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Technical Report: Mercury in the Environment: Implications for Pediatricians

Lynn R. Goldman, MD, MPH, Michael W. Shannon, MD, MPH, and the Committee on Environmental Health

ABSTRACT

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Mercury is a ubiquitous environmental toxin that causes a wide range of adverse health effects in humans. Three forms of mercury (elemental, inorganic, and organic) exist, and each has its own profile of toxicity. Exposure to mercury typically occurs by inhalation or ingestion. Readily absorbed after its inhalation, mercury can be an indoor air pollutant, for example, after spills of elemental mercury in the home; however, industry emissions with resulting ambient air pollution remain the most important source of inhaled mercury. Because fresh-water and ocean fish may contain large amounts of mercury, children and pregnant women can have significant exposure if they consume excessive amounts of fish. The developing fetus and young children are thought to be disproportionately affected by mercury exposure, because many aspects of development, particularly brain maturation, can be disturbed by the presence of mercury. Minimizing mercury exposure is, therefore, essential to optimal child health. This review provides pediatricians with current information on mercury, including environmental sources, toxicity, and treatment and prevention of mercury exposure.

INTRODUCTION

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In response to the Food and Drug Administration Modernization Act of 1997,[1] the US Food and Drug Administration (FDA) has been reviewing the use of mercury in regulated biological products. In June 1999, the FDA notified the American Academy of Pediatrics

that some infants given routine immunizations could exceed 1 of 3 federal guidelines for daily exposure to mercury because of the presence of thimerosal, a mercury-containing preservative, in some vaccines.[2] Currently, all vaccines in the recommended vaccination schedule do not contain thimerosal as a preservative. This technical report provides additional information about the sources, exposures, and toxicity of the 3 forms of mercury in the environment and implications for pediatricians.

SOURCES OF MERCURY IN THE ENVIRONMENT

Everyone is exposed to small amounts of mercury.[3,4] Mercury occurs in 3 forms: the metallic element (Hg^0 [quicksilver or elemental mercury]); inorganic salts (Hg^{1+} [mercurous salts] and Hg^{2+} [mercuric salts]); and organic compounds (methylmercury, ethylmercury, and phenylmercury). Solubility, reactivity, biological effects, and toxicity vary among these forms.

Naturally occurring mercury sources include cinnabar (ore) and fossil fuels, such as coal and petroleum. Environmental contamination has resulted from mining, smelting, and industrial discharges. Mercury in the air is deposited into the water. Bacteria in lake, stream, and ocean sediments can convert elemental mercury to organic mercury compounds (eg, methylmercury), which may then accumulate as fish move up the food chain (Fig 1). This is what occurred in Minamata Bay, Japan, in the 1950s when a factory discharged large quantities of a mercury catalyst into the bay. There were 41 deaths and at least 30 cases of profound brain injury in infants born to mothers who ingested contaminated fish during pregnancy.[5] States have issued advisories about consumption of fish from contaminated waters. Large, long-lived, predatory ocean fish, such as tuna, swordfish, and shark, may have increased methylmercury content because of exposure to natural and industrial sources of mercury.

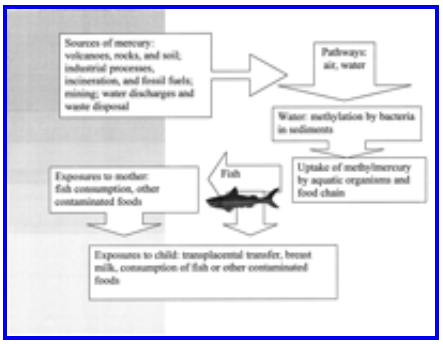

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Fig. 1. Sources of mercury and its conversion to organic mercury compounds.

