

Medications in the Breast-Feeding Mother

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Prescribing medications for a breast-feeding mother requires weighing the benefits of medication use for the mother against the risk of not breast-feeding the infant or the potential risk of exposing the infant to medications. A drug that is safe for use during pregnancy may not be safe for the nursing infant. The transfer of medications into breast milk depends on a concentration gradient that allows passive diffusion of nonionized, non-protein-bound drugs. The infant's medication exposure can be limited by prescribing medications to the breast-feeding mother that are poorly absorbed orally, by avoiding breast-feeding during times of peak maternal serum drug concentration and by prescribing topical therapy when possible. Mothers of premature or otherwise compromised infants may require altered dosing to avoid drug accumulation and toxicity in these infants. The most accurate and up-to-date sources of information, including Internet resources and telephone consultations, should be used. (Am Fam Physician 2001;64:119-26.)

Physicians receive little education about breast-feeding and even less training on the effects of maternal medications on the nursing infant.¹ Yet, concern about potential harm to the nursing infant from maternal medications is often cited as a reason to advise discontinuation of breast-feeding. Overwhelming evidence demonstrates the benefits of breast-feeding and the deleterious effects that can result from premature weaning.² This article provides information to facilitate medication use in breast-feeding mothers.

Transfer of Medications into Breast Milk

The mammary tissue in the breast is composed of clusters of milk-producing alveolar cells surrounding a central lumen. The transfer of medication into breast milk is driven primarily by a concentration gradient that allows passive diffusion of nonionized and free (non-protein-bound) medication.³

The drug concentration in breast milk is

largely determined by the maternal serum drug concentration. This serum concentration tends to be lower with medications that have large volumes of distribution and fluctuates more with medications that have short half-lives. Retrograde diffusion of the drug from breast milk to plasma may remove a medication from the milk even if the mother has not emptied her breasts.³ Medications that are highly protein bound, that have large molecular weights or that are poorly lipid-soluble tend not to enter the breast milk in clinically important quantities.

In the early postpartum period, large gaps between the mammary alveolar cells allow many medications to pass through this milk that may not be able to enter mature milk. These gaps close by the second week of lactation.³ The nursing infant's drug exposure depends on the drug's concentration in the breast milk and the amount of breast milk consumed by the infant.^{4,5} The pharmacologic activity of the medication depends on its absorption, distribution, metabolism and elimination by the infant. *Table 1*^{2,3} lists ways to minimize the risk of toxicity to infants from maternal medications.

General Guidelines and Resources

Specific information from high-quality studies of individual medications in lactation is rarely available, and misinformation

Drug exposure in the nursing infant depends on the concentration of the drug in the breast milk and the amount of breast milk consumed by the infant.

TABLE 1

Minimizing Potential Risk to Nursing Infants from Maternal Medications

General considerations

Avoid drug therapy when possible.

Use topical therapy when possible.

Medications that are safe for use directly in an infant of the nursing infant's age are generally safe for the breast-feeding mother.

Medications that are safe in pregnancy are not always safe in breast-feeding mothers.

Use reliable references for obtaining information on medications in breast milk.

Medication selection

Choose medications with the shortest half-life and highest protein-binding ability.

Choose medications that are well-studied in infants.

Choose medications with the poorest oral absorption.

Choose medications with the lowest lipid solubility.

Medication dosing

Administer single daily-dose medications just before the longest sleep interval for the infant, usually after the bed-time feeding.

Breast-feed infant immediately before medication dose when multiple daily doses are needed.

