AMERICAN ACADEMY OF PEDIATRICS

Committee on Drugs

The Transfer of Drugs and Other Chemicals Into Human Milk

ABSTRACT. The American Academy of Pediatrics places emphasis on increasing breastfeeding in the United States. A common reason for the cessation of breastfeeding is the use of medication by the nursing mother and advice by her physician to stop nursing. Such advice may not be warranted. This statement is intended to supply the pediatrician, obstetrician, and family physician with data, if known, concerning the excretion of drugs into human milk. Most drugs likely to be prescribed to the nursing mother should have no effect on milk supply or on infant well-being. This information is important not only to protect nursing infants from untoward effects of maternal medication but also to allow effective pharmacologic treatment of breastfeeding mothers. Nicotine, psychotropic drugs, and silicone implants are 3 important topics reviewed in this statement.

INTRODUCTION

A statement on the transfer of drugs and chemicals into human milk was first published in 1983,[1] with revisions in 1989[2] and 1994.[3] Information continues to become available. The current statement is intended to revise the lists of agents transferred into human milk and describe their possible effects on the infant or on lactation, if known (Tables 1–7). If a pharmacologic or chemical agent does not appear in the tables, it does not mean that it is not transferred into human milk or that it does not have an effect on the infant; it only indicates that there were no reports found in the literature. These tables should assist the physician in counseling a nursing mother regarding breastfeeding when the mother has a condition for which a drug is medically indicated.

BREASTFEEDING AND SMOKING

In the previous edition of this statement, the Committee on Drugs placed nicotine (smoking) in Table 2, "Drugs of Abuse-Contraindicated During Breastfeeding." The reasons for placing nicotine and, thus, smoking in Table 2 were documented decrease in milk production and weight gain in the infant of the smoking mother and exposure of the infant to environmental tobacco smoke as demonstrated by the presence of nicotine and its primary metabolite, cotinine, in human milk.[4–12] There is controversy regarding the effects of nicotine on infant size at 1 year of age.[13,14] There are hundreds of compounds in tobacco smoke; however, nicotine and its metabolite acotinine are most often used as markers of tobacco exposure. Nicotine is not necessarily the only component that might cause an increase in respiratory illnesses (including otitis media) in the nursing infant attributable to both transmammary secretion of compounds and environmental exposure. Nicotine is present in milk in concentrations between 1.5 and 3.0 times the simultaneous maternal plasma concentration,[15] and elimination half-life is similar—60 to 90 minutes in milk and plasma.[7] There is no evidence to document whether this amount of nicotine presents a health risk to the nursing infant.

The Committee on Drugs wishes to support the emphasis of the American Academy of Pediatrics on increasing breastfeeding in the United States. Pregnancy and lactation are ideal occasions for physicians to urge cessation of smoking. It is recognized that there are women who are unable to stop smoking cigarettes. One study reported that, among women who continue to smoke throughout breastfeeding, the incidence of acute respiratory illness is decreased among their infants, compared with infants of smoking mothers who are bottle fed.[16] It may be that breastfeeding and smoking is less detrimental to the child than bottle feeding and smoking. The Committee on Drugs awaits more data on this issue. The Committee on Drugs therefore has not placed nicotine (and thus smoking) in any of the Tables but hopes that the interest in breastfeeding by a smoking woman will serve as a point of discussion about smoking cessation between the pediatrician and the prospective lactating woman or nursing mother. Alternate (oral, transcutaneous) sources of nicotine to assist with smoking cessation, however, have not been studied sufficiently for the Committee on Drugs to make a recommendation for or against them in breastfeeding women.

PSYCHOTROPIC DRUGS

Anti-anxiety drugs, antidepressants, and neuroleptic drugs have been placed in Table 4, "Drugs for Which the Effect on Nursing Infants is Unknown but May Be of Concern." These drugs appear in low concentrations (usually with a milk-to-plasma ratio of 0.5–1.0) in milk after maternal ingestion. Because of the long half-life of these compounds and some of their metabolites, nursing infants may have measurable amounts in their plasma and tissues, such as the brain. This is particularly important in infants during the first few months of life, with immature hepatic and renal function. Nursing mothers should be informed that if they take one of these drugs, the infant will be exposed to it. Because these drugs affect neurotransmitter function in the developing central

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

nervous system, it may not be possible to predict long-term neurodevelopmental effects.

SILICONE BREAST IMPLANTS AND BREASTFEEDING

Approximately 800 000 to 1 million women in the United States have received breast implants containing silicone (elemental silicon with chemical bonds to oxygen) in the implant envelope or in the envelope and the interior gel. Concern has been raised about the possible effects to the nursing infant if mothers with implants breastfeed. This concern was initially raised in reports that described esophageal dysfunction in 11 children whose mothers had implants.[17,18] This finding has not been confirmed by other reports. Silicone chemistry is extremely complex; the polymer involved in the covering and the interior of the breast implant consists of a polymer of alternating silicon and oxygen atoms with methyl groups attached to the oxygen groups (methyl polydimethylsiloxane).[19] The length of the polymer determines whether it is a solid, gel, or liquid. There are only a few instances of the polymer being assayed in the milk of women with implants; the concentrations are not elevated over control samples.[20] There is no evidence at the present time that this polymer is directly toxic to human tissues; however, concern also exists that toxicity may be mediated through an immunologic mechanism. This has yet to be confirmed in humans. Except for the study cited above, there have been no other reports of clinical problems in infants of mothers with silicone breast implants.[21] It is unlikely that elemental silicon causes difficulty, because silicon is present in higher concentrations in cow milk and formula than in milk of humans with implants.[22] The anticolic compound simethicone is a silicone and has a structure very similar to the methyl polydimethylsiloxane in breast implants. Simethicone has been used for decades in this country and Europe without any evidence of toxicity to infants. The Committee on Drugs does not feel that the evidence currently justifies classifying silicone implants as a contraindication to breastfeeding.

DRUG THERAPY OF THE LACTATING WOMAN

The following should be considered before prescribing drugs to lactating women:

1. Is drug therapy really necessary? If drugs are required, consultation between the pediatrician and the mother's physician can be most useful in determining what options to choose.
2. The safest drug should be chosen, for example, acetaminophen rather than aspirin for analgesia.
3. If there is a possibility that a drug may present a risk to the infant, consideration should be given to measurement of blood concentrations in the nursing infant.
4. Drug exposure to the nursing infant may be minimized by having the mother take the medication just after she has breastfed the infant or just before the infant is due to have a lengthy sleep period.

Data have been obtained from a search of the medical literature. Because methodologies used to quantitate drugs in milk continue to improve, this information will require frequent updating. Drugs cited in Tables 1 through 7 are listed in alphabetical order by generic name; brand names are available from the current *Physicians' Desk Reference*,[23] *USP DI 2001: Drug Information for the Health Care Professional, Volume I*,[24] *and USP Dictionary of USAN and International Drug Names*.[25] The reference list is not inclusive of all articles published on the topic.

