Medications and Breast-Feeding: A Guide for Pharmacists, Pharmacy Technicians, and Other Healthcare Professionals Part III

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Objective: To provide a guide for practicing pharmacists, pharmacy technicians, and other healthcare professionals so that they are able to counsel and advise breast-feeding mothers and fellow healthcare professionals on the safety and use of antiinfectives, vaccines, antiepileptics, benzodiazepines, psychotherapeutic drugs, and radiopharmaceuticals during breast-feeding.

Data Sources: Primary texts used by the breast-feeding community (*Medications and Mothers' Milk, Drugs in Pregnancy and Lactation, Drugs and Human Lactation*) were searched, as well as Micromedex, MEDLINE, PubMed, EMBASE, and EMBASE2 (1984–February 2004).

Study Selection/Data Extraction: Multiple sources were used wherever available to validate the data, and primary articles were used to verify all tertiary source information. Search terms included breast-feeding, lactation, nursing, and medications, as well as specific drug names.

Data Synthesis: Concerns regarding medication use during breast-feeding have caused mothers to either discontinue nursing or not take necessary medications. Complete avoidance of medications or cessation of breast-feeding is often unnecessary. Although there are drugs that can be harmful to nursing infants, breast-milk concentrations of most drugs are insufficient to cause any harm.

Conclusions: Having objective and reliable information on medications enables pharmacists, pharmacy technicians, other healthcare providers, and mothers to make educated decisions regarding drug therapy and breast-feeding.

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The following discussion of medication categories, including infectious diseases medications and vaccines, psychiatric and neurology agents, and radiopharmaceuticals, will help pharmacists and other healthcare professionals understand which are the optimal drugs within specific categories for breast-feeding mothers to take while minimizing the impact on infants. Drugs for use in ambulatory care, analgesia and anesthesia, and cardiology, as well as general medicines were discussed in Parts I[1] and II[2] of this 3-part series. Data and references supporting the information on each drug are detailed in tables, where applicable. American Academy of Pediatrics' (AAP) recommendations are listed if available.[3]

Infectious Diseases

ANTIINFECTIVES

Fortunately, most antibiotics, for various reasons, are generally considered safe for breast-feeding mothers to take. Infants, as well as mothers, should be monitored for

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possible drug hypersensitivity. The penicillins, macrolides, and β-lactams are present in low breast-milk concentrations. Aminoglycosides are considered usually safe because of poor gastrointestinal tract absorption.

Of the quinolones, ciprofloxacin and ofloxacin are considered usually compatible. Tetracyclines are considered usually compatible because of inactivation by calcium in breast milk.

Sulfonamides and nitrofurantoin should be used with caution in the first month of life due to hyperbilirubinemia considerations in the infant. Of the antifungals, fluconazole and ketoconazole are considered usually compatible. Acyclovir is also considered usually compatible. Despite mutagenic concerns, metronidazole has shown minimal excretion into breast milk and no adverse effects.

Mebendazole exhibits poor gastrointestinal tract absorption in infants, as well as low breast-milk concentrations. Of the antimalarials, the drugs of choice are chloroquine, dapsone, and pyrimethimine. Of the antituberculosis agents, isoniazid and rifampin have the best breast-feeding profiles (Table 1).[4-40]

VACCINES

No vaccine is contraindicated; however, there is a time restriction on polio vaccine, and special rules apply for nursing mothers and the use of smallpox vaccine. It is theoretically safer to administer a killed preparation than a live, attenuated vaccine. However, no studies support this statement, except for conflicting studies concerning rubella vaccine (live, attenuated). In addition, breast-feeding has shown negligible effects on antibody titers of infants.[41] Therefore, breast-feeding women or breast-fed children may safely receive needed vaccines[42] (Table 2).[13,41,43-55]

Psychiatric/Neurology Medications

ANTIEPILEPTICS

Treatment with the traditional antiepileptic drugs (phenytoin, carbamazepine, valproic acid) is considered safe; however, as for all anticonvulsants, observation for potential adverse effects is recommended.[56,57] Phenobarbital should be used with caution; if it is to be discontinued, abrupt weaning should be avoided.

