

## REPORTING NEEDS FOR STUDIES OF ENVIRONMENTAL CHEMICALS IN HUMAN MILK

**Michael N. Bates**

School of Public Health, University of California, Berkeley, California, USA

**Sherry G. Selevan**

U.S. Environmental Protection Agency, Washington, DC, USA

**Susan M. Ellerbee**

University of Oklahoma, College of Nursing, Oklahoma City, Oklahoma, USA

**Lawrence M. Gartner**

Departments of Pediatrics and Obstetrics/Gynecology, University of Chicago, Illinois, and Section on Breastfeeding, American Academy of Pediatrics, Valley Center, California, USA

*Studies of environmental chemicals in human milk have been carried out in many countries, but few have been conducted in the United States. These studies are useful for monitoring population trends in exposure to chemicals, for research into the determinants of environmental chemicals in milk and relationships between the levels found and the health status of the women and their infants, and for risk assessment. This article provides practical advice on data and information reporting for such studies. Participation in these studies comes at a difficult time for the breast-feeding mothers, so it is important that the mothers support the study and its goals. A key goal of any study of environmental chemicals in human milk must be to ensure that the breast-feeding process is not disrupted by unwarranted concerns about harm to the infant from chemicals in human milk. Therefore, it is essential that reporting of information be a two-way process. Information needs to be supplied to participating mothers before, during, and after their participation in the study. Information supplied before participation is necessary to satisfy the ethical requirement for informed consent; information supplied during participation includes advice on express-*

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Address correspondence to Dr. Michael Bates, School of Public Health, 140 Warren Hall, University of California, Berkeley, CA 94720-7360, USA. E-mail: m\_bates@uclink.berkeley.edu

*ing, collecting, and storing milk samples, and how to avoid sample contamination; and information supplied to each participant at the end of the study includes a report of their individual results and a summary of study results and outcomes generally. The key instrument for obtaining data from the participants is the study questionnaire. This needs to be prepared in accordance with principles of good questionnaire development, and preferably should be interviewer administered. The questionnaire content will vary according to the objectives of the study. Although studies of environmental chemicals in human milk are logistically complex and demanding, they are practicable and, with careful planning and execution, yield important data.*

Studies of environmental chemicals in human milk are increasingly common in the published scientific literature. Background levels have been characterized in the populations of many countries (Yrjanheikki, 1989; WHO, 1999). However, to date, relatively few such studies have been carried out in the general population of the United States. All such studies require the collection of relevant information from participants (lactating women), usually with a standardized questionnaire, so that the analytical data on chemicals in milk can be put into proper context and properly interpreted. The purpose of this article is to provide practical advice on the process and format of information collection and reporting, so that the maximum value may be obtained from the analytical data.

As a medium for studying exposure to environmental chemicals, human milk has a number of advantages: Milk can be obtained noninvasively, it has a high proportion of lipid, in which many of these chemicals accumulate, and there is a substantial body of comparative data available from around the world. Also, measurements of chemicals in human milk facilitate assessments of risk to infants. However, studies requiring the collection of human milk are inherently difficult, not least for the participants themselves. Breast-feeding mothers, particularly first-time mothers, face many coping difficulties. Additional requirements for milk sample collection come at an inconvenient time, and will only be successful if participating mothers are supportive of the study and its goals. Apart from that, identification and recruitment of eligible women for such studies are costly and laborious processes for the research team. It is therefore essential that maximal benefit be obtained from the efforts put into such studies.

This article starts from the premise that reporting needs for human milk studies are reciprocal. Not only do the investigators seek information from the participants, but the participants seek information and support from the investigators (Lee & Solimano, 1981). The latter is an aspect of informed consent and ensures that the process of breast-feeding is not disrupted or halted as a result of concerns engendered by the study. Most women are unaware that their milk contains low levels of environmental chemicals, and this knowledge can lead them to question whether they should be breast-feeding at all. The preponderance of evidence is that the benefits of breast-feeding outweigh any risks associated with background levels of environmental chemicals present in the milk (Rogan et al., 1991; AAP, 2001). We

would expect this to be the case in most situations, except for unusual circumstances, when women were exposed to very high levels of potential toxicants. For these reasons, this article deals with the two-way process of reporting needs.

