MEDICAL INTELLIGENCE

CURRENT CONCEPTS

Pollutants in Breast Milk

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ATTENTION has been focused on milk pollution by reports at scientific meetings and federally sponsored conferences, in scientific journals,1,4 and in the lay press. Although brief articles for the clinician have appeared in the pediatric literature,3,4 a detailed outline of the kinds of chemicals found in breast milk, the mechanisms for their presence there, and possible clinical implications has not appeared previously. Since most clinicians are familiar with the benefits of breast feeding,5 they will not be considered here.

Occurrence in Breast Milk

In general, the chemical contaminants that appear in breast milk have high lipid solubility, resistance to physical degradation or biologic metabolism, wide distribution in the environment, and slow or absent excretion rates. Of greatest concern among such chemicals are the organohalides such as polychlorinated biphenyls (PCB's) and dichlorodiphenyl trichloroethane (DDT). Long-term, low-level exposure to the organohalides results in a gradual accumulation of residues in fat, including the fat of breast milk.6 Lactation is the only way in which large amounts of such residues can be excreted.

Reports of organohalide concentrations in breast milk must be interpreted with caution. Breast milk varies widely in its fat content from woman to woman, and the value increases over the course of a feeding. Since these chemicals are virtually all in fat, reported levels may not be comparable from study to study unless the concentration is given on a fat basis or adjusted for fat content. Concentrations in fat will usually be about 30 times higher than concentrations in whole milk.

DDT

Laug et al. reported in 1951 that DDT was present in human milk,11 and that observation was subsequently confirmed by many authors in diverse parts of the United States (Table 1).3 These reports are fairly consistent, showing widespread contamination of milk by DDT and its primary metabolite 1,1-dichloro-2,2-bis ethylene (DDE). It seems reasonable to conclude that such contamination results from ambient rather than specific occupational exposure, and that there are no obvious clinical or dietary predictors.

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PCB’s

A relatively systematic sample of mothers in the United States is available from the 1975 survey of pesticides in mother’s milk sponsored by the Environmental Protection Agency. Of 1038 samples reported by Savage et al.,12 nine (1 per cent) had no contamination, 720 (69 per cent) had levels that were detectable but below 0.050 parts per million (the limit of quantifiable values by their method), and 309 (30 per cent) had levels above 0.05 parts per million on a whole-milk basis. Of these 309, about 20 per cent (6.7 per cent of the entire set) had levels above 0.1 parts per million (Table 2).

Other Compounds

Although there are numerous reports of various chlorinated pesticides in breast milk, the data of Savage are by far the most complete. On the basis of these data, it seems that even the less widespread pesticides, such as dieldrin, heptachlor epoxide (a metabolite of heptachlor), and oxychlordane (a metabolite of chlordane), are breast-milk pollutants (Table 3).

Table 1. DDT Concentration in Breast Milk in the United States.

<table>
<thead>
<tr>
<th>INVESTIGATION</th>
<th>NO. OF SAMPLES</th>
<th>CONCENTRATION FOUND</th>
<th>YEAR COLLECTED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laug et al.11</td>
<td>32</td>
<td>0–770 (130) *</td>
<td>1950</td>
</tr>
<tr>
<td>Quinby et al.24</td>
<td>10</td>
<td>&lt;20–360 (120) *</td>
<td>1960,</td>
</tr>
<tr>
<td>(individual)</td>
<td></td>
<td></td>
<td>1961</td>
</tr>
<tr>
<td>Quinby et al.13</td>
<td>4</td>
<td>120–190 (170) *</td>
<td>1960,</td>
</tr>
<tr>
<td>(pooled)</td>
<td></td>
<td></td>
<td>1961</td>
</tr>
<tr>
<td>Curley and</td>
<td>5</td>
<td>42–113 (770) *</td>
<td>1968</td>
</tr>
<tr>
<td>Kimbrough2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kroger et al.</td>
<td>53</td>
<td>0–6 (2.4) †</td>
<td>1972</td>
</tr>
<tr>
<td>Hagvard et al.10</td>
<td>30</td>
<td>92–575 (326) *</td>
<td>1973</td>
</tr>
<tr>
<td>Wilson et al.11</td>
<td>138</td>
<td>&lt;220–830 (170) *</td>
<td>1973</td>
</tr>
</tbody>
</table>
*Parts per billion on a whole-milk basis. Figures in parentheses denote the mean.
†Parts per million on a fat basis. Figures in parentheses denote the mean.

The occurrence of polybrominated biphenyls (PBB’s) in breast milk has been studied mostly in Michigan.13 The median PBB concentration in fat of breast milk of women in the Lower Peninsula was 0.068 parts per million. Ninety-six per cent of 53 samples from the Lower Peninsula and 43 per cent of 42 samples from the Upper Peninsula contained detectable levels of PBB.