Data on the new generation of antiepileptics are more limited, but their use is not necessarily contraindicated. Virtually all anticonvulsant drugs are excreted into milk in low concentrations.[58] In general, the lowest effective doses should be used, the infant should be monitored for potential adverse effects, and plasma concentrations should be monitored in the mother and in the infant (with as little invasiveness as possible). For nurslings whose mothers are on multiple therapies, there have been reports of poor weight gain, vomiting, and poor sucking[41] (Table 3).[56,57,59-73]

BENZODIAZEPINES

Benzodiazepines can be found in breast milk and infant's serum, potentially causing lethargy, weight loss, and prolongation of physiologic jaundice. In addition, some benzodiazepines have long half-lives. The prescriber should be very selective in deciding which agent to use. Alprazolam, oxazepam, and temazepam appear to have the best breast-feeding profiles. Benzodiazepines with long-acting metabolites, such as diazepam, can accumulate in infants, especially neonates.[41] Short-acting benzodiazepines without active metabolites offer the best choice for use[74] (Table 4).[56,57,61,64,75-88]

PSYCHOTHERAPEUTIC DRUGS

Much controversy has existed on the use of selective serotonin-reuptake inhibitors and tricyclics (to a lesser degree) on their effect on neurobehavioral development of breast-fed infants. Thus, the AAP states that the effect of these antidepressants' use on breast-feeding is unknown, but may be of concern.[3] Despite this controversy, these agents are used during pregnancy and breast-feeding after consideration of the benefits (eg, diminishing the possibility of suicide, positive benefits of breast-feeding itself, bonding between mother and child) and risks of their use. In fact, a review of reported data appears to support their use.[89] In a unique study comparing infants of breast-feeding mothers taking fluoxetine and not taking fluoxetine or tricyclic antidepressants, the authors measured the IQs of all the infants, 16 and 88 months' postnatal.[90] A subset of breast-fed children was analyzed. Children whose mothers took fluoxetine were analyzed at 18–30 months. In both the larger and smaller pools of children, fluoxetine did not produce any effects on neurobehavior.[91] These results have been confirmed with other psychotropic drugs.[92,93]

Sertraline, paroxetine, and fluvoxamine appear to have the best breast-feeding profiles. As for other psychotherapeutic agents, the use of phenothiazines has produced conflicting data, reports vary on haloperidol, and the use of lithium is controversial.

There is extensive literature on use of psychotherapeutic drugs and breast-feeding.[94] Useful guidelines include reviewing risks and benefits of treatment and nontreatment, choosing the drug based on clinical status and prior treatment response, using the lowest effective dose, avoiding polypharmacy, monitoring the patient for symptoms and drug concentrations, and educating mothers on potential adverse effects to note in infants.[95]

Pharmacists, healthcare professionals, and lactation consultants are probably asked more questions for advice on psychotherapeutic agents than any other class of drugs. Cases must be evaluated individually and carefully, taking into account the risks and benefits of both the use of the drug and the benefits of breast-feeding (Table 5).[61,62,89,91,96-145]