Elemental Mercury

Sources Elemental mercury is liquid or vapor at room temperature. In the United States, the largest source of atmospheric mercury vapor is from burning fossil fuels, especially high-sulfur coal. Other sources include chloralkali production (a process that uses mercury in electrolysis of salt to produce hydrogen chloride and sodium hydroxide, chlorine, caustic soda, bleach, and other products), mercury mining and smelting, waste

incinerators (especially medical waste), crematoriums, and volcanoes.[3,6] Elemental mercury in liquid form is found in thermometers, barometers, and other instruments. Dental amalgam, a composite metal that is about 50% mercury, has been used to fill decayed teeth since the 1820s.[7] Fluorescent light bulbs (usually 2- to 4-ft tubes) and disk (button) batteries also contain mercury. Indiscriminate disposal of these items is a major source of environmental mercury contamination when they are buried in landfills or burned in waste incinerators rather than recycled. Elemental and inorganic mercury have been used in folk remedies from around the world. Elemental mercury may be used in homes in rituals, such as those used in Santeria, which is practiced by some immigrants from Haiti and other island nations. In Santeria rituals, elemental mercury is sprinkled around a home as part of magicoreligious ceremonies. Unfortunately, this mercury vaporizes and may expose children and others who reside in the household.

Absorption, Metabolism, and Excretion Elemental mercury readily vaporizes at room temperature. When inhaled, elemental mercury vapor easily passes through pulmonary alveolar membranes and enters the blood, where it distributes primarily to the red blood cells, central nervous system (CNS), and kidneys. In contrast, less than 0.1% of elemental mercury is absorbed from the gastrointestinal tract after ingestion, so it has little toxicity when ingested. Only minimal absorption occurs with dermal exposure.[4] Elemental mercury in contact with tissue oxidizes to mercuric ion, which does not cross the blood-brain barrier well. On the other hand, when elemental mercury is converted to the mercuric form within the CNS, it is less able to diffuse out of the brain. Elemental mercury also crosses the placenta and concentrates in the fetus.[8] In adults, the half-life of elemental mercury is 60 days (range: 35-90 days); excretion is primarily fecal, though some is exhaled.

Toxicity At high concentrations, mercury vapor inhalation produces acute necrotizing bronchitis and pneumonitis, which can lead to death from respiratory failure. Fatalities have resulted from heating elemental mercury in inadequately ventilated areas. Long-term exposure to mercury vapor primarily affects the CNS. The "Mad Hatter," a character in the book *Alice in Wonderland*, was based on the brain disease that commonly affected hat makers who used liquid mercury as a treatment for hat felt. Early nonspecific signs include insomnia, forgetfulness, loss of appetite, and mild tremor and may be misdiagnosed as psychiatric illness. Continued exposure leads to progressive tremor and erethism, a syndrome characterized by red palms, emotional lability, and memory impairment. Salivation, excessive sweating, and hemoconcentration are accompanying autonomic signs. Mercury also accumulates in kidney tissues, directly causing renal toxicity, including proteinuria or nephrotic syndrome. Isolated renal effects may also be immunologic in origin.

Mercury exposure from dental amalgams has provoked concerns about subclinical or unusual neurologic effects ranging from subjective complaints, such as chronic fatigue, to demyelinating neuropathies, including multiple sclerosis. Although amalgam fillings have been suspected of causing clinical toxicity since they were introduced, studies have been hampered by insensitive analytic techniques and idiosyncratic outcome measures. Although dental amalgams are a source of mercury exposure and are associated with slightly higher urinary mercury excretion,[9-11] there is no scientific evidence of any measurable clinical toxic effects other than rare hypersensitivity reactions.[12] An expert panel for the National Institutes of Health has concluded that existing evidence indicates dental amalgams do not pose a health risk and should not be replaced merely to decrease mercury exposure.[13] A controlled trial of amalgam versus glass ionomer with long-term developmental follow-up is currently being conducted, but the results will not be available for several years.

Inorganic Mercury Compounds

Sources Inorganic mercury compounds (salts) have antibacterial, antiseptic, cathartic, and diuretic properties. Examples of inorganic mercury salts are mercurous chloride (calomel) and mercuric oxide. Inorganic mercury has been used in a number of consumer products ranging from teething powders to skin lightening creams, but its use has been banned in the United States. These products are still available on the world market, however.

Absorption, Metabolism, and Excretion Although only about 10% of an ingested mercury salt is absorbed, ingested mercury salts tend to be extremely caustic. A small amount of dermal absorption occurs as well. In adults, the half-life is about 40 days. Excretion is mostly fecal, but with chronic exposure, urinary excretion is somewhat greater.