Physicians who encounter adverse effects in infants who have been receiving drug-contaminated human milk are urged to document these effects in a communication to the Food and Drug Administration (http://www.fda.gov/medwatch/index.html) and to the Committee on Drugs. This communication should include the generic and brand names of the drug, the maternal dose and mode of administration, the concentration of the drug in milk and maternal and infant blood in relation to the time of ingestion, the method used for laboratory identification, the age of the infant, and the adverse effects. Such reports may substantially increase the pediatric community's fund of knowledge regarding drug transfer into human milk and the potential or actual risk to the infant.

TABLE 1. Cytotoxic Drugs That May Interfere With Cellular Metabolism of the Nursing Infant

Drug	Reason for Concern, Reported Sign or Symptom in Infant, or Effect on Lactation	Reference No.
Cyclophosphamide	Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia	26, 27
Cyclosporine	Possible immune suppression; unknown effect on growth or association with carcinogenesis	28, 29
Doxorubicin*	Possible immune suppression; unknown effect on growth or association with carcinogenesis	30
Methotrexate	Possible immune suppression; unknown effect on growth or association with carcinogenesis; neutropenia	31

* Drug is concentrated in human milk.

TABLE 2. Drugs of Abuse for Which Adverse Effects on the Infant During Breastfeeding Have Been Reported*

Drug	Reported Effect or Reasons for Concern	Reference No.
Amphetamine†	Irritability, poor sleeping pattern	32
Cocaine	Cocaine intoxication: irritability, vomiting, diarrhea, tremulousness, seizures	33
Heroin	Tremors, restlessness, vomiting, poor feeding	34
Marijuana	Only 1 report in literature; no effect mentioned; very long half-life for some components	35
Phencyclidine	Potent hallucinogen	36

* The Committee on Drugs strongly believes that nursing mothers should not ingest drugs of abuse, because they are hazardous to the nursing infant and to the health of the mother.
† Drug is concentrated in human milk.

TABLE 3. Radioactive Compounds That Require Temporary Cessation of Breastfeeding*

Compound	Recommended Time for Cessation of Breastfeeding	Reference No.
Copper 64 (^{64}Cu)	Radioactivity in milk present at 50 h	37
Gallium 67 (^{67}Ga)	Radioactivity in milk present for 2 wk	38
Indium 111 (^{111}In)	Very small amount present at 20 h	39
Iodine 123 (^{123}I)	Radioactivity in milk present up to 36 h	40, 41
Iodine 125 (^{125}I)	Radioactivity in milk present for 12 d	42
Iodine 131 (^{131}I)	Radioactivity in milk present 2–14 d, depending on study	43–46
Iodine^{131}	If used for treatment of thyroid cancer, high radioactivity may prolong exposure to infant	47, 48
Radioactive sodium	Radioactivity in milk present 96 h	49
Technetium 99m (^{99m}Tc), ^{99m}Tc macroaggregates, ^{99m}Tc O_4	Radioactivity in milk present 15 h to 3 d	41, 50–55

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

TABLE 4. Drugs for Which the Effect on Nursing Infants Is Unknown but May Be of Concern*

Drug	Reported or Possible Effect	Reference No.
Anti-anxiety		
Alprazolam	None	57
Diazepam	None	58–62
Lorazepam	None	63
Midazolam	—	64
Perphenazine	None	65
Prazepam†	None	66
Quazepam	None	67
Temazepam	—	68
Antidepressants		
Amitriptyline	None	69, 70
Amoxapine	None	71
Bupropion	None	72
Clomipramine	None	73
Desipramine	None	74, 75
Dothiepin	None	76, 77
Doxepin	None	78
Fluoxetine	Colic, irritability, feeding and sleep disorders, slow weight gain	79–87
Fluvoxamine	—	88
Imipramine	None	74
Nortriptyline	None	89, 90
Paroxetine	None	91
Sertraline†	None	92, 93
Trazodone	None	94
Antipsychotic		
Chlorpromazine	Galactorrhea in mother; drowsiness and lethargy in infant; decline in developmental scores	95–98
Chlorprothixene	None	99
Clozapine†	None	100
Haloperidol	Decline in developmental scores	101–104
Mesoridazine	None	105
Trifluoperazine	None	104
OTHERS		
Amiodarone	Possible hypothyroidism	106
Chloramphenicol	Possible idiosyncratic bone marrow suppression	107, 108
Clofazimine	Potential for transfer of high percentage of maternal dose; possible increase in skin pigmentation	109
Lamotrigine	Potential therapeutic serum concentrations in infant	110
Metoclopramide†	None described; dopaminergic blocking agent	111, 112
Metronidazole	In vitro mutagen; may discontinue breastfeeding for 12–24 h to allow excretion of dose when single-dose therapy given to mother	113, 114
Tinidazole	See metronidazole	115

* Psychotropic drugs, the compounds listed under anti-anxiety, antidepressant, and antipsychotic categories, are of special concern when given to nursing mothers for long periods. Although there are very few case reports of adverse effects in breastfeeding infants, these drugs do appear in human milk and, thus, could conceivably alter short-term and long-term central nervous system function.[56] See discussion in text of psychotropic drugs.
† Drug is concentrated in human milk relative to simultaneous maternal plasma concentrations.

TABLE 5. Drugs That Have Been Associated With Significant Effects on Some Nursing Infants and Should Be Given to Nursing Mothers With Caution*

Drug	Reported Effect	Reference No.
Acebutolol	Hypotension; bradycardia; tachypnea	116
5-Aminosalicylic acid	Diarrhea (1 case)	117–119
Atenolol	Cyanosis; bradycardia	120–124
Bromocriptine	Suppresses lactation; may be hazardous to the mother	125, 126
Aspirin (salicylates)	Metabolic acidosis (1 case)	127–129
Clemastine	Drowsiness, irritability, refusal to feed, high-pitched cry, neck stiffness (1 case)	130
Ergotamine	Vomiting, diarrhea, convulsions (doses used in migraine medications)	131
Lithium	One-third to one-half therapeutic blood concentration in infants	132–134
Phenindione	Anticoagulant: increased prothrombin and partial thromboplastin time in 1 infant; not used in United States	135
Phenobarbital	Sedation; infantile spasms after weaning from milk containing phenobarbital, methemoglobinemia (1 case)	136–140
Primidone	Sedation, feeding problems	136, 137
Sulfasalazine (salicylazosulfapyridine)	Bloody diarrhea (1 case)	141

* Blood concentration in the infant may be of clinical importance.

