"Autism Spectrum Disorders:
An Update of Federal Government Initiatives and
Revolutionary New Treatments of Neurodevelopmental Diseases "

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Autism, The Misdiagnosis of Our Future Generations

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Over the last 15 years, the incidence of Autism has rapidly increased in the industrialized nations with the United States and the United Kingdom having the sharpest rise.

> *The incidence of Autism has increased from approximately 1 in 10,000 in 1990 to 1 out of 166, representing over a 5,700% increase in just the last 15 or so years. In some states, the incidence is now 1 in 80 and we now have over 1.5 million children diagnosed with Autism in the United States.*

A lot of attention has been given regarding the link between mercury and autism, with mercury being the possible factor underlying the etiology of this condition. The issue of whether mercury plays a role in Autism or other neurodevelopmental disorders has been the subject of long debate and extreme political discourse but the evidence is overwhelmingly obvious to even the simplest of intellects, once the data is objectively reviewed.

The prevalence of mercury in our society is endemic in nature. The association of mercury with chronic disease in the US "medical literature" exists but is very anemic. However, when searching under Toxline under the Agency for Toxic Substances and Disease Registry (ATSDR), a division of Centers for Disease Contorl (CDC), one finds all scientific literature which also includes didactic literature, NOT just the "medical literature". Not surprisingly to advanced researchers and physicians, the association of mercury to chronic diseases is well documented in the didactic scientific literature.

The search for the association between mercury and cardiovascular disease, the number one killer in the industrialized world, revealed 358 scientific papers exemplifying the relationship. The search for the association between mercury and cancer, the number two killer in the industrialized world at the time of this writing, revealed 643 scientific papers exemplifying the relationship. Both of these conditions represent 80% cause of all deaths in the industrialized world, according to the WHO (World Health Organization) as published in 1998. But the association of mercury with neurodegenerative diseases is the most significant, with the references numbering 1445.

The inevitable question is how do we get exposed to mercury? The sources surround us, from mercury amalgams in our teeth, to the contamination of our water sources, inhalation of combustion from fossil fuel, fish that we consume, contaminated water supplies, virtually all vaccinations, and via breast milk, just to name a few. So if mercury is so devastating, why is it allowed to be in our flu shots, vaccines, foods, etc.? This is the "million dollar" question, although it is quite evident to the well informed that the answer will be found somewhere along the money trail.

Increased exposure to mercury through thimerosal containing vaccines is one of the most important issues at hand. Thimerosal (also known as Marthiolate sodium, Mercurothiolate, Thiomersalate and a host of other names) is the common name of a substance known as ethyl mercurithiosalicylic acid. The overburdening knowledge that thimerosal is converted to ethyl mercury (a substance reportedly hundreds, if not a thousand times more destructive than inorganic mercury) in less than one minute after being introduced into the body, should give great concern to those appointed to protect the public. Yet, it is virtually ignored. Why is this highly toxic substance still allowed to be a constituent of our vaccines used to inoculate our precious children, our own future generations?

For example, the MSDS (material safety data sheet) on thimerosal from Eli Lilly, documented on their own letter head as far back as July 13, 1991 clearly states that thimerosal is a "product containing a chemical known to the State of California to cause birth defects or other reproductive harm". Yet Eli Lilly continues to use thimerosal in the manufacturing process for vaccines.

> *Further more, we inoculate our children starting on the day they are born, introducing multiple vaccines with exponentially higher contents of mercury (thimerosal) into their vulnerable and delicate physiologies, with full knowledge that their biliary systems are in a state of development for the first year of life and represent the primary method of normal mercury excretion in a non-challenged system. Under the heading of "Health Hazard Information", the Eli Lilly MSDS goes on to say:*
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> > ***"Effects, including signs and symptoms of exposure: Topical allergic dermatitis has been reported. Thimerosal contains mercury. Mercury poisoning can occur and topical hypersensitivity reactions may be seen. Early signs of mercury poisoning in adults are nervous system effects, including narrowing of the visual field and numbness in the extremities. Exposure to mercury in utero and in children can cause mild to severe mental retardation and mild to severe motor coordination impairment."***

However, the vaccine issue must not overshadow the cumulative mercury exposure experienced by the patient during gestation and early infancy. These additional exposures besides the vaccine history include but are certainly not limited to dietary mercury content, dental amalgam fillings which contribute greatly to the maternal mercury load, Rhogam (immunoglobulin) administration to mother during gestation, inoculations for tetnus toxoid, exposure to combustion of fossil fuels, water contamination, and mercuric compounds used in skin products.

There is absolutely no reason for the use of a mercury based preservative in the use of human vaccinations. Even the American Veterinarian Society had thimerosal removed from animal vaccinations due to the known toxicity of mercuric compounds over 15 years ago. Unfortuantely, as a society we are virtually ignorant to the severe biological burden which mercury places on our physiology.

The CDC reported findings from the NHANES study in 2003 regarding the disturbing fact that 1 out of 6 women of child bearing age were found to be toxic for mercury. It is a widely accepted fact that during gestation, the vast majority of nutrients are diverted to the fetus to support growth. As the nutrient and mineral supply is being shunted from the mother to the fetus, it should be intuitively obvious that all divertible substances including those that are beneficial and potentially harmful, will also be preferentially diverted to the fetus. This was further confirmed at the EPA's National Forum on Contaminants in Fish when EPA biochemist Kathryn R. Mahaffey reported researchers in the last few years had conclusively shown mercury levels in a fetus's umbilical cord blood are 70 percent higher than those in the mother's blood. It becomes painfully clear that if 1 out of every 6 women giving birth in our country has toxic levels of mercury, some if not most of that mercury is being shunted to the developing fetus. The maternal mercury load therefore must significantly contribute to the prenatal mercury levels, even more disturbing when recognizing and accounting for the exponentially devastating effect this concentrated mercury shunting would have on a developing brain.

Furthermore, according to an "Autism Alarm Release" reported in early 2004 by the US Department of Health and Human Services (DHHS), the Centers for Disease Control (CDC) and the American Academy of Pediatrics, one of out ever 6 children born in the United States suffer from some type of developmental disorder and/or behavioral problem. It does not take a proverbial "rocket scientist" to make a correlation between the 1 of 6 children having neurological problems and 1 of 6 mothers being mercury toxic. Virtually all neurological issues with children that occur post partum are associated with some level of mercury, including, but not limited to ADD, ADHD, PDD and ASD.

On July 14, 2005, a well respected, privately funded, non-profit research organization known as the Environmental Working Group (EWG), released a report entitled "BodyBurden, The Pollution in Newborns". The EWG tested umbilical cord blood from newborn babies for 413 industrial chemicals, pollutants and pesticides and found 287 of these substances present in the samples obtained. Mercury was detected in all samples and of the 287 substances found, 180 are known to "cause cancer in humans or animals, 217 are toxic to the brain and nervous system, and 208 are known to cause birth defects or abnormal development in animal tests." Selected components of the executive summary of the report, felt to be pertinent, are provided below.

> ***"In the month leading up to a baby's birth, the umbilical cord pulses with the equivalent of 300 quarts of blood each day, pumped back and forth from the nutrient- and oxygen-rich placenta to the rapidly growing child cradled in a sac of amniotic fluid. This cord is a lifeline between mother and baby, bearing nutrients that sustain life and propel growth.***
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> ***Not long ago scientists thought that the placenta shielded cord blood — and the developing baby — from most chemicals and pollutants in the environment. But now we know that at this***

critical time when organs, vessels, membranes and systems are knit together from single cells to finished form in a span of weeks, the umbilical cord carries not only the building blocks of life, but also a steady stream of industrial chemicals, pollutants and pesticides that cross the placenta as readily as residues from cigarettes and alcohol. This is the human "body burden" — the pollution in people that permeates everyone in the world, including babies in the womb.

In a study spearheaded by the Environmental Working Group (EWG) in collaboration with Commonweal, researchers at two major laboratories found an average of 200 industrial chemicals and pollutants in umbilical cord blood from 10 babies born in August and September of 2004 in U.S. hospitals. Tests revealed a total of 287 chemicals in the group. The umbilical cord blood of these 10 children, collected by Red Cross after the cord was cut, harbored pesticides, consumer product ingredients, and wastes from burning coal, gasoline, and garbage.

Of the 287 chemicals we detected in umbilical cord blood, we know that 180 cause cancer in humans or animals, 217 are toxic to the brain and nervous system, and 208 cause birth defects or abnormal development in animal tests. The dangers of pre- or post-natal exposure to this complex mixture of carcinogens, developmental toxins and neurotoxins have never been studied.

Chemical exposures in the womb or during infancy can be dramatically more harmful than exposures later in life. Substantial scientific evidence demonstrates that children face amplified risks from their body burden of pollution; the findings are particularly strong for many of the chemicals found in this study, including mercury, PCBs and dioxins. Children's vulnerability derives from both rapid development and incomplete defense systems:

- ***A developing child's chemical exposures are greater pound-for-pound than those of adults.***
- ***An immature, porous blood-brain barrier allows greater chemical exposures to the developing brain.***
- ***Children have lower levels of some chemical-binding proteins, allowing more of a chemical to reach "target organs."***
- ***A baby's organs and systems are rapidly developing, and thus are often more vulnerable to damage from chemical exposure.***
- ***Systems that detoxify and excrete industrial chemicals are not fully developed.***
- ***The longer future life span of a child compared to an adult allows more time for adverse effects to arise.***

The 10 children in this study were chosen randomly, from among 2004's summer season of live births from mothers in Red Cross' volunteer, national cord blood collection program. They were not chosen because their parents work in the chemical industry or because they were known to bear problems from chemical exposures in the womb. Nevertheless, each baby was born polluted with a broad array of contaminants.

U.S. industries manufacture and import approximately 75,000 chemicals, 3,000 of them at over a million pounds per year. Health officials do not know how many of these chemicals pollute fetal blood and what the health consequences of in utero exposures may be. Had we tested for a broader array of chemicals, we would almost certainly have detected far more than 287. But testing umbilical cord blood for industrial chemicals is technically challenging. Chemical manufacturers are not required to divulge to the public or government health officials methods to detect their chemicals in humans. Few labs are equipped with the machines and expertise to run the tests or the funding to develop the methods. Laboratories have yet to develop methods to test human tissues for the vast majority of chemicals on the market, and the few tests that labs are able to conduct are expensive. Laboratory costs for the cord blood analyses reported here were $10,000 per sample.

A developing baby depends on adults for protection, nutrition, and, ultimately, survival. As a society we have a responsibility to ensure that babies do not enter this world pre-polluted, with 200 industrial chemicals in their blood. Decades-old bans on a handful of chemicals like PCBs, lead gas additives, DDT and other pesticides have led to significant declines in people's blood levels of these pollutants. But good news like this is hard to find for other chemicals.

The Toxic Substances Control Act, the 1976 federal law meant to ensure the safety of commercial chemicals, essentially deemed 63,000 existing chemicals "safe as used" the day the law was passed, through mandated, en masse approval for use with no safety scrutiny. It forces the government to approve new chemicals within 90 days of a company's application at an average pace of seven per day. It has not been improved for nearly 30 years — longer than any other major environmental or public health statute — and does nothing to reduce or ensure the safety of exposure to pollution in the womb.

Because the Toxic Substances Control Act fails to mandate safety studies, the government has initiated a number of voluntary programs to gather more information about chemicals, most notably the high production volume (HPV) chemical screening program. But these efforts have been largely ineffective at reducing human exposures to chemicals. They are no substitute for a clear statutory requirement to protect children from the toxic effects of chemical exposure.

In light of the findings in this study and a substantial body of supporting science on the toxicity of early life exposures to industrial chemicals, we strongly urge that federal laws and policies be reformed to ensure that children are protected from chemicals, and that to the maximum extent possible, exposures to industrial chemicals before birth be eliminated. The sooner society takes action, the sooner we can reduce or end pollution in the womb."

Mercury causes damage by various mechanisms which include: competitive and noncompetitive inhibition of enzyme activity by reversibly or irreversibly binding to active sulfur, binding at the sites off and displacing other divalent cations, like magnesium, zinc, copper, and manganese causing a disruption of enzyme systems, disrupting critical electron transfer reactions, and complexing molecules and inducing a change in structure or conformation which causes them to be perceived as foreign by the body's immune defense and repair system (hapten reactions) resulting in hypersensitivity that can potentiate or exacerbate autoimmune reactions. Mercury alters biological systems because of its affinity for sulfhydryl groups which are functional parts of most enzymes and hormones. Tissues with the highest concentrations of sulfhydryl groups include the brain, nerve tissue, spinal ganglia, anterior pituitary, adrenal medulla, liver, kidney, spleen, lungs heart and intestinal lymph glands. But most relevant to us for the purposes of this hearing is that mercury has been clearly shown to causes a denudation of the neurofibrils resulting in direct and devastating damage to the neuronal cells.

Children diagnosed with Autism suffer from acute mercury toxicity secondary to huge exposure while in utero (maternal amalgam load, dietary factors, maternal inoculations, Rhogam injections, etc.) and early on in life (vaccinations preserved with thimerosal, etc.). Adults diagnosed with Alzheimer's suffer from chronic, insidious mercury toxicity secondary to exposure over a long time (amalgam load, inhalation of mercury vapors, combustion of fossil fuels, dietary factors, etc.). By addressing and eliminating the mercury "spark", these secondary "fires" become far easier to clinically manage and the improvements realized from the treatment of the resulting imbalances become easier to maintain.

Children with Autism (mercury toxicity) have many resulting imbalances in their systems, including but not limited to significant allergies, opportunistic infections such as systemic

candidiasis, hormonal imbalances, gastrointestinal dysbiosis, immune dysfunctions such as immuno-suppression or significant allergies, nutritional deficiencies, etc. However these are what I refer to as the "fires" of autism. All these, and other "fires" of autism result from one major "spark". Mercury! Successfully addressing these "fires" will accomplish transient improvement but until the "spark" (mercury) that constantly re-ignites these "fires" has definitively been eliminated, any improvement will be short lived at best. Mercury is NOT the fire. It is however, the spark that ignites and constantly re-ignites these "fires". Mercury is the underlying common denominator and exacerbates the destructive nature of other metals and compounds, contributing in various ways to all the problems from which these children suffer.

Once again, the most relevant issue remains that mercury has clearly been shown to causes a denudation of the neurofibrils resulting in direct damage to the neuronal cells. In addition, mercury exposure leads to many secondary clinical problems resulting from the aforementioned mechanisms of damage, such as immunosuppression, allowing for opportunistic infections, allergies, GI dysbiosis, etc. Addressing all other issues in children with Autism or PDD is analogous to attempting to put out fires without addressing the cause of the fire itself. The fire will keep re-igniting unless the "spark" is eliminated. It is the elimination of this "spark", ie mercury, for which we now have an easy and effective solution. Along with some supportive therapies, Autism and certain other chronic neurodegenerative diseases such as Alzheimer's can be fully and permanently reversed if appropriately treated. This is NOT theory. It has already been clinically validated on a repetitive basis and the evidence is irrefutable.

The reason for some individuals to have severe damage from mercury where others do not have serious adverse neurological deficits extends due to various factors which include biological individuality and genetic predisposition. In addition, factors such as the type of toxicity exposure the individual was exposed to makes an enormous difference. Was it inhaled, ingested, injected or exposed on their skin? What type of mercury exposure did the individual receive? Was it organic or inorganic mercury? If it was organic, was it ethyl mercury or methyl mercury? How frequent was the exposure to the source of toxicity? Was there a significant maternal load present prior to birth? Was the situation exacerbated by the mother being inoculated, or having Rhogam administration either during gestation or even, prior to conception? How many vaccine administrations took place and over what period of time? What about the diet? How about the proximity to industrial sites, and exposure to combustion of fossil fuel? As you can see, the variables are extensive. But the treatment is essentially the same. The only difference is the extent of continuity of treatment.

First however, let us answer the question why some people are affected while others show no manifestations of mercury toxicity, despite living in the same environments. In our case, the discussion will be limited to mercury, which is considered to be the second most toxic metal known to man but this explanation is applicable to most other heavy metals as well. Most individuals exposed to mercury as well as other heavy metals, have the ability to at least begin the process of eliminating these heavy metals out of their system. But not everyone has this ability and the extent of variability in the ability of an individual to detoxify their systems will determine the severity of the symptoms of toxicity. Slides #10 to #14 show the typical individual who can get rid of mercury with appropriate treatments. Despite having been exposed to severe levels of mercury vapor, this patient named Robin T. was able to detoxify once

appropriately treated with DMPS. Her mercury level was almost 22 fold greater or 2200% more than what is considered to be safe but with appropriate treatments, her levels returned to normal and her symptoms of mercury toxicity resolved in a relatively short period of time.

However, patients with impaired detoxification pathways do not show similar results on testing. Their bodies are unable to release the mercury and/or other metals and on testing, the mercury does not appear. The basis of our treatment protocol for children diagnosed with autism was determined by my clinical observation that certain individuals were unable to detoxify mercury like the vast majority of people appear to have the ability to do so. Slides #16 to # 21 show the case of Karen D. who showed no appreciable levels of mercury despite appropriately being "challenged" with DMPS by two different physicians over a year apart. In Karen D.'s case, she could not detoxify her system effectively despite being treated appropriately with the correct diagnostic methods.

Karen D. was 34 years old when she presented to me with multiple complaints including pain, glactorhea (milk coming out of her breast), ataxia (abnormal gait while walking), dysphagia (painful swallowing), inability to articulate with a new onset of stuttering, arrhythmia, chest pain, myalgias (muscle aches), artharalgias (joint pain), hirtuism (facial hair), cephalgia (headache), insomnia (inability to sleep), fatigue, malaise (general feeling of sickness), depression, anxiety and suicidal ideations due to being unable to "live like this anymore." On presentation, the patient had notified me she had seen 16 other physicians in the previous 5 years and if I could NOT help her, she would "take care" of the problems herself because she could no longer live this way. The level of mercury measured during each of Karen D.'s tests was inversely proportionate to the amount of mercury remaining in her system. It is important to note that this patient received treatments every week but the test results were obtained only every 20 weeks. Despite this disparity between treatments and testing, we see a dramatic and steady increase in mercury levels on testing, directly correlated with significant clinical improvements and alleviations of symptoms.

Karen D. needed to have persistent treatment for a period of almost 2 years, as seen on slides #16 to #21. However, as you will notice, Karen's mercury levels continued to exponentially RISE until her last test which shows the results dramatically drop. What is most interesting is that as the test results revealed a consistently ***increasing*** level of mercury while the patient began to dramatically improve on a clinical basis. The reason the levels of mercury actually rose in each subsequent test, is that this testing method only determines how MUCH mercury and/or other metals we are able to remove. As treatment continued, we were effectively able to remove a greater quantity of mercury during each and every treatment.

The answer to the question of why some people are able to effectively release mercury and/or show absolutely no manifestations of mercury toxicity despite having lived in the same exact environments and had the same level of exposure to metals while others are severely affected with serious clinical manifestations, is not as difficult to answer as one would initially believe when the multiple variables are considered, which include the types of exposure, methods of exposure, duration of exposure, the biological individuality and genetic predisposition. Each one of these variables introduces numerous additional possibilities into the equation. For instance, if we discuss just the genetic predisposition for the inability to excrete metals, we are faced with

numerous possibilities. Drs. Michael Godfrey, et al, reported one such variable explaining the variability of individuals in detoxifying mercury in a landmark paper published in the Journal of Alzheimer's Disease in 2003, entitle "Apolipoprotein E Genotyping as a Potential Biomarker for Mercury Neurotoxicity".

> ***"Apolipoprotein-E (apo-E) genotyping has been investigated as an indicator of susceptibility to heavy metal (i.e., lead) neurotoxicity. Moreover, the apo-E epsilon 4 allele is a major risk factor for neurodegenerative conditions, including Alzheimer's disease (AD). A theoretical biochemical basis for this risk factor is discussed herein, supported by data from 400 patients with presumptive mercury-related neuro-psychiatric symptoms and in whom apo-E determinations were made. A statistically relevant shift toward the at-risk apo-E ε 4 groups was found in the patients (...0 001). The patients possessed a mean of 13.7 dental amalgam fillings and 31.5 amalgam surfaces. This far exceeds the number capable of producing the maximum identified tolerable daily intake of mercury from amalgam. The clinical diagnosis and proof of chronic low-level mercury toxicity has been difficult due to the non-specific nature of the symptoms and signs. Dental amalgam is the greatest source of mercury in the general population and brain, blood and urine mercury levels increase correspondingly with the number of amalgams and amalgam surfaces in the mouth. Confirmation of an elevated body burden of mercury can be made by measuring urinary mercury, after provocation with 2,3, dimercapto-propane sulfonate (DMPS) and this was measured in 150 patients. Apo-E genotyping warrants investigation as a clinically useful biomarker for those at increased risk of neuropathology, including AD, when subjected to long-term mercury exposures. Additionally, when clinical findings suggest adverse effects of chronic mercury exposure, a DMPS urine mercury challenge appears to be a simple, inexpensive procedure that provides objective confirmatory evidence. An opportunity could now exist for primary health practitioners to help identify those at greater risk and possibly forestall subsequent neurological deterioration."***

The Apo E genotype is just one example of the variable defining genetic predisposition for the inability to clear metals. For example, other genetic predispositions for the inability to clear metals besides Apo E would include a deficiency of MTHFR (methyl tetrahydrofolate reductase enzyme), glutathione reductase enzyme deficiency, or a broad spectrum methylation defect. But for each one of these defined components and biomarkers showing a genetic predisposition for the inability to excrete metals, there are probably a 100 other genetically influenced pathways and predisposition factors that modern science has simply not uncovered yet. And this is only relevant for the metals. Further confabulating variables introduced into the picture would include the persistent organic pollutants and the burden they invoke on the biological system, the extent of which has already been discussed.

Until the spark is eradicated, the fire will continue to re-start and damage the brain and result in further "fires" in vital areas such as the immune system. And the only solution for these non-eliminators is to effectively remove the mercury while repairing and enhancing the damaged elimination and detoxification pathways. It is important to note that this patient received treatments every week but the test results were obtained only every 20 weeks. Despite this disparity between treatments and testing, we see a dramatic and steady ***increase*** in mercury levels on testing, directly correlated with significant improvements clinically and alleviations of symptoms.

We started treating children with Autism first in 1996. By 1997, we were being referred patients by a pediatric neurologist, who was following a mutual patient and observed significant changes in the child's behavior after implementation of our treatments. However, by the end of 1998,

taking care of children with special needs proved more than I wished to handle. Although we had far better success than the traditional approach, our treatments had not been responsible for "normalizing" any children or returning them to a "neurotypic" state. The emotional component was also overwhelming, just having to deal with the pain and frustration of the parents of these children. As a result, we stopped accepting new patients with the diagnosis of Autism or any type of developmental delay before the start of 1999.

On January 25, 1999, my son Abid Azam Ali Buttar was born. By the time he was 14 or 15 months old, he was already saying "Abu" which means father in Arabic, and a few other words such as "bye bye". But by the age of 18 months, my son had not only failed to progress in his ability to speak, but had also lost the few words he had been saying. As he grew older, I began to worry more and more that he was suffering from a developmental delay. He exhibited the same characteristics that so many parents with children that have developmental delays have observed, such as stemming, walking on tip toes, and lack of eye contact. Sometimes I would call to him but his lack of response would convince me there must be something wrong with his hearing. Certain sounds would make him cringe and he would put his hands on his ears to block the obvious discomfort he was experiencing. He would spend hours watching the oscillation of a fan. But through all this, when he would make eye contact with me, his eyes would say, "I know you can do it Dad". The expression he would give me, for just an instant, would be that of a father encouraging his son.

The oceans of tears that I cried and the hours that I spent trying to determine what was happening to my son are no different than that of any other parent in the same situation. The only difference was that I was one of only a 190 some doctors throughout the US board certified in clinical metal toxicology. And if this was metal related as was a theory that I had read, I should know how to fix this problem. I tested him and re-tested him and tested him again, searching for mercury. Slides # 23 to 27 show the results of my son's test and how his system showed no appreciable levels of mercury. But the older he became, the more obvious it became that my son was not developing as he was meant to be developing. My son was not meant to be this way and that was the only one thing that I knew for certain. From the time Abie lost his speech which was around 18 months or so, until 36 months of age, he had absolutely no verbal communication except for the one syllable that he would utter, "deh", on a repetitive basis.

About the same time while desperately searching for the cause of the same ailment that had afflicted so many of my own patients previously, I had been invited to present a lecture regarding some of our research on IGF-1 and the correlation with cancer. I had notified the conference that I was too busy to present this lecture but when I learned that Dr. Boyd Haley was also scheduled to present at this conference, I changed my schedule and agreed to lecture just so I could meet and discuss my son's situation with Dr. Haley. That meeting turned out to be one of the key elements which resulted in our development and subsequent current protocol for treating children with autism, autism like spectrum and pervasive developmental delay. My son was the first one who went through this protocol once safety had been established. Dr. Haley told me of a study that had at the time, not yet been published.

Just before the turn of the century, Holmes, Blaxill and Haley did a study assessing the level of mercury measured in the hair of 45 normally developing children versus 94 children with

neurodevelopmental delays diagnosed as Autism using DSM IV criteria. The finding showed that the Autistic children had 0.47 parts per million of mercury in their hair where as the normally developing children had 3.63 parts per million, more that 7 times the same level of mercury as the Autistic children. Opponents of the mercury-neurodegeneration camp used this opportunity to state that this study clearly showed that mercury had NOTHING to do with Autism or any other neurodegenerative condition. However, they completely missed the point of the study. For the reader, the conclusion of the study is obvious, and in part, is reproduced below.

> ***"The reduced levels of mercury in the first baby haircut of autistic infants raise clear questions about the detoxification capacity of a subset of infants. Despite hair levels suggesting low exposure, these infants had measured exposures at least equal to control population, suggesting that control infants were able eliminate mercury more effectively. In the case of autistic infants, those in our sample were exposed to higher levels of mercury during gestation, through dental amalgams or Rho D immunoglobulin injections in the mother. The addition of multiple postnatal exposures to mercury in childhood vaccines would have more severe consequences in infants whose detoxification capacity is reduced or who may be closer to a dangerous threshold exposure. In the case of control infants, mercury hair levels were strongly affected by exposure levels, suggesting that detoxification and excretion played an important role in ensuring normal development in children with elevate toxic exposure relative to peers. If reduced overall mercury elimination is related to hair elimination, then autistic infants will retain significantly higher levels of mercury in tissue, including the brain, than normal infants. In light of the biological plausibility of mercury's role in neurodevelopmental disorders, our study provides further insight into one possible mechanism by which early mercury exposures could increase the risk of autism.."***

These findings were published in the International Journal of Toxicology in 2003. Understanding these findings, along with my clinical experience with the case of Karen D. as previously detailed, led me to the conclusion that a more aggressive method of treatment was necessary compared to the DMSA and various other treatments I had to date employed in the attempt to document high levels of mercury in my son, which up to this point, had not been successful. The first two attempts with DMPS as a challenge treatment were unsuccessful, the first due to difficulty catching the urine since Abie was only 2 years old at the time, and the other due to loss of the urine specimen while being delivered to the laboratory. The third try with DMPS, which represented the 6th test we did on my son with all previous tests showing no appreciable levels of mercury, resulted in the findings on slide #29, the results that were reported to me on his 3rd birthday. His mercury level was over 400% that of safe levels. It is important to note that this level was only indicative of what we were able to "elicit or sequester" out of him. His actual levels were far greater.

I started Abie's treatments on his 3rd birthday, using a rudimentary version of the current TD-DMPS (DMPS in a transdermal base) that my partner, Dr. Dean Viktora and I had played around with a few years previously. By the age of 41 months, 5 months after initiating treatment with the TD-DMPS, my son started to speak, with such rapid progression of his speech that his speech

therapist was noted to comment how she had never seen such rapid progress in speech in a child before. Today at the age of 5, Abie is far ahead of his peers, learning prayers in a second language, doing large mathematical calculations in his head, playing chess and already reading simple 3 and 4 letter words. His attention span and focus was sufficiently advanced to the point of being accepted as the youngest child into martial arts academy when he was only 4. His vocabulary is as extensive as any 10 year old's, and his sense of humor, power to reason and ability to understand detailed and complex concepts constantly amazes me. This was the preliminary basis for the initiation of our retrospective study which came about as a result of the extraordinary results obtained in the treatment of my son Abie, and the subsequent treatment of 31 other children treated in the same manner.

The retrospective Autism study consisted of 31 patients with the diagnoses of autism, autism like spectrum, and pervasive developmental delay. Inclusion criteria was simple, including an independent diagnosis of the above mentioned conditions from either a neurologist or pediatrician, and the desire of the parent to try the treatment protocol using TD-DMPS. All patients reviewed had been sequentially treated as they presented to the clinic and only those patients whose parents who did not wish to be treated with the TD-DMPS were not included. As a side note, of all the parents presented with this option of treatment with DMPS, only one did not wish to be treated with DMPS. Some of the older children (over the age of 8) were treated with IV administration of DMPS and their data was obviously not included in this retrospective analysis. However, it's important to note how willing parents were to get their children better.

All 31 patients were tested for metal toxicity using four different tests: urine metal toxicity and essential minerals, hair metal toxicity and essential minerals, RBC metal toxicity, and fecal metal toxicity, all obtained from Doctor's Data Laboratory. These tests were performed at baseline, and repeated at 2 months, 4 months, 6 months, 8 months, 10 months, 12 months, and then every 4 months there after. All 31 patients showed little or no level of mercury on the initial baseline test results. Slide #37 shows an example of a baseline test result of one participant in the study showing very little mercury. In addition, all study patients had chemistries, CBC with differentials, lipid panels, iron, thyroid profiles and TSH drawn every 60 days. Further specialized testing also included organic acid testing (OAT test) from Great Plains Laboratory and complete diagnostic stool analysis (CDSA) from Doctor's Data Laboratory. If indicated, IgG mediated food allergy testing was also obtained but was not routinely performed.

Compared to the baseline results all 31 patients showed significantly higher levels of mercury as treatment continued. Slide #39 shows significantly higher mercury levels in this same study patient after two months of treatment with the TD-DMPS, with results showing approximately a 350% increase from previous baseline levels. The improvements in the patients in the study correlated with increased yield in measured mercury levels upon subsequent testing. Essentially, what was noted was that as more mercury was eliminated, the more noticeable the clinical improvements and the more dramatic the change in the patient.

The manifestations of this evidence for clinical improvements included many observations but were specifically quantifiable with some patients who had no prior history of speech starting to speak at the age of 6 or 7, sometimes in full sentences. Patients also exhibited substantially improved behavior, reduction and eventual cessation of all stemming behavior, return of full eye

contact, and rapid potty training, sometimes in children that were 5 or 6 but had never been successfully potty trained. Additional findings reported by parents included improvement and increase in rate of physical growth increased, as well as the child beginning to follow instructions, becoming affectionate and social with siblings or other children, seeking interaction with others, appropriate in response, and a rapid acceleration of verbal skills. The results in many of these children has been documented on video and other physicians involved with this protocol have been successfully able to reproduce the same results.

DMPS, or dimercaptopropane – 1 sulfonate, is a primary chelator for mercury and arsenic. Slide 42 shows the chemical structure of DMPS. DMPS has pitfalls as well as advantages. The pitfalls include oral dosing which is the usual recommended dosing because it is approximately 50% to 55% absorbed by the gastrointestinal mucosa. As a result of already compromised gastrointestinal function and dysbiosis noted in most of these children, there is also be a decreased absorption of the DMPS when dosed orally, and with the severe gut vacillations prevalent in our society, DMPS by mouth becomes impractical. Most of the children that have taken the DMPS orally for more than 1 week continuously, begin complaining of abdominal pain, cramping and other GI distress. We tried the oral DMPS for almost 6 weeks before eliminating it as a possible therapeutic method. Intravenous methods of application were not an option in children so young, although is the preferred method I have used in my clinical practice for my adult patients with mercury toxicity.

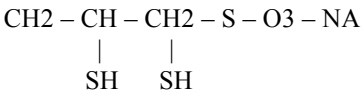
All study patients were also monitored for renal function, and mineral depletion. The key to success with this study was the constant and continuous "pull" of mercury by being able to dose it every other day and the compliance of patient and parents. Each patient was put on a protocol consisting of the transdermal DMPS (TD-DMPS). Transdermal DMPS is DMPS conjugated with a number of amino acids, delivered in highly specialized micro-encapsulated liposomal phospholipid transdermal base with essential fatty acids. The frequent dosing is one of the most important components of the TD-DMPS. It is important to note that DMPS is highly oxygen reactive and is very unstable when exposed to air. This and many other issues of delivery, stabilization, and oxidation have all been successfully identified and resolved over the last two years with the final result now pending patent. In addition, certain other components have been added to the TD-DMPS to potentiate the efficacy of treatment, such as the addition of various amino acids and glutathione.

There are a number of agents that have been demonstrated to have clinical utility in facilitating the removal of mercury from someone who has demonstrated clinical signs and symptoms of mercury toxicity. The most important part of this systemic elimination process, however, is the removal of the source of mercury. Once this has been completed, treatment for systemic mercury detoxification can begin. The following is a summary of the most effective agent with the best safety profile we have so far found (combination of GSH with DMPS) as well as the most commonly used agent (DMSA).

A. <u>DMPS</u>

1. The chemical name is Sodium 2,3 dimercaptopropane-1-sulfonate, this water soluble dimercaprol has 2 active sulfhydryl sites that form complexes with heavy metals such as zinc, copper, arsenic, mercury, cadmium, lead sliver, and tin.

2. The chemical structure of DMPS is:



3. DMPS was developed in the 1950's by the Soviets as an antidote for the chemical warfare agent Lewisite.

4. It became commercially available in 1978, being produced by the German pharmaceutical company Heyl.

5. There has been extensive research in both safety and effectiveness of this drug in the 50 years of its existence and it is now considered to be the most effective therapy for the treatment of mercury toxicity, as mercury is bound to sulfur groups throughout the body and is therefore difficult to remove. The sulfur groups on this compound readily unseat the mercury from its attachment to sulfur in our tissues, then this compound is excreted through the kidneys unchanged.

6. DMPS is widely available throughout the United States as a compounded bulk drug and has been recognized by the FDA in that capacity.

7. DMPS is very safe when used properly. Side effects are very rare, but may include allergic reactions such as skin rashes. Most important is to monitor and supplement with appropriate doses of zinc and copper as these minerals are bound readily by DMPS in the same way as it binds mercury. This should be done prior to commencement of any DMPS treatment regimen, then periodically throughout the process.

8. DMPS can be taken orally, as over 50% is absorbed. Most trained chelation physicians in the United States utilize intravenous challenges, whereas most European physicians will challenge with oral DMPS.

9. Currently, there are a number of different professional medical organizations that teach physicians the appropriate methods of effectively chelating toxic metals. These include the International College of Integrative Medicine, American College for Advancement of Medicine and Integrative Therapeutics in Anti-Aging to name a few. These organizations periodically conduct workshops on mercury toxicity specifically with emphasis on both basic science knowledge and clinical evaluation and treatment.

10. With the increased concern of mercury toxicity as an environmental health threat and in recognition of the need to increase basic science research and clinical treatment of heavy metal toxicity, the American Board of Clinical Metal Toxicology (ABCMT) was recently formed as an evolution of the American Board of Chelation Therapy. This Board will now expand greatly the educational opportunities for physicians interested in this health problem and offer certification procedures that will expand

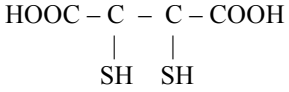
even further the work that has already been done. ABCMT will certify physicians as being competent and proficient in clinical removal of heavy metal toxicity.

11. As a result of the work of these organizations, a general protocol for the use of DMPS has been established which most certified physicians follow.

B. <u>DMSA</u>

1. 2,3 dimercaptosuccinic acid is also a dithiol, like DMPS, and therefore is more effective than EDTA in removing mercury.

2. Structure:



3. This chelator is an oral agent that is reportedly effective in removing both lead and mercury and is used frequently to treat children.

4. DMSA removes mercury both by way of the kidneys, though urine, and the liver, through bile and then the intestines. It is however, only 20% absorbed through the gastrointestinal tract.

5. DMSA has several disadvantages relative to DMPS:
    a. DMPS remains in the body for a longer time than DMSA, therefore it is able to more thoroughly bind to mercury and eliminate greater amounts per treatment.
    b. DMPS acts more quickly than DMSA.
    c. DMPS is given intravenously, intramuscularly, or orally, and now, transdermally, while DMSA is strictly an oral preparation. Preliminary evaluation of DMSA transdermally showed no evidence of efficacy.

6. DMSA is now thought to be potentially harmful if used in patients with excessively high levels of mercury. Therefore, DMSA is recommended for use only late in the mercury elimination process after the peripheral tissue load of mercury has been reduced by DMPS.

In our observation, DMSA did not show efficacy in removing mercury or in clinical improvement in children diagnosed with autism or PDD. Slides #26 and #29 show a comparison in the effect of pulling out mercury, completed less than 30 days apart in my son's case. The yield of DMPS compared to DMSA for removal of mercury in this example was 10 to 1. There is an intriguing explanation provided by Boyd Haley, DSc, to support my clinical observations to the lack of efficacy observed with the use of DMSA in treating children with autism and developmental delays. DMSA stands for dimercapto-succinic acid. Succinic acid is a major

substrate in the citric acid cycle and DMSA is an analog of succinic acid with the only difference consisting of two sulfer groups in DMSA versus two hydroxyl groups (OH-) in succinic acid.

Therefore, DMSA would most likely act as an inhibitor of the enzyme in the citric acid cycle that uses succinic acid as a substrate. This would result in DMSA actually acting as a competitive inhibitor of succinic acid and in turn, would lead to a slowing down of, or inhibition of the citric acid cycle. Succinate produces FADH2 which is directly coupled to the electron transport chain and leads to ATP production. The competitive inhibition of this succinic acid by DMSA would thus, eventually result in an inhibition of ATP production leading to decreased energy utilization causing a significant burden and impaired ability of the physiological system to function correctly.

In our clinical experience, the only effective method that has resulted in the consistent, slow and safest method of removal of mercury resulting in the elimination of this "spark" in the pediatric population is the TD-DMPS that was originally formulated only for the purposes of treating my son's developmental delay. Since it's implementation, we have now successfully treated scores of patients, many of whom have completely recovered but all of whom have improved since the implementation of this treatment. These results have been duplicated by other physicians involved with the care of patients with neurodegenerative disease processes.

Slide 47 shows a newspaper article in the Charlotte Observer with a picture showing one of my patient's mother administering transdermal DMPS to her son's forearms. Slide 48 gives more information on metal toxicity and represents the focus of the majority of my post graduate medical career revolving around the issue of the effective clinical treatment of heavy metal toxicity.

Summary:

The underlying common denominator in chronic neurodegenerative disease seems to be either decreasing vascular supply (less blood to the brain) or accumulation of heavy metals, specifically mercury. The inability of an individual to eliminate toxic metals, especially mercury, is directly related to the level of neurodegeneration experienced. In the young patient population suffering from autism or pervasive developmental delay, the vascular supply is not an issue. The underlying pathology of children with autism and the geriatric population with Alzheimer's is of the same etiology, specifically mercury toxicity.

Both these patient populations suffer from the inability to excrete mercury as a result of a genetic predisposition resulting from various factors. This allele appears to be associated with the inability to get rid of mercury from the system. If these patient populations inhabited a complete mercury free environment, they would not have the problems associated with autism or Alzheimer's. When the mercury is successfully removed from their systems, these individuals begin to significantly improve due to a cessation of the destruction and denudation of the neurofibrils, as evidenced by steady improvement in cognitive function.

Mercury is the "spark" that causes the "fires" of autism as well as many other neurodegenerative diseases including PDD, ADD, ADHD and Alzheimer's. Autism is the result of high mercury

exposure early in life versus Alzheimer's where there is a chronic accumulation of mercury over a life time. A doctor can treat ALL the "fires" but until the "spark" is removed, there is minimal hope of complete recovery with most realized improvements being transient at best. Mercury is the underlying common denominator of all the problems from which these children suffer due to impairment of their excretory pathways. And the only solution for these non-eliminators is to effectively remove the mercury while repairing and enhancing the damaged elimination and detoxification pathways. Concomitantly addressing the GI tract is vital if the goal of treatment is to achieve permanent recovery.

Once the process of mercury removal has been effectively initiated, the source of damage is now curtailed and full recovery becomes possible. Complete recovery can now be attained and further enhanced by utilizing various additional essential therapies including nutrition, hyperbarics, etc. It is my hope and prayer, along with the hopes and prayers of all clinicians who are cognizant of these facts, that the US Congress will act quickly and decisively and put an end to this legalized and tolerated mass modern genocide by outlawing the use of mercury based preservatives in all childhood and adult vaccines.

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Full submission of testimony with supporting data and references to follow.

For an updated power point presentation with audio, available from the internet, the reader can go to www.nomercury.org and click on the research tab on the left hand side of the page. Follow the link to the presentation.

Addendum:

Recently I was invited to present at an Autism conference held in Verona, Italy, by Dr. Bergenti, a neurologist who heads the Public Health department in Verona. He shared with me that he "had to invite" me because he had witnessed with his own eyes the substantial clinical improvements in patients using TD-DMPS. These changes were also noted by other staff members including the other neurologists and psychologists on his staff. In order to insure a balanced program, he also invited a reportedly well published pediatrician who was opposed to the idea of removing metals and routinely states that there is no "scientific evidence" supporting that mercury causes autism or even is a contributory cause. Fortunately for him, I was asked to present first so I could not respond to many of the absurdities and half truths stated during his lecture. But during the round table discussion that followed, all that needed to be said was said and it was clearly obvious by the enthusiastic response from the audience as to who they supported and with whom they agreed.

But what was most absurd, was that this reportedly well respected doctor who is well published, spent more than 30 minutes of his presentation quoting multiple epidemiological studies and various statistical data trying to convince the audience that a known neurotoxin injected into the body of new born babies was NOT responsible for causing neuronal damage. Think about that statement for just a second. My response to this physician was why don't doctors and researchers spend half the time used in defending the use of ethylmercury in the pediatric population, to effectively address the issues revolving around autism? If we did, we would have eradicated the poisoning of our children years ago. But instead, we spend an inordinate amount of energy conducting expensive studies, manipulating the data and jumping through statistical hoops to justify the use of mercury in humans, a substance considered to be the second most damaging substance known to man according to the Environmental Protections Agency (EPA).

The absurdity of inoculating a newborn with hepatitis B vaccine is a case in point that should make our regulatory bodies raise an eyebrow of concern while further infuriating the parents of children damaged by this iatrogenic and governmentally condoned act of mandatory vaccination. Hepatitis B, as even a 1st year medical student knows, primarily affects a select patient population with the highest risk in prostitutes, IV drug users and health care providers due to the exposure to blood products and exposure to this high risk population. It is also widely known and accepted that the Hepatitis B vaccination is only effective for 10 years. Are we really so concerned that our children will begin to prostitute themselves or start using IV drugs or for that matter, become a doctor or nurse during their first 10 years of life? The only reason that health care providers are inoculated for Hepatitis B in the first place is because they risk exposure to blood products of this high risk patient population while working in the hospital environment.

It is important to recognize that this argument is not the argument against vaccinations, but rather, one against the indiscriminant use and irresponsible manner in which vaccination programs have been implemented and promoted. This is an issue regarding a safe method of administering vaccinations at appropriate intervals against potentially destructive childhood pathogens to prevent childhood death. However, past track records show us that the vaccination program in our country has a history of improprieties and blatant mismanagement resulting in increased morbidity and mortality. An example of the above is clearly evidenced with the controversy surrounding whole cell pertussis vaccines versus acellular pertussis vaccines. Upon the advent of the acellular pertussis vaccine and cessation of the whole cell variety, the incidence of SIDS (Sudden Infant Death Syndrome) was dramatically reduced by 50%.

The viral, bacterial and fungal issues endemic in the autism spectrum disorder patients should come as no surprise to anyone. These microbes are opportunistic in nature and will certainly be found in any immunocompromised individual. Mercury has one of the most significant immunosuppressive effects of any substance found in nature and when combined with other metals, the destructive nature increase exponentially. It should come as no surprise that when you inject an immunosuppressive agent such as mercury into an individual who already has an impaired ability to eliminate (detoxify) such a toxic substance, and then you add an attenuated virus (vaccine), you will provide the perfect opportunity for this weakened virus to set up house. I believe that if you check these children diagnosed with ASD further, you will find other

significant biological burdens such as spirochetes, mycoplasma and parasites along with the increased viral, bacterial and fungal load.

The chronic nature of heavy metal accumulation within the biological system and the resulting implications are simply not recognized by the vast majority of the medical profession. Furthermore, the synergistic destructiveness of these heavy metals is completely unappreciated by conventional toxicologists. For example, a study published in the Journal of Toxicology and Environmental Health in 1978 by Schubert, Riley and Tyler showed the LD 1 of lead and LD 1 of mercury in the same population was 100% fatal. In order to appreciate the meaning of this study, it is necessary for the reader to understand some background information first.

LD stands for "lethal dose" and is measured from 1 to 100. An LD 7 of substance X would therefore indicate the amount of substance X necessary to kill 7 out of a 100 people to whom substance X was administerd.. An LD 73 of substance Y would thus indicate the amount of substance Y necessary to kill 73 out of a 100 people. What Schubert et al. showed was that if you take an LD 1 of lead (ie, sufficient amount of lead to kill one out of a 100 people) and an LD 1 of mercury (ie, sufficient amount of mercury to kill one out of a 100 people) and put both these into the same 100 patient population, you will kill all 100 individuals. The destructive nature of these metals and the synergistic nature of their induced damage gives the reader an idea of how truly dangerous these heavy metals can end up being.

For those who do not believe what you have read, your skepticism is understood. You've been told that if something sounds too good to be true, it usually is. But in the rare case, sometimes it IS true. This is one of those times. Do not believe everything you hear or read. I do not expect you to take my word for it. In fact, you should not believe anything that anyone says, including me. Chances are that if you were personally affected by what you have read, you are already a victim of listening and believing someone else that mercury amalgams in your teeth were safe or the vaccinations for your children were safe. If you have been personally affected, then you, of all people, should know the price of listening to the wrong information. Search for the truth yourself and be careful as to who you choose to believe.

For those who are in a position of influence such as doctors, governmental officials and public leaders, remember that your words carry more weight and the public is depending on your honesty and your knowledge. If you are not knowledgeable, do not speak and confuse those whose lives are being affected. But if you do give misinformation, be forewarned. You risk your own reputation and your stature as the public is more and more made aware of the truth.

For video evidence or to obtain further information, the reader is invited to go to either www.drbuttar.com or www.nomoreautism.com and view the proof with your own eyes. Look at the videos of children diagnosed with autism before treatment and after treatment and reach your own conclusion.

Other resources you may find useful are www.MedicalRewind.com, www.FactsOnToxicity.com and www.The9Steps.com (now an international best selling book, translated into 9 languages).

Autism: A Unique Type of Mercury Poisoning

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Lyn Redwood, R.N., M.S.N., C.R.N.P., Woody McGinnis, M.D.

ABSTRACT

Autism is a syndrome characterized by impairments in social relatedness, language and communication, a need for routine and sameness, abnormal movements, and sensory dysfunction. Mercury (Hg) is a toxic metal that can exist as a pure element or in a variety of inorganic and organic forms and can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism. Thimerosal, a preservative frequently added to childhood vaccines, has become a major source of Hg in human infants and toddlers. According to the FDA and the American Academy of Pediatricians, fully vaccinated children now receive, within their first two years, Hg levels that exceed safety limits established by the FDA and other supervisory agencies. A thorough review of medical literature and U.S. government data indicates (i) that many and perhaps most cases of idiopathic autism, in which an extended period of developmental normalcy is followed by an emergence of symptoms, are induced by early exposure to Hg; (ii) that this type of autism represents a unique form of Hg poisoning (HgP); (iii) that excessive Hg exposure from thimerosal in vaccine injections is an etiological mechanism for causing the traits of autism; (iv) that certain genetic and non-genetic factors establish a predisposition whereby thimerosal's adverse effects occur only in some children; and (v) that vaccinal Hg in thimerosal is causing a heretofore unrecognized mercurial syndrome.

SYNOPSIS

A review of medical literature indicates that the characteristics of autism and of mercury poisoning (HgP) are strikingly similar. Traits defining or associated with both disorders are summarized in *Table A* immediately following the *Table of Contents* and are discussed and cited in the body of this document. The parallels between the two diseases are so thorough as to suggest, based on total Hg injected into U.S. children, that many cases of autism are a form of mercury poisoning.

For these children, the exposure route is childhood vaccines, most of which contain thimerosal, a preservative which is 49.6% ethylmercury by weight. The amount of mercury a typical child under two years receives from vaccinations equates to 237.5 micrograms, or 3.53×10^{17} molecules (353,000,000,000,000,000 molecules). Most such vaccinal Hg may not be excreted and instead migrates to the brain.

The total amount injected into infants and toddlers (i) is known to exceed Federal safety standards, (ii) is officially considered to be a "low" level; whereby (iii) only a small percentage of exposed individuals exhibit symptoms of toxicity. In fact, children who develop Hg-related autism are likely to have had a predisposition derived from genetic and non-genetic factors.

Importantly, the timings of vaccinal Hg-exposure and its latency period coincide with the emergence of autistic-symptoms in specific children. Moreover, excessive mercury has been detected in urine, hair, and blood samples from autistic children; and parental reports, though limited at this date, indicate significant improvement in symptoms subsequent to heavy-metal chelation therapy.

The HgP phenotype is diverse and depends upon a number of factors – including type of Hg, route of entry into the body, rate and level of dose, individual genotype, and the age and immune status of the patient. Historically, variation among these factors has caused slightly different manifestations of mercurialism; Mad Hatter's disease, Minamata disease, acrodynia, and industrial exposures provide examples.

The pathology arising from the mercury-related variables involved in autism – intermittent bolus doses of ethylmercury injected into susceptible infants and toddlers – is heretofore

undescribed in medical literature. Therefore, in accord with existing HgP data and HgP's ability to induce virtually all the traits defining or associated with autism spectrum disorders, we hypothesize that many and perhaps most cases of autism represent a unique form of mercury poisoning.

This conclusion and its supporting data have important implications for the affected population of autistic individuals and their families, for other unexplained disorders with symptoms similar to those of heavy metal intoxication, for vaccine content, and for childhood vaccination programs. Due to its high potential for neurotoxicity, thimerosal should be removed immediately from all vaccine products designated for infants and toddlers.

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Table A:
Summary Comparison of Characteristics
of Autism & Mercury Poisoning

	Mercury Poisoning	**Autism**
Psychiatric	Social deficits, shyness, social withdrawal	Social deficits, social withdrawal, shyness
Disturbances	Depression, mood swings; mask face	Depressive traits, mood swings; flat affect
	Anxiety	Anxiety
	Schizoid tendencies, OCD traits	Schizophrenic & OCD traits; repetitiveness
	Lacks eye contact, hesitant to engage others	Lack of eye contact, avoids conversation
	Irrational fears	Irrational fears
	Irritability, aggression, temper tantrums	Irritability, aggression, temper tantrums
	Impaired face recognition	Impaired face recognition
Speech,	Loss of speech, failure to develop speech	Delayed language, failure to develop speech
Language &	Dysarthria; articulation problems	Dysarthria; articulation problems
Hearing	Speech comprehension deficits	Speech comprehension deficits
Deficits	Verbalizing & word retrieval problems	Echolalia; word use & pragmatic errors
	Sound sensitivity	Sound sensitivity
	Hearing loss; deafness in very high doses	Mild to profound hearing loss
	Poor performance on language IQ tests	Poor performance on verbal IQ tests

Sensory	Abnormal sensation in mouth & extremities	Abnormal sensation in mouth & extremities
Abnormalities	Sound sensitivity	Sound sensitivity
	Abnormal touch sensations; touch aversion	Abnormal touch sensations; touch aversion
	Vestibular abnormalities	Vestibular abnormalities
Motor Disorders	Involuntary jerking movements – arm flapping, ankle jerks, myoclonal jerks, choreiform movements, circling, rocking	Stereotyped movements - arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements
	Deficits in eye-hand coordination; limb apraxia; intention tremors	Poor eye-hand coordination; limb apraxia; problems with intentional movements
	Gait impairment; ataxia – from incoordination & clumsiness to inability to walk, stand, or sit; loss of motor control	Abnormal gait and posture, clumsiness and incoordination; difficulties sitting, lying, crawling, and walking
	Difficulty in chewing or swallowing	Difficulty chewing or swallowing
	Unusual postures; toe walking	Unusual postures; toe walking
Cognitive Impairments	Borderline intelligence, mental retardation - some cases reversible	Borderline intelligence, mental retardation - sometimes "recovered"
	Poor concentration, attention, response inhibition	Poor concentration, attention, shifting attention
	Uneven performance on IQ subtests	Uneven performance on IQ subtests
	Verbal IQ higher than performance IQ	Verbal IQ higher than performance IQ
	Poor short term, verbal, & auditory memory	Poor short term, auditory & verbal memory
	Poor visual and perceptual motor skills, impairment in simple reaction time	Poor visual and perceptual motor skills, lower performance on timed tests
	Difficulty carrying out complex commands	Difficulty carrying out multiple commands

	Word-comprehension difficulties	Word-comprehension difficulties
	Deficits in understanding abstract ideas & symbolism; degeneration of higher mental powers	Deficits in abstract thinking & symbolism, understanding other's mental states, sequencing, planning & organizing

(iv)

Unusual	Stereotyped sniffing (rats)	Stereotyped, repetitive behaviors
Behaviors	ADHD traits	ADHD traits
	Agitation, unprovoked crying, grimacing, staring spells	Agitation, unprovoked crying, grimacing, staring spells
	Sleep difficulties	Sleep difficulties
	Eating disorders, feeding problems	Eating disorders, feeding problems
	Self injurious behavior, e.g. head banging	Self injurious behavior, e.g. head banging
Visual	Poor eye contact, impaired visual fixation	Poor eye contact, problems in joint attention
Impairments	"Visual impairments," blindness, near-sightedness, decreased visual acuity	"Visual impairments"; inaccurate/slow saccades; decreased rod functioning
	Light sensitivity, photophobia	Over-sensitivity to light
	Blurred or hazy vision	Blurred vision
	Constricted visual fields	Not described
Physical Disturbances	Increase in cerebral palsy; hyper- or hypo-tonia; abnormal reflexes; decreased muscle strength, especially upper body; incontinence; problems chewing, swallowing, salivating	Increase in cerebral palsy; hyper- or hypotonia; decreased muscle strength, especially upper body; incontinence; problems chewing and swallowing
	Rashes, dermatitis/dry skin, itching; burning	Rashes, dermatitis, eczema, itching
	Autonomic disturbance: excessive sweating, poor circulation, elevated heart rate	Autonomic disturbance: unusual sweating, poor circulation, elevated heart rate

Gastro-intestinal	Gastroenteritis, diarrhea; abdominal pain, constipation, "colitis"	Diarrhea, constipation, gaseousness, abdominal discomfort, colitis
Disturbances	Anorexia, weight loss, nausea, poor appetite	Anorexia; feeding problems/vomiting
	Lesions of ileum & colon; increased gut permeability	Leaky gut syndrome
	Inhibits dipeptidyl peptidase IV, which cleaves casomorphin	Inadequate endopeptidase enzymes needed for breakdown of casein & gluten
Abnormal Biochemistry	Binds -SH groups; blocks sulfate transporter in intestines, kidneys	Low sulfate levels
	Has special affinity for purines & pyrimidines	Purine & pyrimidine metabolism errors lead to autistic features
	Reduces availability of glutathione, needed in neurons, cells & liver to detoxify heavy metals	Low levels of glutathione; decreased ability of liver to detoxify heavy metals
	Causes significant reduction in glutathione peroxidase and glutathione reductase	Abnormal glutathione peroxidase activities in erythrocytes
	Disrupts mitochondrial activities, especially in brain	Mitochondrial dysfunction, especially in brain
Immune Dysfunction	Sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies, asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
	Can produce an immune response in CNS	On-going immune response in CNS
	Causes brain/MBP autoantibodies	Brain/MBP autoantibodies present
	Causes overproduction of Th2 subset; kills/inhibits lymphocytes, T-cells, and monocytes; decreases NK T-cell activity; induces or suppresses IFNg & IL-2	Skewed immune-cell subset in the Th2 direction; decreased responses to T-cell mitogens; reduced NK T-cell function; increased IFNg & IL-12

(v)

CNS	Selectively targets brain areas	Specific areas of brain pathology;

Structural Pathology	unable to detoxify or reduce Hg-induced oxidative stress	many functions spared
	Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
	Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
	Causes abnormal neuronal cytoarchitecture; disrupts neuronal migration & cell division; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, increased glial cells; depressed expression of NCAMs
	Progressive microcephaly	Progressive microcephaly and macrocephaly
	Brain stem defects in some cases	Brain stem defects in some cases
Abnormalities in Neuro-chemistry	Prevents presynaptic serotonin release & inhibits serotonin transport; causes calcium disruptions	Decreased serotonin synthesis in children; abnormal calcium metabolism
	Alters dopamine systems; peroxidine deficiency in rats resembles mercurialism in humans	Possibly high or low dopamine levels; positive response to peroxidine (lowers dopamine levels)
	Elevates epinephrine & norepinephrine levels by blocking enzyme that degrades epinephrine	Elevated norepinephrine and epinephrine
	Elevates glutamate	Elevated glutamate and aspartate
	Leads to cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus & cerebellum	Cortical acetylcholine deficiency; reduced muscarinic receptor binding in hippocampus
	Causes demyelinating neuropathy	Demyelination in brain
EEG	Causes abnormal EEGs, epileptiform activity	Abnormal EEGs, epileptiform activity
Abnormalities/	Causes seizures, convulsions	Seizures; epilepsy
Epilepsy	Causes subtle, low amplitude	Subtle, low amplitude seizure

	seizure activity	activities
Population	Effects more males than females	Male:female ratio estimated at 4:1
Charact-eristics	At low doses, only affects those geneticially susceptible	High heritability - concordance for MZ twins is 90%
	First added to childhood vaccines in 1930s	First "discovered" among children born in 1930s
	Exposure levels steadily increased since 1930s with rate of vaccination, number of vaccines	Prevalence of autism has steadily increased from 1 in 2000 (pre1970) to 1 in 500 (early 1990s), higher in 2000.
	Exposure occurs at 0 - 15 months; clinical silent stage means symptom emergence delayed; symptoms emerge gradually, starting with movement & sensation	Symptoms emerge from 4 months to 2 years old; symptoms emerge gradually, starting with movement & sensation

(vi)

II. COMPARISON OF BIOLOGICAL ABNORMALITIES

Like the similarities seen in observable symptoms, parallels between autism and mercury poisoning clearly exist even at cellular and subcellular levels. These similarities are summarized in tables after each individual section.

a. Biochemistry

Sulfur: Studies of autistic children with known chemical or food intolerances show a low capacity to oxidize sulfur compounds and low levels of sulfate (O'Reilly & Waring, 1993; Alberti et al, 1999). These findings were interpreted as suggesting that "there may be a fault either in the manufacture of sulfate or that sulfate is being used up dramatically on an unknown toxic substance these children may be producing" (O'Reilly and Waring, 1993). Alternatively, these observations may be linked to mercury, since mercury preferentially forms compounds with molecules rich in sulfhydryl groups (--SH), such as cysteine and glutathione, making them unavailable for normal cellular and enzymatic functions (Clarkson, 1992). Relatedly, mercury may cause low sulfate by its ability to irreversibly inhibit the sulfate transporter Na-Si cotransporter NaSi-1 present in kidneys and intestines, thus preventing sulfate absorption (Markovitch and Knight, 1998).
Among the sulfhydryl groups, or thiols, mercury has special affinity for purines and pyrimidines, as well as other subcellular substances (Clarkson, 1992; Koos and Longo, 1976). Errors in purine or pyrimidine metabolism are known to result in classical autism or autistic features in some cases (Gillberg and Coleman, 1992, p.209; Page et al, 1997; Page & Coleman, 2000; The Purine Research Society), thereby suggesting that mercury's disruption of this pathway might also lead to autistic traits.

Likewise, yeast strains sensitive to Hg are those which have innately low levels of tyrosine synthesis. Mercury can deplete cellular tyrosine by binding to the SH-groups of the tyrosine uptake system, preventing colony growth (Ono et al, 1987), and Hg-depleted tyrosine would be particularly significant in cells known to accumulate mercury (e.g., neurons of the CNS, see below). Similarly, disruptions in tyrosine production in hepatic cells, arising from a genetic condition called Phenylketonuria (PKU), also results in autism (Gillberg & Coleman, 1992, p.203).

Glutathione: Glutathione is one of the primary means through which the cells detoxify heavy metals (Fuchs et al, 1997), and glutathione in the liver is a primary substrate by which body clearance of organic mercury takes place (Clarkson, 1992). Mercury, by preferentially binding with glutathione and/or preventing absorption of sulfate, reduces glutathione bioavailability. Many autistic subjects have low levels of glutathione. O'Reilly and Waring (1993) suggest this is due to an "exotoxin" binding glutathione so it is unavailable for normal biological processes. Edelson and Cantor (1998) have found a decreased ability of the liver in autistic subjects to detoxify heavy metals. Alternatively, low glutathione can be a manifestation of chronic infection (Aukrust et al, 1996, 1995; Jaffe et al, 1993), and infection-induced glutathione deficiency would be more likely in the presence of immune impairments derived from mercury (Shenkar et al, 1998).

Glutathione peroxidase activities were reported to be abnormal in the erythrocytes of autistic children (Golse et al, 1978). Mercury generates reactive oxygen species (ROS) levels in cells, which increases ROS scavenger enzyme content and thus glutathione, to relieve oxidative stress (Hussain et al, 1999). At high enough levels, mercury depletes rat hepatocytes of glutathione (GSH) and causes significant reduction in glutathione peroxidase and glutathione reductase (Ashour et al, 1993).

Mitochondria: Disturbances of brain energy metabolism have prompted autism to be hypothesized as a mitochondrial disorder (Lombard, 1998). There is a frequent association of lactic acidosis and carnitine deficiency in autistic patients, which suggests excessive nitric oxide production in mitochondria (Lombard, 1998; Chugani et al, 1999), and again, mercury may be a participant. Methylmercury accumulates in mitochondria, where it inhibits several mitochondrial enzymes, reduces ATP production and Ca2+ buffering capacity, and disrupts mitochondrial respiration and oxidative phosphorylation (Atchison & Hare, 1994; Rajanna and Hobson, 1985; Faro et al, 1998). Neurons have increased numbers of mitochondria (Fuchs et al, 1997), and since Hg accumulates in neurons of the CNS, an Hg effect upon neuronal mitochondria function seems likely - especially in children having substandard mercury detoxification.

Table XI: Abnormalities in Biochemistry Arising from Hg Exposure & Present in Autism

Mercury	**Autism**
Ties up sulfur groups; Prevents sulfate absorption; Low sulfate levels; Has special affinity for purines and pyrimidines; Errors in purine and pyrimidine metabolism can lead to autistic features; Depletes cellular tyrosine in yeast	PKU, arising from disruption in tyrosine production, results in autism; Reduces bioavailability of glutathione, necessary in cells and liver for heavy metal detoxification; Low levels of glutathione; Decreased ability of liver to detoxify heavy metals; Can cause significant reduction in glutathione peroxidase and glutathione reductase; Abnormal glutathione peroxidase activities in erythrocytes; Disrupts mitochondrial activities, especially in brain Mitochondrial dysfunction, especially in brain.

b. Immune System

A variety of immune alterations are found in autism-spectrum children (Singh et al, 1993; Gupta et al, 1996; Warren et al, 1986 & 1996; Plioplys et al, 1994), and these appear to be etiologically significant in a variety of ways, ranging from autoimmunity to infections and

vaccination responses (e.g., Fudenberg, 1996; Stubbs, 1976). Mercury's effects upon immune cell function are well documented and may be due in part to the ability of Hg to reduce the bioavailability of sulfur compounds:

> "It has been known for a long time that thiols are required for optimal primary in vitro antibody response, cytotoxicity, and proliferative response to T-cell mitogens of murine lymphoid cell cultures. Glutathione and cysteine are essential components of lymphocyte activation, and their depletion may result in lymphocyte dysfunction. Decreasing glutathione levels profoundly affects early signal transduction events in human T-cells" (Fuchs & Schöfer, 1997).

Allergy, asthma, and arthritis: Individuals with autism are more likely to have allergies and asthma, and autism occurs at a higher than expected rate in families with a history of autoimmune diseases such as rheumatoid arthritis and hypothyroidism (Comi and Zimmerman, 1999; Whitely et al, 1998). Relative to the general population, prevalence of selective IgA deficiency has been found in autism (Warren et al); individuals with selective IgA deficiency are more prone to allergies and autoimmunity (Gupta et al, 1996). Furthermore, lymphocyte subsets of autistic subjects show enhanced expression of HLA-DR antigens and an absence of interleuken-2 receptors, and these findings are associated with autoimmune diseases like rheumatoid arthritis (Warren et al). These observations suggest autoimmune processes are present in ASD (Plioplys, 1989; Warren et al); and this possibility is reinforced by Singh's findings of elevated antibodies against myelin-basic protein (Singh et al, 1993).

Atypical responses to mercury have been ascribed to allergic or autoimmune reactions (Gosselin et al, 1984; Fournier et al, 1988), and genetic predisposition for Hg reaction may explain why sensitivity to this metal varies so widely by individual (Rohyans et al, 1984; Nielsen & Hultman, 1999). Acrodynia can present as a hypersensitivity reaction (Pfab et al, 1996), or it may arise from immune over-reactivity, and "children who incline to allergic reactions have an increased tendency to develop acrodynia" (Warkany & Hubbard, 1953). Those with acrodynia are also more likely to suffer from asthma, to have poor immune system function (Farnesworth, 1997), and to experience intense joint pains suggestive of rheumatism (Clarkson, 1997). Methylmercury has altered thyroid function in rats (Kabuto, 1991).

Rheumatoid arthritis with joint pain has been observed as a familial trait in autism (Zimmerman et al, 1993). A subset of autistic subjects had a higher rate of strep throat and elevated levels of B lymphocyte antigen D8/17, which has expanded expression in rheumatic fever and may be implicated in obsessive-compulsive behaviors (DelGiudice-Asch & Hollander, 1997).

Mercury exposure frequently results in rheumatoid-like symptoms. Iraqi mothers and children developed muscle and joint pain (Amin-Zaki, 1979), and acrodynia is marked by joint pain (Farnesworth, 1997). Sore throat is occasionally a presenting sign in mercury poisoning (Vroom and Greer, 1972). A 12 year old with mercury vapor poisoning, for example, had joint pains as well as a sore throat; she was positive on a streptozyme test, and a diagnosis of rheumatic fever was made; she improved on penicillin (Fagala and Wigg, 1992). Acrodynia, which is almost never seen in adults, was also observed in a 20 year old male with a history of sensitivity reactions and rheumatoid-like arthritis, who received ethylmercury via injection in gammaglobulin (Matheson et al, 1980). One effective chelating agent, penicillamine, is also effective for rheumatoid arthritis (Florentine and Sanfilippo, 1991).

Mercury can induce an autoimmune response in mice and rats, and the response is both dose-dependent and genetically determined. Mice "genetically prone to develop

spontaneous autoimmune diseases [are] highly susceptible to mercury-induced immunopathological alterations" (al-Balaghi, 1996). The autoimmune response depends on the H-2 haplotype: if the strain of mice does not have the susceptibility haplotype, there is no autoimmune response; the most sensitive strains show elevated antibody titres at the lowest dose; and the less susceptible strain responds only at a medium dose (Nielsen & Hultman, 1999). Interestingly, Hu et al (1997) were able to induce a high proliferative response in lymphocytes from even low responder mouse strains by washing away excess mercury after pre-treatment, while chronic exposure to mercury induced a response only in high-responder strains.

Autoimmunity and neuronal proteins: Based upon research and clinical findings, Singh has been suggesting for some time an autoimmune component in autism (Singh, Fudenberg et al, 1988). The presence of elevated serum IgG "may suggest the presence of persistent antigenic stimulation" (Gupta et al, 1996). Connolly and colleagues (1999) report higher rates in autistic vs. control groups of elevated antinuclear antibody (ANA) titers, as well as presence of IgG and IgM antibodies to brain endothelial cells. On the one hand, since mercury remains in the brain for years after exposure, autism's persistent symptoms may be due to an on-going autoimmune response to mercury remaining in the brain; on the other hand, activation and continuation of an autoimmune response does not require the continuous presence of mercury ions: in fact, once induced, autoimmune processes in the CNS might remain exacerbated because removal of mercury after an initial exposure can induce a greater proliferative response in lymphocytes than can persistent Hg exposure (Hu et al, 1997).

In sera of male workers exposed to mercury, autoantibodies (primarily IgG) to neuronal cytoskeletal proteins, neurofilaments (NFs), and myelin basic protein (MBP) were prevalent. These findings were confirmed in rats and mice, and there were significant correlations between IgG titers and subclinical deficits in sensorimotor function. These findings suggest that peripheral autoantibodies to neuronal proteins are predictive of neurotoxicity, since histopathological findings were associated with CNS and PNS damage. There was also evidence of astrogliosis (indicative of neuronal CNS damage) and the presence of IgG concentrated along the bbb (El-Fawal et al, 1999). Autoimmune response to mercury has also been shown by the transient presence of antinuclear antibodies (ANA) and antinucleolar antibodies (ANolA) (Nielsen & Hultman, 1999; Hu et al, 1997; Fagala and Wigg, 1992).

A high incidence of anti-cerebellar immunoreactivity which was both IgG and IgM in nature has been found in autism, and there is a higher frequency of circulating antibodies directed against neuronal antigens in autism as compared to controls (Plioplys, 1989; Connolly et al, 1999). Furthermore, Singh and colleagues have found that 50% to 60% of autistic subjects tested positive for the myelin basic protein antibodies (1993) and have hypothesized that autoimmune responses are related to an increase in select cytokines and to elevated serotonin levels in the blood (Singh, 1996; Singh, 1997). Weitzman et al (1982) have also found evidence of reactivity to MBP in autistic subjects but none in controls.

Since anti-cerebellar antibodies have been detected in autistic blood samples, ongoing damage may arise as these antibodies find and react with neural antigens, thus creating autoimmune processes possibly producing symptoms such as ataxia and tremor. Relatedly, the cellular damage to Purkinje and granule cells noted in autism (see below) may be mediated or exacerbated by antibodies formed in response to neuronal injury (Zimmerman et al, 1993).

T-cells, monocytes, and natural killer cells: Many autistics have skewed immune-cell subsets and abnormal T-cell function, including decreased responses to T-cell mitogins (Warren et al, 1986; Gupta et al, 1996). One recent study reported increased neopterin levels in urine of autistic children, indicating activation of the cellular immune system (Messahel et al, 1998).

Workers exposed to Hg_o exhibit diminished capacity to produce the cytokines TNF (alpha) and IL-1 released by monocytes and macrophages (Shenkar et al, 1998). Both high dose

and chronic low-level mercury exposure kills lymphocytes, T-cells, and monocytes in humans. This occurs by apoptosis due to perturbation of mitochondrial dysfunction. At low, chronic doses, the depressed immune function may appear asymptomatic, without overt signs of immunotoxicity. Methylmercury exposure would be especially harmful in individuals with already suppressed immune systems (Shenker et al, 1998). Mercury increases cytosolic free calcium levels [Ca2+]i in T lymphocytes, and can cause membrane damage at longer incubation times (Tan et al, 1993). Hg has also been found to cause chromosomal aberrations in human lymphocytes, even at concentrations below those causing overt poisoning (Shenkar et al, 1998; Joselow et al, 1972), and to inhibit rodent lymphocyte proliferation and function in vitro.

Depending on genetic predisposition, mercury causes activation of the immune system, especially Th2 subsets, in susceptible mouse strains (Johansson et al, 1998; Bagenstose et al, 1999; Hu et al, 1999). Many autistic children have an immune portrait shifted in the Th2 direction and have abnormal CD4/CD8 ratios (Gupta et al, 1998; Plioplys, 1989). This may contribute to the fact that many ASD children have persistent or recurrent fungal infections (Romani, 1999).

Many autistic children have reduced natural killer cell function (Warren et al, 1987; Gupta et al, 1996), and many have a sulfation deficiency (Alberti, 1999). Mercury reduces --SH group/sulfate availability, and this has immunological ramifications. As noted previously, decreased levels of glutathione, observed in autistic and mercury poisoned populations, are associated with impaired immunity (Aukrust et al, 1995 and 1996; Fuchs and Schöfer, 1997). Decreases in NK T-cell activity have in fact been detected in animals after methylmercury exposure (Ilback, 1991).

Singh detected elevated IL-12 and IFNg in the plasma of autistic subjects (1996). Chronic mercury exposure induces IFNg and IL-2 production in mice, while intermittent presence of mercury suppresses IFNg and enhances IL-4 production (Hu et al, 1997). Interferon gamma (IFNg) is crucial to many immune processes and is released by T lymphocytes and NK cells, for example, in response to chemical mitogens and infection; sulfate participates in IFNg release, and "the effector phase of cytotoxic T-cell response and IL-2-dependent functions is inhibited by even a partial depletion of the intracellular glutathione pool" (Fuchs & Schöfer, 1997). A mercury-induced sulfation problem might, therefore, impair responses to viral (and other) infections - via disrupting cell-mediated immunity as well as by impairing NK function (Benito et al, 1998). In animals, Hg exposure has led to decreases in production of antibody-producing cells and in antibody titres in response to inoculation with immune-stimulating agents (EPA, 1997, review, p.3-84).

Table XII: Summary of Immune System Abnormalities in Mercury Exposure & Autism

Mercury	**Autism**
Individual sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies and asthma, autoimmune-like symptoms, especially rheumatoid-like ones	More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies
Can produce an immune response, even at low levels; can remain in CNS for years	Indications of on-going immune response in CNS
Presence of autoantibodies (IgG) to neuronal cytoskeletal proteins, neurofilaments, and myelin basic protein; astrogliosis; transient ANA and AnolA	Presence of autoantibodies (IgG and IgM) to cerebellar cells, myelin basis protein
Causes overproduction of Th2 subset; diminishes capacity to produce TNF(alpha) and IL-1; kills lymphocytes, T-cells, and monocytes; inhibits lymphocyte production; decreases NK T-cell activity; may induce or suppress IFN(gamma) and IL-2 production	Skewed immune-cell subset in the Th2 direction and abnormal CD4/CD8 ratios; decreased responses to T-cell mitogens; increased neopterin; reduced NK T-cell function; increased IFN(gamma) and IL-12

c. CNS Structure

Autism is primarily a neurological disorder (Minshew, 1996), and mercury preferentially targets nerve cells and nerve fibers (Koos and Longo, 1976). Experimentally, primates have the highest levels in the brain relative to other organs (Clarkson, 1992). Methylmercury easily crosses the blood-brain barrier by binding with cysteine to form a molecule that is nearly identical to methionine. This molecule - methylmercury cysteine - is transported on the Large Neutral Amino Acid across the bbb (Clarkson, 1992).

Once in the CNS, organic mercury is converted to the inorganic form (Vahter et al, 1994). Inorganic mercury is unable to cross back out of the bbb (Pedersen et al, 1999) and is more likely than the organic form to induce an autoimmune response (Hultman and Hansson-Georgiadis, 1999). Furthermore, although most cells respond to mercurial injury by modulating levels of glutathione, metallothionein, hemoxygenase, and other stress proteins, "with few exceptions, neurons appear to be markedly deficient in these responses" and thus more prone to injury and less able to remove the metal (Sarafian et al, 1996).

While damage has been observed in a number of brain areas in autism, many functions are spared (Dawson, 1996). In mercury exposure, damage is also selective (Ikeda et al, 1999; Clarkson, 1992), and the list of Hg-affected areas is remarkably similar to the neuroanatomy of autism.

Cerebellum, Cerebral Cortex, & Brainstem: Autopsy studies of carefully selected autistic individuals revealed cellular changes in cerebellar Purkinje and granule cells (Bauman and Kemper, 1988; Ritvo et al, 1986). MRI studies by Courchesne and colleagues (1988; reviewed in ARI Newslett, 1994) described cerebellar defects in autistic subjects, including smaller vermal lobules VI and VII and volume loss in the parietal lobes. The defects were present independently of IQ. "No other part of the nervous system has been shown to be so consistently abnormal in autism." Courchesne (1989) notes that the only neurobiological abnormality known to precede the onset of autistic symptomatology is Purkinje neuron loss in the cerebellum. Piven found abnormalities in the cerebral cortex in seven of 13 high-functioning autistic adults using MRI (1990). Although more recent studies have called attention to amygdaloid and temporal lobe irregularities in autism (see below), and cerebellar defects have not been found in all ASD subjects studied (Bailey et al, 1996), the fact remains that many and perhaps most autistic children have structural irregularities within the cerebellum.

Mercury can induce cellular degeneration within the cerebral cortex and leads to similar processes within granule and Purkinje cells of the cerebellum (Koos and Longo, 1976; Faro et al, 1998; Clarkson, 1992; see also Anuradha, 1998; Magos et al, 1985). Furthermore, cerebellar damage is implicated in alterations of coordination, balance, tremors, and sensations (Davis et al, 1994; Tokuomi et al, 1982), and these findings are consistent with Hg-induced disruption in cerebellar synaptic transmission between parallel fibers or climbing fibers and Purkinje cells (Yuan & Atchison, 1999).

MRI studies have documented Hg-effects within visual and sensory cortices, and these findings too are consistent with the observed sensory impairments in victims of mercury poisoning (Clarkson, 1992; Tokuomi et al, 1982). Acrodynia, a syndrome with symptoms similar to autistic traits, is considered a pathology mainly of the CNS arising from degeneration of the cerebral and cerebellar cortex (Matheson et al, 1980). In monkeys, mercury preferentially accumulated in the deepest pyramidal cells and fiber systems.

Mercury causes oxidative stress in neurons. The CNS cells primarily affected are those which are unable to produce high levels of protective metallothionein and glutathione. These substances tend to inhibit lipid peroxidation and thereby suppress mercury toxicity (Fukino et al, 1984). Importantly, granule and Purkinje cells have increased risk for mercury toxicity because they produce low levels of these protective substances (Ikeda et al, 1999; Li et al, 1996). Naturally low production of glutathione, when combined with mercury's ability to deplete usable glutathione reserves, provides a mechanism whereby mercury is difficult to

clear from the cerebellum -- and this is all the more significant because glutathione is a primary detoxicant in brain (Fuchs et al, 1997).
Mercury's induction of cerebellar deterioration is not restricted to high-doses. Micromolar doses of methylmercury cause apoptosis of developing cerebellar granule cells by antagonizing insulin-like growth factor (IGF-I) and increasing expression of the transcription factor c-Jun (Bulleit and Cui, 1998).
Several researchers have found evidence of a brainstem defect in a subset of autistic subjects (Hashimoto et al, 1992 and 1995; McClelland et al, 1985); and MRI studies have revealed brainstem damage in a few cases of mercury poisoning (Davis et al, 1994). The peripheral polyneuropathy examined in Iraqi victims was believed to have resulted from brain stem damage (Von Burg and Rustam, 1974).
Amygdala & Hippocampus: Atypicalities in other brain areas are remarkably similar in ASD and mercury poisoning. Pathology affecting the temporal lobe, particularly the amygdala, hippocampus, and connected areas, is seen in autistic patients and is characterized by increased cell density and reduced neuronal size (Abell et al, 1999; Hoon and Riess, 1992; Otsuka, 1999; Kates et al, 1998; Bauman and Kemper, 1985). The basal ganglia also show lesions in some cases (Sears, 1999), including decreased blood flow (Ryu et al, 1999).
Mercury can accumulate in the hippocampus and amygdala, as well as the striatum and spinal chord (Faro et al, 1998; Lorscheider et al, 1995; Larkfors et al, 1991). One study has shown that areas of hippocampal damage from Hg were those which were unable to synthesize glutathione (Li et al, 1996). A 1994 study in primates found that mercury accumulates in the hippocampus and amygdala, particularly the pyramidal cells, of adults and offspring exposed prenatally (Warfvinge et al, 1994).
The documenting of temporal lobe mercury provides a direct link between autism and mercury because, as cited previously, (i) mercury alters neuronal function, and (ii) the temporal lobe, and the amygdala in particular, are strongly implicated in autism (e.g., Aylward et al, 1999; Bachevalier, 1994; Baron-Cohen, 1999; Bauman & Kemper, 1985; Kates et al, 1998; Nowell et al, 1990; Warfvinge et al, 1994). Bachevalier (1996) has shown that infant monkeys with early damage to the amygdaloid complex exhibit many autistic behaviors, including social avoidance, blank expression, lack of eye contact and play posturing, and motor stereotypies. Hippocampal lesions, when combined with amygdaloid damage, increases the severity of symptoms.
Also noteworthy is the fact that amygdala findings in autism and mercury literatures are paralleled in fragile X syndrome, a genetic disorder wherein many affected individuals have traits worthy of an autism diagnosis. These traits include sensory alterations, emotional lability, appetite dysregulation, social deficits, and eye-contact aversion (Hagerman). Not only are fraX-related proteins (FRM1, FMR2) implicated in amygdaloid function (Binstock, 1995; Yamagata, 1999), but neurons involved in gaze- and eye-contact-aversion have been identified within the primate temporal lobe and amygdaloid subareas (Rolls 1992, reviewed in Binstock 1995). These various findings in ASD, mercury poisoning, and fragile X suggest that amygdaloid mercury is a mechanism for inducing traits central to or associated with autism and the autism-spectrum of disorders.
Neuronal Organization & Head Circumference: Several autism brain studies have found evidence of increased neuronal cell replication, a lowered ratio of glia to neurons, and an increased number of glial cells (Bailey et al, 1996). Based on these and other neuropathological findings, autism can be characterized as "a disorder of neuronal organization, that is, the development of the dendritic tree, synaptogenesis, and the development of the complex connectivity within and between brain regions" (Minshew, 1996).
Mercury can interfere with neuronal migration and depress cell division in the developing brain. Post-mortem brain tissue studies of exposed Japanese and Iraqi infants revealed "abnormal neuronal cytoarchitecture characterized by ectopic cells and disorganization of cellular layers" (EPA, 1997, p.3-86; Clarkson, 1997). Developmental neurtoxicity of Hg may

also be due to binding of mercury to sulfhydryl-rich tubulin, a component of microtubules (Pendergrass et al, 1997). Intact microtubules are necessary for proper cell migration and cell division (EPA, review, 1997, p.32-88).
Rat pups dosed postnatally with methylmercury had significant reductions in neural cell adhesion molecules (NCAMs), which are critical during neurodevelopment for proper synaptic structuring. Sensitivity of NCAMs to methylmercury decreased as the developmental age of the rats increased. "Toxic perturbation of the developmentally-regulated expression of NCAMs during brain formation may disturb the stereotypic formation of neuronal contacts and could contribute to the behavioral and morphological disturbances observed following methylmercury poisoning" (Deyab et al, 1999). Plioplys et al (1990) have found depressed expression of NCAM serum fragments in autism.
Abnormalities in neuronal growth during development are implicated in head size differences found in both autism and mercury poisoning. In autism, Fombonne and colleagues (1999) have found a subset of subjects with macrocephaly and a subset with microcephaly. The circumference abnormalities were progressive, so that, while micro- and macrocephaly were present in 6% and 9% respectively of children under 5 years, among those age 10-16 years, the rates had increased to 39% and 24% respectively. Another study, by Stevenson et al (1997), had found just one subject out of 18 with macrocephaly who had this abnormality present at birth. The macrocephaly in autism is generally believed to result from "increased neuronal growth or decreased neuronal pruning." The cause of microcephaly has not been investigated.
The most detailed study of head size in mercury poisoning, by Amin-Zaki et al (1979), involved 32 Iraqi children exposed prenatally and followed up to age 5 years. Eight (25%) had progressive microcephaly, i.e., the condition was not present at birth. None had developed macrocephaly, at least at the time of the study. The microcephaly has been ascribed to neuronal death or apoptosis from Hg intoxication.

Table XIII: CNS Lesions
in Mercury Poisoning & Autism

Mercury Poisoning	**Autism**
Primarily impacts CNS	Neurological impairments primary
Selectively targets brain areas - those unable to detoxify heavy metals or reduce Hg-induced oxidative stress	Specific areas of brain pathology; many functions spared
Damage to Purkinje and granular cells	Damage to Purkinje and granular cells
Accummulates in amygdala and hippocampus	Pathology in amygdala and hippocampus
Causes abnormal neuronal cytoarchitecture; interferes with neuronal migration and depresses cell division in developing brains; reduces NCAMs	Neuronal disorganization; increased neuronal cell replication, small glia to neuron ration, increased glial cells; depressed expression of NCAMs
Head size differences: progressive microcephaly	Head size differences: progressive microcephaly and macrocephaly
Brain stem defects in some cases	Brain stem defects in some cases

d. Neurons & Neurochemicals
The brains of autistic subjects show disturbances in many neurotransmitters, primarily serotonin, catecholamines, the amino acid neurotransmitters, and acetylcholine. Mercury poisoning causes disturbances in these same neurotransmitters: primarily serotonin, the catecholamines, glutamate, and acetlycholine.
Serotonin: Serotonin synthesis is decreased in the brains of autistic children and increased in autistic adults, relative to age-matched controls (Chugani et al, 1999), while whole blood serotonin in platelets is elevated regardless of age (Leboyer; Cook, 1990). Autistic patients frequently respond well to SSRIs as well as Risperidone (McDougal; 1997; Zimmerman et al, 1996). Likewise, a number of animal studies have found serotonin abnormalities from mercury exposure. For example, subcutaneous administration of methylmercury to rats

during postnatal development increases tissue concentration of 5-HT and HIAA in cerebral cortex (O'Kusky et al, 1988).
Findings about serotonin abnormalities in mercury literature implicate interactions between mercury and intracellular calcium as well as mercury and sulfhydral groups:

> Many researchers have documented disruptions of intra- and extra-cellular calcium in neurons from mercury exposure (Atchison & Hare, 1994), including thimerosal (Elferink, 1999), and calcium metabolism abnormalities have been identified in autism (Plioplys, 1989; Coleman, 1989).
>
> Intracellular concentrations of Ca2+ are critical for controlling gene expression in neurons and mediating neurotransmitter release from presynaptic vesicles (Sutton, McRory et al, 1999). 5-HT re-uptake activity and intrasynaptic concentration of 5-HT are regulated by Ca2+ in nerve terminals. Methylmercury causes a rapid, irreversible block of synaptic transmission by suppression of calcium entry into nerve terminal channels (Atchison et al, 1986). Thimerosal inhibits 5-HT transport activity in particular through interaction with intracellular sulfhydryl groups associated with Ca2+ pump ATPase (Nishio et al, 1996), for example, by modifying cysteine residues of the Ca(2+)-ATPase (Sayers et al, 1993; Thrower et al, 1996).

Dopamine: Studies have found indications both of abnormally high and low levels of dopamine in autistic subjects (Gillberg & Coleman, 1992, p288-9). For example, Ernst et al (1997) reported low prefrontal dopaminergic activity in ASD children, while Gillberg and Svennerholm (1987) reported high concentrations of homovanillic acid (HVA), a dopamine metabolite, in cerebro-spinal fluid of autistic children, suggesting greater dopamine synthesis. Pyridoxine (vitamin B6) has been found to improve function in some autistic patients by lowering dopamine levels through enhanced DBH function (Gillberg & Coleman, 1992, p289; Moreno et al, 1992; Rimland & Baker, 1996). Dopamine antagonists such as haloperidol improve some antipsychotic symptoms in ASD subjects, including motor stereotypies (Lewis, 1996).
Rats exposed to mercury during gestation show major alterations in synaptic dynamics of brain dopamine systems. The effects were not apparent immediately after birth but showed a delayed onset beginning at the time of weaning (Bartolome et al, 1984). A variety of mercuric compounds increase the release of [3H]dopamine, possibly by disrupting calcium homeostasis or calcium-dependent processes (McKay et al, 1986). Minnema et al (1989) found that methylmercury increases spontaneous release of [3H]dopamine from rat brain striatum mainly due to transmitter leakage caused by Hg-induced synaptosomal membrane permeability. SH groups may also be involved in the inhibition of dopamine binding in rat striatum (Bonnet et al, 1994). Pyridoxine deficiency in rats causes acrodynia, with features similar to human acrodynia (Gosselin et al, 1984).
Epinephrine and norepinephrine: Studies on autistic subjects have consistently found elevated norepinephrine and epinephrine in plasma, which suggests elevated levels of these transmitters in brain, as plasma and CSF norepinephrine are closely correlated (Gillberg and Coleman, 1992, p.121-122). Recently, Hollander et al (2000) have noted improvement in function in about half of their ASD subjects with administration of venlafaxine, a norepinephrine reuptake inhibitor. Mercury also disrupts norepinephrine levels by inhibiting sulfhydryl groups and thus blocking the function of O-methyltransferase, the enzyme that degrades epinephrine (Rajanna and Hobson, 1985). In acrodynia, blocking this enzyme

resulted in high levels of epinephrine and norepinephrine in plasma (Cheek, Pink Disease Website). In rats, chronic exposure to low doses of methylmercury increased brain-stem norepinephrine concentration (Hrdina et al, 1976).
Glutamate: It has been observed that many autistics have irregularities related to glutamate (Carlsson ML, 1998). In autism, glutamate and aspartate have been found to be significantly elevated relative to controls (Moreno et al, 1992); and in a more recent study of ASD subjects, plasma levels of glutamic acid and aspartic acid were elevated even as levels of glutamine and asparagine were low (Moreno-Fuenmayor et al, 1996).
Mercury inhibits the uptake of glutamate, with consequent elevation of glutamate levels in the extracellular space (O'Carroll et al, 1995). Prenatal exposure to methylmercury of rats induced permanent disturbances in learning and memory which could be partially related to a reduced functional activity of the glutamatergic system (Cagiano et al, 1990). Thimerosal enhances extracellular free arachidonate and reduces glutamate uptake (Volterra et al, 1992). Excessive glutamate is implicated in epileptiform activities (Scheyer, 1998; Chapman et al, 1996), frequently present in both ASD and mercurialism (see below).
Acetylcholine: Abnormalities in the cortical cholinergic neurotransmitter system have recently been reported in a post mortem brain study of adult autistic subjects (Perry et al, 2000). The problem was one of acetylcholine deficiency and reduced muscarinic receptor binding, which Perry suggests may reflect intrinsic neuronal loss in hippocampus due to temporal lobe epilepsy (see section below for discussions of epilepsy and ASD/Hg). Mercury alters enzyme activities (Koos and Longo, 1976, p.400), including choline acetyltransferase, which may lead to acetylcholine deficiency (Diner and Brenner, 1998), or Hg may inhibit acetylcholine release due to its effects on Ca2 homeostasis and ion channel function (EPA, 1997, p.3-79). In rats, chronic exposure to low doses of methylmercury decreased cortical acetylcholine levels (Hrdina et al, 1976). Methylmercury has also been found to increase spontaneous release of [3H]acetylcholine from rat brain hippocampus (Minnema et al, 1989) and to increase muscarinic cholinergic receptor density in both rat hippocampus and cerebellum, suggesting upregulation of these receptors in these selected brain regions (Coccini, 2000).
Demyelination: Evidence of demyelination has been observed in the majority of autistic brains (Singh, 1992). This is true of mercury poisoning as well. Mild demyelinating neuropathy was detected in two girls (Florentine and Sanfilippo, 1991), and an adult showed axonal degeneration with Hg-related demyelination (Chu et al, 1998). Methylmercury can alter the fatty acid composition of myelin cerebrosides in suckling rats (Grundt et al, 1980).

Table XIV: Abnormalities in Neurons & Neurochemicals from Mercury & in Autism

Mercury	**Autism**
Can increase tissue concentration of serotonin in newborn rats; causes calcium disruptions in neurons, preventing presynaptic serotonin release and inhibiting serotonin transport activities	Serotonin abnormalities: decreased serotonin synthesis in children; over-synthesis in adults; elevated serotonin in platelets; positive response to SSRIs; calcium metabolism abnormalities present
Alters dopamine systems; disrupts calcium and increases synaptosome membrane permeability, which affect dopamine activities; peroxidine deficiency in rats results in acrodynia	Indications of either high or low dopamine levels; positive response to peroxidine by lowering dopamine levels; positive response to dopamine antagonists
Increases epinephrine and norepinephrine levels by blocking the enzyme which degrades epinephrine	Elevated norepinephrine and epinephrine; positive response to norepinephrine reuptake inhibitors
Elevates glutamate; decreases glutamate uptake; reduces functional activity of glutamatergic system	Elevated glutamate and aspartate

Alters choline acetyltransferase, leading to acetylcholine deficiency; inhibits acetylcholine neurotransmitter release via impact on calcium homeostasis; causes cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus and cerebellum
Abnormalities in cholinergic neurotransmitter system: cortical acetylcholine deficiency and reduced muscarinic receptor binding in hippocampus causes demyelating neuropathy
Demyelation in brain

e. EEG Activity/Epilepsy

Abnormal EEGs are common in mercury poisoning as well as autism. In one study, half the autistic children expressed abnormal EEG activity during sleep (reviewed in LeWine, 1999). Gillberg and Coleman (1992) estimate that 35%-45% of autistics eventually develop epilepsy. A recent study by LeWine and colleagues (1999) using MEG found epileptiform activity in 82% of 50 regressive-autistic children. EEG abnormalities in autistic populations tend to be non-specific and consist of a variety of epileptiform discharge patterns (Nass, Gross, and Devinsky, 1998).
Unusual epileptiform activity has been found in a variety of mercury poisoning cases (Brenner & Snyder, 1980). These include (i) the Minamata outbreak - generalized convulsions and abnormal EEGs (Snyder, 1972); (ii) methylmercury ingestion through contaminated pork - all four affected children had epileptiform features and disturbances of background rhythms; two had seizures (Brenner & Snyder, 1980); (iii) mercury vapor poisoning - abnormal EEG in a 12 year old girl (Fagala and Wigg, 1992) and slower and attenuated EEGs in chloralkali workers with long term exposure (Piikivi & Tolonen, 1989); and (iv) exposure from thimerosal in ear drops and through IVIG - EEG with generalized slowing in an 18 month old girl with otitis media (Rohyans et al, 1984) and a 44 year old man (Lowell et al, 1996). More recently, Szasz and colleagues (1999), in a study of early Hg-exposure, described methylmercury's ability to enhance tendencies toward epileptiform activity and reported a reduced level of seizure-discharge amplitude, a finding which is at least consistent with the subtlety of seizures in many autism spectrum children (LeWine, 1999; Nass, Gross, and Devinsky, 1998).
Processes whereby neuronal damage is induced by epileptiform discharges are elucidated in a number of studies, many of which focus upon brain regions affected in autism. Importantly, neuronal damage in the amygdala can be an "ongoing delayed process," even after the cessation of seizures (Tuunanen et al, 1996, 1997, 1999). Alterations of cerebral metabolic function last long after seizures have occurred. In a model of seizure-induced hippocampal sclerosis, Astrid Nehlig's group describes hypometabolism having its regional boundaries "directly connected" to seizure-damaged locus (Bouilleret et al, 2000). That Hg increases extracellular glutamate would also contribute to epileptiform activity (Scheyer, 1998; Chapman et al, 1996).
These findings support a rationale:

> In susceptible individuals, mercury can potentiate or induce Hg-related epileptiform activity, which can have lower amplitude and be harder to identify. Furthermore, this low-level but persisting epileptiform activity would gradually induce cell death in the seizure foci and in brain nuclei neuroanatomically related to the seizure foci.

These studies have a more direct relevance to the possibility of Hg-induced cases of autism (i) because the amygdala are implicated in regard to core traits in autism, as described above, and (ii) because mercury finds its way into the amygdala (see above). Furthermore, these theoretical relationships are consistent with SPECT imaging studies by Mena,

Goldberg, and Miller, who have demonstrated areas of regional hypoperfusion neuroanatomically associated with trait deficits in autism-spectrum children (Goldberg et al, 1999).

Table XV: EEG Activity & Epilepsy in Mercury Poisoning & Autism

Mercury Poisoning	Autism
Causes abnormal EEGs and unusual epileptiform activity	Abnormal EEG activity; epileptiform activity
Causes seizures, convulsions	Seizures; epilepsy
Causes subtle, low amplitude seizure activity	Subtle, low amplitude seizure activities

III. MECHANISMS, SOURCES & EPIDEMIOLOGY OF EXPOSURE

a. Exposure Mechanism

Vaccine injections are a known source of mercury (Plotkin and Orenstein, 1999), and the typical amount of mercury given to infants and toddlers in this manner exceeds government safety limits, according to Neal Halsey of the American Academy of Pediatrics (1999) and William Egan of the Biologics Division of the FDA (1999).

Most vaccines given to children 2 years and under are stored in a solution containing thimerosal, which is 49.6% mercury by weight. Once inside humans, thimerosal (sodium ethylmercurithio-salicylate) is metabolized to ethylmercury and thiosalicylate (Gosselin et al, 1984). The vaccines mixed with this solution are DTaP, HIB, and Hepatitis B (Egan, 1999). Thimerosal is not an integral component of vaccines, but is a preservative added to prevent bacterial contamination. Many vaccine products are available without the thimerosal preservative; however, these alternatives have not been widely used (Egan, 1999). In addition, thimerosal is used during the manufacturing process for a number of vaccines, from which trace amounts are still present in the final injected product (FDA, personal communication; Smith-Kline press release on Hepatitis B, March 31, 2000).

Since at least 1977 clinicians have recognized thimerosal as being potentially dangerous, especially in situations of long term exposure (Haeney et al, 1979; Rohyans et al, 1984; Fagan et al, 1977; Matheson et al, 1980). For nearly twenty years the US government has also singled out thimerosal as a potential toxin (FDA, 1982). In response to the Food and Drug Administration (FDA) Modernization Act of 1997, which called for the FDA to review and assess the risk of all mercury containing food and drugs (*MMWR*, 1999, July 9), the FDA issued a final rule in 1998 stating that over-the-counter drug products containing thimerosal and other mercury forms "are not generally recognized as safe and effective" (FDA, 1998). In December 1998 and April 1999, the FDA requested US vaccine manufacturers to provide more information about the thimerosal content in vaccines (*MMWR*, 1999, July 9); and in July 1999, the CDC asked manufacturers to start removing thimerosal from vaccines and rescheduled the Hepatitus B vaccine so it is given at 9 months of age instead of at birth (CDC, July 1999). In November 1999, the CDC repeated its recommendation that vaccine manufacturers move to thimerosal-free products (CDC, November 1999).

Importantly, based on the CDC's own recommended childhood immunization schedule (and excluding any trace amounts), the amount of mercury a typically vaccinated two year old child born in the 1990s would receive is 237.5 micrograms; and a typical six month old might receive 187.5 micrograms (Egan, 1999). These amounts equate to 3.53×10^{17} molecules and 2.79×10^{17} molecules of mercury respectively (353,000,000,000,000,000 and 279,000,000,000,000,000 molecules). Since thimerosal is injected during vaccinations, the mercury is given intermittently in large, or 'bolus', doses: at birth and at 2, 4, 6, and approximately 15 months (Egan, 1999). The amount of mercury injected at birth is 12.5 micrograms, followed by 62.5 micrograms at 2 months, 50 micrograms at 4 months, another 62.5 micrograms during the infant's 6-month immunizations, and a final 50 micrograms at about 15 months (Halsey, 1999).

Although infancy is recognized as a time of rapid neurological development, to the best of our belief and knowledge, there are no published studies on the effect of injected ethylmercury in intermittent bolus doses in infants from birth to six months or to 2 years (Hepatitis Control Report, 1999; *Pediatrics*, 1999; EPA, 1997, p.6-56). In contrast, four government agencies have set safety thresholds for daily mercury exposure based on ingested fish or whale meat containing methylmercury. Two of these guidelines are based on adult values and two are for pregnant women/fetuses (Egan, 1999). Applying these guidelines to a bolus dose scenario (see Halsey, 1999 for bolus vs. daily dose discussion), the sum of Hg-doses given at 6 months of age or younger, correlated to infant weights, exceed all of the Hg-total guidelines for all infants. The 2 month dose is especially high relative to the typical infant body weight. Halsey (1999) has calculated the 2 month dose to be over 30 times the recommended daily maximum exposure, with babies of the smallest weight category receiving almost three months worth of daily exposures on a single day. Halsey's observation is all the more important because even at doses which were not previously thought to be associated with adverse affects, mercury has resulted in some damage to humans (Grandjean et al, 1998). Given that ethylmercury is equally neurotoxic as methylmercury (Magos et al, 1985), and that injected mercury is more harmful than ingested mercury (EPA, 1997, p.3-55; Diner and Brenner, 1998), the amount of injected ethylmercury given to young children is cause for concern. The potential for Hg-induced harm is compounded by the special vulnerability of infants (Gosselin et al, 1984). Mercury, which primarily affects the central nervous system, is most toxic to the developing brain (Davis et al, 1994; Grandjean et al, 1999; Yeates and Mortensen, 1994), and neonates exposed to methyl (organic) mercury have been shown to accumulate significantly more Hg in the brain relative to other tissues than do adults (EPA, 1997, p.4-1). Mercury may also be more likely to enter the infant brain because the blood-brain barrier has not fully closed (Wild & Benzel, 1994). In addition, infants under 6 months are unable to excrete mercury, most likely due to their inability to produce bile, the main excretion route for organic mercury (Koos and Longo, 1976; Clarkson, 1993). Bakir et al (1973) have shown that those with the longest half-time of clearance are most likely to experience adverse sequelae, while Aschner and Aschner (1990) have demonstrated that the longer that organic mercury remains in neurons, the more it is converted to its inorganic irreversibly-bound form, which has greater neurotoxicity.

b. Population Susceptibility

Nearly all children in the United States are immunized, yet only a small proportion of children develop autism. The NIH (Bristol et al, 1996) estimates the current prevalence of autism to be 1 in 500. A pertinent characteristic of mercury is the great variability in its effects by individual. At the same exposure level of mercury, some will be affected severely, while others will be asymptomatic or only mildly impaired (Dale, 1972; Warkany and Hubbard, 1953; Clarkson, 1997). A ten-fold difference in sensitivity to the same exposure level has been reported (Koos and Longo, 1976; Davis et al, 1994; Pierce et al, 1972; Amin-Zaki, 1979). An example of variability in children is the mercury-induced disease called acrodynia. In the earlier half of this century, from one in 500 to one in 1000 children exposed to the same chronic, low-dose of mercury in teething powders developed this disorder (Matheson et al, 1980; Clarkson, 1997), and the likelihood of developing the disease "appears to be dominated more by individual susceptibility and possibly age rather than the dose of the mercury" (Clarkson, 1992). Given the documented inter-individual variability of responses to Hg, and the young age at which exposure occurs, the doses of mercury given concurrently with vaccines are such that only a certain percentage of children will develop overt symptoms, even as other children might have trait irregularities sufficiently mild as to remain unrecognized as having been induced by mercury.

c. Sex Ratio

Autism is more prevalent among boys than girls, with the ratio generally recognized as approximately 4:1 (Gillberg & Coleman, 1992, p.90). Mercury studies have consistently shown a greater effect on males than females, except in instances of kidney damage (EPA, 1997). At the highest doses, both sexes are affected equally, but at lower doses only males are affected. This is true of mice as well as humans (Sager et al, 1984; Rossi et al, 1997; Clarkson, 1992; Grandjean et al, 1998; McKeown-Eyssen et al, 1983; see also review in EPA, 1997, p.6-50).

d. Exposure Levels & Autism Prevalence

Perhaps not coincidentally, autism's initial description and subsequent epidemiological increase mirror the introduction and use of thimerosal as a vaccine preservative. In the late 1930s, Leo Kanner, an experienced child psychologist and the "discoverer" of autism, first began to notice the type of child he would later label "autistic." In his initial paper, published in 1943, he remarked that this type of child had never been described previously: "Since 1938, there have come to our attention a number of children whose condition differs so markedly and uniquely from anything reported so far, that each case merits…a detailed consideration of its fascinating peculiarities." All these patients were born in the 1930s. Thimerosal was introduced as a component of vaccine solutions in the 1930s (Egan, 1999). Not only does the effect of mercury vary by individual, as noted above, it also varies in a dose-dependent manner, so that the higher the exposure level, the more individuals that are affected. At higher dose levels, the most sensitive individuals will be more severely impaired, and the less sensitive individuals will be only moderately impaired, and the majority of individuals may still show no overt symptoms (Nielson and Hultman, 1999). The vaccination rate, and hence the rate of mercury exposure via thimerosal, has steadily increased since the 1930s. In 1999 it was the highest ever, at close to 90% or above, depending on the vaccine (CDC, 1999, press release). The rate of autism has increased dramatically since its discovery by Kanner: prior to 1970, studies showed an average prevalence of 1 in 2000; for studies after 1970, the average rate had doubled to 1 in 1000 (Gillberg and Wing, 1999). In 1996, the NIH estimated occurrence to be 1 in 500 (Bristol et al, 1996). A large increase in prevalence, yet to be confirmed by stricter epidemiological analysis, appears to be occurring since the mid-1990s, as evidenced by several state departments of education statistics reflecting substantial rises in enrolment of ASD children (California, Florida, Maryland, Illinois, summarized by Yazbak, 1999). These increases have paralleled the increased mercury intake induced by mandatory innoculations: in 1991, two vaccines, HIB and Hepatitis B, both of which generally include thimerosal as a preservative, were added to the recommended vaccine schedule (Egan, 1999).

e. Genetic Factors

ASD is one of the most heritable of developmental and psychiatric disorders (Bailey et al, 1996). There is 90% concordance in monozygotic twins and a 3-5% risk of autism in siblings of affected probands (Rogers et al, 1999), a rate 50 to 100 times higher than would be expected in the general population (Smalley & Collins, 1996; Rutter, 1996). From 2 to 10 genes are believed to be involved (Bailey et al, 1996).

Individual differences in susceptibility to mercury are said to arise from genetic factors and these too may be multiple in nature (Pierce et al, 1972; Amin-Zaki, 1979). They include innate differences in (i) the ability to detoxify heavy metals, (ii) the ability to maintain balanced gut microflora, which can impair detoxification processes, and (iii) immune over-reactivity to mercury (Nielson and Hultman, 1999; Hultman and Nielson, 199; Johansson et al, 1998; Clarkson, 1992; EPA, review 1997, p.3-26). Many autistic children are described as having (i) difficulties with detoxification of heavy metals (Edelson & Cantor, 1998), possibly due to low glutathione levels (O'Reilly and Waring, 1993), (ii) intestinal microflora imbalances that can impede excretion (Shattock, 1997), and (iii) autoimmune dysfunction (Zimmerman et al, 1993). These characteristics might be reflective of the underlying "susceptibility genes" that predispose to mercury-induced sequelae and hence to autism.

As noted above, autism family studies show an exceptionally high concordance rate of 90% for identical twins. Most environmental factors, such as a postnatal viral infection, tend not to be present at exactly the same time or at the same level or rate for each twin. This would cause a difference in phenotype expression, and thus postnatal environmental influences in general reduce the concordance rate for identical twins. However, given the extremely high vaccination rate and the high likelihood of vaccination of one twin at the same time and with the same vaccines as the other twin, mercury-induced autism via vaccination injection, even though it is an environmental factor, would still lead to the high concordance rate seen in twins.

Furthermore, among identical twin pairs, the 90% concordance rate is for the milder phenotype: if one twin has pure classic autism, there is (i) a 60% chance that the other twin will have pure classic autism; (ii) a 30% chance that the other twin will exhibit some type of impairment falling on the autism spectrum, but with less severe symptoms; and (iii) a 10% chance the other twin will be unimpaired. The difference in symptom severity among the 40% of monozygotic pairs who do not exhibit classic autism may arise from either (i) a different vaccination history within pairs, or (ii) the tendency of thimerosal to "clump" or be unevenly distributed in solution, so that one twin might receive more or less mercury than the other. One study found a 62% difference in the mercury concentration of ampoules drawn from the same container of immunoglabulin batches containing thimerosal (Roberts and Roberts, 1979).

f. Course of Disease

Age of onset: Autism emerges during the same time period as infant and toddler thimerosal injections during vaccinations. As noted above, the recommended childhood vaccination schedule from 1991 to 1999 has called for injections of thimerosal starting at birth and continuing at 2, 4, 6, and approximately 15 months (Halsey, 1999); a similar schedule occurred prior to this time but for DTP alone. In the great majority of cases, the more noticeable symptoms of autism emerge between 6 and 20 months old - and mostly between 12 and 18 months (Gillberg & Coleman, 1992). Teitelbaum et al (1998), who have claimed the ability to detect subtle abnormalities at the youngest age so far, have observed these abnormalities at 4 months old at the earliest, the exception being a "Moebius mouth" seen at birth in a small number of subjects.

Symptoms of mercury poisoning do not usually appear immediately upon exposure, although in especially sensitive individuals or in cases of excessive exposure they can (Warkany and Hubbard, 1953; Amin-Zaki, 1978). Rather, there is generally a preclinical "silent stage," seen in both animals and humans, during which subtle neurological changes are occurring (Mattsson et al, 1981). The delayed reaction between exposure and overt signs can last from weeks to months to years (Adams et al, 1983; Clarkson, 1992; Fagala & Wigg, 1992; Davis et al, 1994; Kark et al, 1971). Consequently, mercury given in vaccines before age 6 months would not in most individuals lead to an observable or recognizable disorder, except for subtle signs, prior to age 6-12 months, and for some individuals, symptoms induced by early vaccinal Hg might not emerge until the infant had become a toddler (Joselow et al, 1972).

A few autism researchers have suggested a prenatal onset for autism (Rodier et al, 1997; Bauman & Kemper, 1994), which would preclude a vaccinal-mercury etiology. Others, however, have evidence that suggest post-natal timings (Bailey, 1998; Courchesne, 1999; Bristol Power, NICHD, Dateline Interview, 1999). The general consensus at this point is that the timing cannot be determined (Bailey et al, 1996; Bristol et al, 1996); and, further, that there is "little evidence" that prenatal or perinatal events "predict to later autism" (Bristol et al, 1996), even though clustering of adverse effects (suboptimality factors) are associated with autism (Prechtel, 1968; Bryson et al, 1988; Finegan and Quarrington, 1979). There is also a general agreement that, in the great majority of cases, autistic signs emerge among

infants and toddlers who had looked "normal", developed normally, met major milestones, and had unremarkable pediatric evaluations (Gillberg & Coleman, 1992; Filipek et al, 1999; Bailey et al, 1996), so that autism presents as an obvious deterioration or regression, either before age two or before age three (Baranek, 1999; Bristol Power, NICHD, Dateline Interview, 1999; LeWine, 1999).

It is worthwhile to note that early and intensive educational and behavioral intervention can produce dramatic gains in function, and the gains made by these children "may be somewhat unique among the more severe developmental disabilities" (Rogers, 1996). This phenomenon further suggests that autism arises from an environmental overlay rather than being purely an organic disease. Additionally, at least one study has reported that "re-education and physical treatment" can improve outcomes in mercurialism (Amin-zaki, 1978).

Emergence of symptoms: The manner in which symptoms emerge in many cases of autism is consistent with a multiple low-dose vaccinal exposure model of mercury poisoning. From a parent's and pediatrician's perspective, such an individual is a "normal" looking child who regresses or fails to develop after thimerosal administration. Clinically relevant symptoms generally emerge gradually over many months, although there have been scattered parental reports of sudden onset (Filipek, et al, 1999). The initial signs, occurring shortly after the first injections, are subtle, suggesting disease emergence, and consist of abnormalities in motor behavior and in sensory systems, particularly touch sensitivity, vision, and numbness in the mouth (excessive mouthing of objects) (Teitelbaum et al, 1998; Baranek, 1999). These signs persist and are followed by parental reports of speech and hearing abnormalities appearing before the child's second birthday (Prizant, 1996; Gillberg & Coleman, 1992), that is, within several months of when additional and final injections are given. Finally, in year two, there is a full blossoming of ASD traits and a continuing regression or lack of development, so that the most severe expression of symptoms occurs at approximately 3-5 years of age. These symptoms then begin to ameliorate (Church & Coplan, 1995; Wing & Attwood, 1987; Paul, 1987). The exceptions are the subset of those with regression during adolescence or early adulthood, which may involve onset of seizures and associated neurodegeneration (Howlin, 2000; Paul, 1987; Tuunanen et al, 1996, 1997, 1999).

As in autism, onset of Hg toxicity symptoms is gradual in some cases, sudden in others (Amin-Zaki et al, 1979 & 1978; Joselow et al, 1972; Warkany and Hubbard, 1953). In the case of organic poisoning, the first signs to emerge are abnormal sensation and motor disturbances; as exposure levels increase, these signs are followed by speech and articulation problems and then hearing deficits (Clarkson, 1992), just like autism. Once the mercury source is removed symptoms tend to ameliorate (though not necessarily disappear) except in instances of severe poisoning, which may lead to a progressive course or death (Amin-Zaki et al, 1978). As in autism, epilepsy in Hg exposure also predicts a poorer outcome (Brenner & Snyder, 1980).

Long term prognosis: The long term outcomes of ASD and mercury poisoning show the same wide variation. Autism is viewed as a lifelong condition for most; historically, three-fourths of autistic individuals become either institutionalized as adults or are unable to live independently (Paul, 1987). There are, however, many instances of partial to full recovery, in which autistic traits persist in a much milder form or, in some individuals, disappear altogether once adulthood is reached (Rogers, 1996; Church & Coplan, 1994; Szatmari et al, 1989; Rimland 1994; Wing & Attwood, 1987).

Upon exposure, mercury entering the bloodstream tends to accumulate in tissues and organs, primarily the brain (Koos and Long, 1976; Lorscheider et al, 1995). Once inside tissues, and particularly the brain, mercury will linger for years, as shown on X rays of a poisoned man 22 years after exposure (Gosselin et al, 1984), as well as autopsies of humans with known mercury exposure (Pedersen et al, 1999; Joselow et al, 1972) and primate studies (Vahter et al, 1994). The continued presence of mercury in organs and the

CNS in particualr would explain why autistic symptoms might persist, why researchers such as Zimmerman or Singh would detect an on-going immune reaction, why epilepsy might not emerge until adolescence, or why sulfate transporters in the intestine or kidney might continue to be blocked.
Nevertheless, despite the continued presence of Hg in tissue, the degree of recovery from mercurialism varies greatly. Even in severe cases, there are reports of full or partial recovery (e.g., Adams et al, 1983; Vroom & Greer, 1972; Amin-Zaki et al, 1978). In less severe cases, especially those in which exposure occurs early in life, the more severe symptoms may ameliorate over time, but milder impairments remain, especially neurological ones (Feldman, 1982; Yeates & Mortensen, 1994; Amin-Zaki, 1974 & 1978; Mathiesin et al, 1999; Vroom and Greer, 1972; EPA 1997, pp.3-10, 3-14, and 3-75). The wide variation in outcome is believed to be due, again, to individual sensitivity to mercury, in this case, the ability of some victims to develop "immunity" or a "tolerance" to Hg even when the metal is still present in tissue (Warkany & Hubbard, 1953).

Course of Disease:
Typical Autism & Ingested Organic Mercury
Typical Autism Progression & Thimerosal Administration

Birth 2 mos 4 mos 6 mos 15 mos 2 yrs 3-5 yrs 6-18 yrs Adults
Hg dose Hg dose Hg dose Hg dose Hg dose
Delay (no signs) Delay (no signs) subtle signs - move-ment subtle signs - sensory definite signs -hearing & speech full array of symptoms Height of symptom severity Symptom ameliora-tion Occasion-al full or partial recovery

Temporal & Dose-Response Relationship for Effects of Ingested Methylmercury
Hg dose Delay (no signs) 1st sign - sensory 2nd sign - move- ment 3rd sign - speech/ art-iculation 4th sign - hearing full array of symp-toms Symptom ameliora-tion (or death) full or partial recovery

g. Thimerosal Interaction with Vaccines

As noted above, for most ASD children symptom onset is gradual, but for a significant minority it is sudden. Additionally, many parents believe there is a connection between their child's autism and his or her immunizations. The Cure Autism Now Foundation, for example, reports that half the parents who call its hotline mention such a connection (Portia Iversen, CAN president, personal communication). The association extends not only to the mercury-containing vaccines - DTP/DTaP, HIB, and Hepatitis B - but also to those without thimerosal, particularly the MMR (Bernard Rimland, president, Autism Research Institute, personal communication). Parents may describe a variety of post-vaccine scenarios: a fever followed by a short recovery period and then a more gradual symptom onset; onset of symptoms immediately and suddenly after inoculation with or without fever; or even a mildly impaired child whose condition worsened after vaccination (CAN Parent Advisory Board Internet list; St. John's Autism Internet list).
While it is possible that any temporal association between vaccination and emergence of autism is due to chance, Warkany and Hubbard, who successfully proved the connection between acrodynia and mercury poisoning to the medical community 50 years ago, offer alternate explanations. In their 1953 article in *Pediatrics*, they made the following points:

> (a) They noted that high fever accompanied by a rash after mercury administration can be signs of a "typical, acute, mercurial reaction," and "acrodynia may follow, immediately or after short intervals, acute idiosyncratic reactions to mercury." This reaction was independent of hypersensitivity to mercury, as detected from skin tests, as they

reported that only 10% of acrodynia victims responded positively to Hg on patch tests.

Thus in ASD, the fevers and deteriorations seen by parents immediately after a thimerosal-containing vaccine injection may be a systemic reaction (and not a hypersensitivity response) to the mercury content, and this reaction may subsequently progress to the emergence of autism, just as topical mercury administration produced fever and then acrodynia over 50 years ago.

(b) Warkany and Hubbard provided some tentative observations that the administration of a vaccine, irrespective of whether or not it contains thimerosal, can set off a reaction to any mercuric compound that may also be given to a child, which in the case of acrodynia, would be topical mercury in powders or rinses. This inter-reactivity might explain the pronounced effects from the MMR among subsequently-diagnosed autistic children:

> "[One patient] underwent a fourteen day course of antirabies injections six weeks before outbreak of acrodynia. Ten days after completion of the therapy she was treated with ammoniated mercury ointment and subsequently acrodynia developed...[In another case] antirabies treatment preceded the disease by three months. In several children various immunization procedures preceded the onset of acrodynia in addition to [topical] mercurial exposure. This could be purely coincidental or the vaccination material may play a role as an accessory factor. It is noteworthy that many vaccines and sera contain small amounts of mercury as preservatives which are injected together with the biologic material. These small amounts of mercurial compounds could act as sensitizing substances. In several instances vaccination against smallpox preceded the development of acrodynic symptoms, and some patients were exposed to bismuth, arsenic, lead, and antimony in addition to mercury. Such observations deserve attention."

(c) Finally, these two researchers observed that some individuals would react to mercury and then, upon re-exposure, not show any effects, i.e., they had acquired an unexplained tolerance to it. In other cases, Hg sensitivity would be maintained. Rarely, though, would reactivity occur with the first dose: "more often the patient tolerates several" before the reaction occurs.

> "The organism can harbor appreciable amounts of mercury while remaining in perfect health, and then, for unknown reasons, these innocuous stores of mercury become toxic. It seems in such cases as if the barriers which held the mercury in check break down

without provocation, or as if the mercury had been converted from a nontoxic to a toxic form..."

In ASD, this delayed sensitivity would explain why some might develop autism later, not after the first few vaccines, and it would also explain in part why the more vaccines that are given, the more likely it is that a given individual will develop a reaction since there are more "sensitizing" opportunities. Importantly, in susceptible individuals, the reactions described by Warkany and Hubbard are likely to occur if mercury's presence occurred via injected thimerosal.

IV. DETECTION OF MERCURY IN AUTISTIC CHILDREN

In the past, hair, urine, or blood tests from autistic subjects have mostly found lead rather than mercury (Wecker et al, 1985), but this is likely due (i) to lead's pervasiveness in our environment, coupled with autistic children's pica tendencies and general inability to detoxify *any* heavy metal (LaCamera and LaCamera, 1987; Edelson & Cantor, 1998); (ii) to the difficulty in detecting Hg, especially in older children exposed early in life, since remaining mercury is sequestered in tissue; and (iii) to the greater affinity of standard chelators used in challenge tests (e.g., DMSA) for lead over mercury, making lead more readily detectable in such exams (Frackelton and Christenson, 1998).

More recently, a number of parents of younger autistic children, in whom mercury is more likely to be detectable, have reported higher than expected levels of mercury in hair, blood, and urine samples. Cases studies are listed below, and more are in the process of documentation. Several parents have also noted improved function after chelation.

The Case Studies

We are providing data from several retrospective case studies of autistic children with associated tissue mercury burdens. In each case we have tried to identify potential sources of exposure, although we have not been able to identify the exact amounts in some cases due to inadequate documentation. This information does not purport to be a rigid scientific study, but rather an initial effort to demonstrate that there may be a problem with mercury toxicity in children with autism. Our primary objective is to show that considerable amounts of mercury are found in the bodies of some autistic children. The data we present were derived from many sources: hair, urine and blood. Some of the samples were baseline and others were obtained utilizing a provocative agent, either DMPS or DMSA. Typically a single dose of DMPS will provoke more mercury from the tissue than a single oral dose of DMSA. Excretion levels will also vary depending on the amount of DMPS or DMSA given. There are also variations among these factors in the case studies.

Identifier: 0001SM **Sex**: M **Age**: 5 **DOB**: 4-25-94

Prenatal and Postnatal History: Premature contractions, which required bedrest during the 2nd and 3rd trimesters. Scheduled C-section at term with good apgars. Birth weight 8 lbs. 3 oz. Vomiting milk based formula, which subsided with a switch to soy formula at 2 months.

Developmental Landmarks: Completely normal development, meeting all developmental milestones until 20 months of age. Speech present with two word phrases.

Regression and Symptoms: At 20 months an unexplained loss of speech and eye contact (lateral gaze). He began lining up trains, developed

preservations, and showed a marked decrease in attention. Diagnosed autistic at 26 months of age. Formal psychological evaluation at 30 months found expressive speech at 14-16 months, cognitive at 12-18 months, fine motor at 18 months, and play skills at 12 months. He was described as withdrawn with alternating inattention or repetitive manipulation of objects.

Exposure Sources: He received multiple vaccines with thimerosal preservatives his first year, including influenza vaccine. The documented exposure the first year was 136.5mcg mercury. Mother with 1 amalgam filling and minimal dietary exposure. Child with no dietary exposure the first year of life. Families estimated consumption of seafood 3 times monthly.

Mercury Levels: Hair mercury 2.6 mcg with a norm reference of less than 2mcg. DMPS provacation (3mg per kg. IV) 7-7-99 resulted in 87 mcg mercury per g urinary creatine. Intermittent treatment with oral DMSA continued for 2 months with normalization of hair mercury levels.

Response to Treatment: Parents claim significant improvement in speech and behavior, also documented on neuropsychological evaluation on 1-14 and 1-21-00. "His ability to use language for social purposes has clearly increased and he could maintain exchanges for several turns without excessive difficulty. He has improved in his ability to initiate interactions and invitation to other children to play. Academic function at or above grade level. Impressive and highly encouraging rate of progress."

Identifier: 0002CM **Sex**: M **Age**: 5 **DOB**: 12-1-94

Prenatal and Postnatal History: Unremarkable prenatal course. Birth weight 8lbs.8oz.

Maintained above the 95th percentile for height and weight the first year of life.

Developmental Landmarks: All early developmental landmarks - crawling, walking, and talking - were obtained on schedule.

Regression and Symptoms: Child went from age appropriate to severe autistic regression between 18 to 20 months. He lost speech, eye contact and became inattentive and withdrawn. Symptoms at 3 years include extreme thirst, echolalia, toe walking, high pain threshold, sleep disturbances, hyperactivity and obsessive behaviors.

Exposure Sources: No maternal amalgam history and minimal dietary exposure. He received all recommended vaccines, although without manufacturer data we are unable to calculate total exposure at this time. Known exposure from hepatitis B vaccine, 37.5 mcg mercury.

Mercury Levels: Hair mercury was 2.21ppm at 3 years and 3 months of age with a lab reference of 0-1.5ppm. DMPS provocation utilizing 3 mg. DMPS/kg given IV revealed:

46 micrograms of mercury / g creatine on 12-18-98

86 micrograms of mercury / g creatine on 3-25-99

46 micrograms of mercury / g creatine on 7-27-99

36 micrograms of mercury / g creatine on 9-30-99

Normal reference for urinary mercury 0-3 micrograms / g creatine.

Between DMPS infusions the child received DMSA 100 mg. orally two days a week, with glutathione 75 mg. twice daily, glycine 900 mg. on day prior to DMSA and glycine 900 mg. on DMSA treatment days.

Response to treatment: On 3-22-00 the parents reported marked behavioral improvement, particularly over the past two months. He now responds to his name and follows instructions. He has developed original speech without echolalia, and obsessive behaviors have declined.

Identifier: 0003HC **Sex**: M **Age**: 3yr. 11mo. **DOB**: 4-11-96

Prenatal and Postnatal History: Prenatal history was unremarkable. Infant was thought to be 4 weeks premature, although birth weight was that of a term infant at 8lbs. 6oz. He developed jaundice shortly after birth and was treated with phototherapy. He was briefly given antibiotics for a suspected infection the first 3 days of life.

Developmental Landmarks: Parents report that his development was normal until 12 months. He was crawling but did not begin to walk until 18 months of age with the support of a walker.

Regression and Symptoms: Some concerns at 13 months, marked regression at 16 months. Six to seven spoken words in use at 12 months were entirely lost. Vacant stares predominated and he began biting his hands. Officially diagnosed autistic at 2 1/2 years of age.

Exposure Sources: Mother had 8 amalgams. He also received exposure via vaccine, but total dose is not available at this time.

Mercury Levels: Hair mercury at 2 years 7 months was below detection limits. DMSA provacative protocol with 10 mg per kg per dose three times daily for three days with 24 hr urine screen for heavy metals day 2 revealed:

3.2 micrograms of mercury / g creatine on 6-21-99

28 micrograms of mercury / g creatine on 9-13-99

13 micrograms of mercury / g creatine on 10-12-99

Normal lab reference 0-3 mcg Hg per g creatine.

Response to treatment: Parents feel certain that DMSA chelation has resulted in improvement in their son. They noticed almost immediate improvement during the three days of treatment along with dramatic improvement the past six months. He is "much more with it and curious about his world". Although he is still not talking, he is having frequent vocalizations. He just started running for the first time 6 weeks ago.

Identifier: 0004WR **Sex**: M **Age**: 6 **DOB**: 2-2-94

Prenatal and Postnatal History: Prenatal history unremarkable with the exception of breech presentation. C-section preformed and apgars were 9 and 10. Birth weight, 8lbs.

11oz. Normal postnatal course.

Developmental Landmarks: He easily met and exceeded all early developmental landmarks and was described as a pleasant, happy baby.

Regression and symptoms: Shortly after his first birthday he developed numerous infections and was hospitalized for a respiratory illness. He received antibiotics, steroids, and oxygen and was discharged on day three. By 15 months he had lost speech and interaction. At 18 months he developed a very limited diet with bouts of bloody, culture negative diarrhea. Officially diagnosed autistic at 5 yrs, although he had been receiving services for autism from the school system since age 3.

Exposure sources: This child received all early vaccines with thimerosal preservative. At 2 months of age he received 62.5 mcg of mercury which represented a 125 fold increase above EPA guidelines based on his weight. This occurred again at 4 months, 62.5 mcg mercury and 50 mcg mercury at 6 months, 11 months 12.5mcg mercury and at 18 months, 50 mcg mercury for a total of 237.5 mcg of mercury. Mother also reports 5 dental amalgams and minimal dietary exposure. Child has never eaten fish or seafood.

Mercury Levels: Hair analysis from 20 months revealed 4.8 ppm mercury with a reference range of 0-1ppm and aluminum 40.2 with a reference of 0-9ppm. Note this sample was not sent for analysis until the child was already 5 1/2 years at which time the mother became aware of his early mercury exposure from vaccines. A subsequent analysis at 5 ½ years revealed normal levels of mercury and elevated lead 1.14 ppm with a normal reference 0-0.5, aluminum 23.2, and antimony 0.017 with reference of 0-0.03 and bismuth 0.19 with reference of 0-0.11. Initial treatment with oral DMSA removed 17 mcg per g creatine lead with reference 0-15 mcg per g creatine. Oral cyclic chelation was continued for 5 cycles with lead again present at 15 mcg per g creatine down to normal levels at the 5th cycle.

Response to treatment: Parents report marked improvement with each round of chelation. The last two cycles were not as pronounced as the first 3

cycles of treatment. An increase in spontaneous language and a general overall increase in all areas of functioning were also noted.

Identifier: 0005ZH **Sex**: M **Age**: 10 **DOB**: 5-28-89

Prenatal and Postnatal History: Unremarkable pre- and postnatal course. Term vaginal delivery. Pitocin given for failure to progress. Birth weight 7 lbs. 14 oz., good apgars.

Developmental Landmarks: Mother reports he was a very alert and pleasant infant who easily obtained all his early developmental landmarks with the exception of crawling. He progressed directly to walking at 8 ½ months. He began to babble and had developed some speech the first year of life, which did not progress.

Regression and Symptoms: Parents were concerned about his speech delay but attributed it to other factors. He also developed a very picky diet with a preference for starches. He also would line up toys and repeat phrases but was not officially diagnosed autistic until 5 years of age.

Exposure Sources: Mother with multiple dental amalgams. DPT vaccine known to have mercury 25 mcg per dose at 2,4,and 6 months. Child did eat fish sticks as a toddler but parents switched to only farm raised fish.

Mercury Levels: A 24 hour heavy metal challenge at 9 years of age removed 67 mcg of mercury. Unfortunately, the parents were not able to financially afford further treatment at that time.

Identifier: 0006MA **Sex**: M **Age**: 4 ½ yrs. **DOB**: 8-24-95

Prenatal and Postnatal History: Uncomplicated pregnancy, term vaginal delivery, apgars 9 and 10, birth weight 7 lbs. 6 oz. Quickly learned to breast feed, unremarkable postnatal history.

Developmental Landmarks: Easily met all early developmental milestones. Described as being very social with good eye contact. He was saying Mama, bye-bye, and babbling at 14 months.

Regression and Symptoms: According to the parents, at 16 to 17 months he began to slide into his own world. He stopped responding to his name and making eye contact. He also lost language and social interactions. Parents also report muted emotions.

Exposure Sources: This infant was exposed to 100 mcg mercury the first six months of life via vaccines. No dietary exposure from seafood or fish to the child. Mother with 9 amalgam fillings and only occasional fish consumption during pregnancy.

Mercury Levels: Hair analysis without mercury detection. Heavy metals challenge urine 8.6 mcg / g / creatine with a norm reference of 0-2.5 mcg / g

/ creatine at 3 years 8 months of age. He is currently undergoing cyclic chelation therapy with oral DMSA.

Response To Treatment: Parents report that his level of awareness, eye contact, emotions, and receptive and expressive language have all improved since starting the chelation program.

Identifier: 0007EK **Sex**: M **Age**: 5 **DOB**:12-10-94

Prenatal and Postnatal History: Uncomplicated prenatal and postnatal history. Birth weight 8 lbs., apgars 9 and 9.

Developmental Landmarks: Easily met all early milestones. Parents report precocious language skills. At 10 months he was talking with phrases "oh, there it is."

Regression and Symptoms: At 12 months there was a major and obvious reversal in behavior. Speech, social interaction, and laughter began to fade away rapidly. He began toe walking, lost eye contact, grew inattentive, and developed repetitive behaviors.

Exposure Sources: Mother with 8 dental amalgams, no fish consumption. Infant received thimerosal in vaccines, but unable to calculate exposure at this time. At 3 years of age 8 amalgam fillings were placed with an initial improvement in behavior for 3 weeks, then a decline to a level much worse than before the dental work with progressive decline.

Mercury Levels: Prior to chelation non-detectable, 12-27-99. DMPS IM + oral DMSA/EDTA and DMSA/EDTA supp. (unspecified doses).

2-19-99 41 mcg / g creatine of urinary mercury.

DMSA supp. 250mg bid were used 3 x week, every other week subsequent to provocation testing. Oral DMSA provocation for urinary Hg pending.

Response to Treatment: Multiple dietary and secretin infusions are concurrent to the DMPS/DMSA chelation, but mother is firmly convinced that the latter are contributing to excellent behavioral and somatic gains. Improvement in eye contact within 2 days of DMSA is evident. Improvement in speech, sociability and playing with toys are seen consistently right after DMSA and are reported to be on a gradual upward trend. A full sentence was uttered on or about 3-1-00.

In addition to the above case studies, we have collected preliminary data on three autistic children who have not undergone chelation. These children also exhibit elevated levels of mercury.

Data on Non-Chelated ASD Children

Age Sex Mercury level and source of sample

2 ½ yrs. Female Heavy metal hair analysis 5.6ppm (ref.range 0-2)
4 ½ yrs. Male Hair analysis 1.2ug/g (ref. <0.4) PRBC 18.4 (ref <9)
5 yrs. Male Hair analysis 1.8 ppm PRBC 18.3 (ref.<9)

Discussion

Several observations from these case studies deserve mention. One is that all of the children experienced a regressive form of autism. Other findings are that (i) low levels of mercury in hair may be associated with large amounts of mercury excretion on provocation and (ii) initial levels of provoked mercury may not be as high as subsequent ones. Mercury in the hair will only reflect a current or recent exposure of approximately one year or the body's active detoxification of mercury. This was evident in a child with non-detectable levels of mercury in the hair and positive levels on provocation.

In the case studies there is also a trend of higher numbers for mercury in younger children (20 month hair sample of 4.8 ppm and 2 ½ year hair sample of 5.6 ppm). This may be related to the fact that the testing was performed closer to the time of exposure. Hair levels of mercury greater than 5.0 ppm are considered diagnostic for mercury poisoning (*Applied Toxicology*, 1992). Among the majority of these case studies much more modest elevations of mercury, if detected at all, were associated with high levels of provoked mercury.

There are no standards for provoked levels of mercury in children in the context of behavioral disorders. Therefore, we surveyed a large number of physicians treating adults with chronic health problems diagnosed as secondary to mercury. These clinicians advise that tolerable limits may vary according to the general health of the patient and associated health problems. All consulted agreed that in adults excretion of 50 mcg of mercury per gm creatine after intravenous DMPS challenge is worrisome. We submit that the concern level for children should be even more stringent. High levels of mercury are demonstrated in some children without a history of fish consumption, amalgam burden, or known environmental exposure, suggesting the role of vaccines as a contribution to body burden.

The families who submitted these case histories wanted to tell their stories because their children are noticeably improved after treatment for mercury. Whether this improvement was sudden or gradual, the parents are convinced that lessening the mercury and heavy metal burden has helped their child. They ask us to request support for much needed research in this area.

DISCUSSION

How reasonable is it to claim that the most common form of autism, where there is normal development and then regression, could be caused by mercury poisoning? There are several reasons to believe that this process has indeed occurred.

Diagnostic Criteria Are Met

Medical literature demonstrates that mercury can induce autism-spectrum traits, and this association extends to mercury’s localization within specific brain nuclei. In attempting to address "the totality of the syndrome" (Bailey et al, 1996), we have shown that every major characteristic of autism has been exhibited in at least several cases of documented mercury poisoning, and that every major area of biological and neurological impairment implicated in ASD has been observed with Hg exposure. Recently, government-directed studies have revealed that the amount of mercury given to infants receiving vaccinations exceeds safety levels. The timing of mercury administration via vaccines coincides with the onset of autistic symptoms. Case reports of autistic children with measurable mercury levels in hair, blood, and urine indicate a history of mercury exposure along with inadequate detoxification. Thus the standard criteria for a diagnosis of mercury poisoning in autism, as outlined at the beginning of this paper, are met. In other words, mercury toxicity is a significant contributing factor or primary etiological factor in many or most cases of autism.

Unique Form Would be Expected, Implicates Vaccinal Thimerosal

Symptoms manifested in mercury poisoning are diverse and vary by the interaction of variables such as type of mercury, age of patient, method of exposure, and so forth. Thus, although it could be argued that in all the thousands of cases of past Hg poisonings, no instance of autism could be found, such an argument fails to take into account the possibility of unique expression. It would be comparable to saying that, because in all the cases of Minamata disease no instance of acrodynia could be found, then acrodynia could

not be caused by mercury poisoning. Since there are no case reports or systematic studies in the literature of the effects of intermittent bolus doses of injected ethylmercury on "susceptible" infants and toddlers, it would be reasonable to expect that symptoms arising from this form of mercury poisoning would present as a novel disease. In fact, given the high neurotoxicity of organic mercury, its known psychological effects, and the age at which it has been given in vaccines, it would almost be a given that the "novel disease" would present as a neurodevelopmental disorder like autism.

Conversely, the fact that autism meets the diagnostic criteria for mercury poisoning, yet has never been described as a mercury-induced disease, requires that the disorder must arise from a mode of mercury administration which has not been studied before. This would rule out other known sources of Hg like fish consumption or occupational mercury hazards, as these have been well characterized. It is possible that another under-investigated mercury route, such as maternal Hg exposures (e.g., from vaccinations, thimerosal-containing RhoGam injections during pregnancy, or dental fillings) or infant exposures to thimerosal-containing eardrops or eyedrops, might be a factor, and this cannot be ruled out.

Historical Precedent Exists

There is a precedent for large scale, undetected mercury poisoning of infants and toddlers in the syndrome that came to be known as acrodynia or pink disease. For over 50 years, tens of thousands of children suffered the bewildering, debilitating, and often life-long effects of this disease before its mercury etiology was established, as Ann Dally relates in *The Rise and Fall of Pink Disease* (1997, excerpts):

> "Acrodynia is a serious disease that was common, at least in children's clinics, during the first half of the present (20th) century. Reports abound of children too miserable to acknowledge their mothers, such as the child who kept repeating, "I am so sad." One unhappy mother was quoted as saying, "My child behaves like a mad dog." In most cases the condition improved spontaneously, but was often regarded as chronic. Mortality varied from 5.5% to 33.3% and was usually about 7%. Most physicians who speculated on the causes of pink disease believed in either the infective or the nutritional theory. No one seems to have suggested that it might be due to poisoning. It was a tradition to advise student doctors to treat cases of difficult teething with the mercury powders that were eventually to be revealed as the cause of the disease. The ill-effects of mercury on the mouth had been known at least since the time of Paraclesus, but it was not until 1922 that the pediatrician, John Zahorsky, commented on the similarity between pink disease and mercury poisoning. He dismissed rather than pursued his new idea of possible mercury poisoning and suggested a theory that was more in tune with current fashion. Most doctors, even those skilled in the use of calomel, associated mercury poisoning with adults (syphilis, industrial poisoning, hatters shakes) rather than with infants. By 1935 the disease was seen in every children's out-patient clinic.
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> The mystery began to be solved in 1945 by Dr. Josef Warkany, of the Cincinnati Children's Hospital. He and his assistant found large amounts of mercury in the urine of a child with pink disease. They did not publish their findings until 1948, but it is noteworthy that the news seems not to have spread through the small and tightly knit pediatric world, where everyone knew everyone else. It was probably because the idea was unfashionable and contrary to the conventional wisdom. The theory that mercury poisoning caused pink disease was gradually accepted, but against resistance, particularly by older men and those in powerful positions. Mercury was withdrawn from most teething powders after 1954, initially through voluntary

> action by the manufacturers because of adverse publicity and probably in the hope of avoiding statutory prohibition. Pink disease almost disappeared. Later in the decade the theory was widely accepted and soon pink disease was no longer part of the usual pediatric out-patient clinic."

Thus, like acrodynia before it, autism may in fact be "just another" epidemic of mercury poisoning, this time caused by childhood vaccinal mercury rather than infant teething powders.

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The priorities and methods of research experts in the autism and mercury fields have prevented the association between mercurialism and ASD to be recognized until recently. The effects on humans of mercury-containing medicinals and home remedies used to be studied quite regularly by medical researchers (Warkany and Hubbard, 1953); but since, aside from vaccinal thimerosal, such products have declined dramatically in number since the 1950s and 1960s, most mercury researchers today focus on biochemical studies or environmental sources like fish and coal plants. Some mercury experts seem surprised to learn that Hg is present in infant vaccines (authors' personal experience), and as recently as 1997, when the EPA released its massive review of extant mercury research, vaccines were not even mentioned as a potential source. Thus it is not surprising that mercury experts have never investigated thimerosal as they have, say, contaminated whale meat consumption in the Faroes Islands or Hg exposure among Amazonian goldminers.

Likewise, it is not surprising that neither mercury experts nor autism professionals have ever investigated autism as a possible disease of mercury exposure. Since its discovery by Kanner, autism has been characterized in almost exclusively psychological terms. The descriptions have been such that the symptoms would be essentially unrecognizable as manifestations of poisoning to any mercury expert not looking closely. A perfect example is Kanner himself, who recorded feeding problems and vomiting in infants and concluded: "Our patients, anxious to keep the outside world away, indicated this by the refusal of food." Bruno Bettleheim, who dominated autism discourse in the 1950s and 1960s and blamed the entire disorder on "refrigerator mothers" who forced the withdrawal of the child, asserted, "the source of the anxiety is not an organic impairment but the child's evaluation of his life as being utterly destructive" (1967, reported in ARI Newsletter). In 1987, Robert Sternberg would propose a "unified theoretical perspective on autism" by defining the disorder in terms of a "triarchic theory of intelligence," and in the same publication Lorna Wing and Anthony Attwood would write:

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In the latter part of the 1990s, the situation on both sides changed. Congressional mandate led to the public quantification of the cumulative amount of mercury in vaccines, raising interest in understanding its effects. Parent organizations like CAN and NAAR, working with the NIH and other researchers, engineered an autism research agenda which is more heavily focused on underlying physiological mechanisms of the disease. With parents

already suspecting a vaccine-autism link, the environment was right for investigations focused on the link between vaccinal mercury and autism.

MEDICAL & SOCIETAL IMPLICATIONS

Affected Population

The NIH (1999, web site) estimates that there are nearly half a million Americans who suffer from autism, a devastating, debilitating, and lifelong disorder. Given the role of thimerosal as a major contributing factor in ASD, basic and clinical research efforts should be focused on understanding how mercury leads to autism in susceptible individuals and on finding effective methods to address the resulting Hg damage. Such research might focus on the following areas, with others undoubtedly still to be identified:

(a) Chelation methods which will work across all body tissues and especially the brain. The current standard chelators - DMPS and DMSA - appear unable to cross the blood-brain barrier. Other promising but less studied chelators like alpha lipoic acid can cross the bbb (Fuchs et al, 1997) and should be studied in autism.

(b) Mechanisms to induce immunity to Hg and which might possibly reverse the Th2 shift or IFNg expression which mercury causes. The work of Hu and colleagues suggests that Hg can cause an immune reaction in any individual, but some are protected by a counteractive immunosuppressive response, and Warkany and Hubbard have pointed out that individuals who are Hg-sensitive can later become "immune". It may be possible to engineer these responses in autistic individuals through careful research.

(c) Mechanisms which might reverse Na-Si transporter blockage in the intestines and kidney, thereby normalizing sulfate absorption.

(d) Techniques to eliminate the Hg-induced epileptiform activities found in the majority of autistic children, as outlined by LeWine et al.

(e) Stem cell applications in autism to repair brain damage that occurred during development.

Other Disorders

As pointed out by David Hartman (1998), mercury's ability to cause a wide range of common psychiatric disturbances should be considered in their diagnosis, and it might also be productive in developing hypotheses about and designing research studies for these other disorders. The disorders might include depression, OCD, dementia, anxiety, ADHD/ADD, Tourette's, and schizophrenia. Mercury may play a role in the etiology of some cases of these conditions. Conversely, investigating mercury's wide ranging effects upon neurobiological processes may lead to a quicker understanding of the organic etiologies in these other diseases which are now seen with increasing frequency.

Vaccination Programs

Universal compliance with the recommended vaccine schedule is a governmental, medical, and societal goal, since "vaccines save lives" (CDC). Our goal is not to negatively impact childhood immunization rates. Instead, we have been careful to distinguish between thimerosal and vaccines. Thimerosal is not a vaccine; it is a preservative. Except for trace amounts, vaccines without thimerosal are currently available for all routinely recommended immunizations for children under 6 years (Institute for Vaccine Safety, 1999). Furthermore, it is possible to remove mercury from existing products. Merck, for example, delivered and received FDA approval for a thimerosal-free Hepatitis B vaccine in a record-breaking two

months from the time the FDA publicly encouraged manufacturers to develop thimerosal-free alternatives (Pless, 1999; Merck, 1999). Thus, any issues being raised here are related to how vaccine programs are run, not with vaccines themselves.
The issues, of course, are: (i) first, how thimerosal was allowed to remain a component of the immunization program, even after 1953 when Warkany and Hubbard specifically named vaccinal mercury as a possible factor in acrodynia, or 1982 when the FDA issued a notice singling out thimerosal as especially neurotoxic as well as ineffective as a preservative (Federal Register, 1982); and (ii) second, why thimerosal remains in over 30 vaccine products today (FDA, 1999), and why the FDA, as of March 2000, has only "encouraged" rather than required the vaccine manufacturers to remove the thimerosal (William Egan personal communication). Although the CDC has stated that no adverse effects from thimerosal have been found other than hypersensitivity reactions, the sad fact is there have been no direct studies on the long term effects of intermittent bolus doses of ethylmercury injected in infants and toddlers. As Altman and Bland have aptly demonstrated (1995), "absence of evidence is not evidence of absence."
These lapses in vaccine program oversight suggest that vaccine safety studies need to be bolstered. Current practice is to track adverse reactions only if they occur within one month of the vaccination. The experience with mercury clearly shows that an adverse event may not manifest for months if not years. Studies on adverse reactions must involve long term tracking of patients; they should investigate the impact of multiple injections as well as compare reactions to vaccines with and without various additives; and sample sizes need to be large enough to include especially sensitive groups. Finally, the FDA should require manufacturers to remove all remaining thimerosal from their vaccines immediately, so that another child is not lost to this terrible disease.

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MEDICAL & SOCIETAL IMPLICATIONS

Affected Population

The NIH (1999, web site) estimates that there are nearly half a million Americans who suffer from autism, a devastating, debilitating, and lifelong disorder. Given the role of thimerosal as a major contributing factor in ASD, basic and clinical research efforts should be focused on understanding how mercury leads to autism in susceptible individuals and on finding effective methods to address the resulting Hg damage. Such research might focus on the following areas, with others undoubtedly still to be identified:

(a) Chelation methods which will work across all body tissues and especially the brain. The current standard chelators - DMPS and DMSA - appear unable to cross the blood-brain barrier. Other promising but less studied chelators like alpha lipoic acid can cross the bbb (Fuchs et al, 1997) and should be studied in autism.

(b) Mechanisms to induce immunity to Hg and which might possibly reverse the Th2 shift or IFNg expression which mercury causes. The work of Hu and colleagues suggests that Hg can cause an immune reaction in any individual, but some are protected by a counteractive immunosuppressive response, and Warkany and Hubbard have pointed out that individuals who are Hg-sensitive can later become "immune". It may be possible to engineer these responses in autistic individuals through careful research.

(c) Mechanisms which might reverse Na-Si transporter blockage in the intestines and kidney, thereby normalizing sulfate absorption.

(d) Techniques to eliminate the Hg-induced epileptiform activities found in the majority of autistic children, as outlined by LeWine et al.

(e) Stem cell applications in autism to repair brain damage that occurred during development.

Other Disorders

As pointed out by David Hartman (1998), mercury's ability to cause a wide range of common psychiatric disturbances should be considered in their diagnosis, and it might also be productive in developing hypotheses about and designing research studies for these other disorders. The disorders might include depression, OCD, dementia, anxiety, ADHD/ADD, Tourette's, and schizophrenia. Mercury may play a role in the etiology of some cases of these conditions. Conversely, investigating mercury's wide ranging effects upon neurobiological processes may lead to a quicker understanding of the organic etiologies in these other diseases which are now seen with increasing frequency.

Vaccination Programs

Universal compliance with the recommended vaccine schedule is a governmental, medical, and societal goal, since "vaccines save lives" (CDC). Our goal is not to negatively impact childhood immunization rates. Instead, we have been careful to distinguish between thimerosal and vaccines. Thimerosal is not a vaccine; it is a preservative. Except for trace amounts, vaccines without thimerosal are currently available for all routinely recommended immunizations for children under 6 years (Institute for Vaccine Safety, 1999). Furthermore, it is possible to remove mercury from existing products. Merck, for example, delivered and received FDA approval for a thimerosal-free Hepatitis B vaccine in a record-breaking two months from the time the FDA publicly encouraged manufacturers to develop thimerosal-

free alternatives (Pless, 1999; Merck, 1999). Thus, any issues being raised here are related to how vaccine programs are run, not with vaccines themselves.
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These lapses in vaccine program oversight suggest that vaccine safety studies need to be bolstered. Current practice is to track adverse reactions only if they occur within one month of the vaccination. The experience with mercury clearly shows that an adverse event may not manifest for months if not years. Studies on adverse reactions must involve long term tracking of patients; they should investigate the impact of multiple injections as well as compare reactions to vaccines with and without various additives; and sample sizes need to be large enough to include especially sensitive groups. Finally, the FDA should require manufacturers to remove all remaining thimerosal from their vaccines immediately, so that another child is not lost to this terrible disease.

DISCUSSION
How reasonable is it to claim that the most common form of autism, where there is normal development and then regression, could be caused by mercury poisoning? There are several reasons to believe that this process has indeed occurred.
Diagnostic Criteria Are Met
Medical literature demonstrates that mercury can induce autism-spectrum traits, and this association extends to mercury's localization within specific brain nuclei. In attempting to address "the totality of the syndrome" (Bailey et al, 1996), we have shown that every major characteristic of autism has been exhibited in at least several cases of documented mercury poisoning, and that every major area of biological and neurological impairment implicated in ASD has been observed with Hg exposure. Recently, government-directed studies have revealed that the amount of mercury given to infants receiving vaccinations exceeds safety levels. The timing of mercury administration via vaccines coincides with the onset of autistic symptoms. Case reports of autistic children with measurable mercury levels in hair, blood, and urine indicate a history of mercury exposure along with inadequate detoxification. Thus the standard criteria for a diagnosis of mercury poisoning in autism, as outlined at the beginning of this paper, are met. In other words, mercury toxicity is a significant contributing factor or primary etiological factor in many or most cases of autism.
Unique Form Would be Expected, Implicates Vaccinal Thimerosal
Symptoms manifested in mercury poisoning are diverse and vary by the interaction of variables such as type of mercury, age of patient, method of exposure, and so forth. Thus, although it could be argued that in all the thousands of cases of past Hg poisonings, no instance of autism could be found, such an argument fails to take into account the possibility of unique expression. It would be comparable to saying that, because in all the cases of Minamata disease no instance of acrodynia could be found, then acrodynia could not be caused by mercury poisoning. Since there are no case reports or systematic studies in the literature of the effects of intermittent bolus doses of injected ethylmercury on "susceptible" infants and toddlers, it would be reasonable to expect that symptoms arising from this form of mercury poisoning would present as a novel disease. In fact, given the

high neurotoxicity of organic mercury, its known psychological effects, and the age at which it has been given in vaccines, it would almost be a given that the "novel disease" would present as a neurodevelopmental disorder like autism.
Conversely, the fact that autism meets the diagnostic criteria for mercury poisoning, yet has never been described as a mercury-induced disease, requires that the disorder must arise from a mode of mercury administration which has not been studied before. This would rule out other known sources of Hg like fish consumption or occupational mercury hazards, as these have been well characterized. It is possible that another under-investigated mercury route, such as maternal Hg exposures (e.g., from vaccinations, thimerosal-containing RhoGam injections during pregnancy, or dental fillings) or infant exposures to thimerosal-containing eardrops or eyedrops, might be a factor, and this cannot be ruled out.

Historical Precedent Exists

There is a precedent for large scale, undetected mercury poisoning of infants and toddlers in the syndrome that came to be known as acrodynia or pink disease. For over 50 years, tens of thousands of children suffered the bewildering, debilitating, and often life-long effects of this disease before its mercury etiology was established, as Ann Dally relates in *The Rise and Fall of Pink Disease* (1997, excerpts):

> "Acrodynia is a serious disease that was common, at least in children's clinics, during the first half of the present (20th) century. Reports abound of children too miserable to acknowledge their mothers, such as the child who kept repeating, "I am so sad." One unhappy mother was quoted as saying, "My child behaves like a mad dog." In most cases the condition improved spontaneously, but was often regarded as chronic. Mortality varied from 5.5% to 33.3% and was usually about 7%. Most physicians who speculated on the causes of pink disease believed in either the infective or the nutritional theory. No one seems to have suggested that it might be due to poisoning. It was a tradition to advise student doctors to treat cases of difficult teething with the mercury powders that were eventually to be revealed as the cause of the disease. The ill-effects of mercury on the mouth had been known at least since the time of Paraclesus, but it was not until 1922 that the pediatrician, John Zahorsky, commented on the similarity between pink disease and mercury poisoning. He dismissed rather than pursued his new idea of possible mercury poisoning and suggested a theory that was more in tune with current fashion. Most doctors, even those skilled in the use of calomel, associated mercury poisoning with adults (syphilis, industrial poisoning, hatters shakes) rather than with infants. By 1935 the disease was seen in every children's out-patient clinic.
>
> The mystery began to be solved in 1945 by Dr. Josef Warkany, of the Cincinnati Children's Hospital. He and his assistant found large amounts of mercury in the urine of a child with pink disease. They did not publish their findings until 1948, but it is noteworthy that the news seems not to have spread through the small and tightly knit pediatric world, where everyone knew everyone else. It was probably because the idea was unfashionable and contrary to the conventional wisdom. The theory that mercury poisoning caused pink disease was gradually accepted, but against resistance, particularly by older men and those in powerful positions. Mercury was withdrawn from most teething powders after 1954, initially through voluntary action by the manufacturers because of adverse publicity and probably in the hope of avoiding statutory prohibition. Pink disease almost disappeared. Later in the decade the theory was widely accepted and soon pink disease was no longer part of the usual pediatric out-patient clinic."

Thus, like acrodynia before it, autism may in fact be "just another" epidemic of mercury poisoning, this time caused by childhood vaccinal mercury rather than infant teething powders.

Barriers Preventing Earlier Discovery Are Removed

The priorities and methods of research experts in the autism and mercury fields have prevented the association between mercurialism and ASD to be recognized until recently. The effects on humans of mercury-containing medicinals and home remedies used to be studied quite regularly by medical researchers (Warkany and Hubbard, 1953); but since, aside from vaccinal thimerosal, such products have declined dramatically in number since the 1950s and 1960s, most mercury researchers today focus on biochemical studies or environmental sources like fish and coal plants. Some mercury experts seem surprised to learn that Hg is present in infant vaccines (authors' personal experience), and as recently as 1997, when the EPA released its massive review of extant mercury research, vaccines were not even mentioned as a potential source. Thus it is not surprising that mercury experts have never investigated thimerosal as they have, say, contaminated whale meat consumption in the Faroes Islands or Hg exposure among Amazonian goldminers.

Likewise, it is not surprising that neither mercury experts nor autism professionals have ever investigated autism as a possible disease of mercury exposure. Since its discovery by Kanner, autism has been characterized in almost exclusively psychological terms. The descriptions have been such that the symptoms would be essentially unrecognizable as manifestations of poisoning to any mercury expert not looking closely. A perfect example is Kanner himself, who recorded feeding problems and vomiting in infants and concluded: "Our patients, anxious to keep the outside world away, indicated this by the refusal of food." Bruno Bettleheim, who dominated autism discourse in the 1950s and 1960s and blamed the entire disorder on "refrigerator mothers" who forced the withdrawal of the child, asserted, "the source of the anxiety is not an organic impairment but the child's evaluation of his life as being utterly destructive" (1967, reported in ARI Newsletter). In 1987, Robert Sternberg would propose a "unified theoretical perspective on autism" by defining the disorder in terms of a "triarchic theory of intelligence," and in the same publication Lorna Wing and Anthony Attwood would write:

> "Sometimes young autistic children will stand in a dejected posture, with tears streaming down their faces, as if they suddenly felt their helplessness in the face of a world they cannot understand."

Even as recently as 1995, a typical slate of articles in the dominant *Journal of Autism and Developmental Disorders* (April 1995) would consist of eight psychological pieces (example: "Generativity in the Play of Young People with Autism") and one biomedical one (on biopterin). Thus biomedical research in autism existed, but it was mostly relegated to the margins as psychology held center stage, and the symptomatic characteristics of autism continued to be presented in accord with psychological biases.

In the latter part of the 1990s, the situation on both sides changed. Congressional mandate led to the public quantification of the cumulative amount of mercury in vaccines, raising interest in understanding its effects. Parent organizations like CAN and NAAR, working with the NIH and other researchers, engineered an autism research agenda which is more heavily focused on underlying physiological mechanisms of the disease. With parents already suspecting a vaccine-autism link, the environment was right for investigations focused on the link between vaccinal mercury and autism.

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Rational for Using DMPS

Sodium 2,3-dimercaptopropane-1-sulfonate challange test for mercury in humans: II. Urinary mercury, porphyrins and neurobehavioral changes of dental workers in Monterrey, Mexico.

Gonzalez-Ramirez D, Maiorino RM, Zuniga-Charles M, Xu Z, Hurlbut KM, Junco-Munoz P, Aposhian MM; Dart RC, Diaz Gama JH, Echeverria D et al.

J Pharmacol Exp Ther 272(1):264-274 (1995)

ABSTRACT: "The sodium salt of 2,3-dimercaptopropane-1-sulfonic acid (DMPS) challange test (300 mg p.o. after an 11-hr fast) was given in Monterrey, Mexico to dental and non-dental personnel. Urine samples were collected and analyzed for total mercury. The mean mercury urinary excretion (+/- S.E.) for 6 hr before and 6 hr after DMPS administration for 10 dental technicians, who formulate amalgam, was 4.84 micrograms +/- 0.742 and 424.0 micrograms +/- 84.9; for 5 dentists, who use amalgam in their practice, 3.28 micrograms +/- 1.11 and 162.0 micrograms +/- 51.2; and for 13 nondental personnel, 0.783 microgram +/- 0.189 and 27.3 micrograms +/- 3.19. The urinary coproporphyrin levels before DMPS administration, which are indicative of renal mercury content, were quantitatively associated with the urinary mercury levels among the three study groups after DMPS administration. This was not so if the urinary mercury level before DMPS administration was compared with the urinary coproporphyrin concentration. The urinary mercury level after DMPS administration is a better indicator of exposure and renal mercury burden than is the mercury level measured in the urine before DMPS is given. Regression

analysis showed that the coefficient of urinary mercury was statistically and adversily associated with complex attention (switching task), the perceptual motor task (symbol-digit substitution), symptoms and mood. The easily performed DMPS-mercury challenge test is useful for monitoring dental personnel for mercury vapor exposure."

Mercury Toxicity and the Use of DMPS Chelation

by John C. Cline, M.D., B.Sc.,C.C.F.P.

Medical Director -- Oceanside Medical Clinic

History of Dental Amalgams

For the past two centuries, mercury amalgam use in dentistry has increased in popularity as the preferred tooth filling material.(1,2,3) However, when mercury amalgam was initially introduced into North America in the 1830s, its use was vehemently opposed by the dental licensing authority, the American Society of Dental Surgeons and official policies were adopted to prohibit the use of this material. Their concern was focussed upon the safety of placing mercury into humans since many toxic effects of mercury were well known; including dementia and loss of motor coordination. In spite of this official prohibition, several dentists continued to use mercury amalgam and some were subsequently suspended for malpractice. The popularity of this inexpensive, durable and easy to work with material continued to rise amongst dentists and by 1856, there were so many dentists using mercury amalgam that the American Society of Dental Surgeons was disbanded by overwhelming opposition to their policy surrounding amalgam fillings. Following this, in 1859 the American Dental Association was founded on the premise that mercury amalgam was a safe and desirable tooth filling material. Because of the low cost of amalgam, dentistry was now available to the masses for the first time. By 1895, the mercury amalgam mixture of metals was modified and this formula continues to be used to this day, with a typical mixture containing 50% metallic mercury, 35% silver, 9% tin, 6% copper, and a trace of zinc. Mercury amalgam continues to be the material preferred by 92% of dentists for restoring posterior teeth.(4,5) and over one hundred tons of mercury is now used in dentistry in the U.S. each year.

Mercury release from dental amalgams

The basic premise for regarding the amalgam filling as safe was the assumption that the amalgamation process resulted in a stabilization of the normally volatile mercury. This premise has now been shown to be entirely false. Since the 1980s, it has been well established that mercury vapor is continuously released from amalgam fillings. The release of this vapor into the mouth increases immediately after chewing(6) or tooth brushing(7) and can result in a daily absorbed dose of mercury which exceeds the excretory capacity via the urine and stool. It has now been well established and published by several authorities, including the World Health Organization, that amalgam tooth fillings are, by far, the major source of mercury exposure for the general population.(8) This was recently reiterated by Health Canada in its 1995 position paper on dental amalgam.(9) According to the World Health Organization's expert committee, the daily human exposure to mercury vapor from amalgam fillings ranges from 3micrograms to 17micrograms as compared to a maximum of 2.6micrograms from all other sources. It is disturbing to note that mercury was recently removed from latex paint in North America due to the health risks associated with inhalation of mercury vapor from the paint. Exposure to mercury from

paint was estimated to be 4.6micrograms per day for approximately two weeks following application of the paint.(10) If mercury in latex paint was clearly considered such a health risk, why are amalgam fillings such a source of scornful dialog amongst the dental and medical community when amalgams are a much greater source and a far more persistent source of inhaled mercury?

Pharmacokinetics of inhaled mercury

Mercury vapor released from dental amalgams is efficiently absorbed through the alveoli. Following absorption through the lungs, elemental mercury vapor (Hg0) is only found very transiently in the blood. Due to its high lipid solubility elemental mercury is rapidly transported through cell membranes (including cell membranes of the cells comprising the blood-brain barrier). Once inside metabolically active cells, elemental mercury (Hg0) is then oxidized by catalase to form ionic mercury (Hg2+). Ionic mercury (Hg2+) is not lipid soluble and it therefore results in a high degree of retention of absorbed mercury and a tissue half life ranging from days to decades depending on the particular organ.(11,8,12,13,14,15) This phenomenon clarifies why, studies have repeatedly demonstrated that after placement of amalgam fillings, blood and urinary mercury levels remain relatively low even though many organs develop concentrations of mercury many times greater than that of the blood.(16,17,18) Thus, blood or non-challenged urinary mercury levels bear little relationship to the total body burden of mercury gradually acquired from amalgam fillings.(19)

Biochemical effects of inhaled mercury

Once mercury enters the cell, it ultimately becomes bound covalently to the sulfhydryl groups found in glutathione, and to a lesser degree to cysteine, biotin, lipoic acid, coenzyme A as well as to other protein sulfhydryl groups. The major intracellular sulfhydryl compound in mammals is the tripeptide glutathione. Glutathione and the glutathione rich enzyme, glutathione peroxidase are probably the most important antioxidant defenses in most species including the human.(20) Mercury has been shown to cause a marked reduction in glutathione production and glutathione peroxidase activity and thus it may result in a marked rise in oxidative stress within the brain and other organs.(21,22,23) Apart from the loss of antioxidant protection from mercury induced inhibition of glutathione and glutathione peroxidase, mercury results in a marked increase in free radical generation through Fenton reactions and other mechanisms.(22)

In addition to its key role in antioxidant defenses, glutathione is also a critical component in the liver's detoxification mechanisms. Enzymes within the liver must form conjugates between glutathione and certain toxic metabolites, organic xenobiotics, and heavy metals to enable these toxins to be eliminated from the body. This process of glutathione conjugation makes toxic molecules more water soluble and enables their excretion via the bile or through the kidney. If liver glutathione production is markedly inhibited, as occurs when mercury accumulates within hepatocytes, mercury and numerous other toxic substances may more readily accumulate throughout the body because the excretion of such substances are significantly impaired.(24,25,26,22) Furthermore, because the majority of mercury is excreted through the stool and urine as a glutathione conjugate, individuals with long standing body burdens of mercury (and thus depleted glutathione production) may not demonstrate elevated levels of mercury in the urine, blood or stool when specimens are gathered in the absence of a challenge with an appropriate metal chelating agent. Thus, tissue biopsy of target organs or a provocation test measuring urinary mercury after the administration of a chelating agent, may be the only valid means to assess chronic mercury body burden.(27,28,29,30)

Uptake and distribution of inhaled mercury

Numerous studies have been performed demonstrating the body tissue uptake and distribution of mercury from dental amalgams. Studies using whole body imaging in primates with dental amalgams have clearly demonstrated that the amalgams result in high levels of mercury in the kidney, intestinal tract, brain, liver, and other organs. (31,16) Of great concern are human fetal and neonatal studies which demonstrate that mercury concentrations in kidney, liver, and brain correlate significantly with maternal amalgam surfaces.(32) Furthermore, a recently published study has firmly established the presence of mercury from dental amalgam in the milk of nursing mothers.(33)

Clinical effects of inhaled mercury

The impact of chronic, low level mercury exposure is now known to adversely impact numerous other cellular and organ system processes.(19) Ionic mercury is antigenic and may contribute significantly to autoimmune processes.(34,35) Mercury is also immunotoxic and it may result in immune suppression and allergy.(36,37,38,39) Recent research has also demonstrated that multiple strains of antibiotic resistant bacteria develop rapidly in the gut and oral cavity of both humans as well as non-human primates following the placement of amalgam fillings.(40)

Amalgam fillings have been shown to contribute to mercury accumulation in human and animal kidneys and this has been associated with a significant decrease in renal function.(41,42) Human fertility has also been shown to be significantly impacted by low level exposure to mercury vapor. A recent study examining 7000 dental assistants demonstrated that this group experiences a fertility rate approximately 40% less than that of women who have no occupational exposure to mercury.(43)

Of perhaps greatest concern is the potential role of low level, chronic mercury exposure upon central nervous system function. It is now well established, that amalgam derived mercury accumulates in monkey and human brain tissues.(41,31,13) Mercury has been shown to concentrate selectively in human brain regions involved with memory function and it may play a significant role in the etiology of Alzheimer's disease.(44,45) Other reports have shown subclinical motor and neuropsychological deficits amongst dentists and dental workers as compared to control subjects.(46,47) Mounting evidence has lead some to suggest that, in fact, mercury from amalgams may play a highly significant role in the etiology of numerous mental illnesses and neuropsychological disorders.(48, 49,50,51,52,53)

Pharmacology of DMPS (Dimaval¦ 2,3-dimercapto-1-propane sulfonate, Na+)

DMPS (sodium salt of 2,3-dimercapto-1-propane sulfonic acid) is not a new drug. It was developed in the former Soviet Union in 1958. In 1978, DMPS became available to the western world following its synthesis and production by the German pharmaceutical company, Heyl.54 DMPS is a chelating agent in the group of dithiols, along with dimercaprol (BAL, British anti-Lewisite) and succimer (DMSA, 2,3-dimercaptosuccinic acid).

DMPS has been used extensively in Europe and on a limited basis in North America as a treatment for mercury (55), arsenic (56) or lead intoxication (57). It is a registered drug in Germany and, in fact, due to its long record of safety, is now available without prescription.(28) When compared with D-penicillamine and N-acetyl-DL-penicillamine, DMPS was the most effective agent to clear mercury from the blood of victims of the Iraqi mercury disaster in the 1960's. (58)

In addition to its safety and utility as an agent for detoxification, DMPS has been used frequently as an agent to approximate mercury body burden.(56,59) As described above, resting urine or blood levels of mercury bear little relationship to body burden of mercury in cases of long standing, low level intoxication, such as that which may occur from dental amalgams.(27),

There is a great wealth of scientific literature on the use of DMPS as both a diagnostic tool and a treatment agent in cases of acute and chronic heavy metal intoxication. Much of the European literature surrounding DMPS has been summarized in the English language in a thorough scientific monograph which is in its sixth edition.60 This monograph forms the basis for the rational use of DMPS by clinicians throughout the world. This monograph also formed the basis for the FDA sanctioned, multicentered trial on the use of DMPS in the evaluation of mercury body burden and response to mercury detoxification therapy in polysymptomatic patients with dental amalgams. (As an aside, Dr. Cline was a participant in the official training program for researchers participating in this multicentered trial and he achieved a mark in the 90th percentile range on the examination required for participation).

In the DMPS monograph, there is extensive reference to the work being done by European clinicians in the treatment of the polysymptomatic patient suffering from demonstrable mercury body burden. DMPS is initially used to assess the body burden of mercury and other heavy metals through provocation testing. Several methodological variations of this test are described. Because of the high degree of patient compliance, and because this methodology is in keeping with the pharmacokinetics of DMPS, I have elected to use the provocation testing methodology advocated by the German toxicologist, M. Daunderer, M.D.(61, 60) In this methodology, DMPS is given as a slow IV push. The patient then provides the first voided specimen after one to one and one half hours. The urine is then sent overnight to a toxicology laboratory. Mercury and other heavy metals are reported as micrograms metal per gram of urinary creatinine. The creatinine compensates for variations in urinary dilution. This has proven to be a simple test to perform, with a high degree of patient compliance. The quantity of heavy metal returned has generally correlated well to the symptom severity of the patients I have seen. Furthermore, the changes in metal excretion with this provocation test have corresponded well to the changes in symptom severity of the patients which I have seen. The provocation test forms a rational approach to the use of DMPS. When high quantities of toxic metals are no longer found with provocation urine testing, the DMPS is of no further value and its use may discontinued.

As mentioned previously, the pharmacology of DMPS has been extensively described.(54,28) Both oral and parenteral preparations of this agent are available. Pharmacokinetic data on both preparations are available.(62,63) The parentaral from of this agent allows for better control over the dosage in highly sensitive patients (the treatment can be interrupted if the patient experiences adverse effects). The parenteral route also avoids transport of metals from the gut to the liver through the portal circulation and may be better tolerated by the highly sensitive patient.

The metabolism of DMPS has also been studied thoroughly. DMPS is excreted largely through the urine. Before its excretion, DMPS is biotransformed largely to acyclic and cyclic disulfides. This mode of biotransformation may suggest one advantage of DMPS over the other dithiol chelator, DMSA (succimer). As opposed to DMPS, DMSA is biotransformed almost completely to a cysteine conjugate. Because of this, DMSA may lead to further depletion of cysteine and glutathione stores, which are often already low in metal toxic patients.(64,62,65,23) DMPS undergoes both renal and biliary excretion.(66) DMPS is distributed in both an intracellular and extracellular manner.(66,67,68) However, Unlike most other chelating agents, such as BAL and EDTA, DMPS does not cross the blood brain barrier and does not redistriute mercury to the brain(28).

The toxicity of DMPS is well known and, in this regard, it provides very distinct advantages to the officially approved dithiol chelator, Dimercaprol (BAL). Although BAL continues to be stockpiled by the military in preparation for chemical warfare attack with the arsenical nerve gas, lewisite, it is 300 times more toxic than DMPS, has no corresponding challenge test and it clearly causes redistribution of metals to the brain.(69) Animal studies on the acute and chronic toxicity of DMPS have been carried out and the results illustrate the safety of this agent and its wide therapeutic window.(60) Numerous human studies have failed to uncover any significant adverse impacts of DMPS upon human renal function, liver function, cardiovascular system, blood, immune system,

G.I. tract or any other organs or systems. Minor or avoidable side effects such as local irritation at the site of parenteral infusion or hypotension with overly rapid infusion of the agent have been reported.(60)

Rationale For Using DMPS:

The scientific rationale for using DMPS in determining the body burden of and the removal of mercury and other heavy metals has been outlined above. The clinical rationale for using DMPS in people suffering from idiopathic polysymptomatic disorders such as fibromyalgia and chronic fatigue syndrome is as follows. Current scientific understanding of these disorders suggests that the etiologies are multifactorial and may have significant environmental components including accumulation of heavy metals in key target organs. Most patients coming to my clinic with these chronic disorders have already attended several practitioners and have tried all sorts of therapies, usually to no avail. These patients are well educated regarding the various possible underlying etiologies and want to explore the possibility that heavy metals may be an underlying factor. I have observed that in most individuals in which mercury and other heavy metals are present, that a major improvement in their health usually occurs when they undergo detoxification using DMPS. This is in keeping with the observations made by numerous clinicians in Europe and in the USA by the principle investigators in the multicenter phase III, FDA approved clinical trial mentioned earlier. Finally, I want to emphasize that DMPS is not being utilized as the sole treatment in individuals suffering from these disorders, but rather it is being utilized as a method to relieve the patient of significant physiological stresses by decreasing the body burden of heavy metals. Although further research is clearly required in this area, my clinical experience over the last year in using DMPS has convinced me that this valuable agent has a key role to play in the management of highly disabling and previously intractable cases of chronic fatigue syndrome and fibromyalgia. There are many patients in my practice who are now healthy productive citizens instead of hopeless invalids, thanks to the use of DMPS administered in a safe manner.

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Mercury Threat To Fetus Raised

By Guy Gugliotta

A new government analysis nearly doubled the estimate of the number of newborn children at risk for health problems because of unsafe mercury levels in their blood. Environmental Protection Agency scientists said yesterday that new research had shown that 630,000 U.S. newborns had unsafe levels of mercury in their blood in 1999-2000. The key factor in the revised estimates is research showing differences in mercury levels in the blood of pregnant women and their unborn children. In a January 26 presentation at EPA's National Forum on Contaminants in Fish, in San Diego, EPA biochemist Kathryn R. Mahaffey said researchers in the last few years had shown that mercury levels in a fetus's umbilical cord blood are 70 percent higher than those in the mother's blood.

"We have long known that the effects of methyl mercury on the fetal nervous system are more serious" than on adults, Mahaffey said in a telephone interview yesterday. "But we did not

routinely measure [umbilical] cord blood. We had thought that the mother and the fetus had the same level." Jane Houlihan, a vice president of the Environmental Working Group, noted that the study "for the first time . . . calculated the number based on children's blood levels, not mothers'. The EPA
analysis is showing that even if even if the mother is below the danger zone, she can give birth to a baby that's over the limit."

Mercury, a heavy metal, is a highly toxic substance that can seriously damage neurological tissue. Poisoning can lead to learning disabilities, lower intelligence and overall sluggishness. Fetuses, infants and young children are especially vulnerable. Recent advisories from EPA and the Food and Drug Administration have cautioned pregnant women on the dangers of eating tuna and other large predatory fish and shellfish, whose tissues absorb elevated levels of mercury. EPA has said the largest U.S. sources of mercury contamination are coal-fired power plants, whose annual atmospheric emissions contain 48 tons of mercury. Much of it drifts into the ocean. The Bush administration is proposing a new regulation requiring power plants to cut mercury emissions 29 percent by 2007 and 70 percent by 2018.
Environmental advocates say the industry can achieve significantly deeper reductions. Mahaffey, a top scientist in EPA's Office of Prevention, Pesticides and Toxic Substances, said she began developing her new estimates of the number of infants at risk by studying research published last year from New Jersey and Maine. The information helped her revise the formula used to extract data from a survey conducted by the Centers for Disease Control and Prevention in 1999-2000 on mercury levels in pregnant women's blood. The new formula showed that one out of six pregnant women had mercury levels in their blood
of at least 3.5 parts per billion, sufficient for levels in the fetus to reach or surpass the EPA's safety threshold of 5.8 parts per billion. In 1999-2000, the last year for which government data are available, this meant that 630,000 children were at risk instead of the original estimate of 320,000.

CDC Vaccine Data Leads Scientists to Shocking Discovery

CHILDREN 27-TIMES MORE LIKELY TO DEVELOP AUTISM WITH EXPOSURE TO MERCURY CONTAINING VACCINES, FINDINGS REVIEWED AT TODAY=S IOM MEETING IN DC
Washington, Feb 9/PRNewswire/ B Today, the Institute of Medicine will hold a one-day meeting to review important new research on the link between thimerosal, a mercury-based preservative in vaccines, and neurodevelopmental disorders such as autism. One of the larger studies under review comes from the CDC=s own Vaccine Safety Datalink. Under independent investigation, CDC=s data concludes children are 27-times more likely to develop autism after exposure to three thimerosal-containing vaccines (TCVs), than those who receive thimerosal-free versions. The findings are not only disturbing to government officials like U.S. Rep. Dave Weldon, M.D. (R-FL), who is also scheduled to speak before the IOM panel they suggest autism via TCVs has a higher relative risk than that between lung cancer and smoking, which according to the American Cancer Society is only 22 for men and 11 for women. This absolutely confirms what parents have been saying for years,@ says Jo Pike, President, National Autism Association. Like Pike, thousands of parents have reported sharp regressions in their children following a TCV and many of those children have gone on to receive a label of autism. An easy mistake to make since the symptoms of autism and mercury poisoning are almost identical.
Dr. Mark Geier is the lead investigator in the discovery. A medical doctor with a Ph.D. in

genetics, he along with fellow researcher, David Geier will discuss their findings of the CDC data in front of an IOM panel. Among a host of other physicians and researchers presenting will be Dr. Jeff Bradstreet. He will discuss the results from his peer-reviewed study which concluded that urinary mercury concentrations were six times higher in children with autism vs. normal age/vaccine-matched controls.
The presentation will begin at 8:00 AM at The National Academy of Sciences, Auditorium 2100 C Street NW. Dr. Mark Geier and David Geier are scheduled to present their findings at 12:15. Weldon speaks at 8:00. Bradstreet at 4:00. For an agenda, go to http://www.iom.edu/event.asp?id=17047. For information about the National Autism Association, go to www.nationalautism.org

Typical Course of an Autistic patient

1. Hepatitis B immunization at 12 hours after birth. DPT immunization at 4 and 8 weeks*; oral polio immunization also at 4 and 8 weeks, again at 3 months. Schedule now being changed; children will receive 2 doses of live attenuated oral polio and 2 doses killed polio; oral polio can cause disease; only killed polio is used in Europe.
2. Because of great decrease in cell-mediated immunity (CMI) in infants, the vaccines lower CMI further; one decreases CMI by 50%; two together by 70%. Longest safety trial of of the triple vaccine (MMR, all live attenuated viruses) was three weeks.
3. Repeated immunizations with 3 vaccines simultaneously, e.g., pneumococcus, hemophilus, etc. from 4 weeks to 12 or 18 months. Repeat DPT is given at 12 months.* All these triple vaccines markedly impair CMI.
4. Resultant decrease in CMI predisoposes to recurrent viral infections, especially otitis media, since CMI controls response to viruses (also fungi [e.g., *Candida*], parasites [e.g., leishmaniasis], mycobacteria [e.g., tuberculosis, even if drug resistant, and leprosy].
5. When infections occur, bacterial cultures rarely performed, yet infants repeatedly given antibiotics. Antibiotics are of asbsolutely no help in viral infections; in some countries, antibiotic administration without a prior cultutre is considered malpractice.
6. Antibiotics wipe out helpful bacteria in the gut (e.g., lactobacilli, bifidobacteria) which have important protective functions, including prevention of infection by yeast, pathogenic bacteria, and/or parasites. The protection is provided in part by the helpful bacteria clinging to the intestinal cell wall, thus preventing pathogenic microorganisms from getting to it. The pathogenic bacteria compete with the body for vitamin B-12 and perhaps other vitamins and minerals.
7. After helpful bacteria wiped out, Candida usually develops. Candida produces toxin. However its main deleterious effect is avid binding of coenzyme q10, usually at barely adequate levels in the diet of normals to begin with, to a far greater extent than by normal tissues. Candida is not the cause of increased intestinal permeability, except in rare instances, since substances passing into the body enter via the small intestine (jejeunum) whereas Candida is almost always confined to the large intestine (but if present in jejeunum, can be life-threatening).
8. The Candida infection is usually treated with ketoconazole or similar anti-yeast antibiotic.
9. Ketoconazole and similar compounds impair patient's liver function as shown by liver detoxification profile. This could also be a factor in increased intestinal permeability, because the liver also synthesizes the J piece (joining piece) that binds two molecules of IgA antibodies together to form secretory IgA, which protects the intestinal tract from a variety of damaging agents; severe diminution of secretory IgA predisposes to increased intestinal permeability. Furthermore, since the blood vessels from the colon go directly to the liver via the enterohepatic circulation, the various toxins from microorganisms and undigested food in the colon go directly to the liver and impairs the latter's detoxification mechanisms and its production of enzymes. (The liver produces the vast majority of the hundreds of different body enzymes necessary for normal metabolism.).

10. Decrease in production of the liver enzymes (phosphosulfotransferase and cytochrome p450 family) causes failure to break food proteins (including gluten and casein) into peptides. The intact proteins cross into circulation, and antibodies** are formed against them. The antibodies complex with the antigen to form antigen-antibody complexes, that in turn can enter various organs and seek out cells with receptors for antigen-antibody complexes, e.g., cells of the joints (causing arthritis), muscles (causing myalgia), or brain (causing cognitive dysfunction).

*DPT immunization in inbred mice has been shown to result in decrease synthesis of cytochrome p450 and of phosphosulfotransferase and of the messenger RNA's necessary for their production.
**If antibodies are not detectable, this may be due to immune complex in antigen access.

Prevention

1. The law states that infants with immune defects should not receive immunizations. But no pediatricians test for immune deficiency before giving immunizations. They are always given out of convenience for pediatricians at well-baby follow-ups at 4 and 8 weeks in this country.
2. Defer Rubella vaccine in males completely, in females defer until age when menses begins. Rubella is only a mild disease in the developed countries, with mild fever and "spots" for three days. Reason for females taking it a menses is because if Rubella occurs in the first trimester of pregnancy the child will develop severe congenital defects starts to prevent congenital defects. If administered during first or second trimester do not give to women for at least 2½ years following delivery of last child, as the vaccine virus is present in respiratory secretions for seven days and can cause disease.
3. Defer other immunizations until age 4 (except for tetanus and diphtheria toxoid which should be given at 2½ years).
4. Obtain IgG antibody titers from cord blood to all vaccines currently in use and store away a sample of serum so they can be tested for vaccines which will be introduced later (we are introducing 1-2 new immunizations each year). If any of the IgG antibody to DPT, MMR, polio (and in the British Commonwealth countries 16 Coxsackie viruses), get IgM on infant from the stored serum (divided into 2 parts), and the mother, father and the sib of closest age should be tested for IgG and IgM antibodies to the relevant virus.
5. Do not take influenza vaccines or other new vaccines. Ask the physician if the vaccine bottle contains mercury (thiomerol or alum [which boosts the response to various immunizing agents]). Also ask physician to obtain vaccines free of these. Repeat injections of these agents can cause all kinds of immunologic aberrations.
6. Nurses in newborn nurseries should not receive rubella vaccine. Rubella immunization of nurses in Philadelphia 12 years ago, because of several cases of rubella in newborn infants, resulted in a micro-epidemic of CFIDS.

Treatment of Autistic Spectrum Disorders

A. Non Specific Therapies (i.e. not limited to one disorder within the autism spectrum)

1. Toxic metals besides Mercury, such as Tin, Nickle, Antimony and Arsenic may contribute to this disorder as well. The removal of mercury is essential to achieve recovery, achievable with the TD-DMPS. If deficient trace minerals on screening hair analysis or on urinary challenge testing are noted, replacement of these essential minerals is mandatory. Remember, heavy metals will probably not show on testing in autism spectrum disorders since these patients by definition are non-excreters. The metals, especially mercury, will have to be “challenged” out of them using a potent chelator specific for mercury. Also measure content of metals and minerals in drinking water for ongoing toxicity.

2. For Candida infections give Diflucan, asynthesized antifungal, but only if Candida is demonstrated in stool, urine, finger- and toe-nails, and/or vagina, etc., or if serum Candida detection test gives highly positive results. If present in stool, patient's own Candida should be tested against specific antifungals and six natural substances to see which of these the organism is mosr subseptible. *Lactobacillus acidophilus* and thermophilic bacteria to eradicate and put good bacteria back in the bowel. If refractory, use Candida-specific transfer factor.
3. If serious reaction to the immunization, measure antigen-antibody complexes by four methods. If elevated: (a) plasmapheresis or (b) Theoretical: a method that has been used for Digitalis toxicity: Couple antibody to offending toxin or vaccine virus to Sephadex Columns and pass plasma through this to remove anti-toxin or vaccine and return plasma to patient (if this is difficult to understand, it does not differ that much from dialysis for kidney failure.)
4. At age 15 months, get IgG titers to measles, mumps, rubella, HHV-6, DPT (all 3), cytomegalovirus, antibody to the "early" antigen EBV, also mycoplasma fermentens and chlamydia. (TF's available for most of these).
5. Often increased intestinal permeability; if present, correct by appropriate dietary means (can be determined by very simple test). For most severe increased intestinal permitability, restrict diet to rice-based milk-free, wheat-free, corn-free, and sugar-free diet containing amino acids and proteins (astronauts' diet) for three months.
6. Comprehensive Stool Analysis (e.g., Great Smokies Diagnostic Laboratories-GSDL) for pathogenic bacteria, yeast, and parasites. If present, test sensitivity to natural agents and antibiotics; use those agents to which patient's pathogens are most sensitive. If chymotrypsin is subnormal in the stool, add oral enzymes, preferably alphazyme or gammazyme. If stool pH is alkaline and patient complains of upper abdominal distress, add betaine (tri-methylglycine). Take sublingual vitamins and zinc.
7. Test for malabsorption, especially if stools float or are intermittently light colored. If so, oral vitamins and minerals are only partially absorbed; administer such sublingually.

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Mercury damages nerve cells

by Neal Ozano

U of C researcher records destruction of essential structures

A University of Calgary researcher knows exactly how your fillings can wreck your brain cells. Professor of physiology and biophysics Dr. Fritz Lorscheider recently found and recorded the damage caused to neurons by the mercury contained in mercury amalgam fillings. He said people should take notice of these findings. "We need to take mercury exposure much more seriously," he said. Mercury exposure has long been connected with Alzheimer's Disease, a gradual degeneration of cognitive and memory

abilities. Lorscheider's study found a correlation: tissue from the brains of Alzheimer's patients looks much like that of rats and snails exposed to elemental mercury.

According to the study, the mechanics of damage happen at the sub-cellular level, affecting the structure of proteins that support cell walls and membranes. "Tubulin, a cell-wall protein, forms long chains called microtu-bules, which are the scaffolding necessary for the cell walls and membrane to have shape," said Lorscheider. "When [the proteins are damaged] it causes the structure [of the microtubules] to degenerate, and you end up with stripped neurons, which appear clumped in Alzheimer's." Lorscheider, along with U of C professor Naweed Syed and undergraduate Christopher Leong, researched and recorded the degeneration. The team chose to do their research on snails, since tubulin is similar in all living things.

"It's the same protein in rats, snails and humans," said Lorscheider. "We chose the snail. It only has 28 to 30 neurons, but they're large, which allows us to isolate them." In 1997, Lorscheider and colleagues at the University of Kentucky found that mercury vapour caused "brain molecular lesions caused by an inability by neurons to polymerize tubulin. "We looked at Alzheimer's brain tissue and age-matched control tissue from recently-deceased humans. [The Alzheimer's tissue] had the same molecular lesions as [the mercury-tainted] tissue. These lesions were found in 80 percent of the Alzheimer's samples, but none of the control.
Mercury is a known neurotoxin, but it wasn't known why until the publication of [the current] paper." Lorscheider said sources of mercury include food, air and water, but a major source of mercury in humans are dental amalgam fillings, which are composed of 50 percent elemental mercury. "In our human subjects, 65–70 per cent of the mercury excreted [through urine] is from amalgams. Amalgam fillings are certainly a major source." A major component of the research was the production of a film showing neuron degeneration. Produced through the Learning Commons with the same technology as was used to create Disney's Fantasia 2000, the five-minute film was a "very powerful tool" in the presentation. For more information, visit movie.common.ucalgary.ca/mercury

Retrograde degeneration of neurite membrane structural integrity of nerve growth cones following in vitro exposure to mercury

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Inhalation of mercury vapor (Hg°) inhibits binding of GTP to rat brain tubulin, thereby inhibiting tubulin polymerization into microtubules. A similar molecular lesion has also been observed in 80% of brains from patients with Alzheimer disease (AD) compared to age-matched controls. However the precise site and mode of action of Hg ions remain illusive. Therefore, the present study examined whether Hg ions could affect membrane dynamics of neurite growth cone morphology and behavior. Since tubulin is a highly conserved cytoskeletal protein in both vertebrates and invertebrates, we hypothesized that growth cones from animal species could be highly susceptible to Hg ions. To test this possibility, the identified, large Pedal A (PeA) neurons from the central ring ganglia of the snail *Lymnaea stagnalis* were cultured for 48 h in 2ml brain conditioned medium (CM). Following neurite outgrowth, metal chloride solution (2 µl) of Hg, Al, Pb, Cd, or Mn (10^{-7} M) was pressure applied directly onto individual growth cones.

Timelapse images with inverted microscopy were acquired prior to, during, and after the metal ion exposure. We demonstrate that Hg ions markedly disrupted membrane structure and linear growth rates of imaged neurites in 77% of all nerve growth cones. When growth cones were stained with antibodies specific for both tubulin and actin, it was the tubulin/ microtubule structure that disintegrated following Hg exposure. Moreover, some denuded neurites were also observed to form neurofbrillary aggregates. In contrast, growth cone exposure to other metal ions did not effect growth cone morphology, nor was their motility rate compromised. To determine the growth suppressive effects of Hg ions on neuronal sprouting, cells were cultured either in the presence or absence of Hg ions. We found that in the presence of Hg ions, neuronal somata failed to sprout, whereas other metalic ions did not effect growth patterns of cultured PeA cells. We conclude that this visual evidence and previous biochemical data strongly implicate Hg as a potential etiological factor in neurodegeneration. *NeuroReport 12*:733-737 © 2001 Lippincott Williams & Wilkins.

Key words: Mercury; Microtubules; Neurite growth cone; Neurodegeneration; Neurofbrillary aggregates; Tubulin.

INTRODUCTION

Growth cones located at the tip of developing mid regenerating neurites are responsible for neurite extension, axonal pathfinding mid target cell selection in the nervous system. Actin and tubular that comprise the bulk of growth cone cytoskeleton are highly sensitive to various environmental cues that are present in the extracellular milieu of growth cones. A growth permissive environment facilitates growth cone assembly whereas various growth inhibitory molecules dissemble microtubular structure, induce growth cone collapse mid neurite retraction [1]. Microtubules, a principal protean of the cytoskeleton, are composed of polymerized tubular dimer subunits. Brain neurons require intact microtubules for axoplasmic transport, membrane structure, mid normal neurite outgrowth; the cytoskeletal architecture being dependent upon microtubular stability [2,3]. Methylmercury (MeHg) is a potent neurotoxicant, mid its effects on microtubule integrity during CNS neuronal development are well documented [4].

Attention has also focused on potential CNS toxicity resulting from chronic exposure to another predominant toxic mercury species, that of mercury vapor (Hg°); the principal source being dental amalgam tooth fillings [5]. Approximately 70 % of all Hg ions in human urine originate solely from amalgam [6]. Recently, we have reported that inhalation exposure of rats to Hg° causes disruption of brain microtubule metabolism by inhibiting the polymerization of tubular molecules. Such polymerization is dependent upon the ability of GTP nucleotide to band to (3tubulai, banding that is markedly reduced by the presence of Hg ions. A similar in viva molecular lesion was observed in brains of 80 % of Alzheimer disease (AD) patients, but was not seen in brains from age-matched control patients [7].

Since the amino acid sequence of tubular from all animals brains (vertebrates and Invertebrates) is highly conserved, with > 97 % sequence homology across animal species [8], the present investigation employs a well-established snail neuronal culture model [9] to study microtubule metabolism in the presence of Hg. The development of time-lapse imaging techniques for intact isolated neurons, using cell culture systems, has allowed the direct observation of axonal microtubule structure mid protean synthesis at the neurite growth cone [10,11]. Therefore, the primary objective of the present study was to determine whether the marked Inhibition in microtubule metabolism following Hg° exposure, tie measured at the molecular level [7], could

actually be directly observed by imaging the membrane dynamics of neurite growth cone activity in the presence or absence of Hg ions or other toxic heavy metals.

MATERIALS AND METHODS

Animals: An established stock of the fresh water snail *Lymnaea stagnalis* derived from that of the Department of Biology at the Free University of Amsterdam was used. Animals were maintained in an aerated, filtered pond water aquarium at room temperature in the University of Calgary Animal Resources Centre and were fed lettuce tie described by Ridgeway et al. [12]. In all experiments, central rang ganglia were used for neuronal cell isolation mid to make brain conditioned media (CM). Snails with a shell length of 2530mm (3-4 months old) were used in all experiments.

Cell culture: Animals were de-shelled mid anesthetized for 10min in normal *Lymnaea* saline ((hi mM): 51.3 NaCl, 1.7 KCl, 4.0 $CaCl_2$ and 1.5 $MgCl_2$; buffered in HEPES to pH 7.9) containing 10 % Listerine. All primary cell culture procedures from tine point forward were carried out in a laminar flow hood to prevent Infection of culture samples from air-borne microorganisms. Anesthetized snails were pained down in a dissection dish containing antibiotic saline (ABS) (autoclaved normal *Lymnaea* saline; gentamycin 150 dug/ml) mid their CNS removed tie described previously [9,12]. The isolated central rang ganglia were washed in plastic culture dishes (Falcon; Becton Dickinson, Meylan Cedex, Prance; 35 x 10mm) containing ABS to ensure an aseptic culture [9]. Three consecutive 10-15min washes were completed, each in a culture dish containing 3m1 ABS. Brains were then transferred into a culture dish with 3m1 defined media (DM; 50% L-15 medium with added inorganic salts (in mM): 40 NaCl, 1.7 KCl, 4.1 $CaCl_2$, 1.5 $MgCl_2$, 10 N-2 hydroethyl-piperzine-n'-2-ethanesulfonic acid, pH 7.9; and 20 pM gentamycin; (Gibco BRL, Gaithersburg, MD; special order) containing bug trypsin (2 mg/ml to yield a 0.2 % volume solution; Type T-4665; Sigma, St. Louis, MO), mid left at room temperature (18-20°C) for 23min. Following tine enzyme treatment, the central rang ganglia were placed Into a 0.2% volume trypsin Inhibitor (Type 1-S; Sigma)/DM solution mid left for 15min. The brains were then transferred to a dissection dish containing high osmolarity DM (750 VI of 1 M glucose added to 20 ml DM to yield a 180-190m0em solution) and pinned down dorsal surface up. Pine forceps were used to remove the outer and timer connective tissue sheathes surrounding each ganglion. A Sigmacote (Sigma)-treated glass capillary pipette was attached to polyethylene tubing and sterilized with 70% ethanol for 5min. Following tine sterilization, a micro-syringe (Gilmont, Model GS1100) was connected to the tube and the pipette/tubing/syringe system rinsed thoroughly with ABS prior to being filled with high osmolarity DM. A micromanipulator was used to maneuver the pipette tip overtop a Pedal A (PeA) neuron cell body and gentle suction pressure was applied through the micro-syringe to isolate the neuron from its ganglion. This PeA neuron was then gently flushed Into a poly-L-lysine coated glass coverslip/culture dish [12,13] containing brain conditioned media (CM, described below). Three to five neurons were plated ~5-10 soma diameters apart per dish mid were left undisturbed overnight to allow for cell attachment mid neurite outgrowth.

To prepare CM, 12 isolated central ring ganglia, washed seven times in ABS, were incubated in Sigmacote-treated glass culture dishes containing 6ml DM for 3 days tie described by Wong *et al.* [13]. These ganglia were then removed from the culture dish mid the CM (first time) was discarded. The ganglia were incubated for an additional 4 days in fresh DM and removed. This medium (second time) was filtered (0.22 μm pore; Nalgene) mid placed in a poly-L-lysine-coated plastic culture dish. The ganglia were added (2/ml filtered media) and the dish incubated

for one additional day. These ganglia were then discarded mid the culture dishes with tine CM were used immediately.
Application of heavy metal solutions: Only neurone with well-developed neurites were used for experimentation to ensure a well established microtubule cytoskeletal structure. PeA cells were allowed to extend neurites for 2448h. after plating in CM before exposure to a heavy metal solution. Heavy metal chloride salts of mercury, aluminum, lead, cadmium, mid manganese were obtained from J.T. Baker (Phillipsburg, NJ; room temperature solubilities in water respectively (g/100ml): 6.9, 69.9, 0.99, 140, 151) to make the experimental solutions used. Stock solutions were made in 5.0m1 Falcon sterile centrifuge tubes with autoclaved normal *Lymnaea* saline at room temperature (18-20°C) to obtain a concentration of 1 x 103 M. This stock solution was then serially diluted, also in normal *Lymnaea* saline, to obtain a final working experimental solution concentration of 1 x 10-7 M. Mercury chloride stock and experimental solutions were made fresh every few days due to a moderate lose of ions adsorbed on the container surfaces. The 1 x 10-7 M heavy metal solutions were loaded Into wide-bore, firepolished glass microinjection pipettes mid delivered via pressure ejection into the CM in a region adjacent to growth cones at 2-5 pen using an Eppendorf microinjector (Model 5242). Rattier than using a pulse ejection, the holding pressure of the microinjector was set at 2 pen to deliver a constant stream of experimental solution for 20min. The volume of metal solution delivered to the culture dish (containing 2m1 CM solution) was estimated tie 2 VI. A peristaltic pump (Gilson, Model Minipuls -2) was used to provide a constant flow (400 µl/min) of sterile normal *Lymnaea* saline through the cell culture dish during heavy metal exposure. Neurone were observed as controls for 40min prior to heavy metal treatment and for an additional Albumin after the cessation of mercury ejection into the culture.
Imaging*:* Neurone were viewed with a Zeiss Axiovert Model 135) inverted microscope using a x40 objective. A time lapse video recording of the neurite growth cones during heavy metal exposure was captured using a CCD camera (Hitachi Denshi, Japan, Model KP-M1U) connected to a time-lapse frequency VCR (Panasonic model no. AG 6720A) set at 1 frame/e using Sony VHS SP tape. Linear growth rates for neurite growth cones were estimated using a stage micrometer scale.
A section of the video tape was converted to Betacam SP tape mid a digitized edition was developed by the Advanced Media for Learning unit at the University of Calgary's Learning Commons. Tape editing was performed with a Media 100 XS System, version 4 (Media 100, Marlboro, MA) and compressed for web delivery with Media Cleaner Pro, version 4 (Terran Interactive, Los Gatos, CA). The supporting animation was created with Softimage, version 3.8 sp 2 (Avid Technology Inc., Tewksbury, MA). This digital tape is replayed at a normal VHS speed of 30 frames/e mid can be accessed for web viewing at http://movies.commons.ucalgary.ca/mercury [14].
Immunostaining*:* RITC, Bodipy mid FITC phalloidins (Molecular Probes Inc.) were used to label P-actin. Tublin was visualized with anti-(3tubulin, a mouse monoclonal antibody obtained from Boehringer-Mannheim. The secondary antibodies were obtained from Vector Labs Inc. Cultured cells were fixed for 30 man with 4 % paraformaldehye in PBS containing 3mM EGTA and 0.02% glutaraldehyde, then permeabilized in 0.5 % NP-40. The preparations were subsequently raised in PBS mid incubated for 1 h at room temperature with 25 units fluorescein phalloidin diluted with 20 VI PBS. The cells were raised with PBS mid incubated with (1:100) (3-tubulin diluted in PBS for 1 h. The cultures were then raised mid incubated with 1:20 dilutions of either FITC or rhodamine conjugated anti-mouse IgM for 1 h. Coverslips were

mounted in PBS/glycerol (15-85%) containing 1%-n-propylgalate. Growth cones were viewed wider a Zeiss (Axioekop) fluorescent microscope mid photographed with a 35 mm camera.
Fig. 1. Digital images of cultured nerve growth cones from identified *Lymnaea neurons* before (a), during (b) and after (c) mercury exposure.

a **b** **c**

The arrow indicates the same reference point in all three images. Bar=30XXXm. Neurons were cultured in the presence of brain conditioned medium and allowed to exhibit outgrowth. Following 24-48h neurite outgrowth, growth cone behavior was monitored for 40 min with time-lapse video imaging (a). Individual growth cones were subsequently subjected to Hg which was pressure applied locally under a fast perfusion system for 20 min (b). Hg exposure induced growth cone collapse within 10min (b). Neurite retraction continued under an additional 30 min of observation (c).

RESULTS

To test for both immediate and chronic effects of Hg ions on growth cone morphology and behavior, individually identified neurone from a homogeneous population of Pedal A cluster were isolated in vitro mid maintained in primary cell culture. All neurone cultured in the presence of CM exhibited robust outgrowth over night. Figure la-c shows sequential digital photographs, without image enhancement, of typical nerve growth cones from intact neurone cultured in 2ml media before, during mid after the addition of 2 µl of a 10^{-7} M Solution of $HgCl_2$. The tip of the microejection pipette is visible in Pig. 1b. Within a few minutes of Hg exposure, not only did the growth cone cease its motility but it also exhibited robust collapse mid retraction (Fig. lc). Consistent with tine image (Fig. lc) the denuded neurofibrils eventually formed neurofibrillary aggregates, an observation reflected in the enlarged bulbous bone structure that resulted from neurite retraction following growth cone collapse. This figure is from our June 1, 1999 experiment where tape frame times 15:41:31, 15:58:58, mid 16:15:41 were selected. The entire film sequence, illustrating the dynamics of neurite membrane disassembly mid retraction following Hg exposure, is available on the web [14]. The average linear growth rate for three of these growth cones was determined to be +28 µm/h before Hg exposure, compared to -102 µm/h during and -146 µm/h after Hg exposure. We have repeated tins experiment with similar results for -40 different neuron cultures wider the same conditions over a 2-year period. In these cultures, on average, ~77 % of all nerve growth cones were affected by Hg.

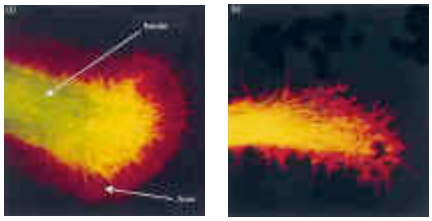
To test for the specificity of the effects of Hg ions on growth cone morphology, we next sought to determine whether other metalic ions such as Al, Th, Cd or Mn (10-7M chloride) would also alter neurite membrane integrity. Despite multiple exposure to the above ions, the growth cone morphology and behavior remained unperturbed suggesting that these ions do not affect growth cone cytoskeleton (n=3 different cultures for each metal, data not shown).

Because Hg ions have previously been shown to effect tubular polymerization, we next asked whether Hg-induced degeneration of growth cone structure involved actin/tubular architecture of newly assembled cytoskeletal elements. Specifically, neurons were cultured and allowed to extend neurites. Following neurite outgrowth, individual growth cones were exposed to Hg ions mid following collapse, these were fixed and processed for actin/tubular immunofluorescence.

We found that as compared with their control, untreated counterparts (Fig. 2a), the Hg ion treated growth cones exhibited a high degree of disintegration of tubulin/microtubule structure (Pig. 2b). These data demonstrate that Hg-induced degeneration of growth cone structure probably involves microtubular disassembly.

Taken together, the above findings demonstrate that Hg ions exert growth suppressive effects on the growth cone of PeA neurons. To test the extent of these effects, PeA cells were cultured in the presence of Hg ions mid the extent of total neurite outgrowth (sprouting) was measured after 48h. Consistent with our hypothesis we found that neurons cultured in the presence of Hg ions failed to initiate neurons (4.6 $\pm$ 2.4 % sprouting), whereas control neurons extended robust outgrowth (93.4 $\pm$ 3.1 % sprouting). These data, shown in Table 1, thus demonstrate that the effects of Hg ions are not restricted to individual growth cones, rattier they prevent neurite initiation from the entire neuron.

Fig. 2. Fluorescent images of cultured nerve growth cones double-stained with antibodies against actin (red-rhodamine) and tubulin (greenfluorescene) before (a) and after (b) mercury exposure.



a **b**

DISCUSSION

The results of the investigation described herein clearly demonstrate that exposure to Hg ions markedly disrupts the membrane structural integrity of neurites mid the growth cones of identified neurons. This phenomenon appears to be specific for Hg, since exposure to four other heavy metals had no observable effect on either growth cone morphology or individual neurites. These findings are consistent with earlier biochemical evidence demonstrating that microtubule metabolism is compromised in the presence of Hg ions because Hg inhibits GTP nucleotide binding to (3-tubulin, a requisite step for tubulin polymerization in the formation of microtubules [7]. We believe that the Hg-induced disassembly of the neurite membrane, as seen in the present study, is a physical manifestation of a disrupted microtubulin polymerization cycle.

The question arises as to whether tins Hg-induced retrograde degeneration of the neuron membrane is solely the result of disruption in microtubule metabolism. Previous evidence indicates that the autoradiographed 45 kDa band of rat brain cortex proteins showed no change in GTP nucleotide banding in the presence of Hg [7]. This protean band is primarily composed of actin, another *cytoskeletal* protein involved al growth cone motility and which is ATP nucleotide-specific, mid tile band also contains lesser amounts of glutamine synthetase mid creatine kinase. Dully *et al. [15]* have previously demonstrated that Hg had no effect on GTP balding to actin. This supports tile interpretation al tile present study that tile structural disassembly of tile neurite membrane, observed herein, is a direct effect of Hg on tubular rattler titan actin; an interpretation confirmed by tile immunostaining evidence presented in this report. These results do not, however, rule out other neurite constituents as potential targets for Hg. For example, neuromodulin (also known as B-50 or GAP-43), present in tile cytoskeleton mid inner plasma membrane surface of tile growth cone, also helps stabilize tile *neurite cell* membrane mid

is involved in neurite outgrowth [16,17]. ADP ribosylation, an essential process in brain metabolism of cytoskeletal and growth associated proteins, is markedly inhibited after both *in vitro* mid *in vivo* exposure *to* inorganic Hg [18].

Table 1. Sprouting assay of neurite outgrowth.

	No.Cells plated	No.Cells sprouted	% sprouted
		CM dish	
I	10	9	90
2	13	13	100
3	8	7	87
4	9	9	100
S	10	9	90
		Average 93.4+3.1	
		CM +Hg dish	
I	14	I	7
2	12	0	0
3	9	I	11
4	21	I	5
S	10	0	0
		Average 4.6+2.4%	

The actual Hg concentration present in our neuronal cultures was indeed lower titan 10^{-7}M because of a dilution effect in the culture media. The Hg concentrations to which these neurone were exposed were of tile same order of magnitude as Hg levels reported al human mid animal brains after chronic exposure to Hg^{o} (reviewed al [5]).

Although more titan three-quarters of all Hg-exposed growth cones that we imaged showed evidence of neurite membrane disassembly, tile absence of any response by some growth cones may reflect maturational changes in microtubules. This interpretation is supported by rationale proposed by *Reuhl et al.* [4] al which they suggest that less differentiated developing neurone may be more *susceptible* to microtubule disruption al tile *presence of* MeHg.

It has been claimed that microtubule assembly is defective in AD brains. However, the relationship between tile paired helical filaments characteristic of neurofibrillary tangles al AD brains mid microtubule instability is unclear [19]. Given tile species differences between human mid snail neurone, tile aggregation of denuded neurofibrils observed in tile present study, following Hg exposure, may not be directly analogous to lesions seen al AD brains.

Recently, Escheverria *et al.* [20] have reported a variety of neurobehavioral effects in dental personnel resulting from chronic low-level exposure to Hg°. Their report is confirmed by tile results of several other clinical investigations conducted by tile same group. We suggest that tile cellular findings al tile present study, revealing that Hg disrupts tile integrity of tile neurite membrane al growth cones of intact neurone, may implicate Hg as a potential etiological factor in neurodegeneration that could ultimately be observed as altered neurobehavior.

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Acknowledgements: The authors thank the Alberta Heritage Foundation for Medical Research (AHFMR) for studentship support of C.E. during the course of there investigations. We also thank AHFMR, and the Medical Research Council of Canada for neuroscience research support of N.S., and the International Academy of Oral Medicine and Toxicology for provision of funds (F.L.) to produce the digital video film.
source: http://www.neuroreport.com/ 30mar01

Dear Ms Lamas,

Thank you very much for your articles about autism in today's Herald. I am a pediatrician in Aventura, and our practice has seen over 800 autistic patients over the past 3 years. I find that the majority of children with autism have underlying biochemical abnormalities, and we perform testing and therapies to identify and treat these abnormalities. I would very much like to go over with you the details of this, and provide you with literature to substantiate these findings.

In your article, the discussion you present on the vaccine issue is erroneous. The Lancet article you quote from 1998 has nothing to do with thimerosal, it was solely relating autism and the MMR vaccine. The scientists you mentioned that retracted their conclusion did so not out of dispute of the evidence that Dr Wakefield presented in that article, (evidence that both Dr. Wakefield and now at least 2 other groups have substantiated), but because it recently came out that part of Dr Wakefield's research was funded by a group that was trying to sue the vaccine companies. Many doctors, including myself, find this rather hypocritical, considering that most studies that have concluded that vaccines are safe, including the one you quoted regarding the Denmark study, had investigators with ties to vaccine manufactures.

As for the mercury issue itself, there are 3 irrefutable points. 1) the effects of mercury toxicity mimics many of the symptoms of autism. 2) the amount of mercury the average infant would have received up until 3 years ago exceeded the EPA's safe level for mercury exposure by at least 50x, and 3) when we do

testing for mercury on autistic children, the majority of them are found to have elevated levels.

Vaccines aside, there are many other consistent findings in these children, including sensitivities to particular foods like wheat and dairy, vitamin deficiencies, abnormal amino acid metabolism, trace mineral imbalances, and the presence of pathological yeast and bacteria residing in their intestines. All of these finding are verifiable by laboratory testing.

I think that it is very important for families to know that autism is treatable by finding these underlying abnormalities, ad that they do not need to resort in all cases to psychotropic medicines and likely institutionalizing them as they get older. As mentioned, I would very much like to share this information with you, and can provide families that will be happy to tell their stories and how their children have either recover or significantly improved with these therapies.

Sincerely,

David Berger, MD
Board Certified Pediatrician

Mercury damage seen in kids of fish eaters

By Maggie Fox
Reuters — Feb. 11, 2004

WASHINGTON — Children whose mothers eat seafood high in mercury while pregnant can suffer irreparable brain damage, researchers reported on Friday.
The report comes the same week as the U.S. Environmental Protection Agency doubled its estimate of how many newborns had unsafe levels of mercury in their blood.
The study, done by an international group led by researchers at the Harvard School of Public Health, also showed that children exposed to mercury in the womb may suffer permanent damage to their heart function.
"We found that both prenatal and postnatal mercury exposure affects brain functions and that they seem to affect different targets in the brain," Philippe Grandjean, who led the study, said in a statement.
Grandjean and colleagues studied more than 1,000 mothers and children living in Denmark's Faroe Islands. Residents there eat large amounts of fish, much of it contaminated with mercury.
They measured mercury in umbilical cord blood taken from the children at birth and then in hair samples taken at ages 7 and 14.
Most of the mothers were suffering from mercury contamination, with their own hair levels at childbirth on average above 1 microgram per gram, the limit recommended by the EPA and the independent, nongovernment National Research Council.

Brain signal irregularities

Writing in the Journal of Pediatrics, Grandjean and colleagues in Denmark and Japan said they put electrodes on the heads of the children to measure electrical signals in the brain. They found delays in brain signaling, and the higher the mother and child's mercury load at birth, the more distinct the irregularities.
They also found these neurological changes affected heart function. The children with the most mercury in their blood were less capable of maintaining the normal variability of the heart rate needed to secure proper oxygen supply to the body, Grandjean's team found.
Earlier this week an EPA researcher published a report doubling the estimates of how may U.S. infants have unsafe levels of mercury in their blood.
The researcher, Kathryn Mahaffey, estimated that 630,000 infants were born in a 12-month period between 1999 and 2000 with blood mercury levels higher than 5.8 parts per billion, the EPA's level of concern. This is more than double the previous estimate of 300,000 infants.
"It is important to note that this estimate is preliminary in nature, and is based on recently available information about mercury in umbilical cord blood versus maternal blood," Mahaffey said in a statement.

"EPA is still reviewing these new studies and their potential implications."
Jane Houlihan of the Environmental Working Group said the study showed the government needs to limit emissions by coal-burning power plants, which are the top source of mercury contamination in the United States.
Her group called for the Food and Drug Administration to issue a list of fish that are lower in mercury and thus safer for pregnant women to eat, such as wild salmon and haddock.
The EPA says the most contaminated fish include shark, tilefish, king mackerel and swordfish.
Sources of healthy omega-3 fatty acids other than fish include walnuts and flaxseed oil, and some fortified foods.

Homeland Security

In the 1990s, despite credible research and opposition by qualified physicians, the massive push began to vaccinate infants and toddlers with multiple doses for many diseases and vaccines that had questionable science backing up the licensing. One of the biggest concerns was the MMr and MMr II vaccine. Numerous medical reports published in prestigious medical journals have cited major complications resulting from the MMR vaccine, including retardation, chronic seizures, inflammatory bowel disease, hearing loss, chronic arthritis, encephalitis and aseptic meningitis.

MMR is closely linked to America's raging epidemic of autism spectrum disorders. One in every 300-500 U.S. children now develops autism. In 1978, only one child in 10,000 developed autism. Late onset autism causes previously normal babies to develop severe abdominal cramping, hyperactivity, learning and social disabilities, along with abnormally aggressive behavior. Studies conducted by British scientist Dr. Andrew Wakefield show a significant correlation between autism and the MMR vaccine. Wakefield found that the MMR vaccine increases the permeability of the bowel, causing "leaky gut syndrome."

Toxin-laden fecal matter is then allowed to escape the digestive tract and enter the bloodstream. Once in the blood, the toxins travel to the brain where they damage sensitive brain tissues leading to the development of autism. Dr. Wakefield also found that autistic children develop inflamed bowel nodules causing indigestion and liver damage from toxic overload. His findings have been corroborated by Irish molecular biologist John O'Leary, who found measles virus in the gut of 96% of vaccinated autistic children and in 75% of children with Crohn's Disease. According to Congressman Dan Burton (R-IN), Chairman of the Government Reform Committee, physicians and a growing number of parents believe that autism affecting their children is related to a mercury preservative used in numerous vaccines.

This preservative is called thimerosal, and it contains mercury, a known neuro-toxin. Thimerosal is still present in some vaccinations and surprisingly - virtually all flu shots. Writing in the Spring 2001 American Association of Physicians and Surgeons journal, Medical Sentinel, Joseph Mercola, M.D. stated: “Immunizations contribute to the enormous and tragic increase in autism in this country, and it is time physicians take a stand on this issue and defend the patient's right to choose. It seems imperative,” states Mercola, “that the first step for physicians who have not carefully studied this issue is to become informed.” First Coast News had a shocking release earlier this week on the issue of thimerosal and autism: "The Centers for Disease Control published a study last fall repudiating any possible link between thimerosal and developmental problems like autism in children. However, First Coast News has obtained non-published documents that show the CDC DID have data supporting such a link-- but kept it from the public. "Documents released through the Freedom of Information Act, detail the transcript of a meeting held in June of 2000 between members of the CDC, the FDA, and representatives from the vaccine industry."

The reported number of autism cases is being described as epidemic and growing. As parents struggle to provide treatment for their autistic children, the Bush Administration has taken steps to keep these parents in the dark by petitioning a federal court to keep all documents from the American people on hundreds of cases of autism believed caused by childhood vaccines. On November 25, 2003, department of Justice lawyers asked a U.S. Court of Federal Claims to "to seal the documents, arguing that allowing

their automatic disclosure would take away the right of federal agencies to decide when and how the material should be released."

How does Homeland Security play into this unfolding tragedy for untold numbers of children and their parents? The Homeland Security Bill contained two paragraphs in the 475-page document that immunizes vaccine manufacturers against the threat of lawsuits. Specifically, pharmaceutical maker Eli Lilly & Company benefits from such immunity because prior to President Bush signing the bill into law, they were the target of a massive class action lawsuit on behalf of autistic children. The parents of these children believe that the mercury (thimerosol) added to vaccines as a preservative caused their child's brain damage. President Bush signed the Homeland Security Bill into law, effectively snuffing out parents ability to sue the pharmaceutical companies individually and leaving them with brain damaged children and financial hardship.

Supporters of this new law maintain that it was necessary because all these lawsuits could have driven vaccine makers out of business. Opponents point out that by shifting the lawsuits from state courts to the Federal Court of Claims, it represents a financial boon for pharmaceutical companies because dollar awards will come from the government and widespread industry fees than than from individual companies. It is unclear how this lawsuit immunity bonanza for the pharmaceutical industry has anything to do with homeland security, bio-terror attacks or keeping America safe from terrorists. Last summer, President Bush appointed Sidney Taurel, Chairman and CEO of Eli Lilly to the Homeland Security Advisory Council.
Since 1989, Eli Lilly alone has given a whopping $5.9 million to congressional campaigns with 3/4ths of the money going to GOP candidates. In the last election election cycle, eighty percent of Republican candidates got the lion's share of the $1.6 million contributed by Eli Lilly who developed thimerosal and has profited handsomely from sales over the past 40 years. Thimerosal isn't the only drug linked to other adverse effects on children. Back in February 2001, News 8 Investigates (Dallas-Ft. Worth area) covered questionable science at the root of getting vaccines approved in this country. One of the newer vaccines scrutinized was RotaShield which was given to the newborn son of Melynda Shay. This particular vaccine promised in its advertisements that RotoShield would help prevent childhood diarrhea. Within days after inoculation, Ms. Shay's newborn's bowels were dangerously obstructed to the point of possibly rupturing.

Federal regulators from the CDC finally discovered more than 100 other infants like Ms. Shay's son had all suffered the same problem and RotoShield was pulled off the market. On the very same day RotoShield was pulled, the CDCs Vaccine Advisory Committee drafted a recommendation for another new vaccine called Prevnar. Clinical trials of Prevnar tested in 38,000 California children produced the following results according to the drug company's own documentation: children receiving Prevnar with other vaccines had more seizures, more rashes, higher fevers and other side effects than children who received the control vaccine.

Some wonder how these vaccines ever get approval and into the marketplace? Congressman Dan Burton's congressional hearings last summer provided some disturbing information that could provide at least some insight on the matter: at least half the members of vaccine committees at both the FDA (Food and Drug Administration) and the CDC had financial ties to drug companies that are developing different versions of the Rotavirus vaccine. More hearings are scheduled for this spring.

Prior to 1970, the prevalence of autism was one in 2000; in 1970 it was one in 1000; in 1996 the NIH estimated it to be one in 500; in 2000, the prevalence of autism is now estimated as one in 150. Parallels have been drawn between

vaccine thimerosal and autism. Evaluation of the amount of mercury eliminated in the urine from a series of administrations of a mercury chelator is intriguing. A significant portion of the known dose of vaccine mercury was eliminated. With the knowledge that mercury is very difficult to eliminate from the body, especially from the central nervous system, this would not be expected. This information suggests a preexisting burden of mercury prior to vaccination

The Danger of Mercury in Vaccines causing BRAIN DAMAGE in Infants–Autism etc.

Mercury supposedly is no longer being used in the manufacturing of vaccines but it is still in lots of vaccines on the shelf and can be very harmful to anyone but particularly infants. It is shocking to learn about the probable cause of autism by the mercury preservative (thimerosal) in vaccines. It is more shocking to read the information about this at: http://www.altcorp.com/thimerosal.htm. Perhaps the best way to warn parents of the potential danger in vaccines is through this letter both by mail and the Internet getting the information out to thousands if not millions. If you will send this letter on to those you know and ask them to also send it on we will probably save numerous children from autism and other learning disorders.

SAVING THE BRAIN OF ONE BABY SHOULD BE WORTH THE EFFORT.

We have unwittingly harmed many infants with mercury in vaccines probably causing autism and other learning disabilities. Vaccine manufacturers started using an organic form of mercury called thimerosal as a preservative in vaccines in the 1930s. Mercury is very poisonous and the most powerful neurotoxin. Autism was first identified in children born after 1930. When vaccines became mandated in the 1980s in this country and many more children were vaccinated and at an earlier age the rate of autism went up dramatically. The rate of autism in England did not increase in the same fashion until the 1990s, but England did not mandate vaccines until the 1990s. The rate of learning disabilities other than autism in this country has been skyrocketing and no one knows the extent to which mercury in vaccines contributes.

This is not to suggest that you not have your children vaccinated but rather you either be sure that the vaccine being given is free of mercury or if not discuss with your Doctor delaying vaccinations, have them given one at a time and give your child supplemental vitamin C and plenty of water for several days thereafter. Details are provided below including footnote references at the end. Please be sure to read the next section regarding suggestions and questions to discuss with your pediatrician.

The amount of mercury in these vaccines is significant. A small child receives three vaccines at one time as is often done the amount of mercury is at a dangerously high level. You would think the FDA would have required proof of safety but recent congressional hearings (July 18, 2000), revealed that was not the case. After the hearings the Chairman of the Committee on Government Reform, Rep. Dan Burton requested that the FDA ban thimerosal (mercury) from vaccines but the FDA declined to do so.

DISCUSSIONS WITH YOUR PEDIATRICIAN

The American Academy of Pediatricians has suggested that mercury be taken out of all vaccines for children, but at the same time has stated that the amount of mercury contained in vaccines is insignificant and does not cause harm. Additionally the pediatricians deny that there has been an increased rate in autism. As a parent you however are the one who gets to make the decisions about the timing of the vaccines which your baby or toddler receives in consultation with your Doctor.

Suggested Questions for Your Doctor:

1.) Can you obtain the vaccines my child needs without any mercury (thimerosal) in them? Does the label clearly indicate no mercury (see the list of names mercury is used under at the bottom).

2.) If not, I want to know (1) how much thimerosal is going to be in the injection my child receives (2) is this a safe amount (3) as my child's Doctor what level is unsafe.

The USEPA standard is 0.1 micrograms per kilogram of body weight per day. This equates to 7.0 micrograms for the 70 kilogram (154 pound) adult. A child could receive as much as 237.5 micrograms of mercury from vaccines, in doses of up to 25.0 micrograms. Thus, administration of a single vaccine to a child would greatly exceed the USEPA adult standard.

3.) What are the risk and benefits of delaying for a few months?

4.) If you are telling me there is no risk, will you put that in writing and insure that my child will not be injured by these vaccines which you want to give.

A very thorough presentation of all the evidence and issues on both sides regarding mercury and vaccines can be found at:: http:/www.autism-mercury.com. For those of you who do not have ready access to the Internet, some additional evidence is set out below.

ADDITIONAL EVIDENCE ON AUTISM AND MERCURY

We have long looked with ridicule and almost laughter speculating that the Roman Empire fell because they allowed their food and beverages to be contaminated with lead causing mental problems among the people. We however in the 21st century continue to inject our babies with mercury which is one-hundred more times more neurotoxic than lead.

Manufacturers are being urged to reduce or eliminate thimerosal as a preservative in pediatric vaccines. The concern is that the cumulative amount of mercury from thimerosal could exceed safe limits in infants. Currently, infants get up to twelve shots in their first six months. One way to reduce thimerosal exposure is to delay hepatitis B vaccination from birth until two to six months but ONLY if the mother is negative for hepatitis B. Use thimerosal-free vaccines when possible.

A growing number of parents of autistic children think that autism is caused by mercury in vaccines! This was the topic of the hearing conducted by the Government Reform Committee of the US House of Representatives on 18 July 2000. The hearing was entitled "Mercury in Medicine - Are We Taking Unnecessary Risks?" The thrust of the committee was on the use of mercury (thimerosal) in vaccines. Testimony was provided by parents of autistic children, physicians and scientists. The information presented was overwhelming!

One physician provided documentation on her treatment of autistic children with mercury chelators. The treatment resulted in a marked improvement in the symptoms of autism and a large provoked increase in urine mercury. Other witnesses provided documentation on the appearance of autism following vaccinations concerning thimerosal. Others detailed the amount of mercury (thimerosal) received from vaccinations, which far exceeded existing mercury exposure standards (for adults).

It was also pointed out that prior to 1970, the prevalence of autism was one in 2000; in 1970 it was one in 1000; in 1996 the NIH estimated it to be one in 500; in 2000, the prevalence of autism is now estimated as one in 150. Parallels were drawn between vaccine thimerosal and autism. Evaluation of the amount of mercury eliminated in the urine from a series of administrations of a mercury chelator is intriguing. A significant portion of the known dose of vaccine mercury was eliminated. With the knowledge that mercury is very difficult to eliminate from the body, especially from the central nervous system, this would not be expected. This information suggests a preexisting burden of mercury prior to vaccination.

There are several organizations dedicated to the investigation of autism. These include Cure Autism Now (CAN), Defeat Autism Now (DAN), and the Autism Research Institute (ARI). All of these seem convinced that mercury is a cause, if not the primary cause of autism.

ARI [www.autism.com/ari] has provided a 70-page document entitled "Autism: A Unique Type of Mercury Poisoning." This document details the correlation's between autism and mercury poisoning, symptom by symptom. Twenty-two of these pages are published scientific references, establishing the connection between mercury and autism. The Synopsis states: "The parallels between the two diseases are so thorough as to suggest, based on total Hg injected into US children, that many cases of autism are a form of mercury poisoning."

In the section Diagnosing Mercury Poisoning in Autism, the document states:

1) Observation of impairments in many but not all of the following domains: (a) movement/motor disorder, (b) sensory abnormalities, (c) psychological and behavioral disturbances, (d) neurological and cognitive deficits, (e) impairments in language, hearing, and vision and (f) miscellaneous physical presentations such as rashes and unusual reflexes.
2) Known exposure to Hg (a) at a level that has been documented as causing impairment in similar individuals under similar circumstances, and (b) at approximately the same time as the symptoms emerge, with allowances given for the latency period. It should be noted that the dose which is considered "toxic" vs. "safe" is unresolved among toxicologists; some researchers feel that any amount of exposure is "unsafe."

3) Detectable levels of mercury in urine, blood, or hair. Importantly because mercury can clear from biological samples before the patient feels symptoms or is tested, the lack of detectable mercury is not cause for ruling out mercury poisoning; and conversely, detectable levels have been observed in unaffected individuals.

4) Improvement in symptoms after chelation. While many patients' symptoms resolve with chelation, some clearly poisoned individuals do not improve. Other exposed subjects have also been known to improve without intervention.

This final point is interesting. Already, positive results from the chelation of mercury for the treatment of autism have been found. All autism groups agree that a genetic factor is involved, as it is with most pathological conditions. Moreover, it is possible that a preexisting body burden of mercury (as from the mercury fillings of mothers) could predispose a child to adverse effects from vaccine mercury.

Mercury is the most toxic of the heavy metals, more toxic than cadmium, lead, or arsenic. Elemental mercury is among the hazardous chemicals listed by the US Environmental Protection Agency and the US Agency for Toxic Substances and Disease Registry. A recent joint "national alert" published by both (the ATSDR and EPA) warns that "short-term or long-term exposures to metallic mercury can lead to

serious health problems."

Asthma and Vaccinations: Dr. Michel Odent, the respected British obstetrician and researcher, made an accidental discovery during some research into the effects of breastfeeding. Working at the Primal Health Research Center in New London, Dr. Odent observed that of the 450 children in his study, 11% of the children who had received the pertussis vaccination suffered from asthma, as compared with only 2% of the children who had not been vaccinated. Although the number of subjects is small, the asthma rate was five times higher in the vaccinated children.

Dr. Odent commented: "I am amazed by our lack of knowledge and still more by our lack of concern about the possible long-term side effects of vaccinations. It would take a century to evaluate the effects of the large number of vaccinations given to infants." The debate over vaccinations often centers around the immediate, obvious reactions. The real question--the question that is being ignored--is the long-term effect of wholesale vaccination on the immune system and on the gene pool. (by Gene A Franks - From: http://babyparenting.about.com/gi/dynamic/offsite.
htm?site=http://www.pwgazette.com/asthma.htm)

Exposure to mercury may precipitate an extraordinarily broad spectrum of symptoms. Casarett and Doull's: The Basic Science of Poisons (Exhibit 46, p. 584) stresses that "[t]here is increasing emphasis on the use of biologic indicators of toxicity such as heme enzymes in lead toxicity, renal tubular dysfunction in cadmium exposure, and neurologic effects in mercury toxicity to serve as guidelines for preventive or therapeutic intervention."; and (Id., p. 605): "No other metal better illustrates the diversity of effects caused by different biochemical forms than does mercury." Gerstner and Huff add that "[m]ercury poisoning presents a variety of clinical pictures, depending on chemical structure and amount of toxic material as well as on length of exposure time and individual sensitivity." These, and other toxicologic references, establish that symptoms and history of exposure are prime factors in the diagnosis of mercury intoxication, and that numerous symptoms have been documented to result from exposure to mercury. For additional Scientifically proven facts about mercury (as used in dental fillings) go to: www.algonet.se/~leif/FUSCIFCT.html

The American Medical Association has published a critique of the use of mercury in vaccines which concludes there may be excessive exposure. Limiting Infant Exposure to Thimerosal in Vaccines and Other Sources of Mercury."" Neal A. Halsey, MD (1999). JAMA 282:1763-1766. Go to: http://www.altcorp.com/SlideShows/Thimerosal/sld012.htm

I f you want to believe it is safe read: An Assessment of Thimerosal Use in Childhood Vaccines By Leslie

K. Ball, Robert Ball, and R. Douglas Pra, PEDIATRICS Vol. 107 No. 5 May 2001, pp. 1147-1154 which concludes: "(S)ome infants may be exposed to cumulative levels of mercury during the first 6 months of life that exceed EPA recommendations. Exposure of infants to mercury in vaccines can be reduced or eliminated by using products formulated without thimerosal as a preservative.
(http://www.altcorp.com/thimassess.htm)

The CDC claims that there is no harm and vaccines with mercury (thimerosal) are rare but rare is not good enough for our babies. Go to:
http://www.cdc.gov/nip/vacsafe/concerns/thimerosal/faqs-availfree.htm

Thimerosal Synonyms
((O-Carboxyphenyl)thio)ethyl mercury sodium salt; Elcide 75; Elicide; Ethyl(2-mercaptobenzoato-S)mercury sodium salt; O-(Ethylmercurithio)benzoic acid sodium salt; Ethylmercurithiosalicylic acid sodium salt; Ethylmerkurithiosalicilan Sodny (Czech); Ethyl (sodium O- ercaptobenzoato) mercury; Mercurothiolate; Mercury, Ethyl(2-Mercaptobenzoate-S)-, sodium salt; Merfamin; Merthiolate; Merthiolate salt; Merthiolate sodium; Mertorgan; Merzonin; Merzonin sodium; Merzonin, sodium salt; SET; Sodium Ethylmercuric Thiosalicylate; Sodium O-(ethylmercurithio)benzoate; Sodium Ethylmercurithiosalicylate; Sodium Merthiolate; Thimerosalate; Thimerosol; Thimersalate; Thiomerosal; Thiomersal; Thiomersalate
1. The Merck Index, 12th ed., p. 1590, #9451 (1996).
2. Martindale The Extra Pharmacopoeia, 30th ed., 804 (1993).

The following information was generated from the Toxicology Literature Online Databank (TOXLINE), a database of the National Library of Medicine's TOXNET system (http://toxnet.nlm.nih.gov) on July 6, 2003.

Query: The chemical name mercury was identified.
The following terms were added from ChemIDplus:
quecksilber
mercurio
mercure
liquid silver
kwik
hydrargyrum
colloidal mercury
CAS Registry Number: 7439-97-6

1
TITLE:
Relationship Between Catalase Activity And Uptake Of Elemental Mercury By Rat Brain

AUTHORS:
Eide I
Syversen TLM

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 52, No. 3, pages 217-223, 16 references, 19831983

ABSTRACT:
The effect of catalase activity on the uptake of mercury (7439976) in the brain was investigated in Sprague-Dawley-rats. Animals were pretreated with 0.18 grams per milliliter 3-amino-1,2,4-triazole (61825) injected into the lateral ventricle of the brain or by intraperitoneal injection 10 to 180 minutes prior to mercury treatment. A solution of mercury-chloride (51312244) and stannous-chloride (7772998) was prepared and the clear supernatant was injected into the right external jugular vein, together with radiolabeled mercury-chloride. Blood was collected from the right ventricle of the heart. Hearts were perfused with saline. Brains, liver, and kidney were removed and homogenates were prepared. Radioactive mercury was determined by scintillation spectrometry. Catalase activity was determined. Brain catalase activity was reduced by 48 percent 75 minutes after intravenous injection of 3-amino-1,2,4-triazole, and there was no significant effect on mercury uptake of the brain. Activity of catalase in liver and kidney was extensively depressed, and mercury content, especially in liver, was significantly increased. Injection of 3-amino-1,2,4-triazole into the lateral ventricle of the brain caused a significant decrease in brain mercury uptake. Catalase activity in liver and kidney was not affected by intraventricular injection of 3-amino-1,2,4-triazole. Ethanol also caused significant decreases in mercury uptake of brain. There was a linear relation between brain mercury uptake and injected mercury. When stannous-chloride was injected intravenously after injection of mercury-chloride, brain mercury content was not altered compared to injection of mercury alone, where blood content of mercury was slightly increased. The authors conclude that uptake of mercury by brain is linearly dependent on activity of brain catalase and the injected amount of elemental mercury. Uptake of mercury by brain is limited by the oxidation rate in brain tissue.

2
TITLE:
Mercury Distribution in the Mouse Brain after Mercury Vapour Exposure

AUTHORS:
Warfvinge K

SOURCE:
International Journal of Experimental Pathology, Vol. 76, No. 1, pages 29-35, 18 references, 1995

ABSTRACT:
The distribution of mercury (7439976) in the brains of mice exposed to mercury vapor was examined. Seven to 8 week old inbred female SJL-mice were exposed to 0.5mg/m3 mercury vapor 19 hours per day (hr/day) (group-A), 1mg/m3 mercury vapor for 3hr/day (group-B), 0.3mg/m3 mercury vapor 6hr/day (group-C), or 1mg/m3 mercury vapor 1.5hr/day (group-D) for 10 weeks. Control mice were exposed to clean air. The mice were killed after 10 weeks and the brains were removed. The caudal half of the right hemisphere was analyzed for mercury by a computerized automated mercury analyzer. The remaining brain tissues were sectioned and analyzed for mercury by an autometallographic based histochemical technique. Brain mercury concentrations in group-A, group-B, group-C, and group-D mice averaged 6.4, 6.3, 1.6, and 0.64 micrograms per gram (microg/g), respectively. The average brain mercury concentration in the controls was 0.01microg/g. Mercury was found in the capillary walls in the brains of group-A, group-B, and group-C mice. The ependyma lining the ventricles and plexus choriodeus of brains in group-A and group-B animals contained mercury. Mercury was distributed through all brain areas in group-A and group-B animals, although the amounts of mercury visualized within the cells varied. The density of mercury containing cells was lower in group-B mice. In group-C mice, the lamina cellularum of the olfactory bulb, layer-V of the neocortex, the white matter, the nucleus caudatus/putamen, Purkinje cells, and nuclei in the thalamus, brainstem, and cerebellum contained mercury. In group-D mice, only the white matter and brainstem nuclei contained mercury. Mercury was not visualized in the brains of control mice. The author concludes that the white matter and other brain structures are targets for mercury accumulation in a mercury sensitive mouse strain.

3
TITLE:
An exposure and risk assessment for mercury

AUTHORS:
Epa working group

SOURCE:
TA:Environmental Protection Agency PG:214 p YR:1981 IP: VI:EPA-440/4-85-011

ABSTRACT:

Risk considerations - Humans: Of concern are the neurological disturbances and fetal brain damage occurring at relatively low mercury levels in man. Attempts have been made to correlate these blood levels with doses that are also shown in the table. The lowest reported effect levels are based on epidemiologic data and thus represent only obvious effects occurring in the population. Other, more subtle effects may result from lower levels of mercury exposure. The tolerable level of 0.43 ug/kg/day was estimated by use of several different methods as described in Chapter V. Other adverse effects that may be of concern include chromosomal damage, teratogenic effects, and reduction in male fertility. Although these effects have been observed in animals, or in human cells in vitro, the significance of these findings to human health effects is unknown. The types of fish eaten by persons with a mercury intake exceeding 0.43 ug/kg/day include both freshwater and saltwater species (see Table 34). Possible sources of mercury for freshwater species containing high mercury concentrations include natural sources, chloralkali plants, mining, copper smelters, and power plants. Electric lamp, battery, instrument, and paint manufacturers may also be sources in local areas. Sources contributing to large bodies of water, like the Great Lakes, would be numerous. Fetuses: Fetal brain damage has been shown to result from mercury exposure to the mother, as discussed in Chapter V, 4, c. Minimum effects levels have not yet been established, but clinical evidence of fetal brain damage has been observed in a study involving 20 mother-infant pairs when peak maternal hair mercury concentration rose above 100 mg/kg (estimated to be equivalent to 400 ng/ml blood concentration). In a separate incident, severe fetal brain damage was correlated with a peak maternal hair concentration of 186 mg/kg. However, it has been estimated that the earliest effects of mercury toxicity would be observable in the most sensitive adult population at blood levels in the range of 200-500 ng/g. Taken in conjunction with the fact that neurological effects have not always been obvious in mothers of infants with clinical evidence of brain damage from mercury, there is some basis for inferring that minimum effects levels for fetal brain damage may be less than or equal to 200 ng/ml maternal blood concentrations. Children: The risk to children due to mercury exposure may be of concern due to the indications of higher susceptibility of this subpopulation. Because relatively little is known regarding the dose-response relationship for mercury in children, detailed exposure analyses were not included for them. However, the risk to children should be at least as great as that for adults. Biota: Monitoring data obtained in 1979 indicate that mercury levels in surface waters at a number of locations are above the laboratory threshold for sublethal effects on the "most sensitive" aquatic species. However, LC50 values for "most sensitive" species are generally more than 10 times the average river basin concentrations. Fish-eating wildlife living near contaminated waters may be at significant risk due to bioaccumulation of mercury in fish. The lowest concentration at which effects were observed in an aquatic organism was < 0.01 ug/l CH_3HgCl, a chronic effects value for Daphnia magna. Growth was inhibited in rainbow trout at CH_3HgCl concentrations as low as 0.04 ug/l. Adverse

effects on reproduction occurred in brine shrimp at CH3HgCl concentrations of 1 ug/l. In marine finfish, sublethal effects were observed in 10 ug/l HgCl2 and CH3HgCl in the mummichog, and in 10 ug/l HgCl2 in the winter flounder. The minimum effects concentrations for a marine diatom was 0.1 ug/l for three different organic forms of mercury. Rainbow trout were again the most sensitive fish in acute bioassays, with LC50 values of 5.1 ug/l and 33 ug/l for phenylmercuric acetate and HgCl2, respectively. For all other groups of organisms, only toxicity data for inorganic mercury were found. The LC50 for Daphnia was 5 ug/l. The mummichog was the only marine fish tested for acute toxicosis, and had a minimum LC50 of 200 ug/l. The most sensitive marine invertebrate was apparently the mysid shrimp, with an LC50 of 3.6 ug/l. Studies indicate that the toxicity of mercury increases with increasing water temperature. Some species, particularly estuarine organisms, may be more susceptible to mercury as salinity decreases. It has been suggested that increasing temperature and decreasing salinity act synergistically to increase absorption rates, thus rendering an aquatic organism more susceptible to mercury toxicosis. Selenium appears to mitigate the adverse effects of mercury on aquatic organisms as it does for humans. However, the mechanism is not well understood. Aquatic organisms may be at risk due to mercury exposure in some locations. However, methylmercury, which is the more toxic form in the laboratory, is found only at very low levels in the natural waters. The risk to aquatic organisms cannot be quantified with the available data. However, the lack of evidence of fish kills associated with mercury suggests that risk due to mercury is low. Studies of the effects of mercury on terrestrial organisms have been limited. Dietary concentrations of 3 mg/kg methylmercuric chloride produced adverse reproductive effects in mallards and black ducks. Oral doses of 13 mg/kg and 60 mg/kg were lethal to goshawks and ducklings, respectively. Most terrestrial organisms do not appear to be at risk, except perhaps in the vicinity of anthropogenic sources. Elevated mercury residues have been found in plant and animal specimens collected near chlor-alkali plants, although no toxic responses have been reported. Piscivorous mammals and birds may be exposed to more mercury than other animals due to their position in the food chain. Mercury can appear in a variety of compounds, both inorganic and organic, in the environment. The evidence suggests that the organic compounds (particularly alkyl- and phenylmercurics) are more toxic than inorganic forms, and that methymercury is more ubiquitous than inorganic forms. Studies of the effects of mercury on terrestrial organisms have been limited. Dietary concentrations of 3 mg/kg CH3HgCl produced adverse reproductive effects in mallards and black ducks; oral doses of 13 mg/kg and 60 mg/kg were lethal to goshawks and ducklings, respectively. Residues of 0.6 mg/kg and 10 mg/kg in maize seedlings resulted in growth inhibition in the shoots and roots, respectively. Fate and distribution on the environment: Mercury is virtually ubiquitous in the environment though elevated levels are found consistently near anthropogenic sources and occasionally near natural sources. Mercury levels is uncontaminated freshwater and saltwater are generally low (0.04 ug/l to 0.3 ug/l). Values

of up to about 50 ug/l mercury have been reported for water in contaminated areas. Sediment levels range from -0.05 mg/kg in unpolluted areas to over 2.0 mg/kg near industrial sources of contamination. Rocks and uncontaminated soils contain 0.02 mg/kg to 0.15 mg/kg mercury, with concentrations of up to 250 mg/kg reported for sites near natural mercury deposits. Atmospheric mercury in remote areas is primarily in the form of a vapor and is usually in the elemental form. The ratio of mercury vapor to mercury adsorbed to particulates is quite variable in urban areas. Background concentrations range from 1 ng/m3 to 50 ng/m3 while urban levels vary from 2 ng/m3 to 60 ng/m3. Freshwater fish usually have slightly higher mercury levels (0.05 mg/kg to 1.80 mg/kg) than do marine fish (below 0.3 mg/kg). Terrestrial biota also contain detectable levels of mercury. Trees and herbaceous growth in unpolluted areas have concentrations ranging from 0.02 mg/kg to 0.03 mg/kg, with levels up to 1.25 mg/kg in areas contaminated by anthropogenic or natural sources of mercury. Levels in birds and mammals vary depending on such parameters as species and geographical region. Feeding habits can also influence mercury accumulation in mammals and birds. Environmental Fate: Mercury

4
TITLE:
Mercury and mercury compounds

AUTHORS:
Anonymous

SOURCE:
TA:IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans PG:239-345 YR:1993 IP: VI:58

ABSTRACT:
Exposure data Mercury occurs at low concentrations in the Earth's crust, mainly in sulfide ores (cinnabar), from which it has been extracted for a variety of uses for many centuries. Common applications of metallic mercury are as a cathode in the electrolytic production of chlorine, in dental amalgams in the extraction of gold from ore concentrates, in electrical equipment and in devices for measuring temperature and pressure. Mercury compounds have been used as fungicides in paints and on seeds and grains, as antiseptics, in electrical applications, and as catalysts and intermediates. Workers are exposed to mercury by inhalation, principally to metallic mercury but also to inorganic and organic mercury compounds. Occupations in which the highest exposures occur include mercury mining, work in chloralkali and alkaline battery plants and production of devices for measuring temperature and pressure. Lower exposures have been measured for people employed in hospital laboratories and dental clinics. Exposures have been measured by both ambient air monitoring and biological monitoring. Nonoccupational sources of exposure to mercury include food (methylmercury compounds, mainly in aquatic

organisms) and dental amalgam fillings (metallic mercury). These exposure levels are usually lower than those typically detected in occupational settings. Human carcinogenicity data Metallic mercury and inorganic mercury compounds A cohort study in a nuclear weapons factory in the USA on exposure to metallic mercury showed no difference in risk for lung cancer in exposed and unexposed subcohorts from the same factory. In a nested case-control study at two nuclear facilities in the USA, the risk for cancers of the central nervous system was not associated with estimated levels of exposure to mercury. A cohort study of chloralkali workers in Sweden identified a two-fold, significant excess risk for lung cancer and some nonsignificant excess risks for cancers of the brain and kidney. Lung cancers also occurred in an almost two-fold excess in Norwegian chloralkali workers, whereas the numbers of cases of cancer of the brain and kidney were close to those expected. In both studies, asbestos and smoking were judged to be the main determinants of the excess risk for lung cancer. In a study of male and female dentists and female dental nurses in Sweden, a two-fold risk for brain tumours was found in each of the three cohorts. No such risk appeared among dentists or medical and dental technicians in a US study of military veterans; these groups had excess risks for pancreatic and colon cancer, respectively. In an Australian case-control study of brain tumours and amalgam fillings, there was a decreased risk for gliomas and no effect was seen with regard to meningiomas. The risk for lung cancer was found to be higher among individuals with silicosis who had been working in US mercury mines than in subjects with silicosis who had worked elsewhere. This finding was based on small numbers, however, and the confidence limits overlapped. A case-control study in Italy indicated an excess risk for lung cancer among women in the felt-hat industry who had heavy exposure to mercury but also to arsenic. In a population-based case-control study from Canada, risk for prostatic cancer was associated with exposure to mercury compounds in general and the risk for lung cancer with exposure to metallic mercury. Organomercury compounds Studies in Minamata, Japan, on causes of death in populations with high exposure to mercury included areas with a high prevalence of methylmercury poisoning. The only clear indication of an increased cancer risk was in the most informative of these studies, in which excess mortality from cancer of the liver and cancer of the oesophagus was found in the area with the highest exposure, together with an increased risk for chronic liver disease and cirrhosis. Consumption of alcoholic beverages was known to be higher than average in the area. A cohort study of individuals in Sweden with a licence for seed disinfection with mercury compounds and other agents found no excess of brain cancer. Of the three Swedish casecontrol studies on exposure to mercury seed dressings and soft-tissue sarcomas, only one showed an odds ratio above unity; in all three studies, the confidence intervals included unity. For malignant lymphomas, there was a slightly but nonsignificantly elevated odds ratio for exposure to mercury seed dressings, but other exposures had higher odds ratios and, consequently, potential confounding. Animal carcinogenicity data Mercuric chloride was tested for carcinogenicity in

two studies in mice, by oral gavage and by administration in the drinking-water; only the study by gavage was adequate for an evaluation of carcinogenicity. Mercuric chloride was also tested in one study in rats by oral gavage. In mice, a few renal adenomas and adenocarcinomas occurred in males only. In rats, a few renal adenomas occurred in females; there was a dose-related increase in the incidence of squamous-cell papilloma of the forestomach in males, and a few papillomas were seen in females. Dose-related hyperplasia of the forestomach was seen in both males and females. Methylmercury chloride was tested for carcinogenicity in three studies in mice and two studies in rats by oral administration in the diet. In all three studies in mice, the incidence of renal adenomas and adenocarcinomas was increased in males. In the two studies in rats, no increase in tumour incidence was reported. In another study in mice given methylmercury chloride, a significant number of renal tumours was found in intact male mice and a few renal tumours were found in gonadectomized male and female mice that also received testosterone propionate: no renal tumour was found in male or female gonadectomized mice that did not receive testosterone propionate. Other relevant data After inhalation, about 70-80% of metallic mercury vapour is retained and absorbed. Little metallic mercury is taken up in the gastrointestinal tract, and less than 10% is absorbed. Metallic mercury passes into the brain and fetus. In the body, metallic mercury is oxidized to mercuric mercury, which binds to reduced sulfhydryl groups. The kidney is the main depository following exposure to both metallic and mercuric mercury. Mercuric mercury is eliminated mainly in urine and faeces; it is also excreted in milk. In humans, inorganic mercury compounds have two half-times: one lasts for days or weeks and the other much longer. Mercury concentrations in urine, blood and plasma are useful for biological monitoring. Methylmercury compounds present in seafood are almost completely absorbed from the gastrointestinal tract and are distributed to most tissues. The methylmercury compounds bind to reduced sulfhydryl groups; a fraction is converted to mercuric mercury, the extent of conversion differing among species. Methylmercury compounds are excreted mainly in the bile; in the intestine, some mercury is biotransformed into inorganic mercury compounds and excreted in the faeces. Methylmercury compounds pass into the fetus and are excreted in milk. In humans, methylmercury compounds have a single biological half-time of approximately two months. Concentrations in blood and hair are useful for monitoring exposure to methylmercury compounds. Following intense exposure to metallic mercury vapour, lung damage occurs; gastrointestinal and renal tubular necrosis occur after ingestion of mercuric mercury. Long-term exposure to metallic mercury causes encephalopathy and renal damage; chronic exposure to mercury mercury causes renal tubular damage. Immunologically based glomerulonephritis can occur. In rats, mercuric chloride may cause immunosuppression. Effects on the immune system vary considerably among rodent strains. Inorganic mercury is a cause of allergic contact dermatitis. The nervous system is the main target organ for methylmercury compounds, but interspecies differences exist; in some species, there are also effects on the kidney.

Some selenium compounds affect the kinetics of inorganic and methylmercury compounds and have a protective ef

5
TITLE:
Different Histochemical Findings in the Brain Produced by Mercuric Chloride and Methyl Mercury Chloride in Rats

AUTHORS:
Suda I
Eto K
Tokunaga H
Furusawa R
Suetomi K
Takahashi H

SOURCE:
Neurotoxicology, Vol. 10, No. 1, pages 113-125, 22 references, 1989

ABSTRACT:
The chemical form of accumulated tissue mercury (7439976) after exposure to inorganic and organic mercury was examined in rats and mice. Male Wistar-rats were injected subcutaneously (sc) with 0 or 5mg/kg methylmercuric-chloride (115093) (MMC) or 0, 0.5, or 1.0mg/kg mercuric-chloride (7487947) for up to 12 days. Animals were killed 7 days after the last dose and the brain, liver, and kidney were removed and assayed for total and inorganic mercury. Brain, liver, and kidney sections were also assayed for mercury granules using a histochemical technique. Male Wistar-rats and ddY-mice were injected sc with 0 or 5mg/kg MMC for 4 or 8 days. Animals were killed 1 to 53 days after the last dose and the brain, kidney, and liver were removed and analyzed as before. In mercuric-chloride treated rats, mercury accumulated in the brain, liver, and kidney in a dose related manner. Approximately 99.9 percent of the accumulated mercury was inorganic mercury. In MMC treated rats both total and inorganic mercury accumulated in the tissues in a dose dependent manner. Mercury granules were found in the brains of rats given mercuric-chloride, but not MMC. Maximum accumulations of total mercury in the brain occurred in rats and mice 8 days after dosing and decreased rapidly thereafter. Peak accumulations of inorganic mercury occurred on day 28. Similar decreases in total mercury content and slow accumulations of inorganic mercury also occurred in the kidney and liver. The accumulation of mercury granules in the brain indicated a temporal pattern similar to that of inorganic mercury. In the brains of mercuric-chloride treated animals the granules were detected in the nerve cells, choroid plexus, and phagocytes. In the brains of MMC treated animals the granules appeared primarily in the phagocytes and ependyma. The authors conclude that the appearance of mercury granules in the tissues corresponds to inorganic mercury, but not organic mercury.

6
TITLE:
The uptake of mercury in the brains of mamals exposed to mercury vapor and to mercuric salts.

AUTHORS:
Berlin Fazackerley J
Nordberg G

SOURCE:
Arch. Environ. Health; 18(5), 719-29, 1969; (REF:8)

ABSTRACT:
HAPAB Brain uptake of mercury was studied in rats, rabbits and squirrel monkeys to assess the differential effects of mercury vapor and an injected mercuric salt. Twelve rats (about 200 g), six squirrel monkeys (about 350 g) and eight rabbits (about 3 kg) were exposed to radioactive mercury vapor in an exposure chamber with controlled oxygen, carbon dioxide and water vapor. After exposure, body burden of mercury was immediately assessed by scintillation counter. Sacrifice was either immediately after exposure or at 1-, 4-, 8-, 16- and 32-day intervals. For each exposed animal, a paired animal was injected i.v. with the same amount of mercury as mercuric nitrate; sacrifice was as above. After death, the brains wer quickly removed and frozen at -80 C and then prepared for autoradiographic examination. Two monkeys and two rabbits had the femoral artery and vein cannulated for extracorporeal exposure of blood to mercury vapor. The monitoring and measuring systems are described in detail and the apparatus used is schematically issultrated. All of the animals exposed to mercury vapor showed a brain content ten times greater than those injected with mercuric salt. Autoradiography of the squirrel monkey showed great similarities in mercury distribution in the brain tissue for both forms of mercury: the highest uptake was in the gray matter with quantitative differences in mercury uptake between the subortical nuclei and the cortical layers. In contrast, the area postrema did not show this order of magnitude in difference of mercury uptake between the vapor an salt form of mercury. The in vivo extracorporeal experiment demonstrated that mercury vapor can be taken up by the blood directly. Binding of mercury to an organic radical in the lung, for example, is not a necessary condition for high brain uptake of mercury. In the animals exposed to mercury vapor, the red blood cells accounted for a higher mercury concentration than in the animals injected with the mercuric salt. The data suggest that high brain uptake in mercury vapor exposure may be due to the differences in the way that the blood transports mercury. There is further indication that the higher brain uptake of mercury in vapor form is a general phenomenon among mammals. TOXICOLOGY AND PHARMACOLOGY 69/08/00, 259 1969

7
TITLE:
Uptake of mercury by the brain

AUTHORS:
Magos L

SOURCE:
Brit. J. Ind. Med.; 25(4), 315-8, 1968; (REF:11)

ABSTRACT:
HAPAB A study was conducted to determine whether elemental mercury is transported as such by the blood to the brain, or whether it is first oxidized to mercuric ions. A technique for injecting metallic mercury intravenously in aqueous solution was developed and is described in detail. Utilizing this method, female rates were injected with 0.1 mcg of metallic 203-labeled mercury into the jugular cannula. Another group of rats was similarly injected with mercuric chloride. All rats except two were decapitated at set times after injection and blood, brain, kidneys, lungs and heart were analyzed for mercury. Two animals were anesthetized with 70 mg/kg diethyl barbituric acid and 30 sec after the injection blood was collected from the chest cavity. Results showed that after injection of metallic mercury, exhalation of mercury started immediately and lasted about 15 sec. After 30 sec, nearly 20% of the dosage administered had been exhaled and the concentration of mercury in the brain was nearly as high as in the blood. After injection of mercuric chloride, only 2% mercury was exhaled and 30 sec after the injection, the lungs, brain and heart uptake was much less. Furthermore, the blood of the animals given metallic mercury retained only 6% of the injected dose in contrast to the 45% remaining in the blood of those given mercuric chloride. The disappearance of mercury from the blood of anesthetized rats was nearly as fast as in the unanesthetized animals and very much faster than in rats given mercuric chloride. The percentages of mercury found in the tissues changed very little from 0.5 to 5 min after the injection of metallic mercury and the ratio of concentrations, brain:blood, was high. After injection of mercuric chloride, the percentages found in the blood and brain decreased and in the kidneys increased with time after injection and the ratio brain:blood was only one-tenth of that after metallic mercury. It was concluded that oxidation of mercury in the blood was, therefore, not instantaneous and the rapid transport of the unconverted metallic mercury to the brain and its subsequent rapid diffusion from the blood was responsible for the high level of mercury in the brain after exposure to mercury vapor. TOXICOLOGY AND PHARMACOLOGY 69/02/00, 46 1968

8
TITLE:
Comparison of Mercury Accumulation among the Brain, Liver, Kidney, and the Brain Regions of Rats Administered Methylmercury in Various Phases of

Postnatal Development

AUTHORS:
Sakamoto M
Nakano A

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 55, No. 4, pages 588-596, 24 references, 1995

ABSTRACT:
Mercury (7439976) distribution among organs and brain regions was investigated in adult male and female Wistar-rats after treatment with a nontoxic level of methylmercury (22967926) during different developmental phases. Groups of rats were administered 1mg/kg/day of methylmercury-chloride (115093) for 10 consecutive days starting on postnatal days one, 14, or 35; the groups were designated as PD1, PD14, or PD35. Although the weights of body, kidney and liver in PD1 rats ranged about 7 to 12% of those in PD35, the brain weighting PD1 rats were about 50% of that in PD35 rats. The brain/body weight ratios differed remarkably according to the postnatal phases. The brain/body weight ratios in PD1 rats were about two and five times as high as those in PD14 and PD35 rats, respectively. The mercury distribution was comparatively uniform among the organs in PD1 rats, and the difference in the mercury distribution became very evident with development of the postnatal phase. The mercury concentration in the brain was highest in PD14 rats, followed by PD1 and PD35 rats. The percentage of total mercury administered in the brain was highest in PD1 rats and decreased with the postnatal phase. The mercury concentration and percent of total mercury administered in the kidney increased markedly with the postnatal phase. The blood mercury levels in PD14 and PD35 rats were higher than in PD1 rats. The percent of the total mercury administered in the brain was highest in PD1 rats and decreased with development. The kidney mercury levels increased markedly with the postnatal phases. The authors suggest that the difference in mercury concentration among the brain regions appears to be important in determining the selectivity of the effects in the case of adult Minamata disease, but cannot be the only cause of variation in the sensitivity of the regions.

