MERCURY (HG) AND METHYLMERCURY

Trace element

Chemical forms

Mercury is found in various inorganic and organic forms and is persistent in the environment (WHO, 2008). While relatively chemically inert, mercury occurs in three valence states: elemental mercury (Hg) also known as metallic mercury, monovalent mercurous ion (Hg^{+}) and divalent mercuric ion (Hg^{++}). Elemental mercury and the divalent ion are the most important in nature. There are also several organic mercury compounds; by far the most common in the environment and in the aquatic food-chain is methylmercury (MeHg) (FAO/WHO, 2011).

Methylation of inorganic mercury occurs in aquatic systems by the presence of macrophytes and different sulfate-reducing bacteria. The mechanism of abiotic methylation involves humic and fulvic acids and a photochemical process (Forsyth et al., 2004).

Contamination source

Mercury is a naturally occurring element found in air, water, and soil. It is distributed throughout the environment by both natural and anthropogenic (human) processes (WHO, 2008).
Mercury occurs at low concentrations in the earth's crust, mainly in sulfide ores (cinnabar), from which it has been extracted for a variety of uses for many centuries. Common applications of metallic mercury are as a cathode in the electrolytic production of chlorine, in dental amalgams, in the extraction of gold from ore concentrates, in electrical equipment and in devices for measuring temperature and pressure. Mercury compounds have been used as fungicides in paints and on seeds and grains, as antiseptics, in electrical applications, and as catalysts and intermediates (IARC, 1997).
Mercury is found naturally in trace amounts in the environment: basically rejected by the earth's crust in the air, it is then dispersed in the soil, water and sediment. It also broadcasts in nature because of releases caused by human activity: mining, metallurgy, processing of paper pulp, waste combustion and fossil fuels in particular (AFSSA, 2004).
Very volatile in its elemental form is as result of chemical changes that mercury is toxic and readily bioaccumulated. Present at low concentrations in water or sediment in its methylated form, it can focus very strongly in aquatic organisms, its content tends to rise throughout the food chain, each time a species eats another (AFSSA, 2004).
Inorganic mercury is very volatil. Methyled forms are easily bioaccumable. Methylmercury (MeHg) is easily absorbed but not easily excreted by living organisms. Present at low concentrations in water or sediment in its methylated form, it can concentrated in aquatic organisms and more specially in carnivorous fish (AFSSA, 2002).

Analytical methods

It has been reported that methylmercury may be decomposed in some food matrices with repeated freezing and unfreezing (particularly in bivalves). However, relatively little is known about the effect of storage on the stability of methylmercury in food samples (FAO/WHO, 2011).

Following acidic digestion of samples, cold vapour atomic absorption spectrometry (CV-AAS) or cold vapour atomic fluorescence spectrometry (CVAFS) has been widely used for the determination of total mercury in several food matrices (FAO/WHO, 2011).

Basically, all the speciation methodology is generally targeted on the separation and determination of methylmercury, and there has been no conclusive identification of other species of mercury.
Extraction of the mercury species from its matrix requires an aggressive treatment, such as acid digestion, distillation or alkaline extraction, with the option of applying ultrasonic or microwave energy to assist in the procedure. Extraction is one of the most critical steps, because two conflicting issues need to be addressed: obtaining high extraction efficiency and preventing losses. In alkaline media, methylmercury appears to be more stable than in acid media, with proteins being easily hydrolysed (FAO/WHO, 2011).

Toxicity

The factors that determine the occurrence and severity of adverse health effects include: the chemical form of mercury; the dose; the age or developmental stage of the person exposed (the fetus is considered to be the most susceptible); the duration of exposure; and, the route of exposure (inhalation, ingestion, and dermal contact). Dietary patterns can increase exposure to a fish-eating population when fish and seafood are contaminated with mercury (WHO, 2008).

The primary targets for toxicity of mercury and mercury compounds are the nervous system, the kidneys, and the cardiovascular system. It is generally accepted that developing organ systems (such as the fetal nervous system) are the most sensitive to toxic effects of mercury. Fetal brain mercury levels appear to be significantly higher than in maternal blood and the developing central nervous system of the fetus is currently regarded as the main system of concern as it demonstrates the greatest sensitivity. Other systems that may be affected include the respiratory, gastrointestinal, hematologic, immune, and reproductive systems (WHO, 2008).

