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GREAT LAKES HUMAN HEALTH STUDIES: NEUROBEHAVIORAL EFFECTS

GREAT LAKES HUMAN HEALTH EFFECTS RESEARCH PROGRAM STUDIES UNDERWAY

In May 1997, a conference was held in Montreal to discuss the findings of a series of studies on the human health effects of environmental exposures to pollution. Subsequent to the passage of the U.S. Great Lakes Critical Programs Act of 1990, the Agency for Toxic Substances and Disease Registry (ATSDR) has funded numerous research projects as a part of the Great Lakes Human Health Effects Research Program. In Canada, there are also a number of research studies on pollution-related health effects that have been conducted or funded by Health Canada. The Health Conference of May 1997 was cosponsored by both agencies, and it provided an opportunity for scientists and policy-makers to gather and discuss the findings of this new body of research.

The series of studies that are currently funded under the ATSDR's program include epidemiological research, studies of exposure to environmental pollutants, and projects to improve analytical or quality control methods in environmental exposure assessment. Several existing cohorts, including the New York Sport Angler cohort and the Mohawk Indian cohort, are being utilized in studies of human exposure to persistent toxic chemicals. Several ATSDR-funded studies are assessing health effects of pollutants from environmental exposures, and these studies are described in more detail here. Additional studies have been funded to develop new methodology for toxicity assessment, and for developing quality control procedures for existing analytical methods.[1] While this series of studies was highlighted in the recent conference, research projects are also being conducted or funded by numerous other agencies, and findings from a number of studies by Canadian researchers were presented. In the health studies, various effects are under study. Neurobehavioral changes are emphasized in this summary, because there is growing evidence that low-level exposures to contaminants can result in subtle endocrine or neurological changes that may lead to neurobehavioral impairment.

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A quarterly summary of recent findings in the scientific literature on human health effects and environmental pollutants, with an emphasis on pollutants of the Great Lakes ecosystem. Prepared under the direction of the Health Professionals Task Force of the International Joint Commission. This newsletter does not represent the official position of the International Joint Commission.

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PRELIMINARY FINDINGS FROM GREAT LAKES HEALTH RESEARCH

A number of the ATSDR-funded studies will assess neurobehavioral effects in infants or older adults. The initial findings of the ***Oswego Newborn and Infant Development Project***[2] were published in 1996, and additional results were presented at the Montreal conference. This cohort includes approximately 150 mother-child pairs in each of three three fish consumption categories. The first published report of neurobehavioral effects from this cohort uses the results of the Neonatal Behavioral Assessment Scale tests that were administered at 12-24 and 25-48 hours after birth. The change scores from these tests indicate that the high fish group babies demonstrated a greater number of abnormal reflexes and less mature autonomic response (e.g. more startles and tremors), and there was some evidence of less developed attention to visual and auditory stimuli. At the Health Conference, preliminary results of additional testing at age 24 months with an infant behavioral questionaire were presented. Changes were found in overall and four of six behavioral scales in the assessment of infant temperment – activity level, fear, smiling and laughter, and soothability – at higher levels of fish consumption, but the differences for individual scales lost statistical significance when controlling for demographic and other variables. Significant effects were seen in several behavioral categories on the Neonatal Behavioral Assessment Scale when analyzed by recency of fish consumption: habituation, orientation, autonomic and reflexes. The authors conclude that their findings generally support those of the Michigan study.[3]

The ***New York State Angler Study***[4] was initiated in 1991; during the recruitment phase, over 20,000 anglers and their wives or partners have responded to a questionnaire that includes information on reproductive and medical histories, and frequencies with which some foods are eaten. In a subsample of participants, blood, hair and urine samples have been collected to determine levels of lead, mercury and some PCBs. Additional studies planned include a study of the health of infants of cohort members, and the researchers are also collecting breast milk samples from lactating women for exposure studies. At the Health Conference, a research design for analyzing effects on the immune system were presented.[5] Additional concern has been raised that older people may represent another population highly susceptible to the neurobehavioral dysfunction following exposure to environmental contaminants. Toxicological studies have found that PCB exposure is associated with decreased dopamine levels, and there is substantial loss (up to 60-70%) of dopamine-using nervous system cells in the normal aging process. A greater than normal loss of such cells may result in Parkinson's disease and impaired cognitive function.

In a study of the ***Cognitive and Motor Effects of PCB Exposure in Older People from the Michigan Fisheater Cohort***,[6] Illinois researchers recruited 572 fisheaters (24+ lbs/year) and 419 nonfisheaters from the members of the cohort established previously by the Michigan Department of Public Health who are now at least 50 years of age. Blood samples were drawn to determine levels of PCBs, DDE and 10 other contaminants in 180 of the subjects. Questionnaires were administered to obtain demographic and fish consumption data. A two-hour battery of tests of motor function, memory and learning, executive functions, and visual-spatial functions was administered. PCB levels were found to be higher in the fisheater group, and higher levels were also found of lead and mercury, though the levels were low in both groups. Results from the fine motor function tests were presented at the Health Conference. High exposure to PCBs/DDE was associated with decreased performance on fine motor function tests, but the associations were not significant when adjusted for demographic and other correlated factors.[7]

In the study of ***Great Lakes Fish as a Source of Maternal and Fetal Exposure to Chlorinated Hydrocarbons***,[8] Illinois researchers recruited approximately 80 pregnant African-American women from the Chicago area, and the cohort was divided into subgroups that consume sport-caught fish, store-purchased fish, and no fish; many also consume wild fowl and game. Upon delivery, sample of maternal and cord blood, placenta, infant meconium, adipose tissue (if cesarean) and breast milk (where available) were collected. Future studies will include include measurements of behavioral, endocrinological, and immunological function in the children.