Information from Hale TW. Medications and mothers' milk: 1999-2000. 8th ed. Amarillo, Tex.: Pharmasoft Medical, 1999, and Lawrence RA, Lawrence RM. Breastfeeding: a guide for the medical profession. 5th ed. St. Louis: Mosby, 1999.

abounds. The safety of a medication during pregnancy does not necessarily imply safety during breast-feeding because the nursing infant must independently metabolize and excrete the medication. In addition, information in the *Physicians' Desk Reference* regarding breast-feeding is often inaccurate.^{2,3}

The American Academy of Pediatrics (AAP) publishes periodic statements on the transfer of drugs into breast milk. These statements classify many medications used in lactating women based on their safety for nursing infants. Most medications that are listed

are included in the safest category—Maternal Medication Usually Compatible with Breast-feeding.⁶ Limitations of this work include infrequent updates (approximately every five years), little detail on the medications and omission of many medications. *Table 2* lists resources that contain more comprehensive information. *Medications and Mothers' Milk* can be especially useful in the office setting because it is inexpensive, is updated annually and details theoretic and documented effects of maternal medications on the breast-feeding infant.

Fortunately, for certain common conditions, general recommendations can be made regarding the use of medications in the treatment of nursing mothers. Greater precaution is advised when prescribing medications for mothers of premature or otherwise compromised infants or newborns in the first week of life than for older, healthy infants.

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Specific Conditions

ALLERGIC RHINITIS

Pseudoephedrine (Sudafed) is excreted in breast milk in small amounts. According to the AAP, its use is compatible with breast-feeding although it may cause decreased milk production.^{6,7} Diphenhydramine (Benadryl), which is frequently prescribed for children, is also excreted in breast milk in small quantities. Either of these medications can cause lethargy or irritability in infants. To reduce the risk to the infant, the mother can take these medications immediately after breast-feeding. The new, nonsedating antihistamines are not well-studied in breast-feeding and are not rated by the AAP. Because they have fewer effects on the central nervous system and are safe for use in children, these antihistamines are preferred for short-term use in breast-feeding women.⁷ For long-term treatment, nasal steroids or cromolyn (Intal) are safer alternatives.^{7,8}

ASTHMA

Inhaled steroids for the treatment of asthma achieve very low levels in maternal plasma and are of no concern for the breast-feeding mother. Fluticasone (Flovent) has the lowest serum levels of the inhaled steroids. Oral steroids such as prednisone (Deltasone) and prednisolone (Delta-Cortef) penetrate into the breast milk poorly and are safe for short-term use. When daily dosages exceed 20 mg, prednisolone may be preferred over prednisone because it has only one peak in activity while prednisone has two peaks in activity—one for the pro-drug (prednisone) and the other for the drug (prednisolone).⁸ Infant exposure can be minimized by withholding nursing for four hours after taking the medication.^{3,7}

CARDIOVASCULAR

Diuretics and beta blockers, commonly preferred antihypertensives, are safe for use in lactating women, with some precautions. In

Inhaled steroids prescribed for asthma achieve very low levels in maternal plasma and are safe for breast-feeding mothers to use.

general, it is preferable to avoid high dosages of any one medication by either changing medications or adding an additional agent.⁹

Low dosages of thiazide diuretics (e.g., 25 mg per day or less of hydrochlorothiazide [Esidrix]) are excreted in small amounts into the breast milk but do not suppress lactation and, consequently, are compatible with nursing.^{6,9} Beta blockers vary widely in the amount excreted into breast milk. Propranolol (Inderal), metoprolol (Lopressor) and labetalol (Normodyne) are excreted in small quantities and are compatible with breast-feeding even in compromised infants. Atenolol (Tenormin), nadolol (Corgard) and sotalol (Betapace) are excreted in higher

TABLE 2
Resources for Information on Medication Use
in Breast-Feeding Women

Books

- Gerald G. Briggs. *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*. 5th ed. Baltimore: Williams & Wilkins, 1998.
- Thomas W. Hale. *Medications and Mothers' Milk*. 8th ed. Amarillo, Tex.: Pharmasoft Medical Publishing, 1999.
- Thomas W. Hale. *Clinical Therapy in Breastfeeding Patients*. Amarillo, Tex.: Pharmasoft Medical Publishing, 1999.
- Ruth Lawrence. *Breastfeeding: A Guide for the Medical Profession*. 5th ed. St. Louis: Mosby, 1999.
- Jack Newman, Theresa Pitman. *Dr. Jack Newman's Guide to Breastfeeding*. Toronto: Harper Collins Publishing, 2000.