Toxicity Absorption of ingested mercury salts can be fatal. Ingestion is usually inadvertent or with suicidal intent. Gastrointestinal ulceration or perforation and hemorrhage are rapidly produced, followed by circulatory collapse. Breakdown of intestinal mucosal barriers leads to extensive mercury absorption and distribution to the kidneys. Mercury salts are very toxic to the kidneys, causing acute tubular necrosis, immunologic glomerulonephritis, or nephrotic syndrome. Central neuropathy can also occur from mercury salt exposure. Acrodynia (painful extremities), also known as pink disease, seems to be a hypersensitivity response to mercury and was initially reported among infants exposed to calomel teething powders containing mercurous chloride[14] (cases also have been reported in infants exposed to the organic mercury compound phenylmercury used as a fungicidal diaper rinse[15] and in children exposed to mercury in interior latex paint[16,17]). A maculopapular rash, swollen and painful extremities, peripheral neuropathy, hypertension, and renal tubular dysfunction develop in affected children. Individual susceptibility is poorly understood.

Organic Mercury Compounds

Sources Organic compounds include methylmercury, ethylmercury, and phenylmercury. All 3 of these agents have been produced as industrial compounds, primarily as biocides, and some have been marketed as pesticides. Organic mercury compounds are also found in 2 once-common household antiseptics: Mercurochrome (merbromin) and Merthiolate (thimerosal). Methylmercury is the best known, because it is the predominant form of organic mercury found in the environment. Generally, methylmercury in the environment is formed by microorganisms from elemental mercury deposited from the air or discharged into water from natural or human sources. Consumption of fish is the primary route of exposure to organic mercury for children older than 1 year. The methylmercury content of fish varies by species and size of fish and harvest location. The top 10 commercial fish species (canned tuna, shrimp, pollock, salmon, cod, catfish, clams, flatfish, crabs, and scallops), which represent about 85% of the seafood market, contain a mean mercury level of approximately 0.1 μg/g. Methylmercury has been used as a fungicide on seed grains and is also an industrial waste. When grain accidentally treated with a mercury fungicide was eaten by people in Iraq during a famine in the 1970s, mercury poisoning occurred in hundreds of people.[18]

Ethylmercury, in the form of thimerosal, was formerly used as a topical antiseptic and has also been used as an effective preservative for killed vaccines and other biological agents for medical therapy. Thimerosal contains 49.6% mercury by weight and is metabolized to ethylmercury and thiosalicylate. Before fall

1999, there was 25 μg of mercury in each 0.5-mL dose of most diphtheria and tetanus toxoids and acellular pertussis vaccines as well as some *Haemophilus influenzae* type b, influenza, meningococcal, pneumococcal, and rabies vaccines. In addition, there was 12.5 μg of mercury in each dose of the hepatitis B vaccine. The reference doses* established by federal agencies were between 0.1 and 0.4 μg/kg/d.[6,19] Assuming that the toxicity of ethylmercury is similar to that of methylmercury, the exposure from a single vaccination could potentially exceed federal guidelines for that day and, with routine immunization, a cumulative dose of up to 75 μg of mercury by 3 months of age and 187.5 μg by 6 months of age could have been received. As a precautionary measure, the Academy, along with the American Academy of Family Physicians, the Advisory Committee on Immunization Practices, and the US Public Health Service issued a joint recommendation that thimerosal be removed from vaccines as quickly as possible.[2,20] Currently, all vaccines in the recommended childhood immunization schedule do not contain thimerosal as a preservative.

