World Health Organization Working Group on the Assessment of Health Risks for Infants from Exposure to PCDDs, PCDFs and PCBs.

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On Nov. 20-22, 1995, 12 scientific representatives from 6 different countries met in Denmark to reassess the health risks to infants associated with perinatal exposure to polyhalogenated aromatic compounds. The meeting was organized by the WHO European Centre for Environment and Health, partially funded by the Danish Ministry of Health, with Dr. Ulf G. Ahlborg serving as chairman and Dr. John Christian Larson as vice-chairman. Prior to the meeting, a draft document entitled "Assessment of Health Risks for Human Infants from Exposure to PCDDs, PCDFs and PCBs", prepared by Dr. Abraham Brouwer for the WHO European Centre for Environment and Health, was distributed and served as the basis for the working group consultation.

Following discussions on previous WHO EURO initiatives related to the current consultation, the working group reviewed current information on the main sources of environmental loading for the contaminants in question, PCDDs, PCDFs and PCBs, and estimations of human exposures. Dioxins and furans are thought to enter the environment primarily through pyrolysis activities (municipal and hazardous waste incineration, metal smelting/refining) and as unintentional trace contaminants formed during the manufacture, use and disposal of chlorinated organic compounds. For example, pentachlorophenol (PCP) use was considered as a possible major source of PCDDs/DFs for industrialized countries. Due to discrepancies in dioxin/furan environmental mass balance equations, it was stressed that continuing effort should be directed towards identifying previously unrecognized sources (i.e., PVC manufacturing).

Unlike dioxins/furans, PCBs were specifically produced for use in a large number of industrial processes (additives, flame retardants, dielectric fluids etc.). Worldwide production of PCBs has been estimated at up to one billion kilograms with over a million kilograms thought to annually enter the environment via mobile environmental reserves (1).

The structural basis for establishing activity relationships between PCDDs/DFs and PCBs was reviewed, along with the criteria and limitations of the "toxic equivalency factor" (TEF) concept. Based on interim TEFs suggested for "dioxin-like" PCBs (2) and previously documented TEFs for PCDDs/DFs (3), the human adult exposures to these compounds was estimated to be in the range of 1-2 pg total TCDD toxic equivalents (TEQs)/kg bw/day (1994-95). As non-occupational exposure to these chemicals is influenced almost entirely by diet, increased consumption of contaminated lipid-rich

foods will increase exposure and body burdens. For human infants, exposure to these contaminants begins in utero, but quantitatively the majority of transfer of the parent compounds occurs via lactation. Infants who breast feed will generally have body burdens of these contaminants exceeding those of the mothers.

The next phase of the workshop dealt with a review of developmental effects attributed to these contaminants which have been observed in experimental studies and in a limited number of epidemiologic investigations. Based on the proceedings from a 1994 European Environmental Research Organization (EERO) Workshop on the developmental toxicity of polyhalogenated aromatic hydrocarbons (4), the working group discussed the variety of reproductive (sexual behaviour and endocrine-related), neurologic (behaviourial and biochemical) and immunologic effects which have been observed in primarily rodent offspring following perinatal exposure to these contaminants. The majority of the experimental studies involved single or multiple dosing regimes during embryogenesis with single congeners or commercial PCB mixtures.

The primary epidemiologic studies which were considered by the working group included the Oriental rice oil poisoning episodes (Yusho and Yu-Cheng), the Michigan sportfish eaters and North Carolina Breast Milk and Formula Project cohorts and the recent Dutch breast milk studies.

The final discussion focused on future recommendations and whether sufficient information existed to allow for the working group to develop a health risk evaluation based on the previous reviews. For the exposure assessment, it was concluded that in a number of industrialized countries, there has been a significant decline (up to 50%) in the levels of PCDDs/DFs and possibly PCBs in breast milk which is probably reflective in part on remedial actions taken to control input into the environment. It has been clearly demonstrated that TCDD and certain PCBs are capable of inducing a variety of persistent functional developmental effects in offspring of experimental animals (primarily rodents) following perinatal exposure, at dose ranges which do not induce appreciable maternal toxicity. However, hazard evaluation from the experimental studies was thought to be partially hampered due to: pharmacokinetic extrapolations (estimated steady-state body burdens from single dose/time point experiments), single congener study designs vs. actual complex environmental mixtures, limited mechanistic determinations and a species/strain-specific nature to certain of the observed effects. Of the epidemiologic studies considered, the most severe developmental effects were associated with the oriental rice oil poisonings. However, it was noted that the effects observed in the infants were the result of high exposure to a contaminant mixture with a unique congener profile (PCBs, PCDFs, PCQs, PCTs) with maternal body burdens (TCDD TEQs) up to two orders of magnitude greater than those associated with environmental exposures. Methodological concerns and discrepancies in the neurodevelopmental results between the Michigan sportfish eaters and North Carolina Breast Milk and Formula Project cohorts were thought to limit their strength in terms of providing positive evidence of an association between exposure to PCBs and adverse effects. Current results from the Dutch breast milk studies were also reviewed. While the majority of the mental/psychomotor and clinical effects observed were considered subtle and within the normal population range, the significance of the findings warranted continued follow up in combination with additional related ongoing studies (Faroe Island, Canadian Inuit, Great Lakes anglers).

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At the end of the meeting, final recommendations by the working group included:

- source identification and environmental input controls, in particular air emissions, were considered the most effective way of reducing human exposure to these contaminants;
- the benefits of breast feeding combined with decreasing levels of these contaminants in breast milk support continued endorsement;
- reassessment of the 1992 WHO TDI for TCDD of 10 pg/kg bw/day, based on the concept of developing harmonized toxic equivalency factors for PCDDs/PCDFs, PCBs and additional "dioxin-like" compounds.

References

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3. NATO/CCMS Report 176, 1988.
4. Brouwer, A. et al., Eur. J. Pharmacol., 293:1-40, 1995.