Telephone advice

Yale-New Haven Hospital Lactation Center: 716-275-0088 (9 a.m. to 5 p.m. EST weekdays)

Internet resources

- Dr. Hale's Breastfeeding Pharmacology Page (<http://www.neonatal.ttuhsu.edu/lact>)
- Case Western Reserve University (<http://www.breastfeedingbasics.org>)
-

Propranolol, metoprolol and labetalol are safe to use while breast-feeding even if the infant is compromised.

amounts, which can lead to hypotension, bradycardia and tachypnea in the infant.⁹

Sustained-release nifedipine (Procardia XL) and verapamil (Calan SR) are excreted into breast milk in amounts that are less than the therapeutic dosage for children. Although diltiazem (Cardizem CD) is rated compatible with breast-feeding by the AAP, the levels found in breast milk are higher than the levels for other calcium channel blockers, so safer alternatives are preferred.^{3,6} Captopril (Capoten) and enalapril (Vasotec) are excreted into breast milk in small amounts. These medications are rated compatible with nursing by the AAP, although they have been studied less than other alternatives.^{3,6} Because neonates are highly sensitive to the effects of angiotensin-converting enzyme (ACE) inhibitors, their use by breast-feeding mothers in the first month of their infants' lives may be of concern.⁷ Hydralazine (Apresoline) is excreted in amounts far less than the pediatric dosage and

is safe, especially for short-term use following delivery.^{3,6}

DIABETES

Insulin is not excreted into breast milk and is considered safe for use during breast-feeding.¹⁰ Based on studies of the distribution of first-generation sulfonylureas into breast milk, the AAP considers tolbutamide (Orinase) to be compatible with breast-feeding.^{6,11} Information on other diabetic agents is less complete. Glyburide (Micronase) and glipizide (Glucotrol) are highly protein-bound (92 to 99 percent), second-generation sulfonylureas. The nature of their protein binding is nonionic and, therefore, they are less likely to be displaced by other drugs and unlikely to pass into breast milk.¹¹ If any of the sulfonylureas are used, it is important to monitor the nursing infant for signs of hypoglycemia, such as increased fussiness or somnolence.

The alpha-glucosidase inhibitors, such as acarbose (Precose), have low bioavailability, large molecular size and water solubility, so they are unlikely to be excreted into breast milk in clinically significant amounts.¹¹

Because of the potential for serious side effects (e.g., lactic acidosis, hepatotoxicity) in adults, it may be advisable to avoid the use of metformin (Glucophage) and thiazolidinediones (e.g., rosiglitazone [Avandia], pioglitazone [Actos]) until more information is available on their use in breast-feeding.

EPILEPSY

Although anticonvulsants are excreted into breast milk, most mothers who require the use of these drugs can safely breast-feed their infants.^{12,13} Determination of maternal serum drug levels may be a useful adjunct to clinical monitoring of the infant when evaluating the drug exposure of the infant.

Phenytoin (Dilantin) and carbamazepine (Tegretol) are compatible with breast-feeding.^{6,8,10,12} Although the AAP considers valproic acid and its derivatives (valproic sodium and divalproex sodium) to be compatible with

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breast-feeding, some experts recommend against their use during breast-feeding because of the potential for fatal hepatotoxicity in children younger than two years.^{6,10,12}

During breast-feeding, anticonvulsants other than phenobarbital and primidone (Mysoline) are preferred because the slow rate of barbiturate metabolism by the infant may cause sedation.^{6,10,12} Infant serum levels may be helpful in monitoring toxicity.

