Journal of
TRAVEL MEDICINE

Breastfeeding Travelers: Precautions and Recommendations

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DOI: 10.1111/j.1708-8305.2009.00362.x

With increased travel globally, more women travel while breastfeeding their infants as well as during pregnancy. The transfer of drugs and chemicals into human milk differs from transfer via umbilical cord during pregnancy. Because there is little evidence-based literature on recommendations for breastfeeding travelers, we review factors that influence drug passage into breast milk and available safety data on common medications that may be encountered by breastfeeding travelers. Biologic and immunologic events in the mother may affect the breastfeeding infant. We review those that are relevant to the breastfeeding woman who is preparing to travel. We also review the use of vaccines in breastfeeding women and the mechanisms by which they could affect the infant.

Breastfeeding: Physiology

Physiologic changes that occur with breastfeeding involve the hormones oxytocin and prolactin. The hyperplasia of milk ducts and production of immunologically rich human milk occur through the feedback mechanism of suckling. Changes to the mother's immune system following vaccine administration should not differ from the non-breastfeeding state, though little research has been directed to this question. Breast milk does not adversely impact the response to vaccines administered directly to the infant.[1,2]

Specific antibody responses to travel-related vaccines have not been studied in nursing mothers.

Maternal plasma volume expands by 50% through pregnancy and returns to normal level in most women by 8 weeks postpartum.[3] This increases the volume of distribution of drugs administered, related to the amount of protein binding of the given compound.

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Passage of Drugs into Breast Milk

Although most medications transfer into human milk, many are found at low concentrations in breast milk and are relatively safe for the infant. The clinician should consider the risk of the drug versus the benefit of breastfeeding for the infant. Maternal, drug, and infant factors influence the amount of drug available to the nursing infant.

The factors influencing drug transfer from maternal circulation into breast milk include ionization, lipid solubility, molecular weight, half-life of drug, fat content of milk, maternal plasma protein binding, and blood level attained in the maternal circulation.[4] Plasma protein binding affects the degree of drug penetration into breast milk. Although the protein-bound fraction remains in the maternal circulation, unbound drug can be transferred into human milk. Thus, the higher the percentage of protein binding, the less likely the drug will enter maternal milk.

Most drugs enter human milk as a result of equilibrium forces that lead to passive diffusion across the alveolar bilayer membranes and into the milk compartment. Low molecular weight drugs (<200 kd) transfer easily into human milk, but high molecular weight drugs are virtually excluded from human milk.[5,6] Once drugs enter breast milk, close equilibrium is maintained between the plasma and milk compartments with diffusion into and out of milk as a function primarily of the maternal plasma level.[7] Drugs with greater lipid-solubility diffuse across the membranes into breast milk and result in greater transfer into breast milk. The rate of transfer of lipid-soluble drugs into breast milk is generally quicker than water-soluble drugs that must pass through pores to cross cell membranes.[5] Colostrum (milk formed within the first few days of lactation) has lower fat content than mature milk.[8] Thus, drugs with high lipid solubility achieve a greater concentration in mature milk. As the mother's serum concentration drops from metabolism and excretion of drug, the concentration of drug in the breast milk may redistribute back in the mother's bloodstream. Maternal

plasma pH is 7.4 but the mean pH of breast milk is 7.2.[9] Drugs that are weak bases are un-ionized in the maternal circulation and can easily pass into breast milk; however, upon entrance into breast milk, they may become ion-trapped in breast milk. On the other hand, drugs that are weak acids will exhibit minimal diffusion into breast milk. Drugs with longer half-lives are more likely to accumulate in the mother and infant than agents with shorter half-lives.[6]

There are different methods for estimating the potential amount of drug that an infant obtains through breastfeeding.[6,8] The milk-to-plasma (M/P) ratio provides an estimate of the drug's distribution between maternal milk and plasma. Generally, the M/P ratio correlates directly with the amount of drug found in breast milk. An M/P ratio lower than 1.0 suggests that little drug will be transferred into breast milk. Unfortunately, the M/P ratio may be misleading as it is subject to variability.[9] Calculating the relative infant dose (RID) provides an estimate of the weight-normalized dose relative to the mother's dose.[6,10] The RID is calculated as follows:

$$\text{RID} = \frac{\text{Infant dose(mg/kg/d)}}{\text{Maternal dose(mg/kg/d)}} \times 100$$

The infant dose is calculated from the drug concentration in the breast milk and multiplied by the total volume of milk that is ingested by the infant. The RID is expressed as a percentage of the maternal dose. Generally, the RID should not exceed 10% of the maternal dose; for pre-term infants, the RID should be less than 10% due to the infant's immature hepatic and renal systems.

Oral bioavailability of the drug is another important factor to consider in both mother and infant.[6] As drug enters breast milk and is ingested, it must pass through the infant's gastrointestinal (GI) tract before absorption. Some drugs are destroyed within the GI tract and thus are not bioavailable in the infant[11]; drugs that are not destroyed in the infant's GI tract benefit from a short gastric emptying time which reduces the exposure time of the drug and minimizes the potential of an adverse reaction. One must also consider the frequency of feedings and volume of breast milk ingested when considering bioavailability. Of note, variations occur in an infant's ability to metabolize, excrete, and respond to medications (ie, idiosyncratic reactions, allergic sensitization).[10] Premature and full-term infants may not have full renal and liver function and some infants have immature GI function. Thus, it is essential to evaluate the infant's ability to handle small amounts of medication before prescribing a medication for a breastfeeding woman.

