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Human Health Risks Due to Consumption of Chemically Contaminated Fishery Products

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A small proportion of fishery products contaminated with appreciable amounts of potentially hazardous inorganic and organic contaminants from natural and environmental sources seem to pose the greatest potential for toxicity to consumers of fishery products in the United States. Health risks due to chemicals (e.g., modest changes in the overall risk of cancer, subtle deficits of neurological development in fetuses and children) are difficult to measure directly in people exposed to low levels. Immunocompetence may increase cancer risk. Inferences about the potential magnitude of these problems must be based on the levels of specific chemical present, observations of human populations and experimental animals exposed to relatively high doses, and theories about the likely mechanisms of action of specific intoxicants and the population distribution of sensitivity of human exposure. Lognormal distributions were found to provide good descriptions of the pattern of variation of contaminant concentrations among different species and geographic areas; this variability offers a solution for reduction of exposure through restricting harvest of aquatic animals from certain sites and by excluding certain species. Available information suggest that risks are not generally of high magnitude; nevertheless, their control will significantly improve public health. The following recommendations will help to reduce risk to humans: existing state and Federal regulations and environmental monitoring must be strengthened and enforced to improve the quality of the environment; a program of shared responsibility where Federal agencies develop a set of monitoring and inspection practices and state governments are responsible for site closures and issuing advisories should be established; research and public education by government agencies and health professionals should be expanded; mandatory labeling should be considered for specific contaminants; and a better system requiring international agreements should be developed to identify country of origin of imported fishery products and to harmonize product safety and quality.

Introduction

Finfish and shellfish accumulate chemicals from their environment; the extent of accumulation depends on such factors as geographic location, species, feeding patterns, solubility and liphophilicity of the chemicals, and their persistence in the environment (*1*). Inorganic contaminants with the greatest potential of toxicity include antimony, arsenic, cadmium, lead, mercury, selenium, and sulfites. Organic contaminants that seem to pose sufficient risk include polychlorinated biphenyls, dioxins, several chlorinated hydrocarbon insecticides, certain processing-related contaminants such as nitrosamines and chlorination products, and aquaculture-related chemicals. Chemicals also can become more concentrated through bioaccumulations, which can either be organ specific or related to fat concentration (e.g., methylmercury in muscle tissue or PCBs in fatty tissues). The problem of assessing human health risks is complicated by the fact that usually more than one contaminant is present in consumable tissues (*2,3*). In some cases, however, the contribution of specific congeners with similar mechanisms of action toward the overall activity of a sample can be made by the use of toxicity equivalence testing and congener-specific analysis (*5*). Although the number and variety of chemical residues are substantial, a small minority contribute the bulk of risk, which can be assessed quantitatively (*4*).

Older concepts, which have shaped the legislative agendas within food protection agencies in the United States, suggest sharp distinction between safe and unsafe levels of exposure to important categories of environmental toxicants. These ideas are gradually giving way to a more quantitative (although still uncertain) concept of risk. Although increased understanding indicates that certain categories of risk cannot be eliminated entirely, the

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tools for societal control of these risks should be adopted to reflect tradeoffs between the cost of forgoing certain portions of food resources and potential health risks (*1*).

Health Effects

A system for biological damage mechanisms intended to sort adverse effects according to the kinds of events likely to occur at either subclinical dosage levels, or preclinical stages divides health hazards into the following categories: *a*) Effects resulting from overwhelming body compensatory process where response is mostly reversible. These are further subdivided into traditional acute toxicity (e.g., paralytic shellfish poisoning, puffer fish poisoning, many teratogenic effects) and traditional chronic toxicity (e.g., methylmercury or lead poisoning, inhibition of heme synthesis enzymes, effects on some measures of kidney and neurological functions). *b*) Effects resulting from irreversible or poorly reversible insidious processes. These are further subdivided into molecular biological (stochastic) effects (e.g., mutagenesis, most carcinogenesis and some teratogenesis) and chronic cumulative effects [e.g., Parkinson's and Alzheimer's diseases, emphysema, atherosclerosis (*6*)].

Trace Metals of Greatest Potential Toxicity

An inorganic contaminant's potential for producing toxicity is classified as major, modest, minor, or no toxic potential based on potency for producing effects and accessibility of the toxicant, among other parameters. Criteria for identifying contaminants of public health concern in the aquatic environment include persistence, bioaccumulation potential, toxicity to humans, sources of contaminants in certain areas, and high concentration of contaminants in consumed fishery products for such areas (*1*).