Effects on the nervous system (especially the developing nervous system) appear to be the most sensitive toxicological endpoint observed following exposure to elemental mercury and methylmercury, while damage to the kidneys is the key end-point in exposure to inorganic mercury compounds (WHO, 2008).

Methylmercury (MeHg) is the most toxic form. Organic forms are more toxic than inorganic forms.

Over 90% of MeHg is absorbed through the gastrointestinal tract and rapidly transferred into the bloodstream due to its high lipophilicity (Ceccatelli et al., 2010). The methylmercury compounds bind to reduced sulfhydryl groups; a fraction is converted to mercuric mercury, the extent of conversion differing among species (IARC, 1997). MeHg is able to cross the blood–brain and placenta barriers, which make it neurotoxic and teratogenic (Ceccatelli et al., 2010). Methylmercury compounds are excreted mainly in the bile; in the intestine, some mercury is biotransformed into inorganic mercury compounds and excreted in the faeces (IARC, 1997). Methylmercury compounds pass into the fetus and are excreted in milk. In humans, methylmercury compounds have a single biological half-time of approximately about 1.5 to 2 month (EFSA, 2004). Concentrations in blood and hair are useful for monitoring exposure to methylmercury compounds (IARC, 1997).

The neurotoxicity of MeHg has been known since the poisoning of the population in Minamata, Japan, in the 1960s and since two other massive contamination episodes in Niigata, Japan, and Iraq (Eto et al., 2010).

Methylmercury compounds induce adverse effects on human development - most notably microcephaly and deficits in neurological development. Similar effects have been shown in many laboratory species (IARC, 1997). These include neurodevelopmental deficits (NRC, 2000) and likely, cardiovascular effects, particularly increased risk of myocardial infarction (Stern, 2005).
Methylmercury is highly toxic particularly to the nervous system, and the developing brain is thought to be the most sensitive target organ for methylmercury toxicity.
Mercury can cause serious damage to the brain, including psychological disturbances, deafness, loss of sight, ataxia, loss of motor control and general debility (Aschner, 2002).
Methylmercury can cause behavioral problems or mild developmental delays in children exposed in utero or after birth, even in the absence of signs of maternal toxicity (AFSSA, 2004).

Carcinogenicity
Methylmercury compounds are possibly carcinogenic to humans (Group 2B).
Metallic mercury and inorganic mercury compounds are not classifiable as to their carcinogenicity to humans (Group 3).
In making the overall evaluation, the Working Group took into account evidence that methylmercury compounds are similar with regard to absorption, distribution, metabolism, excretion, genotoxicity and other forms of toxicity.

Establishment of Health Based Reference Values
The Committee of JECFA established, in 2003, a Provisional Tolerable Weekly Intake (PTWI) of 1.6 µg/kg body weight (bw) based on two epidemiological studies that investigated the relationship between maternal exposure to mercury and impaired neurodevelopment in their children. Neurodevelopment was considered to be the most sensitive health outcome and development *in utero* the most sensitive period of exposure. Calculation of the PTWI was based on an average BMDL/NOEL of 14 mg/kg (14 µg/g) for concentrations of mercury in maternal hair in the studies of

neurodevelopmental effects in cohorts of children from the Faroe Islands and the Seychelles (FAO/WHO, 2006).
The Committee of JECFA considered this PTWI to be sufficient to protect the developing fetus, the most sensitive subgroup of the population. The Committee also reaffirmed its position that fish are an important part of a balanced nutritious diet and that this has to be appropriately considered in public health decisions when setting limits for methylmercury concentrations in fish (FAO/WHO, 2006).

The Committee of JECFA established a PTWI for inorganic mercury of 4 µg/kg bw (FAO/WHO, 2011). The new PTWI for inorganic mercury is considered to be applicable for dietary exposure to total Hg from foods other than fish and shellfish. For dietary exposure to mercury from fish and shellfish, the previously established PTWI of 1.6 µg/kg bw for MeHg should be applied.