9
TITLE:
Mercury Neurotoxicity: Mechanisms of Blood-Brain Barrier Transport

AUTHORS:
Aschner M
Aschner JL

SOURCE:

Neuroscience and Biobehavioral Reviews, Vol. 14, No. 2, pages 169-176, 109 references, 1990

ABSTRACT:

The role of blood/brain barrier transport in mercury (7439976) neurotoxicity was discussed. The characteristics of the blood/brain barrier were described. The blood/brain barrier is a specialized layer of endothelial cells which separate the central nervous system (CNS) from the blood. Despite its specialized nature, the blood/brain barrier cannot prevent the transport of toxicants from the blood to the brain which have the same transport properties as nutrients, therapeutic agents, or hormones. The properties of mercury relevant to membrane toxicity were discussed. These included the effects of mercury on passive ion permeability, carrier mediated ion transport, and inhibition of amino acid and sugar transport systems. Cerebral blood flow and blood/brain barrier integrity were considered. The transport of mercurials across the blood/brain barrier was discussed. Inorganic mercury and mercury vapor are distributed in a similar pattern in the organs and tissues. Mercury vapor because of its high lipophilicity can dissolve in the blood and penetrate the blood/brain barrier. Once inside the brain it is oxidized to divalent mercury (Hg+2). Accumulation of Hg+2 in the brain leads to neurotoxicity. Methylmercury has a high affinity for sulfhydryl groups and forms methylmercury/thiol conjugates. These conjugates are able to pass the blood/brain barrier because of their structural similarity to L-amino acids, especially L-methionine. The authors conclude that the toxicity of mercurials to the CNS depends not only on the functioning of the blood brain barrier but their transport properties. Organic mercurials such as methylmercury are able to cross the blood/brain barrier because of their ability to mimic sulfhydryls.

10

TITLE:

An Analysis of Autopsy Brain Tissue from Infants Prenatally Exposed to Methylmercury

AUTHORS:

Lapham LW
Cernichiari E
Cox C
Myers GJ
Baggs RB
Brewer R
Shamlaye CF
Davidson PW
Clarkson TW

SOURCE:

Neurotoxicology, Vol. 16, No. 4, pages 689-704, 24 references, 1995

ABSTRACT:

In conjunction with the Seychelles Child Development Study (SCDS), mercury (7439976) levels and histopathology were studied in the brains of 32 neonates from the Seychelles. Neonatal brains obtained at autopsy from the Seychelles and 12 referent brains from the United States were examined. No abnormalities were noted in cerebral or cerebellar organization. Brain mercury levels in Seychelles samples varied both between brains for the same brain region and between regions in the same brain. The majority of mercury values ranged from 50 to 250 parts per billion. The majority of brains from Seychelles had mercury values well above those from referent brains. Statistical analysis of different brain regions in Seychelles specimens demonstrated that the frontal region had the lowest mercury levels, the occipital and temporal/hippocampus regions had intermediate levels, and the cerebellum, basal ganglia/thalamus and pons/medulla had the highest levels. Mercury levels were not significantly different between grey matter and white matter. Reactive astrocytes and increased numbers of microglia were identified in the cerebral white matter of many of the Seychelles specimens and in some of the reference brains. No correlation was seen between reactive changes and mercury levels. The authors conclude that no evidence of mercury brain toxicity was identified in this study.

11

TITLE:

Ratio of Organs to Blood of Mercury during its Uptake by Normal and Acatalasemic Mice

AUTHORS:

Ogata M

Aikoh H

SOURCE:

Environmental Research, Vol. 42, No. 2, pages 421-424, 7 references, 19871987

ABSTRACT:

The organ/blood distribution of mercury (7439976) during exposure was studied in normal and acatalasemic mice. Normal and acatalasemic mice were exposed to mercury-203 (13982780) vapor or injected intraperitoneally with mercury-203 or mercury-203 labeled mercuric-chloride (7487947) solution. One hour after treatment, the mice were killed and the brain, heart, kidney, and liver were removed and assayed for total mercury. Blood samples were also analyzed for mercury. Brain/blood mercury ratios were highest in animals exposed to mercury vapor and next highest in those injected with mercury, regardless of their catalase state. Brain/blood, liver/blood, and heart/blood mercury ratios were higher in acatalasemic mice than in normal mice. Kidney/blood ratios were lower in mice injected

with or exposed to metallic mercury vapor than in those injected with mercuric-chloride. The amount of metallic mercury exhaled by acatalasemic mice injected with mercuric-chloride was higher than that of similarly treated normal mice. The authors conclude that metallic mercury in the blood passes through the blood/brain barrier, the brain having a higher concentration of metallic mercury than the blood. The higher blood mercury concentrations and exhaled mercury levels in acatalasemic mice may be explained by assuming that in acatalasemic mice there is sufficient catalase activity to fix metallic mercury as mercuric ion.

12

TITLE:

The Effect of Manganese Administration, Alone or Combined with Zinc, Mercury and Cadmium, on the Tissue Levels of These Elements in Rats

AUTHORS:

Lal S
Gupta SK
Chandra SV

SOURCE:

Toxicology Letters, Vol. 5, No. 3-4, pages 203-206, 6 references, 1980

ABSTRACT:

The effects of manganese (7439965) administration alone or combined with zinc (7440666), mercury (7439976), and cadmium (7440439) on the concentrations of these elements in the brain, liver, and kidney were studied in rats. Male albino-rats were injected intraperitoneally with 4mg/kg manganese as manganous-chloride (7773015), 1mg/kg zinc given as zinc-chloride (7646857), 0.5mg/kg mercury given as mercuric-chloride (7487947), or 0.5mg/kg cadmium as cadmium-chloride (10108642) alone or in combination daily for 30 days. They were then killed and the brain, liver, and kidneys were removed and analyzed for manganese, mercury, zinc, and cadmium. Manganese alone caused significant accumulations of manganese in the brain, liver, and kidney and zinc in the liver and kidneys. Zinc alone caused significant increases in zinc and manganese in all three organs. Manganese plus zinc increased brain manganese concentration and brain, liver, and kidney zinc concentrations and decreased liver and kidney manganese concentrations. Mercury alone induced significant increases in brain, liver, and kidney mercury concentration. Manganese plus mercury significantly decreased hepatic mercury concentration and increased kidney mercury concentration. Manganese concentrations in the examined tissues were not affected. Cadmium alone caused significant increases in brain, kidney, and liver cadmium concentrations. Manganese plus cadmium did not affect brain, liver, or kidney concentrations but significantly enhanced cadmium accumulation in the brain. The authors suggest that the observed changes in brain, liver, and kidney manganese, zinc, mercury, and cadmium

concentration following combined exposure probably reflect interactions at tissue absorption sites or changes in excretory pattern.

13
TITLE:
Elimination Of Brain Mercury In Rats By Multi-agent Tx

AUTHORS:
MORGAN DL

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Currently there is no proven effective treatment to decrease brain mercury levels. Although chelators in combination with various other medicinal agents have been prescribed there is no objective evidence that these treatments are effective. Some drug combinations may in fact increase brain levels by causing a re-distribution of tissue stores. The aim of this study is to determine if brain mercury levels can be reduced by therapeutic treatment with 2,3-dimercaptopropane-1-sulphonate (DMPS), alone and in combination with other agents often prescribed to help eliminate Hg. Experiments were conducted to examine the effects of various combinations of DMPS, ascorbate (ASC) and glutathione (GSH) on mercury levels in the brain. Rats were exposed 2 hours/day for 10 days to 4 mg/m3 mercury vapor. This exposure regimen has been found to result in relatively high levels of mercury in the brain with no obvious neurotoxicity. The rats were removed from the exposure for 7 days to allow the Hg levels to reach equilibrium in the brain. Animals were then treated with DMPS, GSH, or ASC alone, or in various combinations for one week. Initial data indicate that DMPS caused a more rapid elimination of Hg from the brains of exposed rats. GSH and ASC alone or in combination did not appear to increase the efficacy of DMPS. Additional studies were conducted to evaluate the effects of lipoic acid, and insulin in combination with DMSA on elimination of Hg from the brain and kidney of exposed rats. Lipoic acid has been prescribed for autistic children to theoretically remove brain mercury, although there are no data to support this effect. Insulin has been reported to facilitate the transfer of drugs across the blood-brain barrier, and may also facilitate the transfer of free and bound Hg out of the cells. Neither of these compounds improved the efficacy of DMSA in depleting brain Hg.

14
TITLE:
Different histochemical findings in the brain produced by mercuric chloride and methyl mercury chloride in rats.

AUTHORS:

SUDA I
ETO K
TOKUNAGA H
FURUSAWA R
SUETOMI K
TAKAHASHI H

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 10 (1). 1989. 113-125.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The chemical form of mercury reactive by the histochemical technique was studied by using rats and mice treated with mercuric chloride (HgCl2) and methyl mercury chloride (MeHgCl). Mercury granules were demonstrated histochemically in the brain of HgCl2-treated rats with higher levels of inorganic mercury. However, mercury granules were not demonstrated in the brain of MeHgCl-treated rats in spite of a considerably high organic mercury level. In rats and mice with significant biotansformation of injected MeHg to inorganic mercury, the appearance of the peak inorganic mercury level and mercury granules in the brain seemed to occur on the same day. These results suggested that mercury granules in the brain represent inorganic mercury, but not organic mercury. In the brains showing mercury granules, the lowest level of inorganic mercury was 0.12 mug/g in HgCl2-treated rats, 0.14 mug/g in MeHgCl-treated rats and 0.12 mug/g in MeHgCl-treated mice. These values were similar t

15
TITLE:
Relationship Between Catalase Activity And Uptake Of Elemental Mercury By Rat Brain

AUTHORS:
Eide I
Syversen TLM

SOURCE:
Developments in Toxicology and Environmental Science, Vol. 11, Developments in the Science and Practice of Toxicology, pages 491-494, 10 references, 19831983

ABSTRACT:
The importance of catalase activity in the uptake of elemental mercury (7439976) in the brain was studied in rats. Male Sprague-Dawley-rats were treated with 10 microliters aminotriazole (61825) through injection into the lateral ventricle of the brain to inhibit catalase. Aminotriazole was given 10 to 180 minutes prior to injection of elemental mercury intravenously depending on the degree of inhibition desired. Radioactive mercury-chloride was mixed with stannous-chloride for injection. Uptake

of mercury was determined by scintillation spectrometry in brain tissue homogenates of rats killed shortly after injection. Catalase activity was determined through decomposition of hydrogen-peroxide in tissue homogenates. At zero activity of catalase, uptake of mercury was estimated at about 0.057 nanograms per gram wet weight. As catalase activity increased, mercury uptake increased. There was also a linear relation between uptake of mercury by brain and the injected amount of elemental mercury which persisted even in animals with a 52 percent reduction in catalase activity. The authors conclude that administration of aminotriazole, with consequent reduction in catalase activity, reduces mercury uptake in the brain. The rate of mercury oxidation in the brain appears to depend on concentrations of the catalase/peroxide complex and elemental mercury.

16
TITLE:
Localization of Mercury in CNS of the Rat. V. Inhalation Exposure to Metallic Mercury

AUTHORS:
Moller-Madsen B

SOURCE:
Archives of Toxicology, Vol. 66, No. 2, pages 79-89, 31 references, 1992

ABSTRACT:
The autometallographic distribution pattern and target cell localization of mercury (7439976) in the Wistar-rat brain and spinal cord was studied after inhalation of mercury vapor. The rats were exposed to mercury vapor at 50 to 550 micrograms per cubic meter (microg/m3) of air for 4 to 24 hours. Brains, cervical spinal cords, and lungs were removed from sacrificed rats and tissues were prepared for microscopic evaluations. The general distribution of mercury in the central nervous system (CNS) was heterogeneous. Mercury was primarily located in the gray matter of the CNS, in the nuclei of the brain stem and in the brain capillary walls; staining in the latter was pronounced. No mercury deposits were detected throughout the brain and upper cervical spinal cord following exposure to 50microg/m3 mercury for 4 and 8 hours. Only after an exposure period of 4 hours to 500microg/m3 were mercury deposits visible in the choroid epithelial cells visible. A 12 hour exposure to 550microg/m3 was needed before mercury deposits appeared in ependymal cells. The authors suggest that mercury may reach the nervous tissue by crossing the blood/cerebrospinal fluid barrier or the blood/brain barrier of the cerebral capillaries.

17
TITLE:
Doseand Sex-Dependent Alterations in Mercury Distribution in Fetal Mice

Following Methylmercury Exposure

AUTHORS:
Inouye M
Kajiwara Y
Hirayama K

SOURCE:
Journal of Toxicology and Environmental Health, Vol. 19, No. 3, pages 425-435, 21 references, 19861986

ABSTRACT:
The sex dependent and dose dependent alterations of mercury (7439976) distribution in fetal tissue and organs in the course of time after maternal administration of methylmercuric-chloride (115093) was examined using inbred C57BL/6NJcl-mice. The concentration of mercury in the maternal blood and plasma was highest at day one after administration of methylmercuric-chloride, and decreased exponentially in the following days. The plasma level of mercury was always about twice as low as the blood level from day one through five after treatment. Mercury in the brain increased for a certain period, showing a dose dependent effect. The concentration reached the highest levels at 2, 3, 3, and 4 days after doses of 2.5, 5, 10, and 20mg/kg, respectively. In the liver and kidney, the mercury concentration decreased in the course of time without dose dependent variation. In the fetal brain there was also a dose dependent variation in retention of mercury. Mercury reached its highest concentration in the fetal brain earlier than in the maternal brain and was always higher than the concentration in the maternal brain. A statistically significant difference was noted in mercury levels between male and female fetuses in the brain after a maternal dose of 2.5mg/kg; mercury concentration in the brain was higher in females than in males, but not so for the liver or kidney. No significant differences between sexes were noted in any organs examined after administration of the higher doses.

18
TITLE:
Foetal Distribution of Inhaled Mercury Vapor in Normal and Acatalasaemic Mice

AUTHORS:
Ogata M
Meguro T

SOURCE:
Physiological Chemistry and Physics and Medical NMR, Vol. 18, No. 3 pages 165-170, 17 references, 19861986

ABSTRACT:

Organ distribution, including placental and fetal distribution, of mercury (7439976) was determined in normal and acatalasemic mice, in order to investigate the effect of this inborn error of metabolism in the mother on the sensitivity of the fetus to pollutants. Normal and acatalasemic female mice of an inbred strain were exposed to 1.0 milligram/cubic meter metallic mercury vapor for 1 hour in an inhalation exposure chamber, and were sacrificed immediately afterwards. Additionally, normal and acatalasemic mice were injected intraperitoneally with 10 microcuries of mercury-203 as mercuric-chloride (7487947) in saline and sacrificed after 1 hour. Levels of mercury distribution were significantly lower in the blood and lungs, and significantly greater in the brain and liver of metallic mercury exposed maternal acatalasemic mice than in normal maternal mice; mercury concentrations in the fetus, placenta and amniotic sac were significantly higher in the acatalasemic mice than in normal mice. The fetus/blood, placenta/blood and fetus/placenta ratios of mercury concentration in metallic mercury exposed acatalasemic mice were significantly higher than those in normal mice, as were the maternal brain/maternal blood and maternal liver/maternal blood ratios of mercury concentration. In mercuric-chloride injected mice, the placenta/maternal blood, fetus/placenta and fetus/maternal blood ratios of mercury concentration in acatalasemic mice were similar to those in normal mice, as were the maternal brain/maternal blood and maternal liver/maternal blood ratios. In metallic mercury exposed acatalasemic mice, the placenta/maternal blood, fetus/placenta, fetus/maternal blood, maternal brain/maternal blood and maternal liver/maternal blood ratios of mercury concentration were significantly higher than those of mercuric-chloride injected acatalasemic mice. The authors conclude that metallic mercury passes through the blood/brain, blood/liver, and blood/placenta barriers more readily in acatalasemic mice than in normal mice.

19

TITLE:

Distribution of Inorganic Mercury in the Guinea Pig Brain

AUTHORS:

Nordberg GF
Serenius F

SOURCE:

Acta Pharmacologica et Toxicologica, Vol. 27, pages 269-283, 8 references, 19691969

ABSTRACT:

Guinea pigs were exposed to radioactive mercury (7439976) vapor or given intravenous injections of radioactive mercuric-nitrate (10045940) solution, and the animals were sacrificed at various intervals. Mercury levels in the brain were determined by scintillation counting and the

distribution within the brain was illustrated autoradiographically. The uptake of mercury in the brain was several times greater in the vapor exposed animals than in the injected animals, but the distribution of mercury in the brain was similar after both types of administration. The elimination of mercury is different from different parts of the brain and consequently the distribution pattern, a long time after the administration of mercury, is not the same as that found immediately afterwards. Substantial differences were found between the concentrations in different parts of the brain; certain cells in the brain stem still contained particularly high concentrations long after the administration of mercury.

20

TITLE:

Demethylation of Methyl Mercury in Different Brain Sites of Macaca fascicularis Monkeys during Long-Term Subclinical Methyl Mercury Exposure

AUTHORS:

Vahter ME
Mottet NK
Friberg LT
Lind SB
Charleston JS
Burbacher TM

SOURCE:

Toxicology and Applied Pharmacology, Vol. 134, No. 2, pages 273-284, 43 references, 1995

ABSTRACT:

Accumulation of total (T-Hg) and inorganic mercury (7439976) (I-Hg) in different brain regions during long term methylmercury (22967926) (MeHg) and I-Hg exposure was studied in monkeys. Female macaque-monkeys (Macaca-fascicularis) were administered 0 or 50 micrograms per kilogram (microg/kg) methylmercuric-hydroxide (1184572) in apple juice daily for 6, 12, or 18 months (mo). One group given MeHg for 12mo was maintained for another 6mo without MeHg exposure to assess recovery. Another group of monkeys was infused with 0 or 200microg/kg mercuric-chloride (7487947) (HgCl2) daily by an indwelling venous catheter for 3mo. The monkeys were killed at the end of each experimental period and the brains were removed. The cerebellum, occipital pole, pons, motor strip, frontal pole, temporal pole, thalamus, and pituitary gland were dissected out and analyzed for T-Hg and I-Hg. The concentrations of MeHg in the brain regions were determined by subtracting the I-Hg from the T-Hg concentrations. Accumulation of MeHg in the various brain parts occurred to a greater extent in obese monkeys, those weighing 5.0 to 6.1 kilograms (kg), than in normal weight monkeys. In monkeys with normal weights, the MeHg concentrations in each brain region were similar except in the pituitary,

averaging 3.0 micrograms per gram (microg/g) after 6mo, 4.2microg/g after 12mo, and 4.3microg/g after 18mo. MeHg concentrations in the pituitary gland generally averaged about 50% of those in other regions. The average halftime for MeHg to accumulate in the brain sites was around 118 days. In monkeys in the recovery group, MeHg was cleared from all brain sites with an average halflife of approximately 37 days except in the pituitary gland. MeHg clearance from the pituitary could not be determined but appeared to be faster than at other sites. The concentrations of I-Hg in each brain region increased with increasing time of exposure and constituted about 9% of the total brain Hg burden at 6 and 12mo and 12% at 18mo. I-Hg was cleared from most brain sites with halflives of 230 to 540 days. I-Hg concentrations in the brain regions of MeHg exposed monkeys were much higher than in HgCl2 treated animals. The authors conclude that a pronounced, but slow accumulation of I-Hg occurs in the brain as a result of MeHg exposure. The I-Hg is most likely formed by demethylation of MeHg in brain tissues.

21
TITLE:
Mercury

AUTHORS:
Clarkson TW

SOURCE:
Journal of the American College of Toxicology, Vol. 8, No. 7, pages 1291-1295, 4 references, 1989

ABSTRACT:
The environmental fate and toxicity of mercury (7439976) were discussed. The chemical forms and properties of mercury were summarized. The environmental fate of and sources of human exposure to mercury were also reviewed. Anthropogenic sources of mercury included cinnabar mining, biocide production, fossil fuel burning, industrial use of mercury, and use and production of dental materials. Natural sources of mercury included outgassing from the earth's crust, volcanic emissions, and evaporation from the oceans. The atmosphere has been considered to be the major vehicle for mercury transport. Atmospheric transport has been thought to account for the high concentrations of mercury observed in fish which originated from anthropogenic sources. Aside from occupational sources, most human mercury exposures have resulted from dietary sources such as fish and amalgam dental fillings. The disposition of inorganic divalent mercury (Hg+2), mercury vapor, and methylmercury (22967926) in mammalian tissues was discussed. Hg+2 was noted to be distributed throughout the body with the highest concentrations in the kidney cortex. It is excreted primarily in the urine, a fact which makes urinary excretion a useful biological technique. Inhaled mercury vapor was demonstrated to rapidly enter cells where it was oxidized by catalase to

Hg+2. Hg+2 and methylmercury readily cross the blood brain barrier. Methylmercury is incorporated into the hair, with its concentration in the hair proportional to its blood concentration. Methylmercury was noted to be excreted primarily in the feces and in the bile, part of which is reabsorbed. The remainder was degraded to Hg+2. Biological damage caused by Hg+2, mercury vapor, and methylmercury was discussed. Acute exposure to Hg+2 caused death as a result of damage to kidney cells and cardiovascular collapse. Low doses damaged the immune response of kidney cells. Methylmercury primarily affects the brain, inducing focal damage in adults and diffuse damage in developing brains after in-utero exposure. Prenatal effects were induced by exposures considerably lower than those causing adult poisoning.

22

TITLE:

Brain, Kidney and Liver 203Hg-Methyl Mercury Uptake in the Rat: Relationship to the Neutral Amino Acid Carrier

AUTHORS:

Aschner M

SOURCE:

Pharmacology and Toxicology, Vol. 65, No. 1, pages 17-20, 17 references, 1989

ABSTRACT:

This study investigated the transport of methyl-mercury (22967926) (MeHg) across the blood/brain barrier (BBB) and explored the relationship between the L-neutral amino acid carrier transport system and the translocation step of MeHg into the brain. The possibility that this system may be uniformly operative in other tissues such as the kidney and liver was also examined. Female Long-Evans-rats were infused with MeHg in the external jugular vein in one of five treatment regimes each including 0.05 millimolar (mM) methyl-mercury-chloride (115093) combined with: saline; 0.1mM L-cysteine; 0.1mM L-cysteine and 0.1mM L-methionine; 0.1mM L-leucine; or 0.1mM L-cysteine, and 0.1mM L-leucine. Animals were sacrificed at 3 minutes, or at 7 or 96 hours following exposure. Mercury concentrations in the brains of L-cysteine treated animals were significantly higher than in saline treated animals at all three times. The L-cysteine-mediated brain mercury uptake was consistently abolished by the coinjection or coinfusion of methyl-mercury with L-cysteine and L-methionine. No significant differences were noted in kidney and liver mercury concentrations in any of the treatment groups compared with controls, at any of the tested times. No statistical difference was noted in the percentage of diffusible mercury, nonprotein bound, at each sacrifice time irrespective of the treatment used. The authors conclude that methyl-mercury L-cysteine conjugates in the plasma may share a common transport step with the L-neutral amino acid carrier transport system and

that there is present in the brain capillaries a transport system able to selectively mediate methyl-mercury uptake across the capillary endothelial cell membrane.

23
TITLE:
Mercury In Mouse Brain After Inhalation Of Mercury Vapour And After Intravenous Injection Of Mercury Salt

AUTHORS:
Berlin M
Johansson LG

SOURCE:
Nature, Vol. 204, No. 4953, pages 85-86, 4 references, 19641964

ABSTRACT:
The effect of inhaled mercury (7439976) vapor was compared with intravenous injection of mercuric-nitrate (10045940) on mercury uptake in brains of mice. One group of animals was exposed to 10 milligrams per cubic meter radioactive mercury vapor for 4 hours. A comparable concentration of mercury was injected intravenously as radioactive mercuric-nitrate into group 2. At intervals ranging from 1 hour to 32 days, animals were sacrificed and whole body autoradiography was performed on half of each animal. Mercury concentrations were determined by densitometric comparison with standard isotopic measurements. From the other half of the animal, brain, liver, kidney, and other organs were removed and the radiation levels were determined by scintillation counting. Autoradiograms revealed that brain mercury uptake was about 10 time greater in animals inhaling mercury compared with animals intravenously injected with mercury. Scintillation count findings were comparable with autoradiogram results. The authors conclude that brain mercury uptake is much greater when mercury is inhaled than when administered intravenously.

24
TITLE:
Effect of Mercuric Chloride Intoxication and Dimercaprol Treatment on delta-Aminolevulinate Dehydratase from Brain, Liver and Kidney of Adult Mice

AUTHORS:
Emanuelli T
Rocha JBT
Pereira ME
Porciuncula LO
Morsch VM
Martins AF

Souza DOG

SOURCE:
Pharmacology and Toxicology, Vol. 79, No. 3, pages 136-143, 46 references, 1996

ABSTRACT:
The effects of mercuric-chloride (7487947) intoxication and dimercaprol (DM) treatment on delta-aminolevulinate-dehydratase (ALAD) and on mercury (7439976) distribution in brain, liver, and kidney of adult mice were investigated. Mice received one daily injection of 0, 2.3, or 4.6mg/kg mercury-chloride for 3 consecutive days. On the fourth day they were injected once with 0.25 millimole/kilogram DM. Mercury and DM had no effect on brain or liver weight. The mice treated with the highest dose of mercury showed a significant increase in renal weight and renal to body weight ratio, regardless of DM treatment. Cerebral ALAD was not inhibited by mercury. The renal enzyme was inhibited 33% by the 2.3mg/kg dose and 40% by the 4.6mg/kg dose. DM alone caused an 18% inhibition of renal ALAD. DM did not reverse the inhibition caused by the 2.3mg/kg dose and enhanced the inhibition of the renal enzyme caused by 4.6mg/kg mercury. The liver enzyme was inhibited 25% by 4.6mg/kg mercury, and DM did not reverse this inhibition. At the 2.3mg/kg dose, mercury increased in the kidney and DM was unable to remove it. At the 4.6mg/kg dose, mercury increased in the liver. DM promoted mercury to increase in the liver and brain. Mice injected with 4.6mg/kg showed an increase in serum urea, indicating impaired renal function. The authors conclude that DM does not protect the sulfhydryl enzyme ALAD from mercury intoxication in-vivo, and DM tends to increase the toxicity of mercury at the molecular level.

25
TITLE:
Mercury

AUTHORS:
WHO Working Group

SOURCE:
TA:Environmental Health Criteria PG:1-131 YR:1976 IP: VI:1

ABSTRACT:
Two cycles are believed to be involved in the environmental transport and distribution of mercury. One is global in scope and involves the atmospheric circulation of elementary mercuric vapour from sources on land to the oceans. However, the mercury content of the oceans is so large, at least seventy million tonnes, that the yearly increases in concentration due to deposition from the global cycle are not detectable. The other cycle is local in scope and depends upon the methylation of inorganic mercury mainly from anthropogenic sources. Many steps in this cycle are

still poorly understood but it is believed to involve the atmospheric circulation of dimethylmercury formed by bacterial action. The methylation of inorganic mercury in the sediments of lakes, rivers, and other waterways and in the oceans is a key step in the transport of mercury in aquatic food chains leading eventually to human consumption. Methylmercury accumulates in aquatic organisms according to the tropic level, the highest concentrations being found in the large carnivorous fish (biomagnification). Alkylmercury fungicides used as seed dressings are important original sources of mercury in terrestrial food chains. Mercury is passed first to seed eating rodents and birds and subsequently to carnivorous birds. Accumulation of methylmercury in aquatic and terrestrial food chains represents a potential hazard to man by consumption of certain species of oceanic fish, or fish or shellfish from contaminated waters, and of game birds in areas where methylmercury fungicides are used. Experimental studies on the effects of mercury: Reversible and irreversible toxic effects may be caused by mercury and its compounds, depending upon the dose and duration of exposure. Reversible behavioural changes may be produced in animals by exposure to mercury vapour. Methylmercury compounds produce irreversible neurological damage in animals. Many of the neurological signs seen in man have been reproduced in animals. Methylmercury is equally toxic to animals whether it is given in the pure chemical state or in fish where it has accumulated naturally. A latent period lasting weeks or months is observed between cessation of exposure and onset of poisoning. Morphological changes have been seen in the brain before onset of signs. This phenomenon has been referred to as "silent damage". Animal data support epidemiological evidence from Japan, that the fetus is more sensitive than the adult. Little is known about the physical and chemical factors affecting the toxicity of mercury. Selenium is believed to be protective against inorganic and methylmercury compounds Epidemiological and clinical studies: The classic symptoms of poisoning by mercury vapour are erethism (irritability~ excitability, loss of memory, insomnia), intentional tremor, and gingivitis. Most effects of mercury vapour are reversible on cessation of exposure, although complete recovery from the psychological effects is difficult to determine. Recovery may be accelerated by treatment with penicillamine and unithiol (2,3,dimercaptopropansulfonate). Studies of occupational exposure to mercury vapour reveal that the classic symptoms of mercurialism do not occur below a time-weighted average mercury concentration in air of 0.1 mg/m3. Symptoms such as loss of appetite and psychological disturbance have been reported to occur at mercury levels below 0.1 mg/m3. The most common signs and symptoms of methylmercury poisoning are paraesthesia, constriction of the visual fields, impairment of hearing, and ataxia. The effects are usually irreversible but some improvement in motor coordination may occur. Complexing and chelating agents may be useful in prevention if given early enough after exposure but BAL is contraindicated in cases of methylmercury poisoning as it leads to increased brain levels of mercury. Epidemiological investigations have been made on populations in whom the

intensity and duration of exposure to methylmercury through diet differs, for example, a population in Iraq having high daily mercury intakes (as high as 200 ug/kg/day) for a brief period (about 2 months), populations in Japan having lower daily intakes with exposure for several months or years, and several fish-eating populations having daily intakes of mercury usually below 5 ug/kg but with exposure lasting for the lifetime of the individual The results of these studies indicate that the effects of methylmercury in adults become detectable in the most sensitive indiViduals at blood levels of mercury of 20-50 ug/100 ml, hair levels from 50-120 mg kg, and body burdens between about 0.5 and 0.8 mg/kg Observations on the Minamata outbreak in Japan indicate that the e us is more sensitive to methylmercury than the adult but the difference degree of sensitivity has not yet been established. Evaluation of health risks to man from exposure to mercury and its compounds: Adverse health effects have not yet been identified in workers occupationally exposed to a time-weighted average air concentration of mercury of 0.05 mg/m3. This air concentration is equivalent to an average mercury concentration in blood of 3.5 ug/100 ml and an average mercury concentration in urine of 150 ug/litre on a group basis. The corresponding ambient air concentration of mercury for exposure of the general population would be 0.015 mg/m3. It is estimated that the first effects associated with long-term daily intake of methylmercury should occur at intake levels between 3 an 7 ug/kg/day. The probability of an effect (paraesthesia) at this intake level is about 5% or less in the general population. These figures apply only to adults. Prenatal life may be the most sensitive stage of the life cycle to methylmercury. Furthermore experiments on animals indicate a potential for genetic damage by methylmercury.

26

TITLE:

NEUROTOXIC MECHANISMS IN PRIMARY CNS CELL CULTURES

AUTHORS:

BROOKES N

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ Mercury, including its organic compounds, is a pervasive environmental and occupational neurotoxicant with multiple cellular targets of action. In addition to direct toxic effects on neurons, neurotoxicity results secondarily following impairment of other cell types that control the neuronal microenvironment, notably glia and the vascular endothelial cell layer that constitutes the blood-brain barrier. Astroglia and vascular endothelial cells exhibit mutual trophisms in the expression of differentiated blood-brain barrier properties. Many of these properties can be reproduced in vitro in cell culture. It is proposed to use primary

cultures of mouse cerebral astrcyytes and bovine cerebral capillary endothelial cells as in vitro model systems. These widely studied cell cultures will provide accessibility for the kinetic analysis and characterization of membrane transporters, and for the quantitative analysis of cellular toxicity. The ultimate objective of the proposed research is a detailed understanding of the effects of mercury on the selective permeability and transport properties of the blood-brain barrier and its cellular components, which would serve as a basis for new therapeutic interventions aimed at compensating or reversing these effects of mercury intoxication, or aimed at manipulating rates of mercury entry into or egress from the brain. In pursuit of this objective, the Immediate goal of the research is to elucidate the functional properties and selective toxicity of the carriers that mediate blood-brain barrier transport of amino acids. This research project has demonstrated the high-affinity transport of essential amino acids In astrocytes and Its interaction with the glutamine cycle. Such Interactions are believed underlie the functional regulation by astrocytes of amino acid transport In cerebrovascular endothelium. Therefore, the finding that submicromolar concentrations of mercuric mercury suppress glutamine formation in astrocytes has direct consequences for the entry of essential amino acids to the brain. Coordinated studies of astrocytes and endothelial cells in isolation will allow a quantitative analysis of the comparative toxicology of amino acid carriers. Specifically, the proposed research will explore the selective impairment by mercuric chloride and methylmercury(II) chloride of characterized transport systems for anionic, neutral and cationic amino acids in endothelial cells and astrocytes. In the event of anomalies of transport in primary cerebrovascular cell cultures, alternative systems of bovine retinal or adrenal capillary endothelial cells will be available for comparative investigation. Impairment of transport will be correlated with cell content of mercury. The role of serum constituents in modifying fluxes of mercury in endothelial cells and astrocytes will be explored. Radioactive tracers will be used to measure transport of amino acids, and movement of mercury. High-performance liquid chromatog

27

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28
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AUTHORS:
BROOKES N

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ Mercury, including its organic compounds, is a pervasive environmental and occupational neurotoxicant with multiple cellular targets of action. In addition to direct toxic effects on neurons, neurotoxicity results secondarily following impairment of other cell types that control the neuronal microenvironment, notably glia and the vascular endothelial cell layer that constitutes the blood-brain barrier. Astroglia and vascular endothelial cells exhibit mutual trophisms in the expression of differentiated blood-brain barrier properties. Many of these properties can be reproduced in vitro in cell culture. It is proposed to use primary cultures of mouse cerebral astrcyytes and bovine cerebral capillary endothelial cells as in vitro model systems. These widely studied cell cultures will provide accessibility for the kinetic analysis and characterization of membrane transporters, and for the quantitative analysis of cellular toxicity. The ultimate objective of the proposed research is a detailed understanding of the effects of mercury on the selective permeability and transport properties of the blood-brain barrier and its cellular components, which would serve as a basis for new therapeutic interventions aimed at compensating or reversing these effects of mercury intoxication, or aimed at manipulating rates of mercury entry into or egress from the brain. In pursuit of this objective, the Immediate goal of the research is to elucidate the functional properties and selective toxicity of the carriers that mediate blood-brain barrier transport of amino acids. This research project has demonstrated the high-affinity transport of essential amino acids In astrocytes and Its interaction with the glutamine cycle. Such Interactions are believed underlie the functional regulation by astrocytes of amino acid transport In cerebrovascular endothelium. Therefore, the finding that submicromolar concentrations of mercuric mercury suppress glutamine formation in astrocytes has direct consequences for the entry of essential amino acids to the brain. Coordinated studies of astrocytes and endothelial cells in isolation will allow a quantitative analysis of the comparative toxicology of amino acid carriers. Specifically, the proposed research will explore the selective impairment by mercuric chloride and methylmercury(II) chloride of characterized transport systems for anionic, neutral and cationic amino acids in endothelial cells and astrocytes. In the event of anomalies of transport in primary cerebrovascular cell cultures, alternative systems of bovine retinal or adrenal capillary endothelial cells will be available for comparative investigation. Impairment of transport will be correlated with cell content of mercury. The role of serum constituents in modifying fluxes of mercury in endothelial cells and astrocytes will be explored. Radioactive tracers will be used to measure transport of amino acids, and movement of mercury. High-performance liquid chromatog

29
TITLE:
Speciation of Mercury in the Primate Blood and Brain following Long-Term Exposure to Methyl Mercury

AUTHORS:
Vahter M
Mottet NK
Friberg L
Lind B
Shen DD
Burbacher T

SOURCE:
Toxicology and Applied Pharmacology, Vol. 124, No. 2, pages 221-229, 43 references, 1994

ABSTRACT:
Accumulation, distribution, and form of mercury (7439976) (Hg) was measured in the brains of female Macaca-fascicularis monkeys following chronic exposure to methyl-mercury (22967926) (MeHg) over a period of 6 to 18 months. Total Hg (tHg) blood levels reached a maximum of 1.1 microgram/gram (microg/g) after 4 months exposure to a daily dose of 50 micrograms MeHg/kilogram. The half time accumulation of tHg in the blood was approximately 23 days while elimination half time of tHg blood levels was 26 days following cessation of exposure. Inorganic Hg (iHg), formed from the demethylation of MeHg in-vivo, accumulated similar to tHg levels and subsequently leveled off at 0.08microg/g after 4 months exposure, representing 7% of tHg in blood. Brain site and concentrations of MeHg and iHg were also noted and revealed that occipital pole and thalamus concentrations of MeHg were almost identical throughout the study. iHg concentrations were 1.5, 2.0, 2.5 and 2.8 times higher in the thalamus than at the occipital pole at 6, 12, and 18 months exposure, and 12 months exposure plus 6 months post MeHg exposure, respectively. Clearance of MeHg from the brain was rapid with a 35 day half time, while the concentration of iHg decreased very slowly, with a clearance half time on the order of years. Average tHg concentrations in the two brain sites indicated that 0.7%, 0.5% and 0.4% of the total dose of MeHg was present in the brain following 6, 12, and 18 months of exposure, respectively. For comparison, administration of 200microg/kg HgCl2 (7487947), an inorganic source of Hg, resulted in a steady state Hg blood level of 0.14microg/g after only 1 week and lower uptake of iHg by the brain despite higher blood levels of iHg. The authors conclude that the higher concentrations of iHg observed in MeHg treated monkeys is probably due to demethylation of MeHg in the brain.

30

TITLE:
Methylmercury Induced Alterations in the Nerve Growth Factor Level in the Developing Brain

AUTHORS:
Larkfors L
Oskarsson A
Sundberg J
Ebendal T

SOURCE:
Brain Research: Developmental Brain Research, Vol. 62, No. 2, pages 287-291, 44 references, 1991

ABSTRACT:
The effects of methylmercury on the concentration of nerve growth factor (NGF) in the developing rat brain were investigated. Female Sprague-Dawley-rats were administered methylmercury at 3.9mg/kg as mercury (7439976) in their diet starting 14 weeks before mating and continuing through mating, gestation, delivery, and lactation. After weaning on postnatal day 25 (PND25) the offspring were maintained on the same diet until postnatal day 50 (PND50). Selected offspring were killed on PND25 or PND50 and weighed. Selected dams were killed on PND25 and their brains were removed and assayed for NGF. The concentration of NGF in the hippocampus of the offspring was significantly increased by methylmercury on PND25 and PND50, the increases averaging 50%. Septal NGF concentrations were decreased by 23 to 30% at these times, a significant decrease. Methylmercury did not significantly affect NGF concentrations in the cerebral cortex. Body and brain weights were slightly, significantly increased in methylmercury exposed offspring sampled on PND25. Brain weight was slightly increased in methylmercury treated offspring examined on PND50. Methylmercury caused significant increases in blood and brain mercury concentrations at both time points. The increases in blood mercury were larger than in brain mercury concentration. NGF concentrations in the brains of dams examined on PND25 were not significantly affected by methylmercury. The authors conclude that methylmercury increases the NGF concentration in the hippocampus and decreases NGF concentration in the septum of the developing brain.

31
TITLE:
Mercury Distribution in Cortical Areas and Fiber Systems of the Neonatal and Maternal Adult Cerebrum after Exposure of Pregnant Squirrel Monkeys to Mercury Vapor

AUTHORS:
Warfvinge K
Hua J

Logdberg B

SOURCE:
Environmental Research, Vol. 67, No. 2, pages 196-208, 28 references, 1994

ABSTRACT:
The distribution of mercury (7439976) (Hg) in the neonatal and maternal brain following prenatal Hg vapor exposure was studied in monkeys. Seven timed pregnant squirrel-monkeys were exposed to 0 or 0.5mg/m3 Hg vapor 7 hours/ day or 1mg/m3 Hg vapor 4 or 7 hours/day, 5 days/week during gestation. The total days of exposure ranged from 20 to 84. Five offspring and three dams were killed after delivery. The Hg contents of the cerebral occipital lobes were determined by cold vapor atomic absorption spectrometry. Coronal brain slices were prepared and the distribution of Hg in the precentral and postcentral gyri, visual cortex, hippocampal formation, cortex piriformis, and amygdaloid complex was determined by an autometallographic technique. The distribution of Hg in the claustrum and fiber systems of the corpus callosum, capsula externam capsula extrema, and capsula interna was mapped. Maternal brain Hg concentrations ranged from 0.80 to 2.58 micrograms per gram (microg/g). Offspring brain Hg concentrations varied from 0.20 to 0.70microg/g. In maternal brains, pyramidal cells of layer-III and layer-V in the precentral and postcentral gyri and the visual cortex contained the largest amounts of visualizable Hg. The deeper the pyramidal cells in the layers the more Hg they contained; giant pyramidal cells of the motor cortex of the precentral gyrus contained the most Hg. In neonatal brains, the laminated distribution of Hg seen in maternal brains was absent, except in the visual cortex where the amounts of Hg in layers II, IV, and VI were low. In both maternal and neonatal brains, no Hg was found in the stratum granulosa of the dentate gyrus. The amygdaloid complex almost always contained visualizable Hg. Hg was found in the fiber systems of both maternal and neonatal brains, the concentrations being larger in neonatal brains. The authors conclude that mercury detected in neonatal brains confirms earlier studies which found that mercury vapor can cross the placenta. The results of these studies and similar studies conducted previously in rats were reviewed.

32
TITLE:
DEVELOPMENTAL NEUROTOXICITY OF METALLIC MERCURY

AUTHORS:
WEISS B

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ DESCRIPTION: (Adapted from the Investigator's Abstract) Metallic mercury, a neurotoxicant usually viewed as an occupational hazard, is a more general environmental hazard as well. Although we know a great deal about its effects in adults, our knowledge of its impact on the developing brain is fragmentary. This information gap is disquieting. (1) Many women in the work force are exposed to mercury vapor. (2) Many, perhaps most, women have dental amalgam fillings. These emit mercury vapor. Maternal tissue and fetal levels are correlated with the number of fillings. (3) Mercury is a more common contaminant of indoor environments than is generally recognized. Because of its physical properties it can lurk undetected and continue to evaporate. (4) Young children are considerably more vulnerable to mercury toxicity than adults; the syndrome of Pink Disease is a childhood affliction. (5) Organic mercury compounds are potent disrupters of brain development; some authorities believe that its conversion to the inorganic form in brain cells is the toxic mechanism responsible. (6) The experimental literature devoted to neurobehavioral effects consists of a handful of studies. To enhance our ability to evaluate the risks of metallic mercury to the developing brain, we intend to expose both pregnant rats and neonates to mercury vapor. Pregnant rats will be exposed to air, 30 ug/cubic meter, 100 ug/cubic meter, the OSHA permissible level, and 300 ug/cubic meter. Neonatal rats will be exposed to air, 10, 30, and 100 ug/cubic meter. Exposure will last two hours. The different levels are based on reports indicating widely different sensitivities between prenatal and neonatal exposures. Dam and pup blood levels will be monitored, and tissue assays, especially of brain, will be conducted at selected times. To determine the functional consequences of developmental exposure, three behavioral endpoints will be assayed: (1) The acoustic startle response, which will provide measures of habituation, sensory dysfunction, and the total neuromuscular response pattern to sound. (2) Spontaneous locomotor activity in the rats, a common index of neurotoxicity. (3) Acquisition of schedule-controlled operant behavior. Histochemical techniques will be deployed to map localization of brain mercury deposits.

33

TITLE:

DEVELOPMENTAL NEUROTOXICITY OF METALLIC MERCURY

AUTHORS:

WEISS B

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

DESCRIPTION: (Adapted from the Investigator's Abstract) Metallic mercury, a neurotoxicant usually viewed as an occupational hazard, is a more general environmental hazard as well. Although we know a great deal about

its effects in adults, our knowledge of its impact on the developing brain is fragmentary. This information gap is disquieting. (1) Many women in the work force are exposed to mercury vapor. (2) Many, perhaps most, women have dental amalgam fillings. These emit mercury vapor. Maternal tissue and fetal levels are correlated with the number of fillings. (3) Mercury is a more common contaminant of indoor environments than is generally recognized. Because of its physical properties it can lurk undetected and continue to evaporate. (4) Young children are considerably more vulnerable to mercury toxicity than adults; the syndrome of Pink Disease is a childhood affliction. (5) Organic mercury compounds are potent disrupters of brain development; some authorities believe that its conversion to the inorganic form in brain cells is the toxic mechanism responsible. (6) The experimental literature devoted to neurobehavioral effects consists of a handful of studies. To enhance our ability to evaluate the risks of metallic mercury to the developing brain, we intend to expose both pregnant rats and neonates to mercury vapor. Pregnant rats will be exposed to air, 30 ug/cubic meter, 100 ug/cubic meter, the OSHA permissible level, and 300 ug/cubic meter. Neonatal rats will be exposed to air, 10, 30, and 100 ug/cubic meter. Exposure will last two hours. The different levels are based on reports indicating widely different sensitivities between prenatal and neonatal exposures. Dam and pup blood levels will be monitored, and tissue assays, especially of brain, will be conducted at selected times. To determine the functional consequences of developmental exposure, three behavioral endpoints will be assayed: (1) The acoustic startle response, which will provide measures of habituation, sensory dysfunction, and the total neuromuscular response pattern to sound. (2) Spontaneous locomotor activity in the rats, a common index of neurotoxicity. (3) Acquisition of schedule-controlled operant behavior. Histochemical techniques will be deployed to map localization of brain mercury deposits.

34

TITLE:

The Effect of Various Dietary Fibres on Tissue Concentration and Chemical Form of Mercury after Methylmercury Exposure in Mice

AUTHORS:

Rowland IR
Mallett AK
Flynn J
Hargreaves RJ

SOURCE:

Archives of Toxicology, Vol. 59, No. 2, pages 94-98, 28 references, 19861986

ABSTRACT:

The effects of different forms of fiber such as cellulose (9004346),

pectin (9000695), wheat bran on the body burden, tissue concentration, and chemical form of mercury (7439976) were studied after exposure of mice to methylmercury (22967926). Three week old male BALB/c-mice were fed either a control purified diet or the same diet supplemented with cellulose or pectin (50 grams/kilogram (g/kg)) or wheat bran (50, 150 or 300g/kg) for 3 months and throughout the period of mercury exposure. Methylmercuric-chloride (115093) was radiolabeled and mercury retention was studied by assaying changes in radioactive mercury body burden approximately twice weekly for 4 weeks. The mercury concentration in kidneys, liver, and brain was corrected for the contribution of radioactivity in the residual blood in the tissues. Dietary pectin had no significant effect on mercury concentrations in tissues or gut. Bran, especially at the 30 percent level, generally decreased the mercury concentration particularly in the blood, small intestine, and highly significantly, in the brain where feeding of 30 percent bran was associated with a decrease of 24 percent in mercury concentration. Mercuric mercury concentrations in liver and kidneys of animals fed fiber were higher than in mice fed the fiber free control diet. The concentration of mercuric mercury in the large intestine of the 15 and 30 percent bran fed mice was significantly greater than that in control animals. The percentage of mercury present in the mercuric form in the brains of control animals and those fed 5 or 15 percent bran diets was similar, but mice fed 30 percent bran had significantly higher proportions of inorganic mercury in the brain. The authors conclude that retention of mercury by mice after a single oral dose of methylmercuric-chloride can be modified by diet. The toxicity of methylmercury, which is largely directed against the central nervous system, could be reduced by dietary wheat bran.

35

TITLE:

Foetal and Maternal Distribution of Inhaled Mercury Vapour in Pregnant Mice: Influence of Selenite and Dithiocarbamates

AUTHORS:

Danielsson BRG
Khayat A
Dencker L

SOURCE:

Pharmacology and Toxicology, Vol. 67, No. 3, pages 222-226, 25 references, 1990

ABSTRACT:

The distribution of mercury (7439976) in pregnant C57BL-mice was studied following exposure to selenite, thiram (137268), disulfiram (97778), or diethyldithiocarbamate following inhalation of mercury. The uptake of mercury in maternal brain and fetuses was several times higher after

mercury inhalation than after intravenous injection at corresponding dose levels. Pretreatment with selenite decreased the uptake of mercury in the whole fetus, placenta, and fetal liver, which was also true after mercury inhalation. Simultaneously, very high concentrations of mercury were noted in the lung and in other maternal organs. The decreased fetal and placental concentrations of mercury following inhalation appeared to be a result of an accumulation of mercury in material organs, making less mercury available for transfer to the fetus, rather than being due to an interaction in serum, as was the case with injected ionic mercury. No significant changes in mercury concentration in fetal tissues were noted after pretreatment with dithiocarbamates followed by mercury inhalation. A marked increase in mercury concentration after dithiocarbamate (148185) treatment followed by injection of ionic mercury was noted in most maternal organs, particularly in body fat and brain, while the concentrations decreased in plasma and fetal tissues. The authors suggest that firmer binding of mercury occurs after mercury inhalation, when oxidation of metallic mercury vapor to ionic mercury occurs intracellularly, than after ionic mercury injection.

36

TITLE:

Sex and Age Differences in Mercury Distribution and Excretion in Methylmercury-Administered Mice

AUTHORS:

Hirayama K
Yasutake A

SOURCE:

Journal of Toxicology and Environmental Health, Vol. 18, No. 1, pages 49-60, 18 references, 19861986

ABSTRACT:

Sex differences in the distribution and excretion of mercury (7439976) were evaluated in different strains and at various ages in mice. Sexually mature male and female C57BL/6N-mice and BALB/cA-mice were intravenously administered 5mg/kg methylmercury-chloride (115093) (MMC). Total mercury levels in the blood, brain, liver, kidneys, and urine and feces samples were determined. Urinary mercury levels were higher among males than females by ten fold in C57BL/6N-mice and by two fold in BALB/cA-mice. No significant differences were found in fecal mercury levels. Mercury levels in the blood, brain, and liver were higher in females of both strains, while renal mercury levels were higher in males. Changes in mercury distribution and elimination with time were studied in C57BL/6N-mice sacrificed 1, 3, or 5 days after a single oral administration of 5mg/kg MMC. Urinary mercury levels were higher in males than females 1, 3, and 5 days after MMC administration. Fecal mercury levels were not significantly different between the sexes after 1 day, but

were slightly higher in females after 3 and 5 days. Mercury levels in the brain increased for up to 3 days in both sexes, and then decreased in males only after 5 days. Blood and liver mercury levels decreased with time in both sexes, but were always higher in females than males. Mercury levels in the kidneys were higher in males than females after 1 day, but were approximately equal in males and females after 3 days. The effect of age on sex differences was investigated in C57BL/6N-mice, aged 2, 4, 7, 10, or 45 weeks, administered single oral doses of 5mg/kg MMC. No significant sex differences in mercury distribution and excretion were observed in 2 week old mice. Males, aged 4 to 45 weeks, had higher urinary mercury levels than females. The authors conclude that there are significant sex differences in urinary excretion of mercury in sexually mature mice, which may be related to sex hormones, especially androgens.

37

TITLE:

Summary of the Seychelles Child Development Study on the Relationship of Fetal Methylmercury Exposure to Neurodevelopment

AUTHORS:

Myers GJ
Davidson PW
Cox C
Shamlaye CF
Tanner MA
Marsh DO
Cernichiari E
Lapham LW
Berlin M
Clarkson TW

SOURCE:

Neurotoxicology, Vol. 16, No. 4, pages 711-716, 10 references, 1995

ABSTRACT:

The results of the Seychelles Child Development Study (SCDS) examining the relationship between low level dietary mercury (7439976) exposure and developmental neurotoxicology in children in the Republic of Seychelles who had fetal exposure to methylmercury as a result of a maternal diet high in oceanic fish were reported. An initial pilot study conducted in 804 infants suggested a possible association between fetal mercury exposure and development. Maternal hair mercury levels were used as indices of fetal mercury exposure. A pilot follow up study of 217 children at 66 months of age also suggested the presence of neurologic developmental defects, but the validity of these results was questioned. Based on these pilot studies, a prospective, longitudinal study was conducted on 779 children. Fetal mercury exposure was not found to be associated with neurodevelopment at 6 1/2, 19, or 29 months of age;

however, an inverse relationship between maternal mercury level and activity was noted in boys 20 months of age. The results of a related study examining the histology and mercury levels of 32 brains obtained at autopsy from Seychelles infants did not demonstrate clear evidence of abnormalities. Mercury levels up to 300 parts per billion were identified in brain samples and these correlated well between brain regions. In addition, maternal hair mercury levels correlated well with infant brain mercury levels. The authors conclude that the adverse neurodevelopmental effects identified in the pilot study were dependent on methods of data analysis, and that no definitive effects of maternal mercury exposure on neurodevelopment could be identified through 29 months in the main study.

38

TITLE:

LONG-TERM ORGANIC MERCURY NEUROTOXICITY

AUTHORS:

MOTTET NK

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ The aim of this experiment is to determine the species of mercury compound(s) that are the proximate toxic form by comparing the levels of inorganic (Hg) and methylmercury (MeHg) with morphometric changes. During the present grant period groups of primates were given 50 microgram Hg/kg/day "clinically subtoxic" levels of MeHg orally for 6, 12, 18 months and one group was given HgCl-2 for 3 months. MeHg freely passed through the blood-brain-barrier whereas in an HgCl-2 experiment it did not. Brain and tissue sampling has been completed and specimen analysis is underway. During the proposed grant period we plan to complete the speciation of mercury in 8 brain sites and do morphometry on contralateral paired samples. To date the mercury speciation studies done at the Karolinska Institute in Sweden have revealed that after 6 months exposure to the MeHg the brain Hg levels at 4 sites ranged from 3.0 to 4.0 micrograms/g and at 12 months the level was 4.2-5.0. The % inorganic Hg in the 4 brain sites was on average about 14% both at 6 and 12 months. We have the opportunity to use these valuable and unique samples already collected for mercury speciation in the pituitary, blood, kidney, muscle, fat and thyroid and other visceral tissues. This proposal couples the mercury analytical expertise and mercury metabolism knowledge of the Karolinska Institute group with the primate and morphometry expertise of the University of Washington. Morphometric measurements are also beginning. Extensive efforts at method development have established new and efficient procedures. We have found striking structural changes in the endothelial cells of the brain capillaries and down regulation of neuron organelles throughout. Complete analysis of the data is anticipated by the end of

the proposed grant period.

39
TITLE:
Altered levels of apoptotic and neurotrophic factor mRNA in developing rat brain following exposure to mercury vapor or lead acetate.

AUTHORS:
Chao SL
Haines WT
Barone S Jr
Tilson HA
Beliles RP
Morgan DL
Harry GJ

SOURCE:
Toxicologist 2000 Mar;54(1):71

ABSTRACT:
Both apoptotic and neurotrophic factors play essential roles in the development of the brain and formation of the neural networks. Due to evidence suggesting apoptosis as a mode of action following developmental exposure to mercury and lead, we examined the temporal and regional profiles of mRNA levels for various pro- and anti- apoptotic factors following exposure to either mercury vapor or lead. The mRNA levels for bax, caspase 3, caspase 2, bcl-x, and BDNF (brain derived neurotrophic factor) were examined in the postnatal rat brain following inhalation (nose-only) exposure to mercury vapor (2 mg/m3) at gestational days 6-15 or postnatal (PND 1-21) exposure to lead acetate (0.2%). Our results indicate an elevation in mRNA levels of both apoptotic factors and BDNF that were metal and brain region specific. Following exposure to mercury vapor, mRNA levels for the above factors increased in the cerebellum at PND 21 while levels in the frontal lobe remained unchanged. Following lead acetate exposure, the hippocampus was most affected with significant elevations in caspase 3 and bax observed at PND 12 and post-weaning while bcl-x and BDNF were increased at PND 12. In the cerebellum, mRNA levels for caspase 2, 3, and bax were elevated at PND 9. In the cortex, bcl-x and BDNF mRNA levels were decreased at PND 15. These data indicate both time and region specific responses of the developing nervous system following low level exposure to mercury vapor or lead acetate.

40
TITLE:
Mercury Distribution In Mouse Brain After I.V. Administration Of Bis(methylmercuric) Selenide

AUTHORS:

Naganuma A
Nakajima E
Shigehara E
Tanaka M
Imura N

SOURCE:
Toxicology Letters, Vol. 15, No. 2-3, pages 175-179, 11 references, 19831983

ABSTRACT:
Distribution of mercury (7439976) in the brain after methylmercury (22967926) (MM), MM with selenite (14124675), or bis(methylmercuric)-selenide (4305377) (BS) administration was investigated in mice. Mercury-203 (Hg-203) labeled BS was synthesized from methylmercuric-chloride (115093) (MMC), sodium-selenite (10102188) and reduced glutathione (GSH). The compounds were dissolved in saline containing 15 percent ethanol before administration. Male ICR-mice were injected with Hg-203 labeled MMC alone, Hg-203 labeled MMC with sodium-selenite simultaneously, or with Hg-203 labeled BS into tail vein. Ten minutes and 1 hour and 24 hours after administration, mice were anesthetized and killed by submersion in N-hexane dry ice mixture at -70 degrees-C. Sections of whole body and brain were exposed to X-ray film for 10 to 50 days. Radioactivity in the brain of mice that received Hg-203 labeled MMC and sodium-selenite simultaneously or Hg-203 labeled BS was higher than that of mice that received Hg-203 labeled MMC alone. Significant difference in the distribution of radioactivity was not observed in other organs. Mercury accumulation in brain 10 minutes after Hg-203 labeled MMC with sodium-selenite or Hg-203 labeled BS was the same as that observed 24 hours after administration of Hg-203 labeled MMC. Brain mercury distribution pattern did not change even after 24 hours in the former two groups. The authors conclude that since selenite is known to protect against methylmercury toxicity, increase in mercury compounds in the brain from coadministration of selenite plays a role in further modification of methylmercury toxicity by selenite.

41
TITLE:
LONG-TERM ORGANIC MERCURY NEUROTOXICITY

AUTHORS:
MOTTET NK

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ The aim of this experiment is to determine the species of mercury

compound(s) that are the proximate toxic form by comparing the levels of inorganic (Hg) and methylmercury (MeHg) with morphometric changes. During the present grant period groups of primates were given 50 microgram Hg/kg/day "clinically subtoxic" levels of MeHg orally for 6, 12, 18 months and one group was given HgCl-2 for 3 months. MeHg freely passed through the blood-brain-barrier whereas in an HgCl-2 experiment it did not. Brain and tissue sampling has been completed and specimen analysis is underway. During the proposed grant period we plan to complete the speciation of mercury in 8 brain sites and do morphometry on contralateral paired samples. To date the mercury speciation studies done at the Karolinska Institute in Sweden have revealed that after 6 months exposure to the MeHg the brain Hg levels at 4 sites ranged from 3.0 to 4.0 micrograms/g and at 12 months the level was 4.2-5.0. The % inorganic Hg in the 4 brain sites was on average about 14% both at 6 and 12 months. We have the opportunity to use these valuable and unique samples already collected for mercury speciation in the pituitary, blood, kidney, muscle, fat and thyroid and other visceral tissues. This proposal couples the mercury analytical expertise and mercury metabolism knowledge of the Karolinska Institute group with the primate and morphometry expertise of the University of Washington. Morphometric measurements are also beginning. Extensive efforts at method development have established new and efficient procedures. We have found striking structural changes in the endothelial cells of the brain capillaries and down regulation of neuron organelles throughout. Complete analysis of the data is anticipated by the end of the proposed grant period.

42

TITLE:

Proton Magnetic Resonance Imaging and Phosphorus-31 NMR Studies on the Rat Brain Intoxicated with Methyl Mercury

AUTHORS:

Mitsumori F

Nakano A

SOURCE:

Environmental Research, Vol. 62, No. 1, pages 81-88, 33 references, 1993

ABSTRACT:

Male Wistar-rats were orally administered methyl-mercury (22967926) daily for 12 days at 5mg/kg mercury (7439976). From 14 to 16 days after the start of the administrations, nuclear magnetic resonance (NMR) measurements were performed. The mercury content of the brain was high at 195 micromoles/kilogram (micromol/kg) wet weight, compared to a value of 0.039micromol/kg in the control brain. Proton magnetic resonance imaging (MRI) did not show any changes in the image of cerebrum or cerebellum of the poisoned rat brain. Proton MRI found no degenerative changes in the form of pyknosis and karyorrexhis in the granular layer of the cerebellum.

The authors suggest that the damages may be localized to minute areas smaller than the spatial resolution of the present MRI measurement. The NMR method provides a means to investigate methyl-mercury intoxication in the brain from both anatomical and metabolic aspects. Even though MRI did not distinguish the morphological damage, NMR spectra showed a decrease in phosphocreatine with no change in ATP and intracellular pH in the poisoned brain. The findings demonstrate the damage in energetics in the methyl-mercury poisoned brain.

43

TITLE:

Altered levels of nerve growth factor and its low-affinity p75 receptor in the developing brain following by prenatal exposure to mercury vapour.

AUTHORS:

SÓoderstrÓom S
Ebendal T

SOURCE:

Abstr Soc Neurosci 1994;20(Pt 2):1653

ABSTRACT:

Pregnant rats were exposed to low levels of mercury vapour. The levels of mercury (5-10 ng/g wet weight) found postnatally in the brains of their offspring are comparable with those found in human brains after average mercury exposure. The brains of the pups show an approximately 50% increase of NGF protein in the hippocampus and the cortex at postnatal day 21 with a concomitant decrease to 55% of normal levels in the medial septal area with NGF responsive cholinergic neurons. The levels of mRNA for NGF, p75 LNGFR, p140 trk and ChAT were examined by in situ hybridization histochemistry. There were no significant changes of NGF mRNA measured at P22 in the dentate gyrus following the prenatal mercury vapour exposure. The mRNA level of the NGF high affinity receptor p140 trk was slightly increased in the diagonal band and the medial septum at P22, while the expression of mRNA for the low affinity receptor p75 was significantly reduced to approximately 30% of normal in both the medial septal area and in the diagonal band nucleus. ChAT mRNA was slightly reduced in the diagonal band and the medial septum and was significantly reduced in the striatum. It is suggested that the retrograde transport of NGF from the target to the basal forebrain was interrupted due to the accumulated mercury. Moreover, NGF produced by the fibroblast cell line 3T3 in the presence of organic mercury (MeHgCl2) was found to be doubled when methyl mercury was added at concentrations of 0.1 uM-0.5 uM.

44

TITLE:

Prenatal Coexposure to Metallic Mercury Vapour and Methylmercury Produce Interactive Behavioural Changes in Adult Rats

AUTHORS:
Fredriksson A
Dencker L
Archer T
Danielsson BRG

SOURCE:
Neurotoxicology and Teratology, Vol. 18, No. 2, pages 129-134, 30 references, 1996

ABSTRACT:
The developmental neurotoxicity of combined prenatal exposure to metallic mercury (7439976) and organic mercury was studied in rats. Pregnant Sprague-Dawley-rats were gavaged with 0 or 2mg/kg methylmercury (593748) from days six to nine of gestation or exposed to 0 or 1.8mg/m3 mercury vapor from days 14 to 19 of gestation alone or in combination. The dams were allowed to deliver. The litters were culled to four males. The brains were removed from one pup from each litter, and analyzed for mercury. Physical development up to weaning was evaluated by monitoring body weight gain, pinna unfolding, tooth eruption, and eye opening. Functional behavioral testing up to weaning was performed by evaluating the surface righting reflex and the negative geotaxis orienting responses. Adult behavioral testing was performed when the offspring were 4 to 6 months of age and included evaluations of spontaneous motor activity and spatial navigation learning in a circular swim maze and in a radial arm maze. No treatment related changes were seen in physical or functional development up to weaning. Offspring from dams exposed to metallic mercury showed hyperactivity in locomotion, rearing, and total activity during the spontaneous motor activity evaluation. These effects were potentiated by exposure to methylmercury. Rats exposed to mercury vapor alone or mercury vapor plus methylmercury demonstrated significant performance decrements in the swim maze and the radial arm maze compared to rats exposed to methylmercury alone or the controls. Methylmercury alone did not significantly affect any of the tested behaviors. Mercury accumulated in the brain following all exposures. The highest mercury accumulation was seen in rats exposed to mercury vapor plus methylmercury, followed by mercury vapor, and methylmercury, 12.2, 4.9, and 4.3 nanograms per gram (ng/g), respectively. The average brain concentration in control rats was 1ng/g. The authors conclude that prenatal exposure to mercury vapor causes alterations in spontaneous and learned behaviors. Coexposure to methylmercury, which by itself had no effect, potentiates the effect of mercury vapor.

45
TITLE:
Effects of mercury vapor inhalation on (32P)8N3GTP photolabeling of beta-tubulin in brains of fetal and aged rats.

AUTHORS:
Pendergrass JC
Haley BE
Vimy MJ
Lorscheider FL

SOURCE:
Toxicologist 1998 Mar;42(1-S):195-6

ABSTRACT:
In young (170-250 g) adult male rats (32P)8N3GTP photolabeling on the exchangeable E-site of brain beta-tubulin decreased 41% following inhalation exposure to elemental mercury vapor (Hg0) at 250 ug Hg/m3 for 4 h/d x 14 d (Neurotoxicology 18:315-324, 1997). Soluble tubulin dimers must exchange a bound GDP for GTP in the normal polymerization of brain tubulin into microtubules (MTs). MTs are the main component of neuronal cytoskeleton and disruption of the normal MT polymerization/-depolymerization cycle by neurotoxins (eg. Hg) can result in neuronal death. In the present study, brain cortex homogenates of 11 fetuses exposed in utero from gestational days 7-21 to Hg0 (maternal dose of 250 ug Hg/m3; 4 h/d x 14 d) showed a 13.3% decrease in (32P)8N3GTP-beta-tubulin interactions relative to 13 age-matched controls. (32P)8N3GTP photolabeling of fetal brain beta-tubulin averaged 2681 +/- 91 net cts. +/- SEM in the controls compared to 2324 +/- 55 cts. in the Hg0-exposed group, a significant decrease (p less than 0.01). Fetal brain Hg concentration averaged 76 +/- 4.2 ng Hg/g wet wt. in the Hg0-exposed group vs. 4.1 +/- 0.2 ng in controls, a 19-fold increase (p less than 0.01). In contrast, brains of 6 elderly male rats (18-22 months of age, 858 +/- 30 g) exposed to Hg0 (250 ug Hg/m3; 4 h/d x 14 d) showed no decrease in (32P)8N3GTP-beta-tubulin interactions relative to 6 age-matched controls. Photolabeling of beta-tubulin in brain averaged 6838 +/- 124 net cts. in controls compared to 6835 +/- 203 cts. in the Hg0-exposed group (p greater than 0.05). Despite no decrease in beta-tubulin photolabeling, corresponding brain Hg concentrations in the Hg0-exposed aged rats were 86 fold higher than in controls, 1289 +/- 83 vs. 15 +/- 1.9 ng Hg/g wet wt., respectively (p less than 0.01). We conclude that Hg0 exposure impairs (32P)8N3GTP photolabeling of brain beta-tubulin in fetal rats as occurs in young adult rats. However, similar Hg0 exposure in elderly rats does not produce the same molecular lesion.

46
TITLE:
Teratology of heavy metals: mercury and other contaminants.

AUTHORS:
Inouye M

SOURCE:

Teratology 1989;40(6):652-3

ABSTRACT:

Modern industrialization has introduced harmful metals into our environment. Metal compounds used in pesticides, catalysts or energy end up as residues in food, water and air. Developing embryos and fetuses are generally considered to be more vulnerable to exotic toxicants than adults, and there has been a good deal of speculation that heavy metals can cause teratogenesis. In fact many metals and metalloids have been confirmed to have embryotoxicity in experimental animals, but only a few elements (e.g., mercury, lead, etc.) are known to be human teratogens. Liquid metallic mercury is hardly absorbed from the gastrointestinal tract. Inorganic mercury is also poorly absorbed, i.e. around 2% of ingested mercuric chloride is absorbed. However, inhaled mercury vapor is readily absorbed. Uptake of inorganic mercury by the fetus is very low. An experiment using mice revealed that a significant proportion of mercury is blocked in the yolk sack. Teratogenicity of mercuric chloride in rats and mice is considered to result not from direct action but from either the inhibition of the transport of essential metabolites, or maternal kidney dysfunction. Among the organic mercury compounds, the most accumulated knowledge pertains to methyl-mercury compounds. Ethylmercury has toxicological properties similar to those of methylmercury. Methylmercury is easily absorbed through the intestinal tract and skin, and by inhalation. Methylmercury is shown to cross the human placenta with infantile blood levels in excess of the mother's blood at the time of delivery. Accelerated accumulation of methylmercury in rat and mouse fetuses at the late pregnant stage suggests that the exposure of pregnant females to methylmercury at the late stage of gestation may lead to a greater risk of damage to the fetus. Pathological features of children's brains affected by prenatal methylmercury exposure are the outcome of disturbances in the development of the brain; microcephaly, dilated lateral ventricles, as well as derangement in the fundamental structuring of gray matter as the result of abnormal neuronal migration. Degeneration of already formed nerve cells is involved in some cases. Experiments with guinea pigs have demonstrated that developmental disturbances of the fetal brain, including abnormal neuronal migration, are induced when dams are exposed to methylmercury in early pregnancy; and when dams are exposed in later pregnancy, neurons of the cerebral cortex are involved in focal degeneration. Lead has been show to pass through the human placenta readily, and the concentration in the umbilical cord blood is 80 - 90% as high as that in the maternal blood. At the end of the last century it was recognized that women working in the lead industry are frequently sterile, or have high rates of spontaneous abortions and fetal and neonatal loss. Although nowadays women are no longer allowed to work under conditions where lead intoxication is apt to occur, decreased fertility has been reported in male workers occupationally exposed to lead. A large cohort study suggests that increased exposure to lead from the environment in the

prenatal and early postnatal periods results in deficit mental development. Teratogenicity of many metal compounds such as aluminum, cadmium, chromium, cobalt, indium, nickel, platinum, tellurium, thallium, ytterbium and zinc salts has been confirmed in experimental animals. Thallium and some metalloids (e.g., arsenic, selenium and lithium) appear to be teratogenic for humans.

47
TITLE:
Effect of Methyl Mercury Exposure on the Uptake of Radiolabeled Inorganic Mercury in the Brain of Rabbits

AUTHORS:
Dock L
Mottet K
Vahter M

SOURCE:
Pharmacology and Toxicology, Vol. 74, No. 3, pages 158-161, 17 references, 1994

ABSTRACT:
A study was conducted on the effects of mercury (7439976) on the blood brain barrier in rabbits. New-Zealand-White-rabbits were administered 1 micromole/kilogram (micromol/kg) methyl-mercury-chloride (115093) (MeHg) daily for 3 weeks, followed by a single injection of 0.22micromol/kg radiolabeled mercuric-chloride (7487947) (HgCl). In another experiment, rabbits were administered a single 37.5micromol/kg dose of MeHg intravenously. After 5 minutes or 24 hours, rabbits were administered a single intravenous dose of 0.22micromol/kg radiolabeled mercury-chloride. In the third experiment, rabbits were administered MeHg at 1-micromol/kg and radiolabeled mercury-chloride at 0.25micromol/kg. Urine and feces were collected. Rabbits were killed 24 hours after treatment, and the concentration of labeled mercury in blood and tissue samples was determined. No differences in the mercury concentration in the brain following administration of HgCl were seen between rabbits given subchronic treatment with MeHg or treatment with a single dose. Approximately 0.02% of the dose of HgCl administered was found within the brain of both MeHg pretreated and control rabbits. The authors conclude that MeHg does not appear to damage the blood brain barrier in rabbits.

48
TITLE:
Mercury study report to Congress. Health effects of mercury and mercury compounds.

AUTHORS:
Hassett-Sipple B

Swartout J
Mahaffey KR
Rice GE
Schoeny R

SOURCE:
NTIS Technical Report (NTIS/PB98-124779) (EPA/452/R-97/007) 1997 Dec;5:366 pp.

ABSTRACT:
Section 112(n)(1)(B) of the Clean Air Act (CAA), as amended in 1990, directs the U.S. Environmental Protection Agency (U.S. EPA) to submit to Congress a comprehensive study on atmospheric emissions of mercury. This document, which covers the human health effects of mercury and mercury compounds, is one volume of U.S. EPA's eight-volume Report in response to this directive. Mercury is a naturally occurring element that is found in air, water and soil. It exists in any of three valence states: Hg0 (elemental mercury), Hg2(2+) (mercurous mercury), or Hg2+ (mercuric mercury). Most of the population of the earth have some exposure to mercury as a result of normal daily activities. The general population may be exposed to mercury through inhalation of ambient air, consumption of contaminated food, water, or soil; and/or dermal exposure to substances containing mercury. In addition, some quantity of mercury is released from dental amalgam. The health effects literature contains many investigations of populations with potentially high exposure to mercury, including industrial workers, people living near point sources of mercury emissions, people who consume large amounts of fish, and dental professionals. There also are numerous studies of populations unintentionally exposed to high levels of mercury, such as the Minamata poisoning episode in Japan. Volume IV (An Assessment Exposure to Mercury in the United States) presents measured and predicted mercury exposure for various U.S. populations. The purpose of this volume, Volume V, is to summarize the available health effects information for mercury and mercury compounds and to present U.S. EPA's analysis for two critical pieces of the risk assessment paradigm described by the National Academy of Sciences in 1983. Specifically, this volume contains the hazard identification and dose-response assessments for three forms of mercury: elemental mercury, mercuric chloride (inorganic mercury), and methylmercury (organic mercury). In order to characterize risk for any populations, the evaluations presented in this volume must be combined with the assessment of exposure presented in Volume IV. Volume V is not intended to be an exhaustive survey of the voluminous health effects literature available for mercury. Rather, the purpose is to present a brief survey of the studies relevant for assessing potential human health effects and to present more detailed information on those studies which form the basis for U.S. EPA's hazard identification and dose-response assessments. The three forms of mercury which are emphasized in this volume were selected based on data indicating that these are the predominant forms of mercury to which humans are exposed. In

addition, examination of the published literature indicates that most health data are on these forms. It is acknowledged that certain populations can be exposed to many types of organic mercurials, such as antiseptics and pesticides. Volume V, however, deals with methylmercury except in cases where information on another organic is presented for illustrative purposes.

49
TITLE:
Localization of Mercury in CNS of the Rat. III. Oral Administration of Methylmercuric Chloride (CH3HgCl)

AUTHORS:
Moller-Madsen B

SOURCE:
Fundamental and Applied Toxicology, Vol. 16, No. 1, pages 172-187, 40 references, 1991

ABSTRACT:
An autometallographic technique was applied to sections of the brain and upper cervical spinal cord taken from male Wistar-rats treated orally with methylmercuric-chloride (115093) (CH3HgCl). The purposes of the study were to provide a detailed autometallographic mapping of mercury containing cells; to determine the period of treatment required until mercury (7439976) deposits in the brain were just detectable; and to determine the ultrastructural localization of mercury within the stained cells. CH3HgCl was administered orally at a dose of 20 milligrams/liter. Staining for mercury first appeared in specific nuclei in the brain stem 10 days after the start of treatment. After 4 weeks mercury was fairly evenly distributed within the central nervous system. In the cerebral cortex, staining commenced in piriform and entorhinal cortices, followed by staining in neurons of lamina-III in the isocortex and ultimately all layers were stained after 28 days of treatment. Mercury deposits in the cerebellar cortex were restricted to Purkinje cells, Golgi epithelial cells, and Golgi cells after 20 days of treatment while in the spinal cord the majority of mercury was located in the anterior horn motoneurons. Mercury staining was also noted in scattered ependymal cells and epithelial cells of the choroid plexus. The principal target cells were neurons followed by the glial and ependymal cells. Ultrastructurally the bulk of detectable mercury was localized in lysosomes.

50
TITLE:
Mercury Distribution in the Rat Brain after Mercury Vapor Exposure

AUTHORS:
Warfvinge K

Hua J
Berlin M

SOURCE:
Toxicology and Applied Pharmacology, Vol. 117, No. 1, pages 46-52, 24 references, 1992

ABSTRACT:
The effects of mercury (7439976) vapor exposure on the central nervous system were investigated in rats. Male and female Brown-Norwegian-rats were used in this study. Rats were exposed 7 days/week, 24 hours/day to a mercury concentration of about 1mg/m3. A second group was exposed for 3 days/week for 6 hours/day. Rats were killed after 5 weeks of exposure. In the high and low dose exposure groups, the total amounts of mercury absorped were calculated to be 264 and 35 micrograms/week and 100 grams body weight; mean blood mercury concentrations were 0.25 and 0.09 microgram/gram; and total concentrations in brain were 5.03 and 0.71 micrograms/gram tissue, respectively. Using a method based on chemographic principles, the mercury distribution in the brains of the rats was examined. Mercury was found in the ependyma lining the ventricles, in the plexus choroideus, and in the epithelium covering the surface of the brain. Mercury was noted in the neocortex, in the basal nuclei and in the cerebellar Purkinje cells. The pattern of distribution of mercury after administration of different mercury compounds was considered.

51
TITLE:
Mercury Uptake In Vivo By Normal And Acatalasemic Mice Exposed To Metallic Mercury Vapor (203Hg) And Injected With Metallic Mercury Chloride (203HgCl2)

AUTHORS:
Ogata M
Kenmotsu K
Hirota N
Meguro T
Aikoh H

SOURCE:
Archives of Environmental Health, Vol. 40, No. 3, pages 151-154, 13 references, 19851985

ABSTRACT:
Mercury (7439976) uptake in normal and acatalasemic mice was examined in-vivo. Mice were exposed to radiolabeled metallic mercury vapor for 1 hour at room temperature and then were sacrificed. Blood samples were collected and organs were removed. Mercury content was determined by

scintillation counting. An intraperitoneal injection of radiolabeled metallic mercury was given to a second group of mice. After 1 hour, the mice were sacrificed and processed. Mercury content was determined. A third group of mice was given an intraperitoneal injection of radiolabled mercuric-chloride (7487947). One hour after injection, the mice were processed as above. Mercury concentration in blood, lungs, and kidneys of acatalasemic mice given the metallic mercury injection or exposed to mercury vapor was lower than in normal mice. The concentration of mercury in the brain and liver of the acatalasemic mice was also higher. The blood/brain and blood/liver mercury concentration ratios in acatalasemic mice were significantly higher than in those of normal mice. There was no significant difference in mercury concentration or distribution between normal and acatalasemic mice given the mercuric-chloride injection. The authors conclude that elemental mercury passes through the blood/brain or blood/liver barrier more easily in acatalasemic mice than in normal mice.

52

TITLE:

Hereditary Analysis Of The Strain Difference Of Methylmercury Distribution In Mice

AUTHORS:

Doi R
Tagawa M
Tanaka H
Nakaya K

SOURCE:

Toxicology and Applied Pharmacology, Vol. 69, No. 3, pages 400-406, 30 references, 19831983

ABSTRACT:

Mercury concentration in blood and brain after methyl-mercury (MeHg) administration was studied in various mouse strains. C3HeN-mice and C57BL/6N-mice, their first generation cross (F1), and ICR-mice were intraperitoneally injected with 0.25 to 6.0 milligrams per kilogram (mg/kg) methylmercuric-chloride (115093). After 24 hours, animals were sacrificed, and mercury concentrations in blood and brain were determined. Using a 3.0mg/kg dose, similar experiments were run on C3H/HeN-mice and C57BL/6N-mice, F1 and second generation (F2) crosses, and a back cross, as well as on 14 inbred strains for which the alleles controlling hemoglobin structure were known. Blood and brain mercury increased with increasing MeHg dose. Blood concentrations were significantly higher in C3H/HeN-mice than in other strains at all doses, reaching about 2 times those of C57BL/6N-mice and ICR-mice after 6mg/kg. Brain concentrations were highest in C57BL/6N-mice, but the range in values was much smaller than for blood concentration. F1 crosses had values intermediate between the parent strains for both blood and brain mercury. Brain/blood ratios were

stable at 3mg/kg and higher doses, being about 0.35 in C3H/HeN-mice, 0.4 to 0.45 in the F1 cross and ICR-mice, and 0.7 in C57BL/6N-mice. F2 crosses and the back cross showed a wide distribution range of blood mercury concentrations, and phenotype segregation characteristic of these types of crosses was observed. Among inbred strains, blood mercury concentrations were about 1000 nanograms per gram (ng/g) for C57BL/6N-mice and other strains in which the hemoglobin beta polypeptide chains (Hbb) were controlled by the s-allele, and were about 2000ng/g for C3H/HeN-mice and other strains with the Hbb d-allele. Brain/blood ratios ranged mostly between 0.4 and 0.8 for Hbb s-allele strains and between 0.2 and 0.4 for Hbb d-allele and p-allele strains. The authors suggest that Hbb structure, particularly the number and position of molecular cysteinyl residue, is related to MeHg binding and blood mercury concentration.

53

TITLE:

Environmentally Induced Alterations In Neuron And Glia D

AUTHORS:

HARRY GJ

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

The susceptibility of the developing nervous system to environmental agents has been a major concern with regard to children's health issues. While current exposure levels to environmental agents does not represent an acute injury, disruption to the nervous system may be associated with either a structural alteration in the formation of the neural network and/or in nervous system functioning. It is the goal of this project to develop and validate test methods that will allow us to assess various types of chemical-induced perturbations of the brain during development. The formation and interactions between the various cell types in the brain are critically timed events.Such windows of vulnerability is assummed to be a major component in the differential susceptibility of the developing organism to environmental insult. This project examines chemical induced perturbations during development of the nevous as indicated by alterations in the spatio-temporal expression of mRNA for various developmentally regulated proteins associated with distinct processes of development, distribution of compounds to the nervous system, and the neurobehavioral outcome of such exposure. The specific projects under study include 1) distribution of mercury to the brain of young animals following the intramuscular injection of various mercuricals. 2) alterations in the neurobehavioral functioning following early exposure to the pro-inflammatory cytokine IL-6 as a model of maternal infection and premature delivery. 3) Alterations in neuronal processes in the brain following exposure to compounds that perturb homeostatic maintenance of

thyroid hormone during gestational and postnatal development. With regard to delivery of mercury to the brain following an intramuscular injection of either methyl mercury, ethyl mercury, thimerosal, as compared to an oral administration of methyl mercury demonstrated a distribution pattern distinct between the two routes of exposure suggesting a sequestration of the metal within the muscle resulting a minimal level within the brain. Neuroinflammation in the young mouse brain as generated by a direct delivery of hyper-IL6 to the cortical layer resulted in subtle alterations in neurobehavioral functioning characterized by a hyper-reactivity to environmental stimuli and a relatively inflexibility in learning and performance that continued in the adult animal. Alterations in thyroid hormone levels during gestation and lactation induced by either hexachlorobenzene or PCBs produced distinct patterns of disruption in cerebellar neurons as demonstrated by Golgi staining of neuronal processes. For PCBs this pattern of disruption was transient and may be linked to the period of active development. Early developmental exposure to inorganic lead is known to alter brain development. Based upon our previous studies examining specific neuronal and glia markers following low level lead exposure we initiated a study to examine in a more broad manner the developmental ontogeny of multiple nervous system specific genes using DNA array techniques. One specific finding of these studies was the shift in the developmental pattern for a specific chlorid plexus gene suggesting an early maturation of the chlorid plexus as a protective mechanism against a heavy metal exposure however, the consequences to such an early maturation is yet to be studied. For these studies we have used a number of methods to examine alterations in the developing nervous system following exposure to environmental agents including immunohistochemistry, molecular techniques to examine mRNA levels, as well as assessment of neurobehavioral functioning.

54

TITLE:

Mercury distribution in the mouse brain after mercury vapour exposure.

AUTHORS:

WARFVINGE K

SOURCE:

INTERNATIONAL JOURNAL OF EXPERIMENTAL PATHOLOGY; 76 (1). 1995. 29-35.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Female SJL mice were exposed to mercury vapour 5 days/week for 10 weeks, at a mercury concentration of approximately 0.5 mg/m3, 19 h/ day; 1 mg/m3, 3 h/day; 0.3 mg/m3, 6 h/day or 1 mg/m3, 1.5 h/day. The total mercury concentrations in the brain were 6.4, 6.3, 1.6 and 0.64 mug/g tissue, respectively. The mercury distribution in the brains was examined. Mercury was found in almost the whole brain in the two groups with the highest exposure. In the third

group, mercury was primarily found in the neocortical layer V, the white matter, thalamus, and the brain-stem. In the fourth group, the white matter and the brain-stem were the targets for mercury accumulation. Similarities and differences between rats and mice in the distribution pattern are discussed.

55
TITLE:
An analysis of autopsy brain tissue from infants prenatally exposed to methylmercury.

AUTHORS:
Lapham L
Myers G
Cernichiari E
Baggs R
Brewer R
Shamlaye C

SOURCE:
Neurotoxicology 1994;15(4):958

ABSTRACT:
Following informed consent and clearance by appropriate human studies committees, a total of 55 autopsy brain samples have been collected from infants dying in the Republic of Seychelles. Death was due to various causes and occurred prenatally, perinatally, and during infancy. At the time of autopsy, fresh samples of frontal, temporal and occipital cortex were obtained and fresh frozen at -20 degrees C. The remainder of the brain tissue was immediately preserved in 10% formalin. The brains were transported to the Environmental Health Sciences Center at the University of Rochester School of Medicine. To date, eighteen brains have been cut and blocked for histology. Areas of the brain most frequently sampled were frontal region, occipital region, hippocampus, and basal ganglia/thalamus. Pons/medulla and cerebellum were examined when available. Blocks were embedded in paraffin and stained with hematoxylin-eosin and cresyl violet (Nissl stain). The levels of total and inorganic mercury were measured in sections of brain adjacent to the tissue used for histopathology. Mercury adjustments were made on both fixed and deep frozen samples of brain. The results of both the histopathological examinations and the mercury analyses will be presented and discussed.

56
TITLE:
Effects of Long-Term Treatment with Methyl Mercury on the Developing Rat Brain

AUTHORS:

Lindstrom H
Luthman J
Oskarsson A
Sundberg J
Olson L

SOURCE:
Environmental Research, Vol. 56, No. 2, pages 158-169, 35 reference, 1991

ABSTRACT:
The effects of methylmercury (22967926) on brain development were studied in rats. Female Sprague-Dawley-rats were maintained on diets containing 0 or 3.9mg/kg mercury (7439976) as methylmercuric-chloride (115093) (MMC) starting 14 days before mating and continuing through gestation and lactation up to 3.5 weeks after delivery. After weaning the pups were maintained on the same diets until postnatal day 50. Body weights of the dams after weaning and the pups at postnatal day 50 were recorded. The pups were killed on postnatal day 50 and the brains were removed and weighed. Blood and brain mercury concentrations were measured. The brains were examined for histopathological changes. Brain regions were assayed for changes in astrocyte morphology using an immunohistochemical technique. The brain regions were analyzed for noradrenaline and dopamine. Blood and brain mercury concentrations in the exposed pups were 10.03 and 1.45mg/kg, respectively. The corresponding concentrations in control pups were 0.018 and 0.035mg/kg. MMC did not significantly affect body weight of the dams or pups. MMC caused a slight increase in brain weight. No treatment related histopathological effects or changes in astrocyte morphology were observed. Noradrenaline concentrations were significantly increased by MMC only in the cerebellum. MMC did not affect dopamine concentrations in any of the brain regions. The authors conclude that long term exposure to low doses of methylmercury in developing rats can alter the concentrations of neurotransmitters, as indicated by the increase in cerebellar noradrenaline concentration. The fact that MMC did not affect other morphological or biochemical parameters emphasizes the need for a broad methodological approach for investigating potential detrimental effects of chronic low exposures to environmental pollutants.

57
TITLE:
The effect of pregnancy outcome and fetal brain development of prenatal exposure to mercury vapour.

AUTHORS:
Warfvinge K
Berlin M
LÓogdberg B

SOURCE:

Neurotoxicology 1994;15(4):956

ABSTRACT:

Fourteen pregnant female squirrel monkeys were exposed to mercury vapor (Hg0) 5 days/week from 5-7 weeks of gestation until delivery in an exposure chamber. Hg0 exposure varied from 1 mg/m3 for 22 hr/d (1 monkey), 7 hr/d or 4 hr/d to 0.5 mg/m3 for 7 hr/d or 4 hr/d. Hg concentration in maternal blood ranged 0.05-0.09 ug/g. There was a dose related increase in abortion rate and perinatal mortality in the exposed monkeys compared to unexposed controls. The morphology of perinatally sacrificed or succumbed offspring brains showed signs of migration disturbances such as increased cell density in the cerebral subcortical white matter, abnormal cell collections near the cerebral lateral ventricles. Autometallographically, Hg was preferentially localised in the heteropic cells and in the ventricular aspects of the pseudostratified neuroepithelium. Hg concentration in the brain of exposed offspring ranged 0.01-0.70 ug/g. Automellography of the maternal brains revealed that the pyramidal neurons of the neocortical layer V contained more visualized Hg than the other neurons. In the offspring brains, Hg was visualized throughout the whole neocortex and no laminar distribution pattern was found. In the fiber systems, the offspring brains contained more Hg than the adult brains. In the cerebellum, the Purkinje cells, the Bergmann glial cells, the astrocytes of the medullary layer and the deep cerebellar nuclei were the main targets for Hg accumulation in both maternal and offspring brains.

58

TITLE:

Inorganic mercury

AUTHORS:

WHO working group

SOURCE:

TA:Environmental Health Criteria PG:147 p YR:1991 IP: VI:118

ABSTRACT:

Effects on organisms in the environment: Inorganic mercury is toxic to microorganisms, toxic effects from exposure to 5 ug/l have been reported. The organic forms of mercury are generally more toxic to aquatic organisms than the inorganic forms, however aquatic plants are affected by concentrations of 1 mg inorganic mercury/litre. The 96-h LC50s vary between 33 and 400 ug/l for freshwater fish. Reproduction is affected adversely by mercury. Birds fed inorganic mercury show a reduction in food intake and growth. Effects in humans: Acute inhalation exposure to mercury vapour may be followed by chest pains, dyspnoea, coughing, haemoptysis, and sometimes interstitial pneumonitis leading to death. The ingestion of mercuric compounds, in particular mercuric chloride, has caused ulcerative gastroenteritis and acute tubular necrosis causing death from anuria where

dialysis was not available. The central nervous system is the critical organ for mercury vapour exposure. Subacute exposure has given rise to psychotic reactions characterized by delirium, hallucinations, and suicidal tendency. Occupational exposure has resulted in erethism as the principal feature of a broad ranging functional disturbance. With continuing exposure a fine tremor develops. Initially involving the hands. In the milder cases erethism and tremor regress slowly over a period of years following removal from exposure. Decreased nerve conduction velocity has been demonstrated in mercury-exposed workers. Long-term, low-level exposure has been associated with less pronounced symptoms of erethism. There is very little information available on brain mercury levels in cases of mercury poisoning, and nothing that makes it possible to estimate a no-observed-effect level or a dose-response curve. At a urinary mercury excretion level of 100 ug per g creatinine, the probability of developing the classical neurological signs of mercurial intoxication (tremor, erethism) and proteinuria is high. An exposure corresponding to 30 to 100 ug mercury/g creatinine increases the incidence of some less severe toxic effects that do not lead to overt clinical impairment. In a few studies tremor, recorded electrophysiologically, has been observed at low urine concentrations (down to 25-35 ug/g creati- nine). Other studies did not show such an effect. Some of the exposed people develop proteinuria (proteins of low relative molecular mass and microalbuminuria). Appropriate epidemiological data covering exposure levels corresponding to less than 30-50 ug mercury/g creatinine are not available. The exposure of the general population is generally low, but may occasionally be raised to the level of occupational exposure and can even be toxic. Thus, the mishandling of liquid mercury has resulted in severe intoxication. The kidney is the critical organ following the ingestion of inorganic divalent mercury salts. Occu- pational exposure to metallic mercury has long been associated with the development of proteinuria, both in workers with other evidence of mercury poisoning and in those without such evidence. Less commonly, occupational exposure has been followed by the nephrotic syndrome, which has also occurred after the use of skin-lightening creams containing inorganic mercury, and even after accidental exposure. The current evidence suggests that this nephrotic syndrome results from an immunotoxic response. Until recently, effects of elemental mercury vapour on the kidney had been reported only at doses higher than those associated with the onset of signs and symptoms from the central nervous system. New studies have, however, reported kidney effects at lower exposure levels. Experimental studies on animals have shown that inorganic mercury may induce auto-immune glomerulonephritis in all species tested, but not in all strains, indicating a genetic predisposition. A consequence of an immunological etiology is that, in the absence of dose-response studies for groups of immunologically sensitive individuals, it is not scientifically possible to set a level for mercury (e.g., in blood or urine) below which (in individual cases) mercury-related symptoms will not occur. Both metallic mercury vapour and mercury compounds have given rise to contact dermatitis. Mercurial pharmaceuticals have been responsible for

Pink disease in children, and mercury vapour exposure may be a cause of "Kawasaki" disease. In some studies, but not in others, effects on the menstrual cycle and/or fetal development have been reported. The standard of published epidemio- logical studies is such that it remains an open question whether mercury vapour can adversely affect the menstrual cycle or fetal development in the absence of the well-known signs of mercury intoxication. Recently, there has been an intense debate on the safety of dental amalgams and claims have been made that mercury from amalgam may cause severe health hazards. Reports describing different types of symptoms and signs and the results of the few epidemiological studies produced are inconclusive.

59

TITLE:

Mercury Concentration In The Blood And Organs Of Normal And Acatalasemic Mice After Intraperitoneal Injection Of Metallic Mercury (203Hg)

AUTHORS:

Ogata M

Aikoh H

SOURCE:

Physiological Chemistry and Physics and Medical NMR, Vol. 16, No. 1, pages 71-73, 9 references, 19841984

ABSTRACT:

The tissue distribution of mercury (7439976) was determined following treatment of acatalasemic and normal mice with metallic mercury. Female normal and acatalasemic C3H-mice were intraperitoneally treated with metallic mercury prepared from 203 mercury labeled mercuric-chloride (7487947) and ascorbic-acid. Immediately after injection, the mice were placed in exhalation chambers. Mercury aspirating in the exhaled air was passed through 6 percent potassium-permanganate solution. Ten minutes after injection, the mice were anesthetized with ether and blood samples were withdrawn from orbital veins. Organs were removed and washed in saline. Mercury levels in the tissues were estimated. The total amount of mercury exhaled by acatalasemic mice was 1.6 times higher than that of normal mice. The level of mercury ions in the blood of acatalasemic mice was significantly lower, about 2.4 times less than that of normal mice. Mercury levels in brain and liver, and the brain to blood ratio or liver to blood ratio of mercury in the acatalasemic mice was significantly higher than that of normal mice. The authors conclude that metallic mercury readily passes through the blood brain barrier and blood liver barrier and that blood catalase plays a role in the uptake of mercury.

60

TITLE:

Placental and lactational transfer of mercury from rats exposed to

methylmercury in their diet: speciation of mercury in the offspring.

AUTHORS:
Sundberg J
Oskarsson A

SOURCE:
Journal of Trace Elements in Experimental Medicine 1992;5(1):47-56

ABSTRACT:
The objective of the present investigation was to compare the placental and lactational transfer of mercury after long-term exposure to methylmercury (MeHg) in the diet of rats. Dams were given a diet containing 3.9 ug Hg/g as MeHg during 11 weeks prior to mating, during gestation and lactation. Neonates from MeHg-treated dams either stayed with their mothers until day 15 of lactation or were cross-fostered at birth to dams treated with a control diet. Neonates from dams receiving the control diet were in the same way cross-fostered at birth to dams treated with the MeHg diet. The offspring exposed to mercury only via the placenta had approximately twice as high whole blood concentrations and four times as high brain concentrations of total mercury at 15 days of age compared with offspring exposed only via milk. The total mercury concentration in the blood and brains of offspring exposed prenatally and postnatally corresponded approximately to the additive effect of placental and lactational transfer of mercury. In the offspring exposed only during gestation the mercury in blood was present as MeHg, indicating no or a low degree of demethylation during the suckling period. However, in the blood of offspring exposed only via milk approximately 80% of the total mercury was present as MeHg. Demethylation of MeHg is suggested to occur in the dam, resulting in inorganic mercury being transferred to the offspring via the milk. These results show that the placental transfer of mercury is more efficient than the lactational transfer after long-term exposure to MeHg. As inorganic mercury was present in blood in the sucklings exposed only via milk, this route of exposure to inorganic mercury should not be overlooked.

61
TITLE:
Influence of 2,3 Dimercaptopropane-1-sulfonate and Dimercaptosuccinic Acid on the Mobilization of Mercury from Tissues of Rats Pretreated with Mercuric Chloride, Phenylmercury Acetate or Mercury Vapors

AUTHORS:
Buchet JP
Lauwerys RR

SOURCE:
Toxicology, Vol. 54, No. 3, pages 323-333, 15 references, 19891989

ABSTRACT:

The efficiency of meso-dimercaptosuccinic-acid (DMSA) and 2,3-dimercaptopropanesulfonic-acid (DMPS) to release mercury (7439976) from tissues of male Sprague-Dawley-rats pretreated with different doses of mercuric-chloride (7487947), phenylmercury-acetate (62384), (both given intraperitoneally, ip, 5 times/week during 3 weeks at doses of 0.00625 to 0.5 milligrams of mercury/kilogram body weight) or exposed to different concentrations of mercury vapors was investigated. Inhalation exposures lasted from 5 to 14 days and were followed by 4 to 35 days without mercury exposure before the administration of a chelating agent. The relationship between the tissue concentration of mercury and subsequent increased mercury excretion following administration of the chelating agents was also investigated. The results of the study indicated that mercury accumulated primarily in the kidney when given by inhalation as metallic vapor or by the ip route. Significant accumulations in the brain occurred following exposure to mercuric-chloride at high dose levels of the metallic mercury vapor. The blood brain barrier did not appear in this study to be more permeable to the DMSA-Hg2+ complex than to mercury alone. The authors conclude it does not appear necessary to consider any risk of mercury translocation from peripheral tissues to the brain following administration of DMSA. DMSA primarily mobilized mercury from the kidney and favored its excretion through the urinary tract. The rate of removal was higher following DMPS administration than DMSA. However, the latter is the less toxic of the two agents.

62

TITLE:

Methylmercury Distribution, Metabolism, And Neurotoxicity In The Mouse Brain

AUTHORS:

Vandewater LJS
Racz WJ
Norris AR
Buncel E

SOURCE:

Canadian Journal of Physiology and Pharmacology, Vol. 61, No. 12, pages 1487-1493, 18 references, 19831983

ABSTRACT:

The effects of subchronic methylmercury (MM) treatment was studied in mouse brain. Male Swiss albino-mice were given 10 milligrams per kilogram mercury-203 labeled methylmercury-chloride (115093) (MMC) daily for 1 to 9 days. Behavioral changes were assessed. Animals were killed 24 hours after administration of the last dose of MMC. A blood sample was taken within 1 hour of sacrifice. Total mercury concentration was determined.

The brain was removed, rinsed, fixed in formalin, and dissected. The right brain was used to quantitate total and inorganic mercury concentrations; the left brain was used to assess structural damage. Inorganic mercury quantitation was done by isotope exchange. The left brain underwent histological examination. Twenty percent of the mice given all doses of labeled MMC died in the first 3 days of the experiment, none died during days 4 through 7, and 27 percent died over the last 3 days. Behavioral tests showed MM intoxication by day 6. MM was evenly distributed through the brain except for the anterior cerebral cortex which had significantly higher MM concentrations than the rest of the brain in mice given three, six or nine doses. Inorganic mercury concentrations were highest in cerebellum and lowest in cerebral cortex. Mice given six or nine doses of MMC had a non uniform pattern of structural damage with cerebral cortex showing the greatest and brain stem showing the least damage. Inorganic mercury concentration was significantly correlated with structural damage in the anterior cerebral cortex and the anterior subcortex.

63

TITLE:

Histological Localization of Methylmercury in Mouse Brain and Kidney by Emulsion Autoradiography of 203Hg

AUTHORS:

Rodier PM

Kates B

SOURCE:

Toxicology and Applied Pharmacology, Vol. 92, No. 2, pages 224-234, 23 references, 19881988

ABSTRACT:

Effects on emulsion autoradiography of tissue containing nonradioactive methylmercury (MeHg) were compared with those of radioactive MeHg to test whether grains appearing over mercury (7439976) (Hg) containing samples are due to emissions or to a chemical interaction of Hg with silver grains in the emulsion. In preliminary experiments, retention of Hg in mouse brain and agar samples was investigated by treating BALB/c-mice with mercury-203 labeled methyl-mercury-chloride (115093) and killing them 24 hours later, or by mixing labeled dosing solution with liquid agar to form agar buttons. Tissue processing involved eight steps, and no significant change in Hg concentration in brain was observed while agar buttons showed rapid and total loss of MeHg. Data indicated that even very large samples would show no substantial loss of Hg due to actual removal of Hg from brain tissue. Similar results were observed when kidney tissue was studied. Mean Hg content of brains perfused with glutaraldehyde was 2.08 micrograms per gram, while that for fresh brain was 2.74 micrograms per gram; the difference was not significant. In a primary experiment, mice

were given 8mg/kg Hg as MeHg by gavage, while another group of mice were given the same dose with mercury-203 at 24 microcuries per milliliter (microCi/ml). The experiment was repeated with labeled MeHg at 42microCi/ml. No autoradiographic counts above background were observed in either brain or kidney in cold tissue, while counts from radioactive tissue differed from background in both brain and kidney in each region counted with MeHg of low or high specific activity. No effect of cold MeHg on emulsions or any accumulation of silver was observed. Latent images were produced by radioactive MeHg in a dose dependent fashion. The authors conclude that nuclear emissions alone are responsible for the grains appearing in autoradiographs of tissues labeled with radioactive MeHg.

64
TITLE:
The brain-to-liver mercury ratio increases with aging in mice.

AUTHORS:
MASSIE HR
GRECO ME
VADLAMUDI L

SOURCE:
EXP GERONTOL; 28 (2). 1993. 161-167.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. There was no significant change in the total amount of mercury in organs (lung, heart, kidney, brain, and liver) from male C57BL/6J mice ranging in age from 133 to 904 days of age maintained under conventional conditions with no known source of mercury exposure other than background concentrations. The lowest values were found in the liver and the highest in the grain, with considerable variation in the mercury content between individual mice for all organs examined. The ratio of mercury in the brain to that in the liver, however, was found to significantly increase with aging in an exponential manner. A similar result was found for the ratio of brain to kidney mercury. We conclude that older mice are less able to maintain low brain-to-liver ratios of mercury regardless of the total body content of mercury. Dietary mercury ranging from 200 to 20 000 ppm Hg had little or no influence on the life span of Drosophila fruit flies, suggesting that the effect of mercury is prob

65
TITLE:
The Distribution of Total Mercury in the Brain after the Lateral Ventricular Single Injection of Methylmercury and Glutathione

AUTHORS:

Watanabe H
Shimojo N
Sano K
Yamaguchi S

SOURCE:
Research Communications in Chemical Pathology and Pharmacology, Vol. 60, No. 1, pages 57-69, 13 references, 19881988

ABSTRACT:
The effect of glutathione on the brain distribution of mercury (7439976) (Hg) following dosing with methylmercury was studied in rats. Male Wistar-rats were injected intraventricularly with 5.0 millimolar (mM) methylmercuric-chloride (115093) (MMC) and 0, 5.0, 50.0, or 250.0mM glutathione. They were killed 5 or 12 hours later and the brains were removed and assayed for total Hg. Other brains were dissected into the rhinencephalon, frontal cortex, corpus striatum, midcortex, thalamus and hypothalamus, hippocampus, rear cortex, midbrain, cerebellum, and pons and medulla oblongata and assayed for Hg. Glutathione at 5.0mM sharply increased brain Hg content at both time points. The two higher concentrations inhibited the glutathione induced increase in brain Hg. Whole brain Hg concentrations in rats given 250.0mM glutathione were comparable to those in rats given MMC alone. Highest Hg concentrations occurred in thalamus and hypothalamus at both time points and decreased with increasing distance from the lateral ventricle (the injection site). Glutathione tended to equalize the distribution of Hg in the various brain regions in a dose dependent manner. The authors conclude that glutathione when given in equimolar amounts accelerates the movement of methylmercury into the brain. Excess glutathione inhibits transport of methylmercury into the brain and tends to equalize the distribution of Hg throughout the brain. The is attributed to methylmercury and glutathione forming a 1:1 complex that is converted into a methylmercury/cysteine complex by gamma-glutamyl-transpeptidase in the kidney. The methylmercury/cysteine is transported into the brain. Excess glutathione competitively inhibits this process.

66
TITLE:
Monitoring Methylmercury during Pregnancy: Maternal Hair Predicts Fetal Brain Exposure

AUTHORS:
Cernichiari E
Brewer R
Myers GJ
Marsh DO
Lapham LW
Cox C

Shamlaye CF
Berlin M
Davidson PW
Clarkson TW

SOURCE:
Neurotoxicology, Vol. 16, No. 4, pages 705-710, 17 references, 1995

ABSTRACT:
In conjunction with the Seychelles Child Development Study, mercury (7439976) levels and histopathology were studied in the brains of 32 neonates born to mothers with a high dietary intake of oceanic fish. Brain and blood samples obtained at autopsy from infants who died within a few days after birth, and blood and hair samples obtained from their mothers were analyzed for mercury. Mercury levels were determined in brain tissue from the occipital and frontal cortex, hippocampus, cerebellum, pons/medulla, and basal ganglia/thalamus. Significant associations were seen relating maternal hair mercury concentrations with levels found in all six brain regions examined in the infants. This finding was confirmed in a sequential analysis comparing levels in maternal hair to maternal blood, then to infant blood, and finally to infant brain. The authors conclude that maternal hair mercury levels are useful as an indicator of fetal exposure to methylmercury in populations with a high consumption of oceanic fish.

67
TITLE:
The Comparative Toxicology Of EthylAnd Methylmercury

AUTHORS:
Magos L
Brown AW
Sparrow S
Bailey E
Snowden RT
Skipp WR

SOURCE:
Archives of Toxicology, Vol. 57, No. 4, pages 260-267, 22 references, 19851985

ABSTRACT:
The neurotoxicities and nephrotoxicities of ethylmercury (627441) and methylmercury (22967926) were compared in rats. Porton-Wistar-rats were administered five daily doses of 8.0 milligrams per kilogram (mg/kg) methylmercuric-chloride (115093) or 8.0 or 9.6mg/kg ethylmercuric-chloride (107277) by gastric gavage. The animals were observed for signs of toxicity. Selected animals were killed 3 or 10 days after the last dose,

and blood, brain, and kidney total mercury (the sum of inorganic and organic mercury), inorganic mercury (7439976), and organic mercury concentrations were determined. Brain, spinal cord, and renal tissue were examined for histopathological changes. Both compounds caused body weight loss and coordination disorders. On an equimolar basis, ethylmercury caused significantly greater weight losses; however, ethylmercury caused less severe coordination disorders. The concentration of total mercury and organic mercury was higher in the blood of ethylmercury treated rats and in the brain and kidney of methylmercury treated rats. The proportion of inorganic mercury was higher after ethylmercury treatment. The 9.6mg/kg dose of ethylmercury caused higher blood and brain total mercury concentrations than the 8.0mg/kg dose, but did not increase the kidney concentration above that from the 8.0mg/kg dose. The effects of methylmercury and ethylmercury on the dorsal root ganglia were similar. Methylmercury caused more extensive damage in the granular layer of the cerebellum. Ethylmercury was more nephrotoxic than methylmercury. Pathological damage induced by ethylmercury occurred in the P2 region and more often extended to the P1 and P3 regions than in methylmercury treated rats. The authors conclude that in nephrotoxicity, the concentration of inorganic mercury seems to be more important than the concentration of organic or total mercury. Inorganic mercury of dealkylation of alkylmercury compounds, however, cannot be responsible for cerebellar granular layer in alkylmercury intoxication.

68

TITLE:

Blood and brain mercury levels after chronic gestational exposure to methylmercury in rats.

AUTHORS:

NEWLAND MC
REILE PA

SOURCE:

TOXICOLOGICAL SCIENCES; 50 (1). 1999. 106-116.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Female rats were exposed to 0, 0.5, or 6 ppm Hg (as methylmercuric chloride, 10 rats/group) in drinking water. For half the rats, exposure began 4 weeks before mating and for the others, exposure began 7 weeks before mating. All mating was done with an unexposed male. Maternal exposure continued to post-natal day (PN) 16. Blood and whole-brain mercury concentrations were determined in pups on PN 0 (birth) and PN 21 (weaning). Maternal water consumption was monitored daily during gestation and la e to the nursing pups. Brain mercury in offspring decreased between birth and weaning from 0.49 to 0.045 ppm in the low-dose rats and from 9.8 to 0.53 ppm in the high-dose rats. The brain increased in weight only about 5.5-fold during this time, indicating

that there was minimal mercury exposure and some net loss from brain during this period. Brain:blood ratios averaged about 0.14 at birth and 0.24 at weaning, suggesting differential loss from neural and non-neural tissue. These ratios are high nd cumulative mercury consumption, also expressed on a ppm basis (cumulative mercury consumed divided by maternal body weight at parturition), was not linear but was well described by a power-functionrelationship: Hg = A*(cum exposure)b where the exponent, b, was 1.12 and 1.17 for blood and brain, respectively, at birth. This exponent was indistinguishable from 1.0 for both media at weaning, indicating that the relationship between exposure and blood and brain levels became linear.

69

TITLE:

Effect of Long-Term Sodium Selenite Supplementation on Levels and Distribution of Mercury in Blood, Brain and Kidneys of Methyl Mercury-Exposed Female Mice

AUTHORS:

Glynn AW
Lind Y

SOURCE:

Pharmacology and Toxicology, Vol. 77, No. 1, pages 41-47, 36 references, 1995

ABSTRACT:

A study was conducted to investigate the possibility that changes in the level and distribution of methyl-mercury (22967926) (MeHg) in blood following long term selenium (7782492) (Se) treatment may result in changes in the accumulation and distribution of MeHg in brain and kidney tissues. Female Balb/c-CA-mice were supplemented with 0, 0.6, and 3.0 parts/million Se in tap water for seven weeks. They were then given a single 2 micromole/kilogram oral dose of Me203Hg, followed by continued Se supplementation for 56 days. Dietary supplementation with Se did not produce changes in mercury (7439976) (Hg) accumulation and distribution in the blood cells. Similarly there were no changes in the distribution of Hg and its accumulation in the kidneys. However, Hg levels in the brain did increase in response to the increasing Se status. Hg distribution in the brain was also changed. By 56 days after dosing, 70 to 80% of the administered dose had left the body. However, in the 3 parts/million dose group, the brain still retained higher levels of Hg than was found in the control animals. The authors conclude that Se supplementation does not influence the level and distribution of Hg in the blood and blood cells of MeHg exposed female mice. It did affect both Hg accumulation and intracellular distribution in the brain but not in the kidneys. The authors suggest that the effects in the brain may be caused by tissue specific mechanisms rather than by a more general effect on MeHg level and

distribution in the blood transporting MeHg to the tissues.

70
TITLE:
Methylmercury Poisoning Induces Oxidative Stress in the Mouse Brain

AUTHORS:
Yee S
Choi BH

SOURCE:
Experimental and Molecular Pathology, Vol. 60, No. 3, pages 188-196, 42 references, 1994

ABSTRACT:
The role of oxidative stress in methylmercury neurotoxicity was examined. C57BL/6J-mice were injected intraperitoneally with 2.5mg/kg methylmercuric-chloride (115093) for 3, 7, or 14 days. Selected mice were killed after each dosing period and the brains were removed. Whole brain, mitochondrial, cytosol, and nuclear homogenates were prepared and analyzed for organic mercury, inorganic mercury (7439976), superoxide anion, superoxide-dismutase (SOD), and hydrogen-peroxide. Cerebral and cerebellar tissues were examined for histopathological changes. Most mice sampled on day 14 had developed clinical signs of neurotoxicity such as hindlimb crossing and sluggish motor activity. The concentrations of organic mercury increased progressively in all brain tissues. The highest concentrations were found in the nuclear fraction. Small amounts of inorganic mercury were detected in the mitochondrial and nuclear fractions on day three and in all fractions on days seven and 14. Superoxide concentrations were significantly increased in all brain cellular fractions on day three. The increases persisted in all fractions throughout the study period except in the nuclear fraction. Hydrogen-peroxide concentrations were significantly increased in all fractions except in the mitochondrial and nuclear fractions on day three, the nuclear fraction on day seven, and the cytosolic fraction on day 14. SOD activity in all fractions on day three was comparable to that of the controls. SOD activity was significantly decreased in all fractions except the nuclear fraction on days seven and 14. No treatment related histological changes were seen in the cerebral and cerebellar tissues. The authors conclude that methylmercury poisoning in mice leads to a significant increase in the concentration of reactive oxygen species and a marked decrease in SOD activity in brain tissues. These findings suggest suppression of antioxidant activity and disturbances in the mitochondrial electron transport change may contribute to induction of oxidative stress in the mouse brain during methylmercury poisoning.

71
TITLE:

Differences In The Distribution Of Methyl Mercury In Erythrocytes, Plasma, And Brain Of Japanese Quails And Rats After A Single Oral Dose

AUTHORS:
Clausing P
Riedel B
Gericke S
Grun G
Muller L

SOURCE:
Archives of Toxicology, Vol. 56, No. 2, pages 132-135, 18 reference, 19841984

ABSTRACT:
Tissue distribution of methyl-mercury (22967926) was studied in Japanese quail and rats. Male Japanese-quail and Wistar-rats were administered a single oral dose of 15 milligrams per kilogram 1,2-N,N-bis(methyl-mercury)-p-toluolsulfamide. Blood samples were drawn at 1.5 to 120 hours after dosing and methyl-mercury concentrations in the erythrocytes and plasma were measured. Immediately after collecting the blood samples, the animals were killed, the brains were removed, and brain mercury (7439976) concentrations were determined. Significantly higher mercury concentrations were observed in the plasma and brain of quails and erythrocytes of rats, compared with other tissues. The blood/brain ratio of mercury decreased in Japanese-quail from 5.80 to 1.55 between 24 and 120 hours after dosing, but increased from 5.11 to 11.09 between 24 and 120 hours in rats. The erythrocyte/plasma mercury ratio increased from 131 to 162 in rats and from 31 to 56 in Japanese-quail between 1.5 and 120 hours after dosing. The authors note that their results indicate that care must be taken not to generalize results of methyl-mercury toxicity using the rat as an experimental model.

72
TITLE:
Kinetics of Methyl Mercury in Blood and Brain during Chronic Exposure in the Monkey Macaca fascicularis

AUTHORS:
Stinson CH
Shen DM
Burbacher TM
Mohamed MK
Mottet NK

SOURCE:
Pharmacology and Toxicology, Vol. 65, No. 3, pages 223-230, 39 references, 1989

ABSTRACT:

The pharmacokinetics of blood and brain methylmercury during chronic exposure was studied in monkeys. The study was part of a larger study of the behavioral and morphological effects of methylmercury on female Macaca-fascicularis and their offspring. Pregnant and nonpregnant monkeys were administered 0, 50, 70, or 90 micrograms per kilogram (microg/kg) methylmercury-hydroxide (1184572) orally for up to 1143 days. Blood samples were collected weekly from the monkeys and offspring and assayed for methylmercury. The pharmacokinetic behavior of mercury (7439976) in the blood was analyzed according to a linear, one compartment model utilizing data obtained during the first 112 days of exposure. Selected adult and infant monkeys were killed at various times, and the brains were removed and analyzed for mercury. In nonpregnant adult monkeys the pharmacokinetics of methylmercury in the blood did not vary with dose or length of exposure. The mean blood clearance rate and halflife were 41.0 milliliters per day/kilogram and 24.0 days, respectively. In pregnant adults, blood mercury concentrations in the 90microg/kg group were significantly lower than in the 50 or 70microg/kg animals during all trimesters. The halflives in the 50, 70, and 90microg/kg animals were 23.9, 22.6, and 25.7 days, respectively. The halflives of methylmercury in the blood of infants did not differ significantly from the halflives in maternal blood. The ratios of infant/maternal blood mercury concentrations in the 50, 70, and 90microg/kg groups were 1.59, 1.56, and 1.10, respectively. Brain mercury concentrations in adult and infant monkeys were similar. The highest concentrations were found in the basal ganglia and surrounding tissues. The brain mercury concentrations were similar to those found in humans exposed to methylmercury. The authors conclude that except for a slightly faster blood clearance, the biodisposition of methylmercury in Macaca-fascicularis resembles that of humans.

73

TITLE:

Prenatal exposure to mercury vapor: effects on brain development.

AUTHORS:

Berlin M
Hua J
Logdberg B
Warvinge K

SOURCE:

Toxicologist 1992 Feb;12(1):7

ABSTRACT:

Two collaborating groups in Sweden perform studies on the effect of mercury vapor on fetal brain development, Berlin et al., University of

Lund, and Dencker et al., University of Uppsala. The team in Lund exposes timed pregnant squirrel monkeys to mercury vapor 1 mg/m3 for 3 hours and 6 hours per day 5 days a week. Early abortion, premature birth, low birth weight with a perinatal death have been observed. The fetal blood content of mercury was raised dramatically at the end of the pregnancy exceeding that of the mother at delivery by a factor of at least 5. The content of mercury in mother and offspring as well as brain morphology of offspring will be accounted for. Dencker et al. have exposed rats during gestation to 1 mg mercury/m3. Behavioural studies of the offspring have revealed persistant deviation from the controls and also after neonatal exposure to 50 ug/m3.

74

TITLE:

Behavioural Effects of Prenatal Metallic Mercury Inhalation Exposure in Rats

AUTHORS:

Danielsson BRG
Fredriksson A
Dahlgren L
Teiling Gardlund A
Olsson L
Dencker L
Archer T

SOURCE:

Neurotoxicology and Teratology, Vol. 15, No. 6, pages 391-396, 25 references, 1993

ABSTRACT:

Behavioral effects resulting from prenatal mercury (7439976) vapor exposure were studied in rats. Pregnant Sprague-Dawley-rats were exposed to 1.8mg/m3 mercury vapor for 1 hour (low dose) or 3 hours (high dose) on days 11 through 14 and 17 through 20 of gestation. Based on estimated respiratory minute volume, the dams in the low and high dose groups were exposed to 0.07 and 0.20mg/kg mercury. The dams and offspring were observed for clinical signs of toxicity. Selected offspring were killed 3 to 4 days after birth to determine the mercury content of the brain, liver, and kidneys. The other offspring were observed for pinna unfolding, development of the surface righting reflex, and tooth eruption. Negative geotaxis was evaluated when the offspring were 7 to 9 days old. Spontaneous motor activity, habituation to a novel environment (activity chambers), and radial arm maze learning were assessed 3 and 14 months after birth. Circular water maze learning was evaluated when the pups were 7 and 15 months old. No clinical signs of toxicity were seen in the dams or offspring. Pinna unfolding, surface righting reflex development, and tooth eruption were not affected by mercury exposure. Negative

geotaxis was not affected. Spontaneous motor activities such as locomotion, rearing, and total activity counts were significantly decreased in mercury exposed offspring tested at 3 months. Except for total activity counts, these effects had disappeared by 14 months. Total activity counts were significantly increased in pups exposed to 0.2mg/kg mercury. Performance in the radial arm maze and habituation to a novel environment were significantly impaired by both mercury exposures. Learning in the water maze was not affected. Dose related mercury accumulations occurred in the brain, liver, and kidney except in the brain in the low mercury dose group. The authors conclude that prenatal exposure of rats to mercury vapor induces behavioral changes and learning deficits in the offspring.

75
TITLE:
Effects of Exercise Training on the Distribution of Metallic Mercury in Mice

AUTHORS:
Shimojo N
Arai Y

SOURCE:
Human and Experimental Toxicology, Vol. 13, No. 8, pages 524-528, 19 references, 1994

ABSTRACT:
The impact of exercise enhanced catalase (CAT), glutathione-peroxidase, (GSH) and superoxide-dismutase (SOD) activity on the internal distribution of mercury (7439976) following exposure to mercury vapor was investigated in exercised and sedentary mice. Significantly increased levels of CAT, GSH, and SOD were validated in C3H-He.N-mice trained to swim for 60 minutes per day over a period of 9 weeks compared to a sedentary group. At 0, 24 and 48 hours following mercury exposure, total mercury content was similar in both groups of mice, indicating that exercise conditioning did not affect absorption or excretion of mercury. Significant differences were observed, however, in the organ and blood levels of mercury between exercised and unexercised mice including greater concentrations of mercury in the brain, heart, whole blood, and red blood cells of exercised mice at 24 and 48 hours after exposure and significantly more mercury in the kidneys of sedentary mice after 24 hours of exposure. The authors note that these differences provide evidence of a mechanism in which exercise enhanced CAT and SOD activity in the red blood cells contributes to increased oxidation of and hence increased uptake of mercury in the blood relative to the kidney. The authors also suggest that the higher mercury levels found in the brain and heart of exercised mice may reflect a higher blood concentration of mercury in the zero valency state which tends to collect in the heart and brain.

76
TITLE:
Effects of metal exposure on brain development.

AUTHORS:
Berlin M
LÓogdberg B

SOURCE:
Journal of Trace Elements in Experimental Medicine 1992;5(2):96

ABSTRACT:
The risk of interference with brain development by pre- or postnatal exposure toxenobiotics is often neglected and an overlooked problem in environmental health risk assessment. Several metals are among the substances to which exposure during pregnancy may interfere with fetal brain development. A non primate model for prenatal exposure using the squirrel monkey has been developed. Routines for timed pregnancies, caesarian section, biological monitoring, recording of growth and psychomotor development as well as computerized operant behavior testing have been developed. Reference material of brain morphology at different gestational ages has been collected. This animal model has been applied for studies of prenatal exposure to lead, mercury vapor and methylmercury (MeHg). Morphological changes in brain and persistent behavioral deviations have been observed after prenatal lead exposure (maternal blood lead during pregnancy 30-80 ug/dL). After MeHg exposure (maternal MeHg during pregnancy 0.2-1.5 ug/mL) retarded brain development and migration disturbances as well as persistent behavioral changes were seen. Similar morphological changes were observed after exposure to mercury vapor (maternal blood Hg during pregnancy 0.13-0.22 ug/mL). All types of exposure cause a dose dependent decrease in brain weight and increased abortion rate and perinatal mortality.

77
TITLE:
Methyl Mercury Uptake across Bovine Brain Capillary Endothelial Cells In Vitro: The Role of Amino Acids

AUTHORS:
Aschner M
Clarkson TW

SOURCE:
Pharmacology and Toxicology, Vol. 64, No. 3, pages 293-297, 25 references, 19891989

ABSTRACT:

Factors which regulate the transport of methyl-mercury (MeHg) across the plasma membrane of brain capillaries were examined in in-vitro bovine microvessel preparations. The mercury (7439976) uptake by suspended microvessels was significantly increased following 1 hour coincubations of mercury with methylmercury-chloride (115093) with 0.1 millimolar (mM) L-cysteine at 37 degrees-C. Coincubation of microvessels with 0.1-mM L-cysteine-L-methionine, or with 0.1mM L-cysteine plus the gamma-glutamyl-transpeptidase inhibitor AT-125 abolished this enhanced capillary uptake of mercury. No increase in rat uptake of mercury was noted following 1 hour coincubations of bovine capillaries with mercury with methylmercury-chloride and 0.1mM D-cysteine at 37 degrees or 0.1mM L-cysteine at 0 degrees. The authors conclude that L-cysteine enhances the rate of capillary uptake of MeHg. The accumulation of mercury in the bovine microvessels appears to be a carrier mediated process. Capillary uptake is stereospecific to the L-enantiomorph of cysteine, suggesting selective uptake of MeHg across the blood-brain barrier. The data stress the relationship between the L-enantiomorph neutral amino acid carrier system and MeHg transport across the capillaries. The study suggests that mechanisms of MeHg uptake may be studied using in-vitro paradigms that are employed in an attempt to simplify the in-vivo situation.

78

TITLE:

Mercury Poisoning from Dental Amalgam through a Direct Nose-Brain Transport

AUTHORS:

Stortebecker P

SOURCE:

Lancet, Vol. 1, No. 8648, page 1207, 8 references, 1989

ABSTRACT:

The author expresses concern over hazards of mercury (7439976) in dental practices, particularly relating to the direct pathway for the transport of mercury from the oro/nasal to the cranial cavity, a transport pathway which does not seem to have been considered in recent studies. Approximately 50 years ago it was demonstrated that dental amalgam gave off mercury vapors which may be inhaled, reach the circulation, and enter the body. Even more dangerous are the mercurial fumes settling on the mucous membranes in the upper region of the nasal cavity, being transported directly to the brain and pituitary gland via the olfactory nerves of the valveless cranial venous system. This pathway bypasses the detoxification processes of the liver. Postmortem examinations of dentists have indicated surprisingly high concentrations of mercury in the pituitary glands, concentrations which were out of all proportion to those found in other areas of the brain. These differences can only be explained by assuming that the mercury traveled to these locations by

different pathways in the body, with the pituitary receiving an extra amount of mercury through the direct route from the nasal cavity.

79
TITLE:
Deposition of mercury in fetal and maternal brain.

AUTHORS:
YANG MG
KRAWFORD KS
GARCIA JD
WANG J HC
LEI KY

SOURCE:
PROC SOC EXP BIOL MED; 141 (3). 1972 (RECD 1973) 1004-1007

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Ten 16-day pregnant rats were force-fed a tracer-dose of 203-Hg as methyl mercury chloride. The rat was then killed at 1, 2, 4, or 5 days after force-feeding; the 10 maternal brains and the 114 fetal brains were each separated into several brain parts. The uptake of mercury in the maternal brain was greatest in the cerebrum followed in decreasing order by cerebellum, pons plus midbrain, medulla, and hypothalamus. The uptake expressed as a percentage of the dose remained essentially the same throughout the 5-day period after force-feeding. In the fetal brain the uptake increased more than 3-fold from day 17 to day 21 of fetal life. Expressed on the basis of % of dose per g tissue, the fetal cerebellum contained the highest concentration of mercury when compared to either fetal cerebrum or pons, midbrain plus medulla, or to any maternal brain parts. The total fetal brain mass from an average litter accumulated, during the 1st 2 days after force-feeding, approximately the same percentage of the dose as in the mother's brain. However, during the following 3 days, the total brain mass of each litter had 2.5-3.5 times the uptake level in the mother's brain.

80
TITLE:
Mercury Accumulation in the Squirrel Monkey Eye after Mercury Vapour Exposure

AUTHORS:
Warfvinge K
Bruun A

SOURCE:
Toxicology, Vol. 107, No. 3, pages 189-200, 28 references, 1996

ABSTRACT:

Accumulation of mercury (7439976) in eye tissues following mercury vapor exposure was studied in monkeys. Female squirrel-monkeys were exposed to 0, 0.5, or 1.0mg/m3 mercury vapor 4 or 7 hours per day each week (wk) for 59, 65, or 79 days. This protocol produced 239 to 400 hours of total mercury exposure and produced a cumulative estimated mercury absorption of 1,585 to 2,901 micrograms (microg). Venous blood samples were collected every 4 weeks during exposure and analyzed for mercury. The monkeys were killed 1 month (mo) or 1 or 3 years (yr) after exposure ended and the eyes were removed and enucleated. Five micrometer serial sections of the eyes were prepared and analyzed for mercury using an autometallographic technique. Blood mercury concentrations in the exposed monkeys increased to 0.03 to 0.14microg per milliliter after 4wk of exposure and generally remained stable thereafter. No signs of clinical toxicity were observed. Mercury accumulated to a considerable extent in the nonmyelin containing portion of the optic disc, primarily the capillary walls and glial columns. The largest accumulation of mercury in this area was found in a monkey exposed to 0.5mg/m3 mercury vapor for 400hr, which was processed 1mo after exposure ended. Considerable amounts of mercury accumulated in the pigmented epithelium of the pars plicata of the ciliary body (RPE) and in the inner layer of the retina. No mercury was found in the neural retina. Accumulation of mercury in the total retina (excluding the neural retina) appeared to depend on cumulative mercury dose. The authors conclude that following exposure to mercury vapor, mercury accumulates in the RPE in the eye. This finding indicates that deposited mercury is trapped in melanocytes within the RPE, therefore, keeping it away from the neural retina. The retention time of mercury in the eye appears to be comparable to that in the brain, kidneys, and testes, organs known to have long mercury retention times, on the order of years.

81

TITLE:

Brain and Tissue Levels of Mercury after Chronic Methylmercury Exposure in the Monkey

AUTHORS:

Rice DC

SOURCE:

Journal of Toxicology and Environmental Health, Vol. 27, No. 2, pages 189-198, 23 references, 1989

ABSTRACT:

Data were sought on tissue mercury (7439976) levels, and in particular on brain levels, in adult female cynomolgus-monkeys who had been chronically dosed with methylmercury for 1.7 to 2.5 years and withdrawn from methylmercury about 8 months prior to autopsy. The adult female monkeys were dosed with the equivalent to 10, 25, or 50 micrograms/kilogram/day of

mercury as methylmercuric-chloride (115093) on Mondays, Wednesdays and Fridays. The monkeys were dosed until they reached at least 90 percent of their estimated blood steady state value using a one compartment model. At this point they were bred to untreated males. All who delivered infants had been dosed for at least 600 days and those that did not conceive had been dosed for at least 900 days. There was no indication that pregnancy affected distribution or levels of mercury in these individuals. The brain mercury levels were at least three orders of magnitude higher than those predicted by assuming the half life in brain to be the same as that in blood. There was also a dose dependent difference in half lives for some brain regions. According to the author, these findings clearly suggest that brain half life is considerably longer than blood half life in the monkey under conditions of chronic dosing.

82

TITLE:

Demethylation and Placental Transfer of Methyl Mercury in the Pregnant Hamster

AUTHORS:

Dock L
Rissanen R-L
Vahter M

SOURCE:

Toxicology, Vol. 94, Nos. 1-3, pages 131-142, 31 references, 1994

ABSTRACT:

A study was conducted on the significance of methyl-mercury (22967926) (MeHg) demethylation for the retention, distribution and placental transfer of mercury (7439976) (Hg). Pregnant Syrian-Golden-hamsters were orally administered 1.6 micromole/kilogram mercury-203 (Hg203) labeled methylmercuric-chloride (115093) (MeHgCl) on day two (preimplantation stage) or day nine (organogenesis) of gestation. Urine and fecal samples were collected. The hamsters were killed 1 day prior to expected parturition. The fetuses and placenta were removed. Adult and fetal brain, liver, and kidneys were removed. Hg203 activity in the urine, fecal, and tissue samples was analyzed by gamma counting. The fecal route of excretion predominated at all time points in all animals. The highest concentration of Hg was noted in the adult kidney. The amount of Hg in the fetus corresponded to 1.3% and 4.6% of the maternal dose, when the dams were dosed on day two or day nine of gestation, respectively. Hg distribution in the fetus was more uniform than in the adult and the tissue concentration of Hg was the same as the concentration in the placenta. The fetal brain concentration of Hg was lower than in the adult brain, but the amount of Hg in relation to body burden was about three times higher in the fetal brain than in the adult brain. Pregnant hamsters administered MeHgCl on day nine of gestation excreted the

inorganic Hg in the urine. The highest Hg content was in the adult hamster kidney. The concentration of Hg in the tissues of the fetuses was much lower than in the adult animal, except for the brain. The fraction of inorganic Hg in fetal liver corresponded to 3% of the total amount of Hg while the fraction of inorganic mercury in the placenta was 21%. The authors conclude that the inorganic Hg detected in fetal liver following maternal exposure was possibly from MeHg demethylation in the dam and transplacental transfer of inorganic Hg

83
TITLE:
Alteration of brain proteins on inorganic mercury (Hg) induced neurotoxicity in chick embryo.

AUTHORS:
Kim JS
Choi WS
Choi EJ
Kang YS

SOURCE:
Toxicologist 2001 Mar;60(1):186

ABSTRACT:
The chick embryo can be adopted one of the most appropriate materials for the study of neurotoxicity induced by xenobiotics. It has revealed that exposure Hg in vivo and in vitro disturbs the normal regulation of brain neuronal proteins. The present study is aimed on the introduction of a screening method to evaluate neurotoxicity of metals, and buildup of our knowledge about the molecular mechanism involved in the neurotoxic effects induced by Hg. We intended to explain that the use of chick embryo brain is convenient way for neurotoxicological study and that Hg produces the alteration in the level of chick brain proteins in develop period. Hg was injected into the yolk sac of chick embryo on 6-ED as much as 25 ug and 40 ug. The chick embryo brains were collected just before hatching, and the level of transferred Hg to brain was evaluated using atomic absorption spectrophotometry (AAS). This study examined whether changes in proteins of chick embryo brain following Hg exposure produce using Western blots. Immunostaining for tubulin and tau as well as the brain cell viability in primary culture of chick embryo brain were also performed. Our results revealed that the part of injected Hg was transferred into brain depending on the concentration. The transferred Hg induced the change of brain proteins. The level of total protein was slightly increased at the low concentration of Pb, but decreased by exposure to the high dose. The level of tubulin showed gradual increment by increasing the concentration of Hg; however, Hg did not noticeably vary the level of tau. In addition, these changes were underwent in the primary cultured brain cells examined using immunocytochemistry. These experiments point to the fact that exposure to

Hg in the early develop period exerts influences upon brain proteins included cytoskeleton such as tubulin and tau, and induced different yields depending on the exposed concentration.

84
TITLE:
Increased Brain Uptake Of Mercury Induced By 2,3-Dimercaptopropanol (BAL) In Mice Exposed To Phenylmercuric Acetate

AUTHORS:
Berlin M
Rylander R

SOURCE:
Journal of Pharmacology and Experimental Therapeutics, Vol. 146, No. 2, pages 236-240, 10 references, 19641964

ABSTRACT:
The effect of 2,3-dimercaptopropanol (59529) (BAL) on brain mercury (7439976) concentration was examined in female CBA-mice. Animals were given one intravenous injection of 0.5 milligram per kilogram (mg/kg) radioactive phenylmercuric-acetate (62384) and 0.4mg/kg BAL. Animals were sacrificed either 1 hour or 1, 4, 8, or 16 days after injection. Whole body sagittal sections of 20 micrometer thickness were prepared. In a separate experiment, animals were given consecutive daily subcutaneous injections of 1mg/kg phenylmercuric-acetate and 3mg/kg BAL for 16 days. Brains were removed and radioactivity was measured. Controls in both experiments received concentrations of phenylmercuric-acetate only. BAL treated animals in the first experiment showed higher concentrations of mercury in liver, brain, and muscle and lower concentrations of mercury in the renal cortex. This latter difference decreased with time and was not demonstrable on day 16. Specific results were presented in the form of autoradiograms and histograms. In experiment 2, brains of BAL treated animals retained about twice as much mercury as controls. Mean number of counts per 0.1 gram brain were approximately 221 counts per minute (cpm) for BAL treated animals and approximately 1.8cpm for controls. The authors conclude that more mercury is accumulated in the brain when BAL is administered together with phenylmercuric-acetate than when the latter is given alone.

85
TITLE:
Impairment of the blood - brain barrier in mercury poisoning.

AUTHORS:
Steinwall O
Olsson Y

SOURCE:
Acta Neurol. Scand.; 45(3), 351-61, 1969; (REF:25)

ABSTRACT:
HAPAB The effect of poisoning with mercuric chloride and methylmercuric dicyandiamide on the permeability of blood vessels in rat brain and sciatic nerve, by using the fluorescent Evans blue - protein complex as permeability indicator, was investigated. To demonstrate interference with the blood - brain and the blood nerve exchange of nutrients, the methionine analogue Se-75-selenomethionine was used. Mercuric Chloride was injected in single i.v. or i.p. doses ranging from 2 to 20 mg / 100 g body weights. The organic mercury compound was injected similarly in a dosage of 20 mg / 100 g. The rats were generally allowed to survive 6 to 48 hr with the exception of those rats which received the highest does of mercury, who did not survive for more than 2 to 4 min after treatment. The administration of the tracer,s the sampling, radioassay and histochemical procedures are described in detail. Results indicated that the localization and the character of hte lesions were the same in the animals intoxicated with the organic or the inorganic mercury compound. The vast majority of the mercury - intoxicated rats showed disturbed cerebrovascular permeability manifested by the presence of the red fluorescent tracer within or outside the walls of the blood vessels. In the cerebral parenchyma scattered areas with extravasal fluorescence were present both in the grey and white matter. In most animals both the stroma and the epithelial cells of the choroid plexus as well as the ependymal lining of the ventricles were heavily fluorescent. In the cerebellum scattered leions of similar appearance as in other parts of the brain were observed. Only a few of the rats showed signs of distrubed permerabilty in the sciatic nerves. The Se-75 activity in the nervous tissue in rats doesed with 2 mg or 3 mg / 100 g of mercuric chloride showed lower values in the mercury group for all types of specimens. In normal rats, the concentration in the brain exceeded that in the plasma, whereas in the intoxicated rats the values generally were of the same order or below the plasma level. Therefore, it is likely that impairment of blood - brain barrier functions might constitute important pathogenetic factors in mercuric intoxication, resultings in plasma exudation and presumably distrubed blood - brain exchange of nutrients. TOXICOLOGY AND PHARMACOLOGY 70/05/00, 188 1969

86
TITLE:
Mercury Toxicokinetics in Wistar Rats Exposed to Elemental Mercury Vapour: Modeling and Computer Simulation

AUTHORS:
Falnoga I
Mrhar A
Karba R

Stegnar P
Skreblin M
Tusek-Znidaric M

SOURCE:
Archives of Toxicology, Vol. 68, No. 7, pages 406-415, 55 references, 1994

ABSTRACT:
The toxicokinetics of mercury (7439976) exposure was studied in male Wistar-mice. The mice were subacutely and continuously exposed to mercury vapor in a working area of the Idrija mercury mine. In the first study the rats were exposed for 1, 1.5, 2, 4, 10, 21, and 38 days. Blood samples were taken after 4, 8 and 18 hours of exposure. In the second study the rats were exposed in the mine for 17 days. Subsequent to the exposure, the animals were removed from the mine and the elimination of mercury followed for 42 days. Organs and blood samples were taken at 0, 3, 4, 11, 18, 32, and 46 days post exposure. Urine and feces were collected periodically. At the end of the exposure periods the organ concentrations of mercury decreased in the following sequence: kidneys, thyroid, lungs, brain subsamples, spinal cord and liver, and other organs. The kidneys had over 100 micrograms of mercury/gram of tissue. The other organs registered less than 5 micrograms/gram. About 6 weeks after exposure the concentrations in most organs approached those of the control levels except for the kidney, thyroid, and brain. About 45% of the mercury remained in the thyroid, and about 20% in the kidney and brain. At the start of the postexposure period in the second study a jerky increase of mercury concentration was found in the liver, cerebellum and spinal cord. The authors suggest that mercury was redistributed to these organs in which a steady state had not been achieved. Bacterial conversion of inorganic to organic forms in the oral cavity and gastrointestinal tract may also have been occurring, but the question of possible tissue biotransformation remains open.

87
TITLE:
The Effects Of Methyl Mercury Binding To Microtubules

AUTHORS:
Vogel DG
Margolis RL
Mottet NK

SOURCE:
Toxicology and Applied Pharmacology, Vol. 80, No. 3, pages 473-486, 32 references, 19851985

ABSTRACT:
The interaction between methyl-mercury (22967926) and microtubules was

examined in-vitro. Beef brain and rat brain tubulin samples were prepared by three cycles of polymerization and depolymerization, and microtubules were prepared from the tubulin. Microtubular assembly and disassembly assays were performed in the presence and absence of methyl-mercury-hydroxide (1184572) at 0 to 1.0 millimolar concentrations. Sulfhydryl groups on the tubules were measured and the extent of methyl-mercury binding to the sulfhydryl groups on the microtubules was determined. Methyl-mercury inhibited the polymerization and promoted the depolymerization of bovine and rat brain microtubules in a dose related manner. The assembly of microtubules was totally inhibited at approximately 2 moles of methyl-mercury per tubulin dimer. As the methyl-mercury increased, no other effects were observed until the methyl-mercury/tubulin dimer ratio approached 15:1. At this point a mercury/protein aggregate formed. There were approximately 15 free sulfhydryl groups per dimer and all available free sulfhydryl groups were saturated with methyl-mercury. Methyl-mercury bound to free sulfhydryl groups along the strands as well as on the ends of the microtubules. The authors conclude that methyl-mercury is a potent inhibitor of microtubular assembly and mediates its effects through binding to sulfhydryl groups on the molecule.

88

TITLE:

Mercury in the Rat Hypothalamic Arcuate Nucleus and Median Eminence after Mercury Vapor Exposure

AUTHORS:

Ernst E
Christensen M-K
Poulsen EH

SOURCE:

Experimental and Molecular Pathology, Vol. 58, No. 3, pages 205-214, 32 references, 1993

ABSTRACT:

The fate of mercury (7439976) within the hypothalamic arcuate nucleus and median eminence was studied after exposure to mercury vapor. Twenty adult male Wistar-rats, randomly divided into five groups, were exposed to mercury vapor in an exposure chamber containing two stainless steel wire mesh cages under dynamic air flow conditions. Mercury vapors were allowed to circulate within the chamber for at least 30 minutes before rats were introduced, to allow for equilibration. Rats were fitted within collars to prevent accidental ingestion of mercury. The rats were exposed for 6 hours/day, 5 days/week. Three groups were exposed to 50 micrograms/cubic meter for 1, 4, or 8 weeks. A fourth group was exposed to 400 micrograms/cubic meter for 2 weeks. The fifth group was a control group, exposed in a similar manner to filtered air for 8 weeks. After exposure

the rats were sacrificed, and the brains were removed. Autometallographic development of brain sections was conducted to identify mercury deposits. In exposed rats, mercury was detected in neurons, ciliated ependymal cells, tanycytes, glial cells, and endothelial cells. Control rats contained no identified mercury deposits. In rats exposed to 50 micrograms/cubic meter for 1 or 4 weeks, mercury deposits were not observed in the nucleus arcuatus and median eminence. About 2/3 of the cells in the nucleus were labeled in the 400 micrograms/cubic meter group. Virtually all of the ciliated ependymal cells and the tanycytes were densely labeled.

89
TITLE:
Selenium Concentrations in Brain after Exposure to Methylmercury: Relations between the Inorganic Mercury Fraction and Selenium

AUTHORS:
Bjorkman L
Mottet K
Nylander M
Vahter M
Lind B
Friberg L

SOURCE:
Archives of Toxicology, Vol. 69, No. 4, pages 228-234, 32 references, 1995

ABSTRACT:
A study was conducted on the relationship between brain inorganic mercury (7439976) and selenium (7782492) levels following exposure to methylmercury (22967926). Female monkeys (Macaca-fascicularis) were treated in groups of five with daily oral doses of methylmercury-hydroxide (1184572) (50 micrograms mercury per kilogram body weight in apple juice) for 6, 12, or 18 months. One group was exposed for 12 months, then kept unexposed for 6 months before sacrifice. Another three monkeys were exposed to mercury-chloride (7546307) for 3 months. Concentrations of selenium and mercury in the occipital pole and thalamus were determined. Associations were seen between the concentrations of inorganic mercury and selenium in both the occipital pole and the thalamus in treated animals as well as between inorganic mercury concentrations and methylmercury concentrations. Decreasing levels of selenium were seen with increasing concentrations of methylmercury when inorganic mercury was kept constant. Ninety percent of the variation in selenium concentrations were explained by the statistical model. The authors conclude that selenium appears to play an important role in the retention of mercury by the brain.

90
TITLE:

Accumulation of Inorganic Mercury in Lower Motoneurons of Mice

AUTHORS:
Arvidson B

SOURCE:
Neurotoxicology, Vol. 13, No. 1, pages 277-280, 12 references, 1992

ABSTRACT:
The apparently selective accumulation of mercury (7439976) in certain regions of the brain stem and spinal cord was examined in adult female albino NMRI-mice who had been injected intramuscularly in the right thigh with 30 micrograms of mercuric-chloride (7487947) and sacrificed 2 days, 4 days, 1 week, 4 weeks or 4 months after the injection. Mercury deposits were revealed bilaterally within motoneurons of the anterior horns in sections from the spinal cord at the lumbar and cervical levels. The glial cells were not sites of deposits. The motoneurons on the side of the injection at the lumbar level were more heavily labeled with mercury than were the contralateral side neurons. At the cervical level this distinction did not exist. Mercury accumulation in sections of the lower brainstem showed bilateral deposits within motor nuclei and within the trigeminal mesencephalic nuclei. Tubular cells of the kidney held mercury deposits. At the ultrastructural level mercury was localized to neuronal lysosomes. The deposition of the mercury makes it unlikely that there was a direct uptake of mercury from the blood into the cell bodies of the neurons. The authors suggest that circulating metal/protein complexes could gain access to the motor nerve terminals as they have their peripheral processes outside the blood brain barrier, where they are internalized by endocytosis and subsequently transported with retrograde axonal transport to the cell bodies.

91
TITLE:
Effect of Four Thiol-Containing Chelators on Disposition of Orally Administered Mercuric Chloride

AUTHORS:
Nielsen JB
Andersen O

SOURCE:
Human and Experimental Toxicology, Vol. 10, No. 6, pages 423-430, 42 references, 1991

ABSTRACT:
The effect of thiol containing chelators on retention and distribution of inorganic mercury (7439976) was studied in mice. Female Bom:NMRI-mice were given 5, 200, 300, or 400 micromoles per kilogram (micromol/kg)

mercury-203 (Hg-203) labeled mercuric-chloride (7487947) orally. Fifteen minutes later the animals were given 0 to 1600micromol/kg 2,3-dimercaptopropanol (BAL), N-acetyl-DL-penicillamine (NAPA), 2,3-dimercaptosuccinic-acid (DMSA), or 2,3-dimercapto-L-propane-sulfonate (DMPS) orally or by intraperitoneal (ip) injection. Retention of Hg-203 was determined on days 1, 2, 3, 4, 7, 10, or 14 by whole body counting. Surviving mice were killed on day 14 and the brain, spleen, kidneys, and livers were removed and analyzed for Hg-203 activity. Mercuric-chloride at doses of 200micromol/kg or higher caused a dose related increase in mortality. DMPS and DMSA given ip significantly decreased mercuric-chloride induced mortality. DMPS given orally prevented mercuric-chloride induced mortality. NAPA at 1600micromol/kg significantly reduced mercuric-chloride induced mortality. BAL had no effect on mortality. DMSA and DMPS significantly reduced whole body retention of Hg-203 in mice given 200micromol/kg or more mercuric-chloride on day 14. Oral dosing was more effective than ip injection. NAPA increased whole body Hg-203 retention in mice given 300micromol/kg mercuric-chloride. BAL significantly reduced whole body retention of Hg-203 in mice given 5micromol/kg mercuric-chloride. BAL had only a slight effect in mice given higher mercuric-chloride doses. All chelators except NAPA significantly reduced hepatic mercury deposition. DMSA and DMPA were more effective than BAL. NAPA increased hepatic mercury deposition. When given orally all compounds reduced kidney mercury deposition. Only DMSA reduced renal mercury deposition after ip injection. DMSA and DMPS significantly decreased mercury deposition in the brain and spleen. Neither NAPA nor BAL significantly affected brain or spleen mercury content. The authors conclude that the data confirm the results of previous studies that DMPS is a very efficient oral antidote for inorganic mercury poisoning.

92

TITLE:

Pathological changes in the Brown Norway rat cerebellum after mercury vapour exposure.

AUTHORS:

HUA J
BRUN A
BERLIN M

SOURCE:

TOXICOLOGY; 104 (1-3). 1995. 83-90.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Our previous studies have demonstrated that mercury vapour exposure of Brown Norway rats induced an autoimmune response with development of glomerulonephritis and resulted in mercury deposition in the central nervous system, particularly in the neurons. The

aim of this study was to investigate the effect on the central nervous system. A loss of Purkinje cells accompanied by Bergmann glial cell proliferation was found at a brain mercury level of 0.71 mug/g and became even more pronounced as the exposure dose increased. At a brain mercury level of 5.0 mug/g, a heavy gliosis was present in the brain stem, particularly around the pontine nuclei. In comparison with our previous study, the pathological changes in the brain appeared at the same mercury exposure dose as the glomerulonephritis. However, the location of pathological changes at the mercury level of 0.71 mug/g was not completely in accordance with the mercury distribution in the brain, which might be due to the seq

93

TITLE:

Distribution and Retention of Organic and Inorganic Mercury in Methyl Mercury-Treated Neonatal Rats

AUTHORS:

Thomas DJ
Fisher HL
Sumler MR
Hall LL
Musha P

SOURCE:

Environmental Research, Vol. 47, No. 1, pages 59-71, 29 references, 19881988

ABSTRACT:

The distribution and retention of organic and inorganic mercury (7439976) after treatment with methylmercury were studied in neonatal rats. Seven day old Long-Evans-rats were injected subcutaneously with 1 micromole mercury-203 labeled methylmercuric-chloride (115093). Selected rats were killed on days one to 32 postdosing to determine the tissue distribution of organic and inorganic mercury. Whole body retention of mercury was high during the first 10 days after exposure, 94 percent of the dose still being present after 10 days. Seventy one percent of the dose was present after 32 days. The highest concentrations of mercury in the kidney, liver, brain, pelt, skeletal muscle, and blood occurred 1 to 4 days after dosing. Total mercury concentrations decreased rapidly in all tissues except the pelt after 10 days. The concentration of mercury in the pelt increased over the 32 day period. Except for the pelt the percentage of mercury as organic mercury decreased with increasing time after dosing. The percentage of organic mercury in the pelt remained constant at around 91 percent over the 32 day period. The data were used to develop a compartmental model for the distribution of organic and inorganic mercury in neonatal rats. The model predicted that organic mercury was excreted solely from the blood compartment and inorganic mercury from the liver and

kidneys. Organic mercury was metabolized to inorganic mercury primarily in the liver. Inorganic mercury released by the liver into the blood was taken up by other tissues. The authors conclude that in neonatal rats treated with methylmercury, the pelt serves as a major reservoir for organic and inorganic mercury. Except in the pelt, demethylation of methylmercury to inorganic mercury occurs in all tissues.

94
TITLE:
The importance of organ blood mercury when comparing foetal and maternal rat organ distribution of mercury after methyl mercury exposure.

AUTHORS:
WANNAG A

SOURCE:
ACTA PHARMACOL TOXICOL; 38 (4). 1976 289-298

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Fetal rat brain was previously shown to contain twice as much Hg as maternal brain after maternal methyl mercury injection. When brain Hg is corrected for the Hg present in the blood of the brain, fetal rat brain will contain 4-5 times as much Hg as maternal brain (depending on the stage of gestation) 24 h after maternal methyl mercuric chloride injection. Even when methyl mercuric chloride was injected in the mother about 14 days before term, near-term fetal brain contains 1.4 times as much Hg as the maternal brain. When corrected for Hg in the blood of the organ, fetal rat liver also contains 2.0-2.6 times more Hg than maternal liver, and the fetal kidney contains 13-23 times less Hg than the maternal kidney. The amount of Hg in fetal blood is about 65% of the Hg in maternal blood 24 h after maternal methyl mercuric chloride injection; maternal and fetal bloods contain equal amounts 14 days after injection. Except for the fetal membranes, no inorganic Hg released by biotransformation of methyl mercuric chloride was detected in the fetal-placental unit.

95
TITLE:
Effect of amino acids on brain uptake of methyl mercury.

AUTHORS:
HIRAYAMA K

SOURCE:
TOXICOL APPL PHARMACOL; 55 (2). 1980. 318-323.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. To investigate the effect of amino acids on

the brain uptake of methyl mercury (MM), methyl mercury chloride (MMC), and some amino acids were injected i.v. to Wistar strain male rats (190 | 10 g). One hour after the simultaneous injection of 10 mumol and 100 mumol L-Cys to the rat, brain Hg content increased about 3 times as compared with that after a single injection of MMC alone. This effect of L-Cys was depressed by pre- and post-treatment with L-Phe, but not with L-Lys or L-Glu. BAL (2,3-dimercaptopropanol) also increased the brain uptake of MM. L-Phe did not exert an effect on the increased brain uptake of MM. When 10 mumol MMC was injected to the rat treated with L-Phe or L-Ile (pre-, simultaneous and post-treatment), brain Hg 2 h after the injection was lower than that after the single injection of MMC. At that time, there was no significant difference in blood and plasma mercury concentrations between the L-Phe-treated and nontreated rats. Treatment with L-Lys and L-Glu did not affect the brain Hg content after MMC injection. Brain Hg after the injection of 10 mumol MMC increased with time. The rate of increase was lowered by pre-, simultaneous and post-treatment with L-Phe for 2, 6, 9 and 12 h. When L-Phe injection was started 12 h after MMC injection and continued repeatedly for 12 h, the brain Hg content was low when compared with that after the single injection of MMC. Brain MM uptake is depressed by L-Phe and L-Ile, which are neutral amino acids, and not by L-Lys and L-Glu, which are a basic and an acidic amino acid, respectively.

96

TITLE:

Uptake Of Elemental Mercury By Brain In Relation To Concentration Of Glutathione And Activity Of Glutathione Peroxidase

AUTHORS:

Eide I

Syversen TLM

SOURCE:

Toxicology Letters, Vol. 17, No. 3-4, pages 209-213, 20 references, 19831983

ABSTRACT:

The uptake of elemental mercury (7439976) (Hg) in the brain was investigated in Sprague-Dawley-rats. Rats were given injections of 3.8 or 16.0 milligrams per milliliter (mg/ml) iodoacetate (64697) or 516mg/ml diethylmaleate (141059) into the lateral ventricle of the brain. Intraventricular injection of 60mg/kilogram (kg) radioactive Hg was given 30 minutes after iodoacetate or 60 minutes after diethylmaleate. Injections lasted for 90 seconds and animals were killed 3.5 minutes later. Brains were removed and homogenized. Tissue homogenates were counted in a gamma counter for determination of Hg. Reduced glutathione (GSH), caused by diethylmaleate dosing, and glutathione-peroxidase, caused by iodoacetate administration, were determined in brain homogenates of animals not treated with Hg. Inhibition of glutathione-peroxidase was 19

percent 30 minutes after administration of iodoacetate and GSH was decreased by 20 percent. After exposure to Hg, uptake by brain increased by 66 percent compared with untreated controls. Depletion of GSH by 34 percent with diethylmaleate did not affect Hg uptake by brain. The authors conclude that catalase represents a functional reserve capacity to glutathione-peroxidase in the decomposition of hydrogen-peroxide brain tissue, and an increased hydrogen-peroxide supply to catalase in brain tissue causes an increased oxidation rate of Hg.

97
TITLE:
Retention and distribution of mercury in organs of neonatal guinea pigs after in utero exposure to mercury vapor.

AUTHORS:
Yoshida M
Satoh H
Kojima S
Yamamura Y

SOURCE:
Journal of Trace Elements in Experimental Medicine 1990;3(3):219-26

ABSTRACT:
Mercury retention and distribution in organs of fetal and neonatal guinea pigs after in utero exposure to mercury vapor was investigated. Guinea pigs near term were exposed to mercury vapor at approximately 10 mg/m3 for 150 min. Two hours after exposure, the highest mercury concentration among fetal organs was found in the liver. In the other organs, such as the kidney, brain, heart, and lung, mercury concentrations were not markedly elevated. The neonates were fostered by nonexposed mothers to minimize possible mercury intake through the maternal milk. On days 5 and 10 postpartum, the highest concentration was found in the kidney, followed by the liver, lung, and brain. All the concentrations, except the liver, were clearly elevated when compared with the concentrations in fetuses. Sephadex G-75 gel chromatography showed that a substantial portion of the mercury in the fetal liver soluble fraction was associated with metallothionein. During the neonatal development period, metallothionein levels in the liver decreased and the mercury in the fetal liver soluble fraction was eluted in the high-molecular-weight region. These results suggested that mercury initially bound to hepatic metallothionein is further distributed. Studies on the toxicological significance of mercury, thus distributed, are necessary.

98
TITLE:
Persistent Mercury in Nerve Cells 16 Years after Metallic Mercury Poisoning

AUTHORS:
Hargreaves RJ
Evans JG
Janota I
Magos L
Cavanagh JB

SOURCE:
Neuropathology and Applied Neurobiology, Vol. 14, No. 6, pages 443-452, 20 references, 1988

ABSTRACT:
A case of metallic mercury (7439976) poisoning characterized by persistent nerve cell mercury accumulations was described. A male, aged 50 at death, developed tremors in both hands, drowsiness, constipation, a foul taste in the mouth, and other signs of mercury poisoning after he had worked for 18 months filling mercury thermometers. The tremors spread to his legs and later his whole body during the 3 months preceding hospitalization. A 1400 milliliter (ml) urine sample obtained at the time of hospitalization contained 1015 micrograms (microg) mercury. The blood mercury concentration was 48.1microg per 100ml. An electroencephalogram showed mild diffuse abnormal activity. He was treated with N-acetyl-penicillamine which resulted in a slow, incomplete recovery. A year later his tremors had improved, but he complained of forgetfulness and having odd ideas. He was never reemployed, became an alcoholic, and reported having epileptic fits. He died 16 years after first being treated. An autopsy found no histopathological changes attributable to mercury poisoning. Significantly elevated mercury concentrations were found in the kidney and brain. A large proportion of nerve cells in all brain regions contained lysosomal dense bodies that stained positive for mercury. X-ray analysis confirmed that mercury was present in the lysosomal bodies. Most of the deposited mercury was colloidal and was probably mercuric-sulfide or mercuric-selenide. The authors conclude that it is not possible to determine if the patient's psychoneurotic symptoms reflected the mercury accumulations in his nerve cells.

99
TITLE:
Uptake, Distribution and Immunotoxicological Effects of Mercury in Mice

AUTHORS:
Ryan DM
Sin YM
Wong MK

SOURCE:
Environmental Monitoring and Assessment, Vol. 19, Nos. 1-3, pages 507-517,

20 references, 1991

ABSTRACT:

The uptake, distribution, and immunotoxicity of mercury (7439976) were studied in mice. Female Swiss-albino-mice were administered 6.02 micrograms per gram (microg/g) mercury as mercuric-chloride (7487947) or mercuric-sulfide (1344485), 0.5microg/g mercury as mercuric-chloride, or 324microg/g mercury as mercuric-sulfide orally. The mice were killed 24 hours after dosing to determine mercury concentrations in the blood, intestinal tissue and contents, brain, liver, and kidneys. Other mice were administered 100 parts per million mercuric-chloride or mercuric-sulfide in their drinking water for 55 days. Some mice were killed after day 55 to determine the tissue mercury distribution. Other mice were injected with sheep red blood cells (SRBCs) or Trypanosoma-evansi. Antibody titers and the standard hematological parameters were determined in SRBC treated mice. Survival was monitored in mice injected with T-evansi. Mercury concentrations were significantly elevated in all tissues from mice given a single dose of mercuric-chloride. Except for increases in the intestinal contents and kidneys, tissue mercury concentrations in mice given mercuric-sulfide did not differ significantly from those of untreated mice. Other than in the intestinal tract, the kidneys contained the highest mercury concentrations in mercuric-chloride treated mice, followed by the liver and brain in that order. Fifty five days exposure to mercuric-chloride caused significant accumulations of mercury in all tissues. Mercuric-sulfide did not cause any significant tissue mercury accumulation. Mercuric-sulfide significantly increased antiSRBC titers and white blood cell counts. These effects were not seen in mercuric-chloride treated mice. T-evansi did not cause any deaths in mercuric-chloride or mercuric-sulfide treated mice. The authors conclude that solubility is an important factor that governs uptake of mercury into the body. Mercuric-sulfide appears to be less toxic than mercuric-chloride because of its low solubility.

100

TITLE:

Pathological Changes in the Brown Norway Rat Cerebellum after Mercury Vapour Exposure

AUTHORS:

Hua J
Brun A
Berlin M

SOURCE:

Toxicology, Vol. 104, Nos. 1-3, pages 83-90, 21 references, 1995

ABSTRACT:

The brain morphology was examined in mercury (7439976) vapor exposed

Brown-Norway-rats to establish the effect on the central nervous system. The high dose (HD) group was exposed to mercury vapor for 24 hours a day, 7 days a week at concentrations of about 1mg/m3 of air. The estimated absorbed amount of mercury at the end of the 5 week period was 264 micrograms/week/100 grams body weight. The low dose (LD) group was exposed to the same concentration but for 6 hours a day, 3 days a week for 5 weeks with the estimated amount absorbed being 35 micrograms/week/100 grams body weight. In all organs the mercury concentrations were higher in the HD than in the LD group. The kidney contained much more mercury than the other organs, but the mercury level increased by only 17% between the LD and HD groups, while the brain mercury level increased 608% between LD and HD animals. This was very close to the increase in the absorbed dose, which was 645%. The mercury exposed rats showed some pyknotic cells scattered in the granular layer of the cerebrum and many Purkinje cells undergoing degeneration. The Bergmann astrocytes increased in number in the HD but not in the LD group. In the white matter of cerebellum, GFAP positive cell bodies were increased in both mercury exposed groups. Brainstem sections from the DH group showed a strong GFAP positivity. Direct GFAP positive cell counting indicated that the HD group contained a larger number of GFAP positive cell bodies than the LD group.

101

TITLE:

Mercury distribution in the rat brain after mercury vapor exposure.

AUTHORS:

WARFVINGE K
HUA J
BERLIN M

SOURCE:

TOXICOL APPL PHARMACOL; 117 (1). 1992. 46-52.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Brown Norwegian rats were exposed to mercury vapor at a concentration of approximately 1 mg/m3 for 5 weeks 24 hr/day 7 days a week and 6 hr/day 3 days a week, respectively. The total mercury absorption was calculated to 264 and 35 mug per week and 100 g body weight. The mean blood mercury concentration was 0.25 | 0.03 and 0.09 | 0.01 mug/g, and the total concentration in the brain was 5.03 | 0.73 and 0.71 | 0.10 mug/g tissue, respectively. The mercury distribution in the brains was examined using a method based on chemographic principles. Mercury was found primarily in the neocortex, in the basal nuclei, and in the cerebellar Purkinje cells. This distribution pattern corresponded to the pattern of inorganic mercury described after exposure to methyl mercury. Distribution of mercury after administration of different mercury compounds is discussed.

102
TITLE:
Influence Of Mercury On Uptake Of (3H)Dopamine And (3H)Norepinephrine By Rat Brain Synaptosomes

AUTHORS:
Rajanna B
Hobson M

SOURCE:
Toxicology Letters, Vol. 27, No. 1-3, pages 7-14, 20 references, 19851985

ABSTRACT:
The in-vitro effects of mercuric-chloride (7487947) (MC) and methylmercury-chloride (115093) (MMC) on dopamine and norepinephrine uptake and on the sodium and potassium adenosine-triphosphatase (ATPase) system in rat brain synaptosomes were investigated. ATPase activities in synaptosomes prepared by the ficoll sucrose gradient method from normal, adult male Sprague-Dawley-rats were determined by an enzymatic method, measuring absorbance changes in the reaction mixture spectrophotometrically. Sodium and potassium ATPase activities were determined in the presence of 0 to 5 micromolar (microM) MC and 0 to 100microM MMC. Magnesium (mitochondrial) ATPase activity was measured in the presence of 1 millimolar ouabain, a specific inhibitor of sodium and potassium ATPase. Norepinephrine and dopamine synaptosomal uptake was determined by filtration in the presence and absence of 0 to 30microM MC and 0 to 100microM MMC. MC reduced the activities of sodium and potassium ATPase at a very low concentration compared to MMC. For sodium and potassium ATPase, the median inhibitory concentration (IC50) was 0.6microM for MC and 40microM for MMC. Both mercury compounds inhibited magnesium ATPase although again inorganic mercury was the more potent inhibitor. Inhibitory effects were concentrations dependent for both mercury compounds. The uptake of dopamine was reduced by both mercury compounds in a concentration dependent pattern. Organic mercury was less effective than inorganic mercury in reducing uptake, the IC50 being 2microM for MC and 50microM for MMC. Effects on norepinephrine uptake were similar, the IC50 values for MC and MMC being 5microM and 45microM, respectively. Synaptosomal norepinephrine uptake was more or less completely inhibited when 30microM MC or 100microM MMC were employed. The authors conclude that mercury compounds depress the ATP utilizing and synthesizing systems by inhibiting the sodium, potassium, and magnesium ATPases in brain synaptosomes, the effects of inorganic mercury being more severely toxic than those of organic mercury. Mercury metal may interact with the ATPase system due to its high affinity for sulfhydryl groups.

103
TITLE:
Interaction of Mercury Compounds with Muscarinic Receptor Subtypes in the

Rat Brain

AUTHORS:
Castoldi AF
Candura SM
Costa P
Manzo L
Costa LG

SOURCE:
Neurotoxicology, Vol. 17, Nos. 3/4, pages 735-742, 31 references, 1996

ABSTRACT:
The effects of mercury (7439976) as methylmercury (22967926) (MeHg) and mercuric-chloride (7487947) (HgCl2) on M1 and M2 muscarinic receptor subtypes was evaluated. Brain homogenates were obtained from male Sprague-Dawley-rats and incubated with either labeled telenzepine (TZ), the specific ligand for M1, or labeled AFDX384, the specific ligand for M2. Both MeHg and HgCl2 inhibited the binding of TZ to cortical and hippocampal M1 receptors. In rat cerebral cortex, the inhibition curve of HgCl2 fitted a single site model, and the concentration causing half maximal displacement of TZ was 2.2 micromoles. The curve for MeHg inhibition of TZ showed a biphasic profile, with high and low affinity components of 3.4 and 311 micromoles, respectively. In cerebral cortex, HgCl2 was a more potent displacer of AFDX384 binding to M2 receptors than MeHg. The inhibition curve for HgCl2 was steep, whereas that for MeHg was shallow. MeHg competitively inhibited both M1 and M2 receptor binding, showing a three fold increase of the dissociation constant. In contrast, HgCl2 showed a noncompetitive or mixed inhibition on the binding of TZ and AFDX384. HgCl2 induced a significant reduction of M1 and M2 receptor density. The authors conclude that in rat brain, MeHg and HgCl2 are more potent inhibitors of M1 than of M2 antagonist binding, suggesting that mercury may accumulate in the brain and impair cholinergic transmission at M1 muscarinic receptors.

104
TITLE:
Relation between Exposure Related Indices and Neurological and Neurophysiological Effects in Workers Previously Exposed to Mercury Vapour

AUTHORS:
Ellingsen DG
Morland T
Andersen A
Kjuus H

SOURCE:
British Journal of Industrial Medicine, Vol. 50, No. 8, pages 736-744, 26

references, 1993

ABSTRACT:

The relation between different indices of mercury (7439976) exposure and neurological and neurophysiological results among subjects with past exposure to mercury vapor was studied. The 77 chloralkali workers studied had been previously exposed for an average of 7.9 years to mercury at a concentration of 59 micrograms mercury/cubic meter in the working atmosphere. Individual mean urinary concentration of mercury for each year of exposure was 531 nanomoles mercury/liter. In general the average period of time between examination and the stoppage of mercury exposure was 12.3 years. Measures of cumulative exposure to mercury were associated with both the median sensory nerve conduction velocity and the amplitude of the sural nerve. There was also an association between the years since first exposure to mercury and aspects of the visual evoked response. Alterations in visual evoked response were also noted among previously exposed subjects with postural tremor or impaired coordination. The authors suggest that these findings may indicate an effect of previous exposure to mercury vapor on the nervous system, possibly in the visual pathway, cerebellum, and the peripheral sensory nerves.

105

TITLE:

Retention and distribution of mercury in organs of neonatal guinea pigs after in utero exposure to mercury vapor.

AUTHORS:

Yoshida M
Satoh H
Aoyama H
Kojima S
Yamamura Y

SOURCE:

Journal of Trace Elements in Experimental Medicine 1989;2(2-3):174

ABSTRACT:

Elemental mercury vapor (Hgo) penetrates the placenta barrier more easily than does inorganic mercury, and accumulates in the fetus. In fetal guinea pigs exposed to mercury vapor in utero, the highest mercury concentration was found in the liver, being about 1.5 times greater than that of maternal liver, but mercury concentrations in the brain and the kidney did not differ from those of the non-exposed fetuses. Gel chromatography on the Sephadex G-75 column revealed that a substantial portion of the mercury in the fetal liver was associated with metallothionein (MT)-like protein. Organ mercury distribution in day-5 postpartum neonates differed from that of the fetuses. In neonates, the highest concentration was found in the kidney, followed by the liver, lung, brain and heart, all of which

were higher concentrations than in non-exposed animals, respectively. The elution profile of the soluble fraction of the neonatal liver showed that most mercury was bound to a high molecular weight protein fraction. These results indicate that the mercury metabolism changes during the perinatal period and that studies regarding the toxicity of mercury during this period are necessary.

106
TITLE:
Distribution of Mercury in Neonatal Guinea Pigs after Exposure to Mercury Vapor

AUTHORS:
Yoshida M
Satoh H
Aoyama H
Kojima S
Yamamura Y

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 43, No. 5, pages 697-704, 14 references, 1989

ABSTRACT:
The accumulation and distribution of mercury (7439976) in neonatal animals after exposure to mercury vapor were investigated. Hartley-guinea-pigs, within 12 hours after parturition, were exposed to mercury vapor for 120 minutes in an exposure chamber. Both dams and neonates were exposed. Mercury concentration in the air was determined to be 8 to 10mg/m3. Immediately following exposure, the animals were injected with an anesthetic dose of ketamine-hydrochloride and blood samples were drawn from the heart into heparinized glass tubes. The animals were sacrificed. Elemental mercury that crossed the pulmonary membranes was rapidly oxidized into mercuric ions in the red blood cells. In the blood, the catalase activity was lower in neonates compared to the mothers. Neonatal livers also showed much lower activity of catalase, about one fourth that of the mothers. The mercury concentration in the neonatal whole blood was about 64 percent higher in the neonates than in the mothers. The mercury levels in the plasma of neonates were also two to three times higher than the concentrations in maternal plasma, but the erythrocyte levels were similar. Neonatal concentrations of mercury in the brain were 28 percent higher than in the mother, and 58 percent higher in the lung and 64 percent higher in the heart. Accumulation of mercury in the kidneys was lower in neonates than in mothers. In the liver, mercury concentrations in the neonates were slightly higher or similar to those in the mothers. These findings suggest that if organisms are accidentally exposed to a high concentration of mercury vapor, the central nervous system will be more severely damaged in neonates than in adults.

107
TITLE:
Metabolism of Mercury in Hamster Pups Administered a Single Dose of 203Hg-Labeled Methyl Mercury

AUTHORS:
Dock L
Rissanen R-L
Vahter M

SOURCE:
Pharmacology and Toxicology, Vol. 76, No. 1, pages 80-84, 45 references, 1995

ABSTRACT:
The metabolism of methylmercury (22967926) (MeHg) was studied in neonatal hamsters. Seven day old golden-Syrian-hamsters were injected subcutaneously with 0.4 nanomoles per gram mercury-203 (Hg203) (13982780) tagged MeHg. Whole body retention of Hg203 activity was measured immediately and up to 35 days after MeHg injection by gamma radiation counting as a measure of the MeHg body burden. Selected animals were killed 2, 7, 14, 21, or 28 days after MeHg and the livers, kidneys, and brain were removed, weighed, and analyzed for Hg203 activity. Whole body retention of Hg203 activity decreased in a manner indicative of a two component process. The decrease of the first, rapid component, which represented 60% of the dose, corresponded to a biological halflife of 8.7 days. The halflife for the second, slow component could not be determined from the data. The Hg203 content of the liver and brain decreased with time after the first week post injection. At the 28 day sampling point, the largest concentration of Hg203 occurred in the kidney followed by the liver and brain. Liver, kidney, and brain weights increased 11, five, and 2.5 times, respectively, during the study period by 28 days after dosage. After partitioning into MeHg and inorganic mercury (7439976) derived Hg203, the concentration of inorganic mercury in the liver and kidneys increased with increasing post injection time, although the total Hg203 concentrations decreased. The authors conclude that hamster pups injected with Hg203 tagged MeHg at 7 days of age eliminate Hg203 at a low rate, while brain uptake of Hg203 is greater than that previously measured in adult animals. The data also indicate that hamsters are able to demethylate MeHg within 2 weeks of age.

108
TITLE:
Elimination Pattern Of Methyl Mercury From Blood And Brain Of Rats (Dams And Offspring) After Delivery, Following Oral Administration Of Its Chloride Salt During Gestation

AUTHORS:
Casterline JL Jr
Williams CH

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 7, No. 5, pages 292-295, 5 references, 19721972

ABSTRACT:
The metabolic fate of methyl-mercury (22967926) was studied in rats. One group of pregnant Charles-River-rats was exposed to methyl-mercury in corn oil at 0.1, 0.5, or 2.5 milligrams per kilogram (mg/kg) from days 6 through 15 of gestation. Dams were allowed to litter normally, and the young were weaned at 28 days. All animals were observed for signs of toxicity. Three dams and ten female offspring were killed 30, 60, and 90 days after birth of the offspring. Another group of pregnant rats was exposed at 2.5mg/kg, and dams and offspring were killed 6, 13, and 20 days after birth. Rats were killed and blood was sampled. Brains, red blood cells, and plasma were assayed for methyl-mercury content by gas/liquid chromatography. No overt toxic signs were noted at any time in the dams or offspring. A small but statistically significant growth retardation was noted in offspring of dams exposed to the drug at 2.5mg/kg. Storage of the chemical was the highest in red blood cells, less high in the brain, and at a very low concentration in plasma. There was a steady decrease in methyl-mercury content in red blood cells and brains with time. Overall, clearance rates of methyl-mercury were more rapid in the offspring than in the dams. The authors conclude that there is a potential difference in clearance rates of methyl-mercury after exposure in dams and offspring. The process of elimination is a gradual one.

109
TITLE:
Mercury

AUTHORS:
Lauwerys R

SOURCE:
Encyclopaedia of Occupational Health and Safety, Vol. 2, pages 1332-1334, 4 references, 19831983

ABSTRACT:
Health and safety effects of chronic mercury (7439976) poisoning are reviewed. Mercury is found in nature in the form of sulphide (18496258) as cinnabar (19122793) ore, which has an average mercury content on 0.1 to 4 percent. The most important uses of metallic mercury and its organic compounds include the treatment of gold and silver ores; manufacture of amalgams; manufacture and repair of measurement or laboratory apparatus;

manufacture of incandescent electric bulbs, mercury vapor tubes, radio valves, X-ray tubes, switches, batteries, and rectifiers; laboratory research; photography; plating operations; and paint and artificial silk manufacture. Vapor inhalation is the main route for the entry of metallic mercury into the body; about 80 percent of inhaled mercury is absorbed into the alveoli. The main routes of entry of inorganic mercury are the lungs and gastrointestinal tract. After entry into the body, metallic mercury continues to exist for a short time in metallic form. The kidney and brain are the sites of deposition following exposure to metallic mercury vapors. Inorganic mercury is excreted mainly through the colon and kidneys. Within a group of workers, there is a good correlation between the amount of exposure to mercury and the concentration of metal in the blood and urine. Acute poisoning from mercury vapor inhalation may occur as a result of accidental contamination of poorly ventilated areas, during the extraction of mercury from its ore, or the heating of mercury based alloys. Chronic mercury poisoning usually starts insidiously and affects primarily the nervous system. Ventilation is the main safety measure; workers should be provided with respiratory protective equipment if ventilation is inadequate. Periodic medical examinations should be conducted to detect excessive exposure to mercury or signs of mercury poisoning. In cases of acute poisoning, symptomatic treatment should be supplemented by intramuscular administration of 2,3-dimercaptopropanol (598185).

110

TITLE:

Potential Health Hazard of Use of Mercury in Dentistry: Critical Review of the Literature

AUTHORS:

Enwonwu CO

SOURCE:

Environmental Research, Vol. 42, No. 1, pages 257-274, 95 reference, 19871987

ABSTRACT:

The health hazards of the use of mercury (7439976) in dentistry are reviewed, with special emphasis on the potential danger to patients of mercury vapor released from silver amalgam restorations. Sources of the human burden of mercury are discussed. Metallic mercury vapor and the short chain alkyl mercurials, especially methyl-mercury (22967926), are the most important physicochemical states of mercury to which man is exposed from a health standpoint. There is little available scientific literature on the metabolic fate of inhaled mercury vapor in man. Very little is known of the pharmacokinetics that convert an inhaled dose of elemental mercury vapor to the critical concentration in the brain. The molecular basis for mercury toxicity is considered. Mercury vapor and

methyl-mercury in toxic levels elicit behavioral changes and functional disturbances in the central and peripheral nervous systems, which often serve as sensitive indicators of mercury toxicity. Findings on mercury in dentistry are reviewed. The correlation between blood mercury levels and hand steadiness in dentists is considered. Subclinical polyneuropathies have been found in at least 30 percent of tested dentists having mercury tissue levels of more than 20 micrograms/gram. Skin hypersensitivity to mercury is correlated with duration of exposure in dental students. The potential role of silver amalgam restorations as serious intermittent but chronic sources of human exposure to mercury vapor in patients is assessed. Important areas requiring urgent research attention are listed.

111
TITLE:
Studies On The Toxicity And Metabolism Of Mercury And Its Compounds

AUTHORS:
Brown JR
Jose FR
Kulkarni MV

SOURCE:
Medical Services Journal, Canada, Vol. 23, No. 9, pages 1089-1110, 44 references, 19671967

ABSTRACT:
The toxic effects of mercury (7439976) and its compounds were investigated in male Wistar-rats. Animals were exposed to metallic mercury (7439976) and phenylmercuric-acetate (62384) vapor for 2 hours a day over a period of 5 days or injected with mercuric-chloride (7487947) intramuscularly for 12 days. Exposure to metallic mercury ranged from 1.6 to 12.7 milligrams (mg) of mercury per cubic meter. For phenylmercuric-acetate, the concentration ranged from 1.9 to 10.5mg of mercury per cubic meter. Animals injected with mercuric-chloride were given 1mg of mercury per kilogram (kg). D-penicillamine (52675) was injected intravenously at a daily dose of 100mg/kg and 2,3-dimercaptopropanol (59529) (BAL) at 10mg/kg for a period of 5 days. Urine and feces were collected daily throughout each experiment. At the end of the study, the animals were anesthetized and sacrificed. Specimens of blood, liver, lung, brain, heart, kidneys, testes, spleen, skin, and hair were obtained for comparison of their mercury content. Two animals from each group were used as controls. The blood concentration of mercury rose with exposure to mercury and its compounds and dropped when the mercury source was removed. During mercury exposure when the blood concentration of mercury was high, there was a corresponding increase in the amount of mercury eliminated in the urine. D-penicillamine did not increase the urinary and fecal excretion of mercury, but BAL promoted elimination of mercury through the urine and feces. The authors conclude that urinary and fecal mercury concentrations

increase with exposure and steadily decline when the exposure is stopped. BAL is effective in producing the elimination of mercury from the body.

112
TITLE:
The Effect of Mercurials on Amino Acid Transport and Rubidium Uptake by Isolated Rat Brain Microvessels

AUTHORS:
Tayarani I
Lefauconnier J-M
Bourre J-M

SOURCE:
Neurotoxicology, Vol. 8, No. 4, pages 543-552, 40 references, 19871987

ABSTRACT:
The effects of mercuric-chloride (7487947) (HgCl2) and methylmercury-chloride (115093) (MeHgCl) on the uptake of amino acids and rubidium-86 (14932537) (Rb) by isolated rat brain microvessels (BMV), as well as on the activity of gamma-glutamyl-transpeptidase (GTP), were studied. BMVs were isolated from Sprague-Dawley-rat brain homogenates and preincubated with various concentrations of HgCl2 or MeHgCl for 20 minutes at 37 degrees-C. The radiolabeled amino acids, alanine (ala), phenylalanine (phe), glutamic-acid (glu) or alpha-methylaminoisobutyric-acid (MeAIB) were then added and uptake of radioactivity was determined. The uptake of all four amino acids was reduced by more than 70 percent in the presence of 0.0001 molar (M) MeHgCl, with uptake inhibition of between 10 and 13 percent occurring at 0.00001M. No inhibition of uptake was observed at 0.000001 or 0.0000001M MeHgCl2. MgCl2 at 0.0005M inhibited the uptake of Ala, Phe, MeAIB and Glu by 38, 12, 5 and 10 percent respectively, and caused stimulation of uptake at 0.000001 and 0.0000001M. Uptake of Rb was measured in the presence or absence of 0.001M ouabain. Rb uptake inhibition in the presence of ouabain, with or without prior incubation with MeHgCl2 or MgCl2, was the same as in the presence of 0.0001M concentrations of either mercury compound in the absence of ouabain. The percent stimulation and inhibition of Rb uptake by the mercury compounds at 0.00001, 0.000001 and 0.0000001 in the absence of ouabain were similar to those of the amino acids. No significant difference was observed in the GTP activity between the control and the enzyme treated with either mercury compound. The authors conclude that mercury exhibits an inhibitory effect in BMVs at about 0.00001M, which is similar to the concentration of mercury estimated to be in the brains of victims of the accidental mercury poisoning in Minamata.

113
TITLE:

Legacy of the Mad Hatter.

AUTHORS:
Grant N

SOURCE:
Environment; 11(4), 18-23, 43-4, 1969; (REF:28)

ABSTRACT:
HAPAB The incidence of mercury poisoning has increased during the last two decades. Among the poisonous chemicals involved are the alkyl mercury compounds such as methylmercury which can diffuse more easily through biological membranes than other mercury compounds. Methylmercury penetrates the brain membrane, with the peak mercury concentrations in the brain appearing about 7 days after accumulation peaks in other organs. In poisoning cases related to methylmercury, there occurs a large number of symptoms relating to disturbances of balance and vision indicating that the parts of the brain which control coordination and visual perception are relatively greater targets of accumulation. Pathological examinations have shown that methylmercury causes widespread disintegration of brain cells. The symptoms may not appear until 2 months or more after exposure. The symptoms which at first may not be specific include fatigue, headache and irritability and are followed by tremor, numbness of the arms and legs, difficulty in swallowing, deafness, blurred vision and loss of muscular coordination. Other signs may include slurred speech and impairment of hearing which may make it difficult for the individual to understand what is happening. The victim as a result may become emotionally uncertain and withdrawn. The symptoms of acute mercurial poisoning, which can include muscular atrophy, may resemble those of amyotrophic lateral sclerosis. Poisoning due to methylmercury may result from eating contaminated grain or other foodstuff or being exposed to agricultural sprays containing the compound. Methylmercury has been shown to have a high capacity for penetrating membranes and can cause a great deal of damage in living tissue. Other mercury compounds can change into methylmercury and do the same damage. The consumption of mercury-contaminated food poses a real problem. The occurrence of numerous instances of environmental contamination by mercury emphasizes the need for controls and the necessity of developing an organized system for monitoring mercury. EPIDEMIOLOGY AND TREATMENT 70/12/00, 565 1969

114
TITLE:
Changes in the Number of Astrocytes and Microglia in the Thalamus of the Monkey Macaca fascicularis following Long-Term Subclinical Methylmercury Exposure

AUTHORS:
Charleston JS

Body RL
Bolender RB
Mottet NK
Vahter ME
Burbacher TM

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 127-138, 53 references, 1996

ABSTRACT:
Changes in thalamic cell populations induced by subclinical methylmercury exposure were studied in monkeys. Adult female monkeys (Macaca-fascicularis) were orally administered 50 micrograms per kilogram (microg/kg) mercury (7439976) as methylmercuric-hydroxide (1184572) (MMOH) daily for 6, 12, or 18 months (mo). One group given MMOH for 12mo was maintained for another 6mo without dosing (clearance group). Blood samples were collected periodically to determine the standard hematologic and clinical chemistry parameters. The animals were killed after 6, 12, or 18mo and the brains were removed. The left thalamus was used to determine changes in the numbers of neurons, oligodendrocytes, astrocytes, microglia, endothelial cells, and pericytes utilizing the optical volume fractionator stereological technique. The concentrations of accumulated mercury within the cells were measured by autometallographic methods. The right thalamus was used to determine the concentrations of inorganic and total mercury and methylmercury. No clinical signs of toxicity were seen in the monkeys. No hematologic or clinical chemistry abnormalities were detected. None of the MMOH exposures had any significant effect on the neuron, oligodendrocyte, endothelial cell, and pericyte populations. MMOH decreased the number of astrocytes by 44.6% after 6mo exposure, 23.1% after 12mo exposure, and 21.5% after 18mo exposure. Astrocyte numbers in the clearance group were decreased by 37.2%. The decreases in the 6mo exposure and clearance group were statistically significant. The numbers of microglia were increased by 6.3, 78.5, 228, and 162% in the 6, 12, 18mo exposure and clearance groups, respectively. Only the increases in the 18mo exposure and clearance group were statistically significant. The astrocytes and microglia contained significantly higher concentrations of inorganic mercury than the other cell types. Accumulations of methylmercury in the right thalamus plateaued at around 12mo, whereas the concentrations of inorganic mercury progressively increased. The authors conclude that inorganic mercury accumulating in the brain after long term subclinical methylmercury exposure may be the proximate toxic form of mercury that is responsible for inducing the changes in the astrocyte and microglia populations.

115
TITLE:
A Mortality Study Of Men Exposed To Elemental Mercury

AUTHORS:
Cragle DL
Hollis DR
Qualters JR
Tankersley WG
Fry SA

SOURCE:
Journal of Occupational Medicine, Vol. 26, No. 11, pages 817-821, 5 references, 19841984

ABSTRACT:
A survey of the mortality of workers exposed to elemental mercury (7439976) was conducted. The cohort consisted of 2133 white males who were exposed to mercury vapor between 1953 and 1963 at a facility of Union Carbide Corporation, Oak Ridge, Tennessee. The comparisons consisted of 3260 workers at the same installation who were not exposed to mercury. The vital status of the subjects was determined from Social Security Administration records through 1978. Standardized mortality ratios (SMR) were computed for both the cohort and comparison subjects. Attempts were made to correlate any excess deaths with extent and length of mercury exposure. Extent of exposure was determined from company data on air and urinary mercury concentrations. A total of 378 deaths occurred in the cohort and 710 among the comparisons. Death certificates were obtained for 703 of the comparisons and 371 of the cohort. A statistically significant excess of death from cancer of the lung, SMR of 1.34, and cancer of the brain and other central nervous system tissues, SMR of 2.30, occurred among the unexposed workers. An excess of lung cancer deaths, SMR of 1.34, was also observed among the mercury workers. There was no significant excess of deaths from diseases or cancers of organs considered to be target organs for mercury: liver, brain, central nervous system, and kidney. No excess of deaths could be correlated with extent or duration of mercury exposure. The authors conclude that the excess in mortality observed for cancer of the lung and brain and central nervous system tissues is not related to mercury exposure. The observed mortality pattern must be related to some other factor present in the facility or to some life style factor that is prevalent among workers at the facility.

116
TITLE:
Role of Testosterone in gamma-Glutamyltranspeptidase-Dependent Renal Methylmercury Uptake in Mice

AUTHORS:
Tanaka T
Naganuma A
Miura N
Imura N

SOURCE:
Toxicology and Applied Pharmacology, Vol. 112, No. 1, pages 58-63, 39 references, 1992

ABSTRACT:
The role of renal gamma-glutamyltranspeptidase (GTP) in determining sex and age related differences in renal mercury (7439976) uptake was investigated. Participation of a sex hormone in methylmercury-chloride (115093) (MMC) uptake was also studied. ICR-mice received 1 micromole per kilogram MMC injections at 2, 3, 4, 6, and 8 weeks of age. Male mice received a testosterone injection of 5mg/kg every day for 7 days beginning 7 days after castration. Four week old female mice were injected with testosterone daily for 14 days. Urine and blood samples were collected and kidney, liver, spleen, brain, heart, and lung were removed for weighing. One kidney of each mouse was used for mercury analysis and the other for GTP determination. Four hours after MMC injection, renal mercury accumulation was sex and age dependent. Mercury content was two fold higher in male mice compared to female mice and increased five fold between weeks 2 and 8 in male mice. In brain, heart, lung, and plasma the mercury content slightly but significantly decreased with age. Mercury concentrations in urine were low and unrelated to differences in age and sex. Sex and age patterns were correlated for GTP activity and renal mercury uptake. Renal mercury content and GTP activity in males were decreased to levels in females following castration and returned to control levels after subsequent testosterone treatment. In female mice treated with testosterone, renal GTP activity and mercury content increased to the levels in males. Castration and testosterone treatment did not affect the mercury content in the urine or nonkidney tissues. The authors suggest that testosterone partially controls renal GTP activity and thus affects renal methyl-mercury accumulation.

117
TITLE:
On Estimating Threshold Limits for Mercury in Biological Materials

AUTHORS:
Berlin M

SOURCE:
Acta Medica Scandinavica, Supplement 396, 29 pages, 37 references, 19631963

ABSTRACT:
A brief historical review of the study of occupational exposure to mercury (7439976) is presented and the basis for the present maximum allowable concentration values of mercury compounds is examined. Important factors in the determination of the tolerable body burden of mercury are

discussed, notably the body distribution of mercury after exposure, and the risk of cumulation in different organs. In acute exposure the kidney and liver accumulate much mercury and are hence liable to injury, while recent findings indicate that in chronic exposure to moderate levels of mercury the brain and possibly testes are the critical organs because of a pronounced tendency to cumulation. The possibility of obtaining an index of mercury retention is explored; it is concluded that urinary mercury excretion does not reflect the level of body retention although it may indicate very recent exposure. It is suggested that mercury concentration in biopsies of skin, liver, kidney and colonic mucosa may serve as an index of body retention of mercury.

118

TITLE:

Localization of Mercury in CNS of the Rat. II. Intraperitoneal Injection of Methylmercuric Chloride (CH3HgCl) and Mercuric Chloride (HgCl2)

AUTHORS:

Moller-Madsen B

SOURCE:

Toxicology and Applied Pharmacology, Vol. 103, No. 2, pages 303-323, 54 references, 1990

ABSTRACT:

Mercury (7439976) localization in the central nervous system (CNS) following exposure to methylmercuric-chloride (115093) (MMC) and mercuric-chloride (7487947) (MC) was studied in rats. Adult Wistar-rats were injected intraperitoneally with 0 or 100 micrograms (microg) MC daily for 2 to 100 days. Other rats were injected with 100microg MMC daily for 2 days or 200microg MMC daily for 2 to 50 days. The rats were observed for clinical signs of toxicity. Selected rats were killed at various times and the brain and upper cervical spinal cord were removed and examined for mercury by light and electron microscopy. In rats given cumulative MMC doses of 4000 to 10000microg, progressive coordination disorders such as unsteady gait, hind limb weakness, and hind limb crossing were observed. In MC treated rats, mercury deposits were detected by light microscopy in the spinal cord and cerebrum after 2 days of treatment. Mercury was detected in deep cerebellar nuclei but only after 100 days dosing. In MMC treated rats, mercury was detected in the spinal cord and cerebrum after 10 days dosing and in Purkinje cells and cerebellar deep layer nuclei after 40 daily doses. Electron microscopy revealed heavy mercury deposits in the motor nuclei of the rhombencephalon after either MC or MMC. In MMC treated rats, heavy staining for mercury was seen in laminar layer-III, layer-V, and layer-VI of the cerebral cortex and cerebellar Purkinje, golgi, and golgi epithelial cells. Heavy staining was seen in motoneurons of the spinal cord and glia and in ependymal cell cytoplasm. In MC treated rats, significant staining was

seen in laminar layer-VI of the cerebral cortex. Heavy staining for spinal cord motoneurons was seen. The extent of staining increased with increasing cumulative dose. Ependymal cells were stained to a lesser extent. The cell structure that consistently stained for mercury after either MMC or MC was the cytoplasmic lysosomes. The author concludes that the pattern of mercury distribution in the rat CNS depends on the nature of compound and the length of exposure.

119
TITLE:
Mercury Accumulation in the Eye Following Administration of Methylmercury

AUTHORS:
DuVal G
Grubb BR
Bentley PJ

SOURCE:
Experimental Eye Research, Vol. 44, No. 1, pages 161-164, 18 references, 19871987

ABSTRACT:
Accumulation of mercury (7439976) in the eye following methylmercury exposure was studied in rabbits. Male New-Zealand-White-rabbits were administered methylmercuric-chloride (115093) by surgically implanted osmotic minipumps over a 21 day period. The total dose administered was 21mg/kg. Blood samples were taken initially and at 1 week intervals. At the end of the experiment, 21 days, the rabbits were killed, and the eyes were removed. The lens, cornea, iris/ciliary body, retina, and aqueous and vitreous humors were analyzed for mercury. Brain, liver, blood, and plasma samples were also analyzed for mercury. Mercury concentrations of 12.8, 2.4, 6.0, 3.5, 0.12, and 0.06mg/kg were found in the lens, cornea, iris/ciliary body, retina, aqueous humor, and vitreous humor, respectively. Mercury concentrations in the other tissues were brain 8.1mg/kg, liver 25.3mg/kg, blood 6.2mg/kg, and plasma 0.35mg/kg. Lenses from horses, cattle, and dogs, and human lenses from an eye bank were also analyzed for mercury. Mercury concentrations of 20 to 44 micrograms per kilogram (microg/kg) were found in lenses from four of ten horses and 32 to 96microg/kg in five of nine dogs. No mercury was detected in lenses from cows or humans. The authors suggest that the lens could be an indicator of mercury accumulation in the eye.

120
TITLE:
Mercury

AUTHORS:
Skerfving S

SOURCE:

Biological Monitoring and Surveillance of Workers Exposed to Chemicals, A. Aitio, V. Riihimaki, and H. Vainio, Editors, Washington, D. C., Hemisphere Publishing Corporation, pages 29-39, 38 references, 19841984

ABSTRACT:

Occupational exposure to mercury (7439976) and its compounds was reviewed. Occupational exposure primarily involves exposure to elemental mercury vapor, however, in some situations, considerable exposure to mercuric mercury salts and to organic mercury compounds may also occur. Critical organ and initial toxic effects of elemental mercury vapor exposure were discussed, and metabolism of elemental mercury was considered. Mercury has the ability to pass the blood/brain barrier. It also accumulates in the kidney. Metallic mercury is oxidized to mercuric mercury in the body. Upon evaluating the monitoring of mercury exposure, it was noted that no study has demonstrated a good correlation between air and urinary or blood mercury concentrations. Risk monitoring studies have shown correlations between blood and urinary mercury concentrations and the frequency of symptoms and signs of mercury poisoning. An even stronger correlation has been found between ambient air mercury concentrations and symptomatology. Air mercury concentrations of 100 to 200 micrograms per cubic meter (microg/m3) have been associated with the incidence of tremors. Nonspecific symptoms have been associated with concentrations on the order of 50microg/m3. The World Health Organization has recommended an occupational exposure limit of 25microg/m3 mercury vapor in air.

121

TITLE:

Mercuric Chloride-Induced Alterations of Levels of Noradrenaline, Dopamine, Serotonin and Acetylcholine Esterase Activity in Different Regions of Rat Brain during Postnatal Development

AUTHORS:

Lakshmana MK
Desiraju T
Raju TR

SOURCE:

Archives of Toxicology, Vol. 67, No. 6, pages 422-427, 24 reference, 1993

ABSTRACT:

The effects of mercuric-chloride (7487947) (MC) consumption on levels of brain monoamines and acetylcholinesterase activity in various regions of the brains of Wistar-rats were examined. The rats were fed 4mg/kg mercuric-chloride per day from postnatal day two through day 60 by gastric intubation. MC treatment was then discontinued and the rats were allowed to recover until day 170. Control rats were treated with saline. The MC

treated rats showed deficits in both body and brain weights at 10, 20, and 60 days which recovered to control levels by 170 days. The MC treated group demonstrated elevated noradrenaline (NA) levels in olfactory bulb (OB), visual cortex (VC) and brain stem (BS) regions of the brain, but not in striatum accumbens (SA) or hippocampus (HI). Increased levels of dopamine (DA) were also noted in the OB, HI, VC, and BS, but not in the SA. A decrease was observed in acetylcholinesterase activity in the MC group only in HI and VC at 20 days of age. No behavioral abnormality was outwardly noted in the mercury treated group. However, it was noted that there was a deficiency in performance. After the intake of mercury (7439976) was stopped, all of these changes were reversed. The authors concluded that the exposure to these levels of oral mercury resulted in adaptive neural mechanisms rather than in pathological and irreversible damage.

122

TITLE:

Levels of Hg, Pb and V in brain, kidney, liver and lung of anencephalic fetuses from the Eastern coast of Lake Maracaibo, Venezuela.

AUTHORS:

Tahäan JE
Barrios LC
Marcano L
Granadillo VA
Cubilläan HS
Säanchez JM
Rodriguez MC
De Salazar FG
Salgado O
Romero RA

SOURCE:

Trace Elements and Electrolytes 1996;13(1):7-13

ABSTRACT:

This work describes the levels of mercury (Hg), lead (Pb) and vanadium (V) in brain, kidney, liver and lung of anencephalic (A) and control (C) fetuses from the Eastern coast of Lake Maracaibo (Venezuela) evaluated from April 1993 to July 1994. A relatively high anencephaly rate of 5.1 per 1,000 total births was reported in this area for 1994. A petroleum empire has grown indiscriminately in the region under study, provoking adverse effects in the environment and in humans due to the constant release of these toxicants. Sample analyses were done by cold vapour atomic absorption spectrometry (for Hg), differential pulse anodic stripping voltammetry (for Pb) and electrothermal atomization atomic absorption spectrometry (for V). Twenty stillborn fetuses with anencephaly (mean gestation age 34.4 weeks, range 20-40 weeks) and 20 still born

fetuses without anencephaly (mean gestation age 38.5 weeks range 36-40 weeks), included as controls, were considered for the present study. All births occurred at "Pedro Garcäia Clara" Hospital, a public health care center of Ciudad Ojeda (Lagunilla county). Before the spectrometric and voltammetric determinations, samples were mineralized by microwave heating in high-pressure reactors. For all metals, precision (RSD) was better than 5.3%, for both within- and between-run (day-to-day) analyses, which can be considered adequate for these types of analytical evaluations of real samples. Accuracy was tested by analyzing 4 standard reference materials, supplied by 2 international agencies. The dry-weight metal concentrations (mean +/- 1 SD, ug/g) found in brain, kidney, liver and lung were as follows: Hg (brain, 0.07 +/- 0.01 in A, undetectable in C; kidney, 0.29 +/- 0.05 in A, 0.07 +/- 0.03 in C; liver, 0.33 +/- 0.03 in A, 0.17 +/- 0.08 in C; lung, 0.45 +/- 0.40 in A, 0.12 +/- 0.01 in C); Pb (brain, undetectable in A and in C; kidney, 1.9 +/- 0.3 in A, 0.7 +/- 0.3 in C; liver, 2.1 +/- 0.3 in A, 1.1 +/- 0.5 in C; lung, 3.3 +/- 0.4 in A, 0.5 +/- 0.1 in C); V (brain, 0.25 +/- 0.18 in A, 0.64 +/- 0.28 in C). Mercury and Pb were significantly increased (p less than 0.001) in kidney and liver of anencephalic fetuses. Vanadium was detected exclusively at brain level, being significantly higher in controls (p less than 0.05). Hence, V seems to be the most unlikely of the 3 elements studied to be associated with anencephaly. In conclusion, Hg and Pb are toxic elements present in the Eastern coast's environment that should be seriously considered for cause/effect studies when the etiology of anencephaly in this region is considered. However, this malformation is multifactorial and, thus, a more complete study must be carried out in order to be able to reach conclusive ideas, if this is possible. Meanwhile, anencephaly will continue to be a puzzling disease.

123

TITLE:

Mercury and Its Compounds (Inorganic)

AUTHORS:

Barlow SM

Sullivan FM

SOURCE:

Reproductive Hazards of Industrial Chemicals; London, England, Academic Press, pages 386-406, 47 references, 19821982

ABSTRACT:

The available data on reproductive hazards associated with exposure to inorganic mercury (7439976) compounds were reviewed. Inorganic mercury compounds were used in many products, including: instruments, switches, fluorescent lamps, mercury boilers, mirrors, dental amalgams, electric reactifiers, pharmaceutical agents, and agricultural chemicals. Subcutaneous administration of inorganic mercury or exposure to mercury

vapor disrupted the estrous cycle and reduced fertility in female rodents. Single intraperitoneal injections of organic or inorganic mercury transiently reduced fertility in male rodents, due primarily to an action on spermatogonia and spermatocytes. Exposure of female rats to mercury vapor prior to mating did not affect fertility, but significantly increased postnatal mortality of offspring. Exposure during pregnancy increased the incidence of stillbirths and resulted in almost complete postnatal mortality. There was limited evidence that inorganic mercury was teratogenic in laboratory animals. Reduced libido and potency were reported in men exposed to toxic levels of mercury vapor. There were several reports of menstrual disturbances in women occupationally exposed to mercury vapor. There was inadequate data to assess the effects of inorganic mercury exposure in human pregnancy. Organic and inorganic mercury crossed and were accumulated in the placenta in humans. Mercury was excreted in breast milk at levels lower than maternal plasma levels, but there was some evidence that mercury was more readily absorbed and was retained in the brain of neonates. The authors conclude that there is limited experimental evidence that exposure to inorganic mercury reduces fertility in males and females, and is teratogenic and affects postnatal survival in rats.

124

TITLE:

Methylmercury Exposure during Lactation: Milk Concentration and Tissue Uptake of Mercury in the Neonatal Rat

AUTHORS:

Sundberg J
Oskarsson A
Albanus L

SOURCE:

Bulletin of Environmental Contamination and Toxicology, Vol. 46, No. 2, pages 255-262, 17 references, 1991

ABSTRACT:

The dose dependent transfer of mercury (7439976) into milk and to the neonate was studied in lactating Sprague-Dawley-rats treated with methylmercuric-chloride (115093). The uptake of mercury in tissues and blood was followed in the offspring exposed via milk. On day nine of lactation the mothers received a single oral dose of radiolabeled methylmercuric-chloride. Group-I animals received 0.5mg/kg mercury; Group-II, 3.3mg/kg; Group III, 7.8mg/kg; and Group-IV, 9.4mg/kg. Milk was collected from all dams at 24 and 72 hours after the oral dose. After a nursing period of 72 hours, blood and milk were collected from the dams, and all rats were sacrificed. A linear dose related transfer of mercury from plasma into milk was demonstrated. The relationship at 24 hours indicated that the milk level was approximately 10% of the level in

plasma. The relationship between the mercury concentration in plasma and breast milk after 72 hours was also linear. The mercury concentration in milk remained at a similar level at 72 hours as at 24 hours. There was a linear relationship between the mercury concentration in the erythrocytes and breast milk of the dams. The plasma level of mercury was low compared to the erythrocyte level. A close correlation between the mercury concentrations in the erythrocytes of the dams and their pups at 72 hours was noted. The mercury levels in plasma in the dams and their pups were less strongly correlated. As a dose indicator of the exposure of mercury to pups, the tissue uptake of mercury in the pups was also plotted against the mercury concentration in milk. There was a good correlation obtained, especially in the brain and kidney.

125

TITLE:

Effects Of Trace Metals And Their Derivatives On The Control Of Brain Energy Metabolism

AUTHORS:

Bull RJ

SOURCE:

Biochemical Effects of Environmental Pollutants, Lee, S. D., Editor; Ann Arbor Science Publishers, Inc., Ann Arbor, Michigan, pages 425-440, 27 references, 19771977

ABSTRACT:

The effects of lead (7439921), methyl-mercury (22967926), and their derivatives on brain energy metabolism control were studied in rats. Sprague-Dawley-rats were injected intraperitoneally with lead-chloride (7758954) 6 times over 2 weeks for total doses of 3, 12, or 60 milligrams per kilogram (mg/kg) lead. Animals were killed 2 days after the final injection. Rats had 0.01 to 2mg/kg methyl-mercuric-chloride (115093) injected daily for 14 days. Animals were killed on day 15. Tissue slices approximately 0.34 millimeter thick from the first layer of the cerebral cortex were prepared and measured for respiration, glycolytic rate, and redox state of electron transport intermediates. Some tissues were treated in-vitro with an alkyltin derivative to measure metabolic responses to potassium. Tissues from control and lead treated rats were labeled with calcium-45. The turnover of tissue calcium was measured. Lead in brain tissue and mercury (7439976) in the cerebral cortex were determined by atomic absorption spectrophotometry. Brain concentrations of lead increased 0.6 times for each dose from 3 to 12mg/kg lead and increased 0.5 times between 12 and 60mg/kg lead. Cerebral cortex slices had altered metabolic responses to potassium that first appeared at approximately 0.41 microgram per gram (microg/g) lead and 0.1microg/g mercury. Lead and methyl-mercury treatment increased the rate of nicotinamide-adenine-dinucleotide-phosphate (NADP) reduction relative to

controls in a dose dependent fashion. Respiratory response to potassium was significantly depressed. Lead treated tissues significantly depressed the transient increase of calcium efflux induced by potassium. Mercury content in the cerebral cortex was proportional to the dose administered. Organotin derivatives inhibited the net reduction of NADP; triethyltin (997502) was more potent than dimethyltin (23120992) and dibutyltin (1002535). The author suggests that lead, methyl-mercury, and alkyltin compounds affect brain energy metabolism.

126
TITLE:
Effects of long-term treatment with methyl mercury on the developing rat brain.

AUTHORS:
LINDSTROM H
LUTHMAN J
OSKARSSON A
SUNDBERG J
OLSON L

SOURCE:
ENVIRON RES; 56 (2). 1991. 158-169.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Sprague-Dawley rats were exposed to low doses of methyl mercury (3.9 mg mercury/kg diet), via their dams during gestation and lactation and directly via diet until sacrifice at 50 days postpartum, in order to study possible detrimental effects on CNS development. The methyl mercury exposure of the rats resulted in a brain concentration of 1.45 | 0.06 mg mercury/kg wet weight (mean | SEM). No general toxic effects were observed; body weight was not affected, brain weight was only slightly increased. No discernible general morphological alterations were seen in the brain as evaluated using cresyl violet histology. Furthermore, no effects of GFA-positive astrocytes in brain sections were observed and computerized morphometry of smeared astrocytes from frontal cortex, hippocampus, and cerebellum did not reveal any effects of the methyl mercury treatment. The noradrenaline (NA) and dopamine (DA) systems were also studied. In cerebellum the NA levels were increased (117% of co

127
TITLE:
Research of toxic effects on the quail of methyl mercury and methoxyethyl mercury, organo-mercurial fungicides.

AUTHORS:
Godfrain JC

Rico AG
Burgat-Sacaze V
BenM'Lih D
Braun JP
Benard P

SOURCE:
Rev. Med. Vet. (Toulouse)124(8-9): 1019-1039; 1973(REF:16)

ABSTRACT:
PESTAB The subacute toxicity of methylmercury and methoxyethyl mercury fungicides was studied in quail 5-weeks-old. The animals were fed grains containing ppm of methyl mercury and methoxyethyl mercury silicate (Ceregam), respectively, for 15 days. Total anorexia and cachexia and a 15-day mortality of 60% were determined in the group fed methyl mercury-containing grains. Progressive anorexia, but increased gain of weight were observed in the group fed Ceregam-contaminated grain. Animals which ingested methyl mercury exhibited hypertrophy of the liver, kidney, and intestines; edema of the brain; and immaturity of the genitals. Quails fed Ceregam displayed enteritis, fatty degeneration of the liver, and nephritis. The latter group also showed reduced creatinie, albumin, and uric acid levels. The quails fed methyl mercury-containing grain showed increased cholesterol, total protein, creatinie, and albumin levels and lowered uric acid level. The mercury residue, determined on the 16th day of the experiment in the livers, kidneys, and brains of the methyl mercury-treated animals, was 154 ppm, 128 ppm, and 48 ppm, respectively. The highest mercury levels in the corresponding organs of the Ceregam-treated quails were 29 ppm, 40 ppm, and 3. 31 ppm. Methyl mercury was a nerve poison, while Ceregam primarily caused renal lesions.

128
TITLE:
Sex and Strain Differences of Susceptibility to Methylmercury Toxicity in Mice

AUTHORS:
Yasutake A
Hirayama K

SOURCE:
Toxicology, Vol. 51, No. 1, pages 47-55, 13 references, 19881988

ABSTRACT:
Sex and strain differences in susceptibility to methylmercury (22967926) toxicity were studied in mice. BALB/cA-mice and C57BL/6N-mice were given 0 or 5mg/kg methylmercury-chloride (115093) per day for up to 49 days by gastric intubation. They were observed for clinical signs of toxicity.

Urine and feces were collected and assayed for mercury (7439976). Selected mice were killed at various times between 5 and 43 days and the concentrations of mercury in the brain, liver, kidney, blood, and plasma were determined. All mice died by day 49. C57BL males had the longest survival, followed by C57BL females, BALB females, and BALB males in that order. Body weight loss and decreased consumption of food and water appeared 4 to 7 days before death. Urinary excretion of mercury by C57BL males increased to 15 percent of the dose within 1 week, decreasing thereafter. Urinary mercury excretion by all other mice peaked at less than 5 percent of the dose. Fecal excretion of mercury was similar in all groups. Except for the kidney, there was a monotonous increase in tissue mercury concentrations with time until the onset of toxic symptoms. Brain, blood, and plasma concentrations increased more rapidly after symptoms developed. Renal mercury concentrations increased rapidly during the first 10 days and plateaued thereafter. Tissue mercury concentrations were lowest in C57BL males. The authors suggest that the kidney has two compartments with different uptake rates for methylmercury. The first compartment with a higher uptake rate is easily saturated. Once saturation is achieved, renal function is disturbed. This results in a decrease in urinary excretion of mercury, thereby leading to an accumulation of mercury in the body and the appearance of toxic symptoms.

129

TITLE:

Developmental effects of combined lead, mercury and ethanol exposure on neurophysiological processes in rats.

AUTHORS:

Nagymajtäenyi L
Däesi I
Schulz H
Papp A
Vezäer T

SOURCE:

Neurotoxicology 2000 Aug;21(4):628-9

ABSTRACT:

The results of our previous investigations showed that low dose of lead, mercury administered in the different stages of ontogenesis dose and phase-dependently altered certain neurophysiological processes. In this study the alterations of some neurophysiological parameters of rats simultaneously treated by lead/mercury and ethanol were analyzed. Female Wistar rats (P generation) were treated by gavage with 80.0 and 320.0 mg/kg lead (in form of C4H6O4Pb(3H2O)), 0.4 and 1.6 mg/kg mercury (in form of HgCl2), 5% ethanol in drinking water, or with the combination of the mentioned doses from day 5 to 15 during pregnancy, or from day 5 to 15 of pregnancy + for 4 weeks of lactation, or from day 5 to 15 of pregnancy +

for 4 weeks of lactation + the male offspring (F1 generation) for 8 weeks after weaning. The neurophysiological investigations (ECoG, cortical evoked potentials, etc.) were performed at the age of 12 weeks of F1 rats. The number of newborn rats/litter, their average weight and the body weight gain of the treated rats were lower, but the differences compared to the control were not significant; clinical symptoms of lead, mercury, or ethanol intoxication were not seen even in the groups administered their combination. The electrophysiological parameters were dose-, combination- and treatment variation-dependently changed, in case of the higher lead/mercury dose, and lead/mercury + ethanol administration the alterations compared to the control were significant, compared to the single lead, mercury administration were more, but insignificantly expressed. The results showed that, depending on the period of administration during the development, the combined lead/mercury and ethanol exposure caused considerable neurophysiological alterations of the central and peripheral nervous system without any other toxicological changes. One can suppose that the combination of these chemicals can also be a real, higher risk for human being, especially during the early development of the nervous system.

130

TITLE:

Effects of perinatal methyl mercury exposure on the development of central nervous system and immune function in the rat offspring.

AUTHORS:

Sundberg J
Oskarsson A
IlbÓack NG
LÓarkfors L
LindstrÓom H
Luthman J
Ebendal T
Olson L

SOURCE:

Journal of Trace Elements in Experimental Medicine 1992;5(2):137-8

ABSTRACT:

Effects on the development of central nervous system (CNS) and immune function were studied in the offspring of rats exposed to methyl mercury (MeHg) in the diet. In addition the placental and lactational transfer of mercury was compared and the chemical form of mercury was determined in blood of the offspring. Female rats were given a diet containing 3.9 ug Hg/g as MeHg during 11 weeks prior to mating, during gestation and lactation. The results showed that the placental transfer of mercury was more efficient than the transfer via milk. All mercury in blood of the offspring exposed only via placenta was found as MeHg, whereas

approximately 80% of the total mercury level was found as MeHg in the offspring exposed only via milk. Demethylation of MeHg is suggested to occur in the dam and resulting in inorganic mercury being transferred to the offspring via the milk. The present study indicates that perinatal MeHg exposure does adversely affect the developing immune system of the rat. The lymphoproliferative response to T-cell mitogen was increased in the thymus, but decreased in the spleen. A reduced activity of the natural killer (NK) cells was also observed in the group exposed to mercury both via placenta and milk. The effects of maternal MeHg exposure during the development of the CNS was studied in offspring exposed via placenta and milk and thereafter directly via the diet. This exposure resulted in a brain concentration of 1.5 ug Hg/g tissue. No effects on the morphological maturation of neurons and astrocytes in the brain were found in the present study. However, a slight increase in the noradrenaline level in cerebellum was shown. Furthermore, a decreased level of nerve growth factor was found in the septum and an increased level in the hippocampus. Thus, perinatal MeHg exposure in low doses via the diet could adversely affect the development of the central nervous system and immune function in the rat offspring.

131

TITLE:

The Effect of Cadmium Pretreatment on the Disposition and Excretion of Methylmercury and Trace Elements (Zinc, Copper) in Rats

AUTHORS:

Komsta-Szumska E
Miller DR

SOURCE:

Toxicology and Industrial Health, Vol. 2, No. 4, pages 337-349, 24 references, 19861986

ABSTRACT:

The effect of cadmium (7440439) on disposition and excretion of methylmercury (22967926) was studied in rats. The effects on endogenous zinc and copper concentrations were also investigated. Male Wistar-rats were injected subcutaneously with 0 or 3mg/kg cadmium-chloride (10108642) three times weekly for 4 weeks, then kept 3 weeks without any treatment. They were then given 0 or 3mg/kg mercury-203 (Hg-203) labeled methylmercury orally three times a week for 2 weeks. Urine and feces samples were collected for Hg-203 analysis. The animals were killed on day 64 and plasma, red blood cells (RBCs), kidneys, liver, spleen, cerebrum, and cerebellum were assayed for inorganic and organic mercury, cadmium, zinc, and copper. When given alone, the largest accumulation of methylmercury was found in the RBCs, followed by the kidneys, spleen, liver, cerebrum, cerebellum, and plasma, in that order. Cadmium pretreatment significantly decreased mercury in the kidneys and RBCs, but

had no effect on mercury content in other organs. Cadmium also significantly inhibited demethylation of methylmercury in the kidneys. Cadmium did not affect urinary excretion of total mercury, but increased fecal excretion of total mercury. Cadmium significantly decreased endogenous copper in the spleen, brain (cerebrum and cerebellum), and blood of methylmercury treated rats. Methylmercury alone significantly increased renal copper and decreased copper in the plasma and brain. In animals given cadmium only, copper concentrations in the liver, spleen, and RBCs were reduced. Methylmercury alone increased kidney zinc content and reduced plasma zinc. Cadmium increased kidney, liver, and brain zinc and reduced plasma zinc relative to controls and methylmercury treated animals. The authors conclude that cadmium pretreatment may decrease methylmercury toxicity by increasing fecal mercury excretion and inhibiting formation of inorganic mercury in the kidney.

132

TITLE:

Modulation of Protein Kinase C by Heavy Metals

AUTHORS:

Rajanna B
Chetty CS
Rajanna S
Hall E
Fail S
Yallapragada PR

SOURCE:

Toxicology Letters, Vol. 81, Nos. 2/3, pages 197-203, 38 references, 1995

ABSTRACT:

The in-vitro effects of mercury (7439976) or lead (7439921) were studied on partially purified protein-kinase-C (PKC) of rat brain. PKC was prepared from male Sprague-Dawley-rat brain tissue. The PKC activity of rat brain was found to be significantly inhibited by metal cations in a concentration dependent manner with IC50 of 1.5, 2.12, and 0.22 micromolar (microM) for mercuric-chloride (7487947), lead-acetate (15347576), and methyl-mercuric-chloride (115093), respectively. A significant stimulation of the basal PKC activity was observed in the presence of PS and calcium-chloride. Preincubation of PKC with different concentrations of thiol compounds followed by 1microM mercury or lead reduced the inhibition of both basal and PS stimulated PKC activities. A concentration dependent protection of dithiothreitol against metal inhibition was noted for both basal and PS stimulated PKC. The inhibition of basal PKC by lead was not protected by glutathione, but a concentration dependent protection of glutathione was noted against lead inhibition of phosphatidylserine stimulated PKC. The authors conclude that dithiols but not monothiols effectively protect metal inhibited activity of PKC in rat

brain.

133
TITLE:
Mercury level and histochemical distribution in a human brain with Minamata disease following a long-term clinical course of twenty-six years.

AUTHORS:
TAKEUCHI T
ETO K
TOKUNAGA H

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 10 (4). 1989. 651-658.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Details are given of the mercury level and deposition in a human brain with Minamata disease following a twenty-six year clinical course after the first severe attack in 1956. This is the first report of a case in which the methylmercury level within the brain has returned to normal limits in a severely affected victim. However, the total mercury remained high in the brain, and mercury was clearly demonstrated histochemically in microglial cells or macrophages over wide areas of the brain and in neurons of specific brain areas. Bergmann's glial cells also contained mercury deposits, whereas Purkinje's cells had relatively little or no deposition. Mild deposition of the metal was demonstrable in the epithelial cells of the choroid plexus.

134
TITLE:
Strain Difference of the Mouse in Manifestation of Hydrocephalus following Prenatal Methylmercury Exposure

AUTHORS:
Inouye M
Kajiwara Y

SOURCE:
Teratology, Vol. 41, No. 2, pages 205-210, 16 references, 1990

ABSTRACT:
Strain related differences in the induction of hydrocephalus following prenatal methylmercury exposure were studied in mice. Pregnant B10.D2-mice were dosed orally with 10mg/kg methylmercuric-chloride (115093) (MMC) on days 14 through 17 of gestation. Pups were killed on postnatal day 30 and the brains were removed and examined for hydrocephalus. Brain mercury (7439976) concentrations were determined.

Pregnant DBA/2CrSlc-mice (D2) and C57BL/10SnSlc-mice (B10) were administered 10mg/kg MMC on day 15 of gestation. Neonatal mice were killed on postnatal day 30 and examined for hydrocephalus. Brain mercury concentrations were measured. The weaning rate of newborn B10.D2-mice exposed to MMC was low and most surviving mice developed hydrocephalus. The incidence rates of grossly apparent hydrocephalus in mice exposed on days 14, 15, 16, or 17 of gestation were 67, 88, 75, and 48%, respectively. The incidence rate in control mice was 5%. The brains of some treated mice showed slight dilatation of the lateral ventricles. Prenatal exposure of B10-mice to MMC resulted in a hydrocephalus incidence rate of 54%. The incidence rate in the controls was 0.8%. Hydrocephalus was not detected in D2-mice. Brain mercury concentrations generally ranged from 5.5 to 9.2 micrograms per gram and did not vary significantly between strains. The authors conclude that the susceptibility of mice to methylmercury induced hydrocephalus is genetically controlled.

135

TITLE:

Immunohistochemical Localization of Metallothionein in Organs of Rats Treated with Either Cadmium, Inorganic or Organic Mercurials

AUTHORS:

Tohyama C
Ghaffar A
Nakano A
Nishimura N
Nishimura H

SOURCE:

Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 155-165, 17 references, 1991

ABSTRACT:

The immunohistological localization of metallothionein (MT) in the kidneys and brain of rats treated with cadmium (7440439) (Cd), or inorganic or organic mercury (7439976) (Hg) compounds were examined. Male Wistar-rats were injected with either cadmium at 0.5mg/kg as single or repeated doses, or injected with mercury-chloride (7487947) or methyl-mercury-chloride (115093) at daily doses of 0.74 or 8.0mg/kg, respectively, for 4 days. Kidneys and whole brains were removed from rats for immunohistological staining. MT concentrations in the organs were determined by radioimmunoassay. Cd, copper, and zinc in the kidney, and total and inorganic concentrations of Hg were determined by spectrometric methods. A single dose of Cd resulted in MT staining primarily in the proximal tubular epithelium, while multiple Cd doses resulted in very strong MT immunostaining in both the proximal and distal epithelium. Treatment of rats with inorganic Hg caused a relatively high concentration of MT in

conjunction with increases in Cd, copper, and zinc accumulation in the kidney. MT immunostaining was found in ependymal cells, arachnoid, vascular endothelial cells, pia mater, and some glials in the brain after treatment with either inorganic or organic Hg; other areas showed a minimal amount of MT immunostaining. The authors conclude that the induction of MT in capillary endothelia may suggest its role with barrier function upon induction by heavy metals such as mercury and cadmium.

136
TITLE:
Nondestructive Synchrotron Radiation X-Ray Fluorescence Imaging of Trace Elements on Methylmercury and Selenium Administered Guinea Pigs

AUTHORS:
Shimojo N
Homma S
Nakai I
Iida A

SOURCE:
Analytical Letters, Vol. 24, No. 10, pages 1767-1777, 15 references, 1991

ABSTRACT:
A study was conducted to determine the dynamics of the distribution of mercury (7439976), zinc (7440666), copper (7440508), and selenium (7782492) in the brain of guinea-pigs exposed to methylmercury and selenium. Male Hartley-guinea-pigs were administered methylmercury-chloride (115093) or sodium-selenite (10102188) every day for 10 days subcutaneously at 3mg/kg mercury. Mole ratio of mercury/selenium was 1:1. The animals were sacrificed the day after the last dose. Using nondestructive x-ray fluorescence imaging, two dimensional distributions of mercury, zinc, copper and selenium were determined in the brain. In the brain of the guinea-pigs exposed to methylmercury or both methylmercury and selenium, high correlations were observed between mercury and zinc, copper, and selenium. Much lower correlation was noted for nontreated or animals treated only with selenium. Use of this method caused no damage to the samples. The space resolution of the current method was lower than that of microPIXE. However the current beam size will be very useful in investigating the change of trace element distributions macroscopically.

137
TITLE:
Accelerated Uptake Of Mercury By Brain Caused By 2,3-Dimercaptopropanol (BAL) After Injection Into The Mouse Of A Methylmercuric Compound

AUTHORS:
Berlin M

Jerksell L-G
Nordberg G

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 23, No. 4, pages 312-320, 10 references, 19661966

ABSTRACT:
The effect of 2,3-dimercaptopropanol (59529) (BAL) on brain mercury (7439976) concentrations was investigated in CBA-mice. Two experiments were performed. In the first, mice were injected once intravenously with 0.5 milligram per kilogram (mg/kg) radioactive methylmercuric-dicyandiamide (502396). The treatment group was simultaneously given 0.3mg/kg BAL intravenously. Animals were sacrificed either 1 hour or 1, 4, 8, or 16 days after injection. Sagittal sections of 20 micrometers thickness were isolated and autoradiograms were prepared. In experiment 2, mice were injected intraperitoneally with radioactive methylmercuric-dicyandiamide corresponding to 0.5mg/kg mercury. Animals were injected once daily for 16 days. The treatment group was injected simultaneously intramuscularly with 2mg/kg BAL. After 16 days, the animals were sacrificed and brain, lung, liver, testes, myocardium, and a sample of striated muscle were removed. Tissue radiation levels were measured. Results were presented as autoradiograms and in histogram form. Specific quantitative measures were not given. In general, mercury disappeared rapidly from blood in BAL treated animals and within 1 hour it was distributed throughout the body in a pattern reached only after 8 days in controls. In the treatment group, however, mercury appeared early in the brain and within 24 hours reached the same concentration seen in controls after only 8 days. At 8 or 16 days, mercury distribution in the two groups was almost identical. The authors conclude that mercury penetrates more rapidly into all tissues of animals treated with BAL compared with animals that do not receive BAL treatment.

138
TITLE:
In Vitro and In Vivo Effects of Lead, Methyl Mercury and Mercury on Inositol 1,4,5-Trisphosphate and 1,3,4,5-Tetrakisphosphate Receptor Bindings in Rat Brain

AUTHORS:
Chetty CS
Rajanna S
Hall E
Yallapragada PR
Rajanna B

SOURCE:
Toxicology Letters, Vol. 87, No. 1, pages 11-17, 30 references, 1996

ABSTRACT:

The in-vitro and in-vivo effects of mercury (7439976), methyl-mercury (22967926) (MM), and lead (7439921) were investigated on inositol-1,4,5-trisphosphate (IP3) and inositol-1,3,4,5-tetrakisphosphate (IP4) receptor binding activities in the rat brain. Rats were treated with 25mg/kg lead-acetate (301042), 5mg/kg mercuric-chloride (7487947), or 5mg/kg methyl-mercury-chloride (115093). Lead and MM treatments enhanced the binding of IP3 and IP4 to their receptors in cerebellum in a concentration dependent manner. A similar enhancement in these receptor binding activities was noted on in-vivo treatment with lead or MM except for short term intervals of 3 and 24 hours. Both in-vitro and in-vivo treatments suggest that lead and MM alter both the receptor binding activities which in turn can influence the levels of intracellular calcium concentration in neuronal cells. The authors suggest that lead or MM may be allosterically changing the conformation of IP34 receptor to increase the ligand binding. They also suggest that lead or MM may play a similar role of calcium mediator for these receptors increasing in the ligand binding. Further kinetic studies of these receptors need to be performed./ISOLATION & PURIF

139

TITLE:

Distribution and Excretion of Some Mercury Compounds After Long Term Exposure

AUTHORS:

Ulfvarson U

SOURCE:

Internationales Archiv fuer Gewerbepathologie und Gewerbehygiene, Vol. 19, pages 412-422, 6 references, 19621962

ABSTRACT:

Rats were treated with cyanides, hydroxides and propanediolmercaptides of the methyl mercury, ethyl mercury and propyl mercury cations, in amounts equivalent to 2 micrograms of pure mercury, in order to determine the distribution of the metal in the brain, liver, kidney and blood. The results show that the first 3 members of the homologous series of alkyl mercury salts exhibit great stability of the body between the metal and the organic radical. The methoxyethyl mercury also seems to be stable, while the mercury (7439976) ion in phenyl mercury presents slow chemical changes. The biological half-life of the methyl mercury salts is 15 to 20 days, as compared to 4-10 days for methoxyethyl mercury hydroxide. Half-life data for the unstable mercury-nitrate (10045940) and phenyl-mercury-hydroxide (100572) are difficult to determine.

140

TITLE:
Mercury

AUTHORS:
Battigelli MC

SOURCE:
Environmental and Occupational Medicine, pages 449-463, 67 references, 19831983

ABSTRACT:
Mercury (7439976), some compounds of mercury, and their effects on the human body are reviewed. The uses, the mining and the processing of mercury, and its properties are presented. The biological effects of mercury resulting from exposures by inhalation, ingestion, and cutaneous routes are discussed. Distribution of mercury throughout the body is reviewed for effects on kidney, brain, and blood. Distribution of mercury in tissues and body fluids depends on the solubility of the mercury. Partitioning of mercury in tissue is reviewed. Metal mercury vapor is oxidized in blood and tissues to the divalent ionic form. Inorganic and organic mercury compounds tend to be eliminated with time. The metabolism and excretion of mercury are presented. Dose/response correlations are discussed for inorganic, elemental, and organic mercury compounds. The clinical presentation of elemental and inorganic mercury includes both acute and chronic exposure. Mercurial tremor is the principal and most common result of protracted, intense exposure to these forms of mercury. Five degrees of tremor are described. Erethism is one of the earliest expressions of toxicity. Other disorders are presented. The clinical presentation of exposure to toxic organic compounds is noted for mercurial diuretics, the aryl compounds, and alkyl derivatives. Minamata disease, resulting from toxicity by mercury alkyl compounds, is described. Pathology is reviewed according to the organ or site involved, including the central nervous system, kidneys, oral mucosa, endocrine glands, and respiratory system. Diagnosis of mercury intoxication and diagnostic laboratory data are presented. Treatment methods and their efficacy are reviewed.

141
TITLE:
Effects of Endogenous and Exogenous Thiols on the Distribution of Mercurial Compounds in Mouse Tissues

AUTHORS:
Aihara M
Sharma RP

SOURCE:
Archives of Environmental Contamination and Toxicology, Vol. 15, No. 6,

pages 629-636, 36 references, 19861986

ABSTRACT:

CD-1-mice were treated intraperitoneally with either methylmercuric-chloride (115093) (MeHg) or mercuric-chloride (7487947) (HgCl2), in doses equivalent to 5 and 10 milligrams of mercury (7439976) (Hg) per kilogram to determine the process by which the metal diffused into the central nervous system. Cold vapor absorption spectrometry was used to determine the concentration of Hg in the organs. Treatment with MeHg was followed by an increase of brain mercury up to 3 days after the administration of the compound while the levels of Hg in the blood declined following a 24 hour increase, the same pattern as in the liver and in the kidney; the first order rate of passage of Hg into brain was linear up to 24 hours for both doses used. A stable erythrocyte to plasma ratio, ranging from 5 to 7 was recorded at all times. Treatment with HgCl2 did not result in high Hg levels in the brain; the rate of entry in the brain was linear up to 24 hours after treatment, similar to the rates obtained with both doses of MeHg; initially, Hg was equally distributed in erythrocytes and plasma and then gradually increased. Blood and brain Hg levels were not affected by the administration of L-cysteine while the levels of Hg in the liver and kidneys declined. Treatment with diethylmaleate resulted in glutathione depletion and increased levels of Hg in the brain of animals treated with MeHg, while the levels of Hg declined in the kidney and increased in the blood and in the liver. The authors conclude that exogenous or endogenous thiols such as L-cysteine and glutathione may alter the distribution of mercuric ions in other organs without facilitating its entry in the brain.

142

TITLE:

Preliminary studies on methylmercury biotransformation and clearance in the brain of primates: II. Demethylation of mercury in brain.

AUTHORS:

LIND B
FRIBERG L
NYLANDER M

SOURCE:

J TRACE ELEM EXP MED; 1 (1). 1988. 49-56.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Total and inorganic mercury content was determined in the brains of monkeys exposed daily for 1-3 years to methylmercury (MeHg) via oral intake. A cold vapor atomic absorption spectrophotometry method according to Magos was used for the analysis. Total mercury analysis was performed also by radiochemical neutron activation analysis. Brains from two nonexposed monkeys had 1.4 and 2.3 ng

total Hg/g w.w. Brains from eight monkeys exposed to 50 mug Hg/kg b.w./day for at least 1.5 years contained 4,597-7,017 ng Hg/g w.w. of which 477-1,593 ng Hg/g w.w. was in inorganic form (10-33%). Brains from monkeys who received 90 mug Hg/kg b.w./day for 0.5-1.5 years but were sacrificed 0.5-2 years after the end of exposure had 52-314 ng total Hg/g w.w., of which about 90% was in inorganic form. This indicates a longer biological half-time for part of the inorganic mercury accumulated in the brain. The MeHg used for feeding the monkeys contained a 5% impurity (inorganic Hg), but this doe

143

TITLE:

HgEDTA Complex Inhibits GTP Interactions with the E-Site of Brain beta-Tubulin

AUTHORS:

Duhr EF
Pendergrass JC
Slevin JT
Haley BE

SOURCE:

Toxicology and Applied Pharmacology, Vol. 122, No. 2, pages 273-280, 46 references, 1993

ABSTRACT:

The effect of mercury complex (HgEDTA) on guanosine-triphosphate (GTP) interactions with the E-site of brain beta-tubulin was studied in-vitro. S1 fractions isolated from human brain tissue were incubated with 0 to 101 micromolar (microM) mercury (7439976) (Hg) as mercuric-chloride (7487947) and phosphorus-32 labeled 8-azidoguanosine-5'-triphosphate (AzGTP) in the presence or absence of 94microM EDTA (60004) or magnesium ion (Mg+2) as magnesium-chloride for 5 minutes. The effects on GTP tubulin interaction were assessed by measuring the degree of incorporation of AzGTP into the E-site of tubulin (AzGTP uptake) using a photoaffinity assay and gel electrophoresis. A slight decrease in uptake was induced by 101microM Hg+2. When EDTA was present in the medium with 4 or 10microM Hg+2, the extent of AzGTP uptake was sharply decreased. The combination of EDTA and 4microM Hg+2 completely abolished AzGTP uptake. EDTA alone caused a small decrease in AzGTP uptake. Mg+2 alone increased the extent of AzGTP uptake. In the presence of nonchelated Hg+2, Mg+2 had only a slight effect. S1 fractions from human brain homogenates were incubated with 0 to 6microM preformed HgEDTA in the presence of AzGTP or Mg+2. HgEDTA caused a dose related inhibition of AzGTP uptake. Mg+2 did not significantly alter the inhibitory effect of HgEDTA. S1 fractions from human brain homogenates were incubated with 6.0microM EGTA chelated Hg+2 or Hg+2 chelates formed with malic-acid, citric-acid, pyridinedicarboxylic-acid and AzGTP. HgEGTA caused a significant

inhibition of AzGTP uptake. EGTA alone and the other chelates did not significantly affect AzGTP uptake. Neither HgEDTA nor HgEDTA significantly altered photolabeling of any other GTP proteins in tubulin. The authors conclude that HgEDTA and HgEGTA disrupt the interaction of GTP with the E-site of brain tubulin, the obligatory first step in tubulin polymerization. Since Hg+2 is widespread in the environment and EDTA is widely used in foodstuffs and pharmaceuticals, these mercury complexes may present a serious human health hazard.

144

TITLE:

Rapid Changes in Concentrations of Essential Elements in Organs of Rats Exposed to Methylmercury Chloride and Mercuric Chloride as Shown by Simultaneous Multielemental Analysis

AUTHORS:

Muto H
Shinada M
Tokuta K
Takizawa Y

SOURCE:

British Journal of Industrial Medicine, Vol. 48, No. 6, pages 382-388, 25 references, 1991

ABSTRACT:

Changes in essential element concentration induced by methylmercuric-chloride (115093) (MMC) and mercuric-chloride (7487947) were studied in rats. Male Wistar-rats were injected subcutaneously with 10mg/kg MMC or 1mg/kg mercuric-chloride. Selected rats were killed 3, 6, 12, or 24 hours later and the brain, liver, and kidneys were removed and assayed for sodium, potassium, manganese, calcium, iron, magnesium, aluminum, copper, zinc, and mercury (7439976). Mercury accumulated in the brain, liver, and kidney in a time dependent manner after MMC or mercuric-chloride. The largest accumulation occurred in the kidney. The highest brain zinc concentrations occurred in MMC treated rats 3 hours after dosing. The highest brain calcium concentrations occurred at 12 hours in MMC dosed rats. The highest kidney copper concentrations occurred in mercuric-chloride dosed rats after 24 hours. Maximal kidney zinc concentrations occurred in MMC treated rats 3 hours after dosing. Tissue sodium and potassium concentrations were generally higher in mercuric-chloride treated rats than in MMC dosed rats. Principal component analysis indicated that after mercuric-chloride exposure brain iron and manganese concentrations showed time dependent increases that could be correlated with decreases in kidney copper, potassium, and sodium concentration and liver copper concentration. After MMC treatment brain zinc, manganese, copper, aluminum, and calcium and kidney zinc and copper concentrations showed time dependent increases that could be correlated

with decreases in liver copper concentration. The authors conclude that exposure to MMC and mercuric-chloride at lethal concentrations causes rapid changes in the concentration of certain essential elements in the brain, kidney, and liver.

145
TITLE:
Localization of Mercury in CNS of the Rat. IV. The Effect of Selenium on Orally Administered Organic and Inorganic Mercury

AUTHORS:
Moller-Madsen B
Danscher G

SOURCE:
Toxicology and Applied Pharmacology, Vol. 108, No. 3, pages 457-473, 33 references, 1991

ABSTRACT:
A detailed mapping was conducted of mercury (7439976) containing cells in the central nervous system from rats treated per-os for 3 months with methylmercuric-chloride (115093) or mercuric-chloride (7487947) alone or in combination with sodium-selenite (10102188). The ultrastructural localization of mercury within the identified target cells and the effect of selenite on this localization were determined. Male Wistar-rats were used in the study. In animals treated with methylmercuric-chloride, sodium-selenite induced a conspicuous increase in mercury staining of nerve cell bodies in specific areas of the central nervous system, including laminae III-VI in the cerebral cortex, thalamus, hypothalamus, and brain stem nuclei. The cortical Purkinje cells and nerve cells in the deep nuclei of the cerebellum were targets for appreciable mercury accumulations after methylmercury treatment. Staining was limited to the gray matter in the spinal cord following administration of methylmercury alone. Selenite increased the intensity of the staining and deposits also appeared in the white matter. No staining of the Purkinje cells was noted following treatment with mercuric-chloride alone or combined with selenite. The most intense neuronal staining was noted in sections taken from rats treated with a combination methylmercury-chloride and selenite. In animals treated with mercuric-chloride the same cell types were targets for mercury deposits, although staining was to a significantly lesser degree. Concurrent treatment with selenite had no visible effect on the staining pattern. Selenium treatment delayed the functional toxic effects of methylmercuric-chloride.

146
TITLE:
Mercury vapour kinetics and toxicology

AUTHORS:
Magos L

SOURCE:
Central European Journal of Occupational and Environmental Medicine 1995, Vol.1, No.4, p.319-326. Illus. 21 ref.

ABSTRACT:
Experiments were carried out to determine why inorganic mercury salts are renotoxic and mercury vapour is neurotoxic. Investigations involved use of radiolabelled mercuric salt for the labelling of mercury vapour, separation of elemental and mercuric mercury in blood, intravenous injection of elemental mercury and mercuric mercury into rats, and estimation of mercury vapour in exhaled air. Results indicate that elemental mercury is taken up by the blood by diffusion and owing to a delay between uptake and oxidation, part of the inhaled mercury vapour is able to reach and cross the blood-brain barrier.

147
TITLE:
Changes in Axonally Transported Proteins in the Rat Visual System Following Systemic Methyl Mercury Exposure

AUTHORS:
Aschner M

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 59, No. 2, pages 151-157, 25 references, 19861986

ABSTRACT:
Protein synthesis and axonal transport were analyzed in rat retinal ganglion cells following in-vivo methyl-mercury treatment. Female Long-Evans-rats received methyl-mercury-chloride (115093) at a dose level of 4 milligrams (mg) of mercury (7439976) per kilogram/day (kg/day) for 4 to 6, or 12 days. One eye was injected with 3 microliters tritiated proline 24 hours (hr) after the last treatment. Rats were killed 1 to 8hr later. Axonal transport in the optic nerve and tract was examined by liquid scintillation spectrometry. Rats treated for 5 days at the same dose level were injected with tritiated proline, then sacrificed for autoradiographic examination of axonal transport. In animals treated with 8mg/kg/day for 8 days, the optic nerve, optic tracts, and retinas were analyzed for protein content and aliquots of homogenized samples taken for SDS polyacrylamide gel electrophoresis. In control animals, transported radiolabel reached the lateral geniculate body in 8hr. In methyl-mercury treated rats, radiolabel was found in the lateral geniculate body 4hr after injection. At each sacrifice time, protein bound radioactivity in the retina was greatly increased by methyl-mercury treatment.

Autoradiographic evaluation at 4hr after proline injection showed label density exceeding background levels in the lateral geniculate body only in methyl-mercury treated rats. Methyl-mercury intoxication did not involve extensive changes in polypeptide composition in the cell body or axonal extension. Significant alterations were apparent in growth associated proteins. Brain and blood mercury concentrations increased with increasing exposure in a blood/brain ratio of approximately 13/1. The authors conclude that this exposure regimen appears to offer a suitable experimental model with which to investigate the mechanism of action and cellular response to methyl-mercury induced injury.

148

TITLE:

Symposium on clinical observations on public nuisances and agricultural pesticide poisonings. 3. Organic mercury poisoning.

AUTHORS:

Tokutomi H

SOURCE:

Nippon Naika Gakkai Zasshi; 57(10), 1212-6, 1968; (REF:17)

ABSTRACT:

HAPAB Clinical an/ experimental studies were conducted on alkyl mercury (AM) and phenyl mercury acetate (PMA); the former is the causative agent of Minamata disease and the latter is a major agricultural pesticide. A follow-up was done of 26 to 34 mercury poisoning cases ten years later. Exclusive neurological disorders still persisted with little or no improvement. No human case of PMA poisoning has so far been reported. Determinations of mercury hair levels in farmers and nonfarmers in three control districts in Japan showed that farmers had higher mercury values than nonfarmers. The experimental studies were conducted with cats fed 2 to 4 mg daily of various AM compounds. Within 20 to 30 days, all the animals had died in states of extreme convulsions. Mercury excretion varied with the nature of the tested compound but was higher in the feces than in the urine. The excretion mercury values increased in the latter half of the feeding period which indicated that mercury accumulated in the organs during the first to second weeks. PMA was fed to rats in 0.5, 1.0, 2.0 and 3.0 mg daily for 3 weeks. The results were similar to those obtained with the cats. Mercury levels in the organs from the AM Feeding were heaviest in the order: liver, hair, liver kidneys and brain; from the PMA feeding, the heaviest mercury levels were in the order: kidneys, hair, liver and brain. Histologically, AM caused striking and extensive damage in the cerebellum and cerebrum but slight or little change elsewhere. PMA effected only minor changes. EPIDEMIOLOGY AND TREATMENT 69/12/00, 442 1968

149

TITLE:
Human Brain Disturbance by Methylmercury Poisoning, Focusing on the Long-Term Effect on Brain Weight

AUTHORS:
Takeuchi T
Eto K
Kinjo Y
Tokunaga H

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 187-190, 15 references, 1996

ABSTRACT:
A study of changes in brain weight in victims of environmental methylmercury (22967926) poisoning was conducted. Long term changes in brain weight were evaluated as a marker of brain disturbance, in persons from the Minamata area of Japan who became sick after eating seafood contaminated with methylmercury (Minamata disease) approximately 40 years (yr) earlier. The study material consisted of brains obtained at autopsy between 1970 and 1972 from 417 persons (273 females) who lived in the Minamata area and 2,934 persons (760 females) without any history of brain disease who died from accidental causes (controls). All subjects were at least 30yr old at the time of death. Among the controls, the mean brain weights of the males and females were 1,400 and 1,300 grams (g), respectively. The weights of the brains from the Minamata area residents were decreased compared to those of the controls. The decreases ranged from 80 to 200g. The authors conclude that the reduced brain weights seen in the Minamata area residents are consistent with the view that methylmercury exposure causes long lasting effects on brain weight. Since some of the Minamata residents had systemic disorders such as atherosclerosis and pneumonia, the possibility that these disorders may be associated with decreased brain weights could not be excluded.

150
TITLE:
Follow-up of methylmercury concentration in brain areas of developing rats exposed during prenatal life using cold-vapor absorption spectrometry

AUTHORS:
Braghiroli D
Parenti C
Di Bella M
Monzani A
Zanoli P
et al

SOURCE:

Boll. Chim. Farm.; VOL 129 ISS Jul-Aug 1990, P259-262, (REF)

ABSTRACT:

IPA COPYRIGHT: ASHP The amount of mercury in the brain was 10-100 times higher in rats prenatally exposed to methylmercury than in controls at 21 days of age, while it was equal to controls at 60 days of age. Mercury may or may not correlate with neurotoxicity because it could be present in active or inactive bound form in different brain regions. The data suggest that there is a crucial sensitivity of cells in the different brain areas that may explain the presence of short and long lasting effects after an acute exposure during gestation to a fixed dose of methylmercury.

151

TITLE:

Interactions Between Selenium And Mercury In Mice: Marked Retention In The Lung After Inhalation Of Metallic Mercury

AUTHORS:

Khayat A
Dencker L

SOURCE:

Chemico-Biological Interactions, Vol. 46, No. 3, pages 283-298, 20 references, 19831983

ABSTRACT:

The distribution of mercury (7439976) in the lung following selenite (14124675) pretreatment was studied in mice. Male C57BL-mice were injected intraperitoneally with saline or 10 micromoles per kilogram sodium-selenite (10102188). Mice were then exposed to radioactive mercury vapor for 1 hour. The livers, kidneys, hearts, lungs, and other internal organs were then assayed for radioactivity. Mercury rapidly decreased in the lungs after 24 hours with a concomitant increase in the liver and kidney. In sodium-selenite pretreated animals, the lungs retained mercury 9 times the amount in the controls after 24 hours. The increase of mercury in liver and kidneys was delayed by sodium-selenite pretreatment. Serum mercury concentrations were relatively constant for 24 hours. In the heart and brain mercury concentration did not differ in sodium-selenite pretreated animals and controls. The distribution of mercury in the myocardium, the periportal hepatocytes, or the renal cortex was not different in sodium-selenite pretreated mice. Sodium-selenite pretreatment caused a more marked retention of mercury in animals injected with mercury than in those which had inhaled mercury. The authors conclude that selenite increases mercury retention by intracellular interaction.

152

TITLE:

Elemental and inorganic mercury poisoning.

AUTHORS:
YOSHIDA M

SOURCE:
JAPANESE JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH; 44 (3). 1998. 168-181.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury exists as elemental mercury (liquid mercury or mercury vapor), inorganic mercury salts (mercurous or mercuric), and organic mercury compounds (aryl- or alkylmercury). Due to the different chemical and physiological properties of all forms of mercury the effects of mercury on humans shows quite different clinical pictures. In this paper, mercury vapor and inorganic mercury poisoning are mainly reviewed. Liquid mercury, since it is poorly absorbed from the gastrointestinal tract, is nontoxic. Mercury vapor (Hgo) is absorbed rapidly from the alveolar membrane by inhalation and is accumulated mainly in the brain and kidney. In acute exposure to high concentrations of mercury vapor, the symptoms of respiratory, such as chest pain, cough, hemoptysis, and interstitial pneumonitis occur shortly after inhalation. In chronic exposure to relatively low concentrations of mercury vapor, neurological changes are prominent. The signs and symptoms of mercury vapor poisoning is

153
TITLE:
More about the mercury menace

AUTHORS:
ANON

SOURCE:
Food Cosmet. Toxicol.; 6(3), 397-400, 1968; (REF:24)

ABSTRACT:
HAPAB The fact that metallic mercury is far from harmless when it gets into the circulation and in some cases may be fatal is illustrated by several case histories. Slight exposure to mercury vapor is also hazardous, since its saturated vapor pressure at room temperature is equivalent to 20 mg/cu m, greatly above the recommended safe levels of 0.1 mg/cu m adopted by the UK and the USA and 0.01 mg/cu m adopted by Germany. The fact that inhaled mercury is readily taken up by the brain tissue may explain the appearance of erethism and tremor boserved during occupational exposure to mercury. The effects of mercury vapor are species dependent; e.g., pigeons show a greater mercury tolerance than rats, mice or monkeys. In a Scandinavian study, much of the free mercury inhaled by workers was

found in blood plasma and the urinary excretion of mercury rose markedly. In contrast, after exposure to alkyl mercurials most of the mercury was retained in the red cells and because of the relatively low plasma concentration there was little rise in urinary excretion with increasing blook concentration. An average of 68% of the radioactivity from a 3 mcmole dose of phenyl mercuric acetate appeared in the feces and 12.6% in the urine in 7 days. By contrast, inorganic mercury showed 95% excretion in the feces and 1 to 4% in the urine. The concentration of mercury is higher in the liver and kidney than in lungs and heart. It has been demonstrated that the deposition of mercury in the kidney can be decreased and urinary excretion increased by administration of sodium maleate before sublethal doses of mercury. The mercury content of some fish may be a useful index of contamination of surface waters and mercury from seed dressings can enter the human food chain if such treated seed dressings are fed to pigs. TOXICOLOGY AND PHARMACOLOGY 69/01/00, 17 1968

154

TITLE:

Mercury health effects update. Health issue assessment

AUTHORS:

EPA Working Group

SOURCE:

TA:Environmental Protection Agency PG: YR:1984 IP: VI:EPA-600/8-84-019F

ABSTRACT:

Toxic effects of mercury in man and animals; Vapor of metallic mercury; Occupational studies have shown that chronic exposure to mercury vapor affects primarily the central nervous system and the kidneys. Effects associated with the lowest exposure levels--below 100 ug Hg/m3--produce non-specific symptoms such as introversion, insomnia, and anxiety. Biochemical alterations have been observed in enzymes of plasma and red blood cells, and increases in urinary excretion of specific proteins and enzymes are know to occur. Higher chronic exposure produce more pronounced effects in cognitive function, such as short-term memory loss and changes in personality traits (e.g., increased anxiety and introversion); Effects on both the nervous system and kidney are usually reversible, particularly it the effects are mild. Studies have shown that motor effects reverse more readily than cognitive and neurotic effects. Information is generally lacking on reproductive and developmental effects of inhaled mercury vapor; Inorganic compounds of mercury; Chronic oral intake of mercurous chloride (250 mg/day) resulted in typical signs of mercurialism and chronic renal failure. Chronic oral exposure to mercurous chloride has also caused acrodynia or Pink's disease in children; Compounds of methyl mercury; Methyl mercury primarily damages the central nervous system in both adults and prenatal infants. Prenatal exposure at the lowest recorded

levels produce signs of psychomotor retardation in infants; Ongoing studies indicate (based on estimated blood levels in the mother during pregnancy) that the fetus is about three times more sensitive than the adult to methyl mercury exposure. Effects on the adult central nervous system result from focal damage to specific areas of the brain, principally the cortex of the cerebellum and the visual cortex; Dietary intake levels of methyl mercury that produce irreversible destruction of neurons in the cerebellar and visual cortices leading to permanent signs of ataxia and constriction of the visual field are probably at least twice as high as those levels causing mild symptoms; Human health risk assessment of mercury in air; Direct exposure effects; An analysis of dose-response and dose- effect relationships that current levels of mercury in the atmosphere, irrespective of chemical species, would present a negligible risk of adverse health effects from direct airbone exposure. Current atmospheric levels are believed to be 20 ng Hg/m3 or less; Indirect exposure effects--mercury in the atmosphere has the potential to produce indirect exposure effects through increasing levels of methyl mercury in edible tissues of freshwater fish. As previously noted (see section 2.1.2), the effect of atmospheric mercury on indirect exposures was not considered in the 1973 promulgation because of insufficient information on the environmental fate of airborne mercury. (Shortened)

155
TITLE:
Dental amalgam mercury exposure in rats.

AUTHORS:
GALIC N
PRPIC-MEHICIC G
PRESTER L
BLANUSA M
KRNIC Z
FERENCIC Z

SOURCE:
BIOMETALS; 12 (3). 1999. 227-231.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The aim of this study was to measure the distribution of mercury, in tissues of rats exposed to amalgam over a two months period. Possible interaction of mercury with copper and zinc in organs was also evaluated. Rats were either exposed to mercury from 4 dental amalgams, or fed the diet containing powdered amalgam during two months. Mercury was measured in the kidney, liver and brain, copper in kidney and brain and zinc in kidney. The results showed significantly higher concentrations of mercur than in the control group. We found no significant differences between mercury levels in exposed and control rat's liver. Exposure to mercury from dental amalgams did not alter the

concentrations of copper and zinc in the tissues. Histopathological analyses of rats tissues did not show any pathological changes. These results support previously proposed nose-brain transport of mercury released from dental amalgam fillings.

156
TITLE:
Effects Of Vitamin E, Glutathione And Methylmercury On Distribution And Placental Transfer Of Selenium In Mice

AUTHORS:
Yonemoto J
Naganuma A
Suzuki T
Imura N

SOURCE:
Chemosphere, Vol. 12, No. 7-8, pages 1021-1029, 23 references, 19831983

ABSTRACT:
Selenium (7782492) distribution, and its modification by glutathione (70188), vitamin-E (1406184), and methylmercury (22967926) were investigated in mice. The distribution of selenium and mercury (7439976) (administered as bis(methylmercuric)-selenide (4305377) (BMS) in the fetal/placental complex) was also examined. Pregnant CD1-mice were treated intravenously on day 1 of conception with 0.75 micromoles/kilogram (micromol/kg) radiolabeled sodium-selenite (10102188) in some cases preceded by five daily injections of 50 milligrams/kg (mg/kg) dl-alpha-tocopherol-acetate (vitamin-E) or, 20 minutes before, by 5 millimoles/kg glutathione. One group received only 1.5micromol/kg methyl-mercuric-chloride on day 16, or methyl-mercuric-chloride plus sodium-selenite, or 0.75micromol/kg BMS doubly labeled with selenium-75 and mercury-203. Sixty minutes after injection, radioactivity in blood plasma and erythrocytes, amniotic fluid, fetuses, and maternal organs was measured. Selenium contents in the kidneys (8.71 percent of total dose) and spleen (0.41 percent) of the glutathione pretreated mice were significantly elevated when compared with selenium controls (3.79 and 0.27 percent, respectively) and in the brain and heart of mice injected with BMS (1.20 and 1.76 percent) compared with selenium controls (0.09 and 0.46 percent, respectively). Mercury contents in brain, liver and heart of mice injected with selenium and mercury simultaneously, as well as in brain and heart of BMS injected mice were elevated compared with mercury only controls. Fetal selenium in BMS injected mice was 0.06 percent compared to 0.11 percent for selenium only. Treatments did not significantly affect mercury contents of placenta, amniotic membrane, or fetuses, or selenium and mercury concentrations in maternal blood, erythrocytes, plasma, or amniotic fluid. Selenium concentrations in decreasing order were: uterus, placenta, amniotic membrane and fetus. The

authors conclude that patterns of distribution may differ among selenite metabolites. Apparently BMS formation in-vivo does not provide an explanation for the modified distribution of selenium and mercury after simultaneous administration.

