Conf-950646--12
BNL-61542

Issues in the Assessment of Congenital Health Risks from Mercury in Coal

Frederick W. Lipfert
Department of Applied Science
Brookhaven National Laboratory
Upton, NY 11973

Lawrence Saroff
Clean Coal Technology Program
Office of Fossil Energy
U.S. Department of Energy
Washington, DC

Paul D. Moskowitz
Department of Applied Science
Brookhaven National Laboratory
Upton, NY 11973

This research was performed under the auspices of the United States Department of Energy under Contract No. DE-AC02-76CH00016

INTRODUCTION

The Clean Air Act Amendments of 1990 identify a list of toxic air pollutants for which emission limits are to be considered, including mercury compounds. Mercury (Hg) is one of the elements on this list for which adverse health effects have been convincingly demonstrated in the past, because of several unfortunate poisoning incidents. Hg is distributed throughout the environment as an air pollutant but, at current environmental levels, its toxic effects result mainly from ingestion of fish containing methylmercury (MeHg).[1] There are few permanent sinks for Hg in the environment and emissions from a given source may eventually be dispersed around the planet. Thus, adverse health effects must be considered on scales ranging from local to global.

This paper describes a probabilistic assessment of congenital neurological risks associated with consumption of fish and shellfish containing MeHg and the effects that local coal combustion might have on those risks. Two scenarios were considered with this model: the "baseline" scenario (MeHg from fish consumption without local impacts), and the "impact" scenario (baseline plus local power-plant impact on freshwater fish).

In this paper, we describe the framework and application of the model, including parameters and statistical linkages, the distributions used to represent the parameters, and the statistical methods used to characterize the inherent variability in each individual's diet and the distribution of individuals within a hypothetical population. These factors define the baseline, which is then compared to observations of MeHg in hair in order to demonstrate the model's validity. The incremental effect of local coal combustion is represented by augmenting the distribution of Hg in local freshwater fish by a prescribed amount, which we refer to as the "impact factor." Conventional air pollution dispersion modeling is then used to relate this factor to an appropriate range of powerplant characteristics.

This model framework is intended to retain all the elements of heterogeneity in the human and fish populations, while limiting the variability introduced by poorly understood processes and parameters. For example, using the available data on the distributions of Hg in fish precludes the need to predict bioaccumulation factors, which vary greatly by type of water body, its chemistry, and the fish species of interest. Use of the impact factor effectively limits the effects of propagation of uncertainties from modeling plume dispersion, deposition, and overland transport on the final risk estimates. Instead, these uncertainties are combined into a joint uncertainty as to the exact definition of the power plant to which the impact estimates might apply. In that sense, the "impact" results are generic and do not relate to any specific situation. To establish the validity of the parameters and distributions used in the model, we compare the distribution of measured hair/blood Hg ratios to the distribution of hair Hg in a national sample of U.S. females. The distributions of adverse effects resulting from prenatal exposure are assessed from three different epidemiological studies that used Hg concentrations in maternal hair as an index of exposure. The model is then used to predict the distributions of congenital health risks for the baseline and impact scenarios, as applied to a hypothetical population of heavy fish-eaters in the Upper Midwest.

THE BNL MERCURY RISK ASSESSMENT MODEL

Table 1 summarizes the main elements of the risk assessment model that was developed during this project.[2,3] These elements were combined using the Monte Carlo computing package @RISK[4] with Latin hypercube sampling. The model produces distributions of selected parameters as output, based on operations and transformations performed on the input distributions. If a quantitative exposure-response relationship is available, the distribution of responses can be estimated as one of the outputs. Alternatively, if only discrete data on responses are available as a function of some exposure parameter, the distribution of those

DISCLAIMER

Portions of this document may be illegible in electronic image products. Images are produced from the best available original document.

exposures may be produced in order to facilitate a graphical or point-to-point comparison and hence the likelihood of specific risks.

Fish Consumption Rates and the Distribution of Baseline MeHg Intake

The U.S. population is exposed to MeHg principally through the consumption of fish; an estimated 95% of the U.S. population consumes some fish over the course of a year.[2] Hg deposited into water bodies is methylated and then bioconcentrated as it progresses up the food chain; the highest MeHg levels are found in large predatory fish. Rates of aquatic methylation processes and bioconcentration are typically very uncertain and depend on many factors, including type of water body, adjacent wetlands, pH, and fish species; use of the extant measurements of Hg in fish to establish the baseline removes these sources of uncertainty. In this assessment, the estimated increase in freshwater fish MeHg due to Hg deposition from the hypothetical power plant is assumed to be proportional to the change in local Hg deposition, since all other factors remain constant. Thus, the freshwater portion of the MeHg intake of the populations consuming locally-caught fish near the plant is assumed to increase in proportion to their freshwater fish consumption.

Fish consumption statistics from various sources[2] were used to estimate the population intake of MeHg, in conjunction with data on Hg levels in fish.[5] Surveys and national fishery statistics suggest that the overall average per-capita fish consumption rate in the United States is about 25 g/d (about 1 meal per week), with a 95th percentile level of about 80 g/d. Table 2 gives the statistics of the three dietary fish components assumed, which are based on log-normal distributions; freshwater fish provides the largest source of MeHg intake. However, in the risk assessment model, fish consumption was also linked with body mass and the mean baseline MeHg intake parameter was 0.032 ug/kg/day in terms of body mass. The mean intake parameter for the impact scenario was 0.055 ug/kg/day. Meals of tuna fish are assumed to have a uniform mass distribution from 26-130 g; all other fish portions are assumed to be vary uniformly between 100-300 g. The average correlation between the number of fish meals and body mass in this simulation was 0.66, which is higher than Richardson reported (personal communication, Dec. 1, 1994) from a survey in Canada. That survey only looked at total food consumption for all ages and found a linear correlation of about 0.33 with body mass. The lower correlation could have resulted in part from the nonlinearity introduced by including teenagers in the sample.

Metabolic processes

In contrast to both carcinogenic and irritant air pollutants, the dose* metric of practical concern for MeHg is neither the maximum rate of acute intake or the total accumulated intake but the equilibrium body burden that is attained as a balance between quasi-steady rates of intake and excretion. The concept of the "reference dose" (the amount that may be consumed over a lifetime without adverse consequences) would thus appear to be inappropriate here. The overall body burden of MeHg controls health responses and is directly related to measurable levels of MeHg in blood and hair. Because, as a practical matter with a normal diet, a high body burden of MeHg can only be obtained by eating fish more often, the averaging process that takes place with respect to individual dose increments obtained from eating disparate meals over time is an important feature of the pharmacokinetics. Monte Carlo simulations were used to develop an empirical model of this process, which is given by

$$\log(GSD) = -1.211 + 1.766 \log(GSD_0) + 0.5\log(f^*k) \qquad [1]$$

where GSD and GSD_0 are the geometric standard deviations of the original and modified fish Hg distributions, f is the frequency of consumption, and k is the elimination constant

---

*Although it is common in the literature to refer to the amount ingested as the "dose," strictly speaking, the term should be reserved to indicate the amount received by the target organ, in this case, the brain.