## STUDY OBJECTIVES AND DESIGN

### Study Objectives

The objectives of the study directly determine its design and participant population selection. In turn, these affect both the information collected from the participants and the information reported back to them. Broadly, objectives for human milk studies include:

1. Monitoring exposures to exogenous chemicals (such as pesticides, dioxins, and polychlorinated biphenyls [PCBs]).
2. Research either into the determinants of levels of environmental chemicals in human milk, or into the relationship between levels in milk and the women's or their children's health status.
3. Risk assessment, to evaluate any risks to the child from the environmental chemicals in the mothers' milk.

A study may have more than one of these objectives.

### Types of Study

The study objectives directly influence the design of the study. In brief, the key characteristics of these studies follow.

**Exposure Monitoring** These studies typically compare levels of environmental chemicals in human milk from different areas, in the same areas over different periods of time, or from groups of women known to have different occupational or environmental exposures. Levels may be compared across local areas within a country, or between countries; studies in the same areas repeated at, say, 5- to 10-yr intervals, can be used to investigate trends in levels. Making some assumptions about representativeness of exposures in breast-feeding women, concentrations in milk can provide an indicator of relative levels of general population exposure between areas, and can be used to assess the effectiveness of interventions intended to reduce population exposures. A key characteristic of monitoring studies is that selection criteria for participants often need to be rigorously defined, so that results of studies in different settings and at different times may be validly compared (Sim & McNeil, 1992; Harris et al., 2001; LaKind et al., 2001). The World Health Organization (WHO) has set out recommendations for selection criteria (Yrjanheikki, 1989; WHO, 1999). The advantage in adhering to these criteria is that it is then possible to compare levels of environmental chemicals in human milk across countries. Many studies using these criteria are available in the published literature (Atuma et al.,

1998; Bates et al., 1994, 2002; Cuijpers et al., 2000; Gladen et al., 1999; Harris et al., 1999; Hooper et al., 1998; Romero et al., 2000; Newsome et al., 1995; She et al., 1998; WHO, 1996). Despite the advantages of common participant selection criteria, we do not necessarily endorse the WHO recommendations in their entirety, particularly in regard to the pooling of milk samples. We discuss this aspect in more detail later.

**Research** There are two types of research study. The most common have been etiologic studies to identify determinants of levels of environmental chemicals in human milk. These studies are often combined with general exposure monitoring studies. However, the participant selection criteria used in monitoring studies may limit the extent to which etiologic conclusions can be drawn. Epidemiologic studies (case-control or cohort) are also used to investigate associations between levels of environmental chemicals in milk and the health of the women (e.g., likelihood of breast cancer) (Wolff et al., 2002) or their children (e.g., postnatal developmental effects) (Gladen et al., 1988; Koppe et al., 1989; Jacobsen et al., 1990; Vreugdenhil et al., 2002).

**Risk Assessment** A key component of the risk assessment process is the exposure assessment. Knowledge of environmental chemical levels in human milk, combined with milk volume consumption data, can provide an accurate assessment of infant exposure. In situations where there are elevated levels of potential toxicants in the human milk, women will be concerned about whether they are causing harm to their babies by breast-feeding them (Hatcher, 1982). Risk assessments assist regulatory authorities and mothers to make informed decisions about whether breast-feeding or formula feeding is preferable. This would mainly be important in a situation where there had been an unusually high exposure, such as episodes involving heptachlor exposure from contaminated dairy products in both Hawaii and Arkansas in the 1980s (Baker et al., 1991; Mattison et al., 1992). In most situations, where only normal background exposure is involved, the benefits of breast-feeding would heavily outweigh any potential risks. Other than in situations where unusually high exposure is known or suspected, exposure assessment for risk-assessment purposes may be based on either the results of human milk monitoring studies or research studies. However, participant selection criteria in the original study will inevitably affect the extent to which the risk assessment results can be generalized.

### **Individual or Pooled Milk Samples**

A key issue in human milk study design, particularly monitoring studies, is whether milk samples are to be pooled for chemical analysis or analyzed individually. The main reason why milk samples are pooled for analysis is cost. Some chemical analyses, particularly for polychlorinated dibenzo-*p*-dioxins and dibenzofurans ("dioxins"), are very expensive, and funding may be sufficient only for a few such analyses. The other reason for pooling milk samples is to achieve sufficient milk volume for analysis. The latter reason

is rarely appropriate, as participants are usually able to supply sufficient milk sample for individual analysis, and current analytical methods have a high level of sensitivity.