In the United States, phenylmercury (phenylmercuric nitrate or acetate) was used in latex paint as a pesticide (to prevent mildew growth on walls) and as a paint preservative (to prevent paint discoloration from growth of microorganisms). Phenylmercury and ethylmercury continue to be used as bacteriostatic agents for various topical pharmacologic preparations. Dimethylmercury, a form of organic mercury used only in research laboratories, is highly toxic, causing death after extremely small exposures.[21,22] Thimerosal used to irrigate the external auditory canals in a child with tympanostomy tubes has caused severe mercury poisoning.[23]

Absorption, Metabolism, and Excretion Most organic mercury compounds are readily absorbed by ingestion and inhalation and through the skin, except for phenylmercury, which is not well absorbed after ingestion or dermal contact. In general, organic mercury compounds are lipid soluble, and 90% to 100% is absorbed from the gastrointestinal tract. They appear in the lipid fraction of blood and brain tissue. Organic mercury readily crosses the blood-brain barrier and also crosses the placenta. Fetal blood mercury levels are equal to or higher than maternal levels. Methylmercury appears in human milk. The mean half-life for methylmercury in blood is 40 to 50 days (range: 20-70 days) for adults.[3,24] Ninety percent of methylmercury is excreted through bile in feces. Phenylmercury is rapidly metabolized. Its effects are similar to those of mercury salts.

Toxicity The toxicity of organic mercury compounds is dependent on specific compound, route of exposure, dose, and age of the person at exposure. Organic mercury compounds are most toxic in the CNS, though the kidneys and immune system may also be affected.[3,4,25] Generally, methylmercury and ethylmercury are more toxic than phenylmercury, because they are metabolized more slowly in vivo. Signs of toxicity from acute exposure progress from paresthesias and ataxia to generalized weakness, visual and hearing impairment, and tremor and muscle spasticity to coma and death.

In the developing brain, methylmercury is toxic to the cerebral and cerebellar cortex, causing focal necrosis of neurons and destruction of glial cells. Methylmercury is a known teratogen in the fetal brain; it interferes with neuronal migration and the organization of brain nuclei and layering of the cortical neurons. In the Minamata Bay disaster and the Iraq epidemic, mothers who were asymptomatic or showed mild toxic effects gave birth to severely affected infants. Typically, infants appeared normal at birth, but psychomotor retardation, blindness, deafness, and seizures developed throughout time.[24]

Because the fetus is more susceptible to the neurotoxic effects of methylmercury, investigators have sought to identify subclinical effects among children whose mothers' diets include large amounts of methylmercury and whose levels are higher than are commonly seen in the United States. There have been 3 extensive studies, including the Iraq seed grain cohort and 2 prospective epidemiologic studies, 1 in the Seychelles and 1 in the Faroe Islands. The Iraq study involved higher exposures and less sensitive measures of neurodevelopmental outcome, compared with the other 2 studies. In that study, motor retardation was seen in children whose mothers had hair mercury levels in the range of 10 to 20 parts per million (ppm).[18,24,26]

Studies were conducted in the Faroe Islands and Seychelles to obtain a prospective measure of mercury exposure to and toxicity in children. These 2 studies are providing important information for assessing the hazards of oral methylmercury exposure to children. The Faroe Islands are located southeast of Iceland in the Norwegian Sea. They are inhabited by a homogeneous and isolated population of people who consume small amounts of fish (1-3 meals of cod per week) and have episodic feasts of pilot whale. The fish have very low mercury concentrations, but pilot whale meat has a mean content of methylmercury of 1.9 ppm. The Faroe Islands study enrolled 700 mother and infant pairs at birth and monitored mercury levels in mothers' hair and cord blood, children's hair at 12 and 84 months of age, children's blood at 84 months of age, and neurodevelopmental measures of multifocal, domain-related effects in children at 84 months of age.[27] The Seychelles are equatorial islands in the Indian Ocean inhabited by a stable, cohesive, and homogeneous population of people who eat fish frequently (mean, 12 fish meals per week). The fish have relatively low methylmercury concentrations (mean, < 0.3 ppm). The Seychelles study enrolled 740 mother and infant pairs at birth and monitored mercury levels in mothers' hair and in children's hair at 6, 19, and 66 months of age as well as standardized measures of global neurobehavioral function of children at these times.[28]

There are important similarities and differences between the 2 studies. Both studies included a range of oral mercury exposures that are very relevant to the US population. Mean mercury levels in mothers' hair were 6.8 ppm (range: 0.5-27 ppm) in the Seychelles and 4.3 ppm (range: 0.2-39.1 ppm) in the Faroe Islands. There are no population-based data for the United States, but most US population samples that have been analyzed fall below 1 ppm. The pattern of methylmercury consumption is different, with the Seychelles pattern being more constant and the Faroe Islands pattern being more episodic. Also, pilot whales consumed in the Faroe Islands contain not only methylmercury but also polychlorinated biphenyls (PCBs), which are known to have an adverse effect on neurodevelopment of children.[29] The Faroe Islands study included measurements of PCB levels and controlled for PCBs as a potential confounding variable in addition to variables controlled for in both studies.

