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A Review of the Medical Benefits and Contraindications to Breastfeeding in the United States

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Preface

In its report *Breastfeeding: WIC's Efforts to Promote Breastfeeding Have Increased* (1993), the U.S. General Accounting Office (GAO) recommended that the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (DHHS) develop written policies defining the conditions that would contraindicate breastfeeding and determining how and when to communicate this information to all pregnant and breastfeeding participants of the Special Supplemental Nutrition Program for Women, Infants and Children (WIC). The Maternal and Child Health Bureau, DHHS, and WIC, USDA, developed a plan to respond to GAO's recommendation. In late 1994, MCHB awarded a contract to Dr. Ruth Lawrence, a nationally recognized expert in the area of breastfeeding, to develop a policy document on the medical contraindications of breastfeeding. The policy document was reviewed by other national experts in the field of infectious diseases, environmental toxins, acute and chronic diseases, and metabolic disorders. In July 1996, the policy document was submitted to GAO to assist states in developing policies. To ensure widespread dissemination, the document has been prepared as a technical information bulletin (TIB) for distribution to DHHS and USDA regional offices, state and local health departments, WIC state and local agencies, and other interested organizations and health care providers. USDA is encouraging WIC state agencies to develop policies regarding contraindications to breastfeeding that take into consideration the information presented in this document and that are consistent with the policies of their respective state health departments.

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Benefits and Risks

Benefits

In any statement about breastfeeding and breastmilk (human milk), it is important first to establish breastmilk's distinct and irreplaceable value to the human infant. Breastmilk is more than just good nutrition. Human breastmilk is specific for the needs of the human infant just as the milk of thousands of other mammalian species is specifically designed for their offspring. The unique composition of breastmilk provides the ideal nutrients for human brain growth in the first year of life. Cholesterol, desoxyhexanoic acid, and taurine are particularly important. Cholesterol is part of the fat globule membrane and is present in roughly equal amounts in both cow milk and breastmilk. Maternal dietary intake of cholesterol has no impact on breastmilk cholesterol content. The cholesterol in cow milk, however, has been removed in infant formulas. These elements are readily available from breastmilk, and the essential nutrients in breastmilk are readily transported into the infant's bloodstream. The

bioavailability of essential nutrients (including the microminerals) means that there is great efficiency in digestion and absorption. Comparison of the biochemical percentages of breastmilk and infant formula fails to reflect the bioavailability and utilization of constituents in breastmilk compared to modified cow milk (from which only a small fraction of some nutrients is absorbed).[1]

The presence of living leukocytes, specific antibodies, and other antimicrobial factors protects the breastfed infant against many common infections. Protection against gastrointestinal infections is well documented.[1] Protection against infections of the upper and lower respiratory system and the urinary tract is less recognized, although those infections lead to more emergency room visits, hospitalizations, treatments with antibiotics, and health care costs for the infant who is not breastfed.[2,3]

The incidence of acute lower respiratory infections in infants has been evaluated in a number of studies examining the relationship between respiratory infections and breastfeeding or formula feeding in these infants.[4–6] These studies confirm that infants who are breastfed are less likely to be hospitalized for respiratory infection, and, if hospitalized, are less seriously ill. In a study of infant deaths from infectious disease in Brazil, the risk of death from diarrhea was 14 times more frequent in the formula-fed infant and the risk of death from respiratory illness was 4 times more frequent.[6] The association of wheezing and allergy in relation to infant feeding patterns has also shown a significant advantage to breastfeeding. In a report from a seven-year prospective study in South Wales, the advantage of breastfeeding persisted to the age of seven years in non-atopics, while in at-risk infants who were breastfed the risk of wheezing was 50 percent lower (after accounting for employment status, passive smoking, and overcrowding).[7] Breastfeeding is thought to confer long-term protection against respiratory infection as well, according to these authors.

For decades, growth in infancy had been measured according to data collected on infants who were exclusively formula-fed, until the publication of data on the growth curves of infants who were exclusively breast-fed.[8] The physiologic growth curves of breast-fed infants show a pattern similar to that of formula-fed infants at the 50th percentile, with significantly few breastfed infants in the 90th percentile. This is most evident in the examination of the z scores, which indicate that formula-fed infants are heavier compared to breastfed infants.[9]

Upper and lower respiratory tract infections have been evaluated in case–control studies, cohort-based studies, and mortality studies in both clinic and hospitalized children in many countries of the developed world.[1–3,10,11] The results all show clearly that breastfeeding has a protective effect, especially in the first six months of life. A randomized controlled trial indicated that withholding cow milk and giving soy milk provided no such protective effect.[7] The incidence of acute otitis media in formula-fed infants is dramatically higher than in breastfed infants,[12,13] not only because of the protective constituents of human milk but also because of the process of suckling at the breast, which protects the inner ear.[14] When an infant bottlefeeds, the eustachian tube does not close, and formula and secretions are regurgitated up the tubes. Child care exposure increases the risk of otitis media, and bottlefeeding amplifies this risk.[14]

In addition to the protection provided by breastfeeding against the presence of acute infections, epidemiologic studies have revealed a reduced incidence of childhood lymphoma,[11] childhood-onset insulin-dependent diabetes,[15] and Crohn's disease[16] in infants who have been exclusively breastfed for at least four months, compared to infants who have been fed infant formula. In addition, breastfed infants at high risk for developing allergic symptoms such as eczema and asthma by two years of age show a reduced incidence and severity of symptoms in early

life.[17] Some studies suggest the protective effect continues through childhood.[17–20]

In addition to clinically proven medical benefits, breastfeeding empowers a woman to do something special for her infant. The relationship of a mother with her suckling infant is considered to be the strongest of human bonds. Holding the infant to the mother's breast to provide total nutrition and nurturing creates an even more profound and psychological experience than carrying the fetus in utero.

In studies of young women enrolled in the WIC in Kentucky who were randomly assigned to breastfeed or not to breastfeed and who were provided with a counselor/ support person throughout the first year postpartum, the young women who were randomized to breastfeed changed their behavior.[21,22] They developed self-esteem and assertiveness, became more outgoing, and interacted more maturely with their infants than did the women assigned to formula feeding. The women who breastfed turned their lives around by completing school, obtaining employment, and providing for their infants.

Children who have been breastfed were noted by Newton[23] to be more mature, secure, and assertive, and they progressed further on the developmental scale than non-breastfed children. More recently, studies by Lucas[24] and other investigators[25] have found that premature infants who received breastmilk provided by tube feeding were more advanced developmentally at 18 months and at 7 to 8 years of age than those of comparable gestational age and birthweight who had received formula by tube. Such observations suggest that breastmilk has a significant impact on the growth of the central nervous system. This is further supported by studies of visual activity in premature infants who were fed breastmilk compared to those who were fed infant formula.[26] When similar studies were performed in term infants, visual acuity developed more rapidly in the breastfed infants.[27] Even when docosahexaenoic acid (DHA) was added to formula, the performance by the breastfed infants was still better.[28]

Nourishment with breastmilk is a combination event, in which nutrient-to-nutrient interaction is significant. The process of mixing isolated single nutrients in formula does not guarantee the nutrient or non-nutrient benefits that result from breastfeeding. The composition of human milk is a delicate balance of macronutrients and micronutrients, each in the proper proportion to enhance absorption. Ligands bind to some micronutrients to enhance their absorption. Enzymes also contribute to the digestion and absorption of all nutrients.[1] An excellent example of balance is the action of lactoferrin, which binds iron to make it unavailable for E. coli bacterium (which is dependent upon iron for growth). When the iron is bound, E. coli cannot flourish and the normal flora of the newborn gut, lactobacillus bifidus, can thrive. In addition, the small amount of iron in human milk is almost totally absorbed whereas only about 10 percent of the iron in formula is absorbed by the infant. Examples of multiple functions of proteins in human milk include preventing infection, preventing inflammation, promoting growth, transporting microminerals, catalyzing reactions, and synthesizing nutrients.[29]

Risk/Benefit Ratio

Breastfeeding may provide the mother with several benefits, including reduced risk of ovarian cancer and premenopausal breast cancer.[30–32] Women who breastfeed return to prepregnancy state more promptly than women who do not, and they have a lower incidence of obesity in later life.[29,33] The benefits of breastfeeding are so strong and compelling that very few situations definitively contraindicate breastfeeding. The decision to breastfeed in the presence of a possible contraindication should be made on an individual basis, considering the risk of the complication to the infant and mother versus the tremendous benefits of breastfeeding. The benefits of being breastfed are greater for the

infant born in poverty where crowding, poor environment, and higher infection rates prevail. For example, in developing countries, the death rate from diarrhea and other infections in the first year of life is 50 percent for infants who are not breastfed. Thus, although some studies suggest that breastfeeding when the mother is HIV-positive increases the infant's risk of HIV, at this time, breastfeeding under these circumstances is still recommended in developing countries.[10]

There is general agreement that a woman's increasing number of pregnancies, increasing length of oral contraceptive use, and increasing duration of lactation are protective against ovarian cancer.[34] When the relationship between lactation and epithelial ovarian cancer was studied from a multinational database, short-term lactation was as effective as long-term lactation in decreasing the incidence of ovarian cancer in developed countries where ovulation suppression may be less prolonged in relation to lactation.[35] In a study of African-American women, who are known to have a lower incidence of ovarian cancer, breastfeeding for six months or longer as well as four or more pregnancies and oral contraceptive use had an effect in further reducing the incidence of ovarian cancer.[36]

When researchers controlled for other variables such as age and parity, a reduced risk of breast cancer among premenopausal women who have lactated was reported in a study of over 5,000 cases in the United States.[37] The longer the lactation, the greater the protection. A population-based case–control study of 1,211 cases failed to show such a relationship when duration of breastfeeding was less than 30 weeks. However, the study showed that the younger the woman and the longer the duration of breastfeeding, the greater the protective effect.[38]

The risk of osteoporosis in later life is greatest for women who have never borne infants, somewhat less for those who have borne infants, and measurably less for those who have borne and breastfed infants.[39] The bone

mineral loss experienced during pregnancy and lactation is temporary. Bone mineral density returns to normal following pregnancy and even following extended lactation when mineral density may exceed the original base line.[40] Serum calcium and phosphorus concentrations are greater in lactating than in nonlactating women. Lactation stimulates increases in fractional calcium absorption and serum calcitriol most markedly after weaning.[41] Postweaning concentrations of parathyroid hormone are significantly higher than in other stages and urinary calcium is significantly lower.[42]

Whenever the clinician is confronted by a situation that might suggest a conflict in encouraging breastfeeding, the theoretical risk should be measured against the projected benefits of breastfeeding. The discussion that follows is relevant only when the risk/benefit ratio is considered for individual cases.

Risks Associated with Breastfeeding

There are no nutritional contraindications to breastfeeding infants unless they have special health needs. Infants with intestinal lactase deficiency, galactosemia, or phenylketonuria (PKU) require special diets that reduce the intake of lactose, galactose, or phenylalanine, respectively. Infants with galactosemia require total artificial specific lactose-free formula; infants with PKU may be partially breastfed at the discretion of the physician.[1,43,44] Because of the low level of phenylalanine in breastmilk, the breastfed infant may be given a high proportion of breastmilk and require very little phenylalanine-free formula. The formula-fed infant can tolerate very little regular formula in addition to the phenylalanine-free milk to maintain blood levels of phenylalanine between 5 and 10 milligrams per deciliter. All infants need some phenylalanine in their diet.

Maternal Diet

Breastfeeding is recommended for all infants in the United States under ordinary

circumstances, even if the maternal diet is not perfect.[29] The Institute of Medicine's Subcommittee on Nutrition During Lactation was impressed by the strong evidence that mothers are able "to produce milk of sufficient quantity and quality to support growth and promote the health of infants."[29] Studies reporting volume of milk produced relate the variability to the demand or consumption by the infant and not the dietary intake of the mother.[45] It is known that maternal intake of excess fluids does not increase milk production and may even decrease it.[46]

The need for dietary counseling during lactation is based on the need to replenish maternal stores.[47–49] Regardless of the mother's intake, it is recommended that breastfeeding mothers be screened for nutritional problems and provided with dietary guidance. When a woman is identified with a restrictive eating pattern, she should be counseled to make the necessary changes. Table 1 presents suggested measures for improving nutrient intake under different types of restrictive eating patterns.[29]

TABLE 1
Suggested Measures for Improving the Nutrient Intakes of
Women with Restrictive Eating Patterns

Type of Restrictive Eating Pattern	Corrective Measures
Excessive restriction of food intake (i.e., ingestion of <1,800 kcal of energy per day), which ordinarily leads to unsatisfactory intake of nutrients compared with the amounts needed by lactating women	Encourage increased intake of nutrient-rich foods to achieve an energy intake of at least 1,800 kcal/day; if the mother insists on curbing food intake sharply, promote substitution of foods rich in vitamins, minerals, and protein for those lower in nutritive value; in individual cases, it may be advisable to recommend a balanced multivitamin-mineral supplement; discourage use of liquid weight loss diets and appetite suppressants
Complete vegetarianism (i.e., avoidance of all animal foods, including meat, fish, dairy products, and eggs)	Advise intake of a regular source of vitamin B_{12}, such as special vitamin B_{12}-containing plant food products or a 2.6 µg vitamin B_{12} supplement daily
Avoidance of milk, cheese, or other calcium-rich products	Encourage increased intake of other culturally appropriate dietary calcium sources, such as collard greens for [African Americans] from the southeastern United States; provide information on the appropriate use of low-lactose dairy products if milk is being avoided because of lactose intolerance; if correction by diet cannot be achieved, it may be advisable to recommend 600 mg of elemental calcium per day taken with meals
Avoidance of vitamin D-fortified foods, such as fortified milk or cereal combined with limited exposure to ultraviolet light	Recommend 10 µg of supplemental vitamin D per day

Source: Reprinted with permission from *Nutrition During Lactation.*[29] Copyright 1991 by the National Academy of Sciences. Courtesy of the National Academy Press, Washington, DC.

1. Restriction of total intake to less than 1,800 kilocalories energy per day is associated with reduced intake of vitamins and minerals. In extreme cases where the mother is unable to improve her diet, vitamin supplements can be prescribed.

2. Complete vegetarianism (veganism)—that is, avoidance of all animal protein (meat, fish, dairy products, and eggs)—is commonly associated with diminished maternal body stores of B_6 and B_{12}. It is important to recognize that symptoms may occur in the breastfed infant before they appear in the mother. Supplementation of the mother's diet is the preferred route of treatment, although in symptomatic cases the infant may require direct treatment initially. This is not a contraindication to breastfeeding. A daily vitamin B_{12} supplement of 2.6 micrograms may be necessary for the mother.[50,51]

3. Avoidance of milk and other dairy products is recommended for women with suspected milk allergy or for prevention of certain allergic problems in their offspring. Avoidance of these dairy products is associated with inadequate intake of calcium, although calcium absorption is enhanced during lactation. Low calcium intake does not affect the composition of the milk, but it diminishes maternal bone stores.[52] Dietary counseling should encourage intake of other calcium-rich foods such as greens, nuts, fish with bones, and tofu. Failing adequate calcium intake, calcium supplements totaling 1,200 milligrams per day are recommended.