TABLE 6. Maternal Medication Usually Compatible With Breastfeeding*

Drug	Reported Sign or Symptom in Infant or Effect on Lactation	Reference No.
Acetaminophen	None	142–144
Acetazolamide	None	145
Acitretin	—	146
Acyclovir†	None	147, 148
Alcohol (ethanol)	With large amounts, drowsiness, diaphoresis, deep sleep, weakness, decrease in linear growth, abnormal weight gain; maternal ingestion of 1 g/kg daily decreases milk ejection reflex	4, 149–152
Allopurinol	—	153
Amoxicillin	None	154
Antimony	—	155
Atropine	None	156
Azapropazone (apazone)	—	157
Aztreonam	None	158
B_1 (thiamin)	None	159
B_6 (pyridoxine)	None	160–162
B_{12}	None	163
Baclofen	None	164
Barbiturate	See Table 5	
Bendroflumethiazide	Suppresses lactation	165
Bishydroxycoumarin (dicumarol)	None	166
Bromide	Rash, weakness, absence of cry with maternal intake of 5.4 g/d	167
Butorphanol	None	168
Caffeine	Irritability, poor sleeping pattern, excreted slowly; no effect with moderate intake of caffeinated beverages (2–3 cups per day)	169–174
Captopril	None	175
Carbamazepine	None	176, 177
Carbetocin	None	178
Carbimazole	Goiter	83, 179, 180
Cascara	None	181
Cefadroxil	None	154
Cefazolin	None	182
Cefotaxime	None	183
Cefoxitin	None	183
Cefprozil	—	184
Ceftazidime	None	185
Ceftriaxone	None	186
Chloral hydrate	Sleepiness	187
Chloroform	None	188
Chloroquine	None	189–191
Chlorothiazide	None	192, 193
Chlorthalidone	Excreted slowly	194
Cimetidine†	None	195, 196
Ciprofloxacin	None	197, 198
Cisapride	None	199
Cisplatin	Not found in milk	30
Clindamycin	None	200
Clogestone	None	201
Codeine	None	144, 156, 202
Colchicine	—	203–205
Contraceptive pill with estrogen/progesterone	Rare breast enlargement; decrease in milk production and protein content (not confirmed in several studies)	206–213
Cycloserine	None	214
D (vitamin)	None; follow up infant's serum calcium level if mother receives pharmacologic doses	215–217
Danthron	Increased bowel activity	218
Dapsone	None; sulfonamide detected in infant's urine	191, 219
Dexbrompheniramine maleate with *d*-isoephedrine	Crying, poor sleeping patterns, irritability	220
Diatrizoate	None	221
Digoxin	None	222, 223
Diltiazem	None	224
Dipyrone	None	225
Disopyramide	None	226, 227
Domperidone	None	228
Dyphylline†	None	229
Enalapril	—	230
Erythromycin†	None	231
Estradiol	Withdrawal, vaginal bleeding	232
Ethambutol	None	214
Ethanol (cf. alcohol)	—	

TABLE 6. Continued

Drug	Reported Sign or Symptom in Infant or Effect on Lactation	Reference No.
Ethosuximide	None, drug appears in infant serum	176, 233
Fentanyl	—	234
Fexofenadine	None	235
Flecainide	—	236, 237
Fleroxacin	One 400-mg dose given to nursing mothers; infants not given breast milk for 48 h	238
Fluconazole	None	239
Flufenamic acid	None	240
Fluorescein	—	241
Folic acid	None	242
Gadopentetic (Gadolinium)	None	243
Gentamicin	None	244
Gold salts	None	245–249
Halothane	None	250
Hydralazine	None	251
Hydrochlorothiazide	—	192, 193
Hydroxychloroquine†	None	252, 253
Ibuprofen	None	254, 255
Indomethacin	Seizure (1 case)	256–258
Iodides	May affect thyroid activity; see iodine	259
Iodine	Goiter	259
Iodine (povidone-iodine, eg, in a vaginal douche)	Elevated iodine levels in breast milk, odor of iodine on infant's skin	259
Iohexol	None	97
Iopanoic acid	None	260
Isoniazid	None; acetyl (hepatotoxic) metabolite secreted but no hepatotoxicity reported in infants	214, 261
Interferon-α	—	262
Ivermectin	None	263, 264
K_1 (vitamin)	None	265, 266
Kanamycin	None	214
Ketoconazole	None	267
Ketorolac	—	268
Labetalol	None	269, 270
Levonorgestrel	—	271–274
Levothyroxine	None	275
Lidocaine	None	276
Loperamide	—	277
Loratadine	None	278
Magnesium sulfate	None	279
Medroxyprogesterone	None	201, 280
Mefenamic acid	None	281
Meperidine	None	61, 282
Methadone	None	283–287
Methimazole (active metabolite of carbimazole)	None	288, 289
Methohexital	None	61
Methyldopa	None	290
Methyprylon	Drowsiness	291
Metoprolol†	None	120
Metrizamide	None	292
Metrizoate	None	97
Mexiletine	None	293, 294
Minoxidil	None	295
Morphine	None; infant may have measurable blood concentration	282, 296–298
Moxalactam	None	299
Nadolol†	None	300
Nalidixic acid	Hemolysis in infant with glucose-6-phosphate dehydrogenase (G-6-PD) deficiency	301
Naproxen	—	302
Nefopam	None	303
Nifedipine	—	304
Nitrofurantoin	Hemolysis in infant with G-6-PD deficiency	305
Norethynodrel	None	306
Norsteroids	None	307
Noscapine	None	308
Ofloxacin	None	198
Oxprenolol	None	309, 310
Phenylbutazone	None	311
Phenytoin	Methemoglobinemia (1 case)	138, 176, 312
Piroxicam	None	313
Prednisolone	None	314, 315
Prednisone	None	316

TABLE 6. Continued

Drug	Reported Sign or Symptom in Infant or Effect on Lactation	Reference No.
Procainamide	None	317
Progesterone	None	318
Propoxyphene	None	319
Propranolol	None	320–322
Propylthiouracil	None	323
Pseudoephedrine†	None	324
Pyridostigmine	None	325
Pyrimethamine	None	326
Quinidine	None	191, 327
Quinine	None	296
Riboflavin	None	159
Rifampin	None	214
Scopolamine	—	156
Secobarbital	None	328
Senna	None	329
Sotalol	—	237, 330
Spironolactone	None	331
Streptomycin	None	214
Sulbactam	None	332
Sulfapyridine	Caution in infant with jaundice or G-6-PD deficiency and ill, stressed, or premature infant; appears in infant's milk	333, 334
Sulfisoxazole	Caution in infant with jaundice or G-6-PD deficiency and ill, stressed, or premature infant; appears in infant's milk	335
Sumatriptan	None	336
Suprofen	None	337
Terbutaline	None	338
Terfenadine	None	235
Tetracycline	None; negligible absorption by infant	339, 340
Theophylline	Irritability	169, 341
Thiopental	None	139, 342
Thiouracil	None mentioned; drug not used in United States	343
Ticarcillin	None	344
Timolol	None	310
Tolbutamide	Possible jaundice	345
Tolmetin	None	346
Trimethoprim/sulfamethoxazole	None	347, 348
Triprolidine	None	324
Valproic acid	None	176, 349, 350
Verapamil	None	351
Warfarin	None	352
Zolpidem	None	353

* Drugs listed have been reported in the literature as having the effects listed or no effect. The word "none" means that no observable change was seen in the nursing infant while the mother was ingesting the compound. Dashes indicate no mention of clinical effect on the infant. It is emphasized that many of the literature citations concern single case reports or small series of infants.
† Drug is concentrated in human milk.