If pooling of milk samples is unavoidable, then the pooling should be carried out according to clearly defined criteria, such as the age or ethnicity of the participants, their parity, or their residential area. The interpretation of analytical results from pooled milk samples is seriously limited. It is not possible to draw any conclusions about the variability of individual levels, and factors that determine environmental chemical levels cannot be identified, with the exception of factors that are pooling criteria.

A danger in pooling milk samples is that one of the contributors to a pool may have an unusually high exposure to a particular chemical, leading to unrepresentative chemical measures for the pooled sample to which they contribute. To some extent, this possibility can be guarded against by asking screening questions about known (usually occupational) exposures. For example, in a study of organochlorine pesticide levels in human milk, one might ask whether the woman had any known history of spraying such chemicals. If the answer were affirmative (or even if she were unsure) it would be advisable not to include the milk sample from that woman in the pool. In a study of PCB levels, one might ask whether the woman had been involved in transformer or capacitor design or repair. Despite such precautions, however, it is not possible to be completely sure that women with unrepresentative exposures have not been included. Provided such exposures are uncommon, increasing the number of individual contributors to a particular pool should help to minimize the impact of any such unusually high levels of exposure.

### **Importance of Consultation with Participants and Stakeholders**

Although consultation with potential participants and stakeholder organizations is important in any epidemiological study, it is particularly important in studies aiming to measure levels of environmental chemicals in human milk. Mothers are highly attuned to protecting their babies from any harmful influences. The mere suggestion that there may be contaminants in their milk that could harm their child may be sufficient to turn some women from breast to formula feeding. Such a suggestion could just as likely come from an organization with an interest in motherhood or breast-feeding (a stakeholder organization) that has heard of the study, as from the study team itself. To minimize the likelihood of spread of misinformation, and to ensure the smooth conduct of the study, it is essential to involve all stakeholder organizations and representatives of the participant group in the planning process. It is very important that such consultation begin during the study design, well before it is finalized, rather than after the recruitment of mothers has begun.

Time spent in consultation will pay dividends. Not only will it ensure that there is a supply of willing participants, but also it will minimize the

likelihood of unforeseen difficulties that could disrupt the study after it has begun.

Although consultation may be with stakeholder organizations individually, it is often a good idea to have a general meeting to which all such organizations are invited. At such a meeting, the study proposal would be outlined, and general discussion would take place. Insofar as is reasonable and practicable, investigators should take into account in their study design and conduct any particular concerns that are raised.

## **THE SUPPLY OF INFORMATION TO PARTICIPATING MOTHERS**

This section covers the information that should be supplied to the mothers, before their participation begins (including recruitment), during the study, and at the end of the study.

### **Before Participation**

Any study that includes the collection of milk samples from mothers will require approval by an institutional review board (IRB) (45 CFR, 46:101–409; Merz et al., 1999). Before giving its approval, the IRB will want to be confident that participants are protected from risks, that the benefits of the research outweigh any risks, and that an adequate informed consent process will be used. Potential risks from human milk research include unwarranted disclosure of personal information and the possibility that concerns about the research or its underlying purpose could discourage breast-feeding of babies. Maintenance of confidentiality for personal information is common to most human subject research, but the potential for discouraging breast-feeding is possibly unique to human milk studies. To a large degree, the risk of inhibiting breast-feeding can be mitigated by an adequate informed consent process. However, as discussed in the previous section, it is essential that a wider group of stakeholders be adequately informed and consulted in order to fully minimize this risk.

Central to the supply of information before participation in the study is the informed consent process. Research involving human subjects carried out in the United States, including studies of chemicals in human milk, is required to comply with federal regulations governing such research (45 CFR, 46:101–409). This includes the requirement for informed consent. Although there are circumstances under which such consent may be waived, these are unlikely to apply to studies involving collection of human milk samples. This consent (1) must be obtained in writing, (2) must not be obtained under coercive circumstances, (3) must be in understandable language, and (4) may not involve a waiver of rights. Truthfulness is essential at all times. Table 1 lists elements of the informed consent process that are required and that would be appropriate to a study in which human milk samples were obtained for analysis of environmental chemicals.

Two copies of the consent form giving permission for chemical analyses to be carried out on the milk sample should be signed. This form should contain the necessary information in Table 1. One copy should be provided to the participant. In addition to the written information, potential participants should have the opportunity to ask any questions and have them answered to their satisfaction.