Results from the Faroe Islands study suggested that exposure in utero to mercury at lower levels is associated with subtle adverse effects on the developing brain (highest mercury levels in hair and cord blood were 39.1 ppm and 351 parts per billion, respectively). Memory, attention, and language tests were inversely associated with higher methylmercury exposures in children up to 7 years of age, even after controlling for PCB exposures.[27] Motor function and visual spatial ability were less clearly associated with methylmercury exposure. Adverse effects on development or IQ have not been found in the Seychelles study at up to

66 months of age, although exposures were in the same range as the Faroe Islands study.[28]

A workshop convened by the White House in 1998 found that the Seychelles and Faroe Island studies were well-conducted prospective cohort studies that included appropriate measures of exposure to methylmercury and sensitive developmental endpoints.[30] The workshop noted differences between findings in the studies in that, to date in the Seychelles study, effects have not been observed, whereas in the Faroe Islands study, effects have been observed at the same dosage levels. There are a number of potential explanations for this difference, including episodic versus continuous exposure, ethnic differences in response to methylmercury, or lack of common endpoints in the 2 studies as well as other differences, for example, lifestyle, nutrient intake, or contaminants found in seafood. Both studies measured and could control for a number of important lifestyle factors (ie, smoking, breastfeeding, alcohol use, and socioeconomic status). The Faroe Islands and Seychelles studies are continuing to follow the children throughout time and intend to provide a long-term developmental evaluation. In 1998, Congress directed the National Academy of Sciences (NAS) to carry out a study of methylmercury toxicity to provide recommendations on exposure limits.[19] The study was completed in June 2000 and concluded that, at this time, results of the Faroe Islands study should be used to establish a reference dose for mercury of 0.1 μg/kg/d.

One question that is raised by the difference in findings between the Seychelles and Faroe Islands studies is whether bolus doses of methylmercury administered during sensitive time periods are more likely to cause neurodevelopmental damage than the same doses given cumulatively throughout a time period of several months. This is an issue that needs to be further evaluated in epidemiologic studies or toxicity experiments, because it cannot be resolved within these 2 studies alone.

Ethylmercury, although it may have similar toxicity to methylmercury, has been less studied. When vaccines containing thimerosal have been administered in recommended doses, hypersensitivity has been noted.[31] Very high exposures to thimerosal-containing products—as components of intramuscular injections, used for painting omphaloceles, as a preservative in γ-globulin administered at high-doses or for a long period of time, or as intentionally ingested—have resulted in toxicity, including acrodynia, chronic mercury toxicity, renal failure, and neuropathy.[32-36] In an assay of chronic effects in rats, ethylmercury exposure resulted in renal and neurotoxicity in mature rats similar to exposure to methylmercury.[37] Follow-up studies in infants on the neurodevelopmental toxicity of ethylmercury in vaccines were done by the Centers for Disease Control and Prevention (CDC) using data from the Vaccine Safety Datalink project. The first study, which was based on the medical records of 2 managed care organizations, indicated some correlation between the amount of mercury received in vaccines and the reported diagnoses of language delays, speech delays, attention-deficit/hyperactivity disorder, unspecified developmental delays, and tics. A subsequent study of the medical records from a third managed care organization failed to find these correlations. These 2 studies used data not collected to evaluate these specific hypotheses and were not conclusive. Additional studies are now in progress to further evaluate this issue.[38] However, although such postmarket studies can provide information about the occurrence of frank developmental delays, they would not be expected to detect small subclinical alterations in cognitive function that were reported in the Faroe Islands study.