Wisconsin researchers are conducting the ***Ojibwa Health Study***[9] in

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six Ojibwa reservations in the upper Great Lakes area. Over 600 participants have been recruited and completed a questionnaire regarding fish consumption, health history and environmental risk perception. Approximately 200 have provided hair and/or blood samples for analysis, and future studies will include assessment of neurobehavioral effects.

Canadian researchers reported some findings of nervous system dysfunction in adults that were associated consumption of fish from the St. Lawrence River System.[10] In a group of over 300 adults (20-69 years old) with no workplace exposures, a questionnaire was administered to obtain information on fish consumption and socio-demographic factors. A neurological exam was conducted, and a battery of neurofunctional tests administered. Motor slowing and attention difficulties were found to be related to the frequency of St. Lawrence Lakes fish consumption, after controlling for demographic factors. In addition, the subjects who consumed fish in both summer and winter had poorer test results than those who consume fish during one season.

In addition to the new cohort studies described above, a recent report has presented findings of follow-up testing in the ***Michigan Fish-eaters Cohort***.[11] This cohort was established in 1980-81, when 313 newborns and their mothers were recruited for the initial study. The Jacobsons recently published findings from a follow-up study of the children at 11 years of age. Blood and hair samples were collected from 212 children from the original cohort, and a battery of IQ and achievement tests was administered. Prenatal exposure to PCBs was associated with a significant decrease in full-scale and verbal IQ scores (P=0.02); IQ was 6.2 points lower in the most highly-exposed children than those in the other groups (p=0.007). The authors note that all IQ or achievement test scores were lower in the exposed group, but not all differences were statistically significant. Mercury and lead levels were assessed in this follow-up study, and some effects were found to be associated with these exposures, but the associations with PCBs remained significant when controlling for exposure to these metals. Some neurobehavioral effects were found to be associated with postnatal PCB exposure measures, but these associations were not significant when prenatal exposure measures were included in the model.

Finally, the ***Yu-Cheng*** population represents an older cohort of persons exposed to PCBs and other organochlorine contaminants in rice oil used for cooking; developmental effects have been reported in the children born to Yu-Cheng women. Previous studies of the Yu-Cheng have found little or no correlation between levels of PCBs and the effects observed. In a recent commentary, researchers in Taiwan reported on the initiation of new studies to better define the exposures of Yu-Cheng patients and children.[12] Recent developments in analytical methodology have greatly increased scientists' ability to determine levels of individual organochlorine pollutants in human serum or tissue. The new studies will provide new insight on whether the PCBs, PCDFs or PCDDs are the causative agent of the Yu-Cheng health effects.

OBSERVATIONS FROM STUDIES OF WILDLIFE

Scientists studying wildlife populations were first to draw attention to the potential effects of environmental pollutants. While still few studies have been conducted on human health effects from these exposures, a larger body of literature is available from wildlife studies. These reports have provided evidence for more gross developmental effects than the subtle neurobehavioral changes reported in the U.S. and Canadian studies.

In one recent report, a group of researchers from the U.S. and Canada[13] measured chick deformity rates in over 44,000 cormorant chicks and over 12,000 tern chicks from 1986 to 1991. Deformities included bill defects, incomplete skull, vertebral or neck deformity, clubfoot, spina bifida, lack of tail, dwarfed appendages, and Siamese twins. Overall, the percentage of deformities in each of seven populations ranged from 2.6% to 8.18%. Embryo death was also determined, and both death and deformity rates were found to be correlated with concentrations of dioxin-like chemicals and planar PCBs.

The studies described here are focused on exposures in the Great Lakes region, but wildlife researchers have found organochlorine contamination to be global in nature. A recent report shows that concentrations of the PCBs and the DDT complex were similar in fish-eating birds from an island in the North Pacific to levels in Great Lakes region birds.[14]

OBSERVATIONS

There are indications from human and wildlife studies that environmental exposures to persistent pollutants may cause neurological or behavioral effects, but still few human studies have been completed. The findings presented at the Health Conference 97 indicate that prenatal exposure to such pollutants may result in neuro-behavioral effects later in life, but also that adults may be at risk for neurological effects. In a recent issue of *Neurotoxicology and Teratology*, a series of articles were published as an Open Peer Commentary, and many of the researchers involved in the study of neurobehavioral effects of environmental pollutants offered observations that pertain to the studies now underway.

* Jacobson and Jacobson[15] raised the issue of peak exposures to the fetus that may occur when the mother consumes contaminated foods during pregnancy. The authors cite results of a clinical study in which PCB levels in serum were measured in volunteers after consumption of a PCB-contaminated fish meal. The PCB levels in serum peaked at levels up to five-fold higher than baseline within 10 hours, and gradually declined to the premeal baseline over the subsequent seven days.
* Rice[16] observes that results from laboratory research are not always considered in the overall body of literature regarding neurobehavioral effects of PCBs. She notes that, in these studies, PCB-exposed animals appear to have difficulty in changing response strategies and/or inhibiting inappropriate responses, which is consistent with the findings from the epidemiological studies.
* Paneth[17] offers the cautionary note of determining the extent to which decreased performance on a standardized test, obtained under

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NOTE: (abstract) refers to the abstracts published for Health Conference '97 - Great Lakes/St. Lawrence, available from ATSDR (404-639-6357) or Health Canada (514-283-2306)