Table 1. Antiinfectives

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Aminoglycosides	generally considered safe due to poor GI tract absorption one study of gentamicin in women who delivered by cesarean showed mean milk:plasma ratios of 0.11 and 0.44 at 1 and 7 h postdose detectable gentamicin concentrations found in 5 of 10 infants	gentamicin, kanamycin, streptomycin considered usually compatible	12
Antifungals	no data available on most antifungals nystatin is poorly absorbed in milk ketoconazole monotherapy is probably safe fluconazole is excreted minimally into milk	fluconazole and ketoconazole considered usually compatible; no adverse effects reported	26, 27
Antimalarials (chloroquine, dapsone, pyrimethimine)	infant receives 4.2% of maternal chloroquine dose; generally considered safe pyrimethimine largely excreted into milk; infant receives subtherapeutic dose, which may promote resistance; treat or provide prophylaxis infant separately dapsone's presence in milk may protect infant from leprosy; considered safe except in infants with G6PD deficiency	chloroquine considered usually compatible; no adverse effects reported dapsone considered usually compatible; sulfonamide traces found in infants' urine pyrimethimine considered usually compatible; no adverse effects reported	34
Antituberculosis drugs (isoniazid, rifampin, ethionamide, capreomycin, para-aminosalicylic acid)	isoniazid is safest drug during lactation monitor infant LFTs if using ethionamide; no information on excretion into breast milk if using capreomycin, monitor for hearing loss, eosinophilia, proteinuria, nephrotoxicity; no data on excretion into breast milk para-aminosalicylic acid may increase isoniazid concentrations in infant if mother is receiving both therapies	isoniazid considered usually compatible; no adverse effects reported; however, isoniazid's acetyl metabolite is also excreted and is questionably hepatotoxic rifampin considered usually compatible; no adverse effects reported	13, 38–40
Aztreonam (Azactam)	aztreonam is acidic and has low lipid solubility; unlikely to be excreted extensively in milk peak milk concentrations <1% of peak plasma concentrations in one study drug also has poor oral absorption	usually compatible; no adverse effects reported	25
Cephalosporins	due to low MIC of third-generation drugs, gram-positive colonization and enterocolitis possible; use with caution	cefadroxil, cefazolin, cefotaxime, cefoxitin, cefprozil, ceftazidime, ceftriaxone considered usually compatible; no adverse effects reported	5–8
Chloramphenicol (Chloromycetin)	infant serum concentration 5% that of mother's may cause bone marrow suppression; avoid use if possible	not addressed	6, 7, 19, 20
Clindamycin (Cleocin)	excreted in milk, but amount varies concentration in plasma is higher because of high protein binding	usually compatible; no adverse effects reported	24
Macrolides azithromycin, clarithromycin, dithromycin,	minimal amount present in breast milk; use erythromycin if possible as alternative because of increased documentation and proven safety	not addressed	9
erythromycins	low amounts in milk avoid estolate during first month of infant's life due to possibility of jaundice	usually compatible; no adverse effects reported	9
Mebendazole (Vermox)	breast-milk concentrations in case report were low; poor GI tract absorption by infant all lactating women should be offered treatment	not addressed	36, 37
Metronidazole (Flagyl)	doses up to 400 mg/day have shown moderately high excretion into milk, but no toxicity to infants	effects on breast-feeding unknown, but may be of concern metronidazole is an in vitro mutagen safest to avoid breast-feeding for 12–24 h following a single dose	28–30
Nitrofurantoin (Macrodantin, Macrobid)	actively transported into milk, reaching concentrations much greater than serum concentrations infant dose is <10% of maternal dose caution in infants <1 mo old or those with G6PD deficiency	usually compatible hemolytic disease occurred in an infant with G6PD deficiency	22, 23
Nucleoside analogs acyclovir (Zovirax)	use if possible concentration in milk higher than in maternal serum; drug stays in milk up to 5–6 days after last dose infants can tolerate direct dosing of up to 75 mg/kg without toxicity, so drug is probably safe	drug is concentrated in human milk usually compatible; no adverse effects reported	31, 32
valacyclovir (Valtrex)	readily converted into acyclovir amount in milk 2% less than therapeutic dosing of newborns	not addressed	33

AAP = American Academy of Pediatrics; G6PD = glucose-6-phosphate dehydrogenase; GI = gastrointestinal; LFTs = liver function tests; MIC = minimum inhibitory concentration.

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Radiopharmaceuticals

Administration of any radiopharmaceutical will result in at least some excretion of radioactivity into milk. The amount and time course of excretion varies among radiopharmaceuticals.[146] Any period of interruption depends upon the total radioactivity ingested by an infant having been reduced to an acceptable level. The ideal method would be to assay breast milk for radioactivity and resume breast-feeding when concentrations are safe.[147]

Three options exist in a radiopharmaceutical/breast-feeding situation.

1. Discontinue breast-feeding; this also may be necessary for extended interruptions when milk production is already waning.
2. Interrupt breast-feeding for a short period; a breast pump can be used to express milk to store for use during interruptions.
3. Do not interrupt breast-feeding; interruptions are not always necessary depending upon the radiopharmaceutical administered.