4. Inadequate dietary sources or exposure to ultraviolet light should be managed by increasing maternal vitamin D in the diet or supplementing the mother's diet with 10 micrograms of vitamin D per day.

Dietary fetishes and restrictions can be managed by appropriately adjusting the maternal diet or giving supplements. It is important to monitor maternal compliance with such recommendations since some women adhere to nutritionally unsound diets. If the mother refuses such advice, the infant's diet can be supplemented with adequate amounts of the nutrient in question.[29] Poor maternal diet is not a contraindication to breastfeeding. The urgency of dietary counseling in the lactating woman is to replenish her nutritional stores.

Infectious Diseases and Breastfeeding

In general, acute infectious diseases in the mother are not a contraindication to breastfeeding, if such diseases can be readily controlled and treated.[53] In most cases, the mother develops the infection during breastfeeding. By the time the diagnosis has been made, the infant has already been exposed and the best management is to continue breastfeeding so that the infant will receive the mother's antibodies and other host resistance factors in breastmilk. This is true for respiratory infections such as the common cold. Infections of the urinary tract or other specific closed systems such as the reproductive tract or gastrointestinal tract do not pose a risk for excreting the virus or bacteria in the breastmilk unless there is generalized septicemia. When the offending organism is especially virulent or contagious (as with beta-hemolytic streptococcus, group A), both mother and infant should be treated, but breastfeeding is not contraindicated.[1,53]

There are many agents in breastmilk that protect against infection, and their presence is not affected by nutritional status. Protection against infection is important in the United States, especially among infants exposed to multiple caregivers, child care outside the home, compromised environments, and less attention to the spread of organisms.[3] One of the most important and thoroughly studied agents in breastmilk is secretory immunoglobulin (specifically, secretory IgA), which is pre-

sent in high concentrations in colostrum and early breastmilk and in lower concentrations throughout lactation when the volume of milk is increased.[54] Secretory IgA antibodies may neutralize viruses, bacteria, or their toxins and are capable of activating the alternate complement pathway.[55] The normal flora of the intestinal tract of the breastfed infant, as well as the offspring of all other mammalian species studied until weaning, is bifidobacterium or lactobacillus.[54] These bacteria further inhibit the growth of bacterial pathogens by producing organic acids. This is in striking contrast to the formula-fed infant, who has comparatively little bifidobacterium and many coliforms and enterococci. In addition, although the attack rates of certain infections are similar in breastfed and formula-fed infants in the same community, the manifestations of the infections are much less evident in the infants who are breastfed. This appears to be due to anti-inflammatory agents in breastmilk.[56]

A few specific infectious diseases are capable of overwhelming the protective mechanisms of breastmilk and breastfeeding, as detailed in the discussion that follows.[53,57]

Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome

Clinically effective treatments for human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) are still being developed; therefore, any behavior—including breastfeeding—that increases the risk of transmitting the virus from mother to infant should be avoided in the United States. Even though the value of being breastfed is great, failure to breastfeed does not result in a large increase in mortality among U.S. infants. Not all infants born to U.S. HIV-infected mothers are infected at birth, but present laboratory techniques require several months to identify the newborn who has HIV. It is known from work in Africa that infants with HIV who are breastfed do better than those with HIV who are not breastfed.[59] Fifteen percent of HIV-positive infants in Africa die as a result of the virus in the first year of life if they are protected by breastfeeding, whereas 50 percent of all non-breastfed infants in this population and in the general population die during their first year for lack of the protective constituents of breastmilk.[53,59–61]

Because of the inability to distinguish prepartum, intrapartum, and postpartum transmission of HIV and the dilemma of developing an ethical study with adequate sample size and controls, a computer model was developed to assess the impact of breastfeeding practices on the mortality of children under five years of age in developing countries (using parameter values for a hypothetical East African country).[62] Cessation of breastfeeding in urban areas was projected to result in a 108 percent increase in mortality in children under age five whose mothers were HIV negative at the time of the infant's birth, and a 27 percent additional increase in mortality among those whose mothers were HIV positive. The numbers projected for rural areas were even higher. These calculations support the recommendation in Africa for breastfeeding in the case of maternal HIV.[59,62]

Present studies in the United States that provide HIV-positive women with azidothymidine (AZT) during pregnancy and immediate treatment for their infants at birth have shown improved outcome for these infants, with a reduced rate of infection. Although AZT is not a contraindication for breastfeeding, both mother and infant would require postpartum treatment. A carefully controlled study by the Pediatric AIDS Clinical Trials Group Protocol 076 (ACTG 076) yielded the most important result in clinical AIDS research to date. The study demonstrated that HIV transmission could be prevented in approximately 67 percent of infants when zidovudine (AZT) was administered to the mother both intragestationally and during the intrapartum period, and to the infant during the first six weeks of life.[63]

Much publicity has surrounded the issue of breastfeeding by women who became infect-

ed with HIV while lactating.[58,60,64,65] It seemed initially that most of these cases occurred because of a maternal transfusion with contaminated blood postpartum, so that the pathway of the infant's exposure seemed clear. One study found a 29 percent risk of vertical transmission (mother to infant) if the mother became infected during lactation.[60] In Australia, 3 of 11 infants (27 percent) breastfed for nine months or more by mothers who received contaminated transfusions (and by one mother using contaminated needles) became infected.[66]

In the United States, approximately one-third of infants of infected mothers develop AIDS through vertical transmission. Of the pediatric AIDS cases, 84 percent are due to vertical transmission. There are three points perinatally, however, at which the disease could be transmitted: (1) during intrauterine gestation, (2) during delivery, through blood and secretions, and (3) postnatally, through maternal milk and potentially saliva and tears. Studies have shown postpartum conversion in women without transfusions, probably from sexual activity. Knowing the route of infection in the mother does not establish the route in the infant. In at least four reported cases, infected maternal transfusion did not result in disease in the breastfeeding infant.[65] The potential transmission of HIV-1 through breastfeeding continues to be acknowledged even though it is not well quantified. Recommendations are therefore based on perceived risks and benefits.[57]

Efforts to detect HIV-1 P24 antigen (by the antigen capture method and viral DNA by means of polymerase chain reaction) in the milk of 47 seropositive women identified HIV-1 DNA in 70 percent of specimens at 0–4 days postpartum.[67] Samples collected 6–12 months postpartum yielded a 50 percent capture rate. P24 antigen was detected in 24 percent of the milk samples of 37 seropositive women at 0–4 days postpartum but not in subsequent specimens. The presence of HIV-1 DNA or P24 antigen in milk was not significantly associated with maternal CD4 lympho-

cyte counts, beta$_2$-microglobulin levels, or clinical case criteria.[57] Much is still to be learned about the relationship between breastfeeding and transmission of HIV to the recipient infant and about the associated indicators, since all infants breastfed by HIV-positive mothers do not become infected with HIV.[62,64,68]

An estimation of risk of HIV-1 transmission through the breastmilk of infected mothers was determined in a study of 168 breastfed and 793 formula-fed infants of seropositive women. Odds ratios were determined by duration. This study found that the longer the infant was breastfed beyond the neonatal period (28 days), the greater the risk of acquiring HIV.[68]

In reviewing the role of breastfeeding in HIV infection, the following major issues continue to elude definitive answer:[65]

1. The risk of vertical transmission of HIV through breastfeeding
2. The effect of breastfeeding on HIV-infected infants
3. The effect of breastfeeding on noninfected infants of HIV-infected women
4. The effect of lactation on HIV-infected women
5. The effect of AZT on transmission of HIV through breastfeeding

Advances in treatment during the perinatal period may provide the solution in the next decade. If medication can control viral shedding, breastfeeding with all its benefits may be available to the infants of HIV-infected women receiving treatment.

While studies and reports about HIV infection in the perinatal period continue to accumulate, its association with breastfeeding is still unclear. In the United States, the position of the Centers for Disease Control and Prevention (CDC) with regard to HIV-positive mothers is not to breastfeed. The World Health Organization (WHO) states that, in

developing countries or areas where the risk of infant mortality from infection is great, breastfeeding is recommended even in the event of maternal AIDS.[10] (This position is undergoing review and investigation, which may support or change the current recommendation.) Where the risk of mortality from other infections is not great, mothers with HIV should be counseled on alternatives to breastfeeding.

The American Academy of Pediatrics (AAP) Committee on Pediatric AIDS developed the following recommendations[53] on breastfeeding and transmission of HIV in the United States:

• Women and their health care providers need to be aware of the potential risk of transmission of HIV infection to infants during pregnancy and in the peripartum period, as well as through human milk.

• Documented, routine HIV education and routine testing with consent of all women seeking prenatal care are strongly recommended in order that each woman know her HIV status and the methods available both to prevent the acquisition and transmission of HIV and to determine whether breastfeeding is appropriate.

• At the time of delivery, education about HIV and testing with consent of all women whose HIV status during pregnancy is unknown are strongly recommended. Knowledge of the woman's HIV status assists in counseling on breastfeeding and helps each woman understand the benefits to herself and her infant of knowing her serostatus and the behaviors that would decrease the likelihood of acquisition and transmission of HIV.

• Women who are known to be HIV infected must be counseled not to breastfeed or provide their milk for the nutrition of their own or other infants.

• In general, women who are known to be HIV seronegative should be encouraged to breastfeed. However, women who are HIV seronegative but at particularly high risk of seroconversion (e.g., injection drug users and sexual partners of known HIV-positive persons or active drug users) should be educated about HIV with an individualized recommendation concerning the appropriateness of breastfeeding. In addition, during the perinatal period, information should be provided on the potential risk of transmitting HIV through human milk and about methods to reduce the risk of acquiring HIV infection.

• Each woman whose HIV status is unknown should be informed of the potential for HIV-infected women to transmit HIV during the peripartum period and through human milk and the potential benefits to her and her infant of knowing her HIV status and how HIV is acquired and transmitted. The health care provider needs to make an individualized recommendation to assist the woman in deciding whether to breastfeed.

• Neonatal intensive care units should develop policies that are consistent with these recommendations for the use of expressed human milk for neonates. Current standards of the Occupational Safety and Health Administration (OSHA) do not require gloves for the routine handling of expressed human milk. Gloves, however, should be worn by health care workers in situations where exposure to breastmilk might be frequent or prolonged, such as in milk banking.

• Human milk banks should follow the guidelines developed by the United States Public Health Service, which includes screening all donors for HIV infection and assessing risk factors that predispose to infection, as well as pasteurization of all milk specimens.

Tuberculosis

Breastfeeding is not contraindicated in women with previously positive skin tests and no evidence of disease.[69] In the event of

possible tuberculosis in the mother, the urgent problem is to establish the mother's and infant's status, initiate maternal treatment, and if necessary also initiate treatment in the infant during the diagnostic phase.[69] Diagnostic tests include identification of the tubercle bacilli by culture from sputum or gastric washings or other fluid. The skin test is the only practical tool for identifying infected asymptomatic individuals. A positive reaction is first detectable from as early as three to six weeks to as late as three months after exposure.[53]

If all tests are negative, therapy for the infant can be discontinued. An infant born to a mother with known tuberculosis should be placed on preventive therapy immediately, consisting minimally of daily isoniazid (INH). If the mother has been treated, she may breastfeed.[53]

Differentiation between tuberculosis infection and active disease is important. If infection with Mycobacterium tuberculosis occurs but is contained because of immune responses, delayed hypersensitivity to the bacilli can result in a positive skin test, but the chest roentgenogram (x-ray) is normal and no signs or symptoms characteristic of the disease are present. Individuals with the disease, however, have clinical signs and symptoms and may have a chest x-ray that is characteristic of the disease.[53] The interval between the initial infection and the onset of disease may be weeks to years. Cases of active disease are currently most commonly seen in urban, low-income areas and in non-white racial and ethnic subgroups in the United States. Specific groups with the highest incidence of disease are first-generation immigrants from high-risk countries, Hispanics, African Americans, Asians, American Indians, and Alaskan Natives. The homeless and residents of correctional facilities are at greatest risk. Transmission of the bacillus is usually by inhalation of droplet nuclei produced by an adult or adolescent with cavitational lung disease, and the portal of entry is usually the respiratory tract. Tuberculosis is rarely transmit-

ted from mother to fetus via the placenta or infected amniotic fluid, except in cases of overwhelming maternal disease. Exposure postpartum from active disease would be by droplet formation from intimate contact, not via the breastmilk.

The duration of infectivity is usually a few weeks after initiation of appropriate antibiotic therapy.[53] The success of treatment, however, depends on the drug susceptibilities of the organism, the number of bacilli in infected sputum, and the frequency of the cough. Compliance with treatment is a key factor. The patient is considered noninfectious when the sputum is negative on repeated smears and cultures and the cough disappears. Infants with primary tuberculosis are usually not contagious because their lesions are usually small, few if any bacilli are found in sputum, and cough is minimal or absent.

Treatment of active disease consists of at least six months of therapy. In most cases, INH, rifampin, and pyrazinamide are given for the first two months and INH and rifampin for the next four months.[53,70]

If active disease is discovered during pregnancy, a nine-month course of INH and rifampin is given.[53] Pyrazinamide usually is not given because of inadequate information about its potential teratogenic properties. Ethambutol may be added to the initial regimen if a resistant strain of Mycobacterium tuberculosis is suspected. Isoniazid, ethambutol, and rifampin appear to be relatively safe for the fetus, and the benefit of medication for active disease outweighs the risk. In pregnant women with a positive skin test but no major risk factors, preventive therapy can be postponed until after delivery.[53,70,71]

Breastfeeding is not contraindicated in women with previously positive skin tests and no evidence of disease.[69] An individual with a recent conversion to a positive skin test should be evaluated for active disease with a medical history, physical examination, and chest x-ray. If there is no sign of disease,

breastfeeding can begin or continue. If the mother has suspicious symptoms, especially a productive cough, direct contact with the infant to breastfeed or to bottlefeed should be discontinued until the diagnosis is made. If the mother wishes to breastfeed, she should pump her breasts to establish and maintain her milk supply while evaluation is in process. An electric pump may be required in order to successfully establish the milk supply. If the mother is disease-free, breastfeeding may then proceed, and previously pumped milk may be provided to the infant. If there is disease, appropriate medications should be initiated.[71] Breastfeeding may be initiated or resumed after two or more weeks of adequate maternal therapy. During this time, lactation can be maintained by pumping and saving the milk since the disease is not transmitted via the milk. If it is safe for the mother to be in contact with the infant, she may breastfeed. In developing countries where non-breastfed infants have a 50 percent mortality rate from other infections, breastfeeding should not be interrupted during diagnosis and early therapy. The infant should be treated from the beginning.