TABLE 7. Food and Environmental Agents: Effects on Breastfeeding

Agent	Reported Sign or Symptom in Infant or Effect on Lactation	Reference No.
Aflatoxin	None	354–356
Aspartame	Caution if mother or infant has phenylketonuria	357
Bromide (photographic laboratory)	Potential absorption and bromide transfer into milk; see Table 6	358
Cadmium	None reported	359
Chlordane	None reported	360
Chocolate (theobromine)	Irritability or increased bowel activity if excess amounts (≥16 oz/d) consumed by mother	169, 361
DDT, benzene hexachlorides, dieldrin, aldrin, hepatachlorepoxide	None	362–370
Fava beans	Hemolysis in patient with G-6-PD deficiency	371
Fluorides	None	372, 373
Hexachlorobenzene	Skin rash, diarrhea, vomiting, dark urine, neurotoxicity, death	374, 375
Hexachlorophene	None; possible contamination of milk from nipple washing	376
Lead	Possible neurotoxicity	377–380
Mercury, methylmercury	May affect neurodevelopment	381–383
Methylmethacrylate	None	384
Monosodium glutamate	None	385
Polychlorinated biphenyls and polybrominated biphenyls	Lack of endurance, hypotonia, sullen, expressionless facies	386–390
Silicone	Esophageal dysmotility	17–22
Tetrachloroethylene cleaning fluid (perchloroethylene)	Obstructive jaundice, dark urine	391
Vegetarian diet	Signs of B_{12} deficiency	392

ACKNOWLEDGMENT

The Committee on Drugs would like to thank Linda Watson for her work in reference identification, document retrieval, and manuscript preparation.

REFERENCES

1. American Academy of Pediatrics, Committee on Drugs. The transfer of drugs and other chemicals into human breast milk. *Pediatrics*. 1983;72:375–383
2. American Academy of Pediatrics, Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics*. 1989;84:924–936
3. American Academy of Pediatrics, Committee on Drugs. Transfer of drugs and other chemicals into human milk. *Pediatrics*. 1994;93:137–150
4. Bisdom W. Alcohol and nicotine poisoning in nurslings. *JAMA*. 1937;109:178
5. Ferguson BB, Wilson DJ, Schaffner W. Determination of nicotine concentrations in human milk. *Am J Dis Child*. 1976;130:837–839
6. Luck W, Nau H. Nicotine and cotinine concentrations in the milk of smoking mothers: influence of cigarette consumption and diurnal variation. *Eur J Pediatr*. 1987;146:21–26
7. Luck W, Nau H. Nicotine and cotinine concentrations in serum and milk of nursing mothers. *Br J Clin Pharmacol*. 1984;18:9–15
8. Luck W, Nau H. Nicotine and cotinine concentrations in serum and urine of infants exposed via passive smoking or milk from smoking mothers. *J Pediatr*. 1985;107:816–820
9. Labrecque M, Marcoux S, Weber JP, Fabia J, Ferron L. Feeding and urine cotinine values in babies whose mothers smoke. *Pediatrics*. 1989;83:93–97
10. Schwartz-Bickenbach D, Schulte-Hobein B, Abt S, Plum C, Nau H. Smoking and passive smoking during pregnancy and early infancy: effects on birth weight, lactation period, and cotinine concentrations in mother's milk and infant's urine. *Toxicol Lett*. 1987;35:73–81
11. Schulte-Hobein B, Schwartz-Bickenbach D, Abt S, Plum C, Nau H. Cigarette smoke exposure and development of infants throughout the first year of life: influence of passive smoking and nursing on cotinine levels in breast milk and infant's urine. *Acta Paediatr*. 1992;81:550–557
12. Hopkinson JM, Schanler RJ, Fraley JK, Garza C. Milk production by mothers of premature infants: influence of cigarette smoking. *Pediatrics*. 1992;90:934–938
13. Little RE, Lambert MD III, Worthington-Roberts B, Ervin CH. Maternal smoking during lactation: relation to infant size at one year of age. *Am J Epidemiol*. 1994;140:544–554
14. Boshuizen HC, Verkerk PH, Reerink JD, Herngreen WP, Zaadstra BM, Verloove-Vanhorick SP. Maternal smoking during lactation: relation to growth during the first year of life in a Dutch birth cohort. *Am J Epidemiol*. 1998;147:117–126
15. Steldinger R, Luck W, Nau H. Half lives of nicotine in milk of smoking mothers: implications for nursing. *J Perinat Med*. 1988;16:261–262
16. Woodward A, Douglas RM, Graham NM, Miles H. Acute respiratory illness in Adelaide children: breast feeding modifies the effect of passive smoking. *J Epidemiol Community Health*. 1990;44:224–230
17. Levine JJ, Ilowite NT. Sclerodermalike esophageal disease in children breast-fed by mothers with silicone breast implants. *JAMA*. 1994;271:213–216
18. Levine JJ, Trachtman H, Gold DM, Pettei MJ. Esophageal dysmotility in children breast-fed by mothers with silicone breast implants: long-term follow-up and response to treatment. *Dig Dis Sci*. 1996;41:1600–1603
19. LeVier RR, Harrison MC, Cook RR, Lane TH. What is silicone? *Plast Reconstr Surg*. 1993;92:163–167
20. Berlin CM Jr. Silicone breast implants and breast-feeding. *Pediatrics*. 1994;94:547–549
21. Kjoller K, Mclaughlin JK, Friis S, et al. Health outcomes in offspring of mothers with breast implants. *Pediatrics*. 1998;102:1112–1115