The Office of Nuclear Regulatory Research has put together a useful guide that contains instructions and recommendations on the use of radiopharmaceuticals during breast-feeding.[148] In addition, objective mathematically derived guidelines for the administration of radiopharmaceuticals in nursing mothers have been developed[149] (Table 6).[146,147,149-172]

Summary

For many mothers, the decision to breast-feed is not a simple one. Despite extensive studies documenting the benefits of breast-feeding, many mothers are reluctant to do so, especially when medications are involved. One of the major obstacles to breast-feeding is the lack of encouragement from healthcare professionals. Many physicians are hesitant to recommend breast-feeding in patients on drug therapy for fear of potential infant drug toxicity. There are alternative approaches that can be taken.

In many cases, the benefits of breast-feeding far outweigh the potential medication risk to infants. Although the infant may be exposed to a drug through breast milk, this does not necessarily equate to drug toxicity. Often, the amount of drug or metabolite in milk is negligible or too small to adversely affect the nursling. Although infants have immature metabolizing capacities compared with older children or adults, many drugs can be tolerated by nursing children.

It is important for prescribers, other healthcare professionals, and mothers to be aware of which drugs can be safely used during breast-feeding. Having objective information on medications and their effect on nursing children can enable healthcare providers and mothers to make the most educated choice regarding drug therapy and breast-feeding. ≏

Table 1. Antiinfectives (continued)

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Nucleoside reverse transcriptase inhibitors			
zidovudine (Retrovir)	excreted in milk at high concentrations infant may receive clinical benefits through milk; however, HIV is transmitted through breast milk	not addressed	35
Penicillins	very low amounts found in milk; monitor infant for hypersensitivity	ticarcillin and amoxicillin considered usually compatible; no adverse effects reported	4
Quinolones	highly concentrated in milk (ciprofloxacin may be bound to milk calcium) potential for arthropathies in infant data suggest that ofloxacin and norfloxacin have very low milk concentrations; no specific documentation on levofloxacin	ciprofloxacin and ofloxacin considered usually compatible; no adverse effects reported other quinolones not addressed	13–18
Sulfonamides	avoid use in first month of infant's life or in hemolytic disease due to possibility of jaundice	sulfapiridine and sulfisoxazole considered usually compatible caution in infants with jaundice, G6PD deficiency, or premature infants trimethoprim/sulfamethoxazole considered usually compatible; no adverse effects reported	19–21
Tetracyclines	apparently inactivated by calcium in breast milk 2 case reports of black, discolored milk (probably due to chelation with iron) probably safe	tetracycline considered usually compatible; no adverse effects reported infant absorbs negligible amounts	10, 11

AAP = American Academy of Pediatrics; G6PD = glucose-6-phosphate dehydrogenase.

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Table 2. Vaccines

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
BCG	no data available	not addressed	13
Cholera	maternal vaccination significantly increases antibodies (IgA, IgG) to cholera in milk not contraindicated	not addressed	13, 43, 44
Diphtheria-tetanus-pertussis	inactive bacterial product; no contraindication	not addressed	43
Diphtheria-tetanus toxoid	unlikely that large molecular-weight protein toxoid is excreted into milk	not addressed	43
Haemophilus B	no data on maternal vaccination during lactation available; however, infant immunization recommended at 2 mo immunization during pregnancy resulted in increased antibody titer in milk	not addressed	13, 43, 45
Hepatitis A	no data available, but since inactive viral vaccine, unlikely to be harmful	not addressed	13, 43
Hepatitis B	unlikely harmful; no contraindication; AAP recommends infant vaccination 1–12 h after birth	not addressed	43
Influenza	probably safe; inactive viral vaccine; no reported adverse effects; no contraindication	not addressed	13, 43, 46
Measles	no data available	not addressed	13, 43
Meningococcal	no data available	not addressed	13, 43
Mumps	no data available	not addressed	13, 43
Pneumococcal	no data available on maternal vaccination during lactation vaccination during 30–34 weeks' gestation resulted in elevated milk antibody titer for 5 mo after delivery	not addressed	13, 47
Polio (inactivated)	no data available	not addressed	13
Polio (live)	antibody titer of milk equals that of mother's serum maternal immunization not recommended until infant is 6 wk old because of reduced antibody production for immunization of infants <6 wk old, breast-feeding should be withheld 6 h before and after	not addressed	13, 43, 48–50
Rabies	no data available inactivated vaccine; adverse effects unlikely	not addressed	13, 43
Rubella	recommended for susceptible women during immediate postpartum period 2 studies show that attenuated virus is not passed in milk; however, case reports demonstrate transmission of attenuated virus but no adverse effects case report of infant developing rubella 13 days after maternal vaccination	not addressed	13, 43, 51–55
Smallpox	no data available	not addressed	13, 43
Typhoid killed (injectable) live, attenuated (oral)	no data available; however, killed form preferred	not addressed	13, 44

AAP = American Academy of Pediatrics; BCG = bacillus Calmette-Guérin; Ig = immunoglobulin.