Assessing health risk from consumption of fishery products contaminated with elevated levels of inorganic chemicals is complicated because usually more than one agent is present in consumable tissues, and sometimes the chemical species of a given toxic element present in tissue is unknown (*7*).

Based on these criteria, those metals with major toxicological potential are antimony, arsenic, cadmium, chromium, lead, mercury, and nickel. Contaminants with a modest potential for toxicity include copper, iron, manganese, selenium, and zinc. Those of minor or no toxicity are aluminum, silver, strontium, thallium, and tin.

To assess risk from metal exposure, dose–response data are generated either from animal studies or from occupational or accidental environmental human exposure. Extrapolation from animal studies to the human situation is uncertain, whereas occupational or environmental data allow more accurate assessment. Extensive literature are available on occupational and accidental exposure of humans to four of the five metals identified as potential toxicants (arsenic, cadmium, lead, and mercury) and fewer dose–response data exist for accurate assessment of toxicity due to ingestion of selenium, although poisoning has been documented in humans ingesting selenium (*8–10*). Data are summarized in Table 1.

Existing dose–response data on ingestion of seafood contaminated with metals, however, lack sufficient information to assess the effects of chronic exposures, the sensitivity of certain subpopulations, and interindividual variability. In case of arsenic, the primary form in seafood is organic and has low toxicity in animals; no other data exist for effects in humans. Thus, its potential hazard to humans is questionable (*1*). Knowledge about the chemical form is important in predicting both bioavailability and toxic potential (*11*). Populations at special risk for metal toxicity (e.g., pregnant women, the fetus, the elderly, and subsistence fishers with varying nutrition) may be at

Table 1. Trace metal dose–response data (*1*).

Metal	ADI, mg/day	Toxic body burden, mg	Steady daily intake for toxicity, mg/day	Human half-life	Blood LOAEL	% Gastro-intestinal absorption	Dependence of toxicity on age, sex, reproductive status	Long-term effects	Biomarkers	Tissue LOAEL, ppm	Relative priority as a seafood hazard
Arsenic	Uncertain for seafood	Uncertain for seafood	Uncertain for seafood	<20hr	Uncertain for seafood	Uncertain for seafood	Not reported for seafood	Uncertain for seafood	Uncertain for seafood	Uncertain for seafood	Very low
Cadmium	51–72	Not reported	35	Three phases <200 d, +20 d, 10–30 y	Uncertain poor monitor	5	>50 y and multiparous females	Nephropathy	Urine retinol binding protein	Kidney, 200–285	High
Lead	429	100–400	Uncertain	Three phases 3–4 w, 5–30 y	25 ppb (5–15 ppb in child)	10	Fetus and neonate	Anemia and CNS problems	δ-Aminolevulinic acid (RBC)	Poor	High
Mercury	0.23	25	(0.003 (acute)	70–110 d	0.23 ppb adult (0.1 ppb fetus)	95	Fetus, neonates and pregnant female	Retardation	Porphinurea	Hair pregnant patients, 15–20	High
Selenium	Uncertain for seafood	Not reported	–	Three phases 1 d, 8–20 d, 65–116 d	Uncertain (0.179 ppt)	40–80 as the selenite	Not reported	Uncertain	Not reported	Hair, 0.828	Uncertain

Abbreviations: ADI, acceptable daily intake; LOAEL, lowest observed adverse effect level; d, days; w, weeks; y, years; CNS, central nervous system; RBC, red blood cells.

elevated risk (*3*). The results of these uncertainties have lead to wide variations in acceptable levels of inorganic seafood contaminants among various countries (*12*).

Processing-Related Contaminants

Nitrosamines. Nitrosamines are formed in smoked fishery products and in the human as the result of reduction of nitrites in the stomach by bacteria. The extent of exposure to nitrosamines due to consumption of smoked fish contaminated by nitrites has not been fully determined (*1*).

Aquaculture Chemicals. There is deep concern that a number of known or suspected carcinogens (e.g., furazolidone, nitrofurazone, carofur, chloramphenicol, and silver) that are not registered for use in the United States are used by other nations in aquaculture (*13*). The widespread use of sulfonamides, antibiotics, and nitrofurans worldwide for treating diseased aquaculture products from protozoal, mycotic, and helminthic infections poses a threat to human health due to residue persistence in the edible portion of fishery products (*14*). In addition to intentionally used chemicals, aquaculture products are also susceptible to contamination with pesticides, agriculture runoff water, and sediments. The magnitude of human exposure to these sources has not yet been addressed (*1*).