Vaccines Used in Travelers

Vaccination during breastfeeding protects the mother from vaccine-preventable diseases, indirectly protects the infant by preventing maternal infection, and prevents infection in subsequent pregnancies.[1] Research is needed regarding possible changes in the immune response of breastfeeding women as for pregnant women. Additional questions relevant to vaccinating breastfeeding women are: (1) transfer of live microbes (viruses or bacteria); (2) transfer of specific antibodies that aid or block immunologic response in infant; and (3) transfer of chemicals used in the vaccines.

The major concern regarding live vaccines is that microbes, although attenuated, might pass through breast milk to an infant with little or no immunity. This is the case with smallpox, which can be associated with severe consequences. Among women immunized with rubella vaccine (RA27/3), >69% shed the virus in breast milk, which led to IgA antibodies to rubella in breast milk.[12] Animal and human studies suggest that IgA antibodies in mammary glands, colostrum, and breast milk are induced by specific antigens followed by migration of antigen-reactive precursor cells from intestinal and/or bronchial lymphoid tissues.[12] In 50% of the immunized women, rubella vaccine virus persisted in breast milk up to 10–17 days postimmunization.[13] Of breastfed infants, 56% had rubella virus from nasopharynx or throat (0% in non-breastfed infants) and 25% had transient seroconversion to rubella virus without clinical disease (0% in non-breastfed infants).[13] Therefore, breastfeeding is not a contraindication or precaution to rubella vaccination.

In a study of varicella vaccine, 12 postpartum women received varicella vaccine at least 6 weeks after delivery, and all seroconverted.[14] Over 200 samples of breast milk tested by polymerase chain reaction for varicella vaccine virus were negative, and all infants remained seronegative.[14] Although small, this study supports postpartum vaccination of susceptible women without interruption of breastfeeding.

The second concern is that antibody transferred via human milk may interfere with the infant's response to childhood immunizations, especially oral vaccines. Oral polio vaccines (live) administered to breastfed infants on day 3 of life were capable of producing infection in 57% of infants despite maternal antibodies in colostrum.[15] Antibodies in breast milk inhibited newborns' seroconversion following polio immunization.[16] This effect was temporary and it was considered unnecessary to withhold breastfeeding when administering oral polio vaccines to infants >6 weeks of age.[17]

Moreover, antibody response following rubella vaccine in breastfed infants whose mothers received rubella vaccine postpartum was similar to those in formula-fed infants and infants of naturally immune mothers.[18] Hence, immunization with rubella in breastfeeding women does not suppress the immune response to rubella vaccine in the infant.

Antibody persistence in breast milk may vary depending on antibody type. Women vaccinated during pregnancy with pneumococcal and meningococcal

polysaccharide vaccines had specific IgA type 6B antibodies in colostrum that fell to undetectable levels by 2 weeks, whereas type 19F antibodies were found in breast milk up to 5 months.[19] Because an insignificant amount of antibodies in breast milk pass from the GI tract into infant circulation, these antibodies do not suppress the infant immune response.[20,21]

Preservatives and other components of vaccines have caused concern over their potential effect on infants. Studies have assessed the effect of vaccine components (adjuvants, chemicals, preservatives, and additives) on infants, particularly that of thimerosol. Research has repeatedly refuted the association of adverse effects from thimerosol in vaccines administered directly to infants,[22] and the minute amounts that may possibly pass through breast milk should further reduce concern. Unfortunately, such concerns may lead to interruption of breastfeeding when the mother is immunized. The common Food and Drug Administration label "because many drugs are excreted in human milk, caution should be exercised when administering vaccine to a nursing woman" does little to reassure. Nonetheless, with the exception of smallpox vaccine, breastfeeding is not a contraindication to vaccination (Table 1).

Drugs and Chemicals Used in Travelers

Drugs that breastfeeding travelers may encounter include anti-infectives, antimalarials, high-altitude medications, analgesics, antimotility drugs, and topical preparations. The following section will review available data regarding their safety in breastfeeding infants.

