USING KEPONE TO EXEMPLIFY THE IMPORTANCE OF NATURAL VARIABILITY IN ESTIMATING EXPOSURE TO TOXIC CHEMICALS FROM AQUATIC ENVIRONMENTS

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Abstract—Kepone, decachlorooctahydro-l, 3, 4-metheno-2H-cyclobuta (cd) pentalen-2-one, is a known mammalian carcinogen. From at least 1967 to 1975 when production stopped, it contaminated the Chesapeake Bay. Action levels for kepone in seafood were established by the U.S. Environmental Protection Agency, and various species of finfish, oysters, *Crassostrea virginica*, and crabs, *Callinectes sapidus*, often were found to exceed those levels. Detailed sampling and analyses of biota showed that interspecies variability in concentrations often exceeded an order of magnitude. Further examination of the data showed that much of the variability could be explained by factors such as sex, spawning cycle, and migratory patterns. Estimates of human exposure to kepone-contaminated seafood, and, hence, estimates of risk from consuming it, were quite inaccurate unless natural variability was considered. On the positive side, an understanding of the factors controlling natural variability provided alternative risk-management options to minimize risk by decreasing exposure without totally prohibiting harvest or consumption of the resource.

INTRODUCTION

The major components of a human health-risk assessment are relatively well known. The “Red Book” of 1983 examined how to assess risk to humans from cancer-causing chemicals (NRC 1983). The paradigm set forth in this paper has been expanded and modified over time, but the basic principles have remained. To assess health risk from chemicals, one must determine two things: the potential effects of the chemical and exposure to it.

In order to estimate a chemical’s effect, the hazard and dose/response of the substance must be examined. Hazard is the inherent ability of a substance to cause harm. For instance, a metabolite of benzo(a)pyrene (BaP), a compound formed by the incomplete combustion of fossil fuel, is thought to be a human carcinogen. So, the hazard of the 7-8-dihydroxy-9-10-epoxide of BaP is that it can cause cancer. Dose/response, on the other hand, estimates how much of the substance is required, at the right place and time, to cause a manifestation of the effect.

Once one knows what harm a chemical may inflict and how much is required to do it, an estimate of exposure to that chemical allows a characterization of the risk involved.

Action levels or tolerance levels are often defined as the maximum concentration of a hazardous substance one can have in food without experiencing the ill effects of the substance. In effect, these are regulatory or risk-management tools used by the U.S. Food and Drug Administration (FDA) or the U.S. Environmental Protection Agency (EPA) to limit exposure to hazardous substances from ingestion of contaminated food.

There are numerous difficulties involved in estimating the hazard and dose/response of a chemical to humans. Are the animal models used in toxicity tests appropriate for extrapolating to humans? Is it a zero threshold chemical? Are there sensitive subpopulations, etc.? There are also numerous difficulties in estimating exposure to the chemicals; these are often due to the inhomogeneous nature of the substance in question in the environment. Because a determination of risk can be no more accurate than the most inaccurate number that goes into calculating it (the Significant Figures Paradigm), one must strive to obtain the very best estimates of all components of the assessment process, including exposure.

Natural variability, a particularly difficult aspect of accurately determining exposure to environmental contaminants, is the focus of this manuscript. The much-studied chemical contamination by kepone of the James River system is used to exemplify various aspects of this phenomenon.

BACKGROUND

The James River is a major tributary to the Chesapeake Bay. With its drainage basin of 25 600 km², it delivers 16 percent of the freshwater to the bay. The river is tidal for 160 km, from its mouth near Norfolk, VA, to the fall line at Richmond, VA. The salinity at its mouth is usually near 25 parts per trillion (ppt), and brackish waters extend about 50 km upstream, depending on precipitation within the drainage basin. From this point upstream to Richmond, it is a tidal freshwater river, and from this point to the mouth, it is technically an estuary.

Approximately 110 km upstream, in the tidal freshwater portion of the river, lies Hopewell, VA. From 1966 until 1974,

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the pesticide kepone was manufactured there by Allied Chemical Company and Life Science Products, Inc. Over this period, thousands of kg of kepone entered the river via municipal waste effluents and other point and nonpoint sources. Investigation of the river's bottom sediments led to an estimate of 14 000 kg of kepone being sorbed to the particles. This became the major source of contamination to the biota of the James River and the Chesapeake Bay (Bender and Huggett 1984).