Table 3. Antiepileptics[a]

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Carbamazepine (Tegretol)	infant serum concentrations reported to be 15–65% of maternal serum concentrations average dose infant would ingest is 1.3–8% of maternal dose highest concentration detected in infants was much lower than the recommended concentration for the treatment of seizures in young children 1 case of poor suckling; 2 cases of transient hepatic dysfunction that included cholestatic hepatitis, hyperbilirubinemia, and increased γ-glutamyltransferase	usually compatible; no adverse effects reported	56, 57, 61–63
Ethosuximide (Zarontin)	90% of maternal serum concentration in milk	usually compatible drug does appear in infant serum, but no adverse drug effects reported	68
Felbamate (Felbatol)	excreted into milk use with great caution due to risk of aplastic anemia and acute liver failure lack of evidence for serious toxicity	not addressed	56, 57
Gabapentin (Neurotin)	study by manufacturer shows a milk:plasma ratio of 0.73 no reports of adverse effects use with caution and monitor for potential adverse reactions	not addressed	56, 57
Lamotrigine (Lamictal)	due to extensive passage of drug into milk, infant may achieve pharmacologic effects monitor blood concentrations in infant if adverse effects suspected no adverse effects noted in 6 cases use with caution	effect on nursing infant unknown and may be of concern potential for therapeutic serum concentrations in the infant	61, 69, 70
Oxcarbazepine (Trileptal)	the milk:plasma ratio for drug and its metabolites is ~0.5 no adverse effects reported use with caution because the AAP finds carbamazepine is compatible, oxcarbazepine should also be compatible	not addressed	57, 71
Phenobarbital (Bellatal, Solfoton)	may cause increased sedation and decreased suckling, especially in early neonatal period avoid abrupt weaning at therapeutic doses, infant may ingest 23–156% of weight-adjusted maternal dose because of slow excretion 4–6% of maternal serum concentration is found in milk	use with caution due to occurrences of sedation infantile spasms after weaning from milk; 1 case of methemoglobinemia	56, 57, 66–68
Phenytoin (Dilantin)	based on studies, average milk:plasma ratio ranged from 0.03 to 0.55 with maximum infant dose of 0.03–0.47 mg/kg/day infant would ingest <11% of weight-adjusted maternal dose elimination capacity is increased in neonates of mothers being treated with phenytoin, which contributes to lower infant concentrations	usually compatible; 1 case of methemoglobinemia, drowsiness, and decreased suckling reported (multiple therapy with phenobarbital)	56, 57, 59
Primidone (Mysoline)	70–90% of maternal serum concentration is found in milk; caused feeding difficulties in 2 cases	use with caution due to occurrences of sedation and feeding problems	66–68
Tiagabine (Gabitril)	no human data available; animal studies show excretion of drug and metabolites into milk	not addressed	57
Topiramate (Topamax)	milk:plasma ratio 0.86 for 5 mothers taking up to 400 mg/day; breast-fed infants had very low concentrations no adverse effects observed	not addressed	72
Valproic acid (Depakote, Depakene)	milk concentrations ~15% of maternal dose 1 case report of hematologic adverse effects monitor for symptoms of rash and hematoma 1 case of thrombocytopenia purpura and anemia concentrations in infants considered low	usually compatible; no adverse effects reported	56, 57, 61, 62, 64, 65
Vigabatrin	racemic mixture of *S*-enantiomer (active) and *R*-enantiomer (inactive) has low molecular weight and is not protein bound maximum infant dose is 2–3.6% that of the maternal dose for the *R*-enantiomer and 0.6–0.96% of maternal dose for the *S*-enantiomer no cases of nursing infants exposed to drug use with caution and monitor infant	not addressed	57
Zonisamide (Zonegran)	after a 300-mg dose, amount in milk equal to that in maternal plasma readily transported into milk determine concentrations individually if breast-feeding	not addressed	73

AAP = American Academy of Pediatrics.
[a]Some nurslings whose mothers are receiving antiepileptic therapy have increased sedation and may stop feeding early; this should be closely monitored.

