The measurement of these environmental toxicants or their metabolites has proven useful for assessing human exposure in epidemiologic studies and in surveys. Here, I will give examples using lead and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) as examples. In the United States in the 1970s the impact of the decreased use of tetraethyl lead in gasoline was being debated. In 1976, the National Center for Health Statistics began the second National Health and Nutrition Examination Survey (NHANES II); blood lead measurements were conducted on about 30,000 residents of the U.S. This survey continued until 1980. During that same 1976–1980 time period, the use of lead in gasoline was being decreased. The 1976 NHANES II data revealed that the average blood lead level in the U.S. was about 16 micrograms/dl. Mathematical models predicted that the decrease of lead in gasoline over this 4-year period would result in a decrease in the average blood lead level of about 0.6 μg/dl. When the 1976–1980 blood lead data were plotted, two things were obvious: the decrease was not 0.6 μg/dl but rather over 6 μg/dl and the decrease by year of the average blood levels strongly paralleled those of the lead in gasoline. The good news is that with the continued reduction of lead in gasoline and the ban on the use of lead solder in domestic food cans, the average blood lead level has continued to decrease to less than 3 μg/dl in the 1988–1991 NHANES III. The bad news is that about 1.7 million Americans still have levels that exceed 10 μg/dl. These people tend to be minority, low income, central city residents; the primary source is believed lead-based paint chips. The purpose of this report is not to demean models, but rather to point out that models should be validated against the measurement of the internal dose, when possible.

The next examples are based on the environmental toxicant, dioxin. We have measured dioxin in many epidemiological studies. These measurements require an analytical method that possesses both high specificity and sensitivity. Specificity is required to measure this toxicant in the midst of hundreds of other toxicants, many of which are present at higher concentrations. Sensitivity is needed because dioxin is present in human serum at levels in the parts-per-quadrillion range. Sophisticated sample preparation procedures and high-resolution gas chromatography/high-resolution mass spectrometry meet the necessary requirements. One such application was the health study of veterans of Operation Ranch Hand of the U.S. Air Force in Vietnam. In 1987, the Air Force asked us to validate the exposure index that they developed to assess exposure of these veterans to dioxin – a contaminant in some of the herbicides, such as Agent Orange – that they sprayed over 10–20 % of South Vietnam form 1962–1971. Their exposure index was based on the concentration of dioxin in the herbicides during one's tour of duty times the number of gallons of herbicide sprayed divided by the number of men in each speciality and the time component was the time one spent in Vietnam. We compared this exposure index with the serum dioxin measurement on 150 ground crew members of Operation Ranch Hand. To our surprise, there was no correlation between these two exposure indices. Therefore, any attempt to correlate exposure, based on the Air Force's exposure index, and any adverse health outcome would be flawed. Since then, in support of this study, we have measured dioxin in all participants (Ranch Hand veterans and comparisons) in this study. The exposure index that is now used is the serum dioxin measurement.

We have also been providing the analytical measurements of dioxin in the serum of residents of Seveso, Italy, the site of the largest residential exposure to dioxin. Various endpoints, including preliminary evidence of a change in the sex ratio in newborns, are being evaluated. Without these measurements it would not be possible to accurately assess exposure or certainly furthermore to link it to such endpoints. This study continues.

The main point of this presentation again is not to demean the development and use of mathematical models or exposure indices based on data other than the internal dose, but it is to advocate the use of the internal dose as the exposure index, if possible. If the internal dose cannot be measured on all of the population, it should be measured on a segment of the population in order to validate the derived exposure index. This exposure information should then become a vital and used component of risk assessment.