157
TITLE:
Embryonic And Fetal Death After In Utero Methylmercury Exposure And Resultant Organ Mercury Concentrations In Mice

AUTHORS:
Satoh H
Suzuki T

SOURCE:
Industrial Health, Vol. 21, No. 1, pages 19-24, 6 references, 19831983

ABSTRACT:
The embryotoxicity of methylmercury (22967926) was studied in mice. Female IVCS-mice were fed 15.9 or 31.9 nanomoles per gram methylmercury alone or in combination with 11.4 nanomoles per milliliter selenite (14124675), the selenite being administered in their drinking water, for 30 days prior to mating and up to day 18 of gestation. On day 18, the uterus of each dam was opened and the number of surviving fetuses, dead fetuses, dead embryos, resorptions, and implantation sites was determined. Surviving fetuses were examined for gross abnormalities. Mercury (7439976) concentrations were measured in the maternal brain, maternal liver, maternal kidney, maternal blood, uterus, placenta, amniotic membrane, amniotic fluid, fetal brain, fetal liver, and fetal kidney. Fetal death rates, defined as the number of total embryonic and fetal deaths divided by the total number of implants, were calculated. Attempts were made to correlate the fetal death rates with organ mercury concentrations. Coadministration of methylmercury with selenium (7782492) generally increased the fetal death rate. Gross abnormalities (harelip or cleft palate) occurred in only two fetuses. Selenite increased maternal liver mercury concentrations and decreased maternal kidney mercury concentrations. Selenite had no significant effect on mercury accumulation in any other organs. Fetal death rate was significantly correlated with mercury concentrations in the maternal brain, maternal liver, maternal blood, uterus, amniotic blood and amniotic fluid, and fetal liver. The highest correlation was with the maternal blood and amniotic fluid, the correlation coefficients being approximately 0.9 for both methylmercury and methylmercury plus selenite administration. The authors conclude that maternal blood and amniotic fluid can be used as critical organs for assessing embryotoxic effects of mercury exposure. They recommend further study of the interaction of methylmercury and selenite.

158
TITLE:
Localization of mercury in CNS of the rat: III. Oral administration of methylmercuric chloride.

AUTHORS:
MOLLER-MADSEN B

SOURCE:
FUNDAM APPL TOXICOL; 16 (1). 1991. 173-187.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The distribution and cellular localization of mercury in the in situ brain and upper cervical spinal cord of adult Wistar rats were studied at various time intervals after oral administration of methylmercuric chloride (CH3HgCl; 20 mgsverse sections of the cervical spinal cord were prepared for visualization of the mercury by the autometallographic silver-enhancement method. Following mercury administration there was a latent period before the metal appeared in the tissue. Mercury staining was first detected after 10 days in cell bodies of five specific areas of the brain stem: the mesencephalic nucleus of the trigeminal nerve, the red nuclei, the ventral cochlear nucleus, the superior vestibular nucleus, and the nucleus reticularis pontis caudalis. After 28 days of treatment, a fairly even distribution of mercury was seen in the brain and spinal cord. Longer periods of treatment caused no further increase in the density of mercury within the stained cell bodies. In ce

159
TITLE:
Motor neuron uptake of low dose inorganic mercury.

AUTHORS:
PAMPHLETT R
WALEY P

SOURCE:
JOURNAL OF THE NEUROLOGICAL SCIENCES; 135 (1). 1996. 63-67.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In animals, inorganic mercury can bypass the blood brain barrier and enter motor neurons. We sought to determine the lowest injected dose of mercury that could be detected in mouse motor neurons. Mice were injected intraperitoneally with mercuric chloride in doses from 0.05 to 2 mug/g body weight and studied between 5 days and 18 months after injection. After formalin fixation, 7 mum sections of cerebrum, cerebellum, brain stem, spinal cord and kidney were stained with silver nitrate autometallography. Five days after injection, mercury

granules were detected at doses from 0.2 mug/g upwards in the cell bodies of spinal and brain stem motor neurons, more granules being seen at the higher doses. Mercury granules were also seen in 5% of posterior root ganglion neurons. At doses from 0.05 mug/g upwards mercury was detected 5 days later in renal tubule cells. Mercury was still present in motor neurons 6-11 months after injection, but by this time mercury had been cleared fro

160
TITLE:
Relation between mercury levels in brain and blood or cerebrospinal fluid after mercury exposure.

AUTHORS:
YOSHIDA M
SHIMADA E
ARAI F
YAMAMURA Y

SOURCE:
J TOXICOL SCI; 5 (3). 1980 (RECD. 1981). 243-250.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Rabbits were exposed to Hg vapor, MeHg and HgCl2 respectively and the relationship of Hg concentration in brain to that in blood or CSF was investigated after the termination of exposure. At 1 day post-exposure, the ratio of Hg concentration in brain (mug Hg/g) to that in blood (mug Hg/g) wastio for Hg vapor wasts exposed to Hg vapor, the ratios of Hg concentration in blood to brain or CSF to brain at 1 day and 20 days after termination of exposure were compared. Blood to brain ratio decrease to about 1/10 after 20 days and CSF to brain ratio decreased Hg was eliminated from blood and CSF more rapidly than from the brain. In rabbits administrated MeHg, the ratio of Hg concentration in blood to that in brain was almost unchanged at 1 and 20 days after termination of exposure. There were no differences in the rates of elimination from blood and brain. Elimination of Hg from CSF was more rapid than from brain because the ratio between Hg concentration of CSF to that of brain decreased1/3 after 20 days.

161
TITLE:
Pesticide and mercury levels in pelicans in Idaho.

AUTHORS:
Benson WW
Brock DW
Gavica J
Loomis M

SOURCE:
Bull. Environ. Contam. Toxicol. 15(5): 543-546; 1976.(10 references)

ABSTRACT:
PESTAB. Twelve white pelicans (Pelicanus erythrorhynchos) collected in southern Idaho during early summer of 1974 were analyzed for tissue mercury levels using gas chromatography. The liver tissues contained the highest mercury levels (2.33-32.80 ppm), followed by the kidney (average 3.87 ppm), feathers (average 3.70 ppm), muscle (average 3.41 ppm), heart (average 2.37 ppm), brain (average 1.27 ppm), and bone (average 0.34 ppm). An additional bird, found dead, was examined for organochlorine residues. Total DDT levels ranged from 1498 ppm in the liver to 19 ppm in the brain, BHC ranged from 13.60 ppm in the liver to 0.635 ppm in the brain, heptachlor epoxide ranged from 13.20 ppm in the liver to 0.384 ppm in the brain, and dieldrin ranged from 203.00 ppm in the liver to 4.74 ppm in the brain. These pesticides may have been responsible for the bird's death. The mercury residues in the pelicans may have originated from mercury fungicide compounds used by farmers to treat their wheat seed.

162
TITLE:
Contaminant concentrations and biomarker response in great blue heron eggs from 10 colonies on the upper Mississippi River, USA.

AUTHORS:
Custer TW
Hines RK
Melancon MJ
Hoffman DJ
Wickliffe JK
Bickham JW
Martin JW
Henshel DS

SOURCE:
Environ Toxicol Chem 1997 Feb;16(2):260-71

ABSTRACT:
In 1993, great blue heron (Ardea herodias; GBH) eggs were collected from 10 colonies on the upper Mississippi River (UMR). They were then artificially incubated until pipping and analyzed for mercury, selenium, and organochlorines. Livers of embryos were analyzed for hepatic microsomal ethoxyresorufin-O-dealkylase (EROD) activity and four measures of oxidative stress. Brains were measured for asymmetry and blood was measured for the coefficient of variation of DNA (DNA CV). Organochlorine concentrations were generally low (geometric mean DDE = 1.3 ug/g wet weight; polychlorinated biphenyl (PCB) = 3.0 ug/g;

2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) = 11.5 pg/g). Eggshell thickness was negatively correlated with DDE concentrations. Mercury (geometric mean = 0.8 ug/g dry weight) and selenium (3.1 ug/g dry weight) concentrations in GBH eggs were within background levels. EROD activity was not correlated wtih total PCBs, TCDD, or toxic equivalents (TEQs), based on the relative contribution of individual PCB congeners, dibenzodioxins (PCDDs), and dibenzofurans (PCDFs) to total calculated TEQs. Three of the four measures of oxidative stress were correlated with mercury concentrations. Twenty of 43 (47%) embryo brains were asymmetrical and the embryos with asymmetrical brains had higher EROD concentrations in the liver and higher DNA CV in the blood than embryos with symmetrical brains.

163
TITLE:
Mercury: Major Issues in Environmental Health

AUTHORS:
Clarkson TW

SOURCE:
Environmental Health Perspectives, Vol. 100, pages 31-38, 78 references, 1993

ABSTRACT:
This review considered the hazards associated with methylmercury (MM) in the environment. Topics included pathways of human exposure to MM, disposition of MM, toxic action and dose response relationships in adults, prenatal toxicity, and treatment of MM poisoning. Studies have indicated that MM in the environment is bioaccumulated to a high degree in aquatic food chains, attaining its highest concentrations in edible parts of long lived predatory fish in both fresh and ocean waters. Inorganic mercury (7439976) can be converted to organomercury compounds by microorganisms in the environment. Within a few days of exposure, MM is moved throughout the entire body to its principle target, the brain. In human tissues the biological half life of MM is about 50 days, but there is wide individual variation. Focal damage to discrete anatomical areas of the brain such as the visual cortex and granule layer of the cerebellum characterizes adult poisoning. A latent period of weeks or months may ensue prior to the appearance of signs and symptoms of poisoning. These symptoms include paresthesia, ataxia, constriction of the visual fields, and hearing loss. The prenatal period is the most sensitive stage of the life cycle to the toxicity of MM with children who have been so exposed displaying severe cerebral palsy to subtle developmental delays. The author suggests that MM inhibits those processes in the brain which are specifically involved in development and growth such as neuronal cell division and migration.

164

TITLE:
Na++-ATPase in Rat Brain and Erythrocytes as a Possible Target and Marker, Respectively, for Neurotoxicity: Studies with Chlordecone, Organotins and Mercury Compounds

AUTHORS:
Maier WE
Costa LG

SOURCE:
Toxicology Letters, Vol. 51, No. 2, pages 175-188, 37 references, 1990

ABSTRACT:
The general aim of this study was to determine whether parameters of neurotransmission present in blood cells could serve as peripheral indicators of neurotoxicity, specifically the enzyme Na++-ATPase which is important in regulating membrane function and neurotransmission. To validate the use of measurements of Na+/K+-ATPase in erythrocytes as a marker for the same enzyme in brain, the organochlorine pesticide chlordecone (143500), the organotins triethyltin (997502) and tributyltin (688733), mercuric-chloride (7487947) and methyl-mercury were chosen as chemical probes. Male Sprague-Dawley-rats were used in this study. All the compounds tested were shown to be potent in-vitro inhibitors of brain and erythrocyte Na+/K+-ATPase, yet administration of these compounds in-vivo at high doses produced symptoms of neurotoxicity without a corresponding inhibition of Na+/K+-ATPase. The reasons for the discrepancy between in-vitro inhibition and lack of detectable in-vivo inhibition is not always clear. In the case of triethyltin, mercuric-chloride, and methylmercury, the metal levels present in the brain following administration of neurotoxic doses were not high enough to inhibit Na+/K+-ATPase. No consistent patterns of parallel effects of enzyme activity in brain and erythrocytes was observed following in-vivo administration of various neurotoxic compounds. However, the recent finding of decreased erythrocyte Na+/K+-ATPase activities in workers chronically exposed to mercury (7439976) still suggests that chronic studies may be needed to infer or rule out conclusively a role for erythrocyte Na+/K+-ATPase as a useful peripheral marker for exposure to certain neurotoxicants.

165
TITLE:
Hydrocephalus Following Prenatal Methylmercury Poisoning

AUTHORS:
Choi BH
Kim RC
Peckham NH

SOURCE:
Acta Neuropathologica, Vol. 75, No. 4, pages 325-330, 38 references, 19881988

ABSTRACT:
Hydrocephalus induced by prenatal organic mercury (7439976) poisoning was studied in mice. Pregnant C57BL/6J-mice were injected intraperitoneally (ip) with 0 or 12mg/kg methylmercuric-chloride (115093) (MMC) given in three divided doses on days 14, 15, and 16 of gestation. Other mice were given 2mg/kg MMC in their drinking water daily on gestational days two through 18. Tritiated thymidine was administered on day 16 of gestation. After delivery, surviving offspring were killed on postnatal days ten and 20, and their brains were removed and sectioned. The sections were examined by light and electron microscopy and by autoradiography. Surviving offspring of dams given MMC ip or orally had incidences of grossly apparent hydrocephalus of 10 and 7 percent, respectively. Microscopic examination showed the presence of a slight to moderate degree of hydrocephalus in several brains that appeared normal, increasing the incidence to 25 percent for offspring of dams exposed ip and 10 percent for those dosed orally. No hydrocephalus was seen in brains of offspring of untreated dams. Marked stenosis of the cerebral aqueduct in hydrocephalic brains was observed. The aqueduct was partially blocked by compacted cilia. Cerebral white matter showed edema, spongy degeneration, gross cystic change, and loss of parenchyma. Radiography showed significant abnormalities in the distribution of thymidine labeled postmitotic neurons within the cerebral cortical plate. Large numbers of mercury grains were visible in the cytoplasm and cilia of ependymal cells. The authors conclude that hydrocephalus develops in a significant percentage of offspring as a result of prenatal maternal methylmercury poisoning. The observed aqueductal stenosis is probably the result rather than the cause of hydrocephalus.

166
TITLE:
Blood and brain mercury levels after gestational exposure to methylmercury in rats.

AUTHORS:
Newland MC
Reile PA
Dunn WW

SOURCE:
Toxicologist 1997 Mar;36(1 Pt 2):13-4

ABSTRACT:
Female rats were exposed to 0, 0.5 or 6.4 ppm Hg (as methylmercury, 10/grp) in drinking water at least 4 weeks before mating with an unexposed

male. Maternal exposure continued to post-natal day 16 (PN16). Blood and whole-brain concentrations were determined on PN0 (birth) and PN21 (weaning). Maternal water consumption increased 3-fold through gestation for all groups. Brain Hg in offspring decreased between PN0 and PN21 from 0.49 to 0.045 ppm in the low-dose rats and from 9.8 to 0.53 in the high-dose rats, a decrease approximating the brains' increase in mass. This suggests retention but minimal additional mercury exposure during lactation. Brn:Bld ratios increased from 0.13 to 0.25 in each dose group suggesting differential loss of mercury from neural and nonneural tissue. With this dosing protocol Brn:Bld ratios were higher than the value of 0.06 observed after repeated acute administrations during gestation (Magos & Butler, 1976). There were no differences between male and female offspring. A linear relationship between cumulative exposure estimated from water consumption, and log (brain concentration) at PN0 was obtained: log ((ug Hg)/(g brn)) = 1.2 log (cum. exposure in (ug Hg)/(g body mass)) - 0.18.

167

TITLE:

Mercury in Dentistry

AUTHORS:

Gerhardsson L
Brune DK

SOURCE:

Occupational Hazards in the Health Professions, D. K. Brune and C. Edling, Editors; Boca Raton, Florida, CRC Press, Inc., pages 307-321, 85 references, 1989

ABSTRACT:

A review was presented of the potential hazards associated with mercury (7439976) use in the dental industry. Several studies have demonstrated that mercury vapor is released from amalgam fillings, particularly after chewing. Insertion and removal of amalgam fillings by drilling was noted to increase the excretion of mercury in the urine for several days. The concentration of this mercury was correlated to the number of amalgam fillings in the mouth. A correlation was also noted between the number of amalgam surfaces in the mouth and the concentration of mercury in brain and kidneys. The risks for those employed in this field included external and internal exposure to mercury from the working environment and from their own dental fillings. In a study of 111 dentists and assisting personnel, no correlation was noted between blood mercury levels and handwriting tremor. In a study of 298 dentists, 23 had head and wrist mercury concentrations exceeding 20 micrograms/gram of tissue. Of these 23, 30% revealed electrophysiological evidence of a subclinical polyneuropathy not observed in the referent group. Conduction velocity along the sensory nerve fibers was delayed in an individual intoxicated by

elemental mercury. Behavioral changes, erethism, have also been reported. A study of deceased dentists revealed considerably higher total mercury concentrations in the pituitary glands when compared with referents. In a study of the relationship between mercury exposure and pregnancy outcome, no increased rates of spontaneous abortions or congenital abnormalities were noted in the children of men and women who were occupationally exposed to low versus high levels of mercury.

168
TITLE:
Occurrence Of Alkylmercury Compound In Caustic Soda Factory

AUTHORS:
Yamaguchi S
Matsumoto H
Hoshide M
Matsuo S
Kaku S

SOURCE:
Archives of Environmental Health, Vol. 23, pages 196-201, 6 references, 19711971

ABSTRACT:
An alkylmercury compound from the sludge pits of caustic soda factories in which only metallic mercury had been used in the electrolysis of sodium-chloride, was analyzed. Samples of water and sludge were collected at several sites at two Japanese factories. Total mercury was measured by cold vapor atomic absorption. Identification and determination of alkylmercury was measured by gas chromatography and thin layer chromatography. To confirm the production of methyl-mercury-chloride (115093) during electrolysis of sodium-chloride, methyl-mercury-chloride was measured in several experimental inorganic systems. The crystalline substance obtained was dissolved in water with propylene-glycol and administered subcutaneously to rats once every 2 days at 0.5 milligrams (mg) per day for a total dose of 13mg. Some rats were administered authentic methyl-mercury-chloride; control rats received propylene-glycol only. Rats were sacrificed at signs of ataxia, and the amount of methyl-mercury-chloride in various organs was measured. At one factory, a large sludge pit contained 0.014 parts per million (ppm) methyl-mercury-chloride; at the other factory, a similar pit contained 0.311ppm. The crystalline material obtained when methyl-mercury-chloride was measured in a solution of inorganic mercurials mixed with calcium-carbide had the characteristic odor of methyl-mercury-chloride. When analyzed by atomic absorption, the locus where mercury was found showed the same Rf value as that of methyl-mercury-chloride. Rats administered authentic or experimentally synthesized methyl-mercury-chloride exhibited crossing of hind legs when hung by the

tail. Hind leg crossing was not apparent in control rats. In rats administered synthesized material, methyl-mercury-chloride found in organs ranged from 0.78ppm in the brain to 33.40ppm in the kidney. The authors conclude that demonstration of the possible production of methyl-mercury-chloride in a commonly used inorganic process raises serious questions as to the potential entry of this material into biological systems.

169
TITLE:
Mercury, Organic Compounds Of

AUTHORS:
Berlin M

SOURCE:
Encyclopaedia of Occupational Health and Safety, Vol. 2, pages 1336-1338, 6 references, 19831983

ABSTRACT:
The characteristics of organic compounds of mercury (7439976) are reviewed. The three most important organic compounds in common usage are the alkyls, aromatic hydrocarbons or aryls, and alkoxyalkyls. In medical practice, mercury compounds are used as antiseptics, germicides, diuretics, and contraceptives. They serve as algicides, fungicides, herbicides, and slimacides, and as preservatives in paints, waxes, and pastes. In the chemical industry, they act as catalysts in a number of reactions, and the mercury alkyls are used as alkylating agents in organic synthesis. Examples of aryl mercury compounds are phenylmercuric-acetate (62384) (PMA), nitrate (14797558), oleate (115060), propionate (127208), and benzoate (65850). Absorption on occupational exposure may occur through inhalation of aerosols containing PMA, by the skin on skin contamination, or by ingestion. Phenylmercury (23172374) is transported mainly in blood and distributed in the blood cells, and accumulates in the liver, where it is decomposed into inorganic mercury. Occupational exposure to phenylmercury compounds occurs in the manufacture and handling of products treated with fungicides. The short chained alkyl mercury compounds, like methylmercury (22967926) and ethylmercury (627441), are the most important. Volatile methylmercury compounds are absorbed to about 80 percent upon inhalation of vapor. Methylmercury is transported in the red blood cells, and a small fraction is bound to plasma proteins. Methylmercury is concentrated in the central nervous system; the highest concentration is found in the occipital cortex and cerebellum. Most exposure to organic mercury compounds involves mixed exposure to mercury vapor and the organic compound, as organic mercury compounds decompose and release mercury vapor. Persons who will be exposed to mercury compounds should undergo a preemployment medical examination. In alkyl-mercury poisoning, N-acetylpenicillamine (15537710) or dimercaptosuccinic-acid

(2418146) can be used to mobilize mercury from the brain and enhance excretion.

170
TITLE:
Effect of Subchronic Mercury Exposure on Electrocorticogram of Rats

AUTHORS:
Desi I
Nagymajtenyi L
Schulz H

SOURCE:
Neurotoxicology, Vol. 17, Nos. 3/4, pages 719-724, 14 references, 1996

ABSTRACT:
The effect of subchronic, low levels of mercury (7439976) on the electrophysiological function of the brain was investigated. Male Wistar-rats were treated with 0.4, 0.8, or 1.6mg/kg mercuric-chloride (7487947) for 4, 8, or 12 weeks for 5 days a week. The electrocorticogram (ECoG) was recorded at the end of the treatment periods. The amplitude of the somatosensory ECoGs showed a dose and time dependent decrease that was significant only at the two higher doses after 12 weeks. Significantly lower somatosensory ECoG indices occurred at the two higher doses at 12 weeks. The visual ECoG showed the same tendencies as the somatosensory ones. The decreases of mean amplitudes were significantly different for the two higher doses at 12 weeks. The visual ECoG indices were significantly lower at the two higher doses at 8 and 12 weeks. The auditory ECoG indices decreased significantly at 8 and 12 weeks for the two higher doses. The changes in ECoGs from somatosensory, visual, and auditory centers were nearly the same. The authors conclude that subchronic mercury exposure affects the integrative electrophysiological functions of the brain, which may occur in humans without clinical signs of intoxication.

171
TITLE:
Distribution of Mercury in Rabbits Subchronically Exposed to Low Levels of Radiolabeled Methyl Mercury

AUTHORS:
Petersson K
Dock L
Soderling K
Vahter M

SOURCE:
Pharmacology and Toxicology, Vol. 68, No. 6, pages 464-468, 26 references,

1991

ABSTRACT:

The distribution pattern and in-vivo demethylation of methyl-mercury (MeHg) was studied in female New-Zealand-rabbits subchronically exposed to doses comparable to daily human ingestion of fish containing mercury (7439976) (Hg) at a level of 1mg/kg, the highest marketable level in Sweden. Fifteen rabbits were administered radiolabeled MeHg at a dose of 0.125 micromoles per kilogram (micromol/kg), intravenously twice a week for 9 weeks (wk). Groups of three animals each were sacrificed at 1, 4, 8 and 12wk after cessation of treatment. Excretion of Hg in urine and feces was followed in four animals. Tissues examined were brain regions, liver, kidneys, femur, muscle, skin and fur. Separation of MeHg and inorganic Hg was carried out by ion exchange chromatography. Speciation of Hg was carried out by cold vapor atomic absorption spectrophotometry. Blood levels of Hg were close to steady state after 8wk of administration. Retention of Hg during administration and 12wk after its cessation, was calculated. Cumulative excretion in urine and feces at 3 to 4 days after last treatment was 5% in urine and 54% in feces; after 12wk the Hg in urine increased to 25%, indicating accumulation. Concentrations in tissues were highest in fur, followed by kidney. A marked drop occurred in skin levels at 8 to 12wk after the end of treatment. Hg elimination rate was similar in muscle, brain, and blood (half time (t1/2) of about 12 days), and much slower in liver and kidney (t1/2 of about 28 days). The authors conclude that there is no clear evidence for demethylation of MeHg in the rabbit brain. The inorganic Hg observed in the brain may, at least in part, originate from that produced from MeHg elsewhere in the body.

172

TITLE:

Increased Uptake Of Mercury In Mouse Brain Caused By 2,3-Dimercaptopropanol

AUTHORS:

Berlin M
Ullrebg S

SOURCE:

Nature, Vol. 197, No. 4862, pages 84-85, 5 references, 19631963

ABSTRACT:

The effect of 2,3-dimercaptopropanol (59529) (BAL) on brain mercury (7439976) concentrations was examined in mice. Animals were given 0.4 milligram per kilogram (mg/kg) BAL together with 0.5mg/kg mercury-203 (13982780) or other methylmercuric or phenylmercuric compounds. Controls were given only the mercury compound. Animals were sacrificed after injection. Autoradiograms of whole body saggital sections were prepared. Sample autoradiograms in which phenylmercuric-acetate (62384) was injected

and animals sacrificed 8 days after injection were presented, indicating increased uptake of BAL treated animals. The standard staircase below each section showed density caused by decreasing concentrations of radioisotope. The authors conclude that brain mercury uptake is greater when phenylmercuric or methylmercuric compounds are administered together with BAL rather than when they are given alone. However, autoradiograms do not provide any conclusive evidence to the precise manner in which BAL treatment affects mercury brain uptake.

173
TITLE:
Mercury 203 Distribution in Pregnant and Nonpregnant Rats Following Systemic Infusions with Thiol-Containing Amino Acids

AUTHORS:
Aschner M
Clarkson TW

SOURCE:
Teratology, Vol. 36, No. 3, pages 321-328, 13 references, 19871987

ABSTRACT:
The distribution of mercury (7439976) after systemic infusions of pregnant and nonpregnant rats with methylmercury (22967926) (MeHg) was studied in relation to the role of L-cysteine and L-leucine in MeHg transport. Pregnant (gestational day 17) and nonpregnant Long-Evans-rats were infused into the jugular vein with either 0.1 mole per hour (mol/hr) L-cysteine, 0.1mol/hr L-leucine, or saline for 4 days. At 24, 48, and 72 hours, the rats were switched for 1 hour to an infusion of MeHg labeled with mercury-203 (Hg-203), 50 micromoles per hour. Radioactivity was measured by gamma scintillation spectrometry. After the 4 day period, pregnant rats accumulated significantly greater Hg-203 concentrations compared to nonpregnant rats, possibly because of the greater body weight of the pregnant animals. Hg-203 concentrations in blood, brain, kidney, and liver were lower in pregnant than in nonpregnant rats. For both pregnant and nonpregnant rats, brain concentrations of Hg-203 were significantly higher in L-cysteine treated rats than in controls. In nonpregnant rats only, L-leucine significantly decreased Hg-203 concentrations in brain. The authors conclude that the study lends direct support to the hypothesis that gestation reduces MeHg levels in the mother, presumably because of its accumulation in pups. They further conclude that the results support a working hypothesis that MeHg distribution in both pregnant and nonpregnant animals is closely linked to neutral amino acid carrier transport and metabolism in the central nervous system.

174
TITLE:
Distribution of mercury between maternal, fetal and neonatal tissues

following gestational exposure to elemental mercury vapor in Long-Evans rats.

AUTHORS:
Chanda SM
Barone S Jr
Price HC
O'Connor RW
Beliles RP
Morgan DL

SOURCE:
Toxicologist 1998 Mar;42(1-S):28

ABSTRACT:
The disposition of inhaled mercury vapor (Hg0) in pregnant Long-Evans rats was evaluated in this study. Rats were exposed to 0, 2, 4, 8 mg Hg0/m3 2 hr/day from gestation day 6 (GD6) to GD15. Various maternal and fetal/pup tissues were collected for Hg analyses on GD6, GD10, GD15, PND1, PND14, PND21, PND45 and PND90. Total Hg content was analyzed using cold vapor atomic fluorescence spectrometry. Maternal body weights decreased by 12% and greater than 20% in the 4 and 8 mg Hg0/m3 groups, respectively, following exposure to Hg0. The 8 mg Hg0/m3 group also had an increased incidence of resorptions and decreased litter size. A decreased pup body weight was noted at PND1 only in the 8 mg Hg0/m3 dose group. All pups in the 8 mg Hg0/m3 group were sacrificed at PND1 due to morbidity of dams. There was a dose and time dependent increase in maternal plasma and uterus concentration of Hg during exposure. At PND1 both maternal plasma and uterine Hg levels were 3-8 fold lower than the last day of exposure (GD15). Uterine Hg levels were consistently 3-4 times higher than plasma Hg levels. There was a dose and time dependent accumulation of Hg at GD6 and GD10 in the fetus. At GD15 fetal brain Hg concentration was about 7-9 times lower than maternal plasma Hg levels at GD15. The concentration of Hg in the neonatal brain at PND1 was approximately 4 fold lower than the maternal plasma concentration at PND1. The concentration of Hg in the neonatal brain (ng/g) decreased over time, however, it could still be detected at PND90 following gestational exposure. There was an increase in maternal kidney weight with 4 and 8 mg Hg0/m3 at GD6, 10, and 15. At PND1 there was a dose dependent increase in pup kidney Hg levels. These data will be used to correlate exposure level to changes in neurochemical, neuroanatomical and neurobehavioral endpoints following gestational exposure to mercury vapor.

175
TITLE:
Uptake of Mercury by the Hair of Methylmercury-Treated Newborn Mice

AUTHORS:

Shi C
Lane AT
Clarkson TW

SOURCE:
Environmental Research, Vol. 51, No. 2, pages 170-181, 32 reference, 1990

ABSTRACT:
Uptake of mercury (7439976) by the hair after methylmercury (22967926) exposure was examined in mice. Newborn BALB/c-mice were injected intraperitoneally with mercury-203 (Hg-203) labeled methylmercuric-chloride (115093) (MMC) when they were 0, 2, 5, 8, 13, 20, 30, or 36 days old. The mice were killed 2 days after each dose and the amount of Hg-203 activity accumulated in blood, plasma, pelt (skin plus hair), liver, kidney, and brain was determined. Mice were injected with Hg-203 labeled mercuric-chloride (7487947) on postnatal days eight and 20. The mice were killed 48 hours after dosing and Hg-203 activity in the pelt, blood, and plasma was determined. Other mice were injected with tritium (H3) labeled MMC when they were 18 days old and were killed 48 hours later and the skin was removed. Skin biopsies were taken from the lower part of the dorsal skin and examined by autoradiography. Pelt Hg-203 concentrations increased rapidly from 2 to 8 days, peaking at 8 days, the time of maximum hair growth. The amount of Hg-203 in the pelt at that time represented 40% of the dose. On day 20 when the hair entered a senescent phase the amount of Hg-203 in the pelt dropped to 4%. Pelt Hg-203 activity increased again at day 30 when a second wave of hair growth occurred. Liver and kidney Hg-203 concentrations decreased from day two to eight, increasing thereafter. Brain Hg-203 decreased steadily over the 36 day examination period. MMC derived H3 activity accumulated in hair follicles, particularly in regions containing large concentrations of high sulfur content proteins. The amount of inorganic mercury derived Hg-203 in the pelt was less than half of that of organic mercury. Blood and plasma concentrations of inorganic and organic mercury did not differ significantly. The authors conclude that incorporation into growing anagen hair is the major mechanism by which organic mercury accumulates in hair.

176
TITLE:
Increases in the Number of Reactive Glia in the Visual Cortex of Macaca Fascicularis following Subclinical Long-Term Methyl Mercury Exposure

AUTHORS:
Charleston JS
Bolender RP
Mottet NK
Body RL
Vahter ME

Burbacher TM

SOURCE:
Toxicology and Applied Pharmacology, Vol. 129, No. 2, pages 196-206, 59 references, 1994

ABSTRACT:
The effects of the long term subclinical exposure of methyl-mercury (22967926) (MeHg) and mercuric-chloride (7487947) (IHg) on the cortex of the calcarine sulcus of the adult female Macaca-fascicularis were studied. MeHg was administered orally in a daily dose of 50 micrograms per kilogram body weight to three groups of monkeys for 6, 12, or 18 months, and was administered to a fourth group for 12 months followed by a 6 month clearance stage. The fifth group received IHg for 3 months by constant intravenous perfusion. The monkeys were subsequently killed and brain tissues were removed for analysis by optical volume stereology techniques. For all exposure groups, the reactive glia were the only cells to show a significant increase in number: 72% for the 6 month exposure group, 152% for the 12 month exposure group, 120% for the 18 month exposure group, and 89% for the clearance group. The IHg exposed group showed a 165% increase in reactive glia. The neurons, astrocytes, oligodendrocytes, endothelia, and pericytes did not show a significant change in number for any of the exposure groups. The cortex of the calcarine sulcus showed an increase in volume only for the inorganic treated group, suggesting edema. All treated groups had both organic and inorganic mercury (7439976) present in the brain tissues. The organic treated group had more organic than inorganic mercury present, with the exception of the clearance group, which had more IHg than organic mercury. For the IHg treated group, almost all the mercury present in the tissue was inorganic. It was proposed that the reactive glia were more sensitive to subclinical levels of mercury than the other cells. Since both the clearance and the inorganic exposed groups have lower levels of MeHg, and all groups exhibit the presence of significant IHg, the authors suggest that inorganic mercury is responsible for the increase in the reactive glia.

177
TITLE:
Mercury

AUTHORS:
Zielhuis RL
Stijkel A
Verberk MM
van de Poel-Bot M

SOURCE:
Health Risks to Female Workers in Occupational Exposure to Chemical Agents, Springer-Verlag, Berlin, pages 74-78, 14 references, 19841984

ABSTRACT:

The health risk to women occupationally exposed to mercury (7439976) is reviewed. Metallic, inorganic and long chain organic compounds are considered to have similar toxicokinetic and toxicodynamic properties while short chain organic compounds differ in their effects. The World Health Organization has recommended additional protection for female workers exposed to metallic mercury compounds because of of suggestive evidence of increased risk to pregnancy and offspring. No additional protection is recommended for exposure to inorganic salts and long chain organic compounds. There is some evidence of an effect on menstruation from these compounds but the data is not conclusive. No threshold dose can be stated. The present threshold limit value of 50 micrograms mercury per cubic meter, time weighted average, may result in increased risk to pregnancy and offspring. There is no evidence that women respond differently to the short chain organic mercury compounds than men and there is no evidence of an adverse effect on the female reproductive system, but severe adverse effects on the offspring may occur during pregnancy and lactation. Available data is derived mainly from large epidemics of methyl-mercury (22967926) poisoning in Japan and Iraq. The main risk is retarded development of the central nervous system. Risk increases with dose and complete recovery has never been documented. Mercury is excreted in breast milk. Animal evidence supports the human evidence. The developing brain in-utero and in the neonate accumulates organic mercury more than the brain of the mother. The authors conclude that women of fertile age should not be exposed to methyl-mercury.

178

TITLE:

Distribution Of Mercury In Guinea Pig Offspring After In Utero Exposure To Mercury Vapor During Late Gestation

AUTHORS:

Yoshida M
Yamamura Y
Satoh H

SOURCE:

Archives of Toxicology, Vol. 58, No. 4, pages 225-228, 17 reference, 19861986

ABSTRACT:

The effects of in-utero exposure to mercury (7439976) vapor on the distribution of mercury in offspring were studied in guinea-pigs. Pregnant animals were exposed to 0.2 to 0.3 milligram per cubic meter (mg/m3) mercury vapor for 2 hours per day during late gestation until the animals gave birth. Immediately after parturition, blood samples were drawn from the heart of mothers and pups. Animals were then sacrificed

and brain, heart, lungs, liver, and kidneys were removed for mercury analysis. Erythrocytes were separated from plasma. Pregnant animals were exposed for a total of 4, 5, 7, 10, or 11 days. Mercury concentrations in neonatal brain, heart, lungs, kidneys, plasma, and erythrocytes were much lower than those of maternal organs and tissues. Neonatal liver showed a mercury concentration twice as high as the maternal liver. Mercury concentration ratios of erythrocytes to plasma in offspring were different from those of mothers, being 0.2 to 0.4 for offspring and 1.3 to 3.0 for mothers. The authors conclude that mercury vapor metabolism in fetuses is quite different from that in their mothers.

179

TITLE:

Metallothionein (MT) induction in fetal rat brain and neonatal primary astrocyte cultures by in utero exposure to elemental mercury vapor Hg0.

AUTHORS:

Aschner M
Lorscheider FL
Cowan KS
Conklin DR
Vimy MJ
Lash LH

SOURCE:

Toxicologist 1998 Mar;42(1-S):195

ABSTRACT:

Brain MT protein and mRNA levels were determined in the fetal rat following in utero (gestational days 7-21) exposure to elemental Hg0 (300 ug/Hg/m3; 4 hrs/day). Expression of whole brain MT-I mRNA in full-term fetal rats (Day 21) was significantly increased by in utero exposure to Hg0 compared to controls. This corresponded to a 14-fold increase in fetal brain Hg concentration after in utero Hg0 exposure. In addition, astrocytes from both control and in utero Hg0-exposed fetuses were isolated, and primary astrocyte cultures were established and maintained in vitro for up to 3 weeks without additional experimental intervention. Astrocytes from in utero Hg0-exposed fetuses expressed significantly increased MT-I mRNA after 1, 2, and 3 weeks in culture compared with controls. MT-II mRNA was unchanged at 1 and 2 weeks in culture, but was significantly increased at 3 weeks in cultures derived from Hg0-exposed fetuses. Consistent with the increase in MT mRNA, an increase in astrocytic MT proteins was noted by western blots and immunoreactivity. These studies suggest that in utero exposure to Hg0 induces brain MT gene expression, and that MT mRNAs and proteins are useful quantitative biochemical markers of cytotoxic intrauterine exposure to Hg0. Present studies examine in utero Hg0 exposure effects on glutamine synthetase expression in whole brain and astrocyte cultures.

180
TITLE:
Distribution of Mercury 203 in Pregnant Rats and Their Fetuses Following Systemic Infusions with Thiol-Containing Amino Acids and Glutathione during Late Gestation

AUTHORS:
Aschner M
Clarkson TW

SOURCE:
Teratology, Vol. 38, No. 2, pages 145-155, 50 references, 19881988

ABSTRACT:
The distribution of methylmercury in pregnant rats and their fetuses following systemic infusion with thiol containing amino acids and glutathione was investigated. Pregnant rats with cannulated jugulars were infused continuously with 0 or 0.1 millimolar L-cysteine, L-leucine, or glutathione on days 17 through 21 of gestation. They were infused with 0 or 50 micromolar mercury-203 (Hg-203) tagged methylmercury-chloride (115093) for 1 hour at 24 hour intervals. The dams were killed on gestational day 21 and the fetuses were removed. Total fetal Hg-203 body burdens did not vary significantly between treatment groups. Maternal blood Hg-203 concentrations were similar in all treatment groups. Fetal brain Hg-203 concentrations were significantly elevated in those exposed to cysteine and decreased in those infused with leucine and glutathione. Maternal brain Hg-203 concentrations showed the same pattern as seen in the fetal brains; however, fetal brain Hg-203 concentrations were significantly higher compared to maternal brain concentrations. Maternal and fetal kidney Hg-203 concentrations did not vary significantly across groups; however, renal Hg-203 concentrations were lower in the fetuses. Hepatic Hg-203 concentrations of the dams were not affected by leucine, cysteine, or glutathione. Hepatic Hg-203 concentrations were significantly reduced in fetuses of dams infused with leucine or glutathione. Placental Hg-203 concentrations did not vary significantly across the treatment groups. The authors conclude that chronic infusion of amino acids or glutathione alters the distribution of mercury in adult and developing rats. Cysteine enhances uptake of methylmercury by the brain of both mature and developing rats.

181
TITLE:
Developmental Disturbances of the Fetal Brain in Guinea-Pigs Caused by Methylmercury

AUTHORS:
Inouye M

Kajiwara Y

SOURCE:
Archives of Toxicology, Vol. 62, No. 1, pages 15-21, 21 references, 19881988

ABSTRACT:
The prenatal effects of methylmercury on the fetal brain was studied in guinea-pigs. Pregnant female Hartley-guinea-pigs were orally treated with doses of methylmercuric-chloride (115093) the equivalent of 7.5 milligrams mercury on day 21, 28, 35, 42, or 49 of gestation, and sacrificed on gestational day 63 for analysis of uterine content and fetal organs. Methylmercury treatment results in the abortion of approximately 50 percent of the litters within 6 days of metal administration. The fetal and maternal mercury content of liver, kidney, whole blood, and blood plasma increased with increasing gestational time to metal treatment. Fetal metal content was highest in the liver and lowest in the plasma whereas maternal metal content was highest in the kidney and lowest in the plasma. The fetal brains from dams treated on days 21, 28, and 35 were smaller and showed dilated lateral ventricles, thinning of the cerebral cortex, and size reductions of the nucleus caudatus putamen and hippocampal formation. Fetal brains from dams treated on gestational days 42 or 49 showed significant cerebral degeneration including dysgenetic hydrocephalus with spongy degeneration of the brain mantle, hippocampus, nucleus caudatus putamen, and thalamus. The results indicated that developmental disturbances of the fetal brain, including abnormal neuronal migration, were induced when dams were exposed to methylmercury in early pregnancy. Neurons of the cerebral cortex were involved in focal degeneration when dams were exposed later in pregnancy.

182
TITLE:
Induction by mercury compounds of brain metallothionein in rats: Hg0 exposure induces long-lived brain metallothionein.

AUTHORS:
YASUTAKE A
NAKANO A
HIRAYAMA K

SOURCE:
ARCHIVES OF TOXICOLOGY; 72 (4). 1998. 187-191.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Metallothionein (MT) is one of the stress proteins which can easily be induced by various kind of heavy metals. However, MT in the brain is difficult to induce because of blood-brain barrier impermeability to most heavy metals. In this paper, we have

attempted to induce brain MT in rats by exposure to methylmercury (MeHg) or metallic mercury vapor, both of which are known to penetrate the blood-brain barrier and cause neurological damage. Rats treated with MeHg (40 mumol/kg per day 18 mug/g with slight neurological signs 10 days after final administration, but brain MT levels remained unchanged. However, rats exposed to Hg vapor for 7 days showed 7-8 mug Hg/g brain tissue 24 h after cessation of exposure. At that time brain MT levels were about twice the control levels. Although brain Hg levels fell gradually with a half-life of 26 days, MT levels induced by Hg exposure remained unchanged for > 2 weeks. Gel fractionation revealed that most Hg was in the brain cytosol

183
TITLE:
Effect Of Sodium Diethyldithiocarbamate On Placental Passage And Foetal Distribution Of Cadmium And Mercury In Mice

AUTHORS:
Jasim S
Tjalve H

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 55, No. 4, pages 263-269, 15 references, 19841984

ABSTRACT:
The effect of diethyldithiocarbamate (392745) on the fetal uptake of cadmium (7440439) and mercury (7439976) was investigated in C57Bl-mice. Female mice were mated and labeled mercury or cadmium were intravenously injected on day 18 of gestation. Intraperitoneal injections of 3.4 millimoles per kilogram (mmol/kg) sodium-diethyldithiocarbamate were given 4 hours after mercury or cadmium treatment. Animals were killed 8 hours later and fetuses and placentas were removed. Autoradiography of whole bodies and tissues was performed. Administration of sodium-diethyldithiocarbamate induced increased fetal concentrations of cadmium and mercury. Cadmium was increased 30 to 60 times in some fetal tissues and mercury was increased by 3 to 5 times. The highest relative increase in cadmium concentration was in fetal livers. High concentrations of cadmium and mercury were found in placenta, with a marked decrease in cadmium and a small decrease in mercury seen after treatment. Marked increases in cadmium and mercury were seen in maternal brains after treatment. Marked increases in cadmium and mercury were seen by autoradiography of fetuses. Determination of chloroform and water partition coefficients for cadmium ion and mercury ion showed that highly lipophilic chelates were formed in the presence of sodium-diethyldithiocarbamate. The authors conclude that sodium-diethyldithiocarbamate is able to affect the disposition of cadmium and mercury when administered a considerable time after the metals. Both

cadmium and mercury form highly lipophilic complexes with diethyldithiocarbamate, which is able to release metals already bound to tissues and induce redistribution in the body.

184
TITLE:
Mercury, A Hazardous Waste Problem

AUTHORS:
Weber J

SOURCE:
Journal of Environmental Health, Vol. 45, No. 6, pages 284-287, 16 references, 19831983

ABSTRACT:
Mercury (7439976) as a hazardous waste problem is reviewed. The historical uses of mercury in such areas as art, medicine, industry, and scientific research are summarized. The Romans may have been the first to recognize the hazards of mercury, when in the second century BC they closed down a productive mining area because of health problems among the miners. The physical and chemical properties of elemental mercury and its compounds are discussed. The toxicity of mercury and mercury compounds is considered. The symptoms of poisoning by mercury vapor are neuropsychiatric and include excessive shyness, insomnia, and emotional instability. The target organ for inorganic mercury compounds is the kidney. Organic mercury compounds cross the blood brain barrier and concentrate in the central nervous system, causing sensorimotor symptoms. Industrial contamination of waterways has required the development of methods for removing mercury from industrial waste streams. These methods include precipitation, ion exchange, adsorption on charcoal, solvent extraction, and absorption with sulfides. These methods have significantly reduced the amount of mercury going into waterways. The author concludes that, with proper handling, mercury need not be a hazard to humans or the environment.

185
TITLE:
Entry of low doses of mercury vapor into the nervous system.

AUTHORS:
PAMPHLETT R
COOTE P

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 19 (1). 1998. 39-48.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Inorganic mercury remains within neurons indefinitely and has been implicated in some human neurodegenerative diseases. We were interested in finding the lowest dose of mercury vapor that resulted in mercury deposition in neurons. Female BALB/c mice were exposed to 25 mug mercury/m3 for 2-20 hr or 500 mug mercury/m3 for 5-240 min. To see if female mouse neurons were more susceptible to mercury vapor than male neurons, male and female BALB/c mice were exposed to 50 mug mercury/m3 for 4-24 hr. Mice were perfused with formalin 1-30 weeks after exposure and paraffin sections of brain, spinal cord and kidney were stained for mercury with silver nitrate autometallography. On light microscopy, spinal motor neurons contained mercury granules after 12 hr exposure to 25 mug mercury/m3 or after 30 min exposure to 500 mug mercury/m3. Mercury remained in motor neurons 30 weeks after exposure. In female mice, mercury was seen in motor neurons at half the exposure times of male mice.

186

TITLE:

Diseases Caused by Mercury and Its Toxic Compounds

AUTHORS:

Anonymous

SOURCE:

Early Detection of Occupational Diseases, World Health Organization, Geneva, pages 79-84, 1 reference, 19861986

ABSTRACT:

Toxicity of mercury (7439976) and mercury compounds was evaluated in relation to occupational diseases. According to the authors, exposure to mercury and its compounds may occur during the electrolytic production of sodium and potassium hydroxides and chlorine, in the manufacture and repair of measurement or laboratory equipment, in the manufacture of mercury vapor tubes, x-ray tubes, rectifiers, and in the production of amalgams. Mercury-chloride (7487947) is used as a fungicide to treat bulbs and protect wood. Aryl and alkyl mercury compounds serve as fungicides and disinfectants. Methylmercury (593748) is exceedingly toxic. Vapors of elemental mercury are the major concern for occupational exposures as about 80 percent of the inhaled vapors are absorbed. Most mercury in the body is found in the kidneys, bound to metallothionein, and in the liver. Methylmercury has a strong affinity for the brain. Short term exposures cause irritation of the bronchial mucous membranes, stomatitis with increased salivation, and pneumonitis accompanied by fever and dyspnea. Chronic poisoning produces erethism, tremor, and stomatitis. Neurological and psychic symptoms are characteristic. There is some indication of chromosomal and mitotic aberrations as a delayed effect from mercury exposure. The authors recommend that mercury should be handled in hermetically sealed systems and strict hygienic practices must be

enforced. Technical control measures should be introduced to contain vapors and dust. Protective respiratory devices should be worn.

187
TITLE:
Changes In Fatty Acid Elongation In Developing Mouse Brain By Mercury Comparison With Other Metals

AUTHORS:
Bourre J-M
Dumont O

SOURCE:
Toxicology Letters, Vol. 25, No. 1, pages 19-23, 19 references, 19851985

ABSTRACT:
The effects of inorganic mercury (7439976) and other metals on changes in fatty acid elongation were investigated in-vitro using mouse brain preparations. Microsomal preparations were made from mouse brains. The elongation of coenzyme-A was determined in a reaction mixture at 37 degrees-C for 1 hour. The reaction was stopped by the addition of methanolic potassium-hydroxide. The mixture was saponified and extracted with petroleum. The extracted residue was methylated and fatty acid methyl esters were identified by thin layer and gas chromatography. Fatty acid elongation was inhibited 50 percent at a 50 micromolar (microM) concentration of divalent mercury and 100microM divalent copper (15158119). Among other metal ions tested, only divalent magnesium (7439954) induced inhibition above 5 millimolar. Since mercury and copper were potent inhibitors, sulfhydryl groups were considered involved in the underlying reaction. Additionally, impaired myelination during mercury intoxication could also be due to changes in long chain fatty acid synthesis resulting from enzyme alterations. The authors conclude that inorganic mercury inhibits fatty acid elongation in-vitro but it is not possible to conclude that these results are of significance in-vivo.

188
TITLE:
Accumulation of mercury and its effect on antioxidant enzymes in brain, liver, and kidneys of mice.

AUTHORS:
HUSSAIN S
ATKINSON A
THOMPSON SJ
KHAN AT

SOURCE:
JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B PESTICIDES FOOD

CONTAMINANTS AND AGRICULTURAL WASTES; 34 (4). 1999. 645-660.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. The effect of mercuric chloride (HgCl2) on the activities of catalase, superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR) and its effect on glutathione (GSH) content were evaluated in different organs (liver, kidneys, and brain) of mice after administration at 0, 0.25, 0.5 and 1.0 mg/kg/day for 14 days. The uptake of mercury shows that the kidneys accumulated the highest levels of mercury compare to brain and liver. The enzyme levels varied in mercury treated or mercury accumulation. Glutathione content increased in liver and kidneys of mercury treated mice compared to control. The results showed that the highest oral dose of mercury significantly increased antioxidant enzymes in kidneys and liver. The increased antioxidant enzymes enhance the antioxidant potential of the organs to reduce oxidative stress.

189

TITLE:

The Effect of Mercury Chloride and Methyl Mercury on Brain Microsomal Na+-K+-ATPase after Partial Delipidisation with Lubrol

AUTHORS:

Magour S
Maser H
Greim H

SOURCE:

Pharmacology and Toxicology, Vol. 60, No. 3, pages 184-186, 10 references, 19871987

ABSTRACT:

Lipophilic methyl-mercury (MeHg) and hydrophilic mercury-chloride (7487947) (HgCl2) were used to inhibit Wistar-rat brain Na+-K+-ATPase in-vitro before and after the removal of nonessential lipids to test the hypothesis that the removal of nonessential lipids from Na+-K+-ATPase may differentially affect the toxicity of mercurials. Both mercury compounds inhibited brain microsomal Na+-K+-ATPase. The inhibition caused by either compound was of the noncompetitive type with respect to adenosine-triphosphate suggesting that neither compound reacted at the catalytic center of the enzyme. In an effort to determine whether it was the degree of lipid solubility of the mercurials that was responsible for their differential toxicity, a nonionic detergent Lubrol was added. Lubrol potentiated the inhibitory effect of each mercurial, probably through removal of the bulk lipids outside the catalytic center of the enzyme, making the enzyme more sensitive to inhibition by both compounds. The authors conclude that the lipophilicity of MeHg is not solely responsible for its inhibitory effect on the enzyme.

190
TITLE:
Methyl mercury during late gestation affects temporarily the development of cortical muscarinic receptors in rat offspring.

AUTHORS:
ZANOLI P
TRUZZI C
VENERI C
BRAGHIROLI D
BARALDI M

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 75 (5). 1994. 261-264.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Pregnant Sprague-Dawley rats were treated by gavage with a single dose of 8 mg/kg of methyl mercury on gestational day 15. Offspring of control and treated rats were killed at 14, 21 and 60 days of age. The binding characteristics of muscarinic receptors labelled in cortical membrane preparation by 3H-L-quinuclidinyl benzilate were studied together with the assessment of mercury level in the same brain area. Furthermore, the performance in passive avoidance tasks was evaluated in 8 weeks old rats. Perinatal exposure to methyl mercury significantly reduced the maximum number of muscarinic receptors (Bmax) in the brain of 14 (53%) and 21 day old rats (21%), while this change was no more present in 60 day old rats. This phenomenon seems to be strictly related to the presence of mercury in the cortex since it disappeared with the normalization of mercury levels in the brain. Despite the recovery of muscarinic receptor densities in methyl mercury exposed rats at 8 weeks of a

191
TITLE:
Sexual Differences in the Distribution and Retention of Organic and Inorganic Mercury in Methyl Mercury-Treated Rats

AUTHORS:
Thomas DJ
Fisher HL
Sumler MR
Marcus AH
Mushak P
Hall LL

SOURCE:
Environmental Research, Vol. 41, No. 1, pages 219-234, 27 reference,

19861986

ABSTRACT:

The difference in distribution and retention of organic and inorganic mercury (7439976) (Hg) between male and female rats was investigated. Long-Evans-rats were injected intraperitoneally with Hg-203 labeled methyl-mercury-chloride (115093) (MeHg) at a dose of 1 micromole/kilogram. Rats were killed 1, 2, 4, 10, 32, 64, and 98 days after dosing. Body tissues were tested for Hg content using scintillation counting. Organic Hg was removed by toluene extraction. The inorganic content was estimated by the difference between the total Hg and organic portion. The total Hg burden in male rats decreased from 94.8 after the first postdosing day to 11.0 percent of the injected MeHg dose after 98 days. In female rats, the decline was from 95.4 to 8.6 percent. The percentages of MeHg of total Hg at the first and 98th day were as follows: pelt, 85.8 and 85.0; muscle, 95.3 and 61.0; kidney, 79.6 and 5.9; liver, 85.0 and 26.2; brain, 94.4 and 92.1; blood, 97.0 and 68.4; red blood cells, 98.3 and 73.0; and plasma, 55.2 and 38.0, respectively. The corresponding changes in female animals were as follows: pelt, 81.3 to 81.7; muscle, 96.5 to 51.2; kidney, 81.5 to 24.1; liver, 84.2 to 48.3; brain, 88.4 to 77.5; blood, 97.2 to 65.0; red blood cells, 95.1 to 83.0; and plasma, 55.8 to 79.2. Female rats had a significantly higher concentration of MeHg in the kidney and a lesser concentration in the brain than male rats 98 days after administration.

192

TITLE:

Mercury levels in the tissues of ring-necked pheasants fed two mercurial fungicides.

AUTHORS:

Adams WJ
Prince HH

SOURCE:

Bull. Environ. Contam. Toxicol. 15(3): 316-323; 1976.(16 references)

ABSTRACT:

PESTAB. Adult hen and cock pheasants were fed commercial pellets treated with various levels of methylmercury dicyandiamide or phenylmercuric acetate; the treated diets were given every day in some cases and every third day in others. All birds were sacrificed for mercury analysis on day 74 and fecal material was collected on days 10, 18, and 24 from the hens fed the fungicides daily. The tissue mercury concentrations were significantly elevated over control levels in 7 of 9 hens fed an average of 24.7 mg methylmercury dicyandiamade before death; the highest concentrations were found in the kidney and liver and the lowest concentrations were found in the ovary and brain. Among the cocks, there was a positive correlation between the amount of methylmercury

dicyandiamide consumed and the mercury content of the kidney, breast muscle, and gonad. The concentration of mercury in the hens fed phenylmercuric acetate increased with the amount consumed; the greatest mercury accumulations occurred in the kidney, followed by the liver, gonad, breast muscle, and brain. Among the cocks, only the renal mercury level was correlated with the amount of phenylmercuric acetate consumed. The total mercury levels in the feces tended to increase as the mercury concentration in the food increased, and the concentration in the feces was significantly greater in the phenylmercuric acetate group than in the methylmercury dicyandiamide group.

193
TITLE:
Retention and distribution of mercury in organs of neonatal guinea pigs after in utero exposure to mercury vapor.

AUTHORS:
YOSHIDA M
SATOH H
KOJIMA S
YAMAMURA Y

SOURCE:
J TRACE ELEM EXP MED; 3 (3). 1990. 219-226.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury retention and distribution in organs of fetal and neonatal guinea pigs after in utero exposure to mercury vapor was investigated. Guinea pigs near term were exposed to mercury vapor at approximately 10 mg/m3 for 150 min. Two hours after exposure, the highest mercury concentration among fetal organs was found in the liver. In the other organs, such as the kidney, brain, heart, and lung, mercury concentrations were not markedly elevated. The neonates were fostered by nonexposed mothers to minimize possible mercury intake through the maternal milk. On days 5 and 10 postpartum, the highest concentration was found in the kidney, followed by the liver, lung, and brain. All the concentrations, except the liver, were clearly elevated when compared with the concentrations in fetuses. Sephadex G-75 gel chromatography showed that a substantial portion of the mercury in the fetal liver soluble fraction was associated with metallothionein. During the neonatal development per

194
TITLE:
Demonstration of mercury in the human brain and other organs 17 years after metallic mercury exposure.

AUTHORS:

OPITZ H
SCHWEINSBERG F
GROSSMANN T
WENDT-GALLITELLI MF
MEYERMANN R

SOURCE:
CLINICAL NEUROPATHOLOGY; 15 (3). 1996. 139-144.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A male subject became exposed to metallic mercury vapor at work in 1973. He excreted 1,850 mg Hg/l urine initially. Controls of urine mercury excretion after D-penicillamin administration led to the assumption of a total body clearance of mercury latest since 1976. Subsequently he developed an organic psychosyndrome without detectable signs of classical mercurialism. He never returned to work again and died of lung cancer in 1990. In different organs (brain, kidney, and lung) which were sampled at autopsy elevated levels of mercury were documented by atomic absorption analysis. Histological examination of the tissue by the Danscher and Schroder method, which is specific for mercury, showed a highly positive staining in the majority of nerve cells and cells of other organs. Ultrastructurally mercury could be demonstrated by elemental x-ray analysis within lipofuscin deposits. The lipofuscin content was increased in the mercury positive nerve cells as demonstrated by a st

195
TITLE:
Mercury distribution in cortical areas and fiber systems of the neonatal and maternal adult cerebrum after exposure of pregnant squirrel monkeys to mercury vapor.

AUTHORS:
WARFVINGE K
HUA J
LOGDBERG B

SOURCE:
ENVIRONMENTAL RESEARCH; 67 (2). 1994. 196-208.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Pregnant squirrel monkeys were exposed 5 days/week to mercury vapor at a concentration of 0.5 mg Hg/m3 air for 7 hr/day, or at 1 mg Hg/m3 air for 4 or 7 hr/day. The calculated total mercury absorption ranged between 0.8 and 5.4 mg (range of daily absorption 0.04-0.07 mg). The mercury concentration in the cerebral occipital lobe of the offspring ranged between 0.20 and 0.70 mug/g tissue, and in the mothers between 0.8 and 2.58 mug/g tissue. Mapping of the

distribution of mercury in the neocortical layers of the maternal brains revealed that the pyramidal cells contained more visualized mercury than the other neurons. In addition, the mapping disclosed that the deeper the pyramidal cells were situated the more mercury they contained. In the offspring brains, no laminar distribution pattern was found. In the hippocampal formation, the pyramidal cells again contained more mercury than the other neurons. By contrast, the stratum granulosa of the dentate gyrus was always devo

196

TITLE:

Differential Determination of Ionizable and Unionizable (Inert) Forms of Inorganic Mercury in Animal Tissues

AUTHORS:

Takahashi H
Suetomi K
Konishi T

SOURCE:

Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 181-189, 6 references, 1991

ABSTRACT:

A method was developed to distinguish between inert forms of ionizable inorganic mercury (7439976) (Hg) and unionizable inorganic Hg in animal tissues through the use of hydrogen-peroxide as a reducing agent following alkali digestion. Tissue samples were obtained from rats injected with mercury-chloride (7487947) (HgCl2) or treated concurrently with mercury-sulfide (1344485) or mercury-selenide (11138424) via diet, and analyzed by atomic absorbance spectroscopy. The inert form of Hg was barely detectable from various tissues of rats injected twice with 1mg/kg HgCl2 and killed the following day. An inert fraction of Hg was found in the liver and, to a lesser extent, the kidney of rats killed 14 days later. In rats fed a diet containing sufficient amounts of sulfur (S) and selenium (Se), negligible amounts of Hg were found in the liver and none were detected in the kidney or brain, which suggested a very low contribution of S or Se to the formation of inert inorganic Hg in tissues. When S and Se were supplemented in the diet as L-methionine and sodium-selenite, respectively, the HgCl2 injection 2 weeks before death resulted in an increase of inert organic Hg in the liver and kidney, but not in the brain. Supplementation of Se as selenite increased the amount of unionizable form of Hg in the liver substantially more than addition of S as methionine. Data from Minamata Disease victims were analyzed for inert portions of inorganic and organic Hg; most of the inorganic Hg was present in the cerebrum and cerebellum in the inert form, while ionizable and inert forms were found in the liver and kidney of some cases. While

it is difficult to determine the actual chemical forms of stable mercury compounds and to ascertain which inert Hg compounds are actually stable, the authors conclude that the present method is successful in determining ionizable forms of inorganic Hg in the tissues.

197
TITLE:
Teratology of heavy metals: mercury and other contaminants.

AUTHORS:
Inouye M

SOURCE:
Congenital Anomalies 1989;29:333-44

ABSTRACT:
Modern industrialization has introduced harmful metals into our environment, and there has been a good deal of speculation that heavy metals can cause teratogenesis. In fact many metals have been confirmed to have embryotoxicity in experimental animals, but only a few elements (e.g., mercury, lead, etc.) are known to be human teratogens. Liquid metallic mercury is hardly absorbed from the gastrointestinal tract. Inorganic mercury is also poorly absorbed, i.e., around 2% of ingested mercuric chloride is absorbed. Uptake of inorganic mercury by the fetus is very low. An experiment using mice revealed that a significant proportion of mercury is blocked in the yolk sack. Among the organic mercury compounds, the most accumulated knowledge pertains to methylmercury compounds. Methylmercury is efficiently absorbed through the intestinal tract and skin. It crosses the human placenta with infantile blood levels in excess of the mother's blood, giving rise to a higher risk for the fetus. Pathological features of children's brains affected by prenatal methylmercury exposure are the outcome of disturbances in the development of the brain; microcephaly, dilated lateral ventricles, as well as derangement in the fundamental structuring of gray matter as the result of abnormal neuronal migration. Degeneration of already formed nerve cells is involved in some cases. Lead has been shown to pass through the human placenta readily, and the concentration in the umbilical cord blood is 80-90% as high as that in the maternal blood. A large cohort study suggests that increased exposure to lead from the environment in the prenatal and early postnatal periods results in the deficit of mental development. Teratogenicity of many metal compounds such as aluminum, cadmium, chromium, indium, nickel, platinum, tellurium, thallium, ytterbium and zinc salts has been confirmed in experimental animals. Some metalloids (e.g., arsenic, selenium and lithium) appear to have teratogenic potential for humans.

198
TITLE:

Localization of Mercury in CNS of the Rat. An Autometallographic Study

AUTHORS:
Moller-Madsen B

SOURCE:
Pharmacology and Toxicology, Vol. 75, Supplement 1, pages 7-41, 115 references, 1994

ABSTRACT:
Studies were conducted to establish an autometallographic technique for mercury (7439976) (Hg) localization, assess the regional and cellular localization of Hg in the rat central nervous system (CNS), and examine the effect of selenium (7782492) on Hg distribution in the CNS. Using the autometallographic method, mercury sulfide and mercury selenides in tissues become visible as metallic silver/mercury grains after treatment with a developer. Both light and electron microscopy could be used to examine tissues processed by this method. Studies were conducted on Wistar-rats, NMRI-mice, guinea-pigs, and hedgehogs; rats were used for most studies. Animals were exposed to Hg vapor by inhalation and methylmercuric-chloride (115093) (CH3HgCl) or mercuric-chloride (7487947) (HgCl2) via oral administration or intraperitoneal injection. Ingestion of HgCl2 resulted in a nonuniform localization of Hg. Heavy Hg deposition was observed in the rhombencephalon, nuclei strongly linked with motor function, neurons, and lysosomes of stained cells. Intraperitoneal and oral administration of HgCl2 results were comparable. Inhalation of 50, 500, and 550 micrograms Hg vapor/cubic meter resulted in Hg deposition in the vessel walls of the cerebrum and spinal cord, cytoplasm of neurons, and nerve cells and nuclei of the brain stem, respectively. A uniform, time and dose dependent pattern of Hg distribution was observed after ingestion and injection of CH3HgCl. As with inorganic Hg treatment, localization varied with route of administration. Hg vapor resulted in the most pronounced accumulation of Hg in the CNS. Rats coadministered sodium-selenite (10102188) (Na2SeO3) with HgCl2 did not reveal significant differences in distribution pattern from those administered only HgCl2. Coadministration of Na2SeO3 and CH3HgCl resulted in a uniform distribution of stained cells throughout the brain and upper spinal cord, with an increase in the staining of nuclei of neurons and heavy lysosomal staining. The author concludes that a direct relationship exists between the chemical properties of Hg compounds and the extent and distribution of mercury localization in the CNS, and that the autometallographic technique proves to be a valuable supplement to existing procedures.

199
TITLE:
Mutagenicity And Teratogenicity Of Mercury Compounds

AUTHORS:

Leonard A
Jacquet P
Lauwerys RR

SOURCE:
Mutation Research, Vol. 114, No. 1, pages 1-18, 206 references, 19831983

ABSTRACT:
The mutagenicity and teratogenicity of mercury (7439976) compounds are reviewed. The occurrence and uses of mercury are summarized. Agriculture, use of fossil fuels, and industry are the major sources of pollution by mercury, which is released into the environment as metallic mercury or as inorganic and organic compounds. Metabolism and general toxicity of mercury compounds are discussed. The mutagenicity of mercury compounds is considered. The occurrence of C-mitosis which can result in aneuploidy and polyploidy is the most apparent mutagenic effect of mercury compounds on eukaryotes. Screening and mutagenicity tests with eukaryotes are described. Observations on plant material are discussed. In-vivo chromosome studies are outlined. The production of genetic damage in mammalian germ cells is examined. Teratogenicity of mercury compounds is discussed. Alkyl mercury compounds penetrate the human placenta easily and intra uterine poisoning has frequently occurred. Experimental studies on the teratogenic and neurological effects of alkyl mercury compounds in mammalian species are described. The neurological effects of mercury on the fetal brain are discussed.

200
TITLE:
Biotransformation Of Methylmercury Salts In The Rat Studied By Specific Determination Of Inorganic Mercury

AUTHORS:
Norseth T
Clarkson TW

SOURCE:
Biochemical Pharmacology, Vol. 19, No. 10, pages 2775-2783, 21 references, 19701970

ABSTRACT:
The release of inorganic methylmercury salts was investigated in-vivo and in-vitro. The rate of biotransformation of methylmercury-chloride (115093) in kidney tissue of untreated female Sprague-Dawley-rats was compared with that in animals injected with 4.65 micrograms per gram (microg/g) unlabeled mercuric-chloride. Some rats were pretreated with the same dose of unlabeled mercuric-chloride, followed 5 days later by labeled methylmercury-chloride. Female Sprague-Dawley-rats were intravenously injected with a dose of 0.5 milligram mercury/g mercury-203

labeled methylmercury-chloride. Feces were collected and assayed for mercury. One week post injection, organs were homogenized and mercury concentrations were determined. When exchangeable mercury was measured after in-vitro addition of labeled methylmercury-chloride, values for liver and kidney homogenates were close to 2 percent. However, the exchangeable radioactivity recovered from suspensions of red cells was 4 percent higher than the value obtained for liver and kidney homogenates. Plasma, urine, and bile samples gave values approximately 1 percent lower. Methylmercury-chloride alone gave an inorganic mercury concentration of 1.3microg/g wet weight kidney tissue; labeled mercuric-chloride gave a concentration of 1.30microg/g. Pretreatment with unlabeled mercuric-chloride followed by labeled methylmercury-chloride produced kidney concentrations of 1.21microg mercury/g. One week after methylmercury-chloride injection, 39 percent of radioactivity in kidney was present as inorganic mercury. Inorganic mercury in liver, plasma, and feces averaged 11, 22, and 4 percent, respectively. The brain contained only about 3 percent inorganic mercury. The authors conclude that methylmercury-chloride is slowly converted to inorganic mercury, the slow rate of metabolism creating stringent demands on the analytical method. Release of inorganic mercury is the major biotransformation pathway available for methylmercury salts in rats.

201

TITLE:

Mercury (Hg2+) Decreases Voltage-Gated Calcium Channel Currents in Rat DRG and Aplysia Neurons

AUTHORS:

Pekel M
Platt B
Busselberg D

SOURCE:

Brain Research, Vol. 632, Nos. 1/2, pages 121-126, 34 references, 1993

ABSTRACT:

The effects of mercury (7439976) (Hg) on voltage gated calcium channel currents in rat dorsal root ganglion (DRG) and Aplysia neurons were investigated in-vitro. Primary cultures of DRG neurons from 2 to 3 day old rat pups were exposed to inorganic mercury as mercury-chloride (7487947) using a fast bath perfusion system. Aplysia-californica abdominal ganglions were incubated in artificial sea water, and exposed to mercury-chloride using a rapid perfusion system. Inorganic mercury decreased the voltage gated calcium channel currents irreversibly in the two preparations. In the DRG neuron preparation, the exposure caused a rapid concentration dependent decrease in the L type currents to a steady state. With increasing mercury concentrations, a low membrane current was additionally activated, most obviously at concentrations over 2 micromolar

(microM) Hg2+. The current was irreversible and may have been due to the opening of other ion channels by mercury. A binding of mercury to the channel protein and/or modifying its gating properties was suggested by the current voltage relation of DRG neurons being shifted to more positive values. In the A-californica neurons a continuous decrease of calcium channel currents was observed even with the lowest concentration of mercury used, 5microM. Even with high concentrations, a steady state was not reached and the effect was irreversible with no change occurring on resting membrane currents. No shift was observed in the current voltage relation of the calcium channel currents. The authors conclude that the neurotoxic effects of mercury could be partially due to the irreversible blockage of voltage activated calcium channels.

202

TITLE:

Binding of Mercury to Metallothionein-Like Protein in Fetal Liver of the Guinea Pig Following in Utero Exposure to Mercury Vapor

AUTHORS:

Yoshida M
Aoyama H
Satoh H
Yamamura Y

SOURCE:

Toxicology Letters, Vol. 37, No. 1, pages 1-6, 11 references, 19871987

ABSTRACT:

The possible involvement of metallothionein in the detoxification of mercury (7439976) in fetal liver was investigated using pregnant Hartley-guinea-pigs exposed to mercury vapors for 150 minutes between day 60 and day 65 of gestation. Mercury concentrations in the air ranged from 8 to 11mg/m3. Mercury levels in fetal brain, lungs, heart, kidneys, and whole blood were markedly lower than those in maternal organs and tissues, while levels in fetal liver were higher than in maternal liver. In the maternal liver, most mercury was associated with a high molecular weight protein fraction. About 8 percent was bound to a broad band showing a peak where metallothionein like protein would be expected to elute (molecular weight of about 10,000 to 12,000). No zinc was found in this region. In the fetal liver, more than 50 percent of the eluted mercury was in the metallothionein-like protein fractions. Zinc was also observed in this region. The authors conclude that the finding of such a large amount of mercury associated with metallothionein suggests that zinc or copper is displaced from preexisting metal/thionein complexes by mercury, rather than induction of metallothionein by mercury vapor exposure. Fetal liver metallothionein apparently plays a significant part in reducing the toxicity of mercury vapor to the fetus by reducing distribution to other tissues.

203
TITLE:
The Effects of Dose of Elemental Mercury and First-Pass Circulation Time on Exhalation and Organ Distribution of Inorganic Mercury in Rats

AUTHORS:
Magos L
Clarkson TW
Hudson AR

SOURCE:
Biochimica et Biophysica Acta, Vol. 991, No. 1, pages 85-89, 17 references, 19891989

ABSTRACT:
The effects of dose and distances between the injection sites and the lungs on the exhalation and distribution of mercury (7439976) (Hg) in the body of male Porton-Wistar-rats within 60 seconds after dosing were determined. During the first passage through the lung following an intravenous dose of elemental mercury dissolved in aqueous buffer, the amount exhaled ranged from 10 to 17 percent of the injected dose. The precise amount varied according to the original dose level, 0.11 or 1.1 micrograms of mercury/rat and the injection site, being either jugular vein of tail vein. The total amount of mercury extracted during the 60 second period was in the range of 40 to 49 percent of the dose given. Limiting the availability of elemental mercury to certain tissues depended to a large extent on the oxidation of elemental mercury (Hg-0) to Hg2+. When the injection was given to the jugular vein, the residence time in the blood was short, 0.6 seconds, before passing through the lungs for the first time and 12.9 to 17 percent was exhaled in the this lung pass. This compared to 10.4 to 12 percent being exhaled when the elemental mercury was injected to the tail vein and thus remained in the body longer before it made its first pass through the lungs, 1.8 seconds. Even at 60 seconds after dosing there was a general tendency for certain tissues to have higher values after dosing from the jugular vein as compared to the tail vein. These tissues included the lung, brain, and heart. The authors estimate that the half time for oxidation was 3.3 seconds. Blood levels were lower after elemental mercury injection, particularly after the higher dose level, than after Hg2+ injection, consistent with the model where elemental mercury is in part oxidized by red blood cells with the remainder rapidly diffusing in tissues where it is also oxidized to Hg2+.

204
TITLE:
TOXICITY OF METHYL MERCURY IN A FISH EATING POPULATION

AUTHORS:

CLARKSON TW

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Methyl mercury is considered to be a developmental neurotoxicant. However, contr ary to expected findings, a longitudinal study in the Seychelles has revealed a positive association between increasing mercury levels, measured in maternal hai r prenatally and in infant hair, and enhanced child development. Given that fis h consumption the Seychelles is high, and that fish intakes correlate with hair mercury levels, we hypothesize that certain micronutrients in fish may be (a) be neficial the child development and (b) protective against the neurotoxic effects of methyl mercury. We propose to test this hypothesis in a new study of 250 mot her-infant pairs recruited in the Seychelles during the first trimester and foll owed longitudinally until the infants reach 29 months of age using the most sens itive developmental endpoints available. The four likely micronutrients, based on their levels in fish and their documented roles in brain development and prio ritized in terms of biological plausibility, are the long chain polyunsaturated fatty acids principally docosahexaenoic acid, iodine, iron and the amino acid ta urine. Also, selenium may play a role as a modifier of the toxic action of meth yl mercury and, as such, will be included with mercury as an independent variabl e. Mercury in maternal and infant hair will continue to be used as our primary measure of prenatal and post natal exposures. In addition to direct measures of mercury, micronutrient status and selenium levels in biological samples from mot her and infant, a diet survey including fish consumption will be made at selecte d pre- and postnatal stages of this study. These data will allow us to characte rize metabolic interrelationship between fish intake and levels of mercury and m icronutrients that should further test the plausibility of our hypothesis. This proposed study should break new scientific grounds on the interrelationship betw een nutrition and toxicology. Specifically, we expect that data emanating from t he project to indicate that nutritional variables must be taken into account in any evaluation of the neurotoxicity of methyl mercury when fish is the principal source of human exposure to mercury.

205
TITLE:
The Influence Of Administered Mass On The Subcellular Distribution And Binding Of Mercury In Rat Liver And Kidney

AUTHORS:
Planas-Bohne F
Taylor DM
Walser R

SOURCE:
Archives of Toxicology, Vol. 56, No. 4, pages 242-246, 12 reference, 19851985

ABSTRACT:
The effect of the size of a dose of mercury (7439976) on distribution of the metal in body organs was studied in rats. Sprague-Dawley-rats were administered radiolabeled mercury-chloride (51312244) by intravenous injection via lateral tail vein, producing doses in the range of 0.17 to 1.65 milligrams per kilogram (mg/kg) elemental mercury. After 24 hours, the animals were sacrificed, and tissues were excised, weighed, and analyzed. Mercury content in tissues and subcellular fractions was assayed by gamma ray spectrometry, using a standard containing 1 percent of the injected radioactivity. Activities of mitochondrial and lysosomal enzymes were determined in tissue homogenates. The fraction of the administered dose of mercury deposited in the liver increased 3 fold over the dose range tested, whereas the retained dose in the kidney decreased by a factory of 2. Uptake of mercury in the lung, spleen, brain, thymus, and salivary glands showed no dose dependent variation. In the kidney, there were no apparent changes in the distribution of mercury in subcellular organelles; however, there were decreases in the deposition of mercury in the lysosomal and nuclei cell debris fractions of the liver, with a corresponding sharply dose dependent increase in liver cytosol concentrations. The concentration of mercury bound to metallothionein in liver cytosol was dose dependent. In kidney cytosol, the mass of mercury bound to metallothionein increased with doses up to 0.55mg/kg and thereafter remained relatively constant. The authors suggest that mercury binding to metallothionein in the kidney is saturated at 0.55mg/kg, whereas the saturation point for liver metallothionein is not reached even at the high doses.

206
TITLE:
TOXICITY OF METHYL MERCURY IN A FISH EATING POPULATION

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Methyl mercury is considered to be a developmental neurotoxicant. However, contrary to expected findings, a longitudinal study in the Seychelles has revealed a positive association between increasing mercury levels, measured in maternal hair prenatally and in infant hair, and enhanced child development. Given that fish consumption the Seychelles is high, and

that fish intakes correlate with hair mercury levels, we hypothesize that certain micronutrients in fish may be (a) beneficial the child development and (b) protective against the neurotoxic effects of methyl mercury. We propose to test this hypothesis in a new study of 250 mother-infant pairs recruited in the Seychelles during the first trimester and followed longitudinally until the infants reach 29 months of age using the most sensitive developmental endpoints available. The four likely micronutrients, based on their levels in fish and their documented roles in brain development and prioritized in terms of biological plausibility, are the long chain polyunsaturated fatty acids principally docosahexaenoic acid, iodine, iron and the amino acid taurine. Also, selenium may play a role as a modifier of the toxic action of methyl mercury and, as such, will be included with mercury as an independent variable. Mercury in maternal and infant hair will continue to be used as our primary measure of prenatal and post natal exposures. In addition to direct measures of mercury, micronutrient status and selenium levels in biological samples from mother and infant, a diet survey including fish consumption will be made at selected pre- and postnatal stages of this study. These data will allow us to characterize metabolic interrelationship between fish intake and levels of mercury and micronutrients that should further test the plausibility of our hypothesis. This proposed study should break new scientific grounds on the interrelationship between nutrition and toxicology. Specifically, we expect that data emanating from the project to indicate that nutritional variables must be taken into account in any evaluation of the neurotoxicity of methyl mercury when fish is the principal source of human exposure to mercury.

207

TITLE:

Effects of Buthionine Sulfoximine (BSO) on Mercury Distribution after Hg0 Exposure

AUTHORS:

Kim C-Y
Watanabe C
Satoh H

SOURCE:

Toxicology, Vol. 98, Nos. 1-3, pages 67-72, 26 references, 1995

ABSTRACT:

Pretreatment of mice with buthionine-sulfoximine (BSO) to deplete glutathione (GSH) was performed to determine whether lipid peroxidation and the distribution of mercury (7439976) in tissues after exposure to mercury vapor would be affected. BSO was administered intraperitoneally to male ICR-mice 3.5 hours before mercury exposure. The mice inhaled mercury vapor at 3.2mg/m3 in a chamber for 2 hour. BSO pretreatment significantly decreased the levels of GSH in liver, kidney and lung

tissue. The highest concentration of mercury after exposure to mercury vapor was found in the kidney, and BSO pretreatment significantly decreased mercury concentrations in the kidney, but increased mercury concentrations in the lung, plasma, and liver. BSO pretreatment did not affect mercury uptake by the brain, heart, and red blood cells. Oxidative damage, as monitored by thiobarbituric-acid reactive substances, occurred in the kidney and lung, but were not significantly important. The authors conclude that a decrease in GSH changed the mercury distribution after mercury vapor exposure.

208
TITLE:
The Distribution of Inhaled Mercury (Hg-203) Vapors in the Brain of Rats and Mice

AUTHORS:
Cassano GB
Viola PL
Ghetti B
Amaducci L

SOURCE:
Journal of Neuropathology and Experimental Neurology, Vol. 28, pages 308-320, 20 references, 19661966

ABSTRACT:
Distribution of radioactive labeled mercury (7439976) was studied by means of microautoradiography and chemical analysis, in mice exposed to radioactive mercury vapors 6 hours daily for 10 days. Brain sections of mice and rats showed a greater concentration of radioactivity in the gray than in the white matter. The highest concentration appeared in certain neurons of the cerebellum, the spinal cord, the medulla, the pons, and the midbrain. In the cerebellum, silver grains were selectively localized in the Purkinje cells, and in the neurons of the nucleus dentatus. Analysis of the different chemical fractions of the brain showed that radioactivity can be detected in the water-washing fraction and in the insoluble tissue residue, and that an equilibrium may exist between the radioactivity of these two fractions. Radiomercury was found in free and bound fractions equally distributed in the brain.

209
TITLE:
Brain mercury in neurodegenerative disorders.

AUTHORS:
FUNG YK
MEADE AG
RACK EP

BLOTCKY AJ

SOURCE:
JOURNAL OF TOXICOLOGY CLINICAL TOXICOLOGY; 35 (1). 1997. 49-54.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Background: Trace element neurotoxicity has long been invoked as an etiologic factor for Alzheimer's disease. This study was conducted to determine the concentrations of mercury in seven different brain regions from decreased patients histologically confirmed with Alzheimer's disease or multiple sclerosis as compared to control subjects without known central nervous system and renal disorders. Brain mercury concentrations in all deceased subjects can arise from amalgam restorations, diet, and the working environment. Methods: Autopsy frozen specimens (control, Alzheimer's disease and multiple sclerosis) from seven brain regions, which included frontal cortex, temporal cortex, occipital cortex, putamen, hippocampus, corona radiata and corpus callosum were assayed for the concentrations of selenitun using instrumental neutron activation analysis and mercury using radiochemical neutron activation analysis. Results: We found that the concentrations of mercury and the mercur

210
TITLE:
A developmental profile of trk immunoreactivity in the rat brain is affected by gestational exposure to methyl mercury.

AUTHORS:
Barone S Jr
Haykal-Coates N
Goldey ES
Tilson HA

SOURCE:
Abstr Soc Neurosci 1993;19(Pt 2):1734

ABSTRACT:
The high affinity nerve growth factor receptor, trk has been implicated in neuronal growth and differentiation. In this study we examined the effects of gestational exposure to the developmental neurotoxicant methyl mercury on the developmental profile of immunoreactivity (IR) for this receptor. Long-Evans dams were dosed on gestational days 6-15 (po) with 0, 0.1, 1, or 2 mg/kg methyl mercury dissolved in saline. Pups were sacrificed and perfused with buffered paraformaldehyde on postnatal days (PND) 1, 4, 10, and 21. The brains were sectioned sagittally, stained immunohistochemically, and examined throughout the medial and lateral extent of the brain. The greatest density of immunoreactivity of neural cell bodies was seen in the olfactory bulb, hippocampus, septum, striatum,

nucleus basalis, inferior colliculus, pons, cerebral, and cerebellar cortex, and axonal staining was prominent in the brainstem, neocortex, hippocampus, cerebellum, and olfactory tract. In general the regional pattern of this IR was transient except in the olfactory bulb, hippocampus, cerebellum. In controls, trk IR appeared to peak at PND4, decreasing dramatically on PND10 and decreasing further after PND21. An adult-like pattern was apparent on PND21 with trk IR in the hippocampus and cerebellum. Methyl mercury produced a dose-related decrease which was apparent at PND1, PND10, and PND21 but not at PND4. This decrease in trk IR was not related to overt pathology at the time points examined. The present results characterize the cellular and regional ontogeny of the tyrosine kinase, trk and suggest that developmental exposure to methyl mercury can alter the ontogeny of this trophic factor receptor.

211

TITLE:

Altered levels of neurotrophic factor mRNA in rat frontal lobe and cerebellum during developmental exposure to mercury vapor.

AUTHORS:

Chao SL
Haines WT
Barone S Jr
Tilson HA
Beliles RP
Morgan DL
Harry GJ

SOURCE:

Abstr Soc Neurosci 1998;24(Pt 1):544

ABSTRACT:

Neurotrophic factors play a pivotal role in promoting neuron survival and differentiation. The levels of mRNA for several neurotrophic factors were examined in the developing rat brain following gestational nose-only exposure to mercury vapor (HgVap) at gestational days 6-15 to 2 mg/m3. In the cerebellum, mRNA levels of neurotrophin-3 (NT3) in control animals showed a gradual increase with a peaked level at PND14; ciliary neurotrophic factor (CNTF) and brain-derived neurotrophic factor (BDNF) mRNA levels gradually increased until 21 days; mRNA levels for beta nerve growth factor (betaNGF) remained low throughout development. Following HgVap exposure, CNTF, NT3, BDNF, and betaNGF mRNA levels were significantly increased at distinct timepoints for each factor. In the frontal lobe of controls, CNTF, BDNF, and betaNGF mRNA exhibited a gradual age-related increase. Levels of NT3 mRNA were low and consistent over time. Exposure to HgVap produced a selective increase in NT3 mRNA levels in the frontal lobe with no alterations seen in CNTF, betaNGF, and BDNF mRNA levels. The results, therefore, demonstrate that HgVap at moderate

concentrations can alter levels of neurotrophic mRNA, suggesting possible mechanisms for mercury toxicity in the developing central nervous system.

212
TITLE:
Speciation of mercury in the primate blood and brain following long-term exposure to methyl mercury.

AUTHORS:
VAHTER M
MOTTET NK
FRIBERG L
LIND B
SHEN DD
BURBACHER T

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 124 (2). 1994. 221-229.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Total (T-Hg) and inorganic (1-Hg) mercury in blood and brain of female Macaca fascicularis monkeys, exposed to daily peroral doses of methyl mercury (MeHg; 50 mug Hg/kg body wt) for 6, 12, or 18 months, or to continuous iv infusion of HgCl2 (200 mug Hg/kg body wt) for 3 months, were determined. In normal weight monkeys (2.4-4.1 kg body wt) exposed to MeHg, steady state of T-Hg in blood (1.1 mug Hg/g) was reached in about 4 months. The elimination T1/2 in blood was 26 days. I-Hg constituted 7% of T-Hg in blood. The average concentration of MeHg in occipital pole and thalamus was about 3 mug Hg/g at 6 months and 4.5 mug Hg/g at 12-18 months. Accumulation in brain seemed to be biphasic. Following termination of 12 months exposure, elimination T1/2 for MeHg in brain was 35 days. 1-Hg constituted about 9% of T-Hg in brain at 6-12 months, 18% at 18 months, and 74% at 6 months after termination of exposure. The I-Hg concentrations were somewhat higher in thalamus than in occip

213
TITLE:
Choroid Plexus Protects Cerebrospinal Fluid against Toxic Metals

AUTHORS:
Zheng W
Perry DF
Nelson DL
Aposhian HV

SOURCE:
The FASEB Journal, Vol. 5, No. 8, pages 2188-2193, 28 references, 1991

ABSTRACT:

The ability of the choroid plexus to sequester toxic metals was examined. Male Sprague-Dawley-rats were injected intraperitoneally with 4mg/kg cadmium (7440439) as cadmium-chloride (10108642) (CdCl), 27mg/kg lead (7439921) as lead-acetate (301042), or 1mg/kg mercury (7439976) as mercuric-nitrate (10045940) or methylmercuric-chloride (115093). Male New-Zealand-white-rabbits were injected intravenously with 2mg/kg arsenic (7440382) as sodium-arsenate (7778430). The animals were killed 24 hours later and the lateral choroid plexus, cerebrospinal fluid (CSF), brain cortex, and blood were taken and assayed for lead, cadmium, arsenic, and mercury. The choroid plexus and cortex from cadmium treated rats were analyzed for cadmium-metallothionein (CdMT). Rats were injected with 0, 5.4, 10.8, 16.2, or 27mg/kg lead and killed 0, 4, 8, or 24 hours later to assess the dose and time dependence of lead accumulation in the lateral choroid plexus. The lateral choroid plexus and brain cortex were removed from untreated rats and analyzed for reduced-glutathione (GSH), cystine, and other thiols. The lateral choroid plexus from untreated rats was incubated with cadmium-109 tagged CdCl and artificial CSF in the presence or absence of 1.5 millimolar ouabain (630604) for 10 minutes. The concentrations of lead, mercury, and arsenic in the choroid plexus were 70, 95, and 40 times higher than in the CSF. A significant accumulation of cadmium occurred in the plexus, but cadmium was not detected in the CSF. Choroid plexus lead concentration was 57 times that of the brain cortex. Mercury, lead, and arsenic concentrations in the CSF were 0.013, 0.077, and 0.083 those of the blood. Lead accumulated in the choroid plexus in a dose and time related manner. CdMT could not be detected in the choroid plexus. GSH, free thiol, and low molecular weight thiol concentrations in the choroid plexus were significantly lower than in the brain cortex. Choroid plexus cystine concentrations were significantly higher. Ouabain inhibited cadmium uptake in the choroid plexus by 57%. The authors conclude that the choroid plexus has a definite capacity to sequester toxic heavy metals.

214

TITLE:

Impairment Of The Blood-Brain Barrier In Mercury Poisoning

AUTHORS:

Steinwall O
Olsson Y

SOURCE:

Acta Neurologica Scandinavica, Vol. 45, No. 3, pages 351-361, 25 references, 19691969

ABSTRACT:

The effect of mercury (7439976) on the blood/brain barrier was studied in

rats. Sprague-Dawley-rats were injected intravenously (iv) or intraperitoneally (ip) with mercuric-chloride (7487947) or methylmercuric-dicyandiamide (502396) (MMDC) in doses of 2 to 20 milligrams per 100 grams (mg/100g). The animals were observed for signs of intoxication. Rats were injected with the fluorescent dye Evans-Blue or selenium-75 (Se-75) labeled selenomethionine. The animals were then killed at selected times and the distribution of Evans-Blue or Se-75 in the plasma, cerebellum, cerebral hemispheres, and sciatic nerves was determined. Rats given 2 to 3mg/100g mercuric-chloride ip tolerated the doses well, showing no signs of neurological impairment. Rats given 5 to 20mg/100g mercuric-chloride or MMDC became drowsy within a few minutes. Those given 20mg/100g mercuric-chloride iv died within 2 to 4 minutes. Most of the treated rats showed disturbed cerebrovascular permeability, as indicated by the presence of the dye inside or outside blood vessels in the brain. Scattered areas of fluorescence were found in the cerebellum and cerebral parenchyma. Only a few rats showed signs of disturbed permeability in the sciatic nerve. Se-75 activity in the brain parts and sciatic nerves was lower in treated rats than in control animals. The authors conclude that impairment of the blood/brain barrier functions might be involved in the pathogenesis of mercury poisoning.

215

TITLE:

Gestational exposure to mercury vapor: effects on neurotrophic factor stimulated phosphoinositide hydrolysis and protein kinase C activity.

AUTHORS:

Parran DK
Chanda SM
Morgan DL
Beliles RP
Haykal-Coates N
Freudenrich T
Mundy WR
Barone S Jr

SOURCE:

Toxicologist 1998 Mar;42(1-S):195

ABSTRACT:

Gestational exposure to mercury (Hg) vapor can result in elevated levels of Hg in the brain of fetal and neonatal rats. In the present study, we examined changes in neurotrophin-stimulated phosphoinositide (PI) hydrolysis and Protein Kinase C (PKC) activity after gestational exposure to Hg vapor. Long-Evans dams received nose-only exposure to air or 4 mg Hg/m3 for 2 hr/day from gestational day 6 to 15. Pup cortex and cerebellum were collected on postnatal days (PND) 1, 4, 10, and 21 for PI hydrolysis and PKC activity. In males only, PI hydrolysis was measured as the

accumulation of inositol phosphates (IP) in brain slices from cortex and cerebellum at PND 1 and 4 in the absence (basal) and presence of maximally stimulating levels of agonists. The neurotrophins NT-3 and BDNF (500 ng/mL) produced a 2-3 fold stimulation of IP accumulation in both the cortex and cerebellum on PND1 which decreased on PND4 and was not apparent at PND10. Hg vapor exposure resulted in small increases in both basal and stimulated IP accumulation, except for a decrease in BDNF-stimulated IP accumulation in the cerebellum. PKC activity in cortex and cerebellum was examined in both males and females using the MARCKS PSD peptide. After a decrease in PKC activity from PND1 to PND4, there was an age-related increase in PKC activity on PND10 and PND21. In the cortex, control females had higher PKC activity compared to control males. Hg exposure increased PKC activity by 12-33% in males, but decreased activity (approximately 10%) in females in the cortex. In the cerebellum, PKC activity was similar in control males and females. Hg exposure decreased PKC activity (10-15%) in males and females, with recovery to control levels by PND21 in the cerebellum. Therefore, gestational exposure to Hg vapor appears to affect growth-related signal transduction in neonatal brains.

216

TITLE:

Biochemical Markers of Neurotoxicity. A Review of Mechanistic Studies and Applications

AUTHORS:

Manzo L
Artigas F
Martinez E
Mutti A
Bergamaschi E
Nicotera P
Tonini M
Candura SM
Ray DE
Costa LG

SOURCE:

Human and Experimental Toxicology, Vol. 15, Supplement 1, pages S20-S35, 118 references, 1996

ABSTRACT:

Studies of biochemical markers in peripheral tissues, that relate to nervous system damage, were reviewed to evaluate surrogate indicators of neurotoxicity in tissues that are easily and ethically obtainable from human subjects. Recent pharmacological and psychobiological studies that examined neurotransmitter synthesizing and degrading enzymes, membrane bound receptors, second messengers and other markers found in blood,

plasma and cerebrospinal fluid, were reviewed. Peripheral blood lymphocyte cholinergic muscarinic receptors and calcium signaling, blood polyamines, and myelin basic protein in cerebrospinal fluid were evaluated based on animal studies of neurotoxin exposure. Exposure to the organophosphorus insecticide disulfoton (298044) significantly reduced muscarinic receptor density and acetylcholinesterase activity in rat brain tissue and circulating lymphocytes, although recovery after exposure was slower in brain, for both markers. Triethyltin (997502) administration failed to produce increased levels of myelin basic protein but its toxicity was monitored satisfactorily by auditory and somatosensory responses. Responses peaked at 24 hours with a slow recovery. Polyamine content in red cells, plasma and brain tissue was altered in rats administered convulsant doses of kainic-acid (487796). Treatment of rats with a single dose of drugs such as p-chloroamphetamine, d-fenfluramine, or reserpine, that affect brain serotonergic systems, substantially reduced brain tissue and whole blood serotonin levels. The effects of neurotoxic metals, such as mercury (7439976), on calcium metabolism or second messenger systems were studied in rat splenic lymphocytes. Cytosolic free calcium showed time and dose dependent increases in response to mercury exposure. Data on dopamine-beta-hydroxylase, monoamine-oxidase and serum prolactin, in workers occupationally exposed to lead (7439921), manganese (7439965) or styrene (100425) were also assessed. Observed changes in these indicators were related to specific internal dose indicators for the toxins. The authors conclude that neurochemical markers can augment the predictivity and sensitivity of laboratory tests used in animal studies.

217
TITLE:
Interactions of mercury in rat brain.

AUTHORS:
FALNOGA I
KREGAR I
SKREBLIN M
TUSEK-ZNIDARIC M
STEGNAR P

SOURCE:
BIOL TRACE ELEM RES; 37 (1). 1993. 71-83.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In order to study the metabolism of mercury (Hg), its affinity to metallothionein (MT), and its influence on levels of the essential metals copper and zinc in the brain tissue of rats exposed to elemental mercury (HgO) vapor was investigated. The major findings were: 1. After long-term exposure, about 40% of mercury was found in the brain water-soluble phase (supernatant); 2. In brain supernatant, about

80% of Hg was found in the range of low-molecular-weight proteins; the MT-like protein Hg-Cu-Zn-thionein was isolated and partially characterized; 3. HgO vapor exposure resulted in increased tissue levels of essential Cu and Zn in addition to exogenous Hg; and 4. Experiments showed that HgO vapor exposure can induce the stimulation of rat brain MT synthesis.

218
TITLE:
Demethylation of methyl mercury in different brain sites of Macaca fascicularis monkeys during long-term subclinical methyl mercury exposure.

AUTHORS:
VAHTER ME
MOTTET NK
FRIBERG LT
LIND SB
CHARLESTON JS
BURBACHER TM

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 134 (2). 1995. 273-284.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Total (T-Hg) and inorganic (I-Hg) mercury concentrations were determined in specific brain sites (cerebellum, occipital pole, pons, motor strip, frontal pole, temporal pole, thalamus, and pituitary) of female Macaca fascicularis monkeys exposed to daily peroral doses (50 mug Hg/kg body weight) of methyl mercury (MeHg) for 6, 12, or 18 months, or to continuous iv infusion of HgCl2 (200 mug Hg/kg body wt). In normal weight monkeys (2.4-4.1 kg body wt), the average concentration of MeHg (calculated as T-Hg minus I-Hg) was about the same in all brain sites, except the pituitary - 3.0 mug Hg/g at 6 months, 4.2 mug/g at 12 months, and 4.3 mug Hg/g at 18 months. MeHg concentrations in the pituitary were about 50% of those in the other brain sites. In a group of monkeys that were kept unexposed for 6 months following 12 months of MeHg exposure, T 1/2 for MeHg was about 37 days in all brain sites, with the exception of the pituitary, where it was shorter. The concentration of I-

219
TITLE:
Neurotoxic Effects of Selected Metals

AUTHORS:
Wennberg A

SOURCE:

Scandinavian Journal of Work, Environment and Health, Vol. 20, Special Issue, pages 65-71, 70 references, 1994

ABSTRACT:

In a review of the Nordic Expert Group guidelines for assessing neurotoxicity, the anatomic and functional characteristics of a nerve cell and the neurotoxicity of lead (7439921), manganese (7439965), aluminum (7429905), and mercury (7439976) were reviewed. Lead has been shown to affect the central nervous system (CNS) on many levels including the metabolism, membrane, nerve transmission, and myelin formation level. These effects can result in encephalopathy with ataxia, coma, or convulsions. Lead can penetrate the blood brain barrier. Peripheral nerve function is disrupted. The critical level of blood lead concentrations causing CNS and peripheral nervous system effects in adults appear to be about 30 to 40 milligrams per 100 milliliters (mg/100ml). Children are more susceptible to lead neurotoxicity than adults. Their critical blood lead concentrations appear to be 5 to 10mg/100ml. Manganese can exert acute and chronic neurotoxicity. Acute manganese neurotoxicity is primarily associated with psychiatric symptoms, while chronic manganese neurotoxicity is manifested by a cluster of symptoms that resemble Parkinson's disease: tremor, rigidity, and bradykinesia. Manganese exerts its effects by interfering with transmission in dopaminergic nerve cells in the basal ganglia in the brain. It also impairs oxidative metabolism in brain cells. Aluminum neurotoxicity was discussed with an emphasis on the possible association with Alzheimer's disease (Alz) or a dementia similar to Alz. Epidemiological studies, however, have yet to establish a relationship between aluminum exposure and Alz. Experimental studies have shown that aluminum is a potent neurotoxicant when placed in contact with nerve tissue. Because it is not easily absorbed from the gastrointestinal tract, aluminum can be used at high concentrations in antacids. The basis of its neurotoxicity is not fully understood, although it is known to interfere with cellular metabolism, cell membranes, and nerve transmission. Exposure to organic mercury causes cerebellar ataxia and visual and sensory disturbances. Exposure to mercury vapor or inorganic mercury compounds causes primarily tremors. The mechanism of mercury neurotoxicity probably involves an effect on nerve cell metabolism in the cerebellum and, possibly, the anterior root cells.

220

TITLE:

Mercury poisoning and medical proof.

AUTHORS:

Ganley PM

Porteus BD

SOURCE:

Med. Trial Tech. Quart.; 18(4): 374-406; 1972

ABSTRACT:

HAPAB Widespread disintegration of brain cells, particularly in the area controlling coordination and visual perception, is characteristic of mercury poisoning. In Iraq hundreds of cases of poisoning, with many deaths, were reported due to consumption of homemade bread made from grain dressed with ethyl mercury toluene sulfonamide. Disturbance of speech, cerebellar ataxia, and spasticity were the major symptoms, and kidneys, heart, skin, gastrointestinal tract, and muscles were affected in addition to the nervous system. In New Mexico a number of children suffered permanent brain damage as a result of eating meat from a hog fed mercury-treated seed. Fetal tissue may be quite sensitive to and accumulate mercury in amounts greater than would be expected from levels in the mother. Treatment is generally symptomatic and often unsuccessful. Diagnosis is difficul, especially in cases with minimal initial symptoms. The Porteus Maze Test for intelligence may be a useful diagnostic tool for detecting organic brain damage. Combining newly developed or refined histological and chemical examinations with this test can offer medical proof of the degree of injury from mercury poisoning.

221

TITLE:

Decreased Learning Capacity In Rats Exposed Prenatally And Postnatally To Low Doses Of Mercury

AUTHORS:

Olson K
Boush GM

SOURCE:

Bulletin of Environmental Contamination and Toxicology, Vol. 13, No. 1, pages 73-79, 10 references, 19751975

ABSTRACT:

The effects of prenatal and postnatal exposure to low concentrations of mercury (7439976) on learning capacity were examined in Holtzman-rats. Pregnant animals were fed, from day 1 of gestation, a normal diet supplemented by pacific-blue-marlin giving a 2 parts per million (ppm) concentration of mercury, or a normal diet with tuna and supplemental 2ppm methylmercury-hydroxide (1184572). When pups were born, they were also fed on the same diet as that of their mothers. Early development testing was conducted on pups from days 7 through 17 of age with a swimming test and a righting reflex task, while motivational and learning tests, including a locomotion test and a maze series, were conducted at 45 to 68 days of age. Animals were sacrificed at 68 days of age, and mercury content of the brain, liver, and kidney was determined. No significant differences were seen in weight or appearance of animals of any group.

Retarded maturation was seen in animals fed the marlin diet in the swimming test. All animals performed similarly on the motivational tests. Marlin fed pups showed a learning deficit in performance of the symmetrical maze testing. There were no important differences between the groups in terms of weights of brain, liver, kidney, lung, or heart, and no obvious morphological abnormalities were found in any animals. Rats fed the tuna and methylmercury-hydroxide diet had the highest concentrations of mercury in the brain, liver, and kidney, followed in order by marlin fed rats and then by controls. The authors conclude that the marlin diet had the most deleterious effects on the behavior maturation and learning ability of second generation rats.

222

TITLE:

Influence of Dietary Levels of Protein and Sulfur Amino Acids on the Fate of Methylmercury in Mice

AUTHORS:

Adachi T
Yasutake A
Hirayama K

SOURCE:

Toxicology, Vol. 93, Nos. 2/3, pages 225-234, 19 references, 1994

ABSTRACT:

Mechanisms involved in the effects of dietary protein levels on the biological fate of methylmercury (22967926) (MeHg) were studied. C57Bl/6N-mice were fed normal diets, low protein diets, or low protein diets supplemented with methionine and cystine and the distribution and excretion of orally administered 20 micromolar/kilogram MeHg was examined. Brain mercury levels were increased in both the amino acid supplemented and low protein diet groups with the greatest increase seen in the amino acid supplemented animals. Liver mercury levels were increased and kidney levels decreased in the amino acid group while similar levels were seen in these organs in the other groups. In addition, urinary mercury levels were markedly increased in the group supplemented with amino acids. The uptake of mercury in the brain was increased in the low protein group and further enhanced by amino acid supplementation. Liver uptake was increased in the amino acid group as well. Amino acid supplemented animals also demonstrated increases in mercury levels in the low molecular weight fraction of plasma. Increases in the brain uptake of radiolabeled phenylalanine were seen in low protein diet fed and amino acid supplemented animals. The low protein diet decreased urinary cystine levels and these were restored by amino acid treatment. A greater than 20 fold increase in homocystine was induced by amino acid supplementation as well. The authors conclude that insufficient amounts of sulfur amino acids may account for the alteration in the biological fate of

methylmercury in mice fed a low protein diet.

223
TITLE:
Uptake of inorganic mercury by the human brain.

AUTHORS:
PAMPHLETT R
WALEY P

SOURCE:
ACTA NEUROPATHOLOGICA; 92 (5). 1996. 525-527.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A 24-year-old man injected himself intravenously with metallic mercury in a suicide attempt, and died 5 months later after cutting his wrists. The brain was removed at postmortem and 7-mum paraffin sections were cut from representative blocks. Dense deposits of mercury were found on autometallography in large cortical motor neurons, but in no other cerebral neurons. Smaller mercury deposits were found in the brain stem (in the mesencephalic trigeminal nucleus, noradrenergic neurons, and in neurons for extraocular muscles), the cerebellum (in the dentate nucleus) and in lateral motor neurons in the C2/3 spinal cord. Mercury deposits were found in glial cells in all regions. The finding that elemental mercury enters human cortical motor neurons in preference to other cerebral neurons raises the possibility that this neurotoxin may play a part in the pathogenesis of some human motor neuron diseases.

224
TITLE:
The Effects of Methylmercury Chloride of Low Concentration on the Rat Brain

AUTHORS:
Yamamura K
Maehara N
Ueno N
Ohno H
Kishi R

SOURCE:
Industrial Health, Vol. 24, No. 4, pages 235-241, 15 references, 1986

ABSTRACT:
The effects of low concentrations of methylmercury-chloride (115093) (MMC) on early evoked potentials (EEPs) were studied in rats. Ten or 12 week old male Wistar-rats were fed diets containing 20 micrograms per gram MMC

for 2 or 4 weeks, respectively. Body weights were monitored. The animals were observed for clinical signs of toxicity. EEPs were measured 24 hours after the last MMC feeding. The rats were then killed and the brains were removed. Cerebral mercury (7439976) concentrations were determined. Blood mercury concentrations were also measured. Body weight was not significantly affected by MMC in the 2 week exposure group. Rats in the 4 week exposure group had significantly decreased body weights after 2 weeks MMC exposure. Five of 15 rats exposed to MMC for 2 weeks showed slight hind leg flexion or rotation when held by the tail. Hind leg crossing was not observed. Seven of 16 animals fed MMC for 4 weeks showed hind leg crossing or flexion. EEP latencies were significantly lengthened by 2 or 4 weeks MMC exposure. EEP amplitudes were not significantly affected by MMC. Cerebral mercury concentrations were increased in a time dependent manner. Blood mercury concentrations were significantly increased by MMC. The increases induced by 2 and 4 weeks feeding were similar. The authors conclude that low level organic mercury poisoning causes neurobehavioral changes such as hind leg flexion or crossing and increases in EEP latency in rats.

225

TITLE:

Chronic Encephalopathies Induced by Mercury or Lead: Aspects of Underlying Cellular and Molecular Mechanisms

AUTHORS:

Ronnback L
Hansson E

SOURCE:

British Journal of Industrial Medicine, Vol. 49, No. 4, pages 233-240, 82 references, 1992

ABSTRACT:

Possible molecular mechanisms underlying the symptoms indicative of neuropsychological deficits resulting from long term exposure to low doses of mercury (7439976) or lead (7439921) were examined. It is thought that due to the capacity of astrocytes to regulate the ionic and amino acid concentration in the extracellular micromilieu, brain energy metabolism and cell volume, that impairments of astrocyte function are likely important. These functions have been shown to be under monoaminergic control. Mercury and lead at low doses inhibit the astroglial capacity to take up glutamate and inhibit the activity of glutamine-synthetase, needed to convert glutamate to glutamine in astroglia. At higher metal concentrations the astroglial glutamate uptake is further impaired and the extracellular glutamate might reach concentrations that are cytotoxic to neurones. Some brain regions are particularly vulnerable, specifically the hippocampus, perhaps due to high densities of N-methyl-D-aspartate receptors. Slight noradrenaline and serotonin activation may clinically

ease the situation. Noradrenaline in low concentrations may produced a diminished inhibition by an increased astroglial uptake of gamma-aminobutyric-acid mediated by stimulation of beta receptors.

226
TITLE:
Working with Mercury in Industry

AUTHORS:
Anonymous

SOURCE:
NIOSH, U.S. Department of Health, Education, and Welfare, DHEW (NIOSH) Publication No. 74-120, 6 pages, 19731973

ABSTRACT:
This pamphlet provided information on working with mercury (7439976), including industrial uses, effects of exposure to mercury, methods for controlling mercury exposure, reporting symptoms of mercury exposure, management responsibilities, and worker responsibilities. Mercury and its compounds have been used in medicine, dentistry, the chemical industry, and in the manufacturing of paint, paper, pesticides, and fungicides. The most common cause of mercury poisoning occurring on the job was through the inhalation of mercury vapors. Mercury vaporized at room temperature; when spilled, mercury broke into tiny globules which lodged themselves in cracks and penetrated porous surfaces, increasing the amount vaporized into the air. Most industrial poisoning cases resulted from chronic exposures and were characterized by tremor or shaking of the body and emotional disturbances. Several body functions and organs could be affected in the advanced stages including the kidney, liver, brain, heart and lung. For effective control of mercury at the workplace an efficient ventilation system was necessary. Work processes involving the use of mercury should be enclosed and isolated from the other work areas. Respirators may be necessary for brief periods. Air quality should be continually monitored, physical examinations should be offered periodically to employees, and good housekeeping procedures should be in place at the work site.

227
TITLE:
Ingestion And Retention Of Mercury By Sheep Grazing Near A Chlor-alkali Plant

AUTHORS:
Edwards PR
Pumphrey NWJ

SOURCE:

Journal of the Science of Food and Agriculture, Vol. 33, No. 3, pages 237-243, 9 references, 19821982

ABSTRACT:

Mercury (7439976) exposures and tissue distributions were studied in sheep grazing near a chloralkali factory. A total of 11 ewes and 21 lambs were put to pasture on a field contaminated with mercury as a result of atmospheric emissions, and were kept on the pasture for 23 months under normal agricultural conditions. Rams were put in during months 6 and 18, and breeding performance of the flock was assessed. At various intervals sheep were removed for analysis of mercury content in tissues, milk and blood, and urine and feces, when possible. Some samples were analyzed for methyl-mercury. Grass and air samples were analyzed periodically for mercury content. The following ranges of mercury content in tissues samples were observed: 0.03 to 3.4 milligrams per kilogram (mg/kg) in kidney, less than 0.02 to 1.3mg/kg in liver, 0.01 to 6.3mg/kg to brain, 0.01 to 4.0mg/kg in lung, less than 0.01 to 0.09 in muscle, less than 0.01 to 2.5mg/kg in perinephric fat, less than 0.02 to 0.16mg/kg in mesenteric fat, and less than 0.02 to 8.7mg/kg in dried rumen content. Less than 10 percent of the mercury in tissues was methyl-mercury. Mercury in grass averaged 6.5 and 1.9mg/kg during the winter and summer months, respectively. Mean air levels ranged from 0.06 to 0.32 micrograms per cubic meter per month. No histological changes due to mercury were seen, and reproductive performance was normal. The authors conclude that contamination of grass as a result of atmospheric discharges of inorganic mercury from chloralkali sites poses no hazard to grazing animals or to humans ultimately consuming their flesh.

228

TITLE:

Studies on the Accumulation, Metabolism and Excretion of Inorganic Mercury (Hg-203) After Prolonged Subcutaneous Administration to Rats

AUTHORS:

Friberg L

SOURCE:

Acta Pharmacologica et Toxicologica, Vol. 12, pages 411-427, 4 references, 19561956

ABSTRACT:

Administration of non-radioactive mercury (7439976) for two weeks after the exposure to radioactive mercury entailed increased urinary output of the latter substance, compared with the values in rats given no further injections. Displacement of the radioactive mercury by non-radioactive mercury took place mainly in the kidneys, but also occurred in liver, spleen and blood. No such exchange was demonstrated in the brain. Mercury was excreted in the urine and in the feces. The total twenty-four

hour output of mercury in the urine was on average almost twice that in the feces. The fecal concentration of mercury was higher in the females and the urinary concentration in the males. In an experiment in which the males were considerably heavier than the females, and thus, despite identical mercury dosage per kilogram of body weight, received a higher total dose, the urinary excretion of mercury increased on the whole in proportion to the size of dose administered.

229
TITLE:
Exposure to Mercury via Breast Milk in Suckling Offspring of Maternal Guinea Pigs Exposed to Mercury Vapor after Parturition

AUTHORS:
Yoshida M
Satoh H
Kishimoto T
Yamamura Y

SOURCE:
Journal of Toxicology and Environmental Health, Vol. 35, No. 2, pages 135-139, 11 references, 1992

ABSTRACT:
The risk of mercury (7439976) exposure through breast milk was examined by exposing maternal guinea-pigs to a single high dose of mercury vapor. Pregnant Hartley-guinea-pigs were exposed to mercury vapor (6 to 10 milligrams per cubic meter) for 120 minutes within 12 hours after parturition. On day three, five, or ten postpartum and after collection of milk samples, dams and neonates were sacrificed. Blood and plasma mercury concentrations in exposed dams were much higher than in the controls and decreased with time. Mercury concentrations in breast milk were up to 29 times higher in exposed than in control animals. Elimination of mercury from the milk was considered slow in comparison to that from plasma and whole blood. Blood mercury levels in exposed neonates were slightly higher than in the controls. Brain, lung, kidney, and liver concentrations were higher than in the controls. The highest tissue samples values were exhibited on day five in most exposed animals. With respect to stomach content, mercury concentrations in exposed neonates were greatly elevated on days three and five, but decreased abruptly on day ten when the diet was primarily solid food. The authors conclude that organ distribution indicates that neonates were exposed via milk to inorganic rather than elemental mercury.

230
TITLE:
Toxicokinetics of Mercuric Chloride and Methylmercuric Chloride in Mice

AUTHORS:
Nielsen JB

SOURCE:
Journal of Toxicology and Environmental Health, Vol. 37, No. 1, pages 85-122, 67 references, 1992

ABSTRACT:
Studies on the toxicokinetics of mercuric-chloride (7487947) and methylmercuric-chloride (115093) (MMC) in mice were discussed. Bom:NMRI-mice, CBAom-mice, C3H/TifBom-mice, or C57Bl/6Bom-mice were administered 0 to 100 micromoles per kilogram (micromol/kg) mercury-203 (Hg-203) labeled mercuric-chloride or MMC orally or by intraperitoneal injection. Whole body retention of Hg-203 activity was monitored for up to 30 days. Feces and urine samples were analyzed for Hg-203 activity. Selected mice were killed 14 days after dosing to determine the tissue distribution of mercury (7439976). With mercuric-chloride administration, increased retention was noted for male mice and for intraperitoneal injection. The fractional whole body retention of mercury was inversely related to dose. Fecal elimination of Hg-203 was delayed after administration of 100micromol/kg mercuric-chloride. Clearance of mercuric-chloride was slower after intraperitoneal than after oral administration. The percentage true absorption following oral administration of 1 and 5micromol/kg mercuric-chloride was estimated to be 20 to 25%. Mercury was deposited mainly in the liver, kidneys, and carcass; accumulations were most often dose related. Liver and brain mercury concentrations in most strains were higher in male than female mice. Following administration of MMC, mercury elimination showed first order kinetics during the first 14 days post dosing. Kinetic behavior was independent of dosing route, strain, and sex. Deviation from first order kinetics for periods greater than 14 days was attributed to increasing relative deposition of mercury in the carcass. Whole body mercury retention decreased with increasing dose. Retention in male Bom:NMRI-mice was smaller than in female Bom:NMRI-mice. The highest mercury concentrations were found in the carcass, liver, and kidneys. Kidney mercury accumulation was significantly higher in Bom:NMRI-mice than in C57Bl/6Bom and C3H/TifBom-mice. The author concludes that the toxicokinetics of mercuric-chloride depend on dose, route of administration, and sex. The toxicokinetics of MMC are independent of administration route, strain, or sex. The tissue distribution depends on sex and strain.

231
TITLE:
Normal Mercury Level In Human Embryos And Fetuses

AUTHORS:
Nishimura H

Hirota S
Tanaka O
Ueda M
Uno T

SOURCE:
Biology of the Neonate, Vol. 24, pages 197-205, 27 references, 19741974

ABSTRACT:
Concentrations of mercury (7439976) were measured in human embryos, fetuses, and maternal pubic hair. The normal embryonic and fetal specimens were obtained through induced abortions from mothers with healthy courses of pregnancy who resided in urban districts of the central area of Honshu Island. The specimens consisted of 67 embryos at weeks 5 to 7.5 of development and 28 fetuses at months 4 to 10 of development. Liver, kidney, and cerebrum from 20 infants and adults who had died accidentally served as comparisons for the fetal organs. Analyses of total mercury in embryos, fetuses, maternal pubic hair, and organs was by ultraviolet atomic absorption. Mercury, in concentrations ranging from 0.09 to 1.05 parts per million (ppm) of wet tissue, was detected in all the embryos; there was no definite stage difference in concentrations according to age. Embryos from parents engaged in fishery showed high concentrations of 1.05 and 0.71ppm. Mercury concentrations were obtained in all specimens of fetal organs and ranged from 0.05 to 0.46ppm in the liver, 0.08 to 0.66ppm in the kidney, and 0.03 to 0.51ppm in the cerebrum. There was no trend related to sex. Mercury seemed to be distributed almost evenly in the three fetal organs in month 4 of pregnancy. Third trimester concentrations of mercury in the liver were significantly lower than second trimester concentrations. Third trimester mercury concentrations in fetal kidney and liver were similar to concentrations in those organs for infants, but significantly lower than the respective adult concentrations. No difference was seen among mercury contents of the brains at fetal, infant, and adult stages. Hair mercury contents ranged from 1.42 to 20.67ppm and had no relationship to mercury concentrations in embryos. The authors conclude that placental transfer of mercury occurs as early as 5 weeks after conception in embryos, indicating high sensitivity of embryos to exogenous teratogens.

232
TITLE:
In Vitro Oxidation of Mercury by the Blood

AUTHORS:
Hursh JB
Sichak SP
Clarkson TW

SOURCE:

Pharmacology and Toxicology, Vol. 63, No. 4, pages 266-273, 24 references, 19881988

ABSTRACT:

A method for studying the in-vitro oxidation of low concentrations of mercury (7439976) vapor by erythrocytes with short exposure times was presented. Human whole blood samples or erythrocyte preparations were exposed briefly to radiolabeled mercury vapor, and aerated time sequence samples were analyzed for levels of the oxidized mercuric ion and unoxidized mercury vapor in the blood. The oxidation rate of mercury at 37 degrees-C in samples with a hematocrit of 40 to 42 percent was biphasic with zero order kinetics determined for mercury concentrations greater than 6 nanograms/milliliter (ng/ml) and first order kinetics determined for concentrations less than 6ng/ml. The average values for the rate constants for the regions of zero order and first order kinetics were 1.42 and 0.22 nanograms mercury per minute per milliliter, respectively. The oxidation rate of mercury in whole blood at 20 degrees was twice that of 10 degrees for the region of zero order kinetics, and a linear dose relationship was observed between oxidation and percent hematocrit. The addition of hydrogen-peroxide to the incubation medium increased the oxidation rate of mercury when the mercury vapor concentration was maintained at levels higher than 6ng/ml. The results were discussed with regard to the catalase compound-I oxidation pathway. The authors suggest that extrapolation to in-vivo situations indicate that inhaled mercury reached the brain and other tissues primarily as dissolved vapor in the blood rather than as inorganic mercury ions.

233

TITLE:

The Effect Of 2,3-Dimercaptopropane Sodium Sulfonate On Mercury Retention In Rats In Relation To Age

AUTHORS:

Kostial K
Kargacin B
Blanusa M
Landeka M

SOURCE:

Archives of Toxicology, Vol. 55, No. 4, pages 250-252, 11 reference, 19841984

ABSTRACT:

The effect of sodium-2,3-dimercaptopropane-1-sulfonate (4076022) (DMPS) on the age dependent reduction of inorganic mercury (7439976) retention was investigated in rats. Albino-rats, 2, 6, and 28 weeks old, were administered intraperitoneally (ip) radioactive mercury at 10 microCuries per milliliter per kilogram (kg), which corresponded to 50 micrograms/kg

mercury. The chelating agent DMPS was administered ip at 50 milligrams/kg, 3 times, 1 day after mercury injection and at 24 hour intervals thereafter. Immediately after mercury injection and on days 2, 3, and 6, whole body radioactivity was measured when animals were killed. Liver, kidneys, brain, lungs, femur, hair, and skin were removed and their radioactivity was determined by a scintillation counter. Two week old rats retained a higher fraction of mercury in the whole body but not in all organs than older rats. Mercury retention was lower in kidneys of 2 week old rats than adult rats. DMPS decreased the whole body retention of mercury 1.6, 2.6, and 3.2 times more in treated than in control rats aged 2, 6, and 28 weeks, respectively. Following DMPS administration, mercury retention in kidneys was 1.9, 3.9, and 4.7 times lower in 2, 6, and 28 week old treated rats, respectively, than in their corresponding controls. The efficiency of DMPS in reducing mercury retention in whole body and in kidneys, was dependent upon the age of the animals. In all other organs, mercury was reduced by a factor of 1.4 to 2 and was therefore not age dependent. The authors conclude that the age dependent effect of DMPS may be due to specific features such as immaturity of kidneys or biliary transport, differences in binding affinities, or content of metal carrier proteins.

234

TITLE:

Dental treatment, fish consumption, and mercury exposure during pregnancy in relation to child neurodevelopment.

AUTHORS:

Daniels JL
Rowland AS
Longnecker MP
Cook M
Golding J

SOURCE:

Am J Epidemiol 2001 Jun;153(11):S184

ABSTRACT:

We hypothesized that mercury exposure during pregnancy, especially from dental treatment or fish intake, would adversely affect neurodevelopment among British children born in 1991-92. To evaluate their children, over 5,000 mothers from the Avon Longitudinal Study of Pregnancy and Childhood completed the Denver Developmental Screening Test at 6 and 18 months after birth and the MacArthur Communicative Development Inventory at 15 months. Reported dental treatment and fish intake during pregnancy served as markers of exposure to mercury vapor and methyl mercury, respectively. Cord tissue mercury was measured for 1,100 children. Total mercury levels were higher among those who had dental work and ate fish, but were not associated with development test scores. Neither dental work nor fish

intake was associated with decreased overall developmental test scores (eg: adjusted Denver-18 month mean test scores: dentistry = 71.2, no dentistry = 70.4, p = 0.6). Most developmental scores increased, however, with fish intake (MacArthur: no fish = 123.5, fish less than 1/week = 130.3, fish greater than 1/week = 129.8, trend p less than 0.02). In summary, our developmental tests may have lacked sensitivity to subtle mercury effects. The lack of adverse effects from dental work, however, was reassuring given its association with mercury exposure and infection. Fish intake has been questioned due to mercury exposure; but N-3 fatty acids, such as those in fish oils, improve development of vision and cognitive function. These data suggest that maternal fish intake may benefit neurodevelopment when mercury exposure is low.

235

TITLE:

In Vitro Effect of Organic and Inorganic Mercury on the Serotonergic System

AUTHORS:

Oudar P
Caillard L
Fillion G

SOURCE:

Pharmacology and Toxicology, Vol. 65, No. 4, pages 245-248, 17 references, 1989

ABSTRACT:

The effects of methyl-mercuric-chloride (115093), mercuric-acetate (1600277), mercuric-chloride (7487947), and mercuric-nitrate (10045940) on serotonergic systems prepared from Sprague-Dawley-rat brain cortex were investigated. Cerebral tissues were excised, homogenized, and centrifuged to prepare the synaptosomal fraction. Synaptosomes were loaded with 20 nanomolar tritiated 5-hydroxytryptamine (5-HT) and incubated with appropriate mercury ions. Cortical tissues were homogenized and centrifuged, and the pellet was incubated with tritiated 5-HT and mercury salts in various concentrations. The effect of mercury compounds on 5-HT release was dose dependent, with median effect (EC50) for methyl-mercury at 66.2+/-2 micromolar (microM) and 107+/-16microM concentrations. Mineral mercury salts induced 5-HT release at a lower concentration (EC50, 8.4+/-1.3microM) in the presence of calcium ion. The binding of 5-HT to 5-HT1 sites was inhibited at concentrations of 0.1 to 1,000microM. Median inhibitory concentrations (IC50) were 10.9+/0.6 and 27.8+/-3.2microM for mineral mercury salts and methyl-mercury, respectively. The EC50s for organic and mineral mercury were significantly different, as were the IC50s. The authors conclude that mercury compounds interact with the serotonergic system at high concentrations to deplete neuronal 5-HT, as well as at low concentrations with certain ionic forms.

236
TITLE:
Distribution of mercury in the organms of rats in ethylmercury chloride poisoning.

AUTHORS:
Krylova AN
Naumov VM
Rubtsov AF
IAkovleva VI

SOURCE:
Sudebno-Med. Ekspertiza; 12(4): 34-40, 1969

ABSTRACT:
HAPAB Ethylmercury chloride (EMC), a widely used pesticide, distribution in the organs was investigated in rats after poisoning as dependent on time of death (from several hours to 1 year after administration). An alcohol solution of EMC was given to 94 rats perorally in doses from 20 to 35 mg/kg. Clinical symptoms of mercury poisoning, pathomorphological changes in the internal organs and quantitative mercury distribution in various organs were recorded. The organ distribution of mercury was determined by destrubtion of the organic material by sulfuric and nitrice acids in the presenct of ethanol with subsequent precipitation of mercury in the destructate in for forms of a colored iodide complex of mercury and copper followed by colorimetry (Krylova, 1962). Characteristic posioning signs were a rapidly developing depressive state, refusal of food and progressive fall in weight. Death occurred amidst signs of general emaciation. During the first 24 hr after a toxic dose of EMC, there were pronounced circulatory disorders. On death at 2 to 16 days, necrotic nephrosis, foci of necrosis and fatty dystrophy of the liver were seen. The morphological changes were strongly pronounced during the period of greatest mercury content in the liver and kidneys (10 to 25 days). After 2 to 6 months, the typical EMC poisoning signs were not seen. In acute poisoning, the mercury content of the liver exceeded that of the kidneys. On death at 15 days, mercury in the liver decreased, while it increased in the kidneys; over a 3-month course, the mercury content remained about at one level. Five graphs illustrate mercury distribution and the quantities found over time; tabulated data from the literature are also included on the mercury content in the kidneys, liver and brain of poisoned human subjects. Toxicology and Pharmacology 70/08/00, 355 1969

237
TITLE:
Inhibition of Calcium Transport by Mercury Salts in Rat Cerebellum and Cerebral Cortex In Vitro

AUTHORS:
Yallapragada PR
Rajanna S
Fail S
Rajanna B

SOURCE:
Journal of Applied Toxicology, Vol. 16, No. 4, pages 325-330, 45 references, 1996

ABSTRACT:
A study was conducted examining the effects of mercury (7439976) salts on the calcium pump activity of rat cerebellum and cerebral cortex in-vitro. Calcium-adenosine-triphosphatase (Ca-ATPase) was assayed in synaptic plasma membranes (SPMs) and microsomes isolated from the cerebellum and cerebral cortex of Sprague-Dawley-rats and incubated with different micromolar concentrations of mercury and methylmercury. SPM Ca-ATPase was inhibited by mercuric-chloride (7487947) and methyl-mercury-chloride (115093) in a concentration dependent manner in both cerebellum and cerebral cortex. A significant effect of region was seen. Mercuric-chloride was more effective in inhibiting SPM Ca-ATPase in cerebellum than in cerebral cortex; whereas methylmercury-chloride was more effective in inhibiting SPM Ca-ATPase in the cerebral cortex. Both mercuric-chloride and methylmercury-chloride inhibited microsomal Ca-ATPase in a concentration dependent manner in cerebellum and cerebral cortex with a significant effect for region. Ca-ATPase in SPMs was more sensitive to the mercury salts than Ca-ATPase in microsomes. Both mercuric-chloride and methylmercury inhibited microsomal uptake of calcium in concentration dependent fashions. Calcium uptake in the cerebellum was more sensitive to both mercury and methylmercury than that in the cerebral cortex; mercury was more potent than methylmercury in inhibiting calcium uptake. The authors conclude that both mercury and methylmercury inhibit calcium pumps in SPM and microsomes.

238
TITLE:
Working with Mercury in Industry

AUTHORS:
Anonymous

SOURCE:
NIOSH, U.S. Department of Health, Education, and Welfare, Publication No. 73-11006, 6 pages, 19731973

ABSTRACT:
This pamphlet provided information on working with mercury (7439976),

including industrial uses, effects of exposure to mercury, methods for controlling mercury exposure, reporting symptoms of mercury exposure, management responsibilities, and worker responsibilities. Mercury and its compounds have been used in medicine, dentistry, the chemical industry, and in the manufacturing of paint, paper, pesticides, and fungicides. The most common cause of mercury poisoning occurring on the job was through the inhalation of mercury vapors. Mercury vaporized at room temperature; when spilled, mercury broke into tiny globules which lodged themselves in cracks and penetrated porous surfaces, increasing the amount vaporized into the air. Most industrial poisoning cases resulted from chronic exposures and were characterized by tremor or shaking of the body and emotional disturbances. Several body functions and organs could be affected in the advanced stages including the kidney, liver, brain, heart and lung. For effective control of mercury at the workplace an efficient ventilation system was necessary. Work processes involving the use of mercury should be enclosed and isolated from the other work areas. Respirators may be necessary for brief periods. Air quality should be continually monitored, physical examinations should be offered periodically to employees, and good housekeeping procedures should be in place at the work site.

239

TITLE:

CO2 Narcosis. An Experimental Study

AUTHORS:

Meyer JS
Gotoh F
Tazaki Y

SOURCE:

Neurology, Vol. 11, pages 524-537, 24 references, 19611961

ABSTRACT:

The mechanism by which carbon-dioxide (124389) (CO2) depresses the central nervous system was investigated in monkeys. Anesthetized Macaca-rhesus-monkeys were exposed to 20 to 50 percent CO2 in oxygen while artificial respiration was maintained. Some animals were intravenously injected with 0.6 gram (g) sodium-bicarbonate (144558) or 1.8g of the CO2 binding agent tris(hydroxymethyl)aminomethane (77861) (THAM) during CO2 exposure; others were given repeated intravenous injections of acetic-acid (64197) or hydrochloric-acid (7647010) to induce metabolic acidosis. Electroencephalograph (EEG) recordings, CO2 partial pressure (pCO2), and pH in arterial blood and on the pial brain surface were monitored continuously. When high concentrations of CO2 were inhaled, arterial pCO2 rose rapidly to 60 to 100 millimeters of mercury, arterial pH rapidly decreased to 6.6 to 6.8, brain pCO2 increased after a delay, and brain pH fell as brain pCO2 increased. As brain pH fell below 6.6, EEG slowed to

0.25 to 4.0 cycles per second, often with increases in amplitude followed by progressive decreases to virtual electrical silence. After injection of sodium-bicarbonate during CO2 inhalation, arterial pH rose rapidly to normal values, while arterial and brain pCO2 increased further. The brain usually showed a delayed alkaline shift despite elevated brain pCO2, and EEG improved as the brain became alkaline. During metabolic acidosis, brain pH fell below 6.6, but arterial pH was lowered more transiently; EEG slowing corresponded to the change in brain pH. Intravenous THAM increased arterial and brain pH, lowered arterial and brain pCO2, and improved EEG recordings. The authors conclude that CO2 narcosis is due to a specific property of CO2 on neuronal function, that is, rapid intracellular diffusion and acidosis. EEG changes are strongly related to the pH of brain tissues. THAM appears to be a useful therapeutic measure during CO2 narcosis to restore brain pH and EEG to normal.

240

TITLE:

Combined Effects of Low-Level Methylmercury and X-Radiation on the Developing Mouse Cerebellum

AUTHORS:

Inouye M
Kajiwara Y
Hirayama K

SOURCE:

Journal of Toxicology and Environmental Health, Vol. 33, No. 1, pages 47-56, 24 references, 1991

ABSTRACT:

Inbred BALB/cJcJ-mice were mated and the dams given 8 micrograms (microg) mercury (7439976) as methylmercuric-chloride (115093) per gram (g) body weight by gavage on day 17 of pregnancy as part of a study of the combined effects of radiation and methylmercury exposures on the developing brain. Male pups from mercury exposed and control mothers were exposed to whole body x-radiation at doses of 0.125 or 0.5 gray (Gy) on the next day after birth and sacrificed at intervals. The pyknotic cells increased in incidence following x-radiation. Cell death began to increase 3 hours after exposure to 0.125Gy with or without prenatal mercury exposure, reaching a peak incidence at 6 hours and then decreasing to levels of sham radiated groups by 24 hours. The incidences of cell death 6 hours after exposure to 0.125Gy were not significantly different between mercury exposed and nonexposed animals. In the long term study, cell death of the external granular layer (EGL) caused by 0.5Gy decrease in number and the EGL was reduced in thickness by 24 hours post radiation. All pyknotic cells disappeared by 36 hours and restoration of the EGL was noted by 3 days. Slight retardation of development was noted on days four and five in the cerebella exposed to methylmercury and radiation. The EGL was six

to seven cells thick in the culmen and one to two cells less than noted in other groups. The pup cerebellum retained mercury at levels of 4 to 8microg/g by 4 days after birth following a maternal dose of 8microg/g on day 17 of pregnancy. Neither prenatal methylmercury exposure, postnatal 0.5Gy exposure, nor the combination of the two resulted in a weight gain in the pups.

241

TITLE:

Biochemical Changes In The Rat Cerebellar Cortex Elicited By Chronic Treatment With Methyl Mercury

AUTHORS:

Concas A
Corda MG
Salis M
Mulas ML
Milia A
Corongiu FP
Biggio G

SOURCE:

Toxicology Letters, Vol. 18, No. 1-2, pages 27-33, 21 references, 19831983

ABSTRACT:

The effect of chronic methyl-mercury (22967926) administration on cerebellar neurotransmission was investigated. Male Sprague-Dawley-CD-rats were administered methylmercury-chloride (115093) in drinking water at a concentration of 20 micrograms per milliliter for at least 20 days until 5 days before killing when pure water was substituted. After decapitation, cerebellum was dissected. Benzodiazepine and gamma-amino-butyric-acid binding sites, cyclic guanosine-3,5-monophosphate, adenosine-monophosphate, and gamma-amino-butyric-acid contents, and glutamic-acid-decarboxylase activity in cerebellar cortex were assayed. Maximum binding for diazepam (439145) was 0.65 picomoles/milligram (pmol/mg) protein, and the dissociation constant was 3.4 nanomoles (nmol) in control rats. Comparable values were 0.84pmol/mg and 3.4nmol, respectively, for methyl-mercury treated animals. The maximum binding and dissociation constant for high affinity gamma-amino-butyric-acid binding were 1.02pmol/mg and 7.6nmol, respectively, in control animals and 0.94pmol/mg and 7.7nmol, respectively, in treated rats. Chronic methyl-mercury did not affect gamma-amino-butyric-acid content nor glutamic-acid-decarboxylase activity in the cerebellar cortex. Cyclic guanosine-3,5-monophosphate was reduced by 50 percent in treated rats, but cyclic adenosine monophosphate was not significantly affected. The authors conclude that chronic methyl-mercury treatment increases the total number of benzodiazepine binding sites and decreases significantly the

content of cyclic guanosine-3,5-monophosphate in the cerebellar cortex. The treatment fails to modify gamma-amino-butyric-acid content, glutamic-acid-decarboxylase activity, and gamma-amino-butyric-acid binding sites in the same brain area. The toxicity of the compound seems to be related primarily to an impairment in the function of cell membrane and would thus affect receptors located there. The effect of methyl-mercury on cyclic guanosine-3,5-monophosphate may reflect a decrease in the function of cerebellar neurons elicited by methyl-mercury intoxication.

242

TITLE:

Whole Body And Liver Distribution Of Inhaled Mercury Vapor In The Mouse: Influence Of Ethanol And Aminotriazole Pretreatment

AUTHORS:

Khayat A
Dencker L

SOURCE:

Journal of Applied Toxicology, Vol. 3, No. 2, pages 66-74, 32 references, 19831983

ABSTRACT:

The influence of ethanol (64175) and aminotriazole (61825) pretreatment on the metabolic fate of inhaled mercury (7439976) vapor was investigated in mice. Adult C57BL-mice were exposed to radioactive mercury vapor by inhalation for 1 hour at 1.7 micrograms of mercury or 2.4 microCurie per gram body weight. Another group of mice was injected intravenously with radiolabeled mercuric-chloride (7487947) at the same dose. A third group was pretreated with ethanol at 2 grams per kilogram or aminotriazole at 1 gram per kilogram body weight by intraperitoneal injection. Mice were killed at intervals and some mice were subjected to whole body autoradiography using X-irradiation. Liver, kidneys, lung, heart, brain, eyes, thyroids, fat, testes, adrenals and blood were removed and radioactivity in these tissues was measured in a gamma spectrometer. Inhalation of mercury vapor resulted in accumulation of mercury in the thyroid, adrenal cortex, lung, brain, heart, kidney and liver. Intravenous injection of mercuric-chloride did not reveal any specific pattern of uptake. Ethanol and aminotriazole pretreatment decreased the concentration of mercury in several organs in a differential way. Ethanol inhibited accumulation in adrenals, plasma and red blood cells while aminotriazole did not inhibit accumulation in adrenal or red blood cells. Aminotriazole markedly inhibited accumulation in the thyroid. The authors conclude that mercury is distributed to different organs, but apparently undergoes oxidation; this process may contribute to the differential accumulation seen in various tissues.

243

TITLE:
Mercury and multiple sclerosis.

AUTHORS:
CLAUSEN J

SOURCE:
ACTA NEUROL SCAND; 87 (6). 1993. 461-464.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. It has occasionally been claimed that multiple sclerosis (MS) may be due to a chronic mercury intoxication, e.g. from mercury liberated from dental fillings. Therefore, the present communication compares the mercury content assayed by neutron activation in 8 macroscopically normal areas (frontal lobe) of MS autopsy brains with those of 8 control samples. No significant differences could be traced between the two groups concerning total mercury. However, the lipid-soluble mercury (preferably methyl mercury) expressed per cell unit (DNA) was found significantly decreased in MS. These data may be explained either by a wash-out of lipid soluble mercury due to break-down of the blood-brain barrier in MS or to abnormalities in methylation processes probably related to the vitamin B12 metabolism in MS.

244
TITLE:
Accumulation Of Mercury In Tissues Of Cattle, Sheep, And Chickens Given The Mercurial Fungicide, Panogen 15, Orally

AUTHORS:
Wright FC
Palmer JS
Riner JC

SOURCE:
Journal of Agricultural and Food Chemistry, Vol. 21, No. 3, pages 414-416, 8 references, 19731973

ABSTRACT:
Tissue accumulation of mercury (7439976) after dosing with a mercurial fungicide was studied in cattle, sheep, and chickens. Yearling cattle, yearling sheep, and White-leghorn-chickens were administered Panogen-15 (502396), a fungicide containing 2.2 percent methylmercury-dicyandiamide, orally once daily for up to 70 days (cattle and sheep) and 84 days (chickens). The doses were 15 milligrams per kilogram (mg/kg) for cattle and sheep and 5 or 10mg/kg for chickens. The animals were observed for clinical signs of toxicity. Selected animals were killed weekly and all controls were killed at the end of the study for tissue mercury determinations. Two of 13 cattle showed signs of mild poisoning after 56

and 65 days and 3 of 13 sheep showed signs of poisoning after 42, 56, and 59 days. Signs of intoxication included muscular incoordination, stiffness in hindquarters, and unsteady gait. No ill effects were observed in the chickens. Tissue mercury residues were generally higher in cattle than in sheep, except in the liver. Highest mercury residues in both species were found in the kidney, liver, muscle, and brain. In chickens, highest mercury residues occurred in the liver, followed by the kidney, breast, muscles, and thigh muscle, in that order. The authors conclude that mercury residues in the tissues of animals exposed to panogen-15 could pose a hazard to humans.

245
TITLE:
Oral Mercuric Chloride Exposure in Mice: Effects of Dose on Intestinal Absorption and Relative Organ Distribution

AUTHORS:
Nielsen JB
Andersen O

SOURCE:
Toxicology, Vol. 59, No. 1, pages 1-10, 19 references, 1989

ABSTRACT:
The kinetics and organ distribution of orally ingested inorganic mercury (7439976) were investigated. Male CBAom-mice and Bom-NMRI-mice were given a single oral dose of 1, 5, 25, or 100 millimoles mercuric-chloride (7487947) (HgCl2) labeled with mercury-203. Background radioactivity was counted at 15 minutes after dosing, and whole body counts were repeated at 1, 2, 3, 4, 7, 10, and 14 days after dosing. On day 14, mice were killed, and organ counts were obtained. The Bom-NMRI-mice demonstrated lower fecal elimination than the CBA/Bom-mice. Relative whole body retention at 14 days was lower in mice treated with higher doses of HgCl2, ranging from 2.78 to 1.23 percent of the initial dose in Bom-NMRI-mice, and from 1.71 to 1.01 percent in CBA/Bom-mice. Measured residual body burden increased with increasing treatment dosage, from 26.6 to 1,140 nanomoles mercury per kilogram (nmol/kg) in the Bom-NMRI-mice, and from 15.9 to 950nmol/kg in the CBA/Bom-mice. Mercury was primarily retained in kidneys, liver, and carcass, and increased relative deposition was observed in higher dosage groups in all structures except kidneys, carcass, lungs, and brain. No significant interspecies differences in relative organ distribution was noted; however, relative mercury retention in kidneys, intestines, and brain was higher in CBA/Bom-mice at all dosage levels. The authors conclude that orally and parenterally administered inorganic mercury compounds differ in their toxicokinetics.

246
TITLE:

Behavioural Effects of Neonatal Metallic Mercury Exposure in Rats

AUTHORS:
Fredriksson A
Dahlgren L
Danielsson B
Eriksson P
Dencker L
Archer T

SOURCE:
Toxicology, Vol. 74, Nos. 2/3, pages 151-160, 28 references, 1992

ABSTRACT:
The behavioral effects of neonatal mercury (7439976) vapor exposure were studied in rats. Sprague-Dawley-rat pups were exposed to 0.05mg/m3 mercury vapor for 1 (low dose group) or 4 hours daily (high dose group) from postnatal day (PND) 11 to 17. Selected pups were killed on PND 25 and the brains, livers, and kidneys were removed and analyzed for mercury. Spontaneous motor activity was evaluated when the rats were 2 and 4 months (mo) old. Swim maze learning was evaluated when the rats were 5mo old. Radial arm maze learning was evaluated when they were 6mo old. Brain, liver, and kidney mercury concentrations were 0.063, 0.219, and 6.734mg/kg, respectively, in the high dose group and 0.017, 0.084, and 1.247mg/kg, respectively, in the low dose group. Mercury concentrations in control rat tissues were only 0.002mg/kg. Rats in the high dose group showed increases in spontaneous locomotor and total activity, but a decrease in rearing behavior at 2mo. No exposure related changes in spontaneous motor activity were seen in 2mo old rats in the low dose group. Spontaneous locomotor and total activity and rearing behavior were significantly decreased in high dose 4mo old rats. The low dose caused increased spontaneous locomotor and total activity and decreases in rearing behavior at 4mo. Radial arm maze learning was impaired in a dose related manner. Swim maze learning was not affected. The authors conclude that neonatal exposure to mercury vapor at concentrations near the Swedish threshold limit cause dose and age related behavioral changes.

247
TITLE:
Mercury and selenium content and chemical form in human and animal tissue.

AUTHORS:
Cappon CJ
Smith JC

SOURCE:
J. Anal. Toxicol. 5(2): 90-98 1981 (61 References)

ABSTRACT:

PESTAB. Selected samples of human and animal tissue were examined by gas chromatography to determine the content, chemical form and distribution of mercury and selenium. In homogenized brain tissue methylmercury accounted for 38.7% of the mercury content. Methylmercury comprised 40.2, 57.0, 39.6, 6.0 and 57.1% of the total mercury content in human heart, spleen, liver, kidney and placenta, respectively. Of the total mercury found in seal meat, 62.9% was present as methylmercury. The corresponding figure for dear meat was 24.1%. A significant portion of selenium in all samples was present as selenate, averaging 27.0%. Of the toal mercury content in brain heart and placenta, and in seal liver and meat, 53-80% was water extractable. Only 15-45% of the mercury was extractable from human kidney, liver and spleen, and from deer meat. Inorganic mercury was more extractable than methylmercury, with the exception of human kidney and liver, and deer meat. Of the total selenium, 55-76% was water extractable in all samples with the exception of kidney, liver and deer meat.

248

TITLE:

Public health aspects of environmental contamination with mercury.

AUTHORS:

Kahn E

SOURCE:

In: Agricultural ChemicalsöHarmony or Disc; 1971, pp. 85-90 ; (REF:13)

ABSTRACT:

HAPAB Mercury contamination of the environment is related to the use of organic mercurials as agricultural fungicides. The resulting methyl mercury presents three hazards: poisoning of birds which eat mercury-treated grain; translocation of mercury into food grown from treated seed; and use of treated grain as food by hungry and uneducated people. Swedish naturalists have attributed a decline in populations of certain bird species to the presence of methyl mercury on the grain they eat. When mercury in any form is dumped into waterways, it is methylated by microorganisms and enters the aquatic food chain. Methyl mercury is easily absorbed from the gastro-intestinal tract and adversely affects the central nervous system and tissues of the fetus; brain damage is caused by destruction of the brain cells. The government-set tolerance level of 0.5 ppm for fish is practically worthless because it does not distinguish between safe and dangerous fish and does not take into account the amount of fish a person consumes or the individual susceptibility. 1971

249

TITLE:

The Uptake and Distribution of Methylmercury in the Brain of Saimiri Sciureus in Relation to Behavioral and Morphological Changes

AUTHORS:
Berlin M
Nordberg G
Hellberg J

SOURCE:
Mercury, Mercurials and Mercaptans, M. W. Miller, and T. W. Clarkson, Eds., Charles C. Thomas Publisher, Springfield, Illinois, pages 187-208, 8 references, 19731973

ABSTRACT:
The effects of methylmercury (22967926) (MeHg) were investigated in squirrel-monkeys. The animals received unspecified doses of radiolabeled MeHg in food or by stomach tube for various periods of time. Visual discrimination tests were performed, and blood, brain, and whole body mercury uptake was determined. Blood mercury concentrations increased rapidly for 24 hours, decreased rapidly over the next 3 or 4 days, then declined with a halflife of 50 to 60 days. Blood mercury concentrations were linearly related to dose and body burdens up to 1500 nanograms per gram. More than 95 percent of the ingested MeHg was absorbed, and after 85 days, 50 percent of the body burden was found in the fur. Performance of the visual task was impaired by MeHg; subacute exposure caused a sudden visual impairment, while prolonged exposure caused gradual visual deterioration along with motor and sensory disturbances. Cortical damage was more widespread after slow mercury accumulation. The authors conclude that the redistribution of mercury in monkeys requires at least 1 month, and that this redistribution is related to the development of toxic symptoms.

250
TITLE:
Approved Occupational Health Guide Inorganic Mercury

AUTHORS:
Anonymous

SOURCE:
National Health and Medical Research Council, Commonwealth Department of Health, Australia, Report No. MER-82-93, 11 pages, 19821982

ABSTRACT:
Approved guidelines of the Commonwealth Department of Health for elemental inorganic mercury (7439976) are presented. Toxic effects on workers in the felt hat industry (SIC-2352) through vapor inhalation are noted. The physical properties of inorganic mercury and the sources of exposure are described. Its fat solubility and diffusibility allow rapid transfer across the blood/brain barrier and the placental barrier, resulting in

accumulation in the fetal brain and tissue. Mercury is eliminated in sweat, saliva, urine, and breast milk. The immediate effects of acute mercury poisoning are described, and clinical symptoms after exposure are enumerated. Threshold limits for all except alkylmercury are set at 0.05 milligram per cubic meter. Personal exposure is best assessed by sampling the breathing zone. Procedures for detection and location of spillage are presented, and the establishment of a health surveillance program and recommended action are discussed. Urinary mercury monitoring is preferred to serum mercury monitoring. Detection of concentrations of 300 micrograms per liter (microg/l) in urine should be followed up with clinical examination of the worker. It is recommended that the urinary geometric mean should not exceed 100microg/l in urine. A mercury workplace check list is included.

251

TITLE:

Effects of Methylmercury Exposure during the Second Stage of Rapid Postnatal Brain Growth on Negative Geotaxis and on Delta-aminolevulinate Dehydratase of Suckling Rats

AUTHORS:

Rocha JBT
Freitas AJ
Marques MB
Pereira ME
Emanuelli T
Souza DO

SOURCE:

Brazilian Journal of Medical and Biological Research, Vol. 26, No. 10, pages 1077-1083, 21 references, 1993

ABSTRACT:

The effect of methylmercury (22967926) (MM) exposure during the second stage of rapid postnatal brain development on delta-aminolevulinate-dehydratase (ALAD) specific activity and negative geotaxis behavior of rats was examined. Wistar-rats were bred, and when pups were 8 days old they received daily injections of 0, 2.3, 4.6, 6.9, or 9.2mg/kg MM for 5 days. Rats were anesthetized and killed 24 hours after the last MM injection. Brain, liver and kidney were removed and homogenized. Negative geotaxis was assessed from the third to fifth day of MM injections by placing pups head down on an inclined plane and measuring latency to complete the response. Rats treated with 4.6, 6.9, and 9.2mg/kg MM had body weights significantly lower than control rats. Liver specific activity of ALAD was 20 and four fold higher than that of brain and kidney, respectively. ALAD specific activity from liver and brain of 6.9 and 9.2mg/kg MM treated rats was significantly lower than in control rats, while the kidney enzyme was not affected by any dose of MM.

The reduction was 40% for brain ALAD specific activity and 25% for liver specific activity. Treatment with 6.9 and 9.2mg/kg MM increased the latency to complete the negative geotaxis response compared to control animals. The authors conclude that postnatal exposure to high doses of MM caused an inhibition of brain ALAD and motor impairment in suckling rats.

252
TITLE:
Effects of Methylmercury on the Developing Brain

AUTHORS:
Choi BH

SOURCE:
Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 315-337, 67 references, 1991

ABSTRACT:
Recent findings regarding neurotoxic effects of methylmercury compounds on the developing brain were reviewed and possible mechanisms of methylmercury (22967926) action at the cellular and subcellular levels were considered. The following topics were discussed: the effects of methylmercury on neuronal migration, the effects of methylmercury on neuroepithelial germinal cells in the ventricular zone of the telencephalon of embryonic mice, the effects of methylmercury on cell to cell interactions in the developing brain, studies using rotation mediated aggregation cultures of embryonic brain cells, effects of methylmercury on neural cell adhesion molecule, methylmercury effects on developing astrocytes, effects of methylmercury on excitatory amino acid receptors, hydrocephalus following prenatal methylmercury poisoning, methylmercury effects on endothelial cells and perivascular astroglia of neonatal cerebellum, and the effects of methylmercury on the interplay between proteases and protease inhibitors. The author notes that the vulnerability and sensitivity of the developing brain to the toxic effects of methylmercury are clearly understood. The most immediate concern must be the consumption of methylmercury contaminated food by pregnant women, causing minor nervous system damage in the women themselves, and creating very serious effects in the fetus.

253
TITLE:
Differences In The Uptake Of Cadmium And Mercury By Rat Hepatocyte Primary Cultures Role Of A Sulfhydryl Carrier

AUTHORS:
Gerson RJ
Shaikh ZA

SOURCE:
Biochemical Pharmacology, Vol. 33, No. 2, pages 199-203, 27 references, 19841984

ABSTRACT:
The involvement of a sulfhydryl carrier in hepatocellular uptake of cadmium (7440439) and mercury (7439976) was studied in-vitro. Primary cultures of rat hepatocytes were prepared and exposed to radiolabeled cadmium or mercury in Hanks balanced salt solution (HBSS) or media with or without serum. Metal concentrations and incubation times were varied. Cells were washed and assayed for radioactivity. In addition, cells were preincubated with parachloromercuribenzenesulfonate (PCMBS), N-ethylmaleimide (NEM), or mercury in serum free media before adding cadmium or mercury and measuring uptake. Uptake of both metals was similar in HBSS and serum free medium, and significantly less in serum containing medium. In serum free medium, hepatocytes accumulated 4.3 times more cadmium than mercury during 1 hour; mercury uptake was rapid during the first 5 minutes, then slowed, while cadmium uptake remained rapid for the whole hour. Cadmium uptake was reduced by pretreatment with NEM, PCMBS or mercury, but mercury uptake was unaffected. The authors conclude that a sulfhydryl carrier may facilitate the uptake of cadmium but not mercury by hepatocytes, although mercury can interact with this carrier to block cadmium uptake.

254
TITLE:
The pharmacology of mercury compounds.

AUTHORS:
Clarkson TW

SOURCE:
Ann. Rev. Pharmacol.; 12: 375-406; 1972 ; (REF:145)

ABSTRACT:
HAPAB A comprehensive review (exclusive of the dose-response relationship) of the pharmacology of mercury compounds is presented. Absorption of some mercury compounds is facilitated by the high lipid solubility of several mercurial salts; pulmonary, percutaneous, and gastrointestinal absorption are described. The pattern of organ deposition appears to be related to the toxic effects of various mercurials. Large species differences are seen in exposure to methyl mercury compounds in the red blood cell-to-plasma ratio. The intra-organ distribution in the kidneys and brain has been shown by animal experiments. Attempts to measure the distribution of mercury between subcellular particles are hindered in determining the purity of the cellular particles. Mercury binding sites in tissues, mainly the kidneys

and liver, are described. The concentration of mercury in biological fluids is low, and the identification of biocomplexes has been difficult; Rothstein's work on the transport of mercury from blood to tissues is discussed. Mercury excretion mechanisms are reviewed. Biotransformation of organomercurial compounds, as well as elemental and inorganic mercury, is elucidated. In the case of the short chain alkylmercurials, biotransformation may play an important role in determining the rate of excretion from the body. The effects of mercury on biochemical processes have received a great deal of attention, the greatest effort being directed towards elucidation of those changes associated with mercurial diuresis. 1972

255
TITLE:
Methyl mercury poisoning in Canada.

AUTHORS:
Shephard DAE

SOURCE:
Can. Med. Assoc. J. 114(5): 463,466,467,470,472; 1976.(26 references)

ABSTRACT:
PESTAB. In 1965, an outbreak of methyl mercury poisoning was reported among fishermen and their families in Minamata, Japan. The poisoning appeared to result from the consumption of mercury-contaminated fish from Minamata Bay. Through December 1974, 798 Japanese persons had been verified as having Minamata disease; of these, 107 died. Iraq has had three outbreaks of organic mercury poisoning, all related to the ingestion of grain treated with a methyl mercurial fungicide. A family in New Mexico was crippled by methyl mercury poisoning after eating meat from hogs which had consumed similarly treated seed grain. In contrast, clear-cut evidence of methyl mercury poisoning was not found among Swedes who consumed large amounts of contaminated fish, although nervous system abnormalities were observed. Poisoning may be evident at blood mercury concentrations above 1000 ppb, and concentrations exceeding 3000 ppb are associated with lethal damage; on the other hand, concentrations up to 600 ppb are toxicologically insignificant. Evidence indicates that some Canadians, particularly fish-eating Canadian Indians, have unacceptably high whole-blood concentrations of mercury. Because of the possibility of mercury-induced brain damage in these individuals the responsibility for controlling mercury poisoning should be handled by a single group, the effects of methyl mercury should be further investigated, and a mature philosophical approach to the management of environmental problems should be adopted.

256
TITLE:

Experimental secondary methyl mercury poisoning in the goshawk (Accipiter G. gentillis L.).

AUTHORS:
Borg K JR
Erne K JR
Hanko E JR
Wanntorp H JR

SOURCE:
Environ. Pollution; 1(2): 91-104 1970; (REF:20)

ABSTRACT:
HAPAB The effects of methyl mercury poisoning on the goshawk (Accipiter G. gentillis L.) were investigated in a laboratory |food chain| experiment. Chickens were fed wheat dressed with methyl mercury dicyandiamide (about 8 ppm) for 5 to 6 weeks and then killed. The mercury content, mostly as methyl mercury, of the muscles and livers was about 10 and 40 ppm, respectively. Three hawks (group A) were offered diets of this muscle and liver; one bird (B) was fed muscle; and two hawks (C) were offered diets of untreated chicken muscle and liver. Group A birds died after 30, 38 and 47 days (total mercury intake, about 20 mg/bird); B died after 39 days (total mercury intake, about 20 mg/bird); B died after 39 days (total mercury intake, about 18 mg); and group C birds were killed after 43 and 46 days. The main clinical symptoms of poisoning, which appeared after 2 weeks, were inappetence, muscular weakness, ataxia and weight loss. The chief gross finding on autopsy was muscular atrophy. The control birds, in contrast; were in a good state of nutrition and no gross changes were found. Demyelination and nerve cell degeneration in the cerebellum and the medula oblongata and demyelination of the peripheral nerves were among the pronounced histological changes observed in the poisoned hawks. No lesions were found in the cerebrum. No characteristic histologic changes were found in the controls. Mercury residues, almost exclusively methyl mercury, were high in the liver, kidneys, skeletal muscle and brain tissues (tabulated). Especially high levels were found in the gonads, particularly the testes (up to 280 ppm). The experiment demonstrated that methyl mercury may accumulate in a food chain without a loss in toxicity. 1970

257
TITLE:
The Effects Of Mild Congenital Methylmercury Intoxication On The Metabolism Of 3-Hydroxybutyrate And Glucose In The Brains Of Suckling Rats

AUTHORS:
Menon NK
Lopez RR

SOURCE:
NeuroToxicology, Vol. 6, No. 1, pages 55-61, 29 references, 19851985

ABSTRACT:
The effects of mild congenital methylmercury (22967926) toxicity on the metabolism of 3-hydroxybutyrate (591811) and glucose (50997) in the developing brain were studied in rats. Female Sprague-Dawley-rats were injected intravenously with 10 milligrams per kilogram methylmercury-chloride (115093) on day 4 after impregnation. At 1, 7, 14, and 21 days after birth, pup brain slices were incubated with carbon-14 labeled glucose or 3-hydroxybutyrate. For the leucine study, brain slices in the amount equivalent to 15 milligrams protein were incubated with labeled leucine. The carbon-14 contents of carbon-dioxide, lipids, and protein were determined. The total mercury concentration of weighed, digested tissues were estimated. On day 1, mercury concentration in brains of pups was 1.5 times that in the brains of dams. Methylmercury significantly reduced 3-hydroxybutyrate oxidation at post natal days 14 and 21; glucose oxidation was reduced at post natal day 14 but returned to above normal values by day 21. A reduction in the incorporation of label from both substrate s into total brain lipids occurred during the most rapid phase of myelination. A marked reduction in the incorporation of label from glucose into the protein fraction of methylmercury tested brains occurred. There were no significant difference in the rates of labeled leucine into labeled carbon-dioxide and proteins at post natal days 7 and 14.

258
TITLE:
Studies on the toxicity of phenylmercuric acetate (PMA) in chickens. 1. The effects of administration of PMA on mercury retention in some organs of chickens.

AUTHORS:
Rozycka D

SOURCE:
Rocz. Panstw. Zakl. Hig. 27(3): 287-293; 1976.(21 references)

ABSTRACT:
PESTAB. Mercury accumulation and retention were studied in liver, kidney, brain, and muscle of chickens. The chickens received either 1 mg/kg or 10 mg/kg of PMA every 48 hr during periods of 8, 16, 24, 32, or 40 days. Mercury concentration in the liver and kidney increased in a regular manner over the 40 day test period, and the amount accumulated was directly proportional to the dose given. In muscle tissue an equilibrium was reached after 16 days. Only slight uptake of mercury was noted in the brain. Mercury retention given as a percentage of total dose administered was 0.6% in both the liver and kidney and was not dependent on the amount

of PMA administered. No sex differences were noted concerning accumulation or retention of mercury. Body weight gain showed no differences between treated and control chickens. Mercury intoxication was not noted.

259
TITLE:
Toxicology and carcinogenesis studies of mercuric chloride in F344 rats and B6C3F1 mice (gavage studies)

AUTHORS:
NTP working group

SOURCE:
TA:National Toxicology Program Technical Report Series PG:265 p YR:1993 IP: VI:408

ABSTRACT:
Mercuric chloride is an inorganic compound that has been used in agriculture as a fungicide, in medicine as a topical antiseptic and disinfectant, and in chemistry as an intermediate in the production of other mercury compounds. The widespread use of mercury has resulted in increased levels of mercury in rivers and lakes. Mercuric chloride was evaluated in toxicity and carcinogenicity studies because of its extensive use and its occurrence as an environmental pollutant, and because of the lack of adequate longterm rodent studies. Toxicology and carcinogenesis studies were conducted by administering mercuric chloride (greater than 99% pure) in deionized water by gavage to groups of F344 rats or B6C3FI mice for 16 days, 6 months, and 2 years. Genetic toxicology studies were conducted in Salmonella typhimurium (strains TA98, TA100, TA1535, and TA1537), in mouse lymphoma L5178Y cells, in Chinese hamster ovary cells, and in Drosophila melanogaster. 16-DAY STUDIES: Groups of five rats of each sex received 0,1.25, 2.5, 5,10, or 20 mg mercuric chloride/kg body weight and groups of five mice of each sex received 0, 5,10, 20, 40, or 80 mg/kg in deionized water by gavage for 12 dose days. Two male rats in the 20 mg/kg group died in the first week, as did all male and four female mice from the 80 mg/kg group and one male mouse from the 40 mg/kg group. The final mean body weight of male rats receiving 20 mg/kg was 10% lower than that of the controls; the final mean body weight of 20 mg/kg females was 9% lower than that of the controls. Final mean body weights and body weight gains of dosed mice were similar to those of the controls. Absolute and relative kidney weights of male rats receiving 2.5 mg/kg or greater doses and of female rats administered 5 mg/kg or more were significantly greater than those of the controls. Absolute kidney weights of mice were significantly increased in all male dose groups and in the 40 mg/kg female dose group; relative kidney weights of dosed male and female mice were significantly greater than the controls. Analysis of kidney, liver, and brain tissues for mercury residues revealed that the highest mercury concentration was in the kidneys of rats and mice. Acute renal tubule

nephropathy occurred in dosed rats and was slightly more severe in males than in females. Chemical-related lesions in mice included renal tubule necrosis, inflammation and necrosis of the forestomach, and necrosis of the glandular stomach. 6-MONTH STUDIES: Groups of 10 rats of each sex received 0, 0.312, 0.625, 1.25, 2.5, or 5 mg mercuric chloride/kg body weight in deionized water by gavage for 26 weeks. Groups of 10 mice of each sex received 0,1.25, 2.5, 5, 10, or 20 mg/kg in deionized water by gavage for 26 weeks (males) or 27 weeks (females). No deaths related to mercuric chloride administration occurred in rats or mice. Mean body weight gains of male rats that received 5 mg/kg and all female rat dose groups that received 0.625 mg/kg or greater were significantly lower than the controls. The final mean body weight and body weight gain of male mice in the 20 mg/kg group were significantly lower than those of the controls; final mean body weights and body weight gains of other dosed male mice and all dosed female mice were similar to those of the controls. Absolute and relative kidney weights of all dosed male rats and of female rats that received 0.625 mg/kg or greater were significantly greater than those of the controls. In male mice, absolute kidney weights in the three highest dose groups were significantly increased; no biologically significant differences in organ weights occurred in female mice. Analysis of kidney, liver, and brain tissues for mercury residues revealed the highest mercury concentration in the kidneys of rats and mice. The severity of chronic nephropathy increased with dose in male rats. Cytoplasmic vacuolation of renal tubule epithelial cells was observed in male mice in the 5, 10, and 20 mg/kg groups. No histopathologic changes in female mice were related to chemical exposure. 2-YEAR STUDIES: Groups of 60 rats of each sex received 0, 2.5, or 5 mg mercuric chloride/kg body weight and groups of 60 mice of each sex received 0, 5, or 10 mg/kg in deionized water by gavage 5 days per week for 2 years. The doses were based on decreased weight gains in rats receiving 10 and 20 mg/kg and the decreased weight in male mice receiving 40 mg/kg during the 16-day studies, and on the decreased weight gains and toxicity results seen in the 6-month studies. Increased absolute and relative kidney weights in rats and male mice in the 6-month studies and degenerative renal changes suggested that higher dose levels would result in inadequate survival rates for a 2-year study. 15-Month Interim Evaluations: Relative kidney weights were significantly increased in dosed rats and female mice. The severity of nephropathy was increased in male rats, but not in females. High-dose male and female rats had minimal to mild hyperplasia of the basal cell layer in the forestomach epithelium (diagnosed as acanthosis); this lesion was not found in control or low-dose rats. Male mice had an increased severity of vacuolation of the renal tubule epithelium; no chemical-related lesions occurred in the kidneys of females. The incidence of inflammation of the olfactory epithelium lining the nasal cavity increased in male and female high-dose mice. Survival, Body Weights, and Clinical Signs: Survival of dosed male rats was lower than that of the controls (26/50, 10/50, 5/50); survival of dosed female rats was similar to that of the controls (35/50, 28/49, 30/50). Although more than 60% of the mice in each dose group survived to

study end, survival rates of high-dose male mice and dosed female mice were lower than those of the controls (males: 36/50, 36/50, 31/50; females: 41/50, 35/50, 31/50). The final mean body weights of high-dose male and female rats were 15% and 14% lower than controls, respectively. The mean body weight of low-dose female rats was generally similar to controls throughout the 2-year study; the mean body weight of low-dose male rats was similar to that of the control through week 89. In mice, mean body weights of all male and female dose groups were similar to those of the controls throughout the studies. Pathology Findings: Chronic nephropathy appeared to develop at an accelerated rate and led to decreased survival in both dosed male rat groups. Secondary effects of renal dysfunction in dosed male rats resulted in increased incidences of fibrous osteodystrophy of the bone, mineralization of various tissues, and parathyroid gland hyperplasia. Based on evaluations of single and step sections, the incidence of renal tubule hyperplasia was increased in high-dose male rats (control, 3/50; high-dose, 10/50), but the incidences of renal tubule adenoma in high-dose and control males were similar (4/50, 5/50). Renal tubule hyperplasia was also slightly increased in high-dose female rats (2/50, 5/50) and adenomas were seen in high-dose females, but not in controls (0/50, 2/50). Incidences of forestomach hyperplasia in rats were markedly increased in dosed males (3/49, 16/50, 35/50) and high-dose females (5/50, 5/49, 20/50). Squamous cell papillomas of the forestomach were found in 3 low-dose and 12 high-dose males and in 2 high-dose females. No squamous cell carcinomas were found. The incidence of thyroid follicular cell carcinoma was marginally increased in high-dose male rats (1/50, 2/50, 6/50). However, a corresponding increased incidence in follicular cell adenomas (1/50, 4/50, 0/50) or hyperplasias (2/50, 4/50, 2/50) in males did not occur, and the overall incidence of follicular cell neoplasms was not significantly increased (2/50, 6/50, 6/50). The incidence of nasal mucosa inflammation in male and female rats was increased in the high-dose groups (male: 9/50, 8/47,18/50; female: 0/49, 5/49,15/50) and may have been related to chemical administration. The incidences of mammary gland fibroadenomas were significantly decreased in dosed female rats (15/50, 5/48, 2/50). The incidence and severity of nephropathy were increased in dosed mice; secondary

260
TITLE:
Effect of Mercury on Glutathione and Thyroid Hormones

AUTHORS:
Sin YM
Teh WF
Wong MK
Reddy PK

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 44, No. 4,

pages 616-622, 21 references, 1990

ABSTRACT:

The changes of glutathione (GSH) and thyroid hormones were studied in animals treated with mercuric compounds of different solubilities. Young adult female Swiss-albino-mice were treated with mercuric-chloride (7487947) (HgCl2) or mercuric-sulfide (1344485) (HgS) once a day for 10 days via gavage. Animals were sacrificed 24 hours after the last mercury treatment. The accumulation of mercury into the liver, kidney and brain tissues of the HgCl2 treated mice was significantly higher than in those of the HgS treated mice due to the difference in solubility of the two compounds. The amount of tissue GSH in the liver of HgCl2 and HgS treated mice were similar, showing lower mean values but not significantly different from that of the controls. The amount of tissue GSH in the kidney of HgCl2 treated mice was significantly higher than the controls and this change was not seen in the HgS treated animals. The authors assume that the increase of tissue GSH in both the kidney and brain of the HgCl2 treated mice is most likely derived from the liver via blood circulation. An attempt was made to determine to what extent the circulating thyroid hormones can be affected by the different amount of mercury accumulated in the various studied organs. A decrease of both circulating thyroid hormones T3 and T4 in the HgCl2 treated mice suggests that the deposited mercury had exerted its effect not only on the liver but also possibly on the thyroid and other organs. A similar decrease was found in the circulating T3 in HgS treated mice.

261

TITLE:

Mercury concentrations in autopsy tissues from inhabitants of Tarragona Province, Spain.

AUTHORS:

SCHUHMACHER M
BATISTA J
DOMINGO JL
CORBELLA J

SOURCE:

TRACE ELEMENTS AND ELECTROLYTES; 13 (2). 1996. 75-78.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Mercury levels were determined in 5 tissues of 60 non-occupationally autopsied subjects, mean age 65 years, from Tarragona Province, Spain. The influence of the place of residence, i.e. whether it was a rural or an industrial area, of age, sex, drinking and smoking habits was also evaluated. Average concentrations of mercury in brain, liver, bone, lung, and kidney were 34.1 (12 - 115), 140.2 (15 - 627), 9.8 (2 - 79), 28.5 (2 - 163) and 111.7 (7 - 1,185) mug/kg wet

weight, respectively. No significant differences in mercury concentrations were observed for any of the analyzed tissues in relation to the place of residence. However, the brain levels of mercury increased with the age for both sexes, while in contrast the mercury levels in bone decreased significantly with age. Sex, drinking and smoking habits had no influence on tissue mercury concentrations.

262

TITLE:

Neurotoxic heavy metals lead and mercury disturb N-cadherin expression in embryonic chick cortical cells.

AUTHORS:

Dey PM

Grunwald GB

SOURCE:

Toxicologist 2000 Mar;54(1):71-2

ABSTRACT:

Exposure to heavy metals during embryogenesis disturbs brain development and results in decreased neurological potential. Morphogenesis of the central nervous system is mediated, in part, by the developmentally-regulated expression of the cell adhesion molecule N-cadherin. Appearance of this 130 kDa transmembrane glycoprotein and its associated cytoskeleton-linking proteins at neuronal cell surfaces mediates homophilic adhesion and bi-directional cell signaling during all stages of neurodevelopment. One prominent mechanism by which neural N-cadherin is turned over is by divalent-cation dependent proteolysis, resulting in the generation of truncated membrane-associated forms and soluble N-cadherin (NCAD90) fragments. Experiments were undertaken to determine whether the toxic metals lead and mercury disturb N-cadherin expression in chick cortical cells following exposure to metals using in vitro cell cultures and in purified synaptosomal membrane preparations. Incubation of cultured cortical cells with either 2 or 20 mM mercury chloride for 24 hours resulted in the dose-dependent increase in membrane-associated N-cadherin isoform expression, with significant elevation in levels of both the 130 kDa (at 20 mM) and 110 kDa isoforms (2 and 20 mM) and generation of soluble NCAD90. Lead exposure of cortical cell cultures for one week in either 1 or 5 mM lead chloride resulted in reduced membrane-associated N-cadherin expression, along with significant loss of the N-cadherin cytoskeletal linker protein beta-catenin. Alteration in the developmentally-regulated expression of N-cadherin by lead and mercury may disturb N-cadherin-mediated brain morphogenesis, and could contribute to the neurological defects observed in developmental metal neurotoxicity.

263

TITLE:

Mercury accumulation and glutathione levels in fetuses from mice developmentally exposed to low levels of methylmercury.

AUTHORS:

Thompson SA
Gilbert SG
White CC
Eaton DL
Bloom N
Kavanagh TJ

SOURCE:

International Toxicologist 1995 Jul;7(1):AB# 8-P-1

ABSTRACT:

The developing fetus is particularly susceptible to the toxic effects of methylmercury (MeHg). It has also been shown that the upregulation of glutathione (GSH) may play an important role in mitigating the adverse effects of methylmercury. This study was designed to evaluate methylmercury accumulation and alterations in GSH regulation in the developing fetuses of mice which were developmentally exposed to methylmercury. Female C57Bl/6 mice were exposed to methylmercury in the drinking water at 0, 3, or 10 ppm for 2 weeks prior to breeding and throughout gestation. Mice were evaluated for their reproductive capacity, maternal body weight gain per fetus, and mercury levels in the blood and brain were determined. Fetuses were collected on gestation day 18 and evaluated for changes in body weight, mercury levels, GSH levels and gamma-glutamylcysteine synthetase (gamma-GCS) activity. The reproductive capacity was 50% in the 10 ppm dose group compared to 89% and 100% in the 3 ppm and 0 ppm dose group, respectively. There were no significant differences in the maternal weight gain per fetus in any of the dose groups, but there was a dose dependent decrease in the average fetal weight. Blood and tissue mercury levels showed that the fetus accumulates mercury in a dose dependent manner and levels in the fetus were 40% higher than levels in the maternal brain and at least two times the levels seen in the maternal blood. Preliminary results with HPLC showed a dose dependent elevaton in GSH levels and gamma-GCS activity in the gd 18 fetuses exposed to methylmercury. Based on these results it appears that methylmercury does accumulate in the fetus and that gd 18 fetuses are capable of increasing their GSH levels and gamma-GCS activity in response to maternal methylmercury exposure.

264

TITLE:

Oral and Intramuscular Toxicity of Inorganic and Organic Mercury Chloride to Growing Quail

AUTHORS:
Hill EF
Soares JH Jr

SOURCE:
Journal of Toxicology and Environmental Health, Vol. 20, Nos. 1-2, pages 105-116, 30 references, 19871987

ABSTRACT:
The lethal toxicity of the inorganic compound, mercuric-chloride (7487947), and the organic compound, methyl-mercury-chloride (115093), to Coturnix, or Japanese-quail, was compared from hatching to adulthood by administration of a single acute oral dose, intramuscular injections, or by a 5 day dietary trial. Sublethal toxicity was compared at doses of 0, 5, or 25mg/kg mercury (7439976) (Hg) by evaluation of plasma and brain cholinesterase activity. Organic mercury was more toxic than inorganic mercury in all tests at each age tested. Methyl-mercury-chloride, on the average, was twice as toxic as mercuric-chloride by both acute methods, whereas it was 100 times as toxic by the dietary route. The oral median lethal doses (LD50s) for methyl-mercury-chloride and mercuric-chloride were 18 and 42mg/kg, respectively; the dietary LD50s were 47 and 5086 parts per million, respectively. In sublethal single dose toxicity tests, virtually all birds dosed with 25mg/kg of either of the mercurials manifested clinical signs of toxicity, as described for acute testing; a few animals died. Brain and plasma acetylcholinesterase activity declined initially but recovered by day seven.

265
TITLE:
Effects Of Trisodium Nitrilotriacetate On Cadmium And Methyl Mercury Toxicity And Teratogenicity In Rats

AUTHORS:
Nolen GA
Buehler EV
Geil RG
Goldenthal EI

SOURCE:
Toxicology and Applied Pharmacology, Vol. 23, pages 222-237, 15 references, 19721972

ABSTRACT:
The effects of trisodium-nitrilotriacetate (5064313) (NTA) on cadmium (7440439) and methylmercury (22967926) toxicity and teratogenicity were studied in rats. Mated female Charles-River-rats were administered 0, 0.01, 1, or 4 milligrams per kilogram (mg/kg) cadmium-chloride (10108642) or 0, 0.02, 0.2, or 4mg/kg methylmercury-chloride (115093), or 0, 0.1, or

20mg/kg NTA in their drinking water on days 6 through 14 of gestation. Body weight gain and feed water consumption of the dams were monitored. On day 21, the animals were killed, and the numbers of corpora lutea, implantations, resorptions, and live and dead fetuses were determined. Selected fetuses were examined for malformations. Maternal brain, kidney, and liver tissue sections and one live fetus were assayed for cadmium and mercury (7439976). Cadmium at 0.01 and 1mg/kg at no effects on the dams. The 4mg/kg dose reduced body weight gain. The 1 and 4mg/kg doses increased the number of malformed fetuses, but had no effect on the number of resorptions or live and dead fetuses. NTA did not alter the effects of cadmium. Mercury at 0.02 and 0.2mg/kg had no effect on the dams. The 4mg/kg dose decreased body weight gain. The 4mg/kg dose significantly reduced the number of implantations. A dose/dependent increase in fetal malformations occurred. Mercury plus NTA had no significant effect on the number of abnormal fetuses. Dose/dependent increases in the mercury content of maternal liver, kidneys, and brain and in the fetus occurred. NTA had no effect on the uptake or storage of mercury. The authors conclude that NTA does not enhance the toxicity or teratogenicity of cadmium or mercury.

266

TITLE:

Mercurial-Induced Alterations in Neuronal Divalent Cation Homeostasis

AUTHORS:

Denny MF
Atchison WD

SOURCE:

Neurotoxicology, Vol. 17, No. 1, pages 47-62, 86 references, 1996

ABSTRACT:

The effects of mercurials on neuronal divalent cation homeostasis were reviewed. The general features of mercury (7439976) neurotoxicity were summarized. The toxicity of mercury depends primarily on its chemical form. Divalent mercury (Hg+2) and methylmercury are directly neurotoxic and cause symptoms such as tremors, central nervous system hyperexcitability, and loss of fine motor control and vision, hearing, and speech impairments, sensory disturbances, and weakness in the extremities, respectively. Metallic mercury is neurotoxic by virtue of its being bioconverted in the brain to Hg+2. The effects of Hg+2 and methylmercury on neuronal function indicative of disruption of cation regulation were considered. Hg+2 and methylmercury can block calcium ion (Ca+2) influx through voltage activated Ca+2 channels, decrease endplate potential amplitudes, and increase the frequency of miniature endplate potentials (MEPPs) in nerve muscle preparations, all indicating a disruption of Ca+2 homeostasis. Hg+2 and methylmercury inhibit Ca+2 influx by competitive and noncompetitive mechanisms, respectively. The effects of Hg+2 and

methylmercury on Ca+2 channel function, Ca+2 regulation, and intracellular Ca+2 concentration were discussed. Both Hg+2 and methylmercury decrease nerve evoked release of neurotransmitters, but increase spontaneous neurotransmitter release. Increasing the permeability of nerve terminals to Ca+2 has been shown to shorten the time to onset of the methylmercury induced increases in MEPP frequency. Both Hg+2 and methylmercury increase intracellular Ca+2 concentrations. Methylmercury can induce increases in zinc ion (Zn+2) concentration in brain synaptosomal proteins as well as in the Ca+2 concentration. These increases were mediated by release of Zn+2 from soluble synaptosomal proteins and increases in plasma membrane permeability. The authors conclude that mercurials can disrupt divalent cation homeostasis; however, the toxicological significance of this effect is not clear.

267
TITLE:
Effects of mercury and lead on rubidium uptake and efflux in cultured rat astrocytes.

AUTHORS:
ASCHNER M
CHEN R
KIMELBERG HK

SOURCE:
BRAIN RES BULL; 26 (4). 1991. 639-642.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Astrocytes readily sequester lead and mercury (8, 10, 19, 22). Accordingly, studies were undertaken to assess the effects of lead and mercury on homeostatic functions in neonatal rat brain primary astrocyte cultures. Both inorganic and organic mercury, but not lead, significantly inhibited the initial rate (5 min) of uptake of 86RbCl, used as a tracer for K+, at concentrations of 10-100 muM. Mercury and to a lesser extent lead also stimulated the efflux of intracellular 86Rb+ at 10-500 muM. These observations suggest that the astrocyte plasma membrane may be an important target for lead and mercury, and that relatively low concentrations of these heavy metals should inhibit the ability of astrocytes to maintain a transmembrane K+ gradient.

268
TITLE:
The effect of organic mercury on intrauterine life.

AUTHORS:
MURAKAMI U

SOURCE:

ADV EXP MED BIOL; 27. 1972 301-336

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Minamata disease (MD) originated from consumption of fish and shellfish caught in Minamata Bay, Kyushu, Japan. Minamata Bay was polluted by methyl mercuric sulfide and methyl mercuric chloride through waste water discharged into the river by a vinyl-chloride and acetaldehyde plant. A short history of the victims and the present situation as regards disease manifestations were given. Clinical features of fetal Minamata disease (FMD) in relation to embryo-feto-pathy and characteristics findings in FMD (26 victims) were noted. Relationship of FMD to disturbances in intrauterine life; embryo-feto-pathic effect of Hg compounds; and embryo-feto-toxic and teratogenic effects of organic Hg are reviewed. Alkyl mercury poisoning in intrauterine life exhibits embryo- and feto-pathic effects both in human victims of FMD and in animal experiments. Almost all mothers of children suffering from FMD did not manifest apparent symptoms of MD. The immature brain seems to be more sensitive to alkyl mercury; in particular, the immature brain in which cellular architecture is nearly completed is susceptible. An amount of alkyl mercury insufficient to cause involvement of the brain after birth might possibly cause involvement of the immature brain during intrauterine life.

269

TITLE:

Effects Of Neonatal Mercuric Chloride Administration On Growth And Biochemical Development Of Neuronal And Non-Neuronal Tissues In The Rat: Comparison With Methylmercury

AUTHORS:

Bartolome J
Whitmore WL
Slotkin TA

SOURCE:

Toxicology Letters, Vol. 22, No. 1, pages 101-111, 30 references, 19841984

ABSTRACT:

The effects of neonatal exposure to inorganic mercury (7439976) on biochemical factors involved in tissue growth and on neurotransmitter systems were studied in rats. For the first 21 days after birth, Sprague-Dawley-rat pups were subcutaneously injected daily with saline or 0.5 to 2.5 milligrams per kilogram (mg/kg) mercuric-chloride (7487947). Animals were killed at intervals from 3 to 50 days old. Bodies and organs were weighed, and cytosolic fractions of hypotonic tissue homogenates were assayed for ornithine-decarboxylase activity, an enzymatic marker for general cellular maturation. Brain tissue was analyzed for norepinephrine and dopamine content and turnover, and assayed for uptake of labeled

norepinephrine and dopamine into synaptosomes. All treated animals weighed less than controls from day 20 on. In treated animals, brain weights were reduced 5 to 15 percent from day 20 on; heart, kidney, and liver weights were increased 5 to 22 percent on day 10, then declined to near normal or 10 percent sub normal values by day 50. Compared with controls, ornithine-decarboxylase activity was reduced 15 to 40 percent in brain tissue from day 5 to 15 and was increased up to 60 percent in heart tissue by day 10. It then declined to normal or slightly sub normal values and showed a biphasic pattern in kidney and liver of sharp increase followed by sharp decrease in both the first week and immediately after weaning at day 21. On day 10, brain content and turnover of norepinephrine were elevated 10 percent, and of dopamine were reduced 15 percent. Synaptosomal uptake of dopamine and norepinephrine was increased 40 to 50 percent on day 20 by 2.5mg/kg mercury but was unaffected by 1mg/kg. The authors conclude that alterations in ornithine-decarboxylase activity following mercury exposure are predictive of differential tissue growth effects. The central nervous system is highly sensitive to mercuric-chloride, exhibiting selective neurotransmitter effects.

270

TITLE:

ENVIRONMENTALLY INDUCED ALTERATIONS IN NEURON AND GLIA DEVELOPMENT

AUTHORS:

HARRY GJ

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

During the development of the nervous system, the temporal and spatial regulatio n of gene expression is a critical component of neural and glial growth, develop ment, and interactions. These critically timed events are assumed to be a major component in the differential susceptibility of the developing organism to envir onmental insult. This project examined chemical induced perturbations during dev elopment of the NS as indicated by alterations in the spatio-temporal expression of mRNA for various developmentally regulated proteins associated with distinct processes of development. We have shown by RNase protection assays that lead ac etate alters developmentally regulated structural proteins for neurons and glia in the rat as well as an upregulation of apoptosis genes and brain derived neuro trophic factors. Early exposure to mercury vapors also elevate mRNA levels for a poptosis factors consistent with previous reports of mercury induced apoptosis i n the brain. This technique is being expanded with the establishment of new prob e sets to detect mRNA levels for proteins associated with the various cell types and stages of brain development. Future Research: The developmental related eff ects of chemicals which disrupt thyroid hormone levels, PTU and dioxin, will be examined to

determine any relationship with structural alterations in the nervou s system. Additional studies are based upon events associated with hypoxia-isch emia occurring at preterm birth. These studies will examine the acute toxicity o f interleukin 6 on the early post-natal developing CNS and alteration in the nor mal ontogeny of molecular markers for cortical neuronal network development. - m ouse, rat, brain, development, lead acetate, mercury vapors, hypoxia

271
TITLE:
Milk Transfer and Tissue Uptake of Mercury in Suckling Offspring after Exposure of Lactating Maternal Guinea Pigs to Inorganic or Methylmercury

AUTHORS:
Yoshida M
Watanabe C
Satoh H
Kishimoto T
Yamamura Y

SOURCE:
Archives of Toxicology, Vol. 68, No. 3, pages 174-178, 16 reference, 1994

ABSTRACT:
Milk transfer and tissue uptake of mercury (7439921) (Hg) by suckling offspring following postpartum exposure to inorganic and organic Hg was studied in guinea-pigs. Maternal Hartley-guinea-pigs were injected intraperitoneally with 0 or 1.0mg/kg mercuric-chloride (7487947) or methylmercuric-chloride (115093) (MMC) 12 hours after delivery and were allowed to suckle their offspring for 3, 5, or 10 days. Selected dams and their offspring were killed at these times and the maternal milk and blood, and offspring blood, brain, liver, and kidneys were collected and removed. The maternal blood, plasma, and milk were analyzed for Hg and methylmercury (22967926). Neonatal blood, brain, liver, and kidney Hg concentrations were determined. In dams injected with mercuric-chloride, Hg concentrations in the blood, plasma, and milk decreased rapidly. The milk/plasma Hg concentration ratio was always less than one and showed a marked decrease between days three and five. In dams injected with MMC, methylmercury concentrations in the blood and plasma decreased at a slower rate than in those injected with mercuric-chloride. The ratio of methylmercury to total Hg was initially around 60% and decreased with time. The methylmercury/total Hg concentration ratio in maternal milk was approximately 50% and remained constant over time. In mercuric-chloride exposed offspring, the highest Hg concentrations were found in the kidney, followed by the liver and brain and blood. In MMC exposed neonates, Hg concentrations in the brain, liver, and blood were higher than in mercuric-chloride exposed offspring in whom tissue Hg concentrations peaked on day five and then decreased. Tissue Hg concentrations in MMC

offspring remained constant over the 10 day period. The authors conclude that exposure to Hg by way of breast milk leads to a significant accumulation of Hg in the tissues, the tissue distribution pattern depending on the chemical form of the Hg. Since offspring are very susceptible to the toxic effects of Hg, exposure to Hg compounds by way of maternal milk should be avoided as much as possible.

272

TITLE:

Oxidative Stress in Neurotoxic Effects of Methylmercury Poisoning

AUTHORS:

Yee S

Choi BH

SOURCE:

Neurotoxicology, Vol. 17, No. 1, pages 17-26, 40 references, 1996

ABSTRACT:

Purified cultures of oligodendrocytes, astrocytes, and cerebral cortical and cerebellar granular neurons obtained from embryonic and neonatal rat brains were used to examine the effects of methylmercury-chloride (115093) (MMC) on the rate of oxygen uptake. Once exposed to MMC, the oxygen uptake in all cell types was significantly inhibited. The rate at which oxygen consumption was inhibited varied among different cell types considered, in proportion to the rate at which oxygen had been consumed by each cell type prior to exposure. The faster the normal respiratory rate, the sooner the oxygen uptake was stopped following MMC exposure. Complex specific electron donating substrates were used to stimulate the mitochondria taken from control and MMC injected rat brains in an effort to determine the effects of MMC on mitochondrial electron transport chain activity. Stimulation with complex III (ubiquinol/cytochrome-c-oxidoreductase) caused significant increases in reactive oxygen species and thiobarbituric acid reactive substances along with a reduction in glutathione levels of MMC injected animals. Neither complex I (NADH/ubiquinone-oxidoreductase) or II (succinate/ubiquinone-oxidoreductase) produced these effects, causing the authors to suggest that MMC induces changes in electron transport in the complex III region. Cytochrome-c-reductase was inhibited in a competitive fashion. When cytochrome-c-reductase was preincubated with MMC there was no significant change in the kinetics of cytochrome-c-reductase assay. The authors suggest that mitochondria may be the first target of the neurotoxic effects of methyl-mercury and that the most likely site where excess reactive oxygen species are generated in the brain to cause oxidative stress in methyl-mercury poisoning is the mitochondrial electron transport chain.

273

TITLE:
Regulation of N-cadherin proteolysis in normal and abnormal neural development.

AUTHORS:
Cifarelli CP
Dey PM
Grunwald GB

SOURCE:
Teratology 2000 Jun;61(6):476

ABSTRACT:
Proper development of the central nervous system is dependent, in part, on the regulated expression of cadherin cell adhesion molecules that mediate morphogenesis and cell signaling events. Of specific interest in the developing brain is the expression of N-cadherin, a 130 kDa calcium-dependent transmembrane glycoprotein. Regulation of N-cadherin occurs at both the pre- and post-translational levels, with the latter mechanisms involving divalent cation-dependent proteolysis. Using cell cultures or membrane preparations obtained from chick embryonic brain and retina, we have investigated two distinct pathways by which N-cadherin is proteolyzed under both physiological and pathological circumstances. These pathways yield either a soluble 90 kDa ectodomain (NCAD90) or a 110 kDa membrane-associated fragment. Production of NCAD90 is both pH and Zn2+ dependent, and is accompanied by the generation of a membrane-associated 33.5 kDa fragment whose removal is dependent on proteasome activity. In contrast, production of the 110 kDa form does not appear to be dependent on either a narrow pH range or on Zn2+. Neurotoxic metals, lead and mercury, differentially alter N-cadherin proteolysis in a dose-dependent manner in cortical cell culture, with mercury increasing NCAD90 production and lead decreasing 110 kDa levels. These data suggest that proteolysis is an endogenous mechanism of N-cadherin regulation during normal nervous system development, and that perturbation of these proteolytic pathways may contribute to heavy metal neurotoxicity.

274
TITLE:
Cardiovascular Homeostasis In Rats Chronically Exposed To Mercuric Chloride

AUTHORS:
Carmignani M
Boscolo P

SOURCE:
Archives of Toxicology, Supplement 7, pages 383-388, 9 references, 19841984

ABSTRACT:

The effects of chronic mercury (7439976) exposure on cardiovascular functions were examined in Sprague-Dawley-rats. The rats received 50 micrograms per milliliter mercuric-chloride (7487947) in deionized drinking water. Systolic and diastolic aortic blood pressure (BP) and the maximum rate of rise of the left ventricular pressure were obtained by catheterization of the left carotic artery. Heart rate and electrocardiograms (EKG) were monitored. Cardiovascular responses to bilateral carotid occlusion were evaluated. Concentrations of mercury in the kidney, and copper, zinc, and iron in the brain and kidney were determined by atomic absorption spectrophotometry. Cardiovascular responses of a second group of animals were assessed with a dose of 1 microgram per kilogram (microg/kg) norepinephrine and 0.50microg/kg isoprenaline during intravenous infusion with verapamil or papaverine. Basal BP, heart rate, and EKG pattern remained unchanged. The rise of BP and maximum rate of rise of ventricular pressure observed during bilateral carotid occlusion was greatly reduced. The pressor and inotropic response to norepinephrine was significantly reduced. Mercury exposure caused an increase of copper and zinc in the kidneys and brain. Cardiac inotropism was significantly increased in the second group of rats without changes in heart rate and EKG patterns. Systolic and diastolic BP responses to norepinephrine were reduced and to isoprenaline were increased. The authors conclude that chronic exposure to inorganic mercury induces an increase in cardiac inotropism and may induce hypertension without changing the heart rate.

275

TITLE:

Adenine Nucleotides in Cultured Brain Cells after Exposure to Methyl Mercury and Triethyl Lead

AUTHORS:

Grundt IK
Bakken AM

SOURCE:

Acta Pharmacologica et Toxicologica, Vol. 59, No. 1, pages 11-16, 17 references, 19861986

ABSTRACT:

The doses of methyl mercury (MeHg) and triethyl lead (Et3Pb) which were needed to alter the cellular content of adenine nucleotides were compared to doses which induced morphological alterations in cultured newborn rat brain cells. Different types of cells in the culture seemed to be equally susceptible to the metallo compounds. Within 5 minutes after addition of 28 x 10(-6) molar (M) MeMg as methylmercury-chloride (115093), the total content of adenine nucleotides was reduced. Within 20 minutes the

cellular adenine nucleotide and ATP levels dropped to about one tenth of values measured before exposure. The energy charge (EC) was also reduced. Simultaneous alterations in cell shape appeared using light microscopy. Cell processes degenerated. Reduction of the concentration of MeHg to 16 x 10(-6) M caused similar changes on cell morphology and adenine nucleotide levels. The content of ADP in the cells dropped. However, there was an increase of degradation products from adenine nucleotides as inosine and hypoxanthine. Addition of 8 x 10(-6) M MeHg to the growth medium brought about a slowly progressing degeneration of cellular extensions. In cultures exposed to 3 x 10(-6) M Et3Pb as triethyl-lead-chloride (1067147), the adenine nucleotide content was unchanged during the observation time of 1 hour. Morphological degenerations and loss of cells were observed in the microscope after 15 minutes of exposure. The authors suggest that mitochondrial insufficiency is not a direct primary effect of MeHg or Et3Pb, at least not in cultured brain cells.

276

TITLE:

The Effect Of Organic Mercury On Intrauterine Life

AUTHORS:

Murakami U

SOURCE:

Drugs and Fetal Development, Klingberg, M. A., Editor; Plenum Publishing, New York, pages 301-336, 39 references0000

ABSTRACT:

The effects of organic mercury (7439976) compounds on intrauterine life are reviewed. The origin of fetal Minamata disease is discussed. The disease is caused by the consumption of fish and shellfish caught in Minamata Bay that contain high concentrations of methyl-mercuric-sulfide (25310489) and methyl-mercuric-chloride (115093) from the effluent of a chemical factory. Through April 1971, 134 cases were reported. Of these, 26 were fetal cases. It is noted that most of the mothers showed no symptoms of the disease, which resemble those of cerebral palsy. Clinical findings on some case histories are summarized. These include microcephalia, enlargement of the lateral ventricle, diffuse atrophy of the cerebral hemisphere, and asymmetry of the lateral ventricles. Experimental animal studies with organic mercury compounds are discussed. Neuropathological changes were observed in the offspring and fetuses of the various species studied. The author concludes that organic mercury compounds affect the fetal brain in the early stages of embryonic development. Amounts of the compounds insufficient to cause brain damage after birth can affect the brain of the developing fetus.

277

TITLE:
Mercuric chloride-induced alterations of levels of noradrenaline, dopamine, serotonin and acetylcholine esterase activity in different regions of rat brain during postnatal development.

AUTHORS:
LAKSHMANA MK
DESIRAJU T
RAJU TR

SOURCE:
ARCHIVES OF TOXICOLOGY; 67 (6). 1993. 422-427.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Wistar rats were fed mercuric chloride, 4 mg/kg body weight per day chronically from postnatal day 2 to 60 by gastric intubation. Mercury consumption was then discontinued until 170 days to allow time for recovery. Since mercury caused reduction in body weight, an underweight group was also included besides the normal saline group. Levels of noradrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5-HT) and the activity of acetylcholine esterase (AChE) were assayed in various brain regions in different age groups. By 60 days of age, the mercury group showed elevations of NA levels in olfactory bulb (OB), visual cortex (VC) and brain stem (BS) but not in striatum accumbens (SA) and hippocampus (HI). DA levels were also increased in OB, HI, VC and BS but not in SA. AChE activity was decreased in the mercury group only in HI and VC at 20 days of age. The Mercury group showed no behavioural abnormality outwardly; however, operant conditioning revealed a deficiency in perform

278
TITLE:
The Effect of Selenium on the Biliary Excretion and Organ Distribution of Mercury in the Rat after Exposure to Methyl Mercuric Chloride

AUTHORS:
Alexander J
Norseth T

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 44, No. 3, pages 168-176, 15 references, 19791979

ABSTRACT:
The interaction of selenium compounds and methyl-mercuric-chloride (115093) (MeHgCl) in biliary secretion of rats was studied. The bile duct in female Wistar-rats was cannulated under barbiturate anaesthesia. A single intravenous injection of 4 micromoles radiolabeled MeHgCl was

administered at the end of surgical procedure. The bile was collected for 2 hours. Then sodium-selenite (10102188) (NaSe) was injected intraperitoneally and the bile was collected at periodic intervals. Mercury (7439976) (Hg) secretion was determined by performing counts on urine and feces. The concentration of Hg in bile decreased rapidly after injection of 5 micromoles selenite/kilogram (microM/kg) and remained low even 20 hours after a single dose of NaSe. Biliary Hg concentrations were 7.6 nanomoles/gram (nmol/g) for controls and 0.82nmol/g for NaSe treated rats. A 0.20microM/kg dose of NaSe caused a smaller decrease in Hg, whereas higher doses were equally effective. Seleno-di-N-acetylglycine (SNA) also decreased biliary Hg concentration, but the rate was slower. Seleno-methionine (1464422) at 100 moles/kilogram decreased Hg concentration from 17.9 to 2.8nmol/g. Bile duct cannulated rats had a lower kidney Hg content than controls. The brain, blood, and liver concentrations were not affected by cannulation. NaSe induced a ten fold increase in the brain Hg concentration within 1 hour. The rate of brain Hg increase by SNA was slower. The effects of NaSe and SNA on the Hg decrease in kidney were about the same. NaSe treated rats had lower blood Hg concentration than SNA treated rats. A higher level of Hg was observed in the liver of rats treated with NaSe and SNA. The authors state that the inhibiting effect of selenite and SNA on biliary excretion of mercury cannot completely explain the reduction of kidney mercury content, as the reduction in Se treated rats was more prominent than cannulated rats without treatment.

279

TITLE:

Methylmercury Toxicity in Spontaneously Hypertensive Rats (SHR)

AUTHORS:

Tamashiro H
Arakaki M
Akagi H
Hirayama K
Smolensky MH

SOURCE:

Bulletin of Environmental Contamination and Toxicology, Vol. 36, No. 5, pages 668-673, 17 references, 19861986

ABSTRACT:

A study was performed to delineate the toxicity of methylmercury (22967926) (MeHg) in animals with high blood pressure using the laboratory model of spontaneously hypertensive rats (SHR). Male SHRrj and Wistar-Kyoto-rats (WKY) were treated orally with 5mg/kg per day of methylmercury-chloride (115093) (MMC) for 10 consecutive days. Final mortality rates were not significantly different between the two groups of rats, although death occurred significantly earlier in the MMC treated

SHR. In SHR, the neurological manifestations of hindleg crossing and abnormal gait appeared earlier and the decrease in body weight was more pronounced. On days one and five, the content of total mercury was highest in blood cells, followed by kidneys, liver, brain, and plasma. In both groups of rats, compared to day one, the mercury level in the brain and blood cells increased by day five, while liver, kidney, and plasma levels declined, with the exception of liver of SHR. Between SHR and WKY-rats, there were significant differences in mercury levels in the brain, liver, kidneys, and plasma on day one, and again in liver, kidneys, and blood cells on day five; levels were always higher in SHR, perhaps contributing to the higher mortality. It is suggested that the results indicate that MeHg toxicity can be potentiated in hypertensive animals, and presumably in human hypertensives. The authors conclude that both environmental potentiators of MMC and individual differences in resistance and susceptibility to MMC be considered when setting environmental standards for mercury and for the investigation of dose response or dose effect relationships in humans as well as in animals./METABOLISM

280
TITLE:
FOOD INTAKE, BODY WEIGHT, AND BRAIN HISTOPATHOLOGY IN MICE FOLLOWING CHRONIC METHYLMERCURY TREATMENT

AUTHORS:
BERTHOUD HR
GARMAN RH
WEISS B

SOURCE:
TOXICOL. APPL. PHARMACOL. 1976, 36(1) 19-30

ABSTRACT: EIS: Epidemiology Information System

281
TITLE:
Organ Distribution And Biological Half-Time Of Methylmercury In Four Strains Of Mice

AUTHORS:
Doi R
Kobayashi T

SOURCE:
Japanese Journal of Experimental Medicine, Vol. 52, No. 6, pages 307-314, 20 references, 19821982

ABSTRACT:
The distribution and biological half times of methylmercury (22967926)

were studied in four strains of mice. Male BALB/c-mice, C3H-mice, C57BL-mice, and ICR-mice were injected intraperitoneally with 1 milligram per kilogram methylmercury-chloride (115093). Body weight changes were monitored for 22 days. Selected animals were killed up to 22 days after dosing, and total mercury (7439976) concentrations in the blood, brain, liver and kidneys were measured. These were used to determine the biological half times. BALB/c-mice and C3H-mice showed an 8 percent increase in body weight. The mean body weight of C57BL-mice did not increase. Mean body weights of ICR-mice increased by 2 percent over the experimental period. Blood mercury concentrations were twice as high in BALB/c-mice and C3H-mice as in C57BL-mice and ICR-mice. C57BL-mice had the highest brain mercury concentrations. Kidney mercury concentrations were highest in BALB/c-mice and lowest in C3H-mice. Liver mercury concentrations were similar in all strains. Biological half times of brain methylmercury ranged from 14.9 days in BALB/c-mice to 9.3 days in ICR-mice. Biological half times of blood methylmercury were 7.79 days in C57BL-mice and 3.81 days in ICR-mice. Liver methylmercury half times ranged from 9.49 days in C57BL-mice to 4.36 days in ICR-mice. Kidney methylmercury half times ranged from 8.73 days in BALB/c-mice to 4.54 days in ICR-mice. The authors suggest that anatomical factors such as body weight and relative organ weight may play a role in the chemobiokinetics of methylmercury.

282

TITLE:

Influence Of Diethylmaleate On The Formation Of Bis(methylmercuric)selenide And Methylmercury Distribution In Rats

AUTHORS:

Masukawa T
Nishimura T
Kito H
Iwata H

SOURCE:

Journal of Pharmacobio-Dynamics, Vol. 6, No. 12, pages 950-953, 7 references, 19831983

ABSTRACT:

The effects of diethylmaleate (141059) (DEM) on the formation of bis-(methylmercuric)-selenide (4305377) (BMS) and methylmercury (22967926) distribution were assessed in male Wistar-rats. Animals were injected with 20 micromoles (micromol) of labeled methylmercuric-chloride (115093) (MMC) per kilogram (kg) body weight 1 hour after 0 or 1.2 grams (g)/kg DEM was administered. Sodium-selenite was injected at a dose of 20micromol/kg 1 hour later, and rats were sacrificed 90 minutes after MMC adminstration. Total mercury and benzene extractable mercury in the blood and tissues were determined. Pretreatment with DEM depleted tissue reduced

glutathione (GSH) and completely suppressed the significant increase of BMS produced by selenite injection of MMC treated rats. The inhibitory effect of DEM was also observed in the kidney and brain. Under the same conditions, the characteristic accumulation in the brain and testis of total mercury induced by selenite was markedly inhibited by DEM pretreatment. Total mercury in these tissues is not altered by DEM alone and BMS in the blood existed in the erythrocytes but not the plasma. The authors conclude that the suppressed formation of BMS in the erythrocytes mainly results in the decreased accumulation of total mercury in the brain and testis.

283
TITLE:
The effect of mercury vapour on cholinergic neurons in the fetal brain: Studies on the expression of nerve growth factor and its low- and high-affinity receptors.

AUTHORS:
SODERSTROM S
FREDRIKSSON A
DENCKER L
EBENDAL T

SOURCE:
DEVELOPMENTAL BRAIN RESEARCH; 85 (1). 1995. 96-108.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of mercury vapour on the production of nerve growth factor during development have been examined. Pregnant rats were exposed to two different concentrations of mercury vapour during either embryonic days E6-E11 (early) or E13-E18 (late) in pregnancy, increasing the postnatal concentration of mercury in the brain from 1 ng/g tissue to 4 ng/g tissue (low-dose group) or 11 ng/g (high-dose group). The effect of this exposure in offspring was determined by looking at the NGF concentration at postnatal days 21 and 60 and comparing these levels to age-matched controls from sham-treated mothers. Changes in the expression of mRNA encoding NGF, the low- and high-affinity receptors for NGF (p75 and p140 trk, respectively) and choline acetyltransferase (ChAT) were also determined. When rats were exposed to high levels of mercury vapour during early embryonic development there was a significant (62%) increase in hippocampal NGF levels at P21 accompanied by a 50% decrease

284
TITLE:
Mercury accumulation in the squirrel monkey eye after mercury vapour exposure.

AUTHORS:

WARFVINGE K
BRUUN A

SOURCE:
TOXICOLOGY; 107 (3). 1996. 189-200.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Squirrel monkeys were exposed to mercury vapour at different concentrations and for different numbers of days. The calculated total mercury absorption ranged between 1.4-2.9 mg (range of daily absorption 0.02-0.04 mg). The monkeys were killed at different intervals after the end of exposure (range 1 month-3 years) and the eyes were enucleated. Eyes from four un-exposed monkeys were used as control material. Mapping of the mercury distribution in the eye revealed that the non-myelin-containing portion of the optic disc was densely loaded with mercury deposits, which were mostly confined to the capillary walls and the glial columns. The white matter of the brain does not accumulate mercury at these exposure levels, which might suggest that the myelinization process inhibits the accumulation of mercury. The pigmented epithelium of the pars plicata of the ciliary body and of the retina contained a considerable amount of mercury. This finding indicates that mercury is trappe

285
TITLE:
The Toxicity And Teratogenicity Of Mercuric Mercury In The Pregnant Rat

AUTHORS:
Holt D
Webb M

SOURCE:
Archives of Toxicology, Vol. 58, No. 4, pages 243-248, 24 reference, 19861986

ABSTRACT:
Toxic and teratogenic effects of mercuric mercury (7439976) were studied in pregnant female Wistar-Porton-rats. Animals were dosed with about 20 microCuries per milligram (mg) mercury on days 13 or 20 of gestation. Non pregnant animals served as controls. These animals were sacrificed between 24 hours and 4 days of this treatment, and blood, liver, spleen, kidneys, placenta, and fetuses were removed and assayed for radioactivity. Other animals were dosed with various amounts of mercury during different stages of pregnancy and sacrificed for examination for teratogenic effects and maternal kidney damage. It was found that mercuric mercury was retained mainly in the maternal compartment, and uptake by the conceptus was small. The maternal body burden of mercury, particularly in late gestation, was greater than the whole body burden in the non pregnant

animals. However, the median lethal dose of mercury remained essentially constant throughout pregnancy, ranging between 1.0 to 1.2mg/kilogram (kg). Kidney function became less susceptible to mercury as pregnancy advanced from conception to near term. During mid gestation, the minimum effective teratogenic dose, about 0.79mg/kg mercury, was high in relation to the maternal median lethal dose and the incidence of fetal malformations, mainly brain defects. The authors conclude that fetal defects result not from any direct action of mercury on the conceptus, but from either the inhibition of the transport of essential metabolites from the mother, or from maternal kidney dysfunction.

286
TITLE:
Effect of ethanol pretreatment on mercury distribution in organs of fetal guinea pigs following in utero exposure to mercury vapor.

AUTHORS:
YOSHIDA M
SATOH H
SUMI Y

SOURCE:
TOXICOLOGY; 119 (3). 1997. 193-201.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Ethanol (Et-OH), which is an inhibitor of catalase, reduces oxidation of mercury vapor (Hg0) into ionic mercury (Hg2+). Consequently, exposure of pregnant animals to Hg0 with pretreatment of Et-OH causes penetration of larger amount of Hg0 to the fetus. The fate of Hg0 in the fetus of pregnant guinea pigs, thus penetrated, was investigated. Et-OH pretreatment of the dams resulted in the transfer of more mercury to the fetuses and led to a marked increase in mercury in the fetal liver. Furthermore, according to the mercury distribution in the fetal organs, the animals in the Et-OH-pretreated group fell into two subgroups: a group of fetuses (subgroup 1) had higher mercury concentrations in the brain, heart and kidney compared with the group which was exposed to Hg0 without Et-OH-pretreatment (Hg0 group) and another group (subgroup 2) with similar organ mercury concentrations to that of the Hg0 group. Determination of metallothionein (MT) concentrations showed that MT co

287
TITLE:
The Influence Of An Industrial Complexing Agent On The Distribution And Excretion Of Lead And Mercury

AUTHORS:
Norseth T

Nordhagen A-L

SOURCE:
Developments in Toxicology and Environmental Science, Vol. 1, Clinical Chemistry and Chemical Toxicology of Metals, pages 137-140, 4 references, 19771977

ABSTRACT:
The influence of tetramethylthiouram-disulphide (137268) (TMTDS) on the distribution and excretion of lead (7439921), cadmium (7440439), and mercury (7439976) was investigated in female Wistar-rats. Mercury was given as methyl-mercury (22967926) or inorganic mercury in doses of 1 milligram mercury per kilogram (mg/kg). Cadmium-chloride (10108642) was given in corresponding doses. Lead-nitrate (10099748) was given in doses of 10mg/kg. TMTDS was given as a 0.1 percent addition to the food; treatment was started 2 days before the metal injection. Food intake during the experiments was recorded, and urine and feces were collected daily. Animals were sacrificed after 4 days. Several rats were given carbon-disulfide (75150) (CDS), disulfiram (97778) (DS), or manganese/zinc-ethylenebisdithiocarbamate (Mnn-EBDTC) to compare with TMTDS treatment. TMTDS decreased the excretion of all metals: 30 percent for methyl-mercury, 40 percent for cadmium, and up to 80 percent for inorganic mercury. CDS, DS, and Mn/Zn-EBDTC decreased the excretion of the metals to a lesser extent than with TMTDS. The organ distribution of inorganic mercury was altered by simultaneous exposure to TMTDS. Simultaneous administration of TMTDS with lead caused an increase in blood lead content. TMTDS caused a more than 3 fold increase in the liver and brain concentration of lead. The effect of TMTDS on cadmium distribution was less pronounced than the effects on the other metals tested. CDS, DS, and Mn/Zn-EBDTC changed the organ distribution of all metals tested but to a lesser extent than TMTDS. The authors suggest that exposure to mercury, cadmium, and lead may alter the toxicological evaluation of metal exposure to industrial workers, patients under treatment, and to the general public.

288
TITLE:
Mortality and Cancer Incidence in Chloralkali Workers Exposed to Inorganic Mercury

AUTHORS:
Barregard L
Sallsten G
Jarvholm B

SOURCE:
British Journal of Industrial Medicine, Vol. 47, No. 2, pages 99-104, 28 references, 1990

ABSTRACT:

The mortality and cancer morbidity were examined in Swedish chloralkali workers with long term and previously high exposure to inorganic mercury (7439976). Exposure to asbestos (1332214) was also investigated. The mercury cell process was used for the production of chlorine at eight Swedish chloralkali facilities and the subjects for this study came from these sites. Biological monitoring for mercury exposure began at one facility in 1946 and was adopted at the other sites in about 1960. Steps were taken to reduce exposures during the late 1960s and early 1970s. About 25% of the subjects had an accumulated mercury dose exceeding 1000 micrograms/liter. Of the 1190 subjects, 457 had a possible asbestos exposure as well. The incidence of cancer among this population was twice what would have been expected. No excess for tumors in the brain and kidneys was demonstrable. No dose response relationship could be established for lung cancer and mercury exposure. The increase in lung cancer observed was possibly tied to asbestos exposure. An increased mortality was noted from diseases of the circulatory system allowing at least 10 years latency time. This tendency was seen for ischemic heart diseases and cerebrovascular diseases also, being most evident below the age of 60 years. No dose response relationship was found when cardiovascular mortality was related to the accumulated mercury dose.

289

TITLE:

Renal Mechanisms in the Cardiovascular Effects of Chronic Exposure to Inorganic Mercury in Rats

AUTHORS:

Carmignani M
Boscolo P
Artese L
Del Rosso G
Porcelli G
Felaco M
Volpe AR
Giuliano G

SOURCE:

British Journal of Industrial Medicine, Vol. 49, No. 4, pages 226-232, 34 references, 1992

ABSTRACT:

The mechanisms of renal toxicity which may be involved in the dysfunction of cardiovascular function were examined in male weanling Wistar-rats exposed to mercury (7439976) at dose levels known to cause both arterial hypertension and autoimmune lesions in the kidney. Rats were exposed to 200 micrograms of mercury as mercuric-chloride (7487947) per milliliter of

drinking water for 180 days. At the end of the exposure period the heart rate was not changed but systemic arterial blood pressure was augmented and cardiac inotropism reduced. A mesangial proliferative glomerulonephritis was noted in about 80% of the glomeruli as revealed by light and electron microscopic studies of the kidney. Reduction of the acid-phosphatase activity was noted in tubular cells which was related to functional abnormalities of the lysosomes. The kallikrein activity was slightly reduced in the urine samples of the mercury exposed rats after 24 hours. Proteinuria was not present in all samples. A reduction was observed in plasma renin activity, while angiotensin-I converting enzyme was enhanced. No changes were noted in the plasma aldosterone concentrations. The kidney was the site of most of the mercury accumulation. Mercury content in the heart was higher than that in the brain. The authors conclude that chronic mercury exposure acts on the kidney in a complex fashion which results in modification of systemic hemodynamics.

290

TITLE:

Tissue distribution of (14C)methyl mercury in the lobster, Homarus americanus.

AUTHORS:

GUARINO AM
ANDERSON JB
PRITCHARD JB
RALL DP

SOURCE:

J TOXICOL ENVIRON HEALTH; 2 (1). 1976 13-24

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. (14C)Methyl mercury (a pollutant) was administered by 3 different routes: intrasvascular (i.v.) injection, ingestion and absorption from the ambient water. After i.v. administration (0.1 mg/kg) (14C)methyl mercury was rapidly removed from the plasma, followed by slow loss from the hepatopancreas and a strikingly persistent increase in the amount of radioactivity in the tail muscle. Most (80-90%) of the radioactivity in the hepatopancreas was shown by TLC to be the parent compound, and approximately 10% of this persisted for 6 days after injection. The half-life in this organ was 21 days. One month after i.v. treatment with methyl mercury, the only organs that contained more than 0.1 ppm of this xenobiotic were egg masses, male gonads, heart, brain, intestine and tail muscle. The half-lives for disappearance from sexual organs were greater than 1 mo. After ingestion of (14C)methyl mercury (0.1 mg/kg) in food the hepatopancreas contained most of the administered dose at 6 days (68%), while the stomach (10%), tail muscle (8%) and carcass (15%) contained less. A unique distribution emerged 6 days after exposure

to (14C)methyl mercury-containing ambient water (0.1 ppm). The tail muscle contained most (50%) of the absorbed dose, whereas the hepatopancreas and carcass contained only 23 and 10%, respectively. In view of the small molecular size and high lipid solubility of methyl mercury and the lipophilic properties of the chitin-protein exoskeleton of the lobster, it is likely that significant uptake directly from the water as well as storage of absorbed methyl mercury occurred in the tail region. Residue analysis on untreated lobsters indicated that the egg masses contained the largest amount of methyl mercury (0.1 ppm). The hepatopancreas and carcass (muscle) levels were < 0.05 ppm. (Methyl mercury in human food is of concern.)

291
TITLE:
Distribution of Mercury in the Environment at Almaden, Spain

AUTHORS:
Hildebrand SG
Huckabee JW
Diaz FS
Janzen SA
Solomon JA

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 08, 1981

ABSTRACT:
TD3: An ecological survey of the concentration and distribution of mercury in terrestrial and aquatic systems near the mercury mine at Almaden, Spain, was initiated in 1974. Field studies were completed in 1977, and chemical analyses were completed in 1979. Sample collection at Almaden followed a trophic-level approach in which certain compartments were sampled at a given instant in time (fall 1974, fall 1975, spring 1976, fall 1976, spring 1977). Mean total mercury concentration in terrestrial plants (8 taxa combined) ranged from > 100 mu g/g within 0.5 km of the mine to 1 mu g/g 20 km distant from the mine. Different plant species had different affinities for mercury, but moss species usually had higher total mercury concentration than vascular plants. Woody plants were lower in mercury concentration than forbs. Total mercury concentration in muscle, brain, kidney, and liver tissue from mice was highest at a station near the stream receiving liquid effluent from the mine (mean total mercury at th

292
TITLE:
Effects of chronic intrauterine mercury intoxication on the epileptogenicity of developing rat.

AUTHORS:
Szäasz A
Barna B
Szente M
Kirsch-Volders M

SOURCE:
Epilepsia 1999 Sep;40(Suppl 2):142-3

ABSTRACT:
Rationale: In the present study the effects of chronic, intrauterine organic and inorganic mercury intoxication was investigated on the epileptogenicity of the offspring. Methods: One group of adult Wistar rats was exposed to organic mercury (MeHgCl) and the other group was exposed to inorganic mercury (HgCl2) through the drinking water. Electrophysiological parameters of 3-aminopyridine-induced cortical epileptic activity were measured in mercury-treated 4 weeks old offspring and compared to each other and to those of control animals of the same age. Results: Epileptogenicity was significantly higher in both treated groups, characterized by facilitated expression and propagation of ictal activity and strong tendency to generalization. The numbers and duration of ictal episodes of both mercury-treated animals were higher than in controls. In the HgCl2-treated offspring the amplitude of ictal potentials was higher, while in the MeHgCl-treated group it was lower in comparison to control values. In the HgCl2-treated animals status epilepticus developed more frequently than in the controls, while it did not appear in MeHgCl-treated group. The mercury concentration of the brain, measured at age 4 weeks was significantly higher in both treated animals than in controls. Conclusions: It seems that mercurials impair the cortical inhibition, resulting in enhanced excitability and uncontrolled spread of abnormal activity. The decrease in amplitudes of epileptic discharges in treated animals can be explained by the massive cell death in the developing cortex.

293
TITLE:
(Studies on organic mercury poisoning.)

AUTHORS:
Ishida F JR

SOURCE:
Kumamoto Igakkai Zasshi; 44(7): 638-52 1970; (REF:41)

ABSTRACT:
HAPAB Clinical and experimental studies were carried out to obtain more information on the toxicity of phenylmercury with emphasis on the effects of this type of compound on the nervous system. A patient who had

attempted suicide by ingesting a phenylmercury pesticide was placed under clinical observation. The content of mercury in the patient's hair was estimated using a phenylmercury-containing agricultural pesticide. Further studies on organic mercury poisoning involved administering phenylmercury acetate (PMA) to rats. Ethylmercuric chloride (EMC) served as the control compound. The long-term clinical signs in the dosed animals were observed. The content of mercury in the organs as well as in the stool and urine was determined. Another study involved measuring changes in gamma-aminobutyric acid (GABA) and the activity of glutamic acid decarboxylase (GAD) in the brains of rats that were injected i.p. with methylmercuric chloride (MMC). The patient who had ingested the phenylmercury-containing pesticide displayed no significant neurological manifestations. The farmer's hair contained mercury in an amount higher than that measured in control individuals. No significant neurological signs were noted in PMA-treated rats. The mercury content in the organs of PMA-dosed rats was in the following descending order: fur, kidney, liver, cerebellum and cerebrum. The levels of mercury were markedly higher in the hair of EMC-poisoned rats than they were in the rats given PMA. The amount of mercury excreted by PMA-dosed rats was much higher in the stool than it was in the urine. The data suggest that mercury was accumulated in the body during the early stage of mercury administration. The methylmercury treatment did not significantly affect the content of GABA and the activity of GAD. (Author abstract edited) 1970

294

TITLE:

Medical Implications Of Ingestion Of Mercury

AUTHORS:

Kurland LT
Shibko SI
Kolybye A
Shapiro R

SOURCE:

Environmental Research, Vol. 4, No. 1, pages 9-23, 19711971

ABSTRACT:

The medical implications of methylmercury (22967926) ingestion are reviewed. Outbreaks of methylmercury and other alkylmercury poisonings from ingestion of mercury (7439976) treated grain or contaminated fish are discussed, including clinical features of poisonings. A study of prenatal and postnatal exposure indicates that toxicity can occur during fetal development. Studies of mercury metabolism, distribution, and excretion in humans show that the biologic half life of methylmercury is 70 to 74 days, main activity is in the liver, and excretion is mainly through the feces. Absorption and metabolism of organic mercury compounds in animals are examined. A correlation between dose, body burden, and toxic effects

of methylmercury is indicated. Neurological effects of concentrations of mercury in the brain are discussed. Genetic effects of organic mercury compounds are demonstrated in plants but not in test mammals. The distribution of mercury in blood is discussed. An allowable daily intake of mercury based on a Swedish commission study group of safe concentrations of 0.02 micrograms per gram (microg/g) for whole blood and 6microg/g for hair, is 0.04microg per kilogram. Among the study group recommendations are comprehensive information on fish consumption and correlation of frequency/distribution patterns of fish ingestion with known mercury concentrations to relate to possible neurological responses; to study abortuses and stillborn infants in high risk populations; to elucidate site and mode of cellular action of methylmercury; to perform more animal experiments; to attempt early detection of clinical and subclinical reaction with comprehensive examinations and laboratory procedures; to coordinate epidemiologic studies; and to develop better guidelines of tissue changes and mercury concentrations in accessible tissues.

295

TITLE:

Relationship between catalase activity and uptake of elemental mercury by rat brain.

AUTHORS:

EIDE I

SYVERSEN T LM

SOURCE:

ACTA PHARMACOL TOXICOL; 52 (3). 1983. 217-223.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Uptake of Hg by brain after i.v. injection of elemental Hg was investigated in the rat. Catalase activity was inhibited by aminotriazole either by i.p. injections affecting catalase in most tissues of the animal or by intraventricular (i.c.v.) injections affecting catalase in the brain selectively. Uptake of elemental Hg by rat brain was not influenced by i.p. administration of aminotriazole resulting in 50% inhibition of brain catalase. When the inhibitor was injected i.c.v. in concentrations to give a 50% inhibition of brain catalase, the Hg uptake by the brain was significantly decreased. In the latter case when only brain catalase was inhibited and the supply of elemental Hg to brain was maintained, Hg uptake by brain was porportional to the activity of catalase in brain tissue and to the injected amount of elemental Hg. Contrary to the i.c.v. injection of aminotriazole, in animals receiving aminotriazole i.p. prior to elemental Hg injection, the lower activity of brain catalase may be compensated by an increased supply of elemntal Hg caused by the generally lower oxidation rate in the animal. This view is supported by the finding that Hg uptake by liver increased due to

aminotriazole i.p. although activity of catalse was depressed.

296
TITLE:
Methylmercury Developmental Neurotoxicity: A Comparison of Effects in Humans and Animals

AUTHORS:
Burbacher TM
Rodier PM
Weiss B

SOURCE:
Neurotoxicology and Teratology, Vol. 12, No. 3, pages 191-202, 74 references, 1990

ABSTRACT:
The developmental neurotoxicity of methylmercury (22967926) in humans and animals was reviewed. Qualitative and quantitative comparisons of the neuropathological effects of early methylmercury exposure were discussed. Studies of the brains of human and nonhuman primate infants that had brain methylmercury concentrations of 12 to 20 parts per million (ppm) have revealed similar effects. These consisted of brain atrophy and diffuse sclerotic atrophy of the cerebral cortex, subcortical white matter and basal ganglion, and sparing of the diencephalon. These changes were more severe in nonhuman primates. Similar changes were seen in small mammal brains containing 12 to 20ppm methylmercury. Small mammal brains containing 3 to 11ppm methylmercury were also decreased in size and showed damage to the cortex and cerebellum and loss of myelin. The brains containing methylmercury concentrations below 3ppm were undersized and showed loss of brain cells. There were no data on the neuropathological effects of humans and nonhuman primates having brain methylmercury concentrations below 12ppm. Prenatal exposure to methylmercury that caused brain concentrations of 12 to 20ppm has been shown to cause blindness, deafness, cerebral palsy, mental deficiency, and seizures in all species. Brain methylmercury concentrations of 3 to 11ppm are associated with mental deficiency, abnormal reflexes and muscle tone, and retarded motor development in humans, retarded development of object permanence, visual recognition, memory, and social behavior, and visual disturbances in nonhuman primates, and abnormal behavior in water maze, auditory startle, and escape and avoidance tests in small mammals. Methylmercury brain doses below 3ppm have resulted in delayed psychomotor development in humans and induced abnormal behavior in active/avoidance and operant tests in small mammals. The Environmental Protection Agency (EPA) neurotoxicity test battery and its ability to assess potential risks from methylmercury exposure in humans were discussed. Because the battery uses rats as the test species, its usefulness for predicting human risk was stated as questionable. The pharmacokinetics and effects on the

kidney and peripheral nervous system of methylmercury in rats are different from humans. The authors conclude that neuropathological effects induced by high levels of methylmercury exposure are similar in humans and animals, that data for the neuropathological effects induced by low exposures exist only for small animals, and that EPA neurotoxicity test battery is not useful for assessing human risks to methylmercury.

297
TITLE:
Mercuric chloride-induced reactive oxygen species and its effect on antioxidant enzymes in different regions of rat brain.

AUTHORS:
HUSSAIN S
RODGERS DA
DUHART HM
ALI SF

SOURCE:
JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES; 32 (3). 1997. 395-409.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The present study was undertaken to determine if in vitro exposure to mercuric chloride produces reactive oxygen species (ROS) in the synaptosomes prepared from various regions of rat brain. The effects of in vivo exposure to mercury on antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in different regions of rat brain were also investigated. Adult male Sprague-Dawley (CD) rats were dosed with 0, 1, 2.0 or 4.0 mg HgCl2/kg body weight, for 7 days. One week after the last dose, animals were sacrificed by decapitation, their brains were removed and dissected and frozen in dry ice prior to measuring the activities of these enzymes. The results demonstrated that in vitro exposure to mercury produced a concentration-dependent increase of ROS in different regions of the rat brain. In vivo exposure to mercury produced a significant decrease of total SOD, Cu,Zn-SOD and Mn-SOD activities in the cerebellum of rats treated with diffe

298
TITLE:
The distribution of inhaled mercury (Hg-203) vapors in the brain of rats and mice.

AUTHORS:
Cassano GB
Viola PL
Ghetti B

Amaducci L

SOURCE:
J. Neuropathol. Exptl. Neurol.; 28(2), 308-20, 1969; (REF:20)

ABSTRACT:
HAPAB The distribution of inhaled mercury (Hg-203) was studied by means of microautoradiography and chemical analysis. Mice and rats were exposed to radioactive mercury vapors 6 hr daily for 10 days. Whole - body autoradiography showed that the highest concentrations of radioactivity were in the kidney, brain and myocardium. The brain stem nuclei, the spinal cord, the cerebellar nuclei and the cerebellar cortex exhibited larger amounts of radioactivity than did the cerebral cortex, the basal ganglia and the septum. The walls of the brain ventricles, the choroid plexuses and some areas in close contact with the cerebrospinal fluid showed a high degree of radioactivity. The microautoradiograms showed a similar distribution pattern of Hg-203. The concentrations of radioactivity were found to be greater in the gray than in the white matter. In the cerebellum, silver grains were selectively localized in the Purkinje cells and in the neurons of the nucleus dentatus. Analysis of the different chemical fractions of the brian showed that radioactivity can be detected in the water - washing fraction and in the insoluble tissue residue and tht an equilibrium may exist between the radioactivity of these two fractions. Hg-203 was found in free and bound fractions equally distributed in the brain. Later radioactivity decreased in both fractions after a slight initial increas had occurred in the bound fractions. (AUTHOR ABSTRACT MODIFIED). TOXICOLOGY AND PHARMACOLOGY 70/05/00, 199 1969

299
TITLE:
ENVIRONMENTALLY INDUCED ALTERATIONS IN NEURON AND GLIA DEVELOPEMNT

AUTHORS:
HARRY GJ

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Summary of Work: During the development of the nervous system, the temporal and spatial regulation of gene expression is a critical component of neural and glial growth, development, and interactions. These critically timed events are assummed to be a major component in the differential susceptibility of the developing organism to environmental insult. This project examines the effects of various environmental agents, (e.g. lead acetate, triethyltin, trimethyltin, methyl mercury and mercury vapors, ischemia, electromagnetic fields, AIDs therapeutics, and

dietary manipulation), on the development of the nervous system as indicated by alterations in the spatio-temporal expression of mRNA for various developmentally regulated proteins associated with distinct processes of development (e.g., neuronal migration, neurite extension, synapse formation, and myelination). We have shown that lead acetate alters developmentally regulated structural proteins. Ongoing studies are examining the mRNA for neurotrophins and proteins associated with axonal elongation and synapse formation to further understand the subtle lead induced alteration in the formation of the neural network. Using RNase protection assays we have demonstrated a ontological profile for pro-inflammatory cytokines and neurotrophins in various brain regions. This technique is being expanded with the establishment of new probe sets to detect mRNA levels for proteins associated with the various cell types and stages of brain development. In vitro experiments have shown glial cell cultures to demonstrate a maturation pattern of susceptibility to ischemic injury similar to that seen in vivo with an ischemia-induced up-regulation of mRNA for neurotrophins in young cells that is gradually lost during maturation. Future Research: We will continue to generate developmental profiles for the neurotrophins and pro-inflammatory cytokines in chemical-target brain regions in both the normal brain to establish the normal profile and in brain regions following exposure to known developmental neurotoxicants to assess the feasibility of using this approach to determine developmental neurotoxic potential of a chemical and to further understand the nature of the interdependency of these critically timed events in the formation of the neural network.

300

TITLE:

The developmental profile of PKC isoforms in the rat brain is altered by gestational exposure to methyl mercury.

AUTHORS:

Haykal-Coates N
Goldey ES
Herr DW
Tilson HA
Barone S Jr

SOURCE:

Abstr Soc Neurosci 1993;19(Pt 2):1733

ABSTRACT:

Protein kinase C (PKC) mediated phosphorylation has been implicated in neuronal growth and differentiation (Turner et al., Proc. Natl. Acad. Sci. USA, 1984). Using immunohistochemistry, we examined the effects of gestational exposure to the neurotoxicant, methyl mercury (CH3Hg) on the developmental profile of immunoreactivity (IR) for the calcium-dependent, alpha and beta, and calcium-dependent, epsilon, PKC isoforms. Long-Evans

dams were dosed on gestational days 6-15 (po) with 0, 0.1, 1, or 2 mg/kg CH3Hg dissolved in saline. Pups were sacrificed and perfused with buffered paraformaldehyde on postnatal days (PND) 1, 4, 10, 21, 41, and 85. The brains were sectioned sagittally, stained immunohistochemically, and examined throughout the medial to lateral extent of the brain. The greatest density of immunoreactivity of neural cell bodies was seen in the olfactory bulb, hippocampus, inferior colliculus, pons, cerebral, pyriform, and cerebellar cortex, whereas axonal staining was prominent in the brainstem, internal capsule, corpus callosum, anterior commissure, fornix and olfactory tract. In controls, the IR for each isoform was highest at the earliest time-points examined (PND1-4), decreasing dramatically by PND10, and decreasing further after PND21. In all regions examined in the neonate, the locations of IR for isoforms alpha and epsilon were similar. In contrast to the neonatal alpha and epsilon, there was a different pattern for beta IR in the thalamus, neocortex and olfactory bulbs. The highest dose of CH3Hg produced a persistent increase in regional alpha IR, a decrease in epsilon IR at early time points (PND1-4), and no apparent change on beta IR. These changes in PKC IR were not related to overt pathology at any of the time points examined. The present results characterize the cellular and regional ontogeny of 3 PKC isoenzymes, and suggests that developmental exposure to CH3Hg can alter that ontogeny.

301
TITLE:
Effect of methyl mercury exposure on the uptake of radiolabeled inorganic mercury in the brain of rabbits.

AUTHORS:
DOCK L
MOTTET K
VAHTER M

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 74 (3). 1994. 158-161.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Abstract: Exposure to mercuric compounds at high dose levels has previously been shown to alter the integrity and function of the blood-brain barrier in laboratory animals. In the present study, we have investigated the distribution of intravenously administered inorganic 203Hg in rabbits additionally exposed to MeHg. A single dose of 203HgCl, was administered together with or 5 min. or 24 hr after administration of a single dose (10 or 37.5 mumol/kg b.wt.) of MeHg. In another experiment, 203HgCl was administered to rabbits subchronically exposed to MeHg (1 mumol/kg b.wt. daily for three weeks) 24 hr after cessation of treatment. The integrity of the blood-brain barrier was assayed by measuring the uptake of 203Hg in the brain, as the blood-brain

barrier usually serves to exclude inorganic Hg from the brain. The concentration of 203Hg within the brain was similar in all MeHg-treated rabbits, corresponding to 0.02% of the administered dose, and not different from that of

302
TITLE:
Experimental approaches to developmental toxicity of methylmercury.

AUTHORS:
Inouye M

SOURCE:
Advances in Mercury Toxicology (Rochester Series on Environmental Toxicity) 1991;:339-54

ABSTRACT:
Dozens of babies congenitally affected by methylmercury were born in Minamata, Japan and Iraq. For the most severe cases, where death occurred either in infancy or in childhood, pathological examinations were performed. In cases from Iraq the changes in the brains were the outcome of disturbances of development, more specifically, abnormal neuronal migration and derangement in the fundamental structuring of gray matter. The focal nerve cell destruction typically seen in adult cases of methylmercury poisoning was not encountered (Choi et al., 1978). In cases from Minamata, on the other hand, brain changes were the result of degeneration and decrease in the number of nerve cells. These findings were similar in type to those found in adult patients, and in addition were accompanied by developmental changes (Matsumoto et al., 1965). Our experiment using guinea pigs demonstrated that developmental disturbances of the brain as a result of impaired neurogenesis and abnormal neuronal migration were induced when dams were exposed to methylmercury in early pregnancy. When dams were exposed in later pregnancy, neurons of the cerebral cortex were involved in widespread focal degeneration. These findings confirmed and extended the observations of the human cases. Iraqi cases were affected acutely in the earlier stage of pregnancy, so the fetal brain might be involved in developmental disturbances. The Minamata cases were exposed to methylmercury chronically throughout the pregnancy, and thus both the developmental disturbances and the focal degeneration of neurons might be induced in the same fetal brain. Accelerated placental transfer and fetal accumulation of methylmercury at the late pregnant stage, as demonstrated in animal experiments, might cause the degenerative changes of neurons resembling the adult forms. In addition, hydrocephalus has been detected with a low incidence in congenital Minamata disease sufferers. Experimental studies using inbred mice revealed strain difference in susceptibility to postnatal development of hydrocephalus following prenatal methylmercury exposure. B10.D2 is highly susceptible, C57BL/10 and C57BL/6 are moderately susceptible, and DBA/2, C3H/He and

BALB/c are resistant. This indicates that the susceptibility to methylmercury-induced hydrocephalus is under genetic control.

303
TITLE:
Methylmercury Transport across the Blood-Brain Barrier by an Amino Acid Carrier

AUTHORS:
Kerper LE
Ballatori N
Clarkson TW

SOURCE:
American Journal of Physiology, Vol. 262, No. 5, pages R761-R765, 38 references, 1992

ABSTRACT:
The mechanism of methylmercury (22967926) transport across the blood brain barrier (BBB) was studied in rats. Anesthetized female Long-Evans-rats were injected intraarterially with 0 to 2000 micromolar (microM) mercury-203 (Hg-203) tagged methylmercuric-chloride (115093) complexed with 5, 10, or 20microM L-cysteine (MMys) or D-cysteine (MM/DCys). In some experiments, bovine-serum-albumin (BSA) was used as a complexation agent. Fifteen seconds after dosing the rats were killed and the brains were removed and assayed for the Hg-203 to determine brain uptake of methylmercury. The MM/LCys complex, taken up by the brain much faster than the MM/DCys complex, could be described by a Michaelis constant and maximum velocity of 0.39 millimolar and 33 nanomoles per minute per gram, respectively. Complexation with BSA completely inhibited uptake of methylmercury. Injection with 100microM of tagged MM/LCys and 0 to 1000microM D-methionine or L-methionine indicated that both D-methionine and L-methionine inhibited uptake of Hg-203 activity in a dose dependent manner. In rats injected with 100microM Hg-203 labeled MM/LCys in the presence or absence of 1, 5, or 10 millimolar (mM) of the amino acid analogue 2-aminobicyclo(2.2.1)heptane-2-carboxylic-acid (BCH) or alpha-methylaminoisobutyric-acid, only BCH significantly inhibited uptake of Hg-203 activity. When rats were injected with 0 or 0.002mM Hg-203 labeled methylmercury complexed with glutathione (MM/G) or MM/LCys in the presence or absence of S-ethylglutathione (SEG), significant amounts of MM/G derived Hg-203 activity were taken up by the brain. SEG significantly inhibited uptake of MM/G but not MM/LCys. The authors conclude that methylmercury may cross the BBB as MM/LCys. Plasma MM/G may serve as a source of MM/LCys./METHODS

304
TITLE:
The Effects of Mercuric Chloride on Calmodulin-Mediated Ca+2 Transport in

Rat Brain

AUTHORS:
Clifton GG
Oelsner D
Anderson CR
Pearce CJ
Wallin JD

SOURCE:
American Journal of the Medical Sciences, Vol. 299, No. 1, pages 26-31, 14 references, 1990

ABSTRACT:
Mitochondria were prepared from brains of male Sprague-Dawley-rats and the effect of mercuric-chloride (7487947) on calcium uptake by the isolated rat brain mitochondria was examined. The degree of calcium uptake was shown for control tissues and for tissues exposed to either 0.1 millimolar or 1.0 millimolar mercuric-chloride. The results demonstrated that similar concentrations of mercuric-chloride inhibit both calcium uptake by isolated rat brain mitochondria and calmodulin stimulated calcium/magnesium-ATPase (Cag-ATPase) enzyme activity of the same preparation. Mercuric-chloride inhibition of another calmodulin mediated enzyme system was demonstrated using cAMP phosphodiesterase activity in rat brain. Inhibition of Ca/Mg-ATPase enzyme activity was reversible and preexposure of calmodulin to mercuric-chloride did not impair the ability of calmodulin to stimulate phosphodiesterase activity. The authors conclude that mercuric-chloride reversibly impeded calmodulin mediated pumping mechanisms important in maintaining calcium homeostasis in neural systems. These results provide a plausible, biochemical explanation for the previously noted mercuric-chloride inhibition of arginine vasopressin release and may have extended relevance in other models in which calcium homeostasis and calmodulin function are important.

305
TITLE:
Deferoxamine inhibits methyl mercury-induced increases in reactive oxygen species formation in rat brain.

AUTHORS:
LEBEL CP
ALI SF
BONDY SC

SOURCE:
TOXICOL APPL PHARMACOL; 112 (1). 1992. 161-165.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. It has been suggested that methyl mercury may express its neurotoxicity by way of iron-mediated oxidative damage. Therefore, the effect of deferoxamine, a potent iron-chelator, on methyl mercury-induced increases in reactive oxygen species formation was studied in rat brain. The generation rate of reactive oxygen species was estimated in crude synaptosomal fractions using the probes 2',7'-dichlorofluorescin diacetate and dihydrorhodamine 123. The formation rate of the fluorescent oxidation products was used as the measure of reactive oxygen species generation. Seven days after a single injection of methyl mercury (5 mg/kg, ip), the formaton rate of reactive oxygen species was significantly increased in the cerebellum. Pretreatment with deferoxamine (500 mg/kg, ip) completely prevented the methyl mercury-induced increase in cerebellar reactive oxygen species generation rates. The oxidative consequences of in vitro exposure to methyl mercury (20 muM) were also inhibited by

306

TITLE:

Interaction Of Alkylmercuric Compounds With Sodium Selenite. III. Biotransformation, Levels Of Metallothioneinlike Proteins And Endogenous Copper In Some Tissues Of Rats

AUTHORS:

Brzeznicka EA
Chmielnicka J

SOURCE:

Environmental Health Perspectives, Vol. 60, pages 423-431, 85 references, 19851985

ABSTRACT:

The effects of selenium (7782492) on inorganic mercury (7439976) release from alkylmercuric compounds were examined in rats. Wistar-rats were given doses of methylmercuric-chloride (115093) (Meg) and ethylmercuric-chloride (107277) (Et/Hg) intragastrically 7 times in a 2 week period. Selenium was administered in aqueous solution every day for 14 days. At 24 hours after administration of the last dose of selenium the rats were sacrificed. The content of inorganic and organic mercury was estimated by cold atomic spectroscopy. Ceruloplasmin activity in blood serum was determined by colorimetry. Administration of selenite (14124675) simultaneously with the high dose of methylmercury (22967926) resulted in a decrease of the total mercury content of the liver accompanied by an increase in biotransformation to inorganic mercury. Selenium caused a uniform decrease in the concentrations of both forms of mercury in the kidneys, irrespective of the dose of Me/Hg. The total mercury concentration in the brain was augmented by selenium, but the efficiency of biotransformation remained unchanged. No significant effect of selenium on the efficiency of biotransformation of Et/Hg was found in the kidneys, liver, or brain. Sodium-selenite administered with Me/Hg and

Et/Hg decreased the concentration of ceruloplasmin in the kidneys. Administration of sodium-selenite alone also decreased the ceruloplasmin concentration. The authors conclude that selenium does not accelerate the dialkylation of alkylmercurials.

307
TITLE:
Effects of cadmium and mercury on ovarian maturation in the red swamp crayfish, Procambarus clarkii.

AUTHORS:
REDDY PS
TUBERTY SR
FINGERMAN M

SOURCE:
ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY; 37 (1). 1997. 62-65.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In vivo mercury significantly inhibited ovarian maturation in the red swamp crayfish, Procambarus clarkii. 5-Hydroxytryptamine (5-HT) induced ovarian maturation in vivo. Cadmium and mercury inhibited this 5-HT-induced maturation. Ovarian explants incubated with mercury and either brain or muscle demonstrated significant inhibition of (14C)leucine incorporation into ovarian proteins compared to the corresponding groups incubated without mercury. In the absence of mercury the brain, which contains a gonad-stimulating hormone (GSH), induced significantly more incorporation of this amino acid than occurred in the ovaries incubated with muscle. These metals may have exerted their inhibitory effects by directly inhibiting protein synthesis in the ovaries, inhibiting 5-HT-stimulated GSH release, and preventing the ovaries from responding to this hormone.

308
TITLE:
Comparison of the developmental effects of two mercury compounds on glial cells and neurons in aggregate cultures of rat telencephalon.

AUTHORS:
MONNET-TSCHUDI F
ZURICH M-G
HONEGGER P

SOURCE:
BRAIN RESEARCH; 741 (1-2). 1996. 52-59.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A three-dimensional cell culture system was

used as a model to study the influence of low levels of mercury in the developing brain. Aggregating cell cultures of fetal rat telencephalon were treated for 10 days either during an early developmental period (i.e., between days 5 and 15 in vitro) or during a phase of advanced maturation (i.e., between days 25 and 35) with mercury. An inorganic (HgCl2) and an organic mercury compound (monomethylmercury chloride, MeHgCl) were examined. By monitoring changes in cell type-specific enzymes activities, the concentration-dependent toxicity of the compounds was determined. In immature cultures, a general cytotoxicity was observed at 10-6 M for both mercury compounds. In these cultures, HgCl2 appeared somewhat more toxic than MeHgCl. However, no appreciable demethylation of MeHgCl could be detected, indicating similar toxic potencies for both mercury compounds. In highly differentiated cultures, by contrast, MeHgCl exhibited a highe

309

TITLE:

Effects of Methyl Mercury in Postnatal Developing Rats

AUTHORS:

Sakamoto M
Nakano A
Kajiwara Y
Naruse I
Fujisaki T

SOURCE:

Environmental Research, Vol. 61, No. 1, pages 43-50, 17 references, 1993

ABSTRACT:

The effects of methyl-mercury-chloride (115093) (MMC) on different growth phases were studied in postnatal Wistar-rats. Rats at postnatal days (PD) one, 14, and 35 were divided into six subgroups and treated with 0, 2.60, 3.64, 5.10, 7.14, or 10mg/kg MMC for 10 consecutive days. Determinations were made regarding weight changes and hindlimb crossing effects. Surviving rats were used in rotarod tests. Mercury (7439976) contents of the brains, livers, and kidneys were determined in rats treated with 10mg/kg MMC. Results showed that the mean mercury concentration in the brain was highest in the PD14 rats than in the PD35 and PD1 rats. Concentrations in the liver and kidney were lowest in the PD one rats, rising with postnatal development. Body weight gain declined in a dose dependent fashion in the PD35 rats. In the PD1 rats, the gain was lowered dose dependently but none exhibited weight loss. All PD1 rats receiving 10mg/kg/day MMC died by the eleventh day without signs of hindlimb crossing. In PD14 rats receiving the same dose, weight loss began on day ten and hindlimb crossing was evident on day 11. In PD35 rats, weight loss began on day five and hindlimb crossing appeared from day 12. Rotarod performance was deficient only at 7.14mg/kg/day in the PD35 rats;

it was inhibited dose dependently in PD14 rats. The authors conclude that mercury distribution and MMC effects on weight gain and motor skills differ with respect to postnatal development stage of the rat.

310
TITLE:
In Vitro Evidence for the Role of Glutamate in the CNS Toxicity of Mercury

AUTHORS:
Brookes N

SOURCE:
Toxicology, Vol. 76, No. 3, pages 245-256, 41 references, 1992

ABSTRACT:
The role of glutamate in the central nervous system toxicity of mercury (7439921) was examined. Spinal cord cell cultures prepared from 12 to 13.5 day old CD-1-mouse embryos and astrocyte cell cultures prepared from the cerebral hemispheres of 1 day old CD-1-mice were equilibrated with solutions containing 0 or 100 micromolar (microM) glutamate. The spinal cord cell cultures were then incubated with 0 or 1microM divalent-mercury (Hg+2) from mercuric-chloride (7487947) and the astrocyte cultures were incubated with 0 to 1.00microM Hg+2 for up to 180 minutes. The effects of Hg+2 on clearance of exogenous glutamate from the solutions were determined. The effects on the glutamine and taurine concentrations in the astrocyte cultures were also determined. Spinal cord cell cultures were incubated with 0, 0.1, or 0.2 millimolar glutamate in the presence or absence of 0.1 or 1microM Hg+2. Hg+2 neurotoxicity and glutamate excitotoxicity were assessed by measuring uptake of tritiated 2-deoxy-D-glucose. Hg+2 significantly inhibited clearance of exogenous glutamate from both the spinal cord and astrocyte cell cultures. The inhibitory effect in the astrocyte cultures was dose and time dependent. Glutamine concentrations increased with time in the astrocyte cultures. The rate of increase was inhibited by 0.05microM Hg+2. Taurine decreased in a time related matter in the astrocyte cultures. The rate of decrease was inhibited by 0.05microM Hg+2. Hg+2 showed only slight neurotoxicity in the spinal cord cell cultures in the absence of glutamate. Hg+2 did not alter the excitotoxic response of the cultures to glutamate. The author concludes that the data support the hypothesis that low concentrations of Hg+2 in the brain, following mercury vapor or methylmercury uptake, cause neurotoxicity by selectively inhibiting uptake of synaptically released glutamate. This leads to an increase in glutamate in the extracellular spaces.

311
TITLE:
Placental and lactational transfer of mercury from rats exposed to methylmercury in their diet: Speciation of mercury in the offspring.

AUTHORS:
SUNDBERG J
OSKARSSON A

SOURCE:
J TRACE ELEM EXP MED; 5 (1). 1992. 47-56.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The objective of the present investigation was to compare the placental and lactational transfer of mercury after long-term exposure to methylmercury (MeHg) in the diet of rats. Dams were given a diet containing 3.9 mug Hg/g as MeHg during 11 weeks prior to mating, during gestation and lactation. Neonates from MeHg-treated dams either stayed with their mothers until day 15 of lactation or were cross-fostered at birth to dams treated with a control diet. Neonates from dams receiving the control diet were in the same way cross-fostered at birth to dams treated with the MeHg diet. The offspring exposed to mercury only via the placenta had approximately twice as high whole blood concentrations and fourtimes as high brain concentrations of total mercury at 15 days of age compared with offspring exposed only via milk. The total mercury concentration in the blood and brain of offspring exposed prenatally and postnatally corresponded approximately to the additive effect of plac

312
TITLE:
Trace Element Imbalances in Amyotrophic Lateral Sclerosis

AUTHORS:
Khare SS
Ehmann WD
Kasarskis EJ
Markesbery WR

SOURCE:
Neurotoxicology, Vol. 11, No. 3, pages 521-532, 47 references, 1990

ABSTRACT:
Instrumental neutron activation analysis of the brain, spinal cord, blood cells, serum and nails of Amyotrophic Lateral Sclerosis (ALS) patients was performed to determine the concentration of 15 elements in these samples. Imbalances have been detected in a number of trace and minor abundance elements in ALS tissues. It was noted that some of the changes were probably secondary to the loss of motor neurons in the spinal cord and the associated gross volumetric/gravimetric changes in these tissues. More widespread changes were noted in the concentrations of mercury (7439976) and selenium (7782492) in ALS tissues. The authors caution that the

variation in the mercury concentration need not necessarily indicate active toxicity. It could merely represent an enlarged pool of detoxified mercury or perhaps a labeling of a specific cellular ligand by mercury in ALS. These results should be studied, given the ameliorative effects of selenium on the recognized toxicity of mercury.

313
TITLE:
Comparative study of uptake and tissue distribution of methyl mercury in female rats by inhalation and oral routes of administration.

AUTHORS:
Fang SC

SOURCE:
Bull. Environ. Contam. Toxicol. 24(1): 65-72 1980 (4 References)

ABSTRACT:
PESTAB. The uptake and distribution of methyl mercury by inhalation and oral routes of administration were compared. Female wistar rats were exposed to 203Hg methylmercuric chloride (203Hg-MMC) vapor for 6, 12, 18 and 24 hr to determine uptake as a function of exposure time. In a second experiment, rats were exposed for 24 hr to 50, 100 or 140 nmol 203Hg-MMC l. In a third experiment, rats were given oral doses of either 3 or 9 mumol 203Hg-MMC and sacrificed after 1, 2, 3 or 4 days. Body tissues were analyzed for radioactivity. Mercury concentrations in most organs increased linearly with time of exposure. Blood accumulated mercury the fastest. The relative 203Hg content in each organ or tissue remained fairly constant among the 3 inhaled concentrations. Rats given oral doses showed increased mercury levels on day 1, then a slow decline. The brain was the only exception; levels increased throughout the time of the study. Data suggest that when inhaled, mercury is retained in the blood at a greater rate than when ingested. Analysis of subcellular fractions of liver, kidney, and brain demonstrated no difference in the distribution of 203Hg whether the route of administration was oral or by inhalation.

314
TITLE:
Accumulation of mercury in brainstem nuclei of mice after retrograde axonal transport.

AUTHORS:
ARVIDSON B

SOURCE:
ACTA NEUROL SCAND; 82 (4). 1990. 234-237.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Adult mice injected intramuscularly in the region of the vibrissae muscles on the left side of the nose with a small volume of the mercuric chloride dissolved in distilled water. The animals were killed after 1-6 weeks and fixed by whole-body perfusion. Frozen sections were taken from different levels of the brain stem and from the kidney. The sections were subjected to silver acetate autometallography for visualization of mercury. Mercury was found to accumulate in neurones of the facial nerve nuclei, of the motor trigeminal nuclei and of the trigeminal mesencephalic nuclei of the brain stem, after retrograde axonal transport. Mercury was also demonstrated in proximal tubular cells of the kidney. The mechanism for uptake of mercury at the neuromuscular junctions, and the fate of mercury within neurones are analysed. The possible significance of retrograde metal transport for the development of motor neurone disease is discussed.

315
TITLE:
Localization of mercury in CNS of the rat: IV. The effect of selenium on orally administered organic and inorganic mercury.

AUTHORS:
MOLLER-MADSEN B
DANSCHER G

SOURCE:
TOXICOL APPL PHARMACOL; 108 (3). 1991. 457-473.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The distribution and exact cellular localization of mercury in the brain and upper cervical spinal cord of the adult male Wistar rat has been determined using the autometallographic silver-enhancement technique. A detailed atlas of mercury-containing nuclei following oral administration of HgCl2 (20 mgprepared. The effect of orally administered Na2SeO3 (2 mger-1) on these patterns was investigated. In animals treated with CH3HgCl, sodium selenite induced a conspicuous increase in mercury staining of nerve cell bodies in specific areas of the central nervous system (CNS) including laminae III-VI in the cerebral cortex, thalamus, hypothalamus, and brain stem nuclei. In the cerebellum, the cortical Purkinje cells and nerve cells in the deep nuclei were targets for appreciable mercury accumulations after CH3HgCl. Again, these deposits were increased by coadministration of selenite. In the spinal cord following administration of CH3HgCl alone, stanining was limited to the gr

316
TITLE:
The Effect Of Prenatal Methylmercury Administration On Postnatal Renal Functional Development

AUTHORS:
Smith JH
McCormack KM
Braselton WE Jr
Hook JB

SOURCE:
Environmental Research, Vol. 30, No. 1, pages 63-71, 17 references, 19831983

ABSTRACT:
The effects of prenatal treatment and methyl-mercury (22967926) on postnatal renal functional alterations were examined in Sprague-Dawley-rats. Pregnant rats received intraperitoneal injections of methyl-mercury containing 4 or 6 milligrams per kilogram (mg/kg) mercury (7439976) (Hg) on day 8 or 4mg/kg Hg on days 8, 10, and 12 of gestation. Samples of liver, kidney, and brain were taken from litters on days 1, 7, or 42 post partum and analyzed for Hg concentration. Renal cortical slices were prepared. Organic ion exchange accumulation and glucose synthesis were determined. Renal function was assessed after administration of an antidiuretic hormone. Urinary protein was measured. No effects were seen for prenatal exposure to methyl-mercury. Concentrations of Hg in kidneys, liver, and brain at days 1 and 7 post partum were dose related. No Hg was found in tissues of rats at day 42. Prenatal exposure to methyl-mercury had no effect on postnatal renal function assessed by organic ion exchange accumulation or glucose synthesis. Accumulation of polyaromatic hydrocarbons was significantly different from controls on day 42. Measurement of renal function showed slightly less protein excretion in urine of Hg exposed rats than in controls. There was a decreased ability to eliminate sodium (17341252) ion and water in volume loaded rats. No other effects were found. The authors conclude that postnatal renal effects of prenatal Hg exposure indicate few renal alterations.