22. Semple JL, Lugowski SJ, Baines CJ, Smith DC, McHugh A. Breast milk contamination and silicone implants: preliminary results using silicon as a proxy measurement for silicone. *Plast Reconstr Surg*. 1998;102:528–533
23. *Physicians' Desk Reference*. Montvale, NJ: Medical Economics Company; 2001
24. US Pharmacopeia. *USP DI 2001: Information for the Health Care Professional, Volume I*. Hutchinson TA, ed. Englewood, CO: Micromedex; 2001
25. US Pharmacopeia. *USP Dictionary of USAN and International Drug Names*. Rockville, MD: US Pharmacopeia; 2000
26. Wiernik PH, Duncan JH. Cyclophosphamide in human milk. *Lancet*. 1971;1:912
27. Amato D, Niblett JS. Neutropenia from cyclophosphamide in breast milk. *Med J Aust*. 1977;1:383–384
28. Flechner SM, Katz AR, Rogers AJ, Van Buren C, Kahan BD. The presence of cyclosporine in body tissue and fluids during pregnancy. *Am J Kidney Dis*. 1985;5:60–63
29. Nyberg G, Haljamae, Frisenette-Fich C, Wennergren M, Kjellmer I. Breast-feeding during treatment with cyclosporine. *Transplantation*. 1998;65:253–255
30. Egan PC, Costanza ME, Dodion P, Egorin MJ, Bachur NR. Doxorubicin and cisplatin excretion into human milk. *Cancer Treat Rep*. 1985;69:1387–1389
31. Johns DG, Rutherford LD, Leighton PC, Vogel CL. Secretion of methotrexate into human milk. *Am J Obstet Gynecol*. 1972;112:978–980
32. Steiner E, Villen T, Hallberg M, Rane A. Amphetamine secretion in breast milk. *Eur J Clin Pharmacol*. 1984;27:123–124
33. Chasnoff IJ, Lewis DE, Squires L. Cocaine intoxication in a breast-fed infant. *Pediatrics*. 1987;80:836–838
34. Cobrinik RW, Hood RT Jr, Chusid E. The effect of maternal narcotic addiction on the newborn infant: review of literature and report of 22 cases. *Pediatrics*. 1959;24:288–304
35. Perez-Reyes M, Wall ME. Presence of delta9-tetrahydrocannabinol in human milk. *N Engl J Med*. 1982;307:819–820
36. Kaufman KR, Petrucha RA, Pitts FN Jr, Weekes ME. PCP in amniotic fluid and breast milk: case report. *J Clin Psychiatry*. 1983;44:269–270
37. McArdle HJ, Danks DM. Secretion of copper 64 into breast milk following intravenous injection in a human subject. *J Trace Elem Exp Med*. 1991;4:81–84
38. Tobin RE, Schneider PB. Uptake of 67Ga in the lactating breast and its persistence in milk: case report. *J Nucl Med*. 1976;17:1055–1056
39. Butt D, Szaz KF. Indium-111 radioactivity in breast milk. *Br J Radiol*. 1986;59:80
40. Hedrick WR, Di Simone RN, Keen RL. Radiation dosimetry from breast milk excretion of radioiodine and pertechnetate. *J Nucl Med*. 1986;27:1569–1571
41. Rose MR, Prescott MC, Herman KJ. Excretion of iodine-123-hippuran, technetium-99 m-red blood cells, and technetium-99 m-macroaggregated albumin into breast milk. *J Nucl Med*. 1990;31:978–984
42. Palmer KE. Excretion of 125I in breast milk following administration of labelled fibrinogen. *Br J Radiol*. 1979;52:672–673
43. Honour AJ, Myant NB, Rowlands EN. Secretion of radioiodine in digestive juices and milk in man. *Clin Sci*. 1952;11:447–462
44. Karjalainen P, Penttila IM, Pystynen P. The amount and form of radioactivity in human milk after lung scanning, renography and placental localization by 131 I labelled tracers. *Acta Obstet Gynecol Scand*. 1971;50:357–361
45. Bland EP, Docker MF, Crawford JS, Farr RF. Radioactive iodine uptake by thyroid of breast-fed infants after maternal blood-volume measurements. *Lancet*. 1969;2:1039–1041
46. Nurnberger CE, Lipscomb A. Transmission of radioiodine (I^{131}) to infants through human maternal milk. *JAMA*. 1952;150:1398–1400
47. Robinson PS, Barker P, Campbell A, Henson P, Surveyor I, Young PR. Iodine-131 in breast milk following therapy for thyroid carcinoma. *J Nucl Med*. 1994;35:1797–1801
48. Rubow S, Klopper J, Wasserman H, Baard B, van Niekerk M. The excretion of radiopharmaceuticals in human breast milk: additional data and dosimetry. *Eur J Nucl Med*. 1994;21:144–153
49. Pommerenke WT, Hahn PF. Secretion of radio-active sodium in human milk. *Proc Soc Exp Biol Med*. 1943;52:223–224
50. O'Connell ME, Sutton H. Excretion of radioactivity in breast milk following 99Tcm-Sn polyphosphate. *Br J Radiol*. 1976;49:377–379
51. Berke RA, Hoops EC, Kereiakes JC, Saenger EL. Radiation dose to breast-feeding. *J Nucl Med*. 1973;14:51–52
52. Vagenakis AG, Abreau CM, Braverman LE. Duration of radioactivity in the milk of a nursing mother following 99 mTc administration. *J Nucl Med*. 1971;12:188
53. Wyburn JR. Human breast milk excretion of radionuclides following administration of radiopharmaceuticals. *J Nucl Med*. 1973;14:115–117
54. Pittard WB III, Merkatz R, Fletcher BD. Radioactive excretion in human milk following administration of technetium Tc 99 m macroaggregated albumin. *Pediatrics*. 1982;70:231–234
55. Maisels MJ, Gilcher RO. Excretion of technetium in human milk. *Pediatrics*. 1983;71:841–842
56. American Academy of Pediatrics, Committee on Drugs. Psychotropic drugs in pregnancy and lactation. *Pediatrics*. 1982;69:241–244
57. Oo CY, Kuhn RJ, Desai N, Wright CE, McNamara PJ. Pharmacokinet-