DIOXIN-LIKE AND NON-DIOXIN-LIKE TOXIC EFFECTS OF POLYCHLORINATED BIPHENYLS (PCBs): IMPLICATIONS FOR RISK ASSESSMENT

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SUMMARY

Polychlorinated biphenyls (PCBs) are persistent, bioaccumulative and toxic contaminants in the environment. Individual PCB congeners exhibit different physico-chemical properties and biological activities which result in different environmental distributions and toxicity profiles. The variable composition of PCB residues in environmental matrices and their different mechanisms of toxicity, complicate the development of scientifically based regulations for the risk assessment. Various approaches for the assessment of risks of PCBs have been critically examined. Recent developments in the toxic equivalency factor (TEF) approach for the assessment of toxic effects due to dioxin-like PCBs have been examined. PCB exposure studies which describe non-dioxin-like toxic effects, particularly neuro-behavioral effects and their effective doses in animals were also considered. A comparative assessment of effective doses for dioxin-like and non-dioxin-like effects by PCBs was made to evaluate the relative significance of non-ortho and ortho-substituted PCBs in risk assessment. Using mink as an example, relative merits and implications of using TEF and total PCB approaches for assessing the potential for toxic effects in wildlife was examined.

Key words: dioxin-like activity, polychlorinated biphenyls

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INTRODUCTION

Polychlorinated biphenyls (PCBs) are members of the group of halogenated aromatic hydrocarbons (HAHs), and consist of 209 isomers and congeners with different numbers and positions of chlorine atoms substituted on the biphenyl moiety (1). Although 209 congeners of PCBs are theoretically possible, only about 130 individual congeners have been identified in commercial PCB mixtures at concentrations ≥ 0.05 %. Individual PCB congeners exhibit different physico-chemical properties which result in different profiles for environmental distribution and toxicity. The differences in the composition of PCB residues in environmental matrices has implications

for quantification and hazard evaluation, particularly when considering the differences in the biological activity, both qualitatively and quantitatively, among isomers as well as congeners. Due to the differences in metabolism and/or biodegradation rates of individual congeners, the compositions of the original commercial technical mixtures are different from the compositions of the mixtures which humans or wildlife are exposed. Only a few studies have investigated the effects of environmentally altered mixtures of PCBs. Health risks due to PCB exposure in humans or wildlife has been assessed based on either total PCB concentrations or 2,3,7,8-tetrachlorodibenzo-p-dioxin equivalents (TEQs) using toxic equivalency factors (TEF). The U.S. Environmental Protection Agency (EPA) has adopted the TEF approach as an interim procedure for the calculation of risks of planar PCBs (2, 3). The concept of TEF was developed in the early 1980s for assessing the risks of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) in waste incinerators (4, 5). The TEF model for PCBs presupposes a common mechanism of toxic action and additivity for the toxic effects of the individual congeners in the mixture and that PCBs act through the same mechanism of action as PCDDs/PCDFs. Further, the approach assumes that the dioxin-like effects of PCBs are the critical effects on animals. The critical effects are those that occur at the least concentration and would result in the least allowable total concentration of PCB mixtures.

Here we describe, compare and contrast several approaches to assessing the potential risks of PCBs to which wildlife might be exposed (1). Specifically, the concept of a critical toxicant will be developed based on the determination of mechanisms of actions that are likely to cause biological effects at the lowest concentrations of PCBs. This was done by comparing reference doses (RfDs) for various toxic endpoints. A second level of assessment undertaken was to determine the effects of various environmental fate processes on outcomes of risk assessment based on total PCBs. Recent developments in the TEF approach for the assessment of dioxin-like effects of PCBs are also examined (1). Laboratory PCB-exposure studies for neuro-behavioral effects and their effective doses in animals were compiled (1). A comparative assessment of effective doses for dioxin-like and non-dioxin-like PCBs has been made to evaluate their significance in risk assessment process. Using mink as an example, the relative merits and implications of using the TEQ – and total PCB – approaches for assessing the potential for toxic effects in wildlife were examined.

RISK ASSESSMENT OF PCBs

Traditionally, ecological risk assessments of PCBs have involved comparison of exposure concentration in target species to a reference dose (TRV; equation 1). The TRV is an estimate of daily exposure, which during an entire lifetime, is likely to be without an appreciable adverse effects. The TRV can be expressed as a mass of chemical per unit body mass per unit time (e.g., mg/kg bw/d). Alternatively, doses can be given as maximum acceptable toxicant concentrations (MATCs) or burdens in target tissue (mg) or as dietary exposures expressed as concentrations in the food (mg/kg in the diet).