Phenylmercury is less toxic than methylmercury and ethylmercury. Exposure to phenylmercury has resulted in acrodynia in about 1 per 1000 exposed children. When phenylmercuric acetate was used as a fungicide in latex paint, children who were heavily exposed to painted rooms developed severe acrodynia.[16,17] Consequently, this compound is no longer used in latex paints in the United States.

DIAGNOSIS OF MERCURY POISONING

Diagnosis of mercury poisoning is usually made by obtaining a complete history and performing a physical examination. In addition, laboratory tests may demonstrate increased mercury levels. Background blood mercury levels, however, do not exclude mercury poisoning, because it has a relatively short half-life in blood.

Elemental Mercury

Increased mercury vapor concentrations can be measured in exhaled air from people with dental amalgams, but the biological significance is uncertain. Also unclear is the significance of the slight increase in urinary mercury excretion detected after dental amalgams are placed.

Inorganic Mercury

Inorganic mercury exposure can be measured by determining urinary mercury concentration, preferably using a 24-hour urine collection. Results greater than 10 to 20 μg/L are evidence of excessive exposure, and neurologic signs may be present at values greater than 100 μg/L. However, urinary mercury concentration also does not necessarily correlate with chronicity or severity of toxic effects, especially if the mercury exposure has been intermittent or variable in intensity. Whole blood mercury concentration can be measured, but values tend to return to normal (20 μg/L) within 1 to 2 days after the exposure to metallic mercury vapor ends.

Organic Mercury

Although methylmercury can be measured in blood or hair specimens, collection of specimens requires special mercury-free collection materials and rigorous control of contamination. Such testing is usually conducted in a research setting. In the general population, the mercury level in hair is usually 1 ppm or less.

TREATMENT

The most important and most effective treatment involves identifying the mercury source and ending the exposure. Children who have had mercury poisoning should undergo periodic follow-up neurologic examinations by a pediatrician.

Elemental and Inorganic Mercury

Mercury accumulates in the blood, CNS, and renal tissues and is very slowly eliminated. Severe or symptomatic mercury poisoning can be treated by chelation therapy, but whether it decreases toxic effects or speeds recovery in people who have been poisoned is unclear. Indications for chelation therapy after mercury intoxication are not firmly established.[39] However, chelation therapy is typically reserved for those with

evidence of a large mercury burden demonstrated by biological monitoring (eg, measurement in hair, urine, or blood) or clinical manifestations of severe poisoning. Elimination of elemental and inorganic mercury is greatly enhanced by chelating agents, including succimer, D-penicillamine, and dimercaptopropanesulfonate. Chelating agents increase urinary mercury excretion, but their efficacy is uncertain. Severe mercury poisoning should be treated by or in consultation with a physician who has experience in this area.

Organic Mercury

There is no chelating agent approved by the FDA that is effective for methylmercury or ethylmercury poisoning. Chelation has been used in cases of severe intoxication. Compared with other forms of mercury, organic mercury is significantly more resistant to removal from the body. Moreover, chelation therapy for organic mercury intoxication can be harmful; the agent dimercaprol appears to increase brain mercury concentrations and is contraindicated in the treatment of organic mercury poisoning. The chelator proven to be most effective in the treatment of severe organic mercury poisoning is succimer.[40] Recent data have also identified a role for the drug N-acetylcysteine in the chelation therapy for methylmercury poisoning.[41]

PREVENTION

Many mercury compounds are no longer sold in the United States. Organic mercury fungicides, including phenylmercury (once used in latex paints), are no longer licensed for commercial use. Electronic equipment has replaced many mercury-containing oral thermometers and sphygmomanometers in medical settings. Inorganic salts have limited use as antiseptics, although thimerosal is still available. Recently, the American Hospital Association agreed to phase out mercury use by its members. The purpose is to prevent pollution from mercury emissions from medical waste incinerators, because most of the mercury that is used in hospitals is likely to end up in the waste stream.