(ln[2]/half-life). The GSDs were reduced by about 40% at the mean with this relationship. Figure 1 shows how the (geometric) standard deviation of body burden decreases as the frequency of consumption increases; eating fish more often increases the mean body burden but reduces its variability. One measure of the suitability of this model may be made by comparing the variability of the simulation results with the variability of observations of blood and hair Hg. The observed data from various sources have geometric standard deviations (GSDs) ranging from 1.4 to 2.8; the equivalent values for body burden from our simulations were 1.74 and 2.05, depending on assumptions. Hattis and Silver[6] showed that the large observed variability in effects measured on hair Hg levels is more likely to be the result of heterogeneity in the population than measurement error. If metabolic averaging is not considered, typical MeHg intake GSD values obtained by combining the distributions of Hg concentration and fish consumption can exceed 3.0.[7] Important parameters in this model include the half-life of MeHg in the body and body mass, which are required to predict the equilibrium body burden of MeHg. Conversion to blood and hair concentrations requires other parameters: the fraction of Hg in blood, the volume of blood, and the hair-blood ratio. The nominal blood-body burden ratio was 0.7 with a GSD of 2.0. The distribution of hair/blood ratios was selected to match the 12 studies listed by the U.S. Environmental Protection Agency,[8] which had a weighted mean ratio of 276. A standard deviation of 67 provides a normal distribution that approximately matches the means of the lower 5% (139 vs. 140) and the upper 10% (391 vs. 367) of this set, which totals 921 values.

Power plant characteristics and atmospheric processes

The impact factor selected for this assessment corresponded to an approximate doubling of the background rate of atmospheric Hg deposition (10-20 ug/m^2/y), based on selected power plant characteristics and an annual precipitation rate of 1 m. The geographic setting for this analysis is assumed to be the upper midwestern United States (selected because freshwater fish consumption tends to be higher there). Our previous analysis of atmospheric deposition from power plants was based on estimated peak annual deposition from a hypothetical plant;[2] subsequent data on actual coal-fired power plants of 900-1100 MW_e provided by the U.S. Environmental Protection Agency (W. Peters, personal communication, December 1994) show that the previous estimates were high by about a factor of 3, when averaged across the surface of (hypothetical) water bodies or watersheds of 2-10 km diameter. As a result, the model impact analyses may be regarded as pertaining to a very large power plant (ca. 3000 MW_e) burning coal with average Hg content (0.08 ppm), or a modest-sized plant burning coal with the maximum Hg content found in recent testing, or intermediate combinations. The emission controls (electrostatic precipitator) were assumed to reduce the Hg emissions by about 10%. This results in an estimated total Hg emission rate of 0.180 kg/MW_e/y from the hypothetical plant, comprising elemental, reactive, and particulate Hg species. The reactive and soluble portion (Hg^{++}) was assumed to be 75%.[9] A Gaussian plume dispersion model (the EPA ISCLT-2 model) was used to estimate the local annual average air concentrations of the 3 species out to 50 km and deposition rates were estimated for each within 50 km, assuming flat terrain. These calculations were based on a 1000 MW plant with no wet flue gas clean-up. In modeling deposition, Hg speciation was important because of the variations in water solubility of the different Hg species. Dry deposition was modeled by assuming a value for the dry deposition velocity, defined as the ratio of the deposited flux to the air concentration. Wet deposition was modeled in two different ways, using either the washout ratio (ratio of concentration in precipitation to air concentration) or a dynamic plume depletion algorithm. The model indicates that only about 5-9% of Hg emissions are likely to deposit within the first 50 km of travel, depending on stack height; the balance is assumed to join the global Hg pool. At 50 km, the local Hg deposition from the plant would be about 1% of background levels. The effects of power plant Hg emissions on marine species were assumed to be proportional to their contributions to global background Hg. Assuming an average coal Hg content of 0.08 ug/g and annual coal use of 8×10^8 tons, the contribution of U.S. utilities to the global pool relative to all other Hg sources would be about 1%.[10] We thus assumed that the effect of U.S. utility coal burning on the Hg content of marine fish species is negligible.

The model predicted that this reactive Hg would deposit relatively close to the plant, where its impact may be maximized over a relatively small area (assumed to be a sportfishing lake). In the risk calculations, we combined the uncertainties of all the emissions, transport, and deposition processes and used an impact factor with a range from 50% to 200% (uniform probability distribution) deposition increase over global background. This range reflects the combined uncertainties of Hg emissions, atmospheric processes, and uptake by fish.

The importance of local Hg deposition is supported by measurements in various settings. Anderson and Smith[11] found an increase of about 33% in lake sediment Hg (but not in soil) due to the start-up of a nearby coal-fired power plant. Ferrara *et al.*[12] report the influence of anthropogenic Hg emissions on the local scale. Greenberg *et al.*[13] measured Hg deposition near a large municipal solid waste facility and found a pattern of increased wet deposition of Hg that resembles model predictions.[2]

RESULTS OF BASELINE SIMULATIONS

In order to confirm the suitability of the assumptions made in our model, comparisons were made with a set of hair MeHg concentration data first reported by Smith *et al.*[14] These data were obtained from a "demographically balanced" national sample of women of childbearing age in all 50 states and that had been assembled by the Market Research Corporation of America (MRCA). Hair samples were obtained from 1437 women and were analyzed for MeHg by gas chromatography. Food intake diaries were also completed and the average MeHg intake for the 1009 individuals reporting seafood consumption was about 1 ug/day. The highest recorded MeHg intake was 14.3 ug/d. In order to match this rate of MeHg intake, we deleted the freshwater fish portion of our intake diet distribution; this resulted in very good agreement. The relevant statistics of this simulation are compared to the sample data in Table 3 and the hair Hg frequency distributions are compared in Figure 2. The agreement is seen to be excellent, which validates the model parameter values selected to represent MeHg intake (except for freshwater fish) and the pharmacokinetics. It is also interesting that the observed distributions of MeHg in hair are similar for those who reported eating fish and those who did not.[14] Possible explanations for this unexpected finding include inaccurate diaries, other sources of MeHg, or confusion between Hg and MeHg peaks in the gas chromatography. Smith (personal communication, December 1994) reported a (log-log) correlation between hair Hg and dietary intake of about 0.59; we obtained a value of 0.53 from the simulation. We thus concluded that the baseline parameters selected for these simulations and their frequency distributions were consistent with the available observations.