317
TITLE:
In Vivo Incorporation Of 14C-Leucine Into Brain Protein Of Methylmercury Treated Rats

AUTHORS:
Farris FF
Smith JC

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 13, No. 4, pages 451-455, 7 references, 19751975

ABSTRACT:

The effects of methylmercury (22967926) on in-vivo protein synthesis were investigated. The incorporation of radiolabeled leucine (61905) into brain protein of Sprague-Dawley-rats was studied. Five female rats were given subcutaneous (sc) injections of 1.0 milligram (mg) methylmercury-chloride (115093) after day 15 of gestation to the end of pregnancy. Controls were injected with saline. Forty eight hours after birth, brains from two offspring from each female were used for study. Other offspring were intraperitoneally injected with 2 microCuries carbon labeled leucine before the brain was taken 30 minutes later. In a second experiment, eight rats were given a daily sc injection of 5.0mg methylmercury-chloride and 10mg cysteine (52904) in water. Six controls were given water containing only cysteine. On day 7, rats were anesthetized and injected with leucine. After 90 minutes, rats were killed and brains were removed. Brains were sectioned into hemispheres, midbrain, occipital, and cerebellum. One hemisphere was used to measure brain methylmercury and leucine. The remaining hemisphere and other sections were homogenized and protein was isolated and counted. There were no significant differences in protein synthesis between the offspring of saline and treated females. Brain mercury concentrations were low, between 4.5 to 9.7 parts per million. In the second experiment, adult rats showed signs of severe intoxication including reddening or bleeding around the eyes and nose, weight loss, sluggishness, and hunched posture and loss of hind leg function. Three animals died. The concentration of leucine in whole brain tissue was higher in intoxicated rats than in controls. Leucine incorporation was inhibited in at least three brain regions of treated rats. Protein synthesis was about 75 percent that of controls. The authors conclude that brain protein synthesis is significantly depressed in methylmercury intoxicated rats.

318

TITLE:

Modulation of Monoamine Oxidase Activity in Different Brain Regions and Platelets following Exposure of Rats to Methylmercury

AUTHORS:

Chakrabarti SK
Loua KM
Bai C
Durham H
Panisset J-C

SOURCE:

Neurotoxicology and Teratology, Vol. 20, No. 2, pages 161-168, 63 references, 1998

ABSTRACT:

The effects of methylmercury on brain and platelet monoamine-oxidase (MAO)

were studied in-vitro and in-vivo. Adult male Wistar-rats were gavaged with 5mg/kg methylmercuric-chloride (115093) (MMC) daily for 7 days or 7.5mg/kg MMC daily for 10 days. Rats were killed 24 hours after the last dose. The brains were dissected into the cortex, striatum, hypothalamus, hippocampus, and cerebellum. Synaptosomes were prepared from each brain tissue. The platelets were harvested from the blood samples. The brain tissue synaptosomes and platelets were analyzed for MAO. Brain synaptosomes prepared from the cortex, striatum, hypothalamus, hippocampus, brainstem, and cerebellum of untreated Wistar-rats and platelets harvested from these rats were incubated with 0, 0.5, 1, 2.5, 5, or 10 micromolar (microM) MMC for 30 minutes. The synaptosomes and platelets were assayed for MAO. In-vitro, MMC inhibited MAO activity in the synaptosomes from all brain regions in a concentration dependent manner. The threshold concentration for the effect was around 1microM in each tissue except in the striatum where it was 2.5microM. The median inhibitory concentration was approximately 2.5microM in all tissues. No MAO activity could be detected in the platelets. In-vivo, MMC inhibited MAO activity in synaptosomes from the different brain regions in proportion to the total cumulative dose, 35mg/kg (5mg/kg for 7 days) or 75mg/k (7.5mg/kg for 10 days). Synaptosomes from the hippocampus were the most sensitive followed by those from the hypothalamus, cortex, striatum, cerebellum, and brainstem. Platelet MAO activity was decreased 16.7% by the cumulative 35mg/kg dose and 50% by the cumulative 75mg/kg dose. The authors conclude that methylmercury can inhibit MAO activity in different brain synaptosome preparations to different degrees, but without showing any specificity toward any brain region. Decreases in platelet MAO activity may be a potential biomarker of early methylmercury neurotoxicity in rats.

319

TITLE:

Cations in Malignant and Benign Brain Tumors

AUTHORS:

Hayat L

SOURCE:

Journal of Environmental Science and Health. Part A: Environmental Science and Engineering and Toxic and Hazardous Substance Control, Vol. 31, No. 8, pages 1831-1840, 24 references, 1996

ABSTRACT:

A study was conducted to determine if a correlation exists between environmental exposure to heavy metals such as nickel (7440020) (Ni), vanadium (7440622) (Vn), cadmium (7440439) (Cd), cobalt (7440484) (Co), calcium (7440702) (Ca), lead (7439921), mercury (7439976), tin (7440315), zinc (7440666) and selenium (7782492) (Se) due to oil fires in Kuwait during the Gulf War, and the incidence of benign and malignant brain

tumors. Twenty brain tumor tissue samples were obtained from patients in Kuwait, and prepared for analysis by atomic absorption spectrophotometry. Normal brain tissue served as controls. Higher levels of Ni, Vn, Cd, Co, Ca, and Se cations were found in brain tumor tissue compared to levels in normal brain tissues. Significant increases in concentrations of Ca, Se, Co, and Ni in malignant and benign brain tumors were seen, as well as an incremental increase in Vn levels. The author concludes that the greater concentrations of these metals in brain tissue may be associated with the increased incidence of brain tumors due to the aftermath of the Gulf War.

320
TITLE:
The mercury content among deer and of browsed foliage as a means of ascertaining environmental pollution of the mining regions of Idrija - a case study from Slovenia.

AUTHORS:
GNAMUS A
HORVAT M
STEGNAR P

SOURCE:
ZEITSCHRIFT FUER JAGDWISSENSCHAFT; 41 (3). 1995. 198-208.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Tissue samples from deer and from plants in the area around the world's second largest mercury mine in Idrija, Slowenia as well as soil samples were analyzed for their total contents of mercury and methyl-mercury during the time period 1990 to 1994 (see Figs. 2, 3 and 4, Tab, 4-6). The total mercury contents of the tissues of deer inhabiting the vicinity of the mine were nearly 100 higher than that of controls. The proportions of methyl-mercury as part of total mercury are given in percent. The highest Me-Hg contents are found in samples of brain tissues, with quantities up to 80%. The considerable reduction in mercury mining during the 1970's has not comparably reduced the amount of mercury pollution (Fig. 5 and Tab. 7). The results are compared to those obtained for human tissues from the 1970's and 1980's (Fig. 6) in order to emphasize the suitability of deer as bioindicators.

321
TITLE:
Organ And Cellular Distribution Of Inhaled Metallic Mercury In The Rat And Marmoset Monkey (Callithrix Jacchus): Influence Of Ethyl Alcohol Pretreatment

AUTHORS:
Khayat A
Dencker L

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 55, No. 2, pages 145-152, 24 references, 19841984

ABSTRACT:
The effect of ethyl-alcohol (64175) (EtOH) or aminotriazole (61825) on distribution of inhaled metallic mercury (7439976) was investigated in rats and marmoset-monkeys. Sprague-Dawley-rats received single intraperitoneal doses of saline (control) or 2 grams per kilogram (g/kg) EtOH or 1g/kg aminotriazole. Thirty minutes later they inhaled labeled mercuric-chloride (7487947) vapor for 1 hour and were then killed. Monkeys received saline or 1.5g/kg EtOH injections. Fifteen minutes later they were exposed to 480 microgram/kg of mercury vapors and killed. Whole body autoradiography was performed on both species. Selected tissues and blood were analyzed for radioactivity in a scintillation counter. In control rats and monkeys high concentrations of radioactive mercury were found in several organs indicating a high capacity for oxidizing metallic mercury to the ionic form. Highest activity was seen in the respiratory epithelium, kidney cortex, lung, myocardium, and spleen. Localized high concentrations corresponding to the periportal hepatocytes were seen in liver and in the subscapular adrenal cortex, specifically to the zona glomerulosa where major oxidation of metallic mercury to its ionic form occurs. Pancreas, eye, thyroid and salivary glands also showed high concentrations of mercury. In additional the corpora lutea, grey matter of the brain, and skeletal muscles of monkey showed high mercury accumulation. Low concentrations were seen in blood fat, testis, and epididymis. The effect of EtOH and AT pretreatment were similar in the two species. The authors conclude that metallic mercury is readily oxidized in respiratory tract, liver, and adrenals and in other organs of rats and monkeys.

322
TITLE:
There are two kinds of mercury: Environmental and man-made pollutant.

AUTHORS:
ANON

SOURCE:
Calif. Health; 28(10): 8-10, 14 1971

ABSTRACT:
HAPAB Attention has only recently been focused on environmental contamination from the use of mercury in agriculture and industry. Little is known about the effects this contamination will have on public health and the ecology. In this article, particular attention is given to the problems confronting the California State Interagency Committee on

Environmental Mercury, headed by Dr. Ephraim Kahn of the State Department of Public Health. The Committee, composed of representatives of several state and federal agencies, issued its first report in January 1971. When mercury is deposited in the bottom muds of water bodies, it is converted to methyl mercury. This compound easily enters aquatic and marine food chains, with the result that it eventually accumulates in animal flesh. In humans, it attacks brain cells and fetuses. Methyl mercury poisoning is difficult to diagnose and often irreversible damage has been done before identifiable symptoms appear. According to Dr. Kahn, an autopsy is sometimes the only way to prove methyl mercury poisoning. The Interagency Committee could find no recorded experience regarding the amount of methyl mercury that can be ingested without harm, how long it remains in the system or the danger point in cumulative buildup. Knowledge is so sketchy that the tolerance levels set by various governmental organizations are a |numbers-game,| according to Dr. Kahn. Speaking for the Committee, Dr. Kahn concludes: |We've just now got a fingertip hold on this environmental phase of mercury... We feel that epidemiological and toxicological studies are urgently required.| 1971

323
TITLE:
Milk transfer of inorganic mercury to suckling rats: Interaction with selenite.

AUTHORS:
SUNDBERG J
OSKARSSON A
BERGMAN K

SOURCE:
BIOL TRACE ELEM RES; 28 (1). 1991. 27-38.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The transport of mercury into rat milk, and uptake in the suckling offsrping was studied after peroral administration of inorganic mercury to lactating control rats, and to rats fed selenite in the diet. On day 8, 9, 10, or 11 of lactation, dams were administered a single oral dose of 0.1, 0.4, 0.7, 1.3, or 5.8 mg Hg/kg bw labeled with 203mercuric acetate. There was a linear relationship between mercury concentrations in dam's plasma and milk. The level of mercury in milk was approximately 25% of the level in plasma. After 3 d, milk levels were reduced to half the levels at 24 h. In the suckling offspring, exposed to mercury via milk during 3 d, the mercury level in blood was approximately 1% of the level in maternal blood. Mercury concentration in milk was linearly correlated to the levels in kidney, liver, and brain in the suckling offspring after 3 d exposure to mercury via milk. Selenite treatment of rats, 1.3 mug Se/g diet for 5 mo, resulted in increased transport

324
TITLE:
Renal Ultrastructural Alterations and Cardiovascular Functional Changes in Rats Exposed to Mercuric Chloride

AUTHORS:
Carmignani M
Boscolo P
Preziosi P

SOURCE:
Archives of Toxicology, Supplement 13, pages 353-356, 5 references, 1989

ABSTRACT:
The effects of chronic mercury (7439976) exposure upon renal and cardiovascular function was investigated to examine possible alterations in kidney structure. Male Sprague-Dawley-rats were orally exposed, via drinking water, to 50 micrograms per millimeter mercuric-chloride (7487947) for 350 days. Following the exposure period, aortic blood pressure, heart rate, and maximum left ventricular rate were assessed. Tissue samples and thin kidney sections were both observed by microscopy, while the levels of mercury, zinc, and copper in the heart, brain, liver and kidney were determined by atomic absorption spectrometry. Overall, the results demonstrated that blood pressure and cardiac inotropism were both increased by mercury exposure. Baroreflex sensitivity was decreased following mercury exposure, from 8.4 milliseconds per millimeter of mercury (msec/mmHg) to 3.0msec/mmHg. It was also noted that in the kidney, tissue mercury levels were substantially larger than the levels observed for the control animals (139.7 micrograms per gram (microg/g) versus 0.05microg/g, respectively). Higher tissue concentrations of zinc (27.4microg/g versus 21.7microg/g, respectively) and copper (28.2microg/g versus 5.4microg/g, respectively) were also observed. The authors conclude that their results demonstrate that mercury affects the neurogenic, humoral, metabolic, and immunological mechanisms of the kidney and cardiovascular system.

325
TITLE:
MERCURY AND REPRODUCTIVE HEALTH IN WOMEN DENTISTS

AUTHORS:
SAVITZ DA

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ In the U.S., the number of women of child-bearing age practicing dentistry has dramatically increased over the last 15 years. Information is needed about the effects and mechanisms of known occupational toxins with regard to their manifestations in women's health and reproduction. Of particular concern in dentistry is the chronic low dose exposure to mercury vapor, occurring through the use of mercury in amalgam restorations. Mercury vapor is recognized to readily cross both the brain and placental barriers. Studies of the effect of mercury vapor exposure in animals have shown associations with a variety of serious adverse outcomes, suggesting the possibility of multiple mechanisms of effect. The purpose of this study is to determine if occupational mercury exposure affects the fecundability (time to pregnancy) or risk of spontaneous abortion for women dentists. The sampling frame for this mailed questionnaire will be women who graduated from dental school before 1987, of child bearing age, and are on the list of dentists maintained by the American Dental Association. This restriction enables the current study to relate estimated dental occupational exposures to outcome measures addressing several maternal and fetal consequences. The questionnaire is based on those used in other occupational and reproductive health studies. Some of the confounders an effect modifiers to be studies include; nitrous oxide, smoking, coffee, alcohol, reproductive history, age of the mother at pregnancy, other occupational exposures, and the occupation of the husband/partner. This study will help determine if dental practice patterns involving mercury exposure place the female dentist at increased risk for delay in conceiving or of adverse reproductive outcomes.

326

TITLE:

Current data on use and toxicity of mercury.

AUTHORS:

Festy B

SOURCE:

Tech. Sci. Munic. 68(4): 161-171; 1973(REF:13)

ABSTRACT:

HAPAB. The use and toxicological and ecologic problems of mercury are surveyed. Mercury compounds present in water accumulate through food chains, starting from phytoplankton across fish to piscivorous birds. High concentrations of mercury can occur in the organism of granivorous birds due to ingestion of dressed seeds. The mercury concentrations in birds and fish range from 0. 02 to 1. 4 ppm, and values up to 200 ppm in the liver of birds and fish were measured. Neuropathy with multiple sensory disturbances, salivation, transpiration, ataxia, paralysis of peripheral nerves, and congenital cerebral palsy with mental retardation are among the common consequences of acute poisoning with mercury. Mercury, which accumulates mainly in the liver and brain, is eliminated

from the organism slowly, primarily through the feces. Interaction of mercury with enzyme and membrane proteins and DNA, interference with cell division, induction of chromosome aberrations, and incorporation of mercury in the soluble fraction of the cytoplasm were observed.

327
TITLE:
Congenital Mercury Poisoning

AUTHORS:
Snyder RD

SOURCE:
New England Journal of Medicine, Vol. 284, No. 18, pages 1014-1016, 18 references, 19711971

ABSTRACT:
A case of congenital mercury (7439976) poisoning was investigated. A family, including the pregnant mother, ingested meat from hogs fed seed grain that had been treated with a methyl-mercury (22967926) fungicide. The mother consumed the mercury contaminated meat from month 3 through month 6 of her pregnancy. Examination during month 7 was within normal limits; neurologic findings and visual fields were normal. Her urinary mercury concentrations during months 7 and 8 were markedly elevated at 0.06 and 0.18 part per million (ppm). A 3,062 gram male infant was delivered at term. At 1 minute of life, intermittent gross tremors of the extremities developed which persisted for several days. The cry was weak and high pitched. In other respects the infant appeared normal upon general and neurological examination. The infant was never breast fed, receiving commercial milk and food. Neonatally, urinary mercury concentrations were 2.7ppm at age 1 day, and 2.0ppm at 4 days, but reduced to less than 0.01ppm by 6 weeks of age. An electroencephalogram was within normal limits and electromyography performed at 3 days of age showed normal conduction velocities and muscle action potentials. At 6 weeks, the infant was very irritable with a high pitched weak cry, increased tone in the extremities and cortical thumb posturing. At 3 months of age, the electroencephalogram was abnormal with the widespread occurrence of spike activity more abundant in the left central and parietal regions. By 6 months of age, generalized myoclonic jerks developed and the electroencephalogram was markedly abnormal, with paroxysmal high voltage spike, and spike and slow wave patterns present bilaterally. The author concludes that the infant suffered from transplacental poisoning with organic mercury which suggests a special susceptibility of the developing nervous system to such damage. An asymptomatic woman who ingests organic mercury compounds during pregnancy may produce a neurologically defective infant.

328

TITLE:
Lactational exposure and neonatal kinetics of methylmercury and inorganic mercury in mice.

AUTHORS:
SUNDBERG J
JONSSON S
KARLSSON MO
OSKARSSON A

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 154 (2). 1999. 160-169.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The concentration of mercury in milk and the distribution pattern in the sucking pup was followed over time after administration of a single iv injection of 0.5 mg/kg body wt of 203Hg-labeled methylmercuric chloride or mercuric chloride to lactating mice on Day 10 of lactation. Mercury concentrations in milk of the dams and in whole body, blood, plasma, GI-tract, liver, kidneys, and brain of the offspring were followed up to 11 days after dosing (until lactational Day 21). Following the inorganic mercury dose to the dams, most of the mercury in milk was delivered to the pups during the first 24 h, but the maximum mercury concentration in plasma and tissues of pups was not reached until 7 days after dosing, indicating a prolonged absorption of inorganic mercury in the sucking pup. Pups of dams given methylmercury were exposed to a much lower and constant mercury concentration in milk. The estimated accumulated mercury dose via milk per pup of dams given methylmercury was

329
TITLE:
The effect of sodium selenite, sodium tellurite and sodium sulfite on the retention and distribution of mercury in mice.

AUTHORS:
Eybl V
Sykora J
Mertl F

SOURCE:
Arch. Toxikol.; 25(3/4), 296-305, 1969; (REF:20)

ABSTRACT:
HAPAB Experiments on mice were conducted to study the retention and distribution of mercuric chloride administered i.v. in the organism and the influence on them of s.c. injections of the title sodium compounds. Male H strain mice were divided into groups of 24 animals each. Labeled

mercuric chloride (203- HgC12 with carrier) was given i.v. to the first group; further groups also received the compound i.v. but with simultaneous s.c. administration of one of the salts: sodium selenite, sodium tellurite or sodium sulfite. Al the compounds were dissolved in redistilled water and given in a dose of 0.003 mM/kg (0.1 ml/10 g). Radioactivity was about 3 McCi/mouse. Mercury retention at 0, 24 hr and 7, 14, 21 and 28 days was measured by whole body counting with a sodium iodide scintillation crystal and gamma-spectrometry. Eight mice of each group were sacrificed at 24 hr, 7 and 28 days; blood, brain, heart, lungs, liver, the gastrointestinal tract, kidneys, spleen, femur and testicles were preserved for anaylsis of mercury retention by the same method as for the whole body count. The graph and tabulated data demonstrate that the greatest amount of mercury was retained after the injection of sodium selenite. Sodium tellurite caused an analogous but somewhat weaker reaction. Sodium sulfite had no significant effect on mercury retention. The effect of sodium selenite and sodium tellurite was long-lasting: the respective compounds caused 31.9 and 25.5% retention of the total applied mercury does on day 28 compared to 1.6% for controls for the same period of time. Both these compounds caused considerable alteration in the distribution of mercury in the organs as seen in the tabulated resulted. Sodium sulfite had only insignificant effect on mercury distribution. The effect of the sodium selenite and sodium tellurite was found to depend on the values of their redox potentials. The two compounds are reduced in the animal organism to form compounds of a collodial nature with mercury which in turn are retained in the organism. TOXICOLOGY AND PHARMACOLOGY 70/06/00, 234 1969

330
TITLE:
Pharmacokinetics of Methylmercury in Sheep

AUTHORS:
Kostyniak PJ

SOURCE:
Journal of Applied Toxicology, Vol. 3, No. 1, pages 35-38, 11 references, 19831983

ABSTRACT:
The use of sheep as an animal model for heavy metal intoxication was assessed by a preliminary study of the pharmacokinetics of methylmercury (22967926). Radiolabeled methylmercury was administered by intravenous injection to one 8 month old female Corriedale-sheep at a dose of 9.5 milligrams mercury (7439976) per kilogram body weight. The animal was quarantined for 55 days during which blood, urine, feces, and wool samples were collected. The animal was sacrificed at the end of the experimental period for tissue mercury analysis. Mercury levels were determined by gamma spectrometry. Whole blood and plasma exhibited a biphasic decay of

mercury levels with respective half times of 14.1 and 14.6 days for the slower components and 1.5 and 1.9 days for the faster components. Approximately 12 percent of the whole blood mercury was associated with the plasma fraction. The half time for mercury decay in wool was 15 days based on first order kinetics. The mercury output into feces and wool each accounted for approximately 30 percent of the original body burden. No gross or histological abnormalities were found upon necropsy. Kidney and liver showed the highest tissue concentration of metal, and the mercury level of bile was approximately three times that of plasma. The distribution of mercury in the brain was relatively uniform with concentrations ranging from 1.3 to 2.2 nanograms per gram tissue. The author concludes that the sheep provides a useful animal model for the regional deposition of methylmercury.

331
TITLE:
"Normal" Concentrations of Mercury in Human Tissue and Urine

AUTHORS:
Skerfving S

SOURCE:
Mercury in the Environment, L. Friberg and J. Vostal, Eds; CRC Press, Cleveland, Chapter 6, pages 109-112, 19721972

ABSTRACT:
Summary of normal levels of mercury in persons not occupationally or therapeutically exposed to mercury (7439976). Available data indicate that fish consumption influences levels of mercury. Data are presented by country on normal levels of mercury reported, averaging 5 nanograms per gram in whole blood and 0.5 micrograms per liter in urine. Data on normal levels in brain, liver, and kidneys are too contradictory to substantiate any conclusive normal mercury level. Mercury levels in hair vary from 1.8 microgram per gram to levels three times as high.

332
TITLE:
Percutaneous Absorption of Mercury Vapor by Rats

AUTHORS:
Wunscher U
Roschig M
Friese K-H
Hoffmann P

SOURCE:
Archives of Toxicology, Vol. 65, No. 3, pages 257-259, 9 references, 1991

ABSTRACT:

An investigation was conducted to prove the suitability of the rat tail skin as a model of mercury (7439976) skin uptake. The tail only exposure was described and a subacute exposure study was conducted. The tails of five rats were exposed for 4 weeks, 5 days a week, 6 hours per day to a mercury vapor at a concentration of 1.1mg/m3. The tails of a control group were exposed to air alone using the same type of exposure system. A mercury uptake via the rat tail skin was confirmed. The mercury content of the kidneys of exposed animals was without exception higher than the grand median. An increase in the mercury concentration of the other compartments, including blood, caused by exposure could not be proven. Brain uptake was low, which was explained by the relatively high blood circulation time of the skin compartment. The uptake rate could not be estimated quantitatively by these experiments. Compared to the background level of mercury concentration in biological materials determined in unexposed animals, the skin uptake of exposed animals was very low. The authors conclude that further investigations will be undertaken to identify modifying factors to change the properties of the rat tail skin within a physiological range.

333

TITLE:

Effects of exercise training on the distribution of metallic mercury in mice.

AUTHORS:

SHIMOJO N
ARAI Y

SOURCE:

HUMAN & EXPERIMENTAL TOXICOLOGY; 13 (8). 1994. 524-528.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. The purpose of this study was to correlate exercise induced changes of antioxidant enzymes with the distribution of mercury after mercury vapour exposure in mice. Exercise training consisted of swimming (1 h/day for 5 days/week) for 9 weeks. After 9 weeks of training, swim-trained mice showed significantly elevated levels of catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GSHpx) in their red blood cells, CAT and GSHpx in their kidneys and SOD in the liver. Exercised mice (Ex) and non-exercised mice (N.Ex) were exposed to mercury vapour (3.5 mg m-3) for 1 h. Mercury concentrations were assayed in the blood, brain, heart, lungs, liver and kidneys along with the mercury content of the entire body. The whole body mercury content showed no significant difference in any measurement (immediately, 24 h and 48 h after mercury exposure) between the Ex and N.Ex groups. Mercury concentrations in the Ex group were significantly higher than the N.Ex group in th

334
TITLE:
Placental Transfer And Fetal Distribution Of Cadmium And Mercury After Treatment With Dithiocarbamates

AUTHORS:
Danielsson BRG

SOURCE:
Archives of Toxicology, Vol. 55, No. 3, pages 161-167, 32 references, 19841984

ABSTRACT:
The effects of dithiocarbamate (4384821) treatment on fetal mercury (7439976) and cadmium (7440439) distribution were investigated in rats. Pregnant female C57BL-mice were administered 1 millimole per kilogram diethyldithiocarbamate (392745), disulfiram (97778), or thiram (137268) by oral gavage. Two hours later mice were intravenously injected with 750 nanomoles per kilogram radiolabeled mercuric-chloride (7487947), or cadmium-chloride (10108642) followed immediately by a second oral dose of diethyldithiocarbamate, disulfiram, or thiram. Animals were killed 4 or 24 hours after mercury or cadmium administration. They were autopsied and radioactivity in maternal and fetal organs and tissues were measured. Both elements accumulated in the placenta, cadmium values being approximately 4 times higher than mercury values. The placental concentrations of cadmium were 1000 and 4000 times that of plasma at 4 and 24 hours, respectively. Fetal concentrations were 1 to 10 times higher for mercury than for cadmium in all organs measured. At 4 and 24 hours after treatment, significant differences were seen in all organs of dithiocarbamate treated mice compared to those receiving cadmium alone. At both intervals cadmium concentrations were decreased in liver by all three treatments, but increased 25 to 50 percent in kidney, 10 to 20 times in brain, and 6 to 8 times in adrenals, spleen, and ovaries. In contrast, mercury concentrations in liver were increased by all three treatments at both 4 and 24 hours, but concentrations in liver were decreased as much as 80 percent (thiram at 4 hours). Diethyldithiocarbamate and thiram increased cadmium concentrations in whole fetuses and all fetal organs, but disulfiram decreased fetal cadmium concentrations 33 to 80 percent. With mercury, all dithiocarbamates substantially decreased fetal concentrations. The author concludes that oral dithiocarbamate treatment of pregnant mice has a marked but complex effect on cadmium and mercury distribution in mother and fetus. Pregnant females occupationally exposed to dithiocarbamates should be considered a risk group. Chelate regimens in pregnant females may cause more harm than benefit to the fetus.

335
TITLE:

In vivo inorganic mercury induced inhibition of magnesium-dependent ATPase activity in different regions of the fish brain.

AUTHORS:
BANO Y
HASAN M

SOURCE:
J ANAT SOC INDIA; 41 (1). 1992. 15-23.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Neurotoxic effects of inorganic mercury compound HgCl2 were studied histochemically on Mg2+-ATPase in cerebrum, cerebellum and spinal cord of the cat-fish (Heteropneustes fossilis). The enzyme reaction-product of Mg2+-ATPase depicted heterogenous distribution of enzyme activity which was appreciably high in cerebrum, granular cell layer of cerebellum and spinal cord gray metter. Inorganic mercury intoxication elicited time-dependent inhibition of ATPase in the brain, different part of which showed differential response. These results are well correlated with morphological changes consequent to mercury poisoning (Bano & Hasan, 1992).

336
TITLE:
Sublethal effect of Mercury and lead on monoamine oxidase in different regions of the brain in three freshwater teleosts.

AUTHORS:
SHAFFI SA

SOURCE:
REVISTA ESPANOLA DE FISIOLOGIA; 51 (3). 1995. 125-128.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Effect of mercury and lead at 24 and 48 h was investigated on monoamine oxidase (MAO) activity in different regions of the brain (telencephalon, cerebellum, diencephalon and medulla oblongata) in Labeo rohita, Ham., Clarias batrachus, L. and Channa punctatus, Bloch. Highest rise in MAO activity was recorded in telencephalon with mercury followed by lead. Maximum variations in the level of MAO activity in different regions of the brain were recorded at 24 h exposure. The observed alterations were discussed in relation to different parameters.

337
TITLE:
Mitotic Arrest In The Developing CNS After Prenatal Exposure To Methylmercury

AUTHORS:
Rodier PM
Aschner M
Sager PR

SOURCE:
Neurobehavioral Toxicology and Teratology, Vol. 6, No. 5, pages 379-385, 21 references, 19841984

ABSTRACT:
The effects of methylmercury (22967926) on mitosis in the prenatal central nervous system were studied in mice. On day 12 of gestation pregnant ICR-mice were given a single oral dose of methylmercury at 8 milligrams per kilogram (mg/kg) mercury. Fetuses from treated dams were compared with control fetuses 24 and 48 hours after dosing. Four regions of the developing brain, cerebellum, midbrain, hippocampus, and cerebral cortex, were studied for mitotic activity. Mitotic index, number of proliferative cells and thickness of the proliferative zone were determined, as well as the pattern of mitosis. In a separate experiment, concentrations of mercury-203 were evaluated in dams and fetuses 24 hours after administration of a single gavage dose of 8mg/kg labeled methylmercury solution. Labeled mercury contents of maternal blood and brains and fetuses were determined by gamma spectrometry. General measures of proliferative activity, the thickness of the ventricular layer, the number of proliferative cells, and the mitotic index, were not depressed by methylmercury. At 48 hours after treatment thickness of the proliferative zone and number of cells were measured in the midbrain. Mitotic index was higher in treated cortex at 48 hours. In the midbrain early mitotic figures were similar to controls, but in other brain areas methylmercury was associated with elevated numbers of early mitotic figures. The number of late mitotic figures was depressed by treatment. By 24 hours, concentrations of labeled mercury in the fetuses approached those of the dams. Maternal blood concentrations averaged 11.6 micrograms per gram while whole fetal concentrations were 9.9 micrograms per gram. The authors conclude that neurons formed during gestation are sensitive to methylmercury, with arrest of cells in mitosis. It is not clear whether this arrest results in permanent reduction in neuron number.

338
TITLE:
The neuropsychiatric sequelae of mercury poisoning: The Mad Hatter's disease revisited.

AUTHORS:
O'CARROLL RE
MASTERTON G
DOUGALL N

EBMEIER KP
GOODWIN GM

SOURCE:
BRITISH JOURNAL OF PSYCHIATRY; 167 (1). 1995. 95-98.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Background: The detailed effects of mercury poisoning on cognitive function, brain anatomy and regional brain function are largely unknown. We report the case of a 38-year-old man who was exposed to toxic levels of inorganic mercury. Method: Four years after exposure, the patient was assessed using magnetic resonance imaging (MRI), single-photon emission computerised tomography (SPECT) and detailed neuropsychological evaluation. Results: The patient developed a myriad of physical and psychiatric complaints, including stomatitis, muscle spasm, tremor, skin rash and the psychiatric syndrome known as 'erythism' (Mad Hatter's disease). Neuropsychological evaluation revealed marked and significant deficits of attention concentration, particularly when under time pressure. The MRI scan was unremarkable; however, SPECT revealed hypermetabolism of the posterior cingulate cortex. Conclusions: Mercury poisoning appeared to result in a dysregulation of posterior cingulate cortex,

339
TITLE:
Determination of mercury levels in the brain by neutron activation analysis.

AUTHORS:
Al-Hiti K
Al-Sidi IH
Albedri MB

SOURCE:
Int. J. Appl. Radiat. Isot. 31(9): 563-568 1980 (18 References)

ABSTRACT:
PESTAB. Since mercury has been used extensively as a fungicidal dressing for seeds, it has sometimes been found stored in various organs of man and animals. Brain levels of mercury are often a good indication of total body burdens of this compound. The 368 keV prompt gamma-radiation emitted during the 199Hg(ngamma)200Hg reaction at doses of 102 mrem was monitored to measure brain levels of mercury as low as 100 ppm. Experiments on phantom volunteers and animals showed that the assay was accurate to within +- 3.2%. The parietal region of the skulls was viewed using a 60 cm3 Ge(Li) detector of 2.14 keV resolution at the 60Co line. A metallic mole held the head in position during viewing and spatial consideration was given to dose measurements. Minimum shielding weight was achieved by

experiments with a layered system of tungsten alloy, lead, cadmium, lithium fluoride, boron and paraffin. A two part collimation system also helped to reduce background gamma-radiation.

340
TITLE:
Predator-prey relationships in mummichogs (Fundulus heteroclitus (L.)): Effects of living in a polluted environment.

AUTHORS:
SMITH GM
WEIS JS

SOURCE:
JOURNAL OF EXPERIMENTAL MARINE BIOLOGY AND ECOLOGY; 209 (1-2). 1997. 75-87.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Analysis of prey capture ability of mummichogs, Fundulus heteroclitus (L.) from a mercury-polluted tidal creek compared with conspecifics from an uncontaminated environment showed that the latter captured the prey organism Palaemonetes pugio Holthuis at a significantly faster rate and had significantly lower levels of mercury in their brain tissues. Exposure of uncontaminated fish to conditions similar to those of the polluted creek caused both a reduction in their prey capture rate and an increase in brain mercury to levels similar to those of fish native to the creek. Polluted fish maintained in the laboratory for extended periods failed to show either an increase in prey capture rate or a decrease in their levels of brain mercury. Size-selective predation on grass shrimp was observed among mummichogs from both sites, but did not appear to vary between sites. Videotape analysis of predatory behavior showed that fish from the polluted creek made significantly fewer att

341
TITLE:
ENVIRONMENTALLY INDUCED ALTERATIONS IN NEURON AND GLIA DEVELOPEMNT

AUTHORS:
HARRY GJ

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ During the development of the nervous system, the temporal and spatial regulation of gene expression is a critical component of neural and glial growth, development, and interactions. These critically timed

events are assummed to be a major component in the differential susceptibility of the developing organism to environmental insult. This project examines the effects of various environmental agents, (e.g. lead acetate, triethyltin, trimethyltin, methyl mercury, mercury vapors, and electromagnetic fields, and AIDs therapeutics), on the development of the nervous system as indicated by alterations in the spatio-temporal expression of mRNA for various developmentally regulated proteins associated with distinct processes of development (e.g., neuronal migration, neurite extension, synapse formation, and myelination). We have shown that lead acetate alters developmentally regulated structural proteins. Ongoing studies are examining the mRNA for neurotrophins and proteins associated with axonal elongation and synapse formation to further understand the subtle lead induced alteration in the formation of the neural network. Using RNase protection assays we have demonstrated a ontological profile for pro-inflammatory cytokines and neurotrophins in various brain regions. Lead acetate decreased mRNA levels for tumor necrosis factor alpha (TNFa) and interleukin-1 alpha (IL-1a) in the cerebellum while leaving the neurotrophins unchanged. Developmental mercury vapor exposure decreased TNFa, TNFbeta, and IL-6 in the cerebellum at postnatal day 14 with no alterations in the neurotrophins. This technique is being expanded with the establishment of new probe sets to detect mRNA levels for proteins associated with the various cell types and stages of brain development. In vitro experiments have shown glial cell cultures to demonstrate a maturation pattern of susceptibility to ischemic injury similar to that seen in vivo with a hypoxia-induced up-regulation of mRNA for neurotrophins in young cells that is gradually lost during maturation. Future Research: We will continue to generate developmental profiles for the neurotrophins, pro-inflammatory cytokines, and structural related proteins in brain regions following exposure to known developmental neurotoxicants to assess the feasibility of using this approach to determine developmental neurotoxic potential of a chemical and to further understand the nature of the interdependency of these critically timed events in the formation of the neural network.

342

TITLE:

Distribution and excretion of mercury compounds in rats over a long period after a single injection.

AUTHORS:

Sewnsson A
Ulfvarson U

SOURCE:

Acta Pharmacol. Toxicol.; 26(3), 273-83, 1968; (REF:5)

ABSTRACT:

HAPAB Female albino rats (200 g) were injrected intravenously with

mercuric nitrate, phenyl mercuric hydroxide and methyl mercuric hydroxide tagged with mercury-203. Three rats were used for each observation and the dosage was 100 mcg of mercury/animal in 0.5 ml of water. The animals were killed after 1, 2, 4, 9, 16, 83 and 169 days and the elimination of the compounds and the concentration in the organs at different times were followed for 6 months by means of the scintillation technique. during the whole period, analyses of the radioactivity in the whole body of the living animals were also made. Tabulated data include the concentration of the three test compounds in ng/g of organ and the whole body analyses and estimated biological half- life of the compounds at different times after treatment. It was observed that the rate of excretion changed during the observation period. The =biological hal-life= for mercuric nitrate and phenyl mercuric hydroxide varied from about 5 days when the observation period was 9 days, to about 10 days when the observation was extended to 40 days. For methyl mercuric hydroxide the =biological half-life= was 16 days after observation for 9 days and 26 days when the observation period was 40 days. The distribution in the organs varied during the first part of the test period. The blood concentration decreased from high values in animals killed 1 day after injection to much lower values in animals killed subsequently. At the same time the kidney concentration increased and reached a maximum on the 9th day for mercuri nitrate and phenyl mercuric hydroxide and on the 4th day for methyl mercuric hydroxide. The same relationship was found in the brain and testes for mercuric nitrate and methyl mercuric hydroxide. The elimination from the kidneys, the brain and the testes was slower than from other organs for all compounds. The concentrations in different parts of the brain were similar, though a slightly higher concentration in lobus olfactorius was indicated. After about 100 days the concentrations of mercury compounds reached levels found in controls; however, the relation between the concentrations in the different organs remained the same. TOXICOLOGY AND PHARMACOLOGY 68/12/00 22 1968

343

TITLE:

Interaction and distribution of selenite, mercuric, methoxyethyl mercuric and methyl mercuric chloride in rats: 1. Analysis of brain, liver, kidney and feces.

AUTHORS:

MENGEL H
KARLOG O

SOURCE:

ACTA PHARMACOL TOXICOL; 46 (1). 1980. 14-24.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The interaction of Se with methyl mercury, methoxyethyl mercury and mercuric chloride was studied in a 37 day

experiment with rats. Liver, kidney, brain and feces were analyzed for Hg and Se at the end of the experimental period. Se supplementation increased the retention of Hg in liver, when mercuric chloride was given, in liver and brain when methyl mercury was given, and in all tissues examined when methoxyethyl mercury was given. The Hge molar ratios in the tissues were calculated and vary considerably.

344
TITLE:
Deferoxamine Inhibits Methyl Mercury-Induced Increases in Reactive Oxygen Species Formation in Rat Brain

AUTHORS:
LeBel CP
Ali SF
Bondy SC

SOURCE:
Toxicology and Applied Pharmacology, Vol. 112, No. 1, pages 161-165, 43 references, 1992

ABSTRACT:
Deferoxamine was employed in the study of iron catalyzed oxygen radical reactions in rat brain following in-vivo and in-vitro exposure to methyl-mercury (22967926) (MeHg). Male CR-1-CD-rats were given a single intraperitoneal dose of MeHg (5.0mg/kg) in deionized distilled water. Deferoxamine was dissolved in deionized distilled water and administered as a single intraperitoneal dose of 500mg/kg 1 hour before MeHg administration. Synaptosomal fractions were prepared from excised brain regions and used in assays for reactive fluorescent oxygen species. An assay for ferrioxamine formation was also conducted. The formation of reactive oxygen species was significantly increased in the cerebellum 7 days after the MeHg injection; deferoxamine pretreatment completely prevented this increase. Deferoxamine (100 micromolar (microM)) also inhibited the oxidative consequences of in-vitro exposure to MeHg (20microM). A 20 fold excess of methylmercuric-chloride (115093) or mercuric-chloride (7487947) did not affect the formation of the iron saturated complex ferrioxamine; the suggestion was that the deferoxamine/mercurial complex did not form. The authors conclude that: iron catalyzed oxygen radical producing reactions are associated with MeHg neurotoxicity, that fluorescent probes have potential as a measure of reactive oxygen species formation, and that iron chelator therapy can offer protection against xenobiotic induced oxidative damage.

345
TITLE:
Effect of treatment with mercury chloride and lead acetate during the second stage of rapid postnatal brain growth on delta-aminolevulinic acid

dehydratase (ALA-D) activity in brain, liver, kidney and blood of suckling rats.

AUTHORS:
ROCHA J BT
PEREIRA ME
EMANUELLI T
CHRISTOFARI RS
SOUZA DO

SOURCE:
TOXICOLOGY; 100 (1-3). 1995. 27-37.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The sensitivity of developing rodents to toxic metals differs considerably from that of adults. In the present study, we investigated the in vivo and in vitro effects of inorganic mercury and lead on delta-aminolevulinic acid dehydratase (ALA-D) from brain, liver, kidney and blood of young rats. Eight day-old rats were injected with one or five doses of lead acetate (0, 3.5, or 7.0 mg/kg) or HgCl2 (0, 2.5, or 5.0 mg/kg). In vitro, the IC50 for mercury inhibition of cerebral, renal and hepatic ALA-D was in the 124 to 160 muM range, while values for lead acetate was in the 7 to 12 muM range. The IC50 of blood enzyme for lead (0.8 muM) and mercury (6.5 AM) was significantly lower than that observed for the other tissues. A single dose of lead did not affect the enzyme activity, but a single dose of HgCl2 (5 mg/kg) caused a significant inhibition of ALA-D from kidney (40%, P < 0.01) and liver (25%, P < 0.05). Five doses of lead acetate (3.5 or 7 mg/kg) caused an inhib

346
TITLE:
A preliminary physiological model of inhaled mercury vapor (Hgo) disposition in the pregnant rat.

AUTHORS:
Kohn MC
Morgan DL
Barone S Jr
Beliles RP

SOURCE:
Teratology 1997 Jan;55(1):59

ABSTRACT:
Exposure to Hgo during pregnancy can lead to accumulation of Hg in the fetus and may be associated with neurological deficits in the offspring. The objective of this study is to investigate the toxicokinetics of Hgo

inhalation by the pregnant rat and the potential neurotoxicity of Hgo for neonates exposed in utero. A preliminary physiological model of the disposition of inhaled Hgo was constructed to identify factors which may be responsible for Hgo neurotoxicity. The model included compartments for lung, liver, GI tract, kidney, fat, muscle, skin, brain, and other richly perfused tissues. Partition coefficients for Hg and kinetic parameters for enzymes involved in the production, transport, and reduction of Hg2+ were estimated from literature data. In simulations of experiments in which Hgo was inhaled for 2 or 6 hrs, the model reproduced the terminal total Hg tissue contents, and suggested experiments to resolve questions regarding the disposition of inhaled Hgo. Experiments were conducted to establish a dose-response for inhaled Hgo fetotoxicity and fetal accumulation of Hg. Long Evans rats were exposed to 0, 1, 2, or 4 mg Hgo/m3 for 2 hr/day from gestation day (GD)6 to GD15. After exposure on GD6, 10, 15 and on postnatal day (PND)1, blood, lungs, liver, kidneys, abdominal fat, uterus and brain were collected from dams for Hg analyses. These data will be used to validate the kinetic model for Hgo inhalation by the pregnant rat. Numbers of implantation sites, resorptions, litter size and fetal viability were used to determine developmental toxicity. Hg levels were measured in fetuses and placentas at each gestational time point and also in neonatal brain, kidney, and liver on PND1. These data will be used to refine the pharmacokinetic model for Hgo in the fetus. Toxicity data will be used to set Hgo doses for use in studies examining the potential developmental neurotoxicity of Hgo in the developing rat.

347

TITLE:

Effect of Sex Hormones on the Fate of Methylmercury and on Glutathione Metabolism in Mice

AUTHORS:

Hirayama K
Yasutake A
Inoue M

SOURCE:

Biochemical Pharmacology, Vol. 36, No. 12, pages 1919-1924, 25 references, 19871987

ABSTRACT:

Male and female C57BL/6NJcl-mice were used to determine the effects of hormonal manipulation on tissue distribution and urinary excretion of methylmercury and on glutathione metabolism in the liver and kidney. The mice were castrated and, 10 days later, received subcutaneous daily injections of testosterone-propionate (TP) or estradiol-benzoate (EB) at dose levels of 50mg/kg or 1mg/kg, respectively, for 7 days. Methylmercuric-chloride (115093) at a dose of 5mg/kg was given orally. Control male mice excreted 6.5 times more mercury (7439976) (Hg) in urine

than did control females. Animals treated with TP showed accelerated urinary excretion by a factor of 1.7 and 3.3 for males and females, respectively. Treatment with EB caused depletion of urinary Hg excretion by one third in males. Castrated males showed a lowered excretion of Hg and treatment of these animals with TP increased this excretion level. Fecal excretion of Hg in intact mice showed no sex related differences. Control males had significantly higher renal Hg levels than did females. Mercury levels in the liver and brain were lower in control males. TP treatment increased renal Hg levels in females, but decreased liver and brain Hg in both sexes. Castrated males had Hg distribution in the liver, kidney, and brain at levels similar to intact females. This was reversed by the TP injection. The authors suggest that the marked difference in mercury excretion in males and females is closely correlated with the rate of glutathione turnover in the two sexes.

348

TITLE:

Mercuric Chloride-Induced Reactive Oxygen Species and Its Effect on Antioxidant Enzymes in Different Regions of Rat Brain

AUTHORS:

Hussain S
Rodgers DA
Duhart HM
Ali SF

SOURCE:

Journal of Environmental Science and Health. Part B: Pesticides, Food Contaminants, Agricultural Wastes, Vol. 32, No, 3 pages 395-409, 30 references, 1997

ABSTRACT:

The effects of in-vitro exposure to mercuric-chloride (7487947) on the production of reactive oxygen species (ROS) in synaptosomes prepared from various regions of rat brain, and the effects of in-vivo exposure on antioxidant enzymes in the brain were studied. Adult male Sprague-Dawley-rats were dosed with 1.0, 2.0, or 4.0mg/kg mercuric-chloride intraperitoneally for 7 consecutive days. Rats were sacrificed 1 week after the final dose. A significant increase of ROS was noted following the various exposures in the caudate nucleus and cerebellum. The frontal cortex and hippocampus also showed augmented ROS formation following exposure to 2 to 5 micromolar mercury in-vitro. Dose dependent reductions of total superoxide-dismutase (SOD) and Cu,Zn-SOD activities were noted in the cerebellum of the in-vivo treated animals. The Mn-SOD activity was significantly decreased in the cerebellum at the 4mg/kg dose level. In cerebral cortex or brain stem there were no significant variations in the activities of total SOD, Cu,Zn-SOD, and Mn-SOD. A significant decline was observed in the activity of

glutathione-peroxidase (GPx) in the cerebellum at 4mg/kg dose levels, whereas in brain stem an increased level of GPx activity was noted at 2 and 4mg/kg doses. No changes were observed in GPx activity in the cerebral cortex.

349
TITLE:
In vitro metal inhibition of N-methyl-D-aspartate specific glutamate receptor binding in neonatal and adult rat brain.

AUTHORS:
RAJANNA B
RAJANNA S
HALL E
YALLAPRAGADA PR

SOURCE:
DRUG AND CHEMICAL TOXICOLOGY AN INTERNATIONAL JOURNAL FOR RAPID COMMUNICATION; 20 (1-2). 1997. 21-29.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The in vitro effect of methyl mercury (MM) and lead (Pb) on N-methyl-D-aspartate (NMDA)-specific glutamate receptor binding in neonatal (10 days old) and adult rat brain was investigated. The cerebral cortex was isolated from the neonatal and adult male Sprague-Dawley rats and the synaptic plasma membranes were prepared to study the NMDA-specific glutamate receptor binding by using (3H)-glutamic acid. The metal salts such as methyl mercury chloride and lead acetate were used to study the effect of MM and Pb. Both MM and Pb significantly inhibited the receptor binding in neonatal and adult rat brain in a concentration-dependent manner. MM (IC50:0.95 | 0.08 muM) was more potent in inhibiting the receptor binding than Pb (IC50:60 | 7 muM) in neonatal rat brain. A similar high potency was observed for MM than Pb in adult rat brain but the IC50 values are very high (70 | 6 muM and 300 | 24 muM respectively) indicating less effect compared to neonatal brain. The data suggest t

350
TITLE:
Post-transcriptional elevation of mouse brain Mn-SOD protein by mercuric chloride.

AUTHORS:
KUMAGAI Y
MIZUKADO S
NAGAFUNE J
SHINYASHIKI M
HOMMA-TAKEDA S

SHIMOJO N

SOURCE:
BRAIN RESEARCH; 769 (1). 1997. 178-182.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Alterations in gene expression, protein content and enzyme activity of brain Mn-SOD following mercuric chloride (HgCl2) exposure were examined in ICR male mice. Subcutaneous administration of HgCl2 (1 mg Hg/kg) resulted in a significant increase (4-fold) in the brain Mn-SOD content at 6 h after injection while the total mercury concentration was about 0.11 mug/g of brain. The enhancement of Mn-SOD protein caused by HgCl2 was completely abolished by pretreatment with dexamethasone (3 mg/kg) 1 h prior to HgCl2 administration, suggesting involvement of inflammation in inorganic mercury-induced increase in the antioxidant enzyme. This increase in level of Mn-SOD content coincided with a substantial rise in the enzyme activity; however, Northern blot analysis revealed that the induction of protein level was not due to that of its gene expression. The results of the present study indicate that mouse brain Mn-SOD appears to undergo post-translational modification by the enviro

351
TITLE:
Methyl mercury toxicity in the chick embryo.

AUTHORS:
GREENER Y
KOCHEN JA

SOURCE:
TERATOLOGY; 28 (1). 1983. 23-28.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Toxicity of methyl mercury (mHg) (an environmental pollutant) in the developing chick embryo was investigated. The relationship of dose time of administration (i.e., days 4-9 of development) and body levels of mHg was examined. The LD50 for mHg injected into the yolk sac on day 5 of incubation was 40-50 mug. Embryos dying within 24 h showed increased total body mHg levels when compared to survivors (219 | 67 vs. 105 | 41 mug/g, mean | SD). Absorption was dose-related, with a good correlation between mortality and body, blood and brain levels. Daily analysis of body mHg levels after injection on day 5 showed continued mHg accumulation (0.88 | 0.35 mug/embryo per day). Rate of embryo growth exceeded the rate of mHg absorption, resulting in a progressive decrease in mHg in concentration in tissues (from 94.5 | 34.2 mug/g on day 6 to 45.3 | 13.4 on day 9). Administration after day 5 resulted in a significant reduction in levels of mHg in the brain on day

18 (from 11.4 | 2.1 mug/g when given on day 5 to 8.4 | 2.3 when given on day 9) and in mortality (from 64-33%). Because blood mHg levels remained unchanged, increased brain levels and higher mortality early in embryogensis may reflect facilitated transfer of mHg across a poorly developed blood-brain barrier. Later in development, reduced mortality and lower brain mHg levels correspond to formation of specialized interendothelial junctions and a more effective blood-brain barrier.

352
TITLE:
Mercury in the human brain.

AUTHORS:
Olszewski WA
Pillay KKS
Glomski CA
Brody H

SOURCE:
Acta Neurol. Scand. 50(5): 581-588; 1974.(18 references)

ABSTRACT:
PESTAB. Environmental pollution by mercury is discussed and two cases of elevated level of Hg in human brain attributed to pollution reported. The prevalence of Hg in the environment is increasing. Excessive Hg levels are found in fish and can be released to the environment through the burning of fossil fuel. In 1968, a commission in Stockholm established the upper limit of safe concentration in the brain to be 1.0 ppm, one-tenth of the concentration was presumed to be associated with irreversible injury or death. Fatalities following acute exposure to organic mercurials have been associated with Hg concentrations in the brain as low as 4.0 and 4.5 ppm. Fresh brain tissue from 17 randomly selected autopsies was analyzed for Hg using neutron activation analysis. Two of the patients had levels in excess of 1.0 ppm with no exceptional Hg exposure. Concentrations of Hg in the cerebellum, geniculate bodies, pons, calcarine cortex, and corpus striatum were 4-10 times as high as those observed in other subjects. The increase of Hg deposition was more marked in the thalamus, the frontal polar cortex, and the motor cortex where levels of 15-20 fold were obtained. Both subjects had a history of malignancy without brain metastases, as did about 50% of the other subjects.

353
TITLE:
Differential Effects of Methylmercury, Thiols, and Vitamins on Galactosidases of Nervous and Non-nervous Tissues

AUTHORS:
Vijayalakshmi K

Bapu C
Sood PP

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 49, No. 1, pages 71-77, 11 references, 1992

ABSTRACT:
Levels of two lysosomal enzymes, alpha-galactosidase (AGAL) and beta-galactosidase (BGAL), in various nervous and nonnervous tissues were analyzed during methylmercury (22967926) toxicity, as well as during detoxication with vitamins and thiols. A total of 96 male albino-mice aged 3 months were divided into 24 groups of four animals each. Eight groups (controls) were injected subcutaneously with vehicle (10 millimolar sodium-carbonate and sodium-bicarbonate, pH9.2) and 16 groups were injected with methylmercury-chloride (115093) (MMC) at a daily dose of 1mg/kg body weight for 7 days. Of the latter, two groups were sacrificed on day eight and two groups on day 15 (after 7 days of withdrawal from the MMC); the remaining groups were treated with N-acetyl-DL-homocysteine-thiolactone (NAHT), glutathione (GSH), vitamin-B-complex, vitamin-C, vitamin-B12, vitamin-E, or a mix of the thiols and vitamins. Animals were sacrificed on day 15, and brains, spinal cords, livers, kidneys and testes were removed. Tissues were homogenized, centrifuged, and residues were tested for AGAL and BGAL using the method of Tettamanti and Masserini. Results showed that a daily dose of MMC caused inhibition of both enzymes in brain, spinal cord and testis, an increase of both in the liver, and an increase of BGAL and an inhibition of AGAL in the kidney. The withdrawal groups showed further inhibition of the enzymes in the brain and spinal cord, recovery in the liver, and a recovery of AGAL, with a further increase of BGAL in the kidney. Vitamin administration caused significant recovery in brain and spinal cord, with vitamin-E yielding maximum recovery in the brain, and vitamin B-complex and vitamin-B12 causing maximum recoveries of AGAL and BGAL, respectively, in the spinal cord. Both NAHT and GSH caused significant recovery of enzymes in brain and spinal cord, with variable recoveries in the other organs. Mixed vitamins and thiols also gave mixed results. The authors conclude that vitamins show better results as antidotes in mercury toxicity.

354
TITLE:
Distribution of inhaled mercury (mercury-203) in various organs.

AUTHORS:
PLACIDI GF
DELL'OSSO L
VIOLA PL
BERTELLI A

SOURCE:
INT J TISSUE REACT; 5 (2). 1983 (RECD. 1984). 193-200.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg and its derivatives are toxic for the brain and other organs in both animals and man. The distribution of inhaled 203Hg in body tissues of rats and mice was investigated by means of a micro-autoradiographic technique. Animals were exposed to 203Hg vapors 6 h/day for 10 days, and then sacrificed at different times after the last exposure. Whole-body autoradiograms showed significant uptake of labeled H by the kidney, brain, myocardium, intestine and liver, in decreasing order. Micro-autoradiography demonstrated selective localization of 203Hg in the cytoplasm and processes of neurons, whereas little radioactivity was found in the glial cells of the gray and white matter. High levels of 203Hg were detected in nuclei of the cerebellum, midbrain, pons and medulla, in the Purkinje cells of the cerebellar cortex, and in the epithelium of the ependyma and choroid plexus. In the lung radioactivity appeared to be confined to the erythrocytes of small blood vessels, which may be the carriers of this metal to the brain. In the liver, ingested but not inhaled, radioactivity was concentrated in the reticulo-endothelium. In the kidney, proximal and distal convoluted tubules, but not the medulla or the glomeruli, took up large amounts of inhaled 203Hg. Mercury is distributed to many organs in addition to the brain. It may be transported by circulating red blood cells and it concentrates in the cytoplasm of parenchymal cells.

355
TITLE:
Changes In The Activity Of Hydrolytic Enzymes In The Brain Of Rats Intoxicated By Ethyl-mercury-p-toluene-sulfanilide

AUTHORS:
Kozik MB
Wigowska-Sowinska J

SOURCE:
Folia Histochemica et Cytochemica, Vol. 16, No. 3, pages 263-270, 25 references, 19781978

ABSTRACT:
The histoenzymatic effects of ethyl-mercury-p-toluene-sulfanilide (EMTS) were studied in Wistar-rats. Rats were fed 0.2 gram doses of EMTS for 10 days and sacrificed. Brains were removed and prepared for histological and morphological analysis. The activities of thiamine-pyrophosphatase (TPPase), nonspecific esterase, acetylcholinesterase (AChE), alkaline-phosphatase, acid-phosphatase, butyrylthiocholinesterase, and adenosine-triphosphatase (ATPase) were determined in cryostat sections.

Degenerative changes observed in various areas of the brain were most striking in the Ammon's horn, characterized by massive neuronal losses and intensive neuroglial hyperplasia. A marked increase in TPPase activity was seen in blood vessel walls, cortical neurocytes, basal ganglia, pyramidal cells of the Ammon's horn, Purkinje cells of the cerebellar cortex, and in oligodendrocytes of the corpus callosum, fornix, and internal capsule. AChE activity dropped moderately in dendrites of the pyramidal cells of the Ammon's horn and the granular cells of fascia dentata. A marked decrease in acid-phosphatase activity was seen in fields CA1 and CA2 of the hippocampus and in dentata fascia cells. ATPase activity was markedly reduced in capillary walls of the frontal and parietal lobes and the cerebellar gyri, as well as in the septum lucidum, basal ganglia, and the Ammon's horn. There was little or no change in the activation of other enzymes. The authors conclude that EMTS was less potent than other mercury compounds in inducing alterations in the activity of cerebral hydrolases.

356

TITLE:

The Effects of Glutathione Glycoside in Methyl Mercury Poisoning

AUTHORS:

Choi BH
Yee S
Robles M

SOURCE:

Toxicology and Applied Pharmacology, Vol. 141, No. 2, pages 357-364, 31 references, 1996

ABSTRACT:

The effects of glutathione-glycoside (GSH-glyc) in methyl mercury poisoning were studied. GSH-glyc, a newly synthesized compound, was found to have the structure of an S-glycoside based on mass spectrometry and nuclear magnetic resonance data. The compound was found to be highly effective in raising cellular glutathione (GSH) levels both in-vitro and in-vivo. Intraperitoneal and oral administration of GSH-glyc (40mg/kg) to C57BL/6J-mice raised GSH concentrations in brain and liver to significantly higher levels than normal. Incubation with GSH-glyc resulted in rapid GSH uptake observed by confocal microscopy in both A549-cells and mouse astrocytes in-vitro. Mice receiving daily 5mg/kg doses of methylmercuric-chloride (115093) (MMC) showed severe toxic effects associated with marked depletion of brain and liver GSH, progressing to death in all animals. However, animals primed with GSH-glyc (40mg/kg) and given MMC and GSH-glyc concurrently were devoid of toxic signs. Glucose uptake studies were performed in an attempt to elucidate the mechanism of GSH-glyc transport in mice. Following administration of radiolabeled glucose, the mice were euthanized and

samples of perfused liver and brain tissue homogenates were counted in a scintillation counter. Brain uptake of glucose in the presence of GSH-glyc was significantly reduced compared to controls, while liver glucose uptake was higher in the GSH-glyc group than in controls. The authors conclude that GSH-glyc may prove useful for prophylaxis and therapy of tissue injury induced by various neurotoxic compounds, particularly when the capacity to synthesize or regenerate GSH has been compromised.

357
TITLE:
DEVELOPMENTAL NEUROTOXICITY OF LEAD AND METHYL NERCURY

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Developmental Neurotoxicity of Lead and Methyl Mercury Lead (PB) and methyl mercury (MM) are well known environmental contaminants. Exposure to these metals has been shown to affect developing brains to a greater extent. Children are more sensitive to Pb than adults whereas, both children and adults are sensitive to MM. A number of second messenger systems have been shown to play a key role in the development of the brain. However, the underlying mechanism of neurotoxicity of Pb or MM is not well understood. Our hypothesis is that developmental exposure to Pb or MM affect signal transduction process, possibly related to the modulation of nitric oxide as well as alterations in receptor-mediated phosphoinositide hydrolysis and protein kinase C. In order to test our hypothesis, we propose the following specific aims: a) Low levels of pb or MM exposure to rats during developmental results in alteration of second messenger system; and b) Conduct in vitro studies to determine the direct or indirect effects of Pb or MM on the second messenger systems. Experimental design include: a) Treat the sam perinatally with two doses of Pb (0.1% and 0.2%) or MM (0.01% and 0.02%) through drinking water from gestation day 6 up to weaning (postnatal day 20);b) Determine the neurochemical parameters such as nitric oxide synthase, inositol polyphosphate receptor binding activities, phosphoinositide (PI) hydrolysis, phospholipase C, protein kinase C and nitric oxide-mediated PI hydrolysis in hippocampus, cerebellum and frontal cortex at 2,5,10,15,20,25,30, and 60 postnatal days; c) Study the concentration-response of Pb or MM on the neurochemical parameters listed in b. In this study, nanomolar concentrations of metals will be used; d) Determine the concentrations of Pb and MM in blood and brain of rats in order to correlated in vivo and in vitro results. Two undergraduates and two graduate students will be involved in this research as student research

participants. After an initial period of training, these students are expected to complete certain experiments on their own. The experiences gained in this research will motivate them to choose careers in biomedical Sciences.

358
TITLE:
Changes in the activity of hydrolytic enzymes in the brain of rats intoxicated by ethyl-mercury-p-toluenesulfanilide.

AUTHORS:
KOZIK MB
WIGOWSKA-SOWINSKA J

SOURCE:
FOLIA HISTOCHEM CYTOCHEM; 16 (3). 1978 (RECD. 1979). 263-270.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A histochemical study concerning the activity of brain phosphatases and esterases was undertaken in rats experimentally intoxicated by the fungicide ethyl-mercury-p-toluenesulfanilide (EMTS). Compared with other organic and inorganic mercury compounds, such as corrosive sublimate and calomel, EMTS proved less potent an inducer of alterations in the activity of cerebral hydrolases. Brains of animals intoxicated by EMTS revealed a notable decrease of ATPase and acid phosphatase activity and a moderate drop of AChE activity. Instead, the neuronal TPPase (thiamine pyrophosphatase) activity was distinctly elevated. Degenerative changes of neurons were observed in various regions of the experimental brains, the pyramidal cells of the Ammon's horn being affected most severely.

359
TITLE:
DEVELOPMENTAL NEUROTOXICITY OF LEAD AND METHYL NERCURY

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Developmental Neurotoxicity of Lead and Methyl Mercury Lead (PB) and methyl mercury (MM) are well known environmental contaminants. Exposure to these metals has been shown to affect developing brains to a greater extent. Children are more sensitive to Pb than adults whereas, both children and adults are sensitive to MM. A number of second messenger systems have been shown to play a key role in the development of the

brain. However, the underlying mechanism of neurotoxicity of Pb or MM is not well understood. Our hypothesis is that developmental exposure to Pb or MM affect signal transduction process, possibly related to the modulation of nitric oxide as well as alterations in receptor-mediated phosphoinositide hydrolysis and protein kinase C. In order to test our hypothesis, we propose the following specific aims: a) Low levels of pb or MM exposure to rats during developmental results in alteration of second messenger system; and b) Conduct in vitro studies to determine the direct or indirect effects of Pb or MM on the second messenger systems. Experimental design include: a) Treat the sam perinatally with two doses of Pb (0.1% and 0.2%) or MM (0.01% and 0.02%) through drinking water from gestation day 6 up to weaning (postnatal day 20);b) Determine the neurochemical parameters such as nitric oxide synthase, inositol polyphosphate receptor binding activities, phosphoinositide (PI) hydrolysis, phospholipase C, protein kinase C and nitric oxide-mediated PI hydrolysis in hippocampus, cerebellum and frontal cortex at 2,5,10,15,20,25,30, and 60 postnatal days; c) Study the concentration-response of Pb or MM on the neurochemical parameters listed in b. In this study, nanomolar concentrations of metals will be used; d) Determine the concentrations of Pb and MM in blood and brain of rats in order to correlated in vivo and in vitro results. Two undergraduates and two graduate students will be involved in this research as student research participants. After an initial period of training, these students are expected to complete certain experiments on their own. The experiences gained in this research will motivate them to choose careers in biomedical Sciences.

360

TITLE:

LATE CONSEQUENCES OF PRENATAL EXPOSURE TO METHYL MERCURY

AUTHORS:

WEISS B

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ An extensive literature indicates that the fetal brain is exquisitely sensitive to methylmercury. These data come from a multiplicity of species, including humans. Despite the extent of the current literature, however, two difficult and important questions remain unanswered. First, what are the lifetime consequences of prenatal exposure? Might they remain latent until the brain is stripped of compensatory capacity by the processes of aging? Second, what might be the consequences of lifetime exposure to relatively low levels of methylmercury? Could minute increments of damage cumulate to accelerate the processes of aging in the brain? These questions will be addressed in

mice in an experimental format designed to follow the course of potential neurotoxicity through the lifespan. The mice will be exposed prenatally alone or both prenatally and postnatally. Specified groups will be observed at the age of 3, 9, 15, and 21 months for six-month periods, during which behavioral measures of motor function and cognitive performance will be secured. At the end of the observation period, brains will be examined by quantitative morphological methods to determine the structural consequences of the various exposure scenarios, and histo-chemical methods will be used for mercury localization. Both organic and inorganic content will also be assayed. These data will contribute data essential for a full risk assessment of dietary methylmercury sources, because current human data suggest adverse effects of exposure at surprisingly low levels.

361
TITLE:
LATE CONSEQUENCES OF PRENATAL EXPOSURE TO METHYL MERCURY

AUTHORS:
WEISS B

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ An extensive literature indicates that the fetal brain is exquisitely sensitive to methylmercury. These data come from a multiplicity of species, including humans. Despite the extent of the current literature, however, two difficult and important questions remain unanswered. First, what are the lifetime consequences of prenatal exposure? Might they remain latent until the brain is stripped of compensatory capacity by the processes of aging? Second, what might be the consequences of lifetime exposure to relatively low levels of methylmercury? Could minute increments of damage cumulate to accelerate the processes of aging in the brain? These questions will be addressed in mice in an experimental format designed to follow the course of potential neurotoxicity through the lifespan. The mice will be exposed prenatally alone or both prenatally and postnatally. Specified groups will be observed at the age of 3, 9, 15, and 21 months for six-month periods, during which behavioral measures of motor function and cognitive performance will be secured. At the end of the observation period, brains will be examined by quantitative morphological methods to determine the structural consequences of the various exposure scenarios, and histo-chemical methods will be used for mercury localization. Both organic and inorganic content will also be assayed. These data will contribute data essential for a full risk assessment of dietary methylmercury sources, because current human data suggest adverse effects of exposure at surprisingly low levels.

362
TITLE:
Experimental Approaches to Developmental Toxicity of Methylmercury

AUTHORS:
Inouye M

SOURCE:
Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 339-354, 26 references, 1991

ABSTRACT:
Laboratory animal studies on the neuropathological changes following prenatal methylmercury (22967926) exposure were reviewed and compared with autopsy studies on children congenitally affected by methylmercury poisoning in Minamata, Japan and Iraq. Studies on rats, mice, and guinea-pigs confirmed that developmental disturbances of the fetal brain, which were reported also in the cases from Iraq, were induced when the dams were exposed to methylmercury in early pregnancy. Exposure of guinea-pigs later in pregnancy or rats in the early postnatal period produced widespread neuronal degeneration in the cerebral cortices of fetuses or pups, similar to that seen in the Minamata cases. The findings confirmed that the Iraqi cases were acutely affected in early pregnancy, causing the brain to show developmental disturbance. The Minamata cases were exposed chronically throughout the pregnancy, so both the developmental disturbance and degeneration of neurons were induced in the same fetal brain. The accelerated accumulation of methylmercury in fetuses at the late pregnant stage, as demonstrated in laboratory animals, might cause more conspicuous degenerative changes of neurons resembling the adult forms. Experimental studies using inbred strains of mice revealed that the susceptibility to methylmercury induced hydrocephalus is under genetic control; the author suggests that this may also be true of humans.

363
TITLE:
Neurotoxicity Produced by Intracranial Administration of Methylmercury in Rats

AUTHORS:
Richardson RJ
Murphy SD

SOURCE:
Toxicology and Applied Pharmacology, Vol. 29, pages 289-300, 19 references, 19741974

ABSTRACT:

Methylmercuric-chloride (115093) administered as a single intracranial injection in microgram quantities produced a neurological syndrome in rats within 24 hours that resembled the effects produced by repeated subcutaneous injection of 10 milligrams per kilogram over a period of 7-14 days. Neuromuscular function evaluated semiquantitatively by graded performance in simple strength and coordination tests showed severe impairment at 24 hours in intracranially methylmercury-treated animals, with recovery taking place by 72 hours. Body weight decreased and recovered during a similar time course. Incorporation of tritiated leucine into brain protein was increased significantly at 24 hours as measured in vitro in and in vivo. Incorporation returned to control values by 72 hours after the methylmercury injection. Residual brain mercury (7439976) concentrations at 24 hours were about 5-fold lower than those accompanying overt neurological signs in rats produced by subcutaneous administration. Histological examination of brains from intracranially and subcutaneously dosed rats revealed that the lesions produced by the 2 methods were substantially different. Intracranial injection of methylmercury was found to produce an isolated neurotoxic syndrome similar in some respects to the neurotoxicity seen in systemic intoxications but dissimilar histopathologically.

364

TITLE:

Therapeutic Abilities of Thiol Compounds in the Restoration of Methylmercury-Inhibited Cholesterol and Triglycerides in the Rat's Central Nervous System

AUTHORS:

Sood PP

Vinay SD

SOURCE:

Archives of Environmental Contamination and Toxicology, Vol. 21, No. 2, pages 212-217, 28 references, 1991

ABSTRACT:

The ability of thiols to counter the effects of methylmercury on central nervous system (CNS) cholesterol and triglyceride concentration were studied in rats. Male Wistar-rats were preinjected intramuscularly with 1, or 10mg/kg methylmercuric-chloride (115093) (MMC) for 1 to 15 days. They were injected 0.5 hour after MMC with 40mg/kg N-acetyl-DL-homocysteine-thiolactone (NAHT), or 100mg/kg or 150mg/kg glutathione (70188) for 2, 7, or 15 days. They were killed 7, 8, 15, or 16 days after the last dose and the brains and spinal cords were removed. The brains were dissected into the olfactory bulb, cerebral hemispheres, cerebellum, and medulla oblongata. The brain parts and spinal cord

samples were analyzed for cholesterol and triglycerides. MMC caused significant decreases in cholesterol and triglyceride concentrations in all tissues after only 2 days of treatment. The effects on cholesterol concentration were more pronounced. The greatest decreases in both cholesterol and triglyceride concentration occurred in the olfactory bulb and the least in the spinal cord. Glutathione and NAHT partially countered the MMC induced decreases in cholesterol and triglyceride concentrations in all CNS regions. Neither treatment restored the cholesterol and triglyceride concentrations to the control values. The authors conclude that MMC antagonists such as glutathione and NAHT are not very useful for mobilizing mercury (7439976) or producing a recovery in MMC induced CNS lesions.

365
TITLE:
Sublethal concentrations of mercury in river otters: Monitoring environmental contamination.

AUTHORS:
HALBROOK RS
JENKINS JH
BUSH PB
SEABOLT ND

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 27 (3). 1994. 306-310.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Hair, muscle, and liver mercury concentrations were determined in river otter (Lutra canadensis) carcasses collected from the lower coastal plain and piedmont of Georgia. Mean muscle and hair mercury concentrations were greater ($P < 0.001$) in otters from the lower coastal plain (4.42 and 24.25 mg/kg wet wt, respectively) compared to otters from the piedmont (1.48 and 15.24 mg/kg, respectively). Liver tissue from lower coastal plain otters averaged 7.53 mg/kg mercury. Mean fetus brain and muscle mercury concentrations were 1.03 and 1.58 mg/kg wet wt. respectively, and fetal muscle mercury concentrations were correlated ($r = 0.92$) with maternal muscle mercury concentrations. Comparison of mercury concentrations found in Georgia otters to those associated with adverse effects in otter and mink (Mustela vison), indicate sublethal contamination with concentrations in some individuals approaching that observed in experimentally dosed individuals that developed clinical signs

366
TITLE:
DENTAL AMALGAMS AND NEUROPSYCHOLOGICAL FUNCTION

AUTHORS:
FACTOR-LITVAK PR

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
DESCRIPTION: There is considerable evidence that some mercury from "silver fillings" distributes to body tissues, particularly the brain. Occupational exposure to mercury vapor is associated with increases in the prevalence of tremor, peripheral neuropathy, cerebellar dysfunction, and abnormal measures of balance. Occupational exposure also is associated with deficits in neuropsychological tests of memory and visuospatial ability and increased reports of subjective symptoms and disturbed mood. The investigators propose to address the hypothesis that low dose mercury exposure, derived from amalgams in the mouth, may be associated with evidence of neurological dysfunction and neuropsychological deficits. By conducting a cross-sectional study, the investigators will test whether amalgam-derived mercury is adversely associated with tests of neurological function, visuospatial ability, memory and attention/executive function. The study sample will comprise approximately 750-840 Columbia University personnel, ages 30-49 years. Based on preliminary work, it is known that the cohort will have a wide range of visible amalgam surfaces. Measures of exposure will be urinary mercury concentration and the numbers of amalgam surfaces, total and occlusal. The proposed outcome measures tap a wide range of neurological and neuropsychological functions. A variety of tests will assess four domains of neuropsychological function: visuomotor/visuospatial function, memory, attention and executive function, and vocabulary. A self-reported questionnaire of mood and a symptom checklist will also be administered. In addition, the investigators will collect quantitative measures of postural sway. After control for confounding variables, including measures of social desirability and hypochondriasis, the dose-response relationships between exposure and each functional domain will be described. Results from this study will have potential public health applications. Adverse associations, if found, might lead to less use of mercury amalgams. Alternatively, evidence favoring the null hypothesis would allay widespread fears that a variety of health problems may be associated with amalgam exposure.

367
TITLE:
On the biological half-life of mercury.)

AUTHORS:
Doi R

SOURCE:
Kagaku (Science) (Tokyo)44(8): 514-515; 1974

ABSTRACT:
PESTAB (8 references) (Japanese) jThe biological half life (BHL) of mercury is discussed, mainly based on Al-Shahristani's report on the half life of mercury in hairs of 48 Iraqis intoxicated by a methyl mercury pesticide. Although Al-Shahristani reported a BHL of 72 days as the arithmetic mean, there are 154 days between the individual minimum and the individual maximum, 35-189 days. The individual BHL values fall within the range between the min. and max. value according a definite frequency distribution. The statistical method is indispensable for grasping the whole picture, but it is the individuals of lower resistance who are apt to accumulate mercury and must thus be considered in terms of health problems due to intoxication or environmental pollution, rather than the average individual. It would be a great mistake to consider all Japanese mercury accumulation and intoxication problems based on the average BHL of 70 days. Monitoring for maintenance of the ADI of mercury should be based on the maximum value of the BHL in order to prevent any actual risk of intoxication due to mercury. The control of the ADI for methyl in particular should be based on the maximal BHL in brain. s,

368
TITLE:
Mercury-Selenium Interaction: Distribution and Excretion of 203Hg2+ in Rats after Simultaneous Administration of Selenite or Selenate

AUTHORS:
Cikrt M
Bencko V

SOURCE:
Toxicology Letters, Vol. 48, No. 2, pages 159-164, 16 references, 1989

ABSTRACT:
The effects of selenite and selenate on the distribution and excretion of mercury (7439976) were studied in rats. Female Wistar-rats some with cannulated bile ducts were injected intravenously with mercury-203 (Hg-203) labeled mercuric-chloride (7487947) at a dose equal to 0.16mg/kg mercury (7439976) (Hg). They were injected intraperitoneally with 0 or 0.525mg/kg selenium (7782492) as sodium-selenite (10102188) or sodium-selenate (13410010). Bile, feces, and urine samples were collected for up to 24 hours and assayed for Hg+2. The rats were then killed to determine the tissue distribution of Hg-203. Both sodium-selenite and sodium-selenate significantly reduced cumulative 24 hour urinary and biliary excretion of Hg-203; however, sodium-selenate induced a transient increase in biliary excretion of Hg-203 during the first 2 hours. Sodium-selenite and sodium-selenate decreased the concentration of Hg-203

in the kidney and increased the Hg-203 content of the liver and blood. Sodium-selenite significantly increased accumulation of Hg-203 in the brain. The authors conclude that the mechanisms by which selenium reduces the toxicity of mercury compounds are complex. The differing effects of selenite and selenate on biliary excretion of Hg-203 observed during the first 2 hours after dosing support the notion that reduction of selenate to selenite in the body does not occur rapidly, but takes several hours.

369
TITLE:
Physiological Model for the Pharmacokinetics of Methyl Mercury in the Growing Rat

AUTHORS:
Farris FF
Dedrick RL
Allen PV
Smith JC

SOURCE:
Toxicology and Applied Pharmacology, Vol. 119, No. 1, pages 74-90, 79 references, 1993

ABSTRACT:
The pharmacokinetics of methyl-mercury (22967926) (MeHg) and its metabolite mercuric-mercury were studied in the growing rat. Male Sprague-Dawley-rats averaging approximately 300 grams each were treated with radiolabeled MeHg for studies on mercury (7439976) distribution and examined between 3 and 98 days later. Animals used in metabolism studies were treated with labeled MeHg and whole body radioactivity was monitored daily for 15 days. A model was developed to calculate the concentrations of organic, inorganic, or total mercury in nine body compartments, each representing a major site of mercury accumulation, elimination, and/or effect. MeHg was found to be the dominant mercurial in the brain and blood at all times while both mercurials had similar concentrations in the liver. A significant route of elimination was found to be incorporation of the mercurials into hair with almost 90% of the body burden remaining in the hair at the end of 98 days. Fecal elimination of MeHg accounted for 15% of the original dose and 65% was excreted in the feces as inorganic mercury. Elimination was dominated by biliary secretion with 26% of the demethylation occurring in the liver. Urinary elimination was the most minor elimination pathway examined.

370
TITLE:
Microdetermination of mercury by the oxygen bomb combustion method

AUTHORS:

Fujita M
Takeda Y
Terao T
Hoshino O
Ukita T

SOURCE:
Anal. Chem.; 40(13), 2042-3, 1968; (REF:7)

ABSTRACT:
HAPAB To digest the organic material in the determination of mercury in rice, the combustion was carried out in an oxygen-filled bomb made of stainless steel. No interference from the metal bomb was observed in the mercury determination. The combustion was carried out in the presence of 1.0N nitric acid previously added to the bomb to absorb the oxidation products. The oxidation products were subsequently reduced by addition of hydroxylamine hydrochloride and urea solution. The mercury was extracted with dithizone solution and the mercury dithizonate was submitted to column chromatography, employing an aluminum oxide column, for separation from excess dithizone and was then determined colorimetrically. The absorbance of the eluate at 490 mmicrons was measured using the solvent as reference. By this method, recovery of mercury from rice bran samples to which 0.5 to 1.5 mcg of mercury had been added averaged 93%. To compare the usual wet digestion method with the oxygen-bomb combustion method, samples of unpolished rice grain, rice bran, vegetable oils, normal human hair and liver, kidney and brain of mercury-poisoned rats were analyzed by both methods. Results indicate that theree was no significant difference between values obtained by the two methods. However, advantages of the combustion method are that larger amounts of a sample, 4 g of rice grain and 2 g of rice bran, can be analyzed and the digestion is completed in 15 sec; also, vegetable oils which were hardly digested by the wet digestion method were completely combusted by this method. ANALYSIS 69/01/00, 25 1968

371
TITLE:
Biochemical Basis of the Toxicity of Mercury

AUTHORS:
Sharma DC

SOURCE:
Medical Hypotheses, Vol. 23, No. 3, pages 259-263, 28 references, 19871987

ABSTRACT:
A hypothesis for the biochemical basis of mercury (7439976) toxicity was proposed. According to the author, cells contain numerous binding sites, some of which are vital for normal function of the cells. The vital sites

are sulfhydryl compounds. If mercury binds irreversibly to a vital site, toxicity develops. Coenzyme-A is considered one of the vital cellular components. Mercury toxicity is due, at least in part, to binding to coenzyme-A and the subsequent interference with coenzyme-A-sulfhydrylase functions. Experimental evidence to support the hypothesis was cited. Experimental studies have shown that mercury is accumulated in vital organs that are rich in coenzyme-A, such as the liver, kidney, and brain. Rats dosed with mercuric-chloride (7487947) have shown reduced concentrations of coenzyme-A, cysteine, and glutathione. Some of the clinical symptoms of mercury toxicity can be attributed to a metabolic block of coenzyme-A functions. Mercury induced anemia could be due to impaired heme synthesis resulting from decreased incorporation of succinyl-coenzyme-A. The neurotoxic effects could be due to disruptions of cerebral pyruvate metabolism.

372
TITLE:
Cadmium-109 and methyl mercury-203 metabolism, tissue distribution, and secretion into milk of cows.

AUTHORS:
NEATHERY MW
MILLER WJ
GENTRY RP
STAKE PE
BLACKMON DM

SOURCE:
J DAIRY SCI; 57 (10). 1974 1177-1183

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Metabolism of cadmium-109 and methyl mercury-203 was studied in 6 lactating Jersey cows for 14 days following single tracer oral doses. Most of the cadmium-109 was excreted in feces with only .05% in urine. When the cows were killed 14 to 16 days after dosing, kidney and liver had highest cadmium-109. About .75% of the cadmium-109 was retained in the body with 34% of this in gastrointestinal tract and contents, 32% in liver, and 10% in kidney. In fetal tissues highest cadmium-109 was in kidney, tibia, and liver whereas fetal liver had highest methyl mercury-203. Apparent methyl mercury-203 absorption was 59% with 1.1% in urine. Highest concentration was in kidney, followed by liver, skeletal muscles, heart, smooth muscle, spleen, lung, brain, ovaries, and pancreas. Of total body mercury-203, muscle had about 72% and liver 7%. In 14 days, only .17% of mercury-203 dose was secreted into milk. Cadmium-109 in milk was below detectable limits of .00008% of the dose/day. Feed of cattle kept for meat should be protected from methyl mercury, at least near slaughter. Milk is protected from methyl mercury. In sharp contrast to zinc, little of the ingested cadmium appears in

muscle or milk.

373
TITLE:
The Toxicity of Amalgam: A Preliminary Report

AUTHORS:
Musajo F
Trevisan A
Passi P
Miotti A
Marin VTW
Mattiello G

SOURCE:
Quintessence International, Journal of Practical Dentistry, Vol. 19, No. 11, pages 833-839, 17 references, 19881988

ABSTRACT:
The toxicity of dental amalgam powder was assessed in relation to its mercury (7439976) content. An amalgam containing 575 milligrams of an alloy of silver, copper, and mercury and 660 milligrams of mercury was mixed and condensed and allowed to crystallize in a glass container for 30 days. The amalgam was then subjected to continuous cutting for 1 hour in a nonventilated room, and samples of environmental dust were collected at the level of the operator's and assistant's heads. The toxicity of the amalgam powder was compared to that of mercury using an animal model. Ten adult, male Wistar-Lewis rats were exposed to amalgam powder produced during drilling at a working distance of 40 centimeters from the burr. Another group of rats received an intraperitoneal dose of 1mg/kg of mercuric-chloride (7487947) for 5 consecutive days. Both groups of animals were sacrificed 24 hours post treatment, and the mercury levels of different tissues were quantified. The total amounts of amalgam powder collected from filters placed at the operator and assistant positions of 40 and 80 centimeters from the burr were 0.045 and 0.003mg/m3 respectively. Extrapolation indicated that the Italian threshold limit value of 3.33mg/m3 would be exceeded within 120 minutes at the 40 centimeter position. Exposure of the rats to amalgam powder resulted in an accumulation of mercury in decreasing order in the skin, kidney, spleen, liver, lungs, brain, heart, and testicles. Amalgam powder inhalation was associated with tubulonephrosis and an increase in urinary GGT similar to that observed after treatment with mercuric-chloride.

374
TITLE:
Effects of Lead and Mercury Intoxications on Evoked Potentials

AUTHORS:

Lille F
Hazemann P
Garnier R
Dally S

SOURCE:
Clinical Toxicology, Vol. 26, No. 1, pages 103-116, 45 references, 1988

ABSTRACT:
The effects of mercury (7439976) and lead (7439921) poisoning on visual, auditory, and somatosensory evoked potentials (SEPs) were studied in humans. The cohort consisted of 13 patients, ten males, mean age 37 years, who had been occupationally exposed to lead, nine patients, six males, mean age 29 years, occupationally or accidentally exposed to mercury, and 26 alcoholic patients, 25 males, mean age 35 years. Four lead exposed subjects were alcoholics. The comparisons consisted of 20 healthy males, mean age 37 years. Pattern reversal (PREPs), brain stem auditory potentials (BAEPs), and SEPs were recorded. PREPs in the mercury exposed subjects exhibited an N75 peak latency decrease and an increase in P100145 peak to peak amplitude. The P100/N145 amplitude was also increased in the alcoholic lead exposed subjects. The only abnormal BAEP was an increased peak-I to peak-V latency occurring in one lead exposed and one alcoholic patient. Peripheral velocities of the median nerve were significantly decreased in the lead exposed and alcoholic subjects. The peripheral velocity of the tibial posterior nerve was significantly decreased in the alcoholic patients. Significant increases in central conduction time of the lower limbs occurred in the lead and mercury exposed and alcoholic patients. The SEP amplitudes after upper limb stimulation were increased in all cohort subjects; the greatest increases occurred in the subjects exposed to mercury. The SEP amplitudes and durations were not significantly related to age or length of exposure. The authors conclude that increases in cortical evoked potential amplitudes are not related to a sensory modulating or specific toxic agent. Increases in cortical evoked potentials can be interpreted as an early sign of nervous system injury.

375
TITLE:
DENTAL AMALGAMS AND NEUROPSYCHOLOGICAL FUNCTION

AUTHORS:
FACTOR-LITVAK P

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ DESCRIPTION: There is considerable evidence that some mercury from

"silver fillings" distributes to body tissues, particularly the brain. Occupational exposure to mercury vapor is associated with increases in the prevalence of tremor, peripheral neuropathy, cerebellar dysfunction, and abnormal measures of balance. Occupational exposure also is associated with deficits in neuropsychological tests of memory and visuospatial ability and increased reports of subjective symptoms and disturbed mood. The investigators propose to address the hypothesis that low dose mercury exposure, derived from amalgams in the mouth, may be associated with evidence of neurological dysfunction and neuropsychological deficits. By conducting a cross-sectional study, the investigators will test whether amalgam-derived mercury is adversely associated with tests of neurological function, visuospatial ability, memory and attention/executive function. The study sample will comprise approximately 750-840 Columbia University personnel, ages 30-49 years. Based on preliminary work, it is known that the cohort will have a wide range of visible amalgam surfaces. Measures of exposure will be urinary mercury concentration and the numbers of amalgam surfaces, total and occlusal. The proposed outcome measures tap a wide range of neurological and neuropsychological functions. A variety of tests will assess four domains of neuropsychological function: visuomotor/visuospatial function, memory, attention and executive function, and vocabulary. A self-reported questionnaire of mood and a symptom checklist will also be administered. In addition, the investigators will collect quantitative measures of postural sway. After control for confounding variables, including measures of social desirability and hypochondriasis, the dose-response relationships between exposure and each functional domain will be described. Results from this study will have potential public health applications. Adverse associations, if found, might lead to less use of mercury amalgams. Alternatively, evidence favoring the null hypothesis would allay widespread fears that a variety of health problems may be associated with amalgam exposure.

376

TITLE:

Effects of Maternal Dietary Supplementation with Selenite on the Postnatal Development of Rat Offspring Exposed to Methyl Mercury In Utero

AUTHORS:

Fredriksson A
Teiling Gardlund A
Bergman K
Oskarsson A
Ohlin B
Danielsson B
Archer T

SOURCE:

Pharmacology and Toxicology, Vol. 72, No. 6, pages 377-382, 36 references,

1993

ABSTRACT:

The effects of the addition of selenium (7782492) to the diet on the distribution of mercury (7439976) and postnatal development were examined in rats whose mothers were orally exposed to methyl-mercuric-chloride (115093) during gestation. Female Sprague-Dawley-rats received diets containing either 0.3 parts per million (ppm) or 1.3ppm selenium. After 8 weeks the rats were mated. On gestation days six through nine the pregnant females were dosed with 2 or 6mg/kg methyl-mercury per day. Behavioral testing was performed in the offspring at 2 months of age. The results of the study showed that supplementing the diet with selenium partly antagonized some adverse effects of methyl-mercury such as hypoactivity, particularly in the higher dose group. No changes were noted in physical development or body weight except a tendency to decreased weight in offspring of mothers exposed to 6mg/kg. The glutathione-peroxidase activity was significantly increased in rats fed the selenium supplemented diet. The authors conclude that dietary selenite may provide partial protection against some postnatal toxic manifestations in rat offspring exposed to methyl-mercury in-utero. The mechanism for the protective effect is not clear, but may be related to increased complexation of methyl-mercury to glutathione and other thiols in the brains of the offspring.

377

TITLE:

DENTAL AMALGAMS AND NEUROPSYCHOLOGICAL FUNCTION

AUTHORS:

FACTOR-LITVAK P

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ DESCRIPTION: There is considerable evidence that some mercury from "silver fillings" distributes to body tissues, particularly the brain. Occupational exposure to mercury vapor is associated with increases in the prevalence of tremor, peripheral neuropathy, cerebellar dysfunction, and abnormal measures of balance. Occupational exposure also is associated with deficits in neuropsychological tests of memory and visuospatial ability and increased reports of subjective symptoms and disturbed mood. The investigators propose to address the hypothesis that low dose mercury exposure, derived from amalgams in the mouth, may be associated with evidence of neurological dysfunction and neuropsychological deficits. By conducting a cross-sectional study, the investigators will test whether amalgam-derived mercury is adversely associated with tests of neurological function, visuospatial ability, memory and attention/executive function.

The study sample will comprise approximately 750-840 Columbia University personnel, ages 30-49 years. Based on preliminary work, it is known that the cohort will have a wide range of visible amalgam surfaces. Measures of exposure will be urinary mercury concentration and the numbers of amalgam surfaces, total and occlusal. The proposed outcome measures tap a wide range of neurological and neuropsychological functions. A variety of tests will assess four domains of neuropsychological function: visuomotor/visuospatial function, memory, attention and executive function, and vocabulary. A self-reported questionnaire of mood and a symptom checklist will also be administered. In addition, the investigators will collect quantitative measures of postural sway. After control for confounding variables, including measures of social desirability and hypochondriasis, the dose-response relationships between exposure and each functional domain will be described. Results from this study will have potential public health applications. Adverse associations, if found, might lead to less use of mercury amalgams. Alternatively, evidence favoring the null hypothesis would allay widespread fears that a variety of health problems may be associated with amalgam exposure.

378

TITLE:

Effect Of Methylmercury And Some Metal Ions On Microtubule Networks In Mouse Glioma Cells And In Vitro Tubulin Polymerization

AUTHORS:

Miura K
Inokawa M
Imura N

SOURCE:

Toxicology and Applied Pharmacology, Vol. 73, No. 2, pages 218-231, 44 references, 19841984

ABSTRACT:

The effects of methyl-mercury (22967926) on microtubule inhibition were examined in mouse glioma cells. Tubulin was prepared from porcine brain homogenates. Colchicine (64868) sensitivity of cytoplasmic microtubules from mouse glioma cells were assayed. Tubulin polymerization and depolymerization of microtubules were assayed. Electrophoretic analysis of porcine tubulin preparations showed minor bands in the high molecular weight range. Polymerization of tubulin occurred in the presence of methyl-mercury; viscosity increased quickly and reached a steady state at 20 minutes. The increased viscosity was due to formation of numerous microtubules. Inhibition of polymerization of tubulin was dependent on methyl-mercury concentration; 50 percent inhibition was caused by 0.000076 moles methyl-mercury and by 0.000038 moles mercuric-chloride (7487947). Decreases in viscosity were accompanied by a decrease in number and length

of reconstituted microtubules, depending upon the mercury concentration. Tubulin polymerization was inhibited by colchicine at 0.000006 and 0.0000008 moles in the presence or absence of 4 moles glycerol, respectively. When mouse glioma cells were treated with antiserum, a filamentous network was seen in cytoplasm of all interphase cells, and the spindle and stem bodies of mitotic cells were stained. After incubation with colcemid (477305) before antiserum treatment, only a faint diffused fluorescence staining was seen. After incubation for 30 minutes with methyl-mercury, the density of the fibrous structure of microtubules was thinner than in controls. Microtubule networks disappeared after 1 hour of incubation. The authors conclude that the antiserum contains tubulin specific antibodies. Only methyl-mercury affects cellular microtubules. Other ions interfere with other sites in the cells and can depress tubulin polymerization.

379

TITLE:

Autometallographic Determination of Inorganic Mercury Distribution in the Cortex of the Calcarine Sulcus of the Monkey Macaca fascicularis following Long-Term Subclinical Exposure to Methylmercury and Mercuric Chloride

AUTHORS:

Charleston JS
Body RL
Mottet NK
Vahter ME
Burbacher TM

SOURCE:

Toxicology and Applied Pharmacology, Vol. 132, No. 2, pages 325-333, 37 references, 1995

ABSTRACT:

The distribution by cell type of inorganic mercury (7439976) (Hg) after methyl-mercury (22967926) (MeHg) and mercuric-chloride (7487947) (IHg) exposure was determined to establish the cell types responsible for MeHg demethylation and its subsequent sequestration. Four groups of adult female monkeys were orally MeHg at 50 micrograms (microg) Hg/kilogram (kg) body weight/day for 6, 12, or 18 months (mo); a fifth group was intravenously infused with IHg at a dose of 200microg/kg/day for 3mo. The animals were then killed and brain tissue slabs were prepared for autometallography with excess silver ions labeling Hg deposits. The 6mo MeHg exposed monkeys had significant silver grains distributed across all layers of the cortex. A similar distribution across all cortical layers was present in the 12 and 18mo exposed groups, with the staining intensity tending to be greater. The astrocytes and microglia accumulated high levels of Hg compared to other cell types. Moderate Hg deposits were detected in these cell types at 6mo, which became heavier with longer

exposures. These cells often contained one or several large aggregate grains located in a polar or bipolar arrangement near the nucleus. In the 12 and 18mo MeHg exposed groups, individual cells had obscured nuclei due to heavy labeling. Neurons in the 6mo MeHg exposure group were either unlabeled or labeled finely. By 12 and 18mo, labeling of neurons increased in frequency and amount. The majority of oligodendrocytes, endothelial cells, and pericytes showed no staining of Hg in all MeHg exposure groups. The authors conclude that astrocytes and microglia accumulate both the earliest and largest levels of IHg after long term MeHg exposure. While the mechanism of IHg accumulation after MeHg exposure cannot be determined, other findings suggest the brain is capable of undergoing demethylation. The distribution of IHg in astrocytes and microglia indicates that one or both of these cell types may be involved in the demethylation process.

380
TITLE:
Cerebral Changes In The Course Of Intoxication With Mercury Phenylacetate

AUTHORS:
Kozik MB
Wigowska-Sowinska J

SOURCE:
Experimentelle Pathologie, Vol. 16, pages 267-275, 17 references, 19781978

ABSTRACT:
Morphological and histochemical changes in rat brains intoxicated with subacute and chronic doses of mercury-phenylacetate were studied. Wistar-rats were given intragastrically a daily dose of 0.1 gram mercury-phenlyacetate for 10 days, or 0.05 gram for 30 days. Controls were not treated. Animals were killed and brains were fixed. The activities of thiamine-pyrophosphatase (TPPase), nonspecific esterase (NsE), acetylcholinesterase (AChE), nonspecific cholinesterase, acid-phosphatase, alkaline-phosphatase (AP), and adenosine-triphosphatase (ATPase) were measured. Widespread vacuolization of neurocytes in the basal nuclei, the anterior nucleus of the thalamus, and pyramidal cells of the Ammon's Horn were seen in the subacutely intoxicated group. Degeneration of white matter was noted. Cytoplasmic vacuolization of neurons of many cerebral structures was noted in the chronically intoxicated rats. TPPase activity increased following intoxication with both subacute and chronic doses of mercury-phenylacetate. AChE activity was slightly affected by poisoning. Activities of NsE and AP were not affected. Acid-phosphatase activity decreased in the cortex of Ammon's Horn in both treated groups. ATPase activity dropped in capillaries of many cerebral regions. In chronically intoxicated rats, ATPase activity disappeared entirely in some cases. The authors conclude that the effects of mercury-phenylacetate intoxication are dependent on the duration of

poisoning.

381
TITLE:
Mercury distribution and concentration in tissues of Rhizoprionodon terraenovae shark from the Gulf of Mexico.

AUTHORS:
NUNEZ NOGEIRA G
BAUTISTA ORDONEZ J
ROSILES MARTINEZ R

SOURCE:
VETERINARIA - MEXICO; 29 (1). 1998. 15-21.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In this study mean mercury concentrations were measured in gills (0.66 mg/kg), brain (0.45 mg/kg), liver (0.16 mg/kg), pancreas (0.51 mg/kg), muscle (0.63 mg/kg) and kidney (0.42 mg/kg) dry weight bases from 44 sharks (Rhizoprionodon terraenovae) captured at the seashore from the Gulf of Mexico (Veracruz and Tabasco states). Mercury concentration was measured using both the atomic absorption spectrophotometric and bohydride generation methodologies. A comparison was made between mean mercury concentration in males (0.57 mg/kg) and females (0.75 mg/kg). As well as gills 0.47, muscle 0.64, brain 0.51, kidney -0.81, liver -0.61 and pancreas 0.91 concentration, between length and age of individuals. In order to assess the risk due to consumption of meat from these sharks, the maximum acceptable value of mercury as established by the joint Committee FAO was taken into account and compared to the amount of Hg ingested when shark meat was consumed. With this analysis, it was

382
TITLE:
Neurologic Features of Chronic Minamata Disease (Organic Mercury Poisoning) and Incidence of Complications with Aging

AUTHORS:
Uchino M
Tanaka Y
Ando Y
Yonehara T
Hara A
Mishima I
Okajima T
Ando M

SOURCE:

Journal of Environmental Science and Health. Part B: Pesticides, Food Contaminants, and Agricultural Wastes, Vol. B30, No. 5, pages 699-715, 28 references, 1995

ABSTRACT:
A study was conducted characterizing the neurological and aging related features of Minamata disease (organic mercury poisoning). Neurological status and complications were assessed in a group of 80 Japanese patients with confirmed Minamata disease ranging in age from 26 to 90 years. Several neurologic abnormalities were noted, the most widespread of which were constriction and depression of the visual fields which were identified in 51.9% and 68.4% of the patients, respectively. Other commonly recognized neurologic abnormalities included hearing, coordination, deep tendon reflexes, and sensory sensation disturbances. Eight categories of complications, hypertension and cerebrovascular disease, abnormal brain computed tomography (CT), organic ophthalmologic disorders, organic ear disease, locomotor disease, psychoneurologic disease, serological test for syphilis, and urine analysis were identified. Significant increases in the incidences of hypertension and cerebrovascular diseases, organic ophthalmologic disorders, presbyacusias, and cervical spondylosis deformans were seen with age. Compared with a survey conducted earlier, decreases in the incidences of complicated hypertension and cataracts were seen along with increases in the incidences of abnormal brain CT, presbyacusias, cervical spondylosis deformans, and positive urine sugar tests.

383
TITLE:
Organochlorines, mercury, and selenium in great blue heron eggs from Indiana Dunes National Lakeshore, Indiana.

AUTHORS:
Custer TW
Hines RK
Stewart PM
Melancon MJ
Henshel DS
Sparks DW

SOURCE:
Journal of Great Lakes Research 1998;24(1):3-11

ABSTRACT:
In 1993, 20 great blue heron (Ardea herodias; GBH) eggs (one per nest) were collected from a colony at the Indiana Dunes National Lakeshore, Indiana (INDU). The eggs were artificially incubated until pipping and were then analyzed for organochlorines, mercury, and selenium. Livers of embryos were analyzed for hepatic microsomal ethoxyresorufin-O-dealkylase

(EROD) activity. Brains were measured for asymmetry. Egg-laying began in early April and the mean clutch size was 4.2 eggs per clutch. Organochlorine concentrations were generally low (geometric mean p,p'-DDE = 1.6 ug/g wet weight; polychlorinated biphenyl (PCB) = 4.9 ug/g); however, one egg had elevated concentrations of p,p'-DDE (13 ug/g) and PCBs (56 ug/g). EROD activity in the embryos analyzed from INDU was not elevated. The frequency (11%) of brain asymmetry was low. Eggshells averaged 3.4% thinner than eggshells collected prior to the use of DDT. Mercury (geometric mean = 0.9 ug/g dry weight) concentrations in GBH eggs were within background levels. Selenium (4.0 ug/g dry weight) concentrations in eggs were above background levels, but below a concentration threshold associated with reproductive impairment.

384

TITLE:

Effect of Long-Term Uptake of Mercuric Sulphide on Thyroid Hormones and Glutathione in Mice

AUTHORS:

Sin YM

Teh WF

SOURCE:

Bulletin of Environmental Contamination and Toxicology, Vol. 49, No. 6, pages 847-854, 17 references, 1992

ABSTRACT:

The effects of mercuric-sulfide (1344485) on thyroid hormones and glutathione were studied in mice. Female Swiss-mice were gavaged with mercuric-sulfide at a dose equivalent to 6 micrograms per gram divalent mercury (7439976) daily for 4 weeks. Body weight gain was monitored. Selected mice were killed after 1, 2, 3, and 4 weeks of exposure and the brain, kidneys, and livers were removed and assayed for mercury and glutathione. Blood samples were collected and analyzed for plasma thyroid hormones (T3 and T4). Tissue mercury concentrations were not significantly increased above the control values except in the kidneys of mice analyzed at the end of week one. Plasma T3 concentrations were not significantly affected by mercuric-sulfide. Plasma T4 concentrations were significantly decreased after 1 and 4 weeks of exposure. Glutathione concentrations were significantly increased in the brains of mice examined after 2 and 3 weeks exposure. Mercuric-sulfide did not significantly affect glutathione concentrations in any of the other tissues. Body weight gain was not significantly affected by mercuric-sulfide. The authors conclude that exposing mice to mercuric-sulfide for 4 weeks decreases plasma T4 concentrations without significantly affecting plasma T3 concentrations. This finding suggests that prolonged exposure to mercury could disrupt the activity of thyroid cells or the hypothalamus/pituitary axis.

385
TITLE:
In Vitro Interaction of Heavy Metals with Ouabain Receptors in Rat Brain Microsomes

AUTHORS:
Chetty CS
Stewart TC
Cooper A
Rajanna B
Rajanna S

SOURCE:
Drug and Chemical Toxicology, Vol. 16, No. 1, pages 101-110, 17 references, 1993

ABSTRACT:
The effects of heavy metals on the binding of ouabain to microsomal membranes were studied. Microsomal suspensions prepared from the brains of male Sprague-Dawley-rats were incubated with thio(sulfhydryl) (SH) compounds followed by solutions of mercury (7439976), lead (7439921), or cadmium (7440439) for 5 minutes and the binding of radiolabeled ouabain were determined. A reduction in the metal induced inhibition of ouabain binding was seen following preincubation with SH compounds. Dithiothreitol was the most effective, especially for mercury and lead, in decreasing ouabain inhibition even when used in concentrations as low as 50 micromoles/liter. Cysteine provided partial protection to the effects of the metals at a concentration of 100 micromoles, while glutathione demonstrated partial protection to the effects of mercury but not to the effects of cadmium or lead.

386
TITLE:
Comparative Effects of Inorganic Divalent Mercury, Methylmercury and Phenylmercury on Membrane Excitability and Synaptic Transmission of CA1 Neurons in Hippocampal Slices of the Rat

AUTHORS:
Yuan Y
Atchison WD

SOURCE:
Neurotoxicology, Vol. 15, No. 2, pages 403-411, 30 references, 1994

ABSTRACT:
The effects of inorganic divalent mercury (7439976), methylmercury (22967926) (MM), and phenylmercury (PM) on membrane excitability and

synaptic transmission in CA1 neurons of the hippocampal slices from rat brains were investigated. Hippocampal slices were obtained from the brains of Sprague-Dawley-rats and conventional extracellular recordings were made in the CA1 regions using tungsten electrodes. Population spikes (PSs) and excitatory postsynaptic potentials (EPSPs) were recorded. Mercuric-chloride (7487947) (MC), MM, and PM were added to artificial cerebrospinal fluid (ACSF) just prior to the recordings being made. Results showed that all three mercurials significantly reduced the amplitude of the PSs and eventually blocked them, although their time courses were somewhat different. PM caused biphasic changes in PS amplitude, and seemed to be more effective at 20 micromolar (microM) concentrations. At 100microM, the times to complete block were about the same for PM and MM, and were slower than with MC. However, MC had relatively weak effects on EPSPs, which were never blocked even after 120 minutes exposure to 100microM. MM and PM effects on EPSPs were similar to its effects on PSs. In this case, MM caused a biphasic alteration of EPSPs. The most potent effects were with 20mM PM and, at 100mM, the time to block was intermediate between MM and MC. Reversibility of effects were compared after washing the slices for 90 minutes in ACSF containing D-penicillamine (DP). As washing proceeded, the effects of MC on PSs and EPSPs were reversed. While MM effects on PSs were only partially reversed, EPSPs rapidly returned to control levels. PM effects were not reversed by washing with DP. With low intensity stimuli, washing did not reverse MM and PM blocked PSs, but amplitudes of PSs were increased with higher intensity stimuli, suggesting partial recovery. DP completely reversed the effects of MC on PSs. The authors conclude that the primary effects of the three mercurials on PSs may be due to decreased neural excitability, and may be connected with lipophilicity differences.

387

TITLE:

Analysis of Methyl Mercury Binding Sites on Tubulin Subunits and Microtubules

AUTHORS:

Vogel DG
Margolis RL
Mottet NK

SOURCE:

Pharmacology and Toxicology, Vol. 64, No. 2, pages 196-201, 21 references, 19891989

ABSTRACT:

The localization and affinity of methylmercury binding sites on microtubules were studied in-vitro. Beef brain tubulin was incubated with 10(-5) to 1.4x10(-4) molar (M) mercury-203 labeled methylmercury-hydroxide (1184572) (MMOH) in the presence or absence of soluble (unassembled)

microtubulin protein. The extent of equilibrium and steady state binding was determined. Under equilibrium conditions only one class of methylmercury binding site was seen. It contained approximately 15 sites having an apparent dissociation constant (Kd) of 7.25 micromolar (microM). Under steady state conditions in the absence of microtubule protein only one type of binding site containing 8.85 sites with Kd 39.8microM was observed. In the presence of microtubulin protein only one type of site was observed containing 4.15 binding sites with Kd 19.9microM. Microtubulin protein that had gone through two cycles of polymerization and depolymerization was incubated with 0 to 2x10(-4)M MMOH. The extent of mercury/tubulin dimer binding was determined. The mercury/tubulin dimer ratios in the first cycle protein was 0.96. This represented a steady state assembly level of 46 percent. The second cycle microtubulin protein contained detectable amounts of label which was estimated to be one methylmercury molecule per every two polymeric dimers at a MMOH concentration of 4x10(-5)M. The authors conclude that methylmercury has at least one class of binding sites on tubulin. This class probably consists of free sulfhydryl groups. Methylmercury can bind directly to microtubule subunits, which can then bind to the ends of polymers. The end/binding sites on tubulin dimers are indistinguishable from the surface binding sites.

388

TITLE:

Tissue concentrations of mercury after chronic dosing of squirrel monkeys with thiomersal

AUTHORS:

Blair AMJN
Clark B
Clark AJ
Wood P

SOURCE:

Toxicology; VOL 3 ISS Feb 1975, P171-176, (REF 11)

ABSTRACT:

IPA COPYRIGHT: ASHP No evidence of toxicity was seen when squirrel monkeys were dosed intranasally with saline or 0.002% w/v thiomersal (thimerosal) daily for 6 months. The total amounts of thimerosal given were 418 mcg (low dose group) and 2,280 mcg (high dose group). This was equivalent to 207 and 1,125 mcg mercury. The dose differential was achieved by more frequent administration to the high dose group. Mercury concentrations were significantly raised over control values in brain (high dose group only), liver, muscle and kidney, but not in blood. Concentrations were highest in the kidney, moderate in liver and lowest in brain and muscle. Much of the mercury was present in the inorganic form (37-91%).

389
TITLE:
Induction of apoptosis by mercury compounds depends on maturation and is not associated with microbial activation.

AUTHORS:
MONNET-TSCHUDI F

SOURCE:
JOURNAL OF NEUROSCIENCE RESEARCH; 53 (3). 1998. 361-367.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The earliest sign of neurotoxicity observed after exposure of three-dimensional brain cell cultures to low concentrations of mercury compounds is a microglial reaction. We hypothesized that an induction of apoptosis by mercury compounds could be an activating signal of the microglial reaction. Aggregating brain cell cultures of fetal rat telencephalon were treated for 10 days with either mercury chloride or monomethylmercury chloride at noncytotoxic concentrations during two developmental periods: from day 5 to 15, corresponding to an immature stage, and from day 25 to 35 corresponding to a mature stage. Apoptosis was evaluated by the TUNEL technique. It was found that both mercury compounds caused a significant increase in the number of apoptotic cells, but it exclusively in immature cultures exhibiting also spontaneous apoptosis. Double staining by the TUNEL technique combined with either neuronal or astroglial markers revealed that the proportion of cells undergoing

390
TITLE:
Comparison of the sublethal effect of mercury and lead on visceral dehydrogenase system in three inland teleosts.

AUTHORS:
SHAFFI SA

SOURCE:
PHYSIOL RES; 42 (1). 1993. 7-15.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The sublethal effect of mercury and lead was investigated on visceral (liver, muscle, gill, kidney and brain) succinic, malic and lactic dehydrogenases in Labeo rohita, Clarias batrachus and Chana punctatus in acute experiments. The highest decrease of succinic, malic and lactic dehydrogenase was recorded in the hepatic tissue in comparison to muscle, brain, kidney and gill. This decrease was greater in L. rohita than in C. batrachus or in C. punctatus. Mercury was more

effective than lead. Marked variations in the activities of the three dehydrogenases in dark tissues (liver, kidney) were noted after exposure to mercury than lead in the above mentioned species. The observed dehydrogenase variations are discussed in relation to the breakdown of gas exchange at the lamellar level, to visceral hypoxia, hypoglycaemia, impaired aerobic and anaerobic pathways, formation of a metalloenzyme complex and alterations in mitochondrial electron transport.

391
TITLE:
Essential and non-essential metals in fetuses and infants.

AUTHORS:
Lutz E
Lind B
Vahter M

SOURCE:
Journal of Trace Elements in Experimental Medicine 1992;5(2):123

ABSTRACT:
In developing tissues the access of essential metals is extremely important and the damage by non-essential or toxic elements could affect development. In the central nervous system this damage is irreversible but can remain undetected until the affected functions of the CNS are needed, perhaps months or years later. From epidemiological studies of children exposed to lead and to mercury we know that even a very low chronic exposure can give subtle changes in psychomotor development. Cadmium accumulates in the kidney and so does mercury which apart from the toxic effect seems to induce an autoimmune reaction, glomerulonephritis, in sensitive individuals. There is a lack of data on tissue concentrations of toxic metals in fetuses and infants. In a pilot study of six cases, three fetuses in the second and third trimester and three infants of age up to six months samples from brain and renal tissue have been taken at autopsy for analysis of lead, mercury, cadmium, zinc, copper and selenium. The cases constitute all cases at two clinics in Stockholm during winter 1992-1993.

392
TITLE:
Effects of methyl mercury on protein synthesis in vitro.

AUTHORS:
SYVERSEN T LM

SOURCE:
ACTA PHARMACOL TOXICOL; 49 (5). 1981 (RECD. 1982). 422-426.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Methyl mercury interacts with protein synthesis in vivo and in vitro. A rat brain postmitochondrial supernatant was used for studies in vitro. Inorganic Hg2+ was a more potent inhibitor of protein synthesis than methyl mercury, puromycin or cycloheximide. The inhibitory effect of methyl mercury was potentiated by puromycin. Methyl mercury may cause disintegration of polysomes in brain cells.

393

TITLE:

Retinal Function Of Rats Exposed To Organomercurials

AUTHORS:

Gramoni R

SOURCE:

Neurotoxicity of the Visual System, Merigan, W. H., and B. Weiss, Editors; Raven Press, New York, pages 101-111, 29 references, 19801980

ABSTRACT:

The effects of exposure to organomercurials on retinal function were studied in rats. Adult Wistar-rats were injected subcutaneously with phenylmercury (23172374) at 0.59 milligram per kilogram (mg/kg) per day for 7 weeks. Control rats were injected with physiological saline. Another group of Wistar-rats was injected subcutaneously with 0.4mg/kg/day methylmercury (22967926) 6 days per week for 9 weeks. Electroretinograms (ERGs) of the exposed and control animals were recorded before exposure and once a week for 7 weeks after exposure. Urine samples over a 24 hour period were collected each time ERGs were recorded. Total concentrations of mercury in urine were measured by atomic absorption. After drug injection and ERG analysis, rats were sacrificed. Brain, eyes, liver and kidneys were dissected, and mercury (7439976) content was determined. Localization of mercury in retina was determined by an electron microscopic technique. Mercury contents of brain, eyes, liver, and kidneys were 0.14, 0.08, 2.5, and 30.4 micrograms per gram tissue, respectively. Rats exposed to phenylmercury did not show any differences in ERGs in relation to controls. Electron microscopy revealed electron dense granules in retinas that contained mercury and sulfides. Retinal membranes were the main site of localization. No such granules were present in retinas of control rats. Rats exposed to methylmercury showed altered ERG patterns. Retinal membranes also contained granules. The author concludes that exposure to methylmercury results in functional changes in the retina whereas phenylmercury exposure does not reveal any functional changes.

394

TITLE:

Tissue And Cellular Toxicology Of Metals

AUTHORS:
Goyer RA
Cherian MG

SOURCE:
Developments in Toxicology and Environmental Science, Vol. 1, Clinical Chemistry and Chemical Toxicology of Metals, pages 89-103, 19 references, 19771977

ABSTRACT:
The patterns of cellular injury produced by the toxic metals lead (7439921), cadmium (7440439), and mercury (7439976) are reviewed. A morphological feature of lead poisoning in exposed humans and experimental animal is the intranuclear inclusion body. Lead induced inclusion bodies are common in kidney and liver and have been found in brain and osteoclasts of bone marrow. Mitochondria in proximal tubular lining cells of kidneys in individuals with excessive exposure to lead are morphologically and functionally normal. The decrease in reabsorption of amino acids by the renal tubule that occurs in lead poisoning may be related to the effect of lead on mitochrondria in these cells. Clinical observations have suggested that lead intoxication has an effect on the renin/aldosterone response to sodium deprivation. Cadmium, like lead, has a long life in the body; life long exposure to cadmium increases cadmium content of the renal cortex. Cadmium induced nephropathy from industrial exposure to cadmium reveals that renal tubular necrosis and eventual chronic nephropathy with renal failure occurs when cadmium concentrations reach about 200 micrograms per gram tissue. The metabolism of cadmium is closely related to a low molecular weight protein called metallothionein; metallothionein plays a central role in the ability of cells to accumulate cadmium and may be an important factor in producing the cell injury characteristic of cadmium nephropathy. The brain is the principal target organ for mercury toxicity; individuals with methyl-mercury (22967926) poisoning present clinically with central nervous system symptoms. Mercury produces densities in mitochondria corresponding to the onset of tubular cell necrosis, observed following cadmium/metallothionein injection. The authors conclude that lead, cadmium, and mercury have different patterns of cellular metabolism and produce different patterns of cell injury.

395
TITLE:
The Influence Of Weight And Other Physiological Changes During Pregnancy And Lactation On The Toxicities Of Mercury And Cadmium

AUTHORS:
Magos L
Webb M

SOURCE:

Reproductive and Developmental Toxicity of Metals, Clarkson, T. W., G. F. Nordberg, and P. R. Sager, Editors; Plenum Press, New York, pages 417-436, 37 references, 19831983

ABSTRACT:

The influence of physiological changes during pregnancy and lactation on the toxicities of mercury (7439976) and cadmium (7440439) is reviewed. Depressed weight gain or weight loss is one of the first effects of methylmercury (22967926) poisoning in the rat. The treatment of non pregnant rats with methylmercury results in a weight loss whereas pregnant rats receiving the same treatment continue to gain weight. The ability of the placental/fetal unit to withdraw methylmercury from the maternal body is very limited in time due to its rapid development late in gestation. The uptake of methylmercury by the brain decreases with the progression of pregnancy. Acute exposure to mercury and cadmium shows that the former accumulates in the kidneys and the latter in the liver. Renal damage late in gestation is not a direct effect of cadmium since accumulation in the kidneys of pregnant rats is less than in non pregnant rats. The median lethal dose (LD50) of mercuric-chloride (7487947) does not change during pregnancy, but the acute toxicity of cadmium-chloride (10108642) is significantly increased at the end of pregnancy. Cadmium, but not mercury, produces severe placental hemorrhage possibly due to the much higher concentrations of cadmium late in pregnancy. Lactation is found to decrease the body burden of methylmercury and the intensity of coordination disorders but does not accelerate clearance from the brain. The authors conclude that weight loss indicates non pregnant rats to be more sensitive to methylmercury than pregnant rats, but comparison of coordination disorders would indicate the opposite conclusion.

396

TITLE:

Mortality and cancer incidence in chloralkali workers exposed to inorganic mercury

AUTHORS:

Barregêard L
Sèallsten G
Jèarvholm B

SOURCE:

British Journal of Industrial Medicine Feb. 1990, Vol.47, No.2, p.99-104. 28 ref.

ABSTRACT:

Mortality and cancer incidence were studied in men exposed to inorganic mercury at eight Swedish chloralkali plants where individual biological

monitoring data were available. Urinary mercury excretion has declined from about 200|g during the 1950s to less than 50|g/L today. These workers had also been exposed to chlorine and static magnetic fields. At some of the plants there had been a low degree of exposure to asbestos. In total, 1190 men had been monitored for at least one year between 1946 and 1984. Their mortality and cancer incidence were compared with those of the general male population. Mortality from all causes was not significantly increased. Cardiovascular mortality was slightly increased for no known reason. An excess of lung tumours was seen possibly caused by previous exposure to asbestos. Mortality from non-malignant diseases of the brain and the kidneys, the main target organs in mercury poisoning, was not increased, nor was the incidence of brain tumours (3 observed v 1.1 expected) or kidney tumours (3 observed v 1.9 expected).

397

TITLE:

Translocation and fluxes of mercury in neonatal and maternal rats treated with methyl mercuric chloride during gestation.

AUTHORS:

GARCIA JD
YANG MG
WANG J HC
BELO PS

SOURCE:

PROC SOC EXP BIOL MED; 147 (1). 1974 224-231

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Pregnant rats during the 16th day of gestation were force fed a tracer dose of 203-Hg as methyl mercuric chloride. At arturition, 7, 14, 21, and 28 days after parturition, the 203-Hg radioactivities in the different brain parts and organs of maternal and neonatal rats were determined. The concentration of 203-Hg in the brain, brain parts, and organs of mothers and pups decreased with time after force-feeing. At all time periods, the cerebrum had the greatest quantity of 203-Hg and the pituitary had the lowest in mothers and pups due primarily to the size of the tissue. The blood concentration of 203-Hg in the pups at birth was 27% higher than that of the dams. Similarly, at birth, the concentration of 203-Hg in the different brain parts and organs of the pups, except in the kidney, was higher than corresponding tissues in the dams. Hg pool size in the brain and brain parts of maternal and neonatal rats also primarily reflected the size of the tissues studied. In general, a faster turnover of Hg in the pups was found. The half-life of Hg in the maternal brain, kidneys, liver, and gastrocnemius were 10.79, 27.61, 9.38, and 6.73 days, respectively. In the pups, corresponding half-life values were 10.00, 20.20, 13.50, and 12.86 days. In another study, foster rearing of pups originally contaminated in utero with the

radioactive Hg showed that Hg excreted by pups recirculated to the foster dams. The uptake of 203-Hg in the brain, brain parts and organs of foster dams ranged from 0.0001-0.067% of the original dose administered to the mothers of the contaminated pups.

398
TITLE:
Metallothionein induction in fetal rat brain and neonatal primary astrocyte cultures by in utero exposure to elemental mercury vapor (Hg0).

AUTHORS:
ASCHNER M
LORSCHEIDER FL
COWAN KS
CONKLIN DR
VIMY MJ
LASH LH

SOURCE:
BRAIN RESEARCH; 778 (1). 1997. 222-232.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Brain metallothionein (MT) protein and mRNA levels were determined in the fetal rat following in utero (gestational days 7-21) exposure to elemental mercury vapor (Hg0; 300 mug Hg/m3; 4 h/day). Total RNA was probed on northern blots with (alpha-32P)dCTP-labeled synthetic cDNA probes specific for rat MT isoform mRNAs. The probes for MT-I and MT-II mRNA hybridized to a single band of approximately 550 and 450 nucleotides, respectively. Expression of whole brain MT-I mRNA in full-term fetal rats (day 21) was significantly increased ($P < 0.03$) by in utero exposure to Hg0- compared to nonexposed controls. This corresponded to a 14-fold increase ($P < 0.001$) in fetal brain Hg concentration after in utero Hg0 exposure. In addition, astrocytes from both control and in utero Hg0-exposed fetuses were isolated, and neonatal primary astrocyte cultures were established and maintained in vitro for up to 3 weeks without additional experimental intervention. Astrocyte monolayers d

399
TITLE:
Effects of Methylmercury on Neurotransmitter Release from Rat Brain Synaptosomes

AUTHORS:
Minnema DJ
Cooper GP
Greenland RD

SOURCE:
Toxicology and Applied Pharmacology, Vol. 99, No. 3, pages 510-521, 44 references, 1989

ABSTRACT:
The effects of methyl-mercury (22967926) (MeHg) on the release of several neurotransmitter substances from superfused rat brain synaptosomes under conditions of both spontaneous and depolarization evoked release were described. Adult male Long-Evans-rats exposed to concentrations of MeHg ranging from 0.5 to 5.0 micromolar MeHg demonstrated a concentration dependent increase in the spontaneous release of dopamine from brain striatum, gamma-aminobutyric-acid from the cortex, and acetylcholine from the hippocampus. Calcium influx into the nerve terminal was not induced by MeHg. The spontaneous transmitter release persisted in the presence of low extrasynaptosomal sodium, indicating the effect on the release was not mediated by either sodium, potassium-ATPase inhibition or selective increases in membrane sodium permeability. Small increases were noted in calcium-45 efflux from synaptosomes preloaded with calcium-45. Large increases in calcium-45 efflux were noted from preloaded isolated mitochondria. An increase was noted in the efflux of deoxyglucose phosphate from synaptosomes. The authors suggest that the increase in spontaneous transmitter release is the result of transmitter leakage occurring subsequent to MeHg induced increases in synaptosomal membrane permeability. The possible effects of MeHg on intrasynaptosomal calcium homeostasis can not be ruled out.

400
TITLE:
HEALTH HAZARDS OF METHYLMERCURY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ The overall objective is to more clearly define human health risks from prenatal exposure to methylmercury compounds (MeHg). To achieve this objective, we plan to measure dose-response relationships in human populations exposed to methylmercury and to conduct complementary investigations to characterize more precisely both prenatal and early postnatal body burdens of methylmercury including transport to the target organ, the brain.
The aim of the human studies is to test the hypothesis, developed in our previous study of prenatal exposures in the Iraq population, the subtle psychological and behavioral changes in prenatally exposed children can be quantitatively related to the mothers exposure during pregnancy using

dose- response models. MeHg concentration in head hair has been used as the best indicator of the dose. We plan to directly test the assumption that hair levels indicate levels of methylmercury in the target tissue, the brain, by use of human autopsy data. We plan to examine the mechanisms of transport of MeHg from blood to brain across the blood-brain barrier to better understand the factors that limit the accuracy of hair mercury as a biological monitor of dose to the target tissue. We have preliminary evidence that MeHg crosses the blood-brain barrier on the neutral amino acid carrier as a complex with the thiol-containing amino acid, cysteine.

401
TITLE:
Effects of Neurotoxins on Brain Creatine Kinase Activity

AUTHORS:
Matsuoka M
Inoue N
Igisu H
Kohriyama K

SOURCE:
Environmental Research, Vol. 61, No. 1, pages 37-42, 18 references, 1993

ABSTRACT:
In-vivo studies were conducted in rats to determine the effects of ethylene-oxide (75218) (EO), acrylamide (79061), N,N'-methylene-bis-acrylamide (110269) (bis-acrylamide), and methyl-mercury-chloride (115093) (MMC) on brain creatine-kinase (CK) activity. Male Wistar-rats received 500 parts per million EO for 6 hours three times per week for 4 or 12 weeks. The rats were decapitated 40 hours after the last exposure for removal of brains and spinal cords. Total doses of 400 and 800mg/kg bis-acrylamide or 400mg/kg acrylamide were injected intraperitoneally over an 8 day period. Twenty four hours after the last injection, cerebra, cerebella, and spinal cords were removed. For the MMC exposure, the rats received subcutaneous injections of 10mg/kg/day for 7 days. Eight days after the final dose, the rats were decapitated and sections of the whole brains were dissected. Whole homogenates of the tissues were used for enzyme assays. The results showed that EO inhibited CK activity in the brain and spinal cord after 4 weeks of exposure; activity was further suppressed after 12 weeks. Acrylamide inhibited CK activity in the cerebrum, cerebellum, and spinal cord. Neither EO nor acrylamide inhibited aspartate-aminotransferase (ASAT) or lactate-dehydrogenase (LDH). Bis-acrylamide did not inhibit CK activity in any of the tissues, while MMC inhibited CK as well as ASAT in the anterior and posterior cortex and the midcortex. LDH was inhibited in the midcortex and posterior cortex. The authors conclude that CK alterations may relate to the pathogenesis of distal axonal degeneration

in both the peripheral and central nervous systems.

402
TITLE:
HEALTH HAZARDS OF METHYLMERCURY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ The overall objective is to more clearly define human health risks from prenatal exposure to methylmercury compounds (MeHg). To achieve this objective, we plan to measure dose-response relationships in human populations exposed to methylmercury and to conduct complementary investigations to characterize more precisely both prenatal and early postnatal body burdens of methylmercury including transport to the target organ, the brain.
The aim of the human studies is to test the hypothesis, developed in our previous study of prenatal exposures in the Iraq population, the subtle psychological and behavioral changes in prenatally exposed children can be quantitatively related to the mothers exposure during pregnancy using dose- response models. MeHg concentration in head hair has been used as the best indicator of the dose. We plan to directly test the assumption that hair levels indicate levels of methylmercury in the target tissue, the brain, by use of human autopsy data. We plan to examine the mechanisms of transport of MeHg from blood to brain across the blood-brain barrier to better understand the factors that limit the accuracy of hair mercury as a biological monitor of dose to the target tissue. We have preliminary evidence that MeHg crosses the blood-brain barrier on the neutral amino acid carrier as a complex with the thiol-containing amino acid, cysteine.

403
TITLE:
Effect of Mercuric Chloride on the Kinetics of Cationic and Substrate Activation of the Rat Brain Microsomal ATPase System

AUTHORS:
Rajanna B
Sreeramulu Chetty C
Rajanna S

SOURCE:
Biochemical Pharmacology, Vol. 39, N. 12, pages 1935-1940, 30 references, 1990

ABSTRACT:

An investigation was conducted of the cationic and substrate activation of the rat brain microsomal ATPase system following exposure of mercuric-chloride (7487947) (HgCl2). Male Sprague-Dawley-rats were administered HgCl2. The results indicated that HgCl2 was a potent inhibitor of brain microsomal stimulated ATPase and K+-activated PNPPase. HgCl2 inhibited microsomal (Na+-K+)ATPase and K+-PNPPase noncompetitively with respect to substrate and cation activation, indicating that HgCl2 did interfere with ion transport across cell membranes. The kinetics observed may be due to induced conformational changes in the enzyme complex resulting from binding of HgCl2 at critical sulfhydryl moieties. The present data suggested that the inhibition of (Na+-K+)ATPase in rat brain microsomes was possible due to its interference in the dephosphorylation of the enzyme/phosphoryl complex. Inhibition of K+-PNPPase by HgCl2 further supported this contention. The authors state that the observed effects of HgCl2 on this important enzyme indicate marked alterations in the Na+ pump.

404

TITLE:

Mercury retention in the muscles and internal organs of swine following Granosan poisoning.

AUTHORS:

Alekseeva AA

SOURCE:

Veterinariya; No. 5: 58-60, 1969

ABSTRACT:

HAPAB In August 1967 on two farms in Saratov Province, mass poisoning of pigs with Rranosan occurred as the result of using treated seed barley in the feed for 23 to 30 days. On the =October= Collective Farm in Tatishchevo District, 270 of 414 swine of various ages were affected and had to be slaughtered because of signs of acute mercury poisoning. On the =Fedorov= Collective Farm in Marx District, 211 of 444 fatling gilts were affected. Chemical toxicological tests of the internal organs and of the remaining unused feed showed mercury in large quantities. In subsequent months, further losses occurred among the pigs and the remaining animals showed signs of chronic mercury intoxication. The question was raised of slaughtering the surviving animals and of using their meat for food (Soviet veterinary law does not instruct on this point; however, the Sanitary Rules forbid organomercury compounds in any food product). Pathological material from 48 pigs which died or were slaughtered in the acute and chronic phases of the toxicosis was examined for the content and distribution of mercury. The results, tabulated, showed that mercury accumulated and was retained for a long time in the organism. Especially

high quantities were found in the kidneys, liver, lymph nodes, brain and muscle tissue. The level of excreted mercury fluctuated considerably in individual animals at various times following the poisoning and was apparently related to the amount of contaminated grain consumed and the duration of the intake. Meat from sows and gilts can conditionally be considered for food 10 months after recovery from Granosan poisoning. Suckling pigs, nursing during the time of feeding the treated grain but isolated form the mother at the appearance of clinical signs of toxicosis, can be expediently left for fattening and slaughtered at the age of 5 to 6 months. Their meat can be used as food after the elimination of parenchymatous organs. Epidemiology and Treatment 70/02/00, 64 1969

405
TITLE:
The Effects Of CCl4 On The Accumulation Of Mercury In Rat Tissues After Methylmercury Injection

AUTHORS:
Sato M
Takizawa Y

SOURCE:
Toxicology Letters, Vol. 15, No. 2, pages 245-249, 13 references, 19831983

ABSTRACT:
The hepatic injury caused by carbon-tetrachloride (56235) (CCl4) on accumulation of mercury in rat tissues was investigated. Male Sprague-Dawley-rats were given a single subcutaneous injection of 10 milligrams per kilogram methylmercury-chloride (115093) (MMC) followed by three intraperitoneal injections of 0.5 milliliter CCl4 at 48 hour intervals 2 days after MMC injection; controls were treated with the vehicle only at intervals similar to those for CCl4 treatment. Animals were killed and bled, and brain, liver, kidney, and muscles were removed. Blood was fractionated, and plasma and other tissues were analyzed for mercury contents by flameless atomic absorption spectrophotometry. Total mercury content in the cerebellum and cerebrum was significantly increased following treatment with CCl4 10 and 17 days after a single subcutaneous injection of MMC. The effect was of similar magnitude in both tissues, and the difference with and without CCl4 treatment gradually declined by 30 days after MMC injection. CCl4 produced a moderate but statistically insignificant increase in mercury contents of liver, kidney, muscle, and blood. The authors conclude that the increase in mercury concentrations of the tissues by CCl4 is not tissue specific.

406
TITLE:
Uptake of mercury by the hair of methylmercury-treated newborn mice.

AUTHORS:
SHI C
LANE AT
CLARKSON TW

SOURCE:
ENVIRON RES; 51 (2). 1990. 170-181.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Human hair has unique advantages in monitoring environmental exposures to methylmercury. Using newborn Balb/c mice as a model system, the incorporation of methylmercury into the hair was studied and compared with methylmercury distributions in other tissues. Newborn mice were given intraperitoneal injections of 203Hg-labeled methylmercury at designated times according to hair growth stages of the mouse. Animals were sacrificed 2 days after dosing. Distribution of mercury in pelt and other tissues was measured. The level of mercury in pelt was found to correlate with hair growth. The amount of mercury in pelt peaked when hair growth was most rapid and the total amount of mercury in pelt was significantly higher than that in other tissues, constituting 40% of the whole body burden. However, when the hair ceased growing, the amount of mercury in pelt dramatically dropped to 4% of whole body burden and mercury concentrations in other tissue except brain were elevated. Autor

407
TITLE:
Long-term mercury accumulation in the presence of cadmium and lead in Oreochromis aureus (Steindachner).

AUTHORS:
ALLEN P

SOURCE:
JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES; 30 (4). 1995. 549-567.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of cadmium and lead on chronic mercury accumulation were investigated in O. aureus. After 140 days' exposure the accumulation of mercury in the liver, brain, gill filaments, intestine, caudal muscle, spleen, trunk kidney and eye was analysed. The exposure concentrations were 0.05, 0.10 and 0.20 mg for mercury alone. O. aureus was also exposed to mixtures of 0.05 mg/L mercury with lead (0.05 mg/L and 0.50 mg/L or cadmium (0.05 mg/L) and 0.10 mg/L mercury with 0.10 mg/L cadmium. In food fish, a knowledge of toxic metal accumulation patterns is of great importance because of their contribution to the human diet and, as fishmeal, to the diet of agricultural animals. The trunk

kidney consistently accumulated higher concentrations of mercury than any of the other tissues investigated.

408
TITLE:
Effects of Methylmercury on the Morphogenesis of the Rat Cerebellum

AUTHORS:
Howard JD
Mottet NK

SOURCE:
Teratology, Vol. 34, No. 1, pages 89-95, 29 references, 19861986

ABSTRACT:
Changes in the morphogenesis of rat cerebellum after continuous low dose methylmercury (22967926) exposure throughout gestation and the suckling period were monitored. Female Sprague-Dawley-rats were randomly assigned to control or treatment groups within 24 hours of timed mating. Treatment groups were exposed to 12.5 parts per million methylmercury ad libitum in their drinking water beginning on day two of pregnancy. Samples of maternal liver, pup liver, and pup cerebellum were obtained at birth and at 6, 12, and 18 days postpartum. Samples were analyzed for tissue mercury (7439976) burden by a cold vapor atomic absorption spectroscopy technique. Total cerebellar cell counts were determined for the 6, 12, and 18 day old pups by Coulter counter method. Cerebellar tissue from fetuses and 6, 15, and 24 day old pups were examined histologically. No gross evidence of maternal mercury intoxication was seen at any time during the study and no gross malformations were observed in any rat pup examined. Treatment litters displayed normal size but showed an increase in pup death rate within 48 hours after birth. Although the cerebellum retained its normal gross configuration, the mercury exposure resulted in significant reductions in the total cell population of the pup cerebellum which persisted to day 18 postpartum. Differences in mercury tissue burden in maternal liver and pup liver were significant at 6, 12, and 18 days postpartum but not at birth. Pup cerebellum mercury tissue burden decreased from 15.16 micrograms/gram tissue (microg/g) at birth to 0.85microg/g at day 18 postpartum. Pup liver mercury burden exhibited a similar decline. The authors conclude that impaired cell proliferation is central to the mechanism of mercury toxicity after continuous low dose exposure.

409
TITLE:
Effects of mercury, selenium, and organochlorine contaminants on reproduction of Forster's terns and black skimmers nesting in a contaminated Texas bay.

AUTHORS:
King KA
Custer TW
Quinn JS

SOURCE:
Arch Environ Contam Toxicol 1991;20(1):32-40

ABSTRACT:
Mean mercury (0.40 ug/g), and geometric mean DDE (1.6 ug/g) and polychlorinated biphenyl (PCB) (2.3 ug/g) concentrations in Forster's tern (Sterna forsteri) eggs from Lavaca Bay were higher than those in tern eggs from a reference area in San Antonio Bay, but residues were not correlated with hatching success. Nest success was similar between bays. Selenium levels in Lavaca Bay tern eggs (0.71 ug/g) were also comparable to those in eggs from the reference area (0.68 ug/g). Clutch size (3.1 to 3.4) of Lavaca Bay black skimmers (Rynchops niger) was no different than that (3.4) at a reference colony near Laguna Vista. Nest success was similar among three Lavaca Bay colonies, but success was lower at one Lavaca Bay colony (40%) than at Laguna Vista (65%). Mean mercury (0.46 ug/g) and selenium (0.75 ug/g) concentrations in skimmer eggs from Lavaca Bay were higher than those (0.19, 0.33 ug/g) from Laguna Vista; however, concentrations of neither contaminant were related to hatching success. DDE concentrations in Lavaca Bay skimmer eggs (3.4 ug/g) were similar to those from Laguna Vista (3.2 ug/g) and DDE was negatively correlated with hatching success. PCBs were higher in eggs from Lavaca Bay (1.3 ug/g) than Laguna Vista (0.8 ug/g). Organochlorine and metal contaminants in most eggs were below embryotoxic levels. Eggshell thinning in Forster's terns (7%) and black skimmers (5%) was below that associated with lowered reproduction. DDE and PCBs were detected in 9 Caspian tern (S. caspia) eggs; maximum concentrations were 4.7 and 5.4 ug/g. Caspian tern and least tern (S. albifrons) eggs contained low (less than or equal to 0.9 ug/g) concentrations of mercury and selenium.

410
TITLE:
Experimental study on poisoning by organic mercury compounds.

AUTHORS:
Akitake T

SOURCE:
Igaku Kenkyu; 38(3), 357-78, 1968; (REF:65)

ABSTRACT:
HAPAB Female Wistar-King rats weighing about 180 g were used in assessing the neurological effects of alkyl mercury compounds in combination with various metal salts. Histological observations of changes in the central

nervous system, liver, kidney and body hair were carried out. Experiment I used 0.5 mg or 1.0 mg of ethyl mercury chloride (EMC) perorally administered daily with 1 mg of different metal salts; viz., Ba, Bi, Cd, Co, Cu, Fe, Li, Mg, Mn, Ni, Pb and Zn. Experiment II used 1.0 mg of ethyl mercury phosphate (EMP) daily alone or with a copper salt. Experiment III used 0.5 ml of 0.2% methyl mercury thioacetamide (MMTA) applied directly to the skin. Crossing, ataxia and hindleg weakness were found to be the best indicator signs of onset of neurological disturbances. No neurological symptoms were seen in the rats on 0.5 mg EMC daily for 150 days or in the rats treated with MMTA for 180 days. Daily administration of 1 mg EMC or EMP produced symptoms in 34 to 85 days and 32 to 71 days, respectively. Onset of these neurological symptoms was hastened with 1 mg EMC and 1 mg of the Co salt (about 41 days) but the Fe and Zn salts delayed the symptomatology to about 85 and 77 days, respectively. The metal salts alone produced no neurological signs. Mercury showed a higher degree of accumulation in body hair in the rats on EMC. Histologically, no definite brain changes were noted; in some cases there was degeneration or disappearance of Purkinje's cells, and degeneration of the dentate nuclei in the cerebellum and the gray matter of the spinal cord. The kidney showed degeneration of the cortical tubules in all rats fed the alkyl mercury compounds whether alone on in combination with the metal salts. (Author abstract modified) TOXICOLOGY AND PHARMACOLOGY 69/04/00, 115 1968

411

TITLE:

Toxic Trace Elements and Reproduction

AUTHORS:

Copius Peereboom-Stegeman JHJ

SOURCE:

Toxicological and Environmental Chemistry, Vol. 15, No. 4, pages 273-292, 87 references, 19871987

ABSTRACT:

The effects of trace amounts of cadmium (7440439), mercury (7439976), and lead (7439921) on the reproductive process were reviewed. Studies have indicated that exposure to toxic metals can interfere with implantation or cause disruptions in fetal growth. Such exposures could also produce infertility, cause perinatal mortality, and increase malformations in the offspring. The outcome of the exposure depended on the dosage and the timing. Cadmium has been shown to cause damage to the seminiferous tubules and produce a complete hemorrhagic necrosis of the testis. This metal also interacted with the chromatin decondensation process in sperm heads just prior to fertilization. Cadmium has caused ovarian atrophy, hypertrophia and hyperplasia in the microcirculation, limb malformation, exencephaly, embryonic death and resorption, and impairment of lung,

thymic and skeletal development. Smoking contributed to the cadmium burden of the body and the cadmium content of the placenta. Lead has been shown to affect gonadal development, sexual behavior, potency, pituitary releasing hormones, gonadal hormones, target organ responsiveness, intact menstrual cycling, spermatogenesis, sperm viability and number, fertilization, implantation, embryonic and fetal development, placental integrity, parturition, lactation, postnatal development and maternal to paternal behavior. The toxic effects of mercury vapor included neurological damage and disturbance of vision. The placental transfer of inorganic mercury was low compared with organic mercury. In cases of methylmercury exposure, births were uneventful but within a few months evidence of lethargy, delayed movements, failure to follow visual stimuli and convulsions began to occur. The concentration of mercury in the fetal brain following methylmercury exposure was twice that of the mother.

412
TITLE:
The Kinetics of a Tracer Dose of Methylmercury Compared to that of HgCl2 as Reflected in Hair

AUTHORS:
Berg D
Kollmer WE

SOURCE:
Trace Elements in Medicine, Vol. 5, No. 3, pages 120-122, 12 references, 19881988

ABSTRACT:
A study was made in rats comparing the kinetic deposition of mercury (7439976) in hair following intravenous (iv) or oral administration of methylmercury or mercuric-chloride (7487947). Male Wistar-rats received a dose of about 1.25 milligrams methylmercury or 0.26 milligrams mercuric-chloride. Each compound was labeled with mercury-203 and was given by stomach tube or iv into the tail vein. Whole body retention of radioactivity was measured up to 50 days post exposure, at which time brain, liver, and kidney levels were determined. Hair levels were measured after plucking induced hair growth, at 0 to 10, 20 to 30, and 40 to 50 days after dosing. Fecal excretion of radioactivity was much greater after oral dosing with mercuric-chloride than with methylmercury. Respective biological half lives for the two compounds were 20.9 and 35 days, following oral dosing. A much greater percentage of the initial dose of methylmercury was found in hair compared to the percentage for mercuric-chloride. Changes with time were not significantly different. Oral and iv dosing produced virtually the same transfer to hair for methylmercury. Oral mercuric-chloride showed better transfer to hair than did iv mercuric-chloride, suggesting an intestinal metabolic transformation of the inorganic compound. The authors conclude that the

fraction of mercury in hair relative to the amount absorbed intestinally is larger for methylmercury than for inorganic mercury.

413
TITLE:
MERCURY INTERACTION WITH THE TAURINE TRANSPORT SYSTEM OF RED BLOOD CELLS

AUTHORS:
PRESTON RL

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The overall objective of the proposed research is to identify and characterize the molecular targets and mechanisms of interaction of mercury with membrane transport proteins. We will focus specifically on the interactions of mercury with the Na-dependent taurine transport system in the hemoglobin containing coelomocytes (red cells, RBCs) of the marine polychaete, Glycera dibranchiata. This transport system is similar to taurine transport systems in mammalian tissues such as heart, kidney and brain. In Glycera RBCs, taurine is maintained at exceptional gradients (950:01; 190 mM intracellular taurine: 0.2 mM extracellular taurine). We have shown that this transport protein is very sensitive to inhibition by mercurial. A one minute exposure to 20 muM HgC12 inhibits taurine influx 50%. Studies using reduced sulfhydryl reagents of different molecular size indicated that the reactive sites on the transport protein appear to be partially occluded by the membrane since complete reversal is obtained only with small molecules. Since HgC12 in high chloride media is present predominantly as anionic complexes that are impermeant to membranes, we propose the operational hypothesis that the nonionic HgC12 complex is the form that reacts with taurine sulfhydryl groups lying in membrane spanning regions of the protein. We will test this hypothesis by addressing the following specific aims: (1) Physiologically characterize the form of HgC12 that interacts with the taurine transport system and identify the transport proteins involved in cell volume regulation that are sensitive to interaction with mercury. (2) Clone the Na-dependent taurine transporter from Glycera RBCs. (3) Characterize the interaction of mercurial with the taurine transporter expressed in Xenopus oocytes. Flux measurements on intact RBCs and on oocytes expressing the taurine transport protein will be done using radioisotope methods. The molecular procedures will depend on reverse transcription and PCR of poly(A)+RNA with taurine transport activity identified by expression of taurine transport activity of the mRNA fractions microinjected into Xenopus oocytes. Physiological studies will measure solute contents and net fluxes with a variety of techniques including ion selective electrodes, atomic absorption spectroscopy, HPLC and radioisotopic methods. The results of this study will provide important basic information on the

molecular mechanism of interaction of mercury with the taurine transporter that has a hole in many animals tissues including human cardiac, nerve and kidney tissue.

414
TITLE:
Clinical symptoms of mercury poisoning in man.

AUTHORS:
Bidstrup PL

SOURCE:
Biochem. J.130(2): 59P-61P; 1972(REF:19)

ABSTRACT:
HAPAB. Phenyl mercury compounds and short-chain alkyl mercury compounds, both used extensively to control fungus in the past, produce entirely different clinical symptoms. The former may irritate the skin, but systemic effects are few, and distribution in tissue is similar to that of inorganic mercury. Ethyl and methyl mercury are exceedingly toxic to the nervous system, causing severe generalized ataxia, dysarthria, and concentric constriction of the visual fields. Fatigue, impairment of memory, inability to concentrate, and numbness and tingling of the lips and fingers with slight tremor characterize mild poisoning. The alkyl mercury compounds accumulate in all tissue, particularly the brain, and are eliminated more slowly than inorganic or phenyl mercury compounds.

415
TITLE:
Biochemical aspects of mercury poisoning.

AUTHORS:
Clarkson TW

SOURCE:
J. Occupational Med.; 10(7), 351-5, 1968; (REF:29)

ABSTRACT:
HAPAB Two points of view are recognized in the study of the biochemistry of mercury: the effects on tissue enzymes and biotransformation. Mercury has been shown to combine preferentially with thiol groups and is capable of inhibiting any enzyme containing such groups. At higher concentrations it is a protein precipitant. Recent evidence indicates that mercury, on entering the brain, may become localized in special areas and that, in the liver, mercury damage to the lysosomes may be the primary lesion responsible for cell destruction. Studies of mercury's effect on the kidney have been hampered by rapid transformation between oxidation states or from organic to inorganic states. A review of present knowledge

suggests that emphasis should be placed on the biotransformation and microdistribution of mercury and its compounds in cells and tissues.
TOXICOLOGY AND PHARMACOLOGY 68/09/00, 11 1968

416
TITLE:
MERCURY INTERACTION WITH THE TAURINE TRANSPORT SYSTEM OF RED BLOOD CELLS

AUTHORS:
PRESTON RL

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The overall objective of the proposed research is to identify and characterize the molecular targets and mechanisms of interaction of mercury with membrane transport proteins. We will focus specifically on the interactions of mercury with the Na-dependent taurine transport system in the hemoglobin containing coelomocytes (red cells, RBCs) of the marine polychaete, Glycera dibranchiata. This transport system is similar to taurine transport systems in mammalian tissues such as heart, kidney and brain. In Glycera RBCs, taurine is maintained at exceptional gradients (950:01; 190 mM intracellular taurine: 0.2 mM extracellular taurine). We have shown that this transport protein is very sensitive to inhibition by mercurial. A one minute exposure to 20 muM HgC12 inhibits taurine influx 50%. Studies using reduced sulfhydryl reagents of different molecular size indicated that the reactive sites on the transport protein appear to be partially occluded by the membrane since complete reversal is obtained only with small molecules. Since HgC12 in high chloride media is present predominantly as anionic complexes that are impermeant to membranes, we propose the operational hypothesis that the nonionic HgC12 complex is the form that reacts with taurine sulfhydryl groups lying in membrane spanning regions of the protein. We will test this hypothesis by addressing the following specific aims: (1) Physiologically characterize the form of HgC12 that interacts with the taurine transport system and identify the transport proteins involved in cell volume regulation that are sensitive to interaction with mercury. (2) Clone the Na-dependent taurine transporter from Glycera RBCs. (3) Characterize the interaction of mercurial with the taurine transporter expressed in Xenopus oocytes. Flux measurements on intact RBCs and on oocytes expressing the taurine transport protein will be done using radioisotope methods. The molecular procedures will depend on reverse transcription and PCR of poly(A)+RNA with taurine transport activity identified by expression of taurine transport activity of the mRNA fractions microinjected into Xenopus oocytes. Physiological studies will measure solute contents and net fluxes with a variety of techniques including ion selective electrodes, atomic absorption spectroscopy, HPLC and radioisotopic methods. The

results of this study will provide important basic information on the molecular mechanism of interaction of mercury with the taurine transporter that has a hole in many animals tissues including human cardiac, nerve and kidney tissue.

417
TITLE:
MERCURY INTERACTION WITH THE TAURINE TRANSPORT SYSTEM OF RED BLOOD CELLS

AUTHORS:
PRESTON RL

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The overall objective of the proposed research is to identify and characterize the molecular targets and mechanisms of interaction of mercury with membrane transport proteins. We will focus specifically on the interactions of mercury with the Na-dependent taurine transport system in the hemoglobin containing coelomocytes (red cells, RBCs) of the marine polychaete, Glycera dibranchiata. This transport system is similar to taurine transport systems in mammalian tissues such as heart, kidney and brain. In Glycera RBCs, taurine is maintained at exceptional gradients (950:01; 190 mM intracellular taurine: 0.2 mM extracellular taurine). We have shown that this transport protein is very sensitive to inhibition by mercurial. A one minute exposure to 20 muM HgC12 inhibits taurine influx 50%. Studies using reduced sulfhydryl reagents of different molecular size indicated that the reactive sites on the transport protein appear to be partially occluded by the membrane since complete reversal is obtained only with small molecules. Since HgC12 in high chloride media is present predominantly as anionic complexes that are impermeant to membranes, we propose the operational hypothesis that the nonionic HgC12 complex is the form that reacts with taurine sulfhydryl groups lying in membrane spanning regions of the protein. We will test this hypothesis by addressing the following specific aims: (1) Physiologically characterize the form of HgC12 that interacts with the taurine transport system and identify the transport proteins involved in cell volume regulation that are sensitive to interaction with mercury. (2) Clone the Na-dependent taurine transporter from Glycera RBCs. (3) Characterize the interaction of mercurial with the taurine transporter expressed in Xenopus oocytes. Flux measurements on intact RBCs and on oocytes expressing the taurine transport protein will be done using radioisotope methods. The molecular procedures will depend on reverse transcription and PCR of poly(A)+RNA with taurine transport activity identified by expression of taurine transport activity of the mRNA fractions microinjected into Xenopus oocytes. Physiological studies will measure solute contents and net fluxes with a variety of techniques including ion selective electrodes, atomic

absorption spectroscopy, HPLC and radioisotopic methods. The results of this study will provide important basic information on the molecular mechanism of interaction of mercury with the taurine transporter that has a hole in many animals tissues including human cardiac, nerve and kidney tissue.

418
TITLE:
Effect of Reticuloendothelial System Blockade on the Biotransformation of Methyl Mercury in the Rat

AUTHORS:
Suda I
Takahashi H

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 44, No. 4, pages 609-615, 17 references, 1990

ABSTRACT:
The relationship between the reticuloendothelial system (RES) and the biotransformation of methyl-mercury (MeHg) was examined using four representative blockers: colloidal carbon (CC), trypan-blue (TB), colloidal iron (CFe), and carrageenan (CAR). Male Wistar-rats were administered methylmercury-chloride (115093) intravenously with 1 milligram mercury (7439976) per rat. The inhibited biotransformation of MeHg in RES blocker treated rats was evaluated by measuring the amount of total and inorganic mercury in tissues. RES cell activity was measured by carbon clearance. The decreased amount of inorganic mercury trapped in kidneys and the increased amount of MeHg which accumulated in the brain following pretreatment with CC, TB, and CFe resulted in a decreased metabolism of MeHg. The results indicated that CAR, CFe, TB, or CC treatment could cause an inhibited biotransformation of MeHg in rats, with a concomitant RES blockage. The authors suggest that these findings indicate a meaningful role of RES cells in the biotransformation of MeHg by animal tissues themselves, and suggest that the degree of relevance of the RES pathway in mammalian MeHg metabolism is not so small and that intestinal microflora may not be the major potential site of demethylation of MeHg in the animal body.

419
TITLE:
Elemental Mercury Polyneuropathy

AUTHORS:
Albers JW
Cavender GD
Levine SP

Langolf GD

SOURCE:
NIOSH, U.S. Department of Health and Human Services, Cincinnati, Ohio, Grant No. R01-0H-00707-04, 28 pages, 24 references, 19821982

ABSTRACT:
Peripheral neurotoxicity associated with exposure to inorganic mercury (7439976) vapors was investigated. Clinical neurological evaluations, nerve conduction evaluations, and medical questionnaires and interviews were conducted at three chloralkali factories (SIC-2812). Of the 138 workers examined, 77 had significant potential exposures to mercury. All subjects had been in a mercury control program wherein individuals with monthly spot sample urine mercury concentrations exceeding 50 milligrams per liter were removed from exposure. Of 138 workers, 18 had mild sensory disturbances that were evidenced by significantly reduced clinical distal vibratory and pin sensation, reduced distal strength, and reduced muscle stretch reflexes. Significant differences were also see in tests of vibration, touch, and two point discrimination. Affected subjects were older (average age of 43) and had an average of 13 years on the jobs, compared with an average age of 33 and 8 years on the job for normal subjects. Electrodiagnostic abnormalities were more frequent in subjects with polyneuropathy. Subjects with clinical evidence of polyneuropathy had higher mercury urine indexes. The authors conclude that elemental mercury exposure is associated with a clinically significant sensorimotor polyneuropathy. The degree of neurologic impairment is related to the magnitude of exposure.

420
TITLE:
Effects Of Heavy Metals On Monoamine Uptake And Release In Brain Synaptosomes And Blood Platelets

AUTHORS:
Komulainen H
Tuomisto J

SOURCE:
Neurobehavioral Toxicology and Teratology, Vol. 4, No. 6, pages 647-649, 13 references, 19821982

ABSTRACT:
The effects of metals on neurotransmission of dopamine (DA), noradrenaline (NA), and 5-hydroxytryptamine (5-HT) were determined in Wistar-rat tissues and human blood platelets. Metals or organometal cations tested included cadmium (7440439), cobalt (7440484), copper (7440508), mercury (7439976), manganese (7439965), lead (7439921), tin (7440666), methyl-mercury (22967926), triethyllead (5224237), and tetraethyllead (78002). The high

affinity uptake of the monoamines by synaptosomes was measured using tritiated substrates. Metals were allowed to affect synaptosomes in advance by preincubating synaptosomes with metals before adding the substrate. Spontaneous release from preloaded synaptosomes was studied to assess its role in uptake inhibition. The stability of monoamines was determined. Effects of the most potent metals on 5-HT uptake were tested in human blood platelets. Copper, methyl-mercury, and triethyllead strongly inhibited monoamine uptake. Preincubation of synaptosomes with copper but not with methyl-mercury shifted the dose response curves of 5-HT and of DA uptake to lower concentrations. At concentrations higher than 10 micromoles per liter, copper increased NA uptake, although at lower doses copper inhibited uptake. After preincubation with tissue only copper and methyl-mercury inhibited uptake significantly. Both copper and methyl-mercury increased the spontaneous release of radioactivity from synaptosomes as concentration and time increased. Copper and methyl-mercury inhibited 5-HT uptake by human blood platelets. The authors conclude that parameters involving 5-HT give the most reliable results when assessing heavy metal toxicity.

421
TITLE:
Mercury pollution of fish and other food products. Part 2: Toxicologic aspects of the problem.

AUTHORS:
Canuti A

SOURCE:
Ind. Aliment. (Pinerolo, Italy)12(11): 97-100, 1973

ABSTRACT:
PESTAB (39 references) (Italian) jThe toxicological aspects of mercury pollution in food products, especially in fish, are discussed. The toxicological aspects of atmospheric pollution from mercury are also considered. Mercury poisoning is directly related to the time of exposure, the most affected organs being the liver and kidneys, followed by the digestive tract and the brain. The danger of mercury contamination and poisoning through the food chain and a polluted atmosphere especially in working environments should be emphasized. Atmospheric pollution is due to the formation of volatile organic mercury compounds such as methyl, phenyl, and ethyl mercury formed by action of microorganisms. s,

422
TITLE:
Mercury accumulation and biomagnification in ospreys (Pandion haliaetus) in the James Bay and Hudson Bay Regions of Quebec.

AUTHORS:
DESGRANGES J-L
RODRIGUE J
TARDIF B
LAPERLE M

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 35 (2). 1998. 330-341.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury exposure was examined in adults and nestlings of ospreys (Pandion haliaetus) from lakes, rivers, and hydroelectric reservoirs in northern Quebec between 1989 and 1991 by assessing the amount of mercury transferred from fish to ospreys, which are voracious fish-eaters. The high mercury concentrations detected in adult feathers and tissues (feathers, blood, liver, kidneys, muscles, brain) of nestings indicate an increase in mercury availability at recently constructed hydroelectric reservoirs (10-12 years for the La Grande-2 Reservoir). With mean total mercury levels of 37.3 mg/kg and 1.9 mg/kg in feathers (dry weight) and in blood (wet weight), respectively, contamination rates were, in both tissues, five times higher for chicks born near the La Grande Reservoirs (western sector) than in those reared in natural habitats. Furthermore, the mean quantity of total mercury in 40-day-old chicks reared near a reservoir was 10.5 mg, compared with to 1.6 mg for those rear

423
TITLE:
Enrollment and neurodevelopment at 6 months.

AUTHORS:
Myers G
Marsh D
Cox C
Davidson P
Cernichiari E
Clarkson T
Choisy O
Shamlaye C

SOURCE:
Neurotoxicology 1994;15(4):958

ABSTRACT:
Enrollment of the main cohort in the Seychelles Child Development Study (SCDS) occurred when the children were 6 months (+/- 2 weeks) of age. All children born between 2/89 and 2/90 were eligible to participate and 779

mother-infant pairs were enrolled (48% of those eligible). Evaluation consisted of a medical history (pregnancy, neonatal period, and first 6 months of life), general and neurologic examination, Denver Developmental Screen Test (DDST), Fagan Test, and collection of maternal breast milk, and hair from both mother and infant. A few infants were excluded from the study for medical reasons. Maternal hair samples to recapitulate mercury exposure during pregnancy were available for nearly all children. Total mercury was measured by atomic absorption spectroscopy in the maternal hair segment corresponding to pregnancy. The mean maternal hair mercury was used as the index of exposure and ranged from 0.5 to 26.7 ppm with a mean of 6.8 ppm. Covariates included birth weight, birth order, gender, child's medical history, parental income, education and language, and maternal medical history, smoking, and alcohol ingestion. No correlation between mean maternal hair mercury during pregnancy and the infant's performance on the neurologic examination, DDST, Fagan test at 6 months of age appeared significant. The results will be discussed.

424
TITLE:
Toxicokinetics of methyl mercury in pigs.

AUTHORS:
Gyrd-Hansen N

SOURCE:
Arch. Toxicol. 48(2-3): 173-181 1981 (35 References)

ABSTRACT:
PESTAB. Toxicokinetics of methyl mercury were studied in pigs after iv administration of methyl mercury chloride. The distribution of methyl mercury was slow, taking 3-4 days to be completed. Blood elimination half-life was found to be 25 days. The apparent volume of distribution was 9.8 l/kg, indicating pronounced tissue accumulation of methyl mercury. Highest mercury levels were found in kidney and liver, with lower contents in muscle and brain and very little in adipose tissue. The results indicate that from organs like liver and kidney methyl mercury is eliminated much more slowly than from the blood. Over a period of 15 days 16% of the dose administered was excreted with feces and 0.9% in the urine. (Author abstract by permission, modified)

425
TITLE:
Ultrastructural Alterations Of The Liver Of Pekin Ducks Fed Methyl Mercury-Containing Diets

AUTHORS:
Bhatnagar MK
Vrablic OE

Yamashiro S

SOURCE:
Journal of Toxicology and Environmental Health, Vol. 10, No. 6, pages 981-1003, 51 references, 19821982

ABSTRACT:
Ultrastructural alterations of the livers due to eating diets containing methyl-mercury-chloride (115093) (MeHgCl) were studied in Pekin-ducks. Ducks were fed 0.0, 0.5, 5.0, and 15.0 parts per million (ppm) MeHgCl in diets for 12 weeks. Birds were weighed weekly for 7 weeks and examined daily for symptoms for 12 weeks. Blood samples were analyzed at intervals for mercury (7439976). Animals were killed when paralyzed or at 12 weeks for analysis of mercury residue by atomic absorption spectrophotometry. Liver samples were examined by electron microscopy. Decreases in mean body weights in treated animals up to 7 weeks were not significant. Neurological signs of toxicity, leg paralysis and convulsions were seen in ducks given 15.0ppm beginning at 5 weeks for males and 8 weeks for females. Mercury residues increased linearly with the dose in all tissues examined. The greatest amount of mercury was found in liver and kidney and the least in the brain. Few morphological changes were seen in hepatocytes in the lower dose groups, but in the 15.0ppm group ultrastructural changes included increase in peribiliary liposomal bodies. Lysis of inner and outer membranes of mitochondria was seen. Degenerating Kupffer cells were not infrequent. Ultrastructural variations were not evenly distributed throughout the liver. The authors conclude that 15.0ppm MeHgCl cause ultrastructural changes indicative of toxic injury to the liver.

426
TITLE:
Fetal and maternal distribution of inhaled mercury vapor in pregnant mice: Influence of selenite and dithiocarbamates.

AUTHORS:
DANIELSSON B RG
KHAYAT A
DENCKER L

SOURCE:
PHARMACOL TOXICOL; 67 (3). 1990. 222-226.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The distribution of mercury after inhalation of metallic mercury vapour (6-8 mumol 203Hg0/kg b.wt.) was studied in pregnant mice (day 17 of gestation) after pretreatment with selenite (10 mumol Se/kg b.wt. intraperitoneally 1 hr before inhalation), thiram, disulfiram or diethyldithiocarbamate (1mmol/kg orally 2 hr before

inhalation of Hg0). For comparison, the effects of thiram, disulfiram and diethyldithiocarbamate on the distribution of mercury after administration of ionic mercury (7 mumol 203HgCl2/kg b.wt. intravenously) were also studied. Selenite pretreatment caused a longer retention of mercury in maternal tissues but decreased the foetal concentrations after 203Hg0 inhalation, similarly to what has been shwon previously after administration of ionic mercury (Hg2+). Pretreatment with the three dithiocarbamates markedly increased the uptake in maternal brain and fat and decreased the foetal concentrations after intravenous injection of 203HgCl2. In contrast, no cha

427
TITLE:
The role of Na,K-ATPase in methylmercury-induced teratogenesis.

AUTHORS:
Holmes LS
Okita GT

SOURCE:
Fed. Proc. Fed. Am. Soc. Exp. Biol. 38(3, Pt. 1): 680 1979

ABSTRACT:
PESTAB. Methylmercury (MeHg) has been shown to cause various teratogenic effects to mice exposed in utero. We have looked at the Na,K-ATPase in order to determine the mechanism of mercury caused teratogenesis in brain. We suggest that MeHg may inhibit Na,K-ATPase, thus blocking amino acid transport and causing protein deficiencies in the developing brain. Timed pregnant SVSL/129 mice were injected daily on days 7-12 of gestation with 5 mg/kg of MeHg. Fetal brains from both 19th and 16th day gestation were used. The MeHg concentrations in similar brains were 9.8 and 15.8 ppm, respectively. In order to study the inhibition of Na,K-ATPase, a 86Rb+ tracer for K+ was used. Brain cell suspensions from 19th day fetal brains were incubated with a tracer of Rb+ for 20 min, and uptake of Rb+ into the cell was measured. In tissue taken from the MeHg exposed fetuses, there was a 40% inhibition of Rb+ uptake. In a similar cell suspension system, transport of amino acids was examined. A tracer mixture of labeled amino acids was incubated with the cell suspension from 16th day gestation fetal brains. Both amino acid transport and incorporation of amino acids into protein were significantly inhibited by exposure to MeHg. Therefore, those findings indicate that inhibition of Na,K-ATPase by MeHg may be responsible for the observed fetal brain abnormalities. [Abstract 2387 of the annual meeting of the Fed. Am. Soc. Exp. Biol.] (Author abstract by permission)

428
TITLE:
Methylmercury toxicosis: 1. Relationship between the onset of motor

incoordination and mercury contents in the brain.

AUTHORS:
TAGASHIRA E
URANO T
YANAURA S

SOURCE:
FOLIA PHARMACOL JPN; 76 (2). 1980. 169-178.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Mice were given 1 or repeated administrations of methylmercury chloride (MMC) to determine the sexual differences as related to toxic signs, particularly, motor incoordination and the period to evolvement of toxicity. Male and female mice were given 50.6 mg/kg of MMC (about equal to the LD50 in female mice) orally only once, and changes in general behavior and mortality were observed for the following 13 days. Another group of male and female mice was fed food containing 50 and 100 ppm of MMC for 30 days, respectively. The rotarod performance test was carried out daily during the application period, to compare the onset stages of toxic signs and motor incoordination between the groups. The Hg content of the brain was measured at 1-2 day intervals during the application period. When the animals were given MMC only once, the males began to die at 3 days, 7/8 of the group dying thereafter. There was an obvious sexual difference in the toxicity. When the animals were given MMC admixed with food the females proved more sensitive to the compound both in onset and severity of toxic signs. The onset was seen in the females at the stage when they had ingested about half the amount of the toxic food ingested by the males. The onset and the period in days to the onset of suppressed rotarod performance both in the groups on 50 and 100 ppm were correlated to the daily intake of MMC, the total MMC intake to the onset in the 2 groups being similar. The accumulation of Hg in the brain increased linearly in both groups, with the MMC content of the brain at the onset was about 20 mug Hg/g of brain (on the wet basis), i.e., about twice that of the human brain. The Hg content in the brain of the female mice tended to reach the toxicity threshold earlier than that in the brain of the males.

429
TITLE:
A Study of Metal Ions in the Central Nervous System I. Preliminary Considerations

AUTHORS:
Harris WH
Beauchemin JA
Hershenson HM
Roberts SH

Matsuyama G

SOURCE:
Journal of Neuropathology and Experimental Neurology, Vol. 13, pages 427-434, 32 references, 19541954

ABSTRACT:
The presence or absence of 16 metal ions was determined in eight regions of the human brain. Four human brains obtained at autopsy were divided into eight sections: frontal lobe, parietal lobe, occipital lobe, temporal lobe, Island of Reil (insula), basal ganglia, brain stem, and cerebellum. Sections were wet ashed with nitric-acid, concentrated, and spectrographically analyzed. Calcium (7440702), magnesium (7439954), and lead (7439921) were found in all sections of all four brains. Aluminum (7429905), copper (7440508), cobalt (7440484), mercury (7439976), manganese (7439965), vanadium (7440622), nickel (7440020) and titanium (7440326) were found in every section at least once. Chromium (7440473) and zinc (7440666) were identified in all sections except the insula and the brain stem, respectively. Silver (7440224), bismuth (7440699), and molybdenum (7439987) were not found in any section. Although quantitation of metal concentrations was not carried out, the authors conclude that it is noteworthy that the majority of metals were present in all areas of all the brains examined.

430
TITLE:
Methylmercury

AUTHORS:
Clarkson T

SOURCE:
Fundamental and Applied Toxicology, Vol. 16, No. 1, pages 20-21, 2 references, 1991

ABSTRACT:
The results of various studies concerning the effects of methylmercury (22967926) (MeHg) exposure on the adult and developing nervous system were described. MeHg has been observed to readily cross the placenta. Animal studies have indicated that fetal brain levels of MeHg were about twice as high as those in maternal brain. Experimental evidence in developing animals has suggested that MeHg, assumed to be present in plasma as a complex with the thiol containing amino acid cysteine, was carried across the blood brain barrier on the large neutral amino acid carrier. Prenatal exposure has been observed to produce cerebral palsy in infants even when signs of poisoning were mild or absent in the mother during pregnancy. The effects has been explained by an inhibitory action on two key processes in brain development, neuronal migration and cell division.

This inhibitory action arose from the ability of MeHg to depolymerize microtubules. In less severe cases prenatal exposure has produced delayed achievement of developmental milestones and more subtle neurological disturbances. The author concludes that the special susceptibility of the developing brain to maternal intake of MeHG during pregnancy was indicated to be related to several factors: ease of transport across the placenta; the preferential uptake by the fetal brain; and the inhibitory action on cell division and neuronal migration, both key processes in brain growth.

431
TITLE:
In vivo incorporation of 14C-leucine into brain protein of methylmercury treated rats.

AUTHORS:
Farris FF
Smith JC

SOURCE:
Bull. Environ. Contam. Toxicol. 13(4): 451-455; 1975.(7 references)

ABSTRACT:
PESTAB. Pregnant Sprague-Dawley rats were injected s.c. with 1.0 mg methylmercury chloride at various times throughout their pregnancy. Two days after birth, the brains of some offspring were analyzed for methylmercury content, and some offspring were injected i.p. with 2 muCi 14C-leucine. Incorporation of the latter substance into brain protein was determined 30 min later. In a second experiment, female rats were injected s.c. with 5 mg methylmercury chloride and 10 mg cystein or cystein alone for 3 days; 4 days later, all rats were injected i.v. with 13.9 muCi 14C-leucine and its incorporation into brain protein determined 90 min later. In the first experiment, there was no significant difference in brain protein synthesis between the offspring of control (saline-treated) rats and methylmercury treated rats. The brain methylmercury concentrations of the offspring of the methylmercury-treated females varied from 4.5-9.7 mug/mg. In the second experiment, the methylmercury-treated adults showed signs of severe intoxication. The mean body weight of the poisoned animals at the end of the experiment was 63% that of the controls, and protein synthesis in the poisoned animals was about 75% of that in the controls; leucine incorporation was significantly inhibited in the cerebellum, hemispheres, mid-brain, and occipital region of the poisoned animals. Brain mercury levels were approximately 54 ppm in the poisoned rats.

432
TITLE:
Methylmercury poisoning: Long-term clinical, radiological, toxicological, and pathological studies of an affected family.

AUTHORS:
DAVIS LE
KORNFELD M
MOONEY HS
FIEDLER KJ
HAALAND KY
ORRISON WW
CERNICHIARI E
CLARKSON TW

SOURCE:
ANNALS OF NEUROLOGY; 35 (6). 1994. 680-688.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. For 3 months in 1969 a family in the United States that included a pregnant mother consumed pork containing methylmercury. Children, aged 20, 13, and 8 years and a neonate, developed severe neurological signs. Twenty-two years later, the 2 oldest had cortical blindness or constricted visual fields, diminished hand proprioception, choreoathetosis, and attentional deficits. Magnetic resonance images showed tissue loss in the calcarine and parietal cortices and cerebellar folia. The youngest had quadriplegia, blindness, and severe mental retardation until their deaths. The brain of the 8-year-old who died at age 30 showed cortical atrophy, neuronal loss, and gliosis, most pronounced in the paracentral and parietooccipital regions. The total mercury level in formalin-fixed, left occipital cortex was 1,974 ng/gm as measured by atomic absorption. Regional brain mercury levels correlated with extent of brain damage. A control patient had 38.5 ng of mercury/gm in the occipital

433
TITLE:
A physiologically based pharmacokinetic model for methyl mercury in the pregnant rats and fetus.

AUTHORS:
GRAY DG

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 132 (1). 1995. 91-102.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Current methyl mercury (MeHg) guidelines for human exposure are not adequately protective against developmental effects in the children of women consuming MeHg-contaminated food. There is an urgent need to find ways to use human and/or animal studies of MeHg developmental toxicity to assess human health risk. To this end, a

physiologically based pharmacokinetic model (PBPK) for methyl mercury in the pregnant rat and fetus has been developed. The cell membrane, blood-brain barrier, and the maternal/fetal placental membrane are the primary limitations to the distribution of MeHg in the pregnant rat and fetus. Individual fetal organs were modeled, including the fetal brain. Model results compare well with experimental data indicating that the model can be used to predict maternal or fetal organ MeHg concentrations for many dosing regimes. The model will allow the development of target organ (brain) dose-response relationships from studies of developmental toxicity in the r

434
TITLE:
Development Of Reflexes In Neonatal Mice Prenatally Exposed To Methylmercury And Selenite

AUTHORS:
Satoh H
Yasuda N
Shimai S

SOURCE:
Toxicology Letters, Vol. 25, No. 2, pages 199-203, 20 references, 19851985

ABSTRACT:
Selenite (14124675) modification of methylmercury (22967926) (MM) toxicity was investigated in developing mouse neonates. Male and female CFW-mice were mated. On day 9, pregnant mice were injected subcutaneously with saline, with 30 micromoles per kilogram (micromol/kg) MM, or with 30micromol/kg sodium-selenite (10102188); some mice were coadministered 30micromol/kg MM and 30micromol/kg sodium-selenite. Mice were observed. Pups were inspected after delivery and examined on days 1, 3, and 8. Development of reflexes was evaluated. Pups were weighed and killed after behavioral examination. Brain, kidneys, and liver were collected, and total mercury (7439976) in the organs was determined. Weights of pups in the MM/selenite and selenite groups were significantly lower than controls at birth. On day 8, weights of all treated groups were significantly lower than for saline treated controls. Brain weight for the MM/selenite group was significantly lower on day 1 than for controls. On day 3, mercury concentration in all organs of the MM/selenite group was significantly lower than in the MM only group. On day 8, brain concentration of mercury remained significantly lower than for the MM only group. Mean development scores of righting reflex and walking activity were lowest in the MM group on days 1 and 3. The MM/selenite group developed as well as the other two groups. Righting reflex score of the MM/selenite group was superior to the other two groups on day 1. There were significant interactions of effects of MM and selenite exposure in righting reflex and walking activity scores on day 1. The authors suggest

that administration of selenite prevents the neurotoxicity of prenatal exposure to MM.

435

TITLE:

Methylmercury Effects In Rat, Hamster, And Squirrel Monkey. Lethality, Symptoms, Brain Mercury, And Amino Acids

AUTHORS:

Hoskins BB

Hupp EW

SOURCE:

Environmental Research, Vol. 15, No. 1, pages 5-19, 46 references, 19781978

ABSTRACT:

The effects of methylmercury-chloride (115093) (MMC) were investigated in laboratory animals. Male Sprague-Dawley-rats, male Syrian-hamsters, and squirrel-monkeys were injected intraperitoneally with single doses of up to 8 milligrams (mg) MMC per animal or with five daily doses of 2mg. Animals were watched for morbidity, gait, and appearance changes and were weighed weekly. At 25 days after injection or at imminent death, animals were killed. Tissues were fixed and stained for histological examination. The median lethal dose (LD50) at 24 hours and at 30 days was calculated by probit analysis. Portions of the cerebellum, brain stem and cerebral hemisphere were removed from the skull and weighed. Mercury was determined by atomic absorption. Amino acids were determined by thin layer chromatography of the dinitrophenol derivatives. Gamma-amino-butyric-acid (GABA), glycine, glutamate, and aspartate were identified by comparisons to commercial preparations. Amino acids were quantified by spectrophotometry. LD50s at 24 hours were 11.9mg/kilogram (kg) for rats, 22.4mg/kg for hamsters, and estimated at greater than 17mg/kg for monkeys. LD50s at 30 days were 10.1mg/kg in rats, 15.2mg/kg in hamsters, and estimated between 5.6 and 6.4mg/kg for monkeys. Single MMC doses caused rats to exhibit rapid respiratory and vascular symptoms but no motor changes, whereas five daily 2mg MMC doses caused motor symptoms. Hamsters had no motor changes with single or repeated MMC doses, but weight loss was gradual and steady. Monkeys dosed with 6.4mg/kg had motor difficulty; cumulative doses from 4.7 to 20mg per animal caused motor symptoms and rapid deterioration of coordination and vision. Rats and monkeys had significant amounts of mercury in cerebral hemispheres and in brain stems as compared to controls. GABA increased and glycine, glutamate, and aspartate decreased only in monkeys. The authors conclude that monkeys are a useful though more sensitive model for humans than the rodent.

436

TITLE:
Glutamate: A potential mediator of inorganic mercury neurotoxicity.

AUTHORS:
ALBRECHT J
MATYJA E

SOURCE:
METABOLIC BRAIN DISEASE; 11 (2). 1996. 175-184.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Exposure to mercury vapor (Hgo) produces neurotoxic effects which are for the most part subsequent to its biotransformation in brain to the mercuric cation (Hg2+), which has an exceptionally strong affinity towards the SH groups in proteins. However, neurologic symptoms are often encountered in subjects in which Hg2+ concentration in the brain remains in the submicromolar range, markedly below the anticipated threshold for direct inhibition of cerebral metabolism and function. In this report we review biochemical and morphological evidence obtained in this and other laboratories in tissue culture studies suggesting that in such instances mercury neurotoxicity may be mediated by excitotoxic activity of glutamate (GLU). Mercuric chloride (MC) at 1 mum concentration (or less) inhibits GLU uptake and stimulates GLU release in cultured astrocytes, which in vivo is likely to result in excessive GLU accumulation in the extracellular space of the CNS. Inhibition of GLU uptake a

437
TITLE:
Bioelectric activity of the brain in patients with chronic occupational mercury poisoning.

AUTHORS:
POPOV LI
SAMOKHVALOVA GN

SOURCE:
GIG TR PROF ZABOL; 17 (9). 1973 52-53

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. EEG studies were carried out in 48 patients with chronic occupational poisoning from metallic mercury (dredgers, traction substation workers, dentists). Mild manifestations of poisoning in the form of astheno-vegetative or astheno-neurotic syndrome were seen in 26 persons; in 15, more pronounced astheno-vegetative syndrome was accompanied by polyneuritic disturbances; in 7, more severe mercury poisoning was evident in the form of toxic encephalopathy or toxic encephalopolyneurities. Disturbances of the bioelectric activity of the

brain were detected in almost all patients, which indicated dysfunction of the deep structures of the brain at the level of the mesodiencephalon and disturbance of the reactivity of the cortex of the great hemispheres. Changes in bioelectric activity were observed in almost all patinets, independent of the severity of the syndrome and its clinical characteristics.

438
TITLE:
INHIBITION OF BRAIN TUBULIN-GUANOSINE 5'-TRIPHOSPHATE INTERACTIONS BY MERCURY SIMILARITY TO OBSERVATIONS IN ALZHEIMER'S DISEASED BRAIN

AUTHORS:
PENDERGRASS JC
HALEY BE

SOURCE:
SIGEL, A. AND H. SIGEL (ED.). METAL IONS IN BIOLOGICAL SYSTEMS, VOL. 34. MERCURY AND ITS EFFECTS ON ENVIRONMENT AND BIOLOGY. XLII+604P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ISBN 0-8247-9828-7.; 34 (0). 1997. 461-478.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER LITERATURE REVIEW HUMAN RAT TOXICOLOGY MERCURY ALZHEIMER'S DISEASE TUBULIN BETA-SUBUNIT GTP BRAIN NERVOUS SYSTEM BEHAVIORAL AND MENTAL DISORDERS NERVOUS SYSTEM DISEASE NERVOUS SYSTEM

439
TITLE:
Imbalances of trace elements related to oxidative damage in Alzheimer's disease brain.

AUTHORS:
CORNETT CR
MARKESBERY WR
EHMANN WD

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 19 (3). 1998. 339-346.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Four elements that have been implicated in free-radical-induced oxidative stress in Alzheimer's disease (AD) were measured by instrumental neutron activation analysis (INAA) in seven brain regions from 58 AD patients and 21 control subjects. A statistically significant elevation of iron and zinc was observed in multiple regions of AD brain, compared with controls. Mercury was elevated in AD in most

regions studied, but the high variability of mercury levels in both AD and control subjects prevented the AD-control difference from reaching significance. Selenium, a protective agent against mercury toxicity, was significantly elevated only in AD amygdala. The elevation of iron and zinc in AD brian has the potential of augmenting neuron degeneration through free radical processes.

440
TITLE:
Effects of protein-deficient nutrition during pregnancy and development on developmental hindlimb crossing due to methylmercury intoxication.

AUTHORS:
Chakrabarti SK
Bai C

SOURCE:
Toxicologist 2000 Mar;54(1):80

ABSTRACT:
The effects of methyl mercury intoxication on the clinical neurological signs due to protein-calorie malnutrition in children are not known sufficiently. Timed pregnant Sprague-Dawley rats were fed either a control (20% protein) or low (3.5% protein) diet during gestation and lactation. The pups were separated from their mothers of each diet group on postnatal day 21, and were given the same diets as those of their corresponding mothers. The groups of pups from each diet group were treated either on postnatal day 21, or postnatal day 60 with 7.5 mg methylmercury chloride (MeHgCl) per kg b.w. once daily by gavage for 10 consecutive days and the development of ataxia (hind limb crossing) was monitored. The offspring from protein-deficit diet were found to be more sensitive to MeHg-induced ataxia than those from protein-sufficient diet. Rats fed 3.5% casein diet accumulated more mercury in the different brain regions than those fed 20% casein diet. The rates of protein synthesis in different brain regions of offspring fed the protein-deficient diet were significantly reduced compared to those fed the protein-sufficient diet. However, MeHg treatment did not significantly modify further the rates of such protein synthesis in protein-deficient rats. Thus, increased inhibition of the rates of protein synthesis plus increased accumulation of mercury in different brain regions due to severe protein deficiency may result in increasing susceptibility of developing rats to MeHg-induced ataxia, or hind limb crossing.

441
TITLE:
Pathological study of toxic polyneuropathy: IV. Mercury contents in the peripheral nerves of rats administered by methyl mercury chloride.

AUTHORS:
KAMEDA T

SOURCE:
J KUMAMOTO MED SOC; 45 (10). 1971 1000-1005

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The Hg content of the peripheral nerves was determined using the dithizone method and atomic absorption photometry. Hg was demonstrated in the peripheral nerves as well as in the brain and liver. The rate of Hg contents in the peripheral nerve and brain was 1:2 respectively. Over l0 ppm Hg content was necessary to cause nervous symptoms accompanied by morphological changes in the peripheral nerves. After administration, Hg increased rapidly in the peripheral nerves; it gradually decreased after discontinuance. However, a small amount of Hg (3.1 ppm) remained for 102 days (until the end of the experiment). This presumably resulted in a delay of the peripheral nerve regeneration previously observed. From this experiment it was concluded that methyl mercury penetrates the blood brain barrier.

442
TITLE:
Effect of mercuric chloride and methylmercury chloride exposure on tissue concentrations of six essential minerals.

AUTHORS:
Bogden JD
Kemp FW
Troiano RA
Jortner BS
Timpone C
Giuliani D

SOURCE:
Environ. Res. 21(2): 350-359 1980 (32 References)

ABSTRACT:
PESTAB. There are few data on the effects of mercury exposure on tissue concentrations of essential minerals. Male Sprague-Dawley rats were exposed to mercuric chloride and methylmercury chloride administered via the drinking water. Subsequently, the kidneys, spleen, liver, and brain were analyzed for mercury, calcium, copper, magnesium, manganese, iron, and zinc by atomic absorption spectrophotometry. Significant differences from controls were found for brain copper, kidney copper, and kidney zinc in the mercuric chloride-exposed animals; and for brain iron, kidney copper, kidney iron, kidney magnesium, spleen magnesium, and liver manganese in the methylmercury chloride-exposed rats. There was a 5-fold higher mean kidney copper concentration in the mercuric chloride-exposure

group: this may be related to the induction of renal metallothionein synthesis by mercury. Increased kidney copper may be a manifestation of heavy metal-induced renal toxicity. Both inorganic and methylmercury exposure produce significant changes in tissue concentrations of some essential minerals. (Author abstract by permission)

443
TITLE:
Distribution of mercury in rabbits subchronically exposed to low levels of radiolabeled methyl mercury.

AUTHORS:
PETERSSON K
DOCK L
SODERLING K
VAHTER M

SOURCE:
PHARMACOL TOXICOL; 68 (6). 1991. 464-468.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The metabolism of methyl mercury (MeHg) has been studied in rabbits administered 203Hg-labeled methyl mercuric chloride, 0.125 mumol/kg body weight, twice a week for 9 weeks, by intravenous injection. Twelve weeks after cessation of treatment, about 54% of the administered dose had been excreted in faeces and 5% in urine. After one week, the highest concentration of 203Hg was found in fur (8.6 nmol Hg/g). Substantially lower concentrations were found in kidney (2.5 nmol/g), liver (0.9 nmol/g), brain (0.4 nmol/g), muscle (0.3 nmol/g) and blood (0.1 nmol/g). The rate of elimination of 203Hg from brain, muscle and blood was faster (T1/2 about 12 days) than that from kidney and liver (t 1/2 about 28 days). The relative amount of inorganic Hg in kidney and liver increased with time after cessation of treatment. The highest fractions were 85 and 70%, respectively. In brain, no significant demethylation of MeHg could be detected.

444
TITLE:
ENVIRONMENTALLY INDUCED ALTERATIONS IN NEURON AND GLIA DEVELOPMENT

AUTHORS:
HARRY GJ

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
During the development of the nervous system, the temporal and spatial

regulatio n of gene expression is a critical component of neural and glial growth, develop ment, and interactions. These critically timed events are assummed to be a major component in the differential susceptibility of the developing organism to envi ronmental insult.This project examined chemical induced perturbations during dev elopment of the NS as indicated by alterations in the spatio-temporal expression of mRNA for various developmentally regulated proteins associated with distinct processes of development. We have shown by RNase protection assays that lead a cetate alters developmentally regulated structural proteins for neurons and glia in the rat as well as an upregulation of apoptosis genes and brain derived neur otrophic factors. Early exposure to mercury vapors also elevate mRNA levels for apoptosis factors consistent with previous reports of mercury induced apoptosis in the brain.This technique is being expanded with the establishment of new prob e sets to detect mRNA levels for proteins associated with the various cell types and stages of brain development. Future Research: The developmental related ef fects of chemicals which disrupt thyroid hormone levels,PTU and dioxin, will be examined to determine any relationship with structural alterations in the nervou s system. Additional studies are based upon events associated with hypoxia-ische mia occurring at preterm birth. These studies will examine the acute toxicity of interleukin 6 on the early post-natal developing CNS and alteration in the norm al ontogeny of molecular markers for cortical neuronal network development.

445

TITLE:

Chronic toxicity test of phenylmercuric acetate on rhesus monkey (Macaca mulatta).

AUTHORS:

Abe E

SOURCE:

Baioteku (Biotech); 3(2): 98-104; 1972 ; (REF:6)

ABSTRACT:

HAPAB Four groups of rhesus monkeys, age 2 to 3.5 years, consisting of two males and two females were fed diets containing phenylmercuric acetate (PMA) at the rate of 50, 10, 2 and 0.4 ppm for 48 mo. Dosage levels used were 1.25, 0.25, 0.05 and 0.01 mg PMA/kg/day. Another group was used for control. The criteria of effect included mortality, body-weight change, diet consumption, micropathology, organ-weights, measurements of blood, urine and biochemical parameters and serum antobody formation. Contents of mercury in liver, kidney and brain were measured by dithizon method. None of the criteria measured was significantly altered at any dose level except: infiltration of round cells in Glisson's capsule of liver found in the 50 and 0.4 ppm groups, antibody formation in serum (passive cutaneous anaphylaxis reaction) in all the tested groups and abnormal proliferation

of lymph follicle in kidney in the 2.0 ppm group. Mercury content in brain, liver and kidney was significantly higher in the tested groups than in control and especially in kidney the content ran parallel to the dosage level, the value in the 50 ppm group being 2.07 ppm in brain, 22.85 ppm in liver and 173.8 ppm in kidney. The abnormal proliferations in the kidney could be possibly explained as an allergic phenomenon attributable to PMA because PMA was found to be an antigen. Therefore, it will be necessary to examine the possibility of the occurrence of other allergic disturbances due to PMA, as well as the fate and metabolism of PMA in the animal body in connection with the possibility of formation of methyl mercury in vivo. 1972

446

TITLE:

A Physiologically Based Pharmacokinetic Model for Methyl Mercury in the Pregnant Rat and Fetus

AUTHORS:

Gray DG

SOURCE:

Toxicology and Applied Pharmacology, Vol. 132, No. 1, pages 91-102, 77 references, 1995

ABSTRACT:

A physiologically based pharmacokinetic model that can be used to incorporate rat developmental toxicity into the assessment of methyl-mercury (22967926) (MeHg) risk was developed using pregnant rats and fetuses. The model parameters included data on linear binding constants, membrane transfer constants, biliary transport cellular and extracellular volumes, and plasma flow rates for dams and fetuses from previous studies. Calculations for the model parameters were presented. The model was executed with an intravenous dose of 1mg/kg MeHg at various times during the 22 day gestation period. Fetal red blood cells carried most of the MeHg body burden. MeHg levels rose rapidly in the brain, liver, kidney and red blood cells. Continuous dosing for 98 days simulated a human dietary exposure pattern for MeHg contaminated foods. Maternal skin, muscle, and red blood cells accounted for most of the MeHg burden. Fetal brain contained 0.14% of the total MeHg burden. All fetal organs and the placenta combined contained 3.6% of the total MeHg burden. The results of this model compared well with experimental values. Membrane transfer constants were primarily responsible for short term behavior, whereas linear binding constants were more critical for long term MeHg transport. The model generated fetal brain MeHg profiles for dosing patterns used in rat developmental neurobehavioral studies. Dose response relationships can be scaled to human fetuses to estimate the threshold of MeHg concentrations associated with subtle neurobehavioral effects, such as learning deficits. The author concludes that the model

predicts maternal and fetal MeHg organ concentrations for a variety of dosing patterns.

447
TITLE:
Animal models of autism

AUTHORS:
AMARAL DG

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Autism is a neurodevelopmental syndrome defined by deficits in social reciprocity and communication and by unusual repetitive behaviors. While there is clearly an underlying genetic predisposition, the etiology(ies) of autism is/are currently unknown. Development of animal models of autism have been hobbled by the lack of knowledge concerning its etiology(ies) and by the paucity of data on the characteristic neuropathology of autism, i.e., it is not clear what a successful model of autism would look like. If one focuses on the root deficit in autism, i.e., the impairment of social interaction, however, successful mouse and nonhuman primate models are achievable. The overarching goal of this project is to establish batteries of behavioral tasks that will provide sensitive assessments of normal mouse and rhesus monkey social behavior. With the establishment of the animal models, two hypotheses will be tested: 1) that prenatal and/or postnatal exposure to xenobiotics will decrease normal conspecific social behavior; and 2) that changes in social behavior will be associated with alterations of brain regions, such as the amygdala, that have been implicated in social behavior. Perinatal mice will be parametrically exposed to thimerosal, methyl mercury, and to a mixture of PCB congeners (PCB 153, 180, 118, 138, and 170) to determine whether these xenobiotics alter normal social behavior. Based, in part, on the mouse studies and on information concerning expected environmental exposure in autistic children, neonatal monkeys will also be exposed to thimerosal, methyl mercury and PCBs. The mouse battery of social and cognitive testing will include: Response to maternal separation and relocation; response to maternal separation and relocation; response to novel objects; response to a human intruder; response to social videotapes. A specially designed ethogram will also be used to evaluate maternal < - > infant interactions and to study the emergence and quality of social behaviors through daily dyadic social interactions with "stimulus" animals. At the termination of behavioral testing, morphological changes will be evaluated in brain regions, such as the amygdala, known to be involved in normal social behavior. Additional tissue will be distributed to Core I for analysis of xenobiotic distribution, to Core II for analysis of cytokines and autoantibody production and Core III for altered brain gene

expression.

448
TITLE:
Levels of Hg, Pb and V in Brain, Kidney, Liver and Lung of Anencephalic Fetuses from the Eastern Coast of Lake Maracaibo, Venezuela

AUTHORS:
Tahan JE
Barrios LC
Marcano L
Granadillo VA
Cubillan HS
Sanchez JM
Rodriguez MC
De Salazar FG
Salgado O
Romero RA

SOURCE:
Trace Elements and Electrolytes, Vol. 13, No. 1, pages 7-13, 38 references, 1996

ABSTRACT:
The levels of mercury (7439976) (Hg), lead (7439921) (Pb), and vanadium (7440622) in the brain, kidney, liver and lung of anencephalic fetuses were studied in an effort to provide metal data useful in etiological studies. Twenty stillborn fetuses with anencephaly and 20 stillborn fetuses without anencephaly came from the Eastern coast of Lake Maracaibo, Venezuela, where a relatively high anencephaly rate was noted, 5.1 per 1,000 total births in 1994. Evaluations took place from April 1993 to July 1994. Complete organs were obtained by autopsy from all fetuses within 36 hours of delivery and prepared for analysis. Samples were analyzed by cold vapor atomic absorption spectrometry (for Hg), differential pulse anodic stripping voltammetry (for Pb), and electrothermal atomization atomic absorption spectrometry (for vanadium). Demographic data were obtained by questionnaires. The evidence provided a strong correlation of placental transfer of Hg and Pb and showed higher metal contents in anencephalic fetuses than in controls. Hg and Pb were significantly increased in kidney and liver of anencephalic fetuses. Vanadium was detected exclusively at brain level, being significantly higher in controls. The authors conclude that vanadium seems the most unlikely of the three elements studied to be associated with anencephaly. The authors conclude that Hg and Pb as toxic elements found in the environment should be seriously considered for cause/effect studies of the etiology of anencephaly in this region. They note that this malformation is multifactorial and a more complete study is needed.

449
TITLE:
Effects of Chronic Exposure to Cadmium, Lead and Mercury on Brain Biogenic Amines in the Rat

AUTHORS:
Hrdina PD
Peters DAV
Singhal RL

SOURCE:
Research Communications in Chemical Pathology and Pharmacology, Vol. 15, No. 3, pages 483-493, 36 references, 19761976

ABSTRACT:
Effects of chronic treatment with different doses of cadmium-chloride, methylmercury-chloride, and lead-acetate and of 28 day withdrawal of treatment on the levels of acetylcholine and activity of acetylcholinesterase in cerebral cortex, and concentration of norepinephrine and 5-hydroxytryptamine in brainstem were examined in rats. Exposure to both cadmium and methylmercury produced significant decreases in cortical acetylcholine and brain stem 5-hydroxytryptamine levels. In addition, brainstem norepinephrine concentration was increased in methylmercury treated rats. In contrast, chronic treatment with lead resulted in enhanced cerebrocortical acetylcholine levels but a decreased brainstem norepinephrine concentration. Treatment with cadmium also produced a transient enhancement of striatal dopamine levels. Cadmium induced decreased in brainstem 5-hydroxytryptamine and lead induced accumulation of cortical acetylcholine persisted even after 28 day withdrawal of treatment. The data indicate that chronic exposure to low doses of heavy metals produces differential changes in regional levels of various brain biogenic amines. These changes may represent the early signs of adverse effects on central nervous system function since they occur before any overt symptoms of neurotoxic effects of heavy metals become apparent.

450
TITLE:
Cell Specific Enzyme Markers as Indicators of Neurotoxicity: Effects of Acute Exposure to Methylmercury

AUTHORS:
Kung M-P
Kostyniak PJ
Olson JR
Sansone FM
Nickerson PA
Malone MA

Ziembiec N
Roth JA

SOURCE:
Neurotoxicology, Vol. 10, No. 1, pages 41-52, 27 references, 1989

ABSTRACT:
By comparing the onset of biochemical changes in the brain with the presence of histopathological and overt signs of toxicity, the relative sensitivity of changes in biochemical markers as indices of neurotoxicity were assessed. Male Sprague-Dawley-rats were treated with two doses of the neurotoxic agent methylmercury-chloride (115093) (MMC) in efforts to determine the sensitivity of several cell specific enzyme markers. Comparisons were also made of histopathological changes. The rats exhibited less body weight gain than controls when treated orally at the low dose level of 3.36mg mercury (7439976) per kg body weight. Neuronal and nonneuronal enzyme markers gave no evidence of change in the brain at this dose level. However, a significant increase was noted in the myelin marker, 2',3'-cyclicnucleotide-phosphohydrolase (CNP), along with total enolase activity in the optic nerve. No discernible neuronal lesions were noted in MMC exposed animals at the low dose level. A 20 percent loss in the body weight of treated animals was noted at the high dose level of 7.05mg/kg mercury for 7 days. Partial hindlimb paralysis also resulted. Only tyrosine-hydroxylase (TH), of all the neuronal marker enzymes examined, was decreased in the striatum. An elevation was noted in the cerebellum of the proliferating astroglial marker, glutamine-synthetase (GS). CNP was decreased in both the optic and sciatic nerve. No pathological changes were noted in the light microscopic level in the brain of MMC treated rats. The authors conclude that of the cell specific marker enzymes examined, GS in the cerebellum and TH in the striatum, may be useful biochemical markers for the neurotoxic action of MMC.

451
TITLE:
Developmental neurotoxicology of therapeutics: survey of novel recent findings.

AUTHORS:
Slikker W Jr

SOURCE:
Neurotoxicology 2000 Feb-Apr;21(1-2):250

ABSTRACT:
Therapeutic agents present special challenges to risk assessment because many may represent both risks and benefits to human health. Two agents fitting this description are the HIV therapeutic AZT and the vaccine preservative Thimerosal. Treatment of HIV infected pregnant women with AZT

has decreased the vertical transmission of HIV infection to the infant from 25 to 8%. Safety assessments are incomplete, however, and data suggest that prenatal exposure in rodents may result in cancer or behavioral alterations in the offspring. Recent data in pregnant nonhuman primates and humans suggest that monkey fetal tissue and human cord blood contain AZT incorporated into DNA after maternal AZT treatment. Thimerosal is frequently used in life saving vaccinations including diphtheria-tetanus-pertussis (DTP) and influenza. Thimerosal (sodium ethylmercurithiosalicylate) crosses the blood-brain and placental barriers and results in appreciable mercury content in tissues including brain. Thimerosal contains 49.6% mercury by weight and is metabolized to ethyl mercury and thiosalicylate. Even though Thimerosal has been used as a preservative in biologics and vaccines since the 1930s, recent recommendations by the Food and Drug Administration, Public Health Service and the American Academy of Pediatrics that Thimerosal should be removed from vaccines has heightened concern over the potential for Thimerosal to induce developmental neurotoxicology. These two examples reinforce the need for further study of these important ingredients of therapeutic agents that have both benefits and potential associated risks.

452

TITLE:

Methodological issues in assessing neurobehavioral effects of prenatal exposure to neurotoxicants.

AUTHORS:

Grandjean P
White RF
Weihe P
Debes F
Murata K
Araki S

SOURCE:

Neurotoxicology 2000;21(5):888

ABSTRACT:

Experience with lead, methylmercury and PCBs document that prenatal exposure can cause more serious and more widespread damage than exposures encountered postnatally. Because preventive efforts should aim at protecting the most susceptible individuals, it is important to focus on prenatal exposures. However, research in this area is fraught with difficulties. Exposure assessment should consider toxicokinetic patterns in relation to the time of greatest vulnerability of the brain. Studies have successfully used maternal or cord blood concentrations of the neurotoxicants to characterize in utero exposures. Other biomarkers may also be used, but must consider the risk of exposure misclassification. Choosing the age at neurobehavioral assessment is complex. Even Minamata

disease was not recognized at birth, and tests feasible for small children may overlook subtle deficits. Because the effects of fetal exposure may be persistent, examination age 6-7 years has several advantages. At this age, the children have developed sufficiently to perform a wide variety of neurobehavioral tests, and they are capable of cooperating for many functional tasks. An informative test battery should cover a relevant range of behavioral, cognitive, and neurophysiological functions with the highest possible degree of specificity for the domains involved, high diagnostic sensitivity, and high statistical sensitivity. While IQ and other omnibus tests may be useful, tasks that are more specific in their measurement of cognitive processing abilities may reflect the underlying functional deficits that are most susceptible to the exposure. Feasible neurophysiological tests may be less prone to confounding, but their diagnostic sensitivity may be inferior to that of neuropsychological tests. These considerations have been amplified by a prospective study of 1,000 Faroese children with different degrees of prenatal exposure to methylmercury. The cord-blood mercury concentration was the best risk indicator. At age 7 years, mercury-related neuropsychological dysfunctions were most pronounced in the domains of language, attention, and memory, and to a lesser extent in visuospatial and motor functions. Also, significant mercury-associated delays were seen in the I-III interpeak interval and the peak III latency of the auditory brainstem evoked potentials. These findings emphasize the vulnerability of the developing brain to the effects of methylmercury exposure.

453

TITLE:

Inability of Thiol Compounds to Restore CNS Arylsulfatases Inhibited by Methyl Mercury

AUTHORS:

Vinay SD
Sood PP

SOURCE:

Pharmacology and Toxicology, Vol. 69, No. 1, pages 71-74, 20 references, 1991

ABSTRACT:

The inhibition of arylsulfatase-A and arylsulfatase-B by methyl-mercury-chloride (115093) (MMC) in various brain regions and the protective effects of N-acetyl-DL-homocysteine-thiolactone (NAHT) and glutathione (GSH) were studied in rats. Male Wistar-albino-rats were administered MMC intramuscularly at 1.0 or 10mg/kg for 2, 7, or 15 days. Some groups of rats were injected with either 40 or 80mg/kg NAHT, or 100 or 150mg/kg GSH daily for 2, 7, or 15 days. Rats were sacrificed the day after the end of the dose period. Arylsulfatase activity was subsequently measured in the olfactory bulbs, cerebral hemispheres, cerebellum, and

medulla oblongata. Results showed a dose dependant inhibition of enzyme activity by MMC in all areas after 2 days of dosing. After day 15, the cerebellum's arylsulfatase-A activity was the least inhibited of all areas. With respect to arylsulfatase-B, olfactory bulbs showed the highest inhibition. Neither NAHT or GSH was able to reverse MMC induced inhibition. The authors conclude that MMC has the ability to inhibit arylsulfatases in most parts of the brain and NAHT and GSH were unable to reverse inhibition.

454
TITLE:
Preliminary studies on methylmercury biotransformation and clearance in the brain of primates: I. Experimental design and general observations.

AUTHORS:
MOTTET NK
BURBACHER TM

SOURCE:
J TRACE ELEM EXP MED; 1 (1). 1988. 41-48.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Long-term low dose exposure of female Macaque fascicularis to subneurotoxic levels of methylmercury was maintained through pregnancy and parturition. Exposure duration ranged from 500 days (followed by 500 days of clearance) to 1,050 days. The offspring were observed for behavioral and physical development and have been reported separately. Cage behavior of the adults was recorded biweekly. Blood chemistry, including electrolytes, liver and kidney function tests, hemogram and whole blood total mercury were assayed during a baseline period, experimental period, and at autopsy. Subtle microscopic brain mercury lesions could be seen in some animals with blood levels above 2 ppm. There was increased female reproductive failure at blood levels above 1.5 ppm and behavioral deficits were seen in mid sagittally hemisected and half were frozen at -70êC prior to shipment to the Karolinska Institute in Sweden for brain mercury speciation studies.

455
TITLE:
Comparative study on the inhibition of acetylcholinesterase activity in the freshwater fish Cyprinus carpio by mercury and zinc.

AUTHORS:
SURESH A
SIVARAMAKRISHNA B
VICTORIAMMA PC
RADHAKRISHNAIAH K

SOURCE:
BIOCHEM INT; 26 (2). 1992. 367-375.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of sublethal concentrations of mercury (0.1 mg/l) and zinc (6 mg/l) on acetylcholinesterase activity and acetylcholine content of gill, kidney, intestine, brain, liver and muscle of the freshwater fish Cyprinus carpio at 1, 15 and 30 days of exposure were studied. A significant suppression in acetylcholinesterase activity was recorded in all the organs from both mercury and zinc intoxicated fish at all the exposure periods. Concurrently, a significant increase in the content of acetylcholine in the organs was observed. These changes observed in the organs of mercury treated fish in different exposure periods were in the order 1 > 15 < 30 days and in zinc treated fish 1 > 15 > 30 days. Further, these changes were greater in magnitude in the brain, liver and muscle (non-osmoregulatory organs) than in the gill, kidney and intestine (osmoregulatory organs) in both metal media.

456
TITLE:
The dental amalgam mercury controversy: Inorganic mercury and the CNS; genetic linkage of mercury and antibiotic resistances in intestinal bacteria.

AUTHORS:
LORSCHEIDER FL
VIMY MJ
SUMMERS AO
ZWIERS H

SOURCE:
TOXICOLOGY; 97 (1-3). 1995. 19-22.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury (Hg) vapor exposure from dental amalgam has been demonstrated to exceed the sum of all other exposure sources. Therefore the effects of inorganic Hg exposure upon cell function in the brain and in the intestinal bacteria have recently been examined. In rats we demonstrate that ADP-ribosylation of tubulin and actin brain proteins is markedly inhibited, and that ionic Hg can thus alter a neurochemical reaction involved with maintaining neuron membrane structure. In monkeys we show that Hg, specifically from amalgam, will enrich the intestinal flora with Hg-resistant bacterial species which in turn also become resistant to antibiotics.

457
TITLE:
Mechanisms In Cardiovascular Regulation Following Chronic Exposure Of Male

Rats To Inorganic Mercury

AUTHORS:
Carmignani M
Finelli VN
Boscolo P

SOURCE:
Toxicology and Applied Pharmacology, Vol. 69, No. 3, pages 442-450, 43 references, 19831983

ABSTRACT:
Hemodynamic changes following chronic ingestion of mercury (7439976) were studied in rats. Male weanling Sprague-Dawley-rats received 50 micrograms per milliliter (microg/ml) mercuric-chloride in deionized drinking water for 320 days or were untreated. After exposure, aortic blood pressure (BP), heart rate (HR), and the maximal rate of rise in left ventricular pressure (dP/dt) were monitored during basal conditions, bilateral occlusion of the common carotid arteries for 30 seconds, intravenous injection of agonists, bilateral selective vagotomy at the neck below the nodose ganglion, and intravenous injection of graduated doses of hexamethonium (60264) from 0.65 to 2.5 milligrams per kilogram. Animals were sacrificed, and zinc, copper, and iron were determined in kidney and brain. During baseline, exposed rats had a 30 percent larger maximum dP/dt than controls, but the groups did not differ in BP or HR. Bilateral carotid occlusion increased all parameters, but increases of BP and maximum dP/dt in exposed animals were 45 to 60 percent of those in controls. Increases of BP and maximum dP/dt induced by 1microg/kg norepinephrine (51412) or 0.125 to 2.0microg/kg epinephrine (51434) in exposed animals were 35 to 70 percent of those in controls. Changes in HR did not differ between groups after any manipulation, nor did any parameter after vagotomy or administration of hexamethonium, acetylcholine (51843), angiotensin (1407472), bradykinin (58822), histamine (51456), or serotonin (50679). Compared to controls, the kidneys and brain of exposed animals contained 6.5 and 1.5 times more copper, respectively, and 2.1 and 1.6 times more zinc. The authors conclude that chronic mercury exposure superficially affects cardiovascular reactivity to catecholamines and may interfere with baroreflex mechanisms.

458
TITLE:
Degree of Peroxidative Status in Neuronal Tissues by Different Routes of Inorganic Mercury Administration

AUTHORS:
Anuradha B
Rajeswari M
Varalakshmi P

SOURCE:
Drug and Chemical Toxicology, Vol. 21, No. 1, pages 47-55, 29 references, 1998

ABSTRACT:
A study was conducted to measure the extent of peroxidation and perturbed scavenging systems in the neuronal tissues during mercuric-chloride (7487947) (HgCl2) induced toxicity. Adult female Wistar-rats were administered 0.5mg/kg body weight of HgCl2 by three different routes for a period of 7 days. Group II was treated subcutaneously, group III intramuscularly, and group IV intraperitoneally. The levels of reduced glutathione and glutathione-peroxidase were elevated markedly on intoxication with HgCl2. The intramuscular injection brought about maximal alterations in the levels of reduced glutathione and glutathione-peroxidase. In those dosed intramuscularly, the extent of alteration was significantly higher in nerves than in brain tissues. An enhanced activity of superoxide-dismutase was noted, which may be the cause for the elevated activity of catalase. Basal peroxide levels were high in the intraperitoneally dosed group, followed in decreasing order by group III and group II animals. On the addition of inducers, the extent of peroxidation was almost the same in groups III and IV. All test groups showed almost similar susceptibility to ferrous-sulfate and ascorbate induced peroxidation. The nerves of group III animals showed increased susceptibility to hydrogen-peroxide, indicating oxidative stress on the peripheral neuronal cells. The authors conclude that mercury is detoxified by enzymatic and nonenzymatic antioxidant systems and the extent of increase in these systems is a measure of the degree of damage caused to the neuronal tissues.

459
TITLE:
In vitro and in vivo effects of lead, methyl mercury and mercury on inositol 1,4,5-trisphosphate and 1,3,4,5-tetrakisphosphate receptor bindings in rat brain.

AUTHORS:
CHETTY CS
RAJANNA S
HALL E
YALLAPRAGADA PR
RAJANNA B

SOURCE:
TOXICOLOGY LETTERS (SHANNON); 87 (1). 1996. 11-17.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In vitro and in vivo effects of mercury

(Hg), methyl mercury (MM) and lead (Pb) on (3H)inositol 1,4,5-trisphosphate (IP3) and (3H)inositol 1,3,4,5-tetrakisphosphate (IP4) receptor binding in the Sprague-Dawley rat brain cerebellar membranes were studied. In vitro studies indicate that binding of (3H)IP3 and (3H)IP4 to cerebellar membranes was inhibited by Hg while they were stimulated by MM or Pb in a concentration-dependent manner. MM was more potent (EC50 3.4 muM) than Pb (EC50 18.2 muM) in stimulating the (3H)IP3 receptor binding activity whereas Pb (IC50 30 muM) was more potent than MM (IC50 133 muM) in stimulating the (3H)IP4 receptor binding. When the rats were treated (i.p.) with Hg (5 mg/kg body wt.) or MM (5 mg/kg body wt.) or Pb (25 mg/kg body wt.) for 3 or 24 h, no significant alterations in (3H)IP3 receptor binding were observed in cerebellum and cerebral cortex. But the above treatment of Pb or MM for 3 or 24 h to rats resulted in an increase of (3H)IP4 re

460
TITLE:
The chronic toxicity of inorganic mercury in goats: Clinical signs, toxicopathological changes and residual concentrations.

AUTHORS:
PATHAK SK
BHOWMIK MK

SOURCE:
VETERINARY RESEARCH COMMUNICATIONS; 22 (2). 1998. 131-138.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Chronic mercury toxicity was induced in goats by administering mercuric chloride at too mug/ml in deionized drinking water offered ad libitum for 90 days. Toxic signs of gastrointestinal disturbances and renal dysfunction developed from 43 days onwards without any mortality. The toxicity also induced nephrosis and tubular nephritis; centrilobular necrosis of liver; mild to moderate necrosis in spleen, intestine and lymph node: Zenker's degeneration of cardiac muscles; exudative pneumonia; and pial congestion, oedema and vacuolation in the brain. In addition, hyperaemia, oedema and tissue hemorrhages were evident in most of the organs. The kidneys contained the largest residues of mercury, followed by liver, spleen, intestine, lymph node, skeletal muscles, lungs, heart, brain and the omental fat. The intensity of the cytotoxic changes in the various organs was proportional to the amount of mercury accumulated.

461
TITLE:
Inhibition of Rat Brain Microsomal Na++-ATPase and Ouabain Binding by Mercuric Chloride

AUTHORS:
Chetty CS
Rajanna B
Rajanna S

SOURCE:
Toxicology Letters, Vol. 51, No. 1, pages 109-116, 21 references, 1990

ABSTRACT:
The in-vitro effects of mercuric-chloride (7487947) (HgCl2) on Na++-ATPase and tritium labeled ouabain binding in rat brain microsomes were investigated. Independent and additive actions of HgCl2 and ouabain on Na+/K+-ATPase were studied to determine whether there was any interference between these two inhibitors. Male Sprague-Dawley-rats were used for the preparation of microsomes. HgCl2 inhibited Na+/K+-ATPase effectively at micromolar concentrations. As the enzyme concentration increased and the incubation time lengthened, the degree of inhibition decreased. No change in the percent inhibition of Na+/K+-ATPase activity by HgCl2 was noted in response to variations in the ionic strength of Na+ and K+. Enzyme activity was restored partially by repeated washings. HgCl2 inhibited the binding of ouabain to microsomal membranes in a concentration dependent manner. The study on combined effects of HgCl2 and ouabain showed that the observed percent inhibitions were not equal to the calculated values. The authors conclude that HgCl2 and ouabain did not act concurrently and independently on Na+/K+-ATPase.

462
TITLE:
Methyl mercuric chloride toxicokinetics in mice: II. Sexual differences in whole-body retention and deposition in blood, hair, skin, muscles and fat.

AUTHORS:
NIELSEN JB
ANDERSEN O

SOURCE:
PHARMACOL TOXICOL; 68 (3). 1991. 208-211.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This article reports the time course for deposition of methyl mercury administered as a single oral dose in whole body, total carcass, liver, kidneys, brain, blood, fat, muscle, bone, skin and hair of male and female Bom:NMRI mice. The whole-body elimination initially approximated first order kinetics with half-times around 7 days and 12 days for males and females respectively, although a decreased elimination rate was observed during the last 10 days. The elimination of mercury from carcass was slower than the elimination from the whole-body, causing an increasing relative carcass depositon with time in both male

and female mice and expalining the observed deviation from first order elimination kinetics. Thus, first order kinetics is observed on during 2-3 weeks after dosage. Throughout the experimental period, male mice had significantly lower levels of mercury in both blood, brain and muscles than had female mice, whereas renal deposition of mercury in male mice was s

463
TITLE:
Neuropathology of Methylmercury Intoxication

AUTHORS:
Sato T
Nakamura Y

SOURCE:
Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 355-366, 11 references, 1991

ABSTRACT:
This paper reviewed the minimal toxic dose of methylmercury (22967926) in cynomolgus-monkeys and the selective vulnerability of nerve tissue in cats. A daily dose of 0.9 to 0.23mg/kg methylmercury was administered to four monkeys for 56 to 133 days in group-A and a dose of 0.02 to 0.04mg/kg to five monkeys for 87 to 331 days in group-B. Monkeys in group-A developed clinical symptoms of methylmercury intoxication after administration of a total dose of 12.8mg/kg or more, characterized by weakness of grip, an unsteady and ataxic gait, fine tremor and anorexia. Visual and hearing impairments were detected. Monkeys in group-B did not show any remarkable clinical symptoms but abnormal nystagmus was demonstrated in an electronystagnogram. The concentration of methylmercury in the calcarine cortex of monkeys in group-A was 9.9 to 21.7 micrograms/gram and in group-B monkeys was 0.1 to 8.0 micrograms/gram. No differences were observed in methylmercury concentration between the calcarine cortex and other brain areas. Remarkable degeneration of nerve cells was noted by electron microscopic observation in the cerebral cortex, particularly in the calcarine cortex. A marked loss of mitochondria and endoplasmic reticulum was noted as well. In group-B monkeys, light microscopy revealed slightly atrophic nerve cells in the deep layer of the calcarine cortex. In a study of the influence of methyl-mercury on the binding of WB-4101 to the occipital cortexes of cats, a markedly decreased receptor affinity for alpha-1-norepinephrine was noted in the membrane fraction of the occipital cortex intoxicated with methylmercury.

464
TITLE:

Increased Cytochrome Oxidase Activity of Mesencephalic Neurons in Developing Rats Displaying Methylmercury-Induced Movement and Postural Disorders

AUTHORS:
Dyck RH
O'Kusky JR

SOURCE:
Neuroscience Letters, Vol. 89, No. 3, pages 271-276, 16 references, 1988

ABSTRACT:
The ability of methylmercury (22967926) to produce neurotoxicity in early postnatal rat development was examined. On postnatal day three, Sprague-Dawley-rats received complete aspirative neocortical lesions with the frontal and parietal bones removed, the dura excised, and the neocortex aspirated, after which the animals were sutured and rewarmed. On postnatal day five, the animals in the methylmercury group received subcutaneous injections of 0.01 molar methylmercury-chloride (115093) in 5 milligrams saline daily. Controls received the same daily dose of saline and the weight matched controls were kept within 5 percent of the weight of the test animals. During days 20 through 26, when neurological impairment became apparent, the mercury animals and their matched controls were sacrificed, the brains removed, and coronal sections examined histologically for cytochrome-oxidase (CO). Methylmercury toxicity was first seen around day 15. The neurological impairment symptoms seen during days 20 through 26 were hypertonicity of limb muscles, flexion deformities, myoclonic hindlimb jerking, and generalized motor convulsions. Staining for CO, using thionin in an acetate buffer, uncovered CO positive neurons in the magnocellular red nuclei (RMC) of the methylmercury treated animals alone. Although a normal complement of RMC neurons were found in the mercury group, the decrease of CO levels in the large neurons and a concomitant increase in the smaller neurons were thought to cause the neurological disorders.

465
TITLE:
Effects of Lead and Mercury on Histamine Uptake by Glial and Endothelial Cells

AUTHORS:
Huszti Z
Balogh I

SOURCE:
Pharmacology and Toxicology, Vol. 76, No. 6, pages 339-342, 18 references, 1995

ABSTRACT:

The effects of lead (7439921) and mercury (7439976) on histamine uptake by glial and endothelial cells were examined. Astroglial cells obtained from the hypothalami and endothelial cells derived from cerebral microvessels of neonatal Wistar-CFY-Long-Evans-rats were cultured and incubated with 0 to 100 micromolar (microM) lead-acetate (301042) or mercuric-chloride (7487947) for up to 15 minutes. The effects on uptake of tritium labeled histamine were determined. Lead-acetate and mercuric-chloride at concentrations of 1 to 10microM significantly inhibited uptake of tritiated histamine by astroglial cells in a dose dependent manner. The maximum inhibitory effect for either compound amounted to 65 to 68%. At concentrations of 10 to 100microM, histamine uptake was inhibited by 65 to 68% by both compounds at each dose tested. At 100microM, both compounds significantly increased histamine uptake, the effect of mercuric-chloride being much more pronounced than that of lead-acetate. Lead-acetate and mercuric-chloride at 1 to 10microM weakly inhibited histamine uptake by endothelial cells. Mercuric-chloride at 100microM significantly enhanced uptake of histamine by endothelial cells. The authors conclude that low concentrations of lead ions and mercuric ions significantly inhibit uptake of histamine by astroglial and brain endothelial cells from neonatal rats. The inhibitory effect is more pronounced in astroglial cells. The inhibitory effect could reflect loss of the transmembrane sodium or potassium ionic gradient. High concentrations of mercury stimulate histamine uptake. This could reflect a direct effect on the histamine transporter.

466

TITLE:

Mobilization of methyl mercury in vivo and in vitro using N-acetyl-DL-penicillamine and other complexing agents.

AUTHORS:

AASETH J

SOURCE:

ACTA PHARMACOL TOXICOL; 39 (3). 1976 289-301

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The distribution and excretion of Hg was studied in mice given a single i.v. dose of 5 mumol/kg of methyl mercuric chloride. Oral treatment with N-acetyl-DL-penicillamine (3 mmol/kg per day) removed more Hg from the brain and from the whole body than the corresponding treatment with other complexing agents, and it was also effective on delayed treatment. Even more Hg was removed into the feces and the urine, by higher doses of N-acetyl-DL-penicillamine, and 4 days of treatment with 27 mmol/kg per day of this compound did not give rise to any significant toxic symptoms in the mice. In vitro experiments showed that the chemical affinity of N-acetyl-DL-penicillamine for methyl mercury

was higher than that of the other thiols tested, except D-penicillamine. In contrast to the latter, N-acetyl-DL-penicillamine easily penetrated the cellular membranes, and therefore rapidly removed a substantial fraction of methyl mercury from the blood cells. It is assumed that N-acetyl-DL-penicillamine can reduce the Hg concentration in brain cells by converting the intracellularly non-diffusible methyl mercury into a freely diffusible complex.

467
TITLE:
Effects of PCB and DDE in cormorants and evaluation of PCB residues from an experimental study.

AUTHORS:
Koeman JH
VanVelzen-Blad HCW
DeVries R
Vos JG

SOURCE:
J. Reprod. Fert.19(Suppl.): 353-364; 1973(REF:32)

ABSTRACT:
PESTAB. Tissues of cormorants found dead in various parts of the Netherlands and shot or collected from nests at Naardermeer were analyzed for organochlorines, PCBs, and mercury. Carcasses of the dead birds contained about 0. 5-1 g PCB. High PCB levels were also present in tissues from one cormorant which was shot but in very poor condition; this bird and those found dead had low body weights. Mean brain levels in the birds found dead were: HCB 18 ppm, DDE 13 ppm, PCB 190 ppm, heptachlor epoxide 0. 14 ppm, dieldrin 1. 7 ppm, mercury 1. 50 ppm, and methyl mercury 1. 46 ppm. Corresponding levels for controls were: HCB 0. 65 ppm, DDE 7. 8 ppm, PCB 180 ppm (considered high due to one contaminated bird), heptachlor epoxide 0. 067 ppm, dieldrin 0. 43 ppm, mercury 1. 12 ppm, and methylmercury 1. 10 ppm. Mean PCB levels in the brains of nestlings were 0. 69 ppm. Correlations between eggshell thickness and residue levels were significant for HCB, DDE, and PCB. Shells from eggs that hatched were significantly thicker than shells from eggs that did not hatch in the case of empty shells collected in 1970 from the Naardermeer and Wanneperveen colonies. When cormorants were given PCB orally, 46-79% of the dose administered was retained within the body. Survival times of 55-124 days were correlated with total body PCB contents of 1. 12-4. 85 g. These values were similar to the levels found in the dead cormorants under natural conditions, indicating that PCBs were probably responsible for deaths of those birds.

468
TITLE:

Effect Of Mercuric Chloride Upon Zinc Distribution In The Rat

AUTHORS:
Kossakowski S
Grosicki A

SOURCE:
Bulletin of the Veterinary Institute in Pulawy, Vol. 26, No. 1-4, pages 67-76, 27 references, 19831983

ABSTRACT:
The effect of mercuric-chloride (7487947) upon zinc (7440666) distribution was studied in the rat. Wistar-rats were used in the experiments. Animals were divided into four groups with one group as controls. The remaining groups received a single intragastric (ig) dose of either 6, 12, or 18 milligrams per kilogram mercuric-chloride. After 1 hour, animals received a single ig dose of 0.1 microCurie zinc-65 as zinc-chloride (7646857). Animals were sacrificed at 6 and 24 hours, and at 2, 4, 7, and 14 days after zinc administration. Samples of various organs were obtained and analyzed for zinc content by scintillation counting. For control rats, zinc was found to accumulate in the highest amounts in the small intestine with smaller amounts in the lungs and spleen. The smallest amounts were found in the brain, prostate, blood, heart, thigh muscles, skin, hair, and gonads. Animals dosed with mercury showed characteristic changes in the zinc distribution. In the stomach, the zinc content increased after 6 hours and reached a maximum which was related to the mercury dose. Zinc content in both the small and large intestine was lower for the animals dosed with mercury. In the liver, zinc content was initially lower than for the controls, but after 1 or 4 days zinc content was higher than that found in controls. In the remaining organs, zinc content slightly exceeded or remained the same as in controls. The authors conclude that mercury inhibits zinc uptake from the gastrointestinal tract and its metabolism in the liver, kidneys, spleen, and lungs.

469
TITLE:
The role of catalase for uptake of metallic mercury: 5. Exhalation of metallic mercury from acatalasemic and normal mice intraperitoneally injected with mercuric ion, and the mercuric uptake by acatalasemic and normal mice exposed to metallic mercury vapor.

AUTHORS:
KENMOTSU K

SOURCE:
OKAYAMA IGAKKAI ZASSHI; 96 (5-6). 1984. 519-526.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Exhalation of metallic Hg, from acatalasemic and normal mice injected with mercuric ion (203HgCl2) i.p., and Hg uptake by acatalasemic and normal mice exposed to metallic mercury vapor (203Hg0) were investigated. Exhalation of metallic Hg from acatalasemic mice injected with mercuric ion was higher than that from normal mice. Hg uptake by normal mice exposed to metallic Hg was higher than that by acatalasemic mice. The liver and brain of acatalasemic mice were higher in Hg content than those of normal mice. On the other hand, Hg content in heart, lungs, blood and kidneys of acatalasemic mice was lower than in normal mice. The brain/blood concentration ratio of acatalasemic mice was higher than in normal mice. The distribution of Hg in the organs of acatalasemic mice injected with mercuric ion were similar to those of normal mice. Actalase evidently has an important role in the uptake of metallic Hg. The balance of reduction and oxidation systems influence Hg metabolism.

470

TITLE:

Distribution And Excretion Of Mercury In Rats Intoxicated With Methylmercury Dicyandiamide

AUTHORS:

Rusiecki W
Osicka A

SOURCE:

Acta Poloniae Pharmaceutica, Vol. 29, No. 6, pages 623-628, 14 references, 19721972

ABSTRACT:

The distribution, metabolism, and excretion of a single orally administered dose of methylmercury-dicyandiamide (MMDC) were studied in male Wistar-rats. Animals were given, by gastric sound, 50 percent of the known median lethal dose (LD50) of MMDC, equal to 34 milligrams per kilogram (mg/kg) body weight. Rats were sacrificed at 1 to 12 hours, 1 to 7 days, or 14, 21, or 28 days after treatment. Blood, brains, kidneys, and livers were collected and analyzed for organomercury, and tissues were also examined. Excretion of mercury in feces and urine was determined for 7 days following MMDC administration. It was found that MMDC was rapidly absorbed into the blood and transported into tissues; MMDC was also found to be unchanged absorbed from the alimentary tract into the circulation. MMDC had accumulated in all tissues, particularly in blood, and its concentration in the brain increased progressively. MMDC was slowly excreted in feces and urine, mostly as organic mercury. In the kidneys and liver, a slow breakdown of MMDC to inorganic mercury was noted. The authors conclude that MMDC administered per os to rats is rapidly absorbed into circulation and bound by the tissues; particularly by blood cells.

471
TITLE:
Studies on combined effects of organophosphates and heavy metals in birds. I. Plasma and brain cholinesterase in coturnix quail fed methyl mercury and orally dosed with parathion.

AUTHORS:
Dieter MP
Ludke JL

SOURCE:
Bull. Environ. Contam. Toxicol. 13(3): 257-261; 1975.

ABSTRACT:
PESTAB. The effects of mercury on the toxicity and biochemical effects of parathion were investigated with male coturnix quail (Coturnix coturnix japonica). The birds were fed a sublethal concentration of morsodren (methyl mercury dicijan diamide 4 ppm as methyl mercury) for 18 wk, which resulted in accumulation of 21.0 ppm Hg in the liver and 8.4 ppm in the carcass. Birds fed clean feed and those fed morsodren-treated feed were orally dosed with 2,4,6,8, and 10 mg/kg parathion, and their 48-hour survival times compared. The computed LD 50 was 5.86 mg/kg in birds not fed morsodren and 4.24 in those fed the heavy metal. Cholinesterase in the plasma was already inhibited 90% by parathion alone (1.0 mg/kg oral dose). The effect of morsodren on brain cholinesterase was severe enough to seriously interfere with the diagnosis of organophosphate poisoning, as parathion inhibition of the enzyme in morsodren-fed birds was almost twice that in clean-fed ones.

472
TITLE:
Methyl Mercuric Chloride Toxicokinetics in Mice. II: Sexual Differences in Whole-Body Retention and Deposition in Blood, Hair, Skin, Muscles and Fat

AUTHORS:
Nielsen JB
Andersen O

SOURCE:
Pharmacology and Toxicology, Vol. 68, No. 3, pages 208-211, 7 references, 1991

ABSTRACT:
Sex related differences in the toxicokinetics and tissue distribution of methylmercuric-chloride (115093) (MMC) were studied in mice. Bom:NMRI-mice were given a single 1 micromole per kilogram oral dose of mercury-203 tagged MMC. Selected mice were killed 3, 10, 20, or 30 days

later to determine whole body retention and the tissue distribution of mercury (7439976) (Hg). The Hg body burden decreased with increasing time after exposure. The decrease approximated a first order process. The elimination half times were approximately 7 days in male mice and 12 days in females. Total Hg body burdens in female mice were significantly higher than in males 20 and 30 days post exposure. The relative amount of Hg deposited in the carcass was significantly lower in male mice. Hg levels in the liver, kidney, brain, blood, dermis, fat, and muscles decreased with increasing time after exposure. Hg deposition in the hair increased with increasing time post exposure. Blood, brain, and muscle Hg concentrations were consistently lower in male than in female mice at all times. Adipose tissue Hg concentrations were higher in male mice at 3 days but higher in female mice after 10, 20, and 30 days. Hair Hg concentrations were higher in male mice at 3, 10, and 20 days, but were significantly higher in female mice after 30 days. Renal Hg content was consistently higher in male mice. The authors conclude that the major reason for the observed sex differences in mercury disposition after MMC exposure is due to the difference in carcass deposition.

473
TITLE:
Toxicology of mercury

AUTHORS:
Mazarrasa Mowinckel DFO

SOURCE:
MAPFRE Seguridad 1st Quarter 1988, No.29, p.29-35. 6 ref. Illus.

ABSTRACT:
This article analyses the chemical behaviour of mercury in its various forms, from its entry into the human organism, by means of inhalation or ingestion, its biotransformation, transportation and distribution (kidney, liver, mucous membranes of the intestinal track, spleen, testicles, brain cells) until its elimination and excretion. Some historical references to the illnesses caused by mercury in mines and industry are also included.

474
TITLE:
Metabolism of mercurial compounds.

AUTHORS:
Suzuki T

SOURCE:
Adv. Mod. Toxicol. 2: 1-39 1977 (252 References)

ABSTRACT:

PESTAB. Recent literature dealing with the metabolism of mercury compounds is reviewed. The pulmonary absorption of mercury compounds depends primarily on the volatility, solubility, and particle size of the compound, and the efficiency of gastrointestinal absorption depends on the dose, the form of the compound, and the influence of coexistent substances in food. Topical application of mercurials may also result in serious intoxication, although it us unknown whether the transdermal or follicular pathways of skin absorption are more important. The mercury of various chemical forms is transported by binding to plasma protein or blood cells, except in the case of mercury vapor exposure where the rate of oxidation is not fast enough to prevent some of the elemental mercury from reaching the brain. The placental transfer of mercurials is dependent on the form of the compound and may be influenced by species differences in placental structure and function and by differences in the hematocrit and binding characteristics of the hemoglobins of the fetus and adult. The biotransformation of the different mercury compounds is discussed in detail, as is secretion of these compounds in the bile, urine, and milk. The distribution, accumulation, and toxicity of mercurials are discussed in relation to their metabolic properties.

475

TITLE:

Selected case histories and epidemiologic examples of human mercury poisoning.

AUTHORS:

Gerstner HB
Huff JE

SOURCE:

Clin. Toxicol. 11(2): 131-150 1977 (21 References)

ABSTRACT:

PESTAB. The various types of characteristic clinical pictures resulting from mercury intoxication and the circumstances under which they occur are described, based on illustrative case reports from the literature. Elemental mercury enters the human body through inhalation. Depending on air concentration and exposure time, elemental mercury produces two characteristic clinical pictures: acute pulmonary injury or chronic brain injury. The first is liable to be misdiagnosed as an upper respiratory infection, and the second has an insodious beginning, progressing over many months until total incapacitation is reached. Inorganic mercury compounds enter the human body through food, beverages, and dust inhaled in the air. The classical picture of inorganic mercury poisoning comprises of the superimposure of disturbances, mainly stemming from injuries to the alimentary canal and kidneys. The clinical course and ultimate outcome are determined by renal function. A nephrotic syndrome may also result from chronic intoxication. From the standpoint of public health, the problem of

organomercurials reduces itself essentially to that of methylmercury. The methylmercury syndrome is characterized by insidious onset, long duration of clinical sequelae, guarded prognosis with respect to complete recovery, and almost complete confinement to the central nervous system, particularly the optical cortex and cerebellum. Methylmercury ingestion during pregnancy may have a devastating effect on the central nervous system of the fetus. Epidemic outbreaks of methylmercury poisoning have recurred following widespread ingestion of contaminated fish and dressed seed grain. Epidemic outbreaks of poisonings have also followed widespread ingestion of grain treated with ethylmercury-p-toluene sulfonanilide and grain treated with a mixture of phenylmercury acetate and ethylmercury chloride.

476
TITLE:
Pollution of the Rhine fauna by mercury and organochlorines.

AUTHORS:
Kempf C
Sittler B

SOURCE:
Terre Vie 31(4): 661-669 1977 (12 References)

ABSTRACT:
PESTAB. Fish from the Rhine river, dead birds and eggs found along the river were analyzed for residues of mercury and organochlorine pesticides in connection with a massive death of fish in the river. The mercury levels found in fish were in the ranges of 0.75-1.95 ppm in Rutilus rutilus, 0.8-1.27 ppm in Leuciscus cephalus, 2.36-3.18 ppm in L. leuciscus and 1.77-3.86 ppm in Perca fluviatilis. Mercury was also found in the muscle, brain, liver, plumage, tongue and kidneys of Larus ridibundus, Sterna hirundo, Podiceps cristatus, Anas Platyrhynchos, Bucephala clangula, Aythya fuligula, Ardea cinera, Fulica atra, Buteo buteo, Accipiter nisus and Hirundo rustica. The mercury levels were highest in the kidneys, plumage and liver. The mercury levels found in the eggs were usually below 3 ppm. Hexachlorobenzene, alpha-BHC, DDE and PCB's were found in the birds in the respective ranges of 0.043-107 ppm, 0.029-1.39 ppm, 0.216-20.34 ppm and 0.06-157.58 ppm. The residue levels were highest in the fatty tissues. The increased mortality of fishes and birds is probably explained by the high residue levels found.

477
TITLE:
Evaluation of mercury in hair, blood and muscle as biomarkers for methylmercury exposure in male and female mice.

AUTHORS:

NIELSEN JB
ANDERSEN O
GRANDJEAN P

SOURCE:
ARCHIVES OF TOXICOLOGY; 68 (5). 1994. 317-321.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Recently established reference intervals demonstrate that blood mercury is significantly higher in women than in men. Mercury in blood and hair are both used as biomarkers for human methylmercury exposure and employed in risk assessment without considering possible sex-related differences in toxicokinetics of methylmercury. In an experimental study using male and female mice of three different strains, the validity of mercury in hair, blood and muscle as indicators of methylmercury exposure was evaluated. Significant sex-related differences in the toxicokinetics of methylmercury were observed in the mice and it is concluded that hair and blood levels of mercury are of questionable relevance as indicators of both body burden and target organ concentrations of mercury. However, blood concentrations might be used as an indicator of brain deposition and the correlation improves after corrections due to sex-related differences in toxicokinetics.

478
TITLE:
Distribution of inorganic, aryl and alkylmercury compounds in rats

AUTHORS:
Takeda Y
Junugi T
Hoshino O
Ukuta T

SOURCE:
Toxicol. Appl. Pharmacol.; 13(2), 156-64, 1968; (REF:25)

ABSTRACT:
HAPAB A comparative study on the distribution and excretion of several types of 203-labeled mercury compounds is presented. Mercuric chloride (MC) at a dosage of 3 mg Hg/kg and phenylmercuric chloride (PMC), ethylmercuric chloride (EMC), S-ethylmercuric cysteine (EMCys) and n-butylmercuric chloride (BMC) each at a dosage of 10 mg Hg/kg were administered subcutaneously to 7-week-old male rats. Urine and feces were collected separately and after sacrifice the tissues and organs were removed and radioassayed. The results indicated that the accumulation of mercury in organs and tissues was higher and longer- lasting in the case of alkyl-mercury compounds than of MC and PMC. After administration of both MC and PMC, the highest concentration was found in the kidney and a

rapid decrease in the concentration in organs other than the kidney was observed. After administration of alkylmercury compounds, the highest concentraion of mercury was found in the blood and a gradual accumulation was observed in the kidney. Throughout the observation period (8 days), more than 90% of the alkylmercury compounds in the blood were found in the stroma-free hemolyzate of the erythrocytes, while after 1 or 2 days of administration of MC, mercury in the blood was mainly distributed in the plasma, but thereafter the content in the stroma-free hemolyzate became higher than in the plasma. In the case of PMC, the distribution pattern in the blood in the early stage after administration was similar to that of alkylmercury compounds, but after 4 days the pattern was similar to MC. The amount of mercury excreted via feces and urine was remarkably higher for MC and PMC than that for alkylmercury compounds. The several alkylmercury compounds revealed different metabolic behavior which depended on the carbon-chain length of the alkyl group. In the brain, the ratios for alkylmercury compounds are much larger than those for inorganic or phenylmercury compounds and the differences in the distribution of the ethyl and butyl compound seem to be correlated with the specific neurotoxicity of alkylmercury compounds having short chains. TOXICOLOGY AND PHARMACOLOGY 69/02/00, 53 1968

479

TITLE:

The Pathology Of Arylmercurial Poisoning In Swine

AUTHORS:

Tryphonas L
Nielsen NO

SOURCE:

Canadian Journal of Comparative Medicine, Vol. 34, No. 3, pages 181-190, 12 references, 19701970

ABSTRACT:

The pathology of arylmercurial poisoning was studied in swine. Symptoms were correlated with the exposure and tissue mercury (7439976) content. Healthy piglets from a farm herd were given daily doses of 0.19 to 4.56 milligrams per kilogram (mg/kg) mercury as phenylmercuric-chloride (100561) for up to 90 days. Pigs were killed at the onset of clinical signs of poisoning, in the terminal stages of disease, or at 90 days. Gross lesions were examined and detailed studies were made of affected organs. The brain, intestine, liver, kidney, muscle, skin, blood, urine, and bile were analyzed for mercury content by atomic absorption spectrophotometry. Mercury in excess of 2.28mg/kg was moderately toxic; diarrhea and weight loss were seen in pigs receiving this dose and 4.56mg/kg. The primary gross lesions were necrotic typhlitis and colitis, and nephrosis. These were seen in animals at the highest doses. The mucosa of the intestinal tract of pigs with severe diarrhea were necrotic

and covered by a pseudomembrane covering. Livers were reduced in size. Kidneys of sick animals were swollen, pale yellow and had reduced corticomedullary contrast. Newly regenerated epithelium was seen in tubules at 90 days. The kidney and colon accumulated significantly elevated concentrations of mercury. The authors conclude that rapid metabolism and excretion of the compound tend to protect most tissues. If the dose is sufficiently high, organs involved in excretion are damaged.

480
TITLE:
Effect of mercuric chloride intoxication and dimercaprol treatment on delta-aminolevulinate dehydratase from brain, liver and kidney of adult mice.

AUTHORS:
EMANUELLI T
ROCHA J BT
PEREIRA ME
PORCIUNCULA LO
MORSCH VM
MARTINS AF
SOUZA D OG

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 79 (3). 1996. 136-143.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Dimercaprol is a compound used in the treatment of mercury intoxication, however with low therapeutic efficacy. It is assumed that dimercaprol acts by reactivating target sulfhydryl-containing proteins. In the present investigation we studied the inhibitory effect of mercuric chloride treatment (3 days with 2.3 or 4.6 mg/kg HgCl2, sc) in mice on cerebral. renal and hepatic delta-aminolevulinate dehydratase (ALA-D) activity, and a possible reversal of the effect of mercury by dimercaprol (0.25 mmol/kg, 24 hr after the last mercury injection). Mercuric chloride did not inhibit cerebral ALA-D at the doses injected. Dimercaprol treatment did not restore the normal enzyme activity of the liver after the 25% inhibition caused by 4.6 mg/kg HgCl2. In the kidney, dimercaprol enhanced the inhibitory effect of 4.6 mg/kg mercuric chloride (from 35% after mercury treatment alone to 65% after mercury plus dimercaprol treatment). Mercury content increased in kidney after exposure to 2

481
TITLE:
Combined Toxicity of Ethanol and Methylmercury in Rat

AUTHORS:

McNeil SI
Bhatnagar MK
Turner CJ

SOURCE:
Toxicology, Vol. 53, Nos. 2/3, pages 345-363, 41 references, 19881988

ABSTRACT:
A subacute study was designed to correlate the clinical, biochemical and morphological findings with mercury (7439976) levels in rats exposed to methylmercury and ethanol (64175) simultaneously. Male Wistar-rats were divided into four treatment groups. The rats were gavaged with 5.0 milliliters/kilogram (ml/kg) body weight between 0800 and 1000 hours, five times a week. The gavage for Group 1 consisted of double distilled water; Group 2, 25 percent ethanol (EtOH); Group 3, 2.5mg/kg methylmercury-chloride (CH3HgCl); and Group 4 with 2.5 mg/kg CH3HGCl in 25 percent EtOH. The first overt clinical sign of methylmercury toxicity was anorexia. The concentration of mercury was greatest in the blood, decreasing through the kidney, liver and brain. Neurotoxicity noted in Group 3 rats was not enhanced by the addition of EtOH in Group 4. Groups 3 and 4 had similar clinical signs but Group 3 showed more severe cases of hindlimb crossing, hyperflexia and lack of coordination. The onset of ataxia was sudden, usually around week six, and was not preceded by tail rotation. A greater fecal and urinary excretion of mercury occurred in Group 4 than in Group 3, suggesting that the reduced neurotoxicity may be a result of EtOH stimulating the enzyme systems involved in detoxifying and eliminating mercury. The authors conclude that EtOH does not potentiate the toxicity of CH3Hg under all circumstances. Further studies should be conducted concerning the alteration of nephrotoxicity by ethanol exposure.

482
TITLE:
MERCURY ASSOCIATED NEUROBEHAVIORAL DEFICIT IN CHILDREN

AUTHORS:
GRANDJEAN PA

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Methylmercury is an important contaminant of seafood and freshwater fish worldwide. Although tragic pollution episodes have demonstrated that the fetal brain is particularly susceptible to methylmercury toxicity, the upper limit for safe mercury exposure is unknown. A birth cohort of 1,000 children was formed during 1986 to 87 at the Faroe Islands, where increase exposure to methylmercury is mainly due to consumption of pilot whale

meat. The fishing community is unique and highly suitable for population-based studies or prenatal methylmercury neurotoxicity: Average mercury exposures vary more than a 100-fold within the population, and socioeconomic factors and other confounding variables are of only limited concern. Ninety percent of the children from the cohort went through extensive neurobehavioral examinations at age 7 years, and the results showed mild deficits associated with prenatal exposures that were previously thought to be safe. These data will be scrutinized further statistically and neuropsychologically. In addition, to determine the long-term implications and the potential reversibility of mercury-associated deficits, follow-up of the cohort at age 14 years will be carried out. Neurobehavioral performance will be related to several mercury exposure biomarkers that reflect both prenatal and postnatal exposures. Exposures to polychlorinated biphenyls (PCBs) will also be assessed and analyzed for their possible neurobehavioral effects. Advanced statistical methods will be applied to provide documentation that can be used directly in risk assessment.

483
TITLE:
The effect of toxicokinetics on murine mercury-induced autoimmunity.

AUTHORS:
HULTMAN P
NIELSEN JB

SOURCE:
ENVIRONMENTAL RESEARCH; 77 (2). 1998. 141-148.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury induces autoantibodies to the nucleolar protein fibrillarin (ANoA) in genetically susceptible (H-2AS) mouse strains. This study examines the importance of mercury toxicokinetics for the induction and strength (titer) of these autoantibodies. Female mice of the inbred strains A.SW and B10.S (H-2AS on the A and C57BL/10 genetic background, respectively) and A.TL and B10.TL (H-2Ak on the A and C57BL/10 background) were treated with 203HgCl2 in a dose of 1, 5, or 16 mg Hg drinking water for 56-70 days. Whole-body retention of "Hg was monitored throughout the experimental period. Mercury accumulation in kidney, liver, heart, spleen, and brain was determined at end of the experiment when blood samples were also obtained for determination of ANoA. The drinking water consumption showed a limited variation between the strains and the dose groups. Therefore, intake of mercury did not vary much between the strains at a given dose level. The whole-body retention of mercury

484
TITLE:

EEG Findings in Chlor-Alkali Workers Subjected to Low Long Term Exposure to Mercury Vapour

AUTHORS:
Piikivi L
Tolonen U

SOURCE:
British Journal of Industrial Medicine, Vol. 46, No. 6, pages 370-375, 19 references, 1989

ABSTRACT:
A study of electroencephalographic changes in chloralkali workers exposed to mercury (7439921) vapor was conducted. The cohort consisted of 41 males, mean age 38.1 years, employed for at least 5 years in a Finnish chloralkali facility (SIC-2812). Exposure times ranged from 5 to 27 years, mean 15.6 years. The comparisons consisted of 41 males, mean age 38.1 years, employed at mechanical wood processing factories in Finland. Blood and urine samples were collected and assayed for mercury, and electroencephalographic examinations were performed. The electroencephalograms (EEGs) were examined visually and by a computerized technique. The mean total blood mercury concentrations in the cohort and comparisons were 58.0 and 18.8 nanomoles per liter, respectively. The mean urine mercury concentrations were 11.6 and 1.1 micromoles per mole creatinine, respectively. Visually examined EEGs of the exposed workers showed a higher incidence of abnormalities such as generalized, focal, and paroxysmal disturbances than the comparisons, 24 versus 15 percent; however, the difference was not statistically significant. Computerized EEGs from the exposed workers had significantly slower and more attenuated power spectra than those from the comparisons. The changes were most pronounced in recordings made from the occipital region. The changes were less pronounced in exposed subjects who worked on day shifts than in those who worked on variable shifts. The authors conclude that the slowing and attenuation of computerized EEGs observed in the chloralkali workers reflects long term exposure to low concentrations of mercury vapor. Mental strain associated with shift work exacerbates the electroencephalographic changes.

485
TITLE:
Chemical and toxicological studies of the fungicide phenylmercury acetate. 2. Studies of mercury absorption by some organs in the rat and mercury excretion following poisoning with phenylmercury acetate as compared to mercury chloride.

AUTHORS:
Piechocka J

SOURCE:
Roczn. Panst. Zakl. Hig.; 19(4), 389-93, 1968; (REF:7)

ABSTRACT:
HAPAB Using Kaerber's method for estimation, the LD50 value of phenylmercury acetate in rats was found to be 60 mg/kg of body weight. Mercury absorption and excretion were compared in rats given 1/3 the LD50 of phenylmercury acetate and mercury chloride. Higher body accumulation was found for pheylmercury acetate than for the mercury chloride. Tables present the values determined for brain, kidneys, liver, spleen and blood; the results of urinary and fecal analyses are also given. TOXICOLOGY AND PHARMACOLOGY 69/05/00, 151 1968

486
TITLE:
Magnetic Resonance Imaging (MRI), Neurobehavioral Testing, and Toxic Encephalopathy: Two Cases

AUTHORS:
White RF
Feldman RG
Moss MB
Proctor SP

SOURCE:
Environmental Research, Vol. 61, No. 1, pages 117-123, 34 references, 1993

ABSTRACT:
Cases of toxic encephalopathy examined for cerebral pathology by magnetic resonance imaging (MRI) and for functional deficits by neuropsychological testing were presented. The first patient was a 48 year old man exposed to inorganic mercury (7439976) through his job at a thermometer factory. Starting in 1981, he swept mercury off the floors, repaired machines, and operated a crusher machine which crushed instruments so the mercury could be separated for reuse. In 1984 he developed blurred vision, a rash, weakness, memory loss, rage and irrational behavior, and was treated for mercury poisoning. He was evaluated in 1986. MRI studies revealed mild central and cortical atrophy. Neuropsychological testing showed difficulties incognitive flexibility and tracking, fine manual motor coordination, visuospatial analysis and organization, affect and personality, and memory. The second subject, a 60 year old male laboratory technician, was exposed to 2,6-dimethyl-4-heptanone (108838). He had been exposed to heptanone vapors for about 1 month in 1985 while performing hydraulic stripping experiments on iron ore. He developed a severe headache and a 20 minute vision loss. In 1986, MRI revealed small foci in the pons and white matter and neuropsychological evaluation revealed decrements in writing skills, slowing of visuospatial and visuomotor functioning, and short term memory difficulties. Both forms of

medical evaluation showed changes in the structure and function of white matter that are attributable only to toxic exposure.

487
TITLE:
MERCURY ASSOCIATED NEUROBEHAVIORAL DEFICIT IN CHILDREN

AUTHORS:
GRANDJEAN PA

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Methylmercury is an important contaminant of seafood and freshwater fish worldwide. Although tragic pollution episodes have demonstrated that the fetal brain is particularly susceptible to methylmercury toxicity, the upper limit for safe mercury exposure is unknown. A birth cohort of 1,000 children was formed during 1986 to 87 at the Faroe Islands, where increase exposure to methylmercury is mainly due to consumption of pilot whale meat. The fishing community is unique and highly suitable for population-based studies or prenatal methylmercury neurotoxicity: Average mercury exposures vary more than a 100-fold within the population, and socioeconomic factors and other confounding variables are of only limited concern. Ninety percent of the children from the cohort went through extensive neurobehavioral examinations at age 7 years, and the results showed mild deficits associated with prenatal exposures that were previously thought to be safe. These data will be scrutinized further statistically and neuropsychologically. In addition, to determine the long-term implications and the potential reversibility of mercury-associated deficits, follow-up of the cohort at age 14 years will be carried out. Neurobehavioral performance will be related to several mercury exposure biomarkers that reflect both prenatal and postnatal exposures. Exposures to polychlorinated biphenyls (PCBs) will also be assessed and analyzed for their possible neurobehavioral effects. Advanced statistical methods will be applied to provide documentation that can be used directly in risk assessment.

488
TITLE:
Prolonged Behavioral Effects of In Utero Exposure to Lead or Methyl Mercury: Reduced Sensitivity to Changes in Reinforcement Contingencies during Behavioral Transitions and in Steady State

AUTHORS:
Newland MC
Sheng Y
Logdberg B

Berlin M

SOURCE:
Toxicology and Applied Pharmacology, Vol. 126, No. 1, pages 6-15, 62 references, 1994

ABSTRACT:
The effects of in-utero exposure to lead (7439921) were investigated in monkeys. A new approach using concurrent schedules of food reinforcement was developed for the quantification of behavioral toxicity. The study subjects included 5 to 6 year old squirrel-monkeys. Pregnant squirrel-monkeys were dosed with methyl-mercury (0.7 to 0.9 parts per million (ppm) as mercury (7439976) in maternal blood) or lead (21 to 79 micrograms/deciliter in maternal blood) during the last half to two thirds of the gestation period. When the offspring were 5 to 6 years of age, they were trained to lever press. Separate random interval reinforcement schedules operated independently on two levers. The behavior of monkeys exposed to more than 40 micrograms/deciliter of lead and to methyl-mercury was less sensitive to reinforcement rates and heavily biased. The authors suggest that learning deficits and behavioral changes associated with the methyl-mercury and lead exposures may be related to the toxicants. The blood levels experienced during this study were similar to those which would be anticipated in occupational settings.

489
TITLE:
SUMMARY OF RECENT STUDIES IN JAPAN ON METHYL MERCURY POISONING

AUTHORS:
KOJIMA K
FUJITA M

SOURCE:
TOXICOLOGY 1973, 1(1) 43-62

ABSTRACT: EIS: Epidemiology Information System

490
TITLE:
Residues of mercury in tissues and eggs of chickens given oral doses of Panogen 15.

AUTHORS:
Wright FC
Younger RL
Riner JC

SOURCE:

Bull. Environ. Contam. Toxicol.12(3): 366-372; 1974(REF:11)

ABSTRACT:

PESTAB. A group of 3 roosters and 10 hens received 0. 5 mg/kg mercury as Panogen 15 daily. Tissue analysis showed the kidney had the greatest residue followed by the liver, breast muscle, brain, heart, and ovaries. After dosing had stopped, the residues in both hens and roosters decreased to less than 4. 0 ppm at 100 days. Residues in controls were less than 0. 3 ppm throughout the study. In eggs from treated hens, about 90% of the residue was located in the albumin and the remainder in the yolk. Mercury residues of chickens hatched from eggs of treated hens showed that the dosing caused greatest residues in the kidney and liver. Two hens in the group given mercury died, one after 42 and the other after 90 doses. For 3 days prior to death they became completely anorexic. Leg weakness developed, and the chickens were unable to stand. Both showed severe loss of weight. About 50% of the chickens hatched after the third week of the study had clinical signs of mercurial poisoning at hatch or by 3-5 days after hatch. They developed weakness, incoordination, and tremors of peripheral musculature. Hatchability of fertile eggs of treated hens declined to 30% whereas the control value was 80%. After the first 7 weeks of the study, egg production declined to 19% of pretreatment values. The dosed hens which did manage to maintain relatively high egg production had relatively low residues of mercury in their tissues, suggesting that eggs may be a possible pathway for the elimination of mercury from their bodies.

491

TITLE:

Studies on mercury poisoning in marten (Mustela vison).