Kepone, (decachlorooctahydro-1, 3, 4-metheno-2H-cyclobuta (cd) pentelen-2-one), once intended to control fire ants and cockroaches and eventually used for the banana root borer in Central and South America, is extremely persistent and bioaccumulative (Huggett and Bender 1980). It is also a suspected human carcinogen.

Because kepone was found to be present in the edible portion of finfish, crabs, clams, and oysters inhabiting the James River and adjacent Chesapeake Bay, the EPA, under the auspices of the Federal Insecticide, Fungicide, Rodenticide Act, established action levels for the compound. Based on NOELS from rodent testing and average food consumption patterns, the following levels were originally established: finfish: 0.1 mg per kilogram wet weight; crabs: 0.4 mg per kilogram wet weight; oysters: 0.3 mg per kilogram wet weight. The action level for finfish was later raised to its present level of 0.3 mg per kilogram.

It should be noted that action levels or tolerance levels are enforceable by the FDA only if the contaminated commodity crosses State lines. If the contaminated seafood, in this case, was harvested and sold in Virginia, the Federal government had no jurisdiction. Even so, the Commonwealth of Virginia adopted the Federal action levels for instate public health protection.

The problem that faced the State health regulators was to determine accurately the concentrations that existed in the seafood and to permit or ban fishing in certain areas or for certain species in order to control exposure to kepone. This required an accurate assessment of the kepone concentration distributions in various species by location and time. The findings of numerous sampling expeditions and what is commonly called natural variability are described and exemplified in the remainder of this paper.

KEPONE NATURAL VARIABILITY

Many, if not most, of the commercial species of finfish that inhabit the Chesapeake Bay spend part of each year in the ocean. In the spring, they re-enter the bay and spend several weeks near its mouth, and hence, the James River, to equilibrate to the lower salinities. Some organisms enter the James River and remain throughout the season, and others enter and leave again, migrating to other portions of the bay. Concentrations of kepone in 91 blue fish collected in June 1976 from one location in the bay are presented in figure 1 (Huggett and others 1980). There is an obvious biomodal distribution of concentrations with approximately 40 percent of the animals being above the action level of 0.1 mg per kilogram. These more contaminated animals presumably spent some time in the James River before leaving and grouping with fish that had not. Knowledge of

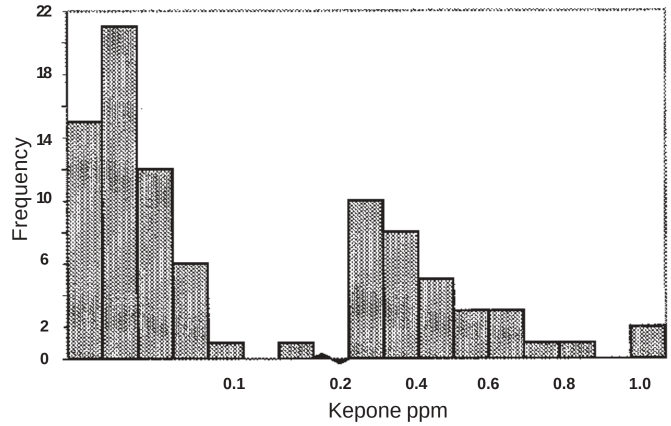

Figure 1—Histogram of kepone concentrations in bluefish from the James River showing bimodal distribution.

the distribution of concentrations greatly increases the accuracy of estimates of exposure from consumption of the fish.

Concentrations of kepone in the edible flesh of aquatic organisms can also be influenced by the sex of the animal, with males often being more contaminated. This is presumably due to the substance being partitioned to the lipid-rich eggs of the females (Huggett 1981). Figure 2 exemplifies this phenomenon. For the American shad, *Alosa sapidissima*, 41 percent of the males contained more than 0.1 mg per kilogram whereas only 6 percent of the females had levels as high.

Blue crabs, *Callenectes sepidus*, from the James River were extensively sampled and analyzed. The difference in concentrations between males and females was striking (fig. 2). As was the case with the American shad, the females continued to show low levels relative to the males. All of the male crabs sampled exceeded the action level of 0.4 mg per kilogram whereas only 11 percent of the females were high. This finding resulted in Virginia allowing commercial harvest and sale of female crabs but not males.