The safety of using antitubercular drugs during lactation depends on the safety of the drug itself for the infant. (Drugs and breastfeeding are discussed fully in the section on medications.) As with most antibiotics, some of these compounds cross into the breastmilk. It is important to note that the infant of a mother who requires antituberculosis medications should also be treated, regardless of feeding mode.[53,70]

Use of these medications during lactation has received some attention.[70] INH is secreted into breastmilk, providing from 6 to 25 percent of the therapeutic dose for an infant. The agent has been found in the suckling infant's urine but not in measurable amounts in the blood. Since INH is given to neonates, it is not considered a contraindication to breastfeeding. While hepatotoxicity has been reported in some infants on full therapeutic doses, it has not been reported in breastfeeding infants.[69]

Pyridoxine (B$_6$) is recommended as an adjunct to therapy with INH in adults and adolescents and in breastfeeding infants of mothers receiving INH. INH has a maternal half-life of about six hours. Food decreases the absorption in the infant, so INH is less well absorbed from the breastmilk. The AAP rating for INH is 6 (i.e., compatible with breastfeeding).[72] The infant's therapeutic dose can be modified to account for a small amount from the breastmilk (16 milligrams/liter).

Rifampin is also secreted into breastmilk in small amounts. It can also be given to infants directly and is considered safe for lactating women. Serum concentrations peak at about three hours after the dose is given. The milk/plasma ratio is less than 1; it is protein bound and only .05 percent of the adult dose reaches the milk. The peak level is estimated to be 4.9 milligrams per liter of milk.[70,71] The AAP rating for the drug is 6 (compatible with breastfeeding). It is important to note that the drug may turn the milk orange, as it does other secretions such as tears, sweat, and urine.

Ethambutol also may be transmitted in breastmilk. Ethambutol is less orally bioavailable (77 percent), the serum concentration peak is three hours, and the milk/plasma ratio of the agent is less than 1. About 1 to 5.7 percent of the therapeutic dose is found in the milk.[1] AAP has given ethambutol a rating of 6 (compatible with breastfeeding).[72]

Pyrazinamide also appears in breastmilk in very small amounts and is readily absorbed orally, but little study has been done on it and the AAP has not rated it. Pyrazinamide is bactericidal and well tolerated by most infants. The agent rarely causes hepatotoxicity in infants or children.[70,71]

Streptomycin in short courses is given a rating of 6 (compatible with breastfeeding) by the AAP. Even though only small amounts of the antibiotic reach the milk, extended treatment with the agent should be avoided because of the potential for ototoxicity.[72]

Mycobacterium tuberculosis rarely causes mastitis or a breast abscess. Local infections, therefore, are not a major factor in the decision to terminate breastfeeding. If it is safe for the mother to be in contact with the infant, it is safe to breastfeed.

Hepatitis

All types of hepatitis are not the same; each type carries different risks of contagion, pathways of exposure, and possible treatments and preventive measures. The major types—A, B, and C—will be discussed separately.

Hepatitis A is an acute illness associated with fever, jaundice, anorexia, nausea, and malaise. It is rarely fulminant and does not become chronic. It is usually transmitted from person to person through fecal contamination and through an oral-fecal route. Food-borne and water-borne epidemics are common and case spread in child care facilities is well documented.[53] When there is exposure to an index case or a food handler with the disease, gamma globulin (GG) 0.02 milliliters/kilogram should be given as soon as possible, but no later than two weeks after exposure.[53]

A newborn infant is rarely infected by vertical transmission from an infected mother during delivery. Universal precautions are the appropriate management for the newborn infant. Breastfeeding is permitted and gamma globulin is given to the infant if the mother developed the disease within two weeks of delivery. Severe disease in newborns has not been reported, with or without gamma globulin.[53] When a mother with hepatitis A has received gamma globulin, breastfeeding is permitted.

Hepatitis B virus (HBV) can cause a wide spectrum of infections from asymptomatic seroconversion to fulminant fatal hepatitis or chronic liver disease in the carrier state. Recent developments in prevention and management have changed the management of infected women during pregnancy and have made breastfeeding safe.[53]

Mandatory prenatal testing for HBV exists in most states, so the mother's status with respect to the disease is known at delivery. All infants born to mothers with active disease or persistent hepatitis B surface antigen (HBsAg) should receive hepatitis B specific immunoglobulin (HBIG) immediately at birth or as soon thereafter as possible. In addition, these infants should be started on the immunization program, receiving their first dose of hepatitis vaccine within 24 hours after birth or at least before hospital discharge. They should receive the second dose at 3 to 4 weeks of age, and the third dose between 6 and 18 months of age.[53] As soon as HBIG is given, breastfeeding may begin. When a mother is unregistered and no prenatal testing has been done, it is recommended that the infant receive HBIG immediately, followed by vaccination with hepatitis B vaccine in the newborn nursery. If there are facilities to quickly test the unscreened mother, the infant can be given the vaccine immediately or within 12 hours after birth and then given HBIG as soon as the results are known to be positive, but no later than one week after birth. Universal vaccination of all infants, including those born to mothers who are HBsAg-negative, is recommended by AAP.[53]

In developing countries, where hepatitis is common and HBIG and vaccine are not available, breastfeeding is recommended because of its tremendous benefits to the infant.[53] In this country, HBIG and vaccination are necessary to remove the remote chance of infection when the mother is HBsAg-positive.[53] Breastfeeding is permitted after the infant receives HBIG. The first dose of hepatitis B vaccine is given before discharge. Table 2 presents the recommended schedule of HBIG and hepatitis B vaccine to prevent perinatal transmission of HBV.

Breastfeeding should not be discouraged in hepatitis C (HCV) carrier mothers without co-infection.[73] Hepatitis C, parenterally transmitted, was originally identified as non-A non-B hepatitis. It is characterized by the insidious onset of jaundice and malaise, with few or no symptoms associated with positive serologic

TABLE 2
Recommended Schedule of Hepatitis B Immunoprophylaxis to
Prevent Perinatal Transmission

Infant born to mother known to be HBsAG-positive

Vaccine Dose and HBIG	Age
First	Birth (within 12 h)
HBIG[†]	Birth (within 12 h)
Second	1–2 mo
Third	6 mo

Infant born to mother not screened for HBsAg

Vaccine Dose and HBIG	Age
First[‡]	Birth (within 12 h)
HBIG[†]	If mother is found to be HBsAg positive, give 0.5 mL as soon as possible, not later than 1 wk after birth
Second	1–2 mo[§]
Third	6–18 mo[‖]

[†] HBIG (0.5 mL) given intramuscularly at a site different from that used for vaccine.

[‡] First dose is same as that for infant of HBsAG-positive mother. Subsequent doses and schedules are determined by maternal HBsAG status.

[§] Infants of HBsAG-positive mothers should be vaccinated at 1 mo of age.

[‖] Infants of HBsAG-positive mothers should be vaccinated at 6 mo.

Source: Adapted with permission from the American Academy of Pediatrics,[53] table 3.19. Copyright American Academy of Pediatrics.

tests on routine screening for insurance, blood donation, or employment.[53] About 50 percent of serologically confirmed individuals develop chronic liver disease including cirrhosis; in rare cases, individuals develop hepatocellular carcinoma. Transmission is by parenteral administration of blood or blood products including some early batches of RhoGAM. Person-to-person spread, including sexual contact, is suspected but not confirmed.[53,74] At risk are parenteral drug users, persons receiving blood transfusions or blood products, health care workers with frequent blood exposure, and household and sexual contact with an infected person.

Diagnosis is made by serologic tests for anti-HCV antibodies. False negative results are rare but false positives are common.[74] The presence of the HCV RNA genome or related antigen in the circulation during infection is a reliable marker for viremia but the analytical methods are not refined or practical. There is no specific treatment, although alpha interferon may be beneficial in a small proportion of cases. Gamma globulin has not been successful for prophylaxis of this infection. HCV causes a slowly evolving disease with major potential for morbidity and mortality associated with chronic liver disease.[75,76]

It has been established that HCV is vertically transmitted from mother to infant, and the risks of transmission are correlated with the level of HCV RNA antibodies in the mother and in the cord blood.[73,75,77–79] Ohto et al.[75]

conducted a series of three independent studies on transmission of hepatitis C virus from mothers to infants. In the first prospective study of 53 antibody-positive mothers and their infants (54 infants, including one set of twins), three of the infants (5.6 percent) became positive within six months. The mothers of these infants were HCV RNA-positive at the time of delivery. None of the infants who were HCV RNA-negative at birth became infected. In the second prospective study, one of six infants born to women with known disease became infected. In the third study, three infected infants were followed retrospectively, and their mothers were all HCV RNA-positive. The titers of HCV RNA in mothers of infected infants were all significantly higher than those of noninfected infants. Other studies have reported 0 to 13 percent of infants born to anti-HCV-positive women to be HCV infected.[80] No woman whose HCV RNA titer was negative or less than 10^6 per milliliter transmitted disease to her infant.[80]

In response to queries, Ohto et al. reported that of a group of 63 infants studied, 6 of the 7 infected infants were breastfed; however, 33 of the 56 noninfected infants were also breastfed; 6 of the 7 mothers of the noninfected infants who were breastfed had HCV RNA in their serum at a titer $\geq 10^6$ per milliliter (i.e., comparable to the titers of mothers with infected infants). The duration of breastfeeding differed between the two groups. Although the findings were not statistically significant, the infected infants nursed 6.6 ± 3.6 months, and the noninfected infants nursed 2.0 ± 2.9 months. When the entire group of 63 infants (for all three studies in the series) was considered, the duration of breastfeeding for the 6 infected breastfed infants was 6.6 ± 3.6 months, compared to 3.3 ± 3.1 months for the 33 noninfected breastfed infants.

Gürakan et al.[76] reported the case of a woman who received an infected blood transfusion at seven months' gestation and delivered an infant who had anti-HCV antibodies and was HCV RNA-positive. Her breastmilk also contained antibodies and HCV RNA. The infant was not breastfed and at four months was antibody- and RNA-negative. Unfortunately, the breastmilk was not analyzed.

In a large prospective study in Italy of mother-to-infant transmission of hepatitis C virus, none of the 94 babies of mothers with anti-HCV alone (without HIV) became infected, and by age one year their titers were negative.[79] Furthermore, 71 (76 percent) of these infants, 23 of whom were born to HCV RNA-positive mothers, remained noninfected although they were breastfed. In this study, co-infection with HIV was associated with HCV infection in the infants. These authors did not feel that breastfeeding was a significant vertical perinatal route of HCV infection.[79]

In a study of 116 infants whose mothers were HCV-positive, 22 of the mothers were also infected with HIV. Of the infants whose mothers were HCV-positive but not HIV-positive, none acquired HIV infection. Of the 22 infants whose mothers were co-infected with HCV and HIV, 8 of the infants (36 percent) acquired HCV and 3 acquired both HCV and HIV. These data support the concept that HIV enhances the risk of neonatal infection.[79]

In a study of 15 mothers with HCV infection, Lin et al.[73] reported that both HCV antibodies and HCV RNA were detected in the colostrum of all 15 mothers. Although the mothers' titers varied from 1:80 to 1:40,000 and the RNA concentrations varied from 10^4 to 2.5 x 10^8 copies/milliliter, the colostral levels were lower. The 11 breastfed infants had no anti-HCV and no HCV RNA at the end of one year. Breastfeeding duration had ranged from three weeks to four months, with a mean of two months. Lin et al. concluded that breastfeeding should not be discouraged in HCV carrier mothers without co-infections and proposed the following explanations:[73,74]

1. HCV levels are too low in colostrum to infect the infant.

2. A small amount of HCV may be inactivated in the infant's gastrointestinal tract.

3. The integrity of the mucosa of the infant may preclude infection by the oral route.

4. There may be neutralization of HCV by antibodies in the colostrum.

Venereal Warts

Venereal warts are epithelial tumors of the skin and mucous membranes of the anogenital area caused by human papilloma virus (HPV).[53] They vary from asymptomatic infection to condylomata acuminata, skin-colored growths with a cauliflower-like surface. In females, the usual sites are cervix, introitus, labia, perineum, vagina, and perianal areas. Typically, they are asymptomatic, but they may cause itching, burning, localized pain, or bleeding. Transmission to the infant could occur during passage through the birth canal. On rare occasions, the warts have been associated with laryngeal papillomas. Lesions have not been reported on the breast. The viruses that cause warts elsewhere are distinct from those causing genital warts.[53] Venereal warts in the genital area are not a contraindication to breastfeeding.

Herpes Viruses

In the human, there are four known herpes viruses: cytomegalovirus (CMV), herpes simplex virus (HSV), herpes varicella-zoster virus (VZV), and Epstein-Barr virus (EBV). CMV, VZV, and EBV are believed to be antigenically related on the basis of cross-reactions observed in immunofluorescent assays.

Cytomegalovirus causes systemic infections that vary with the age and immunocompetence of the host but are predominantly asymptomatic.[53] Although infections acquired postnatally can be similar to those found in infectious mononucleosis, infection is rarely significant except in immunocompromised individuals who are being treated for malignancies, infected with HIV, or receiving immunosuppressive therapy for transplant. Infections acquired transplacentally, during the intrapartum period, or in early infancy may be a problem. Congenital infections usually are asymptomatic but can result in later hearing loss or learning disability. About 5 percent of infected infants have profound involvement with growth retardation, jaundice, microcephaly, intracerebral calcifications, and chorioretinitis.[81] Infections acquired at birth from maternal cervical secretions or breastmilk usually are not associated with symptoms. Infants with congenital or acquired infections usually do better if they are breastfed, because of the continuing supply of maternal antibodies provided in their mother's breastmilk. Infants, usually premature infants infected through CMV seropositive blood, have developed lower respiratory tract infections.[82] Blood products for neonates are now specifically screened for CMV and irradiated.