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Table 4. Benzodiazepines[a]

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Alprazolam (Xanax)	dose in milk is 3% of maternal dose, which is unlikely to have a pharmacologic effect on infants case report of withdrawal symptoms (irritability, crying, sleep disorders) after 9 mo of therapy	effect on breast-feeding unknown, but may be of concern no adverse effects reported	75–77
Clobazam (Frisium)	infant may receive average of 4.6% of maternal dose during short-term treatment drug has an active metabolite, desmethylclobazam, which can accumulate after multiple doses possibly safe; monitor for sedation and poor suckling	not addressed	56, 57
Clonazepam (Klonapin)	excreted into milk 1 infant experienced persistent apnea spells until 10 wk of age; no adverse effects reported in any other infants monitor infants for signs of CNS depression, sedation, and apnea	not addressed	57, 61
Clorazepate (Tranxene)	single 20-mg im dose during labor does not appear to affect infants; repeated dosing could be a problem	not addressed	78
Diazepam (Valium)	drug and active metabolite accumulate in milk, even with low doses infant serum concentrations reported from undetectable to 243 ng/mL choose alternative if possible; if used, monitor the infant closely for lethargy, suckling problems, withdrawal symptoms, and EEG changes	effects on breast-feeding unknown, but may be of concern no adverse effects reported	64, 75, 78–82
Lorazepam (Ativan)	~6% of maternal dose is excreted in milk when used as prelabor medication, full-term infants showed no adverse effects; preterm infants showed poor suckling and hypothermia may delay onset of breast-feeding slightly short course of therapy probably safe	effects on breast-feeding unknown, but may be of concern no adverse effects reported	83, 84
Midazolam (Versed)	0.7% of maternal dose is found in milk after a 15-mg dose may be used safely for a few days; otherwise, use with caution	effects on breast-feeding unknown, but may be of concern	85
Nitrazepam (Mogadon)	excreted into milk; concentration may gradually increase due to long half-life short-term treatment may be safe; long-term treatment needs evaluation monitor infant for sedation and poor suckling	effects on breast-feeding unknown, but may be of concern	56
Oxazepam (Serax)	may be superior to other benzodiazepines (especially diazepam) due to low lipid solubility, short half-life, and no active metabolite 0.1% of maternal dose found in milk no adverse effects reported	not addressed	56, 75, 78, 86
Quazepam (Doral)	amount of maternal dose found in milk ~0.1% after a 15-mg dose; infant would receive ~2.3% of maternal dose no reports involving breast-feeding	effects on breast-feeding unknown, but may be of concern no adverse effects reported	75, 87
Temazepam (Restoril)	found in milk in very small amounts no adverse effects reported, but monitor closely for infant sedation and poor feeding	effects on breast-feeding unknown, but may be of concern	61, 88

AAP = American Academy of Pediatrics; CNS = central nervous system; EEG = electroencephalogram.
[a]Generally, single or repeated low doses are relatively safe in breast-feeding infants. Prolonged, high-dose maternal treatment should be avoided.