AUTHORS:

ZHAO Z

SOURCE:

SINOZOOLOGIA; 0 (9). 1992. 81-86.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. After the adult marten (Mustela vison) was fed crucian carps (Carassius auratus) grown in mercury polluted water for about 250 days and the juvenile marten for about 120 days they would display Hunter-Russell signs. The mercuty content of crucian carp was determined to be 7.6120mg/kg and the mercury content of its food 5.3894mg/kg. The crucian carps constituted about 70 percent of the everyday diet. When the quantity of the crucian carps was reduced to 50 percent of the daily diet, the marten would behave normally and had no minamata for death within one year. The quality of its fur was fine. The marten fed with the contaminated carps accumulated mercury in its organs and the quantities of accumulated mercury were in the following order:

fur, liver, kidney, spleen, muscle, brain, intestines, pancreas, lungs, heart, stomach, fat, blood gonad and bone. The fur was the most affected while the bone the least. When an adult marten retained mercury 332.9mg or a juvenile marten

492
TITLE:
Effects Of Occupational Exposure To Elemental|Mercury On Short-Term Memory Capacity

AUTHORS:
Smith PJ
Langolf GD
Goldberg J

SOURCE:
NIOSH, U.S. Department of Health, Education, and Welfare, 30 pages, 11 references, Grant No. R01-OH-00707-040000

ABSTRACT:
The neurotoxic effects of chronic exposure to elemental mercury (7439976) were investigated in workers in a chloralkali facility. The Wechsler digit span and short term memory (STM) span were used. Tests were given twice, with sessions 3 months apart. Urine samples were taken and 50 percent threshold spans were evaluated as a function of session and urinary mercury content. The Wechsler digit span was not very precise for measuring STM; the variance was high within subjects. There was no significant relationship between Wechsler digit span and urinary mercury concentrations. The 50 percent threshold STM span reduced the within subject variance from 1 to 0.15 digits. The STM span decreased substantially as mercury exposures increased. Decrements in STM span from aging were compared. Exposure to 0.20 milligrams per liter of mercury had the same effect on the 50 percent threshold span as increasing the worker's age from 20 to 44.

493
TITLE:
Pathology Of Chronic Alkylmercurial Poisoning In Swine

AUTHORS:
Tryphonas L
Nielsen NO

SOURCE:
American Journal of Veterinary Research, Vol. 34, No. 3, pages 379-392, 36 references, 19731973

ABSTRACT:

The pathogenesis of chronic alkylmercurial poisoning was studied in swine. Mixed breed pigs were administered ethylmercuric-chloride (107277) (EMC) or methylmercuric-dicyandiamide (502396) (MMD) in doses corresponding to 0.19 to 0.76 milligram per kilogram (mg/kg) mercury (7439976) per day for up to 90 or 60 days, respectively. The animals were observed for clinical signs of poisoning. Selected pigs were killed either preceding or coinciding with the onset of clinical signs and necropsied. Tissue mercury concentrations were determined. Clinical signs consistent with progressive cerebral deficiency, starting with obliviousness to the surroundings, progressing through brief convulsive episodes and culminating in coma, occurred. In pigs given 0.76mg/kg mercury, failure to gain weight was accompanied by anorexia and coincided in most instances with incoordination and knuckling of the front fetlocks. No abnormalities were noted in animals fed 0.19mg/kg mercury. The toxicosis in other animals was primarily related to pathological changes in the nervous system involving neuronal necrosis, secondary gliosis, capillary endothelial proliferation, and degenerative arteriopathy in the blood vessels supplying injured gray matter. Degeneration of hepatocytes and rat renal tubular cells were seen in pigs given MMD or EMC. Degenerative arteriopathy in the submucosa of the esophagus and large intestine were seen in pigs given 0.76mg/kg EMC. The kidney accumulated the largest amounts of mercury, followed by the liver, intestine, brain, muscle, and skin. Tissue mercury concentrations correlated best with dose size, rather than cumulative dose. The authors conclude that MMD and EMC if fed at low concentrations for long periods are highly poisonous to swine.

494

TITLE:

METHYLMERCURY AND ENVIROMENTAL HEALTH

AUTHORS:

Leong L
Olson B
Cooper R

SOURCE:

Journal of Environmental Health 35(5): 436-442; 1973.

ABSTRACT:

HMTC Methylmercury in the environment is examined. Mercury exists naturally in the environment and anthropogenic sources include the roasting of ores, combustion of fossil fuel, and the production of cement. Human contributions are lower than the amount due to natural process. Degassing activities, volcano eruptions, weathering, plowing, or earth excavation are the primary imports of mercury into the environment. United States EPA standards allow the discharge of 5 lb of mercury into the air per day and mercury levels of 0.5 ppb in drinking water. Methylmercury is an alkylorganic mercury. Alkylorganic mercurials do not

degrade in the environment and quickly become cumulative toxins. These compounds have the ability to cross blood-brain barries and destroy nerve cells. Methylmercury enters the body via inhalation, ingestion, or skin absorption. Symptoms of methylmercury poisoning in humans range from numbness and tingling of the hands, feet, or lips to speech, hearing, and visual impairments. Due to enforcement of United States EPA standards, anthropogenic sources of methylmercury are no longer a threat to human or environmental health. (39 ref.)

495

TITLE:

Chronic Methylmercury Toxicosis In Calves

AUTHORS:

Herigstad RR
Whitehair CK
Beyer N
Mickelson O
Zabik MJ

SOURCE:

Journal of the American Veterinary Medical Association, Vol. 160, No. 2, pages 173-182, 18 references, 19721972

ABSTRACT:

The toxicity of methylmercury (22967926) was studied in calves. Six male Holstein-Friesian-calves were administered Ceresan-L (8003370), a commercial product containing 2.89 percent methylmercury-2,3-dihydroxypropylmercaptide and 0.62 percent methylmercury-acetate (108076), in their diet for 91 days. Doses ranged up to 0.4 milligram per kilogram per day. The animals were observed for clinical signs of toxicity. Blood, urine, and hair samples were collected at various times and assayed for mercury (7439976). Standard hematologic and urine chemistry parameters were determined. The animals were killed on day 96 and necropsied. Tissue mercury residues were determined. Final body weights showed an inverse relationship between daily weight gain and cumulative mercury intake. Three calves developed clinical signs of intoxication such as ataxia and neuromuscular incoordination which progressed rapidly to convulsions and a moribund state between 35 and 91 days. No hematologic abnormalities were found. Glucosuria and albuminuria were observed. The other urine chemistry parameters were normal. All calves had limited pneumonia in the ventral portion of the lungs. Focal hemorrhages in the renal cortex and pale kidneys were observed in two calves. Major histopathological changes included a reduction in number of cells in the cerebellar granular layer and toxic nephrosis involving the proximal convoluted tubules. Mercury content of the hair was directly related to the doses through week 5. Mercury residues in the tissues at necropsy were not correlated with the

cumulative dose or onset of clinical symptoms, but were relatively consistent for each animal when residues in the hair, liver, kidney, brain, and semitendinous muscle were compared. The authors suggest that the total mercury dose is more important than daily dose or duration of treatment in causing symptoms of toxicosis in calves.

496
TITLE:
Total mercury levels in selected human tissues, Idahoö1973-74.

AUTHORS:
Gabica J
Benson W
Loomis M

SOURCE:
Pestic. Monit. J. 9(2): 59-63; 1975.(15 references)

ABSTRACT:
PESTAB. Total mercury levels were determined in human tissues taken at autopsy from six hospitals in the three basic geographical areas of Idaho. Of the 242 specimens analyzed, 76 percent contained detectable mercury. Levels were compared with respect to the age, sex, and geographic residence of autopsied individuals. Mean levels detected were 1.04 ppm in kidney tissue, 0.34 ppm in liver, and 0.08 ppm in brain. Mean mercury levels for the three geographical areas were: southeastern Idaho, 0.22 ppm; southwestern Idaho, 0.80 ppm; and northern Idaho, 0.43 ppm. The relatively high means in southwestern Idaho specimens may be related to the preponderance of natural cinnabar deposits in that portion of the state. Mercury levels were higher in women than men for all tissues in both the southwestern and northern areas, but the reverse was true in the southeast. Data was compared with findings of other investigators in an attempt to arrive at backgroound levels of total mercury residues in human tissues. (Author abstract by permission)

497
TITLE:
Mercury levels in a 21-year old black-crowned night heron (Nycticorax nycticorax).

AUTHORS:
Hoffman RD

SOURCE:
Ohio J. Sci. 76(1): 18; 1976.(4 references)

ABSTRACT:
PESTAB. The use of mercury in agricultural practices has helped to raise

the concentrations of mercury in the environment to levels which may be toxic to animals. A 21 yr old female black-crowned night heron with total body weight of 765 g was collected and examined. Organisms in the stomach included two perch and one fresh-water drum. The total mercury concentrations in breast muscle (0.9 ppm), liver (3.1 ppm), brain (0.5 ppm), and primary wing feathers (17.9 ppm) were measured on a wet weight basis, in duplicate. Differences between the concentrations in this particular bird and other herons found earlier indicate that this bird may have been feeding in an area of lower mercury contamination or that the maximum retainable mercury in black-crowned night herons is specific for the individual.

498
TITLE:
Effects of chronic exposure to cadmium, lead and mercury on brain biogenic amines in the rat.

AUTHORS:
HRDINA PD
PETERS D AV
SINGHAL RL

SOURCE:
RES COMMUN CHEM PATHOL PHARMACOL; 15 (3). 1976 483-494

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Effects of chronic (45 days) treatment with different doses of cadmium chloride (0.25 and 1.0 mg/kg per day), methylmercury chloride (0.4 and 4.0 mg/kg per day) and lead acetate (0.2 and 1.0 mg/kg per day) and of 28 day withdrawal of treatment on the levels of acetylcholine (ACh) and activity of acetylcholinesterase (AChE) in cerebral cortex, and concentration of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) in brain-stem were examined in rats. Exposure to both Cd and methylmercury produced significant decreases in cortical ACh and brain-stem 5-HT levels. In addition, brain-stem NE concentration was increased in methylmercury-treated rats. In contrast, chronic treatment with Pb resulted in enhanced cerebrocortical ACh levels but a decreased brain-stem NE concentration. Treatment with Cd also produced a transient enhancement of striatal dopamine levels. Cd-induced decreased in brain-stem 5-HT and Pb-induced accumulation of cortical ACh persisted even after 28 day withdrawal of treatment. Chronic exposure to low doses of heavy metals apparently produces differential changes in regional levels of various brain biogenic amines. These changes may represent the early signs of adverse effects on CNS function since they occur before any overt symptoms of neurotoxic effects of heavy metals become apparent.

499
TITLE:

Uptake of elemental mercury by brain in relation to concentration of glutathione and activity of glutathione peroxidase.

AUTHORS:
EIDE I
SYVERSEN T LM

SOURCE:
TOXICOL LETT (AMST); 17 (3-4). 1983. 209-214.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Uptake of Hg by brain after i.v. injection of elemental Hg was investigated in the rat, after depletion of glutathione or inhibition of glutathione peroxidase in brain tissue. When glutathione in brain was depleted 76% by an intraventricular injection of diethylmaleate, a 13% increase in Hg uptake by brain was observed. After an intraventricular injection of iodoacetate, activity of glutathione peroxidase in brain was inhibited 19% and the content of reduced glutathione was decreased 20%. In these animals Hg uptake by brain increased 66% relative to controls.

500
TITLE:
Mercury vapor inhalation inhibits binding to GTP to tubulin in rat brain: Similarity to a molecular lesion in Alzheimer diseased brain.

AUTHORS:
PENDERGRASS JC
HALEY BE
VIMY MJ
WINFIELD SA
LORSCHEIDER FL

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 18 (2). 1997. 315-324.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Hg2+ interacts with brain tubulin and disassembles microtubules that maintain neurite structure. Since it is well known that Hg vapor (Hg0) is continuously released from "silver" amalgam tooth fillings and is absorbed into brain, rats were exposed to Hg0 4 h/day for 0, 2, 7, 14 and 28 d at 250 or 300 mug Hg/m3 air, concentrations present in mouth air of some humans with many amalgam fillings. Average rat brain Hg concentrations increased significantly (11-47 fold) with duration of Hg0 exposure. By 14 d Hg0 exposure, photoaffinity labelling of the beta-subunit of the tubulin dimer with (alpha32P)8N3GTP in brain homogenates was decreased 41-74%, upon analysis of SDS-PAGE autoradiograms. The identical neurochemical lesion of similar

or greater magnitude is evident in Alzheimer brain homogenates from approximately 80% of patients, when compared to human age-matched neurological controls. Total tubulin protein levels remained relatively unchanged between Hg0 exposed rat brai

501
TITLE:
METHYLMERCURY TRANSPORT ACROSS CELL MEMBRANES

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
DESCRIPTION (from Applicant's Abstract): The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results primarily in neurologic damage characterized by ataxia, sensory disturbances and changes in the mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Approximately 90% of the total excretion in humans or animals exposed to MeHg occurs via the gastrointestinal tract. Gastrointestinal excretion is in turn determined primarily by biliary secretion. Our recent studies provide the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile. These observations not only provide a new framework for understanding transport mechanisms for toxic metals, but also provide a mechanistic basis for the rational design of therapeutic strategies in MeHg intoxication. The overall objective of the proposed studies is to characterize these MeHg transport systems at the cellular and molecular level. Mechanisms of MeHg transport across the luminal and abluminal membranes of brain capillary endothelial cells, the cells that constitute the blood-brain barrier, will be characterized by: A) Testing the role of plasma GSH and of luminal membrane-associated gamma-glutamyltransferase in MeHg uptake into isolated brain capillary endothehal cells. B) Examining the mechanism of MeHg efflux from brain capillary endothelial cells, and C) Examining the molecular mechanism of MeHg-L-cysteine transport on the System L amino acid carrier. We propose to characterize the expression of the brain capillary transporter in Xenopus laevis oocytes, and use the direct expression cloning strategy to identify the cDNA for the transporter. If successful, cloning will yield important structural information on this amino acid carrier, and will allow production of molecular probes with which to define its role in MeHg disposition and

toxicity. Hepatocanalicular transport of MeHg will be examined by: A) Testing whether MeHg-SG is transported across the canalicular membrane into bile by the recently cloned high Km canalicular GSH carrier (RcGshT), and/or by the low Km GSH/glutathione S-conjugate carrier recently identified in our laboratory, and B) Testing whether MeHg is reabsorbed from bile across the canalicular membrane as the cysteine complex on System L carriers.

502
TITLE:
METHYLMERCURY TRANSPORT ACROSS CELL MEMBRANES

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ DESCRIPTION (from Applicant's Abstract): The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results primarily in neurologic damage characterized by ataxia, sensory disturbances and changes in the mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Approximately 90% of the total excretion in humans or animals exposed to MeHg occurs via the gastrointestinal tract. Gastrointestinal excretion is in turn determined primarily by biliary secretion. Our recent studies provide the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile. These observations not only provide a new framework for understanding transport mechanisms for toxic metals, but also provide a mechanistic basis for the rational design of therapeutic strategies in MeHg intoxication. The overall objective of the proposed studies is to characterize these MeHg transport systems at the cellular and molecular level. Mechanisms of MeHg transport across the luminal and abluminal membranes of brain capillary endothelial cells, the cells that constitute the blood-brain barrier, will be characterized by: A) Testing the role of plasma GSH and of luminal membrane-associated gamma-glutamyltransferase in MeHg uptake into isolated brain capillary endothehal cells. B) Examining the mechanism of MeHg efflux from brain capillary endothelial cells, and C) Examining the molecular mechanism of MeHg-L-cysteine transport on the System L amino acid carrier. We propose to characterize the expression of the brain capillary transporter in Xenopus laevis oocytes, and use the direct expression cloning strategy to

identify the cDNA for the transporter. If successful, cloning will yield important structural information on this amino acid carrier, and will allow production of molecular probes with which to define its role in MeHg disposition and toxicity. Hepatocanalicular transport of MeHg will be examined by: A) Testing whether MeHg-SG is transported across the canalicular membrane into bile by the recently cloned high Km canalicular GSH carrier (RcGshT), and/or by the low Km GSH/glutathione S-conjugate carrier recently identified in our laboratory, and B) Testing whether MeHg is reabsorbed from bile across the canalicular membrane as the cysteine complex on System L carriers.

503
TITLE:
METHYLMERCURY TRANSPORT ACROSS CELL MEMBRANES

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ DESCRIPTION (from Applicant's Abstract): The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results primarily in neurologic damage characterized by ataxia, sensory disturbances and changes in the mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Approximately 90% of the total excretion in humans or animals exposed to MeHg occurs via the gastrointestinal tract. Gastrointestinal excretion is in turn determined primarily by biliary secretion. Our recent studies provide the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile. These observations not only provide a new framework for understanding transport mechanisms for toxic metals, but also provide a mechanistic basis for the rational design of therapeutic strategies in MeHg intoxication. The overall objective of the proposed studies is to characterize these MeHg transport systems at the cellular and molecular level. Mechanisms of MeHg transport across the luminal and abluminal membranes of brain capillary endothelial cells, the cells that constitute the blood-brain barrier, will be characterized by: A) Testing the role of plasma GSH and of luminal membrane-associated gamma-glutamyltransferase in MeHg uptake into isolated brain capillary endothehal cells. B) Examining the mechanism of MeHg efflux from brain capillary endothelial cells, and C) Examining the molecular mechanism of

MeHg-L-cysteine transport on the System L amino acid carrier. We propose to characterize the expression of the brain capillary transporter in Xenopus laevis oocytes, and use the direct expression cloning strategy to identify the cDNA for the transporter. If successful, cloning will yield important structural information on this amino acid carrier, and will allow production of molecular probes with which to define its role in MeHg disposition and toxicity. Hepatocanalicular transport of MeHg will be examined by: A) Testing whether MeHg-SG is transported across the canalicular membrane into bile by the recently cloned high Km canalicular GSH carrier (RcGshT), and/or by the low Km GSH/glutathione S-conjugate carrier recently identified in our laboratory, and B) Testing whether MeHg is reabsorbed from bile across the canalicular membrane as the cysteine complex on System L carriers.

504
TITLE:
METHYLMERCURY TRANSPORT ACROSS CELL MEMBRANES

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ DESCRIPTION (from Applicant's Abstract): The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results primarily in neurologic damage characterized by ataxia, sensory disturbances and changes in the mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Approximately 90% of the total excretion in humans or animals exposed to MeHg occurs via the gastrointestinal tract. Gastrointestinal excretion is in turn determined primarily by biliary secretion. Our recent studies provide the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile. These observations not only provide a new framework for understanding transport mechanisms for toxic metals, but also provide a mechanistic basis for the rational design of therapeutic strategies in MeHg intoxication. The overall objective of the proposed studies is to characterize these MeHg transport systems at the cellular and molecular level. Mechanisms of MeHg transport across the luminal and abluminal membranes of brain capillary endothelial cells, the cells that constitute the blood-brain barrier, will be characterized by: A) Testing the role of plasma GSH and of luminal membrane-associated

gamma-glutamyltransferase in MeHg uptake into isolated brain capillary endothehal cells. B) Examining the mechanism of MeHg efflux from brain capillary endothelial cells, and C) Examining the molecular mechanism of MeHg-L-cysteine transport on the System L amino acid carrier. We propose to characterize the expression of the brain capillary transporter in Xenopus laevis oocytes, and use the direct expression cloning strategy to identify the cDNA for the transporter. If successful, cloning will yield important structural information on this amino acid carrier, and will allow production of molecular probes with which to define its role in MeHg disposition and toxicity. Hepatocanalicular transport of MeHg will be examined by: A) Testing whether MeHg-SG is transported across the canalicular membrane into bile by the recently cloned high Km canalicular GSH carrier (RcGshT), and/or by the low Km GSH/glutathione S-conjugate carrier recently identified in our laboratory, and B) Testing whether MeHg is reabsorbed from bile across the canalicular membrane as the cysteine complex on System L carriers.

505
TITLE:
Effects of lead, cadmium and mercury on brain adenylate cyclase.

AUTHORS:
EWERS U
ERBE R

SOURCE:
TOXICOLOGY; 16 (3). 1980. 227-238.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The effects of Pb, Cd and Hg ions on adenylate cyclase activity of rat cerebrum, cerebellum and brain stem were studied in vitro and in vivo. Adenylate cyclase activity in homogenates of cerebellum as well as cerebrum and brain stem was inhibited by micromolar concentrations of these heavy metal ions in vitro. Administration of lead acetate trihydrate (25 mg/kg body wt i.v.) produced an initial increase of adenylate cyclase activity in the cerebellum and brain stem 1 h after injection, followed by a significant decrease of enzyme activity in cerebrum and cerebellum 4 h after the injection. Chronic Pb treatment achieved by feeding Pb containing diets, which generated blood Pb levels of 31.3 | 3.8, 68.8 | 1.5 and 121.5 | 8.6 mug Pb/100 g blood, respectively, produced a significant increase of brain Pb levels and a 10-30% reduction of adenylate cyclase activity in cerebrum, cerebellum and brain stem. Phosphodiesterase activity was reduced under these conditions in the range of 10-20% in cerebellum and brain stem, but not in cerebrum.

506
TITLE:
METHYLMERCURY TRANSPORT ACROSS CELL MEMBRANES

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
DESCRIPTION (from Applicant's Abstract): The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results primarily in neurologic damage characterized by ataxia, sensory disturbances and changes in the mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Approximately 90% of the total excretion in humans or animals exposed to MeHg occurs via the gastrointestinal tract. Gastrointestinal excretion is in turn determined primarily by biliary secretion. Our recent studies provide the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile. These observations not only provide a new framework for understanding transport mechanisms for toxic metals, but also provide a mechanistic basis for the rational design of therapeutic strategies in MeHg intoxication. The overall objective of the proposed studies is to characterize these MeHg transport systems at the cellular and molecular level. Mechanisms of MeHg transport across the luminal and abluminal membranes of brain capillary endothelial cells, the cells that constitute the blood-brain barrier, will be characterized by: A) Testing the role of plasma GSH and of luminal membrane-associated gamma-glutamyltransferase in MeHg uptake into isolated brain capillary endothehal cells. B) Examining the mechanism of MeHg efflux from brain capillary endothelial cells, and C) Examining the molecular mechanism of MeHg-L-cysteine transport on the System L amino acid carrier. We propose to characterize the expression of the brain capillary transporter in Xenopus laevis oocytes, and use the direct expression cloning strategy to identify the cDNA for the transporter. If successful, cloning will yield important structural information on this amino acid carrier, and will allow production of molecular probes with which to define its role in MeHg disposition and toxicity. Hepatocanalicular transport of MeHg will be examined by: A) Testing whether MeHg-SG is transported across the canalicular membrane into bile by the recently cloned high Km canalicular GSH carrier (RcGshT), and/or by the low Km GSH/glutathione S-conjugate carrier recently identified in our laboratory, and B) Testing whether MeHg is reabsorbed from bile across the canalicular membrane as the cysteine complex on System L carriers.

507
TITLE:
The Inhibitory Effects of Nitrous Oxide and Methylmercury In Vivo on Methionine Synthase (EC 2.1.1.13) Activity in the Brain, Liver, Ovary, and Spinal Cord of the Rat

AUTHORS:
Brennt CE
Smith JR

SOURCE:
General Pharmacology, Vol. 20, No. 4, pages 427-431, 26 references, 1989

ABSTRACT:
The effects of nitrous-oxide (10024972) and methylmercury (22967926) on brain, liver, ovary, and spinal cord methionine-synthase activity were examined in rats. Female Sprague-Dawley-rats were injected subcutaneously with 0, 3, or 6mg/kg methylmercury daily for 4 days. Twenty four hours after the last injection they were exposed to a 50:50 mixture of nitrous-oxide and oxygen (7782447) or 100 percent oxygen for 1 hour. Animals were then killed and the brain, liver, spinal cord, and ovaries removed and analyzed for methionine-synthase activity. Methionine-synthase activity was similar in all tissues from rats exposed to pure oxygen. Nitrous-oxide alone induced significant decreases in spinal cord, brain, and liver tissue methionine-synthase activity. Ovarian tissue methionine-synthase activity was also decreased; however, the decreases were statistically significant only at the 90 percent confidence level. The 6mg/kg dose of methylmercury caused a significant decrease in brain methionine-synthase activity and a trend toward decreased methionine-synthase activity in the spinal cord and ovaries. Methylmercury appeared to induce methionine-synthase in the liver. Combined treatment with methylmercury and nitrous-oxide seemed to manifest additive decreases in brain, spinal cord, and ovarian methionine-synthase activity. The authors conclude that the susceptibility of spinal cord and ovarian methionine-synthase to nitrous-oxide is similar to that of brain and liver methionine-synthase. The effect of methylmercury on methionine-synthase may reflect a generalized inhibition of protein synthesis.

508
TITLE:
Studies on combined effects of organophosphates or carbamates and Morsodren in birds. II. Plasma and cholinesterase in quail fed morsodren and orally dosed with parathion or carbofuran.

AUTHORS:
Dieter MP
Ludke JL

SOURCE:
Bull. Environ. Contam. Toxicol. 19(4): 389-395 1978 (7 References)

ABSTRACT:
PESTAB. Six-wk-old Coturnix quail were fed for 18 wk doses of 0.05, 0.50, and 5.0 ppm dry weight Morsodren (methylmercury dicyandiamide) or 1% propylene glycol in turkey feed. Randomly chosen birds from each group were fasted 30 min and dosed orally with a sublethal concentration (0.5 mg/kg) of parathion or carbofuran. Their plasma and brain cholinesterase activities were compared 1 hr later. The only effect of Morsodren on the birds was a 17% reduction of cholinesterase activity in birds fed 5 ppm Morsodren. Parathion caused a 29% inhibition of brain cholinesterase activity in control birds and a progressively greater enzyme inhibition in Morsodren fed birds. The differences between the control and Morsodren fed birds were not significant. Carbofuran dosing in Morsodren fed birds resulted in a significantly greater inhibition (42%) of brain cholinesterase. Mercury levels were proportional to the concentrations fed for 18 wk. Prior mercury exposure rendered carbofuran a more potent brain cholinesterase inhibitor.

509
TITLE:
Differences in the distribution of methyl mercury in erythrocytes, plasma and brain of Japanese quails and rats after a single oral dose.

AUTHORS:
CLAUSING P
RIEDEL B
GERICKE S
GRUEN G
MUELLER L

SOURCE:
ARCH TOXICOL; 56 (2). 1984 (RECD. 1985). 132-135.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Distribution of a single oral dose of methyl mercury (10 mg Hg/kg body wt) was followed from 90 min-120 h in plasma, erythrocytes and brain of Japanese quails and rats. Significantly higher Hg concentrations were observed on plasma and brain of quails and red blood cells of rats. Blood brain ratio decreased in quails from 6 to 2 at 24 and 120 h, respectively; it increased in rats. Erythrocyte/plasma ratio in quails was distribution were accompanied by a > 3-fold higher acute toxicity in quails under adequate experimental conditions.

510
TITLE:

Neurotoxicants and developing brain.

AUTHORS:
Suzuki K
Martin PM

SOURCE:
Developmental Neurotoxicology 1994;:9-32

511
TITLE:
LATE CONSEQUENCES OF PRENATAL EXPOSURE TO METHYLMERCURY

AUTHORS:
WEISS B

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ An extensive literature indicates that the fetal brain is exquisitely sensitive to methylmercury. These data come from a multiplicity of species, including humans. Despite the extent of the current literature, however, two difficult and important questions remain unanswered. First, what are the lifetime consequences of prenatal exposure? Might they remain latent until the brain is stripped of compensatory capacity by the processes of aging? Second, what might be the consequences of lifetime exposure to relatively low levels of methylmercury? Could minute increments of damage cumulate to accelerate the processes of aging in the brain? These questions will be addressed in mice in an experimental format designed to follow the course of potential neurotoxicity through the lifespan. The mice will be exposed prenatally alone or both prenatally and postnatally. Specified groups will be observed at the age of 3, 9, 15, and 21 months for six-month periods, during which behavioral measures of motor function and cognitive performance will be secured. At the end of the observation period, brains will be examined by quantitative morphological methods to determine the structural consequences of the various exposure scenarios, and histo-chemical methods will be used for mercury localization. Both organic and inorganic content will also be assayed. These data will contribute data essential for a full risk assessment of dietary methylmercury sources, because current human data suggest adverse effects of exposure at surprisingly low levels.

512
TITLE:
Abnormal Neuronal Distribution within the Cerebral Cortex after Prenatal Methylmercury Intoxication

AUTHORS:
Peckham NH
Choi BH

SOURCE:
Actal Neuropathologica, Vol. 76, No. 3, pages 222-226, 26 reference, 19881988

ABSTRACT:
The effects of prenatal methylmercury (22967926) intoxication on brain development were studied in mice. Pregnant C57BL/6J-mice were injected intraperitoneally with 0 or 4mg/kg methylmercuric-chloride (115093) (MMC) on days 14, 15, and 16 of gestation. Other mice were administered 0 or 2mg/kg MMC in their drinking water on days two through 16 of gestation. Thirty minutes after the last dose all mice were injected with tritiated thymidine. The dams were allowed to deliver. The offspring were killed on postnatal day ten and the brains were removed. The cerebral cortex was sectioned and the sections were examined by autoradiography and electron microscopy. The cerebral cortex of control offspring had heavily labeled neurons in tight clusters within the upper part of layer-II. In MMC treated mice the radiolabeled neurons were more haphazardly distributed through layers-II and III. The differences were statistically significant. The basic morphological structure of the cerebral cortex in treated mice did not appear to be altered. The authors conclude that prenatal methylmercury intoxication causes abnormal neuronal migration within the developing brain. The observed abnormal distribution of cortical neurons may provide a morphological basis for some of the behavioral abnormalities that are associated with sublethal low dose prenatal methylmercury poisoning.

513
TITLE:
Behavioral changes and mercury concentrations in tissues of rats exposed to mercury vapor.

AUTHORS:
KISHI R
HASHIMOTO K
SHIMIZU S
KOBAYASHI M

SOURCE:
TOXICOL APPL PHARMACOL; 46 (3). 1978 (RECD. 1979). 555-566.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The present study was designed to determine critical brain Hg concentrations associated with specific behavioral

changes during exposure to Hg vapor. Rats exposed to 3 mg Hg/m3 for 3 h, 5 days/wk, for 15-42 wk, showed a decline in conditioned avoidance response. The latency of escape response also increased in pole climb shock escape. The time to the onset of effects varied from 12-39 wk among 14 rats exposed to Hg. All rats recovered to preexposure baseline within 12 wk after the termination of exposure. A significantly poor behavioral performance was noticed in rats with brain Hg concentrations of approximately 20 mug Hg/g. Behavioral recovery was seen when the Hg concentrations decreased to 10 mug Hg/g brain tissue. The critical concentration of inorganic Hg in the brain associated with behavioral changes in the rat ranges from about 10-20 ppm. In spite of the high concentrations of Hg, the nervous tissues of rats with Hg vapor intoxication in this experiment were normal.

514
TITLE:
Mercury levels, production, and hematology in western grebes from three California lakes, USA.

AUTHORS:
ELBERT RA
ANDERSON DW

SOURCE:
ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY; 17 (2). 1998. 210-213.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Twenty-three healthy adult western and Clark's grebes (Aechmophorus occidentalis and Aechmophorus clarkii) were collected at three study sites in California, USA, in 1992: Clear Lake, Lake County; Eagle Lake, Lassen County; and Tule Lake, Siskiyou County. Liver, kidney, breast muscle, and brain were analyzed for total mercury (Hg) concentration (ppm wet weight), and blood was analyzed for various blood parameters. Clear Lake birds (n = 13) had greater Hg concentrations in kidney, breast muscle, and brain than birds from the other two lakes ($p < 0,05$), whereas liver concentrations were not statistically different ($p > 0.05$). Average concentrations for Clear Lake birds were 2.74 ppm for liver, 2.06 ppm for kidney, 1.06 ppm for breast muscle, and 0.28 ppm for brain. The tissue levels of kidney, breast muscle, and brain at the other two study sites were one half the levels found at Clear Lake. These mean tissue levels were near, but below, those known to cause adverse

515
TITLE:
Toxicity of organic mercury compounds: III. Uptake and retention of mercury in several organs of mice by long term exposure of alkoxyethylmercury compounds.

AUTHORS:
YONAHA M
ISHIKURA S
UCHIYAMA M

SOURCE:
CHEM PHARM BULL (TOKYO); 23 (8). 1975 1718-1725

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Uptake and accumulation of alkoxyethylmercury compounds in several organs of mice, in comparison with alkylmercury compounds were studied. Diets containing various organic Hg compounds were continuously fed to mice, and organic Hg in the organs was extracted with dithizone-CCl4 and determined by gas chromatography. Histological studies in mice poisoned by methoxyethylmercury chloride showed a prominent damage of the kidney, and proliferation of glial cells and atrophy of nervous cells in the cerebrum. In all of the compounds administered, the organic Hg was found in the liver and kidney. The ratio of the Hg contents in blood to plasma was higher in ethylmercury chloride than in alkoxyethylmercury compounds. Ethylmercury chloride was rapidly incorporated into the brain, while alkoxyethylmercury compounds were incorporated at much slower rates. The Hg contents in the brain at onset of the neural symptoms were much lower in methoxyethylmercury than in ethylmercury. In the brain after administration of alkoxyethylmercury compounds, Hg was present in an inorganic form in the case of the alkylmercury. Manifestation of the symptoms after exposure of organic Hg compounds is probably not merely related to Hg levels and not always in need of organic forms in the brain.

516
TITLE:
Effects of Metals on PKC-Nitric Oxide Synthase-Glutamate Receptor in the Brain

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Children exposed to Lead (Pb) show memory deficits associated with low levels of intelligence whereas, children and adults are equally sensitive to Methyl Mercury (CH3Hg). The biochemical basis of cognition has been shown to be dependent on proper functioning of two key enzymes in the hippocampus and the cerebellum namely the protein Kinase C (PKC) and Nitric Oxide Synthase (NOS). These enzymes are known to have multiple

isoforms which are modulated by a number of endogenous and exogenous second messengers, neurotransmitters etc. The long term of our research is to delineate the role of PKC-NOS-NMDA complex to understand the mechanism of Pb and CH3HG induced neurotoxicity. The hypothesis to be tested in this proposal is that Pb and CH3Hg mediated developmental neurotoxicity. The hypothesis to be tested in this proposal is that Pb and CH3Hg mediated developmental neurotoxicity is dependent on single or multiple isoforms of PKC and NOS, and the regulation of glutamatergic neurotransmiss ion. The specific aims are: a) environmentally relevant Pb or CH3Hg exposure during the brain development results in changes of PKC and NOS and changes are isoform specific; b) The isoform specifics changes of PKC and NOS by perinatal and changes are isoform specific; b) The isoform specific changes of PKC and NOS by perinatal exposure of Pb and CH3Hg modulate the neurotransmitter pathways critical to cognitive functions; c) the changes in PKC and NOS isoforms, and NMDA receptors are related to the blood and tissue levels of Pb and Hg. The developing brains from rats of Post Natal Day (PND) 5,7, 10, 15, 21, 30, 45, 60 exposed to 1% Pb or 0.01% CH3Hg in deionized distilled drinking beginning at conception through 21 days after limiting will be used. We will study Pb and CH3Hg effects on: a) alpha-PKC, epsilon-PKC and zeta-PKC, b) nNOS, iNOS, and eNOS; c) NMDA specific glutamate receptor, and d) correlate results from these studies with the levels of Pb and CH3Hg in the tissue and blood. At the completion of this project we expect to have provided new information on the mechanism of Pb and CH3Hg neurotoxicity. Furthermore we will have detailed the sensitivity of different isoforms of PKC and NOS to Pb and CH3Hg insult and their influence on the NMDA receptors. All research activities will be appropriately evaluated. A corollary influence of this research will be that Alcorn State University will gain a strong biomedical research base.

517

TITLE:

Evidence that Exposure to Methyl Mercury during Gestation Induces Behavioral and Neurochemical Changes in Offspring of Rats

AUTHORS:

Cagiano R
De Salvia MA
Renna G
Tortella E
Braghiroli D
Parenti C
Zanoli P
Baraldi M
Annau Z
Cuomo V

SOURCE:

Neurotoxicology and Teratology, Vol. 12, No. 1, pages 23-28, 16 references, 1990

ABSTRACT:

Behavioral and neurochemical changes induced by prenatal exposure to methylmercury were studied in rats. Pregnant Sprague-Dawley-rats were administered 8mg/kg methylmercuric-chloride (115093) (MMC) intragastrically on day 15 of gestation. After delivery the ultrasonic vocalization of 4, 8, and 12 day old male pups was tested. Behavioral responsiveness to the dopaminergic agent amphetamine, spontaneous locomotor activity, and passive avoidance behavior was examined 14, 21, and 60 days after birth. Selected pups were killed at these times and the brains were removed. The binding characteristics of dopamine and beta-adrenergic receptors and glutamate receptor sites were studied. Other rats were killed on postnatal days one, 21, and 60 to determine whole brain MMC concentrations. MMC did not significantly affect development of ultrasonic vocalization, spontaneous locomotor activity, or passive avoidance behavior. Exposed rat pups showed an increased response to amphetamine on post natal day 14, but not on day 21 or 60. An increased density of dopamine receptors was found in the striatum on postnatal day 14, but not on day 21 or 60. The binding characteristics of the beta-adrenergic receptors were not affected by MMC. The affinity of glutamate for its binding site was significantly decreased, but the maximum number of binding sites was not affected by MMC. Brain MMC concentrations in the exposed pups were 100 times those of the unexposed pups on post natal day one. They were still significantly elevated on day 21 but had decreased to near the control value by day 20. The authors conclude that the behavioral pattern of MMC exposed rat pups parallels the increase in striatal dopamine receptor densities seen at postnatal day 14 and its normalization by day 60. Prenatal exposure to a high concentration of MMC appears to induce a transient disuse/supersensitivity of the dopaminergic system and decreased functional activity of the glutamatergic system.

518

TITLE:

Sodium, potassium-ATPase in rat brain and erythrocytes as a possible target and marker, respectively, for neurotoxicity: Studies with chlordecone, organotins and mercury compounds.

AUTHORS:

MAIER WE
COSTA LG

SOURCE:

TOXICOL LETT (AMST); 51 (2). 1990. 175-188.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Due to the inaccessibility of human nerve tissue for direct biochemical evaluation, there appears to be a need to identify peripheral markers which will reflect toxicity to the central nervous system by relatively non-invasive means. The aim of this study was to investigate whether the enzyme Na++-ATPase in erythrocytes could be used as a marker for effects on the same enzyme in brain tissue. The compounds chosen to test this hypothesis were the pesticide chlordecone, the organotin compounds triethyltin and tributyltin, mercuric chloride and methyl mercury. All compounds were found to inhibit in vitro Na+/K+-ATPase activity in rat brain (IC50s=0.9-56 muM) and in rat erythrocytes (IC50s=1.2=66 muM) with similar potencies. However, administration of these compounds in vivo at high doses produced no significant inhibition of either brain or erythrocyte Na+/K+-ATPase activity, despite observed symptoms of neurotoxicity. Dialysis experiments indicated that dissociation of the

519
TITLE:
Experimental methyl mercury neurotoxicity: Similar in vivo and in vitro perturbation of brain cell-free protein synthesis.

AUTHORS:
CHEUNG MK
VERITY MA

SOURCE:
EXP MOL PATHOL; 38 (2). 1983. 230-242.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Perturbation of rat brain protein synthesis by methyl mercury chloride (MeHg) was compared in vivo and in vitro. MeHg-stimulated and/or inhibited brain cell-free protein synthesis following in vivo or in vitro administration. Although pretreatment with GSH (glutathione) protected the postmitochondrial supernatant (PMS) from the in vitro inhibition, direct addition of -SH compounds did not reverse the in vivo or in vitro perturbations in synthesis induced by MeHg. Inhibition of synthesis induced by in vivo and in vitro MeHg administration resulted in inactivation of component(s) in brain pH 5 enzymes. Stimulation of amino acid incorporation following in vivo administration of MeHg was apparently associated with the ribosome fraction, but in vitro preincubation of PMS with MeHg produced stimulation associated with the pH 5 enzyme fraction. A model of MeHg neurotoxicity was proposed providing a common molecular locus of interaction in vivo and in vitro.

520
TITLE:
The Toxicity, Distribution and Elimination of Methylmercury in Mice

Following Intracerebral Injection

AUTHORS:
Fair PH
Balthrop JE
Braddon-Galloway S

SOURCE:
NeuroToxicology, Vol. 8, No. 2, pages 281-290, 46 references, 19871987

ABSTRACT:
The toxicity, distribution, and elimination of methylmercury following intracerebral injection were studied in mice. Weanling female ICR-mice were injected intracerebrally (ic) with 0 to 36 micrograms (microg) radiolabeled methylmercuric-chloride (115093) (MMC). The animals were observed for clinical signs of toxicity, and survival was recorded. Selected mice were killed 10 minutes to 7 days after dosing, and brains were removed, weighed, and dissected into various regions. Other mice were injected with labeled MMC as before. Urine and feces were collected daily for 7 days and the radioactivity measured. Treated mice showed signs of neurotoxicity such as ataxia, tremor, partial paralysis, weakened hind limbs with crossing reflex, and tail rotation. These signs appeared after injection with 16microg or higher doses. MMC at doses of 16, 24, and 36microg resulted in 82, 75, and 56 percent survival for 7 days, respectively. All doses caused a significant reduction in body weight; however, brain weight was not affected. MMC was rapidly eliminated from the brain with 40 and 5 percent of the dose remaining after 10 minutes and 7 days, respectively. Highest brain MMC concentrations occurred in the cerebellum. At 10 minutes after dosing, the red blood cells had the highest concentration of MMC, followed by the lungs, kidneys, and spleen. Kidney MMC content increased to five times the concentration of most tissues, maximal concentration occurring after 4 hours. At 7 days post/dosing, the kidney and lung had the highest MMC content. Total fecal and urinary elimination of MMC accounted for 12 and 2 percent of the dose, respectively. The authors conclude that rapid elimination from the brain after ic injection of labeled MMC indicates that the blood brain barrier does not play a significant role in retention of MMC.

521
TITLE:
Methylmercury-Induced Movement and Postural Disorders in Developing Rat: Regional Analysis of Brain Catecholamines and Indoleamines

AUTHORS:
O'Kusky JR
Boyes BE
McGeer EG

SOURCE:
Brain Research, Vol. 439, No. 1/2, pages 138-146, 49 references, 19881988

ABSTRACT:
The effect of methylmercury on the catecholamine and indoleamine content of brain tissues was studied in developing rats. Matched litters of 5 day old Sprague-Dawley-rats were injected subcutaneously with 6.26 milligrams per kilogram methylmercury-chloride (115093) (MMC) daily until one of three stages of toxicity were reached. The stages were defined as reduced weight gain (stage-I), a weight loss persisting for 12 to 24 hours (stage-II), and the onset of neurological symptoms (stage-III). These corresponded to postnatal days 15, 18 to 21, and 22 to 24, respectively. Selected animals were killed at these times, the brains were removed and weighed, and separated into the cerebral cortex, caudate/putamen (CAUD), and spinal cord. The cerebral cortex, CAUD, and spinal cord were assayed for norepinephrine, serotonin, 5-hydroxyindoleacetic-acid (HIAA), dopamine, 3,4-dihydroxyphenylacetic-acid (DOPAC), and homovanillic-acid (HVA). MMC significantly decreased brain weights. In the spinal cord, MMC induced significant increases in the concentrations of norepinephrine, serotonin, and HIAA in stage-II and stage-III of toxicity. The HIAA/serotonin ratio was also significantly increased. No dopamine, DOPAC, and HVA were detected. In the CAUD, tissue concentrations of HIAA and norepinephrine were significantly increased by MMC in stage-II and stage-III. Dopamine concentrations were significantly decreased at stage-II and stage-III of toxicity. In the cerebral cortex, serotonin and HIAA concentrations were significantly increased by MMC at stage-II and stage-III. The norepinephrine concentration was significantly decreased below that of weight matched controls in stage-I and stage-II of toxicity. The authors conclude that the pathogenesis of methylmercury induced movement and postural disorders in developing rats includes selective changes in central catecholaminergic and serotonergic neurotransmission systems.

522
TITLE:
Effects of the polychlorinated biphenyl Aroclor 1242 on locomotor activity and on the neurotransmitters dopamine and norepinephrine in the brain of the gulf killifish, Fundulus grandis.

AUTHORS:
Fingerman SW
Russell LC

SOURCE:
Bull. Environ. Contam. Toxicol. 25(2): 682-687 1980 (18 References)

ABSTRACT:
PESTAB. A study of the effects of the PCB Aroclor 1242 on

neurotransmitters is presented. Included is a literature review of the effects of several pesticides on similar systems. In the brain of the killifish Fundulus grandis, norepinephrine (NE) levels decreased (controls = 2.5 mug/g, treated = 0.61 mug/g) when brain levels of Aroclor 1242 were 0.6 mug/g. The dopamine (DA) levels also decreased (controls = 0.91 mug/g, treated = 0.44 mug/g) when brain levels of Aroclor 1242 reached 0.4 mug/g. In other studies cited, dieldrin caused a depletion of both NE and DA in mallard ducks, but caused no changes in mice. Another investigation found that sublethal doses of methyl mercury decreased the levels of NE and DA in rats. DDT, however, caused a decrease of NE but no change in DA levels in rats. DDT and parathion both decreased NE and DA brain levels in goldfish. DDE and dieldrin reduced DA and NE levels in ring doves. It appears, therefore, that the effects of Aroclor 1242 are similar to those of several pesticides with respect to the action on the brain neurotransmitters dopamine and norepinephrine.

523
TITLE:
Brain acetylcholinesterase activity studies in some fish species collected from a mercury contaminated estuary.

AUTHORS:
SHAW BP
PANIGRAHI AK

SOURCE:
WATER AIR SOIL POLLUT; 53 (3-4). 1990. 327-334.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In an attempt to investigate the impact of the discharge of Hg contaminated effluent from a chlor-alkali industry into the Rushikulya river esturary, brain AChE activity was measured in three fish species, S. sihama, A. nenga and S. argus, sampled from the contaminated water of the estuary. The residual Hg levels in the brain tissue of the fishes were also determined. The maximum brain residual Hg level, 0.072 | 0.205 mg kg-1 ww, was recorded in S. sihama. The inhibition of the AChE activity observed in that species was as much as 26.48% when compared to the normal enzyme activity. The levels of inhibition in that species was as much as 26.48% when compared to the normal enzyme activity. The levels of inhibition observed in the other two fish species, A. nenga and S. argyus, were also more than the 10% index level suggested. A significant negative correlation observed between the brain residual Hg levels and the AChE activity levels suggested the use of fish brain AChE

524
TITLE:
Organochlorine and mercury residues in the harp seal (Pagophilus groenlandicus).

AUTHORS:
Jones D
Ronald K
Lavigne DM
Frank R
Holdrinet M
Uthe JF

SOURCE:
Sci. Total Environ. 5(2): 181-195; 1976.(37 references)

ABSTRACT:
PESTAB. Samples of blubber, liver, kidney, and brain from ten male, six female neonatal, and four lactating female harp seals (Pagophilus groenlandicus) were analyzed for DDT, dieldrin, PCB, and total mercury. The methyl mercury levels in the blood were also determined. Biocide deposition was not significantly different in 10-day-old male and female pups, and 10-day-old pups did not differ significantly from those aged 14 days or more in the hepatic biocide levels. However, the residue levels of DDT, TDE, DDE, and dieldrin tended to decrease with age. There was no clear relationship between biocide levels in the 6-18-yr-old lactating adults and the levels in their pups. Younger adults (6-7 yr) had higher levels of PCB and total DDT in their blubber than older females (10-18 yr). Wide intraspecific variation was noted in the organochlorine and mercury residue levels, although pups taken in 1973 had lower organochlorine residues than those taken from the same area in 1971. The results indicate that detectable amounts of organochlorine and mercury residues are able to cross the placenta in the harp seal.

525
TITLE:
Time dependent tissue distribution of mercury-203 in the white rat and Anabas testudineus, a freshwater teleost.

AUTHORS:
BOSE S
GHOSH P
GHOSH S
CHAUDHURY S
BHATTACHARYA S

SOURCE:
BIOMED ENVIRON SCI; 5 (4). 1992. 355-361.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The distribution of mercury, an environmentally important toxicant, has been evaluated in a time dependent

manner in different tissues of white rat and a freshwater teleost, Anabas testudineus. Sampling was performed at 15 min, 2, 6 and 48 h post injection (im) of 203Hg mercuric nitrate. Radioactivity of the 5% tissue homogenate, serum and bile was measured in a Gamma Counter. The rate of 203Hg accumulation is higher in fish immediately after administration which, however, is more or less of equal rate in the later period of observation in both the experimental animals. Partitioning of 203Hg occurs in a species specific manner with higher levels recorded in the brain and gonad of white rat. Spleen, liver and kidney, however, are the major tissues to accumulate mercury in both the species. The present study highlights that kidney is the target site of mercury retention with a higher kidney/liver ratio of mercury.

526
TITLE:
Chronic Accumulation of Cadmium in the Edible Tissues of Oreochromis aureus (Steindachner): Modification by Mercury and Lead.

AUTHORS:
ALLEN P

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 29 (1). 1995. 8-14.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The influence of mercury and lead on cadmium accumulation was investigated by exposing the fish Oreochromis aureus, or Blue Tilapia, to two heavy metals simultaneously. The chronic accumulation profile of cadmium in the liver, brain, gill filaments, intestine, caudal muscle, spleen, trunk kidney, and gonads was determined for exposure to cadmium alone and with lead or mercury. O. aureus was exposed to cadmium alone at 0.05 and 0.10 mg, and mixtures of 0.05 mg/L cadmium with 0.05 mg/L mercury or lead (0.05 and 0.50 mg/L). Little research has previously been carried out on the long-term interaction between these heavy metals and their effects on tissue accumulation of heavy metals. In a food fish such as O. aureus, a knowledge of toxic metal accumulation patterns is of great importance. The highest levels of cadmium were consistently accumulated by the kidney, and the presence of other mercury or lead did not change this trend. The spleen, intestine, and liver also accum

527
TITLE:
Interaction Of Alkylmercuric Compounds With Sodium Selenite. II. Metabolism Of Methylmercuric Chloride Administered Alone And In Combination With Sodium Selenite In Rats

AUTHORS:

Brzeznicka EA
Chmielnicka J

SOURCE:
Environmental Health Perspectives, Vol. 60, pages 411-421, 71 references, 19851985

ABSTRACT:
The effect of sodium-selenite (10102188) on the metabolism of methylmercuric-chloride (115093) (MeHg) was investigated in rats. Female Wistar-rats were given a dose of either 0.25 or 2.5 milligrams per kilogram mercury-203 labeled MeHg intragastrically or intravenously every other day for 2 weeks. A dose of 0.5 milligram per kilogram sodium-selenite was given intragastrically every day. Total excretion of mercury (7439976) in feces and urine was monitored daily. At 24 hours after the last dose of MeHg, rats were sacrificed. Mercury was determined directly in urine, feces, and tissues using a scintillation counter. Perfused liver and kidneys were fractionated. Mercury was assayed radiochemically in column eluates and protein concentration was monitored by measurements of absorption at 280 and 250 nanometers. Irrespective of the dose or route of administration, the same percent of the cumulative dose of MeHg was excreted in urine and feces. In repeated exposures to MeHg, its concentrations in individual tissues increased approximately proportionally to the administered dose. Sodium-selenite affected the concentration of MeHg in the rat kidney significantly only when the selenium was in excess of the mercury. The ratio of MeHg concentrations in tissues to blood were very similar for both routes of administration and both doses, especially in the case of such vital organs as the brain, liver, and kidney. The authors conclude that forecasting MeHg concentration in rat tissues is possible by determining its concentration in the blood and taking the effect of sodium-selenite into consideration.

528
TITLE:
Health effect of exposure to metallic mercury vapours in workers engaged in the production of chlorine and acetic aldehyde I. Evaluation of the general health condition.

AUTHORS:
MAREK K
ZAJAC-NEDZA M
ROLA E
WOCKA-MAREK T
LANGAUER-LEWOWICKA H
WITECKI K

SOURCE:
MEDYCYNA PRACY; 46 (2). 1995. 101-109.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Physical, neurological and psychological examinations as well as laboratory tests were performed in the group of 147 workers, engaged in the production of chlorine, acetic aldehyde and soda lye, exposed to metallic mercury vapours and in the control group (n=49). In the evaluation of laboratory tests, morphology of peripheral blood, liver function tests and lipid balance were analysed in the first part of the work. Electroencephalography, electrocardiography and chest X-ray were also performed as auxiliary examinations. There was a certain percentage of cases with symptoms of organic damage; of the brain mostly in the form of cerebellar syndrome. Psychological organic tests proved to be of little value in the evaluation of effects of exposure to mercury. The results suggest that occupational exposure to metallic mercury vapours can enhance the risk of hypertension and myocardial failure. Harmful effect of occupational exposure to metallic mercury vapour on the respirato

529

TITLE:

Soft-tissue accumulation of lead in the Blue Tilapia, Oreochromis aureus (Steindachner), and the modifying effects of cadmium and mercury.

AUTHORS:

ALLEN P

SOURCE:

BIOLOGICAL TRACE ELEMENT RESEARCH; 50 (3). 1995. 193-208.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. The interaction of mercury and cadmium with lead was investigated by exposing Oreochromis aureus to two heavy metals simultaneously. The chronic accumulation profile of lead was determined by analyzing the liver, brain, gill filaments, intestine, caudal muscle, spleen, trunk kidney, and gonads following exposure to lead alone and in mixtures with mercury and cadmium. Nominal exposure concentrations of lead were 0.05, 0.10, 0.50, and 1.00 mg. Mixtures of lead (0.50 or 0.05 mg/L) with cadmium (0.05 mg/L) and lead (0.50 or 0.05 mg/L) with mercury (0.05 mg/L) were also used. Following 140 d of exposure to lead, the highest concentrations of lead consistently accumulated in the trunk kidney. The concentration of lead in the kidney was decreased by coexposure to mercury or cadmium, but increased in the muscle and liver. Under all exposure regimes, the median concentration of lead in the muscle exceeded safety levels recommended for human consumption. In a food fish, such as O

530

TITLE:

Effects of Systemic Methyl Mercury-Adulterated Water Consumption on Fast

Axonal Transport in the Rat Visual System

AUTHORS:
Aschner M

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 59, No. 5, pages 349-355, 23 references, 19861986

ABSTRACT:
Fast axonal transport was measured after the onset of neurological impairment in adult Long-Evans-rats exposed to methyl-mercury (22967926) (MeHg) adulterated water in order to examine rate of protein synthesis in the retina and flow of protein bound radioactivity along the visual system. Daily intake of tap water containing 54 micrograms/milliliter mercury (7439976) (Hg) decreased over the first 2 weeks, and increased just before the onset of symptoms. Hind limb cross quickly succumbed to paralysis; forelimbs did not exhibit significant neurological alterations. Pattern of displacement of protein bound radioactivity was studied 8 hours after intraocular injection of H3-proline (147853) in animals drinking adulterated water, in animals directly injected with 9.04 micrograms methyl-mercury-chloride (115093) into the vitreous body, and in animals given 4mg/kg Hg orally for 4 to 6 days. After 8 hours, the first visual relay at the level of the lateral geniculate body had counts exceeding background level. MeHg consuming rats showed an increase in protein synthesis in the retina, but decreased protein bound radioactivity in the optic nerve and other parts of the visual system. Protein levels in the axon were significantly and inversely decreased. Injection of MeHg directly into the eye depressed both protein synthesis in the retina and the quantity propagated into the nerve. Rate of retinal protein synthesis increased after systemic treatment. Nerve fiber did not show similar increases. Accumulation in the peripheral nervous system did not exceed accumulation of the central nervous system. Results did not indicate that fast axonal transport rate is blocked at the onset of MeHg induced neurological deficits. Abnormal transport capacity may be a factor.

531
TITLE:
Mercury distribution in American alligators (Alligator mississippiensis) in Florida.

AUTHORS:
HEATON-JONES TG
HOMER BL
HEATON-JONES DL
SUNDLOF SF

SOURCE:

JOURNAL OF ZOO AND WILDLIFE MEDICINE; 28 (1). 1997. 62-70.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Thirty American alligators (Alligator mississippiensis), including 24 wild-caught and six control captive farm-raised alligators, were analyzed for whole body mercury contamination. Wild-caught animals were collected from Water Conservation Area 3 in the Everglades ecosystem (n = 12) and from Alachua, Brevard, and Collier counties outside the Everglades (n = 12). Using cold-vapor atomic absorption spectrophotometry, samples of brain, cervical spinal cord, liver, paired kidneys, paired testes, paired ovaries, paired oviducts, heart, lungs, spleen, bile, tail and leg muscle, and tail and leg scales were analyzed on a wet weight basis to determine mercury concentration. Mercury was consistently detected in all specimens except for bile: Farm-raised alligators, fed a commercially prepared diet, contained very low mercury concentrations in all tissues analyzed. In comparison with alligators from outside the Everglades, Everglades alligators had significantly elevated concent

532

TITLE:

Combined oral treatment with racemic and meso-2,3-dimercaptosuccinic acid for removal of mercury in rats.

AUTHORS:

KOSTIAL K
RESTEK-SAMARZIJA N
BLANUSA M
PIASEK M
JONES MM
SINGH PK

SOURCE:

PHARMACOLOGY & TOXICOLOGY; 81 (5). 1997. 242-244.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Racemic dimercaptosuccinic acid (DMSA) was found more efficient than the meso-isoform in enhancing the removal of mercury in rats. However, racemic-DMSA has recently been found more toxic. The efficiency of combined oral treatment with the two isoforms of DMSA for removal of mercury has now been evaluated. Female albino rats were treated orally for four days with meso- (M) and/or racemic- (R) DMSA (1 mmol/kg each), five days after a single intraperitoneal administration of 203Hg with 0.5 mg HgCl2/kg. The animals were divided into six groups according to the number of treatments with each isomer: control (untreated), 4M, 1R+3M, 2R+2M, 3R+1M, and 4R. Whole body, kidney, liver and brain mercury contents were measured nine days after 203Hg administration. In all treated groups retention in the whole body and

kidneys was greatly reduced. The groups treated with racemic-DMSA, regardless of the number of doses, showed a greater removal of mercury than the group treated with me

533
TITLE:
Cross-fostering study of methyl mercury retention, demethylation and excretion in the neonatal hamster.

AUTHORS:
NORDENHALL K
DOCK L
VAHTER M

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 82 (3). 1998. 132-136.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The cross-fostering technique was used in order to compare methyl mercury (MeHg) metabolism in hamsters following prenatal (in utero) and neonatal (lactational) exposure. Pregnant Syrian golden hamsters were administered radiolabeled MeHg on day 12 of gestation. The offspring was nursed by foster mothers unexposed to MeHg, while the pups from the unexposed animals were nursed by the MeHg-administered animals. Under these conditions, each pup in the litter received a dose of MeHg in utero corresponding to 0.9% of the maternal dose. The average amount of mercury found in the pups exposed via milk corresponded to 4.5% of the total body burden of the foster dam at the onset of lactation. This was about half the amount received by the pups exposed in utero. The total body burden of mercury, and the amount of mercury in the liver, brain and kidney of the pups exposed in utero began to decrease at seven days of age. The rate of decrease differed among the tissues and was lowes

534
TITLE:
MERCURY IN MOTOR NEURONS AFTER EXPOSURE TO OCCUPATIONALLY SAFE LEVELS OF MERCURY VAPOUR

AUTHORS:
PAMPHLETT R
COOTE P

SOURCE:
XIIITH INTERNATIONAL CONGRESS OF NEUROPATHOLOGY, PERTH, WESTERN AUSTRALIA, AUSTRALIA, SEPTEMBER 7, 1997. BRAIN PATHOLOGY; 7 (4). 1997. 1390.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER MICE
ADULT MERCURY TOXIN MERCURY VAPOUR MOTOR NEURONS SHORT-TERM EXPOSURE WHO
MERCURY EXPOSURE LEVELS OCCUPATIONAL SAFETY TOXICOLOGY NERVOUS SYSTEM

535
TITLE:
THE TOXICOLOGY OF MERCURY

AUTHORS:
CLARKSON TW

SOURCE:
CRITICAL REVIEWS IN CLINICAL LABORATORY SCIENCES; 34 (4). 1997. 369-403.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM LITERATURE REVIEW HUMAN CHILD TOXICOLOGY
MERCURY TOXIN MERCURY VAPOR METHYLMERCURY COMPOUNDS NEUROTOXIN INORGANIC
MERCURY BRAIN DAMAGE PRENATAL MERCURY EXPOSURE NERVOUS SYSTEM DISEASE
TOXICITY

536
TITLE:
Effect of Mercury on Rabbit Myelin CNP-ase In Vitro

AUTHORS:
Domanska-Janik K
Bourre JM

SOURCE:
Neurotoxicology, Vol. 8, No. 1, pages 23-32, 32 references, 19871987

ABSTRACT:
The effects of mercury compounds and other heavy metals on the activity of 2',3'-cyclic-nucleotide-3'-phosphodiesterase (CNPase) in rabbit brain myelin were investigated. Rabbit myelin fraction was incubated in the presence of various inorganic and organic heavy metals. Mercuric-chloride (7487947) (HgCl2) was the most potent inhibitor of CNPase. Exposure to 5 micromole concentrations of HgCl2 for 5 minutes (min) caused 40 percent inhibition of CNPase; complete inhibition was observed after 45min exposure. Methylmercury (593748) caused a 30 percent inhibition after 5min, and a 90 percent inhibition after 45min of preincubation. CNPase activity equivalent to 15.6 micrograms (microg) of myelin protein was blocked by 1 nanomole HgCl2, whereas activity of only 9.9microg protein was blocked by 1 nanomole methylmercury. HgCl2 induced inhibition of CNPase was completely reversed by the hydrophobic low molecular weight thiol, lipoic-acid, but could not be blocked by prior addition of

lipoic-acid. Prior addition of lipoic-acid did prevent the inhibition of CNPase by methylmercury. The CNPase inhibition caused by short term exposure (5min) to methylmercury was completely reversible by both hydrophilic and hydrophobic low molecular weight thiols, while the CNPase inhibition after long term exposure (45min) was only partially reversed by low molecular weight thiols. The other heavy metals studied, lead (7439921) and tin (7440315), had negligible effects on myelin CNPase activity, even at concentrations 100 fold greater than the mercurials. The authors conclude that the biphasic CNPase inhibition of methylmercury suggests that it has more than one mechanism of CNPase inhibition.

537
TITLE:
A study on transfer of phenylmercuric acetate to newborn rats through dam's milk.

AUTHORS:
YUYAMA A
NAKANOWATARI J
MATSUSAKA N
KOBAYASHI H

SOURCE:
J FAC AGRIC IWATE UNIV; 11 (1). 1972 (RECD 1973) 29-36

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Phenylmercuric acetate (PMA) was administered i.v. in a single dose to female rats immediately after parturition. It was estimated in newborns nursed by these rats at 1, 3, 5, 7 and 10 days after the administration, 1 infant being used at 1 time. Every dam might always nurse 10 babies during the experimental period. PMA was estimated in urine samples and organs were harvested from dams killed 10 days after the administration. The amounts of total and organic mercury were determined by measured mercury dithizonate photometrically. The cumulative amounts of total Hg transferred to the newborn through dam's milk increased until 5 days after the administration of PMA. They were almost the same at 7 and 10 days as at 5 days. The mean amount of total Hg contained in 1 newborn at 10 days was about 0.8% of the dose administered. A peak of Hg concentration was recognized at 5 days. No organic mercury was found in any newborn examined. Total Hg was excreted in the urine of dams over a period of 24 h after the administration of PMA. It decreased gradually in amount at 2 days and later with the lapse of time. Very small amounts of organic mercury were found in the urine of the dams soon after the administration of PMA, but not after 5 days. In the dams at 10 days after the administration of PMA, the Hg concentration of the kidney was remarkably high, or more than 5x that of the liver, the brain or the mammary gland. The velocity of PMA metabolism is rapid in rats, and the majority of the Hg discharged in milk through the mammary

gland may be inorganic mercury.

538
TITLE:
Effects of lead and mercury intoxications on evoked potentials

AUTHORS:
Lille F
Hazemann P
Garnier R
Dally S

SOURCE:
J. Toxicol. Clin. Toxicol.; VOL 26 ISS 1-2 1988, P103-116, (REF 45)

ABSTRACT:
IPA COPYRIGHT: ASHP The effects of lead and mercury intoxications on pattern reversal, brain stem auditory and somatosensory evoked potentials in 22 patients occupationally or accidentally exposed to lead or mercury compounds, compared with alcoholics and normal controls, are described. Peripheral conduction velocities were decreased in lead exposed workers and alcoholics, but not modified in mercury exposed patients.

539
TITLE:
The effect of selenium on the biliary excretion and organ distribution of mercury in the rat after exposure to methyl mercuric chloride.

AUTHORS:
ALEXANDER J
NORSETH T

SOURCE:
ACTA PHARMACOL TOXICOL; 44 (3). 1979. 168-176.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The influence of Se compounds on the biliary excretion and organ distribution of Hg after injection of methyl mercuric chloride (4 mumol/kg) was tested. Selenite, seleno-di-N-acetylglycine and seleno-methionine strongly inhibited biliary excretion of Hg. Selenite even in a molar dose of 1/40 of the methyl mercury dose inhibited the biliary excretion of Hg. The less toxic seleno-di-N-acetylglycine was needed in larger molar doses and did not act as rapidly as selenite. Biliary excreted methyl mercury is partly reabsorbed in the gut. Subsequently a part of it is deposited in the kidney, since drainage of the bile lowered the kidney content of Hg. Rats given Se compounds in combination with bile drainage showed further reduction of the kidney Hg content than bile duct drainage alone. The demonstrated lowering effect of

Se compounds on kidney Hg content cannot be completely explained by an inhibition of bilary excretion of Hg. The Ag concentration in the brain was increased by the Se compounds, the effect being dependent on the Se dose reaching a maximum at an equimolar selenite: methyl mercury dose ratio. The mechanisms by which Se influences methyl mercury kinetics are discussed.

540
TITLE:
Health effects related to prenatal exposure to methylmercury.

AUTHORS:
Grandjean P
Weihe P
White RF

SOURCE:
Toxicol Lett 1999 Jun;109(Suppl 1):7

ABSTRACT:
Neurotoxicity may occur in children exposed to methylmercury during early life, but the dose-response relationship has been controversial. New evidence has appeared from the Faroe Islands, Madeira, and the Brazilian Amazon. In the Faroes, we measured mercury concentrations in maternal hair at parturition and in cord blood. At a follow-up examination of 917 children (90% of the cohort) 7 years later, mercury-related neuropsychological dysfunctions were seen, especially in attention, language and memory. Significant associations remained after exclusion of children with maternal hair-mercury concentrations above 1O ug/g. At very low exposure levels, an effect on blood pressure was also seen. The peak III latency of the brainstem auditory evoked potentials showed delays at increased exposures, and this finding was replicated in examinations of 149 children attending first grade in a Madeiran fishing community. Likewise, Brazilian children exposed to mercury downstream from gold-mining fields showed mercury-associated decrements on neuropsychological tests of motor function, attention, and visuospatial performance. The effects on nervous system function associated with prenatal methylmercury exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe.

541
TITLE:
Does pollution control require that agriculture be deprived of organomercurial fungicides?

AUTHORS:
Charmet F

SOURCE:
Phytoma ; 24(243): 14-18; 1972

ABSTRACT:
HAPAB The environmental effects of organomercurial fungicides used for seed treatment are reviewed. Although organomercurial fungicides have a relatively low acute toxicity, they are chronic poisoning hazards due to their accumulation in tissue, especially in the kidney, liver, and brain. Some harmless mercury compounds present in the environment are transformed into the extremely toxic methyl mercury. The fraction of total mercury used for the production of organomercurial fungicides is 3.8%. Organomercurial fungicides used for seed treatment scarcely affect the natural mercury level of the soil, and crops from treated hseeds have mercury levels far below the maximum allowable concentrations, 0.5 ppm in the U.S. Poisonings with organomercurial fungicides are almost exclusively due to the use of contaminated seed material for human or animal consumption.

542
TITLE:
Determination of microgram quantities of mercury in organic material.

AUTHORS:
Piechocka J

SOURCE:
Roczn. Panst. Zakl. Hig.; 19(3), 291-301, 1968; (REF:44)

ABSTRACT:
HAPAB A method has been developed for assaying for microgram quantities of mercury, whether in organic or inorganic form, in organic materials. The materials tested were biological tissues such as kidney, spleen, brain, blood, etc. and products such as milk, cheese, apples, potatoes, beer, etc. The procedure is based on the enzymatic transformation of the sample, followed by its oxidation with potassium permanganate in the presence of sulfuric acid. Mercury is then determined by titration and extraction using a chloroform solution of dithizone. Recovery depends on the sample tested but ranges from 70 to 100% with 20 mcg of added mercury. Statistical analysis of the tabular data presented showed insignificant straggling of the results for individual samples with the same mercury content level. (Author abstract modified) ANALYSIS 69/03/00, 92 1968

543
TITLE:
Amyotrophic lateral sclerosis

AUTHORS:
Currier RD

Haerer AF

SOURCE:
Arch. Environ. Health; 17(5), 712-9, 1968; (REF:13)

ABSTRACT:
HAPAB A total of 31 patients, all with definite amyotrophic lateral sclerosis (ALS) and a frequent positive history of exposure to metallic toxins in their work, were studied. Analysis for lead, mercury and arsenic were done on 24 hr urine specimens, the serum and cerebrospinal fluid pyruvate in several patients was investigated, necropsy tissues from two patitnts were analyzed for lead and mercury and the effect of therapy with chelating agents was evaluated. Tabulated data present the occupational profiles of the 31 patients, their history of exposure to toxic agents, the concentrations of lead, mercury and arsenic in their urine before treatment with chelating agents, the heavy metal excretions of patients with and without history of exposure to each metal and a summary of exposure history, treatment regimens and metal determinations in the urine of 21 patients. Results show that the metals were not often present in abnormal amounts in 24 hr urine specimens and there appeared to be no correlation of the history of exposure to the amount of toxin found. Serum and cerebrospinal fluid pyruvate studies performed on 5 and 7 patients, respectively, were within normal ranges. Treatment of five patients with calcium disodium edetate, four with penicillamine and three with thioctic acid did not produce any consistent changes in lead and mercury concentrations and the treatment did not change the course of the disease. Necropsy tissue studies in 2 patients showed normal concentrations of lead and mercury in spinal cord, liver, kidney, bone and brain. While the possibility does exist that exposure to heavy metals or arsenic at an earlier time in life may have initiated a process of abiotrophy, it must be concluded from present data that no relationship has been shown between exposure to the substances analyzed and the amyotrophic lateral sclerosis in this group of patients. EPIDEMIOLOGY AND TREATMENT 69/01/00, 9 1968

544
TITLE:
Comparative Action of Methylmercury and Divalent Inorganic Mercury on Nerve Terminal and Intraterminal Mitochondrial Membrane Potentials

AUTHORS:
Hare MF
Atchison WD

SOURCE:
Journal of Pharmacology and Experimental Therapeutics, Vol. 261, No. 1, pages 166-172, 48 references, 1992

ABSTRACT:

The effects of methylmercury (22967926) (MeHg) and inorganic divalent mercury (7439976) (Hg++) on plasma and mitochondrial membrane potentials were studied. Synaptosomes were prepared from the brains of Sprague-Dawley-rats exposed to MeHg or Hg++ concentrations ranging from 1 to 20 micromolar (microM). Membrane potentials were determined by fluorescence measurements after the addition of the carbocyanine dye. Dose dependent increases in fluorescence were seen after exposure to either MeHg or Hg++, with significant changes seen with concentrations of 10microM or more. Depolarization of the mitochondria with sodium-azide resulted in a 92% increase in fluorescence. Increased fluorescence was seen using 10 or 20microM MeHg and 5microM Hg++ in normal or depolarized synaptosomes. As the concentration of Hg++ was increased to 10 and 20microM, significantly more fluorescence was seen from normal synaptosomes compared with depolarized synaptosomes. The addition of tetrodotoxin or divalent cobalt had no effect on the actions of MeHg or Hg++. Measurements of the dose dependent depolarization of the plasma membrane calculated by the fluorescence response to depolarization of synaptosomes pretreated with MeHg or Hg++ correlated with the plasma membrane potentials calculated using direct measurements of fluorescence increases.

545

TITLE:

Fetal Methylmercury Study in a Peruvian Fish-Eating Population

AUTHORS:

Marsh DO
Turner MD
Smith JC
Allen P
Richdale N

SOURCE:

Neurotoxicology, Vol. 16, No. 4, pages 717-726, 40 references, 1995

ABSTRACT:

The relationship between low level dietary mercury (7439976) exposure and fetal neurotoxicology was studied in 131 infants in Mancora, Peru who had fetal exposure to methylmercury as a result of a maternal diet high in marine fish. Maternal hair mercury levels were used as an index of fetal mercury exposure. History of labor and delivery, the developmental progress of the infants, and the general and neurologic health of the infants was evaluated. The mean maternal hair methylmercury level was 7.05 parts per million. A high degree of correlation was seen between maternal hair methylmercury levels at the time of birth and newborn hair methylmercury levels. No evidence of developmental or any other abnormalities was identified in any of the infants. Possible reasons for

the lack of adverse effects of fetal mercury exposure seen in this study in contrast to those reported in other studies of fetal methylmercury exposure were discussed.

546
TITLE:
Mercury

AUTHORS:
Campbell D
Gonzales M
Sullivan JB Jr

SOURCE:
Hazardous Materials Toxicology, Clinical Principles of Environmental Health, J. B. Sullivan, Jr., and G. R. Krieger, Editors; Williams and Wilkins, Baltimore, Maryland, pages 824-833, 23 references, 1992

ABSTRACT:
The toxicological aspects of exposure to mercury (7439976) (Hg) in its elemental, inorganic, and organic forms were reviewed. About 70,000 workers are exposed annually to Hg, and the general population is exposed to Hg via food such as fish. Release of about 2000 metric tons per year takes place from mining and ore smelting. The general mode of toxicologic action involves the binding of Hg to sulfhydryl groups, thereby inactivating cellular enzymes and carbohydrate metabolism at the pyruvic-acid level. Inhaled elemental Hg vapor causes bronchitis and acute pneumonitis. Hg is quickly absorbed and passes through the blood brain barrier to accumulate in the central nervous system (CNS). Chronic elemental Hg exposure produces a classic triad of tremor, gingivitis, and erethism. Exposure to inorganic salts of Hg is by the oral route. These salts are corrosive and produce necrotic mucosal damage of the gastrointestinal tract. Organic mercurials are used in chemical research and as pharmaceuticals. Exposure is primarily dietary, from fish in polluted streams and rivers. Epidemiological studies of organomercury exposures in Iraq and Japan were discussed. The absorption of organic mercurials and the resulting CNS, dermal, renal, respiratory, gastrointestinal and hematologic effects were described. Chronic and longterm effects, as well as the metabolism and elimination of these compounds were addressed. Other aspects discussed were teratogenicity, the diagnosis and and management of Hg toxicity, and biologic and environmental monitoring. A summary of international and national regulations pertaining to Hg and its compounds was provided.

547
TITLE:
Selective Determination of Inorganic Mercury and Methylmercury in Tissues by Continuous Flow and Cold Vapor Atomic Absorption Spectrometry

AUTHORS:
Atallah RH
Kalman DA

SOURCE:
Journal of Analytical Toxicology, Vol. 17, No. 2, pages 87-92, 22 references, 1993

ABSTRACT:
Methodology for the selective determination of inorganic mercury (7439976) (InHg) and methylmercury (MeHg) in solubilized animal tissues using continuous flow and cold vapor atomic absorption spectrometry was described. The procedures for the solubilization of tissues as well as inorganic and organic Hg determinations were described. Tissues used were kidney, liver and brain of rats dosed orally with MeHg at 5 or 10 parts per million in the drinking water for up to 30 weeks. The use of sodium-borohydride as reductant enabled determination of total Hg. When stannous-chloride was used as reductant, InHg was selectively determined in the presence of MeHg. The difference between the two determinations yielded the MeHg values. The recoveries were over 95% for both InHg and MeHg. The results suggested negligible matrix interference. To validate the recoveries of MeHg from tissues of exposed rats, the results were compared with those from a method that utilized solvent extraction of MeHg with toluene followed by gas chromatography. Comparative MeHg values for kidneys of two exposed rats were 20.0 versus 22.5 and 25.5 versus 29.0, respectively, with the two techniques. The authors conclude that the system can be used to rapidly differentiate InHg and organic mercury in tissues. However, while the method does not permit ready quantitation of Hg species at background levels, it is applicable if a larger volume of sample and a prior concentration step are used.

548
TITLE:
Mercury and mink: II. Experimental methyl mercury intoxciation.

AUTHORS:
WOBESER G
NIELSEN NO
SCHIEFER B

SOURCE:
CAN J COMP MED; 40 (1). 1976 34-45

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Adult female mink were fed rations containing 1.1, 1.8, 4.8, 8.3 and 15.0 ppm Hg as methyl mercury chloride over a 93 day period. Histopathological evidence of injury was present in all

groups. Mink fed rations containing 1.8 to 15.0 ppm Hg developed clinical intoxication within the experimental period. The rapidity of onset of clinical intoxication was directly related to the Hg content of the ration. Hg concentration in tissue of mink which died were similar, despite differences in Hg content of the diets and time of death. The average Hg concentration in the brain of mink which died was 11.9 ppm. The lesions of methyl mercury poisoning are described and criteria for diagnosis are discussed.

549
TITLE:
LEVELS OF MERCURY AND PATHOLOGICAL CHANGES IN PATIENTS WITH ORGANOMERCURY
POISONING.

AUTHORS:
AL-SALEEM T

SOURCE:
BULL. W.H.O. 1976, 53(SUPPL.) 99-104

ABSTRACT: EIS: Epidemiology Information System

550
TITLE:
Evidence for Delayed Neurotoxicity Produced by Methylmercury

AUTHORS:
Rice DC

SOURCE:
Neurotoxicology, Vol. 17, Nos. 3/4, pages 583-596, 30 references, 1996

ABSTRACT:
The sensory, cognitive, and motor deficits produced by methylmercury in humans and animals were reviewed. Delayed neurotoxicity following methylmercury exposure was observed in mice manifested as neuromuscular deficits and atrophy. Delayed neurotoxicity in monkeys was manifested as impaired clumsiness and delayed somatosensory function and motor function. Humans exposed to methylmercury showed delayed neurotoxicity, expressed as difficulty in performing daily activities with time. Delayed neurotoxicity could have occurred from mercury stored in the body, specifically the nervous system; when damaged neurons or other nervous system cell types died prematurely; or when normal cells compensated for damaged cells and underwent accelerated aging. The half life of mercury in the brain was longer than in blood after methylmercury exposure. Inorganic mercury was concentrated in reactive glia following chronic low level methylmercury exposure in monkeys. The author concludes that

delayed neurotoxicity symptoms in animals and humans may represent the first definitive evidence for delayed neurotoxicity produced by an environmental toxicant.

551
TITLE:
An incident of poisoning by granosan in pigs.

AUTHORS:
Gorlov IF

SOURCE:
Veterinariya (Moscow)2: 102-103; 1974

ABSTRACT:
PESTAB Accidental poisoning of pigs by granosan-contaminated wheat is described. The pigs were fed mud wheat that was, unintentionally contaminated by granosan dust settling on the grains in the silo. The symptoms of poisoning (depression, anorexia, tremor of the skeletal muscles, spasms, and death) occurred first on the 35th day of the poisoning. Focal venous stasis in the skin, cyanosis of the conjunctiva and mucosa of the oral cavity, discoloration of the intestines and liver, enlargement of the kidneys, hyperemia of the spleen and lungs, and cerebral edema were determined on autopsy. Chemical analyses of muscle, liver, and kidney samples revealed mercury contents ranging from 22 to 48 mg/kg in these organs. The mercury level in the wheat was 5. 3-12 mg/kg. Mercury was detected in the brain and the parenchymatous organs for over 300 days, while no mercury was found in the muscles after 200 days. Unithiol, administered at a rate of 1 ml 5% solution per 10 kg body weight for 10 days, accelerated the elimination of mercury from the organism.

552
TITLE:
Mercury poisoning from mercurochrome therapy of an infected omphalocele

AUTHORS:
Yeh TF
Pildes RS
Firor HV

SOURCE:
Clin. Toxicol.; VOL 13 ISS Nov 1978, P463-467, (REF 12)

ABSTRACT:
IPA COPYRIGHT: ASHP A neonate with an infected omphalocele developed mercury poisoning after being treated locally for 5 days with merbromin (mercurochrome; I). Extensive skin peeling with bullous lesions, edema,

and fever developed 3 days after I therapy. The infant died on the ninth day. Autopsy revealed evidence of heavy metal poisoning of the kidney, excessive mercury levels in the blood, and in tissues of the brain, kidney, and liver.

553
TITLE:
MERCURY POISONING.

AUTHORS:
CLARKSON TW

SOURCE:
DEV. TOXICOL. ENVIRON. SCI. 1977, 1() 189-200

ABSTRACT: EIS: Epidemiology Information System

554
TITLE:
Mercury-selenium interactions in the environment.

AUTHORS:
Saroff L
Lipfert W
Moskowitz PD

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 19, 1996

ABSTRACT:
TD3: The Clean Air Act Amendments of 1990 require the U.S. Environmental Protection Agency (EPA) to consider the need to control emissions of trace elements and compounds emitted from coal combustion, including coal-fired power plants. Concern has been expressed about emissions of mercury and arsenic, for example, since health effects may be associated with exposure to some of these compounds. By and large, effects of trace element emissions have been considered individually, without regard for possible interactions. To the extent that the relevant environmental pathways and health endpoints differ, this mode of analysis is appropriate. For example, arsenic is considered a carcinogen and mercury affects the brain. However, there may be compelling reasons to consider emissions of mercury (Hg) and selenium (Se) together: (1) Both Se and Hg are emitted from power plants primarily as vapors. (2) Hg and Se are both found in fish, which is the primary pathway for Hg health effects. (3) Se has been shown to

555
TITLE:
Methylmercury neurotoxicity in Amazonian children downstream from gold

mining.

AUTHORS:
GRANDJEAN P
WHITE RF
NIELSEN A
CLEARY D
DE OLIVEIRA SANTOS EC

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 107 (7). 1999. 587-591.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In widespread informal gold mining in the Amazon Basin, mercury is used to capture the gold particles as amalgam. Releases of mercury to the environment have resulted in the contamination of freshwater fish with methylmercury. In four comparable Amazonian communities, we examined 351 of 420 eligible children between 7 and 12 years of age. In three Tapajo's villages with the highest exposures, more than 80% of 246 children had hair-mercury concentrations above 10 mug/g, a limit above which advers children had hair-mercury concentrations below 10 mug/g. Although average exposure levels may nothave changed during recent years, prenatal exposure levels are unknown, and exact dose relationships cannot be generated from this cross-sectional study. However, the current mercury pollution seems sufficiently severe to cause adverse effects on brain development.

556
TITLE:
Toxicokinetics of methyl mercury in pigs.

AUTHORS:
GYRD-HANSEN N

SOURCE:
ARCH TOXICOL; 48 (2-3). 1981. 173-182.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Toxicokinetics of methyl mercury were studied in pigs after i.v. administration. The distribution of methyl mercury was slow, taking 3-4 days to be completed. Blood elimination half-life was 25 days. The apparent volume of distribution was 9.8 l/kg, indicating pronounced tissue accumulation of methyl mercury. Highest Hg levels were found in kidney and liver, with lower contents in muscle and brain and little in adipose tissue. From organs like liver and kidney, methyl mercury was eliminated more slowly than from the blood. Over 15 days, 16% of the dose administered was excreted with feces and 0.9% in the urine.

557
TITLE:
Mercury vapor inhalation studies: mechanisms of endocrine disruption.

AUTHORS:
Davis BJ
Price HC
O'Connor RW
Rowland AS
Morgan DL

SOURCE:
Toxicologist 1998 Mar;42(1-S):103

ABSTRACT:
Elemental mercury (Hg0) has been used in dental amalgam for more than 150 years, yet little is known about the potential health consequences of this chemical. Epidemiological studies finding menstrual cycle abnormalities among women occupationally exposed to Hg0 prompted us to investigate the mechanisms of reproductive toxicity of Hg0 in the female rat. Nose-only Hg0 vapor inhalation exposures were conducted on 80-90 day old regularly cycling rats. The dose-response of Hg0 effects on the estrous cycle was evaluated by exposing rats to 0, 1, 2, or 4 mg/m3 Hg0 2 hr/day for 8 days. Vaginal smears were evaluated daily. Prolonged estrus cycles were observed in the 2 and 4 mg/m3 dose groups. Serum hormone levels were unchanged and there was no histopathological evidence of toxicity in kidney, brain, or lung. Tissue Hg levels correlated with exposure concentration and duration. To establish the cause for altered estrous cycles, rats were exposed to 2 mg/m3 Hg0 for 8 days beginning when they were in metestrus. A lengthening of the cycle was detected and morphological changes were observed in the corpora lutea (CL) after exposure for 6 days. To determine if changes in the CL correlated with a functional defect, rats were exposed to Hg0 and evaluated for pregnancy outcome. There were no significant effects on pregnancy rate, or numbers of implantation sites when rats were exposed to 1, 2, or 4 mg/m3 Hg0 for 8 days prior to breeding or for 8 days after breeding. Although exposure to Hg0 vapor altered estrous cyclicity, no significant effects were observed on fertility in the rat.

558
TITLE:
Proconvulsive effects of chronic developmental exposure to methyl mercury in rats.

AUTHORS:
Szente M
Szäasz A
Barna B

DeVisscher G
Galbäacs Z
Kirsch-Volders M

SOURCE:
Int J Dev Neurosci 1998 Oct;16(6):571

ABSTRACT:
The effects of chronic, maternal methyl mercuric chloride (MeHgCl) intoxication on the development and spread of cortical epileptic activity was investigated. Adult female Wistar rats were exposed to MeHgCl through the drinking water (0.375 mg/kg/day). Exposure was begin a week before of mating and continued through gestation and the sucking period to the time of experiment. Electrophysiological parameters of aminopyridine-induced cortical seizure activity were measured in mercury treated 4 weeks old offspring and compared to those of control values of the same age. The mercury content of the brain tissue was measured after each experiment. Chronic intrauterine MeHgCl treatment exerted proconvulsive effects in offsprings, which was indicated by shorter latency of seizure onset, highly facilitated expression and propagation of primary and secondary electrical ictal activity, strong tendency to generalization and progress into status epilepticus. The number of ictal periods increased significantly, and their duration was longer in comparison to values measured in control animals. We conclude, that the mechanisms which are responsible for initiation, maintenance and propagation of synchronous, rhythmic activity are influenced by mercury treatment. The most potent targets for mercurials are the voltage- and ligand-gated ionchannels. A relatively selective degeneration of GABAergic inhibitory interneurons was also detected in the cerebral cortex in mercurial treated animals. In addition the lack of adequate inducible defense mechanism against electrophilic toxins, could be critical in the developing nervous system and could be associated with the wide range of developmental disorders during prenatal and early postnatal mercury exposure.

559
TITLE:
Cadmium, Zinc and Mercury

AUTHORS:
Schroeder HA

SOURCE:
American Petroleum Institute, Washington, D.C., Air Quality Monographs, Monograph Number 70-16, 48 pages, 70 references, 19711971

ABSTRACT:
Exposures, both natural and artificial, of civilized man to zinc (7440666), cadmium (7440439) and mercury (7439976) have been evaluated in

biogeochemical and biochemical terms. Zinc, an essential metal, has a low order of toxicity. Cadmium, on the contrary, has toxic manifestations at almost all levels of exposure, for it accumulates in human kidney and liver, causing hypertension, irritates lung, producing emphysema, and at higher exposures causes renal damage. Mercury is more toxic and alkyl derivatives are very toxic to brain. Zinc and cadmium in air are the results of industrial pollution. Mercury has polluted waters in local areas. Abatement of zinc will result in abatement of cadmium in air. Present air levels of zinc are no cause for concern, but cadmium levels represent a present hazard to human health. Mercury in ambient air is generally tolerable.

560
TITLE:
Localization of mercury in CNS of the rat: II. Intraperitoneal injection of methylmercuric chloride and mercuric chloride.

AUTHORS:
MOLLER-MADSEN B

SOURCE:
TOXICOL APPL PHARMACOL; 103 (2). 1990. 303-323.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The autometallographic method has been used to determine the precise localization of mercury in the brain and spinal cord of adult Wistar rats which had been treated with repeated ip injections of methylmercuric chloride (CH3HgCl; 0.2 to 10.0 mg) or mercuric chloride (HgCl2; 0.2 to 10.0 mg). The distribution of mercury was uneven following administration of HgCl2, while it was fairly homogeneous following CH3HgCl. With both compounds, however, heavy deposits of mercury were present in the motor nuclei of rhombencephalon. In contrast, cerebellar Purkinje cells, Golgi cells, and Golgi epithelial cells only contained mercury in sections from rats exposed to CH3HgCl. In cerebral sections from rats exposed to CH3HgCl, staining intensity in cortical cells varied among the layers, being greatest in laminae III, V, and VI. On the other hand, sections from rats exposed to HgCl2 showed only staining in scattered cells of lamina VI. Following administration of either compound, mer

561
TITLE:
Neurotoxicity Of Certain Environmental Substances

AUTHORS:
Taylor JR

SOURCE:

Clinics in Laboratory Medicine, Vol. 4, No. 3, pages 489-497, 15 references, 19841984

ABSTRACT:

The neurotoxicity of some environmental substances is reviewed. Lead (7439921) is discussed with respect to adsorption and distribution in humans. The toxicological effects of lead on heme synthesis, and human neurological disease produced by lead intoxication are examined. Diagnostic tests to confirm the presence of lead are described. Principal sequelae of lead encephalopathy include seizures, mental retardation, and optic atrophy. Treatment is outlined. The absorption and excretion of aluminum (7429905) is discussed. The human neurotoxicity of aluminum is examined with respect to symptoms, and aluminum content in brain. The occurrence of mercury (7439976) is summarized. The absorption and excretion of mercury is discussed. The toxicity of mercury is examined with respect to clinical features of organic and inorganic mercury. Treatment of mercury intoxication involves removal from the source, a sparing effect that selenium and vitamin-E provide, and chelation. Ketones and related solvents are examined and toxicity is analyzed with respect to absorption and excretion. The epidemiology of human ketone and related solvent diseases is noted. Acute and chronic symptoms of ketones are described. Diagnostic tests are discussed. The author concludes that there is an apparent phenomenon of selective vulnerability to these compounds. With the exception of psychoactive drugs, screening tests are misleading and difficult to interpret.

562

TITLE:

Historical methylmercury exposure and developmental toxicity.

AUTHORS:

Reuhl KR

SOURCE:

Neurotoxicol Teratol 2002 May-Jun;24(3):423

ABSTRACT:

It has been 50 years since the first large outbreak of methylmercury in Minamata Bay, Japan entered the public consciousness. The disease was heralded by an increase in the number of infants displaying "cerebral palsy"-like symptoms and was subsequently traced to effluent from a local chemical plant. Several hundred infants were affected. A subsequent outbreak of poisoning in Iraq in 1972 involved thousands of adults and numerous infants. Detailed study of these episodes has provided seminal lessons that have shaped mechanistic toxicology, environmental risk assessment and the development of public policy. Methylmercury can be formed naturally from inorganic mercury by methogenic bacteria in water sediments, bioaccumulates in the food chain and reaches toxic levels in

commercially valuable fish. The pregnant female consuming methylmercury will pass the toxicant to the developing fetus and fetotoxic levels may be achieved in the absence of maternal toxicity, underscoring the importance of rigorous control of exposure. Methylmercury has also proven an important model compound in developmental neurotoxicology. The toxicant's high chemical reactivity toward cellular macromolecules permits the identification of specific targets of injury and the identification of "dose-mechanism" relationships during brain development. Recent concerns regarding potential mercury pollution from natural and anthropogenic sources, and growing evidence of adverse developmental effects on brain function at ever-decreasing concentrations, suggest that methylmercury will remain a major concern for the foreseeable future.

563

TITLE:

Methylmercury effects in rat, hamster, and squirrel monkey; lethality, symptoms, brain mercury, and amino acids.

AUTHORS:

Hoskins BB

SOURCE:

Environ. Res. 15(1): 5-19 1978 (46 References)

ABSTRACT:

PESTAB. Methylmercury is a dangerous byproduct of fungicide application. Sprague Dawley rats, Syrian hamsters, and squirrel monkeys were given 1 mg to 12 mg methylmercury chloride ip. The percentage death rate in 24 hr for rats increased from about 10% at about 7 mg/kg to over 50% at about 10 mg/kg, and reached practically 100% at slightly less than 50 mg/kg. In hamsters, the death rate in 24 hr increased from less than 10% at 10 mg/kg to slightly less than 50% at about 15 mg/kg, increased slowly until about 30 mg/kg, then increased rapidly again. The death rate in 30 days for rats reached nearly 100% at about 20 mg/kg. The death rate in 30 days for hamsters did not become close to 100% until about 50 mg/kg. Monkeys developed severe neurological symptoms but were not killed within 24 hr by doses equivalent to those killing 90% of the rodents. Mercury concentrations in the cerebral hemisphere of rats ranged from 13.74 mug/g in rats with motor symptoms to 0.48 mug/g in rats receiving 1.0 mg methylmercury chloride and having no motor symtpoms. The mercury concentration in the cerebral hemisphere of monkeys was 1.86 mug/g in a monkey given 2 mg methylmercury chloride and 6.76 mug/g in a monkey given 8 mg methylmercury chloride. Glutamate, glycine, aspartate, and GABA levels did not differ significantly among the three brain areas or between control and symptomatic rats. Glutamate content in the cerebral hemisphere was 1.54 mum/g in the control monkey but undetectable in two dosed monkeys. Aspartate content in the cerebral hemisphere was 2.70 mum/g in the control, but was not detected in two dosed monkeys. Glycine content in

the cerebral hemisphere was 0.44 mug/g in the control, 1.05 mug/g in the monkey receiving 3 mg methylmercury chloride, and undetectable in two monkeys receiving higher doses. The gamma-amino butyric acid content in the cerebral hemisphere was 1.0 mum/g in the control and as high as 4.6 mum/g in dosed monkeys.

564
TITLE:
Changes in the activity of hydrolytic enzymes in the brain of rats intoxicated by ethyl-mercury-p-toluene-sulfanilide.

AUTHORS:
Koziz MB
Wigowska-Sowinska J

SOURCE:
Folia Histochem. Cytochem. 16(3): 263-270 1978 (25 References)

ABSTRACT:
PESTAB. Twenty adult Wistar rats were fed ig with 0.2 g of ethyl-mercury-p-toluene sulfanilide for 10 consecutive days. Degenerative changes were noted in the neurons of various regions of the rat brain. Massive neuronal losses were seen within the Ammon's horn. Distinctly reduced ATPase and acid phosphatase activities were noted in the exposed animals. Moderate declines were seen in the AChE activity. A definite rise in neuronal TPPase activity was observed along with a slight elevation of NsE activity. The pyramidal cells of the Ammon's horn as well as those of the second and fourth cortical layers of the frontal and parietal lobes demonstrated the highest vulnerability with respect to ethyl-mercury-p-toluenesulfanilide.

565
TITLE:
Metabolism of mercury in hamster pups administered a single dose of 203Hg-labeled methyl mercury.

AUTHORS:
DOCK L
RISSANEN R-L
VAHTER M

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 76 (1). 1995. 80-84.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Golden Syrian hamster pups were administered a single subcutaneous dose of 203Hg-labeled methyl mercury (MeHg), 0.4 nmol/g body weight, seven days after birth, and were sacrificed 2, 7, 14,

21 or 28 days later. The excretion of 203Hg followed a biphasic elimination pattern with an average half-time of 8.7 days for the rapid component. The slow component had a much longer half-time and probably reflects binding of 203Hg to growing hair. The concentration of 203Hg in the liver. kidneys and brain two days after administration was 0.44. 0.38 and 0.19 nmol/g, respectively. The retention of 203Hg was higher in the kidney than in the liver and the brain. The content of inorganic 203Hg in the liver and kidneys increased the first weeks after administration, demonstrating that hamsters are able to demethylate MeHg before two weeks of age.

566
TITLE:
Concentration Of Metallothionein In Major Organs Of Rats After Administration Of Various Metals

AUTHORS:
Waalkes MP
Klaassen CD

SOURCE:
Fundamental and Applied Toxicology, Vol. 5, No. 3, pages 473-477, 22 references, 19851985

ABSTRACT:
The concentration of metallothionein (MT) in rat organs after metal exposure was investigated. Male Sprague-Dawley-rats were given intraperitoneal injections of cadmium (7440439), chromium (7440473), iron (7439896), lead (7439921), manganese (7439965), mercury (7439976), nickel (7440020) and zinc (7440666) dissolved in water. Twelve hours after the dose, brain, heart, kidney, liver, lung, pancreas, spleen, stomach, and intestines were analyzed for MT. Zinc produced the highest MT increase of the metals, especially in the pancreas. MT was not increased in the brain by any metal. Zinc increased MT in the liver 44 times, and in the intestine 86 times. Cadmium and mercury also increased MT significantly in the liver, pancreas, and intestines. Only cadmium and zinc produced increases in MT in the lung, heart, stomach, and spleen. The lungs were the least responsive to the heavy metals. Cadmium, mercury, nickel, and zinc resulted in increased MT concentrations in the kidneys. The liver was the only organ that had increased MT concentrations for all metals. The authors conclude that MT helps to regulate zinc, particularly in the liver.

567
TITLE:
Effects Of Environmental Temperatures On The Toxicity Of Methylmercury In Rats

AUTHORS:
Yamaguchi S
Shimojo N
Sano K
Kano K
Hirota Y
Saisho A

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 32, No. 5, pages 543-549, 9 references, 19841984

ABSTRACT:
The influence of temperature on methylmercury (22967926) toxicity and tissue concentrations was studied in rats. Male Wistar-rats were acclimated to 22 degrees-C for 15 days and were then subcutaneously injected with 5 milligrams per kilogram methylmercury-chloride (115093) every 3 days for 60 days. During the treatment period, groups of treated and control rats were housed at 33, 22, and 11 degrees. The animals were observed for death, food and water intake, and hind leg crossings. Every 15 days, some treated animals in each temperature group were killed and brain, blood, and kidney were analyzed for total mercury (7439976) and methylmercury. Among treated animals, all high temperature rates produced death by day 45; none of the moderate temperature rats died, and 20 percent of low temperature rats died in the last 15 days. Counting only the initial observation of hind leg crossing in each treated rat, cumulative crossings reached 15 by day 35 at the high temperature, 13 by day 41 at the moderate temperature, and 9 by day 51 at the low temperature. On days 30 and 45 in particular, total mercury content of tissues in the high temperature group were 30 to 100 percent higher than moderate temperature blood and kidney values and low temperature blood and brain values. Low temperature kidney mercury was also elevated compared to the moderate temperature value. Methylmercury content followed similar patterns. Compared to same temperature controls, food intake of treated rats was reduced about 30 percent in all temperature groups, while water intake was reduced 40 percent at the high temperature but only 10 percent at the low temperature. The authors conclude that toxicity findings on methylmercury can be confounded by environmental temperatures. The results have implications for the establishment of threshold limit values for workplace exposure.

568
TITLE:
Mercuric Ions are Potent Noncompetitive Antagonists of Human Brain Kainate Receptors Expressed in 'Xenopus oocytes'.

AUTHORS:
Umbach JA

Gundersen CB

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 07, 1991

ABSTRACT:
TD3: Kainate receptors are one of the major subtypes of excitatory amino acid receptors in the vertebrate central nervous system. Using Xenopus oocytes injected with RNA from human temporal cortex, it is possible to detect electrophysiologically the expression of this receptor subtype in these cells. Ions of the group IIb elements, particularly mercuric ions, are highly potent, noncompetitive inhibitors of these human brain kainate receptors. Mercury-containing sulfhydryl reagents are also very effective, irreversible blockers of the kainate-gated currents of these oocytes. The recovery of kainate-activated currents after washout of Hg2+ is slow and incomplete relative to that seen after treatment either with Cd2+ ir Zn2+. Cysteine or dithiothreitol can accelerate this recovery of kainate-inducible currents after Hg2+ inhibition. Besides the toxicological implications of these results, mercury compounds may be useful for future studies of the structure and physiology of the kainate receptor-channel c

569
TITLE:
Metal Toxicity in the Central Nervous System

AUTHORS:
Clarkson TW

SOURCE:
Environmental Health Perspectives, Vol. 75, pages 59-64, 55 references, 19871987

ABSTRACT:
The central nervous system (CNS) toxicity of lead (7439921) (Pb) and mercury (7439976) (Hg) was reviewed. Studies have indicated that the effects of Pb on the CNS range from acute encephalopathy to chronic, subtle change in behavior and cognition. Pb disrupts heme synthesis, interferes with neurotransmitters, effects calcium metabolism and transport, increases the production of miniature endplate potentials, and affects mitochondrial respiration. The mitochondrial uptake causes the damage to the blood brain barrier. Pb produces electron dense inclusion bodies in renal cell nuclei. The inclusion bodies protect the cell, in particular the mitochondria, from the toxic effects of Pb. The sequence of clinical signs after exposure to Hg is paresthesia, ataxia and other indications of the loss of coordination, and constriction of the visual field. The damage to the CNS is limited to specific focal areas, such as the granule cells of the cerebellum and the neurons in the interstices of

the visual cortex. Hg cation has a high affinity for the SH groups and inhibits SH group containing enzymes. Methyl-mercury (593748) (MeHg) inhibits protein synthesis in the brain. It has been suggested that certain cells are susceptible to damage because they cannot repair initial damage done to protein synthesis in the developing nervous system. Hg affects cell migration and cell division. MeHg causes rapid depolymerization of microtubules in the cytoskeleton by reacting with the SH groups on tubulin monomers. The author concludes that the knowledge of the mechanism of action of Pb and Hg has developed in parallel with, and in most cases as a result of, advances in basic biology.

570
TITLE:
Distribution of mercury in organs of McGraw-Mallard ducks given methyl mercury chloride.

AUTHORS:
HOUGH EJ
ZABIK ME

SOURCE:
POULT SCI; 51 (6). 1972 (RECD 1973) 2101-2103

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Heart, brain, liver, kidney, breast and thigh tissues of McGraw-Mallard ducks which were given oral doses of methyl mercury (MeHg) chloride ranging from 0-19 mg. MeHg/kg body weight were analyzed for total Hg by atomic absorption techniques. Kidney and liver accumulated the highest levels of Hg and the rate of increase with increasing levels of MeHg administered was higher than the levels in the other tissues. Hg levels in breast, thigh, brains, and heart were not significantly different. Regression equations for all 6 tissues are illustrated.

571
TITLE:
Impact of sublethal concentration of mercury on nitrogen metabolism of the freshwater fish, Cyprinus carpio (Linnaeus).

AUTHORS:
SIVARAMAKRISHNA B
RADHAKRISHNAIAH K

SOURCE:
JOURNAL OF ENVIRONMENTAL BIOLOGY; 19 (2). 1998. 111-117.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Exposure of the freshwater fish, Cyprinus

carpio, to a sublethal concentration of mercury (0.1 mg/l) resulted a progressive decrease in soluble, structural and total proteins in the liver, brain and muscle on days 1 and 15, but their levels significantly regained on day 30. Corresponding to the fluctuations in proteins, an elevation was observed in the levels of free amino acids and in the activities of protease, amino transferases (AlAT & AAT) and GDH. Ammonia level in the liver and blood increased progressively on days 1 and 15 and regressed on day 30; the urea level, however, increased over time of exposure. In brain and muscle though ammonia level increased (day 1 > 15 > 30) with a corresponding decrease in urea level (day 1 < 15 < 30), these changes were insignificant. All these observations revealed an initial high proteolysis in the tissues of the fish on sublethal mercury intoxication with a recovery on long-term exposure to a period of 30 days, Among

572
TITLE:
Organochlorines, mercury, and selenium in great blue heron eggs from Indiana Dunes National Lakeshore, Indiana.

AUTHORS:
CUSTER TW
HINES RK
STEWART PM
MELANCON MJ
HENSHEL DS
SPARKS DW

SOURCE:
JOURNAL OF GREAT LAKES RESEARCH; 24 (1). 1998. 3-11.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In 1993, 20 great blue heron (Ardea herodias; GBH) eggs (one per nest) were collected from a colony at the Indiana Dunes National Lakeshore, Indiana (INDU). The eggs were artificially incubated until piping and were then analyzed for organochlorines, mercury, and selenium. Livers of embryos were analyzed for hepatic microsomal ethoxyresorufin-O-dealkylase (EROD) activity. Brains were measured for asymmetry. Egg-laying began in early April and the mean clutch size was 4.2 eggs per clutch. Organochlorine concentrations were generally low (geometric mean p,p'-DDE = 1.6 mug/g wet weight; polychlorinated biphenyl (PCB) = 4.9 mug/g); however, one egg had elevated concentrations of p,p'-DDE (13 mug/g) and PCBs (56 mug/g). EROD activity in the embryos analyzed from INDU was not elevated. The frequency (11%) of brain asymmetry was low. Eggshells averaged 3.4% thinner than eggshells collected prior to the use of DDT. Mercury (geometric mean = 0.9 mug/g dry weight) concentrations

573
TITLE:
Methyl Mercury-Induced Nonselective Blocking of Phosphorylation Processes as a Possible Cause of Protein Synthesis Inhibition In Vitro and In Vivo

AUTHORS:
Kuznetsov DA
Zavijalov NV
Govorkov AV
Sibileva TM

SOURCE:
Toxicology Letters, Vol. 36, No. 2, pages 153-160, 14 references, 19871987

ABSTRACT:
The ability of methyl-mercury (22967926) (MeHg) to nonselectively inhibit various phosphorylation reactions was tested. Three tests systems used were an in-vitro translation system in the presence of excess ATP, inorganic phosphate (Pi), and IC50 MeHg; in-vivo protein phosphorylation in mouse liver and brain; and in-vivo orthophosphate administration to MeHg treated mice. The inhibition of cell free translation by MeHg directly correlated with the suppression of ATP synthesis from ADP and orthophosphate by creatine-kinase. Addition of 5 millimolar (mM) ATP to the cell free system restored the translation activity. Pi added to the cell free system containing 5mM ATP resulted in a significantly greater reactivation of translation. Intraperitoneal orthophosphate buffer injection in-vivo did not stimulate either protein synthesis or phosphorylation in mouse brain or liver, but pretreatment with orthophosphate did prevent MeHg induced effects on the same parameters in the same tissues. Orthophosphate administration was less effective in correcting MeHg induced disorders when given after MeHg treatment. The authors conclude that the toxic effects of MeHg on phosphorylation reactions and protein synthesis are based on nonselective inhibition of certain phosphorylating enzymes culminating in a tissue ATP deficiency.

574
TITLE:
PRIMATE DEVELOPMENTAL EFFECTS OF METHYL MERCURY

AUTHORS:
BURBACHER TM

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Methylmercury (MeHg) continues to be a major global environmental problem. The International Program of Chemical Safety lists mercury as

one of the six most dangerous chemicals to the world's environment. This competitive renewal application describes a 5 year plan aimed at examining the long-term neurotoxic effects of in utero MeHg exposure using the nonhuman primate and rodent animal model. During the initial 3 years of the plan, operant testing of two groups of adult macaca fascicularis: one exposed in utero to MeHg, the other unexposed controls will take place at the University of Washington to test 2 hypotheses related to the effects of early MeHg exposure on adult memory and visual function. At this time, studies of rodents will be carried out at the University of Rochester to test the hypothesis that lesions induced by in utero exposure to MeHg are exacerbated by CNS changes associated with normal aging. At the end of the three years, the results of the behavioral tests of the primates and the neuroanatomical studies of rodents will be reviewed to direct further studies of the primate colony. For the present plan, the primate colony will be sacrificed at the end of year 3 and studies to test 5 hypotheses related to the long-term neuroanatomical and neurochemical effects of in utero MeHg will be conducted during years 4 and 5. All of the hypotheses that will be tested are based on the results developmental assessments of the MeHg exposed and control macaca fascicularis from our laboratory and from the laboratory of Rice et al. (1989). To test the primate neurobehavioral hypotheses, assessments of Delayed Spatial Alteration, Delayed Nonmatch-to-Sample, and Spatial-and Temporal-Visual Contrast Sensitivity will be used. The primate and rodent neuroanatomical hypotheses will be tested by quantifying brains for cell numbers, cell density, and tissue volume; immunocytochemistry will be used to identify growth-controlling cells and astrocytes, and dendritic development will be assessed biochemically by assays of MAP2 (primates only) and morphometrically for dendritic pattern and extent. Finally, the primate neurochemical hypotheses will be tested using autoradiographic techniques to evaluate cholinergic neurotransmission in cortical and subcortical areas related to specific memory pathways and catecholaminergic neurotransmission in the hypothalamic-pituitary axis related to the regulation of growth. While previous studies have reported immediate effects following early MeHg exposure in rodents, macaques, and humans, little is currently known regarding the long-term effects of in utero MeHg exposure on adult and aged animals or humans. The proposed nonhuman primate studies make the best use of the valuable monkey colony, because the studies focus on a set of strongly-supported hypotheses using procedures that are readily available for use with humans. The rodent studies will provide the first results regarding the influence of aging o

575

TITLE:

Quantitative studies of mercury and cadmium deposition in Japanese quail through multiple generations.

AUTHORS:

ESKELAND B

GULLVAG BM
NAFSTAD I

SOURCE:
ACTA AGRIC SCAND; 29 (2). 1979. 113-118.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Deposition of methyl mercury in eggs increases with increasing dose fed to Japanese quail. Hens who got 4 ppm Hg and in addition 5 pp m of Cd in the diet showed augmented Hg deposition in the liver and decreased Hg deposition in the eggs compared with hens who only received 4 ppm Hg in the diet. With 6 ppm Hg and 15 ppm Cd in the diet deposition of Hg in liver and kidney was lower than in those birds who only received Hg. There was instead an augmented Hg deposition in brain and albumen of the egg and very high Hg values were found in the liver of chicks from those eggs (4 times as high as when the parents had received only Hg). The values are discussed with a starting point in the fact that Cd starts metallothionein synthesis in the liver. With the low concentrations of Hg and Cd, the metal binding capacity of the liver cells reduces the amount of Hg transferred to the egg. With the highest doses of Hg and Cd, the metallothionein synthesized in the liver becomes insufficient and there are not enough binding sites to sequester Hg and Cd. Cd does not pass into the egg but binds to the metallothionein present and probably also to some of those sites of the liver and kidney which bound Hg when only Hg was added to the diet. Larger amounts of Hg are then transferred to the brain and to the offspring than when no Cd was added to the diet. During the experiments which involved 6 generations there was a selection of Hg resistant individuals, as the surviving chicks from the groups given 4 ppm methyl mercury in the series of experiments were used in the subsequent experiments. The mortality of newly hatched chicks whose parents were subjected to 8 ppm Hg was reduced from 100 to about 50% after 6 generations of Hg exposure.

576
TITLE:
PRIMATE DEVELOPMENTAL EFFECTS OF METHYL MERCURY

AUTHORS:
BURBACHER TM

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Methylmercury (MeHg) continues to be a major global environmental problem. The International Program of Chemical Safety lists mercury as one of the six most dangerous chemicals to the world's environment. This competitive renewal application describes a 5 year plan aimed at examining

the long-term neurotoxic effects of in utero MeHg exposure using the nonhuman primate and rodent animal model. During the initial 3 years of the plan, operant testing of two groups of adult macaca fascicularis: one exposed in utero to MeHg, the other unexposed controls will take place at the University of Washington to test 2 hypotheses related to the effects of early MeHg exposure on adult memory and visual function. At this time, studies of rodents will be carried out at the University of Rochester to test the hypothesis that lesions induced by in utero exposure to MeHg are exacerbated by CNS changes associated with normal aging. At the end of the three years, the results of the behavioral tests of the primates and the neuroanatomical studies of rodents will be reviewed to direct further studies of the primate colony. For the present plan, the primate colony will be sacrificed at the end of year 3 and studies to test 5 hypotheses related to the long-term neuroanatomical and neurochemical effects of in utero MeHg will be conducted during years 4 and 5. All of the hypotheses that will be tested are based on the results developmental assessments of the MeHg exposed and control macaca fascicularis from our laboratory and from the laboratory of Rice et al. (1989). To test the primate neurobehavioral hypotheses, assessments of Delayed Spatial Alteration, Delayed Nonmatch-to-Sample, and Spatial-and Temporal-Visual Contrast Sensitivity will be used. The primate and rodent neuroanatomical hypotheses will be tested by quantifying brains for cell numbers, cell density, and tissue volume; immunocytochemistry will be used to identify growth-controlling cells and astrocytes, and dendritic development will be assessed biochemically by assays of MAP2 (primates only) and morphometrically for dendritic pattern and extent. Finally, the primate neurochemical hypotheses will be tested using autoradiographic techniques to evaluate cholinergic neurotransmission in cortical and subcortical areas related to specific memory pathways and catecholaminergic neurotransmission in the hypothalamic-pituitary axis related to the regulation of growth. While previous studies have reported immediate effects following early MeHg exposure in rodents, macaques, and humans, little is currently known regarding the long-term effects of in utero MeHg exposure on adult and aged animals or humans. The proposed nonhuman primate studies make the best use of the valuable monkey colony, because the studies focus on a set of strongly-supported hypotheses using procedures that are readily available for use with humans. The rodent studies will provide the first results regarding the influence of aging o

577

TITLE:

Biologically-based dose-response model for methyl mercury developmental toxicity incorporating novel in vivo cell cycling data.

AUTHORS:

Lewandowski TA
Ponce RA
Hong S

Bartell SM
Faustman EM

SOURCE:
Toxicologist 2000 Mar;54(1):292

ABSTRACT:
We are developing a biologically-based dose response model that describes the developmental toxicity of methyl mercury (MeHg) in the developing embryonic rat brain. Key components of the model include biologically-derived rate constants for proliferation of neuroepithelial cells. We are using 5-bromo-2'-deoxyuridine (BrdU) DNA labeling in vivo and flow cytometry to obtain these parameters. We found that in the untreated animal, the fraction of cycling midbrain cells declines from 73 (+/- 4) percent on gestational day (gd) 12 to 10 (+/- 4) percent on gd 16. The estimated cell cycle time increases from 16 hours on gd 12 to 20 hours on gd 16, while the estimated S phase duration increases from 8 hours on gd 12 to 10 hours on gd 16. Similar values were obtained in vitro for rat midbrain cells cultured from gd 12 to gd 14 (Ponce et al., 1994). We are now evaluating the effects of MeHg on cell cycle kinetics in vivo. Preliminary data indicate that dosing on gd l2 to achieve a gd l4 brain concentration of approximately 3 ug/g, results in a significant increase in the fraction of BrdU labeled cells (labeling time = 1.5 hr), suggestive of a slowing of S-phase progression. We are now collecting data on the effect of MeHg on the overall fraction of cycling cells and the cell cycle time. This data will be incorporated into our model and compared to fetal midbrain cell number data being collected in parallel. This will allow us to describe the effect of MeHg on cell cycle progression in vivo and its effects on neural development. We will also assess the utility of in vitro-derived data for modeling, thus improving our knowledge of the uncertainty associated with in vitro to in vivo extrapolation.

578
TITLE:
Disruption of the Potential across the Synaptosomal Plasma Membrane and Mitochondria by Neurotoxic Agents

AUTHORS:
Bondy SC
McKee M

SOURCE:
Toxicology Letters, Vol. 58, No. 1, pages 13-21, 29 references, 1991

ABSTRACT:
A study was undertaken of two neurotoxic agents, toluene (108883) and methyl-mercuric-iodide (143362) on the potential across the synaptosomal limiting membrane and the mitochondrial potential in adult male

CR-1-CD-rats. Synaptosomes were prepared from the whole brain, minus the cerebellum and pons medulla. Rhodamine fluorescence was measured after the depolarization of the plasma membrane or depolarization of the mitochondria, and after 10 minutes of incubation with a toxic agent. The membrane potentials of both mitochondria and plasma membranes were depressed by methyl-mercury in a dose related manner. In additional studies methyl-mercury was administered by a single intraperitoneal injection at a dose of 10mg/kg, and synaptosomes were prepared after 2 days of exposure. No significant effect on either plasma membrane or mitochondrial potential was observed. Toluene also depolarized both mitochondrial and plasma membranes with the effect being dose related. The presence of alpha-tocopherol-succinate, ganglioside-GM1, or deferoxamine was not able to prevent the depolarization of the mitochondria by toluene. Isolated synaptosomes were also exposed to benzene (71432). Benzene exhibited similar, but less potent, results. One hour after treatment with toluene at 1 gram/kilogram intraperitoneally the animals were sacrificed and synaptosomes prepared. The particular vulnerability observed in mitochondria may be due to the disruption of oxidative phosphorylation and may be related to the increase in intrasynaptosomal free ionic calcium that both of these chemicals can induce.

579
TITLE:
Mercuric iodide

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1992. 6p.

ABSTRACT:
Data sheet. Synonym: mercury diiodide. May enter the body by inhalation and through the skin. May irritate the lungs. May damage the kidneys. Mercury poisoning can cause the "shakes", irritability, sore gums, memory loss, increased saliva, metallic taste, personality changes and brain damage. May irritate and burn the eyes causing permanent damage. May irritate and burn the skin and cause skin allergy and grey skin colour.

580
TITLE:
Inhibition of Mitochondrial Ca2+ Release Diminishes the Effectiveness of Methyl Mercury to Release Acetylcholine from Synaptosomes

AUTHORS:
Levesque PC

Hare MF
Atchison WD

SOURCE:
Toxicology and Applied Pharmacology, Vol. 115, No. 1, pages 11-20, 67 references, 1992

ABSTRACT:
Experiments were conducted on the interaction of methyl-mercury (22967926) (MeHg) with nerve terminal mitochondria in rat brain synaptosomes. Synaptosomes were isolated from the brains of Sprague-Dawley-rats and intrasynaptosomal acetylcholine (ACh) was labeled. The synaptosomes were then loaded with tritiated choline and reacted with physostigmine and hemicholinium. The release of labeled ACh was determined and the uptake of choline was measured. A significant inhibition of choline uptake was seen using 100 micromolar (microM) MeHg and a dose dependent increase in the spontaneous release of ACh was seen with 10 or 100microM MeHg. A concentration dependent increase in ACh release was seen following the addition of ruthenium-red (RR). This effect was reduced 10 to 20% in calcium free solutions. The stimulatory effects of MeHg on ACh release were attenuated by preincubation with RR. RR also had a greater quenching effect on the fluorescence seen in predepolarized synaptosomes, than that seen in synaptosomes with intact plasma and mitochondrial membrane potentials. The authors conclude that extracellular calcium is only partially responsible for MeHg induced ACh release, and that MeHg reduces choline uptake into nerve terminals.

581
TITLE:
Interaction between Thiocysteamine and Methylmercury

AUTHORS:
Sumino K
Mio T

SOURCE:
Toxicology of Metals: Clinical and Experimental Research, S. S. Brown and Y. Kodama, Editors; Chichester, Ellis Horwood Limited, pages 339-340, 3 references, 1987

ABSTRACT:
Two experiments were undertaken to determine whether synthetic thiocysteamine (TC) could attack bound methyl-mercury (22967926) (MM) in organs of mice administered MM. The amounts of MM were measured using a gas chromatograph with an electron capture detector. The chemical form of bis-methyl-mercury-sulfide (BMS) was identified using a mass spectrometer with a computer data analytical system. In in-vitro experiments, mice were treated with 15mg/kg of MM, and kidney, liver and brain suspensions

were prepared 3 days later. After addition of 2.5millimolar TC, each suspension was incubated at 37 degrees-C. Ninety percent of the total MM in the kidney was released after a 1 hour incubation. The rate of liberation of MM was 70% in the brain and 45% in the liver. When TC was taken up into the cells, MM in the organs might be released extracellularly in the form of BMS. In in-vivo experiments, TC had little influence on the lethal effect of MM. Subcutaneous injections of 4 milligrams (mg) of TC alone or in combination with 12mg/head of glutathione (GSH) was given to mice every day starting on the third day after administration of 8mg/kg of MM. Administration of TC mixed with glutathione caused high excretion of MM, but TC given alone was less effective. When TC was administered with GSH, about 50% of the total MM in the urine was in the BMS form compared to 10% in the urine of control mice treated with MM alone. This is the first report of an interaction between TC and MM.

582
TITLE:
Astrocytes as Modulators of Mercury-Induced Neurotoxicity

AUTHORS:
Aschner M

SOURCE:
Neurotoxicology, Vol. 17, Nos. 3/4, pages 663-670, 58 references, 1996

ABSTRACT:
The effects of methylmercury (7439976) (MeHg) on astrocytic functions were reviewed. In-vivo, MeHg preferentially accumulated in astrocytes, both in humans and animals. In-vitro, MeHg inhibited glutamate uptake in astrocytes. MeHg on membrane transporters produced astrocytic swelling and release of endogenous glutamate. MeHg caused the expression of metallothioneins (MT) in astrocytes. Western blot analysis revealed a time dependent increase in MT protein synthesis through 96 hours of exposure to MeHg. A time dependent increase in MT immunoreactivity in astrocytes exposed to MeHg was also demonstrated. Preexposure of astrocytes to cadmium-chloride completely reversed the inhibitory effect of MeHg on aspartate uptake, which occurred in MeHg treated astrocytes expressing constitutive MT levels. The author suggests astrocytes may serve a dual role in MeHg intoxication, initially affording protection by sequestering MeHg, and later succumbing to MeHg and swelling and releasing amino acids. The author concludes that future in-vivo research is needed to complement tissue culture results to explore the precise role of astrocytes in MeHg induced neurotoxicity.

583
TITLE:
The Effects of Methylmercury on Endogenous Dopamine Efflux from Mouse

Striatal Slices

AUTHORS:
Kalisch BE
Racz WJ

SOURCE:
Toxicology Letters, Vol. 89, No. 1, pages 43-49, 34 references, 1996

ABSTRACT:
The effects of methylmercury on endogenous dopamine efflux from mouse striatal slices were examined. Right and left striatal sections, sliced sagitally at 300 micrometer intervals, prepared from the brains of adult male Swiss-albino-CD1-mice were perfused in Krebs bicarbonate solution (KRB) containing 0, 10, 50, or 100 micromolar (microM) methylmercury for 40 minutes (min) at 37 degrees-C. In some experiments, KRB minus the calcium-chloride component, was used to assess the dependency of any effect on calcium ion (Ca2+). In other experiments, the slices were perfused with KRB containing potassium-chloride, in place of sodium-chloride, to assess the effect of methylmercury on potassium ion (K+) stimulated dopamine release. Perfusate samples were collected after the 40min exposure period and analyzed for dopamine. Methylmercury induced concentration related increases in spontaneous efflux of dopamine from the slices. The magnitude of the effect did not depend on the presence or absence of Ca2+ in the perfusion medium. Methylmercury enhanced K+ stimulated dopamine efflux from the slices both in the presence and absence of Ca2+. The magnitude of the increase was greater when Ca2+ was present in the perfusate. The authors conclude that methylmercury enhances spontaneous and K+ stimulated efflux of dopamine from mouse striatal slices in a concentration dependent manner. Since threshold methylmercury concentrations capable of causing behavioral and neurochemical alterations in mice have been reported to be in the range of 80 to 160 micromolar total mercury (7439976), the results suggest that changes in dopamine efflux could occur at brain methylmercury concentrations associated with neurochemical and behavioral disturbances.

584
TITLE:
METHYL MERCURY-INDUCED ENCEPHALOPATHY IN MICE

AUTHORS:
MACDONALD JS
HARBINSON RD

SOURCE:
TOXICOL. APPL. PHARMACOL. 1977, 39(2) 195-205

ABSTRACT: EIS: Epidemiology Information System

585
TITLE:
Effect Of Methylmercury Chloride On Sleep Waking Rhythms In Rats

AUTHORS:
Arito H
Hara N
Torii S

SOURCE:
Toxicology, Vol. 28, No. 4, pages 335-345, 13 references, 19831983

ABSTRACT:
The effects of methylmercury-chloride (115093) (MMC) on sleep/waking rhythms were investigated in rats. Unrestricted male Sprague-Dawley-rats were implanted chronically with electroencephalographic and electromyographic electrodes for polygraphic recordings. The light was turned on at 800 hours and off at 2000. Circadian rhythms of wakefulness, slow wave sleep (SS), and paradoxical sleep (PS) and both light and dark phase amounts of wakefulness, SS, and PS were compared before and after administration of MMC. Five days after electrode implantation, rats received 15, 5, or 1.65 milligrams per kilogram (mg/kg) MMC orally on 2 successive days (total doses, 20, 10, 3.3mg/kg). Brain mercury (7439976) concentrations were also measured at various times following dosing. Average wakefulness, SS, and PS of all rats over 4 administration days were 164, 473, and 83 minutes for the light period and 508, 166, and 46 minutes for the dark period, respectively. Circadian rhythms of both SS and wakefulness were entrained squarely with the light/dark cycles. PS, however, reached a maximum at 1600 to 1800 hours and a trough around 400 to 800 hours. The 3.3mg/kg group showed no significant change in sleep/wake parameters. The 10mg/kg group initially displayed a 28 percent decrease in light phase PS and an increase in light phase wakefulness. Both dark phase SS and PS increased, with a decrease in wakefulness; however, these changes returned to baseline by day 19. The 30mg/kg group exhibited prolonged light phase PS at the expense of wakefulness and increased SS and PS during the dark period. The circadian PS rhythm of these rats was shifted, showing a delayed maximum at 2000 to 2200 hours and a delayed trough after 800 hours. Brain mercury concentrations were highest at 10 days after dosing with the highest concentrations in cortex and cerebellum and lowest in pons and medulla. The authors conclude that MMC induces dose dependent changes in sleep/waking patterns with the circadian PS rhythm being selectively vulnerable.

586
TITLE:
Some characteristics of current forms of occupational nervous system diseases of chemical aetiology

AUTHORS:
Antonjuzenko VA
Gnesina EA
Gnelickij GI
Karacarova SV
Kalistova VV

SOURCE:
Gigiena truda i professional'nye zabolevanija Feb. 1987, No.2, p.19-22. 9 ref.

ABSTRACT:
Follow-up of 214 patients with the most commonly encountered types of poisoning (caused by ethylene, vinyl chloride, trichloroethylene, mercury and its compound granosanum-64) as well as with occupational pathology due to antibiotics (penicillin and streptomycin). Neurological symptoms often develop in combination with symptoms of organic lesions of different parts of the brain. Ethylene, vinyl chloride, and trichloroethylene affect mainly the mesencephalon and caudal regions, whereas mercury affects the brain stem and cerebellum. Antibiotics produce circulatory disorders confirmed by visual disorders.

587
TITLE:
Accumulation and tissue distribution of mercury in the guinea pig during subacute administration of methyl mercury.

AUTHORS:
IVERSON F
DOWNIE RH
TRENHOLM HL
PAUL C

SOURCE:
TOXICOL APPL PHARMACOL; 27 (1). 1974 60-69

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. (Methyl mercury (MeHg) contamination of food sources has caused fatal intoxication in man and animals.) Female guinea pigs were dosed orally daily for 71 days with 0.4, 4, 40, or 400 mug Hg/kg given as radiolabeled methyl mercuric chloride. The accumulation of total Hg was followed in 10 tissues at 6 time intervals. After dosing ceased, the decay profiles of Hg were followed for an additional 35 days. The accumulation pattern for Hg was similar for each dose level, and the tissue Hg concentration on day 71 increased in the following order: blood less than cerebellum less than hypothalamus less than calcarine cortex less than frontal lobe less than occipital lobe less than caudate nucleus

less than muscle less than liver less than kidney. Hg accumulation in all tissues, except kidney at the 4-, 40-, and 400- mug/kg dose levels approached steady-state values in the 35-71-day dosing period. The accumulation curves could be fitted by an exponential equation incorporating the Hg half-life obtained from the decay profiles. As the dose level increased, tissue Hg concentrations increased to a greater extent than anticipated. Although doses increased 1000-fold from 0.4-400 mug Hg/kg, kidney concentrations increased 3300-fold after 71 days of dosing. At this time, inorganic Hg (Hg-2+) comprised 42% of the total kidney Hg and 5% of the total liver Hg at the 400 mug/kg dose. Clinical signs of methylmercury (MeHg) intoxication were induced in guinea pigs after dosing daily for 9 days at 5 mg Hg/kg. The activities of 6 enzymes were monitored and cholinesterase (serum), choline acetylase (caudate nucleus) and carboxylesterase (liver) were significantly lower than control values. The total Hg concentration in whole brain was 28 mug/g (wet weight). Animals dosed at 400 mug Hg/kg for 71 days showed no decrease in the activities of the selected enzymes, there was no change in weight gain when compared to the control and there were no signs to Me Hg toxicity. The highest brain Hg concentration after 71 days dosing was 11 mug/g (wet weight) in the caudate nucleus.

588

TITLE:

Maternal and fetal toxicity of methylmercuric chloride administered to pregnant Fischer 344 rats.

AUTHORS:

LEE J-H
HAN D-H

SOURCE:

JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH; 45 (4). 1995. 415-425.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Various doses of methylmercuric chloride (MMC) were administered orally to pregnant Fischer 344 rats on d 7 of gestation. On d 20 of gestation the dams were laparotomized under ether anesthesia, and the fetuses were removed. Maternal body weights were decreased for 2 d and 6 d in rats given 10 and 20 mg/kg MMC, and were continuously decreased for those given 30 mg/kg MMC. Maternal weight gain of each group was decreased to 86.2%, 78.9%, and 61.9% of control group on d 20 of gestation. The reduction of litter weight was greatly enhanced with increasing MMC doses, presumably due to postimplantation loss, which was already increased at high treatment levels. The LD50 of MMC for fetuses was determined to be 16.5 mg/kg. Mercury content in maternal organs was highest in kidney, followed by blood, spleen, liver, and brain, while in fetal organs it was highest in liver. Fetal liver and brain contained more mercury than maternal liver and brain. However, fetal

kidney retained le

589
TITLE:
Mercury Distribution Studies Involving Complexes of Low-Molecular Weight Thiols and Methylmercury

AUTHORS:
Balthrop JE
Wade JL
Braddon-Galloway S

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 37, No. 6, pages 890-898, 12 references, 19861986

ABSTRACT:
A study was performed in ICR-mice to determine if methylmercury (22967926) (CH3Hg) and thiol complexes of CH3Hg are absorbed and distributed in a manner dependent upon the status of a known ameliorative agent of CH3Hg toxicity, selenium (7782492). Studies of blood, brain, liver, kidney, and intestine showed no difference in the distribution of CH3Hg due to the selenium status of the animal nor due to the route of CH3Hg administration (subcutaneous or intraperitoneal). Exposure to each of four complexes of CH3Hg did not alter tissue distribution of CH3Hg as compared to exposure to uncomplexed CH3Hg. About 35 percent of the recovered CH3Hg accumulated in the liver, about 25 percent in kidney and intestine, 15 percent in blood, and 1 percent in brain. Determination of organ CH3Hg concentrations showed no differences due to selenium status nor route of administration. Concentrations were highest in kidney, followed by liver and intestine, blood, and brain. It is suggested that the fact that CH3Hg complexed to thiols is absorbed and distributed in the body in a manner similar to uncomplexed CH3Hg may be due to rapid delivery to the liver via the general circulation. Injected CH3Hg thiol complexes may all be converted to one similar, undefined compound. Since dietary selenium was used, it is possible that metabolic interactions of selenium with CH3Hg may occur only when the metals are concurrently administered.

590
TITLE:
METABOLISM OF METHYLMERCURY IN THE BRAIN AND ITS TOXICOLOGICAL SIGNIFICANCE

AUTHORS:
MOTTET NK
VAHTER ME
CHARLESTON JS
FRIBERG LT

SOURCE:
SIGEL, A. AND H. SIGEL (ED.). METAL IONS IN BIOLOGICAL SYSTEMS, VOL. 34. MERCURY AND ITS EFFECTS ON ENVIRONMENT AND BIOLOGY. XLII+604P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ISBN 0-8247-9828-7.; 34 (0). 1997. 371-403.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER LITERATURE REVIEW HUMAN MONKEY MOUSE RAT RABBIT FETUS ADULT TOXICOLOGY METHYLMERCURY TOXIN SUBCELLULAR EFFECTS METABOLISM BRAIN NERVOUS SYSTEM MERCURY CELLULAR DISTRIBUTION BLOOD-BRAIN BARRIER CELL ADHESION MOLECULES NEURON NEUROTRANSMITTER GLUTATHIONE NERVOUS SYSTEM CIRCULATORY SYSTEM

591
TITLE:
Treatment of methyl mercury poisoning in mice with 2,3-dimercaptosuccinic acid and other complexing thiols.

AUTHORS:
AASETH J
FRIEDHEIM E AH

SOURCE:
ACTA PHARMACOL TOXICOL; 42 (4). 1978 248-252

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Treatment with 2,3-dimercaptosuccinic acid was more effective than N-acetyl-DL-penicillamine and monomercaptosuccinic acid in mobilizing Hg from mice after the injection of methyl mercuric chloride. Dimercaptosuccinic acid treatment started 4 days after the Hg injection and given for 8 days at a dose of 1 mmol SH/kg per day removed more than 2/3 of the Hg in the brain, while acetylpenicillamine and mercaptosuccinate correspondingly removed less than 1/2 of the brain deposits. Neither treatment with 2,3-dimercaptopropanol-1-sulfonate nor with a new thiolated resin, mercaptostarch, mobilized significant amounts of Hg from the brain. Since the toxicity of dimercaptosuccinate seems to be almost as low as that of D-penicillamine this dithiol may provide a potentially useful agent in clinical poisoning due to methyl mercury.

592
TITLE:
Regional Cerebral Glucose Metabolism and Blood Flow during the Silent Phase of Methylmercury Neurotoxicity in Rats

AUTHORS:
Hargreaves RJ
Eley BP

Moorhouse SR
Pelling D

SOURCE:
Journal of Neurochemistry, Vol. 51, No. 5, pages 1350-1355, 39 references, 19881988

ABSTRACT:
Regional cerebral glucose metabolism and blood flow during the silent phase of methylmercury neurotoxicity were studied in rats. Anesthetized male Sprague-Dawley-rats were given 8mg/kg methylmercuric-chloride (115093) (MMC) orally for 6 consecutive days. During the silent phase of intoxication (the asymptomatic phase 1 day after the last dose), glucose flux, cerebral blood flow, glucose utilization, mean arterial blood pressure, heart rate, blood gas concentrations, pH, and body temperature were determined. Cerebral blood flow was determined using radioactive 4-iodoantipyrine. Glucose flux from the blood to the brain was determined by measuring brain uptake of radiolabeled 2-deoxyglucose (2DG). Glucose utilization was evaluated by determining the glucose phosphorylation rate, also using radiolabeled 2DG. MMC did not significantly affect mean arterial blood pressure, heart rate, blood gases, pH, or body temperature. Cerebral blood flow was significantly reduced in MMC treated rats. Significant interregional variations in blood flow occurred, but MMC did not significantly affect blood flow from one brain region to another. Glucose flux and phosphorylation rate were not significantly affected by MMC. The authors conclude that a reduction in cerebral blood flow occurs during the silent phase of methylmercury intoxication; however, this does not seem to be associated with impairment in cerebral glucose supply or phosphorylation.

593
TITLE:
In Vivo and In Vitro Effects of Methylmercury on the Activities of Aminoacyl-tRNA Synthetases in Rat Brain

AUTHORS:
Hasegawa K
Omata S
Sugano H

SOURCE:
Archives of Toxicology, Vol. 62, No. 6, pages 470-472, 18 reference, 19881988

ABSTRACT:
The effects of methylmercury-chloride (115093) were studied on the activities of six aminoacyl-tRNA synthetase species in the brains of adult female Wistar-rats in efforts to understand the action of methylmercury

(MeHg) on protein synthesis. The animals were given subcutaneous injections of methylmercury-chloride at 10mg/kg for 7 consecutive days. Significant reductions in the activities of Asp-tRNA, Leu-tRNA, and Tyr-tRNA synthetases in the brains of treated animals were noted. No change was noted in the Lys-tRNA and Met-tRNA synthetases. Significant increases were noted in the activity of His-tRNA synthetase in the symptomatic phase of MeHg poisoning. The direct addition of MeHg to the assay system in-vitro affected the activities of these six aminoacyl-tRNA synthetases to different extents. There did not appear to be any correlation between in-vitro and in-vivo effects. The authors conclude that the amino acylation of tRNA is one action of MeHg which results in inhibited protein synthesis. The amino acid composition of different cellular proteins may modify the effect of MeHg on the synthesis of these proteins.

594

TITLE:

Methylmercury-Induced Movement and Postural Disorders in Developing Rat: Loss of Somatostatin-Immunoreactive Interneurons in the Stratum

AUTHORS:

O'Kusky JR
Radke JM
Vincent SR

SOURCE:

Developmental Brain Research, Vol. 40, No. 1, pages 11-23, 41 references, 1988

ABSTRACT:

The effects of methylmercury on central nervous system (CNS) neuropeptide somatostatin and glutamic-acid-decarboxylase (GAD) activity were studied in rats. Young Sprague-Dawley-rats were injected subcutaneously daily with 5mg/kg methylmercuric-chloride (115093) (MMC) starting on postnatal day five and continuing until one of three stages of toxicity, defined as gaining weight less rapidly than the controls (stage-I), showing a persistent loss of weight over 24 hours (stage-II), or the onset of symptoms of neurological impairment (stage-III), were reached. Stage-I toxicity occurred on postnatal day 18, stage-II on days 20 to 22, and stage-III toxicity on postnatal days 22 to 25. The animals were killed and the brains were removed and dissected for analysis. Tissues were analyzed for GAD, somatostatin, neuropeptide-Y, or NADPH-diaphorase. All rats in stage-III toxicity exhibited a mixed spastic and dyskinetic syndrome. GAD activity and the somatostatin concentration in the cerebral cortex was significantly decreased in animals in stage-II and stage-III toxicity. Striatum GAD activity and somatostatin were decreased only in stage-III toxicity. MMC did not significantly affect GAD activity or somatostatin content in the thalamus, hypothalamus, hippocampus,

substantia nigra, superior colliculus, cerebellum, or spinal cord. A marked loss of somatostatin and neuropeptide-Y immunoreactive neurons occurred along the dorsolateral half of the caudate/putamen in animals in stage-II and stage-III toxicity. The same pattern of loss was seen by NADPH-diaphorase staining. Surviving NADPH-diaphorase positive neurons were atrophied. The authors conclude that methylmercury induced lesions in the developing CNS involve discrete populations of interneurons in the cerebral cortex and striatum.

595
TITLE:
Effects of Mercuric Chloride on (3H)Dopamine Release from Rat Brain Striatal Synaptosomes

AUTHORS:
Hare MF
Minnema DJ
Cooper GP
Michaelson IA

SOURCE:
Toxicology and Applied Pharmacology, Vol. 99, No. 2, pages 266-275, 38 references, 1989

ABSTRACT:
Brain tissue from adult male Long-Evans-rats was treated with mercuric-chloride (7487947) (HgCl2) at concentrations of 3 to 10 micromolar to investigate the effects of such treatment on dopamine release. A concentration dependent increase was noted in spontaneous tritium labeled dopamine release from purified rat striatal synaptosomes. This increase occurred both in the presence and in the absence of extrasynaptosomal calcium. These findings were similar to those caused by ouabain. Therefore, studies were conducted to determine whether the HgCl2 effects were a result of sodium,potassium-ATPase (Na+,K+-ATPase) inhibition. Such inhibition was noted in lysed synaptosomal membranes exposed to HgCl2. However, even in the presence of 1 millimolar ouabain, HgCl2 still increased dopamine release. The specific inhibitor of sodium ion dependent, high affinity dopamine transport, RM181,182 inhibited ouabain induced dopamine release but had no effect on HgCl2 induced dopamine release. The authors conclude that the actions of mercuric-chloride on spontaneous neurotransmitter release probably do not involve inhibition of Na+,K+-ATPase. They suggest the results are more consistent with a direct effect of HgCl2 on transmitter release or an indirect effect mediated via changes in intracellular calcium ion homeostasis.

596
TITLE:

The protective effect of vitamin E and N,N-diphenyl-p-phenylenediamine against methyl mercury toxicity in the rat.

AUTHORS:
WELSH SO

SOURCE:
J NUTR; 109 (10). 1979. 1673-1681.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The ability of vitamin E (dl-alpha-tocopheryl acetate) to protect against CH3HgCl toxicity in the rat was tested and the mechanism by which protection might occur was investigated. Increasing dietary vitamin E from 50-500 ppm increased growth and survival and decreased toxicity signs in rats poisoned with 10-30 ppm Hg as CH3HgCl in the drinking water. This protective effect was shown in rats fed various levels of Se, as well as in rats depleted of Se. Poisoning with CH3HgCl caused an elevation in plasma lipids. Tocopherol levels in brain, testes, or liver were not influenced by CH3HgCl poisoning. The antoxidant N,N'-diphenyl-p-phenylenediamine (DPPD) was more effective than vitamin E in protecting Se-depleted rats against CH3HgCl toxicity. When DPPD was added to the diet, the Hg concentration decreased in the whole body, brain and liver, but increased in the kidney. DPPD also altered the distribution of total Hg in the body; smaller proportions were found in the brain, lung and testes, whereas greater proportions were found in the kidney, skin and hair. The form of mercury present in the tissues was not affected by DPPD. Vitamin E and DPPD evidently protect against CH3HgCl toxicity by a mechanism that is independent of the Se status of the rat and which may involve altered tissue distribution and/or elimination of Hg.

597
TITLE:
Electron microscopic studies on experimental organic mercury poisoning in the nursling rat brain.

AUTHORS:
Deshimaru M

SOURCE:
Seishin Shinkeigaku Zasshi; 71(5): 506-13, 1969; (REF:15)

ABSTRACT:
HAPAB An experiment was run to learn whether an organic mercury compound could pass through the maternal mammary gland to the nursling rat and damage its brain. A daily dose of 1 mg/rat of methyl methylmercuric sulfide was orally administered to three moter rats immediately after delivery of a total of 25 nursling rats. The increase in body weight of the experimental groups was less than that of the control. On day 17 to

18 after delivery, the brains of the nursling rats were fixed for optical and electron microscopic observation. By optical microscopy, loss and shrinkage of the merve cells was seen in the granular cells and Purkinje cells of the cerebellum and in the small pyramidal cells of the cerebral cortex of the parieto-occipital lobe. By electron microscopy, the granular cells were seen to have irregularly shaped nuclei, a tendency to coagulation of the intranuclear substances, ruptured nuclear membrane, an outflow of intranuclear substances, disappearance of the intracytoplasmic organella and marked Golgi apparatus development. The mitochondria showed no conspicuous changes. The vascular endothelial cells and the vascular foot of glial cells surrounding the lesions had vacuolar formation. The Purkinje cells demonstrated an extremely high electron density in the nucleus and cytoplasmic body, a low electron density and proliferation of the mitochondria, enlargement of the endoplasmic reticulum, proliferation of the membranous structure in the cytoplasm and vacuolization in the nerve cell processes around the lesions. Shrinkage of the nucleus and disappearance of the intracytoplasmic organella were noted in the small pyramidal cells of the cerebral cortex. (Author abstract edited)
TOXICOLOGY AND PHARMACOLOGY 70/07/00, 296 1969

598
TITLE:
Mercury metabolism in Japanese quail: I. The effect of dietary mercury and selenium on their tissue distribution.

AUTHORS:
KLING LJ
SOARES J H JR

SOURCE:
POULT SCI; 57 (5). 1978 1279-1285

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Immature and adult coturnix quail were fed isolated soybean protein diets to which methylmercuric chloride or mercuric chloride (environmental pollutants) were added with or without supplemental Se (Hg antidote) for 7 days. Samples of brain, blood, liver and kidney were analyzed for total Hg and Se via atomic absorption spectrophotometry. Se addition had no effect on the Hg concentration in kidney, brain or blood but did tend to increase the concentration of Hg in the livers of the methylmercuric chloride-treated birds. Se in the presence of methylmercury increased the Se concentration of liver and kidney but had little effect on the Se concentration of brain or blood. Methylmercuric chloride supplementation resulted in increased Se concentration in the blood of the Se supplemented group. All other tissue Se levels were unaffected by the addition of Hg.

599

TITLE:
Interaction of methylmercury and selenium in mouse: Formation and decomposition of bis(methylmercuric) selenide.

AUTHORS:
NAGANUMA A
KOJIMA Y
IMURA N

SOURCE:
RES COMMUN CHEM PATHOL PHARMACOL; 30 (2). 1980. 301-316.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Bis(methylmercuric) selenide (BMS; (CH3Hg)2Se) formation from methylmercury and selenite in rabbit blood was recently reported. In the present experiment in vitro and in vivo formation and decomposition of BMS in mouse were investigated. When methylmercury and selenite were added in vitro to the homogenates, soluble fraction or insoluble fraction of mouse liver, kidney, spleen and brain, a substantial amount of BMS was formed. BMS was formed by the addition of methylmercury into the soluble fraction of liver or kidney obtained from the mouse pre-treated with selenite. BMS was hardly detected in the tissues of mouse i.v. injected with both methylmercury and selenite and even with BMS itself. The experimental results with the rapid decomposition of BMS observed in vitro suggest that the cycle of the formation and the decomposition of BMS may repeatedly occur in vivo. Concentrations of mercury and selenium in the brain of mouse receiving BMS were revealed to be significantly higher than those of the mouse administered with methylmercury and/or selenite, suggesting a possibility that the increase of brain-mercury concentration by the administration of selenite, reported so far by several investigators, is due to the formation of BMS from methylmercury and selenite.

600
TITLE:
Methylmercury in Astrocytes What Possible Significance?

AUTHORS:
Aschner M

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 93-106, 92 references, 1996

ABSTRACT:
Accumulation of methylmercury in astrocytes and its possible physiological significance were discussed. The properties and roles of astrocytes in the central nervous system (CNS) were summarized. The acute effects of methylmercury on astrocyte homeostasis were discussed. Although

methylmercury is known to damage the astrocytic plasma membrane, in the initial stages of exposure, the astrocytes appear to play a protective role for the surrounding microenvironment by sequestering methylmercury, thereby preventing it from interacting with the sulfhydryl groups on neurons. Methylmercury has also been shown to inhibit uptake of excitatory amines by astrocytes, resulting in their concentration increasing in the extracellular fluid. This could trigger a destructive cascade of events that can damage neurons. The possible implications of methylmercury sequestration by astrocytes were considered. Some studies have suggested that the sequestration of methylmercury by astrocytes may result from the ability of methylmercury to induce metallothionine (MT) isoforms and the ability of astrocytes to express MTs. As a result of their inducibility, MTs can provide astrocytes with the means to alleviate, at least temporarily, the toxicity of methylmercury. The general properties of MT isoforms, the distribution of MTs within the CNS, MT gene amplification by mercurials, and the effects of methylmercury on astrocytic MTs were discussed. Methylmercury was found to induce expression of MT in astrocytes. Toxic effects appeared at methylmercury concentrations higher than those at which MT was induced, suggesting that toxicity occurs only after the MT metal binding capacity was saturated. The author concludes that astrocytes play a unique role in brain methylmercury metabolism and are the preferred site for sequestration of methylmercury in the brain.

601
TITLE:
The Developmental Neurotoxicity of Methyl Mercury

AUTHORS:
Weiss B

SOURCE:
Prenatal Exposure to Toxicants, H. L. Needleman and D. Bellinger, Editors; The Johns Hopkins University Press, Baltimore, pages 112-129, 58 references, 1994

ABSTRACT:
A review of the toxic effects of prenatal methylmercury (22967926) (MeHg) exposure was presented. The properties and sources of MeHg were described, including commercial, ecological, and manufacturing sources. A fungicidal seed dressing and fish were the two sources thought to account for most human exposures to MeHg. The absorption, distribution, and excretion of ingested MeHg was discussed; MeHg has been found to easily cross the placenta and accumulate in the brain, among other tissues. Much of the current understanding of the toxic effects of MeHg in humans came from two instances of mass poisonings. The first occurred in a small fishing village in Japan as a result of a diet high in MeHg contaminated fish while the second involved the ingestion of products made from MeHg

treated seed grain. Information gained from these incidents on the relationship between incidence of toxicity and exposure and the pattern of methylmercury induced brain injury were described. Animal studies have provided useful information on the relationship between toxicity and dose rate, the particular susceptibility of developing brains to the effects of MeHg, and behavioral effects resulting from MeHg exposure. Experimental studies have suggested an age related increase in MeHg induced neurotoxic effects in prenatally exposed adult animals. Quantitative studies on risk assessment were reviewed. The results of such studies suggested that levels of MeHg contained in tuna fish may be unhealthy for consumption by pregnant women.

602
TITLE:
The effect of N-acetylated DL-penicillamine and DL-homocysteine thiolactone on the mercury distribution in adult rats, rat foetuses and Macaca monkeys after exposure to methyl mercuric chloride.

AUTHORS:
AASETH J
WANNAG A
NORSETH T

SOURCE:
ACTA PHARMACOL TOXICOL; 39 (3). 1976 302-311

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution and excretion of Hg was studied in pregnant rats given a single i.v. dose of 2 mumol/kg of CH3203HgCl on the 13th day of pregnancy. Oral treatment for 1 wk with N-acetyl-DL-penicillamine (4 mmol/kg per day) increased the Hg excretion in feces (from 45 to 120 nmol) and urine (from 9 to 160 nmol). Such treatment mobilized Hg from all the organs tested, and the fetal and maternal brain levels of Hg were decreased to 1/5 and 1/3 of the controls, respectively. A 4-day period of treatment with N-acetyl-DL-penicillamine started 3 days after the injection of methyl mercury reduced the fetal and maternal brain levels to 1/2 and 2/3 of the controls, respectively. The rapid removal of metal deposits following treatment with N-acetyl-DL-penicillamine is attributed to a free penetration of the complexing thiol into the tissue cells in question. No signs of toxicity were detected in monkeys (Macaca fascicularis) given an effective daily dose of the agent (4 mmol/kg) for 6 days. In contrast N-acetyl-DL-homocysteine thiolactone was toxic in the monkeys. In addition, the latter agent was ineffective in increasing the Hg elimination from the brains of monkeys, rats and rat fetuses.

603
TITLE:

Dosimetric Considerations in Neutron Activation Analysis in Vivo

AUTHORS:
Ettinger KV
Fairchild RG
Cohn SH

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 18, 1982

ABSTRACT:
TD3: The use of filtered low energy neutron beams from reactors and isotopic sources opens new possibilities for detection of trace elements, particularly in the brain. The low values of kerma/neutron in 24 and 2 KeV beams, together with a relatively small value of quality factor made it possible to utilize these for detection of Ca in skull with a negligible dose administered to the patient. Furthermore, for an acceptable radiation dose to the brain and satisfactory eye sparing the levels of mercury in brain can be determined using prompt gamma ray technique at much lower concentrations than in the past. The tailoring of neutron spectrum is finding applications in the detection of calcium in parts of the skeleton, close to the skin. For this and similar applications filtered beams offer better detectability i.e. less dose to the patient. Dose sparing is also achieved if exp 252 Cf replaces Am-Be and Pu-Be sources. (ERA citation 07:023351) Symposium on neutron dosimetry, Munich-Neuherberg, F.R. Germ

604
TITLE:
Health Effects Due to the Emission of Mercury on the Combustion of Coal.

AUTHORS:
Berlin M

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 14, 1984

ABSTRACT:
TD3: This report describes the health risks connected with exposure to different Hg compounds and the relevance of these risks in connection with increased coal combustion in Sweden. The following types of Hg exposure are discussed: 1. exposure to Hg vapor, 2. exposure to inorganic divalent Hg compounds, and 3. exposure to MeHg via intake of fish. Inhalation of Hg vapor results in accumulation of Hg in the nervous system, especially the brain. Exposure to divalent Hg salts through intake of drinking water or food containing Hg of by absorption through the skin can result in renal damage to impairment of renal tubuli function. Recent or ongoing exposure to Hg or inorganic Hg compounds is revealed in the Hg concentration in blood and urine. MeHg in fish is absorbed to more than 90 % in the human

gastrointestinal tract. In the adult, 10 % of the body burden of MeHg is accumulated in the brain, and a larger part is found in the fetal brain. Through epidemiological studies involving assessment of Hg conce

605
TITLE:
Influence of mercury on the anesthetic response to and distribution of thiopental in rats.

AUTHORS:
CHAKRABARTI SK

SOURCE:
J TOXICOL ENVIRON HEALTH; 7 (5). 1981. 765-774.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Pretreatment with HgCl2 (2 mg/kg s.c.) 24 h before administration of thiopental (35 mg/kg i.p.) significantly potentiated the duration of thiopental sleeping time in adult male rats but did not influence the onset time for anesthesia. Plasma concentration of free thiopental was significantly higher in Hg-treated animals 15 and 45 min after thiopental injection (during the period of thiopental anesthesia), with a concomitant increase of free thiopental concentration in the brain at 15 min. Total and free brain thiopental concentrations in Hg-treated rats at the time of awakening were not different from those in saline-treated animals. Urinary thiopental remained unchanged from 0-2 h but increased in the treated urine from 0-27 h. In vitro studies showed a strong inhibition of thiopental binding in 24-h Hg-treated plasma. Prolongation of thiopental anesthesia induced by Hg pretreatment was probably related to changes in the disposition of thiopental in the plasma and brain rather than to an alteration in CNS sensitivity.

606
TITLE:
Comparison of elements in bottlenose dolphins stranded on the beaches of Texas and Florida in the Gulf of Mexico over a one-year period.

AUTHORS:
MEADOR JP
ERNEST D
HOHN AA
TILBURY K
GORZELANY J
WORTHY G
STEIN JE

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 36 (1). 1999.

87-98.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. We analyzed tissue samples from bottlenose dolphins (Tursiops truncatus) that had stranded on beaches in Texas and Florida over a 1-year period starting in September 1991. The concentrations of 10 elements plus methyl mercury (MeHg) were determined in brain, kidney, and liver, and we examined these results for differences based upon age, site, sex, and tissue type. A strong inverse relationship between total mercury (Hg) and the percentage that was MeHg was found in liver, kidney, and brain tissue, presumably due to demethylation of MeHg. A threshold concentration was found for total Hg in brain tissue, indicating that most Hg was present as MeHg up to about 8 years of age. Increases in total Hg after this age were accompanied by an increase in the ratio of total Hg to MeHg, indicating demethylation. Strong relationships were found between total Hg in liver and age and between total Hg and selenium in liver, which have been observed before in many fish- and squid-eating

607
TITLE:
Central cholinergic neurobiology.

AUTHORS:
Jett DA

SOURCE:
Handbook of Developmental Neurotoxicology 1998;:257-74

608
TITLE:
Some Properties Of The Organomercury-Degrading System In Mammalian Liver

AUTHORS:
Lefevre PA
Daniel JW

SOURCE:
FEBS Letters, Vol. 35, No. 1, pages 121-123, 6 references, 19731973

ABSTRACT:
Properties of the organomercury degrading system in the liver were studied in rats and guinea-pigs. Liver, brain, and kidney tissues from sacrificed animals were homogenized. Supernatant was incubated for 30 minutes at 37 degrees-C with an organomercurial agent. Protein was then estimated, and benzene (71432) and ethylene (74851) were identified as products of the reaction of phenylmercury-acetate (62384) (PMA) and methylmercury-chloride (115093) by gas liquid chromatography analysis. The livers, brains, and

kidneys of rats and guinea-pigs have the ability to degrade a variety of organomercury compounds to inorganic mercury. The PMA degrading activity of the hepatic system was markedly stimulated by the addition of dithiothreitol (3483123) or 2-mercaptoethanol (60242) but not by other sulfhydryl compounds. Fractionation of the components in the soluble fraction of rat livers indicated the presence of a high and low molecular weight component, the effects of which were non additive. Only a high molecular weight component was detected in guinea-pig livers. The authors conclude that the livers, brains, and kidneys of rats and guinea-pigs possess the ability to degrade a variety of organomercury compounds to inorganic mercury.

609
TITLE:
Mercury distribution in mouse brain after intravenous administration of bis(methylmercuric) selenide.

AUTHORS:
NAGANUMA A
NAKAJIMA E
SHIGEHARA E
TANAKA M
IMURA N

SOURCE:
TOXICOL LETT (AMST); 15 (2-3). 1983. 175-180.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution of Hg in the brain of mice after i.v. administration of methylmercury, methylmercury with selenite, or bis(methylmercuric) selenide (BMS) was examined by whole-body autoradiography using 203Hg-labeled mercury compounds. The radioactivity in the brain of the mice that received methylmercury and selenite simultaneously, or BMS, was higher than that of the mice that received methylmercury alone, but the differences were not significant.

610
TITLE:
Disruption of Brain Mitochondrial Calcium Sequestration by Methylmercury

AUTHORS:
Levesque PC
Atchison WD

SOURCE:
Journal of Pharmacology and Experimental Therapeutics, Vol. 256, No. 1, pages 236-242, 50 references, 1991

ABSTRACT:

The in-vitro effects of methylmercury (22967926) (MeHg) on calcium transport and respiratory control were examined in mitochondria isolated from rat brain. Uptake of radiolabeled calcium by mitochondria and release of radiolabeled calcium from preloaded mitochondria were measured in the presence and absence of ATP. Calcium release induced by MeHg was measured in the presence and absence of ruthenium-red (RR), a putative inhibitor of the mitochondrial calcium uptake uniporter. Ten micromolar (microM) MeHg reduced mitochondrial calcium uptake by approximately 50%, while 100microM MeHg completely blocked calcium uptake. Exposure of preloaded mitochondria to MeHg resulted in increased calcium efflux. Loading mitochondria with radiolabeled calcium in the presence of RR reduced total uptake of calcium and greatly attenuated MeHg induced release of calcium. The ratio of state-3 to state-4 respiration was measured as a means of assessing the functional integrity of mitochondria. Control ratios of from three to five were only marginally reduced by 2microM MeHg but were greatly reduced by 10 and 20microM MeHg. The authors conclude that concentrations of MeHg that stimulate spontaneous release of transmitter impair mitochondrial respiration, thereby impairing functional integrity and disrupting calcium sequestration. The mechanism by which MeHg increases quantal release of transmitter may involve perturbation of mitochondrial calcium sequestration.

611

TITLE:

Effect of mercury on succinate dehydrogenase activity in vitro in the organs of the freshwater fish, Labio rohita (Hamilton).

AUTHORS:

SREEDEVI P

RADHAKRISHNAIAH K

SOURCE:

GEOBIOS (JODHPUR); 17 (2-3). 1990. 70-72.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Effect of different concentrations of mercury, ranging from 0.5 to 7 mug, on succinate dehydrogenase activity was observed in vitro in the gill, liver, brain and muscle of L. rohita. The activity significantly decreased with 0.5 mug concentration itself in the gill and muscle, but in liver and brain significant suppression was observed at 2.0 mug concentration. The suppression in the activity increased with the increase in concentration, and at 7 mug it reached to 100% in gill, brain and muscle and 62% in liver. The significance of these results is discussed.

612

TITLE:

Effects of cadmium and mercury on sodium, potassium-ATPase and uptake of tritiated dopamine in rat brain synaptosomes.

AUTHORS:
RAJANNA B
HOBSON M
HARRIS L
WARE L
CHETTY CS

SOURCE:
ARCH INT PHYSIOL BIOCHIM; 98 (5). 1990. 291-296.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Effects in vivo of cadmium (Cd), mercury (Hg) and methylmercury (CH3Hg) on Na+-K+ ATPase and uptake of 3H-dopamine (DA) in rat brain synaptosomes were studied. These heavy metals significantly inhibited the Na+-K+ ATPase activity in a dose-dependent manner. Similarly, inhibition of DA uptake by synaptosomes was also observed in rats treated with these metals. Intraperitoneal route of metal administration was found to be more effective than per os treatment. Mercuric compounds compared to Cd elicited a higher inhibition of Na+-K+ ATPase and DA uptake in rat brain synaptosomes.

613
TITLE:
Methylmercury poisoning induces oxidative stress in the mouse brain.

AUTHORS:
YEE S
CHOI BH

SOURCE:
EXPERIMENTAL AND MOLECULAR PATHOLOGY; 60 (3). 1994. 188-196.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. C57BL/6J mice were intoxicated by injection of 2.5 mg/kg body wt of methylmercuric chloride (MMC) daily for 3, 7, and 14 days, and the relative concentrations of superoxide and hydrogen peroxide and the specific activity of superoxide dismutase (SOD) were determined in various cellular fractions of the brain. High brain levels of Hg were associated with significantly increased amounts of superoxide and hydrogen peroxide by Days 3, 7, and 14 and with markedly reduced SOD activity by Days 7 and 14. Such a rise in the levels of reactive oxygen species indicates the induction of oxidative stress within brain tissue. This suggests that suppression of antioxidant activity, including that of SOD and glutathione, together with disturbances in the mitochondrial electron transport chain, may contribute to the induction of oxidative

stress in the mouse brain following MMC poisoning.

614
TITLE:
Enzyme Changes in the Brain, Liver and Kidney Following Repeated Administration of Mercuric Chloride

AUTHORS:
Mehra M
Kanwar KC

SOURCE:
Journal of Environmental Pathology, Toxicology and Oncology, Vol. 7, Nos. 1/2, pages 65-71, 27 references, 19861986

ABSTRACT:
The effects of daily administration of mercuric-chloride (7487947) (HgCl2), injected intraperitoneally at a dose of 1mg/kg/day for 10, 20, or 30 days, on selected enzymes in the liver, kidney, and brain were studied in adult male Swiss-albino-mice. Dose related, tissue specific alterations in enzyme inhibition were observed following treatment with HgCl2. The activity of acid-phosphatase increased in the liver, kidney, and brain. Alkaline-phosphatase activity was substantially elevated in liver and brain, but markedly reduced in kidney. Alterations in ATPase activity were complex and inconsistent; activity varied in different tissues, as well as in the same tissue after different treatments. Glucose-6-phosphatase activity declined progressively and markedly in all tissues after HgCl2 administration. Succinate-dehydrogenase activity also decreased in a dose dependent manner in all tissues, but the decline was more marked in kidney than in brain. The authors conclude that alterations are enzyme specific and vary with duration of exposure.

615
TITLE:
Decrease in Protein Phosphorylation in Central and Peripheral Nervous Tissues of Methylmercury-Treated Rat

AUTHORS:
Kawamata O
Kasama H
Omata S
Sugano H

SOURCE:
Archives of Toxicology, Vol. 59, No. 5, pages 346-352, 40 reference, 19871987

ABSTRACT:

Protein phosphorylation was studied in nervous tissues of rats treated with methylmercury-chloride (115093) for 7 days. Female Wistar-rats were injected subcutaneously with methylmercury-chloride at 10mg/kg/day or vehicle alone (controls). Rats were decapitated at 5 days, 10 days, or 15 days, brain and peripheral nervous tissues were removed and homogenized, and protein fractions were prepared. In brain extracts, protein phosphorylation was elevated in the presence of cyclic-adenosine-3',5'-monophosphate (cAMP), while that in peripheral nervous tissue extracts was unaffected by cAMP. There was evidence of formation of protein bound phosphate. More than 70 percent of the initial ATP remained after 20 seconds of the phosphorylating reaction. Phosphorylation of brain cytosol protein was evident over a wide molecular weight range. Methylmercury only affected MAP-2 and tubulin. Protein phosphorylation was less extensive in peripheral nervous tissues than in the brain, and a cAMP effect was scarcely detected. Protein phosphorylation in peripheral nervous tissues was markedly enhanced in the presence of calcium(2+) or Triton-X-100. Sciatic nerve showed the lowest basal activity per unit amount of protein, and the highest activation by calcium(2+) or Triton-X-100. Decreases in protein phosphorylation were observed in dorsal root ganglion, ventral root, dorsal root, and sciatic nerve. No significant difference in protein concentration of Triton extracts of peripheral nervous tissues was observed between controls and methylmercury treated rats. The yields of myelin fractions from sciatic nerves of control and experimental animals decreased to about 60 percent of the control value at 15 days in the symptomatic period.

616

TITLE:

In Vivo Incorporation of (14C)Leucine into Brain Protein of Mice Treated with Methylmercury and Thiol Complexes of Methylmercury

AUTHORS:

Fair PH
Balthrop JE
Wade JL
Braddon-Galloway S

SOURCE:

Toxicology Letters, Vol. 36, No. 3, pages 213-220, 32 references, 19871987

ABSTRACT:

The effect of methylmercury and methylmercury/thiol complexes on protein synthesis was studied in mice. The purpose of the study was to investigate the influence of thiol complexation of methylmercury on brain protein synthesis. Protein synthesis was chosen as it has been proposed as one of the most sensitive and early indicators of methylmercury intoxication. Weanling female ICR-mice were injected intraperitoneally (ip) with methylmercuric-chloride (115093) (MMC),

methylmercury-glutathione (MMG), or methylmercury-cysteineglycine (MMCG) for 10 days. Dosing was 4 milligrams per kilogram (mg/kg) daily for 8 days and 8mg/kg daily for the remaining 2 days. The mice were weighed and examined daily for signs of intoxication. The animals were killed on day ten. Ninety minutes before death they were injected ip with carbon-14 labeled leucine. The uptake of leucine into brain protein was taken as an index of protein synthesis. By day ten, 50 percent of the mice receiving MMC and 30 percent of those given MMG developed classical symptoms of methylmercury toxicity. MMCG treated mice showed no neurotoxic symptoms. Mice receiving MMC and MMG showed significant weight losses. MMC and MMG significantly decreased the rate of incorporation of leucine by brain protein by 19.3 and 21.0 percent, respectively. The rate of uptake in MMCG treated mice was insignificantly decreased by 8.5 percent. The authors conclude that impairment of brain protein synthesis may depend on the chemical form of methylmercury.

617

TITLE:

Metal Inhibition of Calmodulin Activity in Monkey Brain

AUTHORS:

Vig PJS
Nath R
Desaiah D

SOURCE:

Journal of Applied Toxicology, Vol. 9, No. 5, pages 313-316, 23 references, 1989

ABSTRACT:

The effects of cations of vanadium (7440622) (Vd), cadmium (7440439) (Cd), mercury (7439976) (Hg), aluminum (7429905) (Al), lead (7439921) (Pb), and manganese (7439965) (Mn) on rhesus-monkey brain calmodulin activity were investigated. Samples of cerebral cortex were homogenized and calmodulin depleted synaptic plasma membranes were prepared. Brain fractions with endogenous calmodulin and calmodulin depleted fractions were incubated with various concentrations of aqueous solutions of the test metals for 5 minutes at 37 degrees-C. Calcium and magnesium ATPase and the magnesium ATPase activities were measured on the reaction mixtures to obtain the net calcium ATPase activity. No effect was noted on basal enzyme activity; however, each metal caused significant inhibition in calcium ATPase in brain fractions with calmodulin. Basal enzyme was affected by addition of exogenous calmodulin to to depleted fractions. Median inhibitory concentrations ranged from 3.0 micromoles Hg to 15.8 micromoles Vd; inhibition potency was observed to increase as follows: Hg, Cd, Pb, Mn, Al, Vd. The authors conclude that these toxic metal cations inhibit calmodulin activity in the primate brain.

618
TITLE:
Methylmercury toxicosis: 2. Distribution patterns of mercury at the onset of neurological signs of acute and chronic stages.

AUTHORS:
TAGASHIRA E
URANO T
YANAURA S
IMAEDA K
OHSAWA K

SOURCE:
FOLIA PHARMACOL JPN; 76 (3). 1980. 193-200.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ICR-strain mice (4 wk old) were continually given a low (16 ppm), medium (30 ppm) and high dose (50 ppm) of methylmercury chloride in foods containing this compound, and Hg levels in the blood (separated into blood cells and plasma portion) and various organs at the acute and chronic onsets of Hg poisoning were assayed using an analyzer previously developed. The early onset of severe methylmercury chloride poisoning in female mice was chiefly attributable to sexual differences regarding the amounts of deposited Hg in the brain and other organs; the Hg levels in all organs of the female mice were higher. The Hg level in the blood cells increased gradually with continuation of the diet and parallels were seen between the deposited amounts of Hg in various organs and the length of time the mice ingested this diet. The Hg level in the plasma reached a plateau earlier than the onset time of Hg poisoning. The critical Hg concentration in the blood cells and the brain at the onset of Hg poisoning tended to be low at the chronic stage. In animals on the dose level of 16 ppm, neurological signs evolved at about half the level of the Hg contents in the animals on 50 ppm. The ratios of Hg distribution in the blood and organs to the distribution into the brain at the onset showed a change in the brain/blood ratio; the ratio was higher according to the longer administration of methylmercury. The onset of methylmercury chloride poisoning can be predicted by assessing the level of this compound in the brain, in terms of the application period and the content in blood cells.

619
TITLE:
Differential Effects of Methylmercury on the Phosphorylation of Protein Species in the Brain of Acutely Intoxicated Rats

AUTHORS:
Yagame H
Horigome T

Ichimura T
Uchiyama J
Omata S

SOURCE:
Toxicology, Vol. 92, Nos. 1-3, pages 101-113, 35 references, 1994

ABSTRACT:
The total activity of protein phosphorylation in the brain was determined using female Wistar-rats injected subcutaneously with methylmercury-chloride (115093) (MeHg) at 10mg/kg/day for 7 consecutive days. Rats were killed on day four, nine or 14, and brain cytosol were prepared. Two dimensional electrophoretic analysis of the phosphorylated cytosol fractions from control and MeHg treated rats indicated that MeHg stimulated the phosphorylation activities of some protein species while those of other protein species were either inhibited or not significantly affected. The extent of stimulation or inhibition was not uniform for individual protein species. The patterns of changes in the phosphorylation activities differed with the progress of MeHg intoxication in the animals. The authors conclude that MeHg treatment in-vivo significantly affected the phosphorylation of individual protein species in the brain of the rat, but the total phosphorylation activities were not significantly changed.

620
TITLE:
Methylmercury Efflux from Brain Capillary Endothelial Cells Is Modulated by Intracellular Glutathione but Not ATP

AUTHORS:
Kerper LE
Mokrzan EM
Clarkson TW
Ballatori N

SOURCE:
Toxicology and Applied Pharmacology, Vol. 141, No. 2, pages 526-531, 33 references, 1996

ABSTRACT:
The effects of intracellular glutathione (GSH) and ATP on the modulation of methylmercury efflux from brain capillary endothelial cells was studied. Bovine brain capillary endothelial cells in culture were used to examine the hypothesis that methylmercury is transported out of these cells as a GSH complex. GSH concentration in cultured bovine brain capillary endothelial cells was 13.1 +/3.3 nanomoles/milligram protein. Depletion of intracellular GSH was accomplished by exposure to 1-chloro-2,4-dinitrobenzene or diethyl-maleate. Cells preloaded with

radiolabeled methylmercury-chloride (115093) showed decreased rates of methylmercury efflux when GSH levels were decreased. Incubation of methylmercury preloaded cells with high concentrations of GSH S-conjugates or GSH analogs also inhibited methylmercury efflux, while addition of L-leucine, L-methionine, or L-alanine at 20 millimolar had no effect. Efflux was not affected by depletion of intracellular ATP with 2-deoxyglucose or antimycin-A. The authors conclude that complexation with GSH and subsequent transport of the complex by an ATP independent mechanism may be involved in the transport of methylmercury out of brain capillary endothelial cells.

621
TITLE:
Methylmercury Alters the Tyrosination Status of Tubulin in the Brains of Acutely Intoxicated Rats

AUTHORS:
Ishida Y
Ichimura T
Sumi H
Horigome T
Omata S

SOURCE:
Toxicology, Vol. 122, No. 3, pages 171-181, 45 references, 1997

ABSTRACT:
The effect of methylmercury (22967926) (MeHg) on the tyrosination/detyrosination of alpha-tubulin was examined. Female Wistar-rats were injected with a daily MeHg dose of 10mg/kg for 7 days. Controls received vehicle only. The animals were sacrificed 4 to 14 days following treatment. The brain was excised and the cytosol fraction was isolated. The tubulin tyrosination activity in the brain cytosol fraction was determined by incubating radiolabeled tyrosine with cytosol fraction proteins and measuring the resultant radioactivity in the substrate using liquid scintillation counting. The tubulin-tyrosine-ligase (TTL) activity of the tubulin fraction was determined. The incorporation of radiolabeled tyrosine into tubulin samples pretreated with carboxypeptidase-A was measured in order to quantify tyrosinated and detyrosinated tubulin. The tubulin-tyrosine-carboxypeptidase activity in the brain cytosol fraction was assayed by incubating tyrosinated microtubule protein with the cytosol fraction. Total amounts of alpha-tubulin and beta-tubulin separated by sodium-dodecyl-sulfate polyacrylamide-gel electrophoresis were determined by densitometry and immunoblotting. Tubulin tyrosination activity was markedly higher in the presence of exogenous tubulin than in the presence of the cytosol fraction alone. At 9 and 14 days after treatment, the tubulin tyrosination activity was significantly reduced in rats exposed to MeHg, compared to controls. The TTL activity was also significantly

decreased at 9 and 14 days following exposure. Whereas the amounts of detyrosinated and tyrosinatable tubulin decreased significantly and progressively following MeHg exposure, the amount of preexisting tyrosinated tubulin was not significantly reduced in rats exposed to MeHg. As determined by densitometry and immunoblotting, total amounts of alpha-tubulin and beta-tubulin were not significantly altered following MeHg treatment. Tubulin-tyrosine-carboxypeptidase activity was not affected by MeHg treatment. The authors conclude that MeHg disrupts tubulin tyrosination in the brain cytosol of rats.

622
TITLE:
Inorganic mercury: Selective effects on blood-brain barrier transport systems.

AUTHORS:
PARDRIDGE WM

SOURCE:
J NEUROCHEM; 27 (1). 1976 333-335

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The predominance of CNS symptoms in chronic inorganic mercurial poisoning has long been recognized. The increasing awareness of Hg as an environmental polluter has made it necessary to examine the subclinical effects of this heavy metal on brain metabolism that may precede the gross pathologic picture. Whether mercuric ions exert selective effects on the brain uptake of circulating amino acids, glucose and carboxylic acids was studied in rats. The data suggest a spectrum of effects of inorganic Hg on capillary function in the CNS. Low concentrations of mercuric ions appear to inhibit the active efflux of acid metabolites across the blood brain barrier. Slightly higher doses of Hg depress the influx of circulating amino acids into brain. Higher concentrations inhibit glucose and pyruvate transport and maximal doses of mercuric ions then destroy cerebral capillary wall integrity.

623
TITLE:
Effect of thiocarbamate derivatives on copper, zinc and mercury distribution in rats and mice.

AUTHORS:
AASETH J
ALEXANDER J
WANNAG A

SOURCE:
ARCH TOXICOL; 48 (1). 1981. 29-40.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Oral treatment of rats with tetramethylthiuram disulfide (fungicide) (TMTDS), 0.1% mixed in the food (corresponding to 20-30 mumol daily) for 1 wk, increased the brain levels of endogenous Cu and Zn to 120 and 170%, respectively, of control levels. Mice injected with HgCl2 (2.5 mumol/kg) were used to study the effect of DDC (diethyldithiocarbamate), disulfiram (fungicide), TMTDS or CS2 on heavy metal distribution. Brain levels of Hg were significantly increased in mice given DDC or TMTDS. Disulfiram and CS2 increased brain levels marginally. Pregnant rats exposed to HgCl2 (0.5 mumol/kg) were also included in the studies. Treatment with DDC (0.5 mmol/kg) immediately after Hg injection increased maternal brain concentration of Hg considerably, as measured after 24 and 78 h. Kidney levels were also increased. In the fetuses, the brain and liver levers were transiently increased after treatment with diethyldithiocarbamate. The neurotoxicity of diethyldithiocarbamate and other thiocarbamates may be related to changes in heavy metal metabolism.

624

TITLE:

Effect of four thiol-containing chelators on disposition of orally administered mercuric chloride.

AUTHORS:

NIELSEN JB

ANDERSEN O

SOURCE:

HUM EXP TOXICOL; 10 (6). 1991. 423-430.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Acute toxicity and the disposition of inorganic mercury depends on the route of exposure. Most previous studies on effect of chelators on inorganic mercury toxicity and toxicokinetics employed parenteral administration of both metal and chelator. However, the most prominent routes for human inorganic mercury exposure are the oral or pulmonary. BAL was previously considered the drug of choice in human intoxications with most heavy metals. This recommendation has been questioned during recent years due to the advent of the less toxic hydrophilic BAL analogues DMSA and DMPS. The present study, using oral administration of HgCl2 labelled with 203Hg, demonstrates that DMPS is superior to the other chelators in preventing mortality. Moreover, both DMSA and DMPS are superior to BAL and NAPA in alleviating acute toxicity and in preventing the undesirable distribution of orally administered mercury, especially to the brain. Further, oral administration of these chelators were mo

625
TITLE:
Mortality and cancer incidence in chloralkali workers exposed to inorganic mercury.

AUTHORS:
BARREGARD L
SALLSTEN G
JARVHOLM B

SOURCE:
BR J IND MED; 47 (2). 1990. 99-104.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mortality and cancer incidence were studied in men exposed to inorganic mercury at eight Swedish chloralkali plants where individual biological monitoring data were available. Urinary mercury excretion has declined from about 200 mug/l during the 1950s to less than 50 mug/l today. These workers had also been exposed to chlorine and static magnetic fields. At some of the plants there had been a low degree of exposure to asbestos. In total, 1190 men had been monitored for at least one year between 1946 and 1084. Their mortality and cancer incidence were compared with those of the general male population. Mortality from all causes was not significantly increased (rate ratio = 1.1). Cardiovascular mortality was slightly increased (rate ratio = 1.3; 95% CI 1.0-1.5) for no known reason. An excess of lung tumours was seen (rate ratio = 2.0; 95% CI 1.0-3.8), possibly caused by previous exposure to asbestos. Mortality from non-malignant diseases of the brain and the kidneys, the

626
TITLE:
The evaluation of mental functions in workers exposed to metallic mercury, inorganic lead and carbon disulfide.

AUTHORS:
SIKORA A
LANGAUER-LEWOWICKA H

SOURCE:
MED PR; 43 (2). 1992. 109-121.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The aim of the study was to determine the similarities and differences between the groups of dysfunctions detectable using psychyologic tests in workers exposed to metallic mercury, inorganic lead and carbon disulfide. The study groups included male workers examined in the Clinic of Occupational Diseases of the Institute of Occupational

Medicine in Lodz. The subjects were supposed to the chronically intoxicated with Hg (27 persons), Pb (40 persons) and CS2 (40 persons). A wide variety of tests was used to examine reference groups matched appropriately according to sex, age and level of education. The comparative analysis of results showed that the range and extend of a decrease in psychic functions depend on the type of a neurotoxic agent. The most serious disorders (frequently those of organic brain disease type) were found in subjects exposed to CS2. Exposure to metallic mercury resulted in functional disorders of the psychic sphere, while exposure to inorganic lead ca

627

TITLE:

Interactions Of Calcium, Copper, Iron, And Zinc With Methylmercury And Selenium In Guinea Pig Tissues

AUTHORS:

Komsta-Szumska E
Miller DR

SOURCE:

Biological Trace Element Research, Vol. 6, No. 6, pages 507-517, 19 references, 19841984

ABSTRACT:

The effects of methylmercury (22967926) on the metabolism of calcium (7440702), copper (7440508), iron (7439896), and zinc (7440666) were studied in guinea-pigs. Interactions with selenium (7782492) were also examined. Female guinea-pigs were given a total of 10 doses of methylmercury-chloride (115093) at 3 milligrams per kilogram (mg/kg) every other day for 3 weeks with or without 1.0mg/kg sodium-selenite (10102188), an equimolar dose, given 5 hours after each mercury dose. A group of animals received selenium alone while others were not treated. On days 1, 14, and 28, animals were killed and tissue concentrations of calcium, copper, iron, and zinc were determined by atomic absorption spectrophotometry in the red blood cells, plasma, pancreas, spleen, kidney, liver, cerebellum and cerebrum. At 24 hours the highest concentrations of mercury were in the kidney, liver, red blood cells, spleen, cerebrum, pancreas, cerebellum, and plasma, in decreasing order. Calcium concentrations were significantly higher in the cerebrum of animals given mercury alone, while in the cerebellum they were strikingly lower. In animals receiving selenium, calcium in the brain was essentially normal. The spleen also showed calcium elevation when selenium was not given. For copper the pattern observed in the cerebellum and cerebrum was reversed, but these changes persisted when selenium was given. Increases in the kidney and pancreas of copper concentration persisted in the animals given selenium. Iron in the liver was not affected by mercury with or without selenium. Iron in kidney and spleen

was depressed by methylmercury without regard to selenium. Zinc increased in the cerebrum with or without selenium. The authors conclude that changes in concentrations of some essential elements may be involved in the overall mechanisms of toxicity of methylmercury.

628
TITLE:
Fetal methylmercury poisoning: new data on clinical and toxicological aspects.

AUTHORS:
Marsh DO
Myers GJ
Clarkson TW
Amin-Zaki L
Tikriti S

SOURCE:
Trans. Am. Neurol. Assoc. 102: 69-71 1977

ABSTRACT:
PESTAB. A number of children who were exposed to various levels of methylmercury in utero demonstrated neurological defects. Dose-response relationships were determined of fetal methylmercury poisonings by examining peak concentrations of mercury in maternal hair. Of the 29 children examined, three showed severe neurological deficits, with the others demonstrating mild spastic diplegia. Peak hair concentrations of mercury ranged between 112 and 384 ppm in ten mothers. The following abnormalities were present in the children of these ten mothers with the percentage of children so affected listed: early motor retardation, 50%; delayed speech, 70%; mental retardation, 40%; convulsive disorder by history, 30%; extensor plantar responses at age 4-5 yr, 55%; definite neurological signs other than plantars, 40%; small heads, 40%; and short stature, 70%. The degree to which the same affects were noted in children from 15 other mothers with peak hair concentrations of mercury less than 25 ppm was: 0%, 7%, 7%, 0%, 17%, 7%, 13%, and 14%, respectively. These findings demonstrate a dose-response relationship, and indicate that fetal brain damage can be wroght by considerably lower levels of methyl mercury than had previously been thought possible.

629
TITLE:
Ameliorative capacities of vitamins and monothiols administered alone or in combinations in methylmercury mobilisation in nervous and non-nervous tissues of mice.

AUTHORS:
SOOD PP

VIJAYALAKSHMI K
BAPU C

SOURCE:
CELL MOL BIOL (NOISY-LE-GRAND); 39 (2). 1993. 213-219.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The extent of mercury mobilisation was recorded from various tissues (brain, spinal cord, liver and kidney) of male mice administered with a daily dose of methylmercury chloride (1 mg/kg) for seven days. For this purpose 10 groups of animals were intoxicated. Out of these, one group was sacrificed on 8th day and one group was kept without toxicant for another seven days before sacrificing on 15th day. To the rest of the groups were given a daily dose of N-acetyl-DL-homocysteine thiolactone (NAHT), glutathione (GSH), vitamin B Complex and E, applied either alone or in combinations. All these animals were sacrificed on the 15th day. The mercury clearance rate during thiols, vitamins and their coadministration was examined. Study shows that both the vitamins were able to increase mercury elimination from the nervous and non-nervous tissues. Their combination with NAHT was not suitable as mercury level was increased in all the tissues except kidney as compared to NAHT alone

630
TITLE:
Selective determination of inorganic mercury and methylmercury in tissues by continuous flow and cold vapor atomic absorption spectrometry.

AUTHORS:
ATALLAH RH
KALMAN DA

SOURCE:
J ANAL TOXICOL; 17 (2). 1993. 87-92.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A method has been developed for the determination of inorganic (InHg) and methylmercury (MeHg) in solubilized tissues with continuous-flow (flow injection) cold vapor atomic absorption spectrometry. Kidney, liver, and brain tissues were spiked with MeHg and InHg and solubilized at an elevated temperature in a solution containing 90 g NaOH, 2 g/L L-cysteine, and 4 g/L NaCl. Total mercury determination was achieved by continuous-flow cold vapor atomic absorption spectrometry using an inlet system containing a flow through photo-oxidation reactor and sodium borohydride as the mercury reductant. InHg was selectively determined in the presence of MeHg with this method when using stannous chloride as the reductant. MeHg concentrations were computed as the difference between the values obtained from the two analyses. Recoveries

for spiked tissues were above 95% for InHg and MeHg. Quantitation limits for InHg and total mercury in tissues were 0.4 and 0.6 mug/g, respectively. meH

631
TITLE:
Experimental study on the action of EDTA-liposome to remove mercury from the mice given methylmercury chloride.

AUTHORS:
WANG K-L
YANG H-Y
LI Z-C
ET AL

SOURCE:
CHIN J PREV MED; 27 (1). 1993. 13-15.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. It was reported that experimental study on the action of EDTA-Liposome to remove mercury from the mice given methylmercury chloride showed that elimination of methylmercury chloride from brain, testicle, liver, kidney and blood of mice treated by EDTA-Liposome was more significant than that of mice treated by EDTA alone. Mercury level in feces of EDTA-Liposome treated group increased significantly (P < 0.001). The advantages of treatment with EDTA-Liposome were discussed. Applying EDTA-Liposome is an efficient method in therapy of metal poisoning.

632
TITLE:
Mercury, zinc and selenium bioaccumulation in tissues and organs of Mediterranean striped dolphins Stenella coeruleoalba Meyen: Toxicological result of their interaction.

AUTHORS:
AUGIER H
BENKOEL L
CHAMLIAN A
PARK WK
RONNEAU C

SOURCE:
CELL MOL BIOL (NOISY-LE-GRAND); 39 (6). 1993. 621-634.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Neuron activation analysis of 13 Mediterranean striped dolphins Stenella coeruleoalba showed high mercury

and selenium contaminations of main tissues and organs of these cetaceans. The mercuric contents were excessive, particularly in liver (from 68 to 2272 mug/g dry wt. basis), then in kidney, lung, muscle, heart and brain. The selenium concentrations were also high in liver (from 45 to 1320 mug/g dry wt. basis), then in kidney, lung, muscle, skin and heart. The main way of contamination seems to be the food through trophic network, but skin and lung are also able to play a part which must be elucidated. The average Hge ratios in liver and kidney were respectively 1.82 and 1.59. Linear relationship between mercury and selenium concentrations in tissues and organs, particularly in liver and kidney, were confirmed. The mercury and selenium interaction on a toxicological point of view was established by a statistical approach; in the same way, intervention of zinc, metallo

633
TITLE:
Mercury and selenium in Arctic and coastal seals off the coast of Norway.

AUTHORS:
SKAARE JU
DEGRE E
ASPHOLM PE
UGLAND KI

SOURCE:
ENVIRONMENTAL POLLUTION; 85 (2). 1994. 153-160.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury and selenium concentrations (wet weight) have been determined in samples of liver, kidney and brain of' grey seal (Halichoerus grypus), harbour seal (Phoca vitulina), harp seal (Phoca groenlandica) and ringed seal (Phoca hispida) caught along the Norwegian coast, 114 individuals in all. Significant differences have been found in mercury contamination between the 4 species caught in the same coastal area, Jarfjord, located at the north-east of the Norwegian coast close to the Russian border. Very low hepatic mercury levels were found in the arctic species, ringed and harp seals, ranging from 0.20 to 0.67 and 0.04 to 1.0 mug g-1, respectively, while in the coastal seal species the concentrations were 10 to 40 times higher. The corresponding ranges were 0.7 to 48.3 mug g-1 in grey seals and 0.2 to 19.0 mu g-1 in harbour seals. The median values were 13.5 and 0.7 mug g-1, respectively. The highest levels were found in grey seals, indicating that particularly the st

634
TITLE:
Toxicity and residual aspects of alkylmercury fungicides in livestock.

AUTHORS:

Wright FC
Riner JC
Haufler M
Palmer JS
Younger RL

SOURCE:
Hazard Toxic Subst. 2(1): 331-355 1979 (16 References)

ABSTRACT:
PESTAB. Various species of animals were dosed with mercurial fungicides. Signs of poisoning included lack of appetite, loss of weight, muscular incoordination, unstable gait, and lameness. Rapid accumulation of mercury from the fungicides was noted in all species tested. In the blood of cattle and sheep the levels of mercury were inconsisent. The kidney contained the greatest mercury residues in cattle and sheep with lower levels in the liver, muscle and brain. In the chickens and turkeys the greatest concentration was in the liver, followed by the kidney and muscle, when treated with low doses. At higher dose levels the greatest concentration was present in the kidney with lesser amounts in the liver and muscle. Mercury was present for a long period of time in the hair of livestock.

635
TITLE:
Selenium concentrations in brain after exposure to methylmercury: Relations between the inorganic mercury fraction and selenium.

AUTHORS:
BJORKMAN L
MOTTET K
NYLANDER M
VAHTER M
LIND B
FRIBERG L

SOURCE:
ARCHIVES OF TOXICOLOGY; 69 (4). 1995. 228-234.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Three groups of female monkeys (Macaca fascicularis) were exposed to methylmercury (MeHg, p.o. 50 mug Hg/kg body wt per day) for 6, 12, or 18 months. One group was exposed to MeHg for 12 months and kept unexposed for 6 months before sacrifice. Another group of three monkeys was exposed to HgCl2 i.v. for 3 months. Total and inorganic mercury concentrations in occipital pole and thalamus were determined by cold vapor atomic absorption spectroscopy. Selenium concentrations were analyzed by hydride generation atomic absorption spectroscopy. The

results indicated an association between concentrations of inorganic mercury and selenium in both occipital pole and thalamus in the MeHg-exposed animals. A linear regression model using concentrations of inorganic mercury (nmol/g wet wt) as independent variable, and selenium concentrations (nmol/g wet wt) as the dependent variable showed significant correlations between the variables in both occipital pole and thalamus (r = 0.85 and

636
TITLE:
Effects of lead and mercury of histamine uptake by glial and endothelial cells.

AUTHORS:
HUSZTI Z
BALOGH I

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 76 (6). 1995. 339-342.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of lead and mercury on (3H)-histamine uptake by cultured astroglial and endothelial cells of rat brain were studied. Experimental data showed that both metal ions inhibited the uptake in both cell types of concentrations as low as 1-10 muM. The effects were consistent with non/competitive inhibitions. With either lead or mercury exposure, the inhibition of the uptake was greater in astroglial than in cerebral endothelial cells. Contrary to the above findings, 100 muM of mercuric chloride produced stimulation of histamine uptake and this stimulation was much more pronounced in cultured cerebral endothelial cells than in astroglial cells. Inhibition of (3H)-histamine uptake by lead acetate and mercuric chloride was considered to be association with a loss of the transmembrane Na+ and/or K+ gradient while stimulation of the uptake by high concentration of mercury might be related to a direct effect on histamine transporter. It is noteworthy, that cultured astro

637
TITLE:
Selective involvement of large motor neurons in the spinal cord of rats treated with methylmercury.

AUTHORS:
SU M
WAKABAYASHI K
KAKITA A
IKUTA F
TAKAHASHI H

SOURCE:
JOURNAL OF THE NEUROLOGICAL SCIENCES; 156 (1). 1998. 12-17.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury is thought to be a possible epidemiological factor for the pathogenesis of motor neuron disease, since it has been reported that metallic, inorganic and organic mercury causes a syndrome clinically resembling amyotrophic lateral sclerosis. We administered 10 mg/kg/day methylmercury chloride to adult rats for 10 consecutive days. The hind-limbs became flaccid and atrophic, and 14 out of the 34 rats had died by the 18th day after methylmercury treatment began. Light microscopical examination of the large motor neurons in the spinal anterior horn revealed cytoplasmic vacuolation and loss of Nissl substance on the 14th day, and neuronophagia appeared on the 16th day. On the 18th day, the loss of large motor neurons was almost complete, whereas small to medium-sized neurons were preserved. Silver acetate autometallography to detect mercury revealed the selective accumulation of mercury in the large motor neurons. These findings suggest that although a high dose is r

638
TITLE:
Cerebral changes in the course of intoxication with mercury phenylacetate.

AUTHORS:
KOZIK MB
WIGOWSKA-SOWINSKA J

SOURCE:
EXP PATHOL (JENA); 16 (1-6). 1978. 267-275.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A histoenzymic study of cerebral phosphatases and esterases was performed on rats subjected to experimental intoxication with mercury phenylacetate. Following intragastric application of mercury phenylacetate to experimental animals, decreased activities of cerebral ATPase, acP (acid phosphatase) and AChE (acetylcholinesterase) were observed. The intoxicated animals displayed enhanced cerebral TPPase (thiamine pyrophosphatase) and partially also NsChE (nonspecific cholinesterase) activities. Apart from changes in the histoenzymic pattern of the experimental brains, the ingestion of mercury phenylacetate brought about evident morphological changes in form of neuronal vacuolization and spongious degeneration of the white matter. The extent of morphological and histoenzymic alterations was dependent on the duration of the experimental poisoning.

639

TITLE:
Neuroimmunotoxicology: Humoral assessment of neurotoxicity and autoimmune mechanisms.

AUTHORS:
EL-FAWAL H AN
WATERMAN SJ
DE FEO A
SHAMY MY

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 107 (SUPPL. 5). 1999. 767-775.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The interactions between the nervous and immune systems have been recognized in the development of neurodegenerative disease. This can be exploited through detection of the immune response to autoantigens in assessing the neurotoxicity of environmental chemicals. To test this hypothesis, the following questions were addressed. a) Are autoantibodies to nervous system (NS) antigens detected in populations exposed to environmental or occupational chemicals? In sera of male workers exposed to lead or mercury, autoantibodies, primarily IgG, to neuronal cytoskeletal proteins, neurofilaments (NFs), and myelin basic protein (MBP) were prevalent. These findings were confirmed in mice and rats exposed to either metal. b) Do autoantibodies to NS antigens relate to indices of exposure? In humans exposed to either metal, and similarly in exposed rats, titers of IgG against NFs and MBP significantly c orrelated with blood lead or urinary mercury, the typical indices of exposure. c) Do autoantibodies correlate with sensorimotor deficits? In workers exposed to lead or mercury, a significant correlation was observed between IgG titers and subclinical deficits. Doses of metals used in rat exposures were subclinical, suggesting that autoantibodies may be predictive of neurotoxicity. d) Is the detection indicative of nervous system pathology? In rats exposed to metals, histopathology indicated central nervous system (CNS) and peripheral nervous system (PNS) damage. In addition there was evidence of astrogliosis, which is indicative of neuronal damage in the CNS, and the presence of IgG concentrated along the blood-brain barrier, as indicated by immunostaining for antibodies. e) Are immune responses to NS antigens pathogenic? Immunoglobulin fractions from rat and human sera interfered with n euromuscular function. These studies suggest that the detection of autoantibodies to NS-specific antigens may be used to monitor the development of neurotoxicity to environmental chemicals and that immune mechanisms may be involved in the progression of neurodegeneration.

640
TITLE:
Inhibition of Amino Acid Transport and Protein Synthesis by HgCl2 and

Methylmercury in Astrocytes: Selectivity and Reversibility

AUTHORS:
Brookes N
Kristt DA

SOURCE:
Journal of Neurochemistry, Vol. 53, No. 4, pages 1228-1237, 42 references, 1989

ABSTRACT:
The specificity of the effect of mercuric-chloride (7487947) (HgCl2) on glutamate transport in astrocytes was studied by comparing the susceptibility of other well characterized amino acid transport systems, by measuring protein synthesis and examining some morphological correlates of function. Inhibition of amino acid transport by HgCl2 was selective, whereas methylmercury-chloride (115093) was nonselective. A 50 percent inhibitory concentration of HgCl2 for uptake of alpha-aminoisobutyric-acid by system-A, uptake of alpha-aminoisobutyric-acid or kynurenine by a system-L variant, and uptake of gamma-aminobutyric acid were all two to four fold greater than that for the uptake of glutamate. The submicromolar concentrations of HgCl2 which inhibited glutamate transport also inhibited protein synthesis, but in a rapidly reversible fashion, eliciting only discrete ultrastructural changes. Inhibition of protein synthesis by methylmercury-chloride was irreversible after 1 hour and was marked only at concentrations higher than those that elicited gross morphologic change in the form of bleb like swellings. The findings support the hypothesis that intoxication with elemental mercury vapor can produce brain levels of methylmercury that, while not directly lethal to central nervous system cells, may be neurotoxic by virtue of an excitotoxic mechanism resulting from the inhibition of glial inactivation of glutamate. The importance of the inhibition of glutamate uptake by methyl-mercury was less obvious as it occurred only as part of an apparently nonspecific depression of membrane related function at exposure levels which eventually caused the cultures to detach.

641
TITLE:
Reproductive risks of heavy metals and pesticides in women.

AUTHORS:
Gerhard I

SOURCE:
Reproductive Toxicology 1993;:167-83

ABSTRACT:
Contaminants can influence female fertility at every phase of

reproduction. Fluctuation in the neurotransmitters of the brain can be detrimental to the pulsatile secretion of the gonadotropin-releasing hormone (GnRH). Numerous contaminants can be stored in the pituitary (eg, mercury), causing a change in the gonadotropin production. Other substances (eg, mercury and chloro-organic compounds), are deposited in the adrenal cortex, being high in fat content. This can lead to inhibition of various enzymatic systems and as a result higher androgen levels in the blood as well as partial insufficiency of the adrenal cortex. Hyper- and hypothyroidism can be caused by dioxins, polychlorinated biphenyls (PCB), cadmium or lead. Thus the hypothalamic-pituitary-ovarian-axis can be damaged directly by contaminants, but also, indirectly through changes caused in prolactin, adrenal steroid and thyroid hormone secretion. Contaminants stored in the ovary can influence the production of estradiol and progesterone. Toxins can inhibit the normal development of the oocyte and in certain cases can cause chromosomal aberrations. Numerous contaminants also have an adverse effect on the production of male semen. This is shown by a deficient number of sperms with normal motility, in reduced fertilization capability as well as in morphological and chromosomal aberrations in the spermatogenesis, which leads to abortion, stillbirth and congenital malformation. Even if conception occurs in spite of increased parental contamination, these pregnancies have a higher risk of abortion, congenital malformation, placental insufficiency and premature birth.

642

TITLE:

Monoisoamyl ester of DMSA reduces 203Hg(NO3)2 retention in rats: 1. chelation therapy during pregnancy.

AUTHORS:

Blanuãsa M
Prester L
Piasek M
Kostial K
Jones MM
Singh PK

SOURCE:

Journal of Trace Elements in Experimental Medicine 1997;10(3):173-81

ABSTRACT:

In this study, efficacy of monoisoamyl meso-2,3-dimercaptosuccinate (Mi-ADMS) was tested to mobilize mercury in the period of gestation in rats. Its action was compared to meso-2,3-dimercaptosuccinic acid (DMSA). Pregnant dams (in second third of gestation) received a single intravenous injection of 203Hg(NO3)2 and oral chelating therapy with DMSA or Mi-ADMS 0.5, 24, and 48 hours after that. Each chelator was administered in three single doses of 0.5 mmol/kg body weight on three consecutive days. The

fifth day after 203Hg exposure, retentions were measured in whole body organs, and fetuses. Results (expressed as the percentage of 203Hg dose) showed that all retention values among treated animals were lower than in the control group. Significantly higher reduction of whole body gut, liver, kidney, and brain retentions in Mi-ADMS (to 2-5% of control values) than in DMSA-treated groups (to 37-80% of control values) was found. 203Hg retention in uterus, fetuses, and placentae were reduced to 7-8% in Mi-ADMS and to 41-56% of control value in DMSA group. The major routes of 203Hg excretion after DMSA treatment was urine, whereas fecal excretion was the same as that of controls. After Mi-ADMS treatment, both urinary and fecal 203Hg excretions were approximately 2-3 times higher than the control values resulting in the lowest body retention.

643
TITLE:
EFFECTS OF CERTAIN DIETS ON MERCURY EXCRETION AFTER METHYL MERCURY ADMINISTRATION

AUTHORS:
LANDRY TD
DOHERTY RA
GATES AH

SOURCE:
TOXICOL APPL PHARMACOL; 45 (1). 1978 350-351

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MOUSE DIETARY FACTORS MERCURY KINETICS MERCURY-203 BRAIN BLOOD LIVER

644
TITLE:
EEG findings in chlor-alkali workers subjected to low long term exposure to mercury vapour

AUTHORS:
Piikivi L
Tolonen U

SOURCE:
British Journal of Industrial Medicine June 1989, Vol.46, No.6, p.370-375. 19 ref. Illus.

ABSTRACT:
The cerebral effect of long term (mean 15.6, SD 8.9 years) and low (about 25|g/m|3| air) exposure to mercury vapour was studied in a group of 41 workers in a chlor-alkali plant and in a group of matched controls by electroencephalography (EEG). In the visually interpreted EEGs only a

tendency for an increased number of EEG abnormalities, especially focal ones, could be seen in the exposed subjects. In the computerised EEG (cEEG), however, the exposed workers had significantly slower and more attenuated EEGs than the controls. This difference was most prominent in the occipital region, became milder parietally, and was almost absent frontally. Our results suggest that cEEG may show early effects on the brain of exposure to mercury vapour.

645
TITLE:
Distribution and excretion of mercury in rats intoxicated with methylmercury dicyandiamide.

AUTHORS:
Rusiecki W
Osicka A

SOURCE:
Acta Pol. Pharm. 29(6): 623-628; 1972(REF:14)

ABSTRACT:
PESTAB Methylmercury dicyandiamide administered orally at a dose of 34 mg/kg was rapidly absorbed into the blood and tissues of male rats, with levels in blood exceeding those in tissues for 6 days after intoxication. In kidneys a peak average level of 74. 2mug/kg mercury was observed after three days, and constant levels were noted between the 14th and 28th days. The ratio of free to organic mercury gradually increased in this organ as well as in the liver. Brain accumulated mercury more slowly than liver and kidney, and the average peak level was 16. 0 mug/kg. Only 1. 2% and 3. 5% of the dose were excreted in the urine and feces, respectively, within seven days after administration. Benzene extractable metabolites were not found in urine or feces.

646
TITLE:
Accumulation of mercury in tissues of cattle, sheep, and chickens given the mercurial fungicide, Panogen 15, orally.

AUTHORS:
Palmer J
Riner JC
Wright FC

SOURCE:
J. Agr. Food Chem.; 21(3): 414-416; 1973 ; (REF:8)

ABSTRACT:
HAPAB Yearling cattle and sheep and 6-week-old chickens were given daily

oral doses of the mercurial fungicide Panogen 15 (methylmercury dicyandiamide). Cattle and sheep were given 15 mg of the total formulation per kg of body weight daily to 70 days, and chickens were dosed at both 5 and 10 mg/kg daily to 84 days. Two yearling cattle and three yearling sheep were mildly poisoned in the latter stages of the study. Residues of mercury, determined by atomic absorption spectrophotometry, were generally higher in cattle than in sheep except in the liver. The order of increasing residues in both cattle and sheep was brain, muscle, liver, and kidney. With chickens, however, residues in liver were higher than in kidney in both treatment groups. The residues of mercury in the various tissues of the dosed animals could constitute a hazard to future human consumers. Tissues from control cattle, sheep, and chickens contained no detectable amounts of mercury. (Author abstract reprinted by permission of the American Chemical Society)==

647
TITLE:
203-Hg excretion and tissue distribution in Holstein calves following single tracer intravenous doses of methyl mercury chloride or mercuric chloride.

AUTHORS:
STAKE PE
NEATHERY MW
MILLER WJ
GENTRY RP

SOURCE:
J ANIM SCI; 40 (4). 1975 720-726

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Eight male Holstein calves were given a single tracer i.v. dose of 203-Hg as mercuric chloride or methyl mercury chloride 7 days before sacrifice. Total 7-day fecal and urinary 203-Hg excretions were much higher (p less than .01) from mercuric chloride dosing (28.3 and 8.1% of the dose) than from methyl mercury chloride (6.1 and .4% of the dose). Retention of 203-Hg from mercuric chloride was 2-8 times greater (P less than .01) in kidney, liver, spleen, lung, testicle, rib shaft, tibia joint, tibia shaft, abomasum, small intestine, cecum and large intestine and higher (P less than .05) in pancreas. 203-Hg from mercuric chloride was lower (P less than .01) in brain cerebellum and cerebrum, supraspinatus muscle and heart, and substantially lower (P less than .05) in psoas and semitendinosus muscles. Fifteen min after dosing, whole blood 203-Hg was lower (P less than .01) from mercuric chloride followed by a similar rapid clearance for both 203-Hg forms. Throughout the 7-day period, plasma 203-Hg was greater (P less than .01) from mercuric chloride. In red blood cells, 203-Hg from methyl mercury chloride was higher (P less than .01) during the 1st 2 h after dosing, with no

significant differences thereafter.

648
TITLE:
Combined Effects of Mercury and Hexachlorobenzene in the Rat

AUTHORS:
Lecavalier PR
Chu I
Villeneuve D
Valli VE

SOURCE:
Journal of Environmental Science and Health. Part B: Pesticides, Food Contaminants, and Agricultural Wastes, Vol. B29, No. 5, pages 951-961, 13 references, 1994

ABSTRACT:
The combined toxic effects of mercury (7439921) and hexachlorobenzene (118741) (HCB) were studied. Sprague-Dawley-rats were treated once with 400 or 600mg/kg HCB, 10.0 or 12.5mg/kg mercuric-chloride (7487947) (HgCl2), or a combination of the two and hematological, clinical chemistry, histopathological, and tissue residue analyses were conducted after 14 days. Five rats, one treated with the high dose of HCB, one treated with low doses of HCB and HgCl2, one treated with the high dose of HCB plus the low dose of HgCl2, and two treated with the high doses of both compounds died prior to completion of the study. Treatment with HgCl2 or both chemicals resulted in increases in the activity of lactate-dehydrogenase. Those treated with the high doses of HCB, HgCl2, or a combination of both compounds demonstrated increases in serum cholesterol and phosphorus levels. Significant decreases in serum protein and calcium levels were seen in rats treated with the low dose of HgCl2. Significant hematological changes consisting of decreases in the red cell count and hematocrit were seen in rats treated with HgCl2 alone or in combination with the low dose of HCB. The highest tissue concentrations of HCB in singly treated rats were identified in fat, followed by liver, brain, kidney and serum while mercury was primarily found in the kidney. Evidence of pathology was seen in the liver, thyroid, and thymus of rats treated with HCB and in the kidneys of rats treated with HgCl2. The authors conclude that the toxic effects induced by simultaneous exposure to HCB and HgCl2 appear to additive rather than synergistic.

649
TITLE:
Effects of Methyl Mercury on the Cell Cycle of Primary Rat CNS Cells In Vitro

AUTHORS:

Ponce RA
Kavanagh TJ
Mottet NK
Whittaker SG
Faustman EM

SOURCE:
Toxicology and Applied Pharmacology, Vol. 127, No. 1, pages 83-90, 44 references, 1994

ABSTRACT:
The effects of methyl-mercury (22967926) (MeHg) on the proliferation of primary embryonic rat central nervous system (CNS) cells were examined. Cells treated with colchicine served as a positive control for cell proliferation inhibition. Culture medium containing either MeHg, colchicine, or media alone was added to dishes containing CNS cells from embryonic Sprague-Dawley-albino-rats. Cell cycle distribution histograms of control and treated cultures were determined with flow cytometric DNA content analysis at 0, 12, 24 and 30 hours of incubation. MeHg exposure inhibited neutral-red uptake in the micromass cultures in a time and concentration dependent manner. Cells exposed to MeHg showed an increase in the proportion of G2-phase cells with a corresponding decrease in the S-phase population relative to controls. Cultures treated with colchicine showed a significant accumulation of cells in the G2/M-phase of the cell cycle and a decrease in the proportion of cells in the S-phase of the cell cycle. Exposure to 2 micromolar MeHg inhibited cells in the first G2/M phase, while exposure to 4 micromolar led to an inhibition of cell cycling through any phase. Exposure to colchicine produced an arrest in the G2/M-phase similar to that of exposure to MeHg. The authors conclude that MeHg exerts its primary cell cycle effect in G2/M. Cytotoxicity induced by MeHg cannot be attributed to the cell cycle arrest or inhibition alone because at equivalent levels of G2/M phase inhibition MeHg is more cytotoxic than colchicine. The low neuronal cell counts observed in the brains of infants and animals exposed to MeHg in-utero may result from a combination of mitotic inhibition and cytotoxicity.

650
TITLE:
Effect Of Dietary Methionine On Methylmercury And Atrazine Toxicity

AUTHORS:
Meydani M
Hathcock JN

SOURCE:
Drug-Nutrient Interactions, Vol. 2, No. 4, pages 217-233, 47 references, 19841984

ABSTRACT:

The effects of dietary methionine (63683) on the toxicities of methylmercury-hydroxide (1184572) (MEHG) and atrazine (1912249) were studied in rats. Male Wistar-rats were fed diets with methionine at 0, 0.24, and 0.48 percent for 6 days. In an exposure phase they were then given MEHG at 0.5 or 1.5 milligrams per kilogram (mg/kg) in diet with or without atrazine at 500mg/kg or no additional treatment for up to 5 weeks. Urine was collected periodically for the determination of mercapturic acids and mercury (7439976) excretion. At the end of the experiment, animals were killed and the blood, liver, kidney, and brain were collected for the determination of reduced glutathione (GSH) and oxidized glutathione, glutathione-peroxidase, glutathione-reductase (GSHd), glutathione-S-transferase and mercury. Weight gain was used as an index of toxicity. MEHG at either dose resulted in classic signs of toxicity, with reduced weight gain the major symptom. In blood, but not liver, GSH/peroxidase activity declined with the increase in MEHG. Excess methionine at 0.48 percent did not cause toxicosis or alter weight gain compared with those fed the required methionine amount of 0.24 percent. The greatest weight loss was seen in animals receiving MEHG and atrazine together. The protective effect of excess dietary methionine on weight loss was significant in the group receiving MEHG and atrazine in comparison with other diets. Liver GSH/Rd activity was not changed by any treatment. Atrazine lowered GSH/S-transferase activity in the liver. Mercury excretion after 3 weeks and mercapturic acids in urine were increased by atrazine. Mercury deposition in tissues was increased when there was a deficiency of methionine. The authors conclude that an adaptive process in the rat may prevent depletion of tissue GSH during long term administration of a conjugating agent such as atrazine. Dietary methionine may not lessen the increase in MEHG toxicity caused by atrazine at these concentrations.

651

TITLE:

Methylmercury and environmental health.

AUTHORS:

Leong L
Olson B
Cooper R

SOURCE:

J. Environ. Health35(5): 436-442; 1973(REF:21)

ABSTRACT:

PESTAB Organic mercurials, particularly the alkyl type, are now recognized as potentially fatal toxins when released into the environment. They are not metabolized or eliminated rapidly and, unlike inorganic mercury salts, can cross the blood-brain barrier. The compounds may

enter the body through inhalation, dermal absorption or ingestion. Symptoms, which include numbness in hands, feet or lips; ataxia, disturbances in speech, vision, and hearing; and emotional disturbances, may not appear for months. A standard of 10 mg/m(SUP)3 of air has been established for alkyl mercurials in work environments. Incidents of poisoning from consumption of fish containing methyl mercury in Japan have caused several countries to set limits for mercury in fish (about 1 ppm), ban fishing in certain waterways, and seize commercial catches which exceed these limits. The use of mercury seed dressings is being eliminated because of incidents of accidental consumption of treated seed and toxicity to seed-eating birds.

652
TITLE:
FETAL MINAMATA DISEASE. A NEUROPATHOLOGICAL STUDY OF TWO CASES OF INTRAUTERINE INTOXICATION BY A METHYL MERCURY COMPOUND

AUTHORS:
MATSUMOTO H
KOYA G
TAKEUCHI T

SOURCE:
J. NEUROPATHOL. EXP. NEUROL. 1965, 24(4) 563-574

ABSTRACT: EIS: Epidemiology Information System

653
TITLE:
Alterations in neurochemical and behavioral parameters in the mouse induced by low doses of methyl mercury

AUTHORS:
Salvaterra P
Lown B
Morganti J
Massaro E

SOURCE:
Acta Pharmacol. Toxicol.; VOL 33 ISS Sep 1973, P177-190, (REF 51)

ABSTRACT:
IPA COPYRIGHT: ASHP The effects of controlled single doses of methyl mercury (1, 5 and 10 mg./kg.) on mouse behavior in the open field situation were investigated at fixed times post-injection. Selected glycolytic pathway intermediates, alpha-glycerophosphate, adenine nucleotides and phosphocreatine, were monitored to measure biochemical effects. A good correlation between brain biochemistry and behavioral

effects of methyl mercury was observed and the dose response relationship for behavioral tasks correlated with alterations in levels of metabolic intermediates. These correlations are discussed.

654
TITLE:
THE PROTECTIVE POTENCY OF MARINE ANIMAL MEAT AGAINST THE NEUROTOXICITY OF METHYLMERCURY: ITS RELATIONSHIP WITH THE ORGAN DISTRIBUTION OF MERCURY AND SELENIUM IN THE RAT.

AUTHORS:
OHI G
NISHIGAKI S
SEKI H
TAMURA Y
MAKI T
MINOWA K
SHIMAMURA Y
MIZOGUCHI I
INABA Y
TAKIZAWA Y
KAWANISHI Y

SOURCE:
FOOD COSMET. TOXICOL. 1980, 18(2) 139-145

ABSTRACT: EIS: Epidemiology Information System

655
TITLE:
Neuroimmunotoxicology: Humoral assessment of neurotoxicity and autoimmune mechanisms.

AUTHORS:
EL-FAWAL H AN
WATERMAN SJ
DE FEO A
SHAMY MY

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 107 (SUPPL. 5). 1999. 767-775.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The interactions between the nervous and immune systems have been recognized in the development of neurodegenerative disease. This can be exploited through detection of the immune response to autoantigens in assessing the neurotoxicity of environmental chemicals. To test this hypothesis, the following questions

were addressed. a) Are autoantibodies to nervous system (NS) antigens detected in populations exposed to environmental or occupational chemicals? In sera of male workers exposed to lead or mercury, autoantibodies, primarily IgG, to neuronal cytoskeletal proteins, neurofilaments (NFs), and myelin basic protein (MBP) were prevalent. These findings were confirmed in mice and rats exposed to either metal. b) Do autoantibodies to NS antigens relate to indices of exposure? In humans exposed to either metal, and similarly in exposed rats, titers of IgG against NFs and MBP significantly c orrelated with blood lead or urinary mercury, the typical indices of exposure. c) Do autoantibodies correlate with sensorimotor deficits? In workers exposed to lead or mercury, a significant correlation was observed between IgG titers and subclinical deficits. Doses of metals used in rat exposures were subclinical, suggesting that autoantibodies may be predictive of neurotoxicity. d) Is the detection indicative of nervous system pathology? In rats exposed to metals, histopathology indicated central nervous system (CNS) and peripheral nervous system (PNS) damage. In addition there was evidence of astrogliosis, which is indicative of neuronal damage in the CNS, and the presence of IgG concentrated along the blood-brain barrier, as indicated by immunostaining for antibodies. e) Are immune responses to NS antigens pathogenic? Immunoglobulin fractions from rat and human sera interfered with n euromuscular function. These studies suggest that the detection of autoantibodies to NS-specific antigens may be used to monitor the development of neurotoxicity to environmental chemicals and that immune mechanisms may be involved in the progression of neurodegeneration.

656
TITLE:
MERCURY UPTAKE IN-VIVO BY NORMAL AND ACATALASEMIC MICE EXPOSED TO METALLIC MERCURY VAPOR MERCURY-203 AND INJECTED WITH METALLIC MERCURY-203-LABELED MERCURIC CHLORIDE

AUTHORS:
OGATA M
KENMOTSU K
HIROTA N
MEGURO T
AIKOH H

SOURCE:
ARCH ENVIRON HEALTH; 40 (3). 1985. 151-154.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM CATALASE BLOOD-BRAIN BLOOD-LIVER BARRIER CROSSING

657
TITLE:

Psychiatric aspects of methylmercury poisoning.

AUTHORS:
Maghazaji HI

SOURCE:
J. Neurol. Neurosurg. Psychiat.37(8): 954-958; 1974(REF:13)

ABSTRACT:
PESTAB. In early 1972, thousands of cases of mercury poisoning were reported among Iraqi farmers who had ingested grain treated with methylmercury fungicide. Thy psychiatric manifestations exhibited by 43 such persons were studied. Seven percent of these patients presented themselves to the hospital with complaints suggestive of psychiatric disturbances, and 74. 4% of the 43 cases under study were consistently depressed; clinically, the depressive symptoms were mild to moderate in degree. The blood mercury levels of the depressed patients were higher than the average values for the poisoned patients as a whole, and considerably higher than those of the nondepressed patients. Irritability was observed in 44. 2% of the patients, all but one of whom were under 30 years of age. There was general improvement in the mental states of the hospitalized patients. Mercury binding compounds did not seem to significantly enhance recovery from the depressive state. Differences in the metabolism of inorganic and organic mercury in the brain appear to be responsible for the clinical psychiatric manifestations in the corresponding types of poisoningöthe "mad shaky hatter" as opposed to the "ataxic depressed peasant. "

658
TITLE:
Trace metals in man's environment and their determination by atomic absorption spectroscopy.

AUTHORS:
Norval E
Butler LRP

SOURCE:
S. Afr. Med. J. 48(63): 2617-2626; 1974(REF:129)

ABSTRACT:
PESTAB. Mercury poisonings have occurred in persons eating fish contaminated by methylmercury, wheat seed which had been treated with a pesticide, and contaminated meat from hogs which had consumed mercury in waste seed grain. Methylmercury poisoning causes atrophy of the cerebellar granule cells and preferential injury to the calcerine and other cortical regions. Clinical symptoms include numbness of extremities, lips, and tongue; dysarthria; ataxia of the gait; dysphagia;

deafness; and blurred vision. The compounds cross both the placental and the blood-brain barriers. One of the main sources of mercury pollution has been agricultural. However, mercury compounds for use as fungicides and seed preservatives were removed from the market in South Africa in 1974. It is argued that using only obvious neurological dysfunction tests when setting standards for daily intake is not sufficient. Consideration must be given to possible behavioral, biochemical, carcinogenic, or other subtle effects such as lowered intellectual capacity and premature senility as well as to effects detrimental to the fetus. The agricultural uses of arsenic are limited in this country to the use of arsenic compounds in cattle dips and in sprays used in the citrus industry. Chronic arsenic poisoning, whether through ingestion or inhalation, may cause disturbances of the digestive system, the blood, kidney, and nervous system. Chronic poisoning can also cause bronchitis and skin abnormalities including itching, pigmentation, and cancerous changes.

659

TITLE:

Neurobehavioral performance of Czech school children born in years of maximal air pollution (1982-1983).

AUTHORS:

Otto D
Skalik I
Bahboh R
Hudnell K
Sram R

SOURCE:

Neurotoxicology 1997;18(3):903

ABSTRACT:

Ambient levels of SO2, NOx, PAHs and heavy metals are elevated in Northern Bohemia as a result of intensive mining and combustion of brown coal. SO2 levels, a general measure of air pollution, were highest in 1982 and 1983. Sram (1991) hypothecized that in utero exposure to chemicals causes functional changes in the nervous system expressed as developmental disorders or behavioral impairments. To test this hypothesis, tests from the Neurobehavioral Evaluation System (NES2) were administered to 519 7th-grade children from three districts with varying levels of air pollution. Questionnaires were administered to parents and teachers to assess SES, neonatal health history and school performance. Hair and urine samples were also obtained from children to measure arsenic and mercury exposure. Children from Teplice, the heavily polluted mining district, performed more poorly and were referred more often for assessment of learning disorders than children from Prachatice--an agricultural district-- or Znojmo--a district where natural gas is used for heating and

power generation. Digit span and symbol-digit scores also varied significantly with hair As and Hg levels. DISCLAIMER: This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.

660
TITLE:
Prenatal methyl mercury exposure: 1. Alterations in neonatal activity.

AUTHORS:
ECCLES CU
ANNAU Z

SOURCE:
NEUROBEHAV TOXICOL TERATOL; 4 (3). 1982. 371-376.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Pregnant Long-Evans rats were intubated with 0, 5 or 8 mg/kg of methyl mercury on day 8 or 15 of gestation. Maternal weight gain during gestation was reduced significantly only in those animals that had received 8 mg/kg on day 8 of gestation and had resorbed their litters. In litters tht were delivered, the mercury treatment did not affect litter size or weight gain of the pups in the preweaning period. Methyl mercury content of the 1 day old rat brains was directly related to both the dose and time of treatment. Neonatal activity was significantly elevated on postnatal day 4 in rats treated with 5 mg/kg on day 8 of gestation, on postnatal day 8 in the group that received 8 mg/kg on day 8 of gestation, and on postnatal day 8 and 15 in the group that received 5 mg/kg on day 15 of gestation. Neonatal activity measures can be used as sensitive indicators of low prenatal neurotoxic exposures.

661
TITLE:
Adverse health effects of transplacental exposure to environmental pollutants.

AUTHORS:
Grandjean P

SOURCE:
Placenta 1997 Jul/Aug;18(5/6):A3

ABSTRACT:
Case reports and epidemiological studies suggest that prenatal exposure to certain pollutants may cause irreversible damage to the nervous system. The evidence is most extensive regarding lead. For polychlorinated biphenyls, the picture is complicated because of the involvement of several congeners. Although methylmercury has caused severe cases of congenital poisoning due to contaminated fish or flour, the

dose-relationship is unclear. During 1986-1987, we therefore established a cohort of about 1000 Faroese children whose intrauterine methylmercury exposure was determined by analysis of umbilical cord blood and maternal hair. At the age of 7 years, the children were examined to identify and characterize any neurobehavioural changes and their relationship to the mercury exposure. Clinical examination and neurophysiological testing did not reveal any clear-cut mercury-related abnormalities. Neuropsychological tests showed slight dysfunctions that were most pronounced in the domains of language, attention, and memory, and to a lesser extent in visuospatial, and motor functions. The association with mercury remained after adjustment for covariates and after exclusion of children with maternal hair-mercury concentrations above a presumed safe limit of 10 ug/g. Transplacental methylmercury exposure at exposure levels currently considered safe therefore seems to cause detectable neurobehavioural dysfunction.

662

TITLE:

Effects of Inorganic Mercury on (3H)Dopamine Release and Calcium Homeostasis in Rat Striatal Synaptosomes

AUTHORS:

Hare MF
Rezazadeh SM
Cooper GP
Minnema DJ
Michaelson IA

SOURCE:

Toxicology and Applied Pharmacology, Vol. 102, No. 2, pages 316-330, 32 references, 1990

ABSTRACT:

The effects of inorganic mercury (7439976) (Hg+2) on dopamine release and calcium ion (Ca+2) homeostasis were studied in-vitro. Striated synaptosome homogenates prepared from adult male Long-Evans-rats preloaded with tritium (H-3) were incubated with 0 to 5 micromolar (microM) mercuric-chloride (7487947) in a medium containing 0.025 millimolar (mM) Ca+2. The effect of Hg+2 on spontaneous and depolarization dependent dopamine release was determined. A similar experiment was conducted in the presence of 2mM divalent cobalt (7440484) (Co+2) or 100microM cadmium (7440439) ion (Cd+2). Rat striatal synaptosomes were incubated with 0 to 8microM Hg+2 in a medium containing 0.025 or 1.2mM Ca+2 and 0 or 40microM divalent manganese (Mn+2). The effects on intraterminal Ca+2 were examined using fura-2. Synaptosomal integrity was assessed by measuring leakage of lactate-dehydrogenase (LDH), soluble protein, and H-3 labeled deoxyglucose-6-phosphate (dgluP) into the medium. Synaptosomes preloaded with calcium-45 (Ca-45) were treated with 0 to 8microM Hg+2 and 2microM

Co+2 or 100microm Co+2. Hg+2 at 5microM significantly increased spontaneous but not depolarization dependent dopamine release. Co+2 completely blocked the increase induced by 2microM Hg+2. Cd+2 had no effect. Hg+2 had no effect on intraterminal Ca+2 when buffers containing 1.2mM Ca+2 were used. Hg+2 at 4 and 8microM significantly decreased intraterminal Ca+2 when buffers containing 0.025mM Ca+2 were used. Mn+2 significantly increased quenching of the fura-2 probe in the presence of 4 and 8microM Hg+2. Hg+2 at 2microM increased leakage of synaptosomal dgluP into the medium. Leakage of LDH or soluble protein was not affected by Hg+2. Hg+2 inhibited Ca-45 efflux from synaptosomes in a dose related manner. Co+2 countered th effect of Hg+2, whereas Cd+2 increased Ca-45 effux. The authors conclude that Hg+2 increases spontaneous release of dopamine from rat striatal synaptosomes without increasing intraterminal Ca+2.

663

TITLE:

Epileptogenic Effects Of Pure Metals Implanted In Motor Cortex Of Monkeys

AUTHORS:

Chusid JG
Kopeloff LM

SOURCE:

Journal of Applied Physiology, Vol. 17, pages 697-700, 6 references, 19621962

ABSTRACT:

The clinical epileptogenic effects of 26 pure metals were evaluated in Macaca-mulatta-monkeys. Metals were implanted as pellets or as irregularly shaped fragments into the superficial pre central motor cortex of both cerebral hemispheres. Mercury (7439976) was injected intracerebrally 5 to 10 millimeters below the cortical surface. Monkeys were observed for 12 to 23 months and received periodic testing by intramuscular pentamethylenetetrazole, intravenous picrotoxin, and serial electroencephalograms (EEGs). Seizure responses were graded and EEGs were classified by type and degrees of abnormality. Postmortem examinations were made on brains. Metals that were toxic caused death in treated animals, and included nickel (7440020), antimony (7440360), cadmium (7440439), and thallium (7440280). Pentamethylenetetrazole produced seizures in monkeys treated with antimony, nickel, bismuth (7440699), titanium (7440326), cadmium, tantalum (7440257), zirconium (7440677), vanadium (7440622), and aluminum (7429905). Antimony and nickel were the most reactive. Picrotoxin readily produced seizures in monkeys treated with bismuth, and occasionally in monkeys treated with antimony, nickel, tin (7440315), titanium, cadmium, zirconium, gold (7440575), iron (7439896), vanadium, mercury, molybdenum (7439987), and tungsten (7440337). With the majority of metals, meningeal cerebral cicatrix was

seen at the implantation site with a fibrous capsule that enveloped the metal and was incorporated into the meninges. Lead (7439921) pellets migrated down through the frontal lobe. More extensive tissue reactions were seen with nickel, copper (7440508), mercury, antimony, and cadmium. Spike and sharp wave intensities were seen infrequently, usually in association with slow waves, and occurred with silver (7440224), manganese (7439965), aluminum, and silicon (7440213). The authors conclude that most of the 26 metals were well tolerated after implantation.

664

TITLE:

Effects of mercury on wildlife: a comprehensive review.

AUTHORS:

Wolfe MF
Schwarzbach S
Sulaiman RA

SOURCE:

Environ Toxicol Chem 1998;17(2):146-60

ABSTRACT:

Wildlife may be exposed to mercury (Hg) and methylmercury (MeHg) from a variety of environmental sources, including mine tailings, industrial effluent, agricultural drainwater, impoundments, and atmospheric deposition from electric power generation. Terrestrial and aquatic wildlife may be at risk from exposure to waterborne Hg and MeHg. The transformation of inorganic Hg by anaerobic sediment microorganisms in the water column produces MeHg, which bioaccumulates at successive trophic levels in the food chain. If high trophic level feeders, such as piscivorous birds and mammals, ingest sufficient MeHg in prey and drinking water, Hg toxicoses, including damage to nervous, excretory and reproductive systems, result. Currently accepted no observed adverse effect levels (NOAELs) for waterborne Hg in wildlife have been developed from the piscivorous model in which most dietary Hg is in the methyl form. Such models are not applicable to omnivores, insectivores, and other potentially affected groups, and have not incorporated data from other important matrices, such as eggs and muscle. The purpose of this paper is to present a comprehensive review of the Hg literature as it relates to effects on wildlife, including previously understudied groups. We present a critique of the current state of knowledge about effects of Hg on wildlife as an aid to identifying missing information and to planning research needed for conducting a complete assessment of Hg risks to wildlife. This review summarizes the toxicity of Hg to birds and mammals, the mechanisms of Hg toxicity, the measurement of Hg in biota, and interpretation of residue data.

665

TITLE:
Uptake And Distribution In Mice From Ingesting Soluble And Insoluble Mercury Compounds

AUTHORS:
Sin YM
Lim YF
Wong MK

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 31, No. 5, pages 605-612, 7 references, 19831983

ABSTRACT:
The uptake and distribution of mercury (7439976) (Hg) were studied in mice. C3H-mice were fed mercuric-chloride (7487947), mercuric-sulfide (1344485), or Hg containing Chinese laxative pills. Amounts corresponded to 100 micrograms of divalent mercury (14302875) (Hg+2), and administration was 3 times a week for either 2 or 8 weeks. At the end of the study periods, the mice were killed and Hg concentrations in tissues and organs were determined. Selected tissues were examined for histopathological changes. The kidneys and spleen of the mice fed mercuric-chloride contained the highest concentrations of Hg+2. Hg+2 concentrations after 8 weeks of exposure were 3 to 5 times higher than after 2 weeks of exposure. Other organs with significant concentrations of Hg+2 were the liver and brain. Amounts of Hg+2 in the organs and tissues of mice fed mercuric-sulfide were negligible and not significantly different from amounts in controls after 2 or 8 weeks. No significant Hg+2 concentrations were found in any of the organs or tissues in the mice given laxatives. Hg particles accumulated in cortical region veins of the endothelial cells of the kidney, cells of the alveolar walls of the lungs, red pulp of the lungs, and Kupffer and endothelial cells of the liver. No histopathological changes were observed.

666
TITLE:
A Study On The Biochemical And Biological Behavior Of Methylmercury

AUTHORS:
Doi R
Tagawa M

SOURCE:
Toxicology and Applied Pharmacology, Vol. 69, No. 3, pages 407-416, 43 references, 19831983

ABSTRACT:
Distribution and binding of methyl-mercury (MeHg) in erythrocytes were

studied in various species. Blood was obtained from C3H-mice, C57BL/6N-mice, B6C3F1-mice, and ICR-mice, SD-rats, and humans. Erythrocytes were separated, incubated in 5.55 micrograms per milliliter (microg/ml) methylmercuric-chloride (115093) for 60 minutes, and resuspended in bovine serum albumin (BSA) solution. Release of MeHg into BSA solution was determined at intervals to 60 minutes. Other erythrocytes were incubated with 5.55microg/ml MeHg for 30 minutes, then hemolyzed. Gel filtration was performed on stroma free hemolysates, and chromatographic fractions were analyzed for MeHg. Erythrocytes were obtained from the five mouse strains and humans, rats, goats, dogs, rabbits, and chickens. Hemoglobin was diluted to a 10 micromolar (microM) solution and incubated for 60 minutes with seven serial dilutions of labeled MeHg with a minimum of 5microM. After ultrafiltration, MeHg bound hemoglobin was determined. Release of MeHg from erythrocytes reached maximums of 42 percent in humans, 33 to 37 percent in C57BL-mice and ICR-mice, 18 to 24 percent in B6C3F1-mice and C3H-mice, and 5 percent in SD-rats. The proportion of mercury in the low molecular weight fraction to total mercury was 46 percent in humans, 9 to 29 percent in mice, and 0 percent in SD-rats. Primary binding sites became saturated at lower MeHg concentration and involved cysteinyl residues both outside the alpha 1/beta 1 junction and in the junction. Secondary binding sites occurred only at cysteinyl residues in the junction. There were 2.3 to 8.2 primary binding sites in the various mouse strains; association constants were 9.5 to 30 million for mice, 4.3 to 4.9 million for rats, humans, and goats, and 0.50 to 0.77 million for dogs, rabbits, and chickens. The authors point out that MeHg release rates and distribution in erythrocytes are significantly related to reported blood/brain mercury concentration ratios after MeHg administration.

667

TITLE:

Decreased learning capacity in rats exposed prenatally and postnatally to low doses of mercury.

AUTHORS:

Olson K
Boush GM

SOURCE:

Bull. Environ. Contam. Toxicol. 13(1): 73-79; 1975.(10 references)

ABSTRACT:

PESTAB. Pregnant Holtzman rats and the subsequent offspring were maintained on standard rat chow (controls), on lyophilized, powdered Pacific blue marlin (Makaira ampla) plus rat chow containing 2 ppm mercury per kg diet, or on albacore tuna (Thunnus alalunga) plus rat chow containing 2 ppm total mercury per kg diet. The offspring were tested for swimming ability and righting reflex at 7-17 days of age and for

motivation and maze learning at 45-68 days of age. The marlin-fed rats were significantly smaller than the controls but the three groups did not differ in appearance or age at eye opening. The marlin-fed rats, but not the tuna-fed rats, also showed retarded maturation with respect to swimming behavior and righting reflexes. Similarly, the marlin-fed group showed a significant learning deficit with respect to maze learning in comparison with both the controls and the tuna-fed group. The groups did not differ significantly in the motivational tests. The total mercury concentrations in the brain, kidney, and liver were highest in the tuna-fed group and lowest in the control group, but the organs in the three groups did not differ significantly in terms of weight or morphology. Heavy metal analyses of the tuna and marlin diet revealed a significantly higher concentration of cadmium in the tuna diet, but all heavy metal concentrations were well within allowable minimum daily uptake standards.

668
TITLE:
Mercury contamination of the striped dolphin Stenella coeruleoalba Meyen from the French Mediterranean coasts.

AUTHORS:
AUGIER H
PARK WK
RONNEAU C

SOURCE:
MAR POLLUT BULL; 26 (6). 1993. 306-311.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Total mercury content was determined by neutron activation analysis in tissues and organs of 13 striped dolphins Stenella coeruleoalba Meyen, beached along the French Mediterranean coasts. Analysis showed high values of mercury, with considerable variations according to location and the considered organs or tissues. The highest concentrations were found in the liver (from 68 to 2272 mug g-1 dry wt. basis), then in the lung (from 3 to 396 mug g-1), kidney (from 14 to 341 mug g-1), muscle (from 7 to 155 mug g-1), heart (from 4 to 100 mug g-1) and brain (from 4 to 81 mug g-1). The possible implications of Hg in dolphin death is discussed, and various hypotheses are formulated about the origin of mercury in this sea and its possible uptake by dolphins.

669
TITLE:
The effect of methylmercuric acetate on the rate of disappearance of ethanol from the blood of swine.

AUTHORS:

Coldwell N BBPlatonow

SOURCE:
Toxicol. Appl. Pharmacol.; 14(2), 368-75, 1969; (REF:28)

ABSTRACT:
HAPAB The effect of methylmercuric-203 acetate (MMA) was investigated in relation to ethanol metabolism in and disappearance from the pig liver in vivo, as well as the effect of ethanol on mercury distribution and elimination. Male Yorkshire breed piglets, about 14 kg, in three groups received 1 g/kg i.p. 20% ethanol in aqueous solution plus intracardiac adminstration of 1.5 mg/kg of buffered saline solution, the same i.p. ethanol dosage plus an intracardiac MMA dose equal to 5 mg/kg mercury in buffered saline, or the same intracardiac MMA dose plus 5 ml/kg water i.p. Blood specimens by cardiac puncture were collected at various minute and hourly intervals up to 6 hr post-injection when the animals were sacrificed by decapitation. Mercury accumulation was highest in the kidneys and liver and lowest (in descending order) in the spleen, heart, muscles and brain; ethanol did not affect mercury tissue distribution or its rate of disappearance from the blood. Blood levels of ethanol (administered alone) peaked at 30 min and remained constant for 30 min when ethanol disappeared at a rate of about 16 mg %/ hr; in the presence of MMA, ethanol blood level peaked in 30 min but were 2.4 times higher than those of controls and in 15 min they dropped sharply, disappearing at a constant rate of about 23 mg %/hr. No ethanol was detected in the blood of piglets given MMA. Blood acetaldehyde levels remained quite constant throughout the experiment and appeared unaffected by either ethanol or MMA. From the data, it appears that MMA effects some change, presently unknown, which favors more rapid blood absorption of ethanol and/or a change in the body distribution of ethanol which, in turn, favors increased blood ethanol levels. If this MMA effect is non-specific, it could be used in the study of the pharmacodynamics of drug compartmentalization in laboratory animals. TOXICOLOGY AND PHARMACOLOGY 69/08/00, 272 1969

670
TITLE:
Effects of Neonatal Methylmercury Exposure on Development of Nucleic Acids and Proteins in Rat Brain: Regional Specificity.

AUTHORS:
Slotkin TA
Pachman S
Kavlock RJ
Bartolome J

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 04, 1986

ABSTRACT:

TD3: Exposure of neonatal rats to methylmercury (1 or 2.5 mg/kg SC daily) during the preweaning period caused regionally-specific alterations in DNA, RNA and protein content in brain. In midbrain + brainstem, where neuronal replication and differentiation conclude early, reduced DNA content was prominent at either dose and was apparent well before evidence of general body growth impairment; small deficits in protein content and brain region weight were seen. In contrast, cerebral cortex showed an elevation of DNA in the high dose group and a tendency toward supranormal RNA values at either dose. Journal article, Sponsored by Health Effects Research Lab., Research Triangle Park, NC.

671

TITLE:

Uptake of 203Hg2+ in the olfactory system in pike.

AUTHORS:

BORG-NECZAK K

TJALVE H

SOURCE:

TOXICOLOGY LETTERS (SHANNON); 84 (2). 1996. 107-112.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Inorganic mercury (203Hg2+) was applied to the olfactory chambers or was given i.v. to pike (Esox lucius) and the uptake of the metal in the olfactory system and the brain was examined by autoradiography and gamma spectrometry. Application of 203Hg2+ in the olfactory chambers resulted in an accumulation of the metal in the olfactory nerves and the anterior parts of the olfactory bulbs of the brain. The levels of 203Hg2+ in other brain areas, such as the telencephalon, the optic tecti and the cerebellum, remained low. Application of 203Hg2+ in only one olfactory chamber resulted in an uptake of the metal only in the ipsilateral olfactory nerve and olfactory bulb. Intravenous injection of the 203Hg2+ resulted in a labelling of the olfactory system and the brain, which was much lower than of the blood. These results indicate that the 203Hg2+ is taken up in the olfactory neurones from the olfactory receptor cells in the olfactory rosettes and is transported to the terminal

672

TITLE:

Localization of gamma-glutamylcysteine synthetase mRNA expression in mouse brain following methylmercury treatment using reverse transcription in situ PCR amplification.

AUTHORS:

LI S
THOMPSON SA
WOODS JS

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 140 (1). 1996. 180-187.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In previous studies we reported that prolonged treatment of rats with subtoxic levels of mercury as methymercury hydroxide (MMH) elicited a two- to three-fold increase in renal glutathione (GSH) content and a three- to fourfold increase in the mRNA encoding the catalytically active heavy subunit of gamma-glutamylcysteine synthetase (GCS), the rate-limiting enzyme in GSH synthesis. Since methylmercury is a potent neurotoxicant, we investigated the effect of methylmercury treatment on GSH synthesi and the distribution of GCS mRNA expression in the brain. Male C57B1/6 mice were treated for 3 consecutive days with MMH (3 mg/kg/day, ip). GSH levels in whole brains were increased by twofold 24 hr following the first injection and remained elevated two to three times control levels after two subsequent MMH treatments. Concomitantly, whole brain GCS mRNA levels were increased 2.7-fold 24 hr after the third MMH treatment. Reverse transcription in situ PCR amplification of GCS hea

673
TITLE:
Metallothioneins in brain-The role in physiology and pathology.

AUTHORS:
ASCHNER M
CHERIAN MG
KLAASSEN CD
PALMITER RD
ERICKSON JC
BUSH AI

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 142 (2). 1997. 229-242.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A symposium on the role of brain metallothioneins (MTs) in physiology and pathology was held at the 1996 Annual Society of Toxicology Meeting in Anaheim, California. The objectives of this symposium were to: (1) review the physiologic function of MTs, (2) examine the distribution of brain MTs with particular emphasis on cell-specific localization (neurons vs neuroglia), (3) discuss MT gene responsiveness upon toxic insult with metals, and (4) discuss the potential role of MTs in the etiology of neurodegenerative disorders. Dr.

Cherian discussed the biochemical properties of the MTs, emphasizing structural similarities and differences between the MTs. Dr. Klaassen addressed the expression and distribution of the MTs in brains with special reference to the cell-specific localization of MTs. Dr. Aschner provided data illustrating a potential role for MTs in attenuating the cytotoxicity caused by methylmercury (MeHg) in cultured neonatal astrocytes. Dr. Palmiter discussed t

674
TITLE:
Methylmercury Chloride-Induced and Antagonist-Reverted Succinic Dehydrogenase Changes in the Brain and Trigeminal Ganglia of the Ra

AUTHORS:
Unnikumar KR
Sood PP

SOURCE:
Environmental Research, Vol. 43, No. 1, pages 39-47, 26 references, 19871987

ABSTRACT:
The effect of methylmercury-chloride (115093) (MMC) on the succinic-dehydrogenase (SDH) activity of the forebrain, midbrain, hindbrain, and trigeminal ganglia of young, healthy, male albino-rats was investigated. Forty animals received a dose of 10mg/kg body weight MMC for 2, 7, or 15 days administered by subcutaneous injection. Two separate groups received subcutaneous injections of the chelating agents, N-acetyl-dl-homocysteine-thiolactone (1195160) (NAHTL) or 2,3-dimercaptosuccinic-acid (2418146) (DMSA) at a dose of 40mg/kg in addition to MMC treatment. Another experimental group received MMC treatment for 7 days followed by antagonist treatment for 7 days. The SDH activity of brain and ganglion homogenates was determined by formazan formation. Animals treated with MMC showed a time and dose related inhibition of SDH activity. NAHTL treatment after MMC treatment restored SDH activity, but simultaneous administration of NAHTL resulted in restored enzyme activity only after prolonged treatment at a high dose (15 days, 600mg/kg total dose). DMSA had minimal effects on restoring enzyme activity. All MMC induced effects were significantly greater in the hindbrain than in the forebrain or midbrain. Trigeminal ganglia showed a greater level of MMC induced SDH inhibition than any of the brain areas, and NAHTL administration restored enzyme activity for all treatment regimes. The authors conclude that DMSA would not act as an antidote to methylmercury poisoning in humans.

675
TITLE:
Studies of the In Vitro Effect of Methylmercury Chloride on Rat Brain

Neurotransmitter Enzymes

AUTHORS:
Kung M-P
Kostyniak P
Olson J
Malone M
Roth JA

SOURCE:
Journal of Applied Toxicology, Vol. 7, No. 2, pages 119-121, 21 references, 19871987

ABSTRACT:
The in-vitro effect of methylmercury-chloride (115093) (MM) on the enzymatic activities of the brain marker enzymes choline-acetyltransferase, glutamic-acid-decarboxylase, 2',3'-cyclic-nucleotide-phosphohydrolase, glutamine-synthetase, and enolase was assessed. Whole brain homogenates were prepared from male Sprague-Dawley-rats weighing between 200 and 220 grams. The homogenates were preincubated with various concentrations of MM at room temperature for 15 minutes immediately preceding enzyme determination. The reversibility of MM induced enzyme alterations was investigated by adding dithiothreitol to the preincubation medium and incubating for another 10 minutes prior to enzyme determination. Sodium-thioglycolate was used to assess the reversibility of MM induced effects on choline-acetyltransferase activity. Concentrations of up to 100 micromolar MM had no effect on glutamine-synthetase activity. Decreases in enzyme activity were observed for choline-acetyltransferase, cyclic-nucleotide-phosphohydrolase, glutamic-acid-decarboxylase, and enolase at a dose of 100 micromolar MM. The addition of dithiothreitol or sodium-thioglycolate to the preincubation medium restored enzyme activity to normal following exposure to MM. The authors suggest that MM may interact with essential thiol groups on the inhibited enzymes.

676
TITLE:
MECHANISMS OF MEHG NEUROTOXICITY DURING DEVELOPMENT

AUTHORS:
REUHL KR

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Development of the mammalian brain proceeds via a series of carefully regulated steps; interference with any of these steps has

profound consequences on normal development. Critical to normal morphogenesis is precise temporal expression of cell adhesion molecules (CAMs) and of cytoskeletal modifications which are hallmarks of these steps. Data obtained during the previous funding period indicate that while microtubules are susceptible to methylmercury (MeHg), CAMs are also critically vulnerable to MeHg at specific developmental stages. There is also clear evidence that targeting of CAMs by MeHg leads to an interruption of the essential functional linkage between cell adhesion molecules and the cytoskeleton. Since the nature of impaired brain morphogenesis reflects the developmental step disrupted, and CAMs are differentially expressed at the various stages, it is hypothesized that disturbance of brain development by MeHg is caused by perturbation of CAMs at critical stages or "windows" of neural morphogenesis. The relationships between MeHg, CAMs, and CAM-cytoskeletal linkages will be investigated by addressing the following specific aims: 1) To determine if MeHg acts directly on CAMs, or via CAM biosynthesis, to differentlally alter the expression and function of CAMs at particular developmental stages. 2) To ascertain the mechanism by which MeHg disturbs the linkage between CAMs and cytoskeleton. 3) To develop a model which permits experimental control of CAM expression (using cDNA transfection techniques) to examine critical susceptibilities of CAMs to MeHg and subsequent influences on cytoskeleton. This project represents the first systematic study of the effects of a toxic metal on CAMs during brain development. The specific aims will be addressed using a combination of contemporary molecular and cellular techniques applied to models at the cell (cell culture), tissue (hippocampal or cerebellar slice), and whole animal levels of organization. Members of the calcium-dependent (N-cadherin) and calcium-independent (NCAM, L1) families of CAMs will be examined to determine the effects of MeHg on their expression and modulation, and the integrity of their linkage to cytoskeleton. Immunofluorescence and immunohistochemical microscopy, in situ hybridization, immunoblot analysis, quantitative ELISA, and functional binding assays will be used to provide overlapping approaches to unravelling MeHg-CAM interactions. Finally, the relationship between CAMs and cytoskeleton under normal and toxicant-conditions will be determined in cultured neurons and in 3T3 fibroblasts transfected to express specific CAMs prior to and following chemical perturbation of specific cytoskeletal elements.

677

TITLE:

Behavioral changes in rats following inhalation of mercury vapor.

AUTHORS:

KISHI R

SOURCE:

HOKKAIDO J MED SCI; 53 (6). 1978 (RECD. 1979). 477-488.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Critical brain Hg concentrations associated with specific behavioral changes during exposure to Hg vapor were determined. Rats exposed to 3 mg of Hg/m3 for 3 h, 5 days/wk, for 15-42 wk, showed a decline in conditioned avoidance response. The latency of escape response also increased in pole climb shock escape. The time to the onset of effects varied from 12-39 wk among 14 rats exposed to Hg. All rats recovered to preexposure baseline within 12 wk after the termination of exposure. A significantly poor behavioral performance was noticed in rats with brain Hg concentration oforal recovery was seen when the Hg concentrations decreased to 10 mug Hg/g brain tissue. The critical concentration of inorganic Hg in the brain associated with behavioral changes in the rat rangesHg, the nervous tissues of rats in this experiment with Hg vapor intoxication were normal.

678

TITLE:

From gene to brain.

AUTHORS:

Abel EL

SOURCE:

Behavioral Teratogenesis and Behavioral Mutagenesis 1989;:89-134

679

TITLE:

MECHANISMS OF MEHG NEUROTOXICITY DURING DEVELOPMENT

AUTHORS:

REUHL KR

SOURCE:

Crisp Data Base National Institutes Of Health

ABSTRACT:

RPROJ Development of the brain procedes by a complex and regulated series of morphogenetic steps, disturbance of which results in injury ranging from retardation to gross malformations. The long-term goal of these studies is to better understand the mechanisms by which toxic compounds interfere with brain development. To study these processes, advantage will be taken of the well-recognized developmental neurotoxicity of methylmercury (MeHg). MeHg arrests neuronal migration and inhibits maturation of post-migratory neurons. The hypotheses to be tested are: 1) MeHg damages the microtubular cytoskeleton of neurons and glia, thereby disturbing neural-glial interactions required for neuronal migration and maturation, and 2) MeHg independently perturbs the expression and/or

function of cell adhesion molecules (CAMs) essential for cell migration, aggregation, and differentiation. These hypotheses will be tested using an embryonal carcinoma (EC) cell culture model of differentiating neuroectoderm, murine cerebellar slices in culture, and mice treated with MeHg in vivo. The relative sensitivities to MeHg of microtubules undergoing post-transnational modifications will be studied using indirect immunofluorescence microscopy. Data from the culture system will be compared with MeHg-induced microtubule injury in murine cerebellar explants and in cerebella of postnatally-exposed mice. The relationships between microtubule disassembly, neuronal migration, and neurite formation will be established. In parallel studies, the effects of MeHg on the appearance and function of major CAMs will be assessed in differentiating EC cells, cerebellar explants, and in vivo. The dose-dependent effects of MeHg on cell migration in the EC and cerebellar explant systems will be assessed by time-lapse photomicroscopy, and correlated with microtubule and CAM staining. CAMs will be identified in cultures and in cerebellum sections by immunofluorescence microscopy and by SDS-PAGE. These studies will: 1) determine the relative sensitivities of different classes of interphase microtubules in neurons and astroglia to MeHg-induced disassembly, 2) correlate the pattern of microtubule damage and reversibility with effects on neuron migration and maturation, 3) determine whether function of neuronal and/or glial CAMs is impaired by MeHg, and 4) determine whether CAM involvement contributes to MeHg-induced brain injury.

680
TITLE:
Inorganic vs. organic Hg toxicity in growing rats: Protection by dietary Se but not Zn.

AUTHORS:
JOHNSON SL
POND WG

SOURCE:
NUTR REP INT; 9 (2). 1974 135-147

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Three forms of dietary Hg were tested for interaction with dietary Se and Zn. Se reduced the toxicity of all 3 Hg compounds, reversing the reduction in growth rate. Liver Hg was increased by Se or Zn fed with phenyl Hg. Kidney Se was increased by all 3 Hg compounds. Methyl Hg decreased liver Se while increasing muscle and brain Se. All 3 Hg compounds decreased brain Zn, methyl Hg having the greatest effect. HgCl2 and phenyl Hg increased muscle Zn. Phenyl Hg also increased kidney Zn. Overall, methyl Hg had the greatest number of significant effects, depsite its much lower dosage, 25 ppm in the diet compared to 320 ppm for HgCl2 and phenyl Hg. The most striking

interaction was the effect of methyl Hg on increasing brain Se and Decreasing brain Zn.

681
TITLE:
Tactile-Kinesthetic System of Rats as an Animal Model for Minimal Brain Dysfunction

AUTHORS:
Elsner J

SOURCE:
Archives of Toxicology, Vol. 65, No. 6, pages 465-473, 38 reference, 1991

ABSTRACT:
An operant paradigm was developed for the specific assessment of the tactile kinesthetic system in female Wistar-rats. Prior to pairing, the average daily intake of methylmercury-chloride (115093) amounted to 0.15 to 0.16mg/kg for the lower concentration and 0.43 to 0.48mg/kg for the higher concentration. During gestation these daily doses were 0.10 to 0.23 and 0.31 to 0.64mg/kg respectively and during lactation they were 0.27 to 0.47 and 0.6 to 1.19mg/kg respectively. Two male and two female pups were selected at random for the recording of ultrasonic vocalizations at days 3, 5, 7, 9, 11, 13, and 15. Rats were trained in discrete trials to press a force sensitive level during at least 1 second between two force thresholds of 60 and 80 grams without any feedback other than the rat's own tactile kinesthetic perception. Offspring of rat dams exposed to 1.5 and 5 milligrams/liter methylmercury-chloride in their drinking water from 2 weeks prior to pairing until weaning exhibited a clear performance deficit. Moreover they revealed a dose dependent increase in the percentage of responses in which the force exerted exceeded the upper threshold. The differential reinforcement of force range schedule is proposed as a sensitive tool in experimental behavior teratology for the preclinical assessment of minimal brain dysfunction hazards.

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TITLE:
MECHANISMS OF MEHG NEUROTOXICITY DURING DEVELOPMENT

AUTHORS:
REUHL KR

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Development of the brain procedes by a complex and regulated series of morphogenetic steps, disturbance of which results in injury ranging

from retardation to gross malformations. The long-term goal of these studies is to better understand the mechanisms by which toxic compounds interfere with brain development. To study these processes, advantage will be taken of the well-recognized developmental neurotoxicity of methylmercury (MeHg). MeHg arrests neuronal migration and inhibits maturation of post-migratory neurons. The hypotheses to be tested are: 1) MeHg damages the microtubular cytoskeleton of neurons and glia, thereby disturbing neural-glial interactions required for neuronal migration and maturation, and 2) MeHg independently perturbs the expression and/or function of cell adhesion molecules (CAMs) essential for cell migration, aggregation, and differentiation. These hypotheses will be tested using an embryonal carcinoma (EC) cell culture model of differentiating neuroectoderm, murine cerebellar slices in culture, and mice treated with MeHg in vivo. The relative sensitivities to MeHg of microtubules undergoing post-transnational modifications will be studied using indirect immunofluorescence microscopy. Data from the culture system will be compared with MeHg-induced microtubule injury in murine cerebellar explants and in cerebella of postnatally-exposed mice. The relationships between microtubule disassembly, neuronal migration, and neurite formation will be established. In parallel studies, the effects of MeHg on the appearance and function of major CAMs will be assessed in differentiating EC cells, cerebellar explants, and in vivo. The dose-dependent effects of MeHg on cell migration in the EC and cerebellar explant systems will be assessed by time-lapse photomicroscopy, and correlated with microtubule and CAM staining. CAMs will be identified in cultures and in cerebellum sections by immunofluorescence microscopy and by SDS-PAGE. These studies will: 1) determine the relative sensitivities of different classes of interphase microtubules in neurons and astroglia to MeHg-induced disassembly, 2) correlate the pattern of microtubule damage and reversibility with effects on neuron migration and maturation, 3) determine whether function of neuronal and/or glial CAMs is impaired by MeHg, and 4) determine whether CAM involvement contributes to MeHg-induced brain injury.

683

TITLE:

Methylmercury-Thiol Uptake into Cultured Brain Capillary Endothelial Cells on Amino Acid System L

AUTHORS:

Mokrzan EM
Kerper LE
Ballatori N
Clarkson TW

SOURCE:

Journal of Pharmacology and Experimental Therapeutics, Vol. 272, No. 3, pages 1277-1284, 42 references, 1995

ABSTRACT:

The kinetics and inhibition of methylmercury-L-cysteine (MeHg-L-cysteine) uptake by calf brain endothelial cells were studied to gain insight on how methylmercury (22967926) (MeHg) crosses the blood/brain barrier. Amino acid transport function in cultured cells was determined by the uptake of tritiated L-leucine with a Michaelis constant (Km) of 127 micromolar (microM) and a maximum velocity (Vmax) of 50 picomole per microgram (pmol/microg) DNA per 30 seconds (sec). Uptake was saturable, insensitive to the presence of sodium ion (Na+) or gamma-methylaminoisobutyric-acid (MeAIB), and was inhibited by 2-amino-2-norbornanecarboxylic-acid (BCH). Cells were exposed to 5microM MeHg-L-cysteine or methylmercury-D-cysteine (MeHg-D-cysteine) in the presence of a large excess of the appropriate enantiomer. Temperature dependent and stereospecific uptake exhibiting Michaelis-Menten kinetics was seen for MeHg-L-cysteine. Eadie Hofstee transformation was performed on the data to give an observed Km of 234microM and a Vmax of 57pmol/microg/15sec. The uptake of MeHg-L-cysteine was inhibited by BCH, L-leucine, L-valine, and L-phenylalanine. MeHg-L-cysteine uptake was not affected by Na+, MeAIB, D-glucose or negatively charged L-glutamate. Uptake of tritiated L-leucine was significantly inhibited by MeHg-L-cysteine, modestly inhibited by MeHg-D-cysteine, and unaffected by methylmercury-N-acetyl-L-cysteine and methylmercury-dimercaptopropane. Uptake of methylmercury-DL-homocysteine was slightly lower than uptake of MeHg-L-cysteine while uptakes of the MeHg complexes of N-acetyl-L-cysteine, dimercaptosuccinic-acid and glutathione were significantly lower. The authors conclude that MeHg as MeHg-L-cysteine is transported into brain capillary endothelial cells by the L-carrier.