Simulations were then performed for the cases of interest, with freshwater fish included in the dietary intake as described above. The statistics derived from these simulations are given in Table 4. Figure 3 compares the distributions of body burden and hair Hg as a function of dietary intake, as predicted for the baseline simulation case. Whereas body-burden Hg levels lie in a reasonably tight band, the scatter is greatly increased for hair Hg, varying by 2 orders of magnitude at a given intake level. This variability has important ramifications with regard to the prediction of risk estimates and the ability to develop accurate exposure-response data from observations. Note also that when these predictions are plotted against the number of meals consumed (Figure 3b), the scatter in body burden is reduced at the high end as a result of the metabolic averaging process. These plots confirm that the highest individual hair levels should not be expected to necessarily coincide with the highest individual body burdens or consumption rates, and thus are unlikely to relate to the presence of neurological effects on a 1:1 basis. This situation makes it difficult to fit an accurate exposure-response function to the data. As a further check on the interrelationships in the model, we compared correlations of the log of hair concentration with the MeHg intake per unit of body mass. The simulation produced a correlation coefficient of 0.41, which compares with a correlation of 0.32 between log(hair Hg) and the estimated frequency of fish consumption in the New Zealand data of Kjellstrom *et al.*[15]

These comparisons confirm that, even though hair Hg may be a reliable marker for individual MeHg exposure, the relationships between hair Hg and other measures of MeHg tend to be quite variable across a population. In support of this finding, Pocock *et al.*[16] observed that hair is an unreliable indicator for lead body burden, for example. Note also that the inability to reliably measure low Hg concentrations (below the detection limit) will inevitably adversely affect comparisons with predictions that are made on a logarithmic scale.

HEALTH EFFECTS OF METHYLMERCURY

The central nervous system is the principal target for MeHg, with the potential for effects on sensory, visual, and auditory functions as well as on the neurological development of the fetus; individuals may vary greatly in their responses and in the partitioning of mercury among organs and body storage compartments. This variability, especially the variability of the metabolic half-life of MeHg, then becomes very important in the estimation of the distribution of risks corresponding to a distribution of MeHg intake or to a proposed reference dose level. A probabilistic assessment of risks requires that the probability of exposure at a given level be combined with the probability of experiencing an adverse response at that level. The distribution of exposures generated by our simulation model must thus be matched with the appropriate exposure-response functions.

Previous papers have considered MeHg risks to adults.[2,3] This paper emphasizes effects on children arising from prenatal exposures. The available epidemiological data and their limitations are reviewed briefly; the paper then develops the appropriate distribution of MeHg exposure parameters for comparison with the exposure levels at which adverse effects have been demonstrated.

Health Risks from Prenatal Exposures to MeHg: Methods and Data

Three studies were found in the literature that provided quantitative data suitable for this portion of the assessment. A number of infants were exposed *in utero* during the Iraqi poisoned grain incident of 1971-2. Marsh *et al.*[17] examined 29 Iraqi children, age 4 1/2 to 5, and found that the mothers of the normal children had peak maternal hair Hg levels of 25 ug/g or less (corresponding roughly to average body burdens of 0.14 mg/kg or less). According to the authors, no specific threshold of effects could be identified because of the small sample; the threshold could have been as high as 85 ug/g. Cox *et al.*[18] reported on a much more elaborate analysis of 83 infant-mother pairs from this incident. The mean age of the children was 30 months at the initial interview. They considered frequencies of delayed walking, delayed talking, and of various neurological (CNS) signs. "Increased limb tone and deep tendon reflexes" were the most frequent CNS signs; these symptoms were also noted by Mckeown-Eyssen *et al.*[19] in Cree Indian children at lower maternal hair levels. Note that the definitions of "delayed" walking or talking were somewhat arbitrary and that exact birthdates were sometimes difficult to determine in this population. For this reason, the CNS data were used in our assessment. Cox *et al.* fit logistic and hockey-stick models to these data and developed a data smoothing technique that provided functions of arbitrary shape (Figure 4). The delayed walking and talking exposure-response functions showed a suggestive increase in response around 10 ug/g, with a more definitive rise at around 100 ug/g. The latter point corresponds roughly to the body-burden threshold noted previously for adults. However, the CNS function was more nearly continuous, with the initial rise in response at around 15 ug/g peak maternal hair concentration. The curve-fits to these data presented by Cox *et al.* suggested that, at peak maternal hair levels of 5 ug/g, the risks of CNS signs were about 1-2%, for example.[18]

McKeown-Eyssen *et al.*[19] studied a group of Cree Indians in Northern Quebec in 1978. A total of 247 children, ages 12 to 30 months, were identified in four communities known to have experienced high levels of MeHg exposure. The source was fish contaminated by industrial Hg

discharges. Hair samples were obtained from the mothers and a medical team examined each child for physical and neurological characteristics. The medical team was blinded to the exposure data. Confounding variables considered included amount of time spent "in the bush," maternal alcohol, tobacco, and caffeine consumption, mother's age, lactation, complications of pregnancy and numbers of previous pregnancies. The most frequent neurological finding was "abnormality of tendon reflex," in 13 boys and 14 girls. When combined with 2 cases of increased muscle tone, 15 "cases" were identified among the boys and a statistically significant (p=0.05) relationship was seen with prenatal Hg exposure, in the range from about 2-15 ug/g peak maternal hair concentration. There were no differences in the confounding variables between these 15 and the remaining 82 "controls." No other relationships were seen with Hg in boys, and these conditions were not associated with Hg exposure in girls. However, incoordination was negatively associated (p=0.07) with Hg exposure in girls. We find that this study offers only minimal support to the hypothesis that maternal hair levels around 10 ug/g are associated with deficiencies in childhood neurological development.