Table 5. Psychotherapeutic Drugs

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Bupropion (Wellbutrin, Zyban)	drug accumulates in breast milk at 2–8 times the maternal serum concentration (peak 2 h after dose); no quantifiable drug detected in infant serum no adverse effects noted	effect on breast-feeding unknown, but may be of concern	96, 107, 112–114
Citalopram (Celexa)	infant dose similar to that of fluoxetine monitor closely or choose another SSRI	not addressed	121, 124–127
Clozapine (Clozaril)	accumulation in breast milk 2–3 times the maternal serum concentration advise against breast-feeding due to risk of agranulocytosis in infant	effect on breast-feeding unknown, but may be of concern	96, 142, 143
Fluoxetine (Prozac)	cases of infant irritability, colic, poor feeding, sleep disturbances, seizures associated with maternal use manufacturer recommends against use has longest half-life of SSRIs; thus, most likely to accumulate in milk choose another SSRI if possible	effect on breast-feeding unknown, but may be of concern may cause colic, irritability, feeding and sleep disorders, slow weight gain	89, 91, 96, 101, 107, 115–123
Fluvoxamine (Luvox)	minimally excreted into milk at 0.5% maternal dose; low exposure to infant; no adverse effects reported potentially the safest SSRI; short half-life and no active metabolite in 2 cases, infant fluvoxamine concentrations were too low to be detected (<2.5 ng/mL); infants were reported healthy 2–3 years after the study in 1 case, infant received 0.62% of maternal dose; serum fluvoxamine concentrations were ~45% of mother's no adverse effects seen in any cases	effect on breast-feeding unknown, but may be of concern	107, 123, 131, 132
Haloperidol (Haldol)	reports vary milk concentration is 0.5% of maternal dose no adverse effects seen in infants; however, behavioral changes noted in animal studies	effect on breast-feeding unknown, but may be of concern may cause decline in developmental scores	98–100, 104
Lithium (Eskalith)	toxicity may result due to infant's underdeveloped regulatory and excretory systems monitor for hydration status, lethargy, and cyanosis use with great caution infant serum concentrations 10–50% higher than maternal concentrations	associated with significant adverse effects in nursing infants; should be used with caution 33–50% of therapeutic drug concentrations appear in infant's serum	62, 98, 99, 101–106
Nefazodone (Serzone)	study showed nefazodone passes into milk, but its major metabolites do not infant exposure was <10% of maternal dose; infant serum concentrations were not assessed infants had no abnormalities during study case of infant, whose mother was taking the drug, admitted to the hospital with drowsiness, lethargy, poor feeding, and inability to maintain body temperature; attributed to drug, as all other possibilities were ruled out; dose to infant was ~0.45% of maternal dose long-term effects unknown	not addressed	144, 145
Paroxetine (Paxil)	minimally excreted into breast milk at 1% of maternal dose monitor for insomnia, constipation, diarrhea, or inability to breast-feed no adverse effects noted in 1 infant lower amount to infant than fluoxetine or citalopram and higher amount than sertraline and fluvoxamine case report of no detectable concentrations in infant serum or in breast milk no adverse effects observed; may be optimal choice because of minimal risk	effect on breast-feeding unknown, but may be of concern	122, 123, 128–130
Phenothiazines	conflicting data use lowest possible dose; developmental problems may be associated with higher doses may increase the risk of SIDS in newborns possible drowsiness in infant with chlorpromazine	effect on breast-feeding unknown, but may be of concern chlorpromazine has caused galactorrhea in mother and drowsiness and lethargy in infant, as well as decline in developmental scores	89, 96–100

AAP = American Academy of Pediatrics; SIDS = sudden infant death syndrome; SSRI = selective serotonin-reuptake inhibitor.

(*continued on page 173*)

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Table 5. Psychotherapeutic Drugs (continued)

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
Sertraline (Zoloft)	concentrations undetectable in 4 infants; no adverse effects noted high protein binding probably leads to very low concentrations in milk; metabolite was not measured monitor for symptoms study of 10 lactating women found milk concentrations may exceed plasma concentrations milk:plasma ratio is ~2; infant dose ~2–3% of maternal dose study assessed effect of sertraline on infant serotonin reuptake and found that infant serum 5-HT levels did not significantly change	effect on breast-feeding unknown, but may be of concern	89, 96, 101, 107, 133–139
Tricyclic antidepressants	most evidence says use is not harmful to infants no reports of adverse effects to infants with use of desipramine, amitriptyline, nortriptyline, or imipramine reports of mild CNS effects with clomipramine and sedation and respiratory depression with doxepin (avoid if possible) ideally, use nortriptyline or desipramine in 1 dose at night to minimize exposure	effects of amitriptyline, desipramine, dothiepin, doxepin, imipramine, and nortriptyline on breast-feeding are unknown, but may be of concern; others not addressed	61, 96, 98, 100, 101, 104, 107–111
Venlafaxine (Effexor)	infant concentrations as high as 9% of maternal concentrations metabolite present at low but detectable concentrations in infants no adverse effects noted; monitor for agitation, insomnia, and poor feeding use alternative SSRI if possible	not addressed	130, 140, 141

AAP = American Academy of Pediatrics; CNS = central nervous system; SSRI = selective serotonin-reuptake inhibitor.