684

TITLE:

The kinetics of methylmercury administered repeatedly to rats.

AUTHORS:

MAGOS L
BUTLER WH

SOURCE:

ARCH TOXICOL; 35 (1). 1976 25-39

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Female rats (65-75 days old) were given orally 0.84 or 3.36 mg Hg/kg as methylmercury chloride (MeHgC1) 5 times a wk for 13 and 3 wk, respectively. The proportion of inorganic to total Hg remained as low as 6% in the whole animal though it increased to above 40% in the kidneys. Differences in organ half times and the negative correlation with time for blood to liver, brain and kidney Hg ratios indicated more than 1 compartment for MeHg plus. The brain had a 26-day

half time with a 32% final equilibrium concentration in relation to the body concentrations. Brain concentrations of Hg reported on rats dosed repeatedly with MeHg plus agreed with these values, which justifies their use when experiments are planned to give a certain brain MeHg plus concentration. Half time for the whole body was 34 days but pathological changes-weight loss, tubular damage, slow gastrointestinal passage-disturbed the accumulation curves in the higher dose group. Blood to kidney ratio and uptake of MeHg plus by kidneys also changed significantly.

685

TITLE:

Methylmercury-Induced Changes In The Activities Of Neurotransmitter Enzymes In Nervous Tissues Of The Rat

AUTHORS:

Omata S
Hirakawa E
Daimon Y
Uchiyama M
Nakashita H
Horigome T
Sugano I
Sugano H

SOURCE:

Archives of Toxicology, Vol. 51, No. 4, pages 285-294, 35 references, 19821982

ABSTRACT:

Methylmercury (22967926) (MM) induced changes in the activities of neurotransmitter enzymes were studied in rats. Female Wistar-rats were injected subcutaneously daily with 10 milligrams per kilogram of methylmercury-chloride (115093) (MMC). At selected times, animals were killed and the brain, dorsal root ganglia, and peripheral nerves were excised and assayed for acetylcholinesterase (ACE), choline-acetyltransferase (CAT), tyrosine-hydroxylase (TH), and monoamine-oxidase (MOA) activities. The same nervous tissues were removed from untreated rats and incubated with MMC in unspecified doses. The MMC concentrations required to inhibit ACE, CAT, or MOA activity by 50 percent were determined. MMC caused decreases in CAT activity in the cytosol and synaptosomal fractions of the brain. ACE brain activity was only slightly affected. TH and MOA activities were elevated in the brain, especially in the synaptosomal fractions. MMC caused significant decreases of ACE activity in the dorsal root and CAT activity in the sciatic nerve. The in-vitro concentrations of MMC required to cause inhibition of ACE, CAT, TH, and MOA were much higher than those observed in-vivo. The authors conclude that MM considerably alters the normal pattern of

neurotransmitter metabolism in the nervous system of rats by affecting the neurotransmitter enzyme activities and receptors.

686
TITLE:
NEUROTOXICANT EFFECTS ON CELL CYCLE REGULATION OF NEUROGENESIS

AUTHORS:
CICCO-BLOOM ED

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
DESCRIPTION (provided by applicant) The investigators hypothesize that neurotoxic metals and teratogens disrupt neurogenesis in developing forebrain and hindbrain systems in vitro and in vivo, acting to inhibit proliferation by altering mitogenic growth factor receptors and cell cycles signaling pathways. There are increasing numbers of children who experience problems with learning, social interactions, and self-regulation, and exhibit difficulties with fine and gross motor control. Normal brain development depends on interactions among multiple factors including those from genetic, neurochemical, biochemical, social, and environmental sources. Significantly, recent studies indicate that environmental toxicants injure the developing brain, potentially contributing to cognitive and motor deficits. Toxicants affecting the brain, neurotoxicants, may act at multiple time windows, eliciting immediate stage-dependent effects in specific systems that influence subsequent ontogenetic processes as well. However, while negative effects of neurotoxicants on cell migration, differentiation, and survival have been well-characterized, little is known about the effects on the generation of neurons (neurgenesis) and underlying pathogenetic mechanisms. As child neurologists, the investigators frequently evaluate children for abnormal brain development in clinic, concerned about attention, learning, behavior, and autism spectrum disorders. Further, as a member of the Scientific Advisory Board of the National Alliance for Autism Research (NAAR), a community family advocacy organization, they provide targeted basic and clinical research support. This current proposal represents a new direction for basic research in the investigators laboratory, which has focused on defining mechanisms that control generation of distinct neuronal populations from dividing precursors. Previously, they examined both positive and negative regulators of precursor proliferation in the developing nervous system, defining growth factor and neuropeptide effects in culture and in vivo. Further, they employed neuronal populations in forebrain and hindbrain regions involved in learning, memory and motor functions in the fetus as well as the developing postnatal animal. Based on extensive studies, the investigators now turn attention to the effects of well-characterized

neurotoxicants, including lead and mercury, and model teratogen, valproic acid, on neurogenesis in the embryo and the newborn, defining mediating mitogenic and cell cycle pathways and designing new model systems.

687
TITLE:
Distribution and biotransformation of methyl mercuric chloride in different tissues of mice.

AUTHORS:
MEHRA M
CHOI BH

SOURCE:
ACTA PHARMACOL TOXICOL; 49 (1). 1981. 28-37.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Distribution of 203Hg radioactivity was studied in various organs of adult male and female mice 1 h to 21 days after treating with 203Hg-labeled methyl mercuric chloride (MMC). The amount of methyl mercury (MeHg) and inorganic Hg was also determined by injecting single doses of non-radioactive MMC and measuring total, organic and inorganic Hg content by atomic absorption technique. Photoemulsion histochemical method (PEHM) was used to demonstrate localization of Hg grains in various cellular compartments of organs and tissues. The highest levels of radioactivity were attained at 7 h post-treatment in all organs except brain and testis. The testis showed the highest radioactivity at 1 day and the brain at 2 days post-treatment. MeHg persisted in brain over a longer period but the level was not as high. The content of MeHg and inorganic Hg was maximum in kidneys compared to other organs. The brain and reproductive organs contained the least amount of inorganic Hg. By PEHM, Hg grains were most prominently observed in the sinusoids, Kupfer cells, hepatic cells and bile duct epithelium of liver in the lumen of blood vessels, convoluted and collecting tubules of kidneys and in gastrointestinal epithelium. The pattern of uptake and distribution of MeHg correlated well with the morphological demonstration of Hg grains in tissue sections.

688
TITLE:
Distinctions Of Radioprotective Effect Of Acute Hypoxia On 5-Day-Old Mice Preadapted To Oxygen Deficiency

AUTHORS:
Aytmagambetova BZ
Vygodskaya AL
Korogodina YuV
Petrosyan EP

Yarmonenko SP

SOURCE:
Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina, No. 4, pages 50-54, 24 references, 19781978

ABSTRACT:
The effect of hypoxia on radiation sensitivity was studied in mice. CBA57Bl-mice of varying age (neonate to 8 weeks) were exposed to a hypoxic atmosphere (5 percent oxygen and 95 percent nitrogen). Oxygen partial pressure in the brain and resistance to anoxia, evaluated as the time to death, were measured. Five day old mice exposed to air or the hypoxic atmosphere were irradiated with 0 to 1,200 rads of gamma radiation from a cesium-137 source. Twenty four hours later, the animals were killed and the brain and spleen were removed. Radiation injury was assessed by determining the number of surviving cells in the external granular layer of the cerebellar cortex and the number of surviving splenocytes. Low oxygen partial pressures occurred in the brain of neonatal mice and persisted for up to 2 weeks. Thereafter, the oxygen partial pressure increased, reaching 40 millimeters of mercury by the age of 6 weeks. Resistance to anoxia significantly decreased with age. The decrease occurred prior to elevation of the oxygen partial pressure. Hypoxia demonstrated no radioprotective effect as measured by the number of surviving cerebellar cortex cells. In the spleen, however, there was twice as many splenocytes in mice exposed to 400 and 1,200 rads radiation under hypoxic conditions than in animals exposed to the same doses in air. The authors suggest that the effect of hypoxia on radiosensitivity is not limited to the physical diffusion of oxygen in tissues, but also depends on physiological processes. (Russian)

689
TITLE:
The Hypertensive Response To Soman And Its Relation To Brain Acetylcholinesterase Inhibition

AUTHORS:
Brezenoff HE
McGee J
Knight V

SOURCE:
Acta Pharmacologica et Toxicologica, Vol. 55, No. 4, pages 270-277, 23 references, 19841984

ABSTRACT:
Cardiovascular effects of soman (96640) were investigated in Sprague-Dawley-rats. Blood pressures were recorded in cannulated, anesthetized rats. Various doses of soman were injected by a cannula

inserted into the left jugular vein. Heart rate was monitored. Intracerebroventricular injections were performed through a cannula inserted below the cortex. Acetylcholinesterase (AChE) activity was determined in several brain regions. Brain tissue homogenates were prepared and absorbance was measured. Intravenous injections of soman evoked dose related increases in blood pressure having a very deep slope; the range of responses from threshold to maximum was covered by doses from 10 to 40 micrograms per kilogram (microg/kg). Acute median lethal dose (LD50) varied between 35 and 45microg/kg. Increases in blood pressure of 40 to 70 millimeters of mercury (mm HG) were seen in animals that survived the acute LD50 dose. Heart rates increased in a dose related manner, but the effect was highly variable, with a maximum increase of 58 beats per minute after 35microg/kg soman. Doses required to produce equivalent pressor responses by various routes were: intravenous, 40microg/kg; intramuscular, 50microg/kg; subcutaneous, 70microg/kg; intraperitoneal, 190microg/kg; and intracerebroventricular, 24microg/kg. At less than 70 percent inhibition of AChE, no increase in blood pressure was seen. There was a close correlation between magnitude of pressor response and degree of AChE inhibition in brain stem, cortex, hippocampus, and hypothalamus. The authors conclude that soman increases blood pressure by a central action. Increases in blood pressure produced by cholinesterase inhibitors is not important in determining survival

690
TITLE:
REGULATION OF METAL UPTAKE AND DISTRIBUTION WITHIN BRAIN

AUTHORS:
SMITH QR

SOURCE:
WURTMAN, R. J. AND J. J. WURTMAN (ED.). NUTRITION AND THE BRAIN, VOL. 8. ESSENTIAL FATTY ACIDS AND CHOLINE IN DIETARY LIPIDS: UPTAKE OF ESSENTIAL METALS IN THE BRAIN AND THE BEHAVIORAL EFFECTS OF METAL IMBALANCES: PHARMACOLOGY OF SEROTONINERGIC APPETITE-SUPPRESSANT DRUGS. XI+203P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-88167-628-4.; 0 (0). 1990. 25-74.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM REVIEW BLOOD-BRAIN BARRIER DIET TOXICITY

691
TITLE:
Clinical-morphological changes and diagnosis of poisoning by mercurial preparations in animals.

AUTHORS:
Tishkov AI

SOURCE:
Veterinariya (Moscow) 1: 96-97; 1976.

ABSTRACT:
PESTAB. Four-month-old cocks were fed granosan (0.1 g/day) and/or agrosan (0.1 g/day) for 8-16 day in a study on the toxicity of mercurials. An initial hyperexcitability was followed by depression, asthenia, tremor, paresis, paralysis, blindness, anorexia, hypersalivation, emesis, diarrhea, and cyanosis. Stomatitis, pharyngitis, esophagitis, leukocytosis, thromobocytopenia, reduced serum protein level, and inflammatory, dystrophic, and necrotic changes in the liver, kidneys, and brain were found. Mercury was found in the liver, kidneys, myocardium, skeletal muscles, spleen, esophagus, trachea, lungs, brain, bones, gastrointestinal tract, pancreas, blood, skin, feathers, and testes. Mercury levels of 0.001-0.049 mg% were found in the internal organs of albino mice, guinea pigs and rabbits fed aerial parts of wheat and barley plants grown from seeds dressed with agrosan for 6 months.

692
TITLE:
Milk transfer and tissue uptake of mercury in suckling offspring after exposure of lactating maternal guinea pigs to inorganic or methylmercury.

AUTHORS:
YOSHIDA M
WATANABE C
SATOH H
KISHIMOTO T
YAMAMURA Y

SOURCE:
ARCHIVES OF TOXICOLOGY; 68 (3). 1994. 174-178.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Maternal guinea pigs were injected with mercuric chloride (HgCl2; 1 mg Hg/kg body weight) or methylmercury (MeHg; 1 mg Hg/kg) 12 h after parturition, and exposure of the offspring to mercury (Hg) via breast milk were studied on days 3, 5 and 10 postpartum. Milk Hg concentrations were lower than maternal plasma Hg concentrations regardless of the form of Hg given to the dams. Milk Hg was higher in HgCl2-treated dams than in MeHg-treated dams. In MeHg-treated dams, MeHg was separately determined. While the ratio of MeHg to T-Hg decreased in the dams' plasma, it did not in the milk. There was a strong correlation between milk and plasma T-Hg concentrations in HgCl2 treated dams. In the milk of MeHg-treated dams, the plasma MeHg concentrations correlated better than did the plasma T-Hg concentrations. In the offspring, regardless of the chemical forms of Hg given to the dams, the highest Hg

concentrations were found in the kidney, followed by the liver and the brain. Brain

693
TITLE:
Experimental studies of organic mercury poisoning; the behavior of the Minamata disease casual agent in maternal bodies and its transfer to their infants via either placenta or breast milk.

AUTHORS:
Fujita E

SOURCE:
J. Kumamoto Med. Soc.; 4391), 47-62, 1969; (REF:45)

ABSTRACT:
HAPAB Methyl methylmercuric sulfide considered one of the causal agents of minamata disease, was separately labeled at the sulfur (S) and mercury (Hg) atoms. Each radioactive agent was given orally to pregnant rats in a daily dose of 1 mg/100 g of body weight. The results were as follow. Direct proof was obtained by autoradiography of neonates and suckling rats that the S and Hg of the tested agent were able to penetrate either through the placenta or into the maternal milk. Indirect evidence of this transfer of the agent from the maternal milk. Indirect evidence of this transfer of the agent from the maternal body to the infant was the various disturbances of postnatal development, including dwarf inhibition and neurological disorders. Four factors led to the decutions that the S-Hg bond was dissociated in the maternal body relatively soon after oral ingestion and that both the inorganic sulfate and the mercuric compound without S were tranferred from the maternal body to the infant. These were: 1) a confirmed difference in S and Hg distribution in various tissues of the adult rats; 2) Hg retention was more marked in adult rats in the blood corpuscles than in the plasma; 3) S was excreted in the urine of adult rats mostly as inorganic sulfate, with only traces of organic S Compounds; and 4) S distribution in the autoradiograms of body slices of newborn rats differed from that of Hg. Hg retention was marked in the blood corpuscles but not as much so in the brain tissue of adult rats, as expected. Hg retention in brain tissue was more in the case of long-term administration of small doses of the tested agent (until the onset of neurological signs) than in the case of a single, large dose of the agent. The mercuric compound in the blood corpuscles was bound to hemoglobin but it was easily released from the globin fraction by adding TCA. (Author abstract edited) TOXICOLOGY AND PHARMACOLOGY 69/11/00, 393 1969

694
TITLE:
Changes of Activity and Ultrastructural Localization of Alkaline

Phosphatase in Cerebral Cortical microvessels of Rat After Single Intraperitoneal Administration of Mercuric Chloride.

AUTHORS:
ALBRECHT J
SZUMANSKA G
GADAMSKI R
GAJKOWSKA B

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 897-902.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Inorganic mercury salts administered systemically at low mg/ml doses produce neurotoxic effects without penetrating the cerebral microvascular endothelial cells which form the blood-brain barrier (BBB). This phenomenon promoted investigations testing a hypothesis relating inorganic mercury-induced brain dysfunction to its interference with the BBB transport. In the present study, we tested the effect of a single i.p. administration of mercuric chloride (MC) (6 mg/kg body weight) on the activity and ultrastructural localization of cerebral alkaline phosphatase (AP), a cerebromicrovascular marker enzyme primarily located on luminal plasmalemma of endothelial cells. At 1 h after MC administration, light microscopy revealed a virtual absence of AP in cerebral cortical layers II and III, and its dramatic reduction in the remaining layers. Electron microscopy confirmed the disappearance of the AP reaction product from luminal endothelial cell membranes, and luminal plasmalemm

695
TITLE:
Cellular Respiration During High-Altitude Adaptation Of Rats

AUTHORS:
Dedukhova VI
Mokhova YeN

SOURCE:
Kosmicheskaya Biologiya i Meditsina, Vol. 5, No. 2, pages 31-38, 14 references, 19711971

ABSTRACT:
The effect of high altitude adaptation on cellular respiration was investigated in rats. White-rats were placed into a pressure chamber 6 hours per day for periods of either 20 or 40 days. Pressures within this chamber initially simulated an altitude of 3,500 meters (m), although the majority of the research was conducted at a simulated altitude of 7,000m. Following exposure, all test animals were sacrificed, with the brain being

extracted and immersed in a homogenization medium. Brain homogenates were prepared from the hemispheres alone and were subjected to electron microscope analysis. Cerebral homogenates were also incubated in order to facilitate polarographic registry. An additional study was made of respiration in rat liver mitochondria. Following 12 days of exposure to simulated altitudes ranging from 3,000 to 7,000m, adapted animals exhibited an increase in erythrocyte counts and hemoglobin volumes, together with an increased tolerance to low barometric pressures. Respiration values were inhibited to a greater extent in the mitochondria of experimental animals than in controls. The authors conclude that the decrease observed in oxygen consumption at a pressure of 11 millimeters of mercury is evidently attributable to the reduction of partial oxygen pressure values below 0.1 millimeter of mercury as distance from the sample surface increases, accompanied by a marked decrease in respiration rates. It is further concluded that no changes occur in the oxidation and oxidative phosphorylation systems of tissue mitochondria during high altitude adaptation. The authors recommend that experiments involving the longer residence of test animals at high altitudes, together with the performance of a subsequent comparison between tissue adaptation characteristics and degree of adaptation, be carried out for the purpose of studying the oxidation and oxidative phosphorylation of tissue mitochondria in-vivo. (Russian)

696

TITLE:

Effects of mercury on serotonin concentration in the brain of tilapia, Oreochromis mossambicus.

AUTHORS:

TSAI C-L
JANG T-H
WANG L-H

SOURCE:

NEUROSCIENCE LETTERS; 184 (3). 1995. 208-211.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. In order to know the effect of mercury pollution on the serotonergic system of fish, serotonin concentrations in a discrete brain region of tilapia, Oreochromis mossambicus, were examined. Serotonin concentration was measured using a high performance liquid chromatography system with electrochemical detector. In male fish, the concentrations of serotonin were 1,468 | 0.350, 0.811 | 0.190 and 0.330 | 0.061 mug/g wet tissue in hypothalamus, telencephalon and optic lobe, respectively. The serotonin content was significantly different between each region; the hypothalamus had a higher content than that of the telencephalon and optic lobe. The serotonin concentration in female hypothalamus was 1.102 | 0.112 mug/g wet tissue which was significantly

lower than that in males. However, serotonin concentration in the telencephalon and optic lobe showed no difference between male and female. After exposure to 0.015 and 0.03 ppm HgCl2 for 6 months beginning 7 days posthatching, mal

697
TITLE:
Methyl mercury inhibition of synaptosome and brain slice protein synthesis: In vivo and in vitro studies.

AUTHORS:
VERITY MA
BROWN WJ
CHEUNG M
CZER G

SOURCE:
J NEUROCHEM; 29 (4). 1977 673-680

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Subacute methyl mercury (MeHg) intoxication was induced in adult rats following the daily intragastric administration of 1 mg MeHg/100 g body wt. Decreased (14C)leucine incorporation into cerebral and cerebellar slice protein was found. Weight loss occurred during the latent and neurotoxic phases but pair feeding did not reveal a significant defect in amino acid incorporation into slice protein. There was no decline in synaptosome protein synthesis in vitro during the latent phase but a significant decline in cerebellar and cerebral synaptosome synthesis was found during the neurotoxic phase. MeHg in vitro inhibited cerebral slice and synaptosome protein synthesis at half maximal concentrations of 7.5 and 12.5 muM, respectively. Inhibition of synthesis in synaptosomes was non-competitive with Ki of 4ne or (14C)proline uptake into synaptosomes. There was no significant inhibition of synaptosome basal ATPase or Na + K ATPase at concentrations of MeHg (12 muM) giving half maximal inhibition of protein synthesis. No preferential inhibition of the chloramphenicol (55S) or cycloheximide sensitive components of synaptosome fraction protein synthesis was found, suggesting that the inhibition is common to both mitochondrial and extramitochondrial protein synthesizing systems. Addition of nucleotides and/or atractylate failed to influence protein synthesis and did not reverse the MeHg inhibition. Mannitol, as a replacement for the predominant cation species of the incubation medium, gave 40% inhibition of protein synthesis in the control but protected against further inhibition by MeHg.

698
TITLE:
Effect of long-term sodium selenite supplementation on levels and distribution of mercury in blood, rain and kidneys of methyl

mercury-exposed female mice.

AUTHORS:
GLYNN AW
LIND Y

SOURCE:
PHARMACOLOGY & TOXICOLOGY; 77 (1). 1995. 41-47.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Female Balb/c CA mice were supplemented for seven weeks with 0, 0.6 and 3 p.p.m. Se in tap water and were then exposed to a single oral dose of Me203 Hg (2 mumol/kg). Se supplementation continued for 56 days after MeHg dosage. Supplemented animals showed enhanced activity of glutathione peroxidase in the blood. Twenty-four hr after MeHg dosage, the level and distribution of Hg in blood, blood cells, and kidneys were not influenced by Se exposure. However, in the brain the Hg accumulation was increased and Hg distribution was altered by Se supplementation. Fifty-six days after MeHg dosage, 70% to 80% of the dose had been eliminated from the body, and the brain of the 3 p.p.m. group still had a higher Hg level than the control group. Otherwise, there was no consistent effect of Se supplementation on retention of Hg in the animals. It is indicated that Se influences tissue accumulation and intracellular distribution of Hg through tissue-specific mechanisms rather than thro

699
TITLE:
ASSESSMENT OF THE CENTRAL NERVOUS SYSTEM IN PATIENTS UNDERGOING CHRONIC EXPOSURE TO MERCURY COMPOUNDS

AUTHORS:
OBARA M

SOURCE:
1996 ANNUAL MEETING OF THE NORTH AMERICAN CONGRESS OF CLINICAL TOXICOLOGY, PORTLAND, OREGON, USA, OCTOBER 10-15, 1996. JOURNAL OF TOXICOLOGY CLINICAL TOXICOLOGY; 34 (5). 1996. 589.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER HUMAN PATIENT TOXICOLOGY MERCURY COMPOUNDS HEAVY METALS CHRONIC EXPOSURE BLOOD
BRAIN CENTRAL NERVOUS SYSTEM DYSFUNCTION NEUROLOGY PSYCHOORGANIC SYNDROME
COMPUTED TOMOGRAPHY NEUROPSYCHOLOGICAL EXAMINATIONS PSYCHIATRIC EXAMINATIONS BRAIN ATROPHY NEUROPSYCHOLOGICAL CHANGES POLLUTION TOXICITY NERVOUS SYSTEM DISEASE BEHAVIORAL AND MENTAL DISORDERS DIAGNOSTIC METHOD

DIAGNOSTIC METHODS

700
TITLE:
Mercury-induced lipid peroxidation in the liver, kidney, brain and gills of a fresh water fish, Channa punctatus.

AUTHORS:
RANA S VS
SINGH R
VERMA S

SOURCE:
JAPANESE JOURNAL OF ICHTHYOLOGY; 42 (3-4). 1995. 255-259.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Simultaneous lipid peroxidation and oxidative stress were examined in the liver, kidney, brain and gills of a fresh-water fish, Channa punctatus, after 30 days treatment with inorganic mercury. Although longer exposure caused greater oxidative stress, the degree/rate of injury varied in different organs. Short exposures resulted in increased reduced glutathione (GSH), but longer exposures reduced in all the tissues. The results suggested that the rate of lipid peroxidation did not strictly correspond to oxidative stress. Time dependent effects may represent an early biochemical response, although, the presence of some labile GSH-dependent factors may provide a protective mechanism.

701
TITLE:
Interaction of mercury compounds with muscarinic receptor subtypes in the rat brain.

AUTHORS:
CASTOLDI AF
CANDURA SM
COSTA P
MANZO L
COSTA LG

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 17 (3-4). 1996. 735-741.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The in vitro effects of mercuric chloride (HgCl2) and methylmercury (CH3HgOH) on the M1 and M2 muscarinic receptor subtypes were investigated in rat brain cortical membranes. HgCl2 and CH3HgOH were almost equipotent in inhibiting the binding of (3H)telenzepine to M1 receptors (IC50s = 2.2 and 3.4 muM, respectively).

Conversely, HgCl2 was a thirty-fold more potent inhibitor of (3H)AF-DX 384 binding to M2 sites than CH3HgOH (IC50s = 5 and 149 muM, respectively). In all cases HgCl2 showed steep and monophasic inhibition curves, whereas those of CH3HgOH were biphasic (M1) or shallow (M2). CH3HgOH-induced inhibition of both (3H)telenzepine and (3H)AF-DX 384 binding was of the competitive type, while HgCl2 caused a pronounced reduction of the Bmax value associated with a small change in affinity. CH3HgOH also decreased the affinity of the agonist carbachol for M1 and M2 receptors, while inorganic mercury had minimal effects on the carbachol dose-response curves. These result

702
TITLE:
Studies on membrane permeability. With special reference to the effects of methyl mercury.

AUTHORS:
PEKKANEN TJ

SOURCE:
BOOK; 1971 (RECD 1972) 30

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Membrane permeability studies based on 5 papers from investigations by the author are reviewed. The investigations cover the effect of autolysis at 37 degrees C on acid phosphatase distribution in bovine liver, the effect of bacterial contamination on acid phosphatase distribution during 24 hr autolysis at 37 degrees C in bovine liver slices, and the stability of total acid phosphatase activity in bovine liver at 37 degrees and 4 degrees C. The effects of experimental methyl mercury poisoning on the distribution of acid phosphatase during autolysis in cat liver, on the number of sulfhydryl groups in the rat brain, liver and muscle, on the glucose content of rat erythrocytes, plasma, muscle tissue and liver and on the activity of the TPNH-specific glutathione reductase of rat brain and liver are described. The book contains a detailed review of these investigations, including material used, methods, results, discussion, and general conclusions. A list of references is included.

703
TITLE:
MERCURY TOXICITY AND THE BLOOD-BRAIN FACTOR

AUTHORS:
BARRON DJ

SOURCE:
Crisp Data Base National Institutes Of Health

704
TITLE:
Residues of organochlorine pesticides, polychlorinated biphenyls, and mercury and autopsy data for bald eagles, 1969 and 1970.

AUTHORS:
BELISLE AA
REICHEL WL
LOCKE LN
LAMONT TG
MULHERN BM
PROUTY RM
DE WOLF RB
CROMARTIE E

SOURCE:
PESTIC MONIT J; 6 (3). 1972 (RECD 1973) 133-138

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Thirty-nine bald eagles (Haliaeetus leucocephalus) found sick or dead in 13 States during 1969 and 1970 were analyzed for pesticide residues. Residues of DDE, dieldrin, ploychlorinated biphenyls (PCB's) and mercury were detected in all bald eagle carcasses; DDD residues were defected in 38; DDT, heptachlor epoxide, and dichlorobenzophenone (DCBP) were detected less frequently. Six eagles contained possible lethal levels of dieldrin in the brain, and 1 contained a lethal concentration of DDE (385 ppm) in the brain together with 235 ppm of PCB's. Autopsy revealed that 18 bald eagles were illegally shot; other causes of death were impact injuries, electrocution, emaciation, and infectious diseases.

705
TITLE:
MERCURY TOXICITY AND THE BLOOD-BRAIN FACTOR

AUTHORS:
BARRON DJ

SOURCE:
Crisp Data Base National Institutes Of Health

706
TITLE:
Suppression of Aminoacyladenylate Synthesis by Methyl Mercury In Vitro and In Vivo

AUTHORS:

Kuznetsov DA
Zavijalov NV
Govorkov AV
Richter V

SOURCE:
Toxicology Letters, Vol. 36, No. 2, pages 161-165, 15 references, 19871987

ABSTRACT:
The effect of methyl-mercury (22967926) (MeHg) on the formation of aminoacyladenylates (AAA) was studied in-vivo using male Wistar-rats. The rats were injected intraperitoneally with 50 nanomoles MeHg per gram body weight, and 24 hours later injected with a mixture containing equal amounts of carbon-14 labelled L-amino acids including leucine, serine, lysine, histidine, phenylalanine, and aspartic-acid. The animals were sacrificed 2.5 hours after injection of the labelled amino acids, and the adenylation of the amino acids in brain tissue was examined. Addition of MeHg to an in-vitro system of rat brain homogenate inhibited only the seryl and histidyl types of AAAs. Administration of MeHg in-vivo resulted in a strong inhibition of adenylation of all of the six amino acids studied. The adenylation process was reduced by 75 to 80 percent for all six amino acids following the in-vivo administration of MeHg. The authors concluded that an ATP deficiency induced by the in-vivo administration of MeHg was responsible for the similarity of inhibition among all the amino acids tested and suggested that the nonselective inhibition of phosphorylation processes represented a major molecular mechanism of toxic MeHg effects in-vivo.

707
TITLE:
Central nervous system intoxication from mercurous chloride laxatives

AUTHORS:
Davis LE
Wands JR
Weiss SA
Price DL
Girling EF

SOURCE:
Arch. Neurol. (Chicago); VOL 30 ISS May 1974, P428-431, (REF)

ABSTRACT:
IPA COPYRIGHT: ASHP Two patients developed dementia, erethism, colitis, and renal failure following the chronic ingestion of a laxative containing calomel (mercurous chloride). Brains of both patients showed loss of cerebellar granular cells. Histochemical stains demonstrated mercury granules within the cytoplasm of neurons, particularly those of the

inferior olive and dentate nucleus, and in the choroid plexus. Electron microscopy showed ultradense particles in the basement membrane of the choroid plexus; these were similar to but smaller than those in the kidney, shown by electron diffraction analysis to be mercuric sulfide. Tissue mercury levels were elevated in both cases. In 1 patient, the kidney level was 421 mcg./g., and levels from 21 areas within the brain ranged from 105-0.13 mcg./g. Highest levels were in the inferior olive red nucleus, and choroid plexus.

708
TITLE:
DEVELOPMENTAL EFFECTS OF METHYLMERCURY

AUTHORS:
BURBACHER TM

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Methylmercury (MeHg) continues to be a major global environmental problem. The International Program of Chemical Safety lists mercury as one of the six most dangerous chemicals to the world's environment. This competitive renewal application describes a 5 year plan aimed at examining the long-term neurotoxic effects of in utero MeHg exposure using the nonhuman primate and rodent animal model. During the initial 3 years of the plan, operant testing of two groups of adult macaca fascicularis: one exposed in utero to MeHg, the other unexposed controls will take place at the University of Washington to test 2 hypotheses related to the effects of early MeHg exposure on adult memory and visual function. At this time, studies of rodents will be carried out at the University of Rochester to test the hypothesis that lesions induced by in utero exposure to MeHg are exacerbated by CNS changes associated with normal aging. At the end of the three years, the results of the behavioral tests of the primates and the neuroanatomical studies of rodents will be reviewed to direct further studies of the primate colony. For the present plan, the primate colony will be sacrificed at the end of year 3 and studies to test 5 hypotheses related to the long-term neuroanatomical and neurochemical effects of in utero MeHg will be conducted during years 4 and 5. All of the hypotheses that will be tested are based on the results developmental assessments of the MeHg exposed and control macaca fascicularis from our laboratory and from the laboratory of Rice et al. (1989). To test the primate neurobehavioral hypotheses, assessments of Delayed Spatial Alteration, Delayed Nonmatch-to-Sample, and Spatial-and Temporal-Visual Contrast Sensitivity will be used. The primate and rodent neuroanatomical hypotheses will be tested by quantifying brains for cell numbers, cell density, and tissue volume; immunocytochemistry will be used to identify growth-controlling cells and astrocytes, and dendritic development will be

assessed biochemically by assays of MAP2 (primates only) and morphometrically for dendritic pattern and extent. Finally, the primate neurochemical hypotheses will be tested using autoradiographic techniques to evaluate cholinergic neurotransmission in cortical and subcortical areas related to specific memory pathways and catecholaminergic neurotransmission in the hypothalamic-pituitary axis related to the regulation of growth. While previous studies have reported immediate effects following early MeHg exposure in rodents, macaques, and humans, little is currently known regarding the long-term effects of in utero MeHg exposure on adult and aged animals or humans. The proposed nonhuman primate studies make the best use of the valuable monkey colony, because the studies focus on a set of strongly-supported hypotheses using procedures that are readily available for use with humans. The rodent studies will provide the first results regarding the influence of aging o

709
TITLE:
Developmental neurotoxicology.

AUTHORS:
Harry GJ

SOURCE:
Reproductive and Developmental Toxicology 1998;:211-48

710
TITLE:
Blood-brain barrier: physiological and functional considerations.

AUTHORS:
Aschner M

SOURCE:
Handbook of Developmental Neurotoxicology 1998;:339-51

711
TITLE:
Mercury

AUTHORS:
ANON

SOURCE:
Official Publications of the European Communities, 2985 Luxembourg, Grand Duchy of Luxembourg; International Programme on Chemical Safety (IPCS), World Health Organization, 1211 Genáeve 27, Switzerland, 1992. 2p. Illus.

ABSTRACT:

International chemical safety card. Danger symbol: toxic. Short-term exposure effects: delayed effects; skin absorption; irritation of skin; pulmonary oedema; neurotoxic effects (central nervous system). Long-term exposure effects: may have effects on the cardiovascular system, nervous system, and kidneys; may cause birth defects, specifically brain damage. EC identification number and labelling codes: 080-001-00-0; T; R23-33; S7-44. United Nations number and hazard class: UN 2809 (8; 123; III).

712

TITLE:

Methyl Mercuric Chloride Toxicokinetics in Mice. I: Effects of Strain, Sex, Route of Administration and Dose

AUTHORS:

Nielsen JB
Andersen O

SOURCE:

Pharmacology and Toxicology, Vol. 68, No. 3, pages 201-207, 26 references, 1991

ABSTRACT:

The influence of strain, sex, dose, and route of administration on the toxicokinetics of methylmercuric-chloride (115093) (MMC) was studied in mice. Male and female NMRI:Bom-mice (NMRI) and male C57B1/6JBom-mice (C57B1), C3HiFBom-mice (C3H), or CBA/JBom-mice (CBA) were administered 0 to 25.0 micrograms per kilogram mercury-203 (Hg-203) labeled MMC orally or intraperitoneally. Whole body retention of Hg-203 activity was determined through day 14. The mice were killed on day 14 of exposure to determine the tissue distribution of Hg-203 label. Whole body retention curves were almost linear, indicating that the elimination of MMC followed first order kinetics. Whole body retention of Hg-203 did not vary significantly with the route of MMC administration. The Hg-203 body burdens were significantly lower and the half times for elimination were significantly shorter in male than in female mice. MMC dose was significantly, inversely related to whole body retention and half time. In NMRI, the largest amount of Hg-203 was found in the carcass, followed by the liver and kidney. The tissue distribution was not significantly affected by dose or route of administration. The amounts of Hg-203 deposited in the carcass, liver, stomach, intestines, heart, spleen, lungs, and brain of female mice were higher than in male mice. The amount of Hg-203 in the kidneys of female mice was only half that of male mice. Whole body retention of Hg-203 on day 14 in CBA, C57B1, and C3H amounted to 37, 21, and 18% of the dose, respectively. The differences were statistically significant. The half lives for whole body elimination of Hg-203 in CBA, C57B1, and C3H were 9, 6, and 6 days, respectively. Hg-203 deposited in the brain, liver, and kidneys of CBA was significantly higher than in C57B1 and C3H. The amount of Hg-203 in the kidneys of C57B1 was lower

than in CBA and C3H. The amount of Hg-203 deposited in the carcass of CBA-mice was lower than in C57B1 or C3H. The authors conclude that whole body retention and elimination of MMC is significantly affected by dose. Sex and strain also significantly affect whole body retention and elimination half times. The route of administration does not affect the toxicokinetic behavior of MMC.

713
TITLE:
Effects of perinatal exposure to methyl mercury on functional brain development and neurochemistry.

AUTHORS:
SOBOTKA TJ
COOK MP
BRODIE RE

SOURCE:
BIOL PSYCHIATRY; 8 (3). 1974 307-320

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Methyl mercury chloride was administered orally to pregnant rats throughout the period of organogenesis (days 6-15 of pregnancy). Subsequently, indices of development were followed throughout the 4-wk postnatal period and neurochemical changes were determined in the weanling male offspring. No overt signs of neurotoxicity were noted in either the mothers or pups. Subtle changes were effected in the neonatal sequence of development, involving eye opening and neuromotor coordination, as well as in the neurochemical profile (regional brain pseudocholinesterase activity, serotonin and norepinephrine) of the 28-day-old weanlings.

714
TITLE:
Alterations in Gene Expression due to Methylmercury in Central and Peripheral Nervous Tissues of the Rat

AUTHORS:
Omata S
Terui Y
Kasama H
Ichimura T
Horigome T
Sugano H

SOURCE:
Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New

York, pages 223-240, 33 references, 1991

ABSTRACT:

A study was conducted to investigate the changes in genetic expression and possible differences in rates of protein synthesis resulting from exposure to methylmercury (22967926) (MeHg) in the central and peripheral nervous tissues of the rat. Acute MeHg intoxication was produced by administration of 10mg/kg methylmercury-chloride (115093) in female Wistar-rats for 7 days. The animals were killed on day four (early period), day ten (latent period), or on day 15 (symptomatic period). RNA fractions were obtained from brain matter, and polyadenylated (poly(A)+) messenger RNA (mRNA) was translated in a reticulocyte lysate system in the presence of either sulfur-35 labeled methionine or tritiated leucine. Samples were prepared and analyzed by two dimensional electrophoresis and fluorography; protein spots were extracted and subjected to liquid scintillation counting. The effect of MeHg on protein synthesis in the brain was not uniform, since synthetic activities of some protein species were suppressed while others were elevated or unchanged, and the patterns in protein synthetic rates changed during the progress of MeHg intoxication, despite the fact that equal amounts of poly(A)+ mRNA were added to the reaction mixtures for translation and examination. The authors suggest that the impairment of normal nerve functions may be caused by the unusual elevation or decrease of specific protein species due to MeHg exposure.

715

TITLE:

Electron microscopical study of experimentally induced poisoning due to organic mercury compound; mechanism of development of the morbid change.

AUTHORS:

Miyakawa T
Deshimaru M

SOURCE:

Acta Neuropathol; 14(2): 126-36, 1969; (REF:19)

ABSTRACT:

HAPAB Experimental mercury poisoning was induced in rats in order to study the elctron microscopical findings, especially of the granular cells of the cerebellum, with emphasis on the pathogenesis of such morbid changes. Adult male rats of 100 to 110 g were divided into tow eight-member groups of experimental and control animals. The experimental rats were kept on a daily diet of 15 g/rat of pulverized feed mixed with distilled water and 1 mb/rat of methyl methylmercuric sulfide (MMS). Three animals were sacrificed form each group after dosing with MMS at 10 to 11 mg (12th to 13th day) and 13 to 16 mg (19th th 20th days). MMS treatment was stopped on the 20th day. The remaining animals (two per

group) were killed on the 150th day after the beginning of the experiment. Marked cahnges were observed in the granular cells of the cerebellum at the onset of poisoning signs (overall rough fur, loss of hind leg control when walking followed by a crossing phenomenon of the hind legs). Two major cahnges were noted in these cells. There was a streaming out of the intranuclear substance and a coagulation of the nucleus. This slelctive damage to granular cells was characteristic in the initial stages but in animals killed on the 150th day the changes not only involved the cerebellum but also the cerebrum and the brain stem. The changes observed in the blood brain barrier, vascular satellite cells, glia and synapes were mild when compared with those of the granular cells. No specific correlation was made between vascular distrubution or vascular changes and granular cell changes. GENERAL 70/09/00, 391 1969

716
TITLE:
Disruption by Methylmercury of Membrane Excitability and Synaptic Transmission of CA1 Neurons in Hippocampal Slices of the Rat

AUTHORS:
Yuan Y
Atchison WD

SOURCE:
Toxicology and Applied Pharmacology, Vol. 120, No. 2, pages 203-215, 58 references, 1993

ABSTRACT:
The disruption of membrane excitability and synaptic transmission of CA1 neurons by methyl-mercury (22967926) (MeHg) was investigated in hippocampal slices of the rat brain. Electrophysiological recordings were made in the CA1 region hippocampal slices of Sprague-Dawley-rats exposed to 4, 20, 100 and 500 micromolar (microM) MeHg in artificial cerebrospinal fluid (ACSF). Population spike amplitudes, excitatory postsynaptic potentials (EPSPs), and antidromically activated population spikes were measured. Results showed a biphasic effect of MeHg on low frequency stimulated population spikes. Spike amplitudes initially increased, and then decreased or were blocked, depending on the MeHg concentration. At 4microM MeHg, amplitude increase was small but statistically significant, and no decrease occurred for 180 minutes (min). At higher concentrations, both increase and block occurred faster. A similar biphasic increase followed by decrease or complete block was seen for the EPSP amplitudes and antidromically activated population spikes. MeHg free ACSF washes showed that block of population spikes and antidromically activated population spikes were irreversible, or at best, only partially reversible. EPSPs were partially reversible by washing with ACSF, and totally reversible by D-penicillamine (DPen). Long term potentiation (LTP) remained for 2 hours in the absence of MeHg, but when 100microM MeHg

was applied simultaneously with high frequency stimulation, spike amplitudes increased instantly to 160% of control levels, and a further increase of 40% occurred 2min later. By 49 to 50min after application, spikes were blocked. If MeHg was applied 20min prior to high frequency stimulation, spike amplitudes still increased, suggesting that MeHg did not block LTP. Washing with MeHg free ACSF did not prolong maintenance of LTP. The LTP were irreversible or only partially reversible with DPen. The authors conclude that the biphasic alteration of central neuronal membrane excitability and synaptic transmission are similar to that observed at neuromuscular junctions.

717
TITLE:
Chapter 5: Solid Waste Countermeasures, Section III: Pesticide Pollution.)

AUTHORS:
TokyoMetropolitanGovernment

SOURCE:
IN: Tomin o Kogai Kara Boei Suru Keikaku. (Plans for the Protection of Citizens from Public Nuisance)1973, pp. 305-341

ABSTRACT:
PESTAB Persistence of residues after spraying of organochlorine pesticides decreases in the order of DDT, dieldrin, chlordane, heptachlor, aldrin, endrin, and gamma-BHC (lindane). Emulsions produce the highest residue levels, followed by solution and powder forms. When these chemicals are directly applied to soil, they tend to remain in root vegetables. In general, residues remain in the soil for more than three years. Soil residues decrease in the order of dieldrin, gamma-BHC, heptachlor, and aldrin. Organochlorine pesticides generally tend to accumulate in the fat tissues of the body. Alkylmercury compounds accumulate in the brain, especially in the nerve centers for vision and hearing and in the cerebellum. Phenyl mercurials are more likely to accumulate in the liver and kidneys rather than in the brain. This mercury causes inflammation of the skin. Mercury generally remains in the soil for many years. Pesticide residue standards for 28 vegetables are presented in a table.

718
TITLE:
Meso-dimercaptosuccinic acid, a chelating agent for the treatment of mercury poisoning.

AUTHORS:
FRIEDHEIM E
CORVI C

SOURCE:
J PHARM PHARMACOL; 27 (8). 1975 624-626

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Meso-2,3-dimercaptosuccinic acid (DMS) has low toxicity in mice. Compared with penicillamine, DMS in equal doses was consistently more effective in preventing kidney, liver and brain accumulation of Hg. The efficiency of DMS over penicillamine increased in mouse kidneys when the dose of HgCl2 was decreased from 1.0 to 0.1 mg kg--1. With methylmercury bromide, DMS decreased the kidney concentration of Hg with both levels of Hg doses investigated. This effect was present in mice and guinea-pigs. After the injection of 1.0 mg kg--1 methylmercury bromide to mice the brain Hg concentration was decreased 5X more by 2 days of treatment with 100 mg kg--1 DMS than by 2 days of treatment with 100 mg kg--1 penicillamine; this effect was marginal in mice given 2.5 mg kg--1 methylmercury bromide and 2 days of treatment with 250 mg kg--1 DMA or penicillamine, respectively. Even in this case DMS was more effective in decreasing Hg concentrations in kidney and liver.

719
TITLE:
Essential and Toxic Element Concentrations in Fresh and Formalin-Fixed Human Autopsy Tissues

AUTHORS:
Bush VJ
Moyer TP
Batts KP
Parisi JE

SOURCE:
Clinical Chemistry, Vol. 41, No. 2, pages 284-294, 26 references, 1995

ABSTRACT:
A study was conducted to determine whether element concentrations within a tissue type were homogeneously distributed, whether formalin (50000) fixation changed tissue element concentrations, and to establish a reference range for toxic and essential elements in a range of tissue types collected under routine autopsy conditions. Fresh tissue was collected from 30 human subjects at autopsy. Brain, kidney, liver, heart, skeletal muscle, and bone samples were obtained. Each sample was divided into two portions, one of which was digested and analyzed immediately, while the other portion was subjected to formalin fixation. Tissue digests were analyzed using spectrographic, atomic absorption, emission spectrography, neutron activation, and inductively coupled plasma emission spectroscopic methods. The analyses indicated that the distribution of most elements was homogeneous in the brain, liver, and kidney. Long term storage in formalin had little effect on most element concentrations in

tissue; exceptions to this were noted for aluminum (7429905) and manganese (7439965). The kidney and liver had the highest concentrations of the toxic elements such as cadmium (7440439) and mercury (7439976). The essential elements such as calcium (7440702), magnesium (7439954), copper (7440508), iron (7439896), and zinc (7440666) were uniformly distributed throughout all the organs. A reference range was established for calcium, magnesium, iron, copper and zinc, and for the toxic elements aluminum, arsenic (7440382), cadmium, mercury, manganese and lead (7439921) in seven different tissues. There was no more than a ten fold difference in the tissue concentration of the elements studied among the organs, except for the concentration of iron in liver, and calcium and magnesium in bone. The authors note that the findings in this study are consistent with earlier results from other studies.

720

TITLE:

Exposure to Methyl Mercury Results in Serum Autoantibodies to Neurotypic and Gliotypic Proteins

AUTHORS:

El-Fawal HAN
Gong Z
Little AR
Evans HL

SOURCE:

Neurotoxicology, Vol. 17, No. 1, pages 267-276, 51 references, 1996

ABSTRACT:

Induction of autoantibodies by methylmercury (22967926) was studied in rats. Male Fischer-344-rats were administered 0, 16, or 32 parts per million (ppm) methylmercury in their drinking water for 14 days. Selected rats were killed after 7 or 14 day, and the brains and cardiac blood were obtained. The cortex, cerebellum, and hippocampus were dissected out and analyzed for glial-fibrillary-acid-protein (GFAP) as a marker of neurotoxicity using a sandwich enzyme linked immunosorbent assay (ELISA). The serum was analyzed for autoantibodies raised against nerve system proteins using an ELISA developedspecifically for determining neurofilament triplet protein NF68, NF160, and NF200, myelin-basic-protein (MBP), and GFAP immunoglobulin-G (IgG) and immunoglobulin-M (IgM). Rats given 32ppm methylmercury showed significant decreases in body weight starting after 5 days of exposure. Serum NF68, NF160, and NF200, GFAP, and MBP autoantibodies were detected in rats given methylmercury, but not in control rats. Induction of NF68 and GFAP IgM and MBP IgG autoantibodies after 7 days showed a significant dose response relationship. Induction of NF200 IgM autoantibodies showed a significant dose response relationship after 14 days. A trend toward a time response was seen for NF68 and GFAP IgM and NF200 and MBP IgG induction in rats

given 16ppm, but not 32ppm methylmercury. Cerebellar GFAP levels were significantly elevated after 14 day treatment with 16 and 32ppm methylmercury. GFAP levels in the cortex were significantly decreased after 14 day treatment with 32ppm methylmercury. Hippocampal GFAP levels were not affected by methylmercury. The authors conclude that exposure of rats to methylmercury induces serum autoantibodies raised against nervous system proteins. This suggests that assaying autoantibodies raised against nervous system proteins may provide a method for detecting the early neurotoxic effects of methylmercury exposure.

721
TITLE:
Modification of Methylmercury Toxicity by Selenium in the Developing Nervous System.

AUTHORS:
Chang LW

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 04, 1986

ABSTRACT:
TD3: Golden hamsters (Mesocricetus auratus) were used in the study. Pregnant females were injected intraperitoneally (IP) daily with 2.0 mg/kg body weight of methylmercuric chloride and/or sodium selenide on gestational days 10-15. Control animals were injected similarly with equal volumes of saline solution. The transplacental transfer of mercury, the number and size of the pups, the average brain weights of the pups, neuronal migration, and neuropathology in the cerebellum of the pups were analyzed. It was found that methylmercury crossed the placenta readily and accumulated in the fetus, particularly in the fetal brain. Electron microscopy revealed various degenerative changes in the nerve cells, particularly involving the dendritic processes of the neurons. Such neuronal damage appeared to be permanent and still could be found in animals six months after birth. In sum, methylmercury was found to cross the placental barrier very readily and had a detrimental effect on the developing nervous system

722
TITLE:
Development of Adrenergic Receptor Binding Sites in Brain Regions of the Neonatal Rat: Effects of Prenatal or Postnatal Exposure to Methylmercury.

AUTHORS:
Bartolome JV
Kavlock RJ
Cowdery T
Orband-Miller L

Slotkin TA

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 12, 1988

ABSTRACT:
TD3: In order to understand the effects of developmental exposure to methyl/mercury on the ontogeny of synaptic function, the impact of prenatal or postnatal exposure on acquisition of receptor binding sites for norepinephrine was examined. The actions of the mercurial were both regionally - and receptor subtype-selective and depended upon the maturational profile of each region. Alpha 1 and alpha 2 and Beta-receptor sites in the cerebellum, the region which develops last, were the most vulnerable to methylmercury. In contrast, the same receptor subtypes in the midbrain + brainstem, which develops earliest, were resistant to methylmercury. The cerebal cortex, which matures at a time midway between cerebellum and midbrain + brainstem, also displayed intermediate vulnerability to actions of methylmercury on receptors. Within the cerebellum, prenatal exposure to 1 mg/kg to methylmercury, interfered the most with ontogeny of alpha 1-receptor binding, less so far alpha 2-receptors and least for Beta-recep

723
TITLE:
Methyl mercury inhibition of synaptosome protein synthesis: Role of mitochondrial dysfunction.

AUTHORS:
CHEUNG M
VERITY MA

SOURCE:
ENVIRON RES; 24 (2). 1981. 286-298.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Possible modes of organic Hg inhibition of synaptosome protein synthesis were investigated. CH3HgCl inhibited protein synthesis in synaptosomes harvested from neonatal and adult rat brain cortices. Maximum inhibition occurred when incubations were performed at low synaptosome concentrations (< 1 mg/ml). There was only minor release of lactic dehydrogenase at Hg concentrations producing inhibition of protein synthesis. No change was seen in synaptosome volume at 0-100 muM CH3HgCl. Incubation of neonatal synaptosomes in a Na+- and K+-containing medium with increasing concentrations of CH3HgCl produced decreased K+ content and increased Na+ content. Addition of CH3HgCl to a cell-free, K+-dependent protein-synthesizing system containing brain microsomes from neonatal rats inhibited (3H)Leu incorporation into protein. Incubation of synaptosomes in the presence of methyl mercury

resulted in a dose-dependent decline in ATP. Such a decline in available ATP may account for the observed Hg inhibition in synaptosomal protein synthesis.

724
TITLE:
Studies on the distribution and excretion of (SUP)203 Hg-phenyl mercury acetate administered to animals.)

AUTHORS:
Ogawa E
Suzuki S
Tsuzuki H
Kawajiri M
Kito H

SOURCE:
Kitakanto Igaku (Kitakanto Med. J.)24(1): 57-64; 1974(REF:26)

ABSTRACT:
PESTAB A small amount of (SUP)203 Hg-phenyl mercury acetate ((SUP)203HgöPMA) (muCi/0. 1 ml) was administered orally, intraperitoneally, or subcutaneously to adult male ddN-strain mice. The retention, distribution, and excretion of (SUP)203 Hg were investigated radiochemically for three days. The biological half-life was short, about one-two days in all cases. The daily excretion was usually larger in feces than in urine. The retention after 1 hr of intraperitoneal administration was highest in kidney, attaining a peak after 4 hr. After 1 hr the distribution was in the order kidney GT pancreas GT blood GT liver GT spleen GT brain, and after 24 hr the order was kidney GT liver GT other organs. The subcellular distribution of (SUP)203 Hg in liver and kidney was larger in the supernatant fraction than in other fractions. The effect of acceleration of excretion of (SUP)203 Hg by administration of BAL, once a day for three days after the administration of PMA, was found in kidney, liver, pancreas, spleen, and blood. BAL caused a concentration of (SUP)203 Hg in brain.

725
TITLE:
Alzheimer's disease, dental amalgam and mercury.

AUTHORS:
SAXE SR
WEKSTEIN MW
KRYSCIO RJ
HENRY RG
CORNETT CR
SNOWDON DA

GRANT FT
SCHMITT FA
DONEGAN SJ
WEKSTEIN DR
EHMANN WD
MARKESBERY WR

SOURCE:
JOURNAL OF THE AMERICAN DENTAL ASSOCIATION; 130 (2). 1999. 191-199.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Background. Mercury, Hg, is a neurotoxin that has been speculated to play a role in the pathogenesis of Alzheimer's disease, or AD. Dental amalgam releases low levels of Hg vapor and is a potential source of Hg for a large segment of the adult population. Methods. The authors studied 68 subjects with AD and 33 control subjects without AD to determine Hg levels in multiple brain regions at autopsy and to ascertain the subjects' dental amalgam status and history. The subjects were from central Kentucky and Elm Grove, Wis. The authors conducted dental amalgam assessments during the lives of the majority of subjects and in some subjects at the time of autopsy only. The authors also determined three dental amalgam index scores - Event (placement, repair or removal of amalgam), Location and Time In Mouth - in addition to the numbers of and surface area of occlusal amalgam restorations. The authors determined Hg levels in multiple brain regions and performed full neuropatholog

726
TITLE:
Methyl mercury exposure during post-natal brain growth alters behavioral response to SCH 23390 in young rats.

AUTHORS:
PEREIRA ME
MORSCH VM
CHRISTOFARI RS
ROCHA JBT

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 63 (2). 1999. 256-262.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE WISTAR RAT YOUNG METHYL MERCURY SCH 23390 DOPAMINE D1 RECEPTOR ANTAGONIST BEHAVIORAL RESPONSE BRAIN TOXICOLOGY DEVELOPMENT NERVOUS SYSTEM NERVOUS SYSTEM POST-NATAL GROWTH

727
TITLE:
Distribution of mercury in subcellular fractions of brain, liver and kidney after repeated oral administration of mercury-203-labeled methylmercuric chloride in mice.

AUTHORS:
MEHRA M
CHOI BH

SOURCE:
EXP MOL PATHOL; 35 (3). 1981. 435-447.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Daily oral feeding of 203Hg-labeled methylmercuric chloride-cysteine solution (5 mg/kg body wt) in young adult mice produced reduction of body weight, rough fur, ataxic gait and crossing of the hindlimbs when lifted on the 11th day of feeding. Total body radioactivity decreased to 61% in 1 wk and 74% in 2 wk following the last dose of MeHg. The kidney contained the highest radioactivity (30% of total body) followed by liver (12%) and brain (10%). The supernatant and mitochondrial fractions showed relatively high distribution of 203Hg but declined to similar levels in all fractions at the end of 2 wk following the last dose of MeHg. EM of various fractions revealed considerable contamination by different organelles in some fractions, demonstrating the need for more accurate means of demonstration for Hg in subcellular organelles and for more careful assessment of the data obtained from differential centrifugation of tissue and cells.

728
TITLE:
The effect of lead nitrate on the tissue distribution of mercury in rats treated with methylmercury chloride.

AUTHORS:
CONGIU L
CORONGIU FP
DORE M
MONTALDO C
VARGIOLU S
CASULA D
SPIGA G

SOURCE:
TOXICOL APPL PHARMACOL; 51 (2). 1979. 363-366.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Tissue concentrations of the reduced form of

glutathione in brain, kidney and liver vary in the same relationship as the tissue Hg concentration. Brain glutathione is not influenced by PbN2O6 administration, but kidney and liver glutathione is increased. The administration of PbN2O6 which increased kidney glutathione also resulted in increased kidney Hg deposition. This provides additional evidence that glutathione concentrations in the kidney play a role in control of Hg deposition. (Mercury is a known industrial pollutant.)

729
TITLE:
Effects of sodium selenite on methylmercury distribution in mice of late gestational period.

AUTHORS:
SATOH H
SUZUKI T

SOURCE:
ARCH TOXICOL; 42 (4). 1979. 275-280.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Mercury distribution in pregnant mice, injected s.c. with 1.5 or 15.0 mumol/kg of methylmercury chloride (MeHg) and 0, 1.5 or 15.0 mumol/kg of sodium selenite, was investigated. Selenite increased the retention of Hg in maternal brain in every combination of doses. Selenite also increased Hg concentrations in maternal blood except 1 combination (MeHg 1.5; selenite 1.5 mumol/kg), and the increased Hg was partitioned to red blood cells. The increased mercury retention by selenite was also found in fetal brain.

730
TITLE:
DOSE-DEPENDENT AND SEX-DEPENDENT RESPONSE OF FETAL MICE IN MERCURY DISTRIBUTION FOLLOWING METHYLMERCURY EXPOSURE

AUTHORS:
INOUYE M
KAJIWARA Y
HIRAYAMA K

SOURCE:
FOURTH INTERNATIONAL CONGRESS OF TOXICOLOGY, TOKYO, JAPAN, JULY 21-25, 1986. TOXICOL LETT (AMST); 31 (SUPPL.). 1986. 76.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT RAT BRAIN LIVER KIDNEY TOXICOKINETICS MATERNAL BRAIN MERCURY

731
TITLE:
Antioxidant enzymes: developmental profiles and their role in metal-induced oxidative stress.

AUTHORS:
Hussain S
Ali SF

SOURCE:
Handbook of Developmental Neurotoxicology 1998;:353-69

732
TITLE:
Drug and chemical contaminants in breast milk: effects on neurodevelopment of the nursing infant.

AUTHORS:
Polifka JE

SOURCE:
Handbook of Developmental Neurotoxicology 1998;:383-400

733
TITLE:
BRAIN AND TISSUE LEVELS OF MERCURY AFTER CHRONIC METHYLMERCURY EXPOSURE IN
THE MONKEY

AUTHORS:
RICE DC

SOURCE:
J TOXICOL ENVIRON HEALTH; 27 (2). 1989. 189-198.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN MACACA-FASCICULARIS BRAIN MERCURY LEVEL HALF-LIFE

734
TITLE:
THE OBSERVATION OF BLOOD-BRAIN BARRIER OF ORGANIC MERCURY POISONED RAT A GADOLINIUM DIETHYLENETRIAMINE PENTAACETIC ACID ENHANCED MAGNETIC RESONANCE
STUDY

AUTHORS:
KUWABARA T

YUASA T
HIDAKA K
IGARASHI H
KANEKO K
MIYATAKE T

SOURCE:
BRAIN NERVE (TOKYO); 41 (7). 1989. 681-685.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM INCREASED PERMEABILITY RELAXATION TIME

735
TITLE:
Effect of organic and inorganic mercuric salts on sodium potassium ATPase in different cerebral fractions in control and intrauterine growth-retarded rats: Alterations induced by serotonin.

AUTHORS:
CHANEZ C
FLEXOR MA
BOURRE JM

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 10 (4). 1989. 699-706.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. An intrauterine growth-retarded (IUGR) model based on restriction of blood supply to the rat fetus at the 17th day of pregnancy was studied. We investigated in vitro the effects of thimerosal and mercuric on Na+K+ATPase activity in total brain homogenate, synaptosomes and myelin at weaning. In addition, we evaluated the reversal effect of serotonin on mercury-inhibited Na+K+ATPase activity. The toxicity, terms of inhibition of Na+K+ATPase activity was greater with mercuric chloride than with thimerosal. Synaptosomes and principally myelin were more sensitive to the metal salts than total homogenate. Serotonin stimulated the Na+K+ATPase in total brain homogenate and synaptosomes but inhibited the enzyme in the myelin fraction. This effect was more marked in the IUGR group than in the control group. Serotonin (1 mM) added to total homogenate pretreated with the mercury salts produced variable reversal effects. In the synaptosomal fraction reverse effect was noted with se

736
TITLE:
The effects of age and sex on seven elements in Sprague-Dawley rat organs.

AUTHORS:

UCHINO E
TSUZUKI T
INOUE K

SOURCE:
LAB ANIM; 24 (3). 1990. 253-264.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This study reports age-related changes in 7 element (iron, copper, zinc, manganese, mercury, cadmium and lead) concentrations in the liver, kidney and brain of male and female Sprague-Dawley rats from 1 to 364 days of age. Atomic absorption spectrometry was used for the measurements. Copper, mercury and cadmium in the male and female kidneys increased from weaning until 127 days of age, as did iron concentrations in the female liver and kidney. After 127 days, especially, the copper concentration in the female kidney and cadmium concentration in the male and female kidney increased further. Consistent and statistically significant ($P < 0.05$) sex differences in element concentrations were found for three elements (iron, copper and zinc). Except for the zinc concentration in the liver from 50 to 72 days, iron (in liver and kidney), zinc (in kidney) and copper (in liver, kidney and brain) concentrations in female rats during the adult stage, were all higher than those of

737
TITLE:
Mercury

AUTHORS:
ANON

SOURCE:
Commission of the European Communities, 2920 Luxembourg, Grand Duchy of Luxembourg; International Programme on Chemical Safety (IPCS), World Health Organization, 1211 Genáeve 27, Suisse, 1990. 2p. Illus.

ABSTRACT:
International chemical safety card. Danger symbol: toxic. Short-term exposure effects: delayed effects; skin absorption; irritation of skin; pulmonary oedema; neurotoxic effects (central nervous system). Long-term exposure effects: may have effects on the cardiovascular system, nervous system, and kidneys; may cause birth defects, specifically brain damage. EC identification number and labelling codes: 080-001-00-0; T; R23-33; S7-44. United Nations number and hazard class: UN 2809 (8; 123; III).

738
TITLE:
Mercuric nitrate

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:
Data sheet. May enter the body by inhalation and through the skin. May damage the kidneys. Mercury poisoning can cause the "shakes", irritability, sore gums, increased saliva, personality changes and brain damage. May irritate the eyes and lungs. May irritate and burn the skin and cause skin allergy and grey skin colour.

739
TITLE:
Historical methylmercury exposure and developmental toxicity.

AUTHORS:
Reuhl KR

SOURCE:
Teratology 2002 Jun;65(6):314

ABSTRACT:
It has been 50 years since the first large outbreak of methylmercury in Minamata Bay, Japan entered the public consciousness. The disease was heralded by an increase in the number of infants displaying "cerebral palsy" like symptoms and was subsequently traced to effluent from a local chemical plant. Several hundred infants were affected. A subsequent outbreak of poisoning in Iraq in 1972 involved thousands of adults and numerous infants. Detailed study of these episodes has provided seminal lessons that have shaped mechanistic toxicology, environmental risk assessment and the development of public policy. Methylmercury can be formed naturally from inorganic mercury by methogenic bacteria in water sediments, bioaccumulates in the food chain and reaches toxic levels in commercially valuable fish. The pregnant female consuming methylmercury will pass the toxicant to the developing fetus and fetotoxic levels may be achieved in the absence of maternal toxicity, underscoring the importance of rigorous control of exposure. Methylmercury has also proven an important model compound in developmental neurotoxicology. The toxicant's high chemical reactivity toward cellular macromolecules permits the identification of specific targets of injury and the identification of "dose-mechanism" relationships during brain development. Recent concerns regarding potential mercury pollution from natural and anthropogenic sources, and growing evidence of adverse developmental effects on brain function at ever-decreasing concentrations, suggest that methylmercury

will remain a major concern for the foreseeable future.

740
TITLE:
Renal mechanisms in the cardiovascular effects of chronic exposure to inorganic mercury in rats.

AUTHORS:
CARMIGNANI M
BOSCOLO P
ARTESE L
DEL ROSSO G
PORCELLI G
FELACO M
VOLPE AR
GIULIANO G

SOURCE:
BR J IND MED; 49 (4). 1992. 226-232.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Male weanling Wistar rats received 200 mug/ml of mercury (Hg), as HgCl2, in drinking water for 180 days. At the end of the treatment, systemic arterial blood pressure was augmented, cardiac inotropism was reduced, and heart rate was unchanged. Light and electron microscopical studies of the kidney showed a mesangial proliferative glomerulonephritis in about 80% of the glomeruli. Tubular cells showed reduction of the acid phosphatase activity, which was related to functional abnormalities of the lysosomes. In the 24 hour urine samples of the Hg exposed rats, there was slight reduction of kallikrein activity, but evident proteinuria was not present in all samples. Plasma renin activity was reduced, that of angiotensin I-converting enzyme was augmented, and plasma aldosterone concentrations were unchanged. Mercury was accumulated mostly in the kidney of the Hg treated animals; and the content of Hg in the heart was higher than in the brain. These data show that chronic exp

741
TITLE:
Chronic encephalopathies induced by mercury or lead: Aspects of underlying cellular and molecular mechanisms.

AUTHORS:
RONNBACK L
HANSSON E

SOURCE:
BR J IND MED; 49 (4). 1992. 233-240.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Long term exposure to low doses of mercury or lead can induce neurasthenic symptoms with slight cognitive deficits, lability, fatigue, decreased stress tolerance, and decreased simultaneous capacity. After exposure to higher concentrations permanent neuropsychological deficits can be seen. The present paper gives a new idea of possible molecular mechanisms underlying the symptoms. Impairments of astrocyte function are probably important, especially due to their capacity to regulate the ionic and amino acid concentration in the extracellular micromilieu, brain energy metabolism, and cell volume. Recent results have shown that these functions are under monoaminergic control. Aspects of therapy are outlined.

742

TITLE:

In vitro evidence for the role of glutamate in the CNS toxicity of mercury.

AUTHORS:

BROOKES N

SOURCE:

TOXICOLOGY; 76 (3). 1992. 245-256.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Intoxication with elemental mercury vapor or with methylmercury results in the accumulation of mercuric mercury (Hg2+) in the brain. Submicromolar concentrations of Hg2+ were shown previously to inhibit glutamate uptake in astrocyte cultures selectively and reversibly. This finding suggests that blockade of the inactivation of synaptically released glutamate is a potential mechanism of the CNS toxicity of Ilg2+. The present study shows further that Hg2+ (| 1 muM): (i) markedly inhibits the clearance of extracellular glutamate both by astrocyte cultures and by spinal cord cultures; (ii) reduces glutamine content and export in astrocyte cultures; (iii) has little effect on neuronal viability in spinal cord cultures in the absence of excitotoxic accumulations of glutamate; (iv) does not impair the sensitivity of neurons to the excitotoxic action of glutamate. Also, it is noted that Hg2+ (| 1 muM) has not been shown to impair transmitter release acutely in existing studies

743

TITLE:

Poisoning with alkylmercury compounds.

AUTHORS:

Anonymous

SOURCE:
Br. Med. J. 1(6113): 599-600 1978 (14 References)

ABSTRACT:
PESTAB. The occurrence of poisoning due to mercury compounds used as fungicides is reviewed. The worst outbreaks have been in Iraq, where ethyl mercury p-toluene sulfonanilide (ceresan M) was introduced as a pesticide in seed dressing by the Ministry of Agriculture in 1955. Even though the farmers who received the seed were told not to eat them, some washed the seeds with water and then used them for making domestic bread. The most catastrophic epidemic ever recorded took place in Iraq in the winter of 1971-72, when 6530 patients were hospitalized. Again exposure to alkylmercury occurred due to farmers eating homemade bread made from grain treated with a methylmercury fungicide. The site of damage in methylmercury poisoning leading to the picture of neuropathy seems to be either in the lower brain stem or at some point in the neuromuscular linkage. Visual disturbances occur in about half the cases, and psychological symptoms include headache, sleep disturbances, dizziness, and irritability. Japanese reports on organic mercury poisoning are also noted.

744
TITLE:
How to detect gold, silver and mercury in human brain and other tissues by autometallographic silver amplification.

AUTHORS:
DANSCHER G
STOLTENBERG M
JUHL S

SOURCE:
NEUROPATHOLOGY AND APPLIED NEUROBIOLOGY; 20 (5). 1994. 454-467.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Gold, silver, mercury and zinc bind chemically to Sulphide or selenide ions and create crystal lattices that can be detected in histological sections by a silver amplification technique called autometallography (AMG). The technique specifically magnifies such nanometer-sized catalytic crystals. For each metal, a detailed protocol has been worked out. If several different AMG metals/metal molecules are present in the same tissue, it is possible to distinguish one from another. The AMG technique is based on the capability of small crystal lattices of the aforementioned metals and metal molecules to initiate AMG silver amplification. Electrons released from adhering hydroquinone molecules reduce silver ions that are integrally connected with the crystal lattices. In this manner, particles

consisting of only a few atoms of, say, gold, or molecules of mercury selenide (Figure 1), can be silver amplified to a size at which they can be detected in the electron microscope, or e

745
TITLE:
TOXICITY OF IONIC MERCURY AND ELEMENTAL MERCURY VAPOR ON BRAIN NEURONAL PROTEIN METABOLISM

AUTHORS:
LORSCHEIDER FL
VIMY MJ
PENDERGRASS JC
HALEY BE

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT
SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 955.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT RAT HUMAN ALZHEIMER'S DISEASE

746
TITLE:
MERCURY CONCENTRATION IN THE BLOOD AND ORGANS OF NORMAL AND ACATALASEMIC MICE AFTER INTRAPERITONEAL INJECTION OF METALLIC MERCURY MERCURY-203

AUTHORS:
OGATA M
AIKOH H

SOURCE:
PHYSIOL CHEM PHYS MED NMR; 16 (1). 1984. 71-74.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM LIVER BLOOD-BRAIN BARRIER TOXICOKINETICS METAL TOXICITY

747
TITLE:
A study on the effect of garlic on the toxicity of phenyl mercuric acetate in rats.

AUTHORS:

PARK J-S
CHA C-W

SOURCE:
KOREA UNIV MED J; 21 (3). 1984 (RECD. 1985). 49-58.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Garlic which is consumed as a daily spice in Korea contains abundant amounts of thiol compounds such as -SH and -S-S-radicals. These compounds may be involved in the detoxification mechanism of heavy metal poison by the formation of thiochelate compounds when reacting with heavy metals in the living body. The effect of garlic on the detoxification mechanism of alkyl mercury poisoning in rats was studied. The expermental rats were fed 6 ppm of phenyl mercury in potable water in addition to 3 different concentrations of garlic in pellets (1.70%, 3.35% and 6.70%) which was compared with the control (no Hg and garlic) and the garlic only fed group (no Hg). After rearing for 12 wk with the above prescription, alkaline phosphatase activities in the blood and the accumulation of total Hg in the tissues of target organs of the brain, liver and kidney were measured. Histopathological changes in the tissues of the above organs were observed. Components fo garlic have some roles in detoxificating phenyl mercury poisoning such as decreasing alkaline phosphatae activity, increasing concentration of Hg in target organs and inducing pathological damages to organs.

748
TITLE:
Monoisoamyl and mono-n-hexyl meso-2,3-dimercaptosuccinate in mobilizing 203Hg retention in relation to age of rats and route of administration.

AUTHORS:
KOSTIAL K
BLANUSA M
PIASEK M
PRESTER L
JONES MM
SINGH PK

SOURCE:
JOURNAL OF APPLIED TOXICOLOGY; 15 (3). 1995. 201-206.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Monoisoamyl (Mi-ADMS) and mono-n-hexyl (Mn-HDMS) monoesters of meso-2,3-dimercaptosuccinic acid (DMSA) were given orally or parenterally for the mobilization of inorganic mercury in suckling and older rats. Chelators were administered at a dose of 2days 2 weeks after a single 203Hg injection. Six days later, whole-body, kidney, liver and brain radioactivities were determined in gamma scintillation

counters. Both Mi-ADMS and Mn-HDMS were found to be superior to DMSA in mobilizing mercury from body and organs. The results were similar after oral or parenteral treatment. The efficiency of both monoesters was even higher in younger than in older rats. This is the first report on the mobilization of mercury from the body of sucklings under conditions of late oral treatment.

749
TITLE:
Comparative and interactive effects of mercury, cadmium and lead on tissue GSH levels in Oreochromis aureus (Steindachner): Implications for monitoring heavy metal pollution.

AUTHORS:
ALLEN P

SOURCE:
JOURNAL OF APPLIED ICHTHYOLOGY; 12 (1). 1996. 21-26.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of 45 days exposure to mercury, cadmium and lead on tissue GSH levels were studied in Oreochromis aureus (Steindachner). Liver, brain, gill filaments, intestine and caudal muscle were assayed after exposure to these heavy metals singly, or in combination. Significant increases in intestinal GSH concentrations consistently occurred after exposure to mixtures of heavy metals. Exposure to cadmium or lead did not change hepatic GSH levels, while exposure to two different concentrations of mercury caused significant increases in hepatic GSH.

750
TITLE:
Chronic elemental mercury intoxication: Neuropsychological follow-up case study.

AUTHORS:
HUA M-S
HUANG C-C
YANG Y-J

SOURCE:
BRAIN INJURY; 10 (5). 1996. 377-384.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In initial and follow-up investigations of neuropsychological function in a patient with elemental mercury intoxication, his scores were compared with those of a group of normal control subjects matched for sex, age and education. Each subject received

a comprehensive neuropsychological examination including a personality inventory. On the initial examination the results indicated that the patient had a significant depression of performance intellectual functioning, impairments of attention, non-verbal short-term memory and visual judgement of angles and directions, psychomotor retardation and personality changes including depression, anxiety, desire to be alone, lack of interest and sensitivity to physical problems. Such an impairment picture is compatible with the previous observations of individuals with chronic exposure to elemental, organic or inorganic mercury. The follow-up study was undertaken about 1.5 years later. The results show that the patient's cognitive

751
TITLE:
THE TOXICOLOGY OF MERCURY AND ITS COMPOUNDS

AUTHORS:
CLARKSON TW

SOURCE:
WATRAS, C. J. AND J. W. HUCKABEE (ED.). MERCURY POLLUTION: INTEGRATION AND SYNTHESIS; INTERNATIONAL CONFERENCE ON MERCURY AS A GLOBAL POLLUTANT, MONTEREY, CALIFORNIA, USA, JUNE 1992. XXIII+727P. CRC PRESS, INC.: BOCA RATON, FLORIDA, USA; LONDON, ENGLAND, UK. ISBN 1-56670-066-3.; 0 (0). 1994. 631-641.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER MEETING PAPER HUMAN IMPACT METHYLMERCURY VAPOR ENVIRONMENTAL TOXICOLOGY CONTAMINATION POLLUTION NERVOUS SYSTEM FOOD CHAIN BRAIN DAMAGE

752
TITLE:
PHYSIOLOGY AND TOXICOLOGY OF MERCURY

AUTHORS:
MAGOS L

SOURCE:
SIGEL, A. AND H. SIGEL (ED.). METAL IONS IN BIOLOGICAL SYSTEMS, VOL. 34. MERCURY AND ITS EFFECTS ON ENVIRONMENT AND BIOLOGY. XLII+604P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ISBN 0-8247-9828-7.; 34 (0). 1997. 321-370.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER LITERATURE REVIEW HUMAN GUINEA-PIG RAT TOXICOLOGY MERCURY TOXICITY EXPOSURE BIOTRANSFORMATION ABSORPTION SULFUR SELENIUM BLOOD BRAIN KIDNEY LUNG SKIN PLACENTA

TOXICOKINETICS HYPERSENSITIVITY REACTIONS BLOOD AND LYMPHATICS NERVOUS SYSTEM EXCRETORY SYSTEM RESPIRATORY SYSTEM INTEGUMENTARY SYSTEM REPRODUCTIVE SYSTEM EMBRYONIC STRUCTURE

753
TITLE:
Effects of methyl mercury on the in vivo release of dopamine and its acidic metabolites DOPAC and HVA from striatum of rats.

AUTHORS:
FARO L RF
DURAN R
DO NASCIMENTO J LM
ALFONSO M
PICANO-DINIZ CW

SOURCE:
ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY; 38 (2). 1997. 95-98.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury is a neurotoxic agent that produces different effects on the brain. In the present work, the effects of chronic doses of methyl mercury (MeHg) were studied on the dopaminergic system of the rat striatum, using microdialysis coupled to high-performance liquid chromatography in order to quantify the in vivo release of dopamine (DA) and its acidic metabolites DOPAC and HVA. The administration of an equivalent total dose of 6 mg/kg of MeHg induced significant increases in the striatal release of DA and/or its acidic metabolites, independently of the pattern of administration. These effects are discussed on the base of the release and the metabolization of DA. In conclusion, the effect of MeHg administered under these experimental conditions on the in vivo release of DA and its metabolites seems to have a dose-dependent component and seems to be an accumulative process.

754
TITLE:
Systemic mercury levels caused by inhaling mist during high-speed amalgam grinding.

AUTHORS:
CUTRIGHT DE
MILLER RA
BATTISONE GC
MILLIKAN LJ

SOURCE:
J ORAL MED; 28 (4). 1973 100-104

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. A total of 48 white rats were exposed to amalgam mist produced by grinding an amalgam mercury block 5 cm from each animal. A rapid rise in mercury was noted from a control of 127.2 ngHg/gm to 5060.7 in the lung and 4113.0 in the heart within a period of 32 h. A similar effect may occur in humans during the removal of old amalgam fillings. Comparative amounts were also noted in the liver, brain, and kidneys.

755

TITLE:

Effects of Methylmercuric Chloride of Low Concentration on the Rat Nervous System

AUTHORS:

Yamamura K
Maehara N
Ohno H
Ueno N
Kohyama A
Satoh T
Shimoda A
Kishi R

SOURCE:

Bulletin of Environmental Contamination and Toxicology, Vol. 38, No. 6, pages 985-993, 16 references, 19871987

ABSTRACT:

The neurologic effects of exposure to low concentrations of methylmercury were studied in rats. Male Wistar-rats were fed a diet containing 10 micrograms per gram methylmercury-chloride (115093) (MeHg) for 4, 6 or 8 weeks. A decrease in body weight was observed after 7 weeks of MeHg administration. Flexion and crossing of the hind legs and rotation of the tail, neurologic signs of MeHg poisoning, were observed after 6 and 8 weeks, respectively. Early potential of evoked brain potentials were measured electrophysiologically, and the latency of the primary response was found to be lengthened after 6 weeks of MeHg treatment and was lengthened further after 8 weeks of treatment. The average cerebral mercury (7439976) contents after 6 weeks or 8 weeks of MeHg exposure did not differ significantly, but were significantly higher than in controls or following 4 weeks exposure. Blood concentrations of MeHg were not significantly different in the three treatment groups. Histological examination of the sciatic nerves revealed no pathologic changes in the 4 week exposure group, but sporadic demyelination and degeneration of axons were observed in the 6 week exposure group. More severe demyelination and axonal degeneration were observed after 8 weeks exposure, and mild endoneurial edema was also observed. The authors conclude that there is

considerable risk of accumulation of methylmercury in nervous tissue with chronic exposure to low levels of methylmercury compounds.

756
TITLE:
Uptake of inorganic mercury in the olfactory bulbs via olfactory pathways in rats.

AUTHORS:
HENRIKSSON J
TJALVE H

SOURCE:
ENVIRONMENTAL RESEARCH; 77 (2). 1998. 130-140.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Uptake and transport in the olfactory neurons may be an important means by which some heavy metals gain access to the brain. In the present study we explored whether inorganic mercury (203Hg2+) may be taken up in the CNS via the olfactory pathway. Autoradiography and gamma spectrometry showed that intranasal instillation of 203Hg2+ in the right nostrils of rats resulted in much higher levels of the metal in the right olfactory bulbs than in the left ones. At the side of the application of the 203Hg2+ there was also a labeling of the olfactory nerve bundles projecting to the olfactory bulbs as well as in the olfactory nerve-fibres constituting the olfactory nerve layer of the bulbs, which was not seen on the opposite side. The results also showed that the 203Hg2+ accumulated in the glomerular layer of the bulbs. These data indicate that our results can be ascribed to a movement of the mercury along the olfactory axons to their terminal parts in the glomeruli and not to

757
TITLE:
Effects of Methyl Mercury and Cadmium on the Kinetics of Substrate Activation of (K+)-Paranitrophenyl Phosphatase

AUTHORS:
Ahammad Sahib KI
Moorthy KS
Desaiah D

SOURCE:
Journal of Applied Toxicology, Vol. 7, No. 3, pages 221-226, 23 references, 19871987

ABSTRACT:
A study was undertaken to examine the effects of methyl-mercuric-chloride

(115093) and cadmium-chloride (10108642) on the substrate activation of K+-paranitrophenyl-phosphatase (K+-PNPPase), prepared from brains of Sprague-Dawley-rats. The authors state that the terminal potassium ion dependent dephosphorylation step of the sodium-potassium-adenosine-triphosphatase (Na-K-ATPase) reaction is believed to be catalyzed by K+-PNPPase. The overall reaction of the Na-K-ATPase reaction has been shown to be inhibited by mercury and cadmium compounds, but their effects on the partial reaction have not been studied in detail. The results of this study showed that the enzyme activation by paranitrophenyl-phosphate (PNPP) was inhibited noncompetitively by both metal compounds by their binding to the enzyme/substrate complex. An enzyme/inhibitor/substrate complex was thus formed, and this could not be dephosphorylated. The potassium or PNPP binding sites on the enzyme did not appear to be involved in the binding of the inhibitors. The authors suggest that these heavy metals inhibit the ATPase driven sodium pump by conformational changes in the enzyme, which are caused by binding of the metals to critical sulfhydryl groups.

758

TITLE:

Methylmercury content of selected human tissues over the past 60 years.

AUTHORS:

KEVORKAIN J
CENTO DP
UTHE JF
HAGSTROM RA

SOURCE:

AM J PUBLIC HEALTH; 63 (11). 1973 931-934

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Twenty fixed human autopsy tissue samples, including brain, liver, kidney, and heart, from both sexes and several age groups, and from as far back as 1913, were analyzed by 3 independent laboratories for total mercury content, and by 2 of the 3 for methylmercury content. In addition, 8 fresh frozen samples (including muscle) from 2 recent autopsies were similarly tested. Total mercury levels coincided with the trend noted in an earlier study which revealed marked decrease in total mercury content since the early part of this centruy and a fairly constant level over the post several decades. On the other hand, methylmercury levels in the same tissues were either infinitesimally small or totally undetectable. In view of the major pollution role ascribed to methylmercury these results vitiate the basis, if any, of such a proclamation and underscore the need for sound, more pertinent research before any social or political action is taken.

759

TITLE:
Chronic effects of methylmercury in rats. II. Pathological aspects.

AUTHORS:
ETO K
YASUTAKE A
MIYAMOTO K-I
TOKUNAGA H
OTSUKA Y

SOURCE:
TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE; 182 (3). 1997. 197-205.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Chronic effects of methylmercury (MeHg) were examined pathologically in male Wistar rats fed on diet containing 0, 1 or 5 ppm Hg (as MeHg) for two years. Organs including the central nervous tissues were examined histopathologically using hematoxylin and eosin (H & E), Kluver-Barrera (KB), PAS or phenol-congo red stains. The peripheral nerve system tissues were also examined, using H & E and trichrome stains. Furthermore, immunoglobulins of renal specimens were demonstrated by direct immunofluorescence microscopy. Localization of mercury in the paraffin-embedded sections of the nervous tissue, kidney, liver, pancreas, spleen and testis was demonstrable by the photoemulsion histochemical method. In the 5 ppm group, mercury was readily detectable in tissues of the rats exposed for one year, one and half years, two years and two and half years. Mercury was detected in the cells of the brain such as neurons, neuroglial cells, and phagocytes, and also in most organs, partic

760
TITLE:
EFFECTS OF MERCURY AND LEAD ON PHOSPHOINOSITIDE SYSTEM IN RAT BRAIN

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

761
TITLE:
Behavioral Effects in Pigeons Exposed to Mercury Vapor at a Concentration of 0.1 Mg3

AUTHORS:
Beliles RP
Clark RS

Belluscio PR
Yuile CL
Leach LJ

SOURCE:
American Industrial Hygiene Association Journal, Vol. 28, No. 5, pages 482-484, 6 references, 19671967

ABSTRACT:
The effects of mercury (7439976) (Hg) vapor on the operant behavior of pigeons was investigated. Three male pigeons were trained to a multiple FR-60 FI-15 schedule of reinforcement. After relative behavioral stability was obtained, 2 pigeons were exposed for 6 hours a day for 20 weeks to Hg concentrations of 0.1 milligrams per cubic meter, while 1 pigeon served as a control. Behavior was observed until week 20 when the birds were sacrificed and examined for gross and microscopic changes. No significant changes were observed in behavior or upon gross or histological examination of liver, lung, kidney or brain tissues. No signs of lesions or tremors due to mercury poisoning were found.

762
TITLE:
Excretion of mercury from fish.

AUTHORS:
KIKUCHI T
HONDA H
ISHIKAWA M
YAMANAKA H
AMANO K

SOURCE:
BULL JPN SOC SCI FISH; 44 (3). 1978. 217-222.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The possibility of removing Hg from fish heavily contaminated by methyl mercury was examined in 2 series of rearing experiments using 2 marine spp. of fish, conger eel (Astroconger myriaster) and sea bream (Chrysophrys major). In the 1st series, conger eel, caught from Kagoshima Bay, Japan, which had natural levels of Hg of 1.0 ppm in the muscle tissue, 0.67 ppm in the spleen and 1.8 ppm in the liver, were kept in plain sea water and fed with raw fish flesh for 7 wk. The Hg levels were reduced to 1/2 in 5 wk for the muscle and spleen and in 3 wk for the liver. In the 2nd series, sea bream were fed for 7 wk with pellets containing methyl mercury or mercuric chloride at a level of 1.0 ppm, and subsequently fed with commercial pellet feed or pellets impregnated with a mixture of cysteine, pectin and chitosan for another 7 wk. The Hg concentrations at the end of the 1st feeding period were 0.9

ppm in the kidney and 0.25-0.4 ppm in the muscle, liver, brain and spleen. During the subsequent feeding period, the Hg level was reduced to a level less than 0.2 ppm in every tissue examined, with best results in the group fed with the pellets supplemented by the mixture mentioned. In the case of feeding with pellets containing mercuric chloride, the Hg level in any part hardly reached the level of 0.2 ppm, even after a 7 wk period. Hg in this chemical form may be excreted readily.

763
TITLE:
DENTAL AMALGAMS & NEUROPSYCHOLOGICAL FUNCTION

AUTHORS:
FACTOR-LITVAK P

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
There is considerable evidence that some mercury from "silver" fillings distribu tes to body tissues, particularly the brain. By conducting a cross-sectional st udy of approximately 800 adults, aged 30-49, we will test whether amalgam-derive d mercury is associated with decreased performance on tests of neurological func tion, balance, visuospatial ability, memory, attention/executive function, and r enal function.

764
TITLE:
DENTAL AMALGAMS & NEUROPSYCHOLOGICAL FUNCTION

AUTHORS:
FACTOR-LITVAK P

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
There is considerable evidence that some mercury from "silver" fillings distribu tes to body tissues, particularly the brain. By conducting a cross-sectional st udy of approximately 800 adults, aged 30-49, we will test whether amalgam-derive d mercury is associated with decreased performance on tests of neurological func tion, balance, visuospatial ability, memory, attention/executive function, and r enal function.

765
TITLE:
ASPECTS OF MERCURY II THIOLATE CHEMISTRY AND THE BIOLOGICAL BEHAVIOR OF MERCURY COMPOUNDS

AUTHORS:
CANTY AJ

SOURCE:
BRINCKMAN, F. E. AND JON M. BELLAMA (ED.). ACS (AMERICAN CHEMICAL SOCIETY) SYMPOSIUM SERIES, NO. 82. ORGANOMETALS AND ORGANOMETALLOIDS: OCCURRENCE AND FATE IN THE ENVIRONMENT. SYMPOSIUM. ANAHEIM, CALIF., USA, MAR. 13-17, 1978. XV+447P. ILLUS. AMERICAN CHEMICAL SOCIETY: WASHINGTON, D.C., USA. ISBN 0-8412-0461-6.; 1978 (RECD 1979) 327-338

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN RAT MERCURY POISONING DIMERCAPROL ANTIDOTE BRAIN FAT

766
TITLE:
Biochemical effects of mercury poisoning in rats.

AUTHORS:
DONALDSON ML
GUBLER CJ

SOURCE:
AM J CLIN NUTR; 31 (5). 1978 859-864

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Acute HgCl2 poisoning decreased significantly the pyruvate dehydrogenase (PyDH) and alpha-ketoglutamic dehydrogenese (alphaKgDH) activity in the kidney and liver but not in the brain. Rats receiving 77% of the 2 h LD50 showed 57% of normal renal PyDH activity and 69% of normal renal alphaKgDH activity. Chronic HgCl2 poisoning resulted in an unexpected increase in PyDH and alphaKgDH activity in the kidneys were Hg was most concentrated. In acute methyl mercury injection, no significant effect on PyDH or alphaKgDH activities was observed after 2 days. Less Hg was accumulated in the tissues with methyl mercury poisoning than in the other treatments.

767
TITLE:
Association of mercury exposure with neurobehavioral performance of children in Bohemia.

AUTHORS:
Otto D
Skalik I
Hudnell HK
Ratcliffe J

House D

SOURCE:
Neurotoxicology 1994;15(4):962

ABSTRACT:
Northern Bohemia is one of the most polluted areas in Central Europe. High levels of SO2, NOx, PAHs and heavy metals occur as a result of intensive mining and combustion of brown coal for power generation. Sram (1991) hypothesized that in utero exposure to these chemicals causes functional changes in the nervous system expressed as developmental disorders or behavioral dysfunctions. Seven tests from the Neurobehavioral Evaluation System (Letz 1991) -- finger tapping, hand-eye coordination, continuous performance, visual digit span, symbol-digit substitution, pattern comparison and switching attention tests -- were administered to 774 2nd-grade children (351 from a high-exposure mining district and 423 from an agricultural reference district). Hair and urine samples were obtained from 600 children to assess Hg exposure. Visual acuity, contrast sensitivity and color discrimination were also tested in half of the children. Although hair and urinary Hg levels were well below WHO levels of concern, weak associations of hair Hg and finger tapping, hand-eye coordination, symbol-digit performance and contrast sensitivity were found.

768
TITLE:
Evidence for delayed methylmercury neurotoxicity in monkeys.

AUTHORS:
Rice DC

SOURCE:
Neurotoxicology 1995 Fall;16(3):533-4

ABSTRACT:
Delayed neurotoxicity following developmental exposure to methylmercury was observed in mice two decades ago by Spyker (Fed Proc 34, 1835, 1975), who observed abnormalities including kyphosis, obesity, and severe neurological deficits only as the animals aged. Evidence for delayed neurotoxicity has also come from research in two cohorts of macaque monkeys (Macaca fascicularis) at the Canadian Health Department. One group of monkeys, presently 19 years old, was dosed with 50 ug/kg/day of mercury as methylmercuric chloride from birth to 7 years of age. In another study examining the effects of in utero plus postnatal exposure, females were dosed with 10, 25, or 50 ug/kg/day of mercury as methylmercuric chloride; blood mercury levels averaged 0.37, 0.75, or 1.42 ppm during pregnancy. One, two, and five infants were born from the three dose groups, respectively. One infant in the high-dose group was born with signs of

methylmercury poisoning resembling those of human infants, including motor impairment and nystagmus. When the group of monkeys exposed only postnatally until 7 years of age was 13 years old, individuals began exhibiting clumsiness not present previously. Further exploration revealed that treated monkeys required more time to retrieve treats than did nonexposed monkeys and displayed abnormalities on a clinical assessment of sense of touch in hands and feet, despite the fact that clinical examinations performed routinely during the period of dosing had not yielded abnormal results. This observation was pursued in both groups of monkeys by objective assessment of somatosensory function in the hands: both groups of monkeys exhibited impaired vibration sensitivity. Evidence for delayed neurotoxicity has also come from persons diagnosed with Minamata disease years after cessation of exposure. An interaction between age and the ability of persons with Minamata disease to perform activities of daily living has also been reported (Kinjo et al., Environ Res. 63, 241, 1993). The available body of data is strongly suggestive of delayed neurotoxicity as a result of methylmercury exposure.

769
TITLE:
EFFECTS OF MERCURY AND LEAD ON PHOSPHOINOSITIDE SYSTEM IN RAT BRAIN

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

770
TITLE:
Interventions during individual development of rats affect the behaviour in adulthood: a three-generation study.

AUTHORS:
Schulz H
Nagymajtäenyi L
Däesi I

SOURCE:
Neurotoxicology 1997;18(3):881

ABSTRACT:
The investigated substances (lead, mercury and cadmium) have a different dose- and exposure-time dependent action profile on behavioural pattern of adult male Wistar rats, like spontaneous exploratory behaviour of an open field box, when the individuals exposed during development. There are no compensatory or adaptive mechanisms to eliminate xenobiotical effects throughout the generations. In contrast, it seems they are strengthened.

The developing rats are extremely sensitive to neuro-behavioural damaging by heavy metals during pregnancy whereas further exposure mostly did not intensify the effects. The tested substances exhibit beside their behavioural effects also teratogenic effects on different organs of the adults which interfere directly or indirectly with the well-being of the individuals leading to neuro-physiological malformations and inadequate and/or inadaptive information processing in the central nervous system. The question of interactions between the existing xenobiotics in the biosphere on individuals information processing in the CNS is still open for further investigations.

771
TITLE:
Teratogenic effects of external egg applications of methyl mercury in the mallard, Anas platyrhynchos.

AUTHORS:
HOFFMAN DJ
MOORE JM

SOURCE:
TERATOLOGY; 20 (3). 1979 (RECD. 1980). 453-462.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The embryotoxic potential of external applications of methyl mercury on mallard eggs was investigated to assess the possible impact of Hg transferred from the plumage of effluent-contaminated aquatic birds to their eggs. Eggs were treated on day 3 of development with mu applications of methyl mercury that was dissolved with ethyl acetate into an aliphatic hydrocarbon vehicle. Hg analysis by atomic absorption indicated that almost half of the Hg applied entered the eggs past the shell membranes within several days of treatment. Most mortality occurred within this period at doses of 9 mug of Hg/egg or higher. Decreased embryonic growth resulted with similar doses. A significant incidence of malformations occurred at a dose of 1 mug/egg. These malformations were mainly minor skeletal aberrations and incomplete ossification. With higher doses of Hg, defects included gross external ones such as micromelia, gastroschisis and eye and brain defects. Application of the aliphatic hydrocarbon vehicle did not result in any of these defects.

772
TITLE:
EFFECTS OF MERCURY AND LEAD ON PHOSPHOINOSITIDE SYSTEM IN RAT BRAIN

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

773
TITLE:
PHARMACOKINETICS

AUTHORS:
DEDRICK RL

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and humans. They provide a plausible set of equations that can be used to extrapolate data from animals to humans, and thereby improve chemotherapy and risk assessment. A pharmacokinetic model has been published for the pharmacokinetics of methyl mercury and inorganic mercury derived from it by demethylation in the growing rat. Preliminary consideration has been given to the pharmacokinetics of IBZM to include bound, free, and metabolite concentrations in relevant tissues. Work is well advanced on the development of a pharmacokinetic model for topotecan in the Rhesus monkey. Important features of the model include the reversible opening of the topotecan lactone to an hydroxy acid form, and transport between the plasma and the cerebrospinal fluid. Other research on regional therapy has included discussion of a draft clinical protocol for the administration of AZT into the cerebrospinal fluid for the treatment of AIDS dementia and related transport studies in the rat brain. A draft chapter on intraperitoneal drug administration has been prepared, and calculations suggest that absorption of drugs directly into the surface of the liver may be quantitatively more important than was previously recognized.

774
TITLE:
EFFECTS OF MERCURY AND LEAD ON PHOSPHOINOSITIDE SYSTEM IN RAT BRAIN

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

775
TITLE:
Accidental ethyl mercury poisoning with nervous system, skeletal muscle

and myocardium injury.

AUTHORS:
CINCA I
DUMITRESCU I
ONACA P
SERBANESCU A
NESTORESCU B

SOURCE:
J NEUROL NEUROSURG PSYCHIATRY; 43 (2). 1980. 143-149.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Case reports (4) are presented of patients who ate the meat of a hog inadvertently fed seed treated with fungicides containing ethyl mercury chloride. The clinical, electrophysiological and toxicological, and in 2 of the patients the pathological data, showed that this organic mercury compound has a very high toxicity not only for the brain, but also for the spinal motoneurons, peripheral nerves, skeletal muscles and myocardium.

776
TITLE:
Effects of PrePlus Postnatal Exposure to Methylmercury in the Monkey on Fixed Interval and Discrimination Reversal Performance

AUTHORS:
Rice DC

SOURCE:
Neurotoxicology, Vol. 13, No. 2, pages 443-452, 31 references, 1992

ABSTRACT:
Monkeys were exposed to methylmercuric-chloride (115093) in-utero and postnatally; performance was then assessed on a fixed interval schedule of reinforcement. Female monkeys were exposed to methylmercuric-chloride at 0, 10, 25, or 50 micrograms/kilogram/day, and bred to untreated males. Offspring were treated with the same dose the mother had received. Maternal blood mercury (7439976) levels averaged 0.33, 0.78, or 1.41 parts per million (ppm) for the three dosed groups. Infant blood mercury levels averaged 0.46, 0.93, or 2.66ppm at birth, decreasing slowly to steady state levels of 0.20, 0.25, or 0.60ppm. The assessment of discrimination reversal performance during infancy was negative and therefore performance on a series of discrimination reversal tasks was assessed when these monkeys were juveniles, to determine whether continued exposure to methylmercury would produce deficits on this task. There was no strong indication of differences between treated and control monkeys either as infants or juveniles for the discrimination reversal tasks. Treated

monkeys performed transiently better than controls when first introduced to the task both as infants and juveniles. Marginally longer periods of feeding were noted in the methylmercury treated infants. The author suggests that prenatal plus postnatal exposure to methylmercury did not cause gross intellectual impairment in these monkeys but may have interfered with temporal discrimination.

777
TITLE:
Role of Glutathione in Mercury Disposition

AUTHORS:
Naganuma A
Tanaka T
Urano T
Imura N

SOURCE:
Advances in Mercury Toxicology, T. Suzuki, N. Imura and T. W. Clarkson, Editors; Rochester Series on Environmental Toxicity, Plenum Press, New York, pages 111-120, 14 references, 1991

ABSTRACT:
The complex formation between glutathione (GSH) and methylmercury (22967926) (MeHg) and its metabolism in laboratory animals were discussed. GSH-MeHg complexes have been detected in the brain, liver, red blood cells, and bile, and the role of GSH in the biliary secretion of MeHg was described. The reabsorption of 90% of the administered MeHg in the gut suggested the importance of biliary secretion and the enterohepatic circulation of MeHg in its distribution and toxicity in animals. Interspecies comparisons of biliary secretion of MeHg were made. The difference in biliary secretion of MeHg between species was reflected in total GSH levels and its degradation products in the bile, which included cysteine and cysteinylglycine. The role of GSH in kidney uptake of MeHg was discussed, with emphasis on the effect of 1,2-dichloro-4-nitrobenzene (DCNB) on the renal accumulation of MeHg in mice. DCNB pretreatment in mice depleted concentrations of hepatic GSH, resulting in a reduced renal accumulation of MeHg. The hepatic release of GSH may have influenced MeHg accumulation in the kidney. Pretreatment with acivicin reduced renal uptake of MeHg and caused an increase of MeHg and GSH in the urine. Sex and strain differences were cited as possible factors affected by GSH and gamma-glutamyltranspeptidase in the renal metabolism of MeHg. The authors conclude that hepatic GSH and gamma-glutamyltranspeptidase act as regulatory factors for the accumulation of MeHg in the kidney and may determine sex and strain differences in MeHg distribution.

778
TITLE:

Organochlorine and mercury residues in the harp seal.

AUTHORS:
JONES D
RONALD K
LAVIGNE DM
FRANK R
HOLDRINET M
UTHE JF

SOURCE:
SCI TOTAL ENVIRON; 5 (2). 1976 181-195

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Samples of blubber, liver, kidney and brain, obtained from 10 male, 6 female neonatal and 4 lactating female harp seals (P. groenlandicus), were analyzed for (the environmental contaminants) DDT, dieldrin, PCB (polychlorinated biphenyls) and the total Hg. Methyl mercury levels in blood were also determined. Biocide deposition was not significantly different in female and male 10 day old pups. There were no significant differences in biocide levels in the liver of the 14/+ day old males, but in blubber there were significant differences in dieldrin and DDT. There was no clear relationship between biocide levels in the 6-8 yr old lactating adults and their pups. Younger adult seals (6 and 7 yr) had higher levels of PCB and sigmaDDT (total) levels in their blubber than did older females (10 and 18 yr). Wide intraspecific variation was noted in organochlorine and Hg residue levels. Pups taken in 1973 had lower organochlorine residues than pups taken in the same area in 1971. Preliminary investigation indicates that detectable amounts of organochlorine and Hg residues are capable of crossing the placenta in the harp seal.

779
TITLE:
Reproductive Disorders

AUTHORS:
Hatch MC
Stein ZA

SOURCE:
Occupational Health, Recognizing and Preventing Work-Related Disease, Second Edition, B. S. Levy and D. H. Wegman, Editors; Little, Brown and Company, Boston, pages 415-429, 39 references, 1988

ABSTRACT:
Work related reproductive disorders were reviewed and discussed. The effects of occupational exposures to chemical or physical agents on female

reproductive function were reviewed. Reproductive disorders in women can involve effects on hormones that regulate the menstrual cycle, fecundity and fertility, pregnancy outcome, and teratogenesis. Some studies have suggested that synthetic hormones, mercury (7439976) vapor, and organic solvents can cause menstrual dysfunction. Few studies have investigated the effects on fertility. Some case studies have suggested that exposure to noise, dyes, lead (7439921), mercury, and cadmium (7440439) can cause female infertility. Miscarriages have been associated with exposure to ethylene-oxide (75218) and antineoplastic agents. No conclusive evidence of an association between anesthetic gas exposures and miscarriage has been found despite the large number of studies conducted. Polychlorinated biphenyls exposures have been associated with prematurity and low birth weights. Male reproductive disorders can involve decreases in sexuality, semen quality, and fertility and effects on progeny including childhood cancer. The spermatotoxicity of dibromochloropropane (96128) (DBCP) was discussed. Besides DBCP, ionizing radiation, chlordecone (143500), and carbon-disulfide (75150) have been recognized as being spermatotoxic. Ethylene-dibromide (106934) and hyperthermia have been implicated as causing male infertility. A large number of studies of possible associations between paternal occupation and childhood cancer have been conducted. The most credible association has been a two fold increase in the risk of brain cancer in children whose fathers were exposed to organic solvents. Preventing and controlling occupational exposures that can impact on human reproduction was discussed.

780
TITLE:
Neurobehavioral Effects of Developmental Methylmercury Exposure

AUTHORS:
Gilbert SG
Grant-Webster KS

SOURCE:
Environmental Health Perspectives, Vol. 103, Supplement 6, pages 135-142, 107 references, 1995

ABSTRACT:
A review was undertaken of studies investigating the effects of methylmercury (22967926) (MeHg) exposure on development, current exposure guidelines, and to identify areas in which future research is needed. Mercury has been found to enter the environment from a variety of natural and industrialsources, including volcanic emission, water evaporation, fossil fuel burning, mining, and refuse incineration. Most environmental MeHg is generated via the biotransformation of inorganic mercury. Studies have shown that MeHg is quickly absorbed by the body, and that concentrations in the brain are significantly higher than that in the blood. MeHg has been shown to cross the placenta, and therefore

represents a threat to the developing fetus. In-utero exposure to MeHg has been shown to produce deafness, blindness, and sensory and behavioral deficits. Mental retardation and cerebral palsy have also been attributed to in-utero exposure to MeHg. The number of viable births to pregnant Macaca-fascicularis exposed to MeHg was reduced. The authors conclude that MeHg exposure causes adverse effects on nervous system development, and that stronger regulations on the sale, environmental release, and exposure of MeHg are needed.

781
TITLE:
NEUROTOXICITY OF METHYLMERCURY ACROSS THE LIFESPAN

AUTHORS:
NEWLAND MC

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
DESCRIPTION: (ADAPTED FROM APPLICANT'S ABSTRACT) Fetal exposure to methylmercury (MeHg) has long-lasting effects on sensory-motor function, schedule-controlled behavior, learning (not memory) and sensitivity to certain behaviorally active drugs. Human and animal studies now associate developmental or adult MeHg exposure with age-related declines in certain behavioral functions. Nutritional influences also modify mercury's neurotoxicity, although how these interact through the lifespan is not well understood. This is important both mechanistically and because of concerns that a low RfD for MeHg would decrease consumption of fish, a source of selenium and n-3 fatty acids, especially docosahexanoic acid (DHA). In previous work, rats on a chow diet consuming 40 or 500 mg/kg/day Hg (as MeHg) showed age- and dose-related decrements on high-rate operant behavior, retarded learning, and altered sensitivity to amphetamine and pentobarbital. Proposed studies extend these observations by examining age and diet as modifiers of MeHg's neurobehavioral toxicity. High-rate operant behavior will be examined using a refined procedure (targeted percentile schedule) that maintains high response rates but without lowering reinforcement rates if behavior deteriorates. Concurrent schedule performance in transition, which now can be conducted in single sessions, will be the measure of learning. Fixed-interval (FI) schedule performance will be examined per se and as a baseline for drug challenges. Female rats will start one of three diets (modified semipurified, DHA-enriched, Se-enriched) for two weeks, then MeHg exposure (0. 0.5, or 5 ppm in drinking water) for two weeks, then they will be mated. Maternal rats will continue the diets and mercury exposure to 30 months of age, and their behavior examined under a targeted percentile schedule of reinforcement. During this time they will receive selected drug challenges. At death mercury levels in blood and brain, Se (in the Se cohort) and DHA in the

DHA cohort) will be examined. Offspring will be maintained on the different diets and used as follows: 1) Hg and Se or FA profile determination PN1; 2) FI schedule performance in transition with drug challenges: 3) Targeted percentile schdule performance, and 4) Concurrent schedule performance in transition with drug challenges. Items 2-4 will be conducted as adults and 3-4 to 30 months of age. At death Hg and either Se or FA profiles will be determined, depending on the cohort.

782

TITLE:

Impaired Biliary Excretion and Whole Body Elimination of Methylmercury in Rats with a Congenital Defect in Biliary Glutathione Excretion

AUTHORS:

Ballatori N
Gatmaitan Z
Truong AT

SOURCE:

Hepatology, Vol. 22, No. 5, pages 1469-1473, 23 references, 1995

ABSTRACT:

The possibility of multiple, glutathione independent canalicular transport mechanisms for the excretion of methylmercury (22967926) (CH3Hg) into bile was investigated. Eisai-hyperbilirubinemic-rats (EHBR), incapable of excreting reduced glutathione (GSH) into bile, and female Sprague-Dawley-rats were trachea, jugular vein and bile duct cannulated, and a 5 micromole/kilogram (micromol/kg) dose of radiolabeled methylmercury-chloride (115093) injected into the jugular vein. Bile was collected at 30 minute intervals for 4 hours at which time the liver was perfused and removed. Both glutathione and CH3Hg biliary excretion in EHBR rats were less than 2% of control levels over the course of the experiment. The EHBR rats had higher levels of hepatic glutathione and CH3Hg than control rats. Whole animal mercury-203 (Hg203) levels were measured daily for 17 days following an intraperitoneal dose of 0.5 or 5 micromol/kg of labeled CH3Hg. The biological half lives of the 0.5micromol/kg dose were 18 and 48 days for control and EHBR rats, respectively, and followed a first order elimination process. The half lives for the 5.0micromol/kg dose were 22 and 54 days for control and EHBR rats, respectively. Fecal elimination was the main route of elimination in control and EHBR rats, with the proportion of urinary excretion increasing at the higher dose. Excretion of CH3Hg in feces and urine was lower in EHBR rats. Significantly higher levels of Hg203 were detected in the liver and kidneys of EHBR rats after 17 days, with 24.8% and 1.4% of the administered dose found in the liver of EHBR and control rats, respectively. No significant differences were seen in Hg203 levels in the spleen, heart, brain or whole blood of EHBR and control rats. The authors conclude that elimination of CH3Hg in bile involves a GSH dependent

mechanism that transports a CH3Hg complex across the canalicular membrane.

783
TITLE:
STUDIES ON THE HEALTH EFFECTS OF ALKYLMERCURY IN JAPAN.

AUTHORS:
KAWANISHI S
TSUBAKI T

SOURCE:
STUDIES ON THE HEALTH EFFECTS OF ALKYLMERCURY IN JAPAN. JAPAN: ENVIRONMENT AGENCY, 1975. 217 PP.

ABSTRACT: EIS: Epidemiology Information System

784
TITLE:
INTERACTION OF DIETARY METHYLMERCURY AND SELENIUM ON ACCUMULATION AND RETENTION OF THESE SUBSTANCES IN RAT ORGANS

AUTHORS:
OHI G
NISHIGAKI S
SEKI H
TAMURA Y
MAKI T
MAEDA H
OCHIAI S
YAMADA H
SHIMAMURA Y
YAGYU H

SOURCE:
TOXICOL. APPL. PHARMACOL. 1975, 32(3) 527-533

ABSTRACT: EIS: Epidemiology Information System

785
TITLE:
DIETARY SELENIUM PROTECTION OF METHYLMERCURY INTOXICATION OF JAPANESE QUAIL

AUTHORS:
STOEWSAND GS
BACHE CA
LISK DJ

SOURCE:
BULL. ENVIRON. CONTAM. TOXICOL. 1974, 11(2) 152-156

ABSTRACT: EIS: Epidemiology Information System

786
TITLE:
MINAMATA DISEASE IN CHILDREN

AUTHORS:
HARADA Y
ARAKI Y
SUDOH H
MIYAMOTO Y

SOURCE:
KUMAMOTO DAMON KAISHI 1965, 40(12) 6-14(268-276)

ABSTRACT: EIS: Epidemiology Information System

787
TITLE:
Differential Sensitivity of Neonatal Rat Astrocyte Cultures to Mercuric Chloride (MC) and Methylmercury (MeHg): Studies on K+ and Amino Acid Transport and Metallothionein (MT) Induction

AUTHORS:
Aschner M
Rising L
Mullaney KJ

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 107-116, 39 references, 1996

ABSTRACT:
The effect of mercuric-chloride (7487947) and methylmercury on potassium ion (K+) and amino acid transport and metallothionein induction was studied in astrocyte cultures. Astrocyte cultures prepared from the cerebral cortices of neonatal Sprague-Dawley-rats were incubated with 0 to 100 micromolar (microM) mercuric-chloride or methylmercuric-chloride (115093) (MMC) for 30 minutes (min). The effects on uptake of rubidium-86 (Rb86) tagged rubidium-chloride and tritium (H3) labeled glutamic-acid were determined. Rb86 was used as a tracer for K+. Other rat astrocyte cultures preloaded with Rb86 tagged rubidium-chloride or tritiated D-aspartic-acid (aspartate) were incubated with 0, 2.5, or 10microM mercuric-chloride or 5 or 10microM MMC for up to 50min. The effects on efflux of Rb86 and aspartate derived H3 activity from the cell preparations were determined. Additional rat astrocyte cultures were

incubated with 5 or 10microM mercuric-chloride or MMC for 24hr. The extent of induction of metallothionein was assessed by a Western blotting technique. Mercuric-chloride and MMC inhibited uptake of Rb86 and glutamic-acid derived H3 activity in a dose dependent manner. The concentrations for inhibiting Rb86 uptake by 50% (IC50s) were: mercuric-chloride 4x10(-6) molar (M) and MMC 5x10(-5)M. The IC50s for inhibiting glutamic-acid derived H3 activity uptake were: mercuric-chloride 3x10(-6)M and MMC 2x10(-5)M. Mercuric-chloride and MMC both increased the rate of efflux of Rb86 and aspartate derived H3 activity from the astrocyte cultures, mercuric-chloride being the more effective. Mercuric-chloride also induced a sustained release of Rb86 and H3 activity, whereas the effect of MMC was reversible. Both mercurials caused a dose dependent induction of metallothionein, mercuric-chloride being the more potent inducer. The authors conclude that the effects of mercuric-chloride and MMC on astrocyte ion and amino acid transport support the view that astrocytes mediate mercury (7439976) neurotoxicity.

788
TITLE:
[HEALTH EFFECT OF LONG-TERM DIET MERCURY CONTAMINATED TUNA. PART II. ACCUMULATION AND RETENTION OF MERCURY AND SELENIUM IN ORGANS AND CLINICAL SYMPTOMS.]

AUTHORS:
SHIRAMIZU M
YAMAGUCHI S
KAKU S

SOURCE:
JPN. J. IND. HEALTH 1976, 18(2) 123-135 (JPN)

ABSTRACT: EIS: Epidemiology Information System

789
TITLE:
SELECTED CASE HISTORIES AND EPIDEMIOLOGIC EXAMPLES OF HUMAN MERCURY POISONING.

AUTHORS:
GERSTNER HB
HUFF JE

SOURCE:
CLIN. TOXICOL. 1977, 11(2) 131-150

ABSTRACT: EIS: Epidemiology Information System

790

TITLE:
DISTRIBUTION AND FATE OF MERCURY IN TISSUES OF HUMAN ORGANS IN MINAMATA DISEASE.

AUTHORS:
OKABE M
TAKEUCHI T

SOURCE:
NEUROTOXICOLOGY 1980, 1() 607-624

ABSTRACT: EIS: Epidemiology Information System

791
TITLE:
Poisoning in ferrets by tissues of alkylmercury-fed chickens.

AUTHORS:
Hanko E
Erne
Wanntorp H
Borg K

SOURCE:
Acta Vet. Scand.; 11(2): 268-82 1970; (REF:19)

ABSTRACT:
HAPAB Studies were made to provide experimental evidence for the transfer of alkyl mercury-treated seed to seed-eating bird to predatory mammal along the food chain and to describe the clinical course, pathoanatomical features and tissue mercury distribution in the case of secondary alkylmercury-poisoning in a mammal by way of the food chain. Methylmercury-treated wheat was fed to chickens whose meat (plus some liver) was fed to ferrets. Wheat seed was treated with methylmercury dicyandiamide (MM) to give a mercury (Hg) content of about 8 mg/kg and mixed with a standard feed supplement. The Hg content of the finished feed varied between 5.9 to 14.0 (average 8.2) mg/kg. White Leghorn and Rhode Island chickens received the Hg-containing feed for from 35 to 44 days. During the feeding period, no overt signs of poisoning were seen. Eggs were not laid. The average daily intake of Hg was between about 0.46 and 0.42 mg/kg/day, or a total of 28 and 27 mg/animal according to breed. Total Hg content of chicken muscle and liver and of ferret-tissue was determined by neutron-activation analysis and MM content by gas chromatography. Overall average Hg content of chicken muscle was about 10 mg/kg and of liver 40 mg/kg. Tissue Hg was principally MM. Two groups of six ferrets each were used as experimental and control subjects. The experimental ferrets (in two groups) received two types of ration, both containing muscle and liver of MM-treated chickens. Group A received a

total Hg intake of at most 33 mg/animal;in group B, the total Hg intake amounted to 20 mg/animal at most. The ferrets lost appetite, until almost no food was taken, and lost weight, with marked muscular atrophy being apparent. Clinical signs were manifest in 2 to 3 weeks and were primarily of a neurological nature: limb weakness, trembling, head-twitching, ataxia, paralysis and gradually developing apathy. Late symptoms included periods of excitation, ,yelling' and circular creeping. Death in Group A came within 35 to 36 days and in group B within 58 days. Controls were killed after 37 days. Detailed histopathological study was made of liver, kidney, spleen, pancreas, gonads, digestive tract, vulva, myocardium, skeletal muscle and various parts of the central and peripheral nervous systems. The clinical signs were correlated with marked degeneration in the nervous system, primarily in the cerebellum and the peripheral nerves, but involving to a less degree the cerebrum and spinal cord. The spleen was lymphiodally hyperplastic and there was degeneration of the Graafian follicles in the ovary. High Hg content (principally as MM) was noted in the ferret kidneys, brain, liver, gonads and skeletal muscle, thus giving evidence of transfer and accumulation of alkyl-Hg in toxic form received through the food chain. 1970

792
TITLE:
Mercury Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review,

AUTHORS:
Eisler R

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 15, 1987

ABSTRACT:
TD3: Most authorities agree on six points: (1) Mercury (Hg) and its compounds have no known biological function, their presence in the cells of living organisms is undesirable and potentially hazardous; (2) Forms of Hg with relatively low toxicity can be transformed into forms of very high toxicity, such as methlymercury, through biological and other processes; (3) Hg can be bioconcentrated and biomagnified through food chains; (4) Hg is a mutagen, teratogen, and carcinogen; (5) Some species of fish and wildlife contain normally elevated levels of Hg, not attributable to man's activities. The significance of elevated Hg levels in animal tissues is not fully understood. Usually, however, concentrations in excess of 1,100 Hg/kg fresh weight in kidney, brain, blood, hair, or liver should be considered as presumptive evidence of environmental Hg pollution.

793
TITLE:
Distribution and excretion of mercury ((SUP)203Hg) administered as phenyl mercury ((SUP)203Hg) acetate (PMA) in lactating guinea pigs and its

transfer into the sucklings.)

AUTHORS:
Miyamoto S

SOURCE:
Eiyo To Shokuryo (Food Nutr.)27(3): 109-115; 1974

ABSTRACT:
PESTAB (25 references) (Japanese) jPMA ((SUP)203Hg) of specific activity of 50 muCi/mg, was administered once at the rate of 500 mug/animal p. o. in a capsule to six lactating guinea pigs of the Hartley strain. Another five lactating guinea pigs received the same dose once a day for five consecutive days. The excretion of Hg into feces and urine, the transfer of Hg into milk, the residue of Hg in some organs and blood, and the transfer into sucklings from mother's milk were traced radiochemically. Most of the Hg in PMA administered p. o. was excreted via feces (59. 7% single dose and 61. 7% repeated dose) and urine (13. 2% and 16. 4%). While the transfer of Hg into milk was small (0. 40% for both) it continued during the entire experimental period of 11 days. The amount and concentration of mercury residues were highest in kidney (8. 5-14. 8%, 9. 4-28. 1 ppm), followed by liver (2. 4-2. 8%, 0. 24-1. 5 ppm), and then by other organs. A small amount of Hg was detected in brain. The transfer of Hg from milk to the sucklings was 4. 8% for the single dose and 5. 07% for the repeated dose. The period in which half the amount of administered Hg was excreted was about two or three days. s,

794
TITLE:
Effects of chronic intrauterine mercury intoxication on the epileptogenicity of developing rat.

AUTHORS:
SZASZ A
BARNA B
SZENTE M
KIRSCH-VOLDERS M

SOURCE:
23RD INTERNATIONAL EPILEPSY CONGRESS, PRAGUE, CZECH REPUBLIC, SEPTEMBER 12-17, 1999.YEPILEPSIA; 40 (SUPPL. 2). 1999. 142-143.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM EFFECTS OF CHRONIC INTRAUTERINE MERCURY INTOXICATION ON THE EPILEPTOGENICITY OF DEVELOPING RATYMEETING ABSTRACT MEETING POSTER WISTAR RAT ANIMAL MODEL PUP NERVOUS SYSTEM TOXICOLOGY MERCURY INORGANIC PRENATAL EXPOSURE ORGANIC TOXICITY BRAIN CONCENTRATION

CHRONIC INTRAUTERINE INTOXIFICATION DRINKING WATER ADMINISTRATION EPILEPTOGENICITY ELECTROENCEPHALOGRAPHY EPILEPSY CORTICAL ICTAL ACTIVITY EVALUATION METHOD NERVOUS SYSTEM DISEASE 3-AMINOPYRIDINE-INDUCED FACILITATED EXPRESSION FREQUENCY PROPAGATION DURATION

795
TITLE:
Effect of methyl-mercury administration on the activity of certain enzymes involved in carbohydrate metabolism.

AUTHORS:
BOGHIANU L

SOURCE:
STUD CERCET BIOCHIM; 19 (1). 1976 (RECD 1977) 13-18

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The influence of methyl-mercury administration in rats was studied on the activities of the following rat liver and brain enzymes: phosphorylases a and b, glucose-6-phosphate dehydrogenase (G6PDH), glucose-6-phosphatase, aldolase, lactate dehydrogenase (LDH), succinate dehydrogenase (SD) and succinate oxidase. Methyl-mercury provoked an increase of 41% in the liver activity and an inhibition of 20% in the LDH activity in liver after 30 days of administration. After 60 days of administration the activities of G6PDH and LDH did not present significant changes; the registered results were framed among physiological limits of an adaptating mechanism.

796
TITLE:
Heavy metal poisoning and antidotes.

AUTHORS:
Ogawa E

SOURCE:
Jap. J. Pharmacol.24(Suppl.): 17; 1974

ABSTRACT:
PESTAB. In experiments to determine the effects of principal chelating agents on the elimination of mercury compounds from the living body, tracer doses of the radionuclides were administered p. o. or i. p. , and whole-body radioactivity was measured daily for 3 or 7 days. Immediately after administering nuclides, various chelating agents were given every 24 hr for 3 or 7 days and their effects on the retention, excretion, and distribution of the nuclide examined. EDTA and DTPA were ineffective in treatment of mercury poisoning. Dimercaprol (BAL) decreased the retention of HgCl(SUB)2 and phenylmercuric acetate, but

often increased the mercury concentration in the brain in experiments with phenylmercuric acetate, EMC and MMC. When animals were fasted, all heavy metals tested were retained in the body. When feeding was restored, the body tended to return to a normal state. Thus feeding is important in the absorption, distribution, and elimination of heavy metals.

797
TITLE:
Conduction velocities in methylmercury poisoned patients.

AUTHORS:
VonBurg R
Rustam H

SOURCE:
Bull. Environ. Contam. Toxicol. 12(1): 81-85; 1974(REF:12)

ABSTRACT:
PESTAB. Electrophysiological techniques were used to investigate the human peripheral nervous system in an attempt to improve identification and early diagnosis of persons suffering from mercury poisoning. Fourteen patients with blood mercury levels between 1000 ng/ml and 3900 ng/ml at the height of exposure were examined 7 months post-exposure when blood mercury levels were between 100 and 800 ng/ml. Seven controls were also studied. Results of this study do not support the theory that methylmercury poisoning resembles peripheral polyneuropathy since clinical electrophysiological testing did not detect any consistent abnormalities even in severely afflicted patients. Except for the determination of the threshold for the H reflex, there was no statistically significant difference between patients and controls. This reduced threshold for H reflex suggests the possibility of lower brain stem damage, which would account for ataxia, tremor, dysmetria, the tendency to flex the arms and fist the hands, and emotional outbursts observed in the poisoned patients. This aspect of electrophysiological investigation should be pursued further.

798
TITLE:
THE EFFECT OF VARIOUS DIETARY FIBERS ON MERCURY RETENTION AND MERCURY TISSUE CONCENTRATION AFTER METHYLMERCURY EXPOSURE IN MICE

AUTHORS:
ROWLAND IR
MALLETT AK
HARGREAVES RH

SOURCE:

FOURTH INTERNATIONAL CONGRESS OF TOXICOLOGY, TOKYO, JAPAN, JULY 21-25, 1986. TOXICOL LETT (AMST); 31 (SUPPL.). 1986. 186.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT WHEAT BRAN PECTIN CELLULOSE METHYLMERCURIC CHLORIDE NEUROTOXICITY BRAIN BLOOD SMALL INTESTINE PROPHYLACTIC DIET

799

TITLE:

Acquisition of a multiple DRH extinction schedule of reinforcement in rats exposed during development to methylmercury.

AUTHORS:

Rasmussen EB
Newland MC

SOURCE:

Toxicologist 1999 Mar;48(1-S):149

ABSTRACT:

Female rats were exposed to 0, 0.5 or 6.4 ppm Hg as methylmercury in drinking water beginning at least 4 weeks before mating and ending on postnatal day 16. Female offspring (12 control, 10 low, and 12 high) represented six litters in each group. Concentrations of mercury in the brain for the low and higher-dosed groups were 0.5, and 9.5 ppm respectively at birth and 0.04 and 0.53 ppm at weaning. At 4 mos., female offspring were trained to lever press under Multiple Differential-Reinforcement of-High-Rate Extinction (MULT DRH-N:T EXT) schedules of reinforcement. Under the extinction schedule, lever-pressing had no scheduled consequences. Under the DRH-N:T schedule, a food pellet was delivered whenever N responses occur within T seconds. Two acquisition protocols were examined. First, the DRH parameter imposed in three successive sessions was 3:1, 5:2, and 9:4, values selected so that the same average inter-response time (i.e., rate) was required by the schedules. When the rats did not acquire the schedules in single sessions, as Bornhausen, Musch, & Greim (1980) reported, we implemented each of the three schedules individually until the rats acquired stable performance under each. Acquisition of the schedule was analyzed and marginal effects were apparent. This failed to replicate a similar experiment by Bornhausen et al. (1980) showing effects of mercury on acquisition of a Multiple DRH EXT schedule of reinforcement.

800

TITLE:

Biliary Excretion Of PhenylAnd Methyl Mercury Chlorides And Their Enterohepatic Circulation In Rats

AUTHORS:
Cikrt M
Tichy M

SOURCE:
Environmental Research, Vol. 8, No. 1, pages 71-81, 20 references, 19741974

ABSTRACT:
The biliary excretion and enterohepatic circulation of phenylmercury (23172374) and methylmercury (22967926) were studied in rats. Female Wistar-rats were administered mercury-203 (13982780) (Hg-203) labeled phenylmercury-chloride (100561) (PMC) or methylmercury-chloride (115093) (MMC) intravenously (iv) in doses corresponding to 14 or 88 milligrams per rat divalent mercury, respectively. The animals were killed 24 hours later and the bile, liver, gastrointestinal tract, kidney, urine, feces and brain were assayed for Hg-203. In studies of enterohepatic circulation, Hg-203 labeled PMC was given iv to rats. Bile was collected every 2 hours and administered to other rats (acceptors) through a surgical cannula into the duodenum. Equal doses of PMC were given intraduodenally to control rats. Bile, feces, and urine samples were collected for Hg-103 assay. The animals were killed after 24 hours, and radioactivity in the kidneys, liver, and gastrointestinal tract was determined. Biliary excretion of Hg-203 amounted to 6.9 and 6.2 percent of the dose 24 hours after treatment with PMC or MMC, respectively. Fecal and urinary excretion of radiolabel from PMC was 2.1 and 0.33 percent of the dose, respectively. The corresponding fecal and urinary excretion in MMC dosed animals was 0.21 and 1.03 percent. After PMC, the largest amounts of Hg-203 were found in the liver and kidneys. In MMC treated animals, highest amounts of Hg-203 were found in the gastrointestinal tract. In the enterohepatic circulation experiment, the acceptors absorbed only 20.7 percent of the radiolabel, versus 50.1 percent in the controls. Tissue, urine, and fecal Hg-203 concentrations were higher in the controls. The authors conclude that fecal excretion predominates during the first 24 hours after administering MMC and PMC.

801
TITLE:
CYTOCHEMICAL DEMONSTRATION OF MERCURY DEPOSITS IN TROUT LIVER AND KIDNEY FOLLOWING METHYL MERCURY INTOXICATION DIFFERENTIATION OF TWO MERCURY POOLS
BY SELENIUM

AUTHORS:
BAATRUP E
DANSCHER G

SOURCE:

ECOTOXICOL ENVIRON SAF; 14 (2). 1987. 129-141.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM SALMO-GAIRDNERI SPLEEN BRAIN MUSCLE LYSOSOME TUBULE CELLS GLOMERULAR FILTRATION ELECTRON MICROSCOPY LIGHT MICROSCOPY RADIOLABEL SILVER ENHANCEMENT METHOD

802
TITLE:
Electrophysiological investigations of methylmercury intoxication in humans. Evaluation of peripheral nerve by conduction velocity and electromyography.

AUTHORS:
VonBurg R
Rustam H

SOURCE:
Electroencephalogr. Clin. Neurophysiol. 37(4): 381-392; 1974.(34 references)

ABSTRACT:
PESTAB. In an attempt to elucidate the peripheral nervous symptoms associated with methylmercury intoxication, clinical and electrophysiological studies were conducted on Iraqi patients 7 months after cessation of exposure to this chemical. The fourteen patients had blood levels of mercury up to 3900 ng/ml at the height of the 1972 epidemic. During the current examination, the blood mercury levels ranged from 100 to 800 ng/ml. Evaluation was made of the motor and sensory conduction velocity, sensory threshold and sensory latency, the H reflex of the tibial nerve, and myoneural transmission. The results were negative, perhaps due to the clinical improvement in all patients tested. However, the electrophysiological studies showed evidence suggesting damage to the lower brain stem and a high incidence of interference with myoneural transmission. The exposure of the blood of 4 patients to mercury had exceeded 3300 ng/ml. On electromyographic studies, 3 of these 4 patients demonstrated a myotonic-like response. The results of this study allow the conclusion that humans, moderately to severely intoxicated by methylmercury, may suffer damage to exicitable tissues other than the cerebral cortex and cerebellum.

803
TITLE:
Prenatal Methylmercury Exposure Results in Dendritic Spine Dysgenesis in Rats

AUTHORS:
Stoltenburg-Didinger G

Markwort S

SOURCE:
Neurotoxicology and Teratology, Vol. 12, No. 6, pages 573-576, 33 references, 1990

ABSTRACT:
Histopathological changes in the nervous system that could explain the neurobehavioral abnormalities seen in offspring prenatally exposed to low doses of methylmercury were investigated in rats. Pregnant Wistar-rats were treated by gavage with methylmercury-chloride (115093) at 0.025, 0.05, 0.5, or 5.0mg/kg on days six to nine of gestation. The offspring were subjected to a developmental and behavioral testing battery first performed on day four to 35. Visual discrimination reversal, activity monitoring and auditory startle habituation test were performed on days 60, 120, 180 and 210 postnatally. Ten animals from each dose group were sacrificed at the age of 250 days. The litter size was into the normal range. No differences in physical landmarks were found with the developmental battery. Only the highest dose group showed significantly impaired swimming behavior compared to controls. The most reproducible effect was less nose poking during the intertrial interval in the visual discrimination reversal task by males of the highest dose group. Increased passiveness was noted in these same males. Decreased habituation was noted in the auditory startle response. No differences in brain weights and no malformations were noted. Histopathologically the arborisation of the apical and basilar dendrites of the pyramidal neurons of the treated animals were normal. Spine abnormalities consisted of a reduction of stubby and mushroom shaped spines and a predominance of long and tortuous spines. Dendritic spine dysgenesis implies defective development and may be the pathological feature of the impaired behavior and learning of methylmercury exposed animals.

804
TITLE:
The effect of mercaptodextran and N-acetylhomocystein on the excretion of mercury in mice after exposure to methyl mercury chloride.

AUTHORS:
AASETH J
NORSETH T

SOURCE:
ACTA PHARMACOL TOXICOL; 35 (1). 1974 23-32

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. In order to prevent the reabsorption of biliary excreted mercury in methl mercuric chloride exposed mice, the animals were treated with macromolecular polythiol (mecaptodextran)

synthesized by thiolating a dextran compound using N-acetylhomocysteine thiolactone. The polythiol given in the food at a concentration of 5% reduced the average biological half time of Hg from 11.6 days to 5.9 days. Hg levels in blood, liver and kidney were reduced to about 50% after 10 days as compared to control animals, and the brain level was reduced to about 70%. Fecal excretion of Hg compounds was not changed during 10 days, but the urinary excretion increased by a factor of 5. The effect of the macromolecule seems to be related to N-acetylhomocysteine in that it is released in the gastrointestinal tract, and this compound given alone has the same effect as the macromolecule. Corresponding results can be obtained by the i.v. injection of N-acetylhomocysteine. The mechanism includes the formation in the gastrointestinal tract or in the blood of a N-acetylhomocysteine-methyl-mercuric complex. This complex is easily absorbed when formed in the gastrointestinal tract, and it is easily excreted in the urine.

805
TITLE:
Mercury and vanadium accumulation in river fish.

AUTHORS:
WACHS B

SOURCE:
Z ANGEW ZOOL; 76 (4). 1989. 403-424.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The amounts of mercury and vanadium in 10 organs (muscle, liver, kidney, spleen, brain, heart, gall bladder, fatty tissue, gonads, gills) of river fish were determined. After digestion in conc. supra pure nitric acid at 130ê C the metal determination was carried out by standard methods of flameless atomic absorption spectroscopy. The cold-vapour AAS was used for mercury analysis, and the graphite furnace for the detection of vanadium. The concentrations were related to fresh weight. Most of the specimens have been fished in the Bavarian portion of the upper Danube River (West Germany) (km 2550-2240). Within the period from 1980 to 1989 the Hg-content of Danube River fish is to be found practically at a constant level. 2500 km on the course of the Danube River to the delta the Hg-contamination of fish was also observed as more or less constant. Average content values of the separate annual catches were within the following ranges: 0.12-2.2 mg/kg Hg in muscle; 0.03-0.44 m

806
TITLE:
Effects of methylmercury on the visual system of rhesus macaque (Macaca mulatta). I. Pharmacokinetics of chronic methylmercury related changes in vision and behavior.

AUTHORS:
Finocchio DV
Luschei ES
Mottet NK
Body R

SOURCE:
In: Neurotoxicity of the Visual System. Merigan, W. H., and Weiss, B., eds. (Raven Press: New York, NY): pp. 113-122 1980 (13 References)

ABSTRACT:
PESTAB. Adult female rhesus macaques (Macaca mulatta) were used to test the effects of methylmercury (MeHg) on the visual system, particularly the pharmacodynamic properties. Monkeys were given daily oral doses of MeHg at concentrations of 0, 50, 80, 90, 100 and 125 mug/kg/day. Clinical and behavioral observations were made daily, and every 2 wk mercury analysis (by atomic absorption spectrometry) and laboratory tests (hemogram, serum electrolytes, hepatic and renal function tests, and serum enzyme assays) were carried out. At necropsy, brain, spinal cord and other tissues were examined microscopically. Data showed the body burden of mercury to be proportional to dose. At doses of 0-100 mug/kg/day, the blood concentration reached a steady state, suggesting uptake and clearance of MeHg to follow linear, first-order kinetics. At 125 mug/kg/day, Hg blood levels continued to rise, suggesting a shift to zero-order kinetics. A good correlation was seen between body burden of mercury and degree of neurotoxicity; no toxic symptoms were observed at 50 or 80 mu/kg. At 90, 100 and 125 mug/kg/day doses, observed toxic symptoms included altered mastication, ataxa, and loss of vision. The half-life of MeHg at the 3 lowest doses was approximately 30 days, while at 100 mug/kg/day, the half-life was only 14 days.

807
TITLE:
Inorganic mercurial encephalopathy in discrete brain regions of catfish Heteropneustes fossilis.

AUTHORS:
BANO Y
HASAN M

SOURCE:
BIOMED RES (ALIGARH); 3 (1). 1992. 25-34.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Early neuropathological lesions in discrete regions of the fish brain following exposure to mercuric chloride 1 mg for 24 and 48 h, have been investigated. Wide-spread neuronal degeneration was apparent with the appearance of vacuolated intercellular spaces in the

cerebral cortex. The cerebellum exhibited remarkable loss of granule cells leading eventually to thinning of the cerebellar gray matter.

808
TITLE:
Effects of methylmercury on protein kinase A and protein kinase C in the mouse brain.

AUTHORS:
SAIJOH K
FUKUNAGA T
KATSUYAMA H
LEE MJ
SUMINO K

SOURCE:
ENVIRONMENTAL RESEARCH; 63 (2). 1993. 264-273.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of methylmercury administration on adenosine 3',5'-cyclic monophosphate (cAMP)-dependent protein kinase (protein kinase A) and protein kinase C were investigated by determining their second messenger bindings ((3H)cAMP binding for protein kinase A and (3H)PDBu for protein kinase C) and enzymatic activities in the brains of methylmercury-treated mice. After single administrations of methylmercury (10 mg Hg/kg, sc), no neurological symptoms were observed, while the mercury concentration in the brain reached 5.6 ppm. Neither second messenger bindings nor enzymatic activities of either protein kinase displayed significant changes. When methylmercury was administered repeatedly (10 mg Hg/kgconcentration was 11.7 ppm and the enzymatic activity of protein kinase C was reduced to 75% of the control level without significant change in (3H)PDBu binding. Significant change has not been observed in either (3H)cAMP binding or enzymatic activity of protein kinase A. The

809
TITLE:
ADP-ribosylation of brain neuronal proteins is altered by in vitro and in vivo exposure to inorganic mercury.

AUTHORS:
PALKIEWICZ P
ZWIERS H
LORSCHEIDER FL

SOURCE:
JOURNAL OF NEUROCHEMISTRY; 62 (5). 1994. 2049-2052.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. ADP-ribosylation is an essential process in the metabolism of brain neuronal proteins, including the regulation of assembly and disassembly of biological polymers. Here, we examine the effect of HgCl2 exposure on the ADP-ribosylation of tubulin and actin, both cytoskeletal proteins also found in neurons, and B-50/43-kDa growth-associated protein (B-50-43), a neuronal tissue-specific phosphoprotein. In rats we demonstrate, with both in vitro and in vivo experiments, that HgCl2 markedly inhibits the ADP-ribosylation of tubulin and actin. This is direct quantitative evidence that HgCl2, a toxic xenobiotic, alters specific neurochemical reactions involved in maintaining brain neuron structure.

810

TITLE:

A mutual protective effect of mercury and selenium in Japanese quail.

AUTHORS:

EL-BEGEARMI MM
SUNDE ML
GANTHER HE

SOURCE:

POULT SCI; 56 (1). 1977 313-322

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Dietary interactions between methylmercury (Ch3Hg) and sodium selenite (Na2SeO3) were studied in Japanese quail (Coturnix coturnix japonica). Addition of 0.35-6 ppm Se to diets containing toxic levels of Hg (5-30 ppm Hg) reduced the toxicity of CH3Hg and increased the survival of Japanese quail. The survival increased with increasing levels of Se in the diet. Selenium at 6 ppm did not cause any mortality in males and caused only relatively low mortality in females. However, 12 ppm Se depressed the survival of quail, especially females. No consistent effect of Hg, Se or both was observed on body weight or feed consumption. High levels of Hg reduced egg production, fertility and hatchability, and the addition of Se lessened these effects of Hg. Se in the diet alone (6 or 12 ppm) generally produced lower hatchability and a high percentage of deformed embryos, and 12 ppm Se also depressed egg production. Addition of 5-15 ppm Hg to such Se diets overcame these effects and reduced the percentage of abnormal embryos more than 50%. Analysis of tissues for total Hg showed that Hg was distributed in a pattern typical for alkyl mercurials. Hg levels in Se-protected birds equaled or exceeded the levels in those fed Hg without Se. Se levels in tissues were generally elevated by feeding Hg, especially in brain. Extremely high brain Hg levels, up to 58 ppm were observed in birds fed 15 ppm Hg plus 6 ppm Se for 20 wk prior to sacrifice. The level of Se in the brain of these birds was elevated (4 ppm), but not equimolar to Hg.

811
TITLE:
Neurotoxic effects of mercury: A review.

AUTHORS:
CHANG LW

SOURCE:
ENVIRON RES; 14 (3). 1977 329-373

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The significant literature concerning the neurotoxic effects of Hg, biochemical, physiological and morphological, is reviewed. Hg was found to penetrate and damage the blood-brain barrier very rapidly, leading to a dysfunction of the blood-brain barrier system. Both biochemical and EM histochemical analysis revealed that, intracellularly, Hg was bound to the membranous organelles such as mitochondria, endoplasmic reticulum, Golgi complex, nuclear envelopes and lysosomes. Only very minimal amounts of Hg were found within the nucleus. Biochemical and cytochemical studies also indicated that drastic reduction of neuronal RNA and protein synthesis occurred in Hg-intoxicated animals. Reduction of the protein synthesis was believed to lead to eventual cell death in these neurons. A regain in the neuron RNA level was also observed in prolonged intoxication with mercuric bichloride. Such an observation could also be correlated with the increasing tolerance to Hg toxicity by these animals. Disturbance of the enzymatic systems in the glycolytic pathway in the brain was also reported in Hg-poisoned animals. Neurophysiological study demonstrated abnormal excitation spikes in the Hg-intoxicated neurons. The suggestion that neuronal cell body injury preceded axonal injury was made. The large-caliber myelinated fibers probably were more vulnerable than the smaller nerve fibers to Hg toxicity. Pathological findings on Minamata disease (Japan) were summarized. In experimental models, the sensory neurons in the spinal ganglia and granule cells in the cerebellum were most vulnerable to Hg poisoning. Ultrastructural studies indicated that vacuolar degeneration of the neurons was mainly associated with inorganic Hg intoxication, while coagulative type of degeneration was found mostly in organic Hg poisoning. Degenerative changes in the nerve fibers were also observed. Based on the biochemical, physiological and pathological findings on Hg intoxication, a working hypothesis on the pathogenetic mechanism of Hg on the nervous system is proposed.

812
TITLE:
Selective inhibition of the mouse brain Mn-SOD by methylmercury.

AUTHORS:

SHINYASHIKI M
KUMAGAI Y
HOMMA-TAKEDA S
NAGAFUNE J
TAKASAWA N
SUZUKI J
MATSUZAKI I
SATOH S
SAGAI M
SHIMOJO N

SOURCE:
ENVIRONMENTAL TOXICOLOGY AND PHARMACOLOGY; 2 (4). 1996. 359-366.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Changes in mRNA levels, protein contents and enzyme activities for brain Cu,Zn- and Mn-SOD by methylmercury chloride (MMC) administration, were examined, over a period of 12 days in ICR mate mice. After subcutaneous administration of MMC (10 mg/kg) to mice, brain mercury content reached a maximum at 2 days and remained at that level for at least 5 days. MMC exposure resulted in a time-dependent decrease in the Mn-SOD activity: the enzyme activity at 5 days after exposure to MMC was about 60% of control level whereas this exposure was without effect on the Cu,Zn-SOD activity, indicating differential sensitivity of SOD isozymes to the metal. However, levels of mRNA and protein synthesis for Mn-SOD were unaffected by MMC administration. The direct effect of MMC on the both SOD activities were further examined with purified enzyme preparations. After each SOD isozyme (10 U) was incubated with 0.2 mM MMC for 24 h at pH 7.8, the enzyme activities for Cu,Zn- and Mn-SOD were 90

813
TITLE:
Effects of Hg2+ and CH3Hg+ on Ca2+ fluxes in rat brain microsomes.

AUTHORS:
FREITAS AJ
ROCHA J BT
WOLOSKER H
SOUZA D OG

SOURCE:
BRAIN RESEARCH; 738 (2). 1996. 257-264.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. A permanent increase in cytosolic Ca2+ levels seems to be associated with various pathological situations which may result in cell death. Hg2+ and CH3Hg+ are potent neurotoxic agents, but the precise molecular mechanism(s) underlying their effects are not

sufficiently understood. In the present study we investigated the potential role of Ca2+-ATPase located in the endoplasmic reticulum as a molecular target for mercury. Hg2+ and CH3Hg+ inhibited Ca2+-ATPase and Ca2+ uptake by brain microsomes with similar potencies. However, the inhibitory potency of Hg2+ was higher than that of CH3Hg+, probably reflecting differences in the affinity for the sulfhydryl groups of these compounds. Passive or unidirectional Ca2+ efflux (measured in the absences of Ca2+-ATPase ligands) was increased significantly by CH3Hg+ and Hg2+. Again, the potency of Hg2+ was higher than that of CH3Hg+. Blockers of Ca2+ channels (ruthenium red, procaine, heparin) did not affect the increase in passive

814
TITLE:
Neurological symptoms and mercury concentration in the brain of mice fed with methylmercury salt.

AUTHORS:
SUZUKI T
MIYAMA T

SOURCE:
IND HEALTH; 9 (1-2). 1971 (RECD 1972) 51-58

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The critical concentration of Hg in the brain, necessary to induce neurological symptoms, was tested by feeding methylmercury chloride to mice. After single or repeated preoral administration, death followed the occurrence of neurological symptoms, when the accumulated amount of Hg was more than 30 mug Hg/g. The earliest symptom, lessening of head maintenance in the horizontal position where hung by the tail, was noticed at a brain concentration of 10 mug Hg/g. The group receiving the lowest daily dose (10 mug Hg/g) did not show loss of body weight and neurological symptoms during the observation period up to the 41st day of Hg feeding.

815
TITLE:
Regional Cerebral Blood Flow of Acute Carbon Monoxide Poisoning in Cats

AUTHORS:
Okeda R
Matsuo T
Kuroiwa T
Nakai M
Tajima T
Takahashi H

SOURCE:
Acta Neuropathologica, Vol. 72, No. 4, pages 389-393, 13 references, 19871987

ABSTRACT:
The effects of acute carbon-monoxide (630080) exposure on regional cerebral blood flow (CBF) were studied in cats. Adult cats were exposed to 0.2 to 0.3 percent carbon-monoxide until the carbon-monoxide had induced a drop in aortic blood pressure to 70 or 80 millimeters of mercury, which took about 2.5 hours. Controls consisted of normotensive cats breathing air and cats with hypotension induced by blood depletion and trimetaphan-camsilate. Blood pressure of the aorta and inferior vena cava and carboxyhemoglobin (COHb) content were monitored. Once blood pressure had decreased, carbon-14 labeled antipyrine was injected. The animals were killed at selected times thereafter, the brains were removed, dissected into various regions, and analyzed by autoradiography. The typical response in the cerebral cortex and suprasylvian gyrus consisted of a compensatory increase in CBF as the concentration of COHb increased; however, after 20 to 40 minutes CBF decreased gradually in parallel with a progressive fall in aortic blood pressure. Blood pressure in the inferior vena cava was not involved in regional CBF. CBFs in the caudate, putamen, anterior portion of the pallidum, cerebral cortex, and white matter were significantly below that of the controls. CBFs in the posterior portion of the pallidum, the entopeduncular nucleus, medial, and lateral portions of the hippocampus, superior colliculum, and cerebellar white matter were significantly elevated above the control values, above 100 percent. The authors suggest that the sections of the brain damaged by carbon-monoxide are manifested by reduced regional CBFs.

816
TITLE:
Effect of neurotoxic divalent cations on the activity of the intrinsic nerve ending membrane-associated sialidase of bovine brain.

AUTHORS:
YOHE HC
ROSENBERG A

SOURCE:
NEUROCHEM RES; 3 (1). 1978 101-114

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Exposure to Hg2+ below 10 muM destroyed synaptosomal membrane-associated sialidase of bovine brain in situ. Inhibition by Cu2+ occurred only at relatively higher concentrations, and was demonstrable after the synaptosomal membrane preparation was presaturated with Cu2+. Pb2+ did not inhibit enzymatic activity. Hg2+ did not exert a significant effect on the free energy of association of

monomeric brain gangliosides into aggregates, or on the stability of the aggregate forms, as estimated by ultracentrifugal analysis of the ion-independent moment of ganglioside micelles as a function of concentration. Hg2+ inhibited synaptic membrane sialidase acting both in situ on the native sialocompounds in the membrane, or on exogenous ganglioside. Kinetic analyses of the exogenous activity in membranes exposed to Hg2+ revealed lowered Vmax values but no substantial change in Km for synaptosomal membrane gangliosides. Apparently the powerful inhibitory effect exerted by Hg2+ on nerve ending membrane sialidase is enzyme directed, not substrate directed. Part of the neurotoxic effect of low levels of Hg2+ may stem from an interference with synaptic metabolism by the destruction of membrane-associated sialidase. This enzyme can serve the purpose of modulation of synaptic negative charge density by releasing bound, strongly anionic, sialic acid from highly concentrated sialocompounds in the membrane.

817

TITLE:

Environmental contaminants in tissues of a neonate St. Lawrence beluga whale (Delphinapterus leucas).

AUTHORS:

GAUTHIER JM
PELLETIER E
BROCHU C
MOORE S
METCALFE CD
BELAND P

SOURCE:

MARINE POLLUTION BULLETIN; 36 (1). 1998. 102-108.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Tissue samples of brain, kidney, liver, and blubber from a neonate St Lawrence beluga whale were analyzed for ortho and non-ortho polychlorinated (PCB) congeners, organochlorine (OC) compounds, polychlorinated dibenzo-p-dioxins and -dibenzofurans (PCDDs), and total mercury. As gamma-globulins, which indicate presence of colostrum, were not found in serum of the live neonate, it was unlikely that there had been lactational transfer of environmental contaminants to the neonate. No PCDFs were detected. Of the PCDD congeners, only OCDD was found in all tissues; ranging from 12 pg g-1 lipid in brain to 1138 pg g-1 in liver. Concentrations of PCB (sum of 25 ortho and 4 non-ortho PCBs) and DDT were lowest in brain (1.7 and 0.7 mug g-1 lipid, respectively), intermediate in kidney (4.1 and 2.3 mug g-1) and highest in liver (8.8 and 3.5 mug g-1) and blubber (17.6 and 2.2 mug g-1). PCB 126 was the predominant non-ortho congener. Toxic equivalent 2,3,7,8-TCDD concentrations (TEQ

818

TITLE:

Core--Protein modulators of toxicity

AUTHORS:

GASIEWICZ T

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

The research activities in the Core emphasize biologically active proteins that function as critical regulatory molecules in normal cell processes. These research projects are making contributions toward understanding risk associated with exposures to particular chemicals and to knowledge of the molecular and cellular processes involved in certain diseases. Several sub-themes are included under this central theme: Receptor proteins as molecular sensors, post-transcriptional modification of RNA, proteins involved in Glutathione homeostasis and the role of these in xenobiotic transport and metabolism, and proteins involved in cell cycle regulation as targets for xenobiotics. The investigations are organized into seven projects: 1) Cellular and Molecular Responses to Dioxins Mediated by the Ah Receptor (T. A. Gasiewicz). This project is directed at understanding the molecular and cellular basis by which the Ah receptor mediates the toxicity of structurally-related halogenated hydrocarbons. A secondary objective is to advance knowledge of Ah receptor function especially the role of AhR phosphorylation. Collaborative projects include studies using an AhR-responsive reporter mouse model and molecular actions of AhR and cellular and functional alterations in the immune system. 2) Causes and Consequences of Thymic Atrophy Induced by TCDD and Estrogens (A. E. Silverstone). A major objective of this work is the identification of the cell type(s) that contain the estrogen receptor (ER) and AhR and are activated by TCDD or estrogen to cause thymic atrophy and immunosuppression. These studies will examine either cell cycle arrest, apoptosis, and/or altered cellular differentiation are involved and identification of the gene products involved. A second objective is to use a mouse model of a lupus-like nephritis to identify estrogen and TCDD-induced alterations in T-cell development. 3) Cellular and Molecular Toxicology of Heme Degradation (M. Maines). This research focuses on the heme metabolic pathway enzymes, heme oxygenase (HO) and biliverdin reductase (BVR) to elucidate the physiological functions of the heme degradation products. These studies are examining the biological functions of HO in the brain and cardiovascular system. One hypothesis being tested is that modulation of HO activity by exogenous and endogenous sensors may be involved in steroid-mediated degradation of neurons in brain areas involved in memory and learning. Other studies indicate that CO generated via HO may be a component of the cardiovascular system defense against

impairment induced by nephrotoxic agents. The role of BVR as a defense mechanism against oxidants in the brain. 4) Alteration in RNA processing by Alcohol and its Role in Atherogenic Diseases (H. Smith). This research involves the purification and molecular cloning of auxiliary protein genes involved in RNA editing. Additional studies are testing the hypothesis that ethanol stimulation of apoB mRNA editing results from alteration of enzymes/factors involved in mRNA editing, 5) Glutathione-dependent Metabolism and Plasma Membrane Transport of Xenobiotics (N. Ballatori). The focus of this research is the identification and characterization of cell membrane proteins that mediate the export of GSH adducts, related organic anions and GSH. This group has shown that oatp1, a sinusoidal organic solute transporter in liver functions as a GSH/organic solute exchanger and elucidates a pathway for GSH release in blood plasma. Other studies are defining the role of the y-glutamyl cycle in a mercapturic acid biosynthesis. N-acetylcysteine has been identified as an antidote for methyl mercury. 6) Bioactivation of Halogenated Hydrocarbons (M. W. Anders). A major objective of this research is to investigate the GSH-dependent bioactivation of haloalkanes and the GSH- and b-lyase-dependent bioactivation of haloalkenes. Mechanisms of cysteine S-conjugate induced cytotoxicity and activation of transcription factors in response to changes in cellular redox as a possible step is being considered. The role of mitochondria as an intracellular target is being assessed. 7) Radiation Sensitivity and G2M Delay in Lung Tumor Cells (P. Keng). The central hypothesis to be tested is that IFN-b modulates DNA repair capacity of irradiated human lung tumor cells. The repair of DNA strand breaks is the focus of these studies and the impact of IFN-b on accumulation of cells in G2M following irradiation is being investigated.

819

TITLE:

Mercury in herons, ergrets, and their foods.

AUTHORS:

HOFFMAN RD
CURNOW RD

SOURCE:

J WILDL MANAGE; 43 (1). 1979. 85-93.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Hg concentration levels were measured in herons and egrets and their foods collected in the southwestern Lake Erie region. Primary wing feathers, breast muscle, liver and brain tissues from 42 great blue herons (Ardea herodias), 44 black-crowned night herons (Nycticorax nycticorax), and 43 great egrets (Casmerodius albus) were analyzed. Concentrations were higher in island nesting birds than birds collected at the Winous Point Shooting Club, with primary wing feathers the highest, followed by liver, breast muscle and brain tissues. Hg levels

in breast muscle, liver and brain tissue of adult birds correlated (P < 0.01) within each population. Tissues of adult birds exhibited higher (P < 0.05) Hg concentrations than did tissues from nestlings of the same population. An importance index for each population of birds showing the significance of individual food items as sources of Hg indicated that birds nesting on West Sister Island acquired Hg from fish spp. found more frequently in Lake Erie than in marshes. Hg concentration factors of the Lake Erie marsh ecosystem show a relationship between trophic levels and Hg concentration levels.

820
TITLE:
Distribution of mercury in enzymatically characterized subcellular fractions from the developing rat brain after injections of methylmercuric chloride and diethylmercury.

AUTHORS:
SYVERSEN T LM

SOURCE:
BIOCHEM PHARMACOL; 23 (21). 1974 2999-3007

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Wistar rats were given CH3HgCl (203-Hg-labeled) and (CH3CH2)2Hg in peanut oil i.p. (5.0 mg/kg) every 2nd day from 5 until 27 days of age. A reference group was given identical injections of oil only. The rats appeared normal throughout the experimental period. The brains of the 3 groups were subjected to subcellular fractionation and myelin, nerve-ending particles, mitochondria and microsomes were isolated. Protein, total Hg, inorganic Hg, succinic dehydrogenase and acetylcholinesterase were measured in the fractions. The 2 groups showed an equal Hg content in the brain and the subcellular distribution of Hg showed a correlation with the protein content. The succinic dehydrogenase activity of the mitochondrial fraction was considerably decreased in both Hb groups compared with the reference group. The myelin fraction contained 4 times as much inorganic Hg relative to total Hg compared with other fractions after CH3HgCl injections.

821
TITLE:
Methylmercury alters the developmental pattern of trk and PKC isoforms in the rat brain.

AUTHORS:
Barone S Jr
Haykal-Coates N
Goldey ES

Tilson HA

SOURCE:
Int J Dev Neurosci 1994;12(Suppl 1):80

ABSTRACT:
Nerve growth factor receptor (trk) and protein kinase C (PKC)-mediated phosphorylation play an important role in normal neuronal growth and differentiation, and functional disruption of these kinases may underlie cellular dysmorphology and/or dysfunction resulting from developmental neurotoxicant exposure. Therefore, we examined the effects of exposure to methyl mercury (CH3Hg) on the developmental profile of immunoreactivity (IR) for the trk receptor, the calcium-dependent (alpha and beta) and calcium-independent (epsilon) PKC isoforms. Pregnant Long-Evans dams were dosed on gestational days 6-15 (po) with 0 (saline), 1 or 2 mg/kg/d CH3Hg. The brains were sectioned and stained for Nissl, glial fibrillary acidic protein, trk, and PKC isoforms. Examinations were made on postnatal days (PND) 1, 4, 10, 21 and 85. In controls, the IR for trk and each PKC isoform was highest at the earliest time-points examined, decreasing in many regions by PND10 and decreasing further after PND21. CH3Hg decreased trk IR in a dose-related manner in all regions examined. The 2 mg/kg dose of CH3Hg decreased the IR of PKC isoforms. These changes in IR of growth related kinases were seen in the absence of overt pathology, maternal toxicity or neonatal body weight alterations. The present results localize the cellular and regional ontogeny of trk and 3 PKC isoenzymes, and suggests that exposure to CH3Hg can alter the ontogenetic profile of several growth related kinases in the nervous system.

822
TITLE:
Functional teratogenic effects of chemicals on the developing brain.

AUTHORS:
Swaab DF
Boer K
Mirmiran M

SOURCE:
Fetal and Neonatal Neurology and Neurosurgery 1995;2:263-77

823
TITLE:
Developmental neurotoxic effects of environmental pollutants (heavy metals + organophosphates) in animal experiments.

AUTHORS:
Nagymajtäenyi L
Schulz H

Papp A
Däesi I

SOURCE:
Neurotoxicology 1997;18(3):876

ABSTRACT:
In our previous studies it was stated that the pre- and/or postnatal treatment of low-level inorganic heavy metal compounds (C4H6O4Pb x 3H2O, HgCl2, CdCl2) or organo-phosphorous pesticides (dimethoate, dichlorvos, parathion-methyl) dose and treatment-variation dependently changed the spontaneous and evoked bioelectric functions of rat's brain. In the recent experiment we investigated the combined effects of the low-level, pre- and/or postnatal, parallellous treatment of rats with inorganic heavy metal salts (C4H6O4Pb x 3H2O, HgCl2, CdCl2) and dimethoate. Wistar rats were orally treated by gavage by 80.0, 160.0, and 320.0 mg/kg lead (in form of C4H6O4Pb x 3H2O); 0.4, 0.8, and 1.6 mg/kg mercury (in form of HgCl2); 3.5, 7.0, and 14.0 mg/kg cadmium (in form of CdCl2), and 5.0, 10.0 and 20.0 mg/kg dimethoate. The above mentioned doses were given the female rats in 5-15 days of pregnancy (P variation), or in 5-15 days of pregnancy + for 4 weeks of lactation (P + L variation), or in 5-15 days of pregnancy + 4 weeks of lactation + 8 weeks postweaning (P + L + P variation). The electrophysiological parameters (ECoG, cortical evoked potentials, conduction velocity and refractory periods of peripheral nerve) of male rats of the differently treated groups were investigated at the age of 12 weeks. It was found that the metal + dimethoate combinations dose- and treatment duration-dependently altered both the spontaneous and evoked electrophysiological functions (changed ECoG frequencies, lengthened latencies and durations of evoked potentials, lower conduction velocity of peripheral nerve, etc). The changes caused by the combined treatment of metals and dimethoate were more expressed than in case of single administration of the mentioned compounds. The data showed that the low-level, pre- and postnatal combined exposure of certain metals and an organophosphate considerably affected the bioelectrical function of the nervous system without any signs of intoxication. Our results emphasize the real risk of the continuous (including pregnancy and lactation) low-level metal + organophosphate intake.

824
TITLE:
Effects of low-dose prenatal irradiation on the central nervous system--report of a workshop.

AUTHORS:
ANONYMOUS

SOURCE:
NTIS Technical Report (NTIS/DE92-015171) 1992 Apr;:89 pp.

ABSTRACT:

The workshop traced the historical perspectives and summarized current knowledge on effects of prenatal irradiation on the central nervous system (CNS). Topics included normal and altered morphologic development of the CNS, its functional capacity during postnatal life in experimental animals, as well as results of epidemiologic analyses of data from clinical evaluations of human populations. Background presentations were followed by others that examined current knowledge about changes that occur at the cellular and biochemical level. Finally, descriptions of current approaches used by investigators in the neurosciences and in molecular biology to investigate development of the CNS were presented. This format led to extended discussions that identified areas of agreement, remaining questions, and reasons for discrepancies; considered broad implications; and finally made recommendations for integrated research approaches that would address the effects, disparities, and mechanisms. The initial presentations documented that higher doses of intrauterine irradiation lead to morphologic and functional deficits of the CNS. These effects were observed in clinical and postmortem evaluations of both individuals and human populations and in experimental investigations of laboratory animals. Clinical evaluations in postwar Japan were consistent with these findings, and investigators detected children with reduced head circumference and/or mental retardation among those born to women who received the highest radiation exposures from the atomic bomb detonations. Subsequent analyses determined that there were definite relationships between dose, stage of gestation at exposure, and several measures of CNS dysmorphology and dysfunction in these survivors. This is the only sizable human group that has been evaluated by techniques of population statistics, and conclusions from these analyses serve as the root of many ongoing discussions. In essence, the questions have become whether dose-response relationships for mental retardation or reduced intelligence after exposure in the period from 8 through 16 weeks of gestation are linear, and whether there is a threshold for these effects. In addition to statistical uncertainties these studies are affected by other problems. For example, a number of adverse health and emotional stresses were experienced by the exposed population, which serve to introduce uncertainties into interpretations because of their possible adverse effects on prenatal development or synergy with radiation. One such stress is malnutrition, which may have an effect on birth weight and associated problems of prematurity. The irradiated mothers of mentally retarded children underwent several additional traumas during their pregnancy, including exposure to the blast and heat. In addition to potentially synergistic effects associated with maternal irradiation, there may have been interactions with the effects of other insults, including infection. Studies of experimental animals corroborate that prenatal irradiation produces CNS lesions, that effects tend to be reproducible and dose dependent, and that stage of gestation at exposure determines the specific characteristics and relative sensitivities of most

types of lesions. The altered CNS endpoints in animals ranged from malformations and disrupted histoarchitecture to functional defects of several behaviors, reflexes, and sensory-motor capabilities. The dose levels at which unequivocal permanent damage could be demonstrated, with essentially every endpoint reported, have been in the 0.15- to 0.25-Gy range, both in vivo and in vitro. Techniques used in earlier investigations of morphologic alterations and functional decrements of the CNS following prenatal radiation are crude by current standards, but most details and interpretations are still accepted. Techniques with greater sensitivity have become available to define and correlate lesions with changes in neurofunctional and cognitive measures. These more recently determined endpoints, such as alterations of the cell cycle, histogenic details of neuronal migration, and quantified measures of neuronal and fiber alignment, all yield a similar threshold or no-detectable-effect dose range. The site and identity of cells that die and the time at which they die are being studied to define mechanisms and draw conclusions regarding response relationships. The times and mechanisms of cytolethal processes, removal of dead cells in migrating populations via phagocytosis or apoptosis, and the possibility of sequential death of "different" neuronal "stem cell" populations remain unanswered questions. When appropriate scaling for gestational stage is used as the basis for comparisons, there is remarkable similarity between the development of the human brain and that of other mammalian species. Some categories of functional deficits, such as altered behavior and seizures, are similar and perhaps identical throughout. There is quantitative consistency between radiation effects in humans and animals; the threshold range across species seems to be about 0.15 to 0.25 Gy. There are substantive questions about relations between cognitive and reflex measures and differences between the nature of mental retardation in humans as compared to functional or behavioral changes in experimental animals. In both animals and humans, evidence suggests it is possible to produce primary neural cytotoxic effects, but precise dose-effect relationships have not been determined for individual types of neurons. As with most cell populations, adequate doses to mitotically active cells lead to DNA degradation and lethality. Because the stage of cell cycle at irradiation and whether the cells are pre- or postmitotic are related to time of migration, the nature and magnitude of effects seem to differ with their temporal relationship to these processes. Secondary effects on neuroblasts may be mediated through nonlethal DNA/RNA modification via indirect alteration of the cellular membranes and/or proteins. There is also a possibility of induction of secondary effects in the developing brain by nontraditional mechanisms, but there are no reasons to expect differences among species. These types of processes may include neuronal events that depend on the integrity of other cells and cell populations, such as guidance of migration and localization, as well as the role of proper synaptogenesis in survival. Changing repair and reconstitution capacities during development influence the chronology of cytologic and histologic characteristics and their ultimate functional consequences. The role of

factors that modify injury has not been completely defined and requires quantification. Information from mechanistic studies suggests that CNS lesions are produced by polycytic effects, i.e., ones involving more than a single cell.

825
TITLE:
Identification of mercury in the brain of minamata disease victims by electron microscopic X-ray microanalysis.

AUTHORS:
SHIRABE T
ETO K
TAKEUCHI T

SOURCE:
NEUROTOXICOLOGY (PARK FOR SOUTH); 1 (2). 1979 (RECD. 1980). 349-356.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The brains of acute and protracted Minamata disease (methylmercury intoxication by food poisoning) victims, fixed in formalin for many years, were examined by means of electron microscopic X-ray microanalysis. Hg was identified as round or irregularly shaped, highly electron opaque particles, measuring 10 nm or less in size, in the cytoplasm of nerve cells, astrocytes and endothelial cells, and in the extracellular spaces of the gray and white matter. Hg was most frequently identified with lysosomes in the more severely injured sites of the brain. Hg was thought to be tighly combined with Se, an essential element, and S, probably derived from tissue protein, since Hg was always detected together with Se and S.

826
TITLE:
An ultrastructural study on the bloodbrain barrier dysfunction following mercury intoxication.

AUTHORS:
WARE RA
CHANG LW
BURKHOLDER PM

SOURCE:
ACTA NEUROPATHOL; 30 (3). 1974 (RECD 1975) 211-224

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CH3HgCl (an environmental pollutant) was administered in a single i.p. injection to adult male rats at a dosage of 10 mg/kg body weight. Horseradish peroxidase was systemically injected

into these animals at various time intervals following CH3HgCl administration. Horseradish peroxidase activity as demonstrated by 3,3'-diaminobenzidene conjugation was used as a tracer to study blood-brain barrier dysfunction induced by CH3HgCl. Permeation of tracer into the parenchyma of the CNS was observed ultrastructurally as early as 4-6 h following CH3HgCl administration. Examination of capillary regions in the calcarine cortex and cerebellum at this time also revealed many endothelial cells with mitochondrial injury, increased pinocytotic transport of tracer, and in several instances, widening of lateral leaflet spaces without disruption of tight junctions. At 6 h after the intoxication, many astrocytic end-feet abutting these injured capillaries displayed swelling and tracer accumulation. Horseradish peroxidase activity could be localized within neuronal and glial elements after 10-12 h of CH3HgCl treatment. A newly developed electron microscopic histochemical technique utilizing an ammonium sulfide reaction was also employed to study the distribution of Hg within the blood-brain barrier structures. Localization of Hg corresponded with observed sites of celular injury and tracer extravasation. The observed blood-brain barrier dysfunction was probably due to the impairment of endothelial cells and astrocytic end-feet by Hg ions.

827

TITLE:

Time-dependent accumulation of inorganic mercury in subcellular fractions of kidney, liver and brain of rats exposed to methylmercury.

AUTHORS:

OMATA S
SATO M
SAKIMURA K
SUGANO H

SOURCE:

ARCH TOXICOL; 44 (4). 1980. 231-242.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Accumulation of inorganic Hg in subcellular fractions of the kidney, liver and brain of rats was studied during 48 days after a single injection of 25 mg/kg of methylmercury chloride. The highest ratio of inorganic to total Hg was seen in the cytosol of kidney; 80% of the total was inorganic Hg at day 48. The ratio in the mitochondria and microsomes of kidney attained a maximum level (about 50% of the total as inorganic) at day 26-37. In the liver, the ratio was strikingly low in the cytosol and microsomes as compared to the light and heavy mitochondria, where about 40% of the total was present as inorganic Hg maximally at day 26. The ratio in the brain, determined up to day 15, was very low as compared with the kidney and liver, showing less than 3% of the total in the mitochondria, microsomes and cytosol, and 5.4% in the

myelin fraction. The high accumulation of inorganic Hg in the cytosol of kidney was closely related to metallothionein-like component, while those in the mitochondria and microsomes of kidney and in the mitochondria of liver were exclusively bound to high MW proteins even after deoxycholate treatment.

828

TITLE:

Effects of Methylmercury on Protein Kinase A and Protein Kinase C in the Mouse Brain

AUTHORS:

Saijoh K
Fukunaga T
Katsuyama H
Lee MJ
Sumino K

SOURCE:

Environmental Research, Vol. 63, No. 2, pages 264-273, 32 references, 1993

ABSTRACT:

Methylmercury as methylmercuric-chloride (115093) was administered at 10mg/kg body weight by subcutaneous injection in single dose experiments to 4 week old female Jcl:ICR-mice. In repeated dose experiments, 0.5mg/kg body weight of methylmercury and/or selenium was administered every third day for a total of five doses. Seventy two hours after the last injection, the mice were killed and the brains were removed. Second messenger binding was measured, using tritium labeled adenosine-3',5'-cyclic-monophosphate (cAMP) for protein-kinase-A and phorbol-12,13-dibutylate (PDBu) for protein-kinase-C. Enzymatic activity was measured by incorporation of phosphorus-32 (P32) from gamma-P32-ATP into kemptide for protein-kinase-A and into H1-histone for protein-kinase-C. After the single dose of methylmercury, no signs of toxicity were seen; the methylmercury concentration in the brain was 5.6 parts per million (ppm). After repeated doses of methylmercury (cumulative dose 50mg/kg), the methylmercury concentration was 11.7ppm and some neurological symptoms were noted. After repeated doses of both methylmercury and selenite, the methylmercury concentration was 13.6ppm, while neurological symptoms were decreased compared with methylmercury alone. For protein-kinase-A, neither cAMP binding nor enzymatic activity were significantly altered after single or repeated doses of methylmercury. For protein-kinase-C, PDBu binding was unchanged after single or repeated doses. Enzymatic activity was also unchanged after the single dose, but was significantly reduced in the soluble fraction to 75% of control values after repeated doses. With simultaneous administration of selenite, this decrease was reversed and a nonsignificant increase in PDBu binding was seen. The authors conclude that methylmercury may

inhibit intracellular signal transduction for both protein-kinase-A and protein-kinase-C, resulting in partial concealment of neurological symptoms during early stages of methylmercury toxicity.

829
TITLE:
Effect of mercury compounds on cholineacetyl transferase.

AUTHORS:
DWIVEDI C
RAGHUNATHAN R
JOSHI BC
FOSTER H W JR

SOURCE:
RES COMMUN CHEM PATHOL PHARMACOL; 30 (2). 1980. 381-384.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Methylmercury poisoning exhibits prominent signs and symptoms of the CNS. Mechanism of toxicity was studied using HgCl2 and CH3HgCl given orally by gavage and through drinking water to male albino rats. Rats were sacrificed and brain and diaphragm were analyzed for cholineacetyltransferase (ChAT) activity. Both HgCl2 and CH3HgCl given orally by gavage significantly inhibited ChAT activity (dose related). CH3HgCl produced greater inhibition than HgCl2. CH3HgCl through drinking water also significantly inhibited brain ChAT. Rats did not drink water containing HgCl2. Both HgCl2 and CH3HgCl inhibited ChAT when incubated in vitro with rat brain homogenates. Histopathological studies revealed neural degeneration and necrosis in the cerebrum. Results indicate possible involvement of the cholinergic system during Hg intoxication.

830
TITLE:
Changes of Activity and Ultrastructural Localization of Alkaline Phosphatase in Cerebral Cortical Microvessels of Rat after Single Intraperitoneal Administration of Mercuric Chloride

AUTHORS:
Albrecht J
Szumanska G
Gadamski R
Gajkowska B

SOURCE:
Neurotoxicology, Vol. 15, No. 4, pages 897-902, 31 references, 1994

ABSTRACT:

Changes in the activity and ultrastructural localization of alkaline-phosphatase (ALP) in cerebral cortical microvessels induced by mercuric-chloride (7487947) were studied in rats. Male Wistar-rats were injected intraperitoneally with 6mg/kg mercuric-chloride. Selected rats were killed 1 or 18 hours or 5 days later and the brains were removed. Cerebral cortical sections were prepared and assayed for ALP activity. In control rats, optical microscopy revealed intense uniform staining for ALP throughout all layers of the cortex. One hour after mercuric-chloride, ALP staining was sharply reduced in all of the cortical layers, with the staining virtually disappearing in layer II and III. The overall level of ALP staining was significantly decreased at 18 hours and 5 days post injection, although some staining was visible in layers III and IV at 18 hours and in layers III and V at 5 days. Electron microscopy indicated that in control animals ALP staining was located exclusively in the luminal plasmalemma of the endothelial cells. One hour after mercuric-chloride, ALP staining had virtually disappeared from the luminal plasmalemma and the endothelial cells showed numerous invaginations. The perivascular glia was swollen. ALP staining in the luminal plasmalemma was still decreased at the 18 hour sampling point. If present, it was seen on the abluminal plasmalemma and on the basement membrane. The perivascular glia was still swollen, but to a lesser extent than at 1 hour. Five days post injection, overall ALP staining was still reduced, but moderately strong staining was seen on the abluminal plasmalemma, on the basement membrane, and in the intracellular spaces. This was accompanied by moderate swelling of endothelial cells and numerous invaginations. The authors conclude that the inhibition and subsequent translocation of ALP activity from luminal to abluminal sites induced by mercuric-chloride in cerebral cortical cells support the view that mercuric-chloride may interfere with functioning of the blood brain barrier.

831

TITLE:

Uptake of selenium-75 and its interaction with arsenic, cadmium and mercury in the rat.

AUTHORS:

MANGAL PC
SINGH G

SOURCE:

PROC INDIAN NATL SCI ACAD PART B BIOL SCI; 46 (5). 1980 (RECD. 1981). 615-620.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Tissue uptake, distribution and retention of 75Se in the rat was studied. Maximum activity of 75Se was found in most rat organs within 1-3 h except in the brain and colon where maxima were

reached within 6-8 h post-administration. Graphical analysis of the biological decay of 75Se in rat organs indicated that the decay was a sum of 2 exponentials except in the brain and spleen. In the brain the level of 75Se stayed constant once maximum was reached and in the spleen the decay was single exponential in character. The biological half-lives of 75Se in various rat organs were worked out. The effects of Cd and Hg were more or less similar, but opposite to that of As, suggesting that the uptake of Se, an essential trace elements, was dependent on the level of As, Cd or Hg present concurrently in the biological systems at the time.

832

TITLE:

Effects of Chronic Hypercapnia on Blood Distribution in Organs

AUTHORS:

Schaefer KE

Baker GT

SOURCE:

Submarine Medical Research Laboratory, Naval Submarine Medical Center, Groton, Connecticut, Report No. 603, 22 pages, 38 references, 19691969

ABSTRACT:

The effects of chronic carbon-dioxide (124389) (CO2) exposure on blood distribution were investigated in guinea-pigs. Male Hartley-guinea-pigs were exposed to 15 percent CO2 for periods from 1 hour to 7 days. Blood pH and arterial CO2 tension (PCO2) were measured. Blood content of brain, liver, muscle, and skin was examined by injecting animals intravenously with reconstituted blood tagged with radioactive chromium-51 (14392020) and iodine-125 (14158317). Tissue samples were taken after 15 minutes and examined for red blood cell weight, blood volume, and tissue hematocrit. Results were compared with those from no treatment controls. Brain blood volume increased 30 percent after 1 hour of exposure, remained at this value throughout 7 days of exposure, and returned to initial values after a 1 day recovery. Liver blood volume showed a decrease during the first 3 days of exposure and returned to control values after 7 days of exposure. The fall in liver blood volume was based on a decrease in liver blood plasma volume; red cell volume increased throughout exposure. Muscle blood volume was decreased 30 percent during the first day of exposure, caused by a decrease of both red cell and plasma volume and a decrease in muscle hematocrit. Muscle blood volume subsequently increased to 20 percent above control values. There was a 60 percent rise in skin blood volume after 1 hour of exposure. At 3 and 7 days, skin blood volume decreased to 40 percent below control values; however, hematocrit remained practically constant. Blood pH quickly dropped from 7.4 to 7.0, then gradually rose over several days. PCO2 initially rose from 45 to 123 millimeters mercury and remained elevated throughout the exposure period. The authors conclude that the time course of PCO2 is correlated with that

of brain blood content, while the biphasic changes in the time course of pH parallel the biphasic changes in blood content of muscle, liver, and skin.

833
TITLE:
Uptake of metals in the brain via olfactory pathways.

AUTHORS:
TJALVE H
HENRIKSSON J

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 20 (2-3). 1999. 181-196.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In the olfactory epithelium the dendrites of the primary olfactory neurons are in contact with the nasal lumen, and via the axons these neurons are also connected to the olfactory bulbs of the brain. Materials which come into contact with the olfactory epithelium can be taken up in the primary olfactory neurons and be transported to the olfactory bulbs and even further into other areas of the brain. The present review deals with the mechanism of uptake and transport of metals in the olfactory sy ry pathways. Studies with nickel indicate that this metal, following a transport to the terminal parts of the primary olfactory neurons in the glomeruli of the bulbs, slowly passes to secondary and tertiary olfactory neurons. Cadmium and mercury are transported along the primary olfactory neurons to their terminations in the olfactory bulbs, but these metals appear unable to continue along secondary olfactory neurons. Occupational inhalation of nickel or cadmium can be toxic to t

834
TITLE:
Modification Of The Cardiovascular Effects Of L-Dopa By Decarboxylase Inhibitors

AUTHORS:
Watanabe AM
Parks LC
Kopin IJ

SOURCE:
Journal of Clinical Investigation, Vol. 50, pages 1322-1328, 19 references, 19711971

ABSTRACT:
The cardiovascular effects of L-dopa (59927) and its modification by

decarboxylase inhibitors were investigated in dogs. Dogs were infused with 0.0001 to 0.3 milligrams per kilogram per minute (mg/kg/min) L-dopa and blood pressure (BP) was determined. Decarboxylase inhibitors were intravenously administered at 50mg/kg MK-485 (28875925), or 100mg/kg RO4-4602 (14919778). Dogs pretreated with MK-485 were infused with 0.3mg/kg/min L-dopa and changes in peripheral resistance were studied. Norepinephrine (51412) and dopamine (51616) were also injected. Biochemical analysis of tissues was performed after infusion of tritiated L-dopa. At doses of 0.2 or 0.3mg/kg/min L-dopa, BP increased markedly to 43.3 millimeters of mercury after 45 minutes. Cardiac arrhythmias developed and progressed to ventricular tachycardia or fibrillation. Dogs given MK-485 prior to L-dopa developed hypotension. Hypertension and arrhythmia in dogs given L-dopa were abolished by MK-485 and RO4-4602 pretreatment. A significant decrease in hind limb perfusion pressure occurred after treatment with MK-485 and L-dopa. Mean arterial pressure was significantly lowered by the combination of MK-485 and L-dopa. Sympathetic neuronal function was not affected. Significant amounts of catecholamines were formed from the tritiated L-dopa precursor in hearts, kidneys, and brains. Dogs treated with MK-485 had reduced catecholamines in hearts and kidneys, but not in brains; those treated with RO4-4602 had significant reductions of catecholamines in all three organs. The authors conclude that L-dopa produces opposite effects on BP depending on the accumulation site of its metabolic products. Inhibition of dopa-decarboxylase causes a centrally mediated hypotensive effect. Inhibition of dopa-decarboxylase in the brain abolishes L-dopa effects on BP.

835
TITLE:
Organ specificity of neonatal methyl mercury hydroxide poisoning in the rat: Effects on ornithine decarboxylase activity in developing tissues.

AUTHORS:
BARTOLOME J
CHAIT EA
TREPANIER P
WHITMORE WL
WEIGEL S
SLOTKIN TA

SOURCE:
TOXICOL LETT (AMST); 13 (3-4). 1982. 267-276.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. To determine the organ specificity of neonatal CH3HgOH exposure on biochemical development of its potential target tissues, effects on rat brain, liver, heart and kidney were compared utilizing the ontogenetic pattern of ornithine decarboxylase (ODC)

activity, an early index of perturbation of cellular maturation. CH3HgOH was given daily beginning at birth for up to 21 days, using 3 dose levels (1, 2.5 or 5 mg/kg s.c.). In the brain, CH3HgOH treatment resulted in an initial reduction in ODC followed by a subsequent elevation of activity, a maturational pattern known to be associated with delayed cellular development. In contrast to the effects of CH3HgOH on brain, the pattern obtained in the liver, an initial elevation followed by a subseqeunt decline, was usually associated with compression of the time course of cellular development. In the heart and kidney, CH3HgOH produced sustained elevations of ODC representing prolongation of the developmental period of rapid tissue growth and development; these patterns were associated with tissue hypertrophy which was sustained through the preweaning stage for both tissues and well into the postweaning period for the kidney. Neonatal CH3HgOH poisoning caused organ-specific biochemical lesions which played a role in subsequent effects on overall tissue development.

836
TITLE:
Fetal distribution of mercury following introduction of methylmercury into porcine maternal circulation.

AUTHORS:
KELMAN BJ
WALTER BK
SASSER LB

SOURCE:
J TOXICOL ENVIRON HEALTH; 10 (2). 1982. 191-200.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Tissue samples were obtained from 115 swine fetuses from 10 litters and analyzed for tissue-bound Hg 24 h after mothers were exposed to low levels of methylmercury by i.v. injection. Absorption of Hg by the fetus and placenta increased throughout gestation in concert with increasing fetal weight, as did fetal hepatic Hg. Fetal renal Hg increased throughout gestation but the increase appeared to be much greater than would be expected on the basis of weight increase alone. Blood Hg concentrations did not change significantly. Fetal brain Hg content and concentration increased dramatically toward the end of pregnancy, the gestational period during which the rate of brain growth is greatest in swine. This is important since the brain is especially sensitive to nutritional and, presumably, toxicological preturbation while it is growing most rapidly.

837
TITLE:
Uptake of elemental mercury and activity of catalase in rat, hamster, guinea pig, normal and acatalasemic mice.

AUTHORS:
EIDE I
SYVERSEN T LM

SOURCE:
ACTA PHARMACOL TOXICOL; 51 (4). 1982. 371-376.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Uptake of elemental Hg after inhalation (3.5 mg/m3) and the activity of catalase in brain, liver, kidney and blood were investigated in rat, hamster, guinea pig, and normal and acatalasemic mice. The uptake of Hg in the species investigated varied considerably, being highest in the 2 strains of mice, followed by rat and hamster, and lowest in the guinea pig. The uptake seemed to be more dependent on pulmonary ventilation than on the activity of catalase. The 2 strains of mice were exposed to a wide range of Hg concentrations in air (0.002-3.5 mg/m3). The content of Hg in brain, liver and kidney was linearly dependent on the Hg concentration in the air; in blood this relationship was exponential. At the lower concentrations of Hg in the inhaled air, the Hg level in blood was significantly lower, and in kidney higher in the acatalasemic mice compared to the normal ones. In acatalasemic mice the Hg content in liver was higher at all concentrations investigated; in brain no difference between the 2 strains was found.

838
TITLE:
Neurotransmitter Receptors As Targets For Pesticides

AUTHORS:
Eldefrawi ME
Eldefrawi AT

SOURCE:
Journal of Environmental Science and Health, Vol. B18, No. 1, pages 65-88, 49 references, 19831983

ABSTRACT:
The role of acetylcholine (ACh) neurotransmitter receptors as targets of pesticide affinity is reviewed. Nerve cell neurotransmitter receptor interactions result in a variety of cellular responses, from conductance changes resulting in membrane depolarization or hyperpolarization to induction of catalytic reactions. ACh receptors in the vertebrate nervous system are classified pharmacologically into two general types: nicotinic and muscarinic. For the occupation of receptor sites by the transmitter or agonist to be translated into a cellular response, coupling with a transducer is necessary. Cholinergic transmission in the insect central nervous system is inhibited by both nicotinic and muscarinic drugs. The

muscarinic receptors of mammalian brain and smooth muscles are identified by their specific high affinity binding of antagonists, mainly quinuclidinyl-benzilate (16852816) (QNB). The pharmacologic specificity of binding of QNB to housefly muscarinic receptors is generally similar to those of mammalian brain and smooth muscle. Several organophosphorus and carbamate insecticides bind with high affinities to the nicotinic ACh receptor of the electric organ of the Torpedo ray. A few chlorinated hydrocarbon insecticides and derivatives interact with Torpedo nicotinic ACh receptors at their allosteric or channel sites. The most potent neurotransmitter on both the nicotinic and muscarinic receptors is the acaricide chlorobenzilate (510156). Pyrethrins and synthetic pyrethroids also bind with high affinities to the channel sites of the nicotinic ACh receptor but not to its receptor sites. Organic and inorganic mercury (7439976) compounds also bind to ACh receptors in the Torpedo nicotinic and rat brain muscarinic receptors. The authors conclude that neurotransmitter receptors act as primary or secondary molecular targets for different pesticides.

839
TITLE:
The early effects of methylmercury on the developing rat brain.

AUTHORS:
GEELEN J AG
DORMANS J A MA
VERHOEF A

SOURCE:
ACTA NEUROPATHOL; 80 (4). 1990. 432-438.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of organic mercury compounds on the development of the brain are well known since the exposure of people at a large scale to methylmercury in the Minamata Bay area and in Iraq. The neuropathological examination of the brains of children prenatally exposed revealed dysplasia of the cerebral and cerebellar cortex, neuronal ectopia and several other developmental disturbances. In this experimental study we examined developmental mechanisms involved in methylmercury-induced cerebral anomalies. By examining the fetuses soon after treatment we concentrated in the initial effects of the treatment. The pregnant rats were given 10 mg/kg methylmercury chloride i.p. on day 18. Already at 2 h after administration mitochondrial degeneration occurred in the endothelium of the cerebral capillaries. Subsequently hemorrhages developed interfering with the cellular arrangement in the ventricular zone, with neuronal migration in the intermediate zone and with the development o

840

TITLE:
Nondestructive synchrotron radiation X-ray fluorescence imaging of trace elements on methylmercury and selenium administered guinea pigs.

AUTHORS:
SHIMOJO N
HOMMA S
NAKAI I
IIDA A

SOURCE:
ANAL LETT; 24 (10). 1991. 1767-1778.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The dynamics of the brain distributions of Hg, Zn, Cu and Se in guinea pigs exposed to methylmercury and selenium were examined by X-ray fluorescence imaging utilizing synchrotron radiation. Male Hartley guinea pigs were administered methyl mercury chloride and/or sodium selenite every day for ten days (s.c. 3mg as Hg/kg/day, mole ratio Hg:Se = 1:1). Two dimensional distributions of Hg, Zn, Cu and Se in guinea pig brain were observed by nondestructive X-ray fluorescence imaging. Using the X-ray intensity of each analytical point, correlation coefficients among the distributions of trace elements were calculated. In the brain of the guinea pigs exposed to methylmercury or both methylmercury and selenium, high correlation between Hg and Zn, Cu, Se was observed (r = 0.760 - 0.943), whereas much lower correlation was observed for nontreated or only selenium administered guinea pigs.

841
TITLE:
Insecticides, polychlorinated biphenyls and metals in African lake ecosystems. I. Hartbeesport Dam, Transvaal and Voelvlei Dam, Cape Province, Republic of South Africa

AUTHORS:
Greichus YA
Greichus A
Amman BD
Call DJ
Hamman DCD
Pott RM

SOURCE:
Arch. Environ. Contam. Toxicol. 6(2-3) 6(2-3): 371-383 1977 (32 References)

ABSTRACT:
PESTAB. Concentrations and distribution of chlorinated hydrocarbon

insecticides, polychlorinated biphenyls (PCB's) and some metals were determined in two South African lakes, Hartbeespoort Dam and Voelvlei Dam. Water, bottom sediments, aquatic plants, aquatic insects, fish, fish-eating birds and their eggs were collected. Insecticides and PCB's were analyzed by thin layer and gas chromatography and mass-spectrometry. Analysis of metals was accomplished with atomic absorption spectrophotometry. Metals included arsenic, cadmium, copper, manganese, lead, zinc, and mercury. The insecticide residues most commonly found in both dams were DDE, DDD, DDT, and dieldrin. Hartbeespoort had higher levels than Voelvlei of insecticides and PCB's in all types of samples common to both lakes. Concentrations of PCB's having six or more chlorines increased with an increase in the trophic level. Concentrations of PCB's in the brains of the African birds were greater than the average total concentration of insecticides while the opposite was true for carcasses. Biological magnification of insecticides and PCB's occurred in both lakes. Hartbeespoort Dam had higher levels than Voelvlei for all metals examined in bottom sediments and birds, except for copper in bird carcasses. Mercury levels in bird carcasses ranged from 2- to 5-fold greater than in fish while lead concentrations ranged from 2- to 10-fold greater. (Author abstract)

842
TITLE:
CALCIUM AND CELL DEATH

AUTHORS:
NICOTERA P
ORRENIUS S

SOURCE:
LANGSTON, J. W. AND A. YOUNG (ED.). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, VOL. 648. NEUROTOXINS AND NEURODEGENERATIVE DISEASE; CONFERENCE ON NEUROTOXINS AND THEIR POTENTIAL ROLES IN NEURODEGENERATION, NEW YORK, NEW YORK, USA, MAY 6-8, 1991. XVI+385P. NEW YORK ACADEMY OF SCIENCES: NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-89766-696-8(PAPER); ISBN 0-89766-695-X(CLOTH).; 0 (0). 1992. 17-27.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN BRAIN ISCHEMIA HOMEOSTASIS DISRUPTION NEUROTOXICITY LEAD MERCURY ORGANOTIN

843
TITLE:
Behavioural effects of neonatal metallic mercury exposure in rats.

AUTHORS:
FREDRIKSSON A
DAHLGREN L

DANIELSSON B
ERIKSSON P
DENCKER L
ARCHER T

SOURCE:
TOXICOLOGY; 74 (2-3). 1992. 151-160.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effect of neonatal exposure of rats to mercury vapour (Hg0), at the concentration 0.05 mg/m3, 1 h (low dose) or 4 h (high dose), on the behaviour in adulthood were studied. Exposure occurred on days 11-17 (the period of rapid brain growth). Tests for spontaneous motor activity were performed at the ages of 2 and 4 months. Rats exposed to the high dose Hg0 showed a marked increase in variables locomotion and total activity but a decrease for rearing when tested at 2 months of age. At 4 months of age these rats showed a marked hypoactivity with respect to all three variables. Rats exposed to the low dose showed no significant differences at 2 months compared to controls. However, at the age of 4 months the same pattern (increase in variables locomotion and total activity but a decrease for rearing) already noticed in the high dose group at 2 months was observed. In the spatial learning tasks applied, the radical arm maze and circular swim maze, neonatally exposed pups

844
TITLE:
EFFECTS OF METAL EXPOSURE ON BRAIN DEVELOPMENT

AUTHORS:
BERLIN M
LOGDBERG B

SOURCE:
THIRD INTERNATIONAL CONFERENCE OF THE INTERNATIONAL SOCIETY OF TRACE ELEMENT RESEARCH IN HUMANS (ISTERH), STOCKHOLM, SWEDEN, MAY 25-29, 1992. J TRACE ELEM EXP MED; 5 (2). 1992. 96.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT SQUIRREL MONKEY LEAD MERCURY FETAL TOXICITY ABORTION

845
TITLE:
INFLUENCE OF EXPOSURE TIME ON TISSUE DISTRIBUTION OF MERCURY IN RAINBOW TROUT

AUTHORS:

NIIMI AJ
KISSOON GP

SOURCE:
EIGHTEENTH ANNUAL AQUATIC TOXICITY WORKSHOP, OTTAWA, ONTARIO, CANADA, SEPTEMBER 30-OCTOBER 3, 1991. CAN TECH REP FISH AQUAT SCI; 0 (1863). 1992. 353.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT ONCORHYNCHUS-MYKISS AQUATIC TOXICITY WATER RESOURCES POLLUTION CONTAMINATION GILL LIVER SPLEEN BRAIN KIDNEY MUSCLE METHYL MERCURY CHLORIDE MERCURIC CHLORIDE MORTALITY

846
TITLE:
Electro-magnetic fields in the home environment (color TV, computer monitor, microwave oven, cellular phone, etc) as potential contributing factors for the induction of Oncogen C-fos Ab1, Oncogen C-fos Ab2, integrin alpha5beta1 and development of cancer, as well as effects of microwave on amino acid composition of food and living human brain.

AUTHORS:
OMURA Y
LOSCO M

SOURCE:
ACUPUNCT ELECTRO-THER RES; 18 (1). 1993. 33-73.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects, on normal human subjects, of 3 minutes exposure to electro-magnetic fields (EMFs) emitted from: A) personal computers, B) color television sets, or C) microwave-ovens, or cellular phones were compared by placing the same large sheet of aluminum foil with a square hole or rectangular band-shaped hole at the chest level (or at the side of the head with the cellular phone), with or without grounding the aluminum foil, using the Bi-Digital O-Ring Test Dysfunction Localization and Molecular Identification Methods with cancer related substances (i.e., Oncogen C-fos Ab2 and mercury in the cell nucleus, Integrin alpha5 beta1 in the cell & nuclear membranes, and disappearance of Acetylcholine) as reference control substances. All the above sources of the EMFs not only induced the following various transitional abnormalities on the EMF entry area, but also induced similar abnormalities at the EMF exit area on the back (where the abnormality was found in the same shape

847
TITLE:
Methyl mercury increases intracellular calcium and inositol phosphate

levels in cultured cerebellar granule neurons.

AUTHORS:
SARAFIAN TA

SOURCE:
J NEUROCHEM; 61 (2). 1993. 648-657.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In an effort to explain the previously observed methyl mercury (MeHg)-induced stimulation of protein phosphorylation in cerebellar granule neuron cultures, the effect of MeHg on protein kinase activities in cell-free assays and on second messenger systems in cultured neurons has been examined. Using cell-free assays for several protein kinases, no stimulation of enzyme activity was found at any concentration of MeHg tested. After 24 h exposure, 1-5 muM MeHg was found to have no significant effect on neuronal cyclic AMP levels. In contrast, intracellular levels of Ca2+ and rates of 45Ca2+ uptake were elevated 2.2-fold and 3.6-fold, respectively, by 5 muM MeHg. These effects were not observed with mercuric chloride, triethyllead, or lead acetate. Measurement of inositol phosphate production in granule cell cultures revealed a sensitive, pretoxic effect of MeHg with twofold stimulation following 30-min exposure to 5 muM MeHg and 1.6-fold after 24-h exposure to 3 muM MeHg.

848
TITLE:
Effects of maternal dietary supplementation with selenite on the postnatal development of rat offspring exposed to methyl mercury in utero.

AUTHORS:
FREDRIKSSON A
GARDLUND AT
BERGMAN K
OSKARSSON A
OHLIN B
DANIELSSON B
ARCHER T

SOURCE:
PHARMACOL TOXICOL; 72 (6). 1993. 377-382.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Female Sprague-Dawley rats were fed a control standard diet or a selenite (Se) supplemented diet (1.3 p.p.m. Se) for 8 weeks before mating and during gestation and lactation. Blood glutathione peroxidase activity (GSH-Px) was measured as a biomarker of Se in dames. After mating, the females from two dietary groups were divided

into three subgroups (6 groups with 10 animals in each) given 0 (vehicle), 2 or 6 mg/kg methyl mercury (MeHg) by gavage on days 6-9 of gestation. Day 2 post parturition all litters were standardized to 6 pups per litter and remaining pups were used for determination of blood and brain total Hg contents. Behavioural testing was performed at two months of age. The results of the study showed that supplementing the diet with Se partly antagonized some adverse effects of the MeHg such as hypoactivity especially in the high MeHg dose group. There were no changes in physical development or body weight except a tendency to decreased body weight in offspr

849
TITLE:
Morphology patterns in rats with glomerulonephritis induced by long-term exposure to mercury.

AUTHORS:
ARTESE L
BOSCOLO P
CARMIGNANI M
FELACO M
CARELLI G
SACCHETTONI-LOGROSCINO G
GRILLI A
GIULIANO G

SOURCE:
INT J IMMUNOPATHOL PHARMACOL; 6 (2). 1993. 99-107.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Male Wistar rats, which received 200 mug/ml (Hg), as mercury chloride (HgCl2), in their drinking water for 210 days starting from weaning, showed, in relation to the control animals, increased systolic and diastolic blood pressure and reduced cardiac inotropism. In the rats treated with HgCl2, Hg was more accumulated in the kidney than in the heart and brain. Light and electron microscopy observation showed in most of the Hg-exposed rats hypercellularity and deposition of amorphous material int he mesangium without alterations of the capillary wall. Deposition of IgM in both mesangium and Bowman's capsule was demonstrated by immunofluorescence techniques. In the Hg-exposed animals, glucose-6-phosphate dehydrogenase activity was augmented in all the tubular cells, while acid and alkaline phosphatases were reduced. This study shows that long-term exposure to HgCl2 induces in Wistar rats a mesangial prolipherative glomerulonephritis which is probably related to lysosome al

850
TITLE:

Biochemical changes in the rat cerebellar cortex elicited by chronic treatment with methyl mercury.

AUTHORS:
CONCAS A
CORDA MG
SALIS M
MULAS ML
MILIA A
CORONGIU FP
BIGGIO G

SOURCE:
TOXICOL LETT (AMST); 18 (1-2). 1983. 27-34.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Long-term (20 days) treatment with methyl mercury (MeHg) increased the total number of benzodiazepine binding sites and decreased essentially the content of cGMP in the cerebellar cortex. It failed to modify the content of GABA and cAMP, GAD (glutamic acid decarboxylase) activity and GABA binding sites in the same brain area. The changes in cGMP and benzodiazepine binding sites in the cerebellar cortex were discussed in relation to the motor disturbances associated with MeHg intoxication.

851
TITLE:
Organochlorine and mercury residues in wild animals in Southern Ontario, Canada 1973 - 1974.

AUTHORS:
Frank R
Holdrinet MVH
Suda P

SOURCE:
Bull. Environ. Contam. Toxicol. 22(4-5): 500-507 1979 (12 References)

ABSTRACT:
PESTAB. Red fox, raccoon and striped skunk were collected in Southern Ontario and brain, liver and muscle tissues from each species were examined for chemical residues. Fisher, marten and mink were also collected, but only muscle tissue was available for analysis. All tissues studies gave evidence of p,p'-DDE, PCB, and mercury contamination. p,p'-TDE was present in some tissues. Dieldrin was found in muscle tissue of fisher, marten and mink but not in the other species. Tissues of the six species were negative for aldrin, endrin, heptachlor, heptachlor epoxide or methoxychlor.

852
TITLE:
Pesticides and other persistent chemicals: collection and storage of biological specimens from human populations.

AUTHORS:
Bardodej Z

SOURCE:
In: The Use of Biological Specimens for the Assessment of Human Exposure to Environmental Pollutants. Berlin, A., Wolff, A. H. and Hasegawa, Y., eds. (Martinus Nijhoff:The Hague): pp. 55-63 1979 (28 References)

ABSTRACT:
PESTAB. The dangers of organochlorine pesticides, PCB, and mercury have been uncovered in animal studies and medical examinations of humans occupationally exposed to these substances. They are well known environmental pollutants, and their residues have been measured in food and human adipose tissue. Further studies are needed on different population groups to better understand the toxicity of organochlorine pesticides, PCB, and mercury. The limited knowledge of effects due to chronic exposure to these substances has precluded definite statements on their possible carcinogenicity and mutagenicity. Standardization in sampling, storage, and analysis methods for human epidemiological studies is strongly recommended when investigating the effects of environmental pollutants. Residue data should be maintained on a variety of specimens such as nails, hair, and urine from living subjects and liver, brain and kidney from post-mortem specimens. A storage temperature of -40êC is recommended for samples set aside for future reference. Specimen mailing costs of no more than $10.00 for a domestic shipment and $30.00 for an international shipment are suggested. Studies on humans to monitor environmental pollution in Czechoslovakia are recommended, provided medical ethics, mail, antiepidemic, and customs regulations are respected.

853
TITLE:
DISTRIBUTION OF MERCURY IN THE SOFT TISSUES OF THE BLUE TILAPIA OREOCHROMIS AUREUS STEINDACHNER AFTER ACUTE EXPOSURE TO MERCURY II CHLORIDE

AUTHORS:
ALLEN P

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 53 (5). 1994. 675-683.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE OREOCHROMIS-AUREUS HEAVY METAL LIVER GILLS BRAIN SPLEEN KIDNEY INTESTINE OVARIES TESTES BILE PLASMA MUSCLE TOXICITY WATER POLLUTION AQUACULTURE

854
TITLE:
THE EFFECT OF PREGNANCY OUTCOME AND FETAL BRAIN DEVELOPMENT OF PRENATAL EXPOSURE TO MERCURY VAPOUR

AUTHORS:
WARFVINGE K
BERLIN M
LOGDBERG B

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT
SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 956.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT SQUIRREL MONKEY

855
TITLE:
RETENTION OF INORGANIC MERCURY IN VARIOUS BRAIN SITES OF MACACA FASCICULARIS MONKEYS FOLLOWING LONG-TERM EXPOSURE TO METHYLMERCURY

AUTHORS:
VAHTER M
LIND B
CHARLESTON JS
BURBACHER TM
MOTTET NK
FRIBERG L

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT
SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 959.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MACACA-FASCICULARIS

856
TITLE:
"In Vitro" Effects on Methyl-Mercury on the Nervous System: A Neurotoxicologic Study.

AUTHORS:
CAPO MA
ALONSO CE
SEVIL MB
FREJO MT

SOURCE:
JOURNAL OF ENVIRONMENTAL PATHOLOGY TOXICOLOGY AND ONCOLOGY; 13 (2). 1994. 117-123.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Many of the currently prevailing toxicologic problems are due to the use of organic mercurial compounds in pesticides and fungicides. During recent years, environmental pollution has originated from the incorrect use of these organometals. Methyl-mercury (Me-Hg) is absorbed quickly from the gastrointestinal tract and is distributed to most tissues. The most important effect of Me-Hg is on the nervous tissue and is more relevant in the fetal brain. We were interested in assessing the neurotoxic effects of Me-Hg on the central and peripheral nervous system. Neuronal cells cultures from 14-day-old fetal Wistar rats and ciliary ganglion cells cultures from 8-day-old chick embryos were used. Various Me-Hg concentrations (10-3 M to 10-8 M) were added to these cultures after 36 hr to study the morphologic changes. At 10-3 M and 10-4 M concentrations, cellular degeneration and death in the central nervous system (CNS) were noted. At 10-5 M concentrations, axonal and nerve fiber

857
TITLE:
Methylmercury Stimulates The Exhalation Of Volatile Selenium And Potentiates The Toxicity Of Selenite

AUTHORS:
Yonemoto J
Webb M
Magos L

SOURCE:
Toxicology Letters, Vol. 24, No. 1, pages 7-14, 17 references, 19851985

ABSTRACT:
The interaction of methylmercury (22967926) with selenium (7782492) was studied in rats. Female Wistar-Porton-rats were given

methylmercuric-chloride (115093) at 24 micromoles per kilogram (microm/kg) body weight or sodium-selenite (10102188) at 24microm/kg. Methylmercury was given 1 or 2 hours before selenite or at the same time, or each was given alone. Control animals were tested with saline. Animals were weighed daily for 7 days. For determination of mercury and selenium distribution injection solutions were radiolabeled and selenium was given 1 hour after methylmercury. Animals were killed at 24 hours and radioactivity of organs counted by a gamma scintillation spectrophotometer. The effect of methylmercury on exhalation of selenite was determined with animals given approximately 0.1 microCurie/microm dimethylselenide (593793) and selenium and methylmercury at 1 and 2 hour intervals or simultaneously. Air was pumped into closed cages and through traps to isolate radioactivity which was counted to determine exhalation. Selenite given alone depressed weight gain but methylmercury alone did not. If given before or with selenite it potentiated its effects to an equal degree at all times of administration. Body distribution of selenium was not immediately affected by selenium given 1 hour later but at 24 hours selenium was decreased in lungs, liver and kidneys by their interaction. Brain methylmercury increased while kidney content decreased. Methylmercury stimulated the exhalation of volatile selenium. The increase was higher if both were injected at the same time but even if selenium was given 2 hours later the increase in exhalation was substantial. The authors conclude that the decomposition of methylmercury may result in an overall increase in toxicity of selenite through interaction of mercuric mercury with dimethylselenide.

858
TITLE:
BEHAVIORAL TOXICOLOGY

AUTHORS:
NEEDLEMAN HL

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 103 (SUPPL. 6). 1995. 77-79.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM JOURNAL ARTICLE CHILD LEAD MERCURY METALS ALCOHOL SOLVENT PESTICIDES ENVIRONMENTAL POLLUTION BEHAVIORAL NEUROTOXICOLOGY LEARNING MEMORY BEHAVIORAL TERATOLOGY PRENATAL EXPOSURE
BRAIN DEVELOPMENT

859
TITLE:
Study Of Inorganic Arsenic Methylation By Rat Liver In Vitro: Relevance For The Interpretation Of Observations In Man

AUTHORS:
Buchet JP
Lauwerys R

SOURCE:
Archives of Toxicology, Vol. 57, No. 2, pages 125-129, 19 reference, 19851985

ABSTRACT:
Methylation of inorganic arsenic (7440382) was investigated in-vitro in rat liver. Two to 3 month old male Sprague-Dawley-rats were killed for preparation of whole liver homogenates. Differential separation of hepatic homogenate into nuclear, mitochondrial, lysosomal, and cytosolic fractions was performed by centrifugation. The tissue preparation was incubated with arsenic and various cofactors. Inorganic trivalent and pentavalent arsenic and its methylated forms, monomethylarsonic-acid (124583) (MMA) and dimethylarsinic-acid (144218) (DMA) were determined by atomic absorption spectrophotometry. No methylated arsenic derivatives could be detected without the addition of reduced glutathione and S-adenosyl-L-methionine (SAMe). The addition of vitamin B-12 (68199) enhanced the amount of DMA produced; no significant effects were found on MMA. Increasing the concentration of the cofactors did not increase the yield of arsenic methylated metabolites. The inorganic arsenic methylating capacity of red blood cells and that of whole brain, lung, intestine, and kidney homogenates were insignificant by comparison with that of the liver. Addition of derivatives enhanced the production of the methylated arsenic products by comparison with that produced in the presence of SAMe alone. DMA was produced from MMA; MMA took more than 30 minutes to reach a sufficient concentration in the incubation system to trigger DMA synthesis. At less than 10 percent cytosol concentration, the production of MMA was greater than that of DMA. A 1 millimolar (mM) solution of sodium-diethyldithiocarbamate was a moderate inhibitor; five microliters of trichloroacetonitrile (545062) prevented arsenic methylation. The arsenic dimethylation reaction was highly sensitive to the mercury (7439976) ion; more than 90 percent of the original activity was lost at mercury concentrations of 0.1mM. The authors conclude that the biotransformation of inorganic arsenic by rat liver in-vitro results in the production of a monomethyl and a dimethyl derivative measured as MMA and DMA, respectively.

860
TITLE:
Radiation injury and mercury deposits in internal organs as a result of Thallium-201 chloride intravenous injection for SPECT image: Additional biochemical information obtained in the images of organs from SPECT or PET scans and potential injury due to radiation exposure during long distance flights.

AUTHORS:
OMURA Y
LORBERBOYM M
BECKMAN S

SOURCE:
ACUPUNCTURE & ELECTRO-THERAPEUTICS RESEARCH; 20 (2). 1995. 133-148.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In order to study functional as well as anatomical aspects of various internal organs, SPECT (Single Photon Emission Computerized Tomography) has been used extensively for evaluation of these organs. For SPECT study, intravenous injection of radioactive substances such as technetium-99m (20 millicuries) & thallium-201 chloride (3 millicuries) is commonly used. Although the physical half-life of thallium-201 chloride is 73 hours, its biological half-life is often more than 3.5 times that. Following intravenous injection of thallium-201 chloride it is concentrated in the heart, liver, kidneys, pancreas, thyroid gland, testes or ovaries, and then eventually decays to mercury. Because of its relatively long physical & biological half-lives, thallium-201 chloride may produce mild radiation injury while it remains radioactive. Similar injuries may be induced by technetium-99m (often used for brain SPECT), which radiates Gamma rays (140 KeV), but since its physical half-life i

861
TITLE:
Reproductive And Developmental Toxicity Of Metals

AUTHORS:
Clarkson TW
Nordberg GF
Sager PR

SOURCE:
Scandinavian Journal of Work, Environment and Health, Vol. 11, No. 3, pages 145-154, 28 references, 19851985

ABSTRACT:
The effects on reproduction and development of metals are reviewed. Much research had been done on animals with regard to prenatal exposure to metals, but relatively little in regard to neonates and sucklings. Some effects are specific to the metal: lead (7439921) produces skeletal abnormalities in fetuses, and cadmium (7440439) damages the testes. Methylmercury (22967926) is the only well documented environmental teratogen for humans. Methylmercury affects the central nervous system to produce psychomotor retardation. Fetuses may be 10 times more sensitive to methylmercury than adults. Paresthesia begins to occur at a hair

concentration of 100 micrograms mercury per gram. Methylmercury prevents neuronal migration, brain growth, and cell division by attacking microtubules. The metabolism of mercury, lead, arsenic (7440382), cadmium, and chromium (7440473) is described. Many heavy metals are not metabolized as well by neonates because of the immaturity of their livers. The authors conclude that routes of exposure to heavy metals more closely resembling human exposure must be emphasized in animal research.

862
TITLE:
Synthesis and pharmacological study of a polymer which selectively binds mercury.

AUTHORS:
HARBISON RD
JONES MM
MACDONALD JS
PRATT TH
COATES RL

SOURCE:
TOXICOL APPL PHARMACOL; 42 (3). 1977 (RECD 1978) 445-454

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A polymeric chelating agent (MBP) prepared by condensation of a mercaptoethyl sulfide with a terephthaldicarboxaldehyde exhibited a high degree of specificity for Hg (II) as judged by its ability to reduce rapidly the free metal ion concentration in an aqueous solution. The polymer exhibited a low degree of toxicity (LD50 > 5 g/kg) when administered orally to mice, and it was capable of antagonizing acute methyl Hg-induced lethality. MBP at a level of 1% in food promoted a rapid clearance of Hg from the body after acute administration of methyl mercury. The biological half-life of the metal was reduced from 10.0 days to 4.5 days. The concentration of Hg in various tissues including the brain was reduced 40 to 70% after administration of MBP when compared to contents obtained in animals not treated with MBP.

863
TITLE:
STUDIES ON INHALATION EXPOSURE OF DOGS TO RADIOACTIVE MERCURY VAPOR MERCURY-203

AUTHORS:
CHERIAN MG
VANDER MALLEI R
ALLEN J
VOSTAL JJ

SOURCE:
BURFORD, R. G. INTERNATIONAL CONGRESS ON TOXICOLOGY. ABSTRACTS. TORONTO, ONTARIO, CANADA. 52P. INTERNATIONAL CONGRESS ON TOXICOLOGY: TORONTO, ONTARIO, CANADA.; 1977 35

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT HUMAN TRACHEA LIVER KIDNEY HEART LUNG ERYTHROCYTES BRAIN BLOOD

864
TITLE:
DENTAL AMALGAM AND COGNITIVE FUNCTION IN OLDER WOMEN FINDINGS FROM THE NUN STUDY

AUTHORS:
SAXE SR
SNOWDON DA
WEKSTEIN MW
HENRY RG
GRANT FT
DONEGAN SJ
WEKSTEIN DR

SOURCE:
JOURNAL OF THE AMERICAN DENTAL ASSOCIATION; 126 (11). 1995. 1495-1501.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE HUMAN ELDERLY ROMAN CATHOLIC SISTER TOOTH BRAIN FUNCTION MERCURY VAPOR ADVERSE EFFECT MERCURY
TOXICITY AGE-RELATED NEUROLOGIC DISEASE ALZHEIMER'S DISEASE DEMENTIA PATHOGENESIS OCCLUSAL DENTAL AMALGAM RESTORATIVE MATERIAL TREATMENT NEUROPSYCHOLOGICAL TEST INCIDENCE STATISTICAL ANALYSIS ELM GROVE WISCONSIN USA

865
TITLE:
Neurologic features of chronic Minamata disease (organic mercury poisoning) certified at autopsy.

AUTHORS:
UCHINO M
OKAJIMA T
ETO K
KUMAMOTO T
MISHIMA I
ANDO M

SOURCE:
INTERNAL MEDICINE (TOKYO); 34 (8). 1995. 744-747.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. To better understand the neurologic events related to chronic Minamata disease (organic mercury poisoning), we studied data from 77 patients with Minamata disease as certified at autopsies performed from 1976 to 1994 (mean age: 72.3 years). Major neurologic findings included: sensory impairment in 80.5% of the patients which was limited to the extremities in 42.9%. Impairment of lower extremity coordination was present in 35.8% of the patients, constriction of the visual fields in 28.8%, and retrocochlear hearing loss in 15.3%. There was no correlation between the degree of cerebellar incoordination and the methylmercury concentration in the cerebellum. Compared with the classic type of Minamata disease, the incidence of major neurologic findings was markedly decreased. In light of these findings, supplemental examinations including brain computed tomography (CT), magnetic resonance imaging (MRI), short latency somatosensory evoked potential (SSEP), or tremogram may be

866
TITLE:
Investigations on cerebral mercury from dental amalgam fillings through a direct nose-brain transport.

AUTHORS:
MAAS C
BRUECK W
HAFFNER H-T
SCHWEINSBERG F

SOURCE:
ZENTRALBLATT FUER HYGIENE UND UMWELTMEDIZIN; 198 (3). 1996. 275-291.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The transport of mercury (Hg) from the oro-nasal to the cranial cavity via a direct route was investigated. In 55 deceased persons, Hg concentrations were measured in the olfactory bulb and the trigeminal ganglion, and the number of dental amalgam fillings was assessed. For the purpose of comparison, Hg concentrations were also determined in the occipital lobe cortex, the pituitary gland and the kidney cortex. Quantitative Hg analysis was performed by cold vapor atomic absorption spectroscopy after acid digestion using high pressure microwave treatment. In the olfactory bulb (geom. mean 17.4 mug/kg w. w.), the Hg concentration was significantly higher than in the occipital lobe cortex (geom. mean 9.2 mug/kg w. w.) ($p < 0.0001$). No significant difference was found between the Hg concentration in the trigeminal ganglion (geom. mean 12 mug/kg w. w.) and the occipital lobe cortex (alpha

= 0.005; p = 0.0342). Regression analysis did not reveal a statistically significant

867
TITLE:
Urinary System

AUTHORS:
Goyer RA

SOURCE:
Environmental Pathology, N. Karle Mottet, Editor; New York, New York, Oxford University Press, pages 290-319, 82 references, 19851985

ABSTRACT:
The pathophysiology of the kidney that occurs as a result of exposure to environmental factors, was reviewed. Metal toxicity is reduced by methallothionein and other chelating agents. Most of the pathogenic processes in kidneys are produced by nephrotoxic drugs and chemicals. Acute interstitial nephritis (AIN) occurs as a cell mediated immune response to drugs, particularly to penicillins, thiazides, furosemide (54319), gold salts, and mercury (7439976). AIN is more severe in adult patients. Glomerular lesions may be caused by direct drug or chemical toxicity. Chronic interstitial disease may occur as sequela to severe tubular disease. Lead (7439921) neuropathy may cause reversible decreased absorption of amino acids, glucose, phosphate, and sodium, and an increase in serine production. The chronic effects may result in irreversible tubular cell damage and neoplasia. With age, cadmium (7440439) is accumulated in the kidney. The early effects of cadmium are decreased absorption of amino-acids, glucose, phosphate, and low molecular weight proteins. The late effects are renal tubular acidosis, hypercalciuria, glomerular proteinuria, nephrocalcinosis, renal stones, and interstitial fibrosis. Mercury may produce cell necrosis and renal failure and chronic effects at low doses. Gold salts may cause proteinuria, glomerulonephritis, and tubular cell lesions. Bismuth (7440699) administration results in the formation of nuclear inclusions in proximal renal tubular lining cells. Uranium (7440611) causes injury and necrosis of proximal renal tubules. Nonsteroidal anti inflammatory drugs have been implicated in interstitial nephritis. Volatile hydrocarbons may produce glomerular lesions. Chronic renal failure was found in patients with chronic silicosis. Ethylene-glycol (107211) causes acute brain and kidney toxicity and often permanent renal damage. About 1 percent of heroin addicts develop nephritic disorders. Renal parenchyma, pelvis, and ureter tumors are uncommon, but when present are usually lethal. Bladder tumors frequently develop at multiple sites but due to earlier diagnosis and better therapy, their mortality rate is decreasing. The author suggests that the bladder tumor occurs as a result of saccharin promoting previously initiated cells.

868
TITLE:
Metals and Metalloids Other Than Mercury and Lead

AUTHORS:
Katz GV

SOURCE:
Neurotoxicity of Industrial and Commercial Chemicals, Vol. I, J. L. O'Donoghue, Editor; Boca Raton, Florida, CRC Press, Inc., pages 171-191, 334 references, 19851985

ABSTRACT:
The literature on the neurotoxic effects resulting from occupational exposure to metals (other than lead and mercury) was reviewed. Elevated brain levels of aluminum (7429905) were observed in two cases of encephalopathy reported in aluminum workers. An estimated 1.5 million workers in the U.S. were at risk for occupational exposure to arsenic (7440382), which has been associated with increased incidences of peripheral neuropathies. Arsenic was found to cross the placental barrier and accumulate in the fetal nervous system, resulting in death of the neonate. Mild transient neurologic syndromes characterized by headache and somnolence were reported following acute or chronic occupational exposure to tellurium (13494809). Cases of thallium (7440280) intoxication were reported following occupational exposure to thallium compounds, during the manufacture of rodenticides, separation of industrial diamonds, and disposal of waste products from lead and zinc facilities. Neurologic manifestations of thallium intoxication included: ataxia, lethargy, painful extremities, peripheral neuropathy, multiple cranial nerve palsies, psychosis, convulsions, and coma. Occupational exposure to organotins, used in certain polymers, disinfectants, fungicides, and insecticides, produced transient headaches, visual defects, mental confusion, electroencephalographic changes, epileptic seizures, and loss of consciousness. Neurotoxic effects were associated with accidental poisonings with barium (7440393), bismuth (7440699), cadmium (7440439), cobalt (7440484), gold (7440575), lithium (7439932), platinum (7440064), nickel (7440020), and selenium (7782492); but there were no reports of neurological symptoms resulting from occupational exposure to these metals.

869
TITLE:
REDUCED MERCURY EXCRETION WITH FECES IN GERM-FREE MICE AFTER ORAL ADMINISTRATION OF METHYL MERCURY CHLORIDE

AUTHORS:
NAKAMURA I

HOSOKAWA K
TAMURA H
MIURA T

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 17 (5). 1977 528-533

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. BRAIN LIVER KIDNEY SPLEEN MICROORGANISM METABOLISM INVOLVEMENT

870
TITLE:
Environmental contaminant levels in sharp-shinned hawks from the eastern United States.

AUTHORS:
WOOD PB
VIVERETTE C
GOODRICH L
POKRAS M
TIBBOTT C

SOURCE:
JOURNAL OF RAPTOR RESEARCH; 30 (3). 1996. 136-144.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. We examined contaminant levels in tissue samples of sharp-shinned hawks (Accipiter striatus) collected in the eastern U.S. from 1991-93. We report concentrations of aldrin, cis-nonachlor, p,p'-DDE, dieldrin, heptachlor epoxide, mirex, oxychlordane, PCB, aluminum, lead, and mercury detected in 23 blood, 10 brain, and 31 liver samples. DDE, PCB's, and mercury were detected most often and in highest concentrations. No contaminants were present at concentrations that might cause mortality with the possible exception of one individual with high oxychlordane residues in the liver. It is not known, however, at what levels these contaminants might impair reproduction in sharp-skinned hawks. Migration count data (declining sharp-skinned hawk numbers in the East, stable in the Midwest) coupled with contaminant data (higher DDE levels in blood in eastern sharp-shins than in midwestern) do not rule out the possibility that contaminants may be impairing reproduction in the eastern p

871
TITLE:
Binding of Methylmercury and Methylmercury-Thiol Complexes by Myelin Isolated from Mice of Differing Selenium Status

AUTHORS:
Balthrop JE
Fair PH
Braddon-Galloway S

SOURCE:
Bulletin of Environmental Contamination and Toxicology, Vol. 37, No. 5, pages 783-790, 20 references, 19861986

ABSTRACT:
Experiments were performed to determine the binding characteristics of thiol metabolites of methylmercury to myelin isolated from the central nervous system; possible alteration of such binding by dietary selenium was also investigated. Weanling female ICR Sprague-Dawley-rats were fed either selenium deficient (less than 0.05 micrograms/gram) or selenium control (0.5 microgram/gram) diets for 6 weeks before being used. Myelin preparations from selenium deficient and control rats were incubated with methylmercury complexes of cysteine, homocysteine, glutathione and cysteine-glycine, and methylmercury-chloride (115093). Binding of uncomplexed methylmercury to the myelin proved to be uninterpretable using Scatchard analysis. Scratchard analyses of the binding of thiol complexes of methylmercury to myelin gave typical plots for data representing binding to more than one site. Data were interpreted as indicating a high and a low affinity site. The selenium status of the animal appeared to have no influence on the binding constants. Data suggested that glutathione and its metabolites, when complexed to methylmercury, have a high affinity binding site located on myelin found in the brain. These sites are likely to be the thiol groups located on the myelin proteolipid protein. Uncomplexed methylmercury had less affinity for the myelin and appeared to bind in a nonspecific manner. The authors conclude that the effectiveness of selenium in modifying mercury metabolism has been well established. Data show that selenium in the diet does not influence the binding of methylmercury metabolites to myelin. The ameliorative role of selenium in methylmercury intoxication cannot be explained through an effect on myelin binding of methylmercury.

872
TITLE:
The distribution and tissue retention of mercury-203 in the goldfish (Carassius auratus).

AUTHORS:
WEISBART M

SOURCE:
CAN J ZOOL; 51 (2). 1973 143-150

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Goldfish injected i.p. with 203-Hg (NO3)2 lost mercury at an apparent constant rate resulting in a biological half-life of 568 hr. Correlated with this loss was a linear increase in the amount of Hg in the water. The 203-Hg content in the tissues showed 4 responses. Gallbladder, gonad and spleen tissues showed no significant regressions. Eye, kidney and intestinal tissue manifested significant losses of Hg, but the rate of loss was not significantly different from that of the body as a whole. Gill, heart, skin and swin bladder tissues lost Hg at rates faster than the body was a whole. Brain, liver, muscle and head kidney tissues showed no significant losses of Hg.

873
TITLE:
Interaction of metals with muscarinic cholinoceptor and adrenoceptor binding, and agonist-stimulated inositol phospholipid hydrolysis in rat brain.

AUTHORS:
RAJANNA B
CHETTY CS
RAJANNA S
HALL E
FAIL S
YALLAPRAGADA PR

SOURCE:
COMPARATIVE BIOCHEMISTRY AND PHYSIOLOGY C PHARMACOLOGY TOXICOLOGY & ENDOCRINOLOGY; 116 (2). 1997. 111-116.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In vitro mercury (Hg) or lead (Pb) effectively inhibited the binding of 3H-quinuclidinyl-benzilate (QNB) (a muscarinic cholinoceptor antagonist) and 3H-prazosin (an alpha1-adrenoceptor antagonist) to their receptors in cerebellar and cerebral cortex membranes in a concentration-dependent manner. Hg was more potent than Pb. When the rats were treated with Hg (5 mg/kg body wt) or Pb (25 mg/kg body wt) for 24 hr, a decrease in 3H-prazosin and an increase in 3H-QNB receptor binding were observed in cerebral cortex. There was no alteration in 3H-prazosin binding in cerebellum with the above treatment of metals, but 3H-QNB binding in cerebellum was significantly inhibited by Hg. However, both 3H-prazosin and 3H-QNB receptor bindings were significantly decreased in cerebellum of rats treated for 7 days with Hg (1 mg/kg body wt/day) or Pb (25 mg/ kg body wt/day). But in cerebral cortex of rats treated with these metals for 7 days, a decrease in 3H-prazosin and an increase in 3H

874
TITLE:

THE INFLUENCE OF SELENIUM ON THE DISTRIBUTION OF METHYL MERCURY AND MERCURY CHLORIDE IN THE PREGNANT RAT

AUTHORS:
SASSER LB
JARBOE GE
LAPRADE J

SOURCE:
DRUCKER, HARVEY AND RAYMOND E. WILDUNG (ED.). ERDA (ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION) SYMPOSIUM SERIES, VOL. 42. BIOLOGICAL IMPLICATIONS OF METALS IN THE ENVIRONMENT. PROCEEDINGS OF THE FIFTEENTH ANNUAL HANFORD LIFE SCIENCES SYMPOSIUM. RICHLAND, WASH., USA, SEPT. 29-OCT. 1, 1975. IX+682P. ILLUS. MAPS. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION (AVAILABLE AS CONF-750929 FROM NATIONAL TECHNICAL INFORMATION SERVICE, US DEPARTMENT OF COMMERCE: SPRINGFIELD, VA.). 1977. ISBN 0-87079-104-4.; 1977 478-487

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ANTIDOTE-DRUG BRAIN BLOOD UTERUS PLACENTA FETUS URINARY FECAL

875
TITLE:
High lead exposure and auditory sensory-neural function in Andean children.

AUTHORS:
COUNTER SA
VAHTER M
LAURELL G
BUCHANAN LH
ORTEGA F
SKERFVING S

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 105 (5). 1997. 522-526.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. We investigated blood lead (B-Pb) and mercury (B-Hg) levels and auditory sensory-neural function in 62 Andean school children living in a Pb-contaminated area of Ecuador and 14 children in a neighboring gold mining area with no known Ph exposure. The median B-Pb level for 62 children in the Pb-exposed group was 52.6 mug/dl (range 9.9-110.0 mug/dl) compared with 6.4 mug/dl (range 3.9-12.0 mug/dl) for the children in the non-Pb exposed group; the differences were statistically significant ($p < 0.001$). Auditory thresholds for the Pb-exposed group were normal at the pure tone frequencies of 0.25-8 kHz

over the entire range of B-Pb levels. Auditory brain stem response tests in seven children with high B-Pb levels showed normal absolute peak and interpeak latencies. The median B-Hg levels were 0.16 mug/dl (range 0.04-0.58 mug/dl) for children in the Pb-exposed group and 0.22 mug/dl (range 0.1-0.44 mug/dl) for children in the non-Pb exposed gold mining area, and showed no sig

876
TITLE:
THE EFFECT OF MERCURY ON THE ANESTHETIC RESPONSE AND DISTRIBUTION OF THIOPENTAL IN RATS

AUTHORS:
CHAKRABARTI S
BRODEUR J

SOURCE:
FED PROC; 37 (3). 1978 394

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT URINE BRAIN PLASMA MICROSOMAL ENZYME PROLONGED SLEEPING TIME BINDING PROTEINS

877
TITLE:
Distribution and excretion of the mercury chelating agent sodium 2,3-dimercaptopropane-1-sulfonate in the rat.

AUTHORS:
GABARD B

SOURCE:
ARCH TOXICOL; 39 (4). 1978 289-298

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution and excretion of sodium 2,3-dimercapto-1,3 14C-propane-1-sulfonate as dependent on time was studied in the rat. The highest concentration is found in the kidneys, the lowest in the brain. The excretion is very rapid (T 1/2 (half life) = 19 min) and follows a monoexponential curve during the 1st h after administration. This holds for plasma and most of the organs (liver, spleen, gut, skeleton, muscle, skin). The apparent distribution volume of the radioactivity is equivalent to the volume of the extracellular water. After oral administration, 30-40% is absorbed from the gut. The results lead to the conclusion that a fraction of the drug is weakly bound to plasma- and membrane-proteins. They are discussed with respect to the treatment of heavy metal poisoning.

878
TITLE:
Effects of prenatal methylmercury exposure from a high fish diet on developmental milestones in the Seychelles Child Development Study.

AUTHORS:
MYERS GJ
DAVIDSON PW
SHAMLAYE CF
AXTELL CD
CERNICHIARI E
CHOISY O
CHOI A
COX C
CLARKSON TW

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 18 (3). 1997. 819-829.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury is widespread in the environment and exists in several physical and chemical forms. Prenatal exposure to methylmercury disrupts brain development. The most common mode of prenatal methylmercury exposure is maternal fish consumption. Studies of human prenatal exposure in Iraq following maternal ingestion of methylmercury treated grain suggested that maternal hair mercury concentrations above 10 ppm may be related to delayed developmental milestones and neurological abnormalities. This level of exposure can be achieved by frequent consumption of fish. The Seychelles Child Development Study analyzed developmental milestones similar to those determined in Iraq in a large controlled, prospective study of children exposed prenatally to methylmercury when their mothers ate fish. As part of this ongoing study, cohort children were evaluated at 6.5, 19, 29, and 66 months of age. At 19 months care-givers were asked at what age the child walked (n=720 out of 738) and talke

879
TITLE:
Biochemical Mechanisms of Developmental Neurotoxicity of Methylmercury

AUTHORS:
Slotkin TA
Bartolome J

SOURCE:
Neurotoxicology, Vol. 8, No. 1, pages 65-84, 89 references, 19871987

ABSTRACT:

The literature on the neurobehavioral teratogenic actions of methylmercury (593748) was reviewed. Fetal and neonatal rats exposed to methylmercury were found to have early alterations in a brain enzyme involved in the coordination of cellular maturation, ornithine-decarboxylase. Elevated nucleic acid and protein synthesis indicated a subsequent regional perturbation of cell replication and differentiation. Studies in catecholaminergic pathways indicated that the neurobehavioral disturbances caused by methylmercury exposure were related to postnatal alterations in synaptogenesis and synaptic activity. Neurotransmitter uptake, turnover in presynaptic terminals, and postsynaptic adrenergic receptor binding sites were found to be altered by exposure to methylmercury. The resulting aberrant signal transmission across the synapse disrupted the communication of trophic developmental signals which normally pass from neuron to target tissue. The authors identify the need for further research to elucidate the mechanisms linking developmental abnormalities at the cellular level to the functional consequences.

880
TITLE:
USE OF PYRIDOXINE 4 THIOL IN METHYL MERCURY POISONING AND PHARMACOLOGICAL MECHANISM

AUTHORS:
EDANAMI K
TAKAHASHI H
KURODA T

SOURCE:
FOLIA PHARMACOL JAP; 68 (4). 1972 (RECD 1973) 242P-243P

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT ANTIDOTE-DRUG BRAIN MERCURY LEVELS

881
TITLE:
Contaminant concentrations and biomarker response in great blue heron eggs from 10 colonies on the upper Mississippi River, USA.

AUTHORS:
CUSTER TW
HINES RK
MELANCON MJ
HOFFMAN DJ
WICKLIFFE JK
BICKHAM JW
MARTIN JW
HENSHEL DS

SOURCE:
ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY; 16 (2). 1997. 260-271.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In 1993, great blue heron (Ardea herodias; GBH) eggs were collected from 10 colonies on the upper Mississippi River (UMR). They were then artificially incubated until pipping and analyzed for mercury, selenium, and organochlorines. Livers of embryos were analyzed for hepatic microsomal ethoxyresorufin-O-dealkylase (EROD) activity and four measures of oxidative stress. Brains were measured for asymmetry and blood was measured for the coefficient of variation of DNA (DNA CV). Organochlorine concentrations were generally low (geometric mean DDE = 1.3 mug/g wet weight; polychlorinated biphenyl (PCB) = 3.0 mug/g; 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) = 11.5 pg/g). Eggshell thickness was negatively correlated with DDE concentrations. Mercury (geometric mean = 0.8 mug/g dry weight) and selenium (3.1 mug/g dry weight) concentrations in GBH eggs were within background levels. EROD activity was not correlated with total PCBs, TCDD, or toxic equivalents (TEQs), based on the

882
TITLE:
The Health Canada Great Lakes Multigeneration Study: Summary and regulatory considerations.

AUTHORS:
FEELEY MM
JORDAN SA
GILMAN AP

SOURCE:
REGULATORY TOXICOLOGY AND PHARMACOLOGY; 27 (1 PART 2). 1998. S90-S98.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The Health Canada Multigeneration Study was initiated to determine the consequences in rodents consuming diets containing Lake Ontario (LO) or Lake Huron (LH) chinook salmon over successive generations. Following lyophilization, the contaminant levels in the salmon used in the formulation of the diets for this study exceeded a number of tolerances or guidelines established for contaminants in commercial fish and seafood products (PCBs, dioxin, mirex, chlordanes, mercury). Consumption of the fish diets by rats of two consecutive generations resulted in a variety of effects that can be described as adaptive responses or of limited biological significance. The two exceptions to this were (1) the suggestion of modification of working and reference memory in males of the high-dose groups 20% fish diets, which may have been related to decreases noted in neurotransmitters in several

brain regions in these rats; and (2) an effect on thymus weights noted in the high-dose first g

883
TITLE:
Mercury in alligators (Alligator mississippiensis) in the southeastern United States.

AUTHORS:
JAGOE CH
ARNOLD-HILL B
YANOCHKO GM
WINGER PV
BRISBIN I L JR

SOURCE:
SCIENCE OF THE TOTAL ENVIRONMENT; 213 (1-3). 1998. 255-262.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury methylation may be enhanced in wetlands and humic-rich, blackwater systems that crocodiles and alligators typically inhabit. Given their high trophic level and long life-spans, crocodilians could accumulate significant burdens of Hg. Our objectives were to survey Hg concentrations in alligators from several areas in the southeastern United States to test their utility as sentinels of Hg contamination, to examine relationships among Hg concentrations in various tissues and to look for any differences in tissue Hg concentrations among locations. We measured total Hg concentrations in alligators collected in the Florida Everglades (n = 18), the Okefenokee National Wildlife Refuge, Georgia (n = 9), the Savannah River Site (SRS), South Carolina (n = 49) and various locations in central Florida (n = 21), sampling tissues including blood, brain, liver, kidney, muscle, bone, fat, spleen, claws and dermal scutes. Alligators from the Everglades were mostly juvenile, but H

884
TITLE:
Mercury feeding schedules: Effects on accumulation, retention, and behavior in trout.

AUTHORS:
HARTMAN AM

SOURCE:
TRANS AM FISH SOC; 107 (2). 1978 369-375

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Rainbow trout (Salmo gairdneri) were exposed

to 0.5 and 2.0 mug/g doses of ethyl-mercury (p-toluene sulfonanilide) Ceresan each day for a full year and 2.5 and 10 mug/g doses delivered every 5th day of feeding during the year. A further study extended dose levels from 5.0 to 25.0 mug/g Ceresan given daily. Exposure to the lower doses of Hg for either feeding schedule led to concentrations of Hg in muscle that were similar (regression slope equaled 1) to the average daily index of dose for as long as 6 mo. of feeding. Assessment of concentration in muscle at 9 mo. of feeding showed a breakdown of the effect in all groups except the one receiving 0.5 mug/g of Ceresan daily. Both dose level and schedules influenced the concentrations of Hg in muscle. Daily treatment with higher doses, e.g., 5.0 through 25.0 mug/g, led to dose-related concentrations in Hg in muscle but the regression was greater than one. Orders of Hg concentration in a variety of other tissues differed significantly and were generally related to dose. Fish receiving 10.0 mug/g of Hg every 5 days or 5.0 mug/g or greater doses every day in their feed were unable, with few exceptions, to learn to avoid shock when preceded by a signal-light. But beyond performance on the learning task, there was no evidence of impairment of general behavior nor was there any indication of physical debilitation resulting from any treatment. There appeared to be a fairly rapid loss of Hg from selected tissues (brain, liver, kidney, skin, gill, fin), although estimates of total body burden of Hg remained high after 6 mo. of Hg-free feeding.

885

TITLE:

Radioactive mercury distribution in biological fluids and excretion in human subjects after inhalation of mercury vapor.

AUTHORS:

CHERIAN MG
HURSH JB
CLARKSON TW
ALLEN J

SOURCE:

ARCH ENVIRON HEALTH; 33 (3). 1978 109-114

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The distribution of Hg in red blood cells (RBC) and plasma, and its excretion in urine and feces are described in 5 human subjects during the first 7 days following inhalation of radioactive Hg vapor. A major portion (98%) of radioactive Hg in whole blood is initially accumulated in the RBC and is transferred partly to the plasma compartment until the ratio of Hg in RBC to plasma is about 2 within 20 h. The cumulative urinary and fecal excretion of Hg for 7 days in about 11.6% of the retained dose, and is closely related to the percent decline in body burden of Hg. There is little correlation between either the urinary excretion and plasma radioactivity of Hg, or the specific activities of

urine and plasma Hg, suggesting a mechanism other than a direct glomerular filtration involved in the urinary excretion of recently exposed Hg. Blood Hg levels can be used as an index of recent exposure, while urinary levels may be an index of renal concentration of Hg. There is no reliable index for Hg concentration in the brain. (Hg is a common industrial pollutant.)

886
TITLE:
Effect of Inhibition of Gamma-Glutamyltranspeptidase on Biliary and Urinary Excretion of Glutathione-Derived Thiols and Methylmercury

AUTHORS:
Gregus Z
Stein AF
Klaassen CD

SOURCE:
Journal of Pharmacology and Experimental Therapeutics, Vol. 242, No. 1, pages 27-32, 32 references, 19871987

ABSTRACT:
The relationship between the inhibition of the activity of gamma-glutamyltranspeptidase (GGT) in the liver and kidney of male Sprague-Dawley-rats and the biliary and urinary excretion of methylmercury (MeHg) administered intravenously to the animals in the form of methylmercury-chloride (115093), was investigated. Hepatic, biliary and renal GGT was inhibited by 88, 99 and 97 percent, respectively, following the administration of avicin (AV) to the rats. Enzymatic inhibition was accompanied by a sharp reduction in the excretion of oxidized and reduced biliary glutathione, while the biliary excretion of total glutathione derived thiols and disulfides was unaltered, and the urinary excretion of these thiols exhibited a dose dependent increase. The levels of reduced glutathione in the liver and kidney were not affected by treatment with AV, but the levels of cysteine in these organs declined, following the administration of high doses of AV. The serum of AV treated animals showed increased levels of glutathione, and high concentrations of cystine. The excretion of MeHg in the bile was not affected by the inhibition of GGT, but the urinary excretion of the compound increased 34 times as compared to control values. The levels of MeHg in the liver and kidney of the rats were not affected by AV, but a slight decline was recorded in the brain of the animals. The authors conclude that, as opposed to the kidney, GGT does not have a significant effect on the excretion rates of thiols and that the excretion of MeHg in the bile is affected by the excretion of total glutathione derived thiols.

887
TITLE:
The Role of Biomarkers in Reproductive and Developmental Toxicology

AUTHORS:
Clarkson TW

SOURCE:
Environmental Health Perspectives, Vol. 74, pages 103-107, 20 references, 19871987

ABSTRACT:
The relationship between methylmercury (22967926) concentration in hair and blood was considered along with the application of hair analysis to developing dose response relations for adult exposure and dose response relations for prenatal exposure. Mechanisms of damage to the developing central nervous system were also considered. In a study where volunteers ate fish containing methylmercury for a period of 100 days, a close parallel between blood and hair concentration was noted with about a 20 day lag period in hair levels, during which time methylmercury was entering the hair follicles and appearing above the scalp line. Pregnant women in Iraq during 1971 and 1972 were exposed to bread containing methylmercury. Hair samples taken in January of 1973 indicated clearly that mercury levels could be recapitulated back as far as 1971, prior to the actual exposure. Infants whose mothers had been heavily exposed developed severe cerebral palsy in large numbers. Milder effects were also seen among those not so heavily exposed, primarily representing developmental delays. When the study group was enlarged to 82 mothers and infants in pairs, dose response relations were demonstrable for a number of these effects. Studies of the mechanisms of damage have suggested substantial derangement of the cytoarchitecture of the brain and the inhibition of cell division. The major defect appeared to be faulty development, not destructive focal neuronal damage as has been found in adult poisonings. The author concludes that hair concentrations of methylmercury provide a good biomarker for exposure which can be used to recapitulate blood levels during pregnancy.

888
TITLE:
LEAD AND OTHER NEUROTOXINS AS RISK FACTORS FOR AMYOTROPHIC LATERAL SCLEROSIS

AUTHORS:
KAMEL F

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Exposure to environmental neurotoxins is likely to increase the risk of developing neurodegenerative diseases, either directly or through

interaction with genetic susceptibility factors. Work has begun to assess the role of environmental exposures in the etiology of these disorders. ALS is a progressive neurological disease affecting motor neurons; its etiology is essentially unknown. A protocol has been developed for a case-control study of the role of environmental risk factors in the etiology of ALS. The primary hypothesis is that cumulative lifetime exposure to lead is a risk factor for ALS. Lead exposure will be assessed by measuring bone lead, using the newly developed technology of x-ray fluorescence. Other environmental risk factors which will be investigated include mercury, solvents, and pesticides. Polymorphisms in genes which may increase susceptibility to lead or other neurotoxins will be also be studied. The study will involve interviews and clinical and laboratory assessments for 200 incident ALS patients and 200 clinical controls.

889
TITLE:
PHARMACOKINETICS

AUTHORS:
DEDRICK RL

SOURCE:
Crisp Data Base National Institutes Of Health

ABSTRACT:
RPROJ Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and humans. They provide a plausible set of equations that can be used to extrapolate data from animals to humans, and thereby improve chemotherapy and risk assessment. A pharmacokinetic model has been published for the pharmacokinetics of methyl mercury and inorganic mercury derived from it by demethylation in the growing rat. Preliminary consideration has been given to the pharmacokinetics of IBZM to include bound, free, and metabolite concentrations in relevant tissues. Work is well advanced on the development of a pharmacokinetic model for topotecan in the Rhesus monkey. Important features of the model include the reversible opening of the topotecan lactone to an hydroxy acid form, and transport between the plasma and the cerebrospinal fluid. Other research on regional therapy has included discussion of a draft clinical protocol for the administration of AZT into the cerebrospinal fluid for the treatment of AIDS dementia and related transport studies in the rat brain. A draft chapter on intraperitoneal drug administration has been prepared, and calculations suggest that absorption of drugs directly into the surface of the liver may be quantitatively more important than was previously recognized.

890
TITLE:

The modifying effect of multiple generation selection and dietary cadmium on methyl mercury toxicity in Japanese quail.

AUTHORS:
ESKELAND B
NAFSTAD I

SOURCE:
ARCH TOXICOL; 40 (4). 1978 303-314

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Japanese quails were exposed to dietary methyl mercury chloride in graded amounts from 2-8 ppm through a series of multiple-generation experiments with the experimental periods lasting from 6-12 wk, starting with the experimental diets when the birds were 6 wk old. Cd chloride was added to diets with and without Hg and fed to groups in 3 of the 5 experiments. Hatchability was depressed at 8 ppm Hg. The mortality of chicks from 8 ppm exposed parents was 100% in the 1st 2 generations, while chick mortality at the 4 ppm level in the same experiments was 54-63%. After 6 generations mortality in chicks hatched in 8 ppm group was reduced to about 50%. Cd supplementation at a level of 5 ppm counteracted the Hg-induced toxicity but failed to be effective in preventing the effects of Hg toxicity when added at the 15 ppm level. Significant toxic effects of Cd alone did not occur until the level was raised to 60 ppm. The morphology of Hg-induced encephalopathy was similar to the brain lesions reported in other bird species, with the injuries predominantly being localized to the cerebellar cortex and medulla.

891
TITLE:
Mercury concentrations in tissues of Solea solea treated with HgC12.

AUTHORS:
SERRA R
BARGHIGIANI C
ROSSI A
CATTANI O
CARPENE E

SOURCE:
OEBALIA; 22 (0). 1996. 113-118.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. In injected sole mercury reached a maximum value in the kidney (337 mug/g f.w.) and a minimum in brain and muscle (0.1 mug/g f.w.). In the sole that received Hg via feed, the metal levels were about two orders of magnitude lower.

892
TITLE:
METHYL MERCURY ACCUMULATION IN BRAINS OF PREGNANT NONPREGNANT AND FETAL RATS

AUTHORS:
NULL DH
GARTSIDE PS
WEI E

SOURCE:
LIFE SCI PART II BIOCHEM GEN MOL BIOL; 12 (2). 1973 65-72

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CONGENITAL METHYL MERCURY POISONING

893
TITLE:
MERCURY-203 TISSUE DISTRIBUTION AND EXCRETION WHEN ADMINISTERED INTRA VENOUSLY AS ORGANIC METHYL MERCURY CHLORIDE OR AS INORGANIC MERCURIC CHLORIDE IN HOLSTEIN CALVES

AUTHORS:
STAKE PE
MILLER WJ
NEATHERY MW
GENTRY RP

SOURCE:
FED PROC; 33 (3 PART 1). 1974 660

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MUSCLE BRAIN HEART

894
TITLE:
MERCURY SELENIUM INTERACTION AT CONCENTRATIONS OF SELENIUM AND OF MERCURY
VAPORS AS PREVALENT IN NATURE

AUTHORS:
NYGAARD S-P
HANSEN JC

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 20 (1). 1978 20-23

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. HUMAN WISTAR RAT LUNG BLOOD LIVER BRAIN STRIATED MUSCLE OCCUPATIONAL ENVIRONMENTAL CONTAMINANTS

895
TITLE:
Effects of Methylmercury on Retinoic Acid-Induced Neuroectodermal Derivatives of Embryonal Carcinoma Cells

AUTHORS:
Cadrin M
Wasteneys GO
Jones-Villeneuve EMV
Brown DL
Reuhl KR

SOURCE:
Cell Biology and Toxicology, Vol. 4, No. 1, pages 61-80, 31 references, 19881988

ABSTRACT:
The effect of methylmercury on neuroectodermal cells derived from murine embryonal carcinoma (EC) cells was examined. EC cells were treated with retinoic-acid for 2 days and then exposed to 0.1 micromolar (microM) to 10.0microM methylmercury for periods up to 2 hours. EC cell cultures were then observed for differentiation. Indirect immunofluorescence microscopy was used to determine the effects of methylmercury on the microtubule and intermediate filament systems of neurons and glia. With regard to the reaction to methylmercury, there were at least two populations of microtubules in the neurons. The most sensitive were located in the perikarya. The neurite microtubules were less sensitive and a subpopulation of these was preserved in the complete absence of microtubules in the perikarya. The heterogeneity of microtubules in the neuronal process may be reflected by the relative stability of this subpopulation of neurite microtubules. Even though the response of perikaryal microtubules was relatively predictable in different cells, there was variable preservation of microtubules among cells located in different regions of the aggregate. Cells on the edge of the cell mass lost their microtubules before cells in the interior of the cell mass. Thus the cytoskeleton was partially protected by the physical presence of adjacent cells. The findings support the theory that the microtubule component of the cytoskeleton may be a primary target for methylmercury within cells of the developing brain. Only minor changes were noted in the neuronal commitment. However, microtubules in both neurons and glia were vulnerable to methylmercury and this compound clearly affected the neuroectodermal maturation and neurite growth.

896
TITLE:

Instrumental neutron activation analysis for mercury in dogs administered methylmercury chloride: Used of a low energy photon detector.

AUTHORS:
FRIEDMAN MH
MILLER E
TANNER JT

SOURCE:
ANAL CHEM; 46 (2). 1974 236-239

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg was determined by nondestructive neutron activation analysis in samples of brain tissue from beagles which were fed methylmercury chloride. The mercury concentration was not uniformly distributed throughout the CNS and the fastest rise in concentration occurred in components of the visual system. The analytical procedure was capable of measuring Hg instrumentally and routinely in small samples of biological materials at approximately the 0.2-ppm level within a few days after irradiation with short counting times. Comparative measurements showed that Hg determination based on 197-Hg could be done with greater sensitivity by using a Ge(Li) low energy photon detector rather than a conventional high resolution, high efficiency coaxial Ge(Li) detector.

897
TITLE:
INTERACTION BETWEEN SELENIUM AND INORGANIC MERCURY

AUTHORS:
BERLIN M

SOURCE:
ENVIRON HEALTH PERSPECT; (25). 1978 67-69

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RAT WORKER ANTIDOTE SELENIUM MERCURY COMPLEX METABOLISM BRAIN

898
TITLE:
EFFECT OF LONG-TERM ADMINISTRATION OF D PENICILLAMINE ON SURVIVAL DISTRIBUTION AND ELIMINATION OF MERCURY IN RATS AFTER A SINGLE INJECTION OF METHYL MERCURY HYDROXIDE

AUTHORS:
SWENSSON A
ULFVARSON U

SOURCE:
WORK-ENVIRON-HEALTH; 10 (3). 1973 (RECD 1974) 144-150

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ANTIDOTE-DRUG WEIGHT LOSS NEUROLOGICAL SIGNS BRAIN ACCUMULATION

899
TITLE:
Mercury-induced renal vascular shut-down: Observations in experimental acute renal failure.

AUTHORS:
SHERWOOD T
LAVENDER JP
RUSSELL SB

SOURCE:
EUR J CLIN INVEST; 4 (1). 1974 1-8

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Mercuric chloride introduced into the systemic circulation or directly into the renal artery in (32) dogs led to an immediate and lasting fall in renal blood flow. On arteriography severe cortical ischemia was found. Renal vascular shut-down induced by mercuric chloride is probably concentration dependent, and is not mediated by glomerular filtration. It is possible to protect the kidney from shut-down by an infusion of hyperosmolar mannitol given before mercuric chloride. The no-reflow phenomenon, already documented in the ischemic kidney and brain, probably has a counterpart in mercury induced acute renal failure. Endothelial cell swelling may be an important primary vascular disorder underlying many acute renal failure states.

900
TITLE:
Methylmercury-Induced Movement and Postural Disorders in Developing Rat: High-Affinity Uptake of Choline, Glutamate, and gamma-Aminobutyric Acid in the Cerebral Cortex and Caudate Putamen

AUTHORS:
O'Kusky JR
McGeer EG

SOURCE:
Journal of Neurochemistry, Vol. 53, No. 4, pages 999-1006, 35 references, 1989

ABSTRACT:

The extent to which decreased uptake of choline and gamma-aminobutyric-acid (GABA) at subclinical stages of toxicity contribute to the selective degeneration of GABAergic interneurons at the onset of neurological impairment was studied in Sprague-Dawley-rats. The rats were subcutaneously dosed with methylmercuric-chloride (115093) which caused movement and postural disorders during the fourth postnatal week. Homogenates of cerebral cortex and caudate putamen were prepared to determine the sodium dependent high affinity uptake of radiolabeled choline, glutamate, and GABA. A significant decrease was noted in the uptake of choline in the cerebral cortex (73 to 75 percent) but not in the caudate putamen at the onset of neurological impairment and at one subclinical stage of toxicity. In neither region were there significant differences in glutamate uptake. In the presence of 1 millimolar beta-analine the uptake of GABA was reduced significantly in both the cerebral cortex (55 percent) and caudate putamen at the onset of neurological impairment and at one subclinical stage. This GABA uptake decrease was consistent with earlier studies demonstrating a preferential degeneration of GABAergic neurons in the cerebral cortex and caudate putamen of methylmercury treated animals. The decrease in choline uptake reflected an abnormal development of cholinergic innervation of the cerebral cortex as the high affinity uptake of choline was the rate limiting step for acetylcholine synthesis by cholinergic neurons.

901

TITLE:

(Environmental contamination by mercury (Hg series No. 14): III. Inorganic and organic mercury in human hair and marine fish.)

AUTHORS:

AOKI H

SOURCE:

JAP J HYG; 24 (5-6). 1970 556-562

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The methylmercury level in the hair of 37 fishermen from the middle Oyabe River area was 6.20 4.73 ppm. The highest value was 20.2 ppm. These subjects daily ate fish containing high levels of methylmercury. A Tokyo citizen had 1.86 plus or minus 1.24 ppm (n = 17) of methylmercury in his hair. Groups of helicopter pilots and vegetarians had 4.11 and 1.73 ppm respectively. Corpses of Tokyo citizens, who died suddenly of various causes, contained several ppm of methylmercury in the hair. The concentration in the organs was much less, about 0.01 ppm in the brain and 0.02 0.03 ppm in the liver and kidney. Hair was 1 excretory place for organic Hg, after it was concentrated from circulating blood into an inert form. The highest level of methylmercury in marketed marine fish was found in tuna and yellowtail (approximately 0.4/ppm). Coastal and inland sea fish contained negligible amounts of

methylmercury.

902
TITLE:
Some inter-relationships between vitamin C (L-ascorbic acid) and mercury in the guinea-pig.

AUTHORS:
BLACKSTONE S
HURLEY RJ
HUGHES RE

SOURCE:
FOOD COSMET TOXICOL; 12 (4). 1974 511-516

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Young male guinea-pigs were used to study the interrelationships of L-xyloascorbic acid (vitamin C) and orally administered mercuric mercury (8 mg Hg-2 plus/kg body weight). Hg significantly reduced the concentration of ascorbic acid in the brain, adrenals and spleen of animals receiving maintenance doses of the vitamin. Large doses of ascorbic acid resulted in an increased deposition of Hg in the liver and kidney. Hg administration depressed the growth rate and altered the weights of the liver and kidney, and these changes were not affected by large intakes of ascorbic acid. The Hg-induced adrenal hypertrophy, however, was prevented by large doses of ascorbic acid.