The most extensive data set currently available is that of Kjellstrom *et al.*,[15,20] who selected 73 New Zealand children whose mothers had the highest hair Hg levels during pregnancy, out of a cohort of some 11,000 births. These cases were matched with 164 controls whose mothers had lower hair Hg levels during pregnancy. The analysis then seeks to determine to what extent maternal hair Hg levels may predict the children's IQ at ages 6-7. We performed screening analyses that found 3 outliers (low IQ), and after removing these points, we found a marginally significant relationship (p=0.08) between WISC-R full-scale IQ and the log of average maternal hair Hg during pregnancy:

$$IQ = 0.33\ (\text{years in NZ}) + 0.37\ (\text{child's age}) - 4.7\ (\log[Hg]) + \text{dummy variables for island of origin.} \quad [1]$$

Similar regressions using the fish consumption index instead of log(Hg) were run; the fish consumption variable never achieved a *p* level below 0.25. An analysis of possible thresholds in the IQ exposure-response function suggested threshold values anywhere from 4-10 ug/g average maternal Hair Hg. A separate report[21] provides more details on the reanalysis of the New Zealand data.

Some of the problems with this study include the methods used to select "cases" (exposure rather than outcome), the lack of data on social class, and the possibility of postnatal exposures including exposures to other neurotoxins. Use of only the highest 0.7% of the hair Hg observations to define "cases" may place undue importance on whatever spurious high observations that may have occurred. Nevertheless, the New Zealand data imply that average maternal hair Hg levels above about 3-10 ug/g (4.5-15 ug/g as peak hair levels, based on a factor of 1.5 to convert from average hair Hg to peak Hg levels during pregnancy, as suggested by Kjellstrom *et al.*[15]) may carry the risk of a small decrement in the mental development of the offspring, as typically measured by IQ.

Although each of these studies has flaws, they all support the onset of children's neurological effects at average maternal hair levels around 10 ug/g. The curve-fits to the Iraqi data by Cox *et al.*[18] for CNS signs seem to provide the best quantitative basis for risk assessment.

Estimated Congenital Health Risks

The analysis of congenital health risks proceeds from the same simulations used previously for adults;[2,3] no changes in diet or body weight were assumed for pregnant females. All of the exposure-response information on congenital effects was keyed to maternal hair concentrations. Figure 5 presents the simulated hair MeHg distributions for the baseline and the impact cases, in conjunction with the simulation used previously to compare the model with data from a sample population of females of childbearing age whose intake of MeHg was considerably lower than assumed in this risk assessment.[14] We find that 99% of the average MeHg hair

concentrations are less than 4.5 and 8.1 ug/g for baseline and impact scenarios, respectively, and note that the difference in the two baselines, according to whether (predatory) fresh-water fish are consumed, is larger than the effect of the hypothetical power plant.

The New Zealand data on hair Hg afford an opportunity to compare an observed frequency distribution with the results of our simulation. If we assume that the 73 New Zealand "cases" comprise the upper end of a distribution of 10,930 people (the original cohort), a percentile of 0.67% is obtained at a concentration of 6 ug/g; our simulation predicted 0.46%, which is relatively close and suggests that the two populations may have similar hair Hg distributions. This also suggests that our hypothetical population would include heavy fisheaters, as did the New Zealand cohort.

Estimates of the probability of neurological effects due to prenatal exposure may be made by combining the probabilities of exposure with the probability of effects. Using the data tabulated by Cox *et al.*[18] at a peak maternal hair level of 5 ug/g, we estimated overall risk probabilities of 0.0002 to 0.0004 for the baseline case and 0.0008 to 0.0017 for the impact case. These risk estimates depend somewhat on the intersection point between exposure and response that is selected for evaluation, as well as on the type of curve-fit used to extrapolate the original exposure-response data. These risks are about an order of magnitude higher than the adult paresthesia risks predicted by Lipfert *et al.*[2] based on similar extrapolations, but are two orders of magnitude lower than the levels that are often cited as a "low effect level."[1]

Discussion of Prenatal Risks

This assessment indicates that the margin of safety for consumers of freshwater sportfish may be smaller for congenital effects from prenatal exposures (based on comparison of maternal hair levels) than for adult paresthesias. However, recent results from the Seychelles Islands Child Development Study[22,23] suggest that the margin of safety may actually be substantially larger than indicated by these older epidemiological studies. The Seychelles Study has reported no significant correlation between mean maternal hair total Hg levels (up to about 27 ug/g) and either the results of neurologic examinations at 6 months or with developmental tests at age 19-29 months. However, possible threshold relationships in these data were not evaluated. In addition, Crump *et al.*[24] reanalyzed the Iraqi data on delayed development and report a threshold of 114 ug/g peak maternal hair (with relatively wide confidence limits). Thus, ambiguity exists as to the true threshold for fetal exposure to MeHg. In addition, the clinical significance of the types of neurological effects that have been indicated is unclear.

Earlier we discussed the variability of hair concentrations in relation to blood and body burden levels. Although MeHg hair concentrations are a reliable indicator of exposure for any individual, the relationship between this indicator and fetal brain MeHg levels will vary considerably among individuals comprising a population. Use of hair Hg as the parameter by which exposure is compared to effects thus leads to well-known statistical difficulties, because of the inherent uncertainty in this supposedly error-free variable. Additional random error would be involved if there is a particular time during pregnancy when Hg exposure is critical. As discussed by Thomas *et al.*,[25] such errors may lead to attenuation of the slope of the exposure-response function (when the errors are normally distributed), but they can also obscure the true shape of the function, including the level of the threshold. Future epidemiology studies of congenital MeHg effects should thus strive to use additional maternal or fetal exposure metrics, such as umbilical cord blood concentrations, for example.

One way to place these results in context is by comparison with the (draft) NIEHS criteria identified as "tolerable methylmercury concentrations."[1] Table 5 presents this information, in which various criteria are contrasted with the upper 95th percentiles obtained from the simulations. Note that these criteria employ different parameters or indices of exposure for essentially the same objective: protection of the public from adverse health effects of methylmercury. The FDA set an "action limit" for MeHg in fish at 1 ppm, use of their

consumption rate estimates led to MeHg intakes less than 30 ug/d. Both baseline and impact simulation results are well within this criterion, by a factor of 5 for the baseline, for example.

The WHO "adult" blood and hair concentration criteria[10] are based on avoidance of adult paresthesia; the simulation results indicate wide margins of safety: approximately a factor of 20 for the baseline case. When exposures of pregnant females are considered, the margin for the baseline simulation is a factor of 4-8, which is consistent with the FDA fish Hg criterion. Similar margins of safety are seen with the EPA Lowest Observed Adverse Effect Level (LOAEL) but when this criterion level is reduced by an arbitrary factor of 10 to yield the EPA Reference Dose (RfD), we find no margin of safety, even for the baseline scenario.