The body burden of kepone is somewhat proportional to the duration that the animal is exposed to the substance. Croakers, *Micropogon undulates*, enter the bay from the ocean in early spring and return in the fall. Croakers collected from the James River throughout the summer of 1976 show that kepone concentrations increase with exposure time with no plateauing noted (fig.3) (Huggett and others 1980).

The physiology of the organism, as influenced by temperature, can also affect tissue concentrations. This is exemplified in figure 4, which shows kepone concentrations in eastern oysters, *Crassostrea virginica*, from 1976 through 1980 (Bender and others 1985). During winter, when water temperatures drop, the organisms have less planktonic food available. Their water-filtering rate is drastically reduced, and they metabolize stored body fat. In doing so, some of the lipidophyllic kepone is liberated. As water temperatures rise, feeding increases, and, concurrently, kepone levels increase, thus giving rise to a yearly cycle of concentrations.

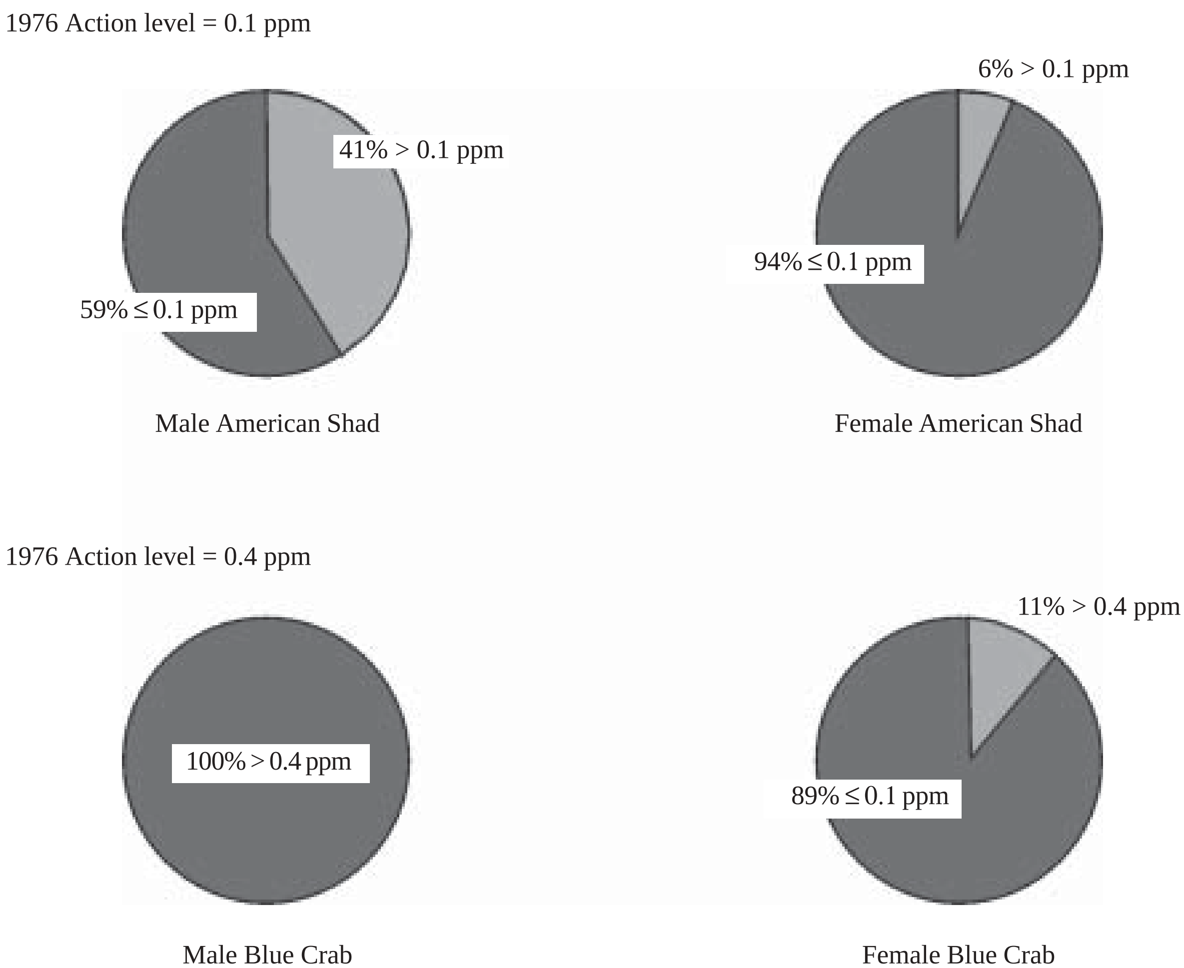

Figure 2—Concentrations of kepone in male and female blue crabs, *Callinectes sapidus*, and American shad, *Alosa sapidissima*.