Products of Chlorination and Sulfites. Chlorine and other halogen compounds are widely used as disinfectants in seafood processing, as well as in the treatment of drinking water and sewage effluents; this process generates some levels of halogenated amines, aromatics, and methanes (*15*). The extent of seafood contamination with hydrogenated compounds and human health risks are uncertain (*1*). Sulfites (e.g., sodium bisulfite or metabisulfite) have been used to prevent discoloration of shrimp in processing plants (*16*). Concern about continued use and labeling of these products has arisen because of potential concern for allerginlike reactions in certain asthmatic people (*17*). No other effective way to treat crustaceans has been developed (*1*).

Organic Compounds

Potential seafood contaminants include chlorinated hydrocarbon pesticides [benzohexachloride (BHC), chlordane, dieldrin, dichlorodiphenyltrichloroethane (DDT), endrin, heptachlor, lindane, monachlor, octachlor, and pentachlorophenol]; industrial chemicals and by-products such as PCBs and dioxins; and, less frequently, pesticides such as carbophenathion, carboxylic acid herbicide 2,4-dichlorophynoxy acetic acid (2,4-D), chlorpyrifos, dacthal (DCPA), diazinon, ethion, ethylene dibromide (EDB), ethyl parathion, malathion, methyl parthion, omethoate, pentchloroaniline, tecnazene, and trifluralin (*18–20*).

Numerous data on finfish and shellfish from domestic freshwater and marine environments show extensive contamination with both organic and inorganic chemicals that are potentially toxic to humans. Although the contamination is widespread, it varies greatly with geographic location and species (*1*). Where data are available, it appears that, in most cases, the distribution of contaminated level fits a lognormal distribution (Fig. 1). See Finney (*21*) and Hattis (*22*) for information on how plots are created.

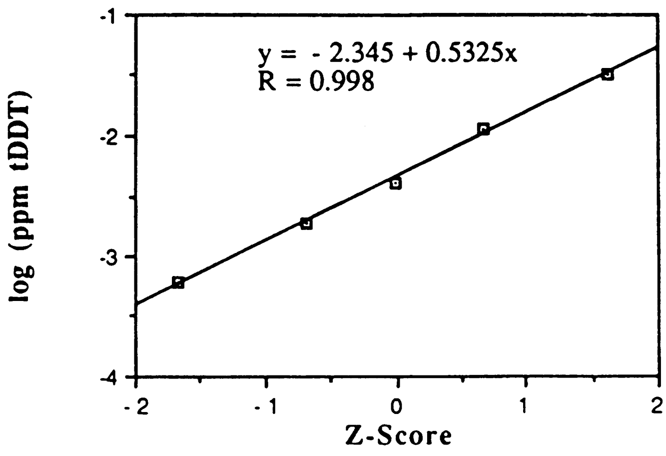

FIGURE 1. Lognormal distribution of wet weight concentrations of DDT and metabolites in bivalves. From Ahmed (*1*).

Except for benzo[*a*]pyrene [BaP], results from epidemiological studies are equivocal concerning the carcinogenicity of several critical pollutants that accumulate in fish [dioxins, furans, HCB, PCBs, etc. (*23*)]. In some cases, however, sufficient animal bioassays are available to support their potential human carcinogenicity, and many of them are considered functional teratogens. These chemicals can also change gene function, turning on and off numerous enzyme systems that control development and activity of the endocrine system; block cell-to-cell communication, upset homeostasis and differentiation, and can modulate both pro-estrogen and anti-estrogen responses (*23*). An association between the activity of the enzyme aryl L hydrocarbon hydroxylase (AHH), which correlates with several toxic responses such as wasting and thymic atrophy in rats, cleft palate in mice, and mild to severe liver porphyria in animals, and the chemicals dioxins, furan, and a number of PCB congeners was observed (*23*).

Potential for Reducing Exposures

There are three potential types of control measures: *a*) the classical approach, now the primary control measure at U.S. Federal agencies, of setting acceptable maximum contaminant levels in seafood, analyzing small fractions of the commercial seafood in interstate commerce, and, where excessive levels are found, seizing products with violative residues; *b*) restriction on harvesting/marketing based on relationships between contaminant levels and species, geographic location, and size; and *c*) labeling and consumer information programs of various types, ranging from general advisories issued by state health departments primarily to sport fishers to possible programs to disclose the origin, or average contaminant levels, for seafood sold in retail outlets.