The ostensible purpose of the factor of 10 used by EPA is to account for variations in observed effects that might result from considering populations larger than those that were available in the original epidemiology data bases, including "sensitive individuals." Presumably, this will protect against an outlier result occurring in a small sample. We would argue that the epidemiological data bases already contain sensitive individuals, since for example, Kjellstrom *et al.*[15] elected the 73 highest hair MeHg concentrations out of a cohort of 11,000. In addition, our simulation was designed to include subsistence fish-eaters as the upper tail of the distribution. To evaluate the problem of sample size, we ran the simulation model repetitively for blood, hair, and body burdens of MeHg and compared the predicted 99th percentiles for 50, 500, and 5000 trials. For our simulations, the largest difference in the 99th percentiles for n=50 and n=5000 was about 40%. Thus EPA's use of a factor of 10 for this purpose is conservative by about a factor of 7. Finally, we note from Figure 3 that essentially the entire range of effective MeHg intake levels only spans about a factor of 20. Thus, use of an arbitrary safety factor of 10 seems unduly conservative.

CONCLUSIONS

This paper has presented a probabilistic framework that seeks to faithfully represent the extant heterogeneity in MeHg while minimizing the effects that parameter uncertainty (i.e., ignorance) might have in unduly widening the confidence limits of the predicted neurological risks. Comparison of predicted and observed hair concentrations of MeHg shows agreement with the average magnitude and with the distribution of values. Use of measured levels of Hg in fish as a baseline obviates the need to predict detailed bioconcentration factors, which can be problematic.[8] Use of an arbitrary factor to represent the increase in local Hg deposition from coal combustion allows a range of possible plant designs, coal types, and atmospheric dispersion and deposition rates to be considered without specifically introducing these uncertainties into the analysis and thus unduly widening the uncertainty range.

Previous assessments found only trivial risks of neurological effects to adults who consume fish containing MeHg on a regular basis.[2,3] The situation is less clear cut with respect to the risks of prenatal exposure, in part because of the lack of data on reliable indicators of fetal exposures in the various epidemiological studies that are currently available.

The assessment found small but finite congenital neurological risks to a heavy fish-eating population, of the order of 10^{-3} to 10^{-4} at average maternal hair Hg levels around 5-10 ug/g, based on the results of three independent studies. The incremental effects of local coal combustion are of the same order as the uncertainty in the risk estimates. The simulations also suggest that maternal hair may not be the best exposure metric to use in population studies, because of its variable relationship with intake and body burden. However, a more recent epidemiological study failed to find significant effects of prenatal exposures at up to 27 ug/g in maternal hair. Pending complete reporting of the data from this and other contemporary epidemiological studies, pregnant females should be advised to exercise caution with respect to consumption of predatory freshwater sportfish.

Important uncertainties remain unresolved, including the role of dynamic changes in diet and seasonal variations (the model only simulates the beginning of fish consumption and the subsequent approach to equilibrium), validation of the distribution of MeHg in blood, possible linkages of half-life with body mass, and the appropriate mean value for MeHg half-life.[26]

ACKNOWLEDGMENTS

We thank Warren Peters of the U.S. Environmental Protection Agency for supplying plume dispersion calculations based on the ISCLT-2 model, and John C. Smith for supplying details of the MRCA hair Hg survey data.

REFERENCES

1. K.R. Mahaffey, NIEHS Report on Mercury (draft). National Institute for Environmental Health Sciences, January 25, 1993.

2. F. Lipfert, P. Moskowitz, V. Fthenakis, M. DePhillips, J. Viren, and L. Saroff, Assessment of Mercury Health Risks to Adults from Coal Combustion, BNL-60435, Brookhaven National Laboratory, May 1994.

3. F. Lipfert, P. Moskowitz, and L. Saroff, Probabilistic Assessment of Health Risks Due to Methylmercury from Coal Combustion: I. Model Framework and Demonstration, NeuroToxicology (submitted).

4. Palisade Corporation, @RISK Users Guide, Newfield, NY, 1988.

5. U.S. Environmental Protection Agency, National Study of Chemical Residues in Fish, EPA 823-R-92-008a, Office of Science and Technology, Washington, DC. 1992.

6. D. Hattis and K. Silver, Human Individual variability - A Major Source of Uncertainty in Assessing Risks for Noncancer Health Effects, Risk Analysis 14:421-31 (1994).

7. A.H. Stern, Re-evaluation of the Reference Dose for methylmercury and Assessment of Current Exposure Levels, Risk Analysis 13:355-64 (1993).

8. U.S. Environmental Protection Agency, Draft Mercury Study Report to Congress, Volume IV, Appendix C (1995).

9. R. Felsvang, R. Gleiser, G. Juip, and K.K. Nielsen, Air Toxics Control by Spray Dryer Absorption Systems, presented at the Second International Conference on managing Hazardous Air Pollutants, Washington, DC, 1993.

10. World Health Organization, Methylmercury, Environmental Health Criteria 101, Geneva, 1990. 144 pp.

11. W.L. Anderson and K.E. Smith, Envir. Sci. Tech 11:75-80 (1977).

12. R. Ferrara, B. Maserti, A. Petrosino, and R. Bargagli, Mercury levels in rain and air and the subsequent washout mechanism in a central Italian region, Atmos. Envir 20, 125-128 (1986).

13. A. Greenberg A *et al.*, Mercury in Air and Rainwater in the Vicinity of a Municipal Resource recovery Facility in Northwestern New Jersey, Proc. 1992 Int. Symp. on Measurement of Toxic and Related Air Pollutants, Durham, NC. Air & Waste Management Assoc., Pittsburgh, PA, 1992.

14. J.C. Smith, M.D. Turner, D.O. Marsh, Hair Methylmercury Levels in Women of Childbearing Age, Report on Project III to National Fisheries Institute, December 1985.

15. T. Kjellstrom, P. Kennedy, S. Wallis, A. Stewart, L. Friburg, B. Lind, T. Wutherspoon, and C. Mantell, Physical and Mental Development of Children with Prenatal Exposure to Mercury from Fish. Stage 2: Interviews and Psychological Tests at Age 6. Report 3642, National Swedish Environmental Protection Board, Solna, Sweden, 1989.

16. S.J. Pocock, M. Smith, and P. Baghurst. Environmental lead and children's intelligence: a systematic view of the epidemiological evidence. BMJ 309:1189-97 (1994).

17. D.O. Marsh, G.J. Myers, T.W. Clarkson, L. Amin-Zaki, S. Tikriti, and M.A. Majeed, Fetal Methylmercury Poisoning: Clinical and Toxicological Data on 29 Cases, Ann.Neurol 7:348-53 (1980).