Investigators may consider providing the participant with some compensation, in the form of a useful gift or even modest financial payment, for the time taken to participate. The level of compensation should never be so large as to be coercive.

**TABLE 1.** Elements of the Informed Consent Process for Breast Milk Studies

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| An explanation of the purpose of the study, including why breast milk is the sample of choice   |
| The name of the organization carrying out the study   |
| The names, positions, and qualifications of key members of the study team   |
| The name of the funding organization  |
| How the study will be conducted (i.e., main procedures)   |
| Eligibility criteria for participation in the study   |
| How many participants will be recruited   |
| What would be asked of participants, including the amount of milk requested, and over what period of time   |
| Whether a questionnaire would be used, how it would be administered, and the topic areas it would cover   |
| What would be done with their milk sample, including storage  |
| What would be done with any left-over milk sample   |
| Any risks associated with participation in the study  |
| Benefits (to participants and to society generally) associated with their participation in the study  |
| Advice that breast-feeding is almost always considered to be the best form of nutrition for a baby, and that the fact that the study is being carried out should in no way be taken as implying anything to the contrary      |
| That information linked to the participant collected during the course of the study would be entirely confidential to members of the study team and then only those team members who needed that information                  |
| That if any results of concern are found, such as very high levels of environmental chemicals in the breast milk, she would promptly be informed and given appropriate advice   |
| That study publications will contain statistical information only and no individual study participant will be identifiable  |
| That participation is entirely voluntary, and she has the right to refuse to participate or withdraw from the study at any time, without any penalty and without affecting the health care that she or her baby would receive |
| The process of withdrawal from the study if she elects to do so   |
| That the investigators can terminate participation in the study at any time, without the participant's consent  |
| A name and contact details for both a study team member and the IRB that approved the study if any questions arise about the research at any time during the course of the study  |
| That she will have the choice of receiving a copy of the analytical data for her breast milk sample and a summary of the study results when available   |
| Whether, as a result of participation in this study, she might be asked to participate in a further study   |

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## **During Study Participation**

Human milk sampling studies often require milk samples to be obtained during a defined period, such as the second month after the birth of the baby. This gives the mother a chance to get used to her new role as a mother and to become accustomed to breast-feeding. Composition of human milk changes over the period of breast-feeding (Macias & Schweigert, 2001), so consistency in the timing of milk sample collection is necessary if results are to be compared to results of other studies. It is common, particularly for first-time mothers, to cease breast-feeding because of the difficulties experienced. So it is in the interests of the participant, her child, and the study for support to be given to mothers to help them maintain breast-feeding. Since participant recruitment for human milk studies is usually best carried out during the pregnancy, it may be appropriate for such support to be given even before the appropriate period for sample collection arrives. The support may be in the form of breast-feeding advice from available physicians, midwives, nurses, or lactation consultants.

For the purposes of milk sample collection, participating women should be given a direct description and demonstration of what they are being asked to do, backed up by written instructions. Key information includes instructions on expressing and collecting the milk sample, avoiding contamination (e.g., with lanolin-containing nipple ointments), and storing the sample before pickup by the study team. Sample collection and storage will usually involve specially cleaned containers, supplied by the study team. It should be made clear whether a breast pump may be used for sample collection, and if so cleaning instructions for the pump should be provided. Participants should be given contact details for a study team member, in case they experience difficulties with their milk sample collection or breast-feeding generally.

## **At the End of the Study**

Supplying a milk sample for the study may add to the difficulties of a mother going through the often difficult process of breast-feeding a newborn child. Consequently, it is entirely reasonable for her to expect, at a minimum, to receive the analytical results for her milk sample. This may help alleviate any anxieties about environmental chemicals that may have been caused by participation in the study. In addition, the participant should be advised of the outcome or main results of the study. Even when full implications of the analytical results are unknown, the study team should provide information on individual levels to the women.

Usually it is sufficient at the end of the study to send each participating mother:

- The analytic results for her own milk sample and the range of results for all study participants, in addition to any appropriate standards that apply (if any exist).
- A summary of the outcomes of the study. It may, at a later stage, be appropriate to send participants copies of published papers, if they should request this.

Since there may be some women who do not want to hear anything further after they have supplied their milk sample, these items should be supplied only if a woman indicates that she wishes to receive them, in response to specific questions in the questionnaire.