Toxicity

Pesticides

The pesticides discussed here are DDT, dieldrin, heptachlor, and chlordane. DDT had wide usage until 1972, when its registration was withdrawn. It is a relatively nontoxic compound for adult human beings. Studies of both occupationally exposed workers and experimentally exposed volunteers in whom doses were considerably above those in the general population have shown little or no evidence of toxicity.14-17 At doses of 16 to 286 mg per kilogram of body weight per day, DDT is acutely poisonous, producing symptoms ranging from mild tremor and vomiting to seizures.16 Although no cases of fatal DDT ingestion have been reported, ingestion of the cyclodiene pesticides (dieldrin, chlordane, and heptachlor) has caused death, typically from convulsions. Hyperirritability and stimulation of the central nervous system are characteristic. Abnormal liver function has been observed in patients recovering from ingestions.18

Some animal species appear to be more susceptible than human beings to the effects of these compounds. DDT is an enzyme inducer in rats; it causes adrenal atrophy in dogs;18 affects the reproductive and hormonal cycles of rats, birds, and other laboratory animals, and is also a carcinogen in mice. All these compounds induce microsomal-enzyme activity in animals and thus may affect drug metabolism. They also produce hepatic dysfunction and may disrupt reproduction through interference with steroid-hormone metabolism. Like DDT, dieldrin is a carcinogen in mice. It should be mentioned that unlike DDT, the cyclodiene are absorbable through intact skin.18

Extrapolation of these results to human beings is difficult. Long-term clinical studies on reproductive capacity, enzyme induction, or carcinogenesis have not been carried out. Newborn babies, who may be

Table 2. Pesticides and PCB Levels in Breast Milk in the United States.12

<table>
<thead>
<tr>
<th>FINDING</th>
<th>DIELDRIN *</th>
<th>HEPTACHLOR *</th>
<th>OXYCHLORDANE *</th>
<th>PCB’s †</th>
</tr>
</thead>
<tbody>
<tr>
<td>parts/billion ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of samples</td>
<td>1436</td>
<td>1436</td>
<td>1436</td>
<td>1033</td>
</tr>
<tr>
<td>% detectable</td>
<td>83</td>
<td>61</td>
<td>74</td>
<td>30</td>
</tr>
<tr>
<td>Mean</td>
<td>164</td>
<td>91</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>Range</td>
<td>14–12,300</td>
<td>16–2050</td>
<td>13–5700</td>
<td>50–4991</td>
</tr>
</tbody>
</table>

*Mean and range are given on samples with >1 part per billion detectable.
†Mean and range are given on samples with >50 parts per billion detectable.
‡On a whole-milk basis.


<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>TYPICAL LEVELS *</th>
<th>FDA ACTION LEVELS FOR COW’S MILK †</th>
<th>ALLOWABLE DAILY INTAKE</th>
<th>DAILY INAKE OF BREAST-FED INFANT ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>parts/billion</td>
<td>kg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dieldrin</td>
<td>1–65,2</td>
<td>7.5,54</td>
<td>0.1,0</td>
<td>0.8</td>
</tr>
<tr>
<td>Heptachlor</td>
<td>8–305,3,32</td>
<td>7.5,35</td>
<td>0.5,06</td>
<td>4</td>
</tr>
<tr>
<td>epoxide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCB’s</td>
<td>40–1001,4</td>
<td>62,54</td>
<td>1,14</td>
<td>14</td>
</tr>
<tr>
<td>DDT (including metabolites)</td>
<td>50–2001,5</td>
<td>50,17</td>
<td>5,17</td>
<td>28</td>
</tr>
</tbody>
</table>

*Levels considered typical in whole milk in the United States. The superscripts are reference numbers, not exponents.
†Assuming 2.5 per cent fat. FDA Action levels represent the limit at or above which FDA will take legal action against a product to remove it from the market.15
‡Intake of a 5-kg infant drinking 700 ml of milk per day. Levels are based on high values given under typical levels.
more susceptible than adults to such toxic effects, have not been studied at all.

**PCB's**

PCB's are industrial chemicals that have been widely used in the electrical industry, particularly as transformer-insulating fluids. Most of the data on the human toxicity of PCB's are from Japan, where food contamination was associated with an epidemic of acne-like rash, headache, nausea, and diarrhea. Patients had eaten considerable amounts of rice oil that was packaged or produced in February 1968 and found to contain 2000 to 3000 parts per million of PCB's. Further investigations revealed that the pipes used to heat the oil contained pinhole leaks that allowed the heat-exchange medium, a PCB mixture, to contaminate the cooking oil. The PCB mixture was also contaminated by other toxic chemicals, making interpretation difficult.

Thirteen children were born to exposed women: one was stillborn, four were small for gestational age, 10 had dark skin pigmentation, four had pigmented gums, nine had conjunctivitis, and eight had neonatal jaundice. PCB's were found in the breast milk of mothers with “Yusho” (oil disease), and children who were breast-fed had higher serum levels than controls. Follow-up of some of these children at about nine years showed slight but clinically important neurologic and developmental impairment. Children whose mothers worked with PCB's and who were breast-fed stored the chemicals for up to 13 years. The level in the children's blood varied with the duration of breast feeding.