903
TITLE:
Organometal-Induced Increases in Oxygen Reactive Species: The Potential of 2',7'-Dichlorofluorescin Diacetate as an Index of Neurotoxic Damage

AUTHORS:
LeBel CP
All SF
McKee M
Bondy SC

SOURCE:
Toxicology and Applied Pharmacology, Vol. 104, No. 1, pages 17-24, 45 references, 1990

ABSTRACT:
An investigation was performed using 2',7'-dichlorofluorescin-diacetate (DCFH-DA) to test two separate hypotheses: whether oxygen reactive species played a role in the neurotoxic mechanisms following in-vivo and in-vitro exposure to methyl-mercury (22967926) (MeHg) and trimethyltin (1631738) (TMT), and whether DCFH-DA was a potential marker for neurotoxicity, and

how it compared to the use of levels of free calcium ion. On days two and seven following a single injection of MeHg at 1mg/kg, a significant increase was noted in the formation rate of cerebellar oxygen reactive species. Two days following a 3mg/kg injection of TMT, hippocampal and frontocortical oxygen reactive species were elevated. The formation of oxygen reactive species was increased following in-vitro exposure to 10 to 20 micromolar (microM) of MeHg. TMT at 5 to 40microM had no effect. No change was noted in the levels of calcium ion in P2 fractions from cerebellum and hippocampus of the animals treated with either MeHg or TMT. The authors conclude that oxygen reactive species are elevated in brain regions, cerebellum for MeHg and hippocampus for TMT, and are believed to be specifically vulnerable to these toxic agents. Oxidative damage may be a mechanism underlying the toxicity of both organometals. DCFH-DA may have potential as an indicator of neurotoxic damage

904

TITLE:

The impact of persistent pollutants on piscivorous and molluscivorous birds.

AUTHORS:

Bothof
De Vries R
Koeman J H
Van Velzen-Blad
Vos J G $

SOURCE:

TNO-Nieuws; 27(10): 561-569; 1972 ; (REF:24)

ABSTRACT:

HAPAB The possible toxic environmental effects of polychlorinated biphenyls (PCB), DDE and other organochlorines, and mercury were studied in four species of aquatic birds. Based on laboratory observations, the mean PCB levels of 190 and 319 ppm found in brain and liver, respectively, of dead cormorants appeared to be responsible for their deaths. Although liver necrosis and hepatic porphyria normally accompany PCB intoxication, neither of these were observed in cormorants. Thinner cormorant eggshells seemed to coincide with high residues of PCBs and DDE. Mercury in these birds was well below the toxic level. Herons appeared to be less susceptible to PCB toxicity than cormorants in laboratory studies. Although herons found dead in the field contained high levels of PCB and some organochlorines, it is unlikely that their deaths resulted from it. Residues in heron eggs and thinning of the shell was similar to those in cormorants. In the sanwich tern pesticide levels have decreased since measures were established to eliminate pollution by pesticide manufacturing plants. DDE appaears to be responsible for eggshell thinning in this species. Eider ducks would be affected by a rise in PCB

contamination although present levels are not considered toxic. No evidence was found in any of the species that breeding was abnormal.

905

TITLE:

Organ clearance of selenium-75-labeled selenium (II) trioxide and mercury-203-labeled mercury(II) chloride administered separately and simultaneously to mice.

AUTHORS:

HANSEN JC
KRISTENSEN P

SOURCE:

TOXICOLOGY; 15 (1). 1979 (RECD. 1980). 1-18.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. A study on organ clearance of Hg (203HgCl2) and Se %W%000006%% given separately or simultaneously in single doses by i.p. injections to mice was performed. The simultaneous administrations are handled in molar ratios (Hge) less than, equal to or greater than 1. Liver, kidneys, spleen and blood contain most of the Hg and Se administered, while heart, lungs, skin, muscles and brain only contain small amounts. Both elements are retained to a higher degree in especially kidneys, liver, spleen and blood when co-administered than when administered alone. In kidneys, clearance rate of Se is independent of Hg administration, with an effective halflife 11.2-13.5 days in accordance with the wholebody elimination. The clearance of Hg is strongly dependent on coadministered Se. At a low molar ratio (Hg/Se | 1) of administered dose clearance rate is identical to that of Se, compared to an effective halflife when administered alone. In liver the effective halflife of Se when administered alone or coadministered with Hg (Hg/Se ratio < 1) is identical to that of kidneys: 11.2-12.5 days. At increasing molar ratios retention of Se increases and clearance rate decreases. A marked decrease in Hg clearance from liver is induced by simultaneously administered Se. The effective halflife becoming extremely long and under certain conditions even an accumulation takes place. Concordant relations are found for liver and spleen. Se in blood is only affected to a minor degree by Hg. Clearance rate for Hg is decreased by Se. At a molar ratio between doses (Hg/Se) \ 1 clearance rate is approximately identical to that of Se. Se metabolism is quantitatively rather than qualitatively influenced by Hg as Hg administration provokes a higher retention of a given dose of Se while clearance rate in kidneys and blood is only influenced by high molar ratios (Hg/Se). Contrary to Se, Hg metabolism is altered both qualitatively and quantitatively as retention as well as clearance rate are influenced by Se in all organs and in all molar ratios given in kidneys and blood. It is assumed that at least 2 mechanisms exist in the metabolic pathways of Hg: binding to metallothionein; and binding to

Se-containing metabolic compounds. As Se induced an increase in Hg retention it is questioned whether Se is beneficial in case of chronic exposure to inorganic Hg. It also implies the question of bioavailability of Se in animal food items.

906
TITLE:
Acquisition of a multiple DRH extinction schedule of reinforcement in rats exposed during development to methylmercury.

AUTHORS:
Rasmussen EB
Newland MC

SOURCE:
Toxicologist 1999 Mar;48(1-S):362

ABSTRACT:
Female rats were exposed to 0, 0.5 or 6.4 ppm Hg as methylmercury in drinking water beginning at least 4 weeks before mating and ending on postnatal day 16. Brain Hg concentrations at birth in cohorts were 0.49 and 9.8 ppm for the two exposure groups. Female offspring were trained to lever press under Multiple Differential-Reinforcement of-High-Rate Extinction (MULT DRH-N:T EXT) schedules of reinforcement. Under the extinction schedule, lever-pressing had no scheduled consequences. Under the DRH-N:T schedule, a food pellet was delivered whenever N responses occur within T seconds. Two acquisition protocols were examined. First, the DRH parameter imposed in three successive sessions was 3:1, 5:2, and 9:4, values selected so that the same average inter-response time (i.e., rate) was required by the schedules. Only ##, ##, and ##% of the control, low-dose, and high-dose rats met the DRH requirement during the third-session. Second, lever-repressing was re-established and the three schedules were imposed until behavior became stable, requiring at least 10 sessions. All but ### animals acquired the response. (A marginal/no effect of mercury was detected?). This failed to replicate a similar experiment by Bornhausen (19**) showing effects of mercury on acquisition a Multiple DRH EXT schedule of reinforcement.

907
TITLE:
Occupational Exposure and Defects of the Central Nervous System in Offspring: Review

AUTHORS:
Roeleveld N
Zielhuis GA
Gabreels F

SOURCE:
British Journal of Industrial Medicine, Vol. 47, No. 9, pages 580-588, 121 references, 1990

ABSTRACT:
An evaluation was conducted to determine indicators for a causal role of parental occupational exposure in the origin of defects of the central nervous system (CNS) in children. Publications concerned with the teratogenic effects of agents used occupationally were extensively evaluated. Both structural and functional disturbances in the developing brain were considered. In spite of a large number of papers addressing this subject, in general, there has been no direct evidence that defects in the CNS in offspring are associated with parental occupational exposure during gestation. The information obtained from nonoccupational investigations, in which a scale of structural and functional defects of the CNS were noted, has not been adequate to form sound conclusions about occupational exposure. The authors conclude however that some hypotheses may be formulated. A causal role of parental occupational exposure in the origin of defects of the CNS is probable for lead (7439921), methylmercury (22967926), and ionizing radiation; possible for cadmium (7440439), organic solvents, anesthetics, and pesticides; and not to be excluded for other chemicals and for nonionizing radiation.

908
TITLE:
BEHAVIOR AS A SENTRY OF METAL TOXICITY

AUTHORS:
WEISS B

SOURCE:
DI FERRANTE, E. (ED.). TRACE METALS: EXPOSURE AND HEALTH EFFECTS; PROCEEDINGS OF THE RESEARCH SEMINAR, GUILDFORD, ENGLAND, JULY 10-13, 1978. VII+262P. PERGAMON PRESS: NEW YORK, N.Y., USA; OXFORD, ENGLAND. ILLUS. ISBN 0-08-022446-6.; 0 (0). 1979 (RECD. 1980). P185-198.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN MACACA-ARCTOIDES SAIMIRI-SCIUREUS BRAIN BLOOD MERCURY LEAD VISUAL DISORDER PARESTHESIA MENTAL RETARDATION

909
TITLE:
Study of mercury intoxication in a teleost fish, Anguilla anguilla: I. Accumulation of mercury in the organs.

AUTHORS:
BOUQUEGNEAU J-M

SOURCE:
BULL SOC R SCI LIEGE; 42 (9-10). 1973 (RECD 1974) 440-446

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A profile of Hg accumulation is established during direct poisoning with HgCl2. The gills are the only organ studied that accumulates Hg in any important fashion, when intoxication is of brief diration. During chronic intoxication, the gills, kidney, spleen, liver and brain are the organs most highly contaiminated. An interpretation of Hg accumulation profiles is proposed, and the possibility of a biolotical test is indicated, based on the assay of Hg in the muscles and liver of the eel.

910
TITLE:
Effects of methylmercury chloride on various cholinergic parameters in vitro.

AUTHORS:
KOBAYASHI H
YUYAMA A
MATSUSAKA N
TAKENO K
YANAGIYA I

SOURCE:
J TOXICOL SCI; 4 (4). 1979 (RECD. 1980). 351-362.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The effects of methylmercury chloride and other Hg compounds on cholinergic parameters were studied in vitro. Methylmercury chloride (MMC) and phenylmercury acetate inhibited mouse choline acetyltransferase (ChA) with 20 muM (I50) (50% inhibition), and mercury nitrate (MN) with 100 muM (I50). All 3 compounds had little effect on cholinesterase activity. MMC inhibited a high affinity choline uptake with 41 muM (Ki) as well as a low affinity choline uptake with 250 muM (Ki). MMC did not affect a spontaneous and K-stimulated ACh release from brain tissue slices incubated in eserinized Krebs-Ringer's solution up to the concentration of 100 muM. Organic mercury compounds, such as methylmercury, are potent inhibitors of the choline uptake systems, as well as ChA activity.

911
TITLE:
Toxins.

AUTHORS:
Henretig F

SOURCE:
Developmental-Behavioral Pediatrics 1999;3:312-20

912
TITLE:
TIME COURSES OF ACCUMULATION OF METHYL MERCURY AND ITS BIOLOGICAL HALF-LIFE IN VARIOUS ORGANS OF RATS ORALLY ADMINISTERED WITH LOW DOSE OF METHYL MERCURY CHLORIDE

AUTHORS:
MASUHARA T
NAKAMURA Y
SATO T

SOURCE:
THE 52ND GENERAL MEETING OF THE JAPANESE PHARMACOLOGICAL SOCIETY, TOKYO, JAPAN, MARCH 26-29, 1979. JPN J PHARMACOL; 29 (SUPPL.). 1979 (RECD. 1980). 130P.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT KIDNEY LIVER BRAIN KINETICS

913
TITLE:
Methylmercury toxicity in riverine children downstream from gold mining in the Amazon Basin, Brazil.

AUTHORS:
Malm O
Grandjean P
Santos EO

SOURCE:
Frontiers in Fetal Health 1999 Dec;1(6):12-3

914
TITLE:
Methyl mercury induces differential ubiquitin-conjugated protein levels in p53 variant mouse embryonal fibroblasts.

AUTHORS:
Sidhu JS
Hong S
Erickson A
Baker A
Robinson J
Vliet P

Faustman EM

SOURCE:
Toxicologist 2003 Mar;72(S-1):67

ABSTRACT:
The ubiquitin-proteasome pathway is critical for the targeting and rapid intracellular degradation of many proteins associated with regulation of cell cycle progression, differentiation, and development. The accumulation of ubiquitinated proteins is usually attributable to a malfunction, inhibition, or overload of this pathway. Recent studies have suggested that various chemical stressors can disrupt critical cell cycle checkpoints, e.g. p53, via increased ubiquitination resulting in cytotoxicity. We examined such a potential mechanism for the environmental contaminant, methyl mercury (MeHg), which causes neurological disorders and disruption of fetal neurodevelopment. Cultures of p53 transgenic mouse embryonal fibroblasts (MEFs) were treated for 0.5, 1, 2, 4, 8 and 24 h with MeHg (0, 0.5, 2.5 uM) and compared to similar treatments with lactacystin, a potent proteosomal inhibitor. Cell extracts were prepared and ubiquitinated protein levels were visualized by western blot analysis using a polyclonal antibody to ubiquitin. Lactacystin induced the accumulation of ubiquitinated proteins in a time-dependent manner irrespective of p53 genotype. In contrast, MeHg treatment (2.5 uM) resulted in a saturated accumulation between 4-24 h in the p53 (+/+) cells. In the (+/-) cells, an equivalent accumulation peaked at 4 h and then declined while the (-/-) cells showed a minor response at early timepoints. MeHg-induced accumulation of ubiquitinated proteins suggests an inhibition of the proteasome by this agent which is qualitatively comparable to that observed with lactacystin. However, the significant disparity in the level of ubiquitinated proteins observed between both agents in the (-/-) suggests a p53-dependent mechanism for MeHg-induced disruption of proteosomal degradation. The toxicant-induced inhibition of this critical cellular function may help explain the aberrant effects associated with MeHg-induced cytotoxicity in neuronal populations of the developing fetal brain.

915
TITLE:
ABNORMAL NEURONAL MIGRATION IN HUMAN FETAL BRAIN DUE TO MERCURY POISONING

AUTHORS:
CHOI BH
LAPHAM LW
AMIN-ZAKI L
SALEEM T

SOURCE:
AM J PATHOL 86:A55,1977

916
TITLE:
Carcinogenic, mutagenic and immunological effects of heavy metals

AUTHORS:
Piechotta W
Witting U
Miebs T
Witting C
Krieg V
Kollmeier H
Seemann J
Wittig P

SOURCE:
Bundesanstalt fèur Arbeitsschutz und Unfallforschung, Postfach 170202, 4600 Dortmund 17, Federal Republic of Germany, 1983. Vol.1: 264p. 300 ref.

ABSTRACT:
The 1st of these 3 reports summarises present knowledge of the harmful effects of lead, cadmium and mercury and reviews the relevant literature: animal experiments, epidemiological studies, in-vitro studies, occupational exposure, defenses against infection, humoral and cellular immunity. Results are summarised in tables. The 2nd report analyses the literature on malignant tumours of occupational origin. Results are tabulated according to the organs and tissues affected: blood and lymphatic tissue, respiratory tract, mesothelioma, digestive system, liver and pancreas, urogenital system, brain, skeleton, skin; occupations and harmful substances are also identified. The 3rd report is a review of various methods of sampling and sample preparation in order to complex and extract heavy metals for flameless atomic absorption spectrophotometry. The metals concerned are: cadmium, chromium, nickel, lead and zinc in human pulmonary, hepatic, splenic and renal tissue. Preferred methods are prese

917
TITLE:
Total mercury concentration in rats fed fish muscle with mercury content.

AUTHORS:
BACCI E
RENZONI A

SOURCE:
BOLL SOC ITAL BIOL SPER; 50 (17). 1974 (1975) 1416-1422

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Fish containing 3 mg/kg Hg were fed to rats. The rats were fed ad libitum and each ingested 30-45 mg Hg/day. After 42 days on this diet, the Hg content of the rat tissues (mg/kg body weight) was as follows: muscle 2.5, heart 4, brain, 1.7, testes 1.5, liver 29, spleen 11, erythrocytes 34. The Hg concentration of untreated control rats never exceeded 0.05 mg/kg body weight. The Hg content of liver and spleen dropped to negligiblr levels 8 days after discontinuation of Hg in the diet. Erythrocyte Hg dropped to 7 mg/kg body weight 11 days after cessation of Hg.

918

TITLE:

Mercury in the environment.

AUTHORS:

Damluji SF
Amin-Zaki L
Elhassani SB

SOURCE:

Brit. Med. J.4: 489; 1972

ABSTRACT:

HAPAB. A Letter-to-the-Editor cites remarkable improvement of function in cases of mercury poisoning in Iraq as evidence that rehabilitation of such victims is possible and that the help of international organizations such as WHO would be valuable. Although cellular necrosis observed in the brain of many victims is clearly irreversible, all cases graded as mild or moderate have made great progress on physical therapy. Many of those completely paralyzed and bedridden began to care for themselves and walk around after several weeks of physical therapy. Partial sight was recovered in some cases and partial hearing in others, even when no drugs were administered.

919

TITLE:

Does Methylmercury Intoxication Induce Arteriosclerosis in Humans? A Pathological Investigation of 22 Autopsy Cases in Niigata, Japan

AUTHORS:

Oyanagi K
Furuta A
Ohama E
Ikuta F

SOURCE:

Acta Neuropathologica, Vol. 83, No. 3, pages 217-227, 25 references, 1992

ABSTRACT:

The effects of exposure to methylmercury (22967926) on the vascular system were studied. Blood vessels from the brain, myocardium, kidney and aorta were obtained at autopsy from 22 patients diagnosed as having methylmercury intoxication and from 36 nonexposed referents. The internal carotid, vertebral, and basilar arteries in subjects under 34 years old showed slight thickenings of the intima. Duplications or interruptions of the internal elastic lamina were also observed. Some intimal thickening was seen in the proximal portion of the coronary arteries and aortas. Sclerotic changes were seen in the cerebral, coronary and renal arteries of patients over 48 years of age; severity increased in subjects over 70. An increase in sclerotic changes was seen in subjects older than 48 who also had hypertension or diabetes mellitus. No differences in arteriosclerotic changes were seen between the methylmercury or referent groups. The authors attributed the neuropathology of methylmercury intoxication to primary neuronal degeneration, not to ischemic changes in the vasculature.

920

TITLE:

Mercury residues in the common pigeon (Columbia livia) from the Jackson, Mississippi, area: 1972.

AUTHORS:

KNIGHT L A JR
HARVEY E J SR

SOURCE:

PESTIC MONIT J; 8 (2). 1974 (RECD 1975) 102-104

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Total Hg in the common pigeon (C. livia) from the Jackson, Mississippi (USA), area was measured by atomic absorption spectrophotometry. Pigeons captured in 1972 from downtown Jackson were killed on the day of capture to determine Hg levels in wild birds in urban environments; others were caged and analyzed for Hg residues weekly or biweekly for 9 wk. Data are presented to show possible pathways by which organisms eliminate this element. Median concentration of mercury in brains of newly captured pigeons was 22 ppb. Claws showed 14-85 ppb Hg. Possible sources of Hg contamination in these birds are (pesticide) treated grains, contaminated weed seeds and naturally occurring mercurials.

921

TITLE:

Tissue content of mercury in rats given methylmercuric chloride orally: Influence of intestinal flora.

AUTHORS:
ROWLAND IR
DAVIES MJ
EVANS JG

SOURCE:
ARCH ENVIRON HEALTH; 35 (3). 1980. 155-160.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The effect of intestinal flora on the absorption and disposition of Hg in tissues was investigated using conventional rats and rats treated with antibiotics (bacitracin, neomycin sulfate and streptomycin sulfate) to eliminate their gut flora. Antibiotic-treated rats given (203Hg)-labeled methylmercuric chloride orally had significantly more Hg in their tissues, especially in kidney, brain, lung, blood and skeletal muscle, and also excreted less Hg in the feces than conventional rats. In the kidneys of the antibiotic-treated rats, the proportion of Hg present as organic Hg was greater than in the kidneys of the conventional rats. The metabolism of methylmercuric chloride by the gut flora reduces the tissue content of Hg. When rats were administered 10 mg methylmercuric chloride/kg per day for 6 days, 4 of 5 of those given antibiotics developed neurological symptoms of toxicity, whereas only 1 of 5 conventional rats given methylmercuric chloride was affected.

922
TITLE:
Identification and Partial Characterization of a Glycoprotein Species with High Affinity for Methylmercury in Peripheral Nervous Tissues of Man and Experimental Animals

AUTHORS:
Ozaki S
Ichimura T
Isobe T
Nagashima K
Sugano H
Omata S

SOURCE:
Archives of Toxicology, Vol. 67, No. 4, pages 268-276, 49 references, 1993

ABSTRACT:
A protein species with high affinity for methylmercury (22967926) (MeHg) was studied to provide new insights into MeHg/protein interactions. Following the binding of radiolabeled methylmercury to the post nuclear or post mitochondrial supernatant fraction of the homogenate of Wistar-rat sciatic nerve, electrophoresis and autoradiography revealed a small amount

of 21 kilodalton (kDa) glycoprotein with high affinity for MeHg in the fraction. Subcellular fractions of DDY-mouse, golden-hamster, guinea-pig, rabbit and human peripheral nervous tissues were also shown to contain the 21kDa glycoprotein which was shown to be localized in the myelin fraction. It was not detected in cellular fractions of brain, spinal cord or nonneural tissues including the kidney and liver. The specific binding activity of the 321kDa glycoprotein with MeHg was 12 to 15 times that of the major myelin protein, Po. Sulfhydryl groups mediated the interaction of the 231kDa glycoprotein with MeHg. The amino acid compositions of the rat and human 21kDa glycoproteins were similar. They were also much different from that of a typical metallothionein. This study demonstrated the presence of a small quantity of a protein species with very high affinity with MeHg. The authors suggest that even though the high affinity of the protein with MeHg does not necessarily result in high functional sensitivity of the protein to the metal, identification and characterization of the protein species exhibiting high affinity with MeHg will provide an experimental approach for elucidation of the in-vivo actions of MeHg.

923

TITLE:

Organochlorine and heavy metal residues in harbor seals (Phoca vitulina) from the Wadden Sea (Netherlands) and their possible effects on reproduction.

AUTHORS:

REIJNDERS P JH

SOURCE:

NETH J SEA RES; 14 (1). 1980 (RECD. 1981). 30-65.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The harbor seal population in the Wadden Sea (Netherlands) decreased significantly and its pup production was low compared to the more stable population in Schleswig-Holstein, Germany. These facts were correlated with an assumed inverse trend of contaminant residue levels in seal tissues. Dead stranded animals were collected in both areas and blubber, liver, brain and kidney analyzed for PCB (polychlorinated biphenyl), o,p'-DDT, p,p'-(DDT + DDE + DDD, dieldrin, aldrin, endrin, endosulfan, alpha-HCH (BHC), beta-HCH, gamma-HCH, HCB (hexachlorobenzene), QCB (pentachlorobenzene), HEPO (heptachlorepoxide) and methyl mercury, Se and Br. High levels of all contaminants except Br occurred together in the seals. An equimolecular relationship was found for Hg and Se but not for Br. A correlation was demonstrated for PCB and total DDT in blubber and kidney. The main metabolite present in the DDT family was DDE. Deposition of contaminants was generally lower in juvenile seals reaching a certain plateau level in older ones. Highest ratios of methyl mercury to total Hg were found in juveniles. Residue levels already

present in stillborn pups indicated transplacental transport of all organochlorines and metals analyzed. Differences in residue levels between Schleswig-Holstein and Denmark and the Netherlands revealed higher values for the latter, especially PCB levels in Dutch adult seals (10-fold higher). Increased PCB and total DDT residue levels with age was present in Dutch seals but absent in Schleswig-Holstein and Danish specimens. Decreased reproductive success of Dutch seal population correlated strongly with high concentrations of PCB in tissues. These compounds interfered with mammalian reproduction and were responsible for low rate of reproduction in Dutch seal population.

924
TITLE:
Experimental trophic chain in a limnic environment: Direct and trophic contamination of a 3rd order consumer (Salmo gairdneri) by methyl mercury: Tissue reparation of metal and incidence of routes of contamination and environmental temperature.

AUTHORS:
RIBEYRE F
BOUDOU A

SOURCE:
WATER AIR SOIL POLLUT; 14 (0). 1980 (RECD. 1981). 349-358.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Analysis of tissue spread of Hg with S. gairdneri after global contamination by methyl mercury showed bioaccumulated metal of a trophic origin. This was significant because length of time for the experiment and environmental temperature were high (18ê C and 30 days). After global contamination, various kinds of organs could be distinguished according to Hg concentration and effect of abiotic factors on accumulation processes. Ecotoxicological behavior of brain and muscle was the same as that of the whole fish. Hg levels were fairly low, but their increase was significant when the temperature of the environment and contamination time were higher. High Hg concentrations and high retention capacity made the posterior intestine an accumulation organ. After 30 days' experimentation, trophic contribution represented over 95% of Hg in that organ. Gills were characteristic of direct contamination. Metal concentrations were independent of environmental temperature and length of time. Figured elements and liver presented the highest Hg concentrations. The influence of experimentation time was slight.

925
TITLE:
THE ACCUMULATION OF OCEANIC CONTAMINANTS IN MARINE MAMMALS

AUTHORS:

HOLDEN AV

SOURCE:
RAPP P-V REUN CONS INT EXPLOR MER; 169. 1975 (RECD 1976) 353-361

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HALICHOERUS-GRYPUS PHOCA-VITULINA PAGOPHILUS-GROENLANDICUS DIELDRIN MERCURY DDT POLY CHLORINATED BI PHENYLS INSECTICIDES METABOLISM FAT KIDNEY HEART MUSCLE BRAIN SPLEEN LIVER

926
TITLE:
(Exposure mode to mercury vapor and body burden in the rat and its decreasing pattern.)

AUTHORS:
FUKUDA K

SOURCE:
JAP J HYG; 26 (2). 1971 257-263

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Rats were exposed to Hg vapor and Hg content in tissues was measured. Two groups were exposed: the HS, high concentration-short term exposure group (6.0 mg/m-3 in Hg concentration x 1 hr in daily duration of exposure, 3.0 x 1 and 1.5 x 1) and the LL, low concentration-long term exposure group (1.0 x 6, 1.0 x 3 and 1.0 x 1.5). Each exposure lasted for 5 days/wk for 2 or 4 consecutive wk in an exposure chamber. Quantitative Hg determination was performed by a dithizone method. Mercury concentration of the lungs of the HS group after both the 2 and 4 wk exposure was higher than that of the lungs of the LL group. That of the other tissues of the HS group was lower than that of the LL group. Hg content in tissues of rats treated by the exposure mode 1.0 x 6 was measured up to 16 wk after the termination of Hg exposure. The Hg content decreased linearly in semilogarithmic scales. The half time of Hg content of the lungs was about 13 days, the shortest and that of the brain was about 210 days, the longest among tissues.

927
TITLE:
Methylmercury Metabolism In Pregnant Mice: Its Modification By Selenium With Particular Reference To Prenatal Toxicity Of These Compounds

AUTHORS:
Suzuki T

SOURCE:
Reproductive and Developmental Toxicity of Metals, Clarkson, T. W., G. F.

Norberg, and P. R. Sager, Editors; Plenum Press, New York, pages 693-723, 75 references, 19821982

ABSTRACT:

Research regarding the protective effects of selenium (7782492) against methylmercury (22967926) toxicity and metabolism in pregnant mice is reviewed. Metabolism studies are included on maternal metabolism, placental transfer, and on embryonic and fetal metabolism. Metabolism of methylmercury and selenium appears to be different in nonpregnant and pregnant females. Simultaneously administered selenite (14124675) does not enhance the placental transfer and fetal accumulation of methylmercury. Mercury concentrations in the fetal brain, however, are elevated by selenite. Methylmercury is easily transferred through the placenta, and fetal organs and tissues do not show appreciable capacity to break down the carbon/mercury bond of methylmercury. The fetal accumulation of selenium is enhanced by administration of methylmercury. Selenium in the form of bis(methylmercuric)-selenide is transferred less easily through the placenta than is selenite. The author concludes that many research problems remain to be solved in the study of the relationship between selenium and methylmercury metabolism in pregnant mice.

928

TITLE:

MINAMATA DISEASE: THE OUTBREAK OF A NEUROLOGIC DISORDER IN MINAMATA, JAPAN, AND ITS RELATIONSHIP TO THE INGESTION OF SEAFOOD CONTAMINATED BY MERCURIC COMPOUNDS

AUTHORS:

KURLAND LT
FARO SN
SIEDLER H

SOURCE:

WORLD NEUROL. 1960, 1(5) 370-391

ABSTRACT: EIS: Epidemiology Information System

929

TITLE:

THE BEHAVIORAL TOXICOLOGY OF METALS

AUTHORS:

WEISS B

SOURCE:

FED. PROC. 1978, 37(1) 22-27

ABSTRACT: EIS: Epidemiology Information System

930
TITLE:
Calcium Channels as Target Sites of Heavy Metals

AUTHORS:
Busselberg D

SOURCE:
Toxicology Letters, Vol. 82/83, pages 255-261, 23 references, 1995

ABSTRACT:
The effects of heavy metals on voltage activated calcium channel currents (VACCCs) and N-methyl-D-aspartate (NDMA) activated channel currents (NACCs) were examined. Dorsal root ganglion (DRG) neurons isolated from 2 to 4 day old rats were used as sources of the VACCCs. Hippocampal neurons, usually CA1 neurons, isolated from 2 to 3 week old rats were used as the sources of the NACCs. The DRG preparations were incubated with zinc (7440666), aluminum (7429905), mercury (7439976), methylmercury, or lead (7439921). Hippocampal slices were incubated with lead or aluminum in the presence or absence of 500 micromolar (microM) aspartate or 1 millimolar (mM) NDMA. The effects on the VACCCs and NACCs were assessed by the patch clamp technique. The DRG preparations were also incubated with lead, aluminum, methylmercury, or zinc and the effects on voltage activated sodium and potassium channel currents were determined. Lead and aluminum caused dose dependent decreases in NACCs in the presence of aspartate or NMDA. The currents were reduced by 50% when exposed to lead concentrations of 20 to 50microM or aluminum concentrations below 50microM. Lead, aluminum, mercury, methylmercury, and zinc reduced the VACCCs in a dose dependent manner. The concentrations causing 50% inhibition (IC50s) of the currents were 0.46, 1.1, 2.6, 69, and 84microM, respectively. When lead, zinc, or aluminum was added simultaneously to the preparations at their IC50 concentrations, they inhibited the VACCCs in an additive manner. Lead, aluminum, or zinc had only a slight effect on the sodium and potassium channel currents, inhibiting them by less than 10%. Methylmercury had a strong effect, the IC50s for reducing the currents through the potassium and sodium channels being 2.6 and 12microM, respectively. The authors conclude that the varying effects of the metals on the VACCCs and NACCs indicate that they produce different actions at the level of the cell membrane.

931
TITLE:
Photosensitization of animals after the ingestion of buckweat.

AUTHORS:
Sheard C

Caylor HD
Schlotthauer C

SOURCE:
J Exp Med, Vol. 47, p. 1013-1028, 1928

ABSTRACT:
1. Following the ingestion of buckwheat (plant or seed) varicolored guinea pigs, white swine and goats exhibited symptoms of photosensitization, the degree of sensitization being in the order given. 2. Rabbits, dogs, white mice and rats did not manifest symptoms of photosensitization. 3. The symptoms and reactions were: agitation, itching, scratching of the ears, weakness, urticaria with sloughing and symptoms similar to those in anaphylaxis. 4. Microscopic examinations showed the lack of marked pathologic changes. The lesions, such as petechial hemorrhage of the lungs, brain, liver, stomach and kidneys, suggest that profound toxemia has been present. 5. Lesions were not found which appeared to be suggestive of malignant neoplasms. 6. Irradiation by a quartz mercury vapor lamp apparently develops a resistance to photosensitization, probably because of increased pigmentation induced by ultra-violet light. 7. From the nature of the physiologic and pathologic reactions produced under various filters and from a consideration of the percentages of transmission of solar energy in the visible spectrum, it would seem that the region of photosensitization lies between 580 millimicrons (yellow) and the red end of the spectrum. This conclusion, moreover, is substantiated by the fact that irradiation by a quartz mercury vapor lamp (which radiates no energy in the visible spectrum at a wave-length greater than 579 millimicrons) produces no symptoms or reactions. 8. Spectrophotometric determinations of alcoholic extracts of grass (non-toxic) and of buckwheat (toxic) show the presence of two additional bands in the absorption spectrum of buckwheat with maxima at about 540 and 600 millimicrons, respectively, together with the common absorption zones at 430 to 490 millimicrons and 630 to 690 millimicrons. 9. Spectrophotometric determinations of blood serums of sensitized animals show, besides the usual absorption bands peculiar to oxyhemoglobin (with maxima at 540 and 580 millimicrons respectively), two zones with maxima at 600 and 660 millimicrons respectively. 10. The fluorescence of chlorophyll per se, as suggested by previous investigators, is not, in all probability, the cause of the sensitization induced by buckwheat. 11. Hematoporphyrine is not the photodynamic substance in all probability. 12. Phylloporphyrine may be the photodynamic substance. In this regard, also, the possibility of cholehematin is not to be ruled out.

932
TITLE:
Methylmercury-Induced Neurotoxicity in Cerebral Neuron Culture is Blocked by Antioxidants and NMDA Receptor Antagonists

AUTHORS:
Park ST
Lim KT
Chung YT
Kim SU

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 37-46, 26 references, 1996

ABSTRACT:
The neurotoxicity of methylmercury was studied in cerebral neuron cultures. The neuroprotective effects of selected antioxidants and N-methyl-D-aspartate (NMDA) receptor antagonists were also investigated. Cerebral neurons obtained from 1 to 3 day old CD-1-mice were incubated with 0 to 40 micromolar (microM) methylmercuric-chloride (115093) (MMC) for 24 hours (hr) or to 0 or 20microM MMC for 1, 2, 4, or 24hr. Other neuron preparations were incubated with 0 or 20microM MMC for 24hr in the presence or absence of the antioxidants 1 to 8 millimolar glutathione, 1 to 40 micrograms per milliliter catalase, 10 to 80microM selenium, 0.1 to 0.8mg/ml cysteine or 1 to 100microM of the NMDA receptor antagonists D-2-amino-5-phosphonovaleric-acid (APV), 7-chlorokynurenic-acid (CKA), 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX), or MK-801. Cytotoxicity was evaluated by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide (MTT) test and a neurofilament enzyme immunoassay (EIA). The MTT test evaluated general cytotoxicity by measuring the extent of cell death. The EIA was an assay specific for nerve cell populations. MMC alone induced dose related increases in cell death as measured by the MTT assay. The 20microM dose decreased cell survival by more that 50% after 24hr. Glutathione, catalase, selenium, cysteine, MK-801, APV, and CKA protected against MMC neurotoxicity in a dose dependent manner, as indicated by both the MTT test and the EIA. The top doses of glutathione, catalase, selenium, cysteine, CKA, and MK-801 completely blocked the neurotoxic effects of MMC. CNQX showed a minimal protective effect at 10 and 25microM, as indicated by the MTT test. No protective effect was detected by the EIA. The authors conclude that MMC can cause lethal toxic effects in cerebral neurons. The neuroprotective effects seen with the antioxidants and NMDA receptor antagonists indicate that the mechanism of MMC neurotoxicity involves oxygen radicals and excitotoxic amino acids.

933
TITLE:
CONGENITAL MINAMATA DISEASE: INTRAUTERINE METHYLMERCURY POISONING.

AUTHORS:
HARADA M

SOURCE:

TERATOLOGY 1978, 18(2) 285-288

ABSTRACT: EIS: Epidemiology Information System

934
TITLE:
Regulatory Volume Decrease in Primary Astrocyte Cultures: Relevance to Methylmercury Neurotoxicity

AUTHORS:
Vitarella D
Kimelberg HK
Aschner M

SOURCE:
Neurotoxicology, Vol. 17, No. 1, pages 117-124, 50 references, 1996

ABSTRACT:
Regulatory volume decrease (RVD) processes and their relevancy to methylmercury neurotoxicity were discussed. Mechanisms associated with astrocytic swelling and RVD were considered. Astrocytic swelling represents a response to a wide variety of pathological states, such as trauma and ischemia, and can occur rapidly. Persistent astrocytic swelling can be viewed as a pathological extension of more limited and controlled volume changes, which are otherwise part of their normal homeostatic function. A number of mechanisms for astrocyte swelling have been proposed. These include swelling associated with acid/base changes, glutamate induced swelling, and potassium ion (K+) induced swelling. A common mechanism of astrocytic RVD involves activation of unselective cation channels by cell swelling, leading to entry of calcium (Ca+2) into the cells, thereby increasing free cytosolic Ca+2 concentrations. The increase in intracellular Ca+2 activates inwardly rectifying Ca+2 dependent K+ channels and phospholipase-A2 and 5-lipooxygenase, which results in changes in the metabolism of eicosanoids. The net result is the loss of intracellular potassium-chloride and taurine, followed by the obligatory water movement, which results in RVD. The effects of methylmercury on the RVD process were discussed. Methylmercury induces astrocytic swelling and inhibits RVD. This effect appears to be related to an increase in cell membrane permeability and retention of intracellular sodium ion.

935
TITLE:
MERCURY AND LEAD CONTENT OF HUMAN BODY TISSUES FROM A SELECTED POPULATION

AUTHORS:
SCHMIDT R

WILBER CG

SOURCE:
MED. SCI. LAW 1978, 18(3) 155-158

ABSTRACT: EIS: Epidemiology Information System

936
TITLE:
NEUROTOXIC RESPONSE OF INFANT MONKEYS TO METHYLMERCURY

AUTHORS:
WILLES RF
TRUELOVE JF
NERA EA

SOURCE:
TOXICOLOGY 1978, 9(1-2) 125-135

ABSTRACT: EIS: Epidemiology Information System

937
TITLE:
METHYLMERCURY: EXPOSURE DURATION AND REGIONAL DISTRIBUTION AS DETERMINANTS
OF NEUROTOXICITY IN NONHUMAN PRIMATES.

AUTHORS:
EVANS HL
GARMAN RH
WEISS B

SOURCE:
TOXICOL. APPL. PHARMACOL. 1977, 41(1) 15-33

ABSTRACT: EIS: Epidemiology Information System

938
TITLE:
Clinical effectiveness of D-penicillamine in chronic mercury poisoning.

AUTHORS:
ALI-ZADE KA
ALEKPEROV II
KASIMOVA FS

SOURCE:
GIG TR PROF ZABOL; (6). 1976 41-42

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Therapy (10-14 days) with daily dose of 600 mg D-penicillinamine in combination with pyridoxine was effective in treatment of (human) occupation-related chronic and preclinical Hg poisoning. It increased the intensity of blood supply to brain vessels, especially in preclinical cases. During therapy, increased Hg secretion with urine was observed. Minor side effects (skin rash) disappeared with termination of administration.

939
TITLE:
HISTOCHEMICAL DEMONSTRATION OF MERCURY IN HUMAN TISSUE CELLS OF MINAMATA DISEASE BY USE OF AUTO RADIOGRAPHIC PROCEDURE

AUTHORS:
SAKAI K
OKABE M
ETO K
TAKEUCHI T

SOURCE:
ACTA HISTOCHEM CYTOCHEM; 9 (1). 1976 103

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT METHYL MERCURY POISONING NERVOUS SYSTEM BRAIN PURKINJE CELLS KIDNEY

940
TITLE:
Influence of Dietary Protein Levels on the Acute Toxicity of Methylmercury in Mice

AUTHORS:
Adachi T
Yasutake A
Eto K
Hirayama K

SOURCE:
Toxicology, Vol. 112, No. 1, pages 11-17, 23 references, 1996

ABSTRACT:
The effects of a low protein diet (LPD) and normal protein diet (NPD) on susceptibility to toxicity by methylmercury (22967926) (MM) was investigated in mice. Male C57BL/6N-mice were orally given 40, 80, or 120 micromoles/kilogram MM and evaluated 40 days later. No mice died on the low MM dose until at least 40 days after administration, whereas the 80

micromoles/kilogram dose killed all mice within 16 days, and the highest dose killed all mice within 7 days. NPD fed mice were more susceptible than LPD fed mice at the high dose. Urinary MM excretion was significantly lower in LPD fed mice than in NPD fed mice at the low dose. In NPD fed mice, urinary MM levels became lower with increased doses, whereas a dose related change did not occur in LPD fed mice. Brain MM levels in LPD fed mice were higher than in LPD fed mice, whereas no difference occurred in MM levels in liver and kidney at any dose. Plasma creatinine levels increased at the medium and high dose in both diets. Plasma activities of aspartate-aminotransferase and alanine-aminotransferase in NPD fed mice increased only at the high dose. The authors conclude that hepatic damage is induced by high dose MM administration in NPD fed mice but not in LPD fed mice, suggesting that the higher susceptibility of the liver to acute MM toxicity in NPD fed mice leads to shorter survival.

941
TITLE:
Meso-dimercaptosuccinic acid a chelating agent for the treatment of mercury and lead poisoning.

AUTHORS:
FRIEDHEIM E
CORVI C
WAKKER CH

SOURCE:
J PHARM PHARMACOL; 28 (9). 1976 711-712

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Experimental findings concerning the effect of DMS (meso-dimercapto succinic acid) on repeated exposures to methylmercuribromide in guinea-pigs and to lead acetate in mice were reported. In the treatment of Hg and Pb poisoning DMS proved more effective than either penicillamine or EDTA in mice or guinea-pigs. In the brain DMS significantly reduced Hg and Pb concentrations while penicillamine had no or an adverse effect.

942
TITLE:
Interference of methyl mercury with monoamine uptake and release in rat brain synaptosomes.

AUTHORS:
KOMULAINEN H
TUOMISTO J

SOURCE:

ACTA PHARMACOL TOXICOL; 48 (3). 1981. 214-222.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Interference of methyl mercury (Met-Hg), a known neurotoxin, with the high affinity uptake and release of tritiated dopamine (DA), noradrenaline (norepinephrine) (NA) and serotonin (5-HT) was studied in vitro in rat striatal, cortical and hypothalamic synaptosomes, respectively. Met-Hg was a potent inhibitor of uptake. IC50 (50% inhibition concentration) were 2.5 muM (DA), 3.2 muM (NA) and 3.4 muM (5-HT) in 2 min incubations. NA uptake was slightly inhibited already at 0.1-1 muM Met-Hg but DA and 5-HT were not. Inhibition was rapid and after 1 min exposure to 3 muM Met-Hg the uptake was totally inhibited. Kinetic pattern of inhibition of DA uptake agreed with the non-competitive type. Spontaneous release of monoamines from preloaded synaptosomes was potent stimulated and dependent on Met-Hg concentration. Sensitivity decreased in the order of DA > 5-HT NA. Apparent inhibition of uptake was probably partly due to the release of the transmitter amine just taken up. Chelation might also contribute to inhibition of NA and DA uptake. Detailed mechanisms of these phenomena remain to be studied but they may explain some of the direct CNS effects of Met-Hg.

943

TITLE:

Methylmercury exposure biomarkers as indicators of neurotoxicity in children aged 7 years.

AUTHORS:

GRANDJEAN P
BUDTZ-JORGENSEN E
WHITE RF
JORGENSEN PJ
WEIHE P
DEBES F
KEIDING N

SOURCE:

AMERICAN JOURNAL OF EPIDEMIOLOGY; 150 (3). 1999. 301-305.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. The mercury concentration in blood or scalp hair has been widely used as a biomarker for methylmercury exposure. Because of the increased risks associated with exposures during prenatal and early postnatal development, biomarker results must be interpreted with regard to the age-dependent susceptibility. The authors compared regression coefficients for five sets of exposure biomarkers in 917 children from the Faroe Islands examined at birth, 1 year, and 7 years. Outcome variables were the result gnificant predictors only of performance on memory for visuospatial information. These findings emphasize the

usefulness of the cord-blood mercury concentration as a main risk indicator. They also support the notion that the greatest susceptibility to methylmercury neurotoxicity occurs during late gestation, while early postnatal vulnerability is less, and they suggest that the time-dependent susceptibility may vary for different brain functions.

944
TITLE:
Delayed evoked potentials in children exposed to methylmercury from seafood.

AUTHORS:
MURATA K
WEIHE P
RENZONI A
DEBES F
VASCONCELOS R
ZINO F
ARAKI S
JORGENSEN PJ
WHITE RF
GRANDJEAN P

SOURCE:
NEUROTOXICOLOGY AND TERATOLOGY; 21 (4). 1999. 343-348.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Methylmercury poisoning may cause constriction of visual fields and deafness, especially if exposure occurs prenatally. However, the risks associated with exposure from contaminated seafood is unclear. We examined 149 children attending first grade in a Madeiran fishing community. As maternal dietary habits were relatively unchanged, current maternal hair concentrations were used as indicator of the child's prenatal exposure to methylmercury (geometric average, 9.64 mug/g (48.2 nmol/g)). After a relationships were seen with the child's own hair-mercury concentration, and other clinicalexaminations revealed no mercury-associated deficits. Neurophysiological evidence of adverse effects on brain function are relatively independent of confounders, and should be considered in the risk assessment of this seafood pollutant.

945
TITLE:
Applications of Neurophysiological Methods in Occupational Medicine. A Review

AUTHORS:
Seppalainen AM

SOURCE:
Scandinavian Journal of Work Environment and Health, Vol. 1, No. 1, pages 1-14, 74 references, 19751975

ABSTRACT:
The application of neurophysiological methods such as electroencephalography (EEG) and electroneuromyography (ENM) in assessing the involvement of the nervous system in occupational exposure is reviewed. EEG shows involvement of the central nervous system, especially dysfunction of the more superficial structures of the brain. ENM differentiates lesions at different sites of the peripheral nervous system and muscles, and includes electromyography and the measurement of nerve conduction velocities. The equipment and measurement capabilities of EEG and ENM techniques are described. The physical and chemical agents causing occupational neurological symptoms include vibration, insecticides, carbon-monoxide (630080), acrylamide (79061), lead (7439921), mercury (7439976), carbon-disulfide (75150), and hydrocarbon solvents. Polyneuropathy is the most common lesion of the peripheral nervous system. It is more striking in distal portions of the nerves in the case of lead, acrylamide, carbon-disulfide and vibration induced neuropathy. Neuropathy due to alkyl-mercury involves the whole length of the sensory axon. Insecticides and carbon-disulfide poisoning causes disturbance in myoneural junctions. Encephalopathy is a potential danger resulting from exposure to carbon-disulphide and other hydrocarbon solvents. The author indicates the usefulness of neurophysiological methods in the study of neurotoxicity of new chemicals, in setting safety norms, in early diagnosis of suspected occupational neurophysiological disease, and in advising workers about their work habits.

946
TITLE:
EFFECTS OF COMBINED ADMINISTRATION OF THIOL COMPOUNDS AND METHYLMERCURY CHLORIDE ON MERCURY DISTRIBUTION IN RATS

AUTHORS:
HIRAYAMA K

SOURCE:
BIOCHEM PHARMACOL; 34 (11). 1985. 2030-2032.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM L CYSTEINE GLUTATHIONE N ACETYL-L-CYSTEINE METHYLMERCURIC CHLORIDE METABOLIC-DRUG BLOOD-BRAIN BARRIER

947
TITLE:
SEX AND AGE DIFFERENCES IN MERCURY DISTRIBUTION AND EXCRETION IN

METHYLMERCURY-ADMINISTERED MICE

AUTHORS:
HIRAYAMA K
YASUTAKE A

SOURCE:
J TOXICOL ENVIRON HEALTH; 18 (1). 1986. 49-60.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN LIVER BLOOD KIDNEY SEX HORMONE-RELATED EXCRETION

948
TITLE:
DISTRIBUTION OF MERCURY IN GUINEA-PIG OFFSPRING AFTER IN UTERO EXPOSURE TO MERCURY VAPOR DURING LATE GESTATION

AUTHORS:
YOSHIDA M
YAMAMURA Y
SATOH H

SOURCE:
ARCH TOXICOL; 58 (4). 1986. 225-228.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN LUNG HEART KIDNEY PLASMA LIVER ERYTHROCYTE CONTAMINATED FISH CONSUMPTION MINAMATA DISEASE

949
TITLE:
SEXUAL DIFFERENCES IN THE DISTRIBUTION AND RETENTION OF ORGANIC AND INORGANIC MERCURY IN METHYLMERCURY-TREATED RATS

AUTHORS:
THOMAS DJ
FISHER HL
SUMLER MR
MARCUS AH
MUSHAK P
HALL LL

SOURCE:
ENVIRON RES; 41 (1). 1986. 219-234.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM LIVER KIDNEY BRAIN PELT SKELETAL MUSCLE

TOXICITY

950
TITLE:
STUDIES ON THE INHIBITION OF BRAIN SYNAPTOSOMAL SODIUM-POTASSIUM ATPASE BY MERCURY CHLORIDE AND METHYL MERCURY CHLORIDE

AUTHORS:
MAGOUR S

SOURCE:
CHAMBERS, P. L., J. TUOMISTO AND C. M. CHAMBERS (ED.). ARCHIVES OF TOXICOLOGY, SUPPL. 9. TOXIC INTERFACES OF NEURONES, SMOKE AND GENES; EUROPEAN SOCIETY OF TOXICOLOGY MEETING, KUOPIO, FINLAND, JUNE 16-19, 1985. X+487P. SPRINGER-VERLAG NEW YORK, INC.: SECAUCUS, NEW JERSEY, USA; BERLIN, WEST GERMANY. ILLUS. PAPER. ISBN 0-387-16589-4; ISBN 3-540-16589-4.; 0 (0). 1986. 393-396.

ABSTRACT: BIOSIS COPYRIGHT: BIOL ABS. RRM RAT

951
TITLE:
Studies on the influence of organic synthetic pesticides on tissue respiration and glucose metabolism in rat brain. Preface and Part 1, tissue respiration.)

AUTHORS:
Kataoka S

SOURCE:
Nippon Hoigaku Zasshi (Jpn. J. Legal Med.)28(1): 24-30; 1974

ABSTRACT:
PESTAB. The influence of six kinds of sythetic organic pesticides, ethylmercuric phosphate, phenylmercuric acetate, parathion, malathion, monofluoroacetamide, and sodium monofluoroacetate, on the cerebral tissue respiration was studied in vitro and in vivo using male Wistar rats. Cerebral cortex slices were immersed into the diluted pesticide, or the pesticides were administered orally at respective doses of 2, 8, 2, 5, 7, and 2 times the LD50 of the pesticides mentioned. After killing the respective rats their cerebral cortex slices were prepared. The respiration was determined via the consumption of oxygen for 60 min in a Warburg apparatus. In vitro both organomercury pesticides showed suppressive action, more markedly for the alkyl mercury than the aryl mercury compounds; both organophosphorus pesticides also showed suppressive action, with a small difference between them; and the organofluorine pesticides showed no marked suppressive action. The results in vivo were: both mercurials showed accentuative action, both

organophosphates showed suppressive action, and both fluorine compounds showed suppressive action, more marked for sodium monofluoroacetate than for monofluoroacetamide.

952
TITLE:
BRAIN RETENTION OF MERCURY IN MICE PRE NATALLY TREATED WITH METHYL MERCURY AND SELENITE

AUTHORS:
SATOH H
SHIMAI S

SOURCE:
22ND ANNUAL MEETING OF THE JAPANESE TERATOLOGY SOCIETY, TOKYO, JAPAN, JULY 8-9, 1982. TERATOLOGY; 26 (1). 1982. 13A.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT ANTIDOTE METABOLIC-DRUG

953
TITLE:
THE EFFECT OF MERCURY CHLORIDE AND METHYL MERCURY ON BRAIN MICROSOMAL SODIUM POTASSIUM ATPASE AFTER PARTIAL DELIPIDIZATION WITH LUBROL

AUTHORS:
MAGOUR S
MAESER H
GREIM H

SOURCE:
PHARMACOL TOXICOL; 60 (3). 1987. 184-186.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT ATP ENVIRONMENTAL POLLUTANT

954
TITLE:
An experimental study on distribution and excretion of ethyl mercury chloride.)

AUTHORS:
Ogawa E
Suzuki S
Tsuzuki H
Kawajiri M

SOURCE:

Kitakanto Igaku (Kitakanto Med. J.)24(4): 229-235; 1974

ABSTRACT:
PESTAB. Large amounts of ethylmercury compounds have been used although they were banned. Radiolabeled ((SUP)203 Hg) ethylmercury chloride suspended in olive oil was administered p. o. to ddN male and Wistar male and female rats. The absorption, retention, excretion, and distribution of radioactivity were traced, as well as the accelerating effect on excretion by addition of several drugs. Findings revealed biological half lives of 4. 4 days in 10 wk old male mice; 10. 1, 9. 3, and 8. 7 days in 6, 8, and 10. 5 wk old male rats, respectively; and 7. 0 days in 10. 5 wk old female rats. Mercury levels decreased in the order kidney, blood, liver, pancreas, spleen, and brain 1 hr after administration. Drugs found effective in accelerating Hg excretion were: DL-penicillamine, 2-mercaptopropionyllysine, and large amounts of glutathione.

955
TITLE:
METALLIC MERCURY IN THE ARTERIAL BLOOD OF NORMAL AND ACATALASEMIC MICE EXPOSED TO METALLIC MERCURY VAPOR

AUTHORS:
OGATA M
MATSUDA A
MEGURO T
AIKOH H

SOURCE:
PHYSIOL CHEM PHYS MED NMR; 19 (2). 1987. 79-82.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN LIVER

956
TITLE:
MERCURY CONCENTRATIONS IN THE HUMAN BRAIN AND KIDNEYS IN RELATION TO EXPOSURE FROM DENTAL AMALGAM FILLINGS

AUTHORS:
NYLANDER M
FRIBERG L
LIND B

SOURCE:
SWED DENT J; 11 (5). 1987. 179-187.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM MERCURY VAPOR

957
TITLE:
The effect of diethyldithiocarbamate on biliary transport, excretion and organ distribution of mercury in the rat after exposure to methyl mercuric chloride.

AUTHORS:
NORSETH T

SOURCE:
ACTA PHARMACOL TOXICOL; 34 (1). 1974 76-87

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Diethyldithiocarbamate (DDC) and disulfiram decrease the biliary excretion of methyl mercuric compounds. The biliary mercury excretion returns to normal after a time period which is dependent on the dose of the inhibiting compound. For some doses of DDC the excretion of Hg increased above control values following the period of inhibition. DDC treatment increased brain, muscle and fur content of Hg. There is an increased retention of Hg in the liver, but decreased amounts of Hg in the kidney. Hg in red cells is not affected. Faecal excretion of Hg decreased as expected because of decreased biliary excretion. The urinary excretion of Hg also decreases, but the mechanism is not clear. Changes in the excretion and organ distribution pattern indicate similar mechanisms for DDC treatment as for bile duct ligation, but DDC probably also changes the organ distribution and excretion by complex formation with some methyl mercuric compound.

958
TITLE:
DISTRIBUTION OF MERCURY IN THE BRAIN AND OTHER ORGANS AFTER CONTINUOUS LATERAL VENTRICULAR INJECTION WITH METHYL MERCURY AND GLUTATHIONE

AUTHORS:
WATANABE H
SHIMOJO N
YAMAGUCHI S

SOURCE:
JPN J IND HEALTH; 30 (1). 1988. 46-47.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT TOXICOKINETICS

959
TITLE:

DISTRIBUTION AND RETENTION OF ORGANIC AND INORGANIC MERCURY IN METHYL MERCURY-TREATED NEONATAL RATS

AUTHORS:
THOMAS DJ
FISHER HL
SUMLER MR
HALL LL
MUSHAK P

SOURCE:
ENVIRON RES; 47 (1). 1988. 59-71.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HEAVY METAL TOXICITY WHOLE BODY CLEARANCE KIDNEY LIVER BRAIN

960
TITLE:
Developmental effects on the central and peripheral nervous system of rats exerted by environmental xenobiotics.

AUTHORS:
Nagymajtäenyi L
Papp A
Vezäer T
Däesi I

SOURCE:
Neurotoxicology 2001;22(4):531

ABSTRACT:
The population of developed parts of the world is continuously exposed by a variety of environmental pollutants including heavy metals like lead, mercury or cadmium, and pesticides like organophosphates. Several of these are neurotoxic, causing biochemical, functional and morphological alterations of the nervous system in animal experiments and in cases of acute or chronic human exposure. Our previous studies (Nagymajtäenyi et al., 1994; Däesi et al., 1996) showed that a 4-12 weeks treatment with lead, mercury and cadmium on one hand, and organophosphate insecticide agents on the other, resulted in considerable dose- and time-dependent changes in certain functional parameters of the central and peripheral nervous system (electrocorticogram, cortical evoked potentials, nerve conduction velocity, etc.). The aim of the present study was to investigate the effects of the above mentioned xenobiotics on nervous system functions of rats when given in different phases of the intra- or extrauterine development. Female Wistar rats (P generation) were treated by gavage with 80.0 or 320.0 mg/kg Pb2+ (Pb-acetate), 0.4 or 1.6 mg/kg

Hg2+ (HgCl2), 3.5 or 14 mg/kg Cd2+ (CdCl2), or 4.5 or 18 mg/kg dimethoate; on days 5-15 of pregnancy, on days 5-15 of pregnancy + 4 weeks during lactation, or on days 5-15 of pregnancy + 4 weeks during lactation + for 8 weeks after weaning in the males of F1 generation. Control groups received saline. At 12 weeks of age, the male F1 from all treatment schedules were prepared. Spontaneous and stimulus evoked activity from the primary somatosensory, visual and auditory cortical area as well as the compound action potential of the tail nerve were recorded. The above mentioned xenobiotics-induced alterations in all of the parameters of central and peripheral nervous functions investigated. Spontaneous activity was depressed, latency of cortical evoked potentials was increased, and conduction velocity of the peripheral nerve was decreased. Depending on dosage and treatment time, some of these changes were statistically significant. These results point to the risk of permanent nervous system damage resulting from exposure to certain environmental xenobiotics during ontogenesis.

961

TITLE:

Effect Of Selenium On Distribution, Demethylation, And Excretion Of Methylmercury By The Guinea Pig

AUTHORS:

Komsta-Szumska E
Reuhl KR
Miller DR

SOURCE:

Journal of Toxicology and Environmental Health, Vol. 12, No. 4, pages 775-785, 21 references, 19831983

ABSTRACT:

The effects of selenium (7782492) (Se) on uptake, distribution, biotransformation, and excretion of methylmercury (22967926) (MeHg) were investigated in guinea-pigs. Animals were given a single oral dose of 10 milligrams per kilogram (mg/kg) labeled MeHg. Some rats received a single oral dose of 3.8mg/kg Se 5 hours later. Animals were sacrificed on days 1, 3, 7, and 13; samples were taken of red blood cells (RBCs), plasma, heart, lung, liver, kidney, spleen, stomach, small bowel, large bowel, skin, muscle, cerebrum, and cerebellum. Kidney and liver homogenates were prepared, and nuclear fractions were obtained. Total protein binding to mercury (Hg) was analyzed. Inorganic and organic Hg content of tissues was assessed by thin layer chromatography. More Hg was eliminated in feces than in urine in both treated groups. The highest concentration of Hg in feces was seen on day 3. More inorganic Hg was present at all times. Excretion of total and inorganic Hg was decreased in feces by Se administration, but elimination of Hg in urine was increased by Se 1 day after administration. At day 1 after administration, the greatest

concentration of total Hg was found in liver, kidney, and RBCs. In the cerebrum the highest concentration of total Hg was found on day 7, but in the cerebellum the highest concentration was found on day 3. Concentration of total Hg in skin on day 13 was 300 percent higher than on day 1. Concentrations of Hg in liver, kidney, and RBCs were significantly lower 24 hours after treatment with Se than in controls; however, total Hg values were significantly higher in cerebrum and cerebellum. Total Hg in spleen, lung, heart, skin, muscle, and stomach of animals treated with Se was significantly higher than in those treated with MeHg alone. Content of Hg in kidney, liver, and cerebrum was associated primarily with nuclear fractions; concentrations in nuclear fractions of kidney and liver decreased from days 1 to 13, but concentrations were still increasing in cerebrum on day 13. The authors conclude that administration of Se with MeHg causes significant decreases in concentration of both total and organic Hg.

962
TITLE:
THE EFFECTS OF DOSE OF ELEMENTAL MERCURY AND FIRST-PASS CIRCULATION TIME ON EXHALATION AND ORGAN DISTRIBUTION OF INORGANIC MERCURY IN RATS

AUTHORS:
MAGOS L
CLARKSON TW
HUDSON AR

SOURCE:
BIOCHIM BIOPHYS ACTA; 991 (1). 1989. 85-89.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM LUNG BRAIN ACCUMULATION

963
TITLE:
BRAIN KIDNEY AND LIVER MERCURY-203 METHYL MERCURY UPTAKE IN THE RAT RELATIONSHIP TO THE NEUTRAL AMINO ACID CARRIER

AUTHORS:
ASCHNER M

SOURCE:
PHARMACOL TOXICOL; 65 (1). 1989. 17-20.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM L CYSTEINE L METHIONINE CAPILLARY ENDOTHELIAL CELL MEMBRANE ENVIRONMENTAL CONTAMINANT GAMMA-SCINTILLATION SPECTROMETRY

964
TITLE:
MERCURY AND ABNORMAL DEVELOPMENT OF THE FETAL BRAIN

AUTHORS:
CHOI BH

SOURCE:
NEUROBIOL TRACE ELEM 2:197-235,1983

965
TITLE:
MERCURY-SELENIUM INTERACTION DISTRIBUTION AND EXCRETION OF MERCURY-203 IN RATS AFTER SIMULTANEOUS ADMINISTRATION OF SELENITE OR SELENATE

AUTHORS:
CIKRT M
BENCKO V

SOURCE:
TOXICOL LETT (AMST); 48 (2). 1989. 159-164.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM DISODIUM SELENATE DISODIUM SELENITE ANTIDOTE-DRUG MERCURIC CHLORIDE LIVER BLOOD BRAIN KIDNEY

966
TITLE:
Methylmercury poisoning.

AUTHORS:
Weiss B
Doherty RA

SOURCE:
Teratology 12(3): 311-314; 1975.(3 references)

ABSTRACT:
PESTAB. Methylmercury is the most toxic compound of mercury, its toxic properties producing sensory malfunctions, motor manifestations, a variety of nonspecific symptoms, and impaired behavioral development and severe brain damage in fetuses and neonates. Toxic exposure to methylmercury occurs primarily via the consumption of contaminated fish or bread prepared from methylmercury-treated seed wheat. Methylmercury also passes freely from mother to fetus, and infants may be exposed by consumption of contaminated mothers' milk. If neurologic criteria are consistent, the only way to definitively confirm a diagnosis of methylmercury poisoning is to establish exposure, particularly by chemical assay. No totally

satisfactory method of treatment has yet been established, and methylmercury poisoning can be prevented only by insuring that the contaminant does not enter food supplies. Thus, methylmercury should no longer be used as a fungicide and the industrial discharge of mercury into the environment should be halted.

967
TITLE:
Urinary excretion of zinc and copper as indicators of alkylmercuric compounds nephrotoxicity in rats.

AUTHORS:
CHMIELNICKA J
NASIADEK M
BRZEZNICKA E
PAPIERZ W
KALUZYNSKI A

SOURCE:
J TRACE ELEM EXP MED; 2 (4). 1989. 331-342.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The purpose of the present study was to determine the dynamics of urinary excretion of Zn and Cu in rats exposed to methylmercuric chloride (MetHg) and ethylmercuric chloride (EtHg). The animals were given (i.g.) 2.5 mg Hg/kg every second day for 6 weeks. Zn and Cu were determined in liver, kidney, brain, blood, and urine by AAS, whereas organic and inorganic mercury were evaluated by cold vapor atomic absorption. The increase of endogenous copper concentration in kidney and endogenous zinc concentration in liver depended on the concentration of inorganic mercury liberated by biotransformation of alkylmercurials. The increased excretion of the essential metals in rats occurred after a 1 week exposure to EtHg and after a 2 week exposure to MetHg. After a 2 week administration of alkylmercuric compounds, changes in kidney histology in the form of vacuolar degeneration of proximal tubules epithelium were observed. Simultaneously, vacuolar degeneration of some neurons and t

968
TITLE:
Evidence that exposure to methyl mercury during gestation induces behavioral and neurochemical changes in offspring of rats.

AUTHORS:
CAGIANO R
DE SALVIA MA
RENNA G
TORTELLA E
BRAGHIROLI D

PARENTI C
ZANOLI P
BARALDI M
ANNAU Z
CUOMO V

SOURCE:
NEUROTOXICOL TERATOL; 12 (1). 1990. 23-28.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. On day 15 of gestation, pregnant Sprague-Dawley rats were orally treated by gavage with 8 mg/kg of methyl mercury (MMC). At day 1 of postnatal life the levels of MMC in whole brain of exposed pups were found to be about 100 times higher than those of saline-exposed rats, while they were near to the control values at 21 days and practically normal at 60 days of age. Behavioral experiments showed that exposure to MMC in late gestation did not affect an any tested time (14, 21 and 60 days) locomotor activity or development of ultrasonic volcalization. An increased response to a challenge dose of amphetamine was, however, detected in MMC-exposed pups at day 14. The phenomenon was no longer evident at day 21 and 60 of age. In parallel, an increased density of dopamine receptors was found in the striatum at 14, but not at 21 and 60, days of age. From these data, we tentatively suggest that a high level of MMC induces a transient phenomenon of disuse-supersensitivity of the do

969
TITLE:
Dental amalgam mercury daily dose estimated from intra-oral vapor measurements: A predictor of mercury accumulation in human tissues.

AUTHORS:
VIMY MJ
LORSCHEIDER FL

SOURCE:
J TRACE ELEM EXP MED; 3 (2). 1990. 111-124.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Recent misconceptions regarding Hg exposure from dental amalgams have been based on several questionable assumptions. The present paper reexamines earlier estimations of Hg daily dose from dental amalgam in order to elaborate and refine the mechanical and volumetric parameters of open-mouth Hg vapor-sampling. This facilitates a comparison with the physiological parameters of human respiration. Corrections for the sampling factors of flow rate and sampling dilution, and the respiratory factor of Hg accumulation in the closed mouth between oral inhalations, reduce our original daily dose estimates by

approximately 50%. Application of a general pharmacokinetic model with our revised Hg daily dose estimates results in predictions for brain, kidney, blood, and urine which approximate tissue Hg measurements reported in subjects with dental amalgams. When tissue Hg predictions are made based upon alternate Hg daily estimates proposed by other investigators, the resultant error

970
TITLE:
Results of environmental pollution monitoring using crows as an indicator.

AUTHORS:
EhimePrefectHygLab

SOURCE:
Ehime Kenritsu Eisei Kenkyusho Nenpo (Annu. Rep. Ehime Prefect. Hyg. Lab.) 37:74; 1975.

ABSTRACT:
PESTAB. Organs from 3 crows (Corvus coronoides japonensis) caught in Iyo city in 1976 were analyzed for isomers of BHC, DDT and its metabolites and PCB as well as mercury, lead and cadmium as indices for environmental pollution monitoring. Total BHC levels in pectoral muscle, adipose tissue, brain, liver and kidney averaged 9.32, 29.14, 2.05, 10.71 and 1.17 ppm respectively (fat basis). Total DDT (in the same order) was 15.43, 12.40, 2.45, 20.22, and 3.94 ppm, respectively (fat basis). Compared to the averages for the whole country these values were higher in the muscle, adipose tissue and liver, especially for beta-BHC and p,p'-DDE. This is due to the fact that in the western part of Japan the accumulation of BHC and DDT is generally higher. No remarkable findings were obtained for mercury, lead, cadmium, and PCB.

971
TITLE:
Use of the fish enzyme system in monitoring water quality: Effects of mercury on tissue enzymes.

AUTHORS:
GILL TS
TEWARI H
PANDE J

SOURCE:
COMP BIOCHEM PHYSIOL C COMP PHARMACOL TOXICOL; 97 (2). 1990. 287-292.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Rosy barb (Puntius conchonius) were exposed to 181 mug/l mercuric chloride for 48 h and the activity of acid and

alkaline phosphatases (AcP and AIP), aspartate aminotransferase (AAT), alanine aminotransferase (AIAT), lactic dehydrogenase (LDH), and acetylcholinesterase (AchE) were measured in vivo in several organs. The AcP activity was inhibited in the liver, gills, kidneys, and gut but stimulated in the gonads. With the exception of kidney, the AIP activity showed an increase in all the organs examined. The AAT and AIAT were generally inhibited in different organs. An increase in LDH activity occurred in the cardiac and skeletal muscles while the AchE activity was considerably lowered in the brain, gills, and liver. In vitro exposure to mercury at concentrations ranged between 10-10 and 10-4 M, inhibited the AIP, AAT, AIAT, LDH, and AchE activities in the tissues examined. The AcP activity was also depressed in all the tissues except in the testes, in which a marginal

972
TITLE:
Tail Rotation, an Early Neurological Sign of Methylmercury Poisoning in the Rat

AUTHORS:
Ohi G
Nishigaki S
Seki H
Tamura Y
Mizoguchi I
Yagyu H
Nagashima K

SOURCE:
Environmental Research, Vol. 16, Nos. 1-3, pages 353-359, 21 references, 19781978

ABSTRACT:
An early neurological sign of methylmercury-poisoning in the rat, tail rotation, is described with reference to chronology of onset, reproducibility of the sign, direction of the rotation, associated pathology of the nervous-system, and possible pathogenesis. Tail rotation, a sustained, vigorous circling of the tail when the animal is held by the trunk, appeared in each of 95 Wistar rats 5 to 6 weeks after continuous exposure to a casein/corn diet that contained 20ppm methylmercury-chloride (115093) and less than 0.1ppm selenium (7782492). When the trunk was turned in a clockwise direction with respect to the long axis of the trunk, the tail swirled in a clockwise direction; when the trunk was turned in counterclockwise direction, rotation also went counterclockwise. Tail rotation appeared 2 to 3 weeks before onset of weight-loss and crossing or ataxia of the hindlegs. The only demonstrable changes in the nervous system at onset of tail rotation involved the peripheral sensory nerves; Meissner type corpuscles contained abnormal

organelles, concentric lamellar bodies resembling myelin that could only be seen with the electron microscope. Mercury levels in the brain at onset were only two thirds as high as levels associated with crossing and ataxia of the hindlegs. Neither the direction nor the velocity of tail rotation was affected by ablation of the visual or inner-ear function. It is suggested that while the mechanism of tail rotation is still unclear, evidence points to its association with peripheral sensory disturbances.

973
TITLE:
DIFFERENTIAL EFFECTS OF ALUMINUM LEAD AND MERCURY ON INOSITOL 1 4 5-TRISPHOSPHATE MEDIATED CALCIUM RELEASE FROM RAT BRAIN MICROSOMES

AUTHORS:
PENTYALA SN
SEKHON BS
TROTTMAN CH
DESAIAH D

SOURCE:
75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J; 5 (4). 1991. A876.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT NEURAL TRANSMISSION HORMONE REGULATION GROWTH FACTOR REGULATION NEUROTOXICITY

974
TITLE:
Durable inhibition of rat cerebral capillary sodium, potassium ATPase after in vivo administration of mercuric chloride.

AUTHORS:
ALBRECHT J

SOURCE:
TOXICOL LETT (AMST); 59 (1-3). 1991. 133-138.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Intraperitoneal administration of a single dose (6 mg/kg body wt.) of mercuric chloride led to a rapid and irreversible inhibition of Na++-ATPase activity in rat cerebral capillaries. The activity measured at 1 h, 18 h and 5 days after injection was, respectively, 53, 44 and 26% of the control. By contrast, Mg2+-ATPase activity in the capillaries remained uninhibited throughout the observation period. Mercuric chloride administration did not affect either of the two enzyme activities in nerve endings, which is consistent with

the inability of the compound to penetrate the blood-brain barrier. The mercuric-chloride-induced impairment of the capillary sodium pump may contribute to disturbances of ion homeostasis in the brain and thus to the neurophysiological abnormalities accompanying this exposure. Direct treatment of the isolated cerebral capillary preparations with mercuric chloride evoked a stronger inhibitory effect on Mg2+-ATPase (IC50 = 0.25 muM) than on Na+/K+-A

975
TITLE:
Distribution of diphenylmercury in the rat.

AUTHORS:
Canty AJ
Parsons RS

SOURCE:
Toxicol. Appl. Pharmacol. 41(2): 441-444 1977 (14 References)

ABSTRACT:
PESTAB. Intraperitoneal injection of diphenylmercury into rats results in a much higher initial concentration of mercury in the brain than that following injection of mercuric chloride or phenylmercuric actate. The concentration in the brain than decreases, and after several days it is similar to that resulting from mercuric chloride and phenylmercuric acetate injection. (Author abstract by permission)

976
TITLE:
Reduced Effectiveness Of The Carotid Baroreflex During Arterial Hypoxia In Dogs

AUTHORS:
Pisarri TE
Kendrick JE

SOURCE:
American Journal of Physiology, Vol. 247, No. 4, pages H623-H630, 33 references, 19841984

ABSTRACT:
The effect of systemic hypoxia on the response to carotid baroreflex stimulation in dogs was investigated. A total of 66 dogs were anesthetized and cannulated in the femoral vein. The carotid sinus nerves were cut, and subjected to 100 millisecond trains of stimulation. Heart rate and arterial pressure were measured, and blood samples were taken. The amount of cardiac slowing produced by nerve stimulation was less than control at an oxygen partial pressure of 67 Torr and below. Suppression

of baroreflex bradycardia was greater at successively lower oxygen partial pressures. The baroreflex suppression during hypoxia occurred over a wide range of nerve stimulation frequencies. During hypoxia before aortic nerve section, carotid sinus nerve stimulation caused heart rate and blood pressure to decrease by 19 beats per minute and 40 millimeters of mercury respectively. After the aortic nerves were cut bilaterally, the heart rate and blood pressure increased to 66 and 70 percent of control levels, respectively. After atropine administration or vagal transection, the heart rate response to baroreflex stimulation during hypoxia was not suppressed. Cutting off the cephalic circulation demonstrated that baroreflex supression was independent of hypoxia of the brain. The authors conclude that an aortic chemoreflex interacts with the baroreflex in the lower brain stem or spinal cord to reduce the effectiveness of the baroreflex during systemic hypoxia.

977
TITLE:
Changes of the sodium potassium ATPase activity in the cerebral cortical microvessels of rat after single intraperitoneal administration of mercuric chloride: Histochemical demonstration with light and electron microscopy.

AUTHORS:
SZUMANSKA G
GADAMSKI R
ALBRECHT J

SOURCE:
ACTA NEUROPATHOL; 86 (1). 1993. 65-70.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Since inorganic mercury salts only poorly penetrate the cerebral microvascular endothelial cells comprising the blood-brain barrier (BBB), their neurotoxicity may be predicted to result from interference with BBB transport enzymes. In the present study, we tested the effect of mercuric chloride (HgCl2) on Na++ ATPase activity, a key enzyme involved in the ion transport in and out of the brain. Routine histochemical staining in conjunction with light and electron microscopy was used to evaluate the changes in the Na+/K+ ATPase activity in cerebral cortical microvessels of rats who received a single intraperitoneal injection of 6 mg/kg HgCl2. At 1 h after HgCl2 administration, light microscopy revealed uniform reduction of the Na+/K+ ATPase reaction in all cortical layers. Electron microscopy confirmed the enzyme reaction to be very weak to completely absent in both the luminal and abluminal endothelial cell membranes, and the luminal plasmalemma showed invaginations and

978

TITLE:
HgEDTA Complex Inhibits GTP Interactions with the E-Site of Brain beta-Tubulin.

AUTHORS:
DUHR EF
PENDERGRASS JC
SLEVIN JT
HALEY BE

SOURCE:
TOXICOLOGY AND APPLIED PHARMACOLOGY; 122 (2). 1993. 273-280.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. We have found that EDTA and EGTA complexes of Hg2+, which conventional wisdom has assumed are biologically inert, are potentially injurious to the neuronal cytoskeleton. Tubulin, a major protein component of the neuronal cytoskeleton, is the target of multiple toxicants, including many heavy metal ions. Among the mercurials, inorganic mercuric ion (Hg2+) is one of the most potent inhibitors of microtubule polymerization both in vivo and in vitro. In contrast to other heavy metals, the capacity of Hg2+ to inhibit microtubule polymerization or disrupt formed microtubules cannot be prevented by the addition of EDTA and EGTA, both of which bind Hg2+ with very high affinity. To the contrary, the addition of these two chelating agents potentiates Hg2+ inhibition of tubulin polymerization. Results herein show that HgEDTA and HgEGTA inhibit tubulin polymerization by disrupting the interaction of GTP with the E-site of brain beta-tubulin, an obligatory step in the polymerization

979
TITLE:
Evaluation of the toxicity of different metal compounds in the developing brain using aggregating cell cultures as a model.

AUTHORS:
MONNET-TSCUHUDI F
ZURICH M-G
HONEGGER P

SOURCE:
TOXICOLOGY IN VITRO; 7 (4). 1993. 335-339.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. To evaluate their toxicity in the developing brain, eight metal compounds, (bismuth sodium tartrate (BiNA-tartrate), CdCl2, CoCl2, HgCl2, dimethyl mercury, NiCl2, TlCl and triethyltin chloride (TET)) were tested in aggregating cell cultures of foetal rat

telencephalon. The compounds were applied to the cultures continuously, either during an early developmental stage (between days 5 and 14) or during and advanced stage of maturation (between days 24 and 34). Changes in the activities of cell type-specific enzymes were used as a criterion for toxicity. A general cytotoxic effect was observed after treatment with either CdCl2, HgCl2 or TET at 10-6 M, and with TlCl at 10-5 M. Selective effects were found with BiNa-tartrate and dimethylmercury. CoCl2 did not modify the parameters tested, whereas a stimulant effect was found with NiCl2. The effects of several compounds were development dependent: HgCl2, TET and TlCl were more toxic in immature cultures, whereas BiNa-tartrat

980

TITLE:

Mechanisms in cardiovascular regulation following chronic exposure of male rats to inorganic mercury.

AUTHORS:

CARMIGNANI M
FINELLI VN
BOSCOLO P

SOURCE:

TOXICOL APPL PHARMACOL; 69 (3). 1983. 442-450.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The possibility that chronic exposure to inorganic Hg may have induced hemodynamic changes in the rat by affecting some neurogenic and/or humoral mechanisms regulating cardiovascular function was verified. Aortic blood pressure, maximum rate of rise of the left ventricular pressure, heart rate and ECG were monitored under pentothal anesthesia in rats which received 50 mug/ml Hg (as HgCL2) in drinking water for 320 days, and in control rats. No pressor or ECG changes were found in Hg-treated animals, which showed increase of cardiac inotropism and decrease of the pressor and inotropic responses to bilateral carotid occlusion. Cardiovascular responses to bilateral vagotomy and i.v. hexamethonium under vagotomy were unchanged in the Hg-exposed rats. In these animals pressor and inotropic responses to i.v. norepinephrine and to higher doses of epinephrine were reduced, while the vascular beta-adrenergic response to 0.125 mug/kg i.v. epinephrine was potentiated. Cardiovascular responses to acetylcholine, angiotensin I, angiotensin II, bradykinin, histamine and serotonin did not differ in the 2 groups of rats. Chronic Hg exposure affected cardiovascular function by interfering with the baroreflex mechanisms and/or the reactivity to catecholamines. Higher amounts of Hg were found in kidney, but the metal was significantly accumulated also in urine, blood and brain. Hg exposure greatly increased the levels of Cu and Zn, but not that of Fe, in brain and kidney. The increased accumulation of Cu and Zn in tissues may have been related to the Hg induced synthesis of metallothionein, a protein

able to bind these essential metals. Zn and Cu may have interacted with Hg in inducing cardiovascular changes.

981
TITLE:
Placental transfer and fetal distribution of cadmium and mercury after treatment with dithiocarbamates.

AUTHORS:
DANIELSSON B RG

SOURCE:
ARCH TOXICOL; 55 (3). 1984. 161-167.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution, in pregnant C57BL mice (day 18 of gestation), of i.v. CdCl2 and HgCl2 (0.75 mumol/kg body wt) was studied, with or without previous dithiocarbamate pretreatment. Diethyldithiocarbamate (DEDTC), disulfiram or thiram (2ere given by gavage 2 h before and immediately after injection of the metals. The mice were sacrificed 4 and 24 h later, and were subjected to autoradiography or impulse counting of excised organs. All dithiocarba the concentration of Cd and Hg in brain and most other maternal organs. While DEDTC and thiram, in that order, strongly increased Cd concentrations in whole fetuses (17-fold at 4 h) and all fetal organs measured, disulfiram caused a decrease in fetal Cd concentrations. For Hg, all dithiocarbamates substantially decreased fetal levels. Disulfiram decreased Hg levels by a factor of 5. The 24 h values confirmed those at 4 h for both elements, although the differences between control and treatment groups were less pronounced. Although the results suggested the formation of lipid-soluble metal-dithiocarbamate complexes in vivo (e.g., increased concentration in brain), this did not necessarily lead to increased fetal levels of the metals. The increased levels of Cd after thiram and DEDTC pretreatment indicated a risk for higher Cd fetotoxicity. Cd was probably released in fetal cells following metabolism of the dithiocarbamate moiety of the complex.

982
TITLE:
A mortality study of men exposed to elemental mercury.

AUTHORS:
CRAGLE DL
HOLLIS DR
QUALTERS JR
TANKERSLEY WG
FRY SA

SOURCE:
J OCCUP MED; 26 (11). 1984. 817-821.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A cohort of 2133 white males who were exposed to elemental Hg vapors between 1953-1963 was followed up through the end of 1978. Death certificates were obtained for 371 of 378 workers reported by the Social Security Administration (USA) as deceased. The mortality experience of this group was compared with the age-adjusted mortality experience of the USA white male population. Mortality had not been studied previously in assessing the long-term health effects of Hg exposure. Standardized mortality ratios (SMR) were calculated for a comparable unexposed worker population to determine the mortality patterns among workers at the same plant who were not involved in the Hg process. Statistically significant excesses of deaths from cancer of the lung (SMR = 1.34; 71 observed, 52.9 expected) and cancer of the brain and other CNS tissues (SMR = 2.30; 13 observed, 5.65 expected) were observed among the plant workers who were not involved in the Hg process. An excess of deaths from cancer of the lung was also observed among the Hg workers (SMR = 1.34; 42 observed, 31.36 expected), although the elevation of this SMR was not statistically significant. Since excesses of lung cancer were evident in both groups of workers, it was not likely that they were related to the Hg exposure and more probable that they were due to some other factor present in the plant or to some life-style factor prevalent among the plant workers. Exposure to Hg vapors at this plant was not related to any excess of deaths from diseases or cancers of organs determined to be target organs for Hg (liver, lung, brain and CNS and kidney). No excesses were found when level of exposure and length of exposure were considered.

983
TITLE:
The outbreak of Minamata Disease (methyl mercury poisoning) in cats on Northwestern Ontario Reserves.

AUTHORS:
TAKEUCHI T
D'ITRI FM
FISCHER PV
ANNETT CS
OKABE M

SOURCE:
ENVIRON RES; 13 (2). 1977 215-228

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Pathological, histochemical and analytical studies confirmed the presence of Minamata Disease in at least 1 of 2 cats that lived on or near Indian Reserves in Northwestern Ontario, Canada.

These symptoms parallel the Japanese experience in the 1950's and raise ominous health considerations for the Indians who share their diet of fish. After being fed a diet that primarily consisted of fish from the English River, 1 cat developed such acute neurological symptoms as an ataxic gait, other abnormal movements, uncontrolled howling and seizures. The total Hg analysis showed high levels in all tissues with 16.4 mg/kg in the brain comparable with symptomatic cats in Japan. A 2nd cat that appeared normal had 6.9 mg/kg in its brain tissues, and pathological studies confirmed the presence of latent Minamata Disease.

984
TITLE:
MERCURY VAPOR EXPOSURE INHIBITS TUBULIN BINDING TO GTP IN RAT BRAIN A MOLECULAR LESION ALSO PRESENT IN HUMAN ALZHEIMER BRAIN

AUTHORS:
LORSCHEIDER FL
VIMY MJ
PENDERGRASS JC
HALEY BE

SOURCE:
EXPERIMENTAL BIOLOGY 95, PART II, ATLANTA, GEORGIA, USA, APRIL 9-13, 1995. FASEB JOURNAL; 9 (4). 1995. A663.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT

985
TITLE:
Apallic syndrome in chronic mercury poisoning.

AUTHORS:
GERSTENBRAND F
HAMDI T
KOTHBAUER P
RUSTAM H
AL BADRI M

SOURCE:
EUR NEUROL; 15 (5). 1977 249-256

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. This report includes 5 cases afflicted by chronic Hg poisoning (due to Hg-treated wheat) which was observed in Iraq in 1972. All 5 cases showed the symptomatology of a severe cerebral damage combined with peripheral nerve lesion. The clinical picture reveals an apallic syndrome or a prestage ensuring in the full-blown picture. The

combination of CNS lesions with polyneuropathy is typical of Hg poisoning with failure of all brain functions and the appearance of brain stem automatism, combined with severe muscular atrophy. When such conditions are established the remission seems to be impossible. The historical as well as the clinical and morphological facts of Minamata disease are reviewed. The different stages of chronic Hg poisoning in Iraq are described.

986
TITLE:
Environmentally hazardous substances and the nervous system.

AUTHORS:
KYVIK KR
MOEN BE

SOURCE:
TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING; 115 (15). 1995. 1834-1838.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The neurons are extremely vulnerable to changes in the local chemical environment, and the nervous system has therefore been given special priority and protection compared with other organ systems. Neurotoxic syndromes may occur when these biochemical conditions are disturbed. The brain is particularly vulnerable to hypoxia, and exposure to toxins that interfere with the intake, transport and utilization of oxygen provoke rapid and major neuronal damage. Compounds crossing the blood-brain barrier may induce both general and extremely localized neurotoxic effects. Today, dramatic and acute neurotoxic manifestations seldom occur in our part of the world. The focus of attention is now directed at the consequences of long-term and low-level exposure. This review presents a general description of some neurotoxic mechanisms, and the clinical effects of a few hazardous substances, ie metals, pesticides, organic solvents.

987
TITLE:
Immunological and brain MRI changes in patients with suspected metal intoxication.

AUTHORS:
TIBBLING L
THUOMAS K-A
LENKEL R
STEJSKAL V

SOURCE:
INTERNATIONAL JOURNAL OF OCCUPATIONAL MEDICINE AND TOXICOLOGY; 4 (2).

1995. 285-294.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Thirty-four patients with central nervous system (CNS) and systemic symptoms suggestive of intoxication from dental amalgam were examined with magnetic resonance imaging (MRI) of the brain (n = 32) and with a Memory Lymphocyte Immuno Stimulation Assay (MELISA) (n = 17). Lymphocyte phenotype was analyzed with flow cytometry (FC) in 22 of the patients. One hundred twenty age-matched patients without CNS symptoms served as controls for the MRI study, seventy-seven healthy subjects with dental amalgam fillings served as controls for the MELISA test, and seventy-five clinically healthy subjects were controls for lymphocyte phenotype determination. Pathological MRI findings were present in 81% of the patients, most of them with signs of degeneration in the basal ganglia, but in none of the controls. The lymphocyte phenotype determination was pathological in 58%. The MELISA showed pathological findings in 88%, of which 60% showed an immune reaction to mercuric chloride, 62% of

988
TITLE:
COMPARISON OF MERCURY ACCUMULATION AMONG THE BRAIN LIVER KIDNEY AND THE BRAIN REGIONS OF RATS ADMINISTERED METHYLMERCURY IN VARIOUS PHASES OF POSTNATAL DEVELOPMENT

AUTHORS:
SAKAMOTO M
NAKANO A

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 55 (4). 1995. 588-596.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE HUMAN MODEL DEVELOPMENTAL TOXICITY EPIDEMIOLOGY

989
TITLE:
MERCURY VAPOR INHALATION INHIBITS BINDING OF GTP TO TUBULIN IN RAT BRAIN A MOLECULAR LESION PRESENT IN ALZHEIMER BRAIN

AUTHORS:
LORSCHEIDER FL
VIMY MJ
PENDERGRASS JC
HALEY BE

SOURCE:
25TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, SAN DIEGO, CALIFORNIA, USA, NOVEMBER 11-16, 1995. SOCIETY FOR NEUROSCIENCE ABSTRACTS; 21 (1-3). 1995. 1723.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER POLYMERIZATION

990
TITLE:
Interaction of heavy metal toxicants with brain constitutive nitric oxide synthase.

AUTHORS:
MITTAL CK
HARRELL WB
MEHTA CS

SOURCE:
MOLECULAR AND CELLULAR BIOCHEMISTRY; 149-150 (0). 1995. 263-265.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This study was designed to evaluate the in vitro effects of transition heavy metal cations on activity of constitutive isoform of nitric oxide synthase (cNOS) in rat brain. NOS activity was determined in the cytosolic fractions of rat cerebral hemispheres by conversion of 3H-L-arginine to 3H-L-citrulline. Different concentrations of mercury (Hg2+), nickel (Ni2+), manganese (Mn2+), zinc (Zn2+), cadmium (Cd2+), lead (Pb2+) and calcium (Ca2+) were tested on NOS activity. While all the cations caused inhibition, there were differences in the apparent inhibition constants (Ki) among the cations. With the exception of calcium ion no other cation required preincubation with the enzyme preparation. These results indicate that while calcium ion modulate cNOS activity at regulatory site(s), inhibitory influence of toxic heavy metal cations may be exerted on the catalytic site(s) either by direct binding to it or by interfering with the electron transfer during catalysis.

991
TITLE:
DEVELOPING BRAIN AS A TARGET OF TOXICITY

AUTHORS:
RODIER PM

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 103 (SUPPL. 6). 1995. 73-76.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM JOURNAL ARTICLE HUMAN LEAD METHYL MERCURY PSYCHOACTIVE DRUGS NEURON PROLIFERATION NEURON MIGRATION POSTNATAL DEVELOPMENT BLOOD-BRAIN BARRIER RECEPTORS TRANSMITTERS SYNAPSES MYELIN PRODUCTION ENVIRONMENTAL POLLUTION DEVELOPMENTAL NEUROTOXICITY X-RAYS

992
TITLE:
ASSESSMENT OF LIVER AND BRAIN ESTERASES IN THE SPOTTED GAR FISH AS BIOMARKERS OF EXPOSURE IN THE LOWER MISSISSIPPI RIVER BASIN

AUTHORS:
OBIH P
HUANG T
JAISWAL R

SOURCE:
EXPERIMENTAL BIOLOGY 96, PART II, WASHINGTON, D.C., USA, APRIL 14-17, 1996. FASEB JOURNAL; 10 (3). 1996. A458.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT LEPISOSTEIDAE-OCULATUS CADMIUM MERCURY LEAD CARBOXYLESTERASE ACETYLCHOLINESTERASE BUTYRYLCHOLINESTERASE BRAIN LIVER TOXICOLOGY IN-VITRO MODEL DEVIL SWAMP PRISTINE REFERENCE SITE TUNICA SWAMP CHLORINATED HYDROCARBON CONTAMINATED ECOSYSTEM

993
TITLE:
Health Risks From Increases In Methylmercury Exposure

AUTHORS:
Mottet NK
Shaw C-M
Burbacher TM

SOURCE:
Environmental Health Perspectives, Vol. 63, pages 133-140, 55 references, 19851985

ABSTRACT:
Studies related to the health effects from increased exposure to methylmercury (22967926) are reviewed. Present knowledge of the human health effects of methylmercury exposure is mainly derived from studies of major outbreaks of human poisonings and experimental studies on primates.

Methylmercury readily passes through such physiological barriers as the blood/brain barrier, the blood/testes barrier, and the placenta. Major pathological effects are on the nervous and reproductive systems and the developing embryo or fetus. The neurotoxicity of methylmercury is well established in both humans and non human primates; lesions in the cerebral and cerebellar gray matter consist of necrosis and lysis of neurons, phagocytosis, and gliosis. At high dose concentrations, the liver, kidneys, and other organs may also have degenerative changes. Although not yet described in humans, a major effect of exposure in female primates is an adverse effect on pregnancy; blood mercury concentrations over 1 part per million are associated with a decreased pregnancy rate and increased abortion rate. Both human and primate studies demonstrate deleterious effects of methylmercury on the developed embryo or fetus, including retarded brain development and the occurrence of a cerebral palsy like behavior in newborns, although the mother may be free of signs of methylmercury toxicity. Further research is needed to define the amount of or concentration at which methylmercury begins to have significant neurotoxic, reproductive, or fetal development effects.

994
TITLE:
ENVIRONMENTAL CONTAMINANTS AND CHOLINESTERASE ACTIVITY IN THE BRAIN OF FISHER MARTES PENNANTI HARVESTED IN NORTHERN WISCONSIN

AUTHORS:
GERSTENBERGER SL
GILBERT JH
DELLINGER JA

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 56 (6). 1996. 866-872.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE MARTES-PENNANTI ERETHIZON-DORSATUM MUSTELA-VISON MERCURY POLYCHLORINATED BIPHENYLS ORGANOCHLORINE COMPOUNDS BLOOD-BRAIN BARRIER REPRODUCTION PREDATION SURVIVAL USA

995
TITLE:
Levels of Hg, Pb and V in brain, kidney, liver and lung of anencephalic fetuses from the eastern coast of Lake Maracaibo, Venezuela.

AUTHORS:
TAHAN JE
BARRIOS LC
MARCANO L

GRANADILLO VA
CUBILLAN HS
SANCHEZ JM
RODRIGUEZ MC
DE SALAZAR FG
SALGADO O
ROMERO RA

SOURCE:
TRACE ELEMENTS AND ELECTROLYTES; 13 (1). 1996. 7-13.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This work describes the levels of mercury (Hg), lead (Pb) and vanadium (V) in brain, kidney, liver and lung of anencephalic (A) and control (C) fetuses from the Eastern coast of Lake Maracaibo (Venezuela) evaluated from April 1993 to July 1994. A relatively high anencephaly rate of 5.1 per 1,000 total births was reported in this area for 1994. A petroleum empire has grown indiscriminately in the region under study, provoking adverse effects in the environment and in humans due to the constant release of these toxicants. Sample analyses were done by cold vapour atomic absorption spectrometry (for Hg), differential pulse anodic stripping voltammetry (for Pb) and electrothermal atomization atomic absorption spectrometry (for V). Twenty stillborn fetuses with anencephaly (mean gestation age 34.4 weeks, range 20 - 40 weeks) and 20 stillborn fetuses without anencephaly (mean gestation age 38.5 weeks, range 36 - 40 weeks), included as controls, were considered for the present

996
TITLE:
Phosphatases and esterases activity in the brain following an acute sublimate intoxication.

AUTHORS:
KOZIK MB
SOSINSKI E
SZCZECH J

SOURCE:
FOLIA HISTOCHEM CYTOCHEM; 15 (2). 1977 87-94

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Experimental studies were performed on rats administered mercury chloride sublimate with a special gastric cannule in a single 6 mg dose for 4 consecutive days. Some changes in the phosphatase and esterase activities were revealed. The diminution of AcP (acid phosphatase), AlP (alkaline phosphatase), ATPase and AChE (acetylcholinesterase) activity and the increase in TPPase (thiamine

pyrophosphatase) activity in the neurocytes and the appearance of NsE (non-specific esterase) activity in many oligodendrocytes were observed. The fall in ATPase activity was observable in cerebral and cerebellar capillaries, which is possibly a manifestation of enzymatic damage to the blood-brain barrier due to a toxic action of mercuric chloride. Attention was drawn to differences in the degree of enzymatic activity between a mercuric chloride intoxication and that with mercurous chloride, and an attempt was made to explain the pathogenetic mechanism of this phenomenon. In the course of sublimate encephalopathy no changes were observed in BuTJ (butyrylthiocholinesterase) activity.

997
TITLE:
EFFECTS OF DRUGS NARCOTICS AND TOXINS ON THE CHEMICAL MATURATION OF THE INFANT BRAIN

AUTHORS:
ALVORD E C JR
SUMI SM

SOURCE:
BERENBERG, SAMUEL R. (ED.). BRAIN, FETAL AND INFANT. CURRENT RESEARCH ON NORMAL AND ABNORMAL DEVELOPMENT. PROCEEDINGS OF A CONFERENCE. PARIS, FRANCE, DEC. 14-16, 1976. XIV+349P. ILLUS. MARTINUS NIJHOFF MEDICAL DIVISION: THE HAGUE, NETHERLANDS. ISBN 90-247-2022-2.; 1977 (RECD 1978) 165-177

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN METHOTREXATE AMINOPTERIN THALIDOMIDE METHYL MERCURY HEXACHLOROPHENE GLIAL FATTY METAMORPHOSIS MYELIN SPECIFIC TOXINS

998
TITLE:
Neurologic Disease

AUTHORS:
Rosenstock L
Cullen MR

SOURCE:
Clinical Occupational Medicine; Philadelphia, Pennsylvania, W. B. Saunders Company, pages 118-134, 11 references, 19861986

ABSTRACT:
Occupational diseases of the nervous system are discussed, including central nervous system disorders such as toxic encephalopathy (either acute or chronic), tumors, and Parkinsonian movement disorders as well as

peripheral nervous system disorders such as toxic polyneuropathy, neuromuscular junction blockade and traumatic disorders including interstitial (vascular related to vibration) and parenchymal (compressive or entrapment mononeuropathy) disorders. Agents which have been shown to produce brain tumors in experimental animals are listed. Occupations in which epidemiologic studies suggest an excess of brain tumors include aluminum (7429905) workers, chemists, lead smelter workers, machinists, medical personnel, oil refinery workers, petrochemical workers, pharmaceutical workers, rubber workers, veterinarians, and vinyl-chloride (75014) workers. Substances which cause peripheral neuropathies fall into the following categories: metals including lead (7439921), arsenic (7440382), mercury (7439976), and thallium (7440280); solvents including hexacarbons, trichloroethylene (79016), and carbon-disulfide (75150); gases such as methyl-bromide (74839) and carbon-monoxide (630080); pesticides and herbicides including chlordecone (143500), some organophosphates, and chlorinated phenol derivatives; and plastics including acrylamide (79061), dimethylaminopropionitrile (1738256), and styrene (9003536). A number of such agents can also cause central neuropathies, including organic solvents, asphyxiant gases, pesticides and heavy metals.

999

TITLE:

Behavioral Effects of Cyclic Dosing with Methylmercury in Pigeons

AUTHORS:

Weisman RG
Freedman NL

SOURCE:

NeuroToxicology, Vol. 7, No. 3, pages 107-120, 16 references, 19861986

ABSTRACT:

Effects of cyclic dosing with methylmercury (MeHg) on psychological functions in pigeons were studied. Male white Carneaux-pigeons were given a high dose (HD), 2.0mg/kg/day, or a low dose (LD), 0.5mg/kg/day, of MeHg. Added to the solution was 2 milligrams L-cysteine to reduce the effect of MeHg on digestion. Each test cycle consisted of a 6 day intubation sequence, followed by a 32 day behavioral testing series. In the last series, there were 28 days of delayed sequence discrimination (DSD), followed by four daily sessions of the feeding test. The steps in the DSD test were as follows: intertrial interval, first stimulus, interstimulus interval, second stimulus, interstimulus interval, third stimulus, retention interval, and test stimulus. Unless pigeons showed signs of acute intoxication, behavioral testing was completed in the fifth series. Impaired discrimination was found in the 2.0mg/kg group, relative to the 0.5mg/kg group. Histological examination found no evidence of significant cell loss in the exposed animals. Pigeons on HD showed signs of

intoxication, while the LD group displayed no signs of abnormal behavior. Experiments with HD tritiated MeHg showed brain MeHg levels between 17.5 and 23.2 parts per million, as determined by scintillation counting and atomic absorption. The authors conclude that performance in the sequence discrimination and feeding task was affected after a cumulative dose of 20mg/kg in the HD group. Sequence discrimination recovered within 3 months after dosing was stopped, but feeding skill remained impaired. A cumulative dose of 86mg/kg in the LD group had no observable effect on task performance.

1000
TITLE:
Development of Adrenergic Receptor Binding Sites in Brain Regions of the Neonatal Rat: Effects of Prenatal or Postnatal Exposure to Methylmercury

AUTHORS:
Bartolome JV
Kavlock RJ
Cowdery T
Orband-Miller L
Slotkin TA

SOURCE:
Neurotoxicology, Vol. 8, No. 1, pages 1-14, 36 references, 19871987

ABSTRACT:
Regional selectivity and subtype specificity of the effects of prenatal and postnatal exposure to methylmercury (593748) on adrenergic receptors in the developing brain were investigated in rats. Pregnant Sprague-Dawley-rats were administered daily subcutaneous injections of 0.5 or 1.0mg/kg methylmercury on gestation days eight through 20. Neonatal rats from unexposed mothers received daily subcutaneous injections of 1.0 or 2.5mg/kg methylmercury for 20 days, starting on the day after birth. In-utero exposure to methylmercury had little or no effect on adrenergic receptor binding in the cerebral cortex and caused a small, but statistically significant, increase in receptor binding in the midbrain and brainstem, but had profound effects on receptor binding in the cerebellum. Within the cerebellum, prenatal exposure to 0.5mg/kg methylmercury increased receptor binding of all adrenergic receptors, but the higher dose produced lower values for binding and actually caused a net reduction in alpha receptor binding. Postnatal exposure produced an initial suppression of adrenergic receptor binding in the cerebral cortex, followed by a dose dependent spike in activity on day six. A similar response was seen in the cerebellum, with the spike in receptor binding occurring somewhat later, on day 15. Higher doses caused a general decrease in alpha-1 receptor binding without an apparent spike. Postnatal exposure had little or no effect on receptor binding in the midbrain and brainstem. The authors conclude that methylmercury exerts a dual spectrum

of action on developing adrenergic receptors, causing promotional effects at low doses and inhibitory effects at higher doses, and that the effects are both regionally and receptor subtype selective and are dependent upon the maturational timetables of each region.

1001
TITLE:
Effects of mercury and selenium on glutathione metabolism and oxidative stress in mallard ducks.

AUTHORS:
HOFFMAN DJ
HEINZ GH

SOURCE:
ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY; 17 (2). 1998. 161-166.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Earlier studies have reported on the toxicity and related oxidative stress of different forms of Se, including seleno-D,L-methionine, in mallards (Anas platyrhynchos). This study compares the effects of Se (seleno-D,L-methionine) and Hg (methylmercury chloride) separately and in combination. Mallard drakes received one of the following diets: untreated feed (controls), or feed containing 10 ppm Se, 10 ppm Hg, or 10 ppm Se in combination with 10 ppm Hg. After 10 weeks, blood, liver, and brain samples were collected for biochemical assays. The following clinical and biochemical alterations occurred in response to Hg exposure: hematocrit and hemoglobin concentrations decreased; activities of the enzymes glutathione (GSH) peroxidase (plasma and liver), glutathione-S-transferase (liver), and glucose-6-phosphate dehydrogenase (G-6-PDH) (liver and brain) decreased; hepatic oxidized glutathione (GSSG) concentration increased relative to reduced glutathione (GSH); and lipid pero

1002
TITLE:
Survival and reproductive success of black ducks fed methyl mercury.

AUTHORS:
FINLEY MT
STENDELL RC

SOURCE:
ENVIRON POLLUT; 16 (1). 1978 51-64

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A diet containing 3 ppm Hg was fed to black ducks (Anas rubripes) for periods of 28 wk during 2 consecutive breeding

seasons. Clutch size, egg production, number of eggs incubated, hatchability and survival of ducklings were lower during both years in hens fed Hg. Reduced hatchability and poor duckling survival were the most harmful effects. During 2 yr, 13 pairs of breeders fed Hg produced only 16 ducklings that survived 1 wk compared with 73 ducklings from 13 pairs of controls. Hg residues in eggs, embryos and ducklings averaged about 30% lower during the 2nd breeding season compared with 1st yr results. Third eggs laid by treated hens contained a mean of 6.14 and 3.86 ppm Hg during the 1st and 2nd yr. Whole embryos that failed to hatch contained means of 9.62 and 6.08 ppm Hg during the 1st and 2nd yr. Brains of dead ducklings contained between 3.25 and 6.98 ppm Hg and exhibited lesions characteristic of Hg poisoning. Relative tissue Hg levels for treated adult breeders were: feathers > liver > kidney > breast muscle > brain. Hg levels in males and females did not differ.

1003
TITLE:
Methylmercury intoxication and histochemical demonstration of NADPH-diaphorase activity in the striate cortex of adult cats.

AUTHORS:
OLIVEIRA RB
GOMES-LEAL W
DO-NASCIMENTO J LM
PICANCO-DINIZ CW

SOURCE:
BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH; 31 (9). 1998. 1157-1161.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of methylmercury (MeHg) on histochemical demonstration of the NADPH-diaphorase (NADPH-d) activity in the striate cortex were studied in 4 adult cats. Two animals were used as control. The contaminated animals received 50 ml milk containing 0.42 mug MeHg and 100 g fish containing 0.03 mug MeHg daily for 2 months. The level of MeHg in area 17 of intoxicated animals was 3.2 mug/g wet weight brain tissue. Two cats were perfused 24 h after the last dose (group 1) and the other animals were perfused 6 months later (group 2). After microtomy, sections were processed for NADPHd histochemistry procedures using the malic enzyme method. Dendritic branch counts were performed from camera lucida drawings for control and intoxicated animals (N = 80). Average, standard deviation and Student t-test were calculated for each data group. The concentrations of mercury (Hg) in milk, fish and brain tissue were measured by acid digestion of samples, followed by reduction of total

1004
TITLE:

EVALUATION OF LIVER AND BRAIN ESTERASES IN THE SPOTTED GAR FISH LEPISOSTEUS OCULATUS AS BIOMARKERS OF EFFECT IN THE LOWER MISSISSIPPI RIVER BASIN

AUTHORS:
HUANG TL
OBIH PO
JAISWAL R
HARTLEY WR
THIYAGARAJAH A

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 58 (5). 1997. 688-695.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE LEPISOSTEUS-OCULATUS SPOTTED GAR FISH BRAIN ACETYLCHOLINESTERASE BIOMARKER LIVER CARBOXYLESTERASE HEXACHLOROBENZENE POLLUTANT HEXACHLOROBUTADIENE HEAVY
METALS POLLUTANTS POLLUTION TOXICOLOGY LOWER MISSISSIPPI RIVER BASIN LOUISIANA USA

1005
TITLE:
Effect of mercury dichloride on some biochemical indices of the brain, blood and liver of the vobla Rutilus rutilus caspicus (Jak.).

AUTHORS:
DOKHOLYAN VK
AKHMEDOVA TP

SOURCE:
VOPR IKHTIOL; 18 (1). 1978 177-180

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Substantial changes occurred in maintenance of the fish R. rutilus caspicus in Hg solutions. In 100 mug/l solutions the fish died; lower concentrations (10 and 5 mug/l) did not lead to death, but produced considerable impairments in the metabolism of substances. Significant increases of ammonia, glutamic acid and amide protein groups and reductions of glutamine and GABA were noted in the brain, with general decrease of protein, blood, albumins and corresponding levels of alpha- and beta-globulins. Blood sugar and glycogen in the liver were reduced. Contamination of the water environment with Hg compounds may lead to a series of physiologico-biochemical changes resulting in reduction of the fish productivity of water bodies.

1006
TITLE:
Further data on heavy metals and organochlorines in marine mammals from German coastal waters.

AUTHORS:
HARMS U
DRESCHER HE
HUSCHENBETH E

SOURCE:
MEERESFORSCHUNG; 26 (3-4). 1977-1978 153-161

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Studies on heavy metals and organochlorines in harbor seals (Phoca vitulina) were continued and extended to other marine mammals (P. hispida (ringed seal), Halichocrus grypus (grey seal), Phocoena phocoena (harbor porpoise), Hyperoodon ampullatus (bottlenose whale) and Delphinapterus leucas (white whale)), found off the German North Sea and Baltic coasts. The results are compared with contamination levels in fish which form the major food source of the marine mammals investigated. Concentrations of Cu, Zn, Cd and Pb in muscle and liver tissues of fish did not differ significantly from corresponding organs of the marine mammals. However, considerably higher amounts of Hg were found in the liver of seals and whales than in fish. Higher Hg concentrations in seals are closely related to the age of the animals. The highest amount of 160 mg/kg (ppm) Hg was found in an adult seal. In contrast to fish a high percentage of total Hg occurs in the inorganic form in seal and whale liver. The degree of contamination with organochlorines (PCB (polychlorinated biphenyl) and total DDT) in seals and whales studied is of the same order of magnitude. Maximum values in seal blubber amount to 27 mg/kg (ppm) for DDT and 564 mg/kg (ppm) for PCB (wet weight). A comparison of fish and marine mammals shows that the pesticide burden in the various tissues is in the first instance a reflection of their lipid content. Seals form an exception, as the DDT and PCB content is comparably lower in the brain than in the liver which contains less fat. This is probably due to a brain barrier against an accumulation of organochlorines.

1007
TITLE:
Detection Limits of Different Approaches in Behavioral Teratology, and Correlation of Effects with Neurochemical Parameters

AUTHORS:
Elsner J
Hodel B
Suter KE

Oelke D
Ulbrich B
Schreiner G
Cuomo V
Cagiano R
Rosengren LE
Karlsson JE
Haglid KG

SOURCE:
Neurotoxicology and Teratology, Vol. 10, No. 2, pages 155-167, 44 references, 19881988

ABSTRACT:
The usefulness of behavioral testing in teratology was demonstrated using a testing battery and automated multivariable test systems. These systems were related to biochemical variables in the brain of offspring from Kfm:WIST-rat dams exposed to methylmercury at dose levels of 0.025, 0.05, and 5.0mg/kg/day on days six to nine of gestation. Offspring were tested with routine developmental and behavioral testing procedures. After these tests were completed, random samples of animals were studied further using auditory startle habituation, visual discrimination and figure 8 activity monitors; wheel shaped activity monitor and spatial alternation operant conditioning; two compartment locomotor activity, passive avoidance and male ultrasonic vocalization during sexual behavior; assays of the weight of different brain areas, along with their glial fibrillary acidic protein and S-100 protein concentrations. The doses which caused behavioral and also neurochemical deficits in exposed offspring were of a low enough level that they did not cause any clinical signs or gross teratogenic effects. The authors conclude that some of the automated multiparametric test systems and neurochemical assays are comparably sensitive to the behavioral testing battery.

1008
TITLE:
Neurophysiological Approaches to the Detection of Early Neurotoxicity in Humans

AUTHORS:
Seppalainen AMH

SOURCE:
CRC Critical Reviews in Toxicology, Vol. 18, No. 4, pages 245-298, 260 references, 19881988

ABSTRACT:
The use of neurophysiological methods in the detection of early neurotoxicity in humans was reviewed. Methods discussed included

electroencephalography, or the recording of the electrical activity of the brain; evoked potentials (EP) which study certain precise functions of the central nervous system such as visual EPs, auditory EPs, or somatosensory EPs; and electromyography, the measurement of nerve conduction velocities. The application of these various neurophysiological methods to determine possible exposure was discussed for the following substances: solvents such as carbon-disulfide (75150), n-hexane (110543), methyl-n-butyl-ketone (591786), toluene (108883), xylene (1330207), halogenated hydrocarbons, styrene (100425), solvent mixtures, other industrial solvents, and alcohol (64175); insecticides including organophosphorus compounds, chlorinated insecticides, and pyrethroids; selected chemicals such as acrylamide (79061), methyl-methacrylate (80626), polychlorinated-biphenyls (1336363), dioxins and phthalates; metals including lead (7439921), mercury (7439976), and arsenic (7440382); and drugs.

1009
TITLE:
Methylmercury transport across cell membranes

AUTHORS:
BALLATORI N

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The overall objective of this laboratory is to identify those factors that underlie human susceptibility to methylmercury (MeHg) poisoning. MeHg is a highly toxic environmental pollutant: clinical and experimental studies demonstrate that exposure to MeHg results in neurologic damage characterized by ataxia, sensory disturbances and changes in mental state. The only way to prevent or ameliorate toxicity once MeHg has been ingested is to accelerate its removal from the body. Our goal is to identify and characterize the mechanisms by which MeHg crosses cell membranes to reach its target sites, or conversely, to be eliminated from the cell. This information is critical both for defining mechanisms of toxicity, and for developing effective biomarkers of exposure and therapeutic strategies. Our previous work provided the first direct demonstration of the mechanism by which MeHg crosses the blood-brain barrier to reach its target tissue, and of the mechanism by which MeHg is transported across the liver cell canalicular membrane into bile, a major route for its excretion. Recent studies have also identified a novel antidote for MeHg, namely N-acetylcysteine (NAC). Our working hypothesis is that NAC enhances urinary MeHg excretion because it leads to the formation of the anionic MeHg-NAC complex, which is a substrate for the renal organic anion transporters. The proposed studies aim to characterize these MeHg transport mechanisms at the molecular and cellular level. Our Specific Aims are: I. Examine the mechanism by which the MeHg-L-cysteine complex is

transported on the L-type amino acid transporters LAT1 and LAT2. II. Test whether the MeHg-glutathione complex (MeHg-SG) is a substrate for some members of the MRP family of transporters. III. Evaluate the molecular mechanism by which NAC stimulates renal excretion of MeHg. IV. Test the hypothesis that urinary excretion of MeHg following an NAC oral challenge may be used as a new biomarker of MeHg exposure.

1010
TITLE:
The effects of thyroid hormone level and action in developing brain: Are these targets for the actions of polychlorinated biphenyls and dioxins?

AUTHORS:
SHER ES
XU XM
ADAMS PM
CRAFT CM
STEIN SA

SOURCE:
TOXICOLOGY AND INDUSTRIAL HEALTH; 14 (1-2). 1998. 121-158.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Alterations in thyroid hormone level or responsivity to thyroid hormone have significant neurologic sequelae throughout the life cycle. During fetal and early neonatal periods, disorders of thyroid hormone may lead to the development of motor and cognitive disorders. During childhood and adult life, thyroid hormone is required for neuronal maintenance as well as normal metabolic function. Those with an underlying disorder of thyroid hormone homeostasis or mitochondrial function may be at greater risk for developing cognitive, motor or metabolic dysfunction upon exposure to substances which alter thyroid hormone economy. Polychlorinated biphenyls (PCBs) and dioxins have been argued to interfere with thyroid hormone action and thus may affect the developing and mature brain. Animal models provide useful tools for studying the effects of thyroid hormone disorders and the effects of environmental endocrine disruptors. The congenitally hypothyroid, hyt/hyt, mouse exhibits a

1011
TITLE:
Methyl mercury, N-CAM expression and dysmorphogenesis.

AUTHORS:
Reuhl KR
Borgeson B

SOURCE:

Toxicologist 1990 Feb;10(1):136

ABSTRACT:

During development, disturbance of neuronal cell adhesion molecules (N-CAMs), membrane glycoproteins vital to normal neural development and maintenance, may lead to defective neuronal migration and/or differentiation. Similar dysmorphic effects are seen following congenital methylmercury (MM) poisoning. The expression and function of N-CAMs were studied in culture to test the hypothesis that MM induces its effects by interfering with N-CAMS. Murine embryonal carcinoma cells differentiated into neurons by treatment with 10(-6) M retinoic acid were exposed to MM (1 - 7.5 uM) for 2 hr on post-commitment day 7. Neurons were then stained with HNK-1 antibody which recognizes N-CAM, and studied by immunofluorescence microscopy. MM treatment resulted in altered distribition of N-CAM on neuronal membranes. N-CAM staining of neurites decreased in a dose-dependent fashion, particularly in peripheral neurites. Loss of N-CAM preceded MM-induced neurite retraction. Perikaryal N-CAM staining was also reduced. Neuron aggregation and neurite fasciculation, processes dependent upon homophilic, homotypic N-CAM binding were markedly impaired by MM, reflecting alterations in membrane adhesion. Removal of MM resulted in reversal of effects on N-CAM staining within 3 hr. These data suggest that MM may alter brain morphogenesis, in part, by perturbing N-CAM dependent cell adhesion.

1012

TITLE:

The effects of organic and inorganic lead and mercury on neurotransmitter high-affinity transport and release mechanisms.

AUTHORS:

BONDY SC
ANDERSON CL
HARRINGTON ME
PRASAD KN

SOURCE:

ENVIRON RES; 19 (1). 1979. 102-111.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The effects of 2 heavy metals upon the high-affinity transport system of certain putative neurotransmitters were studied in adult mouse brain homogenates. C-linked and free ionic forms of Hg and Pb were compared. Tri-n-butyl lead acetate at concentrations as low as 10-6 M severely inhibited the Na-dependent, energy-requiring uptake of a variety of putative neurotransmitters. Dopamine uptake was more affected than other compounds. Ionic Pb (as lead acetate) was several orders of magnitude less toxic than the covalently bound Pb compound. Methylmercuric chloride and mercuric chloride had an intermediate inhibitory effect on

the high-affinity transport system, significant impairment becoming apparent only at around 10-5 M. Both metals stimulated the release of labeled compounds accumulated by high-affinity transport systems in brain homogenates. This stimulation was greater with tributyl lead acetate than with any other compound tested. The effect was independent of and additive to the stimulatory effect of the Ca2+ on neurotransmitter release. Unlike C, heavy metals could effect release of transported compounds in the absence of depolarizing conditions. While Ca-mediated release requires over 0.3 mM Ca2+ to be detected, tributyl lead acetate-mediated release of several putative transmitters was apparent at 5major releasing effects at 5f dopamine was especially strongly affected by covalently bound Pb whose effects could be detected at 10-8 M.

1013

TITLE:

A morphometric analysis of the cerebellum following gestational methylmercury (MeHg) exposure.

AUTHORS:

Flaugher CB
Markowski VP
Rawleigh R
Weiss B
Baggs RB

SOURCE:

Toxicologist 1997 Mar;36(1 Pt 2):14

ABSTRACT:

MeHg may produce neuronal injury by creating an environment of oxidative stress. Glutathione (GSH), a major cellular antioxidant, may combat this oxidative stress by acting as a reducing agent for reactive oxygen species or by conjugating directly with the MeHg via a thiol-mercury interaction. To investigate the interaction between MeHg and GSH, balb/c mice were exposed to 4 ppm MeHgCl in maternal drinking water from gestational day 6 until sacrifice on postnatal day 7, 14, 21, or 30. To confirm that there were MeHg-induced differences in the brains of MeHg-exposed vs control pups, a morphometric investigation was undertaken to examine 5 regions of the cerebellum. Regions 1, 2, 3 and 4 represent the dorsal surface rostral to the rostral side, the caudal side of, and the dorsal surface caudal to the primary fissure, respectively, while Region 5 represents the nodulus. From these regions, the following data were collected and analyzed via 2-way ANOVA: the thickness of the extragranular layer (EGL), intragranular layer (IGL), and molecular layer (ML) and the number of condensed and open nuclei (CN and ON, respectively) within the ML (expressed as nuclei/100,000 u3). Statistically significant differences between treated and control were as follows: Region 1 (R1) showed a main effect of treatment and a treatment-by-age interaction in the EGL and for ON; there

was also a treatment-by-age interaction in R5 for EGL width and for ON. Age was a significant factor in all morphometric measures. In situ hybridization and immunohistochemical studies are continuing in the investigation of GSH metabolism in developing, MeHg-exposed mouse brains because we feel that GSH should react compensatively with MeHg exposure.

1014
TITLE:
Behavioral consequences of a chronic marginal iron deficiency during development in a murine model.

AUTHORS:
Kwik-Uribe CL
Golub MS
Keen CL

SOURCE:
Neurotoxicol Teratol 1998 May/Jun;20(3):366

ABSTRACT:
Marginal iron (Fe) intakes are a common nutritional problem; however, the behavioral consequences of these intakes during development are poorly understood. In this study, Swiss-Webster mice were fed either a control (75 ppm Fe; n = 56) or a marginal Fe diet (12.5 ppm; n = 41) during pre- and postnatal development following a reduction in body iron stores in the dams prior to breeding. On postnatal days (PND) 30, 40, and 50, the animals were subject to a neurobehavioral test battery. The marginal Fe diets had no affect on pregnancy outcome or pup mortality; however, there were significant reductions (10-20%) in body weight in both males and females. At each session, males on the marginal Fe diets responded with a 20-55% reduction in both forelimb and hindlimb strength. Marginal Fe females responded with similar reductions in grip strength; however, by session 3, the hindlimb grip strength of the marginal Fe females was no different than that of control animals. Despite 70-90% lower liver, spleen, and tibia Fe levels in the marginal Fe group, there was no evidence of anemia. Brain Fe was somewhat spared, being only 25-30% lower in the caudate, cerebellum, cortex and brainstem relative to controls. These data are among the first to show that a chronic marginal Fe deficiency during critical periods of brain development can result in behavioral abnormalities even in the absence of anemia.

1015
TITLE:
Occurrence of loosely bound mercury in the blood of guinea pigs treated with methylmercuric chloride.

AUTHORS:
UDA Y

NAKAZAWA Y

SOURCE:
J PHARMACOBIO-DYN; 2 (4). 1979 (RECD. 1980). 245-250.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Guinea pigs were given 203Hg-labeled methylmercuric chloride or mercuric chloride, and the distribution of Hg in the blood, brain and liver was investigated. The methylmercury in the blood and brain was extracted with a chloroform-methanol mixture. Most of the extractable Hg from the blood was detected in the proteolipid fraction by further fractionation. The Hg in the chloroform-methanol extract was also dialyzable against the same solvent. These findings suggest the occurrence of loosely bound Hg in the blood after methylmercury administration.

1016
TITLE:
Intra-uterine growth retardation.

AUTHORS:
Philip AG
Sunshine P

SOURCE:
Fetal and Neonatal Brain Injury: Mechanisms, Management, and the Risks of Practice 1997;2:115-35

1017
TITLE:
Human placenta and embryonic nutrition: importance of environmental and social factors.

AUTHORS:
Miller RK
D'Gregorio RP
Faber W
Asai M
Eisenmann C
Breen J
Czekierdowski A
Jessee L

SOURCE:
Developmental Brain Dysfunction 1994;7:36

ABSTRACT:
The placenta is well known as the conduit for the transfer of the

nutrients (amino acids and carbohydrates) for normal development as well as for the elimination of the waste products. Yet the placenta is also the modulator of the pregnancy, e.g. controlling maternal physiology from being a carbohydrate user to being a fatty acid consumer via human placental lactogen. As part of the modulator role, the human placenta can also be the site for biotransformation of nutrients and drugs to more toxic forms. For years, the study of in utero nutrition and the placenta has concentrated upon small molecules, e.g., amino acids and glucose, to the exclusion of vitamins and in some cases minerals. The transfer and metabolism mechanisms for vitamin A (retinoids) and vitamin B12 (cyanocobalamin) will be examined under in vitro human placental perfusion conditions. Further studies will investigate environmental exposures to metals, e.g. methyl mercury and cadmium, and the importance of dietary and personal habit (smoking) modification to limit exposure to the conceptus utilizing biomarkers of exposure (metal content in blood, tissue and hair) as well as biomarkers of effect (induction of metallothionein). Thus, this presentation will examine the critical role the placenta does play in embryonic nutrition as well as being a site for toxic action.

1018

TITLE:

Developmental neurotoxicity study in rats: a positive control study with dimethylmercury and hydroxyurea.

AUTHORS:

Classen W
Krinke GJ
Weber E

SOURCE:

Neurotoxicology 2001;22(4):530

ABSTRACT:

Dimethylmercury (DMM 6 mg/kg s.c., GD 6-10, group 2; 6 mg/kg s.c., GD 6-10 + 3 mg/kg p.o., PND 1-10; group 3) was administered to mated female Wistar rats. Another group received hydroxyurea (HU 150 mg/kg s.c., GD 9-13). Investigations conducted in pups met the US EPA and OECD test requirements and included: developmental landmarks (opening of eyes, vaginal opening or preputial separation), behavioral ontogeny (surface righting; midair righting, motor activity), functional observational battery, motor activity, startle habituation, passive avoidance, tunnel maze, and neuropathological evaluation (brain weight, histopathology, morphometry). There were no effects on developmental parameters. Behavioral effects observed in offspring of females exposed to DMM were: reduced motor activity at PND 13 and increased activity at PND 60, slightly faster acquisition of a step-through passive avoidance task and improved retention at 24 h retest, higher startle amplitudes at PND 60. Offspring of females exposed to HU developed hydrocephalus leading to early death in

some pups and/or had anophthalmia. During lactation (PND 13, 17, 21) motor activity was increased and female offspring had higher startle amplitudes at PND 60. Both compounds induced morphometric and/or histopathologic changes in cortex, hippocampus and cerebellum. These results demonstrate that study design and test system are adequate to detect a potential developmental neurotoxicity of novel compounds and that a study fulfilling EPA and OECD requirements is technically and logistically feasible.

1019
TITLE:
EFFECTS OF HEAVY METALS ON BRAIN MICRO TUBULES

AUTHORS:
SAKAI S
AIZAWA K
SAITO H
O'HATA S

SOURCE:
32ND ANNUAL MEETING OF THE JAPAN SOCIETY FOR CELL BIOLOGY, KYOTO, JAPAN, NOV. 19-21, 1979. CELL STRUCT FUNCT; 4 (4). 1979 (RECD. 1980). 352.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT CHICK BRAIN TUBULIN MERCURY LEAD ZINC POLYMERIZATION INHIBITION

1020
TITLE:
THE EFFECTS OF METHYL MERCURY BINDING TO MICROTUBULES

AUTHORS:
VOGEL DG
MARGOLIS RL
MOTTET NK

SOURCE:
TOXICOL APPL PHARMACOL 80:473-486,1985

1021
TITLE:
Acute toxicity of methylmercury on glycolytic intermediates and adenine nucleotides of rat brain.

AUTHORS:
PATERSON RA
USHER DR
BISWAS RK
SRETER J

SOURCE:
LIFE SCI PART II BIOCHEM GEN MOL BIOL; 10 (3). 1971 121-128

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ACUTE TOXICITY OF METHYL MERCURY ON GLYCOLYTIC INTERMEDIATES AND ADENINE NUCLEOTIDES OF RAT BRAIN 16056341

1022
TITLE:
Mercury thiocyanate

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:
Data sheet. May enter the body when breathed in and through the skin. May cause "shakes", irritability, sore gums, memory loss, increased saliva, personality change, brain damage, kidney damage, skin allergy and grey skin colour. Irritates the skin and respiratory tract. May damage the eyes.

1023
TITLE:
Mercuric acetate

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:
Data sheet. Can enter the body by inhalation and through the skin. It is a teratogen and should be handled with extreme caution. Mercury poisoning can cause the "shakes", irritability, sore gums, increased saliva, personality changes and permanent brain and kidney damage. May irritate the lungs. May irritate the skin and cause skin allergy and grey skin colour. May irritate and burn the eyes and cause permanent damage.

1024
AUTHORS:
BLAIR A M JN

CLARKE B
CLARKE AJ
WOOD P

SOURCE:
TOXICOLOGY; 3 (2). 1975 171-176

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Squirrel monkeys were dosed intranasally with saline or thiomersal (sodium ethylmercurithiosalicylate, 0.002% w/v) daily for 6 mo. The total amounts of thiomersal fiven during the 6 mo. period were 418 mug (low dose group) and 2280 mug (high dose group). This was equivalent to 207 and 1125 mug Hg. The dose differential was achieved by more frequent administration to the high dose group. Hg concentrations were significantly raised over control values in brain (high dose group only), liver, muscle and kidney, but not in blood. Concentrations were highest in the kidney, moderate in liver and lowest in brain and muscle. Much of the Hg was present in the inorganic form (37-91%). No evidence of toxicity due to thiomersal was seen in any animal. Nevertheless, accumulation of Hg from chronic use of thiomersal-preserved medicines is viewed as a potential health hazard for man.

1025
TITLE:
Distribution and fate of mercury in tissues of human organs in Minamata disease.

AUTHORS:
OKABE M
TAKEUCHI T

SOURCE:
NEUROTOXICOLOGY (PARK FOR SOUTH); 1 (3). 1980. 607-624.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The histochemical distribution and fate of Hg in the nervous system and the other organs were investigated to clarify the neurotoxic factors for pathogenesis of methylmercury poisoning in man. Hg was readily detectable in tissue cells of the brain such as neurons, neuroglial cells and phagocytes and also detected in most organs, particularly in the epithelium of renal tubules, liver cells, epithelium of the thyroid, medullary cells of the adrenal glands, spermatocytes in the testis, epithelium of the pancreas, accessory organs of the skin and epidermis. There were differences in amount of Hg precipitated and its change with time according to the intensity of the lesions and kinds of the organs. There was a great tendency to show a strong residual deposit in the metabolic organs like kidney and liver as well as in the RES while Hg tends to accumulate slowly in the nervous tissues and to remain in them

over longer periods of time. In the brain, the larger the lesion the easier it was to detect Hg by the histochemical method. It was suggested that Hg remaining in the neurons might slowly change during the long course which may result in a gradual decrease of neurons in chronic cases.

1026
TITLE:
Behavioral and biochemical consequences in methylmercury chloride toxicity.

AUTHORS:
ZENICK H

SOURCE:
PHARMACOL BIOCHEM BEHAV; 2 (6). 1974 (RECD 1975) 709-714

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The present experiment was designed to assess the developmental period(s) during which exposure to methylmercury chloride (MMC) would result in permanent learning deficits in rats. In addition, the mercury (Hg) content of the brain at these different stages was measured. Offspring (30 days of age) of mothers exposed during gestation and offspring exposed directly to MMC for 9 days after weaning exhibited the greatest learning deficits on a water escape T maze. These deficits persisted through a retest session 21 days later. Biochemical analysis of brain Hg content indicated that Hg need not be present for these learning deficits to occur.

1027
TITLE:
Hearing: The Effects of Chemicals

AUTHORS:
Rybak LP

SOURCE:
Otolaryngology Head and Neck Surgery, Vol. 106, No. 6, pages 677-685, 48 references, 1992

ABSTRACT:
The effects of exposure to trichloroethylene (79016), xylene (1330207), styrene (100425), hexane (110543), carbon-disulfide (75150), toluene (108883), carbon-monoxide (630080), butyl-nitrite (544161), arsenic (7440382), mercury (7439976), tin (7440315), lead (7439921), and manganese (7439965) on hearing were reviewed. Epidemiological and laboratory animal studies have indicated that trichloroethylene causes hearing loss in occupationally exposed workers and mid to high frequency losses in the brain auditory evoked responses (BAERs) in rats. Xylene and styrene

elevated BAER thresholds in rats following inhalation exposure. Hexane was found to exert primarily neurotoxic effects in both humans and rats. Several epidemiological studies have shown that carbon-disulfide appears to interact with noise to cause sensorineural hearing loss. Laboratory animal experiments indicated that carbon-disulfide had profound effects on BAER latency and amplitude. Epidemiologic and laboratory animal experiments have shown that toluene causes BAER abnormalities. Toluene appeared to interact synergistically with noise to increase the incidence of sensorineural hearing loss. BAER abnormalities have been observed in patients being treated for carbon-monoxide poisoning. Arsenic, the heavy metals, organotin compounds, and manganese have been shown to cause hearing loss or audiometric abnormalities in occupationally and environmentally exposed persons. Butyl-nitrite, used by some drug abusers, has been shown to cause loss of sensitivity to 10 and 40 kilohertz tones in rats.

1028

TITLE:

Toxicological effects of a sublethal concentration of inorganic mercury on the fresh water fish, Tilapia mossambica.

AUTHORS:

PANIGRAHI AK
MISRA BN

SOURCE:

ARCH TOXICOL; 44 (4). 1980. 269-278.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. T. mossambica were exposed to a sub-lethal concentration of 0.5 mg/l of Hg (an industrial pollutant) as HG(NO3)2 in aquaria under controlled laboratory conditions. Main clinical symptoms such as inappetence and ataxia appeared after 2 days of exposure. Blindness was noticed in 60% of the fish after a 10-day exposure. The whole-animal O2 uptake decreased to 27% after an exposure period of 7 days, and remained more or less at this level during the remainder of the 35-day exposure period. When the test fish were transferred to Hg-free, O2-saturated water, the O2 uptake rate recovered to 74% of the initial value. The effects exhibited by the exposed fish were a decrease in protein content, Hb percentage, red blood cell (RBC) count and microhematocrit percentage. A gradual decrease in hematocrit percentage after 1 wk, followed by an increase after 21 days of exposure, was accompanied by an initial enlargement of the RBC, while the subsequent decrease in hematocrit percentage was due to hemolysis of RBC. Hg accumulated more in liver than in brain and muscle, and was depleted more rapidly from the liver than from the brain when the test fish were transferred to Hg-free, O2-saturated water. The physiological and biochemical changes and active metabolic rates were directly related to

the Hg concentrations in the tissues and in the medium.

1029
TITLE:
Reactive Oxygen Species Formation as a Biomarker of Methylmercury and Trimethyltin Neurotoxicity

AUTHORS:
Ali SF
LeBel CP
Bondy SC

SOURCE:
Neurotoxicology, Vol. 13, No. 3, pages 637-648, 41 references, 1992

ABSTRACT:
The formation of reactive oxygen species (ROS) as biomarkers for methylmercury (22967926) (MeM) and trimethyltin (1631738) (TMT) exposure was investigated. Adult C57B1/6N-mice received single doses of 1.0mg/kg MeM or 3.0mg/kg TMT, and CD-rats received single doses of 5.0mg/kg MeM. Mice were sacrificed 48 hours (hr) or one week (wk) after MeM treatment, and 24 and 48hr after TMT treatment. Rats were killed 1wk after MeM treatment. Synaptosomes were prepared from various regions of the brain, and assayed for ROS after incubation with nonfluorescent dichlorofluorescein. Formation of the fluorescent product, dichlorofluorescein (DCF) was monitored by spectrofluorometry. Control assays showed that DCF fluorescence was stimulated by ascorbate or ferrous-sulfate, while deferoxamine inhibited it. Results with the two organometals in-vitro showed that MeM increased the rate of formation of ROS, while TMT was without effect. In-vivo, the rate of ROS formation in both rat and mouse cerebellum increased significantly after MeM treatment. Deferoxamine pretreatment inhibited this increase. In mice, TMT treatment increased ROS formation in the hippocampus and frontal cortex. The authors conclude that the increase in ROS formation in brain areas known to be specifically sensitive to organometals suggests that oxidative mechanisms may beresponsible for the neurotoxic action of these compounds. DCF formation is a sensitive and direct measure of overall oxidative events, and can be used in both in-vitro and in-vivo situations.

1030
TITLE:
(Toxicity of organic mercury compounds: I. Manifestation of the Minamata disease-like symptoms of methoxyethylmercuric chloride.)

AUTHORS:
ISHIKURA S
INOUE N
YONAHA M

SOURCE:
J HYG CHEM; 17 (1). 1971 33-37

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Diet mixed with different organic Hg compounds was fed continuously to dd strain male mice. Hg content in organs was estimated photometrically by the dithizone method after wet digestion of samples with nitric and sulfuric acids. Significant difference was observed in growth curves of mice given methoxyethylmercuric chloride (MEMC) in doses of 1250 and 2500 mu-g Hg/day from that of the control. Specific neural symptoms were observed in almost all the animals. In the case of MEMC, Hg content in the organs was the highest in the liver, followed by the kidney, spleen and brain, in the decreasing order. Accumulation of Hg in the liver increased with an increasing dose. No variation in the amount of accumulated Hg was observed in the kidney. In the case of butylmercuric chloride, accumulation of Hg in the brain was higher than that of MEMC.

1031
TITLE:
Post-mortem findings and clinical signs of dimethyl mercury poisoning in man.

AUTHORS:
PAZDEROVA J
JIRASEK A
MRAZ M
PECHAN J

SOURCE:
INT ARCH ARBEITSMED; 33 (4). 1974 (RECD 1975) 323-328

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A lethal dimethyl Hg poisoning was described in a 28-yr-old chemist who had prepared 6000 g of this compound in the laboratory. Numbness and tingling of the lips, hands and feet developed, as well as ataxia, disturbance of speech, concentric constriction of the visual fields and signs of upper motor neuron lesion. There was no damage to peripheral nerves either in clinical or electromyograph (EMG) examination. The spontaneous daily Hg excretion in urine was 124-142 mug Hg/day. The amount of eliminated Hg was not changed by administration of dimercaptopropanol nor by peritoneal dialysis. Penicillamine, administered at 750 mg/day, increased excretion to 535 mug Hg/day, but with no noticeable clinical effect. Total Hg levels (in mug Hg/g wet weight) were found in various organs as follows: brain 13.2-14.2, kidney 25.6, liver 26.8, spleen 5.4 and muscle 4.67. On post-mortem examination, symmetrical lesions in the cerebral cortex were found, particularly in the

calcarine area. In the cerebellar cortex there was primarily a loss of Purkinje cells. The brain stem and anterior horns of the spinal cord also showed a moderate degree of damage.

1032
TITLE:
STUDIES ON COMBINED EFFECTS OF ORGANO PHOSPHATES AND HEAVY METALS IN BIRDS PART 1 PLASMA AND BRAIN CHOLIN ESTERASE IN COTURNIX QUAIL FED METHYL MERCURY AND ORALLY DOSED WITH PARATHION =56382 =502396/

AUTHORS:
DIETER MP
LUDKE JL

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 13 (3). 1975 257-262

ABSTRACT: HEEP COPYRIGHT: BIOL ABS.

1033
TITLE:
Residues of environmental pollutants and necropsy data for eastern USA ospreys (Pandion haliaetus), 1964-1973.

AUTHORS:
WIEMEYER SN
LAMONT TG
LOCKE LN

SOURCE:
ESTUARIES; 3 (3). 1980. 155-167.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Thirty-three ospreys (P. haliaetus) that were found dead or moribund in the eastern USA between 1964-1973 were necropsied. The brains and carcasses of 26 of these birds were analyzed for organochlorines. The livers of 18 and the kidneys of 7 were analyzed for selected metals. Most adults were recovered in April and May and most immatures were recovered in Aug.-Oct. The adult sex ratio was highly unbalanced in favor of females. Major causes of mortality were impact injuries, emaciation, shooting and respiratory infections. Of special interest were 2 birds with malignant tumors and one with steatitis. Many birds had undergone marked weight losses resulting in mobilization and redistribution of organochlorine residues. Organochlorines were detected in the birds at the following percentages: DDE 100%, polychlorinated biphenyls 96%, DDD 92%, dieldrin 88%, chlordanes (including nonachlors) 82%, DDT 65% and heptachlor epoxide 38%. Organochlorine levels tended to be higher in adults than in immatures. One adult from South Carolina had a

potentially dangerous level of dieldrin in its brain, which might have contributed to its death. Immature ospreys from Maryland had extremely elevated levels of Cu in their livers compared with immatures from other areas and all adults. One immature from Maryland had an elevated As level in its liver, which might have contributed to its death. One adult from Florida that had died of impact injuries had potentially dangerous levels of Hg in both liver and kidney and slightly elevated levels of Cd in these tissues. Additional birds appeared to have been exposed to contamination of the environment by As and Hg. The levels of Cr, Zn and Pb in livers appeared normal.

1034
TITLE:
EFFECTS OF METHYL MERCURY ON DNA SYNTHESIS OF HUMAN FETAL ASTROCYTES A RADIOAUTOGRAPHIC STUDY

AUTHORS:
CHOI BH
CHO KH
LAPHAM LW

SOURCE:
BRAIN RES; 202 (1). 1980. 238-242.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. NOTE CULTURE CENTRAL NERVOUS SYSTEM CELL DEATH BRAIN BODY WEIGHT REDUCTION ELECTRON MICROSCOPY IMMUNO HISTOCHEMISTRY

1035
TITLE:
Tissue distribution of mercury in normal and abnormal young common terns (Sterna hirundo).

AUTHORS:
GOCHFELD M

SOURCE:
MAR POLLUT BULL; 11 (12). 1980 (RECD. 1981). 362-366.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Sixteen young common terns (S. hirundo) from colonies on the south shore of Long Island, New York (USA), had fairly consistent levels and tissue distribution patterns of total Hg in blood, liver, kidney, muscle, brain and feathers. Levels were highest in liver, blood and feathers and were lower in muscle and brain. The latter 2 tissues showed low variability across birds, suggesting that they were more static repositories for Hg compounds. Only slight, non-significicant increases were detected in chicks 10-30 days old compared with 1-9 day

olds. Four chicks with abnormal feather loss had significantly higher Hg levels than 12 normal chicks. Average intercorrelation among tissues was highest for liver (mean r2 = 0.40) and blood (mean r2 = 0.38). Liver was probably the single best tissue to serve as a surrogate for all others, due to high correlation with other tissues, large size and ready availability.

1036
TITLE:
Neurophysiologic and behavioral toxicologic testing to detect subclinical neurologic alterations induced by environmental toxicants.

AUTHORS:
VanGelder GA
Carson TL
Smith RM
Buck WB
Karas GG

SOURCE:
J. Amer. Vet. Med. Ass. 163(9): 1033-1035; 1973(REF:13)

ABSTRACT:
PESTAB Development of adequate methods for the assessment of the dynamic functioning of the nervous system in the intact organism is one of the major challenges of medical research. Historically, the measurement of reflexes and spontaneous brain electrical activity have been used. More recently, nerve conduction tests and quantitative electromyography have been used in clinical and public health situations. Behavioral toxicology is a relatively new specialty that combines the resources of the experimental psychologist and the toxicologist in determining the deleterious effects of drugs and chemicals on behaviors such as learning or memory. Examples are given of the effects of lead and organophosphorus insecticides on peripheral nerve functioning. Experiments are also reviewed that demonstrate the effect of low-level prenatal exposure to mercury and lead on postnatal behavior. The effect of low-level dieldrin exposure on learning behavior in squirrel monkeys is cited as another example of the recent contribution of behavioral toxicology toward a fuller understanding of the effect of common environmental neurotoxicants on brain functioning. (Author abstract by permission)

1037
TITLE:
Computed Tomography in Fetal Methylmercury Poisoning

AUTHORS:
Hamada R

Yoshida Y
Nomoto M
Osame M
Igata A
Mishima I
Kuwano A

SOURCE:
Journal of Toxicology, Clinical Toxicology, Vol. 31, No. 1, pages 101-106, 9 references, 1993

ABSTRACT:
The findings of cerebral computed tomography of patients with fetal methylmercury (22967926) poisoning were reported. The brains of eight young adult patients with histories of transplacental exposure to methylmercury were examined using computed tomography. Neurological alterations were observed in all of the patients. The changes identified included enlargement of cerebral fissures or sulci with or without prominent cisterns along with mild ventricular enlargement. No association could be identified between daily living activities and ventricular enlargement; however, the nonambulatory patients demonstrated the greatest degree of enlargement of longitudinal or Sylvian fissures. One patient demonstrated cavum septi pellucidi, four had enlarged frontal sinuses, and three had increased skull thickness. Compared with the clinical features of the patients, the computed tomographic findings were thought to be mild and indistinct from those associated with cerebral palsy.

1038
TITLE:
Acetylcholinesterase Fluctuations in Central Nervous System of Rat during Methylmercury Intoxication and Chelation Therapy

AUTHORS:
Sood PP
Raghu KG
Bapu C
Vijayalakshmi K

SOURCE:
Journal of Environmental Pathology, Toxicology and Oncology, Vol. 12, No. 3, pages 149-154, 23 references, 1993

ABSTRACT:
This study examined the acetylcholinesterase (AChE) activity in various brain areas during intoxication with methylmercury-chloride (115093) (MMC) to determine if any chelator is able to reinstate the enzymatic level of AChE. Male Wistar-albino-rats were injected intramuscularly with 1mg/kg

and 10mg/kg in two separate sets of animals. The animals were injected over 2, 7, or 15 days. Antagonist treated groups received N-acetyl-DL-homocysteine-thiolactone (NAHT), glutathione (GSH), D-penicillamine,or sodium-selenite 30 minutes after MMC administration. The rats were killed on day three, eight, or 16. The brains were removed and divided into olfactory bulbs, cerebral hemispheres, cerebellum, and medulla oblongata for separate analyses. The degree of AChE activity was determined. After 2 days of treatment with MMC, only a negligible effect was noted on AChE activity. A linear inhibition of the enzyme was observed with increased dosage and duration of MMC administration, which was constant in all the anatomical areas. A slightly stronger enzymatic inhibition was observed with 10mg/kg doses as compared to 1mg/kg. The maximum inhibition of the enzyme after the high dose of MMC was noted on the fifteenth day in the olfactory bulbs, and the minimum in the cerebellum. The low dose MMC caused the maximum inhibition in the spinal cord and the minimum in the cerebral hemispheres during the same time period. The applications of the antagonists showed different effects in different central nervous system regions. However, none of the antagonists demonstrated an appreciable recovery in the AChE level in any of the animal groups, with the exception of GSH and NAHT to some extent. The authors suggest that a search for more effective antagonists to methylmercury (22967926)should be made.

1039

TITLE:

Anodic Stripping Voltammetric Determination of Total Lead in Anencephalic Fetuses after Pressureemperature-Controlled Microwave Mineralization

AUTHORS:

Tahan JE
Marcano L
Romero RA

SOURCE:

Analytica Chimica Acta, Vol. 317, Nos. 1-3, pages 311-318, 22 references, 1995

ABSTRACT:

An anodic stripping voltammetric method for determining lead (7439921) in anencephalic fetuses was developed. The method was developed because of the relatively high anencephaly rate, 5.1 cases per 1,000 births, occurring along the eastern coast of Lake Maracaibo, Venezuela, attributed to high levels of environmental lead pollution. Brain, liver, kidney, and lung fetal tissues, approximately 50 milligrams, after lyophilization were mineralized by digesting them in 8 milliliters (ml) concentrated perchloric-acid in a pressure sealed vessel in a microwave oven for 16 minutes. Microwave irradiation produced a pressure and temperature of 1,260 kilopascals and 190 degrees-C. After cooling to ambient

temperature, the samples were transferred to 50ml polypropylene flasks and diluted to volume with 6 molar acetate buffer. Eight to 10ml aliquots were then analyzed for lead by differential pulse anodic stripping voltammetry (DPSAV) using a hanging drop mercury electrode and a silver/silver-chloride electrode as the reference electrode. The analytical signal was a lead oxidation peak that appeared at -0.45 volts. Calibration plots constructed from analyses of standard solutions were linear up to 100 micrograms (microg) per liter (l) lead. The detection limit was 0.1microg/l, equivalent to 0.03microg per gram (g) lead in a solid sample. Six replicate determinations of kidney tissues that contained 1.5 and 1.3microg/g lead produced relative standard deviations of less than 3.8%. The method was applied to determining lead in brain, kidney, and lung samples from 20 anencephalic and 20 control fetuses. Parallel analyses were performed using electrothermal atomization atomic absorption spectrometry (ETA) for comparison purposes. Dry weight lead concentrations in the anencephalic fetal tissues determined by DPSAV ranged from 0.6 to 2.1microg/g. Lead concentrations in the control tissues varied from 0.5 to 1.5microg/g. The DPSAV data were well correlated with the results obtained by ETA/AAS. The authors conclude that the DPSAV method is a reliable alternative to ETA/AAS for determining lead in solid samples.

1040
TITLE:
Uptake and localization of mercury in the brain of rats after prolonged oral feeding with mercuric chloride.

AUTHORS:
BRUN A
ABDULLA M
IHSE I
SAMUELSSON B

SOURCE:
HISTOCHEMISTRY; 47 (1). 1976 23-29

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Uptake and localization of Hg was studied in rats orally intoxicated with inorganic Hg. By atomic absorption spectrophotometry large quantitative differences were found between test and control animals, particularly relating to blood, kidney and brain. By histochemical demonstration of heavy metals the uptake in the CNS was shown to occur particularly within the cytoplasm of large neurons in the cortex, pons and basal ganglia but also in other neurons, to some extent in the choroid plexus and the vessel walls, and least in the white matter. No lesions were detectable by light microscopy. The Hg was mostly in the methylated form, something that may be explained by gastrointestinal methylation by bacteria. A similar mechanism can be expected in human

chronic inorganic Hg poisoning. (The unlimited use of various Hg compounds as fungicides during the last 30 yr has resulted in widespread contamination of this metal in the environment.)

1041
TITLE:
Some properties of the organomercury-degrading system in mammalian liver.

AUTHORS:
Lefevre PA
Daniel JW

SOURCE:
FEBS (Fed. Eur. Biochem. Soc.) Lett.35(1): 121-123; 1973(REF:6)

ABSTRACT:
PESTAB Tissue homogenates of rat and guinea pig liver, brain, and kidney were studied for their ability to degrade a variety of organomercury compounds to inorganic mercury. All three tissues from both species were able to degrade phenylmercury acetate (PMA), methyoxyethylmercury chloride (MEMC), and PCMB; the guinea pig brain tissues were unable to degrade MEMC and PCMB. The variation in activity of the liver preparations toward all three substrates indicates the presence of at least two systems capable of effecting cleavage of the C-Hg bond. Fractionation of the components in the soluble fraction of the rat liver tissues indicates the presence of high and low molecular weight components, the effects of which are nonadditive. One, a high molecular weight component, was detected in the guinea pig liver. The PMA-degrading activity of the hepatic system was markedly stimulated by the addition of dithiothreitol or 2-mercaptoethanol, but not of other sulfhydryl compounds. Ethylene, benzene, and benzoic acid were products of the reaction with MEMC, PMA, and PCMB, respectively.

1042
TITLE:
Health problems associated with organomercurials.

AUTHORS:
Pazderova J
Cikrt M

SOURCE:
Prac. Lek.25(6): 252-258; 1973(REF:36)

ABSTRACT:
PESTAB. The increasing use of mercury has led to severe contamination of rivers and lakes. Under anaerobic conditions (eutrophic lakes), Hg is mostly insolubilized as HgS, while under aerobic conditions (oligotrophic

lakes), highly toxic alkylmercury is formed, especially at low pH. In man and animals, the less toxic PhMgCl and MeOEtHg SUP+ are found mainly in the liver and kidneys, while the highly toxic MeHgCl and EtHgCl are found in the liver and in the brain; MeHg SUP+ easily crosses the blood-brain and placental barriers. PhHg SUP+ excretion is fairly rapid (50% via digestive tract, remainder mainly via urine). Elimination of alkylmercury is very slow, partly due to its high enterohepatic circulation; interruption of this circulation by administration of synthetic resins containing SH groups is under investigation. The authors have been able to increase elimination of Me(SUB)2HG by administering penicillamine. Alkylmercury compounds principally attack the central nervous system, affecting mainly the cerbral cortex (degeneration of neurons); the basal ganglia are also attacked. Demyelination in the peripheral nervous system is not authenticated. Chromosomal changes have been found in the lymphocytes of patients; genetic effects have not been proven but are suspected. In occupational exposure, PhHgCl has been found in the blood and urine, without signs of clinical intoxication. An international committee has recommended the following maximum allowable concentrations in the atmosphere of the working area: 0. 05 Hg vapor/m(SUP)3, 0. 10 mg PhHg/m(SUP)3; no safe limit for MeHg SUP+ . The Hg concentration in the blood of exposed persons should not exceed 10 mug Hg/100 ml. Fish used for human consumption must not contain more than 0. 03 mg Hg.

1043

TITLE:

Serial Changes in Tissue Carbon Dioxide Content During Acute Respiratory Acidosis

AUTHORS:

Nichols G Jr

SOURCE:

Journal of Clinical Investigation, Vol. 37, pages 1111-1122, 35 references, 19581958

ABSTRACT:

An experiment was conducted to discover where carbon-dioxide (124389) (CO2) is stored in the body and what effect this storage has on the acid base balance of various tissues. Male albino-Wistar-rats and Sprague-Dawley-rats were exposed to an atmosphere of 24 percent CO2 for 30 minutes to 48 hours. Animals were then sacrificed and samples of muscle, brain, and bone were obtained and analyzed for total CO2 content. Whole blood CO2 was also determined. All rats showed hyperpnea and moderate to marked lethargy intermixed with periods of restlessness. Exposure to 24 percent CO2 produced a profound respiratory acidosis with a raise in arterial CO2 pressure and total plasma CO2. The CO2 pressure rose in the first 30 minutes from 36.3 to 180 millimeters of mercury and did not vary

significantly for the remainder of the experiment. Also after 30 minutes, plasma pH changed from 7.47 to 6.92. After 48 hours the plasma pH was 7.10. Total plasma CO2 rose consistently throughout the experiment from 26.7 to 63.9 millimoles per liter after 48 hours. Total CO2 found in muscle tissue reached a peak after 5 hours, rising from 11.7 to 28.1 millimoles per kilogram (mM/kg) of tissue. CO2 in brain tissue followed a similar pattern, rising from 12.7 to 32.5mM/kg; however, bone CO2 content remained the same or declined slightly throughout the experiment. The author concludes that under the conditions of this experiment, carbon-dioxide is stored in soft tissues rather than in bones.

1044

TITLE:

Induction of Growth Arrest and DNA Damage-Inducible Genes Gadd45 and Gadd153 in Primary Rodent Embryonic Cells Following Exposure to Methylmercury

AUTHORS:

Ou YC
Thompson SA
Kirchner SC
Kavanagh TJ
Faustman EM

SOURCE:

Toxicology and Applied Pharmacology, Vol. 147, No. 1, pages 31-38, 43 references, 1997

ABSTRACT:

The effects of methylmercury (22967926) on Gadd gene expression in rodent embryo cell cultures were examined. Cultures of embryonic midbrain (central nervous system (CNS)) and limb bud (LB) cells prepared from 12.5 day old embryos obtained from pregnant Sprague-Dawley-rats were incubated with 0 to 3 micromolar (microM) methylmercury-hydroxide (1184572) (MMOH) for up to 5 days. Cytotoxicity was assessed using the neutral-red dye uptake assay. The effects on cell differentiation measured in CNS cells were assessed by the sulfated proteoglycan/alcian-blue dye staining test. The RNA was extracted from CNS and LB cells and analyzed for expression of Gadd45 and Gadd153 mRNA by a Northern blotting technique. Four week (wk) old female C57BL/6-mice were administered 0, 3, or 10 parts per million (ppm) methylmercury as MMOH in their drinking water for 4wk. At the end of the 4wk exposure period, the animals were killed and the brain, liver, and kidneys were removed. The RNA was extracted from the organs and assayed for expression of Gadd45 and Gadd153 as before. MMOH induced dose related cytotoxicity in CNS and LB cells, the effect being more pronounced in CNS cells. The 1microM dose caused a 84.0% decrease in differentiation of CNS cells after 1 day. MMOH caused concentration related increases in expression of Gadd45 and Gadd153 mRNA in both cell types. The increases

were greater in LB cells following treatment with 1microM MMOH, but greater in CNS cells following treatment with 2microM MMOH. In-vivo, MMOH at 10ppm caused significant increases in Gadd45 mRNA expression in the brain, kidney, and liver. Little if any induction of Gadd153 mRNA was seen in these tissues. The authors conclude that methylmercury increases the level of Gadd45 and Gadd153 expression. Since Gadd genes are known to be involved in cell cycle arrest, activation of Gadd45 and Gadd153 could represent one mechanism by which methylmercury interferes with the cell cycle in adult and developing organisms.

1045
TITLE:
Effects of sodium selenite on distribution and placental transfer of mercuric mercury in mice of late gestational period.

AUTHORS:
SATOH H
SUZUKI T
NOBUNAGA T
NAGANUMA A
IMURA N

SOURCE:
J PHARMACOBIO-DYN; 4 (3). 1981. 191-196.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg distribution and placental transfer in mice were investigated with coadministration of selenite. Pregnant mice, s.c. injected with 1.5 or 15.0 mumol/kg of HgCl2 and 0, 1.3, 12.7 or 25.3 mumol/kg Na2SeO3 on day 16 of gestation, were examined for tissue distribution of Hg 24 h after treatment. Elevated Hg concentrations in blood were found with increasing doses of selenite at the 2 dose-levels of Hg. Decreased accumulation of Hg with increased doses of selenite was found in kidneys and brain. In the liver, the largest amount of Hg was accumulated by approximate-equimolar combinations of doses. The amount of Hg transferred to the fetus was reduced in groups injected with 12.7 mumol/kg of selenite at the 2 dose-levels of Hg. In groups injected with higher dose of Hg, in which fetal organs were measurable for Hg, fetal brain, liver or kidneys of the group of selenite 12.7 mumol/kg contained the least amount of Hg among groups. All mice injected with 15.0 mumol/kg Hg and 25.3 mumol/kg selenite aborted before sacrifice.

1046
TITLE:
Mercury toxicity: Biochemical and physiological alterations in 9 freshwater teleosts.

AUTHORS:

SHAFFI SA

SOURCE:
TOXICOL LETT (AMST); 8 (3). 1981. 187-194.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Fish species (Labeo rohita, Cirrhina mrigala, Catla catla, Heteropneustes fossilis, Clarias batrachus, Mystus seenghala, Channa striatus, C. punctatus, C. marulius) were subjected to various concentrations (5, 10, 15 and 20 ppm) of mercuric nitrate for 4.5 h. The relationship between concentrations of mercuric nitrate and the fall in renal glycogen was inverse. There was an elevation in liver and muscle glycogen at 5 ppm Hg. Brain glycogen increased to < 10 ppm and then decreased. Glucose and lactate levels increased with increasing concentration of Hg and muscle, liver, kidney and brain glycogen decreased. Effects were more marked in major carp than in other species.

1047
TITLE:
Prenatal and lactational exposure to methylmercury affects select parameters of mouse cerebellar development.

AUTHORS:
MARKOWSKI VP
FLAUGHER CB
BAGGS RB
RAWLEIGH RC
COX C
WEISS B

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 19 (6). 1998. 879-892.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Animal studies of the neuropathological effects of prenatal methylmercury (MeHg) seldom use regimens that represent environmental exposures. While acute administration of high doses of MeHg to developing rodents can model some of the outcomes MeHg produces in the human cerebellum, their long-term relevance to cerebellar development is unknown. The present study was undertaken to determine the effect of chronic dietary exposure to MeHg. Pregnant mice were exposed throughout gestation to 0.0 or 4.0 ppm methylmercury in their drinking water. Postpartum exposure of pups and lactating dams continued to postnatal day (PND) 30. On PND7, 14, 21, and 30, several morphometric indices of cerebellar cortex development, as well as blood and brain levels of total Hg, were measured in pairs of male and female littermates. No signs of overt toxicity were observed in the dams or offspring. Blood and brain levels of total Hg were highest in the exposed PND7 offspring

and fell throughout

1048
TITLE:
Life Span and Fine Structural Changes in Oxygen-Poisoned Drosophila Melanogaster

AUTHORS:
Philpott DE
Bensch KG
Miquel J

SOURCE:
Aerospace Medicine, Vol. 45, No. 3, pages 283-289, 34 references, 19741974

ABSTRACT:
Toxicological study of the response of cells to high oxygen tensions which are known to increase lipid peroxidation, to determine the effect of oxygen toxicity on human tissues and animal tissues exposed to artificial atmospheres in diving, aviation, and space vehicles and space suits, and also to get a better understanding of the mechanism of aging. Data are given for the effect of 100% oxygen at 254 millimeters and 760 millimeters of mercury on the longevity of drosophila-melanogaster. Exposure of the flies to 100% oxygen results in loss of vitality and shortening of lifespan. In flies exposed to oxygen for 4 days, electron microscope observation reveals striking brain degeneration and accumulation of dense bodies in other tissues. The fine structural changes suggest that the oxygen poisoning of Drosophila shares some of the characteristics of both accelerated aging and specific attack upon the central nervous system.

1049
TITLE:
The Effect of Carbon Dioxide on Cerebral Blood Flow and Cerebral Metabolism in Dogs

AUTHORS:
Alberti E
Hoyer S
Hamer J
Stoeckel H
Packschiess P
Weinhardt F

SOURCE:
British Journal of Anaesthesia, Vol. 47, pages 941-947, 45 references, 19751975

ABSTRACT:

The effects of changes in arterial carbon-dioxide (124389) tension (PaCO2) on cerebral blood flow (CBF) and oxidative metabolism of the brain were studied in dogs. The dogs were tested under normal conditions, in a state of hypercapnia induced by adding 5 to 7 percent carbon-dioxide to the inspired air, and in a state of hypocapnia induced by hyperventilation. In each state, measurements included PaCO2, CBF, and cerebral metabolic rates and arterial/venous differences for oxygen, carbon-dioxide, glucose, and lactate. From a norm of 36.5 millimeters mercury (mm Hg), PaCO2 rose to 64.7mm Hg in hypercapnia, and fell to 17.8mm Hg in hypocapnia. Hypercapnia increased CBF to 115.7 milliliters per 100 grams per minute from a norm of 61.0, but produced no other significant effects. Hypocapnia decreased CBF to 33.9ml/100g per minute and produced increases of 80 to 90 percent in arterial/venous concentrations for oxygen and glucose, and in venous/arterial concentrations for carbon-dioxide and lactate. No significant changes occurred in cerebral metabolic rates. The authors concludes that hypocapnia produces increased glycolysis in the brain, but this glycolysis may be related to a pH regulatory mechanism rather than to tissue hypoxia.

1050
TITLE:
Methyl mercury binding substances from the brain of experimentally exposed squirrel monkeys (Saimiri sciureus).

AUTHORS:
WINROTH G
CARLSTEDT I
KARLSSON H
BERLIN M

SOURCE:
ACTA PHARMACOL TOXICOL; 49 (3). 1981. 168-173.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Squirrel monkeys were given a single subtoxic dose of 203Hg-labeled methyl mercuric hydroxide. After 3 wk the brains were dissected, homogenized and separated into particulate and soluble fractions by ultracentrifugation. The soluble fractions were further separated into high and low MW components by ultrafiltration. The major part (75%) of the radioactivity was associated with the particulate fraction; high MW compounds in the soluble fraction accounted for 16%. The remainder (9%) was bound to glutathione.

1051
TITLE:
Influence of different doses of mercury on its location in the animal organism.

AUTHORS:
KOSSAKOWSKI S
GROSICKI A
DZIURA A

SOURCE:
MED WETER; 41 (9). 1985 (RECD. 1986). 515-518.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The examinations were carried out on 150 rats (Wistar breed) which were given a radioactive solution of 203HgCl2 orally in a dose of 1, 6, 12, 18, and 24 mg/kg of body weight. The solution was prepared in this way that each 0.5 ml of a Hg sol. contained trace amounts of radioisotope 203Hg/ of radioactivity = 16.7 kBq. Five animals of each group were anesthetized after 3 and 6 hours, 1, 2, 4, and 8 days. The samples of the stomach, jejunum and colon (without a content), liver, kidneys, spleen, heart, skeletal muscles, blood, lungs, brain, testicles, prostate and skin were taken for examinations. The findings indicated that the location of Hg in the organs using the mentioned doses were not changed. The highest amounts of Hg were recorded in the kidneys, liver and spleen, and the lowest in the skeletal muscles and brain. The concentration of Hg in the organs increased along with the doses of Hg, however, the per cent content in all the organs exceeded the per cent increas

1052
TITLE:
Toxicity For Cats Of Methylmercury In Contaminated Fish From Swedish Lakes And Of Methylmercury Hydroxide Added To Fish

AUTHORS:
Albanus L
Frankenberg L
Grant C
Von Haartman U
Jernelov A
Nordberg G
Rydalv M
Schutz A
Skerfving S

SOURCE:
Environmental Research, Vol. 5, No. 4, pages 425-442, 34 references, 19721972

ABSTRACT:
The effects of methylmercury (22967926) (MM) accumulated in fish were studied in cats. Cats were fed homogenates from pike caught in a lake

that had been contaminated with phenylmercury-acetate (62384). Trace amounts of labeled methylmercury-hydroxide (1184572) (MMH) had been sprayed on the fish during blending. Homogenates from uncontaminated pike to which labeled MMH had been added were fed to another group of cats. MM concentrations in both fish homogenates were estimated to be 6 milligrams per kilogram (mg/kg), and the cats were estimated to have ingested 0.45 to 0.47mg/kg mercury (7439976) (Hg) per day. Controls were fed uncontaminated pike for 55 days, and the exposed cats were fed until the onset of symptoms of Hg poisoning. The cats were killed when they showed definite signs of poisoning (usually convulsions) and were autopsied. Gross and histopathological studies were conducted. Distribution of Hg in the tissues was determined. The onset of Hg poisoning symptoms occurred within 60 to 83 days. Pathological effects were limited to the central and peripheral nervous systems. They consisted of degenerative changes in the granular layer of the cerebellar cortex, the peripheral nerves and their dorsal roots, and the cerebral cortex. The Hg was widely distributed in the tissues, and the distribution between the two experimental groups was similar. Fifty eight percent of the whole body burden of Hg was in the pelt; only 1 percent was in the brain. Approximately 100 percent of the Hg was in the form of MM in the brain and muscles, whereas 80 and 62 percent of the Hg was in the form of MM in the liver and kidneys, respectively. The authors conclude that the use of MM salts appears to be relevant in assessing the toxicity of MM in fish.

1053
TITLE:
EFFECTS OF HEAVY METALS ON MONO AMINE UPTAKE AND RELEASE IN BRAIN SYNAPTOSOMES AND BLOOD PLATELETS

AUTHORS:
KOMULAINEN H
TUOMISTO J

SOURCE:
SATELLITE SYMPOSIUM ON ENVIRONMENTAL NEUROTOXICOLOGY: ASSESSMENT OF NERVOUS SYSTEM AND BEHAVIORAL DYSFUNCTION HELD AT THE 1ST WORLD CONGRESS OF THE INTERNATIONAL BRAIN RESEARCH ORGANIZATION, DUSSELDORF, MARCH 29-31, 1982. NEUROBEHAV TOXICOL TERATOL; 4 (6). 1982 (RECD. 1983). 647-650.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM HUMAN RAT COPPER MERCURY TOXICITY IN-VITRO STUDY

1054
TITLE:
EFFECT OF SELENIUM ON THE BODILY DISTRIBUTION OF MERCURY IN RATS

AUTHORS:

NAKANO A
ANDO T
YANAGIHASHI T
TOMARI T

SOURCE:
ACTA MED UNIV KAGOSHIMA; 29 (2). 1987. 55-66.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM METHYLMERCURY TOXICITY SELENITE SELENATE ANTIDOTE-DRUG PROTECTIVE EFFECT BRAIN LEVEL INCREASE LIVER KIDNEY BLOOD-BRAIN BARRIER PERMEABILITY FISH ENVIRONMENTAL POLLUTION

1055
TITLE:
DEVELOPMENTAL DISTURBANCES OF THE FETAL BRAIN IN GUINEA-PIGS CAUSED BY METHYLMERCURY

AUTHORS:
INOUYE M
KAJIWARA Y

SOURCE:
ARCH TOXICOL; 62 (1). 1988. 15-21.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN MORPHOLOGICAL CHANGES CEREBRAL CORTEX NUCLEUS CAUDATUS PUTAMEN HIPPOCAMPAL FORMATION HISTOLOGIC ARCHITECTURE DYSGENETIC HYDROCEPHALUS

1056
TITLE:
METHYL MERCURY UPTAKE ACROSS BOVINE BRAIN CAPILLARY ENDOTHELIAL CELLS IN-VITRO THE ROLE OF AMINO ACIDS

AUTHORS:
ASCHNER M
CLARKSON TW

SOURCE:
PHARMACOL TOXICOL; 64 (3). 1989. 293-297.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BLOOD-BRAIN BARRIER CYSTEINE

1057
TITLE:
Effect Of Arginine Vasopressin, Acetazolamide, And Angiotensin II On CSF

Pressure At Simulated Altitude

AUTHORS:
Senay LC Jr
Tolbert DL

SOURCE:
Aviation, Space, and Environmental Medicine, Vol. 55, No. 5, pages 370-376, 18 references, 19841984

ABSTRACT:
The effects of arginine-vasopressin (113791), acetazolamide (59665), and angiotensin-II (11128997) on cerebral spinal fluid pressures at simulated high altitudes were studied in rats and rabbits. The lateral ventricles of male New-Zealand-rabbits and Brattleboro-rats were cannulated bilaterally. Arginine-vasopressin, acetazolamide, or angiotensin-II were administered in unspecified amounts intraventricularly or intraarterially and the effects on cerebral spinal fluid pressure at ambient pressures, 744 to 755 millimeters of mercury (mm Hg), and reduced pressures, 390 to 356mm Hg, were measured. Pressures of 356 to 390mm Hg were equivalent to altitudes of 2438 to 5486 meters. The animals were exposed to the hypobaric pressures for up to 6 hours. Administration of angiotensin-II was preceded in some experiments by administration of saralasin (34273104). Brain water content and arginine-vasopressin concentrations of the cerebral spinal fluid were determined before and after exposure to the hypobaric pressures. Exposure to simulated high altitudes had no significant effect on the brain water content and the concentration of arginine-vasopressin in cerebral spinal fluid. Intraarterial injection of acetazolamide reduced cerebral spinal fluid pressure at ambient and reduced barometric pressures, whereas intravenous administration had no effect. Arginine-vasopressin when administered at ambient pressures generally decreased the cerebral spinal fluid pressure. When given at hypobaric pressures, the cerebral spinal fluid pressure generally increased. Administration of angiotensin-II elevated the cerebral spinal fluid pressure at both ambient and reduced pressures. When angiotensin-II was preceded by saralasin, the rise in pressure was prevented. The authors conclude that exposure of humans to high altitudes causes fluid shifts and loss of body water. Such loss may trigger production of angiotensin-II, increasing the cerebral fluid pressure. In conjunction with hypoxia, this could contribute to the syndrome of acute mountain sickness.

1058
TITLE:
Brain Lesions In Experimental Methyl Mercury Poisoning Of Squirrel Monkeys (Saimiri Sciureus)

AUTHORS:

Zook BC
Wilpizeski CR
Albert EN

SOURCE:
Animals as Monitors of Environmental Pollutants, National Academy of Sciences, Washington, D.C., pages 151-164, 38 references, 19791979

ABSTRACT:
Neuropathological changes induced by methylmercury (22967926) were studied in monkeys. Methylmercury-chloride (115093) or methylmercury-hydroxide (1184572) was administered orally in doses of 0.12 to 0.74 milligram per kilogram daily to 10 squirrel-monkeys. The purpose of the study was to evaluate vestibular and auditory functions in animals chronically exposed to methylmercury. The animals developed severe signs of neurotoxicity (ataxia, incoordination, abnormal gait, and blindness) within 46 to 98 days, however, and all died or became moribund within the next 4 to 23 days. The brains were removed and examined for pathological changes. The cerebral cortex was severely affected. Cortical lesions consisted primarily of necrosis and disappearance of small granular neurons, and gliosis. Perivascular cuffing and rarefaction of the neuropil were observed. In the cerebral cortex, the most affected areas were, in decreasing order of importance, the striate, pre striate, and temporal cortices of the occipital lobes. The cerebellum was not affected. The authors conclude that squirrel-monkeys fed methylmercury for 50 to 102 days develop neurological signs and cerebral cortical lesions similar to those seen in humans. Unlike humans, the cerebellar cortex is not affected.

1059
TITLE:
Neurotoxic Actions Of Methylmercury On The Primate Visual System

AUTHORS:
Merigan WH
Maurissen JPJ
Weiss B
Eskin T
Lapham LW

SOURCE:
Neurobehavioral Toxicology and Teratology, Vol. 5, No. 6, pages 649-658, 18 references, 19831983

ABSTRACT:
The effects of methylmercury (22967926) on the visual system were investigated in Macaca-nemestrina-monkeys and macaca-arctoides-monkeys. Visual field testing, visual thresholds, spatial contrast sensitivity,

temporal modulation sensitivity, and a visuomotor task were performed. Monkeys were given oral doses of 0.24, 0.3 or 1 milligram per kilogram (mg/kg) methylmercuric-chloride (115093) 2 times per week for 20 to 73 weeks. Mean blood concentrations ranged from 1.56 to 3.1 parts per million (ppm). Monkeys were sacrificed and eyes and brains were examined. A monkey given 1mg/kg methylmercuric-chloride for 20 weeks, with a mean blood concentration of 3.1ppm showed a stable, bilateral concentric constriction of visual fields. Animals with mean blood concentrations of 1.62 and 1.99ppm became acutely ill. Progressive visual field loss occurred before death; loss was not concentric, with greatest loss appearing in superior visual field. Monkeys with mean blood concentrations of 1.56, 1.81, and 2.08ppm showed a transitory field loss that partially resolved when exposure was interrupted. Visual threshold in the animal with blood concentration of 3.1ppm showed selective impairment of temporal modulation sensitivity, reduced low luminance flicker sensitivity and high frequency flicker resolution. Severe tremors were observed in monkeys with mean blood concentrations of 3.1 and 1.81ppm. Monkeys differed dramatically in their ability to perform the visuomotor task. The animal given the highest dose showed marked cortical atrophy in the occipital region, particularly the cortex within the calcarine fissure. Marked degeneration of cortex was also seen in brains of monkeys given 0.25mg/kg for 31.5 weeks and 0.3mg/kg for 20 weeks. Monkeys given 0.24mg/kg for 73 weeks or 0.3mg/kg for 66 weeks showed no change in any portion of the occipital cortex. The authors conclude that long term exposure of macaques to moderate concentrations of methylmercury can produce a visual field constriction similar to that seen in humans.

1060
TITLE:
Effects in vitro of mercury on rat brain magnesium-ATPase.

AUTHORS:
CHETTY CS
MCBRIDE V
SANDS S
RAJANNA B

SOURCE:
ARCH INT PHYSIOL BIOCHIM; 98 (5). 1990. 261-268.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercuric chloride (Hg) in micromolar concentrations inhibited Mg++-dependent ATPase activity in rat brain microsomes. Inhibition was higher in oligomycin-sensitive (O.S.) than oligomycin-insensitive (O.I.) Mg++-ATPase. Hydrolysis of ATP with 15 and 50 mug of microsomal protein for 45 min without and with (2.10-7 M) Hg showed linear rates for 15-20 min. Altered pH vs activity demonstrated comparable inhibitors by Hg in buffered (neutral > acidic > basic)

pH ranges. Inhibition of enzyme activity by Hg was found to be greater at 37ê C than at lower temperatures suggesting positive correlation trend. An uncompetitive inhibition with respect to the activation of Mg++-ATPase, O.S. Mg++-ATPase and O.I. Mg++ ATPase by ATP was indicated by a decrease in apparent Vmax and Km. Mg++-activation kinetic studies indicated that Hg causes uncompetitive inhibition of Mg++-ATPase and O.I. Mg++-ATPase and mixed inhibition of O.S. Mg++-ATPase. Inhibition was partially restored by repea

1061
TITLE:
Mercurous sulfate

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:
Data sheet. May enter the body when breathed in and through the skin. May cause "shakes", irritability, sore gums, memory loss, increased saliva, personality change, brain damage, kidney damage, skin allergy and grey skin colour. Irritates the skin, eyes and respiratory tract.

1062
TITLE:
SEPS OF PATIENTS WITH MINAMATA DISEASE MD THE NEW ANALYSIS METHODS WITH CURVE RESOLUTION

AUTHORS:
NAKANISHI R
YAMANAGA H
TERAMOTO Y
KOGA H
YONEMITU H
MURAYAMA N
IDETA T

SOURCE:
FIRST INTERNATIONAL CONGRESS ON BRAIN ELECTROMAGNETIC TOPOGRAPHY, OSAKA, JAPAN, SEPTEMBER 12-14, 1990. BRAIN TOPOGR; 3 (1). 1990. 259-260.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN METHYL MERCURY POISONING SOMATOSENSORY EVOKED POTENTIALS TOPOGRAPHY

1063
TITLE:
Differential Structural Effects Of Three Behavioral Teratogens

AUTHORS:
Rodier PM

SOURCE:
Developments in Toxicology and Environmental Science, Vol. 11, Developments in the Science and Practice of Toxicology, pages 53-60, 25 references, 19831983

ABSTRACT:
The effects of the teratogens azacytidine (320672), methylmercury (22967926), and nitrous-oxide (10102440) on the central nervous system (CNS) are reviewed. Azacytidine has been tested as a cancer chemotherapy agent because of its property of killing proliferating cells in-vivo. Studies of synchronized cells, measuring incorporation of azacytidine into DNA and RNA, suggest that the early S-phase is critical for effecting differentiation in cultured cells. The effects of azacytidine also extend to any tissue with a high rate of proliferative activity. Methylmercury is neurotoxic in adults and injurious to the developing brain. A single dose of 4 or 8 milligrams of mercury (7439954) per kilogram (mg/kg) as methylmercury causes a rapid change in mitosis in neonatal mouse cerebellum. The proliferating cells appear to enter mitosis at a normal rate but do not complete the process. Prenatal exposure of methylmercury also affects different populations of neurons. Methylmercury toxicity has been described as injuring cerebral vasculature, causing death of some mature neurons and sparing others, causing cell loss in specific regions of the adult CNS, damaging myelin in both mature and developing animals, and having general toxic effects such as inhibiting protein synthesis. Nitrous-oxide has long been known to interfere with cell proliferation in some tissues such as blood and has been evaluated in developing CNS. Neonatal exposure to 4 to 6 hours of 75 percent nitrous-oxide does affect cell production; no effect on mitosis in active CNS regions of prenatal animals has been observed. The author concludes that azacytidine, methylmercury, and nitrous-oxide affect cell production in developing brains and result in permanent deficits in cell numbers.

1064
TITLE:
Choroid plexus protects cerebrospinal fluid against toxic metals.

AUTHORS:
ZHENG W
PERRY DF
NELSON DL
APOSHIAN HV

SOURCE:
FASEB (FED AM SOC EXP BIOL) J; 5 (8). 1991. 2188-2193.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Although heavy metal ions are known to be toxic to the central nervous system (CNS), the mechanisms by which the CNS may protect itself from initial challenges of such toxic ions is unknown. The choroid plexus is the principal site of formation of the cerebrospinal fluid (CSF) which bathes the brain. We have determined in rats and rabbits that after intraperitoneal administration of lead, cadmium, mercury, and arsenic compounds, these toxic metal ions accumulated in the lateral choroid plexus at concentrations of Pb, Hg, and As that were 70-, 95-, and 40-fold higher, respectively, than those found in the CSF. Cd was not detected in the CSF. In addition, concentrations of these heavy metal ions were found to be many fold greater in the choroid plexus than in the brain or blood. The accumulation of Pb in the choroid plexus was dose-dependent and time-related. When the choroid plexus was preincubated, in vitro, with ouabain (1.5 mM), the uptake of Cd from the CSF side of t

1065
TITLE:
Mercuric chloride

AUTHORS:
ANON

SOURCE:
New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:
Data sheet. May enter the body by inhalation and through the skin. May cause mutations and reproductive damage. May damage the kidneys. Mercury poisoning can cause the "shakes", irritability, sore gums, personality changes and brain damage. May cause skin allergy. May irritate and burn the eyes causing permanent damage. May irritate the lungs and cause lung oedema.

1066
TITLE:
Reaction Of Cerebral Ventricles To Antiorthostatic Position And Occlusion Of Jugular Veins

AUTHORS:
Sokolov VI

SOURCE:

Kosmicheskaya Biologiya i Aviakosmicheskaya Meditsina, Vol. 18, No. 4, pages 66-69, 2 references, 19841984

ABSTRACT:

The reactions of cerebral ventricles to anti orthostatic position and occlusion were studied in 20 male subjects. The ventricular system of the brain was examined by means of one dimensional echoventriculometry. The index of the third ventricle (Dvi) and the index of the medial wall of the lateral ventricle (Pmi) were calculated. Ultrasonic probing was performed in the emission mode in the central temporal lead. The cervical veins were occluded by two methods: the simple occlusion test (test 1) consisting of continuous occlusion of veins of the neck including the jugular veins for 5 minutes in the mode of plus 40 millimeters of mercury (mm Hg); and stepped occlusion test (test 2) consisting of occlusion of cervical veins in modes of plus 10 to plus 50mm Hg. Two groups were formed based on a preliminary anti orthostatic test. Only the first group presented dilatation of the cerebral ventricular system in response to head down tilt. Results of the test 1 showed no reliable changes in the Dvi in the second group of subjects during 5 minute occlusion. In the first group, Dvi increased in the first minute. At 3 minutes, the first group presented dilatation of lateral ventricles without reliable changes in the third ventricle. After discontinuing the test 1, the first group presented a 28.3 percent increase in Dvi as compared to the base value. Results of the test 2 showed that the second group presented a reliable fall of spinal fluid pressure with occlusion in modes of plus 30 and plus 40mm Hg. With plus 50mm Hg occlusion, there was a moderate increase in Pmi. The first group showed dilatation of lateral ventricles in the first minute of occlusion of plus 20mm Hg; by the second minute there was a reliable decline of Dvi. Thereafter, an increase of Pmi and a decrease of Dvi were observed. The author suggests that reactions of the ventricular system of the brain have a close functional link with the degree of difficulty in venous efflux from the cranial cavity. (Russian)

1067

TITLE:

Mercuric cyanide

AUTHORS:

ANON

SOURCE:

New Jersey Department of Health, Right to Know Program, CN 368, Trenton, NJ 08625-0368, USA, 1993. 6p.

ABSTRACT:

Data sheet. May enter the body by inhalation and through the skin. May damage the kidneys. Mercury poisoning can cause the "shakes", irritability, sore gums, memory loss, increased saliva, metallic taste,

personality changes and brain damage. May irritate and burn the eyes. May irritate the skin and cause skin allergy and grey skin colour. May irritate the lungs.

1068
TITLE:
EFFECT OF NEUROTOXICANTS ON BRAIN NEUROCHEMISTRY

AUTHORS:
COSTA LG

SOURCE:
TILSON, H. A. AND C. L. MITCHELL (ED.). TARGET ORGAN TOXICOLOGY SERIES: NEUROTOXICOLOGY. XIII+400P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-88167-849-X.; 0 (0). 1992. 101-124.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MAMMAL RAT MOUSE NEUROTRANSMITTER SECOND MESSENGERS PESTICIDES BIOCHEMICAL MARKERS HUMAN ASSESSMENT

1069
TITLE:
MERCURY CONTAMINATION WHAT WE HAVE LEARNED SINCE MINAMATA

AUTHORS:
D'ITRI FM

SOURCE:
FOURTH SYMPOSIUM ON OUR ENVIRONMENT, SINGAPORE, SINGAPORE, MAY 21-23, 1990. ENVIRON MONIT ASSESS; 19 (1-3). 1991. 165-182.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM FISH SEAFOOD HUMAN METHYLMERCURY POLLUTANT HEAVY METAL TOXICITY FOOD CHAIN AQUATIC ECOSYSTEM BRAIN DAMAGE

1070
TITLE:
UPTAKE DISTRIBUTION AND IMMUNOTOXICOLOGICAL EFFECTS OF MERCURY IN MICE

AUTHORS:
RYAN DM
SIN YM
WONG MK

SOURCE:
FOURTH SYMPOSIUM ON OUR ENVIRONMENT, SINGAPORE, SINGAPORE, MAY 21-23, 1990. ENVIRON MONIT ASSESS; 19 (1-3). 1991. 507-518.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM TRYPANOSOMA-EVANSI ANTIPROTOZOAL-DRUG POLLUTANT KIDNEY LIVER BRAIN HEAVY METAL TOXICITY

1071
TITLE:
METHYLMERCURY INTOXICATION CAUSES INCREASE IN REACTIVE OXYGEN SPECIES AND REDUCTION IN SUPEROXIDE DISMUTASE ACTIVITY IN THE MOUSE BRAIN

AUTHORS:
YEE S
CHOI BH

SOURCE:
1992 MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB), PART II, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J; 6 (5). 1992. A1856.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT HYDROGEN PEROXIDE NEUROTOXICITY HEAVY METAL TOXICITY

1072
TITLE:
INTERACTION OF MERCURIC CHLORIDE WITH RAT BRAIN GLUTATHIONE-S-TRANSFERASE AN IN-VITRO STUDY

AUTHORS:
CHETTY CS
RAJANNA B
RAJANNA S

SOURCE:
1992 MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY (FASEB), PART II, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM SOC EXP BIOL) J; 6 (5). 1992. A1856.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT XENOBIOTIC METABOLISM HEAVY METAL TOXICITY

1073
TITLE:
Metals: General Orientation

AUTHORS:
Zielhuis RL
Stijkel A

Verberk MM
van de Poel-Bot M

SOURCE:
Health Risks to Female Workers in Occupational Exposure to Chemical Agents, Springer-Verlag, Berlin, pages 51-57, 30 references, 19841984

ABSTRACT:
Health risks to female workers occupationally exposed to metals in general are reviewed. For most metals there is no relevant data on special health risks of women. The cases of lead (7439921), cadmium (7440439) and mercury (7439976), for which more information is available, are separately considered. Transplacental passage may differ considerably for metals and metal compounds. Accumulation in the placenta may affect offspring. Uptake by the gastrointestinal tract is usually higher in neonates than adults and the blood/brain barrier is generally more permeable. The incidence of spontaneous abortions was increased in a study of females employed in the general metals industry in Finland. Arsenic (7440382) is a metal for which limited data suggests an increased risk to reproduction and offspring. No threshold dose is known. Antimony (7440360) has been suggested as a cause of disturbed menstrual function and low birth weight. Occupational exposure to chromium (7440473) has not been associated with increased risk to reproduction and offspring in humans but high doses induce congenital malformations in animals. Copper (7440508) can increase in the body during pregnancy. The present threshold limit value for manganese (7439965) does not suggest any health risk for women or offspring. Embryotoxicity had been demonstrated for nickel (7440020) in animals. Although firm conclusions have not been drawn for humans, further study is needed to clarify undesirable reproductive effects. No conclusion is possible at present on the health risks to women of selenium (7782492). The authors conclude that greater emphasis is needed to assess specific exposures of women to metals.

1074
TITLE:
NUMBER OF AMALGAM FILLINGS IN PREGNANT RATS AND MERCURY CONCENTRATION IN THEIR FETUSES

AUTHORS:
TAKAHASHI Y
TSURUTA S
HASEGAWA J
KAMEYAMA Y

SOURCE:
JOINT MEETING OF THE 70TH GENERAL MEETING OF THE INTERNATIONAL ASSOCIATION FOR DENTAL RESEARCH (IADR), 40TH ANNUAL MEETING OF THE BRITISH DIVISION OF THE IADR, 1992 ANNUAL MEETING OF THE CONTINENTAL EUROPEAN DIVISION OF THE

IADR, 8TH ANNUAL MEETING OF THE IRISH DIVISION OF THE IADR AND THE 75TH ANNUAL MEETING OF THE SCANDINAVIAN ASSOCIATION FOR DENTAL RESEARCH, GLASGOW, SCOTLAND, UK, JULY 1-4, 1992. J DENT RES; 71 (SPEC. ISSUE). 1992. 571.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT BRAIN LIVER KIDNEY STATISTICS THERAPEUTIC METHOD ANALYTICAL METHOD

1075

TITLE:

The significance of toxic substances in the drinking water.

AUTHORS:

Koch R

SOURCE:

Z. Gesamte Hyg. 23(2): 96-98 1977

ABSTRACT:

PESTAB. General problems of toxic substances in surface water bodies and drinking water are discussed. Water is an ideal vehicle for many environmental chemicals, such as carcinogenic aromatic hydrocarbons, aromatic amines, N-nitroso compounds, pesticides, PCBs, halogenated hydrocarbons, mercury compounds, metals, and antibiotics. The health hazards of small concentrations of environmental chemicals in drinking water can be assessed by long-term experiments in animals or perhaps by epidemiological statistical studies. Many pesticides, especially organochlorine compounds, alkylmercury compounds, lead, and cadmium accumulate in vital organs, such as the kidney, liver and brain. The human toxicological problems and hazards of such accumulation are not yet fully understood and ascertained. Many substances that are nontoxic per se may metabolize to toxic compounds in the body; this was clearly demonstrated for parathion and malathion, which metabolize to the more toxic compounds paraoxon and malaoxon, respectively. A certain protection from the health hazards of environmental chemicals in drinking-water is possible by the establishment of maximum tolerable concentrations on the basis of toxicological data and the performance of drinking-water preparation and residue analytical techniques.

1076

TITLE:

METHYLMERCURY INDUCED STRUCTURAL CHANGES AT SPECIFIC BRAIN SITES OF THE MONKEY MACACA-FASCICULARIS DETERMINED BY MORPHOMETRIC TECHNIQUES

AUTHORS:

CHARLESTON J

CHEN S-W

BOLENDER R
MOTTET K

SOURCE:
THIRD INTERNATIONAL CONFERENCE OF THE INTERNATIONAL SOCIETY OF TRACE ELEMENT RESEARCH IN HUMANS (ISTERH), STOCKHOLM, SWEDEN, MAY 25-29, 1992. J TRACE ELEM EXP MED; 5 (2). 1992. 110.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT ULTRASTRUCTURE ENDOTHELIAL CELL OXIDATIVE CAPACITY NEUROTOXICITY OPTICAL VOLUME FRACTIONATOR

1077
TITLE:
Effect Of Methylmercuric Chloride On Gangliosides Of Mouse Neuroblastoma Cells In Culture

AUTHORS:
Rebel G
P
Prasad KN

SOURCE:
Lipids, Vol. 18, No. 10, pages 664-667, 43 references, 19831983

ABSTRACT:
The effects of methylmercuric-chloride (115093) (MMC) on gangliosides in cultured mouse neuroblastoma cells were studied. Neuroblastoma cells were grown and plated in numbers to obtain similar cell densities at harvest. At 24 hours after plating, MMC at 0, 0.2, and 0.2 micromolar (microM) was added to 250,000 cells, and 0.5 and 1microM MMC was added to 500,000 cells. Media were changed daily, and after 3 days cells were washed, removed, lyophilized, and weighed. Lipids were extracted and the gangliosides were purified and separated by thin layer chromatography. The percentages of the following ganglioside species present in the total were determined: GM1, GM2, GM3, GD3, and GD1a. Total gangliosides decreased slightly with low concentrations of MMC. GM3 content increased by 60 and 36 percent with 0.1 and 0.2microM MMC, respectively, but decreased by 38 and 69 percent with 0.5 and 1microM, respectively. GM2 did not change at low concentrations, but increased by 30 and 38 percent with 0.5 and 1microM, respectively. The other ganglioside species were unaffected by MMC. The authors conclude that MMC induces biochemical alterations in cells which do not exhibit any detectable changes in growth rate or morphology. These changes may account for the subtle alterations in brain functions observed after exposure to low concentrations of organic mercury.

1078

TITLE:
ACCUMULATION OF TOTAL AND INORGANIC MERCURY IN THE PRIMATE BRAIN FOLLOWING LONG-TERM METHYLMERCURY EXPOSURE

AUTHORS:
FRIBERG L
MOTTET K
VAHTER M
BURBACHER T
LIND B

SOURCE:
THIRD INTERNATIONAL CONFERENCE OF THE INTERNATIONAL SOCIETY OF TRACE ELEMENT RESEARCH IN HUMANS (ISTERH), STOCKHOLM, SWEDEN, MAY 25-29, 1992. J TRACE ELEM EXP MED; 5 (2). 1992. 113.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT MACACA-FASCICULARIS NEUROTOXICITY

1079
TITLE:
In vitro interaction of heavy metals with ouabain receptors in rat brain microsomes.

AUTHORS:
CHETTY CS
STEWART TC
COOPER A
RAJANNA B
RAJANNA S

SOURCE:
DRUG CHEM TOXICOL INT J RAPID COMMUN; 16 (1). 1993. 101-110.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This study investigates the influence of heavy metals on ouabain-binding in presence of thiol (sulfhydryl) compounds. The data on in vitro effects of mercury (Hg), lead (Pb) and cadmium (Cd) showed significant inhibition of 3H-ouabain binding to microsomal membrane in a concentration-dependent manner. Maximum inhibition of 3H-ouabain binding was observed at 1 muM for Hg and 100 muM each for Pb and Cd. Preincubation with monothiol (L-cysteine or glutathione) or dithiol (dithiothreitol) protected inhibition of 3H-ouabain binding to the membranes by Hg or Pb. Dithiol but not monothiols partially protected Cd-inhibition. The present data confirm that the heavy metals interact with ouabain receptors in a manner similar to SH-blocking agents and protection of metal-inhibited 3H-ouabain binding

by thiol compounds is metal specific.

1080
TITLE:
MERCURY SPECIATION IN BLOOD AND BRAIN TISSUE FROM MONKEYS INTERLABORATORY COMPARISON OF MAGOS' METHOD WITH OTHER SPECTROSCOPIC METHODS USING ALKYLATION AND GAS CHROMATOGRAPHY SEPARATION AS WELL AS RNAA IN COMBINATION WITH WESTOO'S EXTRACTION METHODS

AUTHORS:
LIND B
BODY R
FRIBERG L

SOURCE:
5TH INTERNATIONAL SYMPOSIUM ON BIOLOGICAL AND ENVIRONMENTAL REFERENCE MATERIALS, AACHEN, GERMANY, MAY 11-14, 1992. FRESENIUS' J ANAL CHEM; 345 (2-4). 1993. 314-317.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MACACA-FASCICULARIS ENVIRONMENTAL TOXIN RADIOCHEMICAL NEUTRON ACTIVATION ANALYSIS ANALYTICAL METHOD

1081
TITLE:
EFFECTS OF NEUROTOXINS ON BRAIN CREATINE KINASE ACTIVITY

AUTHORS:
MATSUOKA M
INOUE N
IGISU H
HOHRIYAMA K

SOURCE:
FOURTH INTERNATIONAL SYMPOSIUM ON NEUROBEHAVIORAL METHODS AND EFFECTS IN OCCUPATIONAL AND ENVIRONMENTAL HEALTH, TOKYO, JAPAN, JULY 8-11, 1991. ENVIRON RES; 61 (1). 1993. 37-42.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT ETHYLENE OXIDE ACRYLAMIDE BISACRYLAMIDE METHYL MERCURY CHLORIDE AXONAL DEGENERATION PATHOGENESIS

1082
TITLE:
Trace metals in the common porpoise, Phocoena phocoena.

AUTHORS:
FALCONER CR

DAVIES IM
TOPPING G

SOURCE:
MAR ENVIRON RES; 8 (2). 1983. 119-128.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg, Cd, Cu and Zn concentrations in brain, liver, kidney, heart and spleen of 26 specimens of the common porpoise (P. phocoena) was presented. Hg and Cd levels in liver and kidneys increased with length of animal, but Cu and Zn levels showed no such trends. The proportion of methylmercury to total Hg (9-57%)in the liver decreased with increasing total Hg concentrations. Pb, Cr, Ni and Co levels were below the analytical detection limits (0.5, 1.0, 1.0 and 2.5 mug/g, respectively).

1083
TITLE:
An outbreak of methylmercury poisoning due to consumption of contaminated grain.

AUTHORS:
Clarkson TW
Amin-Zaki L
Al-Tikrita SK

SOURCE:
Fed. Proc. Fed. Am. Soc. Exp. Biol. 35(12): 2395-2396; 1976.(16 references)

ABSTRACT:
PESTAB. An outbreak of methylmercury poisoning took place in the fall and winter of 1971-72 in Iraq. Six thousand five hundred and thirty cases were admitted to hospitals throughout the country and 459 died in hospital. The outbreak was the result of eating homemade bread prepared from wheat treated with a methylmercury fungicide. The wheat was intended for planting purposes only. Signs and symptoms of poisonings in adults indicate that the major site of action of this form of mercury is the central nervous system. Severe brain damage also resulted from prenatal exposure when the mother ingested large amounts of the contaminated bread. The frequency of signs and symptoms in an exposed population was found to be related to the estimated maximum blood levels, i.e., the concentration in blood at the end of exposure. A small percentage of the population exhibited a significant increase in complaints of paresthesia at maximum blood levels in the range of 240 to 480 ng Hg/ml. At higher blood levels a greater proportion of the population complained of paresthesia and other signs and symptoms became apparent. (Author abstract by permission)

1084
TITLE:
The dynamics of ingested methyl mercury in growing and laying chickens.

AUTHORS:
MARCH BE
POON R
CHU S

SOURCE:
POULT SCI; 62 (6). 1983. 1000-1009.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Growing and laying chickens were fed practical-type diets containing 0, 0.05, 0.15, 0.45 and 1.35 ppm Hg as methyl mercuric chloride. Chicks that had been fed Hg throughout life retained 61, 82, 91 and 95% of the Hg ingested from the respective diets at 8 wk of age. The half-retention times of Hg, following withdrawal of dietary Hg after 8 wk, were 8.4 and 23.4 days, respectively, for liver and kidney in chicks fed 1.35 ppm Hg. Half-retention times in kidney and liver decreased with lower Hg intake, i.e., with lower concentrations in the tissues at the time of Hg withdrawal. Adult laying birds, continuously fed diets containing methyl mercuric chloride, laid eggs with gradually increasing concentrations of Hg until plateau concentrations reflecting the respective dietary concentrations were reached. On withdrawal of HG from the diet, Hg concentrations in the eggs laid by the birds fed 0.05, 0.15, 0.45 and 1.35 ppm declined to reach half of the concentrations at the time of withdrawal in 17, 13, 10 and 9 days, respectively. The half-retention time of Hg in the liver, kidney, heart muscle, pectoral muscle and brain tissue of the adult birds depended on the tissue concentration at the time Hg was withdrawn from the diet and was inversely proportional to initial tissue concentration according to the equation: 1n y = 1.92 - 0.39 1n (7x-5), where x was the initial tissue concentration in ppm and y was half-retention time in weeks, r = -0.95.

1085
TITLE:
The influence of ethyl mercuric p-toluen sulfanilide on the hypothalamic-pituitary system.

AUTHORS:
Wigowska-Sowinska J
Gramza G

SOURCE:
Folia Histochem. Cytochem. 16(2): 161 1978

ABSTRACT:

PESTAB. Wistar rats were fed a single dose of 0.2 g of ethyl mercury p-toluen sulfonamide per day during a 15 day period. Brains and pituitary glands were fixed in Zenker's fluid with the addition of 10% formalin, embedded in paraffin. The Gomori method was used to visualize the neurosecretory substance. Alterations were found in neurocytes of the supraoptic and paraventricular nuclei as well as in the release of neurosecretory material. Some study was given to a possible correlation of these changes with those brought about by other mercuric compounds. [At the 16th Symposium of the Polish Histochemical and Cytochemical Society in a joint meeting with the Polish Anatomical Society.]

1086
TITLE:
Decreasing 203Hg retention by intraperitoneal treatment with monoalkyl esters of meso-2,3-dimercaptosuccinic acid in rats.

AUTHORS:
KOSTIAL K
BLANUSA M
SIMONOVIC I
JONES MM
SINGH PK

SOURCE:
JOURNAL OF APPLIED TOXICOLOGY; 13 (5). 1993. 321-325.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effect of nine monoalkyl esters of meso-2,3-dimercaptosuccinic acid (DMSA) on 203Hg retention after a single i.p. dose was evaluated in 6-7 week-old female albino rats. The monoesters were the monomethyl (MMDMS), monoethyl (MEDMS), mono-n-propyl (Mn-PDMS), monoisopropyl (Mi-PDMS), mono-n-butyl (Mn-BDMS), monoisobutyl (Mi-BDMS), mono-n-amyl (Mn-ADMS), monoisoamyl (Mi-ADMS) and mono-n-hexyl (Mn-HDMS). Dimercaptosuccinic acid or one of the monoesters were administered at a dose of 0.25 mmol kg-1 body wt. twice, i.e. 30 min and 24 h after 203Hg administration. The whole body (WB) radioactivity was determined on the 2nd, 4th and 6th days. The radioactivity in the carcass (C) (whole body without the gastrointestinal tract), liver (L), both kidneys (K) and brain (B) was determined 6 days after 203Hg administration. All treated animals had a significantly lower body burden of mercury than the controls. The reduction of 203Hg retention in WB and other body compartments was

1087
TITLE:
The biochemical and biological behavior of methylmercury.

AUTHORS:
DOI R

TAGAWA M

SOURCE:
TOXICOL APPL PHARMACOL; 69 (3). 1983. 407-416.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The biochemical and biological behavior of methylmercury (MeHg) was investigated by measurement of MeHg release rate from erythrocytes (RBC) of selected animal strains and species, by measurement of the intracellular distribution of MeHg in RBC, and by measurement of the binding affinity of Hb for MeHg. Methylmercury chloride was used throughout the experiments. Significant strain and species differences were found in the release rate of MeHg from RBC of mice, rats, and man and in the distribution of MeHg in RBC. Significant correlations were found between these 2 indices and the brain/blood ratio of Hg concentration 24 h after MeHg injection, i.p. The affinity of Hb for MeHg was examined by ultrafiltration techniques and Scatchard plots. There were Hb with only 1 type of binding site and others with 2 types of binding sites. Both sites were cysteinyl residues. Primary sites involved cysteinyl residues oriented externally at the outside of the alpha1beta1 contact junction and cysteinyl residues in the junction, while secondary sites involved only cysteinyl residues in the junction.

1088
TITLE:
Drugs and the fetus: A consumer's guide by generic and brand name.

AUTHORS:
O'Brien TE
McManus CE

SOURCE:
Birth Fam. J. 5(2): 58-86 1978 (177 References)

ABSTRACT:
PESTAB. The mechanisms of drug transport across the placenta and the difficulties involved in testing for adverse fetal effects of drugs are reviewed. Anti-infective agents, cancer chemotherapy agents, hematologic drugs, cardiovascular drugs, hormones, anaesthetics, vaccines, vitamins, and others are described. Of hematologic drugs, bishydroxycoumarin causes greater anticoagulant effect in the fetus than in the mother, leading to hemorrhage, death in utero, and fetal deformities. Arsenic trioxide, used in a suicide attempt during the last trimester, caused infant death and the infant was found to have high levels of the chemical in the brain, kidney, and liver. Exposure to organic mercury compounds can cause blindness and nervous system malformations such as cerebral palsey and mental retardation. Polychlorinated biphenyls can cause a staining of the skin and mucous membrances as well as growth retardation.

1089
TITLE:
Effects of neonatal malnutrition and perinatal exposure to various pesticides.

AUTHORS:
Sobotka TJ
Cook MP
Brodie RE

SOURCE:
Mater. Med. Pol. 8(2): 152-155; 1976.(13 references)

ABSTRACT:
PESTAB. Model systems used in the neurobehavioral toxicology program employ a multidiscipliary experimental and epidemiologic appraoch. These studies have suggested interactions between nutritional state and toxin response in the case of heavy metals (lead and mercury). Findings have been observed in animals treated with heavy metals which resemble the pharmacobehavioral characteristics in children with minimal brain dysfunction: altered responsiveness to amphetamine, poor learning performance, and alleviation of the performance deficit by amphetamine treatment. Effects of malnutrition alone have been examined in experimental animals. The most characteristic behavioral manifestation of early malnutrition in animals is heightened emotional" responsiveness to stressful conditions. (Note: pesticides per se were not mentioned.)

1090
TITLE:
THE DEVELOPMENTAL PROFILE OF PKC ISOFORMS IN THE RAT BRAIN IS ALTERED BY GESTATIONAL EXPOSURE TO METHYL MERCURY

AUTHORS:
HAYKAL-COATES N
GOLDEY ES
HERR DW
TILSON HA
BARONE S JR

SOURCE:
23RD ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, WASHINGTON, D.C., USA, NOVEMBER 7-12, 1993. SOCIETY FOR NEUROSCIENCE ABSTRACTS; 19 (1-3). 1993. 1733.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER PROTEIN KINASE C NEUROTOXICITY HISTOCHEMISTRY

1091
TITLE:
A DEVELOPMENTAL PROFILE OF TRK IMMUNOREACTIVITY IN THE RAT BRAIN IS AFFECTED BY GESTATIONAL EXPOSURE TO METHYL MERCURY

AUTHORS:
BARONE S JR
HAYKAL-COATES N
GOLDEY ES
TILSON HA

SOURCE:
23RD ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, WASHINGTON, D.C., USA, NOVEMBER 7-12, 1993. SOCIETY FOR NEUROSCIENCE ABSTRACTS; 19 (1-3). 1993. 1734.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER TYROSINE KINASE NERVE GROWTH FACTOR RECEPTOR NEUROTOXICITY HISTOCHEMISTRY

1092
TITLE:
Evaluation of the critical body burden concept based on inorganic and organic mercury toxicity to rainbow trout (Oncorhynchus mykiss).

AUTHORS:
NIIMI AJ
KISSOON GP

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 26 (2). 1994. 169-178.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Subadult rainbow trout (Oncorhynchus mykiss) were exposed to four waterborne concentrations each of 64-426 mug mercuric chloride (HgCl2) and 4-34 mug/L methylmercury chloride (CH3HgCl) until death to evaluate the critical body burden concept. Mean days to death for fish exposed to the highest and lowest concentrations of HgCl2 were 1 and 58 d, and 2 and > 100 d for fish exposed to CH3HgCl. Time to death was an important factor that influenced Hg tissue concentration, and was most evident among fish that died within a few days of exposure. Critical body burdens for Hg could be difficult to establish at the tissue level because no threshold concentrations were clearly indicated among the liver, kidney, spleen, brain, muscle, and gill that were monitored in this study. A critical burden for Hg was derived on a whole body basis for Hg in its organic form. An evaluation of this and other studies suggests whole body

concentrations of 10-20 mg/kg Hg could be lethal to fish.

1093
TITLE:
Pathology of the spinal cord. Chapter 8. Toxic and deficiency diseases.

AUTHORS:
Hughes JT

SOURCE:
Maj. Probl. Pathol. 6: 184-202 1978 (73 References)

ABSTRACT:
PESTAB. Many inorganic poisons affect the nervous system, but usually the effect on the spinal cord is overshadowed by the effect on the brain. The chief examples of heavy-metal poisoning are copper, mercury, and lead. Organic poisons are more common and the list of compounds affecting the nervous system is very long. Tri-o-cresyl phosphate is the most notorious of these compounds whose toxicity apparently is due to selective enzymatic poisoning of certain neurons. A large outbreak occurred in Meknes of Morocco due to the contamination of cooking oil by synthetic lurbicating oil containing o-cresyl phosphate. In such epidemics the clinical picture of an acute polyneuropathy developing over a period of weeks and causing widespread but mainly distal paralysis, first of the lower limbs and later of the hands, developed. Spinal cord involvement either accompanied or followed the peripheral neuropathy and added an upper motor neuron lesion to the paralysis. In spite of the severity of the paralysis, in every outbreak the mortality of the condition has been low and consequently there have been few necropsies. However, the spinal cords examined did show leptomeningeal thickening. White matter degeneration was always present and of variable distribution involving the lateral corticospinal tracts. Changes were much more marked in the lower cord than in the upper segments. Neuronal changes were less striking. There was a reduction of anterior horn cells and those remaining were sometimes pyknotic and lacked Nissel substance.

1094
TITLE:
QUANTITATIVE ANALYSIS OF ZINC COPPER LEAD MOLYBDENUM BISMUTH MERCURY AND ARSENIC IN BRAIN AND OTHER TISSUES FROM MULTIPLE SCLEROSIS AND NONMULTIPLE SCLEROSIS CASES

AUTHORS:
WARREN HV
HORKSY SJ
GOULD CE

SOURCE:

SCI TOTAL ENVIRON; 29 (1-2). 1983. 163-170.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN SMELTING PLANT INDUSTRIAL POLLUTION

1095
TITLE:
BRAIN TRACE ELEMENTS IN ALZHEIMER DISEASE

AUTHORS:
MARKESBERY WR
EHMANN WD

SOURCE:
TERRY, R. D., R. KATZMAN AND K. L. BICK (ED.). ALZHEIMER DISEASE. XVII+472P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ISBN 0-7817-0081-7.; 0 (0). 1994. 353-367.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER HUMAN ELDERLY DEMENTIA NEUROTOXICITY

1096
TITLE:
Environmental contaminants in redheads wintering in coastal Louisiana and Texas.

AUTHORS:
MICHOT TC
CUSTER TW
NAULT AJ
MITCHELL CA

SOURCE:
ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 26 (4). 1994. 425-434.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Whole body and liver analyses indicated that wintering redheads (Aythya americana; n = 70) in coastal Louisiana (one site) and Texas (two sites) were relatively free of contamination with common trace elements, organochlorines, and hydrocarbons. Most trace elements, including As, Cr, Hg, Mg, Mn, Ni, Pb, Se, Sr, and Zn, were within background concentrations in livers; levels of B, Cd, Cu, and Fe were elevated in some specimens. Only one organochlorine, DDE, was detected in redhead carcasses, but its concentration was below reported toxic levels in waterfowl. Body burdens of aliphatic and aromatic hydrocarbons were generally low, but levels of pristane, total

hydrocarbons, and the ratios of phytane:n-octadecane and pristane:n-heptadecane were indicative of possible chronic exposure to petroleum. Based on brain cholinesterase assays, redheads were not recently exposed to organophosphorous or carbamate pesticides. Of 30 elements or compounds tested for seasonal differences,

1097
TITLE:
BEHAVIORAL TOXICOLOGY OF HEAVY METALS

AUTHORS:
GRANDJEAN P

SOURCE:
ZBINDEN, G. ET AL (ED.). APPLICATION OF BEHAVIORAL PHARMACOLOGY IN TOXICOLOGY, MEETING, CAPRI, APRIL, 1982. 91P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS. ISBN 0-89004-902-5.; 0 (0). 1983. P331-340.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN BRAIN CENTRAL NERVOUS DYS FUNCTION ARSENIC CADMIUM MERCURY MANGANESE LEAD THALLIUM OCCUPATIONAL EXPOSURE

1098
TITLE:
MERCURY PROTEIN COMPLEX IN THE BRAIN AND RETINA

AUTHORS:
MUKAI N

SOURCE:
FRANCOIS, J. MONOGRAPHS IN HUMAN GENETICS,; 1972 208

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT ENCEPHALOPATHY

1099
TITLE:
Correlation of metal toxicity with in vitro calmodulin inhibition.

AUTHORS:
COX JL
HARRISON S D JR

SOURCE:
BIOCHEM BIOPHYS RES COMMUN; 115 (1). 1983. 106-111.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A fundamental biochemical process directly and

universally related to the toxicity of metals and metal compounds has not been identified. The toxicity of a series of divalent metal cations in bovine brain preparations correlates well with the metals' ability to inhibit the Ca2+ receptor protein calmodulin (r = 0.986). Because calmodulin regulated a variety of cellular enzymes and processes including intracellular Ca2+ concentrations, calmodulin inhibition may have had value for predicting metal toxicity and for revealing information about the mechanism by which metals induced toxic effects.

1100
TITLE:
Toxic metals in pilot whales (Globicephala melaena) from strandings in 1986 and 1990 on Cape Cod, Massachusetts.

AUTHORS:
MEADOR JP
VARANASI U
ROBISCH PA
CHAN S-L

SOURCE:
CANADIAN JOURNAL OF FISHERIES AND AQUATIC SCIENCES; 50 (12). 1993. 2698-2706.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Concentrations of As, Cd, Cu, Hg, Pb, and Se were measured in 17 adult and 8 fetal pilot whales (Globicephala melaena). Total Hg and Se both occurred in very high concentrations in liver and kidney and in liver were significantly correlated with animal length (and each other) which indicates bioaccumulation over time. Methyl mercury, as a percentage of total Hg, varied inversely with total Hg indicating demethylation was occurring; a one-to-one molar association of Hg and Se was found which is believed to provide protection against Hg toxicity. Arsenic concentrations were relatively low, but Cd concentrations were consistently very high in adult kidney. Lead in adult liver was also correlated with animal length indicating long term bioaccumulation. All non-essential elements were found in critical fetal tissues which indicates maternal transfer occurred. Cadmium in fetal kidney was over 30 times higher than either brain or liver, indicating early differential accumulati

1101
TITLE:
INHIBITION OF RAT BRAIN MUSCARINIC ACETYL CHOLINE RECEPTORS AFTER IN-VIVO TREATMENT WITH METHYL MERCURY AND MERCURIC CHLORIDE

AUTHORS:
ABDALLAH E AM

ABDELFATTAH AS
SHAMOO AE

SOURCE:
27TH ANNUAL MEETING OF THE BIOPHYSICAL SOCIETY, SAN DIEGO, CALIF., USA, FEB. 13-16, 1983. BIOPHYS J; 41 (2 PART 2). 1983. 65A.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM ABSTRACT METAL TOXICITY SULFHYDRYL

1102
TITLE:
A review of axonal transport of metals.

AUTHORS:
ARVIDSON B

SOURCE:
TOXICOLOGY; 88 (1-3). 1994. 1-14.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Neurons have efficient mechanisms for the transport of organelles and chemical substances in axons to the nerve terminals and back to the cell bodies. Enzymes involved in transmitter synthesis, peptide transmitters and their precursors are examples of macromolecules that are transported down the axon, anterogradely. For final degradation and possible reuse, many constituents are transported back to the cell body, retrogradely. Retrograde transport is also a pathway by which certain toxins may bypass the blood-brain barrier and accumulate in neurons. In recent years, it has been shown that certain metals may accumulate in neurons following retrograde transport. The metals for which retrograde transport has been demonstrated include lead, cadmium and mercury. In this article recent findings regarding axonal transport of metals are reviewed. The putative mechanisms involved in the uptake of metals into the nerve terminal and the fate of metals in the cell body are outlined

1103
TITLE:
BLOOD-BRAIN AND BLOOD-NERVE BARRIERS AND THEIR RELATIONSHIPS TO NEUROTOXICITY

AUTHORS:
JACOBS JM

SOURCE:
CHANG, L. W. (ED.). NEUROLOGICAL DISEASE AND THERAPY, 26. PRINCIPLES OF NEUROTOXICOLOGY. XVIII+800P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA;

BASEL, SWITZERLAND. ISBN 0-8247-8836-2.; 0 (0). 1994. 35-68.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER RAT GAMMA-GLUTAMYL TRANSPEPTIDASE CISPLATIN DOXORUBICIN ANTINEOPLASTIC AMIODARONE ANTIARRHYTHMIC SILVER CADMIUM MERCURY GLUTAMATE PYRIDOXINE LEAD 1 3-DINITROBENZENE NEUROPATHY

1104
TITLE:
INDUCTION OF OXIDATIVE STRESS IN THE BRAIN BY NEUROTOXIC AGENTS

AUTHORS:
BONDY SC

SOURCE:
CHANG, L. W. (ED.). NEUROLOGICAL DISEASE AND THERAPY, 26. PRINCIPLES OF NEUROTOXICOLOGY. XVIII+800P. MARCEL DEKKER, INC.: NEW YORK, NEW YORK, USA; BASEL, SWITZERLAND. ISBN 0-8247-8836-2.; 0 (0). 1994. 563-582.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER IRON COPPER MERCURY TOLUENE MYELIN GLUTATHIONE CYTOCHROME P450 EICOSANOID PRODUCTION LIPID PEROXIDATION ACETALDEHYDE GENERATION

1105
TITLE:
MERCURY CAUSES NEURO TOXICITY AT AN INTRA CELLULAR SITE FOLLOWING ENTRY THROUGH SODIUM AND CALCIUM CHANNELS

AUTHORS:
MIYAMOTO MD

SOURCE:
BRAIN RES; 267 (2). 1983. 375-379.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM SULFHYDRYL

1106
TITLE:
Mercury content of human tissues during the twentieth century.

AUTHORS:
KEVORKIAN J
CENTRO DP
HYLAND JR
BAGOZZI WM

VAN HOLLEBEKE E

SOURCE:
AM J PUBLIC HEALTH; 62 (4). 1972 504-513

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Various human tissues and organs from 59 autopsy cases covering the time period of 1913-1970 were analyzed for total Hg content, and 10 individual tissues samples for methylmercury levels. Four different qualified laboratories performed the tests on essentially identical tissue samples. Results were frequently widely divergent. However, several coarse but definite trends indicate that total Hg content of most human organs dropped sharply during the last 60 yr, and that such levels have a biphasic curve throughout an individual's lifetime; namely, peaks in early childhood and middle age. The sharp drop may reflect a cleansing of the general environment of Hg and a diminution of any pollution threat. Methylmercury levels ranged from 0-74% of total Hg levels, and 2 or 3 brain samples showed no methylmercury at all. These are compared with levels reported for various animals.

1107
TITLE:
A case of poisoning of animals by Granosan.

AUTHORS:
Ogurok AP

SOURCE:
Veterinariya; 47(6): 88-89; 1971

ABSTRACT:
HAPAB The symptoms of a fatal mass poisoning incident in hogs, originally mistaken for symptoms of Aujeszky's disease, a disease of the central nervous system, are described. The bioassay for Aujeszky's disease was negative, however, and the discovery of Hg in the liver, brain, kidney and muscles of the diseased animals led to the conclusion that mercury poisoning had occurred. Hogs had been fed barley destined for seed and treated with Granosan. The first symptoms of disease occurred 20 days later. Cattle were less sensitive to Granosan poisoninga 1971

1108
TITLE:
Autometallographic detection of silver in hypothalamic neurons of rats exposed to silver nitrate.

AUTHORS:
STOLTENBERG M
JUHL S

POULSEN EH
ERNST E

SOURCE:
JOURNAL OF APPLIED TOXICOLOGY; 14 (4). 1994. 275-280.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The silver amplification technique, autometallography, has been used to reveal silver accumulation in neurons in the hypothalamus of male Wistar-Kyoto rats. Silver penetrated the blood-brain barrier after exposure to silver nitrate, and differences in staining intensity were found between the hypothalamic nuclei. When using light microscopy, the silver staining of the hypothalamic neurons was highly heterogeneous. Silver was detected exclusively in lysosomes of the loaded neurons. Aspects of this heterogeneous localization are discussed in relation to the distribution of autometallographically developed gold and mercury.

1109
TITLE:
LOCALIZATION OF SILVER AND MERCURY IN HUMAN BRAIN TISSUE

AUTHORS:
RUNGBY J
DANSCHER G
MOLLER-MADSEN B
RESKE-NIELSEN E
HANSEN JC

SOURCE:
7TH EUROPEAN NEUROSCIENCE CONGRESS, HAMBURG, WEST GERMANY, SEPT. 12-16, 1983. NEUROSCI LETT; 0 (SUPPL. 14). 1983. S318.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM ABSTRACT LIGHT MICROSCOPY ELECTRON MICROSCOPY SPECTROPHOTOMETRIC

1110
TITLE:
METHYL-MERCURY ALTERS THE DEVELOPMENTAL PATTERN OF TRK AND PKC ISOFORMS IN
THE RAT BRAIN

AUTHORS:
BARONE S JR
HAYKAL-COATES N
GOLDEY ES
TILSON HA

SOURCE:
10TH BIENNIAL MEETING OF THE INTERNATIONAL SOCIETY FOR DEVELOPMENTAL NEUROSCIENCE, SAN DIEGO, CALIFORNIA, USA, JULY 30-AUGUST 3, 1994. INTERNATIONAL JOURNAL OF DEVELOPMENTAL NEUROSCIENCE; 12 (SUPPL. 1). 1994. 80.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER PROTEIN KINASE C NERVE GROWTH FACTOR RECEPTOR NEUROTOXICITY

1111
TITLE:
Release and inhibition of uptake of 5-hydroxytryptamine in blood platelets in vitro by copper and methyl mercury.

AUTHORS:
TUOMISTO J
KOMULAINEN H

SOURCE:
ACTA PHARMACOL TOXICOL; 52 (4). 1983. 292-297.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Divalent Cu and methyl Hg (Met-Hg) are potent inhibitors of the uptake of 5-hydroxytryptamine (5-HT) in rat hypothalamic synaptosomes in vitro. To assess the usefulness of blood platelets as a peripheral model of central serotonergic nerve endings for neurotoxicological studies, human and rabbit platelets were utilized for comparison. Cu inhibited 5-HT uptake into human platelets when platelets were separated from plasma (the IC50 0.7-0.8 muM). Plasma added with platelets abolished the toxic influence of Cu towards platelets. Met-Hg inhibited 5-HT uptake both in washed platelets (the IC50 0.2 muM) and in platelets added in plasma (the IC50, 10-15 muM). The inhibition of uptake by Met-Hg did not depend on buffer Ca and Mg. At low concentrations of Cu, the uptake tended to be more inhibited in the presence of Ca and Mg. Zn and Hg did not affect 5-HT uptake up to 100 muM. Pb inhibited it transiently (28% at 1 muM) in the presence of Ca and Mg. Met-Hg induced the release of endogenous 5-HT from rabbit platelets when they were in a suspension in Ca-free buffer, but Cu did not, even at 100 muM concentration. Blood platelets give results comparable with brain synaptosomes regarding inhibitory effects of metals on 5-HT uptake provided plasma is decanted. The inhibition of 5-HT uptake by Cu appears to be purely plasma membrane related but Met-Hg may, in addition, induce release of 5-HT from storage granules.

1112
TITLE:

LOCALIZATION OF PKCGAMMA IN THE DEVELOPING RAT BRAIN FOLLOWING EXPOSURE TO METHYL MERCURY

AUTHORS:
HAYKAL-COATES N
SHAFER TJ
MUNDY WR
TILSON HA
BARONE S JR

SOURCE:
24TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, MIAMI BEACH, FLORIDA, USA, NOVEMBER 13-18, 1994. SOCIETY FOR NEUROSCIENCE ABSTRACTS; 20 (1-2). 1994. 44.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER PROTEIN KINASE C-GAMMA NEUROTROPHIC FACTOR RECEPTOR CELLULAR MECHANISM

1113
TITLE:
The oxidation mechanism of metallic mercury in vitro by catalase.

AUTHORS:
OGATA M
AIKOH H

SOURCE:
PHYSIOL CHEM PHYS MED NMR; 15 (1). 1983. 89-91.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Magos et al reported the effect of 3-amino-1,2,4-triazole on Hg uptake by in vitro human blood samples and the Hg contents in blood and brain of rats exposured to metallic Hg vapor. The oxidation of metallic Hg by human blood cells having different catalase activities, hypocatalasemia and acatalasemia, with or without hydrogen peroxide is described. Kudsk found that ethyl alcohol inhibited the uptake of metallic Hg by blood in vitro and in vivo. These findings raise a question as to whether or not the inhibition by ethyl alcohol of the uptake of Hg by the blood is due to a direct reaction between ethyl alcohol and the catalase-hydrogen peroxide complex. The present report deals with the mechanism of metallic Hg oxidation in vitro by catalase using ethyl alcohol.

1114
TITLE:
DISTRIBUTION OF MERCURY WITHIN CHICKEN TISSUES

AUTHORS:
BUSH RS
CAMPBELL LD
MARQUARDT RR

SOURCE:
J ANIM SCI; 34 (5). 1972 916-917

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT LIVER KIDNEY BRAIN

1115
TITLE:
MERCURY ACCUMULATION PROFILES AND THEIR MODIFICATION BY INTERACTION WITH CADMIUM AND LEAD IN THE SOFT TISSUES OF THE CICHLID OREOCHROMIS AUREUS DURING CHRONIC EXPOSURE

AUTHORS:
ALLEN P

SOURCE:
BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY; 53 (5). 1994. 684-692.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE OREOCHROMIS-AUREUS HEAVY METAL LIVER BRAIN GILLS INTESTINE MUSCLE TOXICITY WATER POLLUTION AQUACULTURE

1116
TITLE:
Cellular and subcellular demonstration of mercury in situ by modified sulfide-silver technique and photoemulsion histochemistry.

AUTHORS:
CHOI BH

SOURCE:
EXP MOL PATHOL; 40 (1). 1984. 109-121.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Young adult C57BL/6J mice were injected with 4.0 mg/kg body wt methylmercuric chloride (MMC) for 3 consecutive days for a total of 12.0 mg/kg. Controls received physiological saline in place of MMC. One week following the last injection, the animals were sacrificed. Representative tissue blocks and sections from the brain, kidney and liver were subjected to a modified sulfide-Ag technique (SST) and the photoemulsion histochemical method. Both techniques demonstrated

consistent and distinct localization of Hg gains in cells and subcelluar organelles. These methods were based on the principle that Hg compounds reacted strongly with SH groups in tissues and cells to form Hg-sulfides and also on the affinity of Hg and Ag to form an amalgam when placed in a physical developer or photographic emulsion. Hg in cells was demonstrable without prior treatment of sulfide solution. The methods were simple and reliable when used with proper controls. Specific localization of Hg in cells in situ without disruption of anatomical relationships provided by these methods offered distinct advantages over other methods of Hg determination. It would be possible to conduct a retrospective or prospective study of human autopsy materials and also would allow direct correlation of Hg deposition with pathological changes in cells and subcellular organelles.

1117
TITLE:
PH DEPENDENT INTERACTION BETWEEN METHYL MERCURY CHLORIDE AND SOME MEMBRANE
PHOSPHO LIPIDS

AUTHORS:
LEBLANC RM
JOLY LP
PAIEMENT J

SOURCE:
CHEM-BIOL INTERACT; 48 (2). 1984. 237-242.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM BOVINE BRAIN NEURO TOXICITY

1118
TITLE:
FETAL UPTAKE OF METHYL MERCURY IN SWINE

AUTHORS:
WALTER BK
KELMAN BJ

SOURCE:
FED PROC; 36 (3). 1977 355

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RED CELL BOUND LIVER KIDNEY BLOOD BRAIN

1119
TITLE:

Demethylation and placental transfer of methyl mercury in the pregnant hamster.

AUTHORS:
DOCK L
RISSANEN R-L
VAHTER M

SOURCE:
TOXICOLOGY; 94 (1-3). 1994. 131-142.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The demethylation and placental transfer of methylmercury (MeHg) was studied in Syrian Golden hamsters administered a single oral dose of 203Hg-labeled MeHgCl, 1.6 mumol/kg body weight, on day 2 or 9 of gestation and sacrificed 1 day before expected parturition. In order to evaluate the role of demethylation for transplacental transport of MeHg, four hamsters were administered 203Hg-labeled HgCl2 intravenously on day 9 of gestation. The mean biological halftime of 203Hg in animals administered radiolabeled MeHg was 7.7 days and the fecal route was the main excretory pathway. The fetal content of 203Hg in hamsters administered radiolabeled MeHg on gestational day 2 or 9 corresponded to 1.3% and 4.6% of the administered dose, respectively. The distribution of 203Hg in the fetus was more even than in the dam and the concentration of 203Hg in the fetal brain, liver and kidney was similar to that of the placenta. Inorganic Hg was found in maternal liver (18% of total Hg), ki

1120
TITLE:
Fluctuation of trace elements during methylmercury toxication and chelation therapy.

AUTHORS:
BAPU C
PUROHIT RC
SOOD PP

SOURCE:
HUMAN & EXPERIMENTAL TOXICOLOGY; 13 (12). 1994. 815-823.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The aim of the present investigation was to check the fluctuation in essential elements, such as Na, K, Mg, Mn, Cu, Zn, Cr and Ni in the brain, spinal cord, liver and kidney of mice during methylmercury chloride (MMC) toxication and therapy with monothiols (N-acetyl-DL-homocysteine thiolactone and glutathione) and vitamins (vitamin B complex and E). Mercury deposition and its elimination during chelation therapy were also screened for comparative purposes. The animals

were dosed for 7 days with MMC 1 mg/kg/d and some were then kept without treatment for a further 7 days. Other MMC-treated animals were immediately given one of the above antidotes for 7 days. All the animals were sacrificed on the 15th day. There was a decrease in all elements during MMC toxication with few exceptions, for example, copper was increased in the liver as was sodium in the kidney. Treatment with the thiols and vitamins restored the levels of these elements in certain tissues towards normal, b

1121
TITLE:
EFFECTS OF MERCURY LEAD AND TIN ON BRAIN HEXO KINASE

AUTHORS:
LAI J CK
BARROW HN
CARLSON K C JR
BLASS JP

SOURCE:
68TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ST. LOUIS, MO., USA, APR. 1-6, 1984 FED PROC; 43 (3). 1984. ABSTRACT 1730.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM ABSTRACT RAT NEURO TOXICITY GLYCOLYSIS

1122
TITLE:
Activation of calmodulin by various metal cations as a function of ionic radius.

AUTHORS:
CHAO S-H
SUZUKI Y
ZYSK JR
CHEUNG WY

SOURCE:
MOL PHARMACOL; 26 (1). 1984. 75-82.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The active form of calmodulin is a Ca2+ which occur as environmental pollutant) substitute for Ca2+ to activate calmodulin was determined. Binding of Ca2+ resulted in an altered conformation of calmodulin with an increased quantum yield in its Try fluorescence. Qualitatively similar results were obtained with Zn2+, Mn2+, Cd2+, Hg2+, Sr2+, Pb2+, Tb3+, Sm3+ and La3+. The relative extents of

fluorescence enhancement by these cations were related to their ionic radii; all cations with ionic radii close to Ca2+ (0.99) increased Try fluorescence, whereas those with different ionic radii were not effective, or much less so. The change in calmodulin conformation by the cations was confirmed by its altered electrophoretic mobility on polyacrylamide gels. Cations that change the conformation of calmodulin allow it to stimulate bovine brain phosphodiesterase. The relative extents of stimulation of phosphodiesterase by cations were also related to their ionic radii. The ability of metal cations to inhibit Ca2+ binding was similarly related to their ionic radii. The closer the radius of a metal cation was to that of Ca2+, the more effective was the cation to substitute for Ca2+. The range of effective ionic radii was approximately 1 | 0.2 .
Calmodulin-stimulated phosphodiesterase activity by the cations was reversed by trifluoperazine, an antagonist of calmodulin.

1123
TITLE:
TOXICITY OF METHYL MERCURY IN SHEEP AND IN HENS

AUTHORS:
HILMY MI
RAHIM SA
ABBAS AH
TAKA RY

SOURCE:
FED PROC; 36 (3). 1977 404

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BLOOD KIDNEY BRAIN FUNGICIDE EGG LAYING EXFOLIATIVE DERMATITIS LACTATION SPECTROPHOTOMETRY

1124
TITLE:
ACUTE TOXICITY OF METHYL MERCURY ITS TISSUE DISTRIBUTION AND ELIMINATION IN GUINEA-PIGS

AUTHORS:
DOWNIE RH
IVERSON F
PAUL CJ
TRENHOLM HL

SOURCE:
TOXICOL APPL PHARMACOL; 22 (2). 1972 295

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT ENVIRONMENTAL POLLUTANT BRAIN

ABSORPTION KIDNEY CONCENTRATION LIVER

1125
TITLE:
Effect of dietary methionine on methylmercury and atrazine toxicity.

AUTHORS:
MEYDANI M
HATHCOCK JN

SOURCE:
DRUG-NUTR INTERACT; 2 (4). 1984. 217-234.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Effects of dietary methionine (Met) on the toxicities of methylmercury hydroxide (MeHg) and (the herbicide) atrazine in male Wistar rats were investigated. Three levels of dietary Met (0, 0.24, and 0.48%) 3 levels of MeHg (0, 0.5 and 1.5 mg Hg/kg BW (body weight)) and 2 levels dietary of atrazine (0 and 500 mg/kg of diet) were used in 18 groups of rats arranged in a factorial design. Periodic urine (after 1 and 3 wk of toxicant treatments and at the end) was collected for mercapturic acids and Hg excretion determinations. At the end of the experiment animals were sacrificed and samples of blood, liver, kidney and brain were collected for reduced glutathione (GSH) and oxidized glutathione (GSSG), glutathione peroxidase (GSH-Px), glutathione reductase (GSH-Rd), glutathione S-transferase (GSH S-trans) and Hg analyses. Excess dietary Met had a protective effect on MeHg and atrazine toxicities when weight gain was used as the index of toxicity. Liver weight in response to toxicants was increased in the rats fed lower Met levels. In whole blood but not in liver, GSH-Px activity declined as Hg concentration increased. Liver GSH-Rd activity was not changed by any of treatments. Atrazine lowered liver GSH S-trans activity. Increases in MeHg dose caused a decrease in GSH S-trans activity in rats fed the lowest Met level but increased it with the other diets. The lowest Met level caused greater Hg uptake in the organs. Atrazine caused a significant increase in Hg excretion in urine after 3 wk of exposure but not at the end of experiment. Dietary Met had no effect on liver GSH but increased GSSG and total glutathione in blood. Urinary mercapturic acids excretion was increased by dietary atrazine treatment. Met deficiency, in response to both toxicants, depressed weight gain while increasing deposition of Hg in tissues, increased liver GSH S-trans in presence of atrazine, and, in presence of high MeHg, decreased liver GSH S-trans. Supplementation with Met depressed weight loss, liver weight, deposition of Hg in tissues and prevented depression of blood GSH-Px activity. An adaptive process may exist in the rat to prevent depletion of tissue GSH during chronic exposure to GSH-depleting agents. Dietary Met supplementation may not lessen the potentiation of MeHg toxicity caused by atrazine (at the level we used).

1126
TITLE:
Follow-up studies on hearing disturbance in patients with Minamata disease.

AUTHORS:
FURUTA S
OHYAMA M
MATSUYAMA H
KURONO Y
FUKAMI K
YANO H

SOURCE:
OTOL FUKUOKA; 30 (3). 1984. 435-438.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Cases (25) with Minamata disease were investigated otologically and audiologically. Pure tone audiometries of the patients showed that their hearing thresholds showed gradually high frequency losses. The average pure tone thresholds at 500, 1000, 2000 and 4000 Hz, showed very slight losses, compared with threshold measured 10 yr ago. The thresholds of the stapedial reflex were0 Hz. In all cases, the latency and the amplitude of the auditory brain stem responses were within the normal range. Apparently, the hearing impairment due to chronic organic mercury poisoning was slight in the acoustic nerve passway. The hearing impairment in those cases may be caused by aging rather than by Minamata disease.

1127
TITLE:
THE GLYCOGEN CHANGES IN SOME EMBRYONIC CHICK ORGANS OR TISSUES DUE TO COPPER SULFATE

AUTHORS:
KING DW
HSU JL

SOURCE:
FED PROC; 36 (3). 1977 1330

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT LIVER BRAIN HEART SKELETAL MUSCLE KIDNEY INSULIN ZINC METHYL MERCURY CHLORIDE POISONING COMPARISON

1128
TITLE:

AN ANALYSIS OF AUTOPSY BRAIN TISSUE FROM INFANTS PRENATALLY EXPOSED TO METHYLMERCURY

AUTHORS:
LAPHAM L
MYERS G
CERNICHIARI E
BAGGS R
BREWER R
SHAMLAYE C

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 958.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT HUMAN

1129
TITLE:
CELL POPULATION CHANGES AT SPECIFIC BRAIN SITES OF THE MONKEY MACACA FASCICULARIS FOLLOWING LONG-TERM SUBCLINICAL EXPOSURE TO METHYLMERCURY

AUTHORS:
CHARLESTON JS
BODY RL
BURBACHER TM
VAHTER ME
MOTTET NK

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 959-960.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MACACA-FASCICULARIS

1130
TITLE:
EFFECTS OF MERCURIC CHLORIDE ADMINISTRATION ON RECEPTOR BINDING IN VARIOUS RAT BRAIN REGIONS

AUTHORS:
RODGERS DA
SOLIMAN M RI
ALI SF

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 967.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MOUSE SUPEROXIDE

1131
TITLE:
Metabolism of toxic heavy metals in growing organisms: A review.

AUTHORS:
JUGO S

SOURCE:
ENVIRON RES; 13 (1). 1977 36-46

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Absorption of heavy metals is greatly enhanced in the suckling animal (rat) until weaning. The combined action of a milk diet and a greater nonselective permeability of undeveloped intestinal barrier was proposed as a possible explanation of this phenomenon. Transportability and distribution between organs of several heavy metals in the growing animal are different from those in adults. Most important is the fact that toxic heavy metals such as Pb and inorganic Hg are accumulated in the brain of the immature rat in much greater amounts than in adults, suggesting that at the same uptake level the immature organism could be more severely injured. Spontaneous and provoked (as induced by chelating agents) excretion of heavy metals is lower in the young organism. Greater stability and inertness of heavy metal linkages with body ligands in the growing organism with a consequently lower level of free metal could explain this. Toxicity of heavy metals is lower for the young animal than for adults. This supports the hypothesis about a lower level of free metal and a lower level of active fraction of metal body burden in undeveloped organisms. Although there is lower toxicity of heavy metals in the young animal, there is a much higher absorption rate, lower excretion and an unfavorable distribution in the immature organism. Current standards on permissive daily exposure to toxic heavy metals should be carefully reconsidered, taking into account the specificities of behavior of heavy metals in growing organisms. This study may have human

applications in determining the long term effect of continuous exposure to low concentrations of heavy metals.

1132
TITLE:
EFFECTS OF MERCURIC CHLORIDE EXPOSURE ON NEUROTRANSMITTERS LEVELS IN SPECIFIC RAT BRAIN REGIONS

AUTHORS:
RODGERS DA
SOLIMAN M RI
ALI SF

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 967.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT SPIROPERIDOL QUINUCLIDINYL BENZILATE

1133
TITLE:
INCREASED BRAIN GFAP OCCURS WITH BEHAVIOR AND NEUROMUSCULAR EFFECTS OF CHRONIC ORAL METHYLMERCURY

AUTHORS:
EVANS HL
EL-FAWAL H AN

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 969.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT RAT GLIAL FIBRILLARY ACIDIC PROTEIN

1134
TITLE:
BEHAVIORAL AND BRAIN EFFECTS OF PRENATAL FUMONISIN TREATMENT IN RATS

AUTHORS:
FERGUSON SA
ARROWOOD JW
HOLSON RR
KWON OS
SLIKKER W JR

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 975-976.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT RAT MYCOTOXIN

1135
TITLE:
INHIBITION OF RAT BRAIN NITRIC OXIDE SYNTHASE ACTIVITY BY MERCURIC SALTS

AUTHORS:
DESAIAH D
RAO MR

SOURCE:
MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 976-977.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT NEUROTOXICITY

1136
TITLE:
Experimental study of the processes of decontamination in Salmo gairdneri following direct contamination by 2 mercury derivatives (mercuric chloride and methyl mercuric chloride): Analysis of transfers at organism and organ levels.

AUTHORS:
RIBEYRE F
BOUDOU A

SOURCE:
ENVIRON POLLUT SER A ECOL BIOL; 35 (3). 1984. 203-228.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. To study the bioaccumulation and transfer of Hg compounds within a trophic chain, the decontamination of S. gairdneri was studied following direct contamination with HgCl2 and CH3HgCl. The results obtained for the whole fish at 0, 17, 31, 56, 120 and 250 days were expressed as concentrations and contents. A comparison of the dynamics shown by each compound demonstrated a characteristic exponential decrease in the case of HgCl2. Due to the large incease in fish weight over the 250 day period it was necessary to calculate theoretical dilution concentrations. The kinetics of Hg decrease in the fish was discussed in relation to the concept of biological half-life. The study of the Hg distribution within the main organs of S. gairdneri (liver, brain, gills, muscle, posterior intestine, liver, kidneys, spleen and blood), as measured by concentration (an indicator of ecotoxicological risks) and Hg content (indicating the potential for Hg transfers) from one organ to another permitted their classification according to their different ecotoxicological responses. These responses were varied and dictated by the organ concerned and the Hg compound present. The study of Hg transfer between these organs showed that certain compartments were donors (contamination being rapid and more or less complete) while others were receivers (an increase in Hg content occurring during decontamination). It was possible to group the 16 responses obtained (8 organs and 2 compounds) and to demonstrate 5 main types of ecotoxicological response. For the majority of the compartments studied, a relationship existed between contamination level of the organ and its rate of decontamination. The results obtained for the whole fish were explained by certain key organs which showed high Hg contents.

1137

TITLE:

A SINGLE INJECTION OF TRIETHYLLEAD PRODUCED SELECTIVE NEUROCHEMICAL CHANGES IN RAT BRAIN

AUTHORS:

ALI SF
GHOCH C
BARTOLOMEO A
WALSH TJ

SOURCE:

MEETING ON NEUROTOXICITY OF MERCURY: INDICATORS AND EFFECTS OF LOW-LEVEL EXPOSURE HELD AT THE TWELFTH INTERNATIONAL NEUROTOXICOLOGY CONFERENCE, HOT SPRINGS, ARKANSAS, USA, OCTOBER 30-NOVEMBER 2, 1994. NEUROTOXICOLOGY (LITTLE ROCK); 15 (4). 1994. 977.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT NEUROTOXICANT

1138
TITLE:
Mercury pollution of Lake Erie ecosphere.

AUTHORS:
PILLAY K KS
THOMAS C C JR
SONDEL JA
HYCHE CM

SOURCE:
ENVIRON RES; 5 (2). 1972 172-181

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution of Hg in the ecosphere of Lake Erie, USA, was monitored with a highly sensitive and reliable neutron activation analysis procedure. A variety of samples from the fauna and flora of the lake as well as those from its immediate environment were analyzed for their Hg content. The results of this survey indicate a widespread distribution of Hg in air particulates; coal samples of the region; sediments, plankton/algae and fish samples from the lake; and in the brain tissues of long-time residents of the Lake Errie Basin.

1139
TITLE:
Effect Of An Atmosphere With A High Carbon Dioxide Content On Human Tolerance To Acute Hypoxia And Acceleration

AUTHORS:
Agadzhanyan NA
Shul'zhenko YeB
Vil'-vil'yams IF
Serginenko AV

SOURCE:
Kosmicheskaya Biologiya i Meditsina, Vol. 5, No. 6, pages 57-60, 20 references, 19711971

ABSTRACT:
Human tolerances to acute hypoxia and transverse accelerations following exposure to hypercapnia were studied. Test subjects underwent exposure to a normal atmosphere, to atmospheres with carbon-dioxide contents of 22.8, 30.4, 38, or 45 millimeters of mercury (mm Hg) at a total pressure of 760mm Hg, or to an atmosphere containing carbon-dioxide in a volume of 38mm Hg at a total pressure of 405mm Hg. Body tolerance to acute hypoxia was determined as reserve time at a simulated altitude of 7,500 meters.

Tolerance to transverse accelerations in the back to chest direction was studied by exposing subjects to accelerations in excess of 8 gravities at increments of 0.2 gravity per second with the back of the rotating chair slanted at 78 degrees to the acceleration vector. When carbon-dioxide concentrations were raised to 22.8 through 30.4mm Hg, reserve time increased. In all subjects, altitude tolerance was greater following exposure to hypercapnia. Further carbon-dioxide concentration increases produced an altitude tolerance decrease in all subjects. In most instances, human tolerance to transverse accelerations decreased following exposure to hypercapnic atmospheres. The authors conclude that, up to a certain concentration, hypercapnia in conjunction with hypoxia exerts a stimulating influence on the human body with the intensification of respiratory and cardiovascular system reactions improving blood oxygenation. An increase in partial carbon-dioxide pressure favors oxygen transport from the blood to the tissues and reduces oxygen consumption while the local vasodilating influence exerted by carbon-dioxide increases the supply of blood, enhances oxygen delivery to the brain, heart, and other vitally important organs, and facilitates an increase in tolerance to oxygen deficits. The principal mechanism of the shifts observed is possibly a combination of hypercapnia and respiratory acidosis. Prolonged exposure to an atmosphere with a carbon-dioxide content of more than 30mm Hg reduces human tolerance to acute hypoxia and transverse accelerations. (Russian)

1140
TITLE:
INHIBITION OF CA-2+-ATPASE IN CEREBELLUM CB AND CEREBRAL CORTEX CT OF THE RAT BRAIN BY MERCURY

AUTHORS:
YALLAPRAGADA PR
HALL E
FAIL S
RAJANNA S
RAJANNA B

SOURCE:
EXPERIMENTAL BIOLOGY 95, PART II, ATLANTA, GEORGIA, USA, APRIL 9-13, 1995. FASEB JOURNAL; 9 (4). 1995. A663.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT

1141
TITLE:
THE SPECIFICITY OF TOXICANTS INFLUENCE ON THE BEHAVIOUR OF YOUNG STELLATE STURGEON

AUTHORS:
NIKONOROV SI
VITVITSKAYA LV
VOROB'EVA EI

SOURCE:
DOKLADY AKADEMII NAUK; 338 (4). 1994. 560-563.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE ACIPENSER-STELLATUS COPPER SULFATE CADMIUM CHLORIDE MERCURY CHLORIDE PHENOL DETERGENT ENVIRONMENTAL TOXIN WATER POLLUTION BRAIN FUNCTION MOTOR ACTIVITY LEARNING CONDITIONING BEHAVIOR

1142
TITLE:
Reproductive success of herring gulls nesting on Brothers Island, Lake Ontario, in 1973.

AUTHORS:
TEEPLE SM

SOURCE:
CAN FIELD-NAT; 91 (2). 1977 148-157

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Breeding success and causes of breeding failure were assessed in 1973 in herring gull (Larus argentatus) colony of 34 pairs in eastern Lake Ontario. Breeding synchrony was normal, 13 pairs laid repeat clutches, but 77% of all eggs laid failed to hatch. The number of chicks fledged per pair averaged at least 0.06 but not more than 0.18, an exceptionally low result. Geometric mean concentrations of DDE and PCBs (polychlorinated biphenyls) in 15 eggs that failed to hatch were 134 and 420 ppm dry weight. Concentrations of dieldrin, p,p'DDD, p,p'DDT, heptachlor epoxide, beta-BHC, hexachlorobenzene and Hg were each less than 6 ppm. Arithmetic mean shell thickness of 13 of those 15 eggs was 0.339 mm, and mean thickness index of 11 of those 13 was 1.60; both are low values. Pathological examinations and analyses for organochlorine pesticides and PCBs in brains were conducted on 12 chicks that died. For 11 of the 12, no clear cause of death could be determined. A general association was established between high organochlorine levels and the low breeding success.

1143
TITLE:
BEHAVIOR AND BRAIN CHEMISTRY CORRELATES IN MUMMICHOGS FUNDULUS HETEROCLITUS FROM POLLUTED AND UNPOLLUTED ENVIRONMENTS

AUTHORS:
SMITH GM
KHAN AT
WEIS JS
WEIS P

SOURCE:
SEVENTH INTERNATIONAL SYMPOSIUM ON RESPONSES OF MARINE ORGANISMS TO POLLUTANTS (PRIMO 7), GOTEBORG, SWEDEN, APRIL 20-22, 1993. MARINE ENVIRONMENTAL RESEARCH; 39 (1-4). 1995. 329-333.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING PAPER FUNDULUS-HETEROCLITUS PALAEMONETES-PUGIO DOPAMINE SEROTONIN METABOLITES MERCURY ENVIRONMENTAL POLLUTION TOXICITY LIVER PREY CAPTURE

1144
TITLE:
BRAIN STEM GLIOSIS AND MERCURY IN VICTIMS OF SUDDEN INFANT DEATH

AUTHORS:
KEIM C
DRASCH G
ROTHSCHILD M
WETZEL S
STOLTENBURG G
TUERKER T

SOURCE:
INTERNATIONAL CONGRESS ON SUDDEN INFANT DEATH SYNDROME: THE ROLE OF ENVIRONMENTAL FACTORS IN INFANT MORBIDITY AND MORTALITY, GRAZ, AUSTRIA, MAY 24-27, 1995. EUROPEAN JOURNAL OF PEDIATRICS; 154 (5 SUPPL. 1). 1995. S19.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT HUMAN FETAL BLOOD CONCENTRATION SUDDEN INFANT DEATH SYNDROME

1145
TITLE:
SUBACUTE EFFECTS OF METHYL MERCURY ON RODENT BRAIN GLYCOLYSIS

AUTHORS:
USHER DR
PATERSON RA

SOURCE:
J CELL BIOL; 55 (2 PT 2). 1972 265A

ABSTRACT: HEEP COPYRIGHT: BIOL ABS. RAT

1146
TITLE:
ABNORMAL NEURONAL MIGRATION IN HUMAN FETAL BRAIN DUE TO MERCURY POISONING

AUTHORS:
CHOI BH
LAPHAM LW
AMIN-ZAKI L
SALEEM T

SOURCE:
AM J PATHOL; 86 (2). 1977 55A

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT CONTAMINATED BREAD MATERNAL INGESTION CEREBRAL DYSGENESIS

1147
TITLE:
Sensitivity of the binding sites on glutamate transporters to neurotoxic agents.

AUTHORS:
KIILLINGER S
LI Y
BALCAR VJ

SOURCE:
NEUROREPORT; 6 (9). 1995. 1290-1292.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Autoradiography of (3H)L-aspartate binding to sections of rat brain was used to study the sensitivity of Na+-dependent glutamate transporters to neurotoxic agents such as Zn2+, NH4+, oxygen-containing free radicals and mercuric chloride. Only mercuric chloride was a strong inhibitor in cerebral neocortex, hippocampus, neostriaturn, thalamus and cerebellar cortex. It is concluded that the substrate-binding sites on Na+-dependent glutamate transporters are relatively resistant to direct effects of Zn2+, NH4+ and free radicals but they may depend on the structural integrity of thiol bonds. Direct inhibitory effect of mercury on the binding site could significantly contribute to its long-term neurotoxicity.

1148
TITLE:

BRAIN SLICE TECHNIQUES IN NEUROTOXICOLOGY

AUTHORS:
FOUNTAIN SB
TEYLER TJ

SOURCE:
CHANG, L. W. AND W. SLIKKER, JR. (ED.). NEUROTOXICOLOGY: APPROACHES AND METHODS. XXI+851P. ACADEMIC PRESS, INC.: SAN DIEGO, CALIFORNIA, USA; LONDON, ENGLAND, UK. ISBN 0-12-168055-X.; 0 (0). 1995. 517-535.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER HUMAN ANIMAL HEAVY METALS ACRYLAMIDE ANTICHOLINESTERASES ETHANOL CARBON MONOXIDE HIPPOCAMPUS NEOCORTEX SPINAL CORD ANOXIA HYPOXIA NEUROLOGICAL METHOD

1149
TITLE:
EFFECT OF METALLIC MERCURY AND MERCURIC CHLORIDE ON OXYGEN CONSUMPTION IN RATS

AUTHORS:
KIM MH

SOURCE:
J CATHOL MED COLL; 30 (1). 1977 17-24

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. KIDNEY LIVER DIAPHRAGM BRAIN TESTIS

1150
TITLE:
Mercury in the environment.

AUTHORS:
DAMLUJI SF
AMIN-ZAKI L
ELHASSANI SB

SOURCE:
BR MED J; 4 (5838). 1972 489

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Damage from Hg poisoning is believed to be "irreversible." Less amenable necropsies, especially in cases of prenatal poisoning, have shown extensive cellular necrosis in the brain. However, a remarkable improvement of function is seen in some cases, not only in children who received treatment with chelating agents or polythiol resin

but also in those who had no drug therapy. International organizations could give great help in the field of rehabilitation. WHO should direct its efforts in that way rather than believing that nothing can be done for the large number of crippled patients.

1151
TITLE:
Mercury vapour intoxication.

AUTHORS:
VROOM FQ
GREER M

SOURCE:
BRAIN; 95 (PART 2). 1972 305-318

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Industrial negligence in a thermometer manufacturing company resulted in widespread symptoms of Hg intoxication (HgIn). Nine patients were studied up to 20 mo. after HgIn was recognized. All patients had most of the commonly recognized signs and symptoms of HgIn. Irritability and poor concentration were temporarily noted in all patients. All had some defect in recent memory which was moderate in 5 and severe in 2, and was relatively permanent. The memory defect in these patients is similar to the memory defect with temporal lobe lesions. This memory defect, neglected in the past could readily explain much of the psychic symptoms such as anxiety, depression, irritability, insecurity, decreased socialization, and lack of concentration prominent in these patients. Abnormalities in other neuropsychological tests suggest more generalized cerebral cortical dysfunction. EEG demonstrated diffuse slowing in 5 patients and abnormalities were more marked temporally in 3 patients. Parkinsonian symptoms were noted in 4, but persisted in only 1 patient. Tremor was severe in all patients, incapacitating in most, cut improved dramatically after exposure to Hg was terminated. Four patients had signs or symptoms suggesting involvement of the peripheral nervous system. Electromyographic examination demonstrated abnormalities consistent with denervation in 8 of 9 patients. All of the patients improved. The rapidity and degree of recovery was not apparently influenced by BAL (British-anti-lewisite). The clinical syndromes of organic and inorganic Hg poisoning differ in degree, organic Hg producing more severe involvement.

1152
TITLE:
TRACE ELEMENTS IN SERUM AND TISSUES OF DIALYSIS PATIENTS

AUTHORS:

GALLIENI M
PIETRA R
CANAVESE C
DECOSTANZI E
PADOVESE P
COZZOLINO M
SABBIONI E
BRANACACCIO D

SOURCE:
ANNUAL MEETING OF THE AMERICAN SOCIETY OF NEPHROLOGY, SAN DIEGO, CALIFORNIA, USA, NOVEMBER 5-8, 1995. JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY; 6 (3). 1995. 530.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT HUMAN SILVER ARSENIC GOLD BROMINE CADMIUM COBALT CHROMIUM CESIUM COPPER EUROPIUM MERCURY LANTHANUM MOLYBDENUM RUBIDIUM ANTIMONY SCANDIUM SELENIUM URANIUM TUNGSTEN
ZINC BRAIN HEART LIVER SPLEEN SKIN METABOLISM TOXICITY

1153
TITLE:
The Interaction Of Aluminum And Other Metal Ions With Calcium-Calmodulin-Dependent Phosphodiesterase

AUTHORS:
Richardt G
Federolf G
Habermann E

SOURCE:
Archives of Toxicology, Vol. 57, No. 4, pages 257-259, 20 reference, 19851985

ABSTRACT:
The interaction of aluminum (22537231) (Al+3) and other metal ions with calcium/calmodulin/dependent phosphodiesterase was investigated in-vitro. Activator deficient phosphodiesterase obtained from bovine brain was incubated with Al+3, calcium (14127618) ions (Ca+2), lead (14280503) ions (Pb+2), manganese (16397914) ions (Mn+2), mercury(II) (14302875) ions (Hg+2), or cadmium (22537480) ions (Cd+2), or the calmodulin antagonist chlorpromazine (50533). Basal and calmodulin dependent phosphodiesterase activity were determined. The binding of radiolabeled Ca+2 to calmodulin and its displacement by Ca+2, Al+3, Cd+2, Mn+2, or Pb+2 was measured in a flow/dialysis apparatus. Al+3 in concentrations above 0.00001 molar (M) depressed calmodulin dependent and basal phosphodiesterase activity and completely blocked the activities at 0.01M. Cd+2 and Hg+2 blocked basal

activity at concentrations above 0.01M. Mn+2 stimulated both activities between 0.00001 and 0.001M and depressed them at concentrations above 0.001M. Chlorpromazine inhibited only the calmodulin dependent phosphodiesterase activity. Pb+2 was the most potent displacer of radiolabeled calcium bound to calmodulin, followed by Ca+2, Cd+2, or Mn+2, Al+3, and Hg+2 in that order, Al+3 being at least 10 times less potent than Ca+2. The authors suggest that the hypothesized roles of Al+3 in dialysis encephalopathy and other neurological disorders are not linked with calmodulin.

1154
TITLE:
Electromyographic study of the Minamata disease: Investigations in patients with 10 years' history.

AUTHORS:
NAGAKI J
FURUTA T
OKAMOTO S
OKAJIMA T
TOKUOMI H

SOURCE:
BRAIN NERVE (TOKYO); 24 (7). 1972 821-825

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. As a part of the follow-up study of Minamata disease, electromyography and motor nerve conduction velocity were investigated. Among 29 cases tested, fibrillation voltage in 2, diminution of discharge in 11, grouping voltage in 15 and high amplitude NMU voltage in 7 cases were observed as the abnormal recording. The high amplitude NMU voltage suggested involvement of the motor neurons. Slowing of the motor nerve conduction velocity (below normal: 50 m/sec) was obtained in 2 of 30 cases tested.