Anti-infectives

The most commonly prescribed anti-infectives in the pre-travel consultation are quinolones, macrolides, and occasionally sulfonamides, usually for self-treatment of travelers' diarrhea. Doxycycline, a tetracycline prescribed for chemoprophylaxis of malaria, is also frequently considered in the United States but the World Health Organization (WHO) considers it contraindicated for prophylaxis and treatment for breastfeeding women.[49] As early as 1947, sulfonamides were recognized to pass into milk and persist for days after drug cessation, although studies on sulfanilamide showed no toxic effects in babies.[50] Sulfonamides are generally compatible in breastfeeding but should be used with caution in infants with hyperbilirubinemia.[6] Sulfamethoxazole has a longer half-life than other sulfonamides, ranging from 8 hours in infants to 36 hours in neonates.[51] Sulfisoxazole appears to be the best choice within the drug class because less than 1% of the maternal dose is secreted into human milk.[6] Data regarding tetracycline transfer into human milk have demonstrated limited secretion into breast milk. For example, women taking 2 gm tetracycline daily demonstrated a blood level of 0.65–3.0 μg/mL, while breast milk level was 0.43–2.1 μg/mL.[52] Nursing infants absorbed only 1% of therapeutic dose and probably even less because of protein binding to calcium.[52] Doxycycline, a newer analog of tetracycline, binds less to calcium salts and its overall absorption may be higher than that of tetracycline. The RID of doxycycline would be <6% of the maternal weight-adjusted dose. Harmful effects in breastfed infants have not yet been reported. Short-term use of doxycycline (3–4 wk) is not contraindicated in the United States (although contraindicated per WHO as noted above) but prolonged use is not advised.[6] On the other hand, quinolones were found in high levels in breast milk (ciprofloxacin, pefloxacin, ofloxacin); the breast milk ratio was >75% of serum levels at 2 hours after medication.[53] Because of concerns regarding arthropathy, at that time the authors recommended avoiding quinolones in lactating women.[53] More recently, inhalational and systemic anthrax cases led to the recommendation for initial treatment (including breastfeeding women) with intravenous ciprofloxacin or doxycycline plus one to two more antimicrobial agents.[54] According to the American Academy of Pediatrics (AAP), ciprofloxacin and tetracyclines are usually compatible with breastfeeding because the amounts absorbed by infants are small, but long-term safety is unknown.[55] Azithromycin concentration from the breast milk of a patient being treated with the medication and analyzed by chromatography with electrochemical detection was found to be time dependent; however, this may not be clinically significant[56] (Table 2).

Antimalarials

Chloroquine is a small molecule, a base, that is 60–65% bound in plasma and is excreted in human milk.[69–72] Current data suggest that chloroquine is compatible with breastfeeding.[72] Although adverse effects in breastfed infants have not been reported, close observation is recommended particularly for diarrhea, GI distress, and hypotension.[6] Hydroxychloroquine is a weak base and has a large volume of distribution, which suggests low transfer into milk. A dose of 800 mg hydroxychloroquine given to a woman resulted in 0.0003% of dose secreted in breast milk over 48 hours.[73] Although only a small amount of drug is secreted in breast milk, toxicities can occur with prolonged use (eg, retinal damage). Hydroxychloroquine is primarily metabolized to chloroquine and has a long half-life.[73] Because of its slow elimination rate, hydroxychloroquine can possibly accumulate to toxic amount, and daily hydroxychloroquine should be taken cautiously.[74] The AAP considers hydroxychloroquine to be generally compatible with breastfeeding.

There are no human data regarding the transfer of atovaquone and proguanil into breast milk.

Table 1 Vaccines and their safety/effect on breastfeeding infant

Vaccines	Secretion in breast milk, presence of antibody, antigen, or preservatives	Safety/effect on infant	Contraindication or precaution*	ACIP recommendations and Reference
BCG	No data	No data	Not recommended for use in United States	[23,24]
Cholera (Dukoral)	No data	No data. Inactivated bacterial component and non-toxic subunit of toxin are unlikely to have adverse effect on infant	Not licensed for use in United States but registered in Canada, Europe, New Zealand, Australia, etc.	[25]
Hepatitis A	No data	No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	[24,26,27]
Hepatitis B	No data	No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	[28,29]
Combination hepatitis A/B	No data	No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	[24,30]
Human papillomavirus	No data	No data. Vaccine consists of viral capsid proteins and is unlikely to have adverse effect on infant Among the breastfed infants of women who were vaccinated during the clinical trials, 3.4% developed serious adverse events, including respiratory infections and gastroenteritis or diarrhea. These events were not considered to be due to the vaccine	Not contraindicated	[31]
Immune globulin	No data	No data	Not contraindicated	[24]
Influenza				
Inactivated	No data	No data Inactivated virus vaccine is unlikely to have adverse effect on infant	Considered safe. As recommended by WHO for contact persons. Breastfeeding women should be vaccinated to protect them and reduce the risk of transmitting influenza to their infants because infants and young children are at high risk for influenza complications	[21,32,33,49,]
Live-attenuated	No data Virus that escapes the nasal mucosa is unstable and dies quickly	No data	Considered safe	[6,32]
Japanese encephalitis				
Inactivated (Biken†)		No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	[34]
New inactivated vaccine, Vero-cell derived, approved 2009 (IXIARO)	Contains no thimerosal, gelatin or other stabilizers		Not determined	Personal communication, Ted Tsai

Table 1 (*Continued*)