Setting Maximum Contaminant Levels

The first option outlined above has obvious difficulties. Chemical analyses are both expensive and slow relative to the usual pace of marketing fresh seafood products; thus, only a tiny fraction of products can be screened. Because many of the health effects of chemical contaminants are long-term in nature (i.e., modest increase in the overall risk of cancer, subtle shift in the distribution of birth weights and attained mental performance in offspring, or an increased long-term risk of a chronic cumulative condition such as Parkinson's disease), there is no dividing line between safety and hazard defined on the basis of individual meals. In structuring social control measures to reduce these types of risks, it is important to keep in mind the limitation of long-term average exposures, not simply the reduction of the number of individual items that reach the market above some (arbitrarily defined) cutoff level.

Restriction on Harvesting/Marketing/Size

The second option, restrictions of various kinds on harvesting and marketing, has potential to limit long-term average exposures and the exposures of selected groups for various kinds of toxic effects (e.g., women of childbearing age). Because some geographic areas (e.g., fresh versus salt water), some species and some size classes of aquatic animals have much higher residue levels than others, important quantitative reductions can be made in individual and societal aggregate health risks with measures that would restrict the overall commercial availability of products. If available databases are improved, regulatory agencies will have the potential to better target their efforts, and interested consumers may modify their risks by altering their consumption of specific species of products originating in particular areas. Such targeting should not only include efforts to close or reduce harvesting certain species in high-risk areas, but should also include efforts to reduce the input of contaminants to the local marine environment. A strong effort should be made to develop systems for containment of waste that do not involve atmospheric or aquatic dumping. Coordination of efforts to improve the health of aquatic ecosystems with efforts to improve the safety management of seafood sources will have benefits for both types of societal objectives (*1*).

To illustrate the potential of geographic restrictions on harvesting and marketing, the NOAA Status and Trends data set (*24*) was used to analyze the distribution of several contaminants in specific species of aquatic organisms among different coastal areas, assuming that distributions are lognormal and that in the absence of restrictions all sites would make roughly equal contributions to the specified seafood items to the U.S. food supply (*1*). Results in Table 2 suggest that for most inorganics inshell fish, except lead, the site-to-site variability is small enough that even restricting harvesting to the worst 20% of locations would reduce the population aggregate by less than 50%. On the other hand, for organic contaminants (Table 3), the geographic variability is larger than variability for inorganics. Thus, it is theoretically possible to reduce population dosage delivered by over 50% by restricting harvesting/marketing for only the 5% most contaminated sites. For other cases, restriction of a little more than 10% of the sites would be required to achieve this goal (*1,22*).

Table 2. Illustrative analysis of the potential for reducing the aggregate dosage of specific contaminants from subsets of seafood by restricting harvesting from the sites with the highest contaminant levels: inorganic contaminants (*1*).[a]

	Inorganic contaminants[b]				
Fraction of sites restricted, %	Arsenic	Cadmium	Lead	Mercury	Selenium
1	3.3	4.8	11.5	5.4	2.6
2	5.9	8.3	17.8	9.2	4.8
5	12.2	16.1	29.9	17.5	10.1
10	21.2	26.6	43.6	28.5	18.2
20	36.0	42.7	61.1	44.9	32.0
Site-to-site geometric SD	1.61	1.92	3.05	2.03	1.44
Ratio arithmetic/geometric mean	1.11	1.23	1.86	1.28	1.06

[a]Percentage of total population dosage contributed by highest *N*% if sites of equal contributions to diet are assumed from each site.
[b]Based on concentrations in bivalves (*24*).

Table 3. Illustrative analysis of the potential for reducing the aggregate dosage of specific contaminants from subsets of seafood by restricting harvesting from the sites with the highest contaminant levels: organic contaminants (*1*).[a]

	PCBs		PAHs	DDT and metabolites	
Fraction of sites restricted, %	Bivalves	Fish, edible portions	Bivalves	Bivalves	Fish, edible portions
1	3.3	4.8	11.5	5.4	2.6
1	13.7	14.0	28.4	13.7	28.7
2	20.8	21.1	38.6	20.8	38.9
5	33.7	34.2	54.2	33.8	54.5
10	47.8	48.4	68.1	48.0	68.4
20	65.1	65.6	81.9	65.2	82.1
Site-to-site geometric SD	3.40	3.44	5.75	3.41	5.79
Ratio arithmetic/geometric mean	2.11	2.14	4.61	2.12	4.67

[a]Percentage of total population dosage contributed by highest *N*% if sites of equal contributions to diet are assumed from each site.