The amount of mercury in a single thermometer is usually insufficient to produce clinically significant exposure when ingested. However, the vapor can be absorbed; children, therefore, should not play with metallic mercury. Sporadic cases of acrodynia have resulted from children playing on carpet contaminated by metallic mercury. Once a carpet is contaminated, cleanup can be very difficult, and contaminated carpeting usually must be discarded. In the event of an elemental mercury spill, it is advisable to use a mercury spill kit. If no spill kit is available, parents can use paper to clean the spill, disposing of the material in 2 plastic bags. Vacuuming, which only disperses and volatizes the metal droplets, should be avoided. A parent can call local or state environmental health agencies for assistance. If a significant spill occurs, for example, several cubic centimeters, then consultation with a certified environmental cleaning company is advised.

Most regulatory standards and advisories pertain to the workplace. The Environmental Protection Agency (EPA) has established a standard limit for mercury in drinking water of 2 μg/L, and the FDA has established a standard limit for mercury in bottled drinking water of 2 μg/L. Although there are no regulatory standards for home air, the Agency for Toxic Substances and Disease Registry (ATSDR) suggests that acceptable residential air mercury levels should not exceed 0.05 $\mu g/m^3$.[42]

In recent years, several agencies have been working toward reducing methylmercury exposure via food consumption. Guidelines for maximum exposure to mercury have been established by the EPA at

0.1 μg/kg/d,[6] by the FDA at 0.4 μg/kg/d,[43] and by the ATSDR at 0.3 μg/kg/d.[44] These 3 guidelines, which were developed before publication of NAS recommendations, are based on extrapolations from blood or hair concentrations of mercury in pregnant women and information about the pharmacokinetics of methylmercury to calculate maximum daily oral intakes of methylmercury during pregnancy that were not associated with measurable adverse outcomes in children. These guidelines are not a "bright line" above which levels are dangerous and below which they are safe. Rather, they incorporate uncertainty factors that attempt to ensure a margin of safety between the guideline level and the level at which there would be any harm. The differences in guidelines reflect differences in the studies chosen for calculations of allowable doses as well as differences in judgment about the degree of uncertainty ascribed to variability within the human species. All 3 agencies attempted to incorporate all of the available scientific data. The Iraq study formed the primary basis for the FDA and EPA assessments, which were conducted before publication of the other 2 studies. The 1999 ATSDR assessment was primarily based on the Seychelles study. The NAS recommendation to adopt a reference dose of 0.1 μg/kg/d is under consideration by all 3 agencies.

In March 2001, the CDC reported levels of mercury in blood and hair in a representative sample of the US population.[45] The geometric mean blood mercury levels were 0.3 μg/L for children 1 to 5 years old and 1.2 μg/L for women 16 to 49 years old. Hair mercury levels followed a similar pattern. These mercury levels are primarily a measure of methylmercury. Although the survey could not estimate levels in children with unusual exposure patterns (like high consumption of mercury-contaminated fish), the CDC concluded that children in the general population are well within a safe range for methylmercury exposure. However, the CDC noted many women of childbearing age have mercury levels that are of concern for exposure to the fetus, highlighting the need to reduce methylmercury exposures among women in the general population.

The FDA has set an advisory limit for methylmercury in commercial fish of 1 ppm (1 μg/g)[46] (http://www.cfsan.fda.gov/~dms/mercury.htm). Also in March 2001, the FDA recommended that pregnant women and women of childbearing age should avoid consumption of shark, mackerel, swordfish, and tilefish. Other persons (including children and nursing mothers) should limit consumption of shark, swordfish, and other fish that contain more than 1 ppm mercury to no more than about 7 ounces per week (about 1 serving). For other types of fish, including tuna, the FDA has advised that consumption by children and pregnant women be kept below 12 ounces per week.[47] In some areas of the United States, certain fresh water species (eg, walleye, pike, muskie, and bass) have higher levels of mercury that would result in higher mercury intakes from a meal of fish. Most state health agencies advise limiting intake of freshwater sport fish having mercury concentrations of more than 0.2 to 1 ppm. Current state fish consumption advisories can be found on the EPA Web site (http://www.epa.gov/OST/fish/).