ics in lactating women: prediction of alprazolam transfer into milk. *Br J Clin Pharmacol*. 1995;40:231–236
58. Patrick MJ, Tilstone WJH, Reavey P. Diazepam and breast-feeding. *Lancet*. 1972;1:542–543
59. Cole AP, Hailey DM. Diazepam and active metabolite in breast milk and their transfer to the neonate. *Arch Dis Child*. 1975;50:741–742
60. Dusci LJ, Good SM, Hall RW, Ilett KF. Excretion of diazepam and its metabolites in human milk during withdrawal from combination high dose diazepam and oxazepam. *Br J Clin Pharmacol*. 1990;29:123–126
61. Borgatta L, Jenny RW, Gruss L, Ong C, Barad D. Clinical significance of methohexital, meperidine, and diazepam in breast milk. *J Clin Pharmacol*. 1997;37:186–192
62. Dencker SJ, Johansson G, Milsom I. Quantification of naturally occurring benzodiazepine-like substances in human breast milk. *Psychopharmacology (Berl)*. 1992;107:69–72
63. Summerfield RJ, Nielson MS. Excretion of lorazepam into breast milk. *Br J Anaesth*. 1985;57:1042–1043
64. Matheson I, Lunde PK, Bredesen JE. Midazolam and nitrazepam in the maternity ward: milk concentrations and clinical effects. *Br J Clin Pharmacol*. 1990;30:787–793
65. Olesen OV, Bartels U, Poulsen JH. Perphenazine in breast milk and serum. *Am J Psychiatry*. 1990;147:1378–1379
66. Brodie RR, Chasseaud LF, Taylor T. Concentrations of N-descyclopropylmethylprazepam in whole-blood, plasma, and milk after administration of prazepam to humans. *Biopharm Drug Dispos*. 1981;2:59–68
67. Hilbert JM, Gural RP, Symchowicz S, Zampaglione N. Excretion of quazepam into human breast milk. *J Clin Pharmacol*. 1984;24:457–462
68. Lebedevs TH, Wojnar-Horton RE, Yapp P, et al. Excretion of temazepam in breast milk. *Br J Clin Pharmacol*. 1992;33:204–206
69. Bader TF, Newman K. Amitriptyline in human breast milk and the nursing infant's serum. *Am J Psychiatry*. 1980;137:855–856
70. Erickson SH, Smith GH, Heidrich F. Tricyclics and breast feeding. *Am J Psychiatry*. 1979;136:1483–1484
71. Gelenberg AJ. Single case stuy. Amoxapine, a new antidepressant, appears in human milk. *J Nerv Ment Dis*. 1979;167:635–636
72. Briggs GG, Samson JH, Ambrose PJ, Schroeder DH. Excretion of bupropion in breast milk. *Ann Pharmacother*. 1993;27:431–433
73. Schimmell MS, Katz EZ, Shaag Y, Pastuszak A, Koren G. Toxic neonatal effects following maternal clomipramine therapy. *Clin Toxicol*. 1991;29:479–484
74. Sovner R, Orsulak PJ. Excretion of imipramine and desipramine in human breast milk. *Am J Psychiatry*. 1979;136:451–452
75. Stancer HC, Reed KL. Desipramine and 2-hydroxydesipramine in human breast milk and the nursery infant's serum. *Am J Psychiatry*. 1986;143:1597–1600
76. Rees JA, Glass RC, Sporne GA. Serum and breast-milk concentrations of dothiepin [letter]. *Practitioner*. 1976;217:686
77. Ilett KF, Lebedevs TH, Wojnar-Horton RE, et al. The excretion of dothiepin and its primary metabolites in breast milk. *Br J Clin Pharmacol*. 1992;33:635–639
78. Kemp J, Ilett KF, Booth J, Hackett LP. Excretion of doxepin and N-desmethyldoxepin in human milk. *Br J Clin Pharmacol*. 1985;20:497–499
79. Burch KJ, Wells BG. Fluoxetine/norfluoxetine concentrations in human milk. *Pediatrics*. 1992;89:676–677
80. Lester BM, Cucca J, Andreozzi L, Flanagan P, Oh W. Possible association between fluoxetine hydrochloride and colic in an infant. *J Am Acad Child Adolesc Psychiatry*. 1993;32:1253–1255
81. Burch KJ, Wells BG. Fluoxetine/norfluoxetine concentrations in human milk. *Pediatrics*. 1992;89:676–677
82. Taddio A, Ito S, Koren G. Excretion of fluoxetine and its metabolite, norfluoxetine, in human breast milk. *J Clin Pharmacol*. 1996;36:42–47
83. Brent NB, Wisner KL. Fluoxetine and carbamazepine concentrations in a nursing mother/infant pair. *Clin Pediatr (Phila)*. 1998;37:41–44
84. Isenberg KE. Excretion of fluoxetine in human breast milk. *J Clin Psychiatry*. 1990;51:169
85. Nulman I, Koren G. The safety of fluoxetine during pregnancy and lactation. *Teratology*. 1996;53:304–308
86. Yoshida K, Smith B, Craggs M, Kumar RC. Fluoxetine in breast-milk and developmental outcome of breast-fed infants. *Br J Psychiatry*. 1998;172:175–178
87. Chambers CD, Anderson PO, Thomas RG, et al. Weight gain in infants breastfed by mothers who take fluoxetine. *Pediatrics*. 1999;104(5). Available at: http://www.pediatrics.org/cgi/content/full/104/5/e61. Accessed December 20, 2000
88. Wright S, Dawling S, Ashford JJ. Excretion of fluvoxamine in breast milk. *Br J Clin Pharmacol*. 1991;31:209
89. Wisner KL, Perel JM. Serum nortriptyline levels in nursing mothers and their infants. *Am J Psychiatry*. 1991;148:1234–1236
90. Wisner KL, Perel JM. Nortriptyline treatment of breast-feeding women. *Am J Psychiatry*. 1996;153:295
91. Stowe ZN, Cohen LS, Hostetter A, Ritchie JC, Owens MJ, Nemeroff CB. Paroxetine in human breast milk and nursing infants. *Am J Psychiatry*. 2000;157:185–189
92. Epperson CN, Anderson GM, McDougle CJ. Sertraline and breast-feeding. *N Engl J Med*. 1997;336:1189–1190
93. Stowe ZN, Owens MJ, Landry JC, et al. Sertraline and desmethylsertraline in human breast milk and nursing infants. *Am J Psychiatry*. 1997;154:1255–1260
94. Verbeeck RK, Ross SG, McKenna EA. Excretion of trazodone in breast milk. *Br J Clin Pharmacol*. 1986;22:367–370
95. Polishuk WZ, Kulcsar SA. Effects of chlorpromazine on pituitary function. *J Clin Endocrinol Metab*. 1956;16:292
96. Wiles DH, Orr MW, Kolakowska T. Chlorpromazine levels in plasma and milk of nursing mothers. *Br J Clin Pharmacol*. 1978;5:272–273
97. Nielsen ST, Matheson I, Rasmussen JN, Skinnemoen K, Andrew E, Hafsahl G. Excretion of iohexol and metrizoate in human breast milk. *Acta Radiol*. 1987;28:523–526
98. Ohkubo T, Shimoyama R, Sugawara K. Determination of chlorpromazine in human breast milk and serum by high-performance liquid chromatography. *J Chromatogr*. 1993;614:328–332
99. Matheson I, Evang A, Overo KF, Syversen G. Presence of chlorprothixene and its metabolites in breast milk. *Eur J Clin Pharmacol*. 1984;27:611–613
100. Barnas C, Bergant A, Hummer M, Saria A, Fleischhacker WW. Clozapine concentrations in maternal and fetal plasma, amniotic fluid, and breast milk. *Am J Psychiatry*. 1994;151:945
101. Stewart RB, Karas B, Springer PK. Haloperidol excretion in human milk. *Am J Psychiatry*. 1980;137:849–850
102. Whalley LJ, Blain PG, Prime JK. Haloperidol secreted in breast milk. *Br Med J (Clin Res Ed)*. 1981;282:1746–1747
103. Ohkubo T, Shimoyama R, Sugawara K. Measurement of haloperidol in human breast milk by high-performance liquid chromatography. *J Pharm Sci*. 1992;81:947–949
104. Yoshida K, Smith B, Craggs M, Kumar RC. Neuroleptic drugs in breast milk: a study of pharmacokinetics and of possible adverse effects in breast-fed infants. *Psychol Med*. 1998;28:81–91
105. Ananth J. Side effects in the neonate from psychotropic agents excreted through breast-feeding. *Am J Psychiatry*. 1978;135:801–805
106. Plomp TA, Vulsma T, de Vijlder JJ. Use of amiodarone during pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 1992;43:201–207
107. Havelka J, Hejzlar M, Popov V, Viktorinova D, Prochazka J. Excretion of chloramphenicol in human milk. *Chemotherapy*. 1968;13:204–211
108. Smadel JE, Woodward TE, Ley HL Jr, et al. Chloramphenicol (Chloromycetin) in the treatment of tsutsugamushi disease (scrub typhus). *J Clin Invest*. 1949;28:1196
109. Venkatesan K, Mathur A, Girdhar A, Girdhar BK. Excretion of clofazimine in human milk in leprosy patients. *Lepr Rev*. 1997;68:242–246
110. Tomson T, Ohman I, Vitols S. Lamotrigine in pregnancy and lactation: a case report. *Epilepsia*. 1997;38:1039–1041
111. Gupta AP, Gupta PK. Metoclopramide as a lactogogue. *Clin Pediatr (Phila)*. 1985;24:269–272
112. Kauppila A, Arvela P, Koivisto M, Kivinen S, Ylikorkala O, Pelkonen O. Metoclopramide and breast feeding: transfer into milk and the newborn. *Eur J Clin Pharmacol*. 1983;25:819–823
113. Erickson SH, Oppenheim GL, Smith GH. Metronidazole in breast milk. *Obstet Gynecol*. 1981;57:48–50
114. Heisterberg L, Branebjerg PE. Blood and milk concentrations of metronidazole in mothers and infants. *J Perinat Med*. 1983;11:114–120
115. Evaldson GR, Lindgren S, Nord CE, Rane AT. Tinidazole milk excretion and pharmacokinetics in lactating women. *Br J Clin Pharmacol*. 1985;19:503–507
116. Boutroy MJ, Bianchetti G, Dubruc C, Vert P, Morselli PL. To nurse when receiving acebutolol: is it dangerous for the neonate? *Eur J Clin Pharmacol*. 1986;30:737–739
117. Nelis GF. Diarrhoea due to 5-aminosalicylic acid in breast milk. *Lancet*. 1989;1:383
118. Jenss H, Weber P, Hartmann F. 5-Aminosalicylic acid its metabolite in breast milk during lactation [letter]. *Am J Gastroenterol*. 1990;85:331
119. Klotz U, Harings-Kaim A. Negligible excretion of 5-aminosalicylic acid in breast milk. *Lancet*. 1993;342:618–619
120. Liedholm H, Melander A, Bitzen PO, et al. Accumulation of atenolol and metoprolol in human breast milk. *Eur J Clin Pharmacol*. 1981;20:229–231
121. Schimmel MS, Eidelman AI, Wilschanski MA, Shaw D Jr, Ogilvie RJ,