TRV = NOAEC (or LOAEC)/uncertainty or correction factor [1]

The TRV is estimated by dividing the no observable effect concentration (NOAEC) or the lowest observable effect concentration (LOAEC), which are usually derived from dietary exposure to animals with technical PCB mixtures such as Aroclors, by correction (safety) factors. Here we compare the two methods of risk assessments for complex mixtures of PCBs by calculating HQ values based on total concentrations of PCBs by using the neuro-behavioral effects of di-*ortho*-substituted congeners, which are the primary components of the mixture and comparing these to the HQ values derived by the use of 2,3,7,8-TCDD equivalents (TEQs) that describe the toxicity of the dioxin-like congeners.

A toxic units approach was used to quantify the hazards due to PCB exposure in wild populations based on the NOAEC estimates from laboratory dietary exposure studies (6–8). The Hazards Quotient (HQ) is defined as the ratio of the concentration in the tissue or diet divided by the TRV (equation 2). The units for the HQ are toxic units (TU).

HQ = [Concentration in tissue or diet]/TRV [2]

An HQ of greater than one (1 TU) indicates that the concentration in the diet was expected to be sufficiently great to equal the threshold concentrations to elicit a statistically significant response.

The complex nature of PCB mixtures complicates the risk evaluation for wildlife (9). In order to evaluate risks due to PCBs, a fundamental understanding of the mechanism of action is a prerequisite. At present sufficient evidence is available that there is a common mechanism for non- and mono-*ortho* PCB congeners, involving binding to the Ah-receptor as an initial step. When applying the TEF-concept, the toxicity of these coplanar congeners relative to that of 2,3,7,8-TCDD is determined on the basis of available in vivo or in vitro data. However, it should also be understood that the TEF concept is based on a number of assumptions and has limitations. Studies have also shown that, apart from non- and mono-*ortho* PCBs, *ortho*-substituted nonplanar PCB congeners elicit neuro-toxic effects in exposed animals and in cell cultures. Although a well defined TEFs have not been derived for nonplanar PCB congeners, it appears that at greater exposures these congeners may cause neuro-toxic effects in humans or wildlife. Therefore, for a complete evaluation of risks due to PCBs, consideration of the effects of both *ortho*- and non-*ortho* substituted congeners are needed.

In order to evaluate relative hazards of coplanar and non-coplanar PCBs, concentrations of these congeners were estimated in mink (1). Details of the estimation of PCB concentrations in mink from their diet and dietary threshold values for reproductive and neurotoxic effects are described elsewhere (1). Mink was selected as a surrogate species due to the availability of threshold doses for neurotoxic effects in this species. Based on this example, using mink as a model, it was found that the hazard quotients (HQs) for total weather PCBs, total technical PCBs, TEQs and *ortho*-substituted PCBs were 50, 18, 190 and 5.9, respectively, The HQ values for dioxin-like PCBs were greater than those of non-dioxin-like PCBs, indicating that the coplanar PCBs are the critical in the risk assessment of PCBs. Nevertheless, it should be noted that mink are sensitive to reproductive effects of PCBs (10, 11) and therefore the effects due to coplanar PCBs have been critical. Further, the RfDs derived for non-dioxin-like effects of *ortho*-PCBs in mink were based on adult exposure. Since developing organisms are more sensitive to neuro-toxic effects of *ortho*-PCBs, RfDs from developmental exposures (pre- and/or perinatal) is necessary. However, RfDs for the neuro-toxic effects of *ortho*-PCBs are not available for mink or other wildlife.

Further studies are needed to derive RfDs for neuro-toxic effects of *ortho*-PCBs in wildlife. In any case, laboratory exposure studies with rodents and other mammals and in vitro bioassays have indicated that the neuro-toxic effects have occurred only at great exposures. Therefore, it is considered that TEQs for dioxin-like PCBs are critical in setting environmental quality criteria. In other words, establishment of threshold limits for PCBs based on dioxin-like effects would be able to protect the animals from non-dioxin-like effects.