Occurrence in food

People are exposed to methylmercury mainly through their diet, especially through the consumption of freshwater and marine fish and consumption of other animals that consume fish (such as marine mammals) (WHO, 2008).

The majority of the mercury released in the marine environment is inorganic mercury, but this can be converted to methylmercury by anaerobic bacteria in sediments (Storelli et al., 2004).

The MeHg concentrations in 62 seafood samples representative of consumption in the French population ranged from 1.9 to 588 µg/kg, and the percentage of MeHg varied from 28% to 98% in shellfish and from 84% to 97% in fish (Clémens et al., 2011).
According to the results of the Calypso study (Sirot, Guérin et al., 2008), the most contaminated fish to methylmercury are predator species: swordfish (0.94 µg/g), Emperor (0.57 µg/g), tuna (0.33 µg/g) and eel (0.32 µg/g). Fish with the lowest MeHg levels were anchovy (0.020 µg/g), salmon (0.038 µg/g) and saithe (0.041 µg/g). MeHg represent 67 to 100% of the total mercury in fish.

Fish accumulate MeHg via water and their food source, resulting in a higher concentration in fish and the older ones (mainly predatory fish) than in small fish (Forsyth et al., 2004). The MeHg is the predominant form of mercury in fish (Hastein et al., 2006).

The weighted mean contamination, which was based on all data for the mercury concentration in fish and seafood products sublitted by the Members States, was 109 ± 845 µg/kg; the high standard deviation reflects the wide variations in the analytical results (EFSA, 2004).

Among sample analyzed in the study EAT2 (ANSES, 2011), 95% had Hg concentration below the LOD or LOQ. The higher mean concentration were found in fish (LB=0.133 mg/kg, UB=0.134 mg/kg), chocolate (LB=0.014mg/kg, UB=0.017 mg/kg), mollusks and shellfish (LB=0.014 mg/kg, UB=0.016 mg/kg).

Dietary expsoure assessment

Fish consumption is the main source of human dietary exposure to methylmercury (Forsyth et al. 2004). The level of contamination in fish varies among species. It tends to be higher in those who are at the top of the food chain (large predators).

Sieon (2007) has estimated the mean and 95th percentile dietary exposure of the population of Flemish adolescent to methylmercury at 16.8 and 73.3 ng/kg bw/day. The mean and 95th percentile dietary exposure of the population of adult to methylmercury was estimated to 42.7 and 125.3 ng/kg bw/day (Sioen, 2007). The mean and 95th percentile dietary intake of adolescent seafood consumer was estimated at 26.3 and 90.7 ng/kg bw/day. For adult seafood consumer, the mean and 95th percentile dietary intake was estimated at 45.6 and 128.6 ng/kg bw/day (Sioen, 2007).

The average exposure of the French population to organic mercury (MeHg) through the only consumption of fish and other seafood, is estimated in adults to 0.017 µg/kg bw/day. In children, the average exposure is estimated at 0.022 µg/kg bw/day. At 95th percentile, the exposure is estimated at 0.061 µg/kg bw/day in adults and 0.097 µg/kg bw/day in children. In women of childbearing age, constituting the critical group in terms of effects of MeHg on fetal development, the exhibition is on average 0.019 µg/kg bw/day. At 95th percentile, the exposure is estimated at 0.067 µg/kg bw/day

(ANSES, 2011).

The average exposure of the French population to inorganic mercury through the consumption of other food than seafood in adults is estimated at 0.006 µg/kg bw/day in the lower bound (LB) and at 0.18 µg/kg bw/day under the upper bound hypothesis (UB). In children, the average exposure is estimated at 0.014 (LB) and 0.26 (UB) µg/kg bw/day. At the 95th percentile, the exposure is estimated at 0.026 (LB) and 0.29 (UB) µg/kg bw/day in adults and at 0.05 (LB) and 0.47 (UB) µg/kg bw/day in children (0.02 to 0.53) (ANSES, 2011).

Risk Characterization

The estimated dietary intake of MeHg through seafood by the Flemish population (table 1) is below the PTWI of 1.6 µg/kg bw/week. The intake of MeHg through seafood did not seem to be of toxicological concern.