Size is another important control parameter associated with lipophilic contaminant concentration that may be useful in some cases (e.g., PCB concentration in certain bluefish). In this case, when data for the various sizes are averaged, small bluefish (less than 11.8 in.) average about 0.21 ppm PCB; medium (11.8–19.7 in.) average 0.42 ppm; and large average somewhat over 1.4 ppm (about seven times more than the average concentration in the small category). Ideally, such size-based restrictions could be structured with somewhat different cut points for different geographic areas, depending on local concentration/size data (*1*).

Labeling and Consumer Information Programs, and Advisories

Some people have suggested retail displays of seafood accompanied by a quantitative risk score and a capture geographic location of the species considered for sale to allow the consumer the freedom of choice (*1*). Others have questioned the wisdom of this decision, even with additional public education because this places a burden on people or may require them to devote more time and effort to effectively evaluate health risk and economic choices. Public health authorities have the advantage of scale in gathering information and evaluating the health risks and can also take preventive actions when necessary (*1*).

Opportunities for Reducing Risk

Industry and agriculture are considered primary sources of contamination in sport fish through urban runoff, followed by domestic use and disposal of hazardous chemicals and long range atmospheric transport (*25*). Chemically contaminated sport fish are not regulated by the same regulations used to control fish sold in commercial markets such as the Federal Food, Drug and Cosmetic Act administered by the U.S. Food and Drug Administration (FDA) (*26*). Most states have addressed this issue through fish consumption advisories, based mostly on FDA's tolerance or action levels. Different states use different trigger levels and different advice for fish having similar concentrations of contaminants. Thus, advisories do not provide a comprehensive solution to this problem. In addition, advisories cannot be enforced by local authorities, and they may not reach all segments of affected individuals because they are usually given at the time of purchasing fishing licenses. More importantly, advice has no impact on the source of hazardous chemicals (*1,27*).

Programs to monitor chemical contaminants in seafoods that address human exposure are currently lacking. Programs that specifically address human health impacts of consumption of contaminated recreational fish (advisories) are often irrelevant. Programs intended to regulate chemicals that contaminate all fishery products [the Clean Water Act, Toxic Substance Control Act (TSCA) and Federal Insecticide, Fungicide, Rodenticide Act (FIFRA)] have not eliminated the source of these chemicals (*25*).

An emerging concept, Sunset, stipulates that some chemicals (as well as processes on products associated with them) be eliminated through ban, phase-out, use restriction, or substitution (*28*). Identification of candidate chemicals would take into account their potential of reaching the environment, contaminating foods, and threatening human health. While this is being developed, Federal agencies (U.S. Environmental Protection Agency and FDA) should develop stricter guidelines, including development of a standard, written format and effectively communicate and broadcast these guidelines to sport fishers and require states to follow them when issuing their advisories. Moreover, current regulatory programs addressing environmental toxicants (prohibition of discharges under the Clean Water Act, bans under TSCA, and prohibition of support of banned pesticides under FIFRA) should recognize the health impacts of these substances as a result of consuming fishery products contaminated with them, and commit themselves to regulatory activities that prevent the contamination of fishery products with toxic substances. Strong consideration should also be given to the closure of recreational harvest areas deemed to pose a threat to human health (*25*).

Inspection should continue to be based on shared responsibility between state and Federal agencies, whereby a Federal agency (or agencies) have responsibility for identifying and characterizing risks, establishing methodologies and acceptable levels of undesirable agents, and coordinating and monitoring state inspection programs. In addition, the Federal agency would have primary responsibility for imported products and products in interstate shipment and would establish well-equipped regional laboratories to conduct tests. States, with financial support of Federal sources, would carry out inspections and apply police powers to in-state fishing industry operations by using procedures that meet Federal standards (*1*).

Educational programs should be established for training regulators and industry personnel to be proficient in the regulatory programs under consideration. These programs should be well coordinated across states, with more national guidance and increased consideration of the unique attributes of various geographic regions. Educational programs for safe preparation and service of seafoods in commercial and home settings must be developed and communicated as a part of an integrated program.

As more countries require the equivalency of domestic and imported products, it is apparent that the time has come for the international community to begin a process that would minimize the differences existing among various national regulatory guidelines and approaches. It is also desirable that a better system requiring international agreements be established to identify the country of origins of imported seafood products (*1*).

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