An animal model of potential relevance has been developed at the Wisconsin Primate Research Center. Female rhesus monkeys fed 2.5 parts per million of Araqolar 1248, a PCB mixture, in the total diet had infants with a low birth weight. Breast feeding led to skin changes strikingly similar to those in Yusho babies. Results on developmental testing were abnormal, and early mortality was increased. The breast milk of the lactating monkeys contained 0.15 to 0.40 parts per million PCB's on a whole-milk basis; assuming 4 per cent fat content and complete partitioning, this figure represents about 3.8 to 10 parts per million on a fat basis. Kimbrough has reviewed the animal and human toxicity of the PCB's.

These data should be interpreted cautiously for several reasons. In the first place, the Yusho experience represents a different kind of exposure from the ambient one. The concentrations of the various congeners of PCB were different in the Yusho patients from those in the general population, and toxic impurities in the PCB mixture, including the highly toxic benzofurans, had contaminated the Yusho oil. Secondly, regarding the data on rhesus monkeys, there is much less subcutaneous fat in infant monkeys than in human newborns. Thus, the animals had less depot tissue in which the PCB's could be stored and thus higher doses at target sites for toxicity, such as liver, skin, or brain.

**Intake and "Safe" Levels**

It is very difficult to address the concept of a "safe" level of organohalide compounds. However, both the World Health Organization (WHO) and the Food and Drug Administration (FDA) have set "regulatory" or "allowable" levels for daily intake of several organohalides (Table 3). A typical infant might be exposed to higher levels of any of these chemicals. However, since such standards are often set up to allow a 100-fold or even a 1000-fold "margin of safety," the fact that the infant's intake exceeds the level does not mean that such exposure is toxic.

**Discussion**

Environmental chemicals can be present and concentrated in human tissue as a result of well-documented "bioconcentration" mechanisms. For certain fat-soluble chemicals, nursing infants can be regarded as living at the top of the food chain and are exposed to much more than background levels. Such compounds are virtually absent from the vegetable fat of commercially available foods for infants. A clinical assessment of risk is difficult because, although virtually all studies of the value of breast milk have shown definite benefits, the role of milk contaminants in the production of disease in children is virtually unstudied. It is heartening to note that no case reports of illnesses due to the transmission of environmental chemicals through breast milk have appeared (a case report does exist on occupational chemicals). Although screening (i.e., testing unselected mothers) has not been proposed anywhere in North America, both the state of Wisconsin and the Canadian Ministry of Health have mentioned the possibility of testing the milk of mothers who have potentially high exposure to PCB's or whose breast-fed infants are ill. Both areas have adopted similar "advisory" levels: 0.050 parts per million on a whole-milk basis in Canada and 2.5 parts per million on a fat basis in Wisconsin. However, the "turn-around time" for laboratory analysis is typically six weeks — a period that can represent a considerable portion of an infant's career as a breast feeder — and the clinical usefulness of such testing therefore seems minimal. The clinical importance of such advisory levels is, of course, conjectural, since there are no directly applicable human studies. More conservative recommendations concerning PCB's have also been made: pregnant and lactating women have been advised to avoid sport fish from contaminated waters, the only important dietary source of PCB's remaining, and they have been advised to avoid excessive weight reduction, which might mobilize the chemicals from fat stores. A policy statement from the American Academy of Pediatrics recommends breast feeding and mentions testing for PCB's only in women who have eaten large amounts of sport fish or been occupationally exposed.
Whether environmental chemicals attenuate the benefits of breast feeding is unknown, but breast feeding still seems to be beneficial. Continued efforts to diminish the levels of contaminants and thus the potential harm are needed, as is research on the impact of environmental pollution on the fetus and the newborn.

**REFERENCES**


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**ABNORMAL ADRENERGIC AND CHOLINERGIC SENSITIVITY IN CYSTIC FIBROSIS**

**PAMELA B. DAVIS, M.D., PH.D., JAMES R. SHELHAMER, M.D., AND MICHAEL KALINER, M.D.**

The organ systems most clearly affected by cystic fibrosis are regulated in part by the autonomic nervous system. Abnormal autonomic regulation may contribute to the clinical spectrum of cystic fibrosis.1,2 Previous studies have suggested that alpha-adrenergic regulation may be abnormal in the pupils,3,4 that beta-adrenergic responses are abnormal in leukocytes,5 and that responses to cholinergic agents may be disordered in the submaxillary gland and bronchial smooth muscle.6,7 Thus, abnormalities in all three components of the autonomic nervous system may coexist in cystic fibrosis. One possible explanation for these observations is altered responsiveness of the end organs. To assess this possibility, we examined the responses of patients with cystic fibrosis to administration of alpha-adrenergic, beta-adrenergic, and cholinergic agents.

We found that the patients had abnormal re-

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