Table 6. Radiopharmaceuticals[a]

DRUG	DATA	AAP 2001 RECOMMENDATIONS	REFERENCE
^{18}F-FDG	high uptake into breast milk maximum dose to infant with no interruption period is 0.085 mSv, which is less than the recommended limit of 1 mSv for infant	not addressed	150
Gallium-67 citrate	breast-feeding should be discontinued because it can take ≥2 wk for radioactivity to decrease enough to be safe for the infant	requires temporary cessation of breast-feeding radioactivity present in milk for 2 wk	146, 149, 151–157
Indium-111	maximum exposure to infant without interruption is 0.5 mSv; interruption not necessary	requires temporary cessation of breast-feeding very small amounts present at 20 h	156, 158–160
Iodine-131	discontinue breast-feeding because recommended interruption is excessive (52 days) case of no radioactivity in milk 21 days after oral dose	requires temporary cessation of breast-feeding if used for treatment of thyroid cancer, high radioactivity may prolong exposure to infant	155, 157, 161–163
Iodine-123 sodium iodide	researchers concluded that interruption not necessary (note conflicting AAP recommendation)	requires temporary cessation of breast-feeding radioactivity in milk present for up to 36 h	154, 156
Iodine-125 fibrinogen iodide	breast-feeding should be discontinued	requires temporary cessation of breast-feeding radioactivity in milk present for 12 days	146, 155
Iodine-131 hippuran	breast-feeding should be discontinued	not addressed	146, 155
Iodine-131 sodium iodide	breast-feeding should be discontinued	requires temporary cessation of breast-feeding radioactivity in milk present for 2–14 days, depending upon study	163–166
P-32 phosphate	breast-feeding should be discontinued	not directly addressed	167, 168
Technetium-99m DISIDA	no interruption necessary	not directly addressed	154, 157
Technetium-99m DTPA	consider interruption for 4 h, but interruption not really necessary	not directly addressed	146, 154, 156, 170
Technetium-99m gluconate	no interruption necessary	not directly addressed	154–156
Technetium-99m HAMs	no interruption necessary[153,155] vs interruption for 18 h[156]	not directly addressed	154, 156, 157
Technetium-99m HDP	no interruption necessary	not directly addressed	155
Technetium-99m HMDP	no interruption necessary	not directly addressed	155
Technetium-99m HMPAD	dose to infant calculated to be 0.26 mSv no interruption necessary	not directly addressed	172
Technetium-99m MAA	interruption necessary for 6–24 h	not directly addressed	146, 149, 154–156, 170, 171
Technetium-99m MDP	no interruption necessary	not directly addressed	154, 156
Technetium-99m MIBI	no interruption necessary limit close contact only	not directly addressed	154, 156, 157
Technetium-99m PYP	no interruption necessary[153,155] vs interruption for 18 h[156]	not directly addressed	154, 156, 157
Technetium-99m RBCs	interruption for 12 h (based on in vitro data) no interruption necessary (based on in vitro data)	not directly addressed	154, 156
Technetium-99m SC	no interruption necessary[138,141] vs interruption for 12 h[142]	not directly addressed	154, 156, 157
Technetium-99m TcO_4	interruption necessary for 12–72 h consider measuring radioactivity before starting breast-feeding	requires temporary cessation of breast-feeding radioactivity present for 15 h to 3 days	146, 147, 149, 154–157, 169

AAP = American Academy of Pediatrics; DISIDA = diisopropyl-iminodiacetic acid; DTPA = diethylene triamine penta-acetic acid; gluconate = glucoheptonate; HAM = microsphere; HDP = hydroxydiphosphate; HMDP = hydroxymethylene diphosphate; HMPAD = hexamethylpropylene amine oxime; MAA = macroaggregated albumin; MDP = methylene diphosphate; MIBI = sestamibi; PYP = pyrophosphate; RBCs = labeled red blood cells; SC = sulfur colloid; TcO_4 = pertechnetate.

[a]The ideal is to obtain a series of milk samples to determine individually how long breast-feeding should be interrupted. If not possible, follow the general guidelines shown in the table.

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