Koren G. Toxic effects of atenolol consumed during breast feeding. *J Pediatr*. 1989;114:476–478
122. Thorley KJ, McAinsh J. Levels of the beta-blockers atenolol and propanolol in the breast milk of women treated for hypertension in pregnancy. *Biopharm Drug Dispos*. 1983;4:299–301
123. Kulas J, Lunell NO, Rosing U, Steen B, Rane A. Atenolol and metoprolol. A comparison of their excretion into human breast milk. *Acta Obstet Gynecol Scand Suppl*. 1984;118:65–69
124. White WB, Andreoli JW, Wong SH, Cohn RD. Atenolol in human plasma and breast milk. *Obstet Gynecol*. 1984;63:42S–44S
125. Kulski JK, Hartmann PE, Martin JD, Smith M. Effects of bromocriptine mesylate on the composition of the mammary secretion in non-breast-feeding women. *Obstet Gynecol*. 1978;52:38–42
126. Katz M, Kroll D, Pak I, Osimoni A, Hirsch M. Puerperal hypertension, stroke, and seizures after suppression of lactation with bromocriptine. *Obstet Gynecol*. 1985;66:822–824
127. Clark JH, Wilson WG. A 16-day-old breast-fed infant with metabolic acidosis caused by salicylate. *Clin Pediatr (Phila)*. 1981;20:53–54
128. Levy G. Salicylate pharmacokinetics in the human neonate. In: Marselli PL, ed. *Basic and Therapeutic Aspects of Perinatal Pharmacology*. New York, NY: Raven Press; 1975:319
129. Jamali F, Keshavarz E. Salicylate excretion in breast milk. *Int J Pharm*. 1981;8:285–290
130. Kok TH, Taitz LS, Bennett MJ, Holt DW. Drowsiness due to clemastine transmitted in breast milk. *Lancet*. 1982;1:914–915
131. Fomina PI. Untersuchungen uber den Ubergang des aktiven agens des Mutterkorns in die milch stillender Mutter. *Arch Gynecol*. 1934;157:275
132. Schou M, Amdisen A. Lithium and pregnancy. 3. Lithium ingestion by children breast-fed by women on lithium treatment. *Br Med J*. 1973;2:138
133. Tunnessen WW Jr, Hertz CG. Toxic effects of lithium in newborn infants: a commentary. *J Pediatr*. 1972;81:804–807
134. Sykes PA, Quarrie J, Alexander FW. Lithium carbonate and breast-feeding. *Br Med J*. 1976;2:1299
135. Eckstein HB, Jack B. Breast-feeding and anticoagulant therapy. *Lancet*. 1970;1:672–673
136. Nau H, Rating D, Hauser I, Jager E, Koch S, Helge H. Placental transfer and pharmacokinetics of primidone and its metabolites phenobarbital, PEMA and hydroxyphenobarbital in neonates and infants of epileptic mothers. *Eur J Clin Pharmacol*. 1980;18:31–42
137. Kuhnz W, Koch S, Helge H, Nau H. Primidone and phenobarbital during lactation period in epileptic women: total and free drug serum levels in the nursed infants and their effects on neonatal behavior. *Dev Pharmacol Ther*. 1988;11:147–154
138. Finch E, Lorber J. Methaemoglobinaemia in newborn probably due to phenytoin excreted in human milk. *J Obstet Gynaecol Br Emp*. 1954;61:833–834
139. Tyson RM, Shrader EA, Perlman HH. Drugs transmitted through breast milk. II. Barbiturates. *J Pediatr*. 1938;13:86–90
140. Knott C, Reynolds F, Clayden G. Infantile spasms on weaning from breast milk containing anticonvulsants. *Lancet*. 1987;2:272–273
141. Branski D, Kerem E, Gross-Kieselstein E, Hurvitz H, Litt R, Abrahamov A. Bloody diarrhea—a possible complication of sulfasalazine transferred through human breast milk. *J Pediatr Gastroenterol Nutr*. 1986;5:316–317
142. Berlin CM Jr, Yaffe SJ, Ragni M. Disposition of acetaminophen in milk, saliva, and plasma of lactating women. *Pediatr Pharmacol (New York)*. 1980;1:135–141
143. Bitzen PO, Gustafsson B, Jostell KG, Melander A, Wahlin-Boll E. Excretion of paracetamol in human breast milk. *Eur J Clin Pharmacol*. 1981;20:123–125
144. Findlay JW, DeAngelis RL, Kearney MF, Welch RM, Findlay JM. Analgesic drugs in breast milk and plasma. *Clin Pharmacol Ther*. 1981;29:625–633
145. Soderman P, Hartvig P, Fagerlund C. Acetazolamide excretion into human breast milk. *Br J Clin Pharmacol*. 1984;17:599–600
146. Rollman O, Pihl-Lundin I. Acitretin excretion into human breast milk. *Acta Derm Venereol*. 1990;70:487–490
147. Lau RJ, Emery MG, Galinsky RE. Unexpected accumulation of acyclovir in breast milk with estimation of infant exposure. *Obstet Gynecol*. 1987;69:468–471
148. Meyer LJ, de Miranda P, Sheth N, Spruance S. Acyclovir in human breast milk. *Am J Obstet Gynecol*. 1988;158:586–588
149. Binkiewicz A, Robinson MJ, Senior B. Pseudo-Cushing syndrome caused by alcohol in breast milk. *J Pediatr*. 1978;93:965–967
150. Cobo E. Effect of different doses of ethanol on the milk-ejecting reflex in lactating women. *Am J Obstet Gynecol*. 1973;115:817–821
151. Kesaniemi YA. Ethanol and acetaldehyde in the milk and peripheral blood of lactating women after ethanol administration. *J Obstet Gynaecol Br Commonw*. 1974;81:84–86
152. Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, Clarren SK. Maternal alcohol use during breast-feeding and infant mental and motor development at one year. *N Engl J Med*. 1989;321:425–430
153. Kamilli I, Gresser U. Allopurinol and oxypurinol in human breast milk. *Clin Investig*. 1993;71:161–164
154. Kafetzis DA, Siafas CA, Georgakopoulos PA, Papadatos CJ. Passage of cephalosporins and amoxicillin into the breast milk. *Acta Paediatr Scand*. 1981;70:285–288
155. Berman JD, Melby PC, Neva FA. Concentration of Pentostam in human breast milk. *Trans R Soc Trop Med Hyg*. 1989;83:784–785
156. Sapeika N. Excretion of drugs in human milk: review. *J Obstet Gynaecol Br Emp*. 1947;54:426–431
157. Bald R, Bernbeck-Betthauser EM, Spahn H, Mutschler E. Excretion of azpropazone in human breast milk. *Eur J Clin Pharmacol*. 1990;39:271–273
158. Fleiss PM, Richwald GA, Gordon J, Stern M, Frantz M, Devlin RG. Aztreonam in human serum and breast milk. *Br J Clin Pharmacol*. 1985;19:509–511
159. Nail PA, Thomas MR, Eakin R. The effect of thiamin and riboflavin supplementation on the level of those vitamins in human breast milk and urine. *Am J Clin Nutr*. 1980;33:198–204
160. Roepke JL, Kirksey A. Vitamin B6 nutriture during pregnancy lactation. I. Vitamin B6 intake, levels of the vitamin in biological fluids, condition of the infant at birth. *Am J Clin Nutr*. 1979;32:2249–2256
161. West KD, Kirksey A. Influence of vitamin B6 intake on the content of the vitamin in human milk. *Am J Clin Nutr*. 1976;29:961–969
162. Greentree LB. Dangers of vitamin B6 in nursing mothers. *N Engl J Med*. 1979;300:141–142
163. Samson RR, McClelland DB. Vitamin B12 in human colostrum and milk. Quantitation of the vitamin and its binder and the uptake of bound vitamin B12 by intestinal bacteria. *Acta Paediatr Scand*. 1980;69:93–99
164. Eriksson G, Swahn CG. Concentrations of baclofen in serum and breast milk from a lactating woman. *Scand J Clin Lab Invest*. 1981;41:185–187
165. Healy M. Suppressing lactaton with oral diuretics. *Lancet*. 1961;1:1353
166. Brambel CE, Hunter RE. Effect of dicumarol on the nursing infant. *Am J Obstet Gynecol*. 1950;59:1153
167. Tyson RM, Shrader EA, Perlman HH. Drugs transmitted through breast milk. III. Bromides. *J Pediatr*. 1938;13:91–93
168. Pittman KA, Smyth RD, Losada M, Zighelboim I, Maduska AL, Sunshine A. Human perinatal distribution of butorphanol. *Am J Obstet Gynecol*. 1980;138:797–800
169. Berlin CM Jr. Excretion of the methylxanthines in human milk. *Semin Perinatol*. 1981;5:389–394
170. Tyrala EE, Dodson WE. Caffeine secretion into breast milk. *Arch Dis Child*. 1979;54:787–800
171. Hildebrandt R, Gundert-Remy U. Lack of pharmacological active saliva levels of caffeine in breast-fed infants. *Pediatr Pharmacol (New York)*. 1983;3:237–244
172. Berlin CM Jr, Denson HM, Daniel CH, Ward RM. Disposition of dietary caffeine in milk, saliva, and plasma of lactating women. *Pediatrics*. 1984;73:59–63
173. Ryu JE. Caffeine in human milk and in serum of breast-fed infants. *Dev Pharmacol Ther*. 1985;8:329–337
174. Ryu JE. Effect of maternal caffeine consumption on heart rate and sleep time of breast-fed infants. *Dev Pharmacol Ther*. 1985;8:355–363
175. Devlin RG, Fleiss PM. Captopril in human blood and breast milk. *J Clin Pharmacol*. 1981;21:110–113
176. Nau H, Kuhnz W, Egger JH, Rating D, Helge H. Anticonvulsants during pregnancy and lactation. Transplacental, maternal and neonatal pharmacokinetics. *Clin Pharmacokinet*. 1982;7:508–543
177. Pynnonen S, Kanto J, Sillanpaa M, Erkkola R. Carbamazepine: placental transport, tissue concentrations in foetus and newborn, and level in milk. *Acta Pharmacol Toxicol (Copenh)*. 1977;41:244–253
178. Silcox J, Schulz P, Horbay GL, Wassenaar W. Transfer of carbetocin into human breast milk. *Obstet Gynecol*. 1993;82:456–459
179. Cooper DS. Antithyroid drugs: to breast-feed or not to breast-feed. *Am J Obstet Gynecol*. 1987;157:234–235
180. Lamberg BA, Ikonen E, Osterlund K, et al. Antithyroid treatment of maternal hyperthyroidism during lactation. *Clin Endocrinol (Oxf)*. 1984;21:81–87
181. Tyson RM, Shrader EA, Perlman HH. Drugs transmitted through breast milk. I. Laxatives. *J Pediatr*. 1937;11:824–832
182. Yoshioka H, Cho K, Takimoto M, Maruyama S, Shimizu T. Transfer of cefazolin into human milk. *J Pediatr*. 1979;94:151–152
183. Dresse A, Lambotte R, Dubois M, Delapierre D, Kramp R. Transmam-