Table 1: MeHg dietary exposure for adult and adolescent in Flanders and percentage of the PTWI

Population	Exposition (ng/kg bw/day)	% PTWI
Flemish adolescent consumer - Mean	23.6	10.3
Flemish adolescent population - Mean	16.8	7.3
Flemish adolescent consumer - P95	90.7	39.7
Flemish adolescent population - P95	73.3	32.1
Flemish adult consumer - Mean	45.6	19.9
Flemish adult population - Mean	42.7	18.7
Flemish adult consumer- P95	128.6	56.3
Femish adult population- P95	125.3	54.8

According to the EAT2 study (ANSES, 2011), there is 0.84% of exceedances of the PTWI set for MeHg in adults (0.4, 1.3) and 1.11% in children (0.6, 1.7) in France. In women of childbearing age in particular, there is 0.72% of exceedances of the PTWI (0.4, 1.1). Topics beyond the PTWI are overwhelmingly high consumers of fresh tuna (consumption of 100 to 500 g/week), the species among the most contaminated samples in EAT 2. The risk of MeHg exposure does not pose a major public health problem in France, however, continue efforts should be down to reduce contamination and exposure (ANSES, 2011).

Regarding inorganic mercury, assuming only upper bound hypothesis, there is 1.4% of exceedances of the PTWI in children, but no in adult. Risk associated with exposure to inorganic mercury is not a major public health problem; however, continue efforts should be down to reduce exposures. Moreover, it appears necessary to lower analytical limits for the research of mercury to refine exposure (ANSES, 2011).

The estimated intakes of mercury in Europe vary by country, depending on the amount and the type of fish consumed. The mean intakes are in most cases below the JECFA PTWI but the average intake in some countries exceedes the U.S.-NRC limit of 0.7 µg/kg bw/week. High intakes may also exceed the JECFA PTWI. A probabilistic analysis of the French data indicate that children are more likely to exceed the PTWI than adults (EFSA, 2004).
There may be population-groups in Europe with a frequent consumption of large predatory fish, which are at the top of the food chain (for instance swordfish and tuna) which often have a higher concentration of methylmercury. These population-groups may therefore have higher dietary intakes than those found in populations with a high intake of fish containing low levels of methylmercury (EFSA, 2004).

For the general population, AFSSA (2009) considers that the consumption of fish shows no health risk regarding to the risk associated with methylmercury. Indeed, the contribution of population to methylmercury is lower than the tolerable daily intake defined by the World Health Organization.

Legislation

As a safeguard for human health, guidelines and regulations stipulating maximum permissible levels of mercury in fish (0.50 or 1 mg/kg essentially for predatory fish) and seafood (0.50 mg/kg) have been set by Regulation (EC) No. 629/2008 [EC (2008) Amending Regulation (EC) No. 1881/2006 laying down maximum levels for certain contaminants in foodstuffs. Commission Regulation No. 629/2008, Oj No. 364, 20.12.2006] to limit dietary exposure of consumers.

Recommendations

Recommendations of the JECFA (FAO/WHO, 2011)

There is a need for:

- validated analytical methods for both inorganic mercury and methylmercury applicable in several food matrices;
- more information on the inorganic mercury and methylmercury content of foods as consumed that mainly contribute to overall dietary exposure.

Recommendations of the AFSSA (2009)

In view of the nutritional benefits associated with the consumption of fish (essential fatty acids, proteins, vitamins, minerals and trace elements), AFSSA recommended:

- eating fish twice a week including fatty fish (salmon, mackerel, sardines, anchovies, smoked trout, herring ...)
- to diversify the species of fish consumed.

For pregnant and lactating women and young children (under 30 months), AFSSA (2009) recommended to take special precautions:

- as a precaution to avoid eating the most contaminated fish: sharks, lampreys, swordfish, billfish (swordfish close) and sikis (variety of shark)
- limit consumption of fish likely to be heavily contaminated to 150 g per week for pregnant and lactating women and 60 g per week for children under 30 months.

Recommandations of the ANSES (2011)

- There is a need to implement routine analytical methods for speciation of mercury in foods.

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