Vaccines	Secretion in breast milk, presence of antibody, antigen, or preservatives	Safety/effect on infant	Contraindication or precaution*	ACIP recommendations and Reference
Measles	No data	No data	Not contraindicated	24,35
Mumps	No data	No data	Not contraindicated	24,35
Rubella	Attenuated virus is shed in breast milk up to 10–17 d after immunization	Some breastfed infants had rubella virus from nasopharynx or throat and/or transient seroconversion but no clinical disease	Not contraindicated	12,13,35
Meningococcal Neisseria meningitis, quadrivalent				36
Polysaccharide (Menomune, Mencevax)	No data	No data. Vaccine is capsular polysaccharide and unlikely to have adverse effect on infant	Not contraindicated	24
Conjugate (Menactra)		No data. Vaccine is capsular polysaccharide conjugated to diphtheria toxoid and unlikely to have adverse effect on infant	Not determined	24
Pneumococcal				
23-valent polysaccharide	Increased IgA titers	No data. Vaccine consists of capsular polysaccharides and is unlikely to have adverse effect on infant	Not contraindicated	19,37
Polio				38
Inactivated, enhanced	No data	No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	24
Oral (Sabin)	Poliovirus antibodies are present	Antibodies in colostrums may inhibit the development of immunity to polio if oral polio vaccine were given in the immediate neonatal period	No longer used in the United States	15,17,39,40
Rabies (modern tissue culture vaccines approved by the WHO)	No data	No data. Inactivated virus vaccine is unlikely to have adverse effect on infant	Not contraindicated	24,41
Tetanus-diphtheria pertussis	No data	Pertussis-, diphtheria-, and tetanus-specific antibodies are found in colostrum, but breast milk antibodies "do not enter the neonatal circulation from the intestine in substantial amounts"	Considered safe. In women who have not received Tdap previously, Tdap is encouraged in the immediate postpartum period to protect the women from pertussis and to reduce the risk of exposure to pertussis in the infants	42,43
Tick-borne encephalitis	No data	No data	Registered in Europe, not licensed for use in the United States; use precaution	44
Typhoid				
Injectable, Vi polysaccharide	No data	No data	Not contraindicated	45
Live-attenuated oral	No data	No data	Not contraindicated	45

Table 1 (*Continued*)

Vaccines	Secretion in breast milk, presence of antibody, antigen, or preservatives	Safety/effect on infant	Contraindication or precaution*	ACIP recommendations and Reference
Varicella	12 non-immune women enrolled and received varicella vaccine postpartum. Varicella DNA was not detected by polymerase chain reaction in any of the 217 postvaccination breast milk specimens Another study did not detect varicella gene sequences in the postvaccination breast milk	In the study of 12 breastfeeding women vaccinated against varicella, none of the infants seroconverted	Considered safe. Breastfeeding women without immunity to varicella should be vaccinated	2,14,46,47
Yellow fever	No data	Although transmission to infant has not been reported, vaccination should be avoided due to the theoretical risk of transmitting 17D virus to the breastfed infant Vaccine recipients have viremia with live vaccine virus	Precaution, but to be considered if risk of infection is substantial	48
PPD	No data	Safe	Not contraindicated	

BCG = Bacille Calmette-Guérin; PPD = purified protein derivative.
*The statements "considered safe" and "not contraindicated" are derived from Advisory Committee on Immunization Practices (ACIP) Recommendations for each product. "Considered safe" indicates data are available and support vaccination of breastfeeding women and "not contraindicated" indicates lack of specific contraindication, but vaccine is also not specifically recommended in breastfeeding women.
†No longer being produced; remaining stocks still being used in 2009 but should be replaced by new vaccine.

Table 2 Anti-infective drugs commonly prescribed for travel-related illnesses

Anti-infective	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Antibiotic				
Azithromycin	Yes; accumulates in breast-milk; the estimated infant dose is 0.4 mg/kg/d, which is not clinically significant; RID 6.0%	No adverse effect seen in infants	None reported via breast milk	6,56
Ciprofloxacin	Yes; levels secreted in breast milk vary in studies but current studies suggest that the amount of drug in milk is low; RID: 2.65%	AAP considers usually compatible with breastfeeding; one case of pseudomembranous entercolitis reported in infant of a breastfeeding mother on ciprofloxacin for 6 d (Harmon); probably compatible in breastfeeding (Briggs); concern due to possible arthropathy in newborn animals	Precautions: infant diarrhea; observe infant for gastrointestinal symptoms such as diarrhea; consider alternative antibacterial if available	6,24,53,57–59
Rifaximin	Not known; however, rifaximin is poorly absorbed orally from the mother	Unknown in breastfeeding. Because maternal plasma levels are very low, unlikely that a significant concentration would enter plasma compartment to produce clinically relevant levels in milk; thus, the assumed infant exposure would be minimal	None reported via breast milk	6

Table 2 (*Continued*)

Anti-infective	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Trimethoprim–sulfamethoxazole	Yes for both components (low M/P ratios) Sulfamethoxazole: secreted in small amounts in breast milk and has longer half-life than other sulfonamides (sulfisoxazole has lowest M/P ratio within class). Trimethoprim: average milk levels were 2.0 mg/L and M/P ratio 1.25 and RID: 9.02%	Sulfamethoxazole: appears to be compatible but exercise caution; sulfisoxazole appears to be the best choice within the sulfonamides class. Trimethoprim: AAP considers usually compatible with breastfeeding	Sulfamethoxazole: use in caution in premature neonates that have hyperbilirubinemia and infants with G6PD deficiency. Trimethoprim: long-term use should be avoided if possible because it may interfere with folate metabolism or infant should be supplemented with folic acid	6,60–64
Antifungal				
Fluconazole	Yes; estimated infant dose through breast milk is 0.34 mg/kg/d or 16% of the weight-adjusted maternal dose; RID 16.1%	AAP considers usually compatible with breastfeeding; no untoward effects reported in breastfed infants	Caution in young infants, particularly with poor renal function	65–67
Miconazole	About 1% of dose is absorbed systemically after intravaginal application; thus, unlikely that the limited absorption would produce significant milk levels. Oral absorption of miconazole is only 25%–30%; milk concentrations following oral and IV miconazole have not been reported	Unlikely that levels absorbed by breastfeeding infant would be high enough to cause untoward effects; limited absorption probably limits clinical relevance in breastfed infants	None reported via milk	6
Clotrimazole	Penetration in breast milk unknown; upon intravaginal administration only 3%–10% of drug is absorbed and even less by oral lozenge	Unlikely that levels absorbed by breastfeeding infant would be high enough to cause untoward effects; limited absorption probably limits clinical relevance in breastfed infants	None reported via milk	6
Antivirals				
Neuraminidase inhibitors (oseltamivir, zanamivir)	Unknown	No data	Considered to be compatible with breastfeeding	68
Adamantanes (amantadine, rimantadine)	Secretion in breast milk reported		Contraindicated	