CMV, though not highly contagious, is ubiquitous. For infants, the birth process and child care exposure are the common sites. Effects on the infant are greatest when the mother develops a primary infection during pregnancy. CMV is usually acquired during late adolescence. Young mothers are at greater risk for developing the disease during pregnancy. In a random study of postpartum women, 39 percent had CMV in their milk, vaginal secretions, urine, and saliva.[81] Of the infants who were breastfed, 69 percent developed infections while the antibodies were present in the milk. The infants shed the virus, developed immune responses to the virus, but did not develop disease. Transmission of CMV from breastmilk is related to the duration of breastfeeding. Reactivation of CMV in the breastmilk peaks between 2 and 12 weeks, a time when transplacental antibody is waning. Infants who continue to receive antibody or associated protective factors via the milk rarely manifest any symptoms. Non-breastfed infants can be infected via other secretions, including saliva; they do not receive protective antibodies or other host resistance factors present in breastmilk[82] and may have signifi-

cant residuals of the disease (e.g., micro-cephaly and mental retardation).

Term infants can be breastfed when the mother is shedding virus in her milk because of the passively transferred maternal antibodies. Premature infants with low concentrations of transplacentally acquired maternal antibodies can develop disease from fresh breastmilk containing the virus.[53] Freezing destroys the virus, and breastmilk can be frozen at -20 degrees centigrade for seven days before feeding it to the infant for the first few weeks, until the titer of antibody received via the milk increases. (Some experts consider storage for three days at -20 degrees centigrade adequate.)[53,82]

Herpes simplex virus infection in the neonatal period is often severely debilitating or fatal. It can be manifested as a generalized systemic infection, as localized central nervous system (CNS) disease, or as localized infection of skin, eyes, and mouth. Typical vesicular lesions are helpful diagnostic signs. The infection is most frequently transmitted to the infant during passage through the birth canal when the mother has an infected lower genital tract. In 33 to 50 percent of cases, there is risk of neonatal disease from a primary lesion in the mother. The risk to the infant born to a mother with recurrent HSV is, at most, 3 to 5 percent. Disseminated neonatal disease usually occurs within 14 days of birth.[53]

The cases reported in the literature associating neonatal herpes with breastfeeding have involved lesions on the breast itself.[83,84] HSV cultures are easily obtained and the virus usually grows in a few days; smears of secretions are readily done and serum antibody titers can be obtained. A definitive diagnosis of a suspicious lesion on the breast can be made quickly and breastfeeding withheld temporarily until herpes is ruled out. This is especially important in the first few months of life when the neonate is very prone to serious infection from HSV.[53] It is recommended that women with herpetic lesions on their breasts refrain from breastfeeding until they are completely cleared.

Active HSV lesions elsewhere should be covered and the mother should be instructed to wash her hands carefully before handling the infant. A mother with herpes labialis (cold sore) or stomatitis should wear a disposable surgical mask and wash her hands carefully when touching her newborn until the lesions have crusted and dried. Whether breastfeeding or formula feeding the mother should not kiss or nuzzle her newborn until the lesions have cleared.

Herpes varicella-zoster virus (which causes chicken pox) is one of the most contagious of diseases.[85] The incidence is reported at 5/10,000 pregnancies. As the vaccine becomes more widely used and natural disease less likely, new guidelines may be necessary. Presently, risk of infection to the neonate depends upon when the disease occurs during the mother's pregnancy or postpartum period. Congenital chicken pox, by definition, occurs in neonates younger than 10 days of age and is associated with significant mortality. Varicella virus DNA has been detected in breastmilk, but the spread of disease from mother to infant after delivery is by direct contact, not by feeding. Infants born to mothers who have varicella can develop the infection between 1 and 16 days of life. The usual time interval from onset of rash in the mother to onset in the neonate is 9 to 15 days.

When maternal chicken pox occurs immediately postpartum or within six days of delivery and no lesions are present in the neonate, mother and infant should be isolated from each other. Only half of the neonates will develop the disease, but all of them should receive varicella zoster immune globulin (ZIG) immediately at birth. When the mother becomes noninfectious, she can be with her infant and breastfeed.[53]

Epstein-Barr virus is the principal cause of infectious mononucleosis, which is usually a disease of adolescence and young adult life

and is rarely recognized in infants and young children. An association between pregnancy and EBV has not been established, and breastfeeding is not restricted during Epstein-Barr virus infection.[53]

Toxoplasmosis

Toxoplasmosis is one of the most common infections of humans throughout the world. The protozoan organism is ubiquitous, causing a variety of illnesses previously thought to be due to other agents or unknown causes.[1] The normal host is the cat. The pregnant or lactating woman should not handle kitty litter. Kitty litter should, however, be disposed of daily, as the oocysts are not infective for the first 48 hours after passage. In humans, prevalence of positive serologic test titers increases with age, indicating past exposure, and there is equal distribution in males and females in the United States.[86] The risk to the fetus is related to the time when maternal infection occurs. In the last months of pregnancy, the protozoa are most frequently transmitted to the fetus, but the infection is subclinical in the newborn. Early in pregnancy, transmission to the fetus occurs less often but does result in severe disease. Once the placenta has been infected, it remains so throughout pregnancy.

Toxoplasma gondii (T. gondii) have been isolated from breastmilk, menstrual fluid, placenta, lochia, amniotic fluid, embryo, and fetal brain in 33 percent of the subjects in one series.[86]

Transmission during breastfeeding in humans has not been demonstrated. It is possible that unpasteurized cow milk could be a vehicle of transmission. The human mother, however, would provide appropriate antibodies via her milk. From this information, it appears there is no evidence to support depriving the neonate of breastmilk when the mother is known to be infected with T. gondii.[86]

Mastitis

Mastitis is rarely a cause for discontinuing breastfeeding. It usually does not occur until 10 days postpartum (or later) except in rare cases when the mother has been massaging her breasts or nipples before delivery.[73]

Mastitis is an infectious process in the breast producing localized tenderness, redness, and heat, together with systemic reactions of fever, malaise, and sometimes nausea and vomiting (i.e., flu-like symptoms). Mastitis is usually

TABLE 3
Characteristics of Engorgement, Plugged Ducts, and Mastitis

Characteristics	Engorgement	Plugged Duct	Mastitis
Onset	Gradual, immediately postpartum	Gradual, after feedings	Sudden, after 10 days
Site	Bilateral	Unilateral	Usually unilateral
Swelling and heat	Generalized	May shift/little or no heat	Localized, red, hot, and swollen
Pain	Generalized	Mild but localized	Intense but localized
Body temperature	<38.4°C	<38.4°C	>38.4°C
Systemic symptoms	Feels well	Feels well	Flu-like symptoms

Source: Reprinted with permission from Lawrence,[1] table 8-5.

due to an acute bacterial infection of a duct or lobule of the breast, precipitated by trauma or transient obstruction of the duct due to pressure from a strap or engorgement or poor drainage. It must be distinguished from a plugged duct or engorgement. The key differential points are compared in table 3. Before the development of antibiotics, when women were hospitalized two weeks postpartum, mastitis was epidemic in hospitals. Today, however, mastitis may be acquired in the hospital and then develop during the first four weeks postpartum at home if the mother or infant is colonized with a virulent bacteria. Because treatment is given at home, hospitalization for mastitis is rare and large series are not reported in the literature.

The common bacteria involved are staphylococcus aureus and, less commonly, E. coli. When the infection is bilateral and the mother is especially toxic, the bacteria is usually beta hemolytic streptococcus, and both mother and infant should be treated aggressively. A mother should always be instructed to contact her physician if unusual symptoms occur, so that proper management can be initiated promptly. Inappropriately or inadequately treated cases of mastitis predispose to recurrent or chronic mastitis. Most reports indicate that the cases of acute mastitis that result in poor outcomes, including abscess and recurrent disease, had significant delay between the onset of symptoms and the start of antibiotic therapy.[87,88] Recurrent mastitis can also be traced to inadequate treatment when antibiotics are discontinued before a full 10 to 14 days.

Early management of mastitis should involve early evaluation by the physician, mid-stream cultures of the milk from the affected breast, and antibiotics. The following key points outline the recommended management of mastitis:[73]

1. Continue to breastfeed on both breasts, usually starting with the unaffected side and taking care to totally empty the affected side at each feeding.

2. Ensure bed rest, with the mother's only responsibility being to feed the infant.

3. Select the antibiotic that is effective and safe for the infant. A minimum of 10 to 14 days' treatment will reduce the incidence of recurrence.

4. Apply local treatment of cold packs or warm packs, whichever provide the greatest relief of pain and discomfort.

Abscess formation is rare except when treatment is delayed or discontinued too quickly. If surgical drainage is necessary, breastfeeding should continue; the surgeon may leave a drain in place. Applying firm pressure over the incision will minimize the drainage of milk through the incision during feeding. Between feedings, the surgical drain will continue to drain the abscess.

Selection of the best antibiotic for mastitis depends upon safety and efficacy. In general, antibiotics pass into the milk. If the antibiotic can be given to the infant directly, it is considered safe for use during lactation.[89] Thus, only a very small number of antibiotics should be avoided. These include chloramphenicol, tetracycline, streptomycin, and ciprofloxacin. In most cases, there are sufficient alternatives so that breastfeeding need not be discontinued.[1,72] Generally, breastfeeding should continue during acute mastitis. In rare circumstances when the abscess drains into the duct system, breastfeeding is contraindicated on that breast. Infected lesions on the breast, such as superficial boils, impetigo, and herpes simplex are contraindications to breastfeeding until the lesions clear.

Lyme Disease

Lyme disease has attracted increasing attention since it was identified in the United States in 1975.[53] The greatest concentration of cases is in the Northeast. Lyme borreliosis is a tick-borne infectious disease caused by the spirochete, Borrelia burgdorferi. The spirochete has been found in the fetus during preg-

nancy and results in fetal death if untreated. If the mother is adequately treated during pregnancy, the outcome is good.[90] The mother and infant need not be isolated from each other or from other patients.

If the disease is diagnosed postpartum, the mother should be treated immediately. The spirochete has been found in breastmilk,[91] so the infant should also receive treatment, especially if any symptoms (e.g., rash, fever) develop. Indirect fluorescent antibody and ELISA tests are available. Once maternal treatment has begun, lactation can continue. The treatment prescribed is doxycycline or amoxicillin or the cephalosporins for at least 14 days. If the infant is healthy and the mother has initiated treatment for Lyme disease, the infant can be breastfed.

Human T-Cell Leukemia Virus Type 1

The incidence of human T-cell leukemia virus type 1 (HTLV-1) is increasing in parts of the world such as the West Indies, Africa, and southwestern Japan.[92] There is virtually no transmission from the mother to the fetus, and cord bloods are not found to contain infected cells. On the other hand, infected lymphocytes have been found in the milk of infected mothers. Mathematically, it can be calculated that if 10 percent of cells in human colostrum are T-lymphocytes, and if 1 percent of them are infected, then 1 milliliter of milk will contain 1,000 infected T-cells. In a study in Japan,[93] the incidence of mother-to-child transmission of HTLV-1 was 30 percent among breastfed infants, 10 percent among mixed-fed infants, and nonexistent among formula-fed infants. Though it has not been confirmed whether the presence of infected cells in the milk actually causes disease, future studies may demonstrate that breastmilk and its antibodies are actually protective.

Although HTLV-1 is not increasing in the United States, trends may change. At the present time, it is recommended that, in the United States, the mother with HTLV-1 disease should not breastfeed.

Medication/Prescription Drugs and Street Drugs

Medications

Much concern and anxiety have been expressed regarding the question of medications taken by lactating women and the risk to the suckling infant. In reality, very few drugs are contraindicated during breastfeeding.[72] Each situation should be evaluated on a case-by-case basis by the physician. The important factors include the pharmacokinetics of the drug in the maternal system and also the absorption, metabolism, distribution, storage, and excretion in the recipient infant. Variables that should be considered in the decision include gestational age, chronological age, body weight, breastfeeding pattern, and other dietary practices. Ultimately, the decision is made by assessing the risk/benefit ratio (i.e., the risk of a small amount of the drug compared to the tremendous benefit of being breastfed).[1]

The American Academy of Pediatrics Committee on Drugs has prepared a rating of some of the more common medications that might be prescribed for women while lactating.[72] Following are the numerical ratings:

1. Drugs that are contraindicated during breastfeeding

2. Drugs of abuse: contraindicated during breastfeeding

3. Radioactive compounds that require temporary cessation of breastfeeding

4. Drugs whose effect on nursing infants is unknown but may be of concern

5. Drugs that have been associated with significant effects on some nursing infants and should be given to nursing mothers with caution

6. Maternal medication usually compatible with breastfeeding

7. Food and environmental agents: effect on breastfeeding

Table 4 presents the list of drugs contraindicated for breastfeeding. It is important to note that bromocriptine suppresses the production of one of the main lactogenic hormones, prolactin.[72] However, if a woman has been able to become pregnant and delivers a healthy infant while on bromocriptine for pituitary adenoma, the drug is not a contraindication to breastfeeding her infant. It will be particularly important, however, to monitor her milk production. Thus, bromocriptine should not be rated 1 but rather 5 or 6, and its use in individual cases should be decided by the mother's physician.

Radioactive compounds, if given for diagnostic purposes in a single dose, require temporary cessation of breastfeeding.[1] Once the radioactive compound has cleared the mother's plasma, breastfeeding may be resumed. The time, however, varies from compound to compound. Physiologically, iodine is "pumped" into the milk and has a milk/plasma ratio greater than 1. Radioactive iodine appears in high concentrations in milk. Some radioactive iodine compounds take more time to clear the body than others; for example, iodine 131 (^{131}I) takes two weeks to clear the body, while gallium 67 (^{67}GA) takes only two days.[1] Table 5 lists the radioactive compounds and the time they take to clear from the milk. During this time, the mother should be instructed to pump her milk to maintain her supply, but to discard the milk.

When radioactive compounds are used in multiple doses for therapeutic purposes, it may take weeks or months to clear radioactivity from the milk and breastfeeding usually has to be discontinued. When these compounds are used therapeutically (e.g., ^{131}I used for thyroid malignancy), the primary disease is usually serious, presenting an additional reason to avoid breastfeeding.

TABLE 4
Drugs That Are Contraindicated During Breastfeeding

Drug	Reason for Concern, Reported Sign or Symptom in Infant, or Effect on Lactation
Bromocriptine	Suppresses lactation; may be hazardous to the mother
Cocaine	Cocaine intoxication
Cyclophosphamide	Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia
Cyclosporine	Possible immune suppression; unknown effect on growth or association with carcinogenesis
Doxorubicin*	Possible immune suppression; unknown effect on growth or association with carcinogenesis
Ergotamine	Vomiting, diarrhea, convulsions (doses used in migraine medications)
Lithium	One-third to one-half therapeutic blood concentration in infants
Methotrexate	Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia
Phencyclidine (PCP)	Potent hallucinogen
Phenindione	Anticoagulant: increased prothrombin and partial thromboplastin time in one infant; not used in United States

*Drug is concentrated in human milk.

Source: Adapted with permission from the American Academy of Pediatrics Committee on Drugs,[72] table 1. Copyright American Academy of Pediatrics.