## OBTAINING INFORMATION FROM PARTICIPANTS

There are a number of reasons why information is obtained from participants in human milk studies. These reasons will vary from study to study, depending on the objectives, but include:

- Ensuring eligibility for study participation.
- Confirming eligibility for pooling of milk samples.
- Determining comparability of results with those for other human milk studies.
- Explaining unusual results.
- Identifying determinants of levels of environmental chemicals.
- Identifying potential confounding factors for elevated levels.

### The Study Questionnaire

Other than the milk sample analysis, the primary instrument for data collection in human milk studies is the questionnaire. Key issues to be considered are the mode of administration and the nature of the questions.

**Mode of Administration** Usually for studies of environmental chemicals in human milk there are two possible ways in which the questionnaire may be administered: It may be provided to the participating mother so that she may complete it when time permits, or it may be administered directly by a study team member. Ideally, to minimize response bias, the questionnaire should be administered in the same way to all study participants. For a number of well-recognized reasons, interviewer-administered questionnaires are preferable to self-administered questionnaires (Armstrong et al., 1992). Interviewer-administered questionnaires permit a more complex range of questions, ensure completeness and consistency of answers, and allow some probing, if needed. Appropriate training of study team members in interviewing techniques is essential.

Administration of the questionnaire may most conveniently take place at the time that the participant is given instruction in milk sample collection and provided with appropriate containers. If that is not convenient, questionnaire administration could take place when the milk sample is collected for transport to the laboratory, or if necessary, by telephone.

**The Format and Content of the Questionnaire** The nature and format of the questions will necessarily vary according to the objectives of the study, the study population, and the chemicals for which analyses will be carried out. A number of different questionnaires might be used in a single project: a screening questionnaire to determine whether mothers fit the selection criteria, the primary questionnaire with all the key questions, and,

possibly, a follow-up questionnaire(s) for projects with a longitudinal component. The focus of this section is on the primary questionnaire.

For monitoring studies, consistent questionnaire content is needed for comparability of results from studies in different settings and at different times. Table 2 lists appropriate items and topics that are commonly covered in questionnaires for human milk studies. For studies in which the milk samples will be pooled, a much more limited list of questions, covering mainly eligibility and pooling criteria, would be appropriate. Because of the imposition on the mother during a demanding period, the researcher should limit questions to those that are likely to be useful to the study, rather than taking

**TABLE 2.** Content of Questionnaires for Breast Milk Chemical Studies

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1. All questionnaires should contain:
    - Date, study title, organization name, and version number (if a draft)
    - Page numbers and a space for the participant code number on each page
    - An introduction (including purpose of study [but not study hypotheses], voluntary nature of participation, confidentiality of responses, likely length of interview)
    - Instructions to the interviewer or participant (if self-administered)
    - A final question about anything else the participant wishes to add
    - A statement thanking the participant for her cooperation
  
  2. Questions will usually cover:
    - Date of interview
    - Name of mother
    - Date of birth of child
    - Date of birth of the mother
    - Race/ethnicity
    - Height and weight of mother
    - Birth order of the child
    - Whether a singleton or multiple birth
    - Health of mother, baby, and pregnancy
    - Residential history
    - Whether exclusively breast-feeding, and if not, a measure of the frequency of breast-feeding
    - Some measure of socioeconomic status, such as mother's educational level, usual occupation (of mother and partner), family income (within a range), and so on
    - Availability of refrigerator (for storing samples before collection)
    - Dates of milk collection (if collection has been completed)
  
  3. Depending on the study objectives, questions will often cover:
    - Types of water supply to residences
    - Diet of mother
    - Smoking history
    - Lactation history
    - Mother's medications (prescription and non-prescription)
    - Occupational history, up to, during, and following pregnancy, including chemical exposures
    - Folk medications, alternative treatments
    - Alcohol consumption history
    - Use of domestic products (e.g., solvents, pesticides, others)
    - Hobbies
    - Other exposures of interest (e.g., recreational drugs)
    - Health and reproductive history (including previous abortions)
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advantage of the opportunity to obtain information on as wide a range of topics as possible.

As with all epidemiologic study questionnaires, the wording of questions should be clear, appropriate and unambiguous, and directed to the participant. As a simple illustration, it is better to have a question such as "Do you eat meat?" than "Does the mother eat meat?" This will ensure that the interviewer does not have to reword questions so that they can be directed to the participant, which could lead to each participant answering a slightly different question, in which case the answers might not be directly comparable. Words subject to wide interpretation, such as "urban" and "rural," should be defined in terms of the meaning that they have within the context of the study. Questions should be placed in a logical order, with the most sensitive topics toward the end of the questionnaire.