RID = relative infant dose; M/P ratio = milk/plasma ratio.
*This section summarizes key information and does not include all data on secretion of drug into breast milk.

Malarone, which is a fixed combination of atovaquone and proguanil, is approved for use for treating pediatric patients ≥5 kg. The Centers for Disease Control and Prevention (CDC) recommends that mefloquine be used instead of Malarone in breastfeeding women whose infants weigh <5 kg. Mefloquine is secreted in small amounts into breast milk (approximately 3% of maternal dose).[6] Although no harmful effects have been reported with mefloquine, lactation should be discontinued if neuropsychiatric disturbance (change in sleep or behavior) is suspected in the child. There are no data on the transfer of primaquine into breast milk nor on its use in lactation.[6] Because of its known adverse effects, primaquine is contraindicated during lactation unless both the mother and the infant have documented normal G6PD levels[75] (Table 3).

Miscellaneous Oral Medications: High-altitude, Antimotility, Analgesic, Anti-inflammatory, and Sleep Aid

Medications to prevent or treat acute mountain sickness are sometimes prescribed in travelers, most commonly

Table 3 Antimalarials and their safety or effect on breastfeeding infant

Antimalarials	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/ contraindications	References
Atovaquone	No data regarding transfer into human milk; elimination half-life is shorter in pediatric patients compared with adult patients (1–2 vs 2–3 d, respectively)	Unknown in breastfeeding	None reported via milk	6,49,75
		Approved for use in pediatric patients as chewable tablet formulation as Malarone (atovaquone 62.5 mg and proguanil 25 mg)	CDC recommends that breastfeeding mothers with infants <5 kg use mefloquine instead of Malarone (fixed combination of atovaquone and proguanil)	
			Not recommended by WHO	
Proguanil	Trace quantities found in human milk	Unknown in breastfeeding	None reported via milk	6,24,75
			CDC recommends that breastfeeding mothers with infants <5 kg use mefloquine instead of Malarone (fixed combination of atovaquone and proguanil)	
Chloroquine	Yes; data vary from studies	CDC and AAP consider usually compatible with breastfeeding	None reported; monitor for diarrhea, GI distress, and hypotension	70–72,76
	In recent study, 16 women day 3 to 17–21 postpartum, the estimated absolute and RID were 34 and 15 μg/kg/d and 2.3 and 1% for chloroquine and desethylchloroquine (the active metabolite), respectively			
Doxycycline	Yes; in a study of 15 women, the average doxycycline level in milk was 0.77 mg/L following a 200 mg oral dose; most tetracyclines secreted into milk are bound to calcium, thus limiting absorption; doxycycline is the least bound (20%) and may be better absorbed in comparison with older tetracyclines; RID (4.0%–5.7%)	Data are limited during breastfeeding. No harmful effects reported in breastfeeding infants	Most experts consider short-term use (3–4 wk) compatible with breastfeeding; prolonged use is not advised (refer to CDC), but as per WHO contraindicated	6,24,75,77
		Theoretical concern regarding dental staining and bone growth		
Hydroxychloroquine (HCQ)	Large volume of distribution suggests milk levels low; study of mother receiving 400 mg of HCQ, the M/P ratio was approximately 5.5. RID 2.89%; HCQ is primarily metabolized to chloroquine	AAP considers usually compatible with breastfeeding	Observe for retinal damage; consider the alternative chloroquine, which has more data for malaria chemoprophylaxis and no precaution/contraindication noted for breastfeeding	6,69,73,78
		No harmful effects reported		
Mefloquine	Yes; mefloquine is secreted in small concentrations, approximately 3% of maternal dose; RID 0.22%	No harmful effects reported but discontinue lactation if neuropsychiatric disturbances occur	None reported	6,75,79

Table 3 (*Continued*)

Antimalarials	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/ contraindications	References
			CDC recommends that breastfeeding mothers with infants <5 kg use mefloquine instead of Malarone (fixed combination of atovaquone and proguanil)	
Primaquine	No data on transfer into human milk; maternal plasma levels are low, suggesting that milk levels might be also low	No harmful effects reported	Contraindicated during lactation unless both mother and infant have normal G6PD levels (refer to CDC). Infant should be tested for G6PD before a breastfeeding mother is given primaquine	6,75