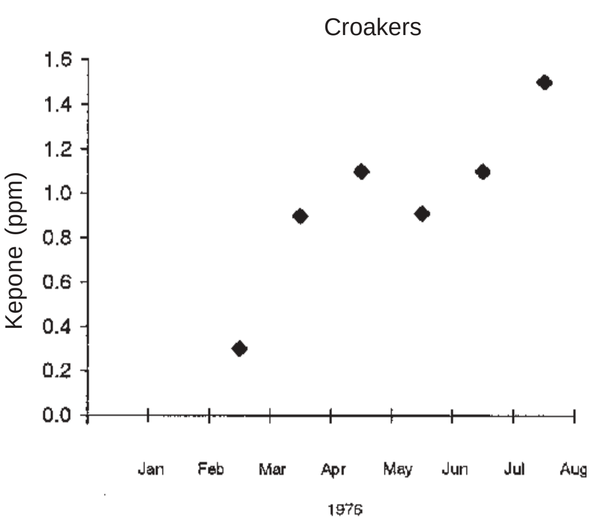

Figure 3—Kepone concentrations in croakers, *Micropogon undulatus*, collected from the James River in 1976.

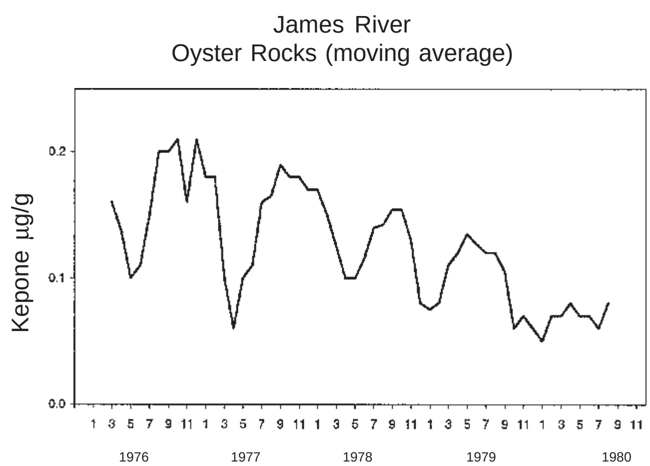

Figure 4—Kepone residues in oysters vs. time.

Figure 4 also shows an overall decline in kepone concentrations over time due to the burial of kepone in the sediments after production of the pesticide was stopped in 1975.

Since the production of kepone stopped in the mid-1970s, the concentrations in seafood have slowly decreased. The harvest of finfish in the James River was totally or partially banned until 1988 when concentrations fell below action levels (Huggett 1989). Table 1 presents data that show that by 1996 the levels were less than one quarter of the action level (Unger, M.A. 2000. Personal communication. Glouster Point, VA: Virginia Institute of Marine Science).

Table 1—Yearly averages of kepone concentrations in striped bass (*Morone saxatilis*) from the James River

Year	Animals analyzed	Mean kepone	Standard deviation
	- - No. - -	*Mg/kg*	
1989	40	0.13	0.03
1990	40	.20	.06
1991	40	.22	.07
1992	40	.20	.07
1993	40	.12	.11
1994	60	.17	.08
1995	60	.16	.07
1996	55	.07	.05

CONCLUSION

Studies designed to determine human exposure to hazardous chemicals from consumption of contaminated foods need to take into account natural variability. Failure to do so may result in inadvertently placing consumers at risk or, on the other hand, imposing harvest restrictions more severe than necessary to protect public health. It is also important to consider natural variability when assessing the effects of hazardous chemicals on the organisms themselves. Partitioning of lipidophyllic compounds to gametes poses a relatively high risk of toxic reproductive effects.

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