Construction of the questionnaire should be done with the final data analysis in mind, so that all necessary data are collected, and in a format that lends itself to the analysis. In that regard, questions with open-ended answers should be kept to a reasonable minimum.

Finally, pretesting the questionnaire on friends and colleagues and pilot testing it on a small sample of mothers are essential to assess clarity and lack of ambiguity of wording before the study has begun. With permission, the questionnaire can include items from well-tested questionnaires from other studies. A questionnaire that has been successfully used in a human milk monitoring study is available on request from the corresponding author for this article.

### **Direct Measurements**

A relationship between fat content of the milk and body mass index, calculated from height and weight of the participant, has been reported (Jensen, 1983). It is preferable to collect data on height and weight of the participant through direct measurement, rather than through self-report. This can be done at the time of interview, using a good quality set of scales and a length measure.

### **CONCLUSIONS**

Studies of environmental chemicals in human milk are logistically complex and demanding, but are quite practicable and very worthwhile, provided the planning and setup are properly carried out. The main issue of concern in such studies is the potential to discourage breast-feeding. Provided that studies include early and ongoing dissemination of appropriate information and advice to participants, breast-feeding may actually be promoted. It cannot be emphasized strongly enough that reporting needs for studies of environmental chemicals in human milk are bidirectional.

This article has attempted to draw upon the experience of previous successful studies, and to present practicable recommendations for planning future studies. We have tried not to be prescriptive, particularly in regard to

questionnaire design, as there is no one way to carry out a human milk study. The final design will depend particularly on the study objectives and the target population.

## REFERENCES

- American Academy of Pediatrics. 2001. AAP Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics* 108:776–789.
- Armstrong, B. K., White, E., and Saracci, R. 1992. Methods of exposure assessment. In *Principles of exposure measurement in epidemiology*, Chap. 2. Monographs in Epidemiology and Biostatistics, Vol. 21. Oxford: Oxford University Press.
- Atuma, S. S., Hansson, L., Johnsson, H., Slorach, S., de Wit, C. A., and Lindstrom, G. 1998. Organochlorine pesticides, polychlorinated biphenyls and dioxins in human milk from Swedish mothers. *Food Addit. Contam.* 15:142–150.
- Baker, D. B., Loo, S., and Barker, J. 1991. Evaluation of human exposure to the heptachlor epoxide contamination of milk in Hawaii. *Hawaii Med. J.* 50:108–112, 118.
- Bates, M. N., Hannah, D. J., Buckland, S. J., Taucher, J. A., and van Maanen, T. 1994. Chlorinated organic contaminants in the breast milk of New Zealand women. *Environ. Health Perspect.* 102 (suppl. 1):211–217.
- Bates, M. N., Thomson, B., and Garrett, N. 2002. Reductions in organochlorine levels in the milk of New Zealand women. *Arch. Environ. Health*, in press.
- Cuijpers, C. E. J., Zeilmaker, M. J., van Eijkeren, J. C. H., and Liem, A. K. D. 2000. Dioxin levels in Dutch human milk: A 50% decrease in 10 years. How will future trends develop? *Organohalogen Compounds* 48:58–61.
- Gladen, B. C., Rogan, W. J., Hardy, P., Thullen, J., Tangelstad, J., and Tully, M. 1988. Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk. *J. Pediatr.* 113:991–995.
- Gladen, B. C., Monaghan, S. C., Lukyanova, E. M., Hulchiy, O. P., Shkyryak-Nyzhnyk, Z. A., Sericano, J. L., and Little, R. E. 1999. Organochlorines in breast milk from two cities in Ukraine. *Environ. Health Perspect.* 107:459–462.
- Harris, C. A., O'Hagan, S., and Merson, G. H. 1999. Organochlorine pesticide residues in human milk in the United Kingdom 1997–8. *Hum. Exp. Toxicol.* 18:602–606.
- Harris, C. A., Woolridge, M. W., and Hay, A. W. 2001. Factors affecting the transfer of organochlorine pesticide residues to breastmilk. *Chemosphere* 43:243–256.
- Hatcher, S. L. 1982. The psychological experience of nursing mothers upon learning of a toxic substance in their breast milk. *Psychiatry* 45:172–181.
- Hooper, K., Petreas, M. X., Chuvakova, T., Kazbekova, G., Druz, N., Seminova, G., Sharmanov, T., Hayward, D., She, J., Visita, P., Winkler, J., McKinney, M., Wade, T. J., Grassman, J., and Stephens, R. D. 1998. Analysis of breast milk to assess exposure to chlorinated contaminants in Kazakhstan: High levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in agricultural villages of southern Kazakhstan. *Environ. Health Perspect.* 106:797–806.
- Jacobson, J. L., Jacobson, S. W., and Humphrey, H. E. 1990. Effects of exposure to PCBs and related compounds on growth and activity in children. *Neurotoxicol. Teratol.* 12:319–326.
- Jensen, A. A. 1983. Chemical contaminants in human milk. *Residue Rev.* 89:1–128.
- Koppe, J. G., Plum, E., and Olie, K. 1989. Breastmilk, PCBs, dioxins and vitamin K deficiency: discussion paper. *J. R. Soc. Med.* 82:416–419.
- LaKind, J. S., Berlin, C., and Naiman, D. Q. 2001. Infant exposure to chemicals in breast milk in the United States: What we need to learn from a breast milk monitoring program. *Environ. Health Perspect.* 109:75–88.
- Lee, J. G., and Solimano, G. 1981. Including mothers in the design of infant feeding research. *Studies Fam. Plan.* 12:173–176.
- Macias, C., and Schweigert, F. J. 2001. Changes in the concentration of carotenoids, vitamin A, alpha-tocopherol and total lipids in human milk throughout early lactation. *Ann. Nutr. Metab.* 45:82–85.