RID = relative infant dose; M/P ratio = milk/plasma ratio; WHO = World Health Organization; CDC = Centers for Disease Control and Prevention.
*This section summarizes key information and does not include all data on secretion of drug into breast milk.

acetazolamide which is a weak acid. Because the pH of breast milk is usually lower than blood, the concentration is expected to be lower in breast milk than blood. When acetazolamide 500 mg bid was given to a nursing mother for 1 week, the infant's daily dose was measured at about 0.06% of the mother's dose. After adjustment for body weight, the infant's dose was 1/130 of mother's dose/kg body weight.[80]

Nifedipine, sometimes used to prevent or treat high-altitude pulmonary edema, is 90% bound to plasma protein, thus only a small amount is available for transfer to milk. Assay of milk from a lactating woman taking nifedipine showed about 0.0027% of a 90 mg daily dose in milk, reaching peak within 1 hour.[81] Thus only an insignificant amount is transferred (<5% of a therapeutic dose); delaying breast feeding for 3–4 hours after taking the drug would further reduce the amount.

Dexamethasone is also used for high-altitude travel. No adverse effects have been reported with small amounts of corticosteroids in breast milk.[74] The AAP considered prednisone/prednisolone safe and compatible with breastfeeding.[55] A woman on high-dose steroids can decrease the amount of steroid in milk by delaying breastfeeding for 4 hours after the dose.

Loperamide is used to treat symptoms of travelers' diarrhea. Samples from six lactating women had extremely small amounts of loperamide and loperamide oxide in plasma and even lower concentrations in breast milk (by radioimmunoassay).[82] A breastfed infant consuming 165 mL/kg of milk daily from a mother who ingests 4 mg bid would get 1/2000 of the therapeutic dose of loperamide and 1/8000 of the dose of loperamide oxide.[83]

Analgesics and anti-inflammatory medications are commonly used by travelers. Aspirin is polar, is acidic, penetrates into breast milk poorly, and is eliminated slowly.[84] Measurement of salicylate excretion by chromatography in nursing mothers showed that it was detectable in milk within 1 hour and peaked in 2–6 hours, suggesting that single doses of aspirin would not lead to clinically significant levels in milk, but repeated doses may be significant due to slow elimination.[85] Breastfed neonates whose mothers take aspirin have been found to have substantial serum salicylate levels; concerns include metabolic acidosis, bleeding, effect on pulmonary circulation, and Reye syndrome.[74] A single dose of 450–650 mg delivers 0.1–21% to the infant over a 24-hour period.[86] AAP cautions the use of aspirin in breastfeeding mothers and recommends avoidance of large doses.[55]

Ibuprofen is highly protein bound, a weak acid, present in ionized form in greater proportion in plasma than in breast milk; no measurable concentration of ibuprofen was detected in the milk of breastfeeding women taking ibuprofen 400 mg every 6 hours.[87] Trace amounts of non-steroidal anti-inflammatory drugs (NSAIDs), which displace bilirubin and lead to increased risk of kernicterus, have been reported in milk. Therefore, NSAIDs are contraindicated in woman breastfeeding a jaundiced neonate.[74] Acetaminophen is an alternative analgesic.

In contrast to aspirin, acetaminophen is hydrophilic and a relatively neutral/weak acid. Acetaminophen is rapidly absorbed and distributed to milk; assay by liquid chromatography showed it to be present in milk by 15 minutes after an oral dose, peak between 1 and 2 hours, with none detected after 12 hours.[86] Codeine is found in higher concentration in milk, being a weak base, highly lipophilic, and has low plasma protein binding.[84]

Some travelers treat water with iodides and a very small amount is excreted in milk.[50] A nursing mother who used povidone–iodine vaginal gel for 6 days (50 mg iodine) noted an iodine odor in her 7½-month-old breastfed infant 2 days later. The infant's serum and urine iodine levels were elevated.[88] Iodine was absorbed through vaginal mucosa, concentrated in breast milk, and reached a level in breast milk eight times that of serum.[88] Acquired hypothyroidism has been reported

in full-term and pre-term breastfed infants whose mothers had topical exposure to iodine.[89,90] It appears prudent to avoid iodine preparations in breastfeeding travelers.

Some travelers request sleep aids. Benzodiazepines are excreted in breast milk.[91] Zolpidem is an imidazopyridine derivative unrelated to benzodiazepine with hypnotic effect, rapid onset, short duration, and usually touted for no residual sleepiness. It has a rapid absorption and short half-life. Zolpidem is detected in breast milk 3 hours after a 20 mg dose at <0.02% of oral dose (milk/plasma ration of 0.13) primarily via passive diffusion.[91] No drug is detected in samples taken at 13 and 16 hours.[91]

Finally, topical products such as *N*,*N*-diethyl-m-toluamide (DEET) and sunscreen may be ingested by breastfeeding infants if they are applied on or near the breast. The infrequent cases of DEET toxicity have been associated with ingestion as well as inhalation and ocular exposure,[92] whereas sunscreens contain myriad chemicals that can potentially cause toxicity when ingested. Breastfeeding women should apply topical products such as repellents and sunscreens at a distance from the breast and wash their hands after their application to avoid ingestion by the nursing infant (Table 4).