The risks of exposure to methylmercury from fish have to be balanced with the health benefits of eating fish. Fish is a source of high-quality protein as well as unsaturated fatty acids and other beneficial nutrients. For some populations, locally caught fish may be the only good alternative for a nutritious diet. If fish with lower mercury levels are available, then it is prudent to substitute these rather than eat fish that have methylmercury advisories or commercial fish, such as swordfish and tuna, which are known to have higher mercury levels.

As a precautionary measure, ethylmercury in vaccines is being reduced or eliminated from vaccine preparations as quickly as manufacturers can alter their production processes and obtain FDA approval for the

reformulated materials. Currently, all vaccines in the recommended childhood immunization schedule do not contain thimerosal as a preservative.

Newer enclosed methods for preparing mercury amalgams have decreased the likelihood of mercury spillage and exposure during dental amalgam preparation. Although Sweden has banned amalgam for use as a dental restorative and other northern European countries are considering doing so, to date, the conclusion in the United States is that the risks are very low and that the available substitutes are not superior. There are a variety of materials, such as composite resins, stainless steel, and gold that do not contain mercury and are approved for use in dental restorations in children. In the specific case of large caries on the occlusal surfaces of molars that do not require a gold or steel crown, there are 4 composite resins currently accepted by the American Dental Association.[48] The chief disadvantage of the resins is their decreased long-term stability. Successful restoration of caries is very dependent on technique, and most dentists have far less experience with these materials than with amalgam. Resins probably do not last as long as amalgam, even when placed expertly. Median life for amalgam fillings is approximately 15 years, whereas composites reportedly last 4 to 5 years.[48] As with amalgam, no long-term studies have been done on composites other than those on their performance as dental material. If parents are extremely concerned about the issue, they can take their children to a dental center that uses resins in children on a regular basis. Because of technique sensitivity, restorations done by inexperienced practitioners may lead to early failure with subsequent loss of tooth material and the possibility of infection and tooth loss. The safety of the chemicals used for resin has not been established in children.

CONCLUSIONS

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1. Mercury in all of its forms is toxic to the fetus and children, and efforts should be made to reduce exposure to the extent possible to pregnant women and children as well as the general population. Pediatricians can contribute to the effort of decreasing the amount of mercury in the waste stream by phasing out mercury-containing devices, such as thermometers and sphygmomanometers, from their offices and other medical facilities and encouraging parents to remove mercury thermometers from their homes.
2. Inorganic and elemental mercury should not be present in the home or other environments of children. Pediatricians need to be aware of traditional folk uses of mercury like in Santeria or in ethnic remedies and work sensitively with such families, who may initially be unwilling to discuss such factors with physicians and with people outside of their cultural group. Public health agencies, community organizations, pediatricians, and other child health providers should work together to identify the diverse cultural practices that may lead to mercury exposure.
3. The most important source of methylmercury exposure is fish consumption by the mother before or during gestation and by young children. Parents can reduce methylmercury exposure to their children by limiting the amount of fish with high mercury content consumed during pregnancy and lactation and amounts eaten by children. Recreational and subsistence fishers need to heed warnings and advisories from state health departments not only about mercury but also about other contaminants, such as PCBs, in fish.
4. As part of an ongoing review of biological products in response to the Food and Drug Administration

Modernization Act of 1997, the FDA is reviewing the use of mercury in biological products and pharmaceutical preparations. It would seem prudent for the FDA to carefully examine all uses of mercury in pharmaceuticals, particularly pharmaceuticals that are used by infants and pregnant women. The FDA is working with the pharmaceutical industry and the medical community to decrease or eliminate exposures to mercury in vaccines and other products.

Lynn R. Goldman, MD, MPH

Staff

Lauri A. Hall

FOOTNOTES

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

* A reference dose is a dosage of a chemical that has been determined to be safe on the basis of available toxicity information. Reference doses are used to provide a basis for establishing safety standards and guidelines.

ABBREVIATIONS

FDA, Food and Drug Administration; CNS, central nervous system; ppm, parts per million; PCBs, polychlorinated biphenyls; NAS, National Academy of Sciences; CDC, Centers for Disease Control and Prevention; EPA, Environmental Protection Agency; ATSDR, Agency for Toxic Substances and Disease Registry.

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