Acknowledgements

We gratefully acknowledge the support of the National Food Safety and Toxicology Center and Institute for Environmental Toxicology at Michigan State University. The preparation of this analysis was supported, in part, by the NIEHS – Superfund Basic Research Program (NIH-ES-04911) and the General Electric Corporation.

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THE IMPACTS OF EXPOSURE TO ORGANIC COMPOUNDS OCCURRENCE OF NATURAL ORIGIN IN THERMAL WATER ON HEALTH IN BÉKÉS, HUNGARY

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SUMMARY

Deep thermal well (75 °C) in Békés county, South East Hungary has been studied. The chemical measurements showed that the thermal water coming from deep geological layers (>800 m) contains up to 117.2, 35.2, 30.2 and 26 µg/l of benzene, toluene, ethylbenzene, and xylenes, respectively. The objectives of this study are: to measure these naturally occurring compounds; estimating to potential risk and hazard index for the population who are using this well mainly for swimming and health baths; assessing the relationship between exposure to environmental chemical and human health; and to stimulate thinking about possible broader uses of risk assessment in identifying and solving public health problems. This paper is not intended as a complete study concerning the four measured compounds. A particular emphasis on benzene which is highly toxic and carcinogenic has been paid. The exposure assessment of benzene based on Risk Assistant model was done. The results showed that the Hazard Quotient (H.Q.) for benzene is more than 1 (requiring actions) and the probability of getting cancer from this exposure is 8E-5 exhibiting high risk for exposed population.

Key words: benzene, exposure assessment, hazard quotient, carcinogenic risk

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INTRODUCTION

Benzene is a monocyclic aromatic compound and is released to the environment from both natural and man-made sources, the latter accounting for the major part of emissions. Benzene concentrations in fresh surface waters are generally less than 1 µg/l (1). Benzene has been placed in Group I of the IARC classification as a human carcinogen (2). Benzene is absorbed via ingestion, inhalation and skin application. Humans may absorb benzene vapours through skin as well as the lungs, of the total dose absorbed by two routes, an estimated 22–36 % enters the body through the skin (3). The new studies found that the personal exposure exceeded indoor concentrations of benzene, which in turn exceeded outdoor concentrations (4). The leukemogenic potential of benzene has been well documented. Biologic evidence suggests that the timing, duration, and concentration of exposure are important independent factors in predicting benzene's hematotoxic effects (5). The acute health effects due to exposure to benzene is well known and the risk is easy to determine. However, the risk associated with chronic health hazards is more difficult to calculate. For this reason a ranking model was developed which made use of a point scoring system. This model highlights those compounds especially benzene which have a great possibility of causing adverse health effects (6) for long time exposure.

METHODOLOGY

Field and laboratory activities including field sampling, and analysis of aquifer materials. Selected unstable properties and chemical constituents were measured at the sampling site. The site located in the south east part of Hungary where many thermal water are found due to geological structure of that area. The different uses of this well are mainly for bathing and swimming after mixing with other sources of water. The volatile monoaromatic hydrocarbons in thermal water were analyzed according to US EPA Method 524.2 by using solid phase microextraction (SPME) and capillary gas chromatography with mass selective detector (CGC/MSD). The computer software RISK*ASSISTANT version 1.1 (1995) is a powerful set of tools and databases for estimating the health risk of various chemicals in the environment. Default input parameters provided by the model are used, whenever possible, instead of a site-specific information. Default parameters for calculating exposure have been extracted from the US EPA exposure factors handbook (7, 8). In our analysis, April 1997, IRIS information was applied and IRIS represents up-to-date official estimate formulated by the EPA.

RESULTS AND DISCUSSION

Chemical concentrations in the environmental medium are needed to determine the magnitude of exposure. The results suggest higher levels of benzene and other components as well. Comparison between the organic compounds obtained in this study with certified or literature values (1, 9 and 10) showed that the current ones are extremely higher, which is important because of their relations to human health.

The predicted indoor and outdoor air concentrations of benzene presented in Table 1 were compared with other previous studies (4,