mary passage of cefoxitin: additional results. *J Clin Pharmacol*. 1983;23:438–440
184. Shyu WC, Shah VR, Campbell DA, et al. Excretion of cefprozil into human breast milk. *Antimicrob Agents Chemother*. 1992;36:938–941
185. Blanco JD, Jorgensen JH, Castaneda YS, Crawford SA. Ceftazidime levels in human breast milk. *Antimicrob Agents Chemother*. 1983;23:479–480
186. Bourget P, Quinquis-Desmaris V, Fernandez H. Ceftriaxone distribution and protein binding between maternal blood and milk postpartum. *Ann Pharmacother*. 1993;27:294–297
187. Lacey JH. Dichloralphenazone and breast milk. *Br Med J*. 1971;4:684
188. Reed CB. A study of the conditions that require the removal of the child from the breast. *Surg Gynecol Obstet*. 1908;6:514
189. Soares R, Paulini E, Pereira JP. Da concentracao e eliminacao da cloroquina atraves da circulacao placentaria e do leite materno, de pacientes sob regime do sal loroquinado. *Rev Bras Malariol Doencas Trop*. 1957;9:19
190. Ogunbona FA, Onyeji CO, Bolaji OO, Torimiro SE. Excretion of chloroquine and desethylchloroquine in human milk. *Br J Clin Pharmacol*. 1987;23:473–476
191. Edstein MD, Veenendaal JR, Newman K, Hyslop R. Excretion of chloroquine, dapsone and pyrimethamine in human milk. *Br J Clin Pharmacol*. 1986;22:733–735
192. Werthmann MW Jr, Krees SV. Excretion of chlorothiazide in human breast milk. *J Pediatr*. 1972;81:781–783
193. Miller EM, Cohn RD, Burghart PH. Hydrochlorothiazide disposition in a mother and her breast-fed infant. *J Pediatr*. 1982;101:789–791
194. Mulley BA, Parr GD, Pau WK, Rye RM, Mould JJ, Siddle NC. Placental transfer of chlorthalidone and its elimination in maternal milk. *Eur J Clin Pharmacol*. 1978;13:129–131
195