1155
TITLE:
Effect of pesticide chemicals on marine organisms.

AUTHORS:
Phillips JH

SOURCE:
In: Agricultural ChemicalsöHarmony or Disc; 1971, pp. 68-79

ABSTRACT:
HAPAB The presence of DDT and mercury in fishery products in recent years has caused concern over the use of organic pesticides. In several cases

pesticide residue levels in marine organisms have been correlated with abnormalities and declines in marine populations. Studies of fish in the Monterey Bay area have shown a range of 0.022-66.0 ppm of DDT derivatives in the liver. Levels of DDT derivatives in the blubber of 40 sea lions ranged from 4,000 to 41 ppm with the median between 500 and 1,000 ppm; the average DDT derivatives in the brain ranged from 10-15 ppm. Water samples were taken below the surface along the West Coast for simultaneous measurements of DDT derivatives in the water and in the phytoplankton. Only 10% of the DDT derivatives were associated with the phytoplankton; the other 90% present a possible burden to benthic organisms. Another study measuring the burden in marine sediments in Monterey Bay indicates an input of DDT by water runoff from the Salinas Valley. Questions raised during the discussion period dealt with the significance of low-level pollution by agricultural chemicals and the interpretation of epidemiologic information. 1971

1156

TITLE:

Dietary Administration Of Nickel: Effects On Behavior And Metallothionein Levels

AUTHORS:

Nation JR
Hare MF
Baker DM
Clark DE
Bourgeois AE

SOURCE:

Physiology and Behavior, Vol. 34, No. 3, pages 349-353, 26 references, 19851985

ABSTRACT:

Dietary nickel (7440020) effects on behavior were studied in rats. Metallothionein was measured in the liver and kidneys of treated rats. Male Sprague-Dawley-rats were fed a diet not allowing for weight gain but not causing starvation related problems. Nickel was added at 0, 10 or 20 milligrams per kilogram (mg/kg). After 14 days on the diet, animals were trained over 61 days in an operant training schedule where lever responding was reinforced every 2 minutes on the average. The accumulation of nickel in the tissues of these animals was determined through atomic absorption spectrometry. Hepatic and renal metallothionein was measured through a standard method using radiolabeled mercury (7439976) added to tissue homogenates. Rats treated at the higher dose lever pressed at a significantly lower rate than untreated animals. Those given 10mg/kg did not react at a significantly different rate than the untreated. There was a dose related increase of nickel in the kidney but analyses of blood, bone, brain, hair, small intestine, liver and testes

did not indicate additional accumulations in these organs with increasing exposure. Hepatic and renal metallothionein were not increased above control values in either group of nickel treated animals. The authors conclude that chronic exposure to 20mg/kg, but not to 10mg/kg, affects the behavior of rats in an operant lever press task. Chronic nickel in the diet did not appear to induce metallothionein in the liver or the kidney.

1157
TITLE:
Mercury concentrations in soil, grass, earthworms and small mammals near an industrial emission source.

AUTHORS:
BULL KR
ROBERTS RD
INSKIP MJ
GOODMAN GT

SOURCE:
ENVIRON POLLUT; 12 (2). 1977 135-140

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Scarcity of data describing Hg concentrations in the biota of an environment subjected to Hg fallout prompted this study around a chlor-alkali works. Atomic absorption spectrometric analysis of top-soils, grass (Festuca rubra), earthworms (Lumbricus terrestris) and atmospheric fallout, within 0.5 km and 10-30 km of the works, showed Hg levels were significantly higher near the works. Woodmice (Apodemus sylvaticus) and bank voles (Clethrionomys glareolus chr.) collected near the works had significantly greater concentrations of total Hg in brain, kidney, liver and hair than controls. The presence of methylmercury in the mammals and L. terrestris is evidence for methylation of the inorganic Hg fallout.

1158
TITLE:
Purkinje cells express neuronal nitric oxide synthase after methylmercury administration.

AUTHORS:
HIMI T
IKEDA M
SATO I
YUASA T
MUROTA S-I

SOURCE:
BRAIN RESEARCH; 718 (1-2). 1996. 189-192.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. To study the effects of chemical injury on the cerebellar nitric oxide synthase (NOS), we administered methylmercury chloride subcutaneously to mice, 10 mg/kg/day for 9 days. In the methylmercury-treated cerebellum, Purkinje cells were positive both for NADPH-diaphorase and for neuronal NOS. Calcium-dependent NOS activity was increased to 160% of the controls. The present study suggests the ability of Purkinje cells to produce NO through the expression of neuronal NOS.

1159
TITLE:
MERCURY LEVELS IN FRESH WATER FISH OF THE STATE OF SOUTH-CAROLINA

AUTHORS:
KOLI AK
WILLIAMS WR
MCCLARY EB
WRIGHT EL
BURRELL TM

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 17 (1). 1977 82-89

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. USA SHAD BASS BLUEGILL CATFISH REDBREAST PIKE MUDFISH GILLS MUSCLE LIVER KIDNEY SKIN BONE SCALES FIN GONADS BRAIN STOMACH SPLEEN HEART BLOOD

1160
TITLE:
OBSERVATIONS ON THE EFFECTS OF METHYL MERCURY CYSTEINE ON THE ADULT RAT BRAIN

AUTHORS:
PFRENDER AR

SOURCE:
ANAT REC; 172 (2). 1972 382-383

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT ELECTRON MICROSCOPY RADIOAUTOGRAPHY PROTEIN SYNTHESIS INTERFERENCE

1161
TITLE:
MATHEMATICAL MODEL OF MERCURY METABOLISM IN THE HUMAN BODY

AUTHORS:
SMIRNOVA PA
TOKIN IB

SOURCE:
GIGIENA I SANITARIYA; 0 (2). 1996. 34-36.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RESEARCH ARTICLE METHYLMERCURY TOXICITY BLOOD SKIN BRAIN LYMPH HEART LIVER LUNGS GASTROINTESTINAL TRACT KIDNEY BONE MARROW SPLEEN LYMPH NODES FOOD CHAIN ENVIRONMENTAL POLLUTION HALF-LIFE THRESHOLD LEVEL

1162
TITLE:
A ROLE OF SELENIUM AGAINST METHYL MERCURY TOXICITY

AUTHORS:
SUMINO K
YAMAMOTO R
KITAMURA S

SOURCE:
NATURE (LOND); 268 (5615). 1977 73-74

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN BLOOD BOVINE SERUM ALBUMIN RAT LIVER KIDNEY BRAIN TUNA MUSCLE

1163
TITLE:
Changes in the number of astrocytes and microglia in the thalamus of the monkey Macaca fascicularis following long-term subclinical methylmercury exposure.

AUTHORS:
CHARLESTON JS
BODY RL
BOLENDER RP
MOTTET NK
VAHTER ME
BURBACHER TM

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 17 (1). 1996. 127-138.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effects of long-term subclinical

exposure to methylmercury on the number of neurons, oligodendrocytes, astrocytes, microglia, endothelial cells and pericytes within the thalamus from the left side of the brain of the monkey Macaca fascicularis has been determined by use of the Optical Volume Fractionator stereological method. The accumulated burden of inorganic mercury(IHg) within these same cell types has been determined by autometallographic methods. Four groups of monkeys were exposed to methylmercury (MeHg; 50 mug Hg/kg body weight/day) by mouth for 6 months, 12 months, 18 months, or 12 months followed by 6 months without exposure (clearance group). Neurons, oligodendrocytes, endothelia, and pericytes did not show a significant change in cell number for any exposure group. Astrocyte cell number exhibited a significant decline for both the 6 month and clearance exposure groups. The microglia, in contrast, showed a significant increase in the 18 month and clearanc

1164
TITLE:
Long ago and far away: A retrospective on the implications of Minamata.

AUTHORS:
WEISS B

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 17 (1). 1996. 257-263.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Minamata claimed entry into the lexicon of toxicology 40 years ago as a definition of methylmercury poisoning, but deposited a legacy of unsolved puzzles that still endures. In fact, they scatter ramifications across the entire domain of neurotoxicology. One puzzle is how the earliest clinical index of adult toxicity, paresthesia, can remain stable, even with continued exposure. Does damage, like body burden, reach a plateau? A second enigma is the question of silent damage to nerve cell populations even more vulnerable than those whose loss of function results in minimal symptoms such as paresthesia. Is there a population of unidentified humans exposed to methylmercury whose deficits might be uncloaked by neurobehavioral test methods that have succeeded in revealing silent toxicity in populations exposed to lead, manganese, and elemental mercury? A third puzzle arises in the context of aging. Attrition of nerve cells occurs naturally as the brain ages but is also accom

1165
TITLE:
HEAVY METAL AND ORGANOCHLORINE CONCENTRATIONS IN TISSUES OF THE LITTLE PENGUIN EUDYPTULA MINOR

AUTHORS:

GIBBS PJ

SOURCE:
DANN, P., I. NORMAN AND P. REILLY (ED.). THE PENGUINS: ECOLOGY AND MANAGEMENT; SECOND INTERNATIONAL PENGUIN CONFERENCE, COWES, VICTORIA, AUSTRALIA, AUGUST 1992. XIX+475P. SURREY BEATTY AND SONS PTY LTD: CHIPPING NORTON, NEW SOUTH WALES, AUSTRALIA. ISBN 0-949324-58-2.; 0 (0). 1996. 393-419.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BOOK CHAPTER MEETING PAPER EUDYPTULA-MINOR QUALITY CONTROL LIVER BRAIN FAT EGGS LEAD CADMIUM ZINC COPPER ARSENIC SELENIUM MERCURY NICKEL INSECTICIDE

1166
TITLE:
THE ROLE OF MERCURIC ION AND METHYL MERCURY ON LIPID PEROXIDATION.

AUTHORS:
TAYLOR TJ
RIEDERS F
KOCSIS JJ

SOURCE:
FED PROC; 32 (3 PART 1). 1973 261

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN KIDNEY HOMOGENATES

1167
TITLE:
TIME DEPENDENT DISTRIBUTION OF MERCURY-203 METHYL MERCURIC CHLORIDE IN WHITE LEGHORN CHICKS

AUTHORS:
MCROBERTS D

SOURCE:
PROC S D ACAD SCI; (56). 1977 (RECD 1978) 254-255

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN LIVER BREAST MUSCLE KIDNEY BLOOD BEAK

1168
TITLE:
THE INFLUENCE OF MERCURY I CHLORIDE ON THE BRAIN HISTO PATHOLOGY AND HISTO ENZYMOLOGY

AUTHORS:
KOZIK M
SZCZECH J
SOSINSKI E

SOURCE:
FOLIA HISTOCHEM CYTOCHEM; 15 (2). 1977 154

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT PHOSPHATASES ESTERASES

1169
TITLE:
EFFECT OF METHYL MERCURY COMPOUNDS ON GLYCOLYSIS IN RAT BRAIN

AUTHORS:
SAKUMA C
UCHIDA S

SOURCE:
SEIKAGAKU; 44 (11). 1972 (RECD 1973) 943

ABSTRACT: HEEP COPYRIGHT: BIOL ABS. ABSTRACT

1170
TITLE:
LEAD MERCURY AND CADMIUM TOXICITY IN CHILDREN

AUTHORS:
ANGLE CR
MCINTIRE MS

SOURCE:
PAEDIATRICIAN; 6 (35). 1977 (RECD 1978) 204-225

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. REVIEW ENVIRONMENTAL CONTAMINANT BONE KIDNEY LIVER NERVOUS TISSUE LUNG BRAIN RED CELLS DIAGNOSIS TREATMENT

1171
TITLE:
Anodic stripping voltammetric determination of total lead in anencephalic fetuses after pressure/temperature-controlled microwave mineralization.

AUTHORS:
TAHAN JE
MARCANO L

ROMERO RA

SOURCE:
ANALYTICA CHIMICA ACTA; 317 (1-3). 1995. 311-318.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The development of a closed-vessel mineralization method for the decomposition of brain, liver, kidney and lung specimens of anencephalic (A) fetuses and controls (C) from the eastern coast of lake Maracaibo, Venezuela, is presented. Digestion was done in a laboratory microwave oven provided with pressure sensing tube and fiberoptic temperature probe to monitor and control pressure and temperature conditions inside the lined digestion vessels. Total lead was subsequently determined by differential pulse anodic stripping voltammetry (DPASV) with a hanging mercury drop electrode, The optimized conditions for maximal pressure and temperature set up were 1260 kPa and 190ê C. Three samples and one blank were routinely prepared for simultaneous digestion. After sample mineralization, the lead oxidation peak appeared at a potential of -0.45 V vs. AggCl, pH 4.70. Lead concentrations obtained by DPASV analysis of the mineralized biological materials were compared with those pro

1172
TITLE:
EFFECT OF SUBCHRONIC MERCURY EXPOSURE ON EEG OF RATS

AUTHORS:
DESI I
NAGYMAJTENYI L
SCHULZ H

SOURCE:
FIFTH MEETING OF THE INTERNATIONAL NEUROTOXICOLOGY ASSOCIATION, PORT LUDLOW, WASHINGTON, USA, JUNE 25-30, 1995. NEUROTOXICOLOGY (LITTLE ROCK); 16 (3). 1995. 548.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER HUMAN ELECTROENCEPHALOGRAPHY NEUROTOXICITY CENTRAL NERVOUS SYSTEM PERIPHERAL NERVOUS SYSTEM BRAIN ELECTRICAL ACTIVITY

1173
TITLE:
440KD ISOFORM OF BRAIN ANKYRIN AS A SENSITIVE MARKER FOR THE NEUROTOXICITY OF METHYL MERCURY

AUTHORS:
KUNIMOTO M

SUZUKI T

SOURCE:
FIFTH MEETING OF THE INTERNATIONAL NEUROTOXICOLOGY ASSOCIATION, PORT LUDLOW, WASHINGTON, USA, JUNE 25-30, 1995. NEUROTOXICOLOGY (LITTLE ROCK); 16 (3). 1995. 552.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MEETING ABSTRACT MEETING POSTER RAT CEREBELLUM MICROTUBULE-ASSOCIATED PROTEIN GLIAL FIBRILLARY ACIDIC PROTEIN NEURON-SPECIFIC PROTEIN

1174
TITLE:
THE DISTRIBUTION OF MERCURY IN THE TISSUES OF FRESH WATER FISH

AUTHORS:
BISHOP JN
NEARY BP

SOURCE:
DRUCKER, HARVEY AND RAYMOND E. WILDUNG (ED.). ERDA (ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION) SYMPOSIUM SERIES, VOL. 42. BIOLOGICAL IMPLICATIONS OF METALS IN THE ENVIRONMENT. PROCEEDINGS OF THE FIFTEENTH ANNUAL HANFORD LIFE SCIENCES SYMPOSIUM. RICHLAND, WASH., USA, SEPT. 29-OCT. 1, 1975. IX+682P. ILLUS. MAPS. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION (AVAILABLE AS CONF-750929 FROM NATIONAL TECHNICAL INFORMATION SERVICE, US DEPARTMENT OF COMMERCE: SPRINGFIELD, VA.). 1977. ISBN 0-87079-104-4.; 1977 452-464

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CHANNEL CATFISH CARP PICKEREL NORTHERN PIKE LAKE TROUT WALLEYE MUSCLE BONE SKIN SCALES LIVER KIDNEY HEART BRAIN GONAD INTESTINE

1175
TITLE:
Astrocytes as modulators of mercury-induced neurotoxicity.

AUTHORS:
ASCHNER M

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 17 (3-4). 1996. 663-669.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The case for significant toxicity of methylmercury (MeHg) to the CNS is strongly supported by both in vivo and

in vitro studies. MeHg perturbs a number of cellular processes which most certainly include astrocytic failure to maintain the composition of the extracellular fluid. Astrocytic predisposition to be damaged by MeHg offers a potential explanation for its neurotoxicity. Consistent with this concept is the ability of astrocytes to preferentially concentrate brain MeHg. The present commentary elaborates on the role of astrocytes in mediating MeHg-induced injuries, detailing their function in maintaining the extracellular concentrations of the excitatory amino acids glutamate and aspartate. It continues with a discussion on the effects of MeHg on astrocytic swelling and the ensuing regulatory volume decrease (RVD). Recent work demonstrating that primary astrocyte cultures constitutively express a cluster of sulfhydryl (-SH)-containing proteins, collectively referred

1176
TITLE:
Effects of Methylmercuric Chloride, Cycloheximide, and Colchicine on the Reaggregation of Dissociated Mouse Cerebellar Cells

AUTHORS:
Jacobs AJ
Maniscalco WM
Finkelstein JN

SOURCE:
Toxicology and Applied Pharmacology, Vol. 86, No. 3, pages 362-371, 23 references, 19861986

ABSTRACT:
The effects of methylmercuric-chloride (115093) (MMC), cycloheximide (66819), and colchicine (64868) on reaggregation of cerebellar cells were studied in mice. Neonatal BALB/c-mice were administered 0 or 3mg/kg MMC orally. Twenty-four hours later, they were killed, and the brains were removed. Cerebellar cells were isolated and the ability of the cells to reaggregate was evaluated by using a cell recognition/cohesion assay. Reaggregation was monitored by measuring cell diameters from low power photomicrographs. In in-vitro experiments, isolated mouse cerebellar cells were incubated with 0 to 4.0 micromolar (microM) MMC, 0 to 10.0microM cycloheximide, or 0 to 10.0microM colchicine. The cell cultures were monitored for reaggregation. In-vivo exposure to MMC disrupted the ability of cerebellar cells to reaggregate. Between 25 and 51 hours (hr) of culturing, exposed reaggregates grew at a faster rate than control cultures, and at 51hr attained average diameters 40 percent greater than controls. In-vitro MMC caused an initial dose related inhibition of reaggregation, the concentration for 50 percent inhibition being 1.5microM through 24hr. Afterwards, a dose dependent acceleration in reaggregation occurred. By 95hr, reaggregates exposed to 1microM MMC had attained mean diameters almost twice that of the controls.

Cycloheximide caused only a dose dependent inhibition of reaggregation. Colchicine caused a dose dependent acceleration of reaggregation similar to that seen in MMC exposure, except there was no initial inhibitory phase. The authors suggest that MMC affects cerebellar cell recognition by a complex process involving an initial decrease in synthesis of specific proteins, followed by changes in microtubules.

1177
TITLE:
EFFECT OF DIETARY CYSTEINE ON TOXICITY TISSUE DISTRIBUTION AND ELIMINATION OF METHYL MERCURY IN THE RAT

AUTHORS:
FARRIS FF
POKLIS A
GRIESMANN GE

SOURCE:
DRUCKER, HARVEY AND RAYMOND E. WILDUNG (ED.). ERDA (ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION) SYMPOSIUM SERIES, VOL. 42. BIOLOGICAL IMPLICATIONS OF METALS IN THE ENVIRONMENT. PROCEEDINGS OF THE FIFTEENTH ANNUAL HANFORD LIFE SCIENCES SYMPOSIUM. RICHLAND, WASH., USA, SEPT. 29-OCT. 1, 1975. IX+682P. ILLUS. MAPS. ENERGY RESEARCH AND DEVELOPMENT ADMINISTRATION (AVAILABLE AS CONF-750929 FROM NATIONAL TECHNICAL INFORMATION SERVICE, US DEPARTMENT OF COMMERCE: SPRINGFIELD, VA.). 1977. ISBN 0-87079-104-4.; 1977 465-477

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ANTIDOTE-DRUG BLOOD SPLEEN BRAIN TESTIS KIDNEY LUNG MUSCLE

1178
TITLE:
Chemical contaminants in harbor porpoise (Phocoena phocoena) from the North Atlantic coast: Tissue concentrations and intra- and inter-organ distribution.

AUTHORS:
TILBURY KL
STEIN JE
MEADOR JP
KRONE CA
CHAN S-L

SOURCE:
CHEMOSPHERE; 34 (9-10). 1997. 2159-2181.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Concentrations of chlorinated hydrocarbons (CHs), such as polychlorinated biphenyls (PCBs), were measured in subsamples taken from different anatomical locations of blubber and liver of three apparently healthy harbor porpoises (Phocoena phocoena) incidentally caught in a gill-net fishery along the northwest Atlantic coast; selected elements (e.g., mercury) were measured in subsamples of liver. The vertical distribution (skin to muscle) of contaminants within blubber was also determined. Additionally, the concentrations of CHs and elements were determined in individual samples of brain, lung, kidney, and testis to assess how the disposition of toxic chemicals may be dependent on the physiological characteristics of a specific organ. Statistical analyses of the results showed that the anatomical location of the blubber or liver sample had no significant effect on concentrations of either CHs in blubber and liver, or of selected elements in liver. However, there were stat

1179
TITLE:
Evaluation of the Q16 questionnaire on neurotoxic symptoms and a review of its use.

AUTHORS:
LUNDBERG I
HOGBERG M
MICHELSEN H
NISE G
HOGSTEDT C

SOURCE:
OCCUPATIONAL AND ENVIRONMENTAL MEDICINE; 54 (5). 1997. 343-350.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Objectives: The questionnaire 16 (Q16) is commonly used to study prevalences of neurotoxic symptoms among workers exposed to organic solvents. It has also been recommended that exposed workers reporting more than six symptoms should be referred for further examination of possible chronic toxic encephalopathy. It would be useful to know whether symptoms reported in the questionnaire also reflect impairment of similar functions measured with objective or semiobjective methods in a formerly highly exposed group. Methods: 135 painters and 71 carpenters answered the Q16, were interviewed about symptoms compatible with an organic brain damage, and took a battery of psychometric tests. A subsample of 52 painters and 45 carpenters were interviewed for psychiatric diagnosis according to Diagnostic and Statistical Manual for Mental Disorders, 3rd version (DSM III) and their vibration thresholds in hands and feet were measured. The entire group was followed up in the register of d

1180
TITLE:
Retrospective assessment of occupational exposure to chemicals in community-based studies: Validity and repeatability of industrial hygiene panel ratings.

AUTHORS:
BENKE G
SIM M
FORBES A
SALZBERG M

SOURCE:
INTERNATIONAL JOURNAL OF EPIDEMIOLOGY; 26 (3). 1997. 635-642.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Background. Occupational hygiene panels are increasingly being used to rate retrospective occupational exposures to chemicals in community-based studies. This study aimed to assess the validity, reliability and feasibility of using such an expert panel in a brain tumour case-control study. Methods. A panel of five experts was recruited to rate exposure to 21 chemicals for 298 job descriptions to investigate the level of agreement. Validity was assessed by comparing the ratings of the experts for 49 of the jobs with objective quantitative exposure data which existed for these jobs. Repeatability was assessed by comparing the results for 50 resubmissions. Results. Specificity was high for reporting that exposure occurred (all above 90%), but sensitivity was variable with values between 48% and 79%. Weaker validity was found for rating exposure level and exposure frequency. The raters showed the greatest inter-rater agreement for exposure to three of the 21 chemicals consi

1181
TITLE:
Disorders of the central nervous system in prolonged experimental poisoning with mercury vapors.

AUTHORS:
TWARDOWSKA-SAUCHA K
ACHTELIK W

SOURCE:
BIUL SLUZBY SANIT EPIDEMIOL WOJEWODZTWA KATOWICKIEGO; 16 (3). 1972 (RECD 1973) 305-316

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Prolonged exposure to Hg vapors leads to CNS damage. Hg blocks activity of enzymes participating in electron transport

and CNS transmission activities. Poisoning with Hg vapors leads to degeneration and intensification of catabolic processes. Histochemical and biochemical changes in the cerebrum and cerebellum resulting from Hg poisoning can lead to metabolic disorders connected with the occurrence of certain symptoms characteristic for brain damage.

1182
TITLE:
Effects of dyeing and printing industry effluent on acid and alkaline phosphatase in few vital organs of a coastal teleost, Periophthalmus dipes.

AUTHORS:
CHHAYA J
THAKER J
MITTAL R
NUZHAT S
MANSURI AP
KUNDU R

SOURCE:
INDIAN JOURNAL OF MARINE SCIENCES; 26 (2). 1997. 186-190.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Experiments were carried out to assess the dose and duration dependent effects of dyeing and printing effluent on the lysosomal enzyme, acid phosphatase and a membrane bound enzyme, alkaline phosphatase in five vital tissues viz. gills, intestine, liver, brain and muscle, of a coastal euryhaline teleost Periophthalmus dipes. Fishes were exposed to different effluent dilution viz. 0.1%, 0.5% and 1% for three test periods (2, 4 and 6 days) and the activity of the enzymes was estimated. The results show both significant inhibition at the lower concentrations and stimulation in the higher effluent concentration. Significant dose and duration dependent changes occurred in the gills whereas, predominant duration dependent changes were noticed in other tissues examined.

1183
TITLE:
EFFECTS OF METHYL MERCURY IN CATS AFTER PRE NATAL OR POST NATAL TREATMENT

AUTHORS:
KHERA KS

SOURCE:
TERATOLOGY; 7 (3). 1973 A-20

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN HISTOLOGICAL CHANGES

1184

TITLE:

The biological half-time of heavy metals: The existence of a third, "slowest" component.

AUTHORS:

SUGITA M

SOURCE:

INT ARCH OCCUP ENVIRON HEALTH; 41 (1). 1978 25-40

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Concentrations of Cd (475 samples), Pb (271) and total Hg (166) were determined in the organs and tissues (heart, pancreas, kidney, liver, brain, skeletal muscle, aorta, bone, bile and urine) of inhabitants of the Tokyo (Japan) metropolitan area. These individuals had no known exposure to abnormally high levels of heavy metals and had died suddenly. Based on the intraorganic accumulation of the heavy metals according to age when they were not experimentally administered, the biological half-time (BHT) was estimated using a mathematical model with differential equations. It was hypothesized that the input of heavy metals into organs is proportional to the amount of food intake according to age (assuming little or no chronological change of heavy metals concentrations in food over several decades), and that the output is proportional to the intraorganic accumulation. The resulting BHT was very long, 10-100 times that computed in a number of studies from observation of the attenuation curve for a relatively short period after the experimental administration of heavy metals to humans or animals. A model consisting of 2 series compartments in 1 organ was devised: the superficial, where heavy metals enter directly and are weakly bound with protein, and the profound, where they enter only via the superficial compartment to be a strongly bound with the constituents. The short BHT obtained by heavy metal administration is associated only with the superficial compartment of the organ, and the long BHT obtained without experimental administration of heavy metals is due to the detour circuit from the superficial to the profound compartments. The ratio of the short BHT to the long BHT is the proportion of the content of a heavy metal in the superficial compartment to the total content in the whole organ. In order to prove the existence of the 2 compartments and to compute their ratios, further studies should be performed. The attenuation curve of the concentration, or of the amount after a single administration of a heavy metal, consists of the rapid component (first) and the slow component (second). The latter has been generally used for computation of BHT. The slowest component is frequently present several years after the first 2. There is a fair chance that the BHT based on the slowest component agrees with the BHT found in the present study.

1185
TITLE:
Increased Free Intrasynaptosomal Ca+2 by Neurotoxic Organometals: Distinctive Mechanisms

AUTHORS:
Komulainen H
Bondy SC

SOURCE:
Toxicology and Applied Pharmacology, Vol. 88, No. 1, pages 77-86, 41 references, 19871987

ABSTRACT:
The effects of neurotoxic organometals on intrasynaptosomal calcium (Ca+2) were studied in-vitro. Synaptosomes obtained from the brains of male Fischer-344-rats were incubated with 2.5 to 30 micromolar (microM) methylmercury-chloride (115093) (MMC), triethyllead-chloride (1067147) (TEL), triethyltin-chloride (994310) (TET), or trimethyltin-chloride (1066451) (TMT) with or without 1 millimolar (mM) calcium-chloride. In some experiments, synaptosomes were pretreated with 50mM potassium ion (K+), 3OmicroM verapamil, or 5microM tetrodotoxin alone or in combination. The effects on free synaptosomal Ca+2 were evaluated. MMC was the most potent stimulator of free intrasynaptosomal Ca+2, increasing the Ca+2 concentration in a dose dependent manner. TEL, TET, and TMT were much less potent. When calcium-chloride was omitted from the medium, neither TEL nor TET increased Ca+2 at all and MMC only marginally. Verapamil inhibited 36 percent of the TEL induced elevation of Ca+2, but had no effect on the stimulation of Ca+2 by MMC or TET. Verapamil inhibited 48 percent of the increase in Ca+2 induced by K+. Tetrodotoxin inhibited by 67 percent the increase in Ca+2 caused by TEL, but had no effect on the increases induced by TET or MMC. Synaptosomes were incubated with MMC, TET, or TEL in the presence or absence of ouabain. Ouabain potentiated the increases in Ca+2 induced by MMC and TET. The authors conclude that neurotoxic derivatives of alkylmetal compounds increase the concentration of free synaptosomal Ca+2. This is due to nonspecific increases in Ca+2 leakage through the plasma membrane in the case of MMC or TET or to specific interferences with mechanisms regulating Ca+2 fluxes through the plasma membrane in the case of TEL.

1186
TITLE:
THE BEHAVIORAL TOXICOLOGY OF METALS

AUTHORS:
WEISS B

SOURCE:
FED PROC; 37 (1). 1978 22-27

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. SAIMIRI-SCIUREUS MACACA-ARCTOIDES RAT PIGEON BLOOD BRAIN BARRIER

1187
TITLE:
Biological monitoring of environmental pollution and human exposure to metals in Tarragona, Spain. II. Levels in autopsy tissues.

AUTHORS:
LLOBET JM
GRANERO S
SCHUHMACHER M
CORBELLA J
DOMINGO JL

SOURCE:
TRACE ELEMENTS AND ELECTROLYTES; 15 (1). 1998. 44-49.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Arsenic (As), beryllium (Be), cadmium (Cd), chromium (Cr), mercury (Hg), manganese (Mn), nickel (Ni), lead (Pb), tin (Sn), thallium (Tl), vanadium (V), and zinc (Zn) concentrations were determined in brain, bone, kidney, liver, and lung of 20 autopsied subjects nonoccupationally exposed to these elements, who at the time of death had lived in Tarragona (Catalonia, Spain) during at least the last 10 years. Results were analyzed in terms of age, sex, and specific place of residence. Beryllium, Cd, Cr, Mn, Ni, Pb, Tl, Sn, V, and Zn were measured by ICP-MS, whereas As and Hg were determined by using hydride generation-MS. Beryllium, Tl, and V were under the respective detection limits. Bone showed the highest concentrations of As, Cr, Ni, Pb, Sn, and Zn. In turn, the highest levels of Cd and Hg were found in kidney, while liver was the organ with the highest Mn concentrations. For most elements, tissue levels were higher in males than in females. No significant differences

1188
TITLE:
Effects of trace elements and mono- and dithiols on mitochondrial monoamine oxidase of rats.

AUTHORS:
REVIS N
HORTON C

SOURCE:
TOXICOL APPL PHARMACOL; 43 (3). 1978 439-448

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The effects of several trace elements (environmental pollutants) on mitochondrial (heart, liver, kidney, brain, adrenals) monoamine oxidase (MAO , (E.C. 1.4.3.4) were studied. Elements were studied at a concentration of 1 mM; only Hg, Cd and Cu were significantly effective in reducing the activity of this enzyme. Of several thiols tested, only dithiothreitol could reverse the inhibition of MAO by these elements. Evidence is also presented to show that cysteine, homocysteine and reduced glutathione inhibit this MAO; dithiothreitol or dithioerythritol evoke stimulatory responses.

1189
TITLE:
Effect of N-Acetyl-DL-homocysteine Thiolactone and 2,3-Dimercaptosuccinic Acid on the Restoration of Alkaline Phosphatase in the Nervous System of Rat During Methylmercury Toxication

AUTHORS:
Sood PP
Unnikumar KR

SOURCE:
Journal of Environmental Pathology, Toxicology and Oncology, Vol. 7, No. 3, pages 21-28, 17 references, 19871987

ABSTRACT:
Tests were carried out to determine the effects of N-acetyl-DL-homocysteine-thiolactone (AHT) and 2,3-dimercaptosuccinic-acid (DMSA) in a dose of 40mg/kg, on the activity of alkaline-phosphatase (AP) in the brain and trigeminal ganglia in male albino-rats treated subcutaneously with methylmercury-chloride (115093) (MMC) at the rate of 10mg/kg daily for periods ranging from 2 to 15 days. The activity of AP in the rats treated with MMC for 2 days increased slightly, while animals treated for 7 and 15 days showed, respectively, 3.83 and 16.48 percent inhibition. Treatment with AHT restored the levels of AP in the MMC treated rats, except in the animals receiving treatment for 15 days. The antagonistic effect of AHT was highly significant at all sites, except in the hindbrain where its effect was only marginally significant. On the contrary, the administration of DMSA had an insignificant effect on the inhibition of MMC induced AP. The authors conclude that the hindbrain of rats is affected more severely by MMC than the other sites evaluated.

1190
TITLE:
ELIMINATION PATTERN OF METHYL MERCURY FROM BLOOD AND BRAIN OF RATS DAMS

AND OFFSPRING AFTER DELIVERY FOLLOWING ORAL ADMINISTRATION OF ITS CHLORIDE SALT DURING GESTATION

AUTHORS:
CASTERLINE J L JR
WILLIAMS CH

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 7 (5). 1972 (RECD 1973) 292-295

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ENVIRONMENTAL DISPERSAL

1191
TITLE:
Prenatal methylmercury exposure and children: Neurologic, developmental, and behavioral research.

AUTHORS:
MYERS GJ
DAVIDSON PW

SOURCE:
ENVIRONMENTAL HEALTH PERSPECTIVES; 106 (SUPPL. 3). 1998. 841-847.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Mercury is present in the earth's crust and is methylated by bacteria in aquatic environments to methylmercury (MeHg). It is then concentrated by the food chain so predatory fish and sea mammals have the highest levels. Thus, consuming seafood leads to exposure. MeHg readily crosses the placenta and the blood-brain barrier and is neurotoxic. The developing fetal nervous system is especially sensitive to its effects. Prenatal poisoning with high dose MeHg causes mental retardation and cerebral palsy. Lower level exposures from maternal consumption of a fish diet have not been consistently associated with adverse neurodevelopmental outcomes. However, most studies have considerable uncertainty associated with their results. Two large controlled longitudinal studies of populations consuming seafood are underway that are likely to determine if any adverse effects can be identified. No adverse associations have been found in the Seychelles, where exposure is mainly from fish

1192
TITLE:
Dietary protein levels cause different effects of methionine supplement on the fate of methylmercury in mice.

AUTHORS:

ADACHI T
HIRAYAMA K

SOURCE:
JAPANESE JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH; 44 (3). 1998. 226-232.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The effect of supplementing methionine (1%) to a 24.8% protein diet (normal protein diet, NPD) or a 7.5% protein diet (low protein diet, LPD) on the fate of methylmercury (MeHg) was investigated after oral administration of MeHg (20 mumol/kg). Hg concentration in the brain was increased by methionine supplement to LPD, but not to NPD. Methionine supplement to both NPD and LPD resulted in increased Hg concentration in the liver but decreased Hg concentration in the kidney. Hg concentrations in the blood and plasma were decreased only by methionine supplement to LPD. Urinary Hg excretion was increased by methionine supplement to both diets, whereas no marked difference in fecal Hg excretion was observed by the supplement. Hg concentration in the plasma low molecular weight (LMW) fraction 2 h after oral administration of MeHg (20 mumol/kg) was increased by methionine supplement to LPD, but not to NPD. This suggests that the ratio of availability of sulfur amino acids for t

1193
TITLE:
Application of covalent affinity chromatography with thiol-disulphide interchange for determination of environmental exposition to heavy metals based on the quantitative determination of Zn-thionein from physiological human fluids by indirect method based on analysis of metal contents.

AUTHORS:
KABZINSKI A KM

SOURCE:
BIOMEDICAL CHROMATOGRAPHY; 12 (5). 1998. 281-290.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. intoxication with heavy metals results in numerous poisonings and diseases. They disturb metabolism of the system, are the source of cancer, degeneration changes and others. As a result of kidney damage the urine of people exposed to heavy metals contains different low molecular weight proteins, oligopeptides and amino acids, indicating pathological changes. One of the proteins is a very specific metallopolythiopolypeptide-metallothionein (MT). Based on earlier investigations, a very good correlations has been found between the contents of metallothionein in urine and plasma and the concentration of heavy metals in the blood, urine, kidneys, liver and brain and general in

level of exposition to heavy metals. The aim of our investigations was to carry out quantitative isolation of Zn-thionein (Zn-Th), in order to determine the level of exposition to heavy metals. For Zn-Th protein isolation by covalent affinity chromatography with thiol-disulphide interchange (CAC-TDI) w

1194
TITLE:
A TRACER STUDY OF THE DISTRIBUTION OF METHYL MERCURY IN PREGNANT RATS

AUTHORS:
ROBKIN MA
KING RB

SOURCE:
TRANS AM NUCL SOC; 17. 1973 95-96

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN LIVER KIDNEY HEART PLACENTA FETUS TERATOGEN

1195
TITLE:
DEVELOPMENTAL NEUROTOXICITY OF LEAD AND METHYL NERCURY

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

1196
TITLE:
Accumulation of mercury and selenium in tissues of kittens fed commercial cat food.

AUTHORS:
BOYER C I JR
ANDREWS EJ
DELAHUNTA A
BACHE CA
GUTENMANN WH
LISK DJ

SOURCE:
CORNELL VET; 68 (3). 1978 365-374

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Kittens, 3 males and 3 females, were fed for 100 days on a commercially canned red meat tuna containing elevated concentrations of Hg and Se while a control group was fed a dry commercial cat food comparatively low in the concentration of these elements. At the end of the feeding trial, concentrations of Hg and Se were markedly higher in blood, bone, brain, kidney, liver, muscle and spleen of the kittens fed the tuna diet as compared to the controls. No behavioral abnormalities or pathological lesions were detected in any of the kittens.

1197
TITLE:
SIMPLIFIED METHOD OF GOLD TONING METAL DETECTION

AUTHORS:
KOYA G

SOURCE:
ACTA HISTOCHEM CYTOCHEM; 4 (4). 1971 (RECD 1972) 247

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN MERCURY CONTAMINATION

1198
TITLE:
DOSIMETRY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

1199
TITLE:
THE INFLUENCE OF AGE ON HEAVY METAL CONCENTRATIONS IN HUMAN TISSUE

AUTHORS:
WEIGERT P
FISCHER H

SOURCE:
NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL; 302 (SUPPL). 1978 R16

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT LEAD COPPER MERCURY CADMIUM MANGANESE ZINC LIVER METABOLISM BRAIN TOXICITY KIDNEYS

1200

TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1201
TITLE:
Physical and Chemical Factors that Increase Vulnerability to Stress or Act as Stressors at Work

AUTHORS:
Lindstrom K
Mantysalo S

SOURCE:
Psychosocial Factors at Work and Their Relation to Health, R. Kalimo, M. A. El-Batawi, and C. L. Cooper, Editors; Geneva, World Health Organization, pages 112-123, 42 references, 19871987

ABSTRACT:
The problem of occupational stress was discussed in relationship to the presence of noise, thermal conditions, vibration, and chemicals as stressors in the work environment. According to the authors, the most commonly present neurotoxic agents in industry are organic solvents. Painting, dry cleaning, degreasing of metals, lamination, gluing, and photogravure printing are tasks which have included solvent exposure. Psychological effects of working with neurotoxic agents included decreased ability to remember or learn along with decreased sensory and motor functions. Exposure to halogenated hydrocarbons has produced impairment of cognitive and psychomotor functions and affective alterations. Aromatic hydrocarbons can cause visuomotor inaccuracy, psychoorganic deterioration, and short term memory effects. Aliphatic hydrocarbons, present in paints, can cause lowered emotionality and less control of behavior and thinking processes. Carbon-disulfide (75150) exposure can occurs during the production of artificial fibers by the viscose method and has produced deterioration in the brain. Carbon-monoxide (630080) can cause fatigue, lack of mental energy, irritability and difficulty in concentrating. Exposure to heavy metals, the most toxic being lead (7439921) and mercury (7439976), may occur in metallurgic processing, in refineries, chloralkali facilities, and certain chemical laboratories, and in the electrical industry. Pesticides, mainly the organophosphorus type, can cause anxiety, dizziness, headache, and tremor and depression. Noise can damage the ear itself, cause mental stress, fatigue, and a slowing of nervous system responses. Vibration and thermal conditions have also been

shown to be stressors. Improvements to be made in the chemical and physical environment of the workplace were noted, along with suggestions for worker education and research in the field.

1202
TITLE:
DOSIMETRY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

1203
TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1204
TITLE:
EFFECTS OF L CYSTEINE CO ADMINISTRATION ON SHORT-TERM MERCURIC CHLORIDE DISTRIBUTION IN RATS

AUTHORS:
THOMAS DJ
O'TUAMA LA

SOURCE:
PHARMACOLOGIST; 20 (3). 1978 177

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT TOXICITY METABOLISM INTRA VENOUS ADMINISTRATION LIVER KIDNEY BRAIN PLASMA MERCURY

1205
TITLE:
DOSIMETRY

AUTHORS:
CLARKSON TW

SOURCE:

Crisp Data Base National Institutes Of Health

1206
TITLE:
Chelation in Metal Intoxication XXVII: Chelating Agents Containing Vicinal Thioether Groups as Antidotes of Lead Toxicity

AUTHORS:
Tandon SK
Sharma BL
Singh S

SOURCE:
Drug and Chemical Toxicology, Vol. 11, No. 1, pages 71-84, 16 references, 19881988

ABSTRACT:
Chelating agents containing vicinal thioether groups were compared with a chelator containing vicinal-mercaptal groups as antidotes of lead (7439921) (Pb) intoxication. Male albino rats were administered 10mg/kg Pb as the acetate by gastric gavage, 6 days a week for 6 weeks. Groups of 6 of the treated rats then received intraperitoneally 0.3 mole per kilogram 4,5-dicarboxy-3,6-dithiaoctanedioic-acid (DMSA), disodium-3,6-dithia-1,8-octanediol-4,5-dicarboxylate (DMES), 2,9-diamino-5,6-dicarboxy-4,7-dithiadecanedioic-acid (DCSA), or alpha-mercapto-beta-(2-thienyl)-acrylic-acid (29529848) (MTA) dissolved in sodium-bicarbonate, or distilled water alone, daily for 3 days. The animals were maintained and urine and feces collected for 4 days, when blood was collected and the animals were killed. DMSA, DMES, and DCSA were about equally effective, but more effective than MTA, in enhancing urinary and fecal excretion of Pb. Administration of Pb significantly inhibited blood delta-aminolevulinic-acid-dehydratase (ALAD), decreased the hemoglobin content, and elevated the levels of blood zinc-protoporphyrin (ZPP) and urinary delta-aminolevulinic-acid (ALA). Treatment with DMSA, DMES, and DCSA partly restored blood ALAD activity and urinary ALA excretion but did not affect the changes in ZPP and hemoglobin. MTA was completely ineffective in reversing the biochemical alterations. DMSA, DMES, and DCSA were equally effective in reducing blood, liver, and kidney levels of Pb; the mobilization of hepatic Pb was far more than blood or renal Pb. MTA was equally potent in depleting renal Pb only. None of the compounds mobilized Pb from the brain. The authors conclude that the chelators with vicinal-thioether groups appear as promising antidotes of Pb intoxication owing to their water solubility, low toxicity, and ability to chelate toxic metals.

1207
TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1208
TITLE:
Interactions of Neurotoxicants with Neurotransmitter Systems

AUTHORS:
Costa LG

SOURCE:
Toxicology, Vol. 49, Nos. 2/3, Part 2, NIOSH Grant No. K01-OH-00054, pages 359-366, 54 references, 19881988

ABSTRACT:
In an effort to better understand the mechanisms of neurotoxicity, research concerning the interaction of toxicants with neurotransmitter systems has been reviewed. Specific examples of chemicals which attack one or more of the parameters of neurotransmission were discussed. One or more of the components of neurotransmission have been shown to be affected by compounds of different chemical classes. Carbon-disulfide (75150) increases the level of dopamine and decreases norepinephrine content in the brain. Particular food colors, heavy metals, organometallic compounds, or pesticides each impair the uptake of neurotransmitters. Three classes of pesticides inhibit neurotransmitter degradation. The organophosphates and carbamates inhibit acetylcholinesterase. The formamidines inhibit monoamineoxidase and interact with alpha2-adrenoceptors. Other pesticides, the type-II pyrethroids and several organochlorines interact with the GABA receptor/ionophore complex. Pyrethroids of both type-I and type-II have as their target the axonal sodium channel. One of the problems in studying neurotoxicants is the fact that they often have more than one target. In addition, the observed effects may actually be the result of nonspecific actions on the cell membrane or on cellular metabolism, making it difficult to measure the effect of the neurotransmitter and to assign particular effects to a specific agent. Even so, the authors stress the importance of neurochemical studies as a support to behavioral, electrophysiological, and pathological studies.

1209
TITLE:
DOSIMETRY

AUTHORS:

CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

1210
TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1211
TITLE:
DOSIMETRY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

1212
TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1213
TITLE:
Systemic mercury intoxication following rupture of a Miller- Abbott tube.

AUTHORS:
BREDFELDT JE
MOELLER DD

SOURCE:
AM J GASTROENTEROL; 69 (4). 1978 478-480

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Following rupture of a Miller-Abbott tube Hg

bag, a 39 yr old woman, postoperative for resection of the right colon for diverticulosis and diverticulitis, developed signs and symptoms of systemic Hg intoxication. A small bowel fistula allowed the metallic Hg to aggregate in retroperitoneal tissues setting up an environment which was conducive to conversion of metallic Hg to divalent Hg, an absorbable product. Analysis of brain, kidney and urine following her death showed markedly elevated Hg levels. This is believed to be the only reported case of such a complication. Clinicians should be wary of elemental Hg in the gastrointestinal tract in patients with suspected or proven enteric fistulas.

1214
TITLE:
Evidence of metal pollution in Cetacea of the western Mediterranean.

AUTHORS:
VIALE D

SOURCE:
ANN INST OCEANOGR; 54 (1). 1978. 5-16.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Whether pollution of the Mediterranean by metals has repercussions on Cetacea by way of their trophic environment was studied. Several important metals entering the sea, Fe, Ti, Cr, V, Cd, Pb and Hg, were assayed in the organs of various beached Cetacea: skin, blubber, muscle, liver, lung, kidney and brain. Fe and Hg were found in abnormally high levels in the liver; Ti is stored in the lung and transgresses the placental barrier; a relatively large amount of Cr is present in nervous tissue; Cd reaches a maximum in the kidney and the highest levels of V are found in the gut. The highest levels found in Cetacea organs are 8le human dietary levels for Fe, and 1500g. Concentrations of Ti found in Cetacea are the highest reported for marine animals; Cr values are 2.5igher than those for other marine species. The number of Cetacean beachings has increased progressively each year and the specific composition is changing; e.g., there has been a considerable increase in beachings of Stenella coeruleoalba.

1215
TITLE:
DOSIMETRY

AUTHORS:
CLARKSON TW

SOURCE:
Crisp Data Base National Institutes Of Health

1216
TITLE:
CORE-- MORPHOLOGY AND HISTOCHEMISTRY

AUTHORS:
RODIER PM

SOURCE:
Crisp Data Base National Institutes Of Health

1217
TITLE:
INTEGRATED ION CURRENT TECHNIQUE OF QUANTITATIVE MASS SPECTROMETRIC ANALYSIS CHEMICAL AND BIOLOGICAL APPLICATIONS

AUTHORS:
MAJER JR
BOULTON AA

SOURCE:
GLICK, DAVID (ED.). METHODS OF BIOCHEMICAL ANALYSIS, VOL. 21. VIII+572P. ILLUS. JOHN WILEY AND SONS: NEW YORK, N.Y., USA; LONDON, ENGLAND.; 1973 (RECD 1974) 467-514

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN URINE RAT BRAIN ATMOSPHERE POLLUTION LEAD TRACE METALS

1218
TITLE:
DEVELOPMENTAL NEUROTOXICITY OF LEAD AND METHYL NERCURY

AUTHORS:
RAJANNA B

SOURCE:
Crisp Data Base National Institutes Of Health

1219
TITLE:
STRUCTURE/FUNCTION OF MEMBRANE PROTEIN CHANNELS

AUTHORS:
MITRA AK

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:

The objective of this proposal is to understand structural details in the bilaye r that relate to transport properties of membrane protein channels. Specificall y, we wish to understand the structure/function relationships for the mammalian water channels AQP1 and AQP4 and the pore-forming anthrax toxin protective antig en by high-resolution electron crystallography. Our specific aims are listed bel ow. AIM I. Examine at the structural level the inhibition of water transport in AQP1 by mercurial compounds. We will apply electron diffraction to quantitate in 3-dimensions structural changes in AQP1 upon mercurial binding. This will al low us to understand AQP1 function based on its modulation by the pharmacologica l inhibitor. AIM II. Examine the structural/functional roles of residues invol ved in the selective water transport in AQP1. We will examine the functional ro les of polar and charged amino acids in the putative membrane-spanning region of AQP1 using a combined functional and structural approach. Amino-acid substitut ions that lead to altered function without structural perturbation will allow us to identify residues critical for water transport. AIM III. Structural studies on the AQP4 water channel. The AQP4 water channel expressed primarily in brain elicits highest osmotic water permeability. We will crystallize AQP4 in the li pid bilayer and use it as a model to understand and identify at the structural l evel factors responsible for diversity in solute transport mediated by aquaporin s. AIM IV. Structural studies on anthrax toxin protective antigen. The structu re of the soluble and membrane-integrated complex of protective antigen (PA63) h eptamers with and without bound lethal factor (LF) will be studied using single particle image analysis and conical-tilt reconstructions. This will allow us to understand the binding of LF and test the proposed porin-like model for the mem brane-embedded domain of PA63. The selective expression of AQP1 and homologous water channels believed to be involved in fluid absorption and/or secretion make s them an important pharmacological target. The pore-forming anthrax toxin has been shown to have a potential for delivery of macromolecules across the bilayer . Thus structural studies on these systems will potentially have impact on stru cture-based drug design.

1220

TITLE:

ACTIVITIES OF BILIVERDIN REDUCTASE-EFFECT OF NEPHROTOXIN

AUTHORS:

MAINES MD

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

Biliverdin reductase (BVR) is a unique dual pH/cofactor-dependent enzyme that ca talyzes the last step in the heme degradation pathway (i,e

reduction of biliverd in to bilirubin). Biliverdin, the substrate for BVR, is generated, with carbon monoxide (CO), in the course of heme degradation by the stress/heat shock family of proteins: heme oxygenase (HO)-1 and HO-2. CO functions as NO. BVR is the ul timate regulator of heme metabolism, in that, biliverdin regulates HO activity i n vivo. Biliverdin is also a liver tumor promoter and inhibits human Herpes vir us-6 replication and HIV-1 proliferation. Bilirubin is a potent antioxidant; lo w levels of serum bilirubin are associated with increased risk of coronary arter y heart disease and retinopathy of prematurity. We are the only laboratory in t he country actively pursuing molecular toxicology research on BVR that, by virtu e of being an -SH-dependent enzyme, is a target for environmental agents and nep hrotoxins. We have now discovered that BVR is a kinase and a protein kinase C (PKC)-interacting and -activating protein and translocates into the nucleus in re sponse to nephrotoxins: such as mercury, bromobenzene and bacterial endotoxins (LPS) as well as in cancerous transformation. In addition, in human kidney tumor s, ischemic rat brain and kidneys, and in kidneys of rats exposed to nephrotoxin s, BVR levels are increased. Also, the ability to produce biliverdin in advance d human prostate tumor cells is increased. PKCs play an important role in the f ield of cancer research and are key components of cellular response to oxidative stress. Based on the ability of BVR to activate PKC, it is likely that BVR pla ys a significant role in modulating a multitude of cellular functions including cell growth and differentiation. The Specific Aims of the proposed studies are 1) To further characterize BVR for molecular properties and requirements of kina se and reductase activities. 2) To further investigate BVR/PKC interaction. 3) To characterize BVR interactive proteins in the cells and to identify the protei ns that interact with BVR under normal and oxidative stress conditions, such as exposure to nephrotoxic agents and cancer. Also, to explore the nuclear functio n of BVR in the context of HO-1's response to oxidative stress. 4) To isolate t he human BVR gene, characterize its promoter region and analyze its regulation b y various toxins and effector agents.

1221

TITLE:

STRUCTURE/FUNCTION OF MEMBRANE PROTEIN CHANNELS

AUTHORS:

MITRA AK

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

The objective of this proposal is to understand structural details in the bilaye r that relate to transport properties of membrane protein channels. Specificall y, we wish to understand the structure/function relationships

for the mammalian water channels AQP1 and AQP4 and the pore-forming anthrax toxin protective antig en by high-resolution electron crystallography. Our specific aims are listed bel ow. AIM I. Examine at the structural level the inhibition of water transport in AQP1 by mercurial compounds. We will apply electron diffraction to quantitate in 3-dimensions structural changes in AQP1 upon mercurial binding. This will al low us to understand AQP1 function based on its modulation by the pharmacologica l inhibitor. AIM II. Examine the structural/functional roles of residues invol ved in the selective water transport in AQP1. We will examine the functional ro les of polar and charged amino acids in the putative membrane-spanning region of AQP1 using a combined functional and structural approach. Amino-acid substitut ions that lead to altered function without structural perturbation will allow us to identify residues critical for water transport. AIM III. Structural studies on the AQP4 water channel. The AQP4 water channel expressed primarily in brain elicits highest osmotic water permeability. We will crystallize AQP4 in the li pid bilayer and use it as a model to understand and identify at the structural l evel factors responsible for diversity in solute transport mediated by aquaporin s. AIM IV. Structural studies on anthrax toxin protective antigen. The structu re of the soluble and membrane-integrated complex of protective antigen (PA63) h eptamers with and without bound lethal factor (LF) will be studied using single particle image analysis and conical-tilt reconstructions. This will allow us to understand the binding of LF and test the proposed porin-like model for the mem brane-embedded domain of PA63. The selective expression of AQP1 and homologous water channels believed to be involved in fluid absorption and/or secretion make s them an important pharmacological target. The pore-forming anthrax toxin has been shown to have a potential for delivery of macromolecules across the bilayer . Thus structural studies on these systems will potentially have impact on stru cture-based drug design.

1222
TITLE:
Core--Neurotoxicology

AUTHORS:
CORY-SLECHTA DA

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The basic research goal of the Neurotoxicology Core is to understand the nature of the effects of environmental chemicals on nervous system function, their consequences over the life span, the mechanisms by which these effects are produced, and the risks they pose to human health. A key element in this goal is to understand the contribution of combined effects of genetic predisposition and environmental chemical exposures on

neurological dysfunctions, particularly as it relates to neurodegenerative diseases. The research within this Core involves both basic neuroscience research and neurotoxicology and explores the age spectrum from development to aging. The general theme of the Core is that both early and late stages of life represent periods of potentially enhanced vulnerability to neurotoxic effects. Embedded within this theme is the emerging concept that neurological effects of toxic exposures may not manifest themselves until years after exposure, and that toxicants interact in complex ways with the genetic composition of the human to influence the nature and severity of functional outcomes. The Core consists of seven members of which five are continuing members and two are new members, drawn from the Departments of Neurology, Environmental Medicine, and Obstetrics-Gynecology. The members have been chosen on the basis of their productivity, commitment to multidisciplinary neuroscience research, and experience in areas of thematic interest to the Center. In the past funding period, the Core was called the Neurobehavioral Toxicology Research Core to reflect its focus on behavioral toxicology. The present Core, now named the Neurotoxicology Core, has expanded its focus to include a broader spectrum of issues, ranging from mechanisms, genetic predispositions and contributions to human diseases, and human risk assessment, while maintaining strengths in behavioral toxicology. Of particular note are the inclusions of sophisticated molecular biology and neurochemistry into the battery of Core skills. The present proposal continues to advance the traditional strengths in metal neurotoxicology, while venturing into several new initiatives as well. A major change is the plan to recruit a new faculty to replace Dr. Cory-Slechta as Core Director. The individual will be selected to further integrate the neurotoxicology and basic neuroscience. Another change is the new initiative into molecular neuroscience and genetic-toxicant interactions, which has been developed through the addition of Drs. Federoff and Gelbard to the Core. This group will focus particularly on toxicant contributions to the development of neurodegenerative disorders. The major thematic areas of the Neurotoxicology Core are the following: 1) Neurochemical mechanism of lead-induced behavioral toxicology (Cory-Slechta). This project examines the neurochemical and neuroanatomical sites through which lead alters neural functions. Work had identified neurotransmitter alterations, neural pathways and behavioral deficits in animal models of lead exposure. 2) Environmental neurotoxicant genetic interaction: murine model (Federoff). This work would test the hypothesis that neurotoxicants interact with yet uncharacterized genetic determinants to produce selective vulnerability. Focusing on the dopamine transporter (DAT), the principal investigator will engineer a population of dopaminergic neurons overexpressing DAT by means of a somatic mosaic approach and directed gene expression to compare the responses of expressing and non-expressing neurons in the same animal. 3) A murine model of genetic and environmental neurotoxicant action (Richfield). This project would look at the role of the alpha-synuclein gene and gene product in Parkinson?s disease using the somatic mosaic approach. Studies will determine whether mice

overexpressing alpha-synuclein show an enhanced dopaminerigic vulnerability when exposed to low does of paraquat. 4) Genotype and phenotype of autism spectrum disorders (Rodier). This project will continue the investigator?s work linking injury during early development (as early as neural tube fusion) and specific genes with the development of the autism disorders. Work will continue to examine the valproic acid model of brain injury (which phenocopies some aspects of autism spectrum disorders), and the toxicant involves the HOX family of genes. 5) The role of inflammation and oxidative stress in human immunodeficiency virus type 1- associated neurologic disease (Gelbard). This project has been investigating how HIV type 1 results in neurotoxicity. In the proposed research, the principal investigator would examine the role of tumor necrosis factor alpha (TNF-a) and platelet activating factor (PAF) in the pathogenesis of neurotoxicity. Future plans include the development of TNF-overexpressing mice by somatic mosaic methods, and subsequent examination of neuronal death under various challenges. 6) Neurobehavioral and developmental effects of methylmercury exposure (Clarkson). This represents a continuation of the large human study of methylmercury exposure via fish and its consequences on development. This is one of two definitive epidemiological studies of human methylmercury exposure, which will continue and expand during the next funding period. In addition, the project director will continue his involvement in a prospective study of mercury exposure via dental amalgams. 7) Persisting functional consequences of neurotoxicant exposure during early development (Weiss). This work will continue studies of developmental exposure to several classes of toxicants. These will include solvents in addition to ongoing work in metals, endocrine disruptors (e.g., TCDD), and drugs (e.g., cocaine).

1223
TITLE:
INFLUENCE OF AGE ON METAL METABOLISM AND TOXICITY

AUTHORS:
KOSTIAL K
KELLO D
JUGO S
RABAR I
MALJKOVIC T

SOURCE:
ENVIRON HEALTH PERSPECT; (25). 1978 81-86

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RAT SUCKLINGS LEAD CADMIUM MERCURY MANGANESE LD-50 MILK DIET BRAIN ACCUMULATION

1224

TITLE:
ACTIVITIES OF BILIVERDIN REDUCTASE-EFFECT OF NEPHROTOXIN

AUTHORS:
MAINES MD

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Biliverdin reductase (BVR) is a unique dual pH/cofactor-dependent enzyme that catalyzes the last step in the heme degradation pathway (i,e reduction of biliverdin to bilirubin). Biliverdin, the substrate for BVR, is generated, with carbon monoxide (CO), in the course of heme degradation by the stress/heat shock family of proteins: heme oxygenase (HO)-1 and HO-2. CO functions as NO. BVR is the ultimate regulator of heme metabolism, in that, biliverdin regulates HO activity in vivo. Biliverdin is also a liver tumor promoter and inhibits human Herpes virus-6 replication and HIV-1 proliferation. Bilirubin is a potent antioxidant; low levels of serum bilirubin are associated with increased risk of coronary artery heart disease and retinopathy of prematurity. We are the only laboratory in the country actively pursuing molecular toxicology research on BVR that, by virtue of being an -SH-dependent enzyme, is a target for environmental agents and nephrotoxins. We have now discovered that BVR is a kinase and a protein kinase C (PKC)-interacting and -activating protein and translocates into the nucleus in response to nephrotoxins: such as mercury, bromobenzene and bacterial endotoxins (LPS) as well as in cancerous transformation. In addition, in human kidney tumors, ischemic rat brain and kidneys, and in kidneys of rats exposed to nephrotoxins, BVR levels are increased. Also, the ability to produce biliverdin in advanced human prostate tumor cells is increased. PKCs play an important role in the field of cancer research and are key components of cellular response to oxidative stress. Based on the ability of BVR to activate PKC, it is likely that BVR plays a significant role in modulating a multitude of cellular functions including cell growth and differentiation. The Specific Aims of the proposed studies are 1) To further characterize BVR for molecular properties and requirements of kinase and reductase activities. 2) To further investigate BVR/PKC interaction. 3) To characterize BVR interactive proteins in the cells and to identify the proteins that interact with BVR under normal and oxidative stress conditions, such as exposure to nephrotoxic agents and cancer. Also, to explore the nuclear function of BVR in the context of HO-1's response to oxidative stress. 4) To isolate the human BVR gene, characterize its promoter region and analyze its regulation by various toxins and effector agents.

1225
TITLE:

Psychologic Effects of Exposure to Solvents and Other Neurotoxic Agents in the Work Environment

AUTHORS:
Ekberg K
Hane M
Berggren T

SOURCE:
Occupational Medicine: Principles and Practical Applications, Second Edition, C. Zenz, Editor; Chicago, Year Book Medical Publishers, Inc., pages 785-795, 67 references, 1988

ABSTRACT:
The psychological effects of occupational exposure to organic solvents and heavy metals were examined. A review of experimental, field, cross sectional, and longitudinal studies of the behavioral effects of exposure to organic solvents, lead (7439921), mercury (7439976), and other neurotoxic agents was presented. A test battery developed by a group of Swedish psychologists to determine diffuse organic brain damage was described. The test evaluated verbal and cognitive abilities, perceptual speed and accuracy, eye hand coordination, and memory. The use of computers as tools for neuropsychological assessment was examined. Current trends in behavioral toxicology were included: better measurement of biological exposures, more direct measurement of biological and psychological processes, identification of physiologic processes that do not require complex mental processing, identification of basic information processes in mental activities, and broadening the types of psychological effects measured.

1226
TITLE:
Impact of nuclear plants on dulcicolous ecosystems.

AUTHORS:
MICHA J-C
GENIN M

SOURCE:
NAT BELG; 59 (6-7). 1978. 149-158.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A study of the environmental impact of the Tihange Nuclear plant (Belgium) on the Meuse River is discussed. Thermal pollution, radioactive contamination of aquatic organisms and chemical pollution are considered. The effect of thermal discharge on biological cycles such as metamorphosis, migration, reproduction and behavior is discussed with special mention of the decreased Dreissena polymorpha

population and changes in Atyaephyra desmaresti and Rutilus rutilus populations. Radioactive contamination of aquatic organisms, accumulation and transfer in trophic chains and somatic and genetic effects are considered for large invertebrates, fish and molluscs. Tests on liver, spleen, brain, fat reserve and testicular function in R. rutilus were performed. Pollution by and accumulation of 137Cs, 60Co, 54Mn, 134Cs, 58Co, 3H and 90Sr are discussed. Chemical pollution as a result of biocides used to protect cooling towers is considered as is redistribution of the toxic metals Zn, Cu, Cd and Hg.

1227

TITLE:

Environmental epidemiology of autism

AUTHORS:

HERTZ-PICCIOTTO I

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

The causes and contributing factors for autism are poorly understood. Evidence suggests that incidence is increasing, but diagnostic changes & improvements may be playing a role. Both genetic and environmental factors appear to play a role. Autopsy studies demonstrate structural changes in the brain and clinical investigations reveal neurophysiologic differences in information processing in autistic vs. normal children. Members of our team recently demonstrated altered levels of certain neuropeptides at birth in children who later developed autism. The proposed case-control study will be the first large-scale epidemiologic investigation of underlying causes for autism and triggers of regression. This study will capitalize on the strengths of the case-control design, which is well suited to examine a broad array of factors for rare conditions that are thought to be multifactorial. Comparisons will be made with both general population controls and mentally retarded children. From California's Department of Developmental Services (DDS) databases and Regional Centers that coordinate services for developmentally disabled persons, we will identify children aged 2 to 5 years, recently diagnosed with autism from two geographic areas in the state. Eligibility will be determined through evaluation by trained professionals using the Autism Diagnostic Interview-Revised and the Autistic Diagnostic Observation Schedule-Generic. A set of general population controls will be matched on gender, age, and community of residence. Another set will be matched to the autistic children with mental retardation, and will consist of children in the DDS database/Regional Center system with mental retardation but not autism. Cognitive and adaptive function will be assessed in all children. Both parents will be interviewed, separately, regarding peri- conceptional, prenatal, and early childhood exposures and

experiences. Interviewers will collect family histories of speech development, social skills, psychological disorders, and behavioral patterns. Blood, urine, and buccal swab specimens will be collected from the index child (case or control), parents, and siblings, and newborn blood spots from the index child will be obtained from the specimen bank maintained by the State of California. Prenatal clinic, delivery, and pediatric medical records for the index child will be obtained. Specimens will be analyzed by the Analytical Biomarkers Core for mRNA of candidate genes and later for specific genetic polymorphisms. The proposed study will be the first major epidemiologic case-control study to examine autism in relation to a broad array of environmental exposures and endogenous susceptibility factors.

1228

TITLE:

Molecular and cellular mechanisms of autism

AUTHORS:

PESSAH IN

SOURCE:

Crisp Data Base National Institutes of Health

ABSTRACT:

The long-term goal of Research Project III is to identify molecular and cellular mechanisms that underlie idiosyncratic responses within autistic children to chemicals to which they are exposed in in utero and during periods of early postnatal brain development. The pressing worldwide concern about the role of vaccine antigens, the mercurial preservative thimerosal, and environmental exposure to mixtures of methylmercury and PCBs, justify detailed analysis of the underlying mechanisms of these factors in autism. We will first focus on three hypotheses relating to synergistic actions of mercurials and PCBs agents, known to be immunotoxic and neurotoxic. The hypotheses to be tested are: Hypothesis I addresses how peripheral blood mononuclear cells (PBMCs) from autistic children exhibit significant differences in their sensitivity and/or pattern of cell activation and cytokine secretion when challenged in vitro with vaccine antigens. How Non-coplanar PCBs of environmental relevance, thimerosal and other environmental agents identified by the Center's units exacerbate these differences will be studied. Hypothesis II determines how organic mercurials (thimerosal and MeHg) and non-coplanar PCBs (PCBs 118, 138, 153, 170, and 180 singly or in combination) act synergistically to influence glia/neural cell signaling pathways leading to altered patterns of dendritic spine growth, dendritic branching and synaptogenesis. Products of antigen- stimulated and control PBMCs (isolated from autistic and non-autistic children) characterized and quantified in Hypothesis I will be used to address their differential effects on neuronal cell growth. Hypothesis III utilizes mice exposed to PCBs and organic

mercurials in vivo (PROJECT II) to assess functional and biochemical changes associated with social behavioral deficits. We will identify differences in patterns of evoked potentials and excitability in hippocampus/amygdala slice preparations from mice that have been perinatally or neonatally exposed to PCBs, organic mercurials, singly or in combination in Project II. We will elucidate the underlying biochemical mechanisms of these effects.

1229
TITLE:
Compartmental analysis for the evaluation of biological half-lives of cadmium and mercury in mouse organs.

AUTHORS:
MATSUBARA-KHAN J

SOURCE:
ENVIRON RES; 7 (1). 1974 54-67

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Repeated observations on the quantitative behavior of 109-Cd and 203-Hg in various mouse organs after a single injection of these tracers revealed the fact that a clear difference of turnover characteristics exists between these nuclides, as was quantitatively determined by the compartmental analysis using electron computer HITAC 5020. Loss patterns of 109-Cd in liver, kidney, and salivary gland fitted the 2-compartment model. In each organ fast and slow biological half-lives were obtained from the 2 observed rate constants. Data from gastrointestinal tissues or contents conformed with the 1-compartment model. Loss patterns of 203-Hg in most mouse organs, except brain, fitted the 1-compartment model with larger rate constants which were more than 10-fold those of 109-Cd. By comparing the parameters obtained in the fitted exponential functions for various organs, it was possible to define the interrelationship of the metabolic flow of the elements in the different organs. In Cd, data from kidneys, livers, and salivary glands of s.c. injected animals were obtained which gave a common value for the parameter reflecting the pool size. Rate constants in kidneys and salivary glands were very small thus giving extremely long biological half-lives. Decay pattern of 109-Cd for the whole body was also examined in detail.

1230
TITLE:
Block of 45Ca Uptake into Synaptosomes by Methylmercury: Ca++and Na+-Dependence

AUTHORS:
Shafer TJ

Atchison WD

SOURCE:
Journal of Pharmacology and Experimental Therapeutics, Vol. 248, No. 2, pages 696-702, 44 references, 19891989

ABSTRACT:
The effect of calcium ions (Ca+2) and sodium ions (Na+) on methylmercury inhibition of Ca+2 uptake by isolated nerve terminals was examined. Synaptosomes prepared from the forebrains of male Sprague-Dawley-rats were incubated with 0 to 300 micromolar (microM) methylmercuric-acetate (108076) (MMA) in the presence of 5 or 41.25 millimolar (mM) potassium-ion (K+) for 10 seconds. The effects on uptake of calcium-45 (Ca-45) labeled Ca+2 were assessed. Under nondepolarizing conditions MMA did not affect Ca-45 uptake at concentrations up to 50microM. MMA at 125 and 250microM significantly decreased Ca-45 uptake. Under depolarizing conditions MMA concentrations above 5microM significantly inhibited Ca-45 uptake in a dose dependent manner. The concentration for 50 percent inhibition (IC50) was approximately 50microM. When the fast and slow phases of Ca-45 uptake were examined separately, the IC50s for both were also 75microM. Rat forebrain synaptosomes were incubated with 50microM MMA in the presence of 41.25mM K+ and 0.01 to 1.15mM extracellular Ca+2. Increasing extracellular Ca+2 only reversed slightly the MMA block of total or fast phase Ca+2 uptake. MMA inhibited slow phase Ca-45 uptake was completed reversed by extracellular Ca+2 concentrations above 0.3mM. Total and fast phase synaptosomal Ca-45 uptake was reduced by about 50 percent by MMA in both Na+ containing and Na+ free buffer solutions. Slow phase Ca-45 uptake was reduced by MMA by 26.1 percent in the Na+ containing buffer and by 96.0 percent in the Na+ free buffer. MMA inhibition of slow phase Ca-45 uptake was not reversed in the Na+ free medium. The authors conclude that methylmercury irreversibly blocks channel mediated Ca+2 uptake into K+ depolarized synaptosomes. Nondepolarized Ca+2 uptake is decreased only by high concentrations of methylmercury.

1231
TITLE:
STRUCTURE/FUNCTION OF MEMBRANE PROTEIN CHANNELS

AUTHORS:
MITRA AK

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The objective of this proposal is to understand structural details in the bilayer that relate to transport properties of membrane protein channels. Specifically, we wish to understand the structure/function relationships

for the mammalian water channels AQP1 and AQP4 and the pore-forming anthrax toxin protective antigen by high-resolution electron crystallography. Our specific aims are listed below. AIM I. Examine at the structural level the inhibition of water transport in AQP1 by mercurial compounds. We will apply electron diffraction to quantitate in 3-dimensions structural changes in AQP1 upon mercurial binding. This will allow us to understand AQP1 function based on its modulation by the pharmacological inhibitor. AIM II. Examine the structural/functional roles of residues involved in the selective water transport in AQP1. We will examine the functional roles of polar and charged amino acids in the putative membrane-spanning region of AQP1 using a combined functional and structural approach. Amino-acid substitutions that lead to altered function without structural perturbation will allow us to identify residues critical for water transport. AIM III. Structural studies on the AQP4 water channel. The AQP4 water channel expressed primarily in brain elicits highest osmotic water permeability. We will crystallize AQP4 in the lipid bilayer and use it as a model to understand and identify at the structural level factors responsible for diversity in solute transport mediated by aquaporins. AIM IV. Structural studies on anthrax toxin protective antigen. The structure of the soluble and membrane-integrated complex of protective antigen (PA63) heptamers with and without bound lethal factor (LF) will be studied using single particle image analysis and conical-tilt reconstructions. This will allow us to understand the binding of LF and test the proposed porin-like model for the membrane-embedded domain of PA63. The selective expression of AQP1 and homologous water channels believed to be involved in fluid absorption and/or secretion makes them an important pharmacological target. The pore-forming anthrax toxin has been shown to have a potential for delivery of macromolecules across the bilayer. Thus structural studies on these systems will potentially have impact on structure-based drug design.

1232

TITLE:

ACCUMULATION AND REMOVAL OF MERCURY-203 IN DIFFERENT REGIONS OF THE RAT BRAIN

AUTHORS:

BUTTERWORTH RF
GONCE M
BARBEAU A

SOURCE:

CAN J NEUROL SCI; 5 (4). 1978 397-400

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. MESO DI MERCAPTO SUCCINIC-ACID ANTIDOTE CHELATOR

1233
TITLE:
Course and validity of regression in autism

AUTHORS:
OZONOFF S

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
The onset of autism occurs at two peak periods. Approximately 2/3 of children with autism display developmental abnormalities within the first year of life, while the other third display a period of mostly normal development, followed by a loss of skills and onset of autism. This Project examines the measurement, predictors, course, causes, and external validity of regression. Four studies compare children with regressive autism to those with early onset autism, non-autistic developmental delays, and typical development, providing a multi-level analysis of the regression phenomenon. Study 1 examines the validity of parent report definitions of regression. All previous studies of regression have employed parent report methods, yet their accuracy is not clear. Parent report measures of regression will be compared to videotapes from the first year of life, analyzed by trained researchers blind to diagnosis using a well-validated coding system of early social-communicative behavior. Study 2 will identify early warning signs of regression. Behaviors from the infant videotapes of children with later regression will be compared to children with typical development and developmental delay to identify early predictors of later regression. Study 3 examines potential causes of regression, including both familial and environmental factors. The potential role of exposure to metals with known neurotoxicity (e.g., mercury), environmental pollutants with suspected neurodevelopmental effects (e.g., PCBs), and immunologic abnormalities (e.g., auto-antigens to brain or other tissue) will be assessed, using specific biological assays, in all 4 groups. Study 4 tests the discriminant validity of regression from early onset autism, using a comprehensive age-appropriate neuropsychological battery that includes tests of all the major domains affected in early autism. These studies will lead to a better understanding of the neurobiological mechanism underlying both regressive and early-onset autism, phenomenological differences between the two, earlier identification of at-risk children, with concomitant earlier intervention, and perhaps in the future, prevention of regression.

1234
TITLE:
Residue analysis in fish.

AUTHORS:
Reichenbach-Klinke HH
Negele RD

SOURCE:
Z. Wasser Abwasser Forsch.; 5(1): 25-28; 1972 ; (REF:16)

ABSTRACT:
HAPAB Fish have been examined by various authors for residues of heavy metals (e.g., copper sulfate, mercury), pesticides (trichlorfon), phenols and antibiotics. The characteristic areolas around the nerve cells of the spinal cord first observed by Kayser et al. in 1962, which are due to pesticide pollution, were found in fish examined subsequently. According to a study by Gakstatter (1968), exposure of goldfish to 0.05 ppm (SUP)14C-aldrin for eight hours resulted in an accumulation of more than 20 ppm in the fatty tissue, and no signs of degradation were noted even months after exposure; nerve cells, too, tend to retain the pesticide concentration, once attained, for long periods of time. Spinal cord, brain, blood, kidneys, and liver began to degrade the pesticide after exposure. In the spinal cord, somewhat more than 14 ppm had accumulated, which fell to 8 ppm after 8 days; the liver had accumulated 5 ppm, which decreased to a little less than 2 ppm after 8 days. In muscle, the concentration went up to nearly 2 ppm, and had dropped back to 1 ppm after 8 days. The kidneys reduced the accumulated concentration of about 4 ppm to about 1 ppm. 1972

1235
TITLE:
THE ROLE OF SODIUM POTASSIUM ATPASE IN METHYL MERCURY INDUCED TERATOGENESIS

AUTHORS:
HOLMES LS
OKITA GT

SOURCE:
FED PROC; 38 (3 PART 1). 1979 680

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MOUSE BRAIN INDUCED PROTEIN DEFICIENCY

1236
TITLE:
BLOOD BRAIN BARRIER DYS FUNCTION FOLLOWING MERCURY INTOXICATION

AUTHORS:
WARE RA

DUDLEY A W JR
CHANG LW

SOURCE:
J NEUROPATHOL EXP NEUROL; 33 (1). 1974 175

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT HUMAN MINAMATA DISEASE

1237
TITLE:
Metropolitan Denver sewage sludge fed to feedlot steers.

AUTHORS:
KIENHOLZ EW
WARD GM
JOHNSON DE
BAXTER J
BRAUDE G
STERN G

SOURCE:
J ANIM SCI; 48 (4). 1979. 735-741.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Feedlot steers received 0, 4 or 12% metropolitan Denver sewage sludge (MDSS) on a dry wt intake basis for a 94 day finishing period. The MDSS was anaerobically digested primary sludge that had been treated with polyelectrolyte to aid in dewatering during vacuum filtration. It was dried to 35% water prior to mixing into the pelleted diet given the steers. Cattle (6 on each treatment) were slaughtered and kidney, liver, muscle, bone, brain, blood, lung, spleen and fat were analyzed for As, Cd, Cu, Hg, Mo, Ni, Pb, Se and Zn. Growth of MDSS animals was less than controls ($P < .025$) because MDSS, apparently, provided no energy. MDSS ingestion caused no pathology. All 10 inorganic elements except Ni were increased in 1 or more body tissues following the 94 day MDSS ingestion. Percentage whole carcass retentions of ingested minerals were estimated as follows: .2% As, .04% Cd, .3% Cu, .07% Hg, .2% Mo, < .006% Ni, .6% Pb, 1.3% Se, .2% Zn, and 32% F. Steers retained low amounts of the toxic heavy metals from MDSS ingestion.

1238
TITLE:
BEHAVIORAL IMPLICATIONS OF PRENATAL AND EARLY POSTNATAL EXPOSURE TO CHEMICAL POLLUTANTS.

AUTHORS:
WEISS B

SPYKER JM

SOURCE:
PEDIATRICS; 53 (5 PT 2). 1974 851-859

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CHILD ANIMAL LEAD POISONING METHYL MERCURY MINIMAL BRAIN DYS FUNCTION

1239
TITLE:
Studies of the persistence of DDT and methyl mercury in the lobster after various modes of administration.

AUTHORS:
Guarino AM
Call J
Rall DP

SOURCE:
Fed. Proc., Fed. Amer. Soc. Exp. Biol.; 31(2): 561; 1972

ABSTRACT:
HAPAB The organ distribution of total (SUP)14C-DDT or (SUP)14C-methyl Hg (MH) was studied in lobsters (Homarus americanus) which had received one of these environmental pollutants by administration either by intravascular or oral routes, or after uptake from ambient sea water. The hepatopancreas contained most of the radioactivity after intravascular injection of DDT, and the half-life for removal from this organ was 46 days. Regardless of the mode of receiving DDT, more than 95% of the absorbed dose remained in the hepatopancreas after 7 days. After intravascular injection the early distribution of (SUP)14C-MH was similar to that of DDT, i.e., high levels occurred in heart, hepatopancreas and gonads at 24 hrs. Large amounts of radioactivity were also present in intestine, brain and gill. Hepatopancreas levels decayed with a half-life of about 14 days while an interesting redistribution of MH occurred where the 33 day levels of tail muscle became about 2-fold higher than those of the 1 day values. Six days after MH was administered with food, 68% of the absorbed dose was present in the hepatopancreas and 5% was in the tail muscle. When MH was added to ambient water these values were 23% for hepatopancreas and 60% for tail muscle. Thus, such comparisons of DDT and MH distribution after 3 modes of entry revealed major differences in handling these compounds by the lobster. (Abstract number 1955, 56th Annual FASEB Meeting, Atlantic City, N. J., April 9-14, 1972, reprinted by permission.)=, 1972

1240
TITLE:

CLINICAL AND NEUROCHEMICAL ASPECTS OF INORGANIC MERCURY INTOXICATION

AUTHORS:
KARK R AP

SOURCE:
VINKEN, P. J. AND G. W. BRUYN (ED.). HANDBOOK OF CLINICAL NEUROLOGY, VOL. 36. INTOXICATIONS OF THE NERVOUS SYSTEM, PART 1. XII+570P. ILLUS. ELSEVIER-HOLLAND BIOMEDICAL PRESS: AMSTERDAM, THE NETHERLANDS; NEW YORK, N.Y., USA. (DIST. IN THE USA BY ELSEVIER/NORTH-HOLLAND, INC.: NEW YORK, N.Y.) ISBN 0-7204-7236-9.; 1979 147-197

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CHILD NEUROPATHY ACRODYNIA ATAXIA LUNG DAMAGE METABOLIC INTERFERENCE HAIR SALIVARY BRAIN CEREBRO SPINAL FLUID TREATMENT

1241
TITLE:
Biologic markers in reproductive toxicology.

AUTHORS:
ANONYMOUS

SOURCE:
NTIS Technical Report (NTIS/PB93-100980) 1989;:401 pp.

ABSTRACT:
Experts are increasingly concerned that exposure to toxic substances in our environment is impairing our reproductive and developmental processes. Biologic markers have emerged as a promising tool for understanding the environmental effects of toxic substances. This report clarifies the underlying concepts of the use of biologic markers in general and explores how a broad range of biologic markers may be the key to our understanding of environmental health effects, particularly in the reproductive field, early enough to make a difference in people's lives. The four major text sections in this book are male reproduction, female reproduction, biologic markers of pregnancy, and biologic markers of neurodevelopment. Each section presents a detailed view of what is understood about human systems--including the most recent research results--and how biologic markers may specifically be applied.

1242
TITLE:
The developmental neurotoxicity of methyl mercury.

AUTHORS:
Weiss B

SOURCE:
Prenatal Exposure to Toxicants: Developmental Consequences (The Johns Hopkins Series in Environmental Toxicology) 1994;:112-29

1243
TITLE:
Transition and heavy metal inhibition of ligand binding to muscarinic acetylcholine receptors from rat brain.

AUTHORS:
ARONSTAM RS
ELDEFRAWI ME

SOURCE:
TOXICOL APPL PHARMACOL; 48 (3). 1979. 489-496.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Several divalent heavy metals interact with muscarinic acetylcholine receptors in neural membranes from rat forebrains in vitro to inhibit the binding of (3H)3-quinuclidinyl benzilate (QNB), a potent and specific receptor antagonist. Hg is the most potent inhibitor with an ID50 (median infective dose) value of 10-7 M for the inhibition of the binding of 10-10 M QNB. Several other metals are less effective with ID50 values between 10-5 and 2owing order: Fe < Ag < Cu < Pb < Cd < Tb < Zn. Co, Mn, La, Ni and Sn are less potent inhibitors (ID50 > 10-3 M). Binding inhibition by Cu, Hg and Cd is competitive and the inhibition by all the metals can be reversed by decreasing the free metal concentration through dilution or chelation by EDTA, dimercaprol or penicillamine. The effects of metals on muscarinic binding are largely independent of temperature. Chaotropic anions (100 mM iodide, thiocyanate, trichloroacetate or nitrate) are similarly without effect on the metal-receptor interaction. The limited effects of sulfhydryl reducing (dithiothreitol, 2-mercaptoethanol and glutathione) and alkylating (N-ethyl maleimide) reagents do not indicate a prominent role for sulfhydryl groups in mediating metal inhibition of muscarinic receptors.

1244
TITLE:
Induction of Metallothionein

AUTHORS:
Klaassen CD
Lehman-McKeeman LD

SOURCE:
Journal of the American College of Toxicology, Vol. 8, No. 7, pages 1315-1321, 63 references, 1989

ABSTRACT:

Metallothionein (MT) and its physiochemical properties were discussed. MT was noted to contain 61 amino acids, of which approximately 33 percent are cysteine. The sulfhydryl groups have the ability to bind a variety of heavy metals, with a maximum capacity of 7 gram atoms per mole protein. Of the most frequently examined metals, the relative binding affinities ranked in decreasing order were silver, mercury, copper, cadmium, zinc, cobalt, and nickel. The MTs were observed to be synthesized in tissues such as the liver, kidney, intestine, muscle, heart, spleen, and brain and were localized in the cytoplasm. MTs were usually detected in biological tissues only in conjunction with overt hepatotoxicity and nephrotoxicity. MTs were observed in high concentrations in rapidly growing and developing tissues and were usually synthesized at low basal levels in mature animals. The physiological function of MT included serving as intracellular storage depots for zinc, copper, and other essential metals, modulating many important processes for which zinc is required, and detoxifying heavy metals by sequestering them. Induction of MT by metals, such as cadmium, resulted in tolerance to the subsequent metal's toxicity developing. Methods for quantitating MT were reviewed. Induction of MT by metals was discussed. Many metals were observed to be capable of inducing MT synthesis, with cadmium and zinc the most effective inducers. MT induction by metals was noted to be regulated at the transcriptional level. MT was also observed to be induced by some organic compounds. The occurrence of MTs in humans was discussed and noted to have been observed in human liver and kidney tissue, with concentrations increasing with age. Smoking was indicated to increase renal MT concentrations, especially in males, but has little effect on hepatic MT.

1245

TITLE:

DIETARY SELENIUM PROTECTION OF METHYL MERCURY INTOXICATION OF JAPANESE QUAIL

AUTHORS:

STOEWSAND GS
BACHE CA
LISK DJ

SOURCE:

BULL ENVIRON CONTAM TOXICOL; 11 (2). 1974 152-156

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. COTURNIX-COTURNIX-JAPONICA LIVER KIDNEY BRAIN EGGS MORTALITY SEX DIFFERENCES

1246

TITLE:

Effect of spironolactone on the biliary excretion and distribution of

metals.

AUTHORS:
KLAASSEN CD

SOURCE:
TOXICOL APPL PHARMACOL; 50 (1). 1979. 41-48.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Pretreatment of rats with spironolactone (75 mg/kg i.p.) 15 min before the i.v. administration of a metal produced a marked alteration in the distribution and biliary excretion of Hg and Cu. The concentration of Hg and Cu in the kidney and plasma was much lower after spironolactone pretreatment but was higher in the blood, heart lung, brain, and other tissues. Spironolactone pretreatment increased the biliary excretion of these 2 metals 3- and 7-fold. Spironolactone had a somewhat opposite effect on Cd and Ag. It increased the concentration of Cd in the kidney; it decreased the biliary excretion of Ag and increased its concentration in the kidney. Spironolactone did not affect all metals; it did not alter the distribution or biliary excretion of Pb Mn or As.

1247
TITLE:
A Therapeutic Profile of Metal Chelators in the Detoxication of Methylmercury Chloride Inhibited Acid and Alkaline Phosphatases in Different Areas of the Central Nervous Systems of Rats

AUTHORS:
Vinay SD
Raghu KG
Sood PP

SOURCE:
Journal of Environmental Pathology, Toxicology and Oncology, Vol. 9, No. 4, pages 351-359, 31 references, 1989

ABSTRACT:
The effects of methylmercury-chloride (115093) (MMC) on acid and alkaline phosphatase activity, and the efficacy of several chelating agents in reversing these effects, were investigated in the central nervous system of male Wistar-albino-rats. Animals were given single daily doses of 5mg/kg MMC over various schedules to yield total doses ranging from 10 to 75mg/kg; controls received no MMC. Chelating antagonists were given at 30 minutes after the MMC dose; these included N-acetyl-dl-homocysteine-thiolactone (1195160) (NAHT), D-penicillamine (52675) (DPA), glutathione (70188) (GSH), and sodium-selenite (10102188) (SS). Total doses of chelators were: NAHT, 160 to 1,200mg/kg; DPA, 160 to 1,200mg/kg; GSH, 200 to 1,500mg/kg; and, SS, 0.72 to 5.40mg/kg. Central

nervous system (CNS) tissues were harvested post mortem for phosphatase activity assays. Acid and alkaline phosphatases were not significantly inhibited until after 7 days of MMC treatment. After 15 days of treatment, maximum inhibition of phosphatases was recorded in the spinal cord and cerebellum. A linear pattern was found with increasing days of treatment. Chelation did not consistently restore acid phosphatase activity throughout the CNS over the maximal 15 day treatment period. NAHT restored acid phosphatase activity in the cerebellum, while SS restored activity to spinal cord and cerebellum; GSH was effective in the cerebellum only in the 7 day group, but in the olfactory bulbs and medulla after 15 days. A similar pattern was found in restoring alkaline phosphatase activity. Neither enzyme was affected by DPA treatment.

1248

TITLE:

Learning and memory deficits induced by prenatal aluminium exposure in rat pups.

AUTHORS:

Lehotzky K
Gonda Z
Täatrai E

SOURCE:

Neurotoxicology 1997;18(3):881

ABSTRACT:

Prenatal administration of neurotoxic agents has been shown to lead to subtle neurobehavioural impairments manifested by developmental delays and subsequent learning deficits - so called minimal brain dysfunction - without morphological abnormalities. Behavioural teratogenic effects have been demonstrated following prenatal exposure to different compounds of lead, mercury, tin and cadmium. Aluminium (Al) has been implicated as a neurotoxic agent, dementia has been correlated to elevated Al levels in Alzheimer's disease and has been related to impaired motor coordination and to a number of cognitive deficits. To determine the neurotoxicity of Al lactate exposure in rat pups, postnatal behavioural effects of 0, 2.5, 5 and 10 mg/kg daily s.c. treatment during gestational days 7th-15th were investigated by using our test battery. The main sign of neurotoxicity was diminished performance and lengthened latency in an avoidance responding task in all treated groups, during acquisition, extinction and reconditioning as well. Neurohistology of pups treated prenatally with top dose showed no alterations in the cerebellar Purkinje cells or in the hippocampus. Lack of neurofibrillary degeneration (tangles) and axonal swelling also strengthened the species differences. Our findings support that Al-lactate is a developmental neurotoxicant and might induce impairment in cognitive and associative functions in a very low dose.

1249
TITLE:
DELAYED EFFECTS OF PRENATAL EXPOSURE TO METHYL MERCURY BRAIN ULTRASTRUCTURE AND BEHAVIOR.

AUTHORS:
SPYKER JM
CHANG LW

SOURCE:
TERATOLOGY; 9 (3). 1974 A37

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MOUSE TERATOGEN ELECTRON MICROSCOPY FIXATION

1250
TITLE:
Pollution disasters in Japan.

AUTHORS:
Ui J

SOURCE:
Laekartidningen; 69(23): 2789-2796; 1972

ABSTRACT:
HAPAB Japan is one of the most polluted countries in the world. Mass poisoning has resulted from mercury, cadmium, and polychlorinated biphenyls (PCBs), the latter having occurred in 1968 with effects still being observed in the victims. PCBs leaked into rice oil from a heat exchanger during the production process, and the rice oil was subsequently ingested. Although some of this "dark oil" had poisoned several chickens prior to the human disaster, the connection between the two incidents was not made until it was too late. The initial symptoms of the poisoning in humans were: inflammatory skin changes; muscular pain and paralysis; delayed symptoms which affected the liver, brain, and respiratory tract. A number of deaths occurred. PCBs are excreted very slowly from the body stores; prognosis for the victims of the poisoning is poor. The PCB content of fish has been found to be much higher in Japan than in other parts of the world. Another source of PCB contamination was found in carbon less copying paper, which when burned releases large amounts of PCBs into the atmosphere. The average value of PCBs in the body fat tissues of Japanese people has been reported as 5 ppm. The corresponding value for one of the rice-oil victims was 13 ppm, which represents a narrow margin for the average Japanese person. 1972

1251

TITLE:
Occupational vestibular damages.

AUTHORS:
ZENK H

SOURCE:
Z AERZTL FORTBILD; 64 (13). 1970 676-678

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Diagnoses of vestibular nerve reactions to industrial poisons by means of combined caloric, rotational and positional tests, and the measurement of nystagmus are presented. The vestibular nerve ties in with nystagmogenic zone in the brain stem, where peripheral stimuli are transformed into oculomotor impulses. The resulting nystagmus may be the only objective method for confirming the dizziness of which the patient complains. Among the noxious agents producing central lesions are Cd, Hg, V and cyanides, narcotic halogenated hydrocarbons (polyvinyl chloride, trichlorethylene and dichloroethane), nitro and amino compounds like nitrobenzene and aniline, and tri-o-cresylo phosphate.

1252
TITLE:
Chronic Toxicity and Carcinogenicity of Methylmercury Chloride in B6C3F1 Mice

AUTHORS:
Mitsumori K
Hirano M
Ueda H
Maita K
Shirasu Y

SOURCE:
Fundamental and Applied Toxicology, Vol. 14, No. 1, pages 179-190, 14 references, 1990

ABSTRACT:
A 2 year, long term methylmercury-chloride (115093) (MMC) feeding study was conducted in B6C3F1-mice. Mice were fed a diet containing MMC at 0.4, 2, or 10 parts per million (ppm) for 104 weeks; during the study, food consumption and body weight were monitored, and mice were observed for general condition. All animals surviving 104 weeks were autopsied, as were those which died or were killed in-extremis. The findings were compared with those of an earlier study regarding chronic toxicity and carcinogenicity in ICR-mice. Neurotoxic signs in the B6C3F1-mice at 10ppm levels were characterized by posterior paralysis in 33 males after 59 weeks and in three females after 80 weeks. A marked increase in mortality

and a remarkable decrease in body weight gain were observed in males after 60 weeks. Both sexes in this dose group developed toxic encephalopathy consisting of neuronal necrosis of the brain and toxic peripheral sensory neuropathy. The males developed chronic nephropathy, testicular atrophy, and glandular stomach ulcers. Females showed increased incidences of chronic nephropathy. Significant increases in the incidence of renal adenoma and/or carcinoma were noted in the proliferative lesions (16/60) and tubular cell hyperplasia (14/60) in males of the 10ppm dose group. Chronic nephropathy also increased in the males of the 2ppm dose group. The authors conclude that the susceptibility of B6C3F1-mice to renal toxicity and renal carcinogenicity is comparable to that of ICR-mice. The B6C3F1-mice were more sensitive to the chronic neurotoxic effects of MMC than were the ICR-mice.

1253
TITLE:
MERCURY EFFECTS FROM CHRONIC AND ACUTE DOSES ON FIXED INTERVAL OPERANT BEHAVIOR OF FEMALE SQUIRREL MONKEYS

AUTHORS:
VITULLI WF

SOURCE:
PSYCHOL REP; 35 (1). 1974 3-9

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. SAIMIRI-SCIUREUS BRAIN SPINAL CORD SENSORI MOTOR DISRUPTION CONDITIONING

1254
TITLE:
Analytic study to evaluate associations between hazardous waste sites and birth defects--final report.

AUTHORS:
Marshall EG
Gensburg LJ
Geary NS
Deres DA
Cayo MR

SOURCE:
NTIS Technical Report (NTIS/PB95-199196) 1995 Jun;:184 pp.

ABSTRACT:
A study was conducted to evaluate the risk of two types of birth defects (central nervous system (CNS) and musculoskeletal (MUS) defects) associated with mothers' potential exposure to solvents, metals, and

pesticides through residence near hazardous waste sites. Relative risks were estimated by comparing the probability of residential exposure among mothers of infants born with a birth defect to mothers of those without major malformations. Subjects were drawn from births in 1983-1986 to residents of 18 urban counties in New York State excluding New York City: cases were reported to the Congenital Malformations Registry and controls were randomly selected from birth certificates. Subjects for the first two birth years were drawn from those included in a preliminary study (Geschwind et al, Am J Epidem 1992;135:1197-1207). Potential residential exposure was rated based on the address at birth. Previously collected data on all inactive hazardous waste sites within the study area (N = 643) were reviewed using a standard assessment method. Areas within one mile of each site were classified according to the probability of exposure (high, medium, or low) to solvents, metals, and pesticides via four pathways (groundwater ingestion, groundwater vapor inhalation, air vapor inhalation, and contact with air iculates). Case and control residences were also rated on proximity to air releases from industrial or commercial facilities and contamination of community water supplies. The environmental ratings for 473 CNS cases, 3,305 MUS cases, and 12,436 controls were combined with data on other potential risk factors for birth defects obtained from birth certificates, such as mother's age, race, and education level. Compared to those with a low probability of exposure, mothers residing in areas classified as having a medium or high probability of exposure to chemicals from hazardous waste sites did not show an increased risk of birth defects in their offspring. After adjusting for potential confounders, the relative risk for CNS defects and exposure to solvents was .84 (95% Confidence Interval (CI): .44-1.6); for CNS and metals, 1.05 (95% CI: .67-1.65); MUS defects and solvents, .92 (95% CI: .78-1.08); and MUS defects and pesticides, .80 (95% CI: .51-1.3). The only environmental factor showing a statistically significant elevation in risk was living within one mile of industrial or commercial facilities emitting solvents or metals into the air. Residence near these facilities showed an elevated risk for CNS defects and solvents (OR = 1.30, 95% CI: 1.02-1.65); and CNS defects and metals (OR = 1.37, 95% CI: 1.05-1.79) but no elevated risks for MUS defects. However, data on possible levels and likely geographic areas of exposure from these facilities were not available. The low percentages of subjects classified as having a greater than low probability of exposure to chemicals from hazardous waste sites (less than 1% for pesticides, 3% for solvents, and 5% for metals) limited the power of the study to investigate the risk of particular pathways, disease subgroups, or geographic areas. Contact with contaminants was classified using data collected for other purposes, and maternal exposure was not confirmed through environmental measurement, However, summary results consistently showed no statistically significant association between the risk of CNS or MUS defects and maternal residential exposures from hazardous waste sites estimated through detailed evaluation of site data. Associations between CNS defect risk and air releases of solvents and metals need to be investigated further

through more specific assessment of exposure.

1255
TITLE:
Rapid solubilization of human body tissues and tissue fluids for microdetermination of heavy metals.

AUTHORS:
GAFFIN SL

SOURCE:
CLIN TOXICOL; 15 (3). 1979 (RECD. 1980). 293-300.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A liquid pressure technique for decomposing and liquifying several different human tissues as a pretreatment for atomic absorption spectroscopy was evaluated. Samples of Pb, Hg, Cu, Zn, Cd, Ni and/or Cr in the ppm concentration range were used to spike samples of human liver, intestine, muscle, lung, brain and/or teeth. All human tissue samples decomposed completely in a 23-ml capacity Teflon-lined decomposition vessel under the following standard conditions: 0.2 g tissue, 2.5 ml nitric acid (64%), 135ê C for 2 h. Recoveries of the various added heavy metals under the above standard conditions by atomic absorption spectroscopy were high, with errors averaged over all the samples of 29.2% for a concentration of 1 ppm, 8.4% for 5 ppm, and 5.7% for 20 ppm. Liquid pressure technique was found to be a simple, rapid, and reliable method for decomposing both hard and soft human tissues for trace metal determinations by atomic absorption spectroscopy.

1256
TITLE:
Workshop on the Qualitative and Quantitative Comparability of Human and Animal Developmental Neurotoxicity, Work Group II Report: Testing Methods in Developmental Neurotoxicity for Use in Human Risk Assessment

AUTHORS:
Buelke-Sam J
Mactutus CF

SOURCE:
Neurotoxicology and Teratology, Vol. 12, No. 3, pages 269-274, 30 references, 1990

ABSTRACT:
A critical evaluation was presented of the EPA stand/alone developmental neurotoxicity proposal. Also specifically considered was the content of a basic screening battery and if developmental neurotoxicity testing should be required routinely for all chemicals and not just for those triggered

by other data. The qualitative and quantitative comparisons of human and animal studies reviewed during the first day of the workshop were used as a common data base from which the Work Group addressed the topic of testing methods in developmental neurotoxicology. Two distinct approaches to developmental neurotoxicity testing were considered: a triggered stand/alone test battery and a routine basic screening battery for inclusion within any requested developmental or reproductive toxicity study. The Group overwhelmingly agreed to address the latter approach. The Group also agreed that a basic screening battery should include evaluation of multiple central nervous system functions, that observed alterations may be indicative of primary or secondary effects on the nervous system, that the test methods selected may differ based on what is known about the agent, and that the protocol for study conduct can be as important as the methods employed. For monitoring offspring development the Group recommended using measures of physical landmarks, brain weights, neuropathology, functional observations, motor activity, reactivity and learning and memory.

1257
TITLE:
Acoustic startle response in the study of developmental toxicity.

AUTHORS:
Hironaka N

SOURCE:
Congenital Anomalies 1999;39(1):3-12

ABSTRACT:
Acoustic startle response (ASR) is a defensive reflex that occurs shortly after presentation of a brief intense acoustic stimulus. It consists of a sudden contraction of facial and skeletal muscle. ASR in rodents is a gross vibration-like movement of the body that is easy to elicit, record, and analyze quantitatively. It can also be used as a reliable and sensitive measure of physiological mechanism of developmental toxicity. The basic neural mechanisms of ASR have been elucidated. The cochlear nucleus and the reticular nucleus of pons are essential to the induction and regulation of ASR amplitude. Fear or anxiety augments ASR (fear potentiation) and functionally involves amygdala. A brief presentation of a weak acoustic stimulus shortly before the presentation of a startling stimulus suppresses ASR (prepulse inhibition). Prepulse inhibition is thought to be regulated by the dopaminergic mesolimbic system. Taken together, these phenomena suggest the use of ASR as a means of modeling anxiety/fear and the sensorymotor abnormalities that may present themselves in a condition such as schizophrenia. In this review, the fundamental behavioral and neural features of ASR are described and major findings in connection with the toxicology of ASR are reviewed. Finally, the significance of ASR in the study of developmental toxicology including

behavioral teratology is discussed.

1258
TITLE:
BRAIN LESIONS IN EXPERIMENTAL METHYL MERCURY POISONING OF SQUIRREL MONKEYS SAIMIRI-SCIUREUS

AUTHORS:
ZOOK BC
WILPIZESKI CR
ALBERT EN

SOURCE:
NIELSEN, S. W., G. MIGAKI AND D. G. SCARPELLI (ED.). ANIMALS AS MONITORS OF ENVIRONMENTAL POLLUTANTS; SYMPOSIUM, STORRS, CONN., USA, 1977. XII+421P. NATIONAL ACADEMY OF SCIENCES: WASHINGTON, D.C., USA. ILLUS. MAPS. PAPER. ISBN 0-309-02871-X.; 0 (0). 1979 (RECD. 1980). P151-164.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN COMPARISON DEATH ORAL DOSE

1259
TITLE:
BEHAVIORAL NEUROCHEMICAL AND METABOLIC CORRELATES OF METHYL MERCURY IN MICE

AUTHORS:
SALVATERRA P
MASSARO EJ
LOWN B
MORGANTI J

SOURCE:
HOEKSTRA, W. G. ET AL. (ED.). TRACE ELEMENT METABOLISM IN ANIMALS, NO. 2. PROCEEDINGS OF THE SECOND INTERNATIONAL SYMPOSIUM. MADISON, WIS., U.S.A., JUNE 18-22, 1973. XXVI+775P. ILLUS. UNIVERSITY PARK PRESS: BALTIMORE, MD., U.S.A.; LONDON, ENGLAND. ISBN 0-8391-0696-3.; 1974 701-704

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. BRAIN GLYCOLYTIC INTERMEDIATES ATP ADP AMP PHOSPHO CREATINE PHOSPHO FRUCTO KINASE

1260
TITLE:
Methylmercury a review of health hazards and side effects associated with the emission of mercury compounds into natural systems.

AUTHORS:

LOFROTH G

SOURCE:
ECOL RES COMM BULL; 4. 1970 1-56

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN FISH MOUSE DROSOPHILA-MELANOGASTER PLANT CELLS PESTICIDE POISONING BRAIN DAMAGE POLLUTED WATER GENETICS METABOLISM OCCUPATIONAL EXPOSURE BODY ACCUMULATION

1261
TITLE:
Worksite Behavioral Research: Results, Sensitive Methods, Test Batteries and the Transition from Laboratory Data to Human Health

AUTHORS:
Anger WK

SOURCE:
Neurotoxicology, Vol. 11, No. 4, pages 629-720, 479 references, 1990

ABSTRACT:
A brief summary of large scale human health disasters and an extensive review of the human behavioral epidemiologic research on neurotoxic effects of chronic exposure to chemicals in the workplace were provided. Health disasters included food adulteration, medical experiments and pharmaceutical errors, short term chemical or radiation exposures, and extended chemical or radiation exposures. The research reveals consistent nervous system effects of industrial chemicals that have been studied since this type of worksite research began in the late 1960's. This is followed by consideration of the methods employed in this field and their relation to regulatory approaches. Approximately 185 epidemiological behavioral neurotoxicology studies have been published through 1989 dealing with workplace exposures to chemicals; about 250 different tests have been administered to exposed workers in primarily cross sectional studies. Statistically significant decrements were reported in 43% of the approximately 1100 test population administrations. Twenty eight different chemicals as well as multiple chemical exposures have been studied. The most extensive findings are seen in research on carbon-disulfide (75150), lead (7439921), mercury (7439976), and multiple solvents exposures. Three or more independent studies have also been reported on workers exposed to styrene (100425) and organophosphates. The results indicated that exposures produced a broad spectrum of cognitive, motor, and affective or personality changes. Functional deficits were most frequently reported in tests of intelligence, memory, spatial relations, coordination, and speed plus coordination. A lack of parallelism between human test methods and the EPA and FDA methods used for preproduction screening in animals; this would make it unlikely that

the widely used human and animal behavioral test batteries could identify disease complexes newly suspected of having a chemical etiology.

1262
TITLE:
BLOOD BRAIN BARRIER PERMEABILITY AND GLUCOSE TRANSPORT DURING CHRONIC MERCURY INTOXICATION

AUTHORS:
BARRY DI
BOLWIG T
HERTZ M
HANSEN J

SOURCE:
9TH INTERNATIONAL SYMPOSIUM ON CEREBRAL BLOOD FLOW AND METABOLISM, TOKYO, JAPAN, MAY 28-JUNE 9, 1979. ACTA NEUROL SCAND SUPPL; 60 (72). 1979. 572-573.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT

1263
TITLE:
Gestational exposure to methylmercury retards operant behavior in transition in adult rats.

AUTHORS:
Newland MC
Reile PA
Langston JL
Paletz EM

SOURCE:
Toxicologist 2002 Mar;66(1-S):130

ABSTRACT:
Evidence is growing that developmental exposure to methylmercury (MeHg), has behavioral effects that extend into adulthood and aging. To study MeHg's prolonged effects on behavioral plasticity, rats were exposed to methylmercury during gestation via maternal drinking water containing 0, 0.5 or 6.4 ppm Hg as MeHg. Exposure began at least four weeks before mating, and continued to postnatal day 16. Brain Hg concentrations were 0.49 and 9.8 ppm at birth in littermates of the rats described here; lactation resulted in no mercury exposure. The behavior of one- and two-year old offspring was maintained under various Concurrent Variable Interval reinforcement schedules in which pressing each of two levers was maintained by independent Variable Interval t schedules of reinforcement,

and t is the average inter-reinforcer interval. During the first 30 minutes of 150 min. sessions, the reinforcement rates on both levers were equal, and the ratio of left to right (L:R) lever presses approximated 1.0. After 30 min. the left lever became rich relative to the right, the right became relatively rich, or there was no change. During sessions in which one lever became rich, responding was tracked as it transitioned to reflect the new allocation of reinforcers. Terminal reinforcer ratios (L:R) used were 9:1, 4:1, 3:1, 1:1, 1:3, 1:4, and 1:9. In controls and most exposed rats, response ratios reflected reinforcer ratios by the end of the session. The transitions of many exposed rats were retarded relative to controls, and in some transitions they went in the wrong direction. The tactic used here greatly reduced the time required to study behavior in transition from a month in previous reports to a single session here.

1264
TITLE:
EFFECTS OF PERINATAL EXPOSURE TO METHYL MERCURY ON FUNCTIONAL BRAIN DEVELOPMENT AND NEUROCHEMISTRY

AUTHORS:
SOBOTKA TJ
COOK MP
BRODIE RE

SOURCE:
BIOL PSYCHIATRY 8:307-320,1974

1265
TITLE:
DEPOSITION OF MERCURY IN FETAL AND MATERNAL BRAIN

AUTHORS:
YANG MG
KRAWFORD KS
GARCIA JD
WANG JC
LEI KY

SOURCE:
PROC SOC EXP BIOL MED 141:1004-1007,1972

1266
TITLE:
ELIMINATION PATTERN OF METHYL MERCURY FROM BLOOD AND BRAIN OF RATS(DAMS AND OFFSPRING)AFTER DELIVERY,FOLLOWING ORAL ADMINISTRATION OF ITS CHLORIDE SALT DURING GESTATION

AUTHORS:
CASTERLINE JL JR
WILLIAMS CH

SOURCE:
BULL ENVIRON CONTAM TOXICOL 7:292-295,1972

1267
TITLE:
NEURAL TUBE DEFECTS AND BRAIN ANOMALIES:A REVIEW OF SELECTED TERATOGENS AND THEIR POSSIBLE MODES OF ACTION

AUTHORS:
MORRISSEY RE
MOTTET NK

SOURCE:
NEUROTOXICOLOGY(LITTLE ROCK,AR) 2:125-162,1981

1268
TITLE:
BRAIN RETENTION OF MERCURY IN MICE PRENATALLY TREATED WITH METHYLMERCURY AND SELENITE

AUTHORS:
SATOH H
SHIMAI S

SOURCE:
TERATOLOGY 26(1):13A,1982

1269
TITLE:
EFFECTS OF MERCURY ON THE GROWTH OF RAT BRAIN ASTROCYTES AND ON THE CHROMOSOME ABERRATION OF CHINESE HAMSTER OVARY CELLS IN CULTURES

AUTHORS:
JOU TC
LIU SM
DENG JF

SOURCE:
VET HUM TOXICOL 28:476,1986

1270
TITLE:
Proceedings of the second Finnish-Estonian Symposium of early effects of toxic substances

AUTHORS:
Hernberg S
Kahn H
Lehtinen S

SOURCE:
Institute of Occupational Health, Haartmaninkatu 1, 00290 Helsinki 29, Finland, 1982. 212p. Illus. 164 ref.

ABSTRACT:
Proceedings of a Symposium organised by the Institute of Experimental and Clinical Medicine in Tallinn, Estonia (USSR), and the Finnish Institute of Occupational health. The texts of 21 papers presented at the symposium are reproduced in English and Russian under 2 main headings: genetic toxicology (implications in occupational health, chromosomal aberrations in offspring of female styrene workers, experimental effects of shale oil on reproductive function, biological monitoring); clinical and experimental neurotoxicity (central nervous function following lead exposure, psychological effects of long-term mercury exposure, neurotoxic properties of n-hexane, injury to brain cells by exposure to sublethal doses of organic solvents).

1271
TITLE:
Occupational neurology

AUTHORS:
Juntunen J

SOURCE:
Institute of Occupational Health, Laajaniityntie 1, 01620 Vantaa 62, Finland, 1983. 217p. Illus. Bibl.

ABSTRACT:
The 17 papers presented at the first International Course on Occupational Neurology (June 1982, Helsinki, Finland) are reproduced. Topics covered include: descriptive, analytic, experimental and theoretical applications of neuroepidemiology to occupational neurology; toxicological mechanisms in nervous system degeneration; occupational exposure to neurotoxic agents in Finland; psychiatric aspects of organic brain syndromes; pathogenic and clinical aspects of polyneuropathies; electrophysiological investigation of toxic neuropathies; alcoholism; exposure to organic solvents and their effects; metals; mercury and lead; physical factors.

1272
TITLE:
Organometallic compounds in relation to pollution.

AUTHORS:
Glockling F

SOURCE:
Anal. Proc. 17(10): 417-422 1980 (7 References)

ABSTRACT:
PESTAB. Four types of organometallic compounds are considered: organosilanes, organolead compounds, organomercurials, and organotin compounds. Organomercurials are used in industry and in agriculture. They are potent compounds with a broad spectrum of effectiveness as fungicides. All soluble mercury compounds are toxic. The monomethyl mercurials are extremely toxic in that they rapidly cause irreversible brain damage. The animal body only slowly excretes the chemicals through the degradation process of demethylation. Various trimethylsilylmethylmercury compounds have been examined and their chemical reactivity was found to be similar to that of the methylmercurials. However, their mammalian toxicity is much lower than that of the methylmercurials, even though they do not undergo extensive dealkylation in the animal body. Organotins are also used as fungicides but have a lower mammalian toxicity than the organomercurials.

1273
TITLE:
Determination of microquantities of mercury in biomaterials with a complex elemental composition (neutron-activation analysis.)

AUTHORS:
BAKULINA LA
SHUSTOV DA

SOURCE:
GIG SANIT; (11). 1974 49-52

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Using neutron-activation analysis a method of determining microquantities of Hg in complex biomaterials was developed. The accuracy and sensitivity of the method with respect to beta-radiation were determined. The method was tested on cattle kidneys, liver, muscle and brain. The Hg preparations were identified on the basis of the half-life and energy of beta- and gamma-radiation.

1274
TITLE:
Analytical problems in the measurement of pesticide residues.

AUTHORS:
Korte F

SOURCE:
IN: Fate of Pesticides in Environment, Gor; 1972, pp. 465-477 ; (REF:21)

ABSTRACT:
HAPAB In measuring pesticide residues analytical data older than a few years or not verified by independent methods should not be trusted. Not only must the parent compounds be subject to analysis, but the conversion products as well. Collection, storage, extraction, and clean-up of representative samples are difficult. Only after an intensified extraction procedure yields no further increase in the amount of pesticide extracted can the procedure be considered adequate. Solvents which coagulate proteins should only be used in the last extraction step. New methods are needed for the recovery of hydrolytic degradation products. Quantitative determination of pesticide residues may be carried out with fairly good results by GLC. Important progress in TLC analysis may be forthcoming from a new scanning microdensitometer equipped with a xenon or xenon-mercury lamp and a monochromator which allows measurements in the range of 200 to 700 mmu. This will enable many substances to be determined on TLC without visualization with spray reagents. The claim that cholinesterase inhibition is a measure of the toxic effect of organophosphate and carbamate insecticides is under attack as an oversimplification. The majority of current analytical methods developed measure on the inhibition of the pseudocholinesterases, which are located in the plasma of most animals. These methods may be useful, especially for screening purposes, to reveal the presence of inhibitors, but must not be regarded as indices of total residue toxicity. Unless identity of response between red blood cell cholinesterase and the esterases of brain and nervous tissue is established, even the determination of red blood cell cholinesterase inhibition will remain unacceptable for toxicologic evaluation of a residue.

1275
TITLE:
Toxic Effects of Lead on Neuronal Development and Function

AUTHORS:
Freedman R
Olson L
Hoffer BJ

SOURCE:
Environmental Health Perspectives, Vol. 89, pages 27-33, 29 references, 1990

ABSTRACT:
The effects of lead (7439921) on neuronal development and function was studied through grafts of brain tissue from rat fetuses which were placed

on the anterior eye chamber of adult hosts. This method permitted histological and physiological analyses which would otherwise have been difficult to perform. Injections of 5 microliters of lead-acetate (301042) into the anterior chamber induced hypernoradrenergic innervation of the central nervous system tissue. In contrast, mercury (7439976) caused marked degeneration of adrenergic nerves. Lead treatment of the host had no adverse effects on endothelial budding and vascularization of the transplants from the host iris. No effects of 1% lead were seen on cerebellar transplant growth at either vigorous growth or final size in oculo stages. Lead-acetate treated animals had Purkinje graft cells which exhibited almost no spontaneous activity; interspike interval histograms showed regular discharge patterns. The authors conclude that the hyperactivity associated with lead exposure in children may be related to increased adrenergic nerve fiber density.

1276

TITLE:

Characterization of Interactions of Methylmercury with Ca2+ Channels in Synaptosomes and Pheochromocytoma Cells: Radiotracer Flux and Binding Studies

AUTHORS:

Shafer TJ
Contreras ML
Atchison WD

SOURCE:

Molecular Pharmacology, Vol. 38, No. 1, pages 102-113, 73 references, 1990

ABSTRACT:

The effects of methylmercury on nerve terminal calcium (Ca+2) channel properties in synaptosomes and pheochromocytoma cells were examined. Synaptosomes prepared from the forebrains of male Sprague-Dawley-rats were incubated with 0 to 100 micromolar (microM) methylmercuric-acetate (108076) (MMA) for up to 30 seconds. The effects on cellular influx of calcium-45 (Ca-45) tagged Ca+2 were evaluated. Synaptosomes were incubated with 0 to 100microM MMA in the presence of Ca-45, strontium-85 (Sr-85), or barium-133 (Ba-133). Undifferentiated or nerve growth factor (NGF) differentiated pheochromocytoma PC12 cells were incubated with 0 to 250microM in the presence of 52.5mM potassium ion (K+). Rat forebrain synaptosomes or PC12 cells were incubated with 0 or 100microM MMA and 0 to 70 picomolar tritiated nitrendipine or omega-conotoxin-GVIA (CgTx). Effects on nitrendipine and CgTx cellular binding were determined. MMA inhibited about 30% of the Ca+2 influx during the first second. After 10 seconds MMA blocked an increasingly larger proportion of channel mediated depolarization induced Ca+2 influx, but not total influx. The extent of blockage increased with increasing degree of depolarization. The degree of blockage was similar for synaptosomes depolarized by K+ or maintained

in a low Ca+2 medium. MMA inhibited influx of Ca-45, Sr-85, and Ba-133 in a dose dependent manner. Nifedipine blocked influx of Ca+2 into undifferentiated and NGF differentiated PC12 cells in a dose dependent manner. MMA inhibited Ca+2 influx into undifferentiated and differentiated PC12 cells dose dependently. MMA significantly decreased the extent of nitrendipine synaptosomal binding. The decrease was due to decreases in binding affinity and binding sites. MMA did not significantly alter CgTx synaptosomal binding, but significantly decreased the extent of CgTx PC12 cell binding.

1277
TITLE:
Toxic responses of the central nervous system.

AUTHORS:
Norton S

SOURCE:
In: Toxicology: The Basic Science of Poisons. Doull, J., Klaassen, C. D. and Amdur, M. O., eds. (Macmillan Publ. Co. Inc.: NY): CH09: 179-205 1980 (196 References)

ABSTRACT:
PESTAB. Toxic responses of the central nervous system are examined. Structural and functional toxicity are considered. Six types of nervous system toxicants are discussed. Anoxia is caused by barbiturates, carbon monoxide, cyanide, azide and nitrogen chloride. Agents causing damage to myelin include hexachlorophene, lead and thallium. Organophosphorus compounds cause peripheral axonopathies. Several episodes of serious poisoning have occurred from unintentional contamination of food by TOCP. Delayed neurotoxicity has been shown to occur in poisoning from DFP, leptofos, and mipafox. Related insecticides, such as parathion and malathion, and carbamate anticholinesterase insecticides, have not been shown to cause neuropathies. Agents causing primary damage to perikarya of peripheral neurons include organomercury compounds. Organomercury compounds more readily affect the sensory cell bodies in the dorsal root ganglion of the spinal cord because of the lack of a blood barrier such as exists over much of the brain capillaries. Neuromuscular junctions of motor nerves are affected by DDT, allethrin and lead. DDT and other similar insecticides caused repetitive firing of the motor end plate through repeated depolarizations of the presynaptic nerve terminal. Repetitive discharge occurs in sensory, central, and motor neurons in DDT poisoned insects. Pyrethrum induces various nervous system effects. Allethrin has effects resembling DDT, causing repetitive firing of the motor end plate. Neurotoxicants causing localized CNS lesions include DDT and mercury.

1278

TITLE:
NEURO PATHOLOGICAL EFFECTS OF MERCURY TOXICATION

AUTHORS:
SIMMAT K
ANTHONY A

SOURCE:
PROC PA ACAD SCI; 45. 1971 (1974) 88-92

ABSTRACT: HEEP COPYRIGHT: BIOL ABS.

1279
TITLE:
Tissue levels in animals and effects caused by chlorinated hydrocarbon insecticides, chlorinated biphenyls, and mercury in the marine environment along the Netherlands coast.

AUTHORS:
Koeman JH
VanGenderen H

SOURCE:
IN: Marine Pollution and Sea Life, Fishing News (Books) Ltd., London,1972, pp. 428-435(REF:14)

ABSTRACT:
HAPAB. Results of studies of the pesticide content in tissues of dead or dying birds are presented. Proof of pesticide lethality can be determined from the residues in the liver and brain. Telodrin was particularly toxic for terns and eiders. Endrin, while present in relatively high concentrations at the lower trophic levels, was found only in low concentration in the tissues of terns and eiders, indicating that this particular insecticide is less hazardous for higher trophic levels. Poisoning of terns occurred in two distinct stages: very soon after hatching, attributed to resorption of the yolk sac; and as the birds learned to fly. It is reasoned that the increased energy used in the attempt to fly released chlorinated hydrocarbons from the fat deposits. The conspicuous increase in death of female eiders at the end of the breeding cycle is explained by the fact that the females took in little or no food during the incubation period, using up the fat stores of their bodies which released the stored chlorinated hydrocarbon residues.

1280
TITLE:
The applicable condition of Magos method for mercury measurement under coexistence of selenium.

AUTHORS:
YAMAMOTO R
SATOH H
SUZUKI T
NAGANUMA A
IMURA N

SOURCE:
ANAL BIOCHEM; 101 (1). 1980. 254-259.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Delayed and incomplete release of Hg0 was reported in liver, blood and spleen, but not in kidneys and brain of mice simultaneously administered HgCl2 and Na2SeO3 for both inorganic and total Hg determination by Magos method. This problem was overcome by the treatment of the tissue homogenate with an equal volume of 45% NaOH containing 1% Cys HCl at 40ê C for more than 30 min and the use of the area under the peak of the Hg release curve on calculation. In the case of CH3HgCl administration instead of HgCl2, the influence of coexistent Se was not observed for Hg determination by Magos method in mice within 24 h after dosing.

1281
TITLE:
The effect of immediate and delayed treatment with 2,3-dimercaptopropane-1-sulfonate on the distribution and toxicity of inorganic mercury in mice and in fetal and adult rats.

AUTHORS:
WANNAG A
AASETH J

SOURCE:
ACTA PHARMACOL TOXICOL; 46 (2). 1980. 81-88.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution and excretion of Hg were studied in mice and rats given a single injection of HgCl2 combined with chelation treatment. BAL-sulf (2,3-dimercaptopropane-1-sulfonate) given i.v. (500 mumol SH/kg) to mice 24 h after the Hg injection (2.0 mumol Hg/kg) reduced the kidney Hg-level significantly, while N-acetyl-DL-penicillamine and BAL (2,3-dimercaptopropanol) did not. Severe kidney damage with oliguria was observed in pregnant as well as in non-pregnant rats after injection of 5 mumol/kg of HgCL2. The gross pathological changes could be avoided with immediate treatment with BAL-sulf (500 mumol SH/kg), and such treatment protected against the oliguric reaction. Treatment delayed for 24 h reduced the renal Hg-levels

significantly, but was ineffective in preventing the kidney damage. This indicates that irreversible changes might have occurred in kidneys cells at this time. The Hg-levels in the brain were either unchanged or lowered in animals given BAL-sulf treatment. BAL-sulf is supposed to act by chelation of Hg2+, particularly in the extracellular space. The complexes formed appears to be rapidly excreted by healthy kidneys. Hg poisoning with severe renal damage is associated with a block in urinary Hg-excretion. The poisoned animals responded on the BAL-sulf treatment with a substantial raise of fecal Hg excretion.

1282
TITLE:
Distribution and excretion of mercury-203 (II) in rats after unitiol, spironolactone and polythiol resin treatment.

AUTHORS:
CIKRT M
LENGER V

SOURCE:
TOXICOL LETT (AMST); 5 (1). 1980. 51-54.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Rats were given 203HgCl2 i.v. at a dose level of 120 mug of Hg2+ per rat. The effect of unitiol (UNI; sodium 2,3-dimercaptopropanesulfonate) and a combined UNI, spironolactone and polythiol resin treatment on whole-body retention, organ distribution and excretion were studied for 48 h. In both treated groups significant increases in excretion and decreases in whole-body retention of 203Hg were observed. In the combination-treated group significantly lower values of 203Hg in plasma, kidney and brain were found.

1283
TITLE:
The effect of manganese administration, alone or combined with zinc, mercury and cadmium, on the tissue levels of these elements in rats.

AUTHORS:
LAL S
GUPTA SK
CHANDRA SV

SOURCE:
TOXICOL LETT (AMST); 5 (3-4). 1980. 203-206.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Manganese chloride was administered alone or in combination with zinc chloride, mercuric chloride and cadmium chloride

i.p. to rats for 30 days to investigate the effect of interaction of these elements on their content in brain, liver and kidney. Significant changes in the accumulation of these metals after combined exposure indicate that metabolic interactions occur. Alterations in the tissue contents of Mn, Zn, Hg and Cd after combined administration may reflect changes at the absorptive sites or in excretory pattern.

1284
TITLE:
Biotransformation of methyl mercuric salts in the mouse studied by specific determination of inorganic mercury.

AUTHORS:
NORSETH T

SOURCE:
ACTA PHARMACOL TOXICOL; 29 (4). 1971 375-384

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. After a single injection of the organomercurial, inorganic Hg was detected in the blood, brain, liver, kidney, spleen and in the intestinal cells. Inorganic Hg was also found in the bile and feces. The results indicated a role of biotransformation in the excretion of Hg after the injection of methyl mercuric salts. Inorganic Hg was preferentially excreted in the feces. Differences in pharmacokinetics of methyl mercuric salts between rats and mice were discussed with regard to differences in biliary excretion and enterohepatic circulation. Species differences should be considered in the evaluation of toxic hazards of methyl mercuric salts.

1285
TITLE:
THE MECHANISM OF OXIDATION OF INHALED MERCURY VAPOR

AUTHORS:
CLARKSON TW
HALBACH S
MAGOS L
SUGATA Y

SOURCE:
BHATNAGAR, R. S. (ED.). MOLECULAR BASIS OF ENVIRONMENTAL TOXICITY; SYMPOSIUM AT THE 176TH NATIONAL MEETING OF THE AMERICAN CHEMICAL SOCIETY. IX+589P. ANN ARBOR SCIENCE PUBLISHERS INC.: ANN ARBOR, MICH., USA. ILLUS. ISBN 0-250-40306-4.; 0 (0). 1980. P419-428.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN DUCK MOUSE RAT BLOOD BRAIN CATALASE

OXYGEN

1286
TITLE:
Modified distribution of methylmercury by additional exposure to elemental mercury or mercuric chloride in mice fed methylmercuric chloride.

AUTHORS:
YAMAMOTO R
SATOH H
SUZUKI T
NOBUNAGA T

SOURCE:
J PHARMACOBIO-DYN; 3 (2). 1980. 80-84.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Male IVCS mice fed pellets containing 8 nmol methylmercuric chloride (MMC)/g feed for 32 days were additionally exposed to elemental Hg vapor (Hgê) or injected mercuric chloride (Hg2+). The modified distribution of accumulated organic Hg was observed 24 h after exposure to inorganic mercurials. The body burden of organic Hg decreased significantly in MMC + Hg2+ treated mice and moderately (not significant) in MMC + Hgê treated mice when compared with MCC treated mice. In spite of the decreased body burden, the organic Hg levels in brain, kidneys and blood of MMC + Hgê treated mice, and in kidneys of MMC + Hg2+ treated mice were elevated. In bile, organic Hg concentration after Hgê of Hg2+ exposure was reduced. The decrease of the blood cells-to-plasma ratio of organic Hg in mice after Hgê exposure is in agreement with the data reported for workers exposed to Hg vapor.

1287
TITLE:
Role of biotransformation in organic mercury neurotoxicity.

AUTHORS:
GALLAGHER PJ
LEE RL

SOURCE:
TOXICOLOGY; 15 (2). 1980. 129-134.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Although the clinical patterns of organic and inorganic Hg poisoning are very different, systemic toxicity experiments have shown that the histological changes in the kidneys and dorsal root ganglia neurons are identical with the 2 classes of compounds. The toxicity of organic mercurials is probably the result of biotransformation

to inorganic Hg. To test this hypothesis, between 10-7 and 10-10 mol of mercuric chloride and methyl mercuric acetate were injected directly into the cerebrum of rats. The comparative size of lesions was estimated anatomically and by reference to blood-brain barrier dysfunction. Inorganic lesions were only slightly larger than those produced by equimolar amounts of organic Hg. Consequently, both organic and inorganic Hg must be regarded as neurotoxic in their own right. Conversion of organic to inorganic Hg certainly occurs but it is not the only mechanism by which organic Hg exerts its toxicological effect.

1288
TITLE:
The protective potency of marine animal meat against the neurotoxicity of methylmercury: Its relationship with the organ distribution of mercury and selenium in the rat.

AUTHORS:
OHI G
NISHIGAKI S
SEKI H
TAMURA Y
MAKI T
MINOWA K
SHIMAMURA Y
MIZOGUCHI I
INABA Y
ET AL

SOURCE:
FOOD COSMET TOXICOL; 18 (2). 1980. 139-146.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The meats of 2 marine animals known to contain high levels of both methylmercury and Se were compared with respect to their protective potencies against the neurotoxicity of methylmercury. The organ distributions of Se and Hg in rats given diets containing these meats was also compared. Weanling rats were fed for 12 wk on a diet containing 17.5 ppm methylmercuric chloride and 1 of 2 levels of Se (0.3 or 0.6 ppm) originating from the meat of sebastes (Sebastes iracundus) or of the sperm whale (Physeter catodon), or from sodium selenite. The protection conferred sebastes meat was roughly equal to that of the selenite regarding growth rate but was considerably greater with respect to the neurological signs. By both criteria, sperm whale meat was less effective than sebastes meat and selenite in providing protection. The organ distribution pattern of Se and Hg showed that Se in the blood, brain and spinal cord was positively correlated with neurological protection, while total Hg and methylmercury in those organs were negatively correlated with neurological protection. The level of protection (delay of

the neurological manifestations by nearly 7 wk) corresponding with the increase in Se levels in the nervous system (from about 1/50 to 1/10 of the methylmercury levels on a molar basis) indicated that the protective mechanism was not simple direct conjugation of Se with methylmercury. It has previously been noted that tuna fish containing high levels of Se provide protection against methylmercury toxicity and it may be that all marine animals rich in both Se and methylmercury afford this protection.

1289
TITLE:
A Study on the Neurobehavioral Effects of Occupational Exposure to Organic Solvents in Korean Workers

AUTHORS:
Lee S-H
Lee SH

SOURCE:
Environmental Research, Vol. 60, No. 2, pages 227-232, 16 references, 1993

ABSTRACT:
A cross sectional neurobehavioral study was conducted among workers exposed to solvents in painting and printing occupations. The subjects included 113 male workers occupationally exposed to solvents and 81 referents who had not been so exposed. The solvent exposed workers were divided into two groups, low exposure and high exposure. Visual perception and memory ability and perceptual/motor speed declined in the exposed group in this study. The results of the Santa Ana dexterity test for preferred hand in the highly exposed group were lower than those in the low exposed group. Only visual memory ability declined in the solvent exposed group. However, the association between digit symbol and solvent exposure was marginally significant after the effects of confounders were controlled. As the exposed group was not exposed to either lead or mercury, these findings suggest an association between solvent exposure and decreased visual perception/memory. The authors are planning a survey which will provide more accurate readings as to the precise level of solvent exposure on an individual basis.

1290
TITLE:
INHALATION UPTAKE OF LOW LEVEL ELEMENTAL MERCURY VAPOR AND ITS TISSUE DISTRIBUTION IN RATS

AUTHORS:
OBERSKI SP
FANG SC

SOURCE:

BULL ENVIRON CONTAM TOXICOL; 25 (1). 1980. 79-84.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. KIDNEY LUNG HEART LIVER BRAIN BLOOD

1291
TITLE:
INHIBITION OF MONO AMINE UPTAKE IN RAT BRAIN SYNAPTOSOMES BY METHYL MERCURY

AUTHORS:
KOMULAINEN H
TUOMISTO J

SOURCE:
2ND INTERNATIONAL CONGRESS ON TOXICOLOGY, BRUSSELS, BELGIUM, JULY 6-11, 1980. TOXICOL LETTERS (AMST); 0 (SPEC. ISSUE 1). 1980. 130.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT DOPAMINE

1292
TITLE:
The effect of N-acetylhomocysteine and its thiolactone on the distribution and excretion of mercury in methyl mercuric chloride injected mice.

AUTHORS:
AASETH J

SOURCE:
ACTA PHARMACOL TOXICOL; 36 (3). 1975 193-202

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The distribution and excretion of Hg was studied in mice given a single i.v. dose of 5 mugmol/kg of CH3HgCl. I.V. treatment with N-acethylhomocysteine (10 mmol/kg) increased the urinary excretion of Hg. The corresponding thiolactone mixed into the feed of the mice was more effective in removing Hg from the body. The toxicity of the thiolactone seemed to be remarkably low compared to other S containing agents. Hg deposited in the brain was mobilized by oral administration of the thiolactone even if the treatment was delayed until 5 days after the injection of CH3HgCl. The formation of a N-acetylhomocysteine-methyl-mercuric-complex is probably responsible for this effect.

1293
TITLE:
DISTRIBUTION AND CONCENTRATION OF MERCURY IN AUTOPSY SPECIMENS OF HUMAN

BRAIN

AUTHORS:
GLOMSKI CA
BRODY H
PILLAY S KK

SOURCE:
NATURE (LOND); 232 (5307). 1971 200-201

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. NOTE FISH WATER POLLUTION

1294
TITLE:
FACTORS AFFECTING MERCURY CONCENTRATIONS IN RECENT AND OLD BATHY DEMERSAL
FISH

AUTHORS:
BARBER RT
WHALING PJ

SOURCE:
ENVIRON HEALTH PERSPECT; 10. 1975 261

ABSTRACT: HEEP COPYRIGHT: BIOL ABS.

1295
TITLE:
Pathology of chronic alkylmercurial poisoning in swine.

AUTHORS:
Tryphonas L
Nielsen NO

SOURCE:
Amer. J. Vet. Res.34(3): 379-392; 1973(REF:36)

ABSTRACT:
HAPAB. The nervous, urinary, and digestive systems of swine were affected by administration of methylmercuric dicyandiamide (MMD) for 60 days and ethylmercuric chloride (granosan) (EMC) for 90 days. The most obvious clinical signs were neurologic. Neuronal necrosis followed by secondary gliosis, capillary endothelial proliferation, and degenerative arteriopathy in the blood vessels supplying injured gray matter (which caused further neuronal necrosis) were observed. EMC was much more toxic than MMD; histopathologic observations indicated that pigs given 0. 38

mg/kg/day would have had clinical signs a short time after termination of the experiment. Mean tissue concentrations reflected doses administered, but a brain mercury level above 7 mug of Hg/g was the best indicator of injury. Levels of Hg found in kidney, liver, and muscle, the most commonly eaten portions of an animal carcass, were high enough to be potentially hazardous to man.

1296
TITLE:
INHIBITION OF CHOLINE ACETYL TRANSFERASE AND CARNITINE ACETYL TRANSFERASE BY CADMIUM AND MERCURY

AUTHORS:
GOODMAN DR
HARBISON RD

SOURCE:
MEETING OF THE AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, ROCHESTER, MINN., USA, AUG. 17-21, 1980. PHARMACOLOGIST; 22 (3). 1980. 199.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MOUSE RAT BRAIN SPERM METABOLISM TOXICITY

1297
TITLE:
Similarities of the In Vivo and In Vitro Effects of Mercuric Chloride on (3H)Ouabain Binding and Potassium Activation of Na++-ATPase in Isolated Rat Cerebral Microvessels

AUTHORS:
Albrecht J
Hilgier W

SOURCE:
Toxicology Letters, Vol. 70, No. 3, pages 331-336, 16 references, 1994

ABSTRACT:
The in-vivo and in-vitro effects of mercuric-chloride (7487947) (MC) on tritium labeled ouabain binding and potassium activation of sodium/potassium-ATPase (Na++-ATPase) activity in rat brain microvessels (RBM) were compared. For the in-vivo study, microvessels were prepared from male Wistar-rats that had been given 6mg/kg MC intraperitoneally 18 hours previously. For in-vitro treatment, MC was added to a suspension of RBM from control animals. Components of the ouabain binding assay were added. Inorganic phosphate liberated from ATP was measured colorimetrically. The potassium ion (K+) levels in the incubation

mixtures were varied. Results showed that MC added in-vitro inhibited ouabain binding to the RBM in a dose dependent manner. In the in-vivo study, the ouabain binding closely paralleled that in the in-vitro study (36% versus 38%, respectively). Increasing K+ concentration from 0 to 20 millimolar (mM) resulted in increased enzyme activity and dropped to submaximal values at 40mM K+. The Michaelis constant for K+ was not affected by either treatment with MC, whereas maximum velocity was decreased substantially in both in-vivo and in-vitro treatments (13.10 to 6.07 and 7.67 micromoles/milligram/hour). The authors conclude that the similarities of the effects of MC on the in-vivo and in-vitro inhibitory effects of ouabain on Na+/K+-ATPase activity, and on K+ activation kinetics suggests that the in-vivo inhibition of the enzyme results from a direct and durable action of mercuric ions on the enzyme.

1298
TITLE:
The inhibition of cerebral high affinity receptor sites by lead and mercury compounds.

AUTHORS:
BONDY SC
AGRAWAL AK

SOURCE:
ARCH TOXICOL; 46 (3-4). 1980 (RECD. 1981). 249-256.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Effect of concentrations of several Pb and Hg compounds on high affinity receptor sites within discrete brain regions was measured in rats. Specific binding of radioactive spiroperidol and quinuclidinyl benzilate to striatal and cortical membranes, respectively, was more severely inhibited in the presence of tri-n-butyl lead acetate than by lead acetate. The hydrophobic organic Pb derivative was able to interfere with receptor structure more readily than lead acetate. HgCl2 was more effective in blocking these 2 neurotransmitter receptor sites than organic methylmercuric chloride. This implied that sulfhydryl groups may be within or proximal to the allosteric binding site. Relative ineffectiveness of all heavy metal compounds studied in blocking the Gly, GABA (gamma-aminobutyric acid) or diazepam receptors indicated that the mechanism of binding may not be similar with different receptor proteins. Since micromolar concentrations of some Pb and Hg compound severely inhibited neurotransmitter binding sites, such a direct interference with postsynaptic events may account for neurological consequences of heavy metal poisoning.

1299
TITLE:
QUANTITATIVE PERSPECTIVES ON THE LONG-TERM TOXICITY OF METHYL MERCURY AND

SIMILAR POISONS

AUTHORS:
WEISS B
SIMON W

SOURCE:
WEISS, BERNARD AND VICTOR G. LATIES (ED.). ENVIRONMENTAL SCIENCE RESEARCH, VOL. 5. BEHAVIORAL TOXICOLOGY. CONFERENCE. ROCHESTER, N.Y., U.S.A., JUNE 1972. XXI+469P. ILLUS. PLENUM PRESS: NEW YORK, N.Y., U.S.A.; LONDON, ENGLAND. ISBN 0-306-36305-4.; 1975 429-437

ABSTRACT: HEEP COPYRIGHT: BIOL ABS.

1300
TITLE:
Accumulation of mercury in certain species of fishes of Lake St-Louis below Beauharnois, Quebec, Canada.

AUTHORS:
GAMACHE P
VALIQUETTE Y
CHODOROWSKI A
PICHET P

SOURCE:
WAT POLLUT RES J CAN; 15 (2). 1980 (RECD. 1981). 143-156.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg contents of young specimens of Perca flavescens and Lepomis gibbosus captured in Lake St. Louis indicated a high degree of variability between individuals of these species. Hg accumulation varied according to the stations and the 2 spp. studied and was not directly linked to the level of Hg in sediments. Mean levels observed were lower than those published for older individuals of the same region, indicating an accumulation with age. Hg content of the brain in Ambloplites rupestris and L. gibbosus varied with the average content in the fish.

1301
TITLE:
Effect of mercury compounds on adult fish and fry of the medaka, Oryzias latipes.

AUTHORS:
SAKAIZUMI M

SOURCE:

J FAC SCI UNIV TOKYO SECT IV ZOOL; 14 (4). 1980 (RECD. 1981). 361-368.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. The dose-survival relationship on HgCl2 (MC) and methyl mercuric chloride (MMC) was studied in the adult fish and fry of O. latipes. Adult fish treated with MC began to die immediately after the beginning of exposure at concentrations above 400 mug Hg/l. At lower concentrations, they began to die after a certain time-lag depending on concentration. The 50% survival time was 3 days at 1000 mug Hg/l, 5 days at 400 mug Hg/l, 26 days at 200 mug Hg/l, 72 days at 100 mug Hg/l and 92 days at 50 mug Hg/l. In the case of MMC, the fish died just after administration at concentrations above 120 mug Hg/l. A certain time-lag depending on concentration was also observed at concentrations lower than 40 mug Hg/l. The 50% survival time was 1 day at 120 mug Hg/l, 18 days at 80 mug Hg/l, 27 days at 40 mug Hg/l, 41 days at 20 mug Hg/l and 51 days at 10 mug Hg/l. Fry just after hatching survived 10 days without food. In a MC solution, mean survival time was shortened to < 5 days at 300 mug Hg/l and to < 1 day at 1400 mug Hg/l. In the case of MMC, mean survival time was 4 days at 50 mug Hg/l and it was shortened to < 1 day at 120 mug Hg/l. Fry were more sensitive than adult fish. The effective concentration of MC was about 10-fold higher than that of MMC in adult fish and fry. Hg accumulation and distribution in 6 different organs (brain, gill, liver, kidney, ovary and testis) were studied in adult fish exposed to MC or MMC at concentrations of 100 and 40 mug Hg/l, respectively. MMC was incorporated more easily than MC. Hg concentration in the kidney and liver was higher than that in other organs for both compounds. The concentration factor in the kidney was 1.5803 on MC and 4.05ere suggested in adult fish.

1302

TITLE:

EFFECTS OF HEAVY METALS ON 5 HYDROXY TRYPTAMINE UPTAKE BY HUMAN BLOOD PLATELETS

AUTHORS:

TUOMISTO J
KOMULAINEN H

SOURCE:

JOINT MEETING OF THE SCANDINAVIAN AND GERMAN PHARMACOLOGICAL SOCIETIES, LUEBECK-TRAVEMUENDE, WEST GERMANY, SEPT. 16-18, 1980. NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL; 313 (SUPPL.). 1980. R68.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT COPPER II METHYL MERCURY BRAIN PROTEIN KINETICS IN-VITRO

1303

TITLE:
METHYL MERCURY CHOLIN ESTERASE INTERACTIONS IN RATS

AUTHORS:
HASTINGS FL
LUCIER GW
KLEIN R

SOURCE:
ENVIRON HEALTH PERSPECT; 12. 1975 127-130

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. CARBARYL INSECTICIDE PLASMA BRAIN ACETYL CHOLIN ESTERASE SEX DIFFERENCE MIXED FUNCTION OXIDASE SYSTEM

1304
TITLE:
MERCURY AND THE NERVOUS SYSTEM

AUTHORS:
CASSITTO MG
GILIOLI R

SOURCE:
G ITAL MED LAV; 2 (3-4). 1980 (RECD. 1981). 181-186.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. REVIEW HUMAN BRAIN BLOOD NEURO PSYCHIC BEHAVIOR VAPOR OCCUPATIONAL HEALTH KINETICS

1305
TITLE:
IN-VITRO MERCURY UPTAKE BY HYPO CATALASEMIC AND ACATALASEMIC MOUSE HEMOLYSATES AND HUMAN ACATALASEMIC HEMOLYSATES

AUTHORS:
OGATA M
KENMOTSU K
NAITO M
MEGURO T
HIROTA N

SOURCE:
IND HEALTH; 18 (4). 1980 (RECD. 1981). 217-220.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. BRAIN ERYTHROCYTE LUNG LIVER KINETICS

1306
TITLE:
Developmental Neurotoxicity: Evaluation of Testing Procedures with Methylazoxymethanol and Methylmercury

AUTHORS:
Goldey ES
O'Callaghan JP
Stanton ME
Barone S Jr
Crofton KM

SOURCE:
Fundamental and Applied Toxicology, Vol. 23, No. 3, pages 447-464, 102 references, 1994

ABSTRACT:
Methods for identification of potential developmental toxicants were tested using offspring of Long-Evans-rats exposed to methylazoxymethanol (590965) (MAM) or methylmercury (22967926) (MM) during gestation. Pregnant rats were administered a single intraperitoneal injection of MAM at 30mg/kg on gestation day 15, or MeHg orally at 1, 2, or 4mg/kg/day from gestation day six to 15. Prenatal exposure to MAM resulted in a reduction of neonatal body weights, but no changes in viability or postnatal survivorship; changes in brain weight with histological alterations of the cortex and hippocampus in particular; a significant increase in the concentration of glial fibrillary acidic protein in the cortex and hippocampus of treated offspring; a slowing in the acquisition phase of a given task; hyperactivity in treated offspring that persisted into adulthood; and reduced startle amplitudes in preweanlings. Prenatal MM exposure at 1, 2, or 4mg/kg on gestational days six to 15 significantly affected only a few endpoints. At the highest dose, fetal and neonatal mortality, and lower neonatal body weights were seen. The authors conclude that while minimal effects of MM may reflect a relative insensitivity of the test species and/or the test methods, the combined results from both chemicals suggest that some procedures not currently required in the developmental neurotoxicity guideline may be helpful in hazard identification.

1307
TITLE:
RETENTION AND DISTRIBUTION OF MERCURY-203 CHLORIDE IN SUCKLING AND ADULT RATS

AUTHORS:
JUGO S

SOURCE:

HEALTH PHYS; 30 (2). 1976 240-241

ABSTRACT: HEEP COPYRIGHT: BIOL ABS.

1308
TITLE:
Molecular and Ionic Mimicry of Toxic Metals

AUTHORS:
Clarkson TW

SOURCE:
Annual Review of Pharmacology and Toxicology, Vol. 32, pages 545-571, 118 references, 1993

ABSTRACT:
A review on oxyanion and divalent metal competition resulting in what has recently been termed molecular mimicry was presented. Molecular mimicry was defined as the binding of a metal cation and a cellular ligand, resulting in a structure so closely mirroring an endogenous substrate that it is then incorporated and used by the cellular metabolic machinery. Such occurrences have been reported for substances such as methylmercury-cysteine which has been found to mimic methionine and to be transported through the blood/brain barrier by an amino acid carrier and taken up by astrocytes, kidney cells, and other tissues, and methyl and inorganic mercury-glutathione complexes which have been reported to mimic conjugates of glutathione and oxidized glutathione resulting in the transport of such complexes out of liver cells and into the bile as well as out of other cells such as kidney and PC-12 cells in-vitro. Another example of molecular mimicry was discussed, involving methylmercury-cysteinylglycine mimicking acylglycines. The possibility of oxyanions of several toxic metals mimicking endogenous anions due to similarities in structure to phosphate, sulfate, and bicarbonate and chloride was discussed. In addition, the importance of ionic mimicry, whereby toxic metals mimic or take the place of essential metals, in the transport and toxicity of such metals at the cellular level was discussed.

1309
TITLE:
Central Effects Of Paraoxon On Haemodynamics In The Cat

AUTHORS:
de Neef JH
Porsius AJ

SOURCE:
Naunyn-Schmiedeberg's Archives of Pharmacology, Vol. 317, No. 2, pages 168-172, 26 references, 19811981

ABSTRACT:

The effects of paraoxon (311455) on the central nervous system were studied in cats. Cats were cannulated through the femoral vein for exposure to drugs. For infusion of drugs through the left and right vertebral artery, right sided thoracotomies were performed. Paraoxon was dissolved in dimethyl-formamide, and cats were exposed through the cannulated arteries or veins. Hemodynamic properties of the central nervous system were monitored by an electromagnetic flowmeter. In a number of experiments, paraoxon was tested in pithed cats. Tritiated dexetimide (21888982) was injected as a marker to follow distribution of the drug in brain tissues. Mean arterial pressure was also measured in cats after exposure to paraoxon. Mean arterial pressure was about 124 millimeters of mercury. Exposure to paraoxon induced dose dependent depressor effects on the central nervous system. Both systolic and diastolic pressure decreased in a dose dependent manner. The maximal decrease was seen at 6 to 8 minutes after exposure. In the pithed cats, paraoxon had no effect on mean arterial pressure under stimulated or unstimulated conditions. The authors conclude that paraoxon elicits changes in hemodynamic parameters within minutes after intravenous exposure in cats.

1310

TITLE:

Methylmercury Acts at Multiple Sites to Block Hippocampal Synaptic Transmission

AUTHORS:

Yuan Y

Atchison WD

SOURCE:

Journal of Pharmacology and Experimental Therapeutics, Vol. 275, No. 3, pages 1308-1316, 39 references, 1995

ABSTRACT:

A study was done to describe the effects of methylmercury (593748) (MeHg) on central synaptic activity. Action potentials and resting membrane potentials were measured in CA1 neurons of Sprague-Dawley-rat hippocampal slices treated with 4 to 100 micromolar methylmercuric-chloride (115093). MeHg caused a concentration and time dependent block of action potentials and depolarization of CA1 neuronal membranes. The effects of MeHg on resting membrane potentials occurred more slowly than on action potentials. The block of action potentials evoked by antidromic stimulation of the alveus occurred faster than the block of action potentials generated by current injection at the cell soma. MeHg also suppressed the responses of CA1 neurons to iontophoresis of glutamate. Inhibitory postsynaptic potentials were more sensitive to MeHg than

excitatory postsynaptic potentials. The authors attribute this to the fact that block of inhibitory postsynaptic potentials occurred prior to block of excitatory postsynaptic potentials. The authors conclude that MeHg acts at multiple sites to block central synaptic transmission.

1311
TITLE:
CHANGES IN OXYGEN CONSUMPTION OF SURVIVING LIVER KIDNEY AND BRAIN SLICES EXPOSED TO METHYL MERCURY

AUTHORS:
LIJOI AF
VON BURG R

SOURCE:
AM ZOOL; 16 (2). 1976 255

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT HUMAN

1312
TITLE:
Mental disorders in mercury poisoning.

AUTHORS:
KOROLENKO TP
PIVEN BN
SHIL'NIKOVA LP

SOURCE:
NAUCHN TR NOVOSIB MED INST; 57 1971 148-154

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Patients (18) aged 27-55 were exposed to Hg for 102 days-20 yr were studied. Common complaints were headaches, mainly in the frontal region, insomnia, irritability, hyperesthesia to sound and light, and deterioration of memory. The neurological characteristics were tremor of the eyelids and extended fingers, increase and nonuniformity of tendon reflexes, hyperhidrosis, and diffuse dermographia rubra. Emotional lability, tearfulness, and affective-anxiety states were noted. Most patients had disorders in perception in the form of visual and auditory hypnagogic hallucinations, more rarely psychosensory disorders and attacks of memory impairments. Epileptiform states were noted in 4 patients. The symptoms are explained by organic effects on the brain.

1313
TITLE:
Chronic Lead Treatment Accelerates Photochemically Induced Platelet

Aggregation in Cerebral Microvessels of Mice, In Vivo

AUTHORS:
Al Dhaheri AH
El-Sabban F
Fahim MA

SOURCE:
Environmental Research, Vol. 69, No. 1, pages 51-58, 26 references, 1995

ABSTRACT:
The effects of chronic lead (7439921) exposure on platelet aggregation in cerebral microvessels were studied in mice. Adult male TO-mice were injected subcutaneously with 0, 0.1, or 1.0mg/kg lead as lead-acetate (301042) daily for 7 days. On day eight, some mice underwent craniotomies and were injected intravenously with sodium-fluorescein dye. Platelet aggregation in the pial microvessels was induced photochemically by irradiating cranial tissues with 44,000 lux candle per square centimeter from a mercury lamp. This treatment produced free radicals in the dye which injured the endothelium microvascular lumen. As a result, platelets began to adhere to the sites of endothelial injury. The times required for the first platelet to adhere to the pial microvessel lumena and for full vascular occlusion to occur were determined using a microscopy/video imaging recording technique. Blood samples were collected from other mice to measure lead concentrations and changes in hematologic parameters. Mean blood lead concentrations in the control mice and the mice injected with 0.1 and 1.0mg/kg lead were 0.19, 0.25, and 0.67 part per million, respectively. A significant decrease in hemoglobin in the 1.0mg/kg group was the only observed hematological effect of lead. Lead exposure significantly shortened the time until the first platelet appeared in pial arterioles in a dose dependent manner. The mean times were 155 seconds (sec) in the control, 113sec in the 0.1mg/kg group, and 71sec in the 1.0mg/kg group. Times until blood flow stoppage and platelet aggregate growth in the arterioles were not affected by lead exposure, varying from 259 to 303 and 129 to 187sec, respectively. Lead exposure did not affect platelet aggregation in pial venules. The authors conclude that lead exposure can increase the risk of cerebrovascular thrombosis.

1314
TITLE:
Neurobehavioural Effects

AUTHORS:
Axelson O

SOURCE:
Epidemiology of Work Related Diseases, C. McDonald, Editor; BMJ Publishing Group, London, pages 165-184, 99 references, 1995

ABSTRACT:

Epidemiological investigations concerning neurobehavioral effects of exposure were summarized in this chapter. Case studies were reviewed, which indicated that such symptoms as poor memory, fatigue, irritability, dizziness, and headache resulted in cases of solvent exposure. Studies were discussed, which revealed that neurobehavioral function was disturbed after occupational exposure to a variety of solvents, including carbon-disulfide (75150), toluene (108883), and xylene (1330207). The debilitating effects of lead (7439921), mercury (7439976), and organophosphate exposure on neurobehavioral parameters were also addressed. Electroencephalography was mentioned as a means of measuring the effects of solvent exposure. A discussion of the epidemiological studies regarding chronic psychoorganic syndromes was also presented. Case/control and cohort studies were reviewed which indicated an increased risk of neuropsychiatric disorders related to solvent exposure. Alcohol abuse was determined in several studies to compound the effects of solvent exposure. Workers such as painters, carpet layers, varnishers, and petroleum workers were found to have a higher risk of developing neuropsychiatric disorders than other workers. No association between Alzheimer's dementia and solvent or lead exposure was determined. Several studies were reviewed which suggested a connection between multiple sclerosis and solvent exposure. While no evidence of a relationship between Parkinson's disease and solvent exposure was found, exposures to manganese (7439965), iron (7439896), aluminum (7429905) and herbicides were related to the disease in several studies. Although some studies indicated an association between either solvent or lead exposure with amyotrophic lateral sclerosis, many inconsistencies among these studies were also discovered. The author concludes that while the existing experimental data supports the epidemiological research, more investigations into the effects of solvent exposure are needed to elucidate the mechanisms and causes of neurobehavioral disorders.

1315

TITLE:

EQUIVALENT BRAIN CONCENTRATIONS OF METHYL MERCURY IN RAT PUPS EXPOSED AT DIFFERENT TIMES DURING GESTATION

AUTHORS:

HUGHES JA
SPARBER SB

SOURCE:

PHARMACOLOGIST; 18 (2). 1976 124

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. ABSTRACT TOXICITY

1316
TITLE:
Clinical picture and treatment of organomercurial pesticide poisoning in children.

AUTHORS:
Ramanauskayte MB
Baublis PP

SOURCE:
Pediatriya Moscow35 (2): 56-60; 1973

ABSTRACT:
PESTAB. (25 references) (Russian) jThe clinical picture and the treatment of acute and chronic poisoning by organomercurial pesticides like granosan in children are described on the basis of a comprehensive clinical material. The acute poisonings were due mostly to handling of granosan or the ingestion of granosan-treated seeds. Intrauterine poisoning in infants was observed. While children on the whole are more susceptible to mercury than adults, the clinical picture of the poisoning was a function of age. Serious functional disorders of the central nervous system, hydrocephalus, cerebral paralysis, and spasms were observed in infants. Toxic encephalomyeloradiculoneuritis with prevalence of the syndromes of lesions of the cerebral cortex, brain stem, cerebellum, myelitis, peripheral neurites, lesions of the motor centers, of the pyramidal tracts, and encephalitis with irregular alpha-rhythm were observed in older children. Epilepsy lasting up to 2 years was observed in 10% of all cases. Prevalence of vegetoneurotic syndromes, tachycardia, bradycardia, arrhythmia, acrocyanosis, lability of the arterial pressure, and reduction of the blood cholinesterase activity were found in older children with chronic poisoning. The lesions of the liver, kidney, heart and gastrointestinal tract were much less pronounced than those of the central nervous system. Sodium thiosulfate, glutamic acid, vitamin B and C complex, glucose, and diuresis are essential for detoxication. s,

1317
TITLE:
THE INDUCTION OF HEME OXIDATION IN VARIOUS TISSUES BY TRACE METALS EVIDENCE FOR THE CATABOLISM OF ENDOGENOUS HEME BY HEPATIC HEME OXYGENASE

AUTHORS:
MAINES MD
KAPPAS A

SOURCE:
ANN CLIN RES SUPPL; 8 (17). 1976 39-46

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. RAT LIVER HEART RENAL CORTEX RENAL MEDULLA LUNGS SPLEEN BRAIN INTESTINAL MUCOSA DELTA AMINO LEVULINIC-ACID SYNTHETASE CHROMIUM IRON NICKEL COPPER ZINC CADMIUM LEAD MERCURY

1318

TITLE:

Metallothionein Content Increased in the Liver of Mice Exposed to Magnetic Fields

AUTHORS:

Satoh M
Tsuji Y
Watanabe Y
Okonogi H
Suzuki Y
Nakagawa M
Shimizu H

SOURCE:

Archives of Toxicology, Vol. 70, No. 5, pages 315-318, 32 references, 1996

ABSTRACT:

The metallothionein (MT) content of tissues of mice exposed to static magnetic fields (SMF) and the induction by SMF of MT in the liver of mice given carbon-tetrachloride (CCl4) were investigated. Groups of BALB/c-mice were exposed to SMF of 3 or 4.7 tesla (T) for 1, 3, 6, 24 or 48 hours (hr). One additional group was immediately exposed to 4.7T SMF for 24hr after subcutaneous injection of 0.5 milliliters/kilogram CCl4 or olive-oil. The MT content of tissues was determined using a mercury binding assay. The liver MT content was significantly increased after exposure to 4.7T SMF for 6, 24 or 48hr, but not for 1 or 3hr. The maximum was reached at 24hr, when MT increased three fold. The MT content of kidney and brain was not affected by 4.7T SMF. Exposure to 3T SMF had no effect at any time. The MT content of liver in mice treated with 4.7T SMF and CCl4 was significantly elevated at 24hr compared with SMF alone. The authors conclude that MT levels in liver may be increased by exposure to strong magnetic fields generated during magnetic resonance imaging or nuclear magnetic resonance, and that exposure to an inducing agent like CCl4 can strengthen the effect.

1319

TITLE:

Lead And Other Neurotoxins As Risk Factors For Amyotroph

AUTHORS:

KAMEL F

SOURCE:
Crisp Data Base National Institutes of Health

ABSTRACT:
Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease affecting the motor neurons of the spinal cord and brain. Degeneration of spinal motor neurons leads to muscular atrophy and weakness, while degeneration of motor neurons in the cerebral cortex leads to hyperreflexia. ALS is rapidly progressive; patients generally die within two to five years of onset. The annual incidence rate of ALS is one to two per 100,000. This rate increases with age and is greater in men than in women. Approximately 5 to 10% of ALS cases have a family history of ALS. In general, the etiology of ALS remains unclear, although genetic factors are involved in the familial form. Environmental exposures have also been considered as potential causes of ALS. Existing evidence has most clearly suggested a role for exposure to heavy metals, particularly lead, although electromagnetic fields and chemical exposures including pesticides and solvents have also been implicated. We conducted a case-control study of ALS in New England from 1993 to 1996. The primary purpose of the study was to evaluate the relationship of lead exposure to ALS. We collected information on occupational, residential, and recreational exposure to lead using a structured interview. In addition, we measured blood and bone lead levels, the latter via in vivo K x-ray fluorescence (K-XRF). To our knowledge, no previous studies have reported bone lead levels in ALS cases measured with this technique. We evaluated the relation of lead exposure to ALS, using both biological measures and interviews, in a case-control study. Cases (N=109) were recruited at two hospitals in Boston, MA. Population controls (N=256) identified by random digit dialing were frequency-matched to cases by age, sex, and region of residence within New England. Risk of ALS was associated with a two-fold increase in self-reported occupational exposure to lead, with a dose-response for lifetime days of lead exposure. Risk of ALS was also associated with elevations in both blood and bone lead levels. These results are consistent with previous reports and suggest a potential role for lead exposure in the etiology of ALS. We also evaluated the relationship of ALS to genetic susceptibility to lead. The ALAD2 allele was associated with decreased lead levels in both patella and tibia, although not with blood lead levels, and with a two-fold increased risk of ALS. In contrast, the vitamin D receptor B allele was not associated with lead levels or ALS.

1320
TITLE:
Influence of selenium on toxicity and metabolism of methylmercury in chicks and quail.

AUTHORS:
SELL JL
HORANI FG

SOURCE:
NUTR REP INT; 14 (4). 1976 439-447

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Experiments were conducted to determine the effects of dietary Se (Se as sodium selenite) on the toxicity of Hg (Hg as methylmercuric chloride) for chicks and Japanese quail. Mortality occurred only among chicks and quail fed 20 ppm Hg. The incidence and severity of signs of Hg toxicity (tremors, loss of balance, etc.) were higher in quail than in chicks. Signs of Hg toxicity and mortality did not occur in chicks or quail when 8 ppm Se was included in the Hg-containing diets. Hg depressed weight gains of chicks significantly, and Se markedly enhanced this effect of Hg. Neither Hg nor Se, alone or in combination, affected gain by quail. Se decreased the proportion of ingested Hg deposited in livers of chicks by nearly 50% as compared with chicks fed Hg but no Se. In contrast, nearly twice as much Hg was present in livers of quail fed Hg and Se than in those of quail fed Hg only. Se also decreased the concentration of Hg in breast muscle of chicks but did not change the Hg levels in muscle of quail or in brains of either species. The weight gain, liver Hg and muscle Hg data indicate that Se modifies the toxicity and metabolism of Hg differently in chicks than in quail.

1321
TITLE:
THE EFFECTS OF HEREDITY AND ENVIRONMENT ON COPPER METABOLISM

AUTHORS:
SCHEINBERG IH

SOURCE:
MED. CLIN. N. AM. 1976, 60(4) 705-711

ABSTRACT: EIS: Epidemiology Information System

1322
TITLE:
Intellectual Impairment in Children Exposed to Polychlorinated Biphenyls In Utero

AUTHORS:
Jacobson JL
Jacobson SW

SOURCE:
New England Journal of Medicine, Vol. 335, No. 11, pages 783-789, 34 references, 1996

ABSTRACT:

A study was conducted examining the effects of in-utero exposure to polychlorinated-biphenyls (PCBs) on intellectual function in school age children. A Wechsler Intelligence Scales for Children Intelligence Quotient (IQ) test was administered to 212 children (mean age 11.0 years) as part of an ongoing study of the effects of in-utero PCB exposure. These children had been born to mothers who had eaten PCB contaminated fish while pregnant. Significantly lower full scale and verbal IQ scores were seen in children who had prenatal exposure to PCBs. This effect was seen primarily in those born to mothers who had had at least 1.25 micrograms/gram PCB in maternal milk. Children in the highest exposure group had IQ scores that averaged 6.2 points lower than those in other dose groups. A relationship between PCB exposure and IQ scores was supported in regression analyses. Lead (7439921) and mercury (7439976) exposure were also significantly associated with poor test performance. No relationship was seen between poor performance and breast feeding. The authors conclude that in-utero exposure to PCBs has long lasting effects on intellectual function.

1323

TITLE:

THE INFLUENCE OF AGE ON HEAVY METAL CONCENTRATIONS IN HUMAN TISSUE

AUTHORS:

WEIGERT P
FISCHER H

SOURCE:

NAUNYN-SCHMIEDEBERGS ARCH. PHARMACOL. (N.D.), 302(SUPPL.) 416

ABSTRACT: EIS: Epidemiology Information System

1324

TITLE:

Effect of heavy metals on dopamine, noradrenaline and serotonin uptake and release in rat brain synaptosomes.

AUTHORS:

KOMULAINEN H
TUOMISTO J

SOURCE:

ACTA PHARMACOL TOXICOL; 48 (3). 1981. 199-204.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. Effects of some heavy metals on the initial high affinity uptake and spontaneous release of triated dopamine (3H-DA), noradrenaline (norepinephrine) (3H-NA) and 5-hydroxytryptamine (3H-5-HT)

were studied in vitro in rat striatal, cortical and hypothalamic synaptosomes, respectively. As uptake inhibitors, metals were inactive in these conditions. At 10 muM Cu2+ was most potent, inhibiting 3H-DA and 3H-5-HT uptake nearly completely while inhibition of 3H-NA uptake varied. 3H-DA uptake was inhibited slightly by Zn2+, sometimes by Sn2+ but never by Co2+, Hg2+ or Mn2+. Pb2+ and Cd2+ increased synaptosomal 3H-DA uptake. 3H-5-HT uptake was affected least while that of 3H-NA showed some diversity, Zn2+ Pb2+ and Sn2+ induced inhibition of 3H-NA uptake by direct interference with 3H-NA. As to the spontaneous release of tritiated amines during short incubation from preloaded synaptosomes. Cd2+ decreased that of 3H-DA at high concentrations but Hg2+, Pb2+, Sn2+ and Zn2+ were ineffective. In vitro, uptake and relase of 3H-DA were more affected than those of other amines. The inhibitory mechanisms of monoamine uptake may include direct effects on synaptosomes and indirect ones by interference with amines themselves.

1325
TITLE:
INCREASED RATE OF FAST AXONAL TRANSPORT IN METHYL MERCURY INDUCED NEUROPATHY

AUTHORS:
WAKABAYASHI M
ARAKI K
TAKAHASHI Y

SOURCE:
BRAIN RES; 117 (3). 1976 524-528

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RAT MYELIN PROTEIN

1326
TITLE:
Target Sites for Anticholinesterases on the Ventral Surface of the Medulla Oblongata: Hypotension Elicited by Organophosphorus Agents,

AUTHORS:
Edery H
Geyer MA
Taylor P
Berman HA

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 10, 1987

ABSTRACT:
TD3: Sensitivity of the ventral surface of the medulla oblongata to

organophorus agents, oxime reactivators, and muscarinic antagonists was examined in order to delineate sites of cholinergic activity in the central nervous system. The exposed ventral surface of the medulla oblongata in anaesthetized cats was treated with the organophosphorus anticholinesterase agents soman and (7-nitro-2-oxa-1,3-diazole) aminopentyl methylphosphonofluoridate (NBD-AP-MFP), a fluorescent active centre-selective probe of acetylcholinesterase. Topical application of soman (1-5 micrograms or NBD-AP-MPF (5-120 micrograms elicited a profound (80-90 mm mercury, long-lasting (0.5-3 h), dose-dependent vasodepression with only minor changes in heart rate and respiration. The vasodepression was rapidly reversed (7 -10 min) upon topical application of muscarinic antagonists (atropine methylnitrate, atropine sulphate) and the bisquaternary oxime HI-6; systemic administration was without effect. Reversal of the hypotension by 1,1'

1327
TITLE:
EFFECT OF MERCURY AND MERSALYL ON TRANSMITTER RELEASE AT THE FROG NEURO MUSCULAR JUNCTION

AUTHORS:
BINAH O
MEIRI U
RAHAMIMOFF R

SOURCE:
ISR J MED SCI; 12 (10). 1976 (RECD 1977) 1219

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT BRAIN MITOCHONDRIA CALCIUM UPTAKE NEUROLOGICAL DISORDERS

1328
TITLE:
Intraorgan Distribution of Chemical Contaminants in Tissues of Harbor Porpoises 'Phocoena phocoena' from the Northwest Atlantic.

AUTHORS:
Stein JE
Tilbury KL
Brown DW
Wigren CA
Meador JP

SOURCE:
Govt Reports Announcements & Index (GRA&I), Issue 10, 1993

ABSTRACT:

TD3: The possible heterogeneous partitioning of chemical contaminants within tissues of marine mammals is a factor affecting whether a tissue sample is representative of the entire organ. The potential partitioning is of particular concern in marine mammals where the analytical sample is quite often a very small proportion of the whole organ. Accordingly, blubber and liver samples were taken from different anatomical locations in these organs of three apparently healthy harbor porpoises (Phocoena phocoena) caught in a gill-net fishery in the northwest Atlantic. Concentrations of chlorinated hydrocarbons (CHs), such as polychlorinated biphenyls (PCBs), DDTs, and chlordanes, were measured in the blubber (n = 7) and liver (n = 5) samples, and selected toxic elements (e.g., mercury, lead, cadmium) were also measured in the liver. Additionally, individual samples were taken from brain, lung, kidney, and gonad to assess the disposition of toxic chemicals within harbor porpoise. Technical memo. See also P

1329
TITLE:
GLUTATHIONE PEROXIDASE RESPONSE IN TISSUES OF RATS FED DIETS CONTAINING FISH PROTEIN CONCENTRATE PREPARED FROM SHARK GALEORHINUS-AUSTRALIS FLESH OF KNOWN MERCURY AND SELENIUM CONTENTS

AUTHORS:
THROWER SJ
ANDREWARTHA KA

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 26 (1). 1981. 77-84.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN ANTIDOTE METABOLIC-DRUG FOOD TOXICITY LIVER BRAIN KIDNEY ERYTHROCYTE

1330
TITLE:
Mercury levels in a 21-year-old black-crowned night heron (Nycticorax nycticorax).

AUTHORS:
HOFFMAN RD

SOURCE:
OHIO J SCI; 76 (1). 1976 18

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. A 21 yr old black-crowned night heron was collected on West Sister Island, Ohio, USA. This female had been banded as a nestling near South Bass Island, Ohio, on June 6, 1952. Organisms in the

stomach included 2 perch (Perca flavescens) and 1 fresh-water drum (Aplodinotus grunniens). Total Hg concentrations in breast muscle (0.9 ppm), liver (3.1 ppm), brain (0.5 ppm) and primary wing feathers (17.9 ppm) were measured on a wet weight basis, in duplicate, using flameless atomic absorption spectrophotometry. Differences in Hg levels between the 21 yr old bird and other black-crowned night herons from the same heronry imply that the 21 yr old bird may have been feeding in an area of lower Hg contamination or that the maximum retainable Hg in black-crowned night herons is specific to an individual.

1331
TITLE:
Morphological investigations in experimental cases of mercuric poisoning in sheep.

AUTHORS:
STOEV S
LAZAROVA S

SOURCE:
VETERINARSKI ARHIV; 68 (5). 1998. 163-171.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. An experiment was carried out to reproduce chronic mercury poisoning in sheep by treating (per os) with sub-lethal doses of 1% mercuric chloride solution. Pathoanatomical and pathomorphological changes in various internal organs were studied in dynamics by using biopsy materials, as well by slaughtering of sheep during the experiment. Macroscopically, livers (extravasations) were established in the region of head, breast and abdomen: suppurative efflux from the nose; erosive stomatitis; shearing of wool; venous congestion in internal organs; necroses, oedema, haemorrhagic and diphtheroid inflammation in rennet, small intestine and colon; yellow-clayey colour of liver; hyperaemia and haemorrhages in kidneys; hyperaemia and oedema in brain envelope and lungs. Histological examination revealed granular or hyaline degeneration in the epithelium of convoluted tubules in cortex in early stages, and thickened basement tubular membranes, as well slight proliferation of connecti

1332
TITLE:
EVIDENCE FOR ESSENTIAL SULFHYDRYL GROUPS IN MUSCARINIC RECEPTOR BINDING SITE REGENERATION OF A FUNCTIONALLY ACTIVE RAT BRAIN MUSCARINIC RECEPTOR AFTER INHIBITION WITH METHYL MERCURY AND MERCURIC CHLORIDE BY D PENICILLAMINE

AUTHORS:
ABDELFATTAH A-S A

SHAMOO AE

SOURCE:
72ND ANNUAL MEETING OF THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, ST. LOUIS, MO., USA, MAY 31-JUNE 4, 1981. FED PROC; 40 (6). 1981. 1707.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT RAT ANTIDOTE METABOLIC-DRUG AUTONOMIC-DRUG NEURO TOXICITY IN-VITRO

1333
TITLE:
EFFECTS OF SUBLETHAL CONCENTRATIONS OF MERCURY IN A TELEOST PUNTIUS-CONCHONIUS BIOCHEMICAL AND HEMATOLOGICAL RESPONSES

AUTHORS:
GILL TS
PANT JC

SOURCE:
INDIAN J EXP BIOL; 19 (6). 1981. 571-573.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. NOTE MYO CARDIUM LIVER BRAIN AGE HYPER GLYCEMIA ERYTHROPENIA HEMO GLOBIN POLYCYTHEMIA

1334
TITLE:
Analysis of permeability of the placenta to inorganic mercury and its accumulation in maternal and fetal tissues in the rat.

AUTHORS:
MARSZALEK K
DABROWSKI Z
MISZTA H

SOURCE:
ACTA BIOL CRACOV SER ZOOL; 23 (0). 1981. 159-166.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Passage of inorganic Hg across the rat placenta was studied in various stages of pregnancy by the administration of 203HgCl2 in a single dose in the course of preimplantation, implantation, at the onset of placental function and after organogenesis. Hg accumulation was determined on the 20th day of pregnancy in maternal and fetal tissue samples from 10 selected organs: heart, liver, lungs, ureter, spleen, smooth muscle, urinary bladder, kidneys, skeletal muscle and brain. A lower radioactivity was observed in the organs of fetuses

whose mothers were injected with 203HgCl2 on days 8 and 12 of pregnancy, indicating that the placenta provides a certain degree of protection.

1335
TITLE:
BATS AND ENVIRONMENTAL CONTAMINANTS A REVIEW

AUTHORS:
CLARKE D R JR

SOURCE:
U S FISH WILDL SERV SPEC SCI REP-WILDL; 0 (235). 1981. 1-27.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. BIRD MAMMAL CARBAMATE INSECTICIDE DDT DIELDRIN POLY CHLORINATED BI PHENYL MERCURY LEAD BRAIN FAT MORTALITY

1336
TITLE:
INHIBITION OF BRAIN CELL RNA SYNTHESIS BY METHYL MERCURY

AUTHORS:
SARAFIAN T
DELLA-SANTINA C
VERITY MA

SOURCE:
69TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ANAHEIM, CALIF., USA, APR. 21-26, 1985. FED PROC; 44 (3). 1985. 743.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT RAT URIDINE PHOSPHORYLATION

1337
TITLE:
EXPERIMENTAL METHYL MERCURY NEUROTOXICITY LOCUS OF MERCURIAL INHIBITION OF BRAIN PROTEIN SYNTHESIS IN-VIVO AND IN-VITRO

AUTHORS:
CHEUNG MK
VERITY MA

SOURCE:
J NEUROCHEM; 44 (6). 1985. 1799-1808.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT TRANSFER RNA POLYURIDYLIC-ACID

PHENYLALANINE RNA RIBOSOMES RADIOLABEL

1338
TITLE:
CHANGES IN FATTY-ACID ELONGATION IN DEVELOPING MOUSE BRAIN BY MERCURY COMPARISON WITH OTHER METALS

AUTHORS:
BOURRE J-M
DUMONT O

SOURCE:
TOXICOL LETT (AMST); 25 (1). 1985. 19-24.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BEHENYL COENZYME A MALONYL COENZYME A MYELIN METAL TOXICITY COPPER

1339
TITLE:
ABNORMALITIES IN GANGLIOSIDES AND OTHER LIPIDS OF MONKEY RABBIT AND HUMAN BRAINS WITH CHRONIC ORGANIC MERCURY INTOXICATION

AUTHORS:
ANDO S
TOYODA Y
NAGAI Y
IKUTA F

SOURCE:
JPN J EXP MED; 55 (1). 1985. 1-6.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ASTROCYTE GRAY MATTER TISSUE PHOSPHATIDYLETHANOLAMINE PHOSPHATIDYLCHOLINE SPHINGOMYELIN

1340
TITLE:
DIFFERENTIAL EFFECTS OF MONOVALENT DIVALENT AND TRIVALENT METAL IONS ON RAT BRAIN HEXOKINASE EC-2.7.1.1

AUTHORS:
LAI J CK
BAKER A
CARLSON K C JR
BLASS JP

SOURCE:

COMP BIOCHEM PHYSIOL C COMP PHARMACOL TOXICOL; 80 (2). 1985. 291-294.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM CHROMIUM COPPER CALCIUM STRONTIUM BARIUM ZINC CADMIUM MERCURY LEAD MANGANESE IRON COBALT NICKEL ALUMINUM NEUROTOXICITY POLLUTION

1341
TITLE:
CONCENTRATION OF METALLOTHIONEIN IN MAJOR ORGANS OF RATS AFTER ADMINISTRATION OF VARIOUS METALS

AUTHORS:
WAALKES MP
KLAASSEN CD

SOURCE:
FUNDAM APPL TOXICOL; 5 (3). 1985. 473-477.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN HEART INTESTINE KIDNEY LIVER LUNG PANCREAS SPLEEN STOMACH TESTIS ZINC NICKEL CADMIUM CHROMIUM IRON LEAD MANGANESE MERCURY

1342
TITLE:
EFFECTS OF CADMIUM MERCURY AND VANADATE ON THE GLUTATHIONE-CONJUGATING ENZYMES IN LIVER KIDNEY LUNG AND BRAIN OF MICE

AUTHORS:
SCHENKE M

SOURCE:
26TH SPRING MEETING OF THE DEUTSCHE PHARMAKOLOGISCHE GESELLSCHAFT (GERMAN
PHARMACOLOGICAL SOCIETY), MAINZ, WEST GERMANY, MAR. 12-15, 1985.
NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL; 329 (SUPPL.). 1985. R33.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT

1343
TITLE:
EFFECTS OF METHYL MERCURY ON THE ACTIVITIES OF SULFHYDRYL CONTAINING ENZYMES IN RAT BRAIN

AUTHORS:
TSUZUKI Y

SOURCE:
JPN J IND HEALTH; 23 (5). 1981. 548-549.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. SUCCINIC DEHYDROGENASE MONO AMINE OXIDASE KINETICS NEURO TOXICITY

1344
TITLE:
Experimental Papilledema: A Study of Cats and Monkeys Intoxicated with Triethyl Tin Acetate

AUTHORS:
Hedges TR
Zaren HA

SOURCE:
Neurology, Vol. 19, pages 359-366, 17 references, 19691969

ABSTRACT:
The pathogenesis of papilledema was investigated in cats and rhesus-monkeys intoxicated with triethyl-tin (997502) (TET). Animals received intraperitoneal injections of 0.1 milligrams per kilogram (mg/kg) TET daily. Animals were observed for neurological deficit and optic nerve abnormalities. A screw cap device was implanted to permit daily monitoring of intracranial pressure (ICP) in monkeys. An open end catheter was used through a burr hole in cats prior to sacrifice. After sacrifice, heads were frozen in liquid nitrogen and removed. Sections were prepared and examined. Neurological and pathological findings were well correlated. The first signs of neurological deficit were seen on day 4 of TET administration with ataxia, followed by weakness and progressing to complete flaccid paralysis. Loss of weight, diarrhea, and hypophagia occurred in cats and monkeys. Terminal ICP readings in cats ranged from a normal value of 3 millimeters of mercury (mm Hg) to 24mm Hg. In monkeys, a terminal ICP of 24mm Hg was recorded. Papilledema was seen in one monkey, but in none of the cats. The degree of pathological change was correlated with the amount of edema in the cerebellum. No ophthalmic evidence of papilledema was seen in cats. In monkeys, an increased degree of edema was seen close to the optic foramina. Edema was most severe in the chiasm. The authors conclude that TET intoxication is an effective means to produce swelling of the white matter of the brain extending into the optic nerve. There is a species difference in which papilledema can be produced in monkeys, but not in cats.

1345
TITLE:
(Late prognosis of accidental poisoning in childhood.)

AUTHORS:
Reddemann H JR
Amendt P JR
Jaehrig K JR

SOURCE:
Deut. Gesundheitsw.; 25(43): 2027-32 1970; (REF:46)

ABSTRACT:
HAPAB Of pediatric interest is the accidental poisoning in children from such agents as drugs, household poisons and insecticides. From 1965 to 1968, at the Universitaets-Kinderklinik in Greifswald (Greifswald University Pediatrics Clinic), 275 cases of poisoning in children were treated. Of this number, 9.1% of the cases were caused by the children ingesting insecticides, such as DDT, mercury and Wofatox (an organophosphate). The symptomatology of the children included autonomic and central nervous (CNS) systems disturbances, headaches and behavioral disturbances. The clinical research conducted on them comprised studies on bilirubin, lipids, serum electrolytes and other hematological tests, in addition to electrocardiogram and electroencephalogram tracings. Calorimetry and paper electrophoresis methods were also employed. Particular attention was devoted to disturbances of the CNS, liver and kidneys. In a study of serious poisoning from insecticides, three children ranging in age from 17 months to 3 years ingested |Mux| (a DDT preparation, an antiant compound and Wofatox. These cases presented neurological involvement. Five insecticide-poisoned children had normal liver and kidney function tests. In one case, the electroencephalogram showed brain tracings similar to meningoencephalitis. The results of the present research suggest that the late prognosis after an acute poisoning is favorable, in general. Serious injuries may be expected in cases of poisoning by such agents as benzene, dichloroethane and carbon monoxide if the diagnosis is delayed. 1970

1346
TITLE:
Poultry poisoning with Granosan.

AUTHORS:
Tishkov AI
Saley P
Vitkalov VP

SOURCE:
Veterinariya; 45:(4) 58; 1968

ABSTRACT:
HAPAB Heavy losses occurred in a poultry-yard due to feed treated with

Granosan. The clinical symptoms observed in chickens on the last day before death were depression, spasm, paralysis of the limbs, swollen heads, and body temperatures of 40.3-41 sMath,eC. Serous edema in the neck region and extremities were found upon autopsy. Mucous edema and hemorrhagic inflamation of the intestine as well as mercury residues in kidneys, livers, to a lesser extent in muscles, skin, brains, lungs, hearts, ovaries, and eggs were ascertained. Depending on the duration and intensity of the exposure, mercuric residues could be detected in tissues as long as 120 days after poisoning. 1968

1347
TITLE:
Animal models for assessing developmental toxicity.

AUTHORS:
Kimmel CA
Kavlock RJ
Francis EZ

SOURCE:
NTIS Technical Report (NTIS/PB91-219154) 1991;:53 pp.

ABSTRACT:
Developmental effects may result from toxic agent exposure of parental gametes prior to conception, during the prenatal period or postnatally up to the time of sexual maturation. These effects are not predictable from the assessment of adult exposures to the same agent. A number of animal models have been used to evaluate the developmental effects of exposure to toxicants, and several of these are exemplified by the standard protocols used by regulatory agencies. Others have been developed to evaluate the effects of toxicants on particular target organs or organ systems. Animal models and principles for the interpretation of data from studies involving prenatal exposure are much further advanced than those involving postnatal exposure. In those experimental animal studies that assess the effects of prenatal exposure, the developing organism is exposed secondarily via the maternal organism which intervenes in the absorption, metabolism and distribution to the embryo/fetal compartment. In postnatal exposure studies, exposure of the developing offspring also may be indirect via maternal milk or direct by dosing of pups. In addition, exposure may occur unintentionally via contaminants on maternal fur or skin, in excretory products following exposure, and/or by access to dosed food or drinking water before weaning. A number of factors may influence the response of pups to toxicant exposure either prenatally or postnatally, e.g., the influence of litter, litter size, handling of pups, maternal care and maternal/infant separation during exposure. Studies designed to compare the sensitivity of developing animals and adults must consider the above factors along with those that more directly influence sensitivity, e.g., metabolic capability, growth and repair processes,

functional maturity, or genetic differences in susceptibility. To illustrate the complexity of postnatal studies, examples derived from developmental neurotoxicity and renal developmental toxicity are presented. In these examples, it can be seen clearly that each organ or functional system has its own unique ontogenetic maturation sequence and the pattern of organ maturation varies across species. Thus, there can be no single laboratory animal model that is most appropriate for predicting the effects of toxicants in the developing human. It is possible, however, to utilize existing data on comparative developmental morphology and physiology to study effects of toxic agents in laboratory animal models for use in human risk assessment, and target organ toxicity in the developing organism should be evaluated in light of these patterns.

1348
TITLE:
Distribution of heavy metals and their age-related changes in the eastern great white egret, Egretta alba modesta, in Korea.

AUTHORS:
HONDA K
MIN BY
TATSUKAWA R

SOURCE:
ARCH ENVIRON CONTAM TOXICOL; 15 (2). 1986. 185-198.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Organ and tissue distribution of eight metals (Fe, Mn, Zn, Cu, Pb, Ni, Cd, Hg) and their age-related changes were investigated in the chick and adult eastern great white egret, Egretta alba modesta, collected in Korea. High concentrations of the metals were found in the liver, kidney, feathers, bone, and skin; low values were found in the muscle and brain. A majority of the metal burdens in the chick and adult egrets existed in the muscle, bone, and feathers; about 50% of the Hg was in the feathers. The concentrations of Fe, Mn, Zn, and Cu in organs and tissues of the chicks characteristically changed with age, and their accumulations depended upon the metabolic turnover. In contrast, the concentrations of Pb, Ni, Cd, and Hg increased with age, suggesting that age or exposure time is a dominant factor. However, the younger stage of the downy chicks showed a rapid accumulation plateau of Pb, Ni, Cd, and Hg, and a dilution effect of these metal concentrations by increased

1349
TITLE:
INTERACTIONS OF METHYL MERCURY WITH MICRO TUBULES

AUTHORS:

SAGER PR
DOHERTY RA
OLMSTED JB

SOURCE:
21ST ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, ANAHEIM, CALIF., USA, NOV. 9-13, 1981. J CELL BIOL; 91 (2 PART 2). 1981. 330A.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT HUMAN FIBROBLAST PORCINE BRAIN

1350
TITLE:
INFLUENCE OF MERCURY ON UPTAKE OF TRITIATED DOPAMINE AND TRITIATED NOREPINEPHRINE BY RAT BRAIN SYNAPTOSOMES

AUTHORS:
RAJANNA B
HOBSON M

SOURCE:
TOXICOL LETT (AMST); 27 (1-3). 1985. 7-14.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM SODIUM POTASSIUM ATPASE ENVIRONMENTAL CONTAMINANT HEAVY METAL POLLUTION

1351
TITLE:
EFFECT OF CALCIUM DEFICIENCY ON HISTOPATHOLOGICAL ALTERATIONS AND METALS CUMULATION IN RATS BRAIN FOLLOWING THE COMBINED INTOXICATION WITH LEAD CADMIUM AND MERCURY

AUTHORS:
MADEJ JA
ZECHALKO A
SZYMCZAK J
BIERNAT J

SOURCE:
BROMATOL CHEM TOKSYKOL; 18 (3). 1985. 173-180.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HISTOPATHOLOGY

1352
TITLE:
EFFECT OF INTERACTION OF MANGANESE WITH CADMIUM MERCURY AND ZINC ON

TYROSINE DOPAMINE AND NOREPINEPHRINE LEVELS OF RAT BRAIN

AUTHORS:
SHUKLA GS
CHANDRA SV

SOURCE:
ANNUAL MEETING AND 2ND CONGRESS OF THE FEDERATION OF ASIAN AND OCEANIAN BIOCHEMISTS, BANGALORE, INDIA, DEC. 14-18, 1980. INDIAN J BIOCHEM BIOPHYS; 18 (4). 1981. 136.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT ANTIDOTE METABOLIC-DRUG NEURO TOXIN ENVIRONMENTAL POLLUTION SYNERGISM ANTAGONISM

1353
TITLE:
Effects Of Metal Pollutants Upon Embryonic Development

AUTHORS:
Ferm VH

SOURCE:
Reviews on Environmental Health, Vol. 1, No. 3, pages 238-259, 96 references, 19741974

ABSTRACT:
Heavy metals and other elements shown to have an effect on embryonic development are reviewed. Two types of studies are considered: accidental exposure to abnormal concentrations of metals from industrial processes, and controlled laboratory exposure. Research on the effects of lead (7439921) shows retarded embryonic development in fish, chicks, frogs, and salamanders. Teratogenic effects are also noted in chicks, with particular changes seen in the nervous system. Lead is also teratogenic in hamsters, rats, and mice. Studies of cadmium (7440439) show fetal toxicity, teratogenic effects in hamsters, and neoplastic effects on mesenchymal tissues in rats. Zinc (7440666) and cadmium appear to have antagonistic effects in reproductive studies. Results of studies of mercury (7439976) on reproduction show toxicity and developmental malformations in chicks, fish, hamsters, and mice. Studies showing arsenic (7440382) to be teratogenic in the chick and the hamster are discussed. Fetal death and chromosomal abnormalities have been demonstrated in humans following chronic arsenic poisoning; however, organic arsenicals have been utilized in great amounts during pregnancy for syphilis without adverse effects. Teratogenic effects of selenium (7782492), lithium (7439932), and tellurium (13494809) are considered. Teratogenic effects of dietary deficiencies of cobalt (7440484), manganese (7439965), copper (7440508), and molybdenum (7439987) are noted. Cases of

synergistic teratogenic effects and protection offered by one metal against another are discussed. The author concludes that the significance of metals in the structure and function of essential enzyme systems must be investigated to understand their role in embryonic development.

1354
TITLE:
TRITIATED DOPAMINE UPTAKE AND TRITIATED HALOPERIDOL BINDING IN STRIATUM AFTER ADMINISTRATION OF METHYL MERCURY TO RATS

AUTHORS:
KOMULAINEN H
TUOMISTO J

SOURCE:
ARCH TOXICOL; 57 (4). 1985. 268-271.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN DISORDER BENZODIAZEPINE RECEPTOR DOPAMINE RECEPTOR SEROTONIN

1355
TITLE:
RESIDUAL MERCURY CONCENTRATION IN BRAIN LIVER AND MUSCLE OF CONTAMINATED FISH COLLECTED FROM AN ESTUARY NEAR A CAUSTIC-CHLORINE INDUSTRY

AUTHORS:
SHAW BP
SAHU A
PANIGRAHI AK

SOURCE:
CURR SCI (BANGALORE); 54 (16). 1985. 810-812.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM WASTE DISPOSAL ENVIRONMENTAL QUALITY WATER POLLUTION

1356
TITLE:
In vivo removal of a few heavy metals in certain tissues of the fish, Notopterus notopterus.

AUTHORS:
VERMA SR
JAIN M
DALELA RC

SOURCE:
ENVIRON RES; 26 (2). 1981. 328-334.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. An evaluation was made of the comparative efficiency of 5 metal-binding agents (NTA (nitrilotriacetic acid), EDTA, DDTA (3,6-dioxaoctamethylenedinitrilotetraacetic acid), DTPA (diethylenetriaminepentaacetic acid) and DDC (sodium diethyldithiocarbamate) in vivo in mobilization of Cr, Ni and Hg from the liver, kidney, gills and brain of the freshwater fish N. notopterus. The maximum and significant ($P < 0.001$) mobilization of Cr by DTPA (54.68%) and EDTA (36.56%) was observed. In the cases of Ni and Hg, the significant ($P < 0.01$ and $P < 0.001$, respectively) mobilizations observed were 56.57% by DDC and 45.52% by EDTA. No definite correlation between the chemical structure or MW of the chelators and their ability to remove the metals from the biological systems was observed.

1357
TITLE:
APPLICATION OF INSTRUMENTAL NEUTRON ACTIVATION ANALYSIS TO THE STUDY OF TRACE METALS IN BRAIN AND METAL TOXICITY

AUTHORS:
LAI J CK
CHAN A WK
MINSKI MJ
LEUNG T KC
LIM L
DAVISON AN

SOURCE:
GABAY, S., J. HARRIS AND B. T. HO (ED.). NEUROLOGY AND NEUROBIOLOGY (NEW YORK), VOL. 15. METAL IONS IN NEUROLOGY AND PSYCHIATRY. XIII+409P. ALAN R. LISS, INC.: NEW YORK, N.Y., USA. ILLUS. ISBN 0-8451-2717-9.; 0 (0). 1985. 323-344.

ABSTRACT: BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN

1358
TITLE:
STUDIES ON THE INTERACTION BETWEEN SELENIUM OXIDE AND SULFUR COMPOUNDS AND
DISTRIBUTION OF RUBIDIUM ZINC COBALT IRON AND MERCURY IN MICE BY INSTRUMENTAL NEUTRON ACTIVATION ANALYSIS

AUTHORS:
CZAUDERNA M
ROCHALSKA M

SOURCE:
INT J APPL RADIAT ISOT; 37 (3). 1986. 211-216.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM LIVER KIDNEY SPLEEN BRAIN MINERAL TOXICITY GLUTATHIONE CYSTEINE CYSTEAMINE METHIONINE

1359
TITLE:
A KINETIC STUDY ON THE METABOLISM OF METHYL MERCURY

AUTHORS:
TAGAWA M
DOI R

SOURCE:
7TH MEETING ON ENVIRONMENTAL POLLUTANTS AND TOXICOLOGY, KOBE, HYOGO, JAPAN, NOV. 13-14, 1980. J PHARM DYN; 4 (5). 1981. S-72.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT HUMAN MOUSE RAT BRAIN ERYTHROCYTE HEMO GLOBIN STRAIN DIFFERENCE MINAMATA DISEASE

1360
TITLE:
A BRIEF HISTORY OF THE INFLUENCE OF TRACE ELEMENTS ON BRAIN FUNCTION

AUTHORS:
SANDSTEAD HH

SOURCE:
AM J CLIN NUTR; 43 (2). 1986. 293-298.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM REVIEW HUMAN LEAD MERCURY TOXICITY IODINE COBALT COPPER IRON MANGANESE ZINC VITAMIN B-12 IODINE DEFICIENCY THYROXINE NERVOUS SYSTEM DISORDER CRETINISM

1361
TITLE:
NEUROBEHAVIORAL SEQUELAE OF SUBCUTANEOUS INJECTION OF METALLIC MERCURY

AUTHORS:
ZILLMER EA
LUCCI K
BARTH JT
PEAKE TH

SOURCE:
FOURTEENTH ANNUAL INTERNATIONAL NEUROPSYCHOLOGICAL SOCIETY MEETING, DENVER, COLO., USA, FEB. 4-8, 1986. J CLIN EXP NEUROPSYCHOL; 7 (6). 1985. 648.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT HUMAN BRAIN INFILTRATION SUICIDE ATTEMPT

1362
TITLE:
UPTAKE OF ELEMENTAL MERCURY AFTER INHALATION

AUTHORS:
EIDE I
SYVERSEN T

SOURCE:
32ND SCANDINAVIAN PHARMACOLOGICAL SOCIETY MEETING, TRONDHEIM, NORWAY, JUNE 29-JULY 1, 1981. ACTA PHARMACOL TOXICOL; 49 (1). 1981. 91.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. ABSTRACT MOUSE RAT HAMSTER GUINEA-PIG BRAIN KIDNEY LIVER BLOOD CATALASE

1363
TITLE:
THE TOXICITY AND TERATOGENICITY OF MERCURIC MERCURY IN THE PREGNANT RAT

AUTHORS:
HOLT D
WEBB M

SOURCE:
ARCH TOXICOL; 58 (4). 1986. 243-248.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HEAVY METAL ENVIRONMENTAL TOXIN BRAIN KIDNEY DAMAGE HISTOPATHOLOGY GLOMERULAR FILTRATION

1364
TITLE:
EFFECT OF HEAVY METAL SALTS ON RAT BRAIN AND LIVER MONOAMINE OXIDASE ACTIVITY

AUTHORS:
KADIISKA M

STANCHEVA S
STOYTCHEV TS

SOURCE:
ACTA PHYSIOL PHARMACOL BULG; 11 (4). 1985 (RECD. 1986). 27-32.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM TYRAMINE 5 HYDROXYTRYPTAMINE BETA PHENETHYLAMINE

1365
TITLE:
VISUALIZATION OF SILVER AND MERCURY IN NERVOUS TISSUE

AUTHORS:
SCHRODER HD
RUNGBY J
THORLACIUS-USSING O
MOLLER-MADSEN B
DANSCHER G
NIELSEN ER
GREGERSEN M

SOURCE:
ANNUAL MEETING OF THE SCANDINAVIAN NEUROPATHOLOGICAL SOCIETY, AARHUS, DENMARK, MAY 17-19, 1985. ACTA NEUROL SCAND; 73 (1). 1986. 95.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT HUMAN BLOOD BRAIN BARRIER

1366
TITLE:
BRAIN TRACE ELEMENTS IN ALZHEIMER'S DISEASE

AUTHORS:
EHMANN WD
MARKESBERY WR
ALAUDDIN M
HOSSAIN T IM
BRUBAKER EH

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 7 (1). 1986. 197-206.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN TRACE ELEMENT TOXICITY BROMINE NITROGEN CHLORINE SODIUM CESIUM POTASSIUM MERCURY RUBIDIUM SEX DIFFERENCE INSTRUMENTAL NEUTRON ACTIVATION ANALYSIS

1367
TITLE:
The Accumulation And Excretion Of Heavy Metals In Organisms

AUTHORS:
Miettinen JK

SOURCE:
Ecological Toxicology Research; Environmental Science Research, Vol. 7, pages 215-229, 33 references, 19751975

ABSTRACT:
The accumulation and excretion of heavy metals are reviewed. Divalent cadmium (22537480) (Cd), divalent mercury (14302875) (Hg), methylmercury (22967926), and divalent lead (14280503) (Pb), their sources in the food chain, and the mode of ingestion and elimination are summarized. In humans, the critical organs for Cd are the kidney and liver. The human critical organ for Hg is the kidney. The critical organ for human exposure to methylmercury is the central nervous system. The critical organ in humans for Pb is the hematopoietic system and the central and peripheral nervous systems. Absorption and elimination of Cd in humans is discussed. The metabolism of Hg and methylmercury in humans is examined. The absorption and elimination of Pb in humans is described. Gastrointestinal absorption of Pb in humans is quite variable, between 1 and 16 percent, and is age dependent, being highest in the young. Pb passes into the brain more easily than Cd, although it does not accumulate there. Blood and urine Pb concentrations reflect exposure well. Blood concentrations are considered to be more reliable, since metabolic factors may affect renal handling of Pb.

1368
TITLE:
CHELATION IN METAL INTOXICATION XIX. ALPHA MERCAPTO-BETA-ARYL ACRYLIC-ACID AS ANTIDOTES TO NICKEL AND LEAD TOXICITY

AUTHORS:
SHARMA BL
KACHRU DN
SINGH S
TANDON SK

SOURCE:
J APPL TOXICOL; 6 (4). 1986. 253-258.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT ALPHA MERCAPTO-BETA-2-FURYLACRYLIC-ACID ALPHA MERCAPTO-BETA-3

4-DIMETHOXYPHENYLACRYLIC-ACID ANTIDOTE-DRUG METABOLIC-DRUG MERCURY URINE FECES BRAIN DELTA AMINOLEVULINIC-ACID DEHYDRATASE DELTA AMINOLEVULINIC-ACID PHARMACODYNAMICS

1369
TITLE:
ARSENIC CADMIUM MERCURY LEAD AND SELENIUM IN SLAUGHTERED ANIMALS A REVIEW OF A DECADE OF INVESTIGATION

AUTHORS:
VAESSEN H A MG
ELLEN G

SOURCE:
TIJDSCHR DIERGENEESKD; 111 (14). 1986. 671-676.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM PORCINE BOVINE KIDNEY LIVER BRAIN MEAT

1370
TITLE:
Mercury accumulation and its effect on fishes.

AUTHORS:
DOKHOLYAN VK
AKHMEDOV AM
AKHMEDOVA TP
SHLEIFER GS

SOURCE:
VOPR IKHTIOL; 21 (3). 1981. 537-547.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Hg accumulation and distribution in fish organs and tissues and its effect on survivability as well as physiological-biochemical indices of the blood and brain were studied in the sturgeon, Acipenser guldenstadti, the roach, Rutilus rutilus caspicus, the Caspian round goby, Neogobius melanostomus affinis, the kutum, R. frisii kutum and the keta, Oncorrhynchus keta. Natural immunity factors were also studied. Experiments were conducted using 150 l tanks (sturgeon, roach, round goby) and small aquariums (kutum, keta) at 20-22ê C and 1-30 day exposures using HgCl2 at 1-100 mug/l. Critical levels of Hg accumulation were determined for each species. The experiments demonstrated that metabolic processes were inhibited or altered and blood protective functions were weakened when Hg accumulation reached critical levels in the fish body.

1371

TITLE:
BIO TRANSFORMATION RATE OF ORGANIC MERCURY COMPOUNDS IN EXPERIMENTAL STUDIES ON ANIMALS

AUTHORS:
BEZEL' VS
ROZENBERG EE

SOURCE:
GIG TR PROF ZABOL; 0 (7). 1981. 49-51.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. NOTE RAT LUNG ADRENAL LIVER MUSCLE SPLEEN BONE BRAIN HEART METAL TOXICITY

1372
TITLE:
GENERATION AND DOSE AS MODIFYING FACTORS OF INORGANIC MERCURY ACCUMULATION
IN BRAIN LIVER AND KIDNEYS OF RATS FED METHYLMERCURY

AUTHORS:
YAMAMOTO R
SUZUKI T
SATOH H
KAWAI K

SOURCE:
ENVIRON RES; 41 (1). 1986. 309-318.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM TISSUE DISTRIBUTION

1373
TITLE:
Congenital Minamata disease accompanied by arachnoid cyst.

AUTHORS:
HIRA K
HARADA M
TAKEHARA S
KABASHIMA K
TATETSU S
FUJIOKA M
YASUTAKE H
OZAKI M

SOURCE:

BRAIN NERVE (TOKYO); 34 (3). 1982. 259-266.

ABSTRACT:

HEEP COPYRIGHT: BIOL ABS. A male infant was born on Dec. 8, 1956, during an outbreak of Minamata disease. His parents ate fish and shell-fish taken from Minimata Bay and suffered from light, incomplete Minimata disease, showing sensory disturbance, constriction of the visual field, muscular weakness, etc. In 1962 Minamata disease was diagnosed. The clinical symptoms included intelligence disturbance, character change, dysarthria, primitive reflexes, strabismus, hypersalivation, ataxia and hyperkinesia, indicating a typical congenital Minamata disease. Until 13 yr old or so, his mental and motor function developed gradually. EEG examination revealed a slow alpha activity on basic pattern and 6-Hz positive spikes in the sleep EEG. The constriction of the visual field was classified. When 15 yr old, he complained of severe heacache and showed irritability and emotional unstability as well as displeasure. His neurological symptoms deteriorated again. CT (computed tomography) disclosed extensive localized low density areas in the right frontal, temporal and parietal region and left frontal and temporal regions. A diagnosis of noncommunicating arachnoid cyst was made by metrimazide CT cisternography. Bilateral cystoperitoneal shunt were carried out. Neither clinical symptoms nor CT scanning findings showed any change despite some relief from the headache. The symptoms are probably due to the arachnoid cyst and the congenital malformations due to organic Hg poisoning during the intrauterine period.

1374

TITLE:

LOCALIZATION OF MERCURY IN CENTRAL NERVOUS SYSTEM OF THE RAT I. MERCURIC CHLORIDE PER OS

AUTHORS:

MOLLER-MADSEN B
DANSCHER G

SOURCE:

ENVIRON RES; 41 (1). 1986. 29-43.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM PURKINJE CELL GLIAL CELL EPENDYMAL CELL ANTERIOR HORN MOTONEURON CEREBELLUM BRAIN SPINAL CORD

1375

TITLE:

DOSE AND SEX-DEPENDENT ALTERATIONS IN MERCURY DISTRIBUTION IN FETAL MICE FOLLOWING METHYLMERCURY EXPOSURE

AUTHORS:

INOUYE M
KAJIWARA Y
HIRAYAMA K

SOURCE:
J TOXICOL ENVIRON HEALTH; 19 (3). 1986. 425-436.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN LIVER KIDNEY HEAVY METAL SEX DIFFERENCE

1376
TITLE:
The correlation between hair and tissue concentration of mercury in mice.

AUTHORS:
SHIMIZU M
NOGUCHI K
JINNOUCHI K
FUJII T
SAIRENJI E

SOURCE:
EISEI KAGAKU; 28 (2). 1982. 78-82.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. The use of human head hair has become of interest as a biological indicator of environmental pollution. Although hair is easily collected and multielement analysis of hair is easily carried out by applying instrumental neutron activation analysis, it is not always clear how the trace element contents in hair represent those in organs and there are unclarified points regarding the correlation between them. A survey of the Hg movement in body hair and tissues of mice was made and the correlation coefficients between them were determined by using 203Hg tracer in HgCl2. The maximum concentration of Hg was obtained in kidney and the minimum value in blood. The Hg concentration in body hair was higher than that in other tissue except kidney. The r between the concentrations in body hair and tissues was 0.864 in kidney, 0.869 in liver, 0.843 in lung, 0.933 in brain, 0.883 in spleen, 0.892 in intestine, 0.890 in thighbone and 0.839 in blood, and a significant correlation was observed between the Hg concentration in hair and in other tissues. By applying compartmental analysis to the data, the difference of turnover characteristics was examined between body hair and other tissues. The regression equation was introduced to calculate the Hg concentration in tissues other than body hair.

1377
TITLE:

AN EXAMINATION OF THE OXIDATION OF MERCURY VAPOR BY RAT BRAIN HOMOGENATE

AUTHORS:
SICHAK SP
MAVIS RD
FINKELSTEIN JN
CLARKSON TW

SOURCE:
J BIOCHEM TOXICOL; 1 (1). 1986. 53-68.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM CATALASE

1378
TITLE:
EFFECTS OF ENDOGENOUS AND EXOGENOUS THIOLS ON THE DISTRIBUTION OF MERCURIAL COMPOUNDS IN MOUSE TISSUES

AUTHORS:
AIHARA M
SHARMA RP

SOURCE:
ARCH ENVIRON CONTAM TOXICOL; 15 (6). 1986. 629-636.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM METHYLMERCURIC CHLORIDE MERCURIC CHLORIDE BRAIN UPTAKE ERYTHROCYTE UPTAKE LIVER KIDNEY GLUTATHIONE THIOL DISTRIBUTION ALTERATION

1379
TITLE:
MERCURY SURVEILLANCE IN SEVERAL CREE INDIAN COMMUNITIES OF THE JAMES BAY REGION QUEBEC

AUTHORS:
DUMONT C
WILKINS R

SOURCE:
FORTUINE, R. (ED.). CIRCUMPOLAR HEALTH 84; SIXTH INTERNATIONAL SYMPOSIUM, ANCHORAGE, ALASKA, USA, MAY 13-18, 1984. XXIV+484P. UNIVERSITY OF WASHINGTON PRESS: SEATTLE, WASH., USA. ILLUS. ISBN 0-295-96202-X.; 0 (0). 1985 (RECD. 1986). 88-91.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN METHYLMERCURY POISONING INDUSTRIAL

POLLUTION FISH CONSUMPTION MAD AS A HATTER MINAMATA DISEASE LIVER KIDNEY BRAIN

1380
TITLE:
MERCURY DISTRIBUTION STUDIES INVOLVING COMPLEXES OF LOW-MOLECULAR WEIGHT THIOLS AND METHYLMERCURY

AUTHORS:
BALTHROP JE
WADE JL
BRADDON-GALLOWAY S

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 37 (6). 1986. 890-898.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MOUSE BLOOD BRAIN LIVER KIDNEY INTESTINE SELENIUM TOXICOKINETICS

1381
TITLE:
HISTOCHEMICAL DISTRIBUTION OF MERCURY IN THE BRAINS OF RESIDENTS IN THE METHYLMERCURY-CONTAMINATED AREA OF MINAMATA

AUTHORS:
TAKEUCHI T

SOURCE:
IIND US-JAPAN HISTOCHEMISTRY AND CYTOCHEMISTRY CONGRESS: THIRTY-SEVENTH ANNUAL MEETING OF THE HISTOCHEMICAL SOCIETY AND TWENTY-SEVENTH ANNUAL MEETING OF THE JAPAN SOCIETY OF HISTOCHEMISTRY AND CYTOCHEMISTRY, SAN FRANCISCO, CALIFORNIA, USA, JUNE 8-13, 1986. ACTA HISTOCHEM CYTOCHEM; 19 (3). 1986 (RECD. 1987). 412.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT HUMAN DIAGNOSIS

1382
TITLE:
RATIO OF ORGANS TO BLOOD OF MERCURY DURING ITS UPTAKE BY NORMAL AND ACATALASEMIC MICE

AUTHORS:
OGATA M
AIKOH H

SOURCE:

ENVIRON RES; 42 (2). 1987. 421-424.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN LIVER HEART

1383
TITLE:
Dose-effect relationship between ethyl alcohol pretreatment and retention and tissue distribution of mercury vapor in rats.

AUTHORS:
KHAYAT AI
SHAIK ZA

SOURCE:
J PHARMACOL EXP THER; 223 (3). 1982 (RECD. 1983). 649-653.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. Pretreatment with ethyl alcohol, 0.5 h before exposure to 0.1 mg/m3 Hg vapor, resulted in markedly lower retention of Hg was compared with the nonalcohol-treated controls. The decrease in whole-body Hg retention was related to the dose of alcohol (0.25-6.0 g/kg). Near maximum reduction in Hg concentration in blood, brain, heart and lung was obtained at a 1 g/kg alcohol dose. Hg concentration in kidney was not significantly reduced even at a 2-g/kg alcohol dose and was significantly elevated in liver up to a 3-g/kg alcohol dose; higher doses of alcohol produced a linear decrease in both renal and hepatic Hg concentrations. A part of the decrease in whole-body Hg level was ascribed to the sedative effect of alcohol as indicated by results from rats treated with pentobarbital. Studies in rats treated with 3-aminotriazole indicated that alcohol probably also acted by inhibition of catalase-mediated oxidation of Hg vapor. Administration of pyrazole resulted in augmentation of the effect of alcohol, suggesting that alcohol itself, rather than its metabolites, was responsible for the inhbition of Hg vapor oxidation.

1384
TITLE:
MECHANISM OF INTERACTION OF METHYL MERCURY AND CADMIUM CHLORIDE WITH SULFHYDRYL GROUPS OF RAT BRAIN SODIUM-PUMP

AUTHORS:
DESAIAH D
AHAMMADSAHIB KI

SOURCE:
71ST ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, WASHINGTON, D.C., USA, MARCH 29-APRIL 2, 1987. FED

PROC; 46 (3). 1987. 557.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT PROTEIN BINDING

1385
TITLE:
MOTOR NEURON DISEASE AND TOXIC METALS

AUTHORS:
CONRADI S
RONNEVI L-O
NORRIS FH

SOURCE:
ROWLAND, L. P. (ED.). ADVANCES IN NEUROLOGY, VOL. 36. HUMAN MOTOR NEURON DISEASES; MUSCULAR DYSTROPHY ASSOCIATION INTERNATIONAL MEETING, SCOTTSDALE, ARIZ., USA, JUNE 7-12, 1981. XIV+577P. RAVEN PRES: NEW YORK, N.Y., USA. ILLUS. ISBN 0-89004-737-5.; 0 (0). 1982. P201-232.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. HUMAN AMYOTROPHIC LATERAL SCLEROSIS BLOOD BRAIN BARRIER AMINO LEVULINIC-ACID SYNTHETASE SELENIUM MERCURY LEAD ENVIRONMENT

1386
TITLE:
FETAL DISTRIBUTION OF INHALED MERCURY VAPOR IN NORMAL AND ACATALASEMIC MICE

AUTHORS:
OGATA M
MEGURO T

SOURCE:
PHYSIOL CHEM PHYS MED NMR; 18 (3). 1986 (RECD. 1987). 165-170.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MERCURIC CHLORIDE BLOOD LUNGS BRAIN LIVER AMNIOTIC SAC PLACENTA

1387
TITLE:
SUPPRESSION OF AMINOACYLADENYLATE SYNTHESIS BY METHYL MERCURY IN-VITRO AND
IN-VIVO

AUTHORS:

KUZNETSOV DA
ZAVIJALOV NV
GOVORKOV AV
RICHTER V

SOURCE:
TOXICOL LETT (AMST); 36 (2). 1987. 161-166.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT ENVIRONMENTAL NEUROTOXIN SERINE HISTIDINE PHENYLALANINE LEUCINE ARGININE ASPARTATE BRAIN CELL

1388
TITLE:
MERCURY LEVELS IN BONAPARTE'S GULLS LARUS-PHILADELPHIA DURING AUTUMN MOLT IN THE QUODDY REGION NEW BRUNSWICK CANADA

AUTHORS:
BRAUNE BM
GASKIN DE

SOURCE:
ARCH ENVIRON CONTAM TOXICOL; 16 (5). 1987. 539-550.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM EGG KIDNEY MUSCLE BRAIN FEATHER AGE METAL POLLUTION

1389
TITLE:
TISSUE DISTRIBUTION OF HEAVY METALS AND THEIR VARIATIONS WITH AGE SEX AND HABITAT IN JAPANESE SEROWS CAPRICORNIS-CRISPUS

AUTHORS:
HONDA K
ICHIHASHI H
TATSUKAWA R

SOURCE:
ARCH ENVIRON CONTAM TOXICOL; 16 (5). 1987. 551-562.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM NICKEL CADMIUM MANGANESE ZINC IRON COPPER COBALT LEAD MERCURY KIDNEY BRAIN LIVER MUSCLE HAIR METAL POLLUTION

1390
TITLE:
EFFECT OF SEX HORMONES ON THE FATE OF METHYLMERCURY AND ON GLUTATHIONE

METABOLISM IN MICE

AUTHORS:
HIRAYAMA K
YASUTAKE A
INOUE M

SOURCE:
BIOCHEM PHARMACOL; 36 (12). 1987. 1919-1924.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ESTRADIOL URINARY EXCRETION KIDNEY BRAIN LIVER PLASMA ERYTHROCYTE SEX DIFFERENCE

1391
TITLE:
PARADOXICAL EFFECT OF METHYL MERCURY ON MITOCHONDRIAL PROTEIN SYNTHESIS IN MOUSE BRAIN TISSUE

AUTHORS:
KUZNETSOV DA

SOURCE:
NEUROCHEM RES; 12 (8). 1987. 751-754.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ENVIRONMENTAL POLLUTANT ATP SYNTHESIS TRANSLATION ACTIVITY

1392
TITLE:
MICROSCOPIC DISTRIBUTION OF ORGANIC VS INORGANIC MERCURY IN NEONATES AND ADULTS EXPOSED TO METHYLMERCURIC CHLORIDE OR MERCURIC CHLORIDE

AUTHORS:
RODIER PM
KATES B
SIMONS R

SOURCE:
TWENTY-SEVENTH ANNUAL MEETING OF THE TERATOLOGY SOCIETY, RANCHO MIRAGE, CALIFORNIA, USA, JUNE 14-18, 1987. TERATOLOGY; 35 (2). 1987. 63A.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT KIDNEY BRAIN

1393
TITLE:

EFFECTS OF METHYL MERCURY ON OPERANT BEHAVIOR

AUTHORS:
LATIES VG
EVANS HL

SOURCE:
SATELLITE SYMPOSIUM ON ENVIRONMENTAL NEUROTOXICOLOGY: ASSESSMENT OF NERVOUS SYSTEM AND BEHAVIORAL DYSFUNCTION HELD AT THE 1ST WORLD CONGRESS OF THE INTERNATIONAL BRAIN RESEARCH ORGANIZATION, DUSSELDORF, MARCH 29-31, 1982. NEUROBEHAV TOXICOL TERATOL; 4 (6). 1982 (RECD. 1983). 683-688.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM PIGEON LONG-LASTING TOXIC CONSEQUENCES FIXED CONSECUTIVE NUMBER SCHEDULE BEHAVIORAL TOXICOLOGY

1394
TITLE:
RETROGRADE AXONAL TRANSPORT OF MERCURY

AUTHORS:
ARVIDSON B

SOURCE:
EXP NEUROL; 98 (1). 1987. 198-203.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT LOWER BRAIN STEM HYPOGLOSSAL NUCLEI TOXINS CRYOSTAT AUTORADIOGRAPHY

1395
TITLE:
NEURO TOXIC EFFECTS IN MERCURY EXPOSED WORKERS

AUTHORS:
TRIEBIG G
SCHALLER K-H

SOURCE:
SATELLITE SYMPOSIUM ON ENVIRONMENTAL NEUROTOXICOLOGY: ASSESSMENT OF NERVOUS SYSTEM AND BEHAVIORAL DYSFUNCTION HELD AT THE 1ST WORLD CONGRESS OF THE INTERNATIONAL BRAIN RESEARCH ORGANIZATION, DUSSELDORF, MARCH 29-31, 1982. NEUROBEHAV TOXICOL TERATOL; 4 (6). 1982 (RECD. 1983). 717-720.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM HUMAN BLOOD URINE NERVE CONDUCTION VELOCITY NEURO PSYCHIATRIC EXAMINATION PSYCHOLOGICAL TESTING SHORT-TERM MEMORY

1396
TITLE:
THE MATRIX EFFECT IN THE COLD-VAPOR ATOMIC ABSORPTION ANALYSIS OF MERCURY IN VARIOUS BIOLOGICAL TISSUES

AUTHORS:
WIGFIELD DC
EATOCK SA

SOURCE:
J ANAL TOXICOL; 11 (4). 1987. 137-139.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM FISH SAMPLE HAIR DIGEST URINE MILK BRAIN TOXICITY

1397
TITLE:
NEURO TOXICITY ANOREXIA AND THE PREFERENTIAL CHOICE OF ANTIDOTE IN METHYL MERCURY INTOXICATED RATS

AUTHORS:
MAGOS L

SOURCE:
SATELLITE SYMPOSIUM ON ENVIRONMENTAL NEUROTOXICOLOGY: ASSESSMENT OF NERVOUS SYSTEM AND BEHAVIORAL DYSFUNCTION HELD AT THE 1ST WORLD CONGRESS OF THE INTERNATIONAL BRAIN RESEARCH ORGANIZATION, DUSSELDORF, MARCH 29-31, 1982. NEUROBEHAV TOXICOL TERATOL; 4 (6). 1982 (RECD. 1983). 643-646.

ABSTRACT:
HEEP COPYRIGHT: BIOL ABS. RRM URINARY EXCRETION ENVIRONMENTAL TOXIN DI MERCAPTO SUCCINIC-ACID BODY WEIGHT BODY BURDEN

1398
TITLE:
THE DISTRIBUTION OF MERCURY IN VARIOUS TISSUES OF GUINEA-PIGS AFTER APPLICATION OF DENTAL AMALGAM FILLINGS A PILOT STUDY

AUTHORS:
FREDIN B

SOURCE:
SCI TOTAL ENVIRON; 66 (0). 1987. 263-268.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN KIDNEY LIVER HEART

1399
TITLE:
MERCURY-203 DISTRIBUTION IN PREGNANT AND NONPREGNANT RATS FOLLOWING SYSTEMIC INFUSIONS WITH THIOL-CONTAINING AMINO ACIDS

AUTHORS:
ASCHNER M
CLARKSON TW

SOURCE:
TERATOLOGY; 36 (3). 1987. 321-328.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN KIDNEY LIVER BLOOD TOXICITY

1400
TITLE:
THE EFFECTS OF ORGANIC MERCURY ON SOME BIOTOXICOLOGICAL INDICATORS IN WHITE RATS

AUTHORS:
ANCA Z
OSSIAN A
SURCEL D
OLINIC A

SOURCE:
REV IG BACTERIOL VIRUSOL PARAZITOL EPIDEMIOL PNEUMOFTIZIOL SER IG; 36 (2). 1987. 113-119.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM KIDNEY LIVER BRAIN ADRENAL TESTICLE THYROID HISTOPATHOLOGY VASCULAR CHANGES ORGAN WEIGHT INCREASE BLOOD GLUCOSE HOMEOSTASIS SERUM CHOLINESTERASE BODY WEIGHT DECREASE

1401
TITLE:
HISTOLOGICAL LOCALIZATION OF METHYLMERCURY IN MOUSE BRAIN AND KIDNEY BY EMULSION AUTORADIOGRAPHY OF MERCURY-203

AUTHORS:
RODIER PM
KATES B

SOURCE:
TOXICOL APPL PHARMACOL; 92 (2). 1988. 224-234.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM TOXICOKINETICS

1402
TITLE:
NIOSH Testimony on Neurotoxic Chemicals by J. R. Froines, June 6, 1979

AUTHORS:
NIOSH

SOURCE:
NIOSH, 17 pages, 1979

ABSTRACT:
This testimony summarized information dealing with worker exposure to neurotoxic chemicals. Following a definition of neurotoxicity, the testimony described some of the investigations on workers exposed to such chemicals on the job in which NIOSH has been involved. Included among the examples were the workers in Hopewell, Virginia, exposed to kepone (143500), who suffered loss of muscle coordination, loss of memory, and an eye movement disorder. Another episode of workers exposed to a pesticide involved leptophos (21609905). At the time of the exposure, leptophos was registered by the Environmental Protection Agency primarily for export. Animals administered a single oral dose showed weight loss, ataxia, and eventual muscle paralysis. Other potentially toxic chemicals were used in the preparation of leptophos including toluene (108883), a neurotoxic solvent. A third incident of worker exposure to pesticides occurred due to the release of o-ethyl-o-p-nitrophenylphenylphosphonothioate (2104645) (EPN), at a manufacturing site in Chicago Heights, Illinois. Neurological signs of distress included muscle weakness and cerebellar signs of toxicity. Cases of worker exposure to the following solvents were also reviewed: methyl-n-butyl-ketone (591786) and carbon-disulfide (75150). Exposures to metals were also reviewed including lead (7439921), arsenic (7440382), and mercury (7439976). Early detection of exposures to neurotoxic agents was briefly considered.

1403
TITLE:
EFFECT OF METHYLMERCURY ON THE LIPID COMPONENTS IN RATS

AUTHORS:
ANDO T
SAKAMOTO M
YAMAGIHASHI T

SOURCE:
ACTA MED UNIV KAGOSHIMA; 29 (2). 1987. 67-74.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MERCURY BIOTRANSFORMATION STARVATION BLOOD CELL FATTY ACID COMPOSITION PLASMA FATTY ACID CONCENTRATION BRAIN CHOLESTEROL CONCENTRATION METHYLMERCURY TOXICITY ENVIRONMENTAL POLLUTION

1404
TITLE:
MECHANISM OF INHIBITION OF RAT BRAIN SODIUM POTASSIUM-STIMULATED ATPASE REACTION BY CADMIUM AND METHYL MERCURY

AUTHORS:
AHAMMADSAHIB KI
RAMAMURTHI R
DESAIAH D

SOURCE:
J BIOCHEM TOXICOL; 2 (FALL-WINTER). 1987. 169-180.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HEAVY METAL TOXICITY TRITIATED OUABAIN PHARMACOLOGICAL TOOL THIOL COMPOUND THERAPY MINAMATA ITAI-ITAI

1405
TITLE:
REGIONAL BRAIN TRACE-ELEMENT STUDIES IN ALZHEIMER'S DISEASE

AUTHORS:
THOMPSON CM
MARKESBERY WR
EHMANN WD
MAO Y-X
VANCE DE

SOURCE:
NEUROTOXICOLOGY (LITTLE ROCK); 9 (1). 1988. 1-8.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN AMYGDALA HIPPOCAMPUS NUCLEUS BASALIS OF MEYNERT MERCURY CESIUM POTASSIUM SODIUM PHOSPHORUS RUBIDIUM IRON SCANDIUM ZINC NEUTRON ACTIVATION ANALYSIS RADIOCHEMICAL ANALYSIS MEMBRANE ABNORMALITY TOXICITY

1406
TITLE:
THE DISTRIBUTION OF TOTAL MERCURY IN THE BRAIN AFTER THE LATERAL VENTRICULAR SINGLE INJECTION OF METHYLMERCURY AND GLUTATHIONE

AUTHORS:
WATANABE H
SHIMOJO N
SANO K-I
YAMAGUCHI S

SOURCE:
RES COMMUN CHEM PATHOL PHARMACOL; 60 (1). 1988. 57-70.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT HEAVY METAL

1407
TITLE:
CHARACTERIZATION AND DEVELOPMENT OF METALLOTHIONEIN IN FETAL LIMB BUDS BRAIN AND LIVER FROM THE MOUSE

AUTHORS:
MUNOZ C
VORMANN J
DIETER HH

SOURCE:
29TH SPRING MEETING OF THE DEUTSCHE GESELLSCHAFT FUER PHARMAKOLOGIE UND TOXIKOLOGIE (GERMAN SOCIETY FOR PHARMACOLOGY AND TOXICOLOGY), MAINZ, WEST GERMANY, MARCH 8-11, 1988. NAUNYN-SCHMIEDEBERG'S ARCH PHARMACOL; 337 (SUPPL.). 1988. R25.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT CADMIUM ZINC COPPER MERCURY BINDING

1408
TITLE:
IN-VITRO EFFECT OF MERCURY AND CADMIUM ON BRAIN CALCIUM ATPASE OF THE CATFISH ICTALURUS-PUNCTATUS

AUTHORS:
REDDY RS
JINNA RR
UZODINMA JE
DESAIAH D

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 41 (3). 1988. 324-328.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM CALCIUM TRANSPORT NEUROTOXICITY WATER

POLLUTION

1409
TITLE:
LONG TERM PERSISTENCE OF MERCURY IN THE BRAIN

AUTHORS:
CAVANAGH JB

SOURCE:
BR J IND MED; 45 (10). 1988. 649-651.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM REVIEW TOXICOKINETICS

1410
TITLE:
THE INTERACTION OF CATIONS WITH ACTIVITY OF SOLUBLE PROTEIN KINASE C FROM MOUSE BRAIN

AUTHORS:
SAIJOH K
INOUE Y
KATSUYAMA H
SUMINO K

SOURCE:
PHARMACOL TOXICOL; 63 (4). 1988. 221-224.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM MERCURY CADMIUM LEAD CALCIUM ENVIRONMENTAL POLLUTANT

1411
TITLE:
IN-VITRO OXIDATION OF MERCURY BY THE BLOOD

AUTHORS:
HURSH JB
SICHAK SP
CLARKSON TW

SOURCE:
PHARMACOL TOXICOL; 63 (4). 1988. 266-273.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN BRAIN CATALASE-COMPOUND I SYSTEM HYDROGEN PEROXIDE TEMPERATURE

1412
TITLE:
EFFECT OF ETHANOL ON THE ACCUMULATION AND EXCRETION OF MERCURY IN RATS

AUTHORS:
ANDO T
WAKISAKA I
YANAGIHASHI T
SAKAMOTO M

SOURCE:
JPN J HYG; 43 (3). 1988. 717-723.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM FECES URINE BRAIN LIVER KIDNEY

1413
TITLE:
DISTRIBUTION OF MERCURY IN THE CARP TISSUES AND ITS BIOLOGICAL EFFECT

AUTHORS:
FILENKO OF
DU SHIHUA
CHEN SYULON
DZHAN YUCHI

SOURCE:
GIDROBIOL ZH; 24 (4). 1988. 63-66.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM GILL LIVER BRAIN LESION TOXICITY

1414
TITLE:
ANALYSIS OF METHYL MERCURY BINDING SITES ON TUBULIN SUBUNITS AND MICROTUBULES

AUTHORS:
VOGEL DG
MARGOLIS RL
MOTTET NK

SOURCE:
PHARMACOL TOXICOL; 64 (2). 1989. 196-201.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN NEUROTOXIN

1415
TITLE:
EFFECTS OF ALUMINUM AND OTHER CATIONS ON THE STRUCTURE OF BRAIN AND LIVER CHROMATIN

AUTHORS:
WALKER PR
LEBLANC J
SIKORSKA M

SOURCE:
BIOCHEMISTRY; 28 (9). 1989. 3911-3915.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT TOXICITY ALZHEIMER'S DISEASE MESSENGER RNA

1416
TITLE:
HEAVY METALS ACCUMULATION AND THEIR EFFECTS ON A FEW ENZYMES IN NOTOPTERUS-NOTOPTERUS

AUTHORS:
CHAND R
SHANKAR JS
KUMAR P
VERMA SR

SOURCE:
UTTAR PRADESH J ZOOL; 8 (2). 1988. 114-123.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM BRAIN KIDNEY MERCURY CADMIUM GLUTAMIC-OXALACETIC TRANSAMINASE GLUTAMIC-PYRUVIC TRANSAMINASE

1417
TITLE:
EEG FINDINGS IN CHLOR-ALKALI WORKERS SUBJECTED TO LOW LONG TERM EXPOSURE TO MERCURY VAPOR

AUTHORS:
PIIKIVI L
TOLONEN U

SOURCE:
BR J IND MED; 46 (6). 1989. 370-375.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN ELECTROENCEPHALOGRAM BRAIN DAMAGE OCCUPATIONAL HEALTH AND SAFETY POLLUTION

1418
TITLE:
KINETICS AND BIOTRANSFORMATION OF MERCURY AND ITS COMPOUNDS

AUTHORS:
CIKRT M

SOURCE:
PRAC LEK; 41 (3). 1989. 112-116.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT RES BLOOD LIVER BRAIN KIDNEY SPLEEN

1419
TITLE:
THE VESTIBULAR SYSTEM AND CEREBELLUM IN ORGANIC MERCURY INTOXICATION AN OTOLARYNGOLOGICAL AND NEUROPATHOLOGICAL INVESTIGATION ON 14 AUTOPSY CASES
IN NIIGATA JAPAN

AUTHORS:
OYANAGI K
OHAMA E
IKUTA F
IGARASHI S
NAKANO Y

SOURCE:
BRAIN NERVE (TOKYO); 41 (7). 1989. 711-717.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN VERMIS DEGENERATION NEURON LOSS GLIOSIS

1420
TITLE:
EFFECTS OF HEAVY METAL CATIONS ON SECOND MESSENGER SYSTEMS IN THE BRAINS OF MICE

AUTHORS:
INOUE Y
SAIJOH K
KATSUYAMA H
SUMINO K

SOURCE:
SUMINO, K. (ED.). ENVIRONMENTAL AND OCCUPATIONAL CHEMICAL HAZARDS, NO. 8; ASIA-PACIFIC SYMPOSIUM ON ENVIRONMENTAL AND OCCUPATIONAL TOXICOLOGY, SINGAPORE, OCTOBER 4-7, 1987. XII+582P. KOBE UNIVERSITY SCHOOL OF MEDICINE: KOBE, JAPAN. ILLUS. MAPS.; 0 (0). 1988. 155-162.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM CADMIUM MERCURY LEAD STRONTIUM BARIUM CALMODULIN PROTEIN KINASE C ACTIVATION

1421
TITLE:
The Interaction Of Selenium With Various Metals In Vitro And In Vivo

AUTHORS:
Naganuma A
Tanaka T
Maeda K
Matsuda R
Tabata-Hanyu J
Imura N

SOURCE:
Toxicology, Vol. 29, No. 1-2, pages 77-86, 35 references, 19831983

ABSTRACT:
The interaction of selenium (7782492) with various metal ions was studied in-vivo and in-vitro. Male CD-1-mice were injected intravenously with 10 micromoles per kilogram (micromol/kg) selenium-75 (14265715) (Se-75) labeled sodium-selenite (10102188) and 0 or 10micromol/kg of 24 other metal ions. Twenty four hours after administration, blood, brain, heart, lung, liver, spleen, kidney, and testis were removed and assayed for Se-75 activity. Four in-vitro reaction systems consisting of heparinized rabbit blood, rabbit blood plasma, and reduced glutathione at concentrations of 50 micromoles per milliliter or 100 nanomoles per milliliter were incubated with Se-75 labeled sodium-selenite at concentrations of 10 nanomoles per milliliter to 0.00001 molar solutions. The distribution of Se-75 activity in the plasma, erythrocytes, and water insoluble fractions was determined. Silver (7440224), monovalent copper (17493866), cadmium (7440439), mercury (7439976), lead (7439921), zinc (7440666), arsenic (7440382), bismuth (7440699), nickel (7440020), trivalent chromium (16065831), divalent platinum (22542105), gold (7440575), and palladium (7440053) ions significantly altered the distribution of selenium in mouse tissues. Manganese (7439965), silver, monovalent and divalent copper (15158119), cadmium, mercuric, lead, zinc, arsenious, divalent cobalt (22541533), nickel, hexavalent chromium (18540299), platinum, gold, thallium (22537560), and palladium ions significantly affected the

in-vitro behavior of selenium. The authors conclude that interaction between selenium and metals usually occurs in animals and regulates their toxicity, physiological activity, and behavior.

1422
TITLE:
KINETICS OF METHYL MERCURY IN BLOOD AND BRAIN DURING CHRONIC EXPOSURE IN THE MONKEY MACACA-FASCICULARIS

AUTHORS:
STINSON CH
SHEN DM
BURACHER TM
MOHAMED MK
MOTTET NK

SOURCE:
PHARMACOL TOXICOL; 65 (3). 1989. 223-230.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM NEUROTOXICITY PHARMACOKINETICS CLEARANCE HALF-LIFE HALF-LIFE ENVIRONMENTAL EFFECT ANIMAL MODEL

1423
TITLE:
IN-VITRO EFFECT OF ORGANIC AND INORGANIC MERCURY ON THE SEROTONERGIC SYSTEM

AUTHORS:
OUDAR P
CAILLARD L
FILLION G

SOURCE:
PHARMACOL TOXICOL; 65 (4). 1989. 245-248.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM RAT BRAIN CORTEX SYNAPTOSOMAL FRACTION INTOXICATION POTENTIAL 5 HYDROXYTRYPTAMINE

1424
TITLE:
Toxicity To Heavy Metals And Relationship To Seizure Thresholds

AUTHORS:
Adler MW
Adler CH

SOURCE:
Clinical Pharmacology and Therapeutics, Vol. 22, No. 5, Part 2, pages 774-779, 28 references0000

ABSTRACT:
The effects of lead (7439921), mercury (7439976), and nickel (7440020) on seizure thresholds were investigated in Sprague-Dawley-rats. Median lethal doses (LD50) were determined for lead-acetate (301042), lead-nitrate (10099748), methylmercury-chloride (115093), mercuric-chloride (7487947), nickel-acetate (373024), and nickel-sulfate (7786814). Thresholds to flurothyl (333368) induced seizures were also determined. Rats were treated with various doses of metal compounds for 2 days, or with daily injections 5 days per week for 6 weeks. Animals were challenged after dosing was completed with flurothyl, and the convulsive threshold was determined. The LD50 per day for 2 days of administration was 215 milligrams per kilogram (mg/kg) for lead-acetate; 65.9mg/kg for lead-nitrate; 11.9mg/kg for methylmercury-chloride; 4.5mg/kg for mercuric-chloride; and about 35 to 40mg/kg for nickel-acetate and nickel-sulfate. There was a significant fall in body weight in animals receiving high doses of all three heavy metals over the 2 day period; there were only four instances of significant alterations in seizure threshold. Elevated thresholds were seen after high doses of nickel-acetate and nickel-sulfate; a decrease was seen with a high dose of lead-nitrate salt. The same effects were seen in animals receiving chronic doses; no significant change in seizure threshold occurred, and body weights were significantly decreased. The authors conclude that high doses of lead can alter brain excitability after short term exposure; however, the specific effect is related to the form in which the metal is administered.

1425
TITLE:
ACCUMULATION OF METHYLMERCURY AND INORGANIC MERCURY IN THE BRAIN

AUTHORS:
FRIBERG L
MOTTET NK

SOURCE:
FIRST INTERNATIONAL MEETING ON MOLECULAR MECHANISMS OF METAL TOXICITY AND CARCINOGENICITY, URBINO, ITALY, SEPTEMBER 19-22, 1988. BIOL TRACE ELEM RES; 21 (0). 1989. 201-206.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN EPIDEMIOLOGY DEMETHYLATION BIOTRANSFORMATION BIOLOGICAL HALF-TIME

1426

TITLE:
HEAVY METAL INDUCED ALTERATIONS IN THE NERVE GROWTH FACTOR LEVEL IN THE RAT BRAIN

AUTHORS:
LARKFORS L
OSKARSSON A
SUNDBERG J
EBENDAL T

SOURCE:
19TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PHOENIX, ARIZONA, USA, OCTOBER 29-NOVEMBER 3, 1989. SOC NEUROSCI ABSTR; 15 (1). 1989. 444.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT DEVELOPMENT ADULTHOOD TOXICITY CHOLINERGIC NEURON DEGENERATION METHYL MERCURY LEAD CHLORIDE ALZHEIMER'S DISEASE

1427
TITLE:
EFFECTS IN-VITRO OF LEAD CADMIUM AND MERCURY ON RAT BRAIN MICROSOMAL POTASSIUM ION P NITROPHENYL PHOSPHATASE AND ITS PROTECTION BY THIOL REAGENTS

AUTHORS:
RAJANNA B
CHETTY CS
RAJANNA S

SOURCE:
74TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, PART II, WASHINGTON, D.C., USA, APRIL 1-5, 1990. FASEB (FED AM SOC EXP BIOL) J; 4 (4). 1990. A1015.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT DITHIOTHREITOL CYSTEINE ATPASE

1428
TITLE:
Histopathological lesions in the body organs of catfish (Heteropneustes fossilis) following mercury intoxication.

AUTHORS:
BANO Y
HASAN M

SOURCE:

J ENVIRON SCI HEALTH PART B PESTIC FOOD CONTAM AGRIC WASTES; 25 (1). 1990. 67-86.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Light microscopic study of different body organs of cat-fish following exposure to HgCl2 0.2 mg in water in 30 days revealed that focal degeneration of liver cells and disorganization of hepatic cords occurred at places. Furthermore, centrilobular atrophy and compensatory hypertropy of some hepatic cells were also observed. In the kidneys disintegration of renal epithelium along with displacement of nuclei, shrinkage of glomeruli, breakdown of Bowman's capsule and heavy infiltration by inflammatory cells were observed. The histopathological changes noted in the intestine included degeneration of lining epithelium, and diminution of goblet cells. Microscopic section of ovaries exhibited reduction of ooplasm leading to formation of atypical oocytes. An increase in the occurrence of atretic oocytes and interfolicular spaces was also discernible. No histopathological lesions could be detected in testes of male fish probably because of the difference in the maturity of the co

1429

TITLE:

Usefulness of fibroblast culture for testing of cattle tissues polluted with heavy metals.

AUTHORS:

WEGLARZ L
DROZDZ M
WARDAS M
KULA B
PAWLACZYK-SZPILOWA M

SOURCE:

ENVIRON RES; 51 (2). 1990. 163-169.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. Cattle tissues (liver, kidney, brain, and lung) that had been polluted with heavy metals were tested for their ability to alter fibroblast culture growth, cellular protein and DNA content, and fibroblast DNA synthesis. At 72 hr of incubation a significant increase in cellular DNA and (14C)thymidine incorporation was noted in the primary cultures as well as in the subcultures compared to controls. Fibroblast cultures also displayed growth inhibition and reduction in protein content. The measurement of basic biochemical parameters of the fibroblast culture may represent a sensitive means of assessing rapidly the activity of heavy metals deposited in the tissues of cattle as a result of their grazing on polluted soil.

1430

TITLE:
(Methyl mercaptophos detection reactions in forensic chemical analysis.)

AUTHORS:
Ikramov LT JR
Tashpulatov AIU JR
Abduvakhabov KA JR

SOURCE:
Farmatsiya (Moscow); 19(6): 70-3 1970; (REF:10)

ABSTRACT:
HAPAB In a search for new specific reactions for detecting methyl mercaptophos for forensic chemical purposes, a series of reagents was examined. It was found that the pesticide in aqueous or alcoholic solutions forms various products with different reagents (data tabulated). Methyl mercaptophos forms the most characteristic microcrystals with reagents of mercury dichloride or dibromide and of iodine chloride (illustrated); the reactions are briefly described. Compounds such as Thiophos (parathion), chlorophos (trichlorfon), Anthio (formothion), atropine, morphine, pilocarpine, etc. do not form similar microcrystals. Phosphamide (dimethoate) and Sayphos (menazon) do form similar microcrystals with iodine chloride but the phosphamide microcrystals take on another form after standing 10 min. The reactions described were tested on methyl mercaptophos isolated from cadaveric material. In a special experiment, a rabbit was perorally poisoned with 3 g of the 30% technical concentrate of methyl mercaptophos in water. The results of the analysis of liver, stomach contents, kidneys, heart, brain, etc. of the rabbit are tabulated. The usefulness of these microcrystal reactions for detecting methyl mercaptophos has been demonstrated, as well as the limits of their sensitiveness for biological materials. 1970

1431
TITLE:
MERCURY NEUROTOXICITY MECHANISMS OF BLOOD-BRAIN BARRIER TRANSPORT

AUTHORS:
ASCHNER M
ASCHNER JL

SOURCE:
NEUROSCI BIOBEHAV REV; 14 (2). 1990. 169-176.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM REVIEW HUMAN ANIMAL PHYSICOCHEMICAL STATE REDOX POTENTIAL KIDNEY

1432

TITLE:
Glutamine synthetase activity of developing astrocytes is inhibited in-vitro by very low concentrations of lead.

AUTHORS:
ENGLE MJ
VOLPE JJ

SOURCE:
DEV BRAIN RES; 55 (2). 1990. 283-287.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. This study has dealt with the inhibition by lead of glutamine synthetase (GS) activity in homogenates of mixed glial primary cultures, 95% enriched in differentiating astrocytes. A 70% inhibition was observed with a lead concentration of only 2.5 muM. Prevention of the inhibition by addition of EDTA or dithiothreitol is compatible with the conclusion that the effect is mediated by binding of lead ion to sulfyhydryl moieties of the enzyme. Among several other cations tested, only mercury, which has a similarly high binding affinity for sulfhydryl moieties, inhibited the enzyme. The inhibitory effect of lead was relatively specific, since no inhibition of another astrocytic marker enzyme, lactate dehydrogenase, of the oligodendroglial marker enzyme, 2',2'-cyclic nucleotide 3'-phosphohydrolase, or of the plasma membrane marker, Na,Ka-ATPase, was observed with concentrations of lead that produced a 70% decrease of GS. Because of the critical role of GS in regulation of extr

1433
TITLE:
Effects of oral meso-2,3-dimercaptosuccinic acid (DMSA) administration on late gestation and postnatal development in the mouse.

AUTHORS:
DOMINGO JL
BOSQUE MA
CORBELLA J

SOURCE:
LIFE SCI; 47 (19). 1990. 1745-1750.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. The present study was conducted to evaluate the effects of meso-2,3-dimercaptosuccinic acid (DMSA) on late gestation and postnatal viability and growth in the mouse. DMSA was given po to four groups of pregnant Swiss mice at 0, 200, 400, and 800 mg/kg/day from day 14 of pregnancy until postnatal day 21. At birth, the following data were recorded: length of gestation, number of live, dead, and abnormal pups,

sex, and individual pup weights. Each pup was weighed again on days 4, 14, and 21 of lactation. Pinna detachment, incisor eruption and eye opening were also monitored. No treatment-related signs of toxicity were noted in any of the dams during the study. No adverse effects on offspring survival or development were evident in the 200 or 400 mg DMSA/kg/day groups. However, on days 14 and 21 of lactation a significant decrease in pup body weight was observed in the 800 mg/kg/day group. Also, a significant increase in the relative weight of the brain was seen in this gro

1434
TITLE:
SELECTIVE QUANTIFICATION OF INORGANIC MERCURY IN TISSUES OF METHYLMERCURY-TREATED RATS

AUTHORS:
YASUTAKE A
HIRAYAMA K

SOURCE:
BULL ENVIRON CONTAM TOXICOL; 45 (5). 1990. 662-666.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ENVIRONMENTAL TOXICOLOGY BRAIN LIVER KIDNEY

1435
TITLE:
Bioaccumulation of metals from nickel works waste in the gull (Larus ridibundus L., 1766).

AUTHORS:
DAROLOVA A
REICHRTOVA E
PAVELKA J

SOURCE:
BIOLOGIA (BRATISL); 44 (6). 1989. 567-574.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Accumulation of components of wastes form nickel works in Larus ridubundus, especially its eggs, was studied in an exposed locality at a distance of about 6 km from the waste deposits and a control locality. Thirty-three eggs from each locality were analysed by atomic absorption spectrometry. Egg shells from the exposed locality showed significantly increased levels of Fe, Ni and Al ($P < 0.0005$) and of Cd ($P < 0.005$); significantly higher levels of Cd ($U < 0.05$) and Ni, Mg, Ca and Hg ($P < 0.005$) were found in egg contents. Analysis of two adult L. ridibundus revealed highest levels of Cr, Pb, Ni, Co, Zn and

Cu in feathers; of Cd and Mo in the livers; of Be, Al, Ca and Mg in the brains; and of Fe in thoracic muscles. Average values of egg length and width and shell thicknesses in egg centre were greater in the exposed locality than in the control one, but the differences were not statistically significant.

1436
TITLE:
Vascular Permeability and Neurotoxicity

AUTHORS:
Jacobs JM

SOURCE:
Environmental Health Perspectives, Vol. 26, pages 107-116, 44 references, 19781978

ABSTRACT:
The selectivity of neurotoxic substances was discussed, with emphasis on the role of vascular permeability. Capillaries in brain and somatic and autonomic peripheral nerves differ from those in other tissues. Their component endothelial cells are closely connected by tight junctions. There is no significant vesicular transport across these cells. Vascular endothelial cells in nonnervous tissues contain an actomyosin/like protein which responds to released histamine, causing cellular contraction and separation. Cerebral endothelial cells do not contain the contractile protein. Capillaries in certain regions have slits or fenestrations allowing rapid exchange of a plasma filtrate through these attenuated regions of the endothelial cells; this may allow toxic substances to pass readily between blood and nervous tissue. Some selective toxic effects in the central nervous system (CNS) may be explained by vascular permeability. Monosodium-glutamate (142472) and aspartame (22839470) damaged the CNS by neuronal degeneration of the arcuate nucleus of the hypothalamus. Tracer techniques showed that blood vessels in dorsal root ganglia were permeable. Fenestrated blood vessels were found to be more numerous in autonomic sympathetic ganglia than in dorsal root ganglia. Dorsal root and nerve-V ganglia were found to be particularly affected by methylmercury (22967926) in rats, rabbits, pigs, and monkeys. Because of high lipid solubility, methylmercury reached ganglion cells rapidly. According to the author, an awareness of the accessibility of particular nerve cells or processes to circulating substances may suggest new ways of assessing neurotoxic effects.

1437
TITLE:
MERCURY INDUCES GTP-TUBULIN INTERACTIONS IN RAT BRAIN SIMILAR TO THOSE OBSERVED IN ALZHEIMER'S DISEASE

AUTHORS:
DUHR E
PENDERGRASS C
KASARSKIS E
SLEVIN J
HALEY B

SOURCE:
75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J; 5 (4). 1991. A456.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT RABBIT POSSIBLE ETIOLOGY

1438
TITLE:
IN-VITRO EFFECTS OF HEAVY METALS ON BRAIN PHOSPHODIESTERASE AND CALMODULIN ACTIVITY

AUTHORS:
CHETTY CS
RAJANNA B
RAJANNA S

SOURCE:
75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J; 5 (4). 1991. A878.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. RRM ABSTRACT RAT NEUROTOXICITY MERCURY CADMIUM LEAD

1439
TITLE:
Mercury modulation of GABA-activated chloride channels and non-specific cation channels in rat dorsal root ganglion neurons.

AUTHORS:
ARAKAWA O
NAKAHIRO M
NARAHASHI T

SOURCE:
BRAIN RES; 551 (1-2). 1991. 58-63.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. The effects of mercuric chloride and methylmercury chloride on the rat dorsal ganglion neurons in primary culture were studied by the whole-cell patch clamp technique. gamma-Aminobutyric acid-induced chloride currents were augmented by mercuric chloride in a potent and efficacious manner; at concentrations of 1 and 10 muM, the current amplitude was increased to 130% and 200% of the control. Methylmercury even at 100 muM did not augment but rather decreased the GABA-induced chloride current. Both mercuric chloride and methylmercury generated slow inward currents by themselves. These currents are not mediated by the GABA-activated chloride channels or by voltage-activated sodium, potassium or calcium channels, and are likely to be due to non-specific cation channels.

1440

TITLE:

Occupational Hazards and Emotional Stress as Related to Morbidity and Mortality of Dentists: A Review of and Comment on Published Research

AUTHORS:

Gift HC

SOURCE:

Bureau of Economic Research and Statistics, American Dental Association, Chicago, Illinois, 40 pages, 47 references, 19771977

ABSTRACT:

The impact of occupational hazards and emotional stress on dentists was discussed. Possible ways of reacting to environmental and occupational stressors were summarized. Research publications dealing with occupational hazards in dentistry, stress in dentists, reactions of dentists to occupational hazards, and morbidity and mortality in dentists were reviewed. Mercury (7439976) and ionizing radiation have been the most frequently studied hazards encountered in the dental setting. Less frequently studied have been bacteriological hazards resulting from air contamination due to equipment used in the operatory and hazards from anesthetics. Viral hepatitis and other infectious diseases are also significant occupational hazards for dentists. It was noted that most studies focusing on stress in dentists are general in nature and contain little in the way of supportive, systematic research. Most studies on the reactions to occupational hazards and morbidity in dentists have been suggestive rather than definitive. Very little evidence of maladaptive behavior that could be attributed to job stress has been found. The mortality studies have shown that dentists are healthy and have an overall death rate that is lower than that of the general population. For example, a recent study found that 73 percent of the deaths in dentists occurred after the age of 64. Some studies have shown a higher that average suicide rate; however, these studies have been based on a death in time design in selected regions with only a few years and a small number

of suicides. The most thorough study using a nationwide cohort indicated that dentists have the same suicide rate as the general population. Some subgroups have shown higher suicide rates as well as excess mortality from brain cancer, cirrhosis of the liver, lymphomas, nephritis, and nephrosis. Future research needs on job stress and morbidity and mortality in dentists were outlined.

1441
TITLE:
Interactions of methylmercury with rat primary astrocyte cultures: Methylmercury efflux.

AUTHORS:
ASCHNER M
EBERLE NB
KIMELBERG HK

SOURCE:
BRAIN RES; 554 (1-2). 1991. 10-14.

ABSTRACT:
BIOSIS COPYRIGHT: BIOL ABS. Methylmercury (MeHg) efflux from rat astrocyte cultures was studied to complement our previous studies on uptake of MeHg in these cells. Exchange with extracellular MeHg was not obligatory for the efflux of (203Hg)MeHg into the extracellular media, because efflux occurred into MeHg-free extracellular media, but stimulation of (203Hg)MeHg net efflux was shown when astrocytes were equilibrated in the presence of 'cold' MeHg and graded concentrations of L-cysteine. Net efflux of MeHg was most rapid for the first 5 min, and approximately 20% of preloaded (203Hg)MeHg was lost from the astrocytes by 60 min. Uptake of (203Hg)MeHgCl was maximal by 30 min and did not increase when the loading period was extended up to 4 h. However, the total amount of intracellular 203Hg that was available for net efflux gradually decreased as the duration of the preloading period increased. MeHg net efflux from astrocytes was unchanged when (203Hg)MeHgCl preloaded astrocytes were equilibrated i

1442
TITLE:
MINAMATA DISEASE A STORY OF MERCURY'S MALEVOLENCE

AUTHORS:
POWELL PP

SOURCE:
SOUTH MED J; 84 (11). 1991. 1352-1358.

ABSTRACT:

BIOSIS COPYRIGHT: BIOL ABS. RRM HUMAN METHYLMERCURY POISONING AQUATIC FOOD CHAIN EXPOSURE ENVIRONMENTAL CATASTROPHE BRAIN DAMAGE DYSPHAGIA HYPERSALIVATION JAPAN

1443
TITLE:
Late aftereffects of nervous system pathology provoked by the action of low ethylmercuric chloride concentrations.

AUTHORS:
Mukhtarova ND

SOURCE:
Gig. Tr. Prof. Zabol. 20(3): 4-7; 1977.(8 references)

ABSTRACT:
PESTAB. Nervous system dynamics and other clinical parameters were examined 1.5-3 yr after exposure in 25 persons exposed repeatedly to low ethylmercuric chloride concentrations. EEG and Asschner-Dagni reflexes were among the clinico-physiological parameters examined, and the biochemical factors included catecholamines, sugar, mercury, and urinary DDT and DDE levels. The nervous system pathology was somewhat altered compared to the earlier examinations. Changes were observed in sympathico-adrenal function. Vascular lesions in the brain resembled transient derangements of cerebral circulation in the vertebro-basilar basin and angiospasms. Diffuse changes were seen in the nervous system, with predominant involvement of hypothalamic cerebral structures and sometimes psychological disturbances.

1444
TITLE:
Evaluation of slaughter products from Granosan-poisoned animals.

AUTHORS:
Saley PI

SOURCE:
Veterinariya; 46(8): 102-103; 1970

ABSTRACT:
HAPAB The largest amounts of residual mercury (Hg) were found in liver, kidney, and brain tissues from chicken and swine given Granosan-contaminated feed for 6 to 12 months. Decrease in Hg was observed 60 days following interruption of contaminated feed administration. Residual amounts of Hg remained in muscular tissue for 60-120 days and in liver and kidney tissue for 300 days following interruption of feeding. Meat, kidney, or liver kept for 2, 3, or 6 months in the refrigerator could not be decontaminated. Mice given swine

liver and kidney containing 20 mg/kg Hg died within 17-20 days; their bodies contained 50-65 mug Hg. Dried feed prepared from swine liver and kidney containing 14 mg/kg Hg was given to 2 month-old cocks for 30 days (7 g meat powder daily). Upon slaughter, their livers contained 16 mug %, kidneys contained 40 mug % and muscles contained 2% Hg respectively. Thus, refrigeration or thermal treatment of meat products from granosan-contaminated feed-treated animals achieved no Hg decontamination. 1970

1445

TITLE:

A Histopathological Study of the Brain of Cats Poisoned with Methylmercuric Compounds

AUTHORS:

Matsumoto KoyaGDeguchiHSonodaMKaiF H

SOURCE:

J. Kumamoto Med. Soc.; 40:1016-22, 1966

ABSTRACT:

HAPAB Methyl mercuric chloride, methyl mercuric iodide, and methyl mercuric hydroxide, in amounts ranging from 0.6 to 2.0 mg Hg/kg/day, were administered orally to 14 cats from 7 to 35 times. When the total quantity administered was 10 mg and over, the cats exhibited nervous symptoms such as ataxic gait, damage to eyesight, and convulsions. Such nervous symptoms are evidence of severe damage to the cerebellar and cerebral cortical cells. Cerebellar damage following administration of mercury compounds is characterized by granular degeneration, necrosis, and shedding. Purkinje cells are also affected. RESEARCH IN TOXICOLOGY AND PHARMACOLOGY 67/01/00, 15 1966