TABLE 5
Radioactive Compounds That Require Temporary Cessation of Breastfeeding*

Drug	Recommended Time for Cessation of Breastfeeding
Copper 64 (^{64}Cu)	Radioactivity in milk present at 50 h
Gallium 67 (^{67}Ga)	Radioactivity in milk present for 2 wk
Indium 111(^{111}In)	Very small amount present at 20 h
Iodine 123 (^{123}I)	Radioactivity in milk present up to 36 h
Iodine 125 (^{125}I)	Radioactivity in milk present for 12 d
Iodine 131 (^{131}I)	Radioactivity in milk present 2–14 d, depending on study
Radioactive sodium	Radioactivity in milk present 96 h
Technetium-99m (^{99m}Tc), ^{99m}Rc macroaggregates, ^{99m}Tc O4	Radioactivity in milk present 15 h to 3 d

*Consult nuclear medicine physician before performing diagnostic study so that radionuclide that has shortest excretion time in breastmilk can be used. Before study, the mother should pump her breast and store enough milk in freezer for feeding the infant; after study, the mother should pump her breast to maintain milk production but discard all milk pumped for the required time that radioactivity is present in milk. Milk samples can be screened by radiology departments for radioactivity before resumption of nursing.

Source: Adapted with permission from the American Academy of Pediatrics Committee on Drugs,[72] table 3. Copyright American Academy of Pediatrics.

Compounds rated 4 or 5 by the American Academy of Pediatrics' Committee on Drugs[72] require individual consideration. Compounds rated 6 are usually compatible with breastfeeding. Drugs of abuse (rated 2) and environmental agents (rated 7) will be discussed separately. The AAP list is not exhaustive, and other resources may need to be consulted. (Additional information is available in other references; see Briggs[89] and Lawrence.[1]) The Breastfeeding and Human Lactation Study Center ([716] 275-0088) provides additional information to professionals through an extensive computer database that is updated continually. Often, more than one drug is available for a given therapeutic need and it may be possible to change the medication to one that is less likely to cross into the milk or that is not well absorbed from the stomach by the infant.

Therefore, before breastfeeding is summarily discontinued, adequate information should be sought and the clinician should consider the risk of the drug versus the benefit of breastfeeding for the infant. The pharmacologic properties of the drug that will affect passage into the milk are often known, even in the absence of extensive studies measuring the actual amount of drug that reaches the breastmilk. If compounds are quickly metabolized by the mother, little trace of the agents may remain in the plasma at feeding time. Thus, such medications are not a problem for the suckling infant. Compounds taken only occasionally by the dose (such as aspirin for headache) are rarely a problem. They clear the maternal plasma in a short period of time and do not accumulate in the infant. If the peak maternal plasma time for the drug is known, this will help in planning dosing times in relationship to feedings. Some medications are so poorly absorbed orally that they are given to the mother by injection or nasal spray. Such drugs have low oral bioavailability and would not be absorbed from the infant's stomach.

The chronologic age and maturity of the infant play an important role in the way compounds are metabolized by the infant; gesta-

tional age has an effect in the first few months of life because of the immaturity of liver metabolism and renal excretion. Thus, a drug that might be of concern for an infant at one week of age might be of little concern at four months.

A number of pharmacologists have attempted to simplify the concept of determining how much drug reaches the infant.[94–96] The three-compartment pharmacologic model of Wilson et al.[95] assumes that breastmilk is the third compartment and only interacts when the infant is feeding and removing milk. This model suggests that the amount of the drug in breastmilk can be calculated if the level of the drug is known in one of the other compartments (e.g., the plasma). When breastmilk is not being removed, the breastmilk compartment equilibrates with compartment two, the interstitial compartment.[95] Application of this model is dependent upon knowing the rate constant for each drug—a factor not readily available.

Another model involves the volume of distribution of the parent compound.[97] The volume of distribution is determined by the total amount of drug in the body divided by the concentration of the drug in the plasma. This assumes the most elementary kinetic model in which the body is a single compartment and the drug is assumed to distribute evenly. Actually, if the volume of distribution of a drug is known, then the amount available to the infant via the milk can be calculated if the weight of the mother and the dose of the drug are known.[97] In general, drugs with a small volume of distribution (≤ 1) have milk/plasma ratios of 1 or higher (that is, some gets into the milk). Drugs with a large volume of distribution and a small dosage have very low concentrations that appear in the milk. The volume of distribution of many common drugs is recorded in the drug index.[1]

Another way of determining risk is the exposure index, which has been described as a function of a coefficient (10 milliliter kilogram^{-1} minute^{-1}). The drug clearance in the infant is expressed as (milliliter kilogram^{-1} minute^{-1}). This concept takes a pharmacokinetic parameter (drug clearance) and a physiochemical parameter (the milk/plasma ratio) to determine infant exposure.[98] Thus, high clearance drugs (those requiring large doses to achieve clinical effect) have lower levels in the milk. Clearance rates, however, are not readily available for most drugs. While these calculations have theoretical significance, they have little practical application in the clinical setting.

In general, only small amounts of medications that are acidic, water soluble, highly protein bound, and with low oral bioavailability pass into milk. Drugs of large molecular size (e.g., insulin, heparin) do not cross the membrane into the milk.

Because of the wide selection of therapeutic medications available today, the clinician can select an alternative medication for the mother if one drug is known to develop high levels in the milk. Antibiotics usually cross into breastmilk to some degree. In general, if the antibiotic is considered safe enough that it could be given directly to the infant, it is considered safe for the mother to use while breastfeeding. Tetracycline and chloramphenicol, for example, should be avoided when the nursing infant is under six months of age. Some antibiotics are not absorbed orally and must be given parenterally (aminoglycosides); thus, little is absorbed from the gastrointestinal track and no threat is posed to the infant receiving a small amount in the breastmilk.

Caffeine, however, is sometimes given directly to infants—especially premature infants—to stimulate them to breathe, but they are only dosed once a day at first because they do not clear it quickly. Thus, small amounts of caffeine consumed more than three to four times a day will accumulate in the infant after a few days and may cause irritability and wakefulness.[99]

Information about a wide group of antihypertensive drugs indicates that a few of them

cross into the milk in high levels (e.g., nadolol, atenolol), while others appear at very low levels (captopril and metoprolol).[100,101] AAP gives atenolol, nadolol, captopril, and metoprolol a rating of 6 (compatible with breastfeeding).

In assessing a specific woman's risk/benefit of breastfeeding her infant, it can be stated that, generally, most medications taken by the mother are considered safe. Those that are contraindicated are listed in tables 4 and 5. Otherwise, the mother should be encouraged to breastfeed, and the health care professional encouraged to seek information about any drug that the mother needs. Usually, the question about a medication comes after lactation is established. Time can be taken to evaluate the best medication to accomplish the therapeutic goal without compromising the infant.

For temporary treatment with a problem drug, the mother can pump and discard her milk during treatment. The infant will need to receive formula by cup or bottle during that time. Metronidazole (Flagyl) used for trichomonas vaginalis and amoebiasis is considered a problem when the infant is under three months of age, because the drug passes into milk.[102] Instead of a 10-day course of therapy, it has been recommended that the drug be given in a 1- to 2-gram dose and that the milk be pumped and discarded for 12 to 24 hours. Metronidazole is occasionally used in newborns for serious infections.[103]

While lists can be helpful in identifying the few compounds that are contraindicated, lack of knowledge about a compound should not be used as a reason to avoid breastfeeding. The health care professional who cares for the infant can determine the safety of the compound by reviewing the available data. The *Physician's Desk Reference* (PDR)[104] is not a reliable source because the manufacturers are required to say that a specific drug or compound is not recommended during lactation unless they have carried out extensive studies on lactating women and their breastfed infants. The PDR can provide information

about molecule size, pH, protein-binding, and other properties. Local poison control centers can also provide additional information, as can other sources (see Briggs[89] and Lawrence[1]).

Street Drugs and Drugs of Abuse

Generally, drugs of abuse are contraindicated during breastfeeding. The AAP presents a list of such items in table 6. Although the contraindication of illicit drugs such as amphetamines, cocaine, heroin, marijuana, and phencyclidine is undisputed, universal agreement has not been reached concerning all of the agents on the list.

Tobacco

While tobacco use and smoking are never recommended, these can be viewed as a matter of risk/benefit ratio: the risk of some nicotine exposure versus the tremendous benefit of being breastfed. Formula-fed infants of mothers who smoke also excrete nicotine and cotinine in their urine. Infants who live in households where adults smoke have a higher incidence of pulmonary problems, especially infections and asthma.[105] Breastfeeding provides some protection from both infection and asthma; breastfed infants of smokers do better than those who are formula fed. Absorption of nicotine is greater from the respiratory tract than from breastmilk. The nicotine absorbed from milk is less than 5 percent of the average daily dose of the adult.[106] The nicotine levels in maternal serum reflect smoking technique and tend to increase with increased depth of inhalation and the number of puffs per cigarette.[106] The risk of sudden infant death syndrome (SIDS) is significantly higher in infants who are not breastfed and whose mothers smoke; in other words, breastfeeding is protective against SIDS when mothers smoke.[107]

Smoking is not a contraindication to breastfeeding. Smoking may adversely affect milk volume, and women who smoke tend to wean sooner. No reports have been published

TABLE 6
Drugs of Abuse: Contraindicated During Breastfeeding*

Drug Reference	Reported Effect or Reasons for Concern
Amphetamine[†]	Irritability, poor sleeping pattern
Cocaine	Cocaine intoxication
Heroin	Tremors, restlessness, vomiting, poor feeding
Marijuana	Only one report in literature; no effect mentioned
Nicotine (smoking)	Shock, vomiting, diarrhea, rapid heart rate, restlessness, decreased milk production
Phencyclidine	Potent hallucinogen

*The Committee on Drugs strongly believes that nursing mothers should not ingest any compounds listed here. Not only are they hazardous to the nursing infant, but they are also detrimental to the physical and emotional health of the mother. This list is obviously not complete; no drug of abuse should be ingested by nursing mothers even though adverse reports may not be in the literature.

[†]Drug is concentrated in human milk.

Source: Adapted with permission from the American Academy of Pediatrics Committee on Drugs,[72] table 2. Copyright American Academy of Pediatrics.

associating nicotine from breastmilk with infant health problems, according to the Institute of Medicine Subcommittee on Nutrition During Lactation.[29] Mothers who smoke should be urged not to smoke in the same room as the infant at any time and not to smoke within two hours of nursing the infant.

Alcohol

Alcohol (ethanol) presents another series of questions. In countries where, for centuries, alcoholic beverages such as wine and beer have been consumed with daily meals, breastfeeding is universal, and no apparent problems have been reported. More recently in the United States, studies have been reported regarding the effect on suckling infants when alcohol is present in the breastmilk. These studies involved the rapid consumption of 40 to 90 milliliters of absolute alcohol by lactating women, who served as their own controls.[108] Blood levels were drawn every 30 minutes for four hours, and levels in the milk paralleled the maternal blood levels. The milk was noted to smell of alcohol at peak levels, paralleling the concentration of alcohol in the milk, which peaked between 30 and 60 min-

utes post maternal ingestion. The infants were observed to suckle more frequently but consumed less milk in the presence of alcohol. The mothers had been unaware of any differences. Few women consume the volume of alcohol or drink with the speed established in these experiments.[109] Alcohol appears in milk if there is alcohol in the serum while nursing. Acetaldehyde, which is the major metabolite of ethanol and believed to be the major source of alcohol toxicity, does not appear in breastmilk.[110]

A study of one-year-old infants received considerable attention in the lay press in 1989, reporting a strong positive association between psychomotor development scores obtained with the Bayley Scales of Infant Development and an approximate measure for exposure to alcohol through breastfeeding.[111] The scores of infants of breastfeeding mothers who drank alcohol occasionally (e.g., one to two drinks per week) did not differ from those of infants breastfed by mothers who never drank. Infants of mothers who drank heavily (a six-pack of beer per day) showed slight gross motor delay at one year. No follow-up has been reported. It is important to note that these infants may well have

been exposed to alcohol in utero and may have been expressing effects of fetal alcohol syndrome. The study did not report details of confounding socioeconomic factors or deficits in maternal interactions, which also affect developmental parameters.

The American Academy of Pediatrics Committee on Drugs lists alcohol as usually compatible with breastfeeding.[72] The Institute of Medicine Subcommittee on Nutrition During Lactation has concluded that no published scientific evidence demonstrates that consumption of alcoholic beverages has a beneficial impact on lactation performance.[29] The Committee on Drugs further suggests that if alcohol is used, intake should be limited to "no more than 0.5 grams of alcohol per kilogram of maternal body weight per day. . . . For a 60-kilogram (132-pound) woman, 0.5 grams of alcohol per kilogram of body weight corresponds to approximately 2 to 2.5 ounces of liquor, 8 ounces of table wine, or 2 cans of beer."[29]

Caffeine

Caffeine consumption is of national interest, and many caffeine-free beverages are available. Beverages that are naturally caffeine-free may differ from those that are decaffeinated. A study done in rats in Costa Rica suggests that other components of coffee itself—exclusive of caffeine—affect iron concentrations when volumes equivalent to three cups of coffee per day are consumed.[112] The chief concern with caffeine is related to the fact that infants in the first few weeks of life do not excrete caffeine rapidly.[1] Only small amounts of caffeine appear in breastmilk, but if the mother consumes considerable caffeine day after day, the caffeine accumulates in the infant. The infant becomes symptomatic (i.e., irritable, wakeful, jittery). Symptoms promptly abate with a decrease in caffeine consumption. Maternal consumption of one to two caffeine-containing beverages per day is not associated with problems.[99] As noted earlier, caffeine is sometimes given directly to infants (especially premature infants) to stimulate

them to breathe, but they are dosed only once a day at first because they do not clear the caffeine quickly.

Herbal and food products

With the blend of cultures and traditions, herbs and herbal teas have become more widely used. Much of the traditional and current use of these herbs surrounds pregnancy, childbirth, and lactation.[113] While many herbal teas contain innocuous flavors, others contain pharmacologically active components that form the basis for folk medicine treatments. A number of natural herbs contain belladonna (atropine) and are recommended to create euphoria and ease pain. Other herbs contain naturally occurring coumarins, which, when taken to excess, can cause bruising and hemorrhage. Comfrey leaves have been a favorite of traditional midwifery but have been banned in Canada and other countries because of the association with veno-occlusive disease and hepatotoxicity.[114]

Licorice, garlic, and ginseng are other herbs with potent pharmacologic properties that enjoy great popularity among certain cultures, but that have been reported to have caused serious problems. Licorice in large amounts alters potassium levels.[115] Garlic has caused serious burns when worn against the skin. Ginseng has been responsible for syncope and altered consciousness.[116]

The clinician should inquire about all foods and beverages when taking a medical history. If an herbal product is being taken in excessive amounts, the contents should be checked. Such "self-medication" has posed many problems and should be evaluated in the breastfeeding mother. The regional poison control center may be able to assist in identifying the active properties of most herbs. The medicinal use of herbs per se is not a contraindication to breastfeeding.

