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Methylmercury and Pregnancy

Volume 12, No. 3, July 2005

Mercury is a naturally occurring substance that exists in a variety of chemical forms.

Elemental (inorganic) mercury is found in thermometers and dental amalgams. Mercury vapor (inorganic) is produced by the burning of fossil fuel, or by volcanic eruption, and is dispersed widely in the atmosphere. It is returned to the Earth's surface via rainwater and undergoes biosynthesis in aquatic environments to become organic mercury, also called methyl mercury (MeHg). Small fish consume the deposited MeHg and bioaccumulation occurs up through the food chain. This issue of Risk Newsletter focuses on the reproductive risks of MeHg mercury. See Risk Newsletter Volume 8 (3) for a reproductive review regarding elemental mercury.

Historical Perspective

High doses of MeHg can cause harmful neurological effects. In adults, MeHg acts on the central nervous system causing an initial sensation of "pins and needles," which may further progress to ataxia, dysarthria, constriction of the visual fields, and hearing loss. The phenotype and insight into effects on fetal development have been documented following various adult MeHg poisonings.

In 1953 it was reported that villagers in Minimata, Japan developed neurological disease following high level exposure to MeHg. A factory located near Miniamata Bay had dumped their inorganic mercury waste into the bay. It was eventually estimated that the amount of mercury dumped exceeded 100 tons (Tedeschi, 1982). Fish consumed the MeHg and the villagers' diet largely consisted of the contaminated fish. Residents experienced ataxia, sensory/motor impairment, speech impairments and visual disturbances (Tedeschi, 1982). There were about 380 confirmed cases of MeHg poisoning with 52 fatalities (Tedeschi, 1982). Additionally, pregnant women consuming the contaminated fish gave birth to infants with cerebral palsy, mental retardation, and seizures. This condition is sometimes referred to as Congenital Minimata Disease.

In 1971, another epidemic of MeHg poisoning occurred in Iraq when grain treated with MeHg as an antifungal agent was mistakenly ground into bread and eaten directly instead of being planted (Moienafshari, 1999). Some 6000 persons were admitted to the hospital and there were over 450 deaths (Clarkson, 2002, Tedeschi, 1982). Again the offspring of pregnant women were noted to have higher rates of microcephaly, cerebral palsy, and sensory impairments.

Based on this Iraqi population, a 5% risk for neurological damage was suggested following mercury levels of 10-20 ug/g in maternal hair. This should be viewed as a tentative estimate since many children born to women with hair levels >100 ug/g had normal outcomes and a more sophisticated re-analysis suggested no adverse neurological damage with maternal hair < 80 ug/g (Bellinger, 2003). In comparison, the average United States diet results in maternal hair concentrations of less than 1 ug/g (McDowell, 2004, Davidson, 2005)

In both the Japan and Iraq populations, neurological disease was noted in children born to mothers with only mild, transient paresthesias (or no signs at all) suggesting a heightened fetal sensitivity (Bellinger, 2003).

Recent population studies

Populations in archipelago environments in which diets consist largely of fish have made possible longitudinal prospective studies of MeHg exposure in non-poisoning situations. While levels of MeHg were comparable between studies, disparate results have made it difficult to draw conclusions regarding safety threshold levels.

The Faroe Islands cohort included 917 children enrolled between 1986 and 1987 who were then evaluated at 7 years of age for cognitive deficits (Grandjean et al., 1997). Pilot whale meat is a staple food in this population and the main source of MeHg exposure. Mercury concentrations were measured in both cord blood and maternal hair (mean 4.27 ug/g). All analyses were carried out using MeHg concentrations from cord blood.

Clinical examination and neurophysiolocial testing did not reveal any obvious mercury related anomalies. However, following multiple regression analysis 9 out of 20 neuropsychological measures showed mercury-associated deficits. Deficits were most apparent in measures of language, attention, and memory, with fewer effects seen in domains of visuospatial and motor functioning.