18. C. Cox, T.W. Clarkson, D.O. Marsh, L. Amin-Zaki, S.A. Tikriti, and G. Myers, Dose-Response Analysis of Infants Prenatally Exposed to Methyl Mercury: An Application of a Single Compartment Model to Single-Strand Hair Analysis. Envir.Res 49:318-32 (1989).

19. G.E. McKeown-Eyssen, J. Ruedt, and A. Neims, Methyl Mercury Exposure in Northern Quebec II. Neurologic Findings in Children, Am.J. Epidem. 118:470-9 (1983).

20. T. Kjellstrom, P. Kennedy, S. Wallis, and C. Mantell, Physical and Mental Development of Children with Prenatal Exposure to Mercury from Fish. Stage 1: Preliminary Tests at Age 4. Report 3080, National Swedish Environmental Protection Board, Solna, Sweden (1986).

21. F.W. Lipfert, Congenital Health Risks from Methylmercury Associated with Coal Combustion, draft Brookhaven National Laboratory Report, December 1994.

22. P.W. Davidson, G. Myers, J. Sloane-Reeves, D. Marsh, C. Shamlaye, and T. Clarkson, Prenatal Exposure to Methylmercury through Maternal Fish Consumption: Neurodevelopment of Seychelles Child Development Cohort at 19 and 29 Months of Age, presented at the 12th International Neurotoxicology Conference, Neurotoxicity of Mercury: Indicators and Effects of Low-Level Exposure, Hot Springs, AR, November 1994

23. G. Myers, D. Marsh, C. Cox, P. Davidson, E. Cernichiari, T. Clarkson, O. Choisy, and C. Shamlaye, The Seychelles Child Development Study: Enrollment and Neurodevelopment at 6 Months, presented at the 12th International Neurotoxicology Conference, Neurotoxicity of Mercury: Indicators and Effects of Low-Level Exposure, Hot Springs, AR, November 1994.

24. K.S. Crump, H.J. Clewell, J.M. Gearhart, A.M. Shipp, A. Silvers, and J. Viren, A New Analysis of the Iraqi Data on *In Utero* Mercury Exposure, presented at the 12th International Neurotoxicology Conference, Neurotoxicity of Mercury: Indicators and Effects of Low-Level Exposure, Hot Springs, AR, November 1994

25. D. Thomas, D. Stram, J. Dwyer, Exposure Measurement Error: Influence on Exposure-Disease Relationships and methods of Correction, Ann.Rev.Public Health 14:69-93 (1993).

26. J.C. Smith, P. Allen, and M. Turner, The kinetics of intravenously administered methylmercury in man, Toxicol Appl Pharmacol 128:251-6 (1994).

Table 1. Features of the BNL Mercury Risk Assessment Model.

Hg emissions	Ratio of Hg^{++} to total Hg is estimated based on Cl^- in coal. Effects of air pollution controls are estimated.
Transport, dispersion, and deposition	Gaussian plume transport and dispersion model for 3 Hg species, up to 50 km. Constant V_d and washout ratio for each Hg species. No atmospheric reactions.
Accumulation in surface waters	The incremental Hg deposition to the watershed is assumed to enter the water body.
Contributions to global background	Any Hg not deposited within 50 km is assumed to enter the global pool and to increase global deposition.
Effects of local sources on fish Hg content	The average Hg in each freshwater fish species is assumed to increase in proportion to the Hg deposition increment.
Background Hg intake from fish, shellfish	The intake distribution (Hg concentration x consumption rate) is based on the sum of log-normal distributions of fresh-water fish, marine species, and canned tuna.
Equilibrium metabolic model	The equilibrium level of the body burden of MeHg is estimated by considering the frequencies of the 3 different types of fish meals, in addition to the total MeHg intake. The distribution of body burden is estimated using probabilistic methods, from distributions of Hg intake, body mass, and half life of Hg, as a baseline and with power plant contributions to MeHg in freshwater fin fish.
Exposure-response functions and risk analysis	Extant epidemiological data are used to establish relationships between MeHg exposure and specific neurological responses. Adult paresthesia was linked to estimated MeHg body burdens from a poisoning incident. Prenatal exposures were linked to maternal hair Hg and assessed from that incident and from two studies on fish-eating populations.
Treatment of uncertainties	Uncertainties due to Hg emissions, transport, chemical reactions, deposition, and uptake by fish are combined and represented by using a probabilistic "impact" factor by which freshwater fish Hg is increased due to local Hg deposition. Uncertainties in the Hg distributions of baseline body burden, blood, and hair concentrations are assessed by comparisons with measurements.

Table 2. Representative Statistics for Components of the Seafood Diet in Northcentral States.

Component	Means		Medians		GSDs*		MeHg Intake#	
	diet g/d	Hg ug/g	diet g/d	Hg ug/g	diet g/d	Hg ug/g	mean ug/d	median ug/d
canned tuna	4.5	0.20	2.7	0.15	2.7	2.16	0.55	0.43
freshw. finfish	10.3	0.28	6.8	0.15	2.5	3.0	1.43	1.09
other marine	9.9	0.077	7.2	0.061	2.0	2.2	0.53	0.44
total seafood	24.7 g/d						2.5	2.05

*GSD = geometric standard deviation;

# denotes simulation output.

Table 3. Comparison of Observed and Predicted MeHg Statistics (n=1000).

parameter	Observed@	Predicted
mean MeHg intake, ug/d	1.0	1.07
median hair concentrations*		
all subjects	0.26 (2.6)#	0.235 (2.56)
fisheaters	0.27 (2.4)	
non fisheaters	0.25 (2.5)	

@ data from Smith et al.[14]

* measured as MeHg but reported as Hg (ug/g)

( ) = geometric standard deviation

Table 4 Distribution Statistics Derived from Simulations (n=5000).