Advice and Precautions for Breastfeeding Travelers

Clinicians advising or treating breastfeeding travelers must balance a mother's health and a nursing infant's safety. Medications (ie, antimalarials) taken by breastfeeding mothers do not give protective drug levels in the infant. Administration of the same drugs to mother and breastfeeding infant does not lead to excessive drug level or toxicity in the infant.

Table 4 Miscellaneous medications indicated for travelers

Medication	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Altitude sickness				
Acetazolamide	Yes; patient receiving 500 mg twice daily, drug concentrations in milk: 1.3 mg/L to 2.1 mg/L and maternal plasma levels ranged from 5.2 mg/L to 6.4 mg/L; RID 2.21%	AAP considers usually compatible with breastfeeding	None reported via milk	6,80
Dexamethasone	Long-acting corticosteroid with greater potency than prednisone (0.75 mg dose is equivalent to 5 mg dose of prednisone). No data on transfer into human milk; however, probably similar to that of prednisone; prednisone RID 2.04%; doses of prednisone as high as 120 mg did not produce clinically relevant milk levels	Unknown for dexamethasone; AAP considers prednisone usually compatible with breastfeeding	Small doses of most steroids are not contraindicated in nursing mothers; with high doses, particularly for extended periods, steroids could potentially produce problems in infant growth and development (no data); monitor for growth and development	6,24,93
		Unlikely that the amount in milk would produce clinical effects unless dexamethasone was used in high doses		
Nifedipine	Yes; two studies indicate varying levels of transfer into breast milk but both generally low; RID 1.9%	AAP considers usually compatible with breastfeeding	None reported via milk	6,81,94
Salmeterol	Long-acting beta-2 adrenergic bronchodilator. No data in lactating women. Maternal plasma levels after inhaled administration are very low or undetectable	Unknown. No reports in lactating women available	None reported via milk	6
Motion sickness				
Dimenhydrinate	No data on transfer into human milk; molecular weight is low enough that excretion into milk is likely	Unknown in breastfeeding	None reported via milk	6,24

Table 4 (*Continued*)

Medication	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Meclizine	No data on transfer into human milk; molecular weight is low enough that excretion into milk is likely	Unknown in breastfeeding. Some medications in the same class such as diphenhydramine and brompheniramine are classified as contraindicated during breastfeeding by manufacturers	None reported via milk	6,24
Scopolamine	No data on transfer into human milk but due to poor oral bioavailability it is thought to be minimal	AAP considers usually compatible with breastfeeding	None reported via milk	50
Antimotility/ antidiarrheal				
Attapulgite	No data on transfer into human milk	Not absorbed after oral administration; problems in humans have not been documented	None reported via milk	
Bismuth subsalicylate	Bismuth salts poorly absorbed from maternal GI tract: no data in human milk; significant levels of salicylate could be absorbed from various products	Effect on nursing infants unknown but may be of concern	Use cautiously in breastfeeding. Best avoided due to systemic salicylate absorption	24,84,95
Diphenoxylate	No data on transfer into human milk; probably secreted in small quantities	Unknown in breastfeeding	None reported via milk but observe for dryness, constipation, and sedation	6,50
Atropine	Only small amounts believed secreted in milk; controversial	AAP considers usually compatible with breastfeeding; use caution	None reported via milk	6,50
Loperamide	Only minimal absorption orally (0.3%) and only very small amounts secreted into breast milk; RID (0.03%)	AAP considers usually compatible with breastfeeding; safe based on study on inactive prodrug	None reported via milk	6,82
Water treatment				
Iodine (iodide)	Concentrated in breast milk	May use per AAP but may affect thyroid activity; goiter	Avoid; consider alternative chlorine	55,88
Chlorine	No data on transfer into human milk	Unknown in breastfeeding	None reported via milk	
Analgesics				
Acetaminophen	Yes; only small amounts secreted into breast milk; wide variations in milk concentrations in different studies but RID is probably less than 6.4% of maternal dose	AAP considers usually compatible with breastfeeding	None reported via milk	6,86,96,97
Aspirin	Very small amounts secreted into breast milk; salicylic acid (active metabolite) penetrated poorly in milk; another study of a patient with rheumatoid arthritis who received 4 gm/d aspirin, none was detected in her milk; another study of a patient consuming chronic aspirin, M/P ratio was 0.08; RID (2.52–9.4%)	Drug associated with significant side effects and should be given with caution per AAP	Because aspirin is implicated in Reye syndrome, it is a poor choice of analgesic to use in breastfeeding mothers	6,84,85,98,99
Ibuprofen	Yes, trace amounts detected in breast milk (less than 6% of maternal dose); a study of 12 women receiving 400 mg doses every 6 h for five doses resulted in breast milk levels less than 1.0 mg/L, the lower limit of the assay; RID 0.65%	AAP considers usually compatible with breastfeeding; ideal analgesic for breastfeeding mothers (Hale)	None reported via milk	6,73,87,100

Table 4 (*Continued*)