Environmental Contaminants

Environmental contamination of breastmilk has been investigated in many sites around the world. In general, chemicals that are lipophilic (dissolve in fat) are found in the lipid fraction of breastmilk. The risk of environmental contaminants in breastmilk is based on a woman's exposure to chemicals. The greater her exposure, the greater the levels in her milk. Women in Vietnam, Turkey, Japan, and Taiwan with high levels of chemicals were exposed to contaminated foodstuffs.[117] Women currently at risk in this country may have had major exposure in an industrial accident. However, a spill of polychlorinated biphenyl in North Carolina did not result in increased levels in mothers' milk.[118] In the lower Michigan Peninsula exposure, polybrominated biphenyls (PBBs) were unintentionally put in cattle feed, thus entering the food chain.[119] More than 90 percent of the residents in this area, including pregnant and lactating women, had measurable amounts in their body fat and breastmilk. In the face of this information, however, few chose to wean their infants.

Herbicides

Agent Orange was a mixture of two pesticides: 2, 4-D and 2, 4, 5-T. The compound 2, 4, 5-T was contaminated during manufacture with 2, 3, 7, 8 TCDD, the best-known dioxin.[120] Agent Orange was widely used as an herbicide in Vietnam.[121] Pooled milk samples from women with high-level exposure in Vietnam contained the dioxin. Although the original data from Vietnam were believed to be flawed technically, nursing infants are known to retain almost all of the 2, 3, 7, 8 substituted dioxins that they ingest from breastmilk. On a body weight basis, nursing infants have a dietary intake of TCDD and its equivalents that is 100 times greater than that of adults.[122] Exposure of the fetus is also significant; however, transfer of dioxin-like compounds across the placenta is incomplete. Exposure of the general public is low, and only industrial workers exposed to dioxins are believed to be at risk for any absorption.[123] Very few workers are exposed to TCDD now. Because testing is still extremely costly, a woman with an inordinate exposure in industry should not breastfeed, but the magnitude of the exposure should first be verified.[124] Exposure to TCDD is not a general concern for breastfeeding women.

Pesticides

The levels of DDT and other insecticides in breastmilk vary with exposure.[125] Since DDT was banned in the United States in 1972, the threat to the average citizen has become minimal. In developing countries, the risk continues in rural areas among agricultural workers. In India, China, Guatemala, and Mexico, rural women have high levels of exposure. The World Health Organization has established pesticide residues limits and recommends a maximum average daily intake (ADI) of DDT and its metabolites of less than 20 micrograms/kilogram body weight from all sources.

From a practical standpoint in the United States, the average woman is not considered at risk for excessive levels of DDT in her breastmilk.[124,126] If there is a possibility of heavy environmental contamination with these compounds, the situation should be discussed with the physician, and, when appropriate, testing can be arranged through a state-approved laboratory before recommending whether the mother should breastfeed. Breastmilk is not considered a major source of DDT by the World Health Organization.

Dichlorodiphenyldichloroethylene (DDE) is the most stable derivative of the pesticide DDT. DDE has been associated with shortened duration of lactation in the general population in North Carolina.[118] A follow-up study was conducted in Mexico, where relatively high DDE levels exist.[127] The authors concluded that DDE may affect women's ability to lactate and postulated that this exposure

may contribute to lactation failure in parts of the world where DDT and DDE are prevalent.

Polychlorinated biphenyls (PCBs) and furans in pregnant Japanese and Taiwanese women who were heavily exposed to contamination produced small-for-gestational-age infants with transient darkening of the skin ("cola babies"). Polybrominated biphenyls (PBBs) are similar compounds and have been associated with a one-time heavy exposure to farm animals through contaminated cattle feed in the lower Michigan Peninsula in 1975.[119] Women in the United States with the greatest risk of high exposure to PCBs or PBBs have worked with or eaten excessive amounts of fish from sport fishing in contaminated waters.[1]

Studies have refuted earlier observations of concern. No information is available in the United States concerning the levels of polychlorinated dibenzodioxins (PCDDs) or polychlorinated dibenzofurans (PCDFs) in anglers who consume a great deal of fish.[128] Others considered by some to be at high risk live near a waste disposal site or have been involved in environmental spills. Except in cases of unusually heavy exposure, however, there is no contraindication to breastfeeding. When there is a question about environmental exposure and safety of breastfeeding, the state health department can be consulted for specific advice or to measure plasma and breastmilk levels. The epidemiologists usually are aware of the risks in a given geographic area and know whether it is necessary to measure breastmilk levels once lactation is fully established. If this sampling is planned far in advance during the pregnancy, little time need be lost. Unless the exposure is unique and excessive, the infant can be breastfed until levels are returned from the laboratory.[1]

Several extensive reviews have been published concerning the dilemma of pollutants in breastmilk.[118,126,129,130] It has been suggested that the body burden at birth can be added to by exposing the infant to small levels in the milk, which may indeed exceed the allowable exposure limits for daily intake, set by the World Health Organization.[131] Breastmilk levels are used epidemiologically as markers of human exposure within a community's exposure because of the close correlation between breastmilk levels and levels in the fat stores. Randomly selected mothers in the Great Lakes region were tested by the state of New York in 1978, and no chemical (PCB, PBB) was found in any breastmilk in a random sampling of residents. Thus, unless the circumstances are unusual, breastfeeding should not be abandoned on the basis of insecticide contamination.[1]

The cyclodiene pesticides and their metabolites detected in breastmilk include aldrin, dieldrin, endrin, heptachlor and its epoxide, chlordane, oxychlordane, and trans-nonachlor. The most abundant and widespread compounds are dieldrin and heptachlor epoxide.[120] Their levels in breastmilk, however, are very much lower than those of DDT, and only a fraction of women have levels above the detection limit.[120] According to Jensen, measurable amounts of aldrin and heptachlor in breastmilk samples are contrary to the fact that these chemicals are transformed to epoxide derivatives (e.g., aldrin to dieldrin) in living organisms and ecosystems.[125] These substances are persistent organo chlorine insecticides of higher toxicity than DDT and have been banned in industrialized countries for over a decade. The only source that might remain is from foodstuffs imported from Third World countries.[124] In the United States, levels in breastmilk have dropped and are reported undetectable.[120] Heptachlor and its epoxide, which have been limited to use in some southern states for termite eradication, have decreased in importance and have not been reported in breastmilk in this country within the last decade.

Technical chlordane, a mixture of 26 compounds, is common in termite control in the southern United States. Oxychlordane and trans-nonachlor have been detected in breastmilk in some regions, including the southeastern United States (0.08 parts per million),

Hawaii, and the Binghamton area of New York State (minimal amount, one pool of seven donors). The most recent measurements were reported in 1985.[120,125,132] In the 1990s, the general public in the United States is not at risk for exposure to the cyclodiene pesticides.

Heavy Metals

Heavy metal exposure such as lead, mercury, arsenic, and cadmium can be related to water supplies, cow milk, and even infant formulas.[133] Typically, breastfed infants are exposed to lower amounts than formula-fed infants because formula is mixed with water that may contain the heavy metal. Lead is a heavy metal that still exists in the environment in older housing, lead pipes, certain industries, and auto exhaust pollutants.

Lead

Lead levels reported from the Third National Health and Nutrition Examination Survey (NHANES III) in 1988–94, compared to NHANES I (1976–75) and NHANES II (1976–80), reveal a drop across all ages.[134] It is presumed that eliminating leaded gasoline and removing lead solder from food and soft drink cans have been responsible for this decrease, along with removing lead-based paint. Low-income Hispanic and African-American children living in major cities have the highest lead levels (≥ 10 micrograms/deciliter).[134]

In the United States, the extensive lead screening program for children has identified individuals before they are symptomatic and has also identified women in their childbearing years because they live in the same environment as children with elevated levels of lead.[135] More women are asking the question: Is it safe for me to breastfeed? Generally, the answer has been: If the blood lead level is less than 40, it is safe to breastfeed because the levels of lead in the milk will be low or undetectable. Considerably less lead passes into the breastmilk than across the placenta.[136] Infants who have been exposed in utero can be expected to lose lead if their daily intake via breastmilk is less than 5 micrograms per day.[137] If a woman has an elevated lead level, it is wise to measure the infant's serum and the milk, even if the maternal level is less than 40 micrograms/deciliter. Milk levels are one-tenth to one-fifth of maternal levels. County or state health department laboratories usually have lead screening programs. The home environment should be evaluated if the mother's level is above 10 micrograms/deciliter, and a program to reduce the mother's level of lead should be initiated. In studies comparing feeding methods, formula-fed infants have higher lead levels than breastfed infants.[100] Breastfeeding is not contraindicated unless the maternal level of lead exceeds 40 micrograms/deciliter.[134]

Mercury

Mercury was a major contaminant in the Iraqi wheat exposure, and also in some parts of the Great Lakes from industrial exposure in the 1970s.[138,139] Exposure of the general public is limited to industrial exposure of specific workers to organic mercury, and dietary exposure to organic mercury (usually methyl mercury) from seafood. Amalgam from dental fillings is a small exposure for many in the United States. A freak exposure occurred when a metallic mercury spill from a large thermometer was cleaned up with the family vacuum cleaner. The mercury remained in the dust bag and was gradually vaporized and inhaled by the family each time the vacuum was used. Most exposures are identified because symptoms develop.

The neurodevelopmental study of Seychellois children following in utero exposure to methyl mercury from a maternal fish diet showed no association between maternal hair mercury level during pregnancy and an adverse neurodevelopmental outcome of the infant at six months.[140] At 19 and 29 months after the subjects' births, the results showed possible association between high levels of

TABLE 7
Summary of Medical Contraindications to Breastfeeding in the United States

Problem	OK to Breastfeed in U.S.?	Conditions
INFECTIOUS DISEASES		
Acute infectious disease	Yes	Respiratory, reproductive, gastroitestinal infections
HIV	No	HIV positive
Active tuberculosis	Yes	After mother has received 2 or more weeks of treatment
Hepatitis		
Hepatitis A	Yes	As soon as mother receives gamma globulin
Hepatitis B	Yes	After infant receives HBIG, first dose of hepatitis B vaccine should be given before hospital discharge
Hepatitis C	Yes	If no co-infections (e.g., HIV)
Venereal warts	Yes	
Herpes viruses		
Cytomegalovirus	Yes	
Herpes simplex	Yes	Except if lesion on breast
Varicella-zoster (chicken pox)	Yes	As soon as mother becomes noninfectious
Epstein-Barr	Yes	
Toxoplasmosis	Yes	
Mastitis	Yes	
Lyme disease	Yes	As soon as mother initiates treatment
HTLV-1	No	
MEDICATION/PRESCRIPTION DRUGS AND STREET DRUGS		
Antimetabolites (see table 4)	No	
Radiopharmaceuticals (see table 5)		
Diagnostic dose	Yes	After radioactive compound has cleared mother's plasma
Therapeutic dose	No	
Drugs of abuse (see table 6)	No	Exceptions: cigarettes, alcohol
Other medications	Yes	Drug-by-drug assessment
ENVIRONMENTAL CONTAMINANTS		
Herbicides	Usually	Exposure unlikely (except workers heavily exposed to dioxins)
Pesticides		
DDT, DDE	Usually	Exposure unlikely
PCBs, PBBs	Usually	Levels in milk very low
Cyclodiene pesticides	Usually	Exposure unlikely
Heavy metals		
Lead	Yes	Unless maternal level ≥40 mg/dL
Mercury	Yes	Unless mother symptomatic and levels measurable in breastmilk
Cadmium	Usually	Exposure unlikely
Radionuclides	Yes	Risk greater to bottlefed infants

Note: This table provides a brief summary. Each situation must be decided individually. Contraindications are rare in the United States.

exposure and activity levels in males, with other parameters being unrelated to mercury levels. This study involved a population in which 90 percent were breastfed in the first week of life and 50 percent were still being breastfed at 6 months. The breastfeeding correlations have not been analyzed at this time.[140] However, there were no adverse outcomes related to mercury.

Cadmium

Cadmium has been measured in fetuses in Japan, where cadmium intake is higher, presumably from industrial exposure, heavy smoking, and exposure from contaminated rice. No clear-cut cases of cadmium exposure through breastmilk have been reported.[122] Itai-Itai disease is believed to be due to cadmium, but it may have other etiologies. Cadmium exposure has not been an issue in the United States; the major concern related to cadmium intake is cigarette smoke. Heavy metals are not a usual risk for breastfed infants. Any woman with an exposure should be evaluated by her physician. Heavy metals are rarely a contraindication for breastfeeding, and only under special circumstances of exposure.[141]

Radionuclides

Radionuclides have been followed environmentally since the nuclear age began. The deposition of strontium in the deciduous teeth of infants in St. Louis was much greater in formula-fed infants than in breastfed infants in 1964. In the aftermath of the Chernobyl nuclear explosion, breastmilk was found to be lower in strontium 90 and iodine 131 than cow milk and other parts of the food chain and the water supply.[142]

In summary, in the United States, except under unusual circumstances of environmental exposure in individual cases, breastfeeding is not contraindicated because of environmental hazards and may be safer than formula mixed with water.

Conclusion

As stated in the introduction, breastmilk provides more than just good nutrition—its unique composition provides the ideal nutrients for human brain growth and protects the infant against infection. Breastfeeding has distinct, species-specific, irreplaceable value that is ideal for the infant's growth, development, and emotional well-being. It is important, however, for health care professionals to be aware of those rare situations when the mother should be counseled not to breastfeed. Table 7 summarizes the information presented in this paper concerning medical contraindications to breastfeeding in the United States. Breastmilk should not be withheld from any infant unless absolutely necessary.

References

1. Lawrence RA. 1994. *Breastfeeding: A Guide for the Medical Profession* (4th ed.). St. Louis, MO: C.V. Mosby Company.

2. Cunningham AS, Jelliffe DB, Jelliffe EFP. 1991. Breast-feeding and health in the 1980s: A global epidemiologic review. *Journal of Pediatrics* 118:659–666.

3. Hanson LA, Adlerberth I, Carlsson B, Castrignano SB, Dahlgren U, Jalil F, Khan SR, Mellander L, Eden CS, Svennerholm AM, et al. 1989. Host defense of the neonate and the intestinal flora. *Acta Paediatrica Scandinavica* 351(Suppl.):122–125.