Of note, they saw effects even when they excluded children with maternal hair mercury concentrations above 10 ug/g. Fish in the Seychelle Islands have similar MeHg concentrations as do fish in the United States, however, fish consumption is greater with an average of 12 weekly fish meals versus one or less for the United States (Myers et al., 2003). The Seychelles archipelago cohort consisted of 643 mother-child pairs enrolled between 1989 and 1990. Prenatal exposure to MeHg was detemined by measuring total Hg in maternal hair during pregnancy. Children were followed for 9 years and evaluated for neurocognitive, language, memory, motor, perceptual-motor, and behavorial functions through specific testing. The authors controlled for caregiver IQ, socioeconomic status, and home environment stimulation. The mean prenatal total MeHg exposure was 6.9 ug/g.

Only 2 of 21 end points were associated with prenatal MeHg exposure, namely, improved scores on the hyperactivity domain of the Connor's teacher rating scale and decreased performance on the grooved pegboard non-dominant hand in males only. Based on further analysis, these findings were thought to be due to chance. The authors concluded that their study did not support the hypothesis that there is a neurodevelopmental risk from prenatal MeHg exposure resulting solely from ocean fish consumption (Myers et al., 2003).

While both studies are high quality with regard to methodology , there are several possible explanations for the incongruent results between the Faroe and Seychelle Island studies (Davidson, 2005). For example, sources of MeHg exposure differed; whale meat in the Faroe Islands and ocean fish in the Seycelle Islands. Pilot whale meat has much higher levels of mercury than other seafood and the blubber also contains more polycholorinated biphenyls (PCBs) and other chemicals.

Measurement procedures also differed between studies. Cord blood concentrations used in the Faroe Island cohort are indicative of concentrations only in the third trimester, whereas MeHg concentrations in maternal hair used in the Seycelle study indicate exposure throughout pregnancy.

This difference may reflect effects of episodic versus long-term exposure. The disparate results could also lie in population differences in genetic, nutritional, and social-environmental areas (Bellinger, 2003). Daniels et al. (2004) evaluated maternal fish consumption and very early offspring cognitive development in a cohort of 7421 British children born in 1991-1992. Mercury levels were measured in cord tissue in 1054 children. Maternal and child fish intake was assessed by patient questionnaire and developmental tests were performed at 15 and 18 months of age. Maternal fish intake was categorized into rarely or never, once per 2 weeks, 1-3 times per week, and 4 or more times fore week. The authors assumed the each fish meal averaged 4.5 ounces.

Maternal fish intake was associated with increased umbilical cord mercury concentrations but the overall cord mercury levels were low (median 0.01ug/g wet weight) and not associated with developmental outcomes. Maternal fish intake during pregnancy was actually associated with a subtle but consistently higher developmental scores for language comprehension and social activity compared to women who did not eat fish. The association was strongest for women eating fish, 1-3 times per week. The authors concluded that fish intake could subtly enhance early child development. However, it cannot be known from this study whether it was the fish consumption itself or an associated factor, such as an overall better diet or better caregiving, that contributed to the outcome.

FDA Advisory

The March 2004 advisory from the U.S. Food and Drug Administration (FDA) and the Environmental Protection Agency made the following recommendations for women who may become pregnant, pregnant women, nursing mothers, and young children:

·Avoid shark, swordfish, king mackeral, and tilefish (larger fish with longer life spans accumulate the highest levels of MeHg)

·Eat up to 12 ounces (2 average meals) of other cooked fish weekly

·Commonly eaten fish that are low in mercury include but are not limited to canned light tuna, shrimp, salmon, catfish, and pollock

·http://www.cfsan.fda.gov/~frf/sea-mehg.html contains mercury level listing of other fish

·Since albacore (”white”) tuna has more mercury than canned light tuna, when choosing two meals of fish and shellfish, eat up to 6 ounces (one average meal) of albacore tuna per week.

·Check local advisories about the safety of fish caught by family and friends in your local lakes, rivers, and coastal areas. If no advice is available, eat up to 6 ounces (one average meal) per week of fish you catch from local waters, but don’t consume any other fish during that week.

One weeks’ consumption does not significantly alter the body mercury levels so these are “on average” guidelines

Summary

Fish is an important source of protein and omega 3 fatty acids before, during, and after pregnancy. In order to accrue the benefits of fish but maintain lower mercury levels, an average of 12 ounces of certain fish per week is recommended. This FDA recommendation is thought to be conservative given the lack of consensus findings of adverse neurological effects with non poisoning situations. While MeHg can be measured in hair (chronic exposure) or blood (recent exposure), a risk assessment based on the results is unclear so routine pregnancy testing is not recommended.

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