Medication	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Sleep aid				
Zolpidem	Yes; study of five lactating women receiving 20 mg daily, the amount of drug recovered in breast milk 3 h after administration ranged from 0.004% to 0.019% of the total dose administered; breast milk clearance of zolpidem is very rapid and undetectable by 4–5 h after dosing	AAP considers usually compatible with breastfeeding	Monitor for infant sedation, lethargy, and changes in feeding habits	24,91
Diphenhydramine	No data on levels in breast milk; small levels are thought to be secreted into breast milk	Manufacturer does not recommend use in breastfeeding; concern for increased sensitivity of newborn or infant to effects	Not ideal use in breastfeeding; non-sedating antihistamines are generally preferred	6,24,101,102
Melatonin	Normal hormone that is known to be passed into human milk; amount of melatonin in human milk is about 35% of maternal level but can range to as high as 80%. Effect of orally administered melatonin in newborns is unknown. In a group of 10 breastfeeding mothers, nighttime maternal serum levels averaged 280 pmol/L, milk levels averaged 99 pmol/L	No data on the use of oral melatonin in breastfeeding	Because effects of exogenous melatonin on lactation are unknown, best to avoid based on lack of safety information	6,24,103
Topicals				
DEET (*N*,*N*-diethyl-m-toluamide)	Unknown if transfers into human milk. However, because it is very lipophilic with a large volume of distribution, some probably enters milk compartment. DEET is absorbed through the skin at variable concentrations (5%–17%). DEET concentrations can vary from product to product. "Family" line products contain the least amount of DEET (7%) compared with "deep woods" DEET product that can contain concentrations as high as 70%	No data in breastfeeding. Currently, no evidence that the use of DEET by lactating women poses health hazards to infants	Avoid the use of concentrated solutions (>25%) over large surface areas of body if breastfeeding	6,75,104
Permethrin	Unknown if transfers into human milk. Although molecular weight is low, minimal systemic absorption and rapid metabolism suggest minimal transfer into milk	No report describing topical use of permethrin in breastfeeding	None reported via milk	24,75

Table 4 (*Continued*)

Medication	Secretion in breast milk, amount/ concentration*	Safety/effect on infant	Precautions/contraindications	References
Picaridin	Unknown regarding transfer into human milk	No data in breastfeeding; EPA has classified picaridin as not likely to be a human carcinogen. AAP has not issued recommendation or opinion in children	None reported via human milk	
Oil of lemon eucalyptus-active ingredient: p-menthane 3, 8-diol (PMD)	Unknown regarding transfer into human milk	No data in breastfeeding. According to the label, oil of lemon eucalyptus products should not be used in children <3 yr of age. AAP has not issued recommendations or opinion in children	None reported via human milk	
Sunscreen products (numerous products available on the market with different chemicals)	Unknown regarding transfer into human milk	Unknown if sunscreen products with oxybenzone, which is well absorbed through the skin, are transferred to appreciable levels into breast milk to cause an adverse effect in the infant	None reported in human milk	75,105,106

RID = relative infant dose; M/P = milk/plasma ratio; EPA = Environmental Protection Agency
*This section summarizes key information and does not include all data on secretion of drug into breast milk.

Adequate hydration should be emphasized, especially for travel to high altitudes or hot environments. Breastfeeding travelers may be at greater risk of mosquito bites at night, if they get up frequently and leave mosquito netting to nurse or go to the bathroom, as was the case with pregnant women.[107] Increased attractiveness to mosquitoes, per se, has not been documented.

Empiric treatment of travelers' diarrhea is important. Many diseases are spread by fecal-oral route and careful hand washing (and avoidance of contamination of skin around breasts, nipples, and baby's mouth) is critical. Medications prescribed for travelers' diarrhea should be reviewed for excretion in breast milk and used accordingly. Breastfeeding travelers may need to pump milk if separated from the infant. Electric pumps need compatible electric current supply. Manual pumps are reliable, though more time-consuming to operate. Meticulous attention to the cleanliness of the breast pump and breast hygiene are important to avoid mastitis. The traveler should be advised of findings that suggest mastitis: fever, chills, flulike myalgia, and variable breast findings of an erythematous wedge or localized tenderness. Predisposing factors to development of this painful condition include engorgement, infrequent or disrupted feeding schedule, rapid weaning, maternal stress, and fatigue. Infection may or may not be associated with the inflammation. Treatment should be directed at the most common pathogen, *Staphylococcus aureus*. Methicillin-resistant *S. aureus*, to date, has rarely been reported as the cause.[108,109] In addition, intertrigo on the under surface of the breast may occur in hot climates, necessitating antifungal treatment. Milk storage and reliable refrigeration are also crucial considerations. If reliable storage and transport are unavailable, the traveler should discard the milk rather than risk feeding the infant the contaminated milk. The traveler should also be aware of cultural aspects and expectations of breastfeeding at the destination. Potential adjustments of feeding style in a culturally sensitive manner may be addressed at a pre-travel visit.

Conclusion

Breastfeeding women and their infants can travel safely, but need special attention to protect the infant. A critical goal is to maintain adequate hydration. Geographic areas where clean water and sanitation are lacking pose particular hurdles to any traveler and are especially difficult for the breastfeeding woman. Careful planning and assessment of local resources are important to preserve the health of infant and mother.

Acknowledgments

The authors thank Drs I. Dale Carroll and Robert Steffen, and Brenda Phipps, BS, IBCLC, for their thoughtful review of the manuscript and helpful comments.

Declaration of Interests

The authors state that they have no conflicts of interest to declare.

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