	------baseline------			-------impact------		
parameter	mean	median	95%	mean	median	95%
body mass, kg	73	71	104	73	71	104
half life, days	72	68	118	72	68	118
# meals in 5 half-lives	43	36	87	43	36	87
intake, ug/d	2.5	2.0	5.7	4.3	3.5	10.6
intake parameter, ug/kg/d	0.032	0.029	0.061	0.055	0.047	1.22
body burden, mg/kg	0.0033	0.0027	0.0072	0.0057	0.0046	0.0135
blood concentration, ug/L	0.0029	0.0020	0.0086	0.0050	0.0032	0.015
hair concentration, ug/g	0.82	0.54	2.42	1.40	0.86	4.64

Table 5. Comparison of Simulation Results with NIEHS Criteria[1]

	NIEHS	simulation results	
Parameter	Criterion	Baseline 95%-ile	Impact 95%-ile
Hg intake (ug/d) based on FDA fish limit (1 ppm)	30	6	11
WHO (adults) blood Hg (ug/L)	200	9	15
hair Hg (ug/g)	50	2.4	4.6
WHO (congenital) hair Hg (ug/g)	10-20	2.4	4.6
EPA LOAEL (ug/kg/d)	0.3	0.06	0.12
EPA RfD (ug/kg/d)	0.03	0.06	0.12

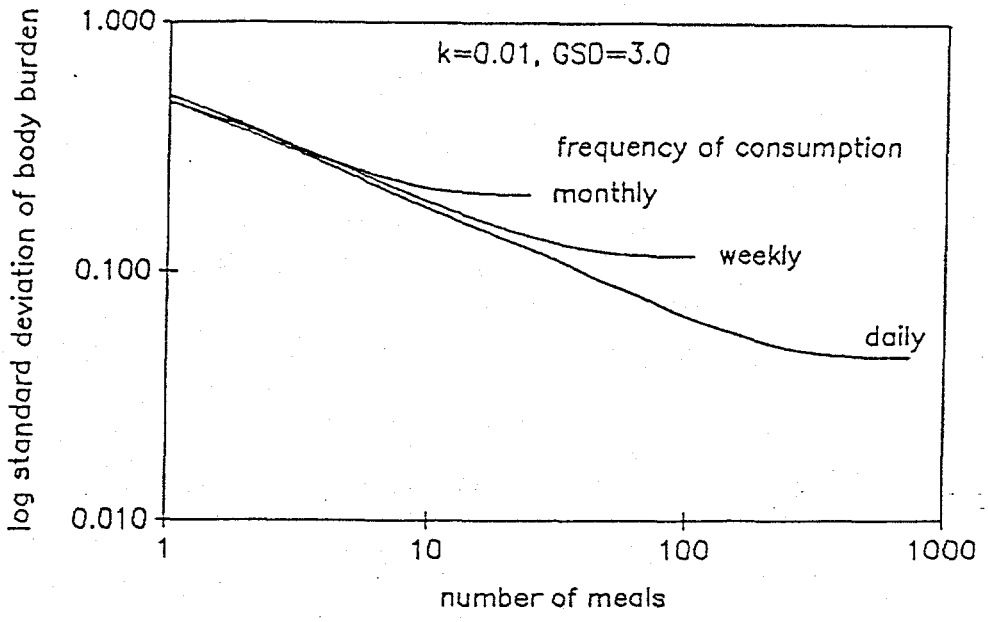

Figure 1. Simulated reduction in the standard deviation of body burden as a function of number of fish meals consumed in the time to reach equilibrium, with an underlying GSD of 3.0 (k = elimination constant).

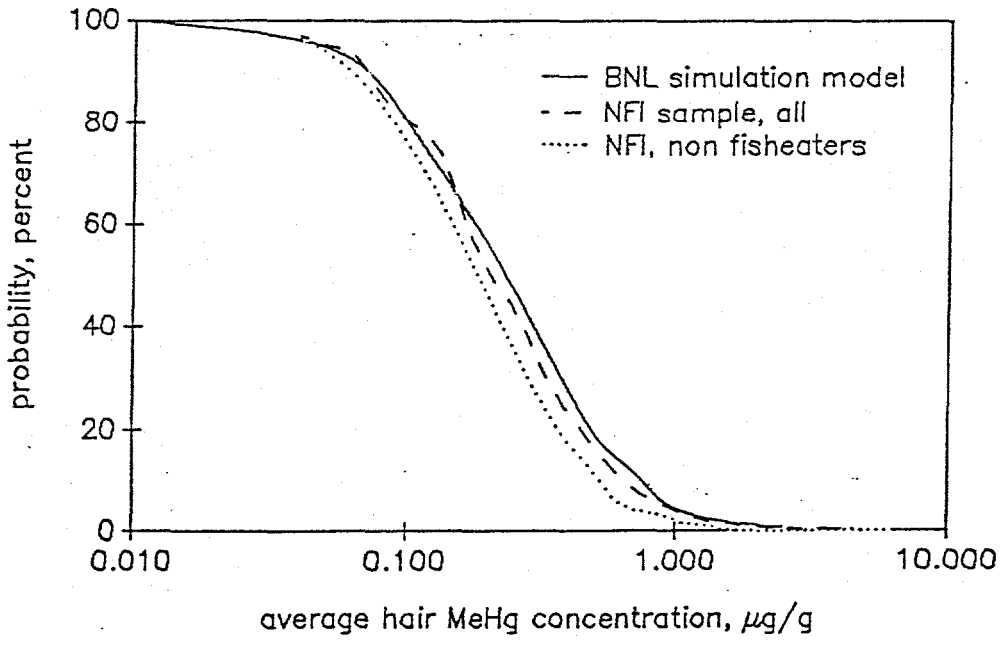

Figure 2. Comparison of simulated and measured distributions of MeHg in hair. NFI data are from Smith *et al.*[14]