Specific Categories of Medications

ANTIBIOTICS

Penicillins and cephalosporins, which are excreted in milk in trace amounts, are compatible with breast-feeding.⁶ A remote possibility exists that the child will experience an allergic reaction to the antibiotic or develop diarrhea caused by changes in gut flora. Trimethoprim-sulfamethoxazole (Bactrim, Septra) is compatible with breast-feeding,⁶ but its use should be avoided when nursing infants are younger than two months because of its potential for causing increased bilirubin levels.³

Tetracycline is excreted in small amounts in breast milk, but the calcium in breast milk limits its absorption. Although tetracycline is compatible with breast-feeding, other antibiotics are preferred, especially for long-term use.^{3,6} Newer derivatives such as doxycycline (Vibramycin) or minocycline (Minocin) should be avoided because of higher absorption by infants and toxicity in children (e.g., dental staining, decreased bone growth).⁷ Quinolones have not been well studied in breast milk and are not rated by the AAP. They should be used in the breast-feeding mother only when other, better-studied options cannot be used and after the risks and benefits have been assessed.³

Metronidazole (Flagyl) is rated by the AAP as a drug whose effect on infants is unknown, but it may be of concern because older studies found its use in pregnancy to be associated with mutagenicity.⁶ Nevertheless, the amount transferred to the infant through breast milk is much lower than the therapeutic dosage for

During breast-feeding, anticonvulsant drugs other than phenobarbital and primidone are preferred because the slow rate of barbiturate metabolism by the infant can result in sedation.

infants, and no adverse effects have been reported from exposure through breast milk.³ Following a 2-g dose, cessation of breast-feeding for 12 to 24 hours is recommended by the AAP.^{3,6} Topical preparations of metronidazole (MetroGel-Vaginal) produce very low serum concentrations in the mother and are not a concern.³

Fluconazole (Diflucan) is commonly prescribed for yeast infections of the nipple in breast-feeding mothers. It is present in breast milk, but the nursing infant can only ingest 5 percent of the usual pediatric dosage.³ Although limited information is available, topical antifungal agents, such as clotrimazole (Gyne-Lotrimin) or miconazole (Monistat) produce very low maternal serum concentrations, and their use should pose little risk to the nursing infant.³

ANTIDEPRESSANTS

Maternal depression is known to have an adverse effect on parenting and infant development.¹⁴ Tricyclic antidepressants have been shown to have little to no effect on the breast-feeding infant, although the AAP finds most tricyclic agents to be of possible concern.^{3,7} Taking a single daily dose at bedtime will limit the infant's exposure to the medication. The selective serotonin reuptake inhibitors (SSRIs) are generally the first choice of treatment for depression. Sertraline (Zoloft) is likely to be the safest choice among them because it has been studied extensively and because drug levels found in nursing infants are usually minimal.^{7,12}

Fluoxetine (Prozac) use during pregnancy has been well-studied, and many new mothers are already taking it at delivery. Its use during breast-feeding is controversial, however. Flu-

Because of the long half-life of its metabolite, meperidine is not the preferred analgesic in breast-feeding mothers, although morphine, codeine and hydrocodone are usually considered safe for short-term use.

oxetine's long half-life and potential for accumulation in breast milk has prompted some recommendations to avoid its use in women who are breast-feeding young infants.³ Colic and fussiness have been attributed to elevated serum concentrations of fluoxetine and its metabolite in nursing infants.⁴ Results from a

recent study showed a decrease in the level of fluoxetine and its metabolite in the early weeks of life in nursing infants whose mothers were maintained on fluoxetine throughout pregnancy and breast-feeding. This decrease implies an absence of accumulation of fluoxetine during exposure from breast milk.¹⁵ No long-term studies of neurologic outcomes of children with breast milk exposure to SSRIs are available. These children should be observed closely.

At this time, it seems prudent to choose an SSRI with the lowest plasma levels in infants, such as sertraline (Zoloft) or paroxetine (Paxil).^{7,14} Another option is to measure

TABLE 3
Medications Commonly Prescribed for Maternal Ailments During Breast-Feeding