- Mattison, D. R., Wohlleb, J., To, T., Lamb, Y., Faitak, S., Brewster, M. A., Walls, R. C., and Selevan, S. G. 1992. Pesticide concentrations in Arkansas breast milk. *J. Ark. Med. Soc.* 88:553–557.
- Merz, J. F., Leonard, G. B., and Miller, E. R. 1999. IRB consent and review in human tissue research. *Science* 283:1647–1648.
- Newsome, W. H., Davies, D., and Doucet, J. 1995. PCB and organochlorine pesticides in Canadian human milk—1992. *Chemosphere* 30:2143–2153.
- Rogan, W. J., Blanton, P. J., Portier, C. J., and Stallard, E. 1991. Should the presence of carcinogens in breast milk discourage breastfeeding? *Regul. Toxicol. Pharmacol.* 13:228–240.
- Romero, M. L., Dorea, J. G., and Granja, A. C. 2000. Concentrations of organochlorine pesticides in milk of Nicaraguan mothers. *Arch. Environ. Health* 55:274–278.
- She, J., Petreas, M. X., Visita, P., McKinney, M., Sy, F. J., Winkler, J. J., Hooper, K., and Stephens, R. D. 1998. Congener-specific analysis of PCBs in human milk from Kazakhstan. *Chemosphere* 37:431–442.
- Sim, M. R., and McNeil, J. J. 1992. Monitoring chemical exposure using breast milk: A methodological review. *Am. J. Epidemiol.* 136:1–11.
- Vreugdenhil, H. J., Lanting, C. I., Mulder, P. G., Boersma, E. R., and Weisglas-Kuperus, N. 2002. Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age. *J. Pediatr.* 140:48–56.
- Wolff, M. S., Berkowitz, G. S., Brower, S., Senie, R., Bleiweiss, I. J., Tartter, P., Pace, B., Roy, N., Wallenstein, S., and Weston, A. 2002. Organochlorine exposures and breast cancer risk in New York City women. *Environ. Res.* 84:151–161.
- World Health Organization. 1996. *Levels of PCBs, PCDDs and PCDFs in human milk: Second round of WHO-coordinated exposure study.* Environmental Health in Europe Series No. 3. Copenhagen: World Health Organization.
- World Health Organization. 1999. *Levels of PCBs, PCDDs and PCDFs in human milk. Draft protocol for third round of exposure studies.* Bilthoven, the Netherlands: World Health Organization European Centre for Environment and Health.
- Yrjanheikki, E. J. 1989. *Levels of PCBs, PCDDs and PCDFs in breast milk.* Environmental Health Series No. 34. Copenhagen: World Health Organization, Regional Office for Europe.