4. Pisacane A, Graziano L, Zona G, Dolezalova H, Cafiero M, Coppola A, Scarpellino B, Ummarino M, Mazzarella G. 1994. Breast feeding and acute lower respiratory infection. *Acta Paediatrica* 83:714–718.

5. Beudry M, Dufour R, Marcoux S. 1995. Relation between infant feeding and infections during the first six months of life. *Journal of Pediatrics* 126:191–197.

6. Victora CG, Smith PG, Vaughan JP, Nobre LC, Lombardi C, Teixeira AM, Fuchs SM, Moreira LB, Gigante LP, Barros FC. 1987. Evidence for protection by breastfeeding against infant deaths from infectious diseases in Brazil. *Lancet* 2(8554):319–322.

7. Burr ML, Limb ES, Maguire MJ, Amarah L, Eldridge BA, Layzell JC, Merrett TG. 1993. Infant feeding, wheezing, and allergy: A prospective study. *Archives of Disease in Childhood* 68:724–728.

8. Dewey KG, Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B. 1992. Growth of breast-fed and formula-fed infants from 0 to 18 months: The DARLING Study. *Pediatrics* 89(6, Pt. 1):1035–1041.

9. Dewey KG, Peerson JM, Brown KH, Krebs NF, Michaelsen KF, Persson LA, Salmenpera L, Whitehead RG, Yeung DL. 1995. Growth of breast-fed infants deviates from current reference data: A pooled analysis of US, Canadian, and European data sets. World Health Organization Working Group on Infant Growth. *Pediatrics* 96(3, Pt. 1):495–503.

10. *HIV and breast-feeding* [press release, World Health Organization, No. 30]. 1992, May 4. Geneva, Switzerland: World Health Organization.

11. Davis MK, Savitz DA, Graubard BI. 1988. Infant feeding in childhood cancer. *Lancet* 2(8607):365–368.

12. Alho OP, Koivu M, Sorri M, Rantakallio P. 1990. Risk factors for recurrent acute otitis media and respiratory infection in infancy. *International Journal of Pediatric Otorhinolaryngology* 19:151–161.

13. Aniansson G, Alm B, Andersson B, Hakansson A, Larsson P, Nylen O, Peterson H, Rigner P, Svanborg M, Sabharwal H, et al. 1994. A prospective cohort study on breastfeeding and otitis media in Swedish infants. *Pediatric Infectious Disease Journal* 13:183–188.

14. Lawrence R. 1995. The clinician's role in teaching proper infant feeding techniques. *Journal of Pediatrics* 126:S112–S117.

15. Virtanen SM, Räsänen L, Aro A, Lindstrom J, Sippola H, Lounamaa R, Toivanen L, Tuomilehto J, Akerblom HK. 1991. Infant feeding in Finnish children less than 7 years of age with newly diagnosed IDDM. Childhood Diabetes in Finland Study Group. *Diabetes Care* 14:415–417.

16. Koletzko S, Sherman P, Corey M, Griffiths A, Smith C. 1989. Role of infant feeding practices in development of Crohn's Disease in childhood. *BMJ* 298:1617–1618.

17. Merrett TG, Burr ML, Butland BK, Merrett J, Miskelly FG, Vaughan-Williams E. 1988. Infant feeding and allergy: 12-month prospective study of 500 babies born into allergic families. *Annals of Allergy* 61:13–20.

18. Gruskay FL. 1982. Comparison of breast, cow and soy feedings in the prevention of onset of allergic disease: A 15-year prospective study. *Clinical Pediatrics* 21:486–491.

19. Kern RA. 1939. Prophylaxis in allergy. *Annals of Internal Medicine* 12:1175–1188.

20. Burr ML, Limb ES, Maguire MJ, Amarah L, Eldridge BA, Layzell JC, Merrett TG. 1993. Infant feeding, wheezing and allergy: A prospective study. *Archives of Disease in Childhood* 68:724–728.

21. Bryant CA. 1986. *Overcoming Breastfeeding Barriers.* Paper presented at U.S. Department of Health and Human Services Region IV nutrition conference, Building Support Networks for Breastfeeding, Atlanta, GA.

22. Gussler JD, Bryant CA, eds. 1984. *Helping Mothers to Breastfeed: Program Strategies for Minority Communities.* Lexington, KY: Nutrition and Health Education division, Lexington-Fayette County Health Department.

23. Newton N. 1971. Psychological differences between breast and bottle feeding. *American Journal of Clinical Nutrition* 24:993–1004.

24. Lucas A, Morley R, Cole TJ, Lister G, Leeson-Payne C. 1992. Breast milk and subsequent intelligence quotient in children born preterm. *Lancet* 339:261–264.

25. Johnson DL, Swank PR, Howie VM, Baldwin CD, Owen M. 1996. Breastfeeding and children's intelligence. *Psychological Reports* 79:1179–1185.

26. Neuringer M, Reisbick S, Janowsky J. 1994. The role of n-3 fatty acids in visual and cognitive development: Current evidence and methods of assessment. *Journal of Pediatrics* 125:S39–S47.

27. Jorgensen MH, Hernell O, Lund P, Holmer G, Michaelsen KF. 1996. Visual acuity and erythrocyte docosahexaenoic acid status in breast-fed and formula-fed term infants during the first four months of life. *Lipids* 31:99–105.

28. Jonsbo F, Jorgensen MH, Michaelsen KF. 1995. The importance of n-3 and n-6 fatty acids for visual function and development in newborn infants. *Ugeskrift for Laeger* 157:1987–1991.

29. National Academy of Sciences, Institute of Medicine, Food and Nutritional Board, Committee on Nutritional Status During Pregnancy and Lactation, Subcommittee on Nutrition During Lactation. 1991. *Nutrition During Lactation: Summary, Conclusions, and Recommendations.* Washington, DC: National Academy Press.

30. Byers T, Graham S, Rzepka T, Marshall J. 1985. Lactation and breast cancer. Evidence for a negative association in premenopausal women. *American Journal of Epidemiology* 121:664–674.

31. MacMahon B, Lin TM, Lowe CR, Mirra AP, Ravnihar B, Salber EJ, Trichopoulos D, Valaoras VG, Yuasa S. 1970. Lactation and cancer of the breast: A summary of an international study. *Bulletin of the World Health Organization* 42:185–194.

32. Sowers MF, Corton G, Shapiro B, Jannausch ML, Crutchfield M, Smith ML, Randolph JF, Hollis B. 1993. Changes in bone density with lactation. *JAMA* 269:3130–3135.

33. Rebuffe-Scrive M, Enk L, Crona N, Lonnroth L, Abrahamsson L, Smith U, Bjorntorp P. 1985. Fat cell metabolism in different regions in women. Effect of menstrual cycle, pregnancy, and lactation. *Journal of Clinical Investigation* 75:1973–1976.

34. Whittemore AS. 1994. Characteristics relating to ovarian cancer risk: Implications for prevention and detection. *Gynecologic Oncology* 55(3, Pt. 2):S15–S19.

35. Rosenblatt KA, Thomas DB. 1993. Lactation and the risk of epithelial ovarian cancer. The WHO Collaborative Study of Neoplasia and Steroid Contraceptives. *International Journal of Epidemiology* 22:192–197.

36. John EM, Whittemore AS, Harris R, Itnyre J. 1993. Characteristics relating to ovarian cancer risk: Collaborative analysis of seven U.S. case–control studies. Epithelial ovarian cancer in black women. Collaborative Ovarian Cancer Group. *Journal of the National Cancer Institute* 85:142–147.

37. Newcomb PA, Storer BE, Longnecker MP, Mittendorf R, Greenberg ER, Clapp RW, Burke KP, Willett WC, MacMahon B. 1994. Lactation and a reduced risk of premenopausal breast cancer. *New England Journal of Medicine* 330:81–87.

38. Brinton LA, Potischman NA, Swanson CA, Shoenberg JB, Coates RJ, Gammon MD, Malone KE, Stanford JL, Daling JR. 1995. Breastfeeding and breast cancer risk. *Cancer Causes and Control* 6:199–208.

39. Melton LJ III, Bryant SC, Wahner HW, O'Fallon WM, Malkasian GD, Judd HL, Riggs BL. 1993. Influence of breastfeeding and other reproductive factors on bone mass later in life. *Osteoporosis International* 3:76–83.

40. Kalkwarf HJ, Specker BL. 1995. Bone mineral loss during lactation and recovery after weaning. *Obstetrics and Gynecology* 86:26–32.

41. Kalkwarf HJ, Specker BL, Heubi JE, Viera NE, Yergey AL. 1996. Intestinal calcium absorption of women during lactation and after weaning. *American Journal of Clinical Nutrition* 63:526–531.

42. Cross NA, Hillman LS, Allen SH, Krause GF, Vieira NE. 1995. Calcium homeostasis and bone post-weaning: A longitudinal study. *American Journal of Clinical Nutrition* 61:514–523.

43. Clark BJ. After a positive Guthrie–what next? Dietary management for the child with phenylke-tonuria. 1992. *European Journal of Clinical Nutrition* 46 (Suppl. 1):S33–S39.

44. Ernest AE, McCabe ERB, Neifert MR, O'Flynn ME. 1980. *Guide to Breastfeeding the Infant with PKU* (DHHS Publication No. 79-5110). Washington, DC: U.S. Government Printing Office.

45. Thomas MR, Kawamoto J. 1979. Dietary evaluation of lactating women with or without vitamin and mineral supplementation. *Journal of the American Dietetic Association* 74:669–672.

46. Dusdieker LB, Booth BM, Stumbo PJ, Eichenberger JM. 1985. Effect of supplemental fluids on human milk production. *Journal of Pediatrics* 106:207–211.

47. Prentice AM, Roberts SB, Prentice A, Paul AA, Watkinson M, Watkinson AA, Whitehead RG. 1983. Dietary supplementation of lactating Gambian women. I. Effect on breast-milk volume and quality. *Human Nutrition Clinical Nutrition* 37:53–64.

48. Rasmussen KM. 1988. Maternal nutritional status and lactational performance. *Clinical Nutrition* 7:147–155.

49. Rasmussen KM, Habicht JP. 1989. Malnutrition among women: Indicators to estimate prevalence. *Food and Nutrition Bulletin* 11:29–37.

50. Herbert VD, Colman N. 1988. Folic acid and vitamin B_{12}. In ME Shils, VR Young, eds., *Modern Nutrition in Health and Disease.* Philadelphia, PA: Lea and Febiger.

51. Sneed SM, Zane C, Thomas MR. 1981. The effects of ascorbic acid, vitamin B_6, vitamin B_{12}, and folic acid supplementation on the breast milk and maternal nutritional status of low socioeconomic lactating women. *American Journal of Clinical Nutrition* 34:1338–1346.

52. Greer FR, Tsang RC, Levin RS, Searcy JE, Wu R, Steichen JJ. 1982. Increasing serum calcium and magnesium concentrations in breast-fed infants: Longitudinal studies of minerals in human milk and in sera of nursing mothers and their infants. *Journal of Pediatrics* 100:59–64.

53. American Academy of Pediatrics, Committee on Infectious Diseases. 1997. *1997 Red Book: Report of the Committee on Infectious Diseases.* Elk Grove Village, IL: American Academy of Pediatrics.

54. Hanson LA, Ahlstedt S, Andersson B, Carlsson B, Fallstrom SP, Mellander L, Porras O, Soderstrom T, Eden CS. 1985. Protective factors in milk and the development of the immune system. *Pediatrics* 75:172–176.

55. Cooperstock M, Zedd AJ. 1983. Intestinal flora of infants. In DJ Hentges, ed., *Human Intestinal Microflora in Health and Disease* (pp. 79–99). New York, NY: Academic Press.

56. Goldman AS. 1993. The immune system of human milk: Antimicrobial, anti-inflammatory, and immunomodulating properties. *Pediatric Infectious Disease Journal* 12:664–671.

57. Ruff AJ. 1994. Breast milk, breastfeeding, and trans-mission of viruses to the neonate. *Seminars in Perinatology* 18:510–516.

58. Van de Perre P, Lepage P, Homsy J, Dabis F. 1992. Mother-to-infant transmission of human immunodeficiency virus by breast milk: Presumed innocent or presumed guilty? *Clinical Infectious Diseases* 15:502–507.

59. Oxtoby MJ. 1988. Human immunodeficiency virus and other viruses in human milk: Placing the issues in broader perspective. *Pediatric Infectious Disease Journal* 7:825–835.

60. Palasanthiran P, Ziegler JB, Stewart GJ, Stuckey M, Armstrong JA, Cooper DA, Penny R, Gold J. 1993. Breast-feeding during primary maternal human immunodeficiency virus infection and risk of transmission from mother to infant. *Journal of Infectious Diseases* 167:441–444.

61. Ruff AJ, Coberly J, Halsey NA, Boulos R, Desormeaux J, Burnley A, Joseph DL, McBrien M, Quinn T, Losikoff P, et al. 1994. Prevalence of HIV-1 DNA and p24 antigen in breast milk and correlation with maternal factors. *Journal of Acquired Immune Deficiency Syndromes* 7:68–73.

62. Del Fante P, Jenniskens F, Lush L, Morona D, Moeller B, Lanata CF, Hayes R. 1993. HIV, breast-feeding and under 5 mortality: Modelling the impact of policy decisions for or against breast-feeding. *Journal of Tropical Medicine and Hygiene* 96:203–211.

63. Connor EM, Mofenson LM. 1995. Zidovudine for the reduction of perinatal human immunodeficiency virus transmission: Pediatric AIDS Clinical Trials Group Protocol 076—Results and treatment recommendations. *Pediatric Infectious Disease Journal* 14:536–541.

64. Cutting WA. 1994. Breast-feeding and HIV: A balance of risks. *Journal of Tropical Pediatrics* 40:6–11.

65. Davis MK. 1991. Human milk and HIV infection: Epidemiologic and laboratory data. In J Mestecky et al, eds., *Immunology of Milk and the Neonate* (p. 271). New York, NY: Plenum Press.

66. Ziegler JB, Cooper DA, Johnson RO, Gold J. 1985. Postnatal transmission of AIDS-associated retrovirus from mother to infant. *Lancet* 1(8434):896–898.

67. Newburg DS, Linhardt RJ, Ampofo SA, Yolken RH. 1995. Human milk glycosaminoglycans inhibit HIV glycoprotein gp 120 binding to its host cell CD4 receptor. *Journal of Nutrition* 125:419–424.

68. de Martino M, Tovo PA, Tozzi AE, Pezzotti P, Galli L, Livadiotti S, Caselli D, Massiromi E, Ruga E, Fioredda F, et al. 1992. HIV-1 transmission through breast-milk: Appraisal of risk according to duration of feeding. *AIDS* 6:991–997.