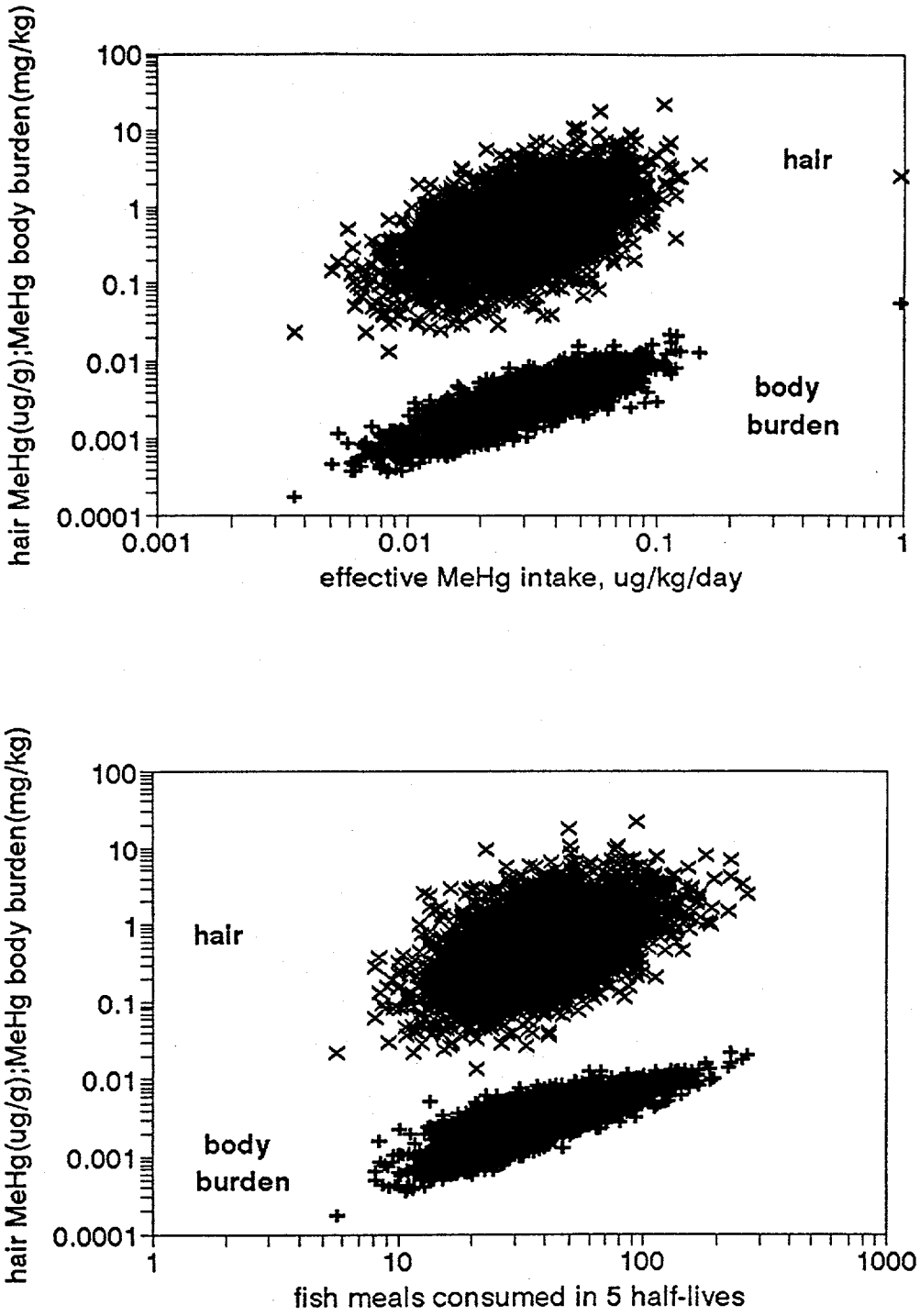

Figure 3. Simulated relationships between MeHg body burden and hair content and intake. (a) as a function of dietary intake. (b) as a function of frequency of consumption.

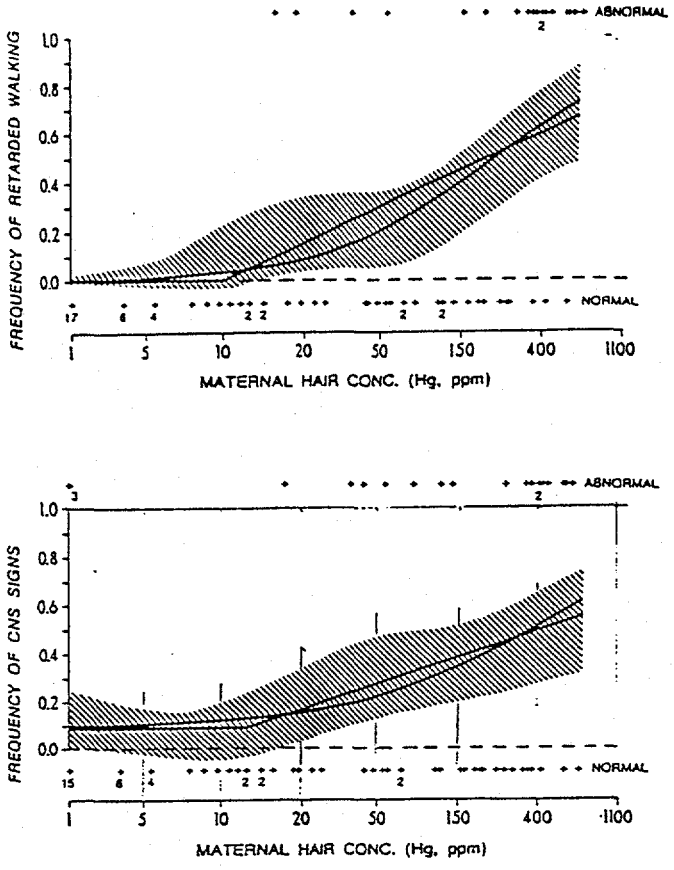

Figure 4. Dose-response functions for the Iraqi data on prenatal exposures. (a) late walking. (b) central nervous system signs. The solid lines are logit and hockey-stick fits; the shaded area represents 95% confidence limits from nonparametric smoothing analysis.
Source: Cox *et al.*[18] (permission requested).

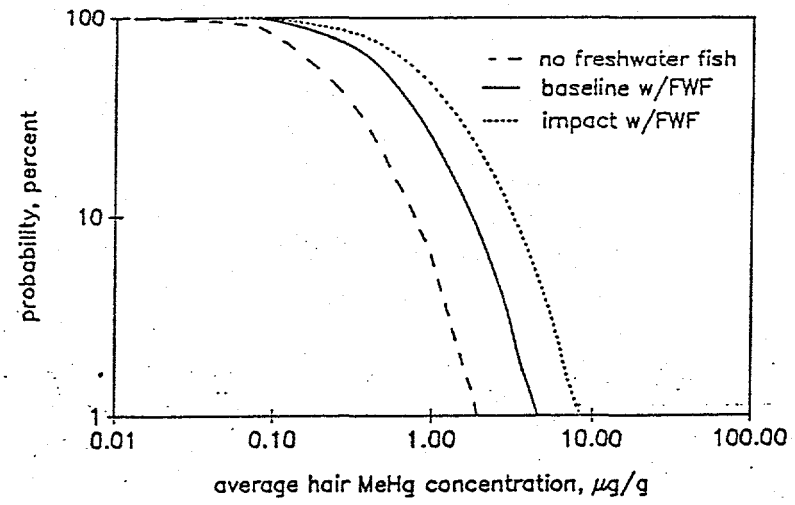

Figure 5. Monte Carlo simulations of average hair concentrations of MeHg resulting from fish consumption, based on 5000 trials.