<i>Condition</i>	<i>Recommended agents</i>	<i>Alternative agents</i>	<i>Use with caution</i>
Allergic rhinitis	Beclomethasone (Beconase) Fluticasone (Flonase) Cromolyn (Nasal crom)	Cetirizine (Zyrtec) Loratadine (Claritin) Sedating antihistamines Decongestants	
Cardiovascular	Hydrochlorothiazide (Esidrix) Metoprolol tartrate (Lopressor) Propranolol (Inderal) Labetalol (Normodyne)	Nifedipine (Procardia XL) Verapamil (Calan SR) Hydralazine (Apresoline) Captopril (Capoten) Enalapril (Vasotec)	Atenolol (Tenormin) Nadolol (Corgard) Sotalol (Betapace) Diltiazem (Cardizem CD)
Depression	Sertraline (Zoloft) Paroxetine (Paxil)	Nortriptyline (Pamelor) Desipramine (Norpramin)	Fluoxetine (Prozac)
Diabetes	Insulin Glyburide (Micronase) Glipizide (Glucotrol) Tolbutamide (Orinase)	Acarbose (Precose)	Metformin (Glucophage) Thiazolidinediones
Epilepsy	Phenytoin (Dilantin) Carbamazepine (Tegretol)	Ethosuximide (Zarontin) Valproic sodium (Depakote)	Phenobarbital
Pain	Ibuprofen (Motrin) Morphine Acetaminophen (Tylenol)		Naproxen (Naprosyn) Meperidine (Demerol)
Asthma	Cromolyn (Intal) Nedocromil (Tilade)	Fluticasone (Flovent) Beclomethasone (Beclonvent)	
Contraception	Barrier methods	Progestin-only agents	Estrogen-containing contraceptives

Information from references 3, 6 through 12 and 15 through 18.

serum concentrations of the SSRI and major metabolites in the infant at two to six weeks postpartum to verify that the medication is not accumulating. If the mother has taken fluoxetine during pregnancy, an infant serum level of fluoxetine and norfluoxetine at about six weeks should reflect drug accumulation from the breast milk instead of continued presence of the prenatal medication.¹⁵

ANALGESICS

Of the nonsteroidal anti-inflammatory drugs (NSAIDs), ibuprofen (Motrin) is the preferred choice because it has poor transfer into milk and has been well-studied in children. Long half-life NSAIDs such as naproxen (Naprosyn), sulindac (Clinoril) and piroxicam (Feldene) can accumulate in the infant with prolonged use.⁷

Epidural use of bupivacaine (Marcaine), lidocaine (Xylocaine), morphine, fentanyl (Sublimaze) and sufentanil (Sufenta) is generally safe in breast-feeding mothers.^{8,15,16} Morphine, codeine and hydrocodone are considered compatible with breast-feeding by the AAP.⁶

Meperidine (Demerol) is not the preferred analgesic for use in breast-feeding women because of the long half-life of its metabolite in infants. Repeated exposure to analgesic agents, especially meperidine, may result in drug accumulation and toxic effects in young or compromised infants because of their underdeveloped hepatic conjugation.¹⁶ When possible, mothers should breast-feed their infants before taking the medication, and low to moderate dosages should be used.^{3,7,17}

CONTRACEPTIVE AGENTS

Hormones contained in combination oral contraceptive pills (OCPs) are not harmful to infants but, because estrogen diminishes the maternal milk supply, these products should be avoided in breast-feeding mothers whenever possible, especially during the first two months of breast-feeding. Progestin-only contraceptives are preferable, although these also may decrease milk supply. Delaying the use of

OCPs, including the progestin-only mini-pill, until six weeks after starting breast-feeding and then using a progestin-only mini-pill (such as Micronor) will allow the mother to assess the drug's effect on her milk supply. If the medication is well-tolerated, repository medroxyprogesterone (Depo-Provera) can be used. When appropriate, the use of an intrauterine contraceptive device or other barrier method of birth control is ideal.⁷

ANESTHETIC AGENTS

Although limited information is available regarding anesthetic agents and their compatibility with breast-feeding, use of propofol (Diprivan), thiopental sodium (Pentothal) and enflurane (Ethrane), should result in negligible amounts of drug exposure to the nursing infant.^{16,18} In general, the healthy term infant can safely nurse as soon after surgery as the mother is awake and alert.⁷

Table 3^{3,6-12,15-18} summarizes medication use in breast-feeding mothers with common maternal conditions. *Table 4*^{5,6} lists medications that are not recommended for use in breast-feeding mothers.

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TABLE 4
Medications Not to Be Used in Breast-Feeding Mothers

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