69. Snider DE Jr, Powell KE. 1984. Should women taking antituberculosis drugs breast-feed? *Archives of Internal Medicine* 144:589–590.

70. Holdiness MR. 1984. Antituberculosis drugs and breast-feeding [letter]. *Archives of Internal Medicine* 144:1888.

71. Holdiness MR. 1984. Clinical pharmacokinetics of the antituberculosis drugs. *Clinical Pharmacokinetics* 9:511–544.

72. American Academy of Pediatrics Committee on Drugs. 1994. The transfer of drugs and other chemicals into human milk. *Pediatrics* 93:137–150.

73. Lin HH, Kao JH, Hsu HY, Ni YH, Chang MH, Huang SC, Hwang LH, Chen PS, Chen DS. 1995. Absence of infection in breast-fed infants born to hepatitis C virus–infected mothers. *Journal of Pediatrics* 126:589–591.

74. Weiland O, Schvarcz R. 1992. Hepatitis C: Virology, epidemiology, clinical course, and treatment. *Scandinavian Journal of Gastroenterology* 27:337–342.

75. Ohto H, Terazawa S, Sasaki N, Hino K, Ishiwata C, Kako M, Ujiie N, Endo C, Matsui A, et al. 1994. Transmission of hepatitis C virus from mothers to infants. *New England Journal of Medicine* 330:744–750.

76. Gürakan B, Oran O, Yigit S. 1994. Vertical transmission of Hepatitis C virus [letter]. *New England Journal of Medicine* 331:399.

77. Nagata I, Shiraki K, Tanimoto K, Harada Y, Tanaka Y, Okada T. 1992. Mother-to-infant transmission of Hepatitis C virus. *Journal of Pediatrics* 120:432–434.

78. Ogasawara S, Kage M, Kosai K, Shimamatsu K, Kojiro M. 1993. Hepatitis C virus RNA in saliva and breastmilk of hepatitis C carrier mothers [letter]. *Lancet* 341:561.

79. Zanetti AR, Tanzi E, Paccagnini S, Principi N, Pizzocola G, Caccamo ML, D'Amico E, Cambie G, Vecchi L. 1995. Mother-to-infant transmission of hepatitis C virus. Lombardy Study Group on Vertical HCV Transmission. *Lancet* 345:289–291.

80. Alter MJ. 1994. Transmission of hepatitis C virus—Route, dose, and titer. *New England Journal of Medicine* 330:784–786.

81. Dworsky M, Yow M, Stagno S, Pass, RF, Alford C. 1983. Cytomegalovirus infection of breast milk and transmission in infancy. *Pediatrics* 72:295–299.

82. Yeager AS, Palumbo PE, Malachowski N, Ariagno RL, Stevenson DK. 1983. Sequelae of maternally derived cytomegalovirus infections in premature infants. *Journal of Pediatrics* 102:918–922.

83. Quinn PT, Lofberg JV. 1978. Maternal herpetic breast infection: Another hazard of neonatal herpes simplex. *Medical Journal of Australia* 2:411–412.

84. Sullivan-Bolyai JZ, Fife KH, Jacobs RF, Miller Z, Corey L. 1983. Disseminated neonatal herpes simplex virus type I from maternal breast lesion. *Pediatrics* 71:455–457.

85. Gershon AA. 1990. Chickenpox, measles and mumps. In JS Remington, JO Klein, eds., *Infectious Diseases of the Fetus and Newborn Infant* (3rd ed.). Philadelphia, PA: WB Saunders.

86. Remington JS, Desmonts G. 1990. Toxoplasmosis. In JS Remington, JO Klein, eds., *Infectious Diseases of the Fetus and Newborn Infant* (3rd ed.). Philadelphia, PA: WB Saunders.

87. Matheson I, Aursnes I, Horgen M, Aabo O, Melby K. 1988. Bacteriological findings and clinical symptoms in relation to clinical outcome in puerperal mastitis. *Acta Obstetrica et Gynecologica Scandinavica* 67:723–726.

88. Thomsen AC. 1982. Infectious mastitis and occurrence of antibody-coated bacteria in milk. A*merican Journal of Obstetrics and Gynecology* 144:350–351.

89. Briggs GG, Freeman RK, Yaffe SJ. 1994. *Drugs in Pregnancy and Lactation* (4th ed.). Baltimore, MD: Williams and Wilkins.

90. Stiernstedt G. 1990. Lyme borreliosis during pregnancy. *Scandinavian Journal of Infectious Diseases.* 71(Suppl.):99–100.

91. Schmidt BL, Aberer E, Stockenhuber C, Klade H, Breier F, Luger A. 1995. Detection of Borrelia burgdorferi DNA by polymerase chain reaction in the urine and breast milk of patients with Lyme borreliosis. *Diagnostic Microbiology and Infectious Disease* 21:121–128.

92. Ando Y, Saito K, Nakano S, Kakimoto K, Furuki K, Tanigawa T, Hashimoto H, Moriyama I, Ichijo M, Toyama T. 1989. Bottle-feeding can prevent transmission of HTLV-1 from mothers to their babies. *Journal of Infection* 19:25–29.

93. Hino S. 1989. Milk-borne transmission HTLV-1 as a major route in the endemic cycle. *Acta Paediatrica Japanica* 31:428–435.

94. Wilson JT. 1983. Determinants and consequences of drug excretion in breast milk. *Drug Metabolism Reviews* 14:619–652.

95. Wilson JT, Brown RD, Cherek DR, Dailey JW, Hilman B, Jobe PC, Manno BR, Manno JE, Redetzki HM, Stewart JJ. 1980. Drug excretion in human milk: Principles, pharmacokinetics and projected consequences. *Clinical Pharmacokinetics* 5:1–66.

96. Wilson JT, Brown RD, Hinson JL, Dailey JW. 1985. Pharmacokinetic pitfalls in the estimation of the breast milk/plasma ratio for drugs. *Annual Review of Pharmacology and Toxicology* 25:667–689.

97. Peterson RG, Bowes WA Jr. 1983. Drugs, toxins and environmental agents in breast milk. In MC Neville, MR Neifert, eds., *Lactation, Physiology, Nutrition, and Breastfeeding.* New York, NY: Plenum Press.

98. Huxtable RJ. 1992. The myth of beneficent nature: The risks of herbal preparations. *Annals of Internal Medicine* 117:165–166.

99. Rivera-Calimlim L. 1987. The significance of drugs in breast milk. Pharmacokinetic considerations. *Clinics in Perinatology* 14:51–70.

100. Devlin RG, Duchin KL, Fleiss PM. 1981. Nadolol in human serum and breast milk. *British Journal of Clinical Pharmacology* 12:393–396.

101. Devlin RG, Fleiss PM. 1981. Captopril in human blood and breast milk. *British Journal of Clinical Pharmacology* 21:110–113.

102. Erickson SH, Oppenheim GL, Smith GH. 1981. Metronidazole in breast milk. *Obstetrics and Gynecology* 57:48–50.

103. Heisterberg L, Branebjerg PE. 1983. Blood and milk concentrations of metronidazole in mothers and infants. *Journal of Perinatal Medicine* 11:114–120.

104. *Physicians' Desk Reference* (49th ed.). 1995. Montvale, NJ: Medical Economics Data Production Company, Medical Economics Company, Inc.

105. Schulte-Hobein B, Schwartz-Bickenbach D, Abt S, Plum C, Nau H. 1992. Cigarette smoke exposure and development of infants throughout the first year of life: Influence of passive smoking and nursing on cotinine levels in breast milk and infant's urine. *Acta Paediatrica* 81:550–557.

106. Steldinger R, Luck W, Nau H. 1988. Half lives of nicotine in milk of smoking mothers: Implications for nursing [letter]. *Journal of Perinatal Medicine* 16:261–262.

107. Klonoff-Cohen HS, Edelstein SH, Lefkowitz ES, Srinivasan IP, Kaegi D, Chang JC, Wiley, KJ. 1995. The effect of passive smoking and tobacco exposure through breast milk on sudden infant death syndrom. *JAMA* 273:795–798.

108. Mennella JA, Beauchamp GK. 1991. The transfer of alcohol to human milk: Effect on flavor and the infant's behavior. *New England Journal of Medicine* 325:981–985.

109. Jones AW. 1992. Alcohol in mother's milk. *New England Journal of Medicine* 326:766–767.

110. Kesäniemi YA. 1974. Ethanol and acetaldehyde in the milk and peripheral blood of lactating women after ethanol administration. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 81:84–86.

111. Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, Clarren SK. 1989. Maternal alcohol use during breast-feeding and infant mental and motor development at one year. *New England Journal of Medicine* 321:425–430.

112. Neville MC, Walsh CT. 1995. Effects of xenobiotics on milk secretion and composition. *American Journal of Clinical Nutrition* 61(Suppl. 3):687S–694S.

113. Stuart M, ed. 1979. *The Encyclopedia of Herbs and Herbalism.* New York, NY: Crescent Books.

114. Dubick MA. 1986. Historical perspectives on the use of herbal preparations to promote health. *Journal of Nutrition* 116:1348–1354.

115. Davis EA, Morris DJ. 1991. Medicinal uses of licorice through the millennia: The good and plenty of it. *Molecular and Cellular Endocrinology* 78:1–6.

116. Ridker PM. 1987. Toxic effects of herbal teas. *Archives of Environmental Health* 42:133–136.

117. Rogan WJ, Ragan NB. 1994. Chemical contaminants, pharmacokinetics, and the lactating mother. *Environmental Health Perspectives* 102(Suppl. 11):89–95.

118. Rogan WJ, Gladen BC, McKinney JD, Albro PW. 1983. Chromatographic evidence of polychlorinated biphenyl exposure from a spill. *JAMA* 249:1057–1059.

119. Poland RL, Cohen SN. 1980. The contamination of the food chain in Michigan with PPB: The breastfeeding question. In AR Liss, ed., *Drugs and Chemical Risks to the Fetus and Newborn.* New York, NY: Alan R. Liss, Inc.

120. Jensen AA. 1991. Levels and trends of environmental chemicals in human milk. In AA Jensen, SA Slorach, eds., *Chemical Contaminants in Human Milk* (pp. 45–198). Boca Raton, FL: CRC Press.

121. Schecter A, Gasiewicz TA. 1987. Health hazard assessment of chlorinated dioxins and dibenzofurans contained in human milk. *Chemosphere* 16:2147–2154.

122. Jensen AA, Slorach SA. 1991. Assessment of infant intake of chemicals via breast milk. In AA Jensen, SA Slorach, eds., *Chemical Contaminants in Human Milk.* (pp. 215–222). Boca Raton, FL: CRC Press.

123. Lindstrom G, Hooper K, Petreas M, Stephens R, Gilman A. 1995. Workshop on perinatal exposure to dioxin-like compounds. I. Summary. *Environmental Health Perspectives* 103(Suppl. 2):135–142.

124. Kimbrough RD. 1991. Toxicological implications of human milk residues as indicated by toxicological and epidemiological studies. In AA Jensen, SA Slorach, eds., *Chemical Contaminants in Human Milk* (pp. 271–284). Boca Raton, FL: CRC Press.

125. Jensen AA. 1991. Occupational chemicals in human milk. In AA Jensen, SA Slorach, eds., *Chemical Contaminants in Human Milk* (pp. 216–217). Boca Raton, FL: CRC Press.

126. Rogan W, Gladen B. 1983. Monitoring breast milk contamination to detect hazards from waste disposal. *Environmental Health Perspectives* 48:87–89.

127. Gladen BC, Rogan WJ. 1995. DDE and shortened duration of lactation in a northern Mexican town. *American Journal of Public Health* 85:504–508.

128. Kimbrough, RD. 1991. Consumption of fish: Benefits and perceived risk. *Journal of Toxicology and Environmental Health* 33:81–91.

129. Wickizer TM, Brilliant LB. 1981. Testing for polychlorinated biphenyls in human milk. *Pediatrics* 68:411–415.

130. Wolff MS. 1983. Occupationally derived chemicals in breast milk. *American Journal of Industrial Medicine* 4:259–281.

131. Stephens RD, Rappe C, Hayward DG, Nygren M, Startin J, Esboll A, Carle J, Yrjanheikki EJ. 1992. World Health Organization International Intercalibration Study on dioxins and furans in human milk and blood. *Analytical Chemistry* 64:3109–3117.

132. Jensen AA. 1991. Transfer of chemical contaminants into human milk. In AA Jensen, SA Slorach, eds., *Chemical Contaminants in Human Milk* (pp. 1–8). Boca Raton, FL: CRC Press.

133. Dabeka RW, Karpinski KF, McKenzie AD, Bajdik CD. 1986. Survey of lead, cadmium and fluoride in human milk and correlation of levels with environmental and food factors. *Food and Chemical Toxicology* 24:913–921.

134. Blood lead levels—United States, 1988–1991. 1994. *Morbidity and Mortality Weekly Report* 43:545–548.

135. Dillon HK, Wilson DJ, Schaffner W. 1974. Lead concentrations in human milk. *American Journal of Diseases of Children* 128:491–492.

136. Ellenhorn MJ. 1997. *Medical Toxicology* (2nd ed., pp. 1565–1566). Baltimore, MD: Williams & Wilkins.

137. Ong CN, Phoon WO, Law HY, Tye CY, Lim HH. 1985. Concentrations of lead in maternal blood, cord blood and breast milk. *Archives of Disease in Childhood* 60:756–759.

138. Amin-Zaki L, Elhassani S, Majeed MA, Clarkson TW, Doherty RA, Greenwood M. 1974. Intra-uterine methylmercury poisoning in Iraq. *Pediatrics* 54:587–595.

139. Amin-Zaki L, Elhassani S, Majeed MA, Clarkson TW, Doherty RA, Greenwood M. 1974. Studies of infants postnatally exposed to methylmercury. *Journal of Pediatrics* 85:81–84.

140. Meyers GJ, Marsh DO, Davidson PW, Cox C, Shamlaye CF, Tanner M, Choi A, Chernichiari E, Choisy O, Clarkson TW. 1995. Main neurodevelopmental study of Seychellois children following in utero exposure to methylmercury from a maternal fish diet: Outcome at six months. *Neurotoxicology* 16:653–664.

141. Giroux D, Lapointe G, Baril M. 1992. Toxicological index and the presence in the workplace of chemical hazards for workers who breast-feed infants. *American Industrial Hygiene Association Journal* 53:471–474.

142. Gori G, Cama G, Guerresi E, Cocchi G, Dalla Casa P, Galtavecchia E, Ghini S, Tonelli D. 1988. Radioactivity in breast milk and placentas during the year after Chernobyl accident [letter]. *American Journal of Obstetrics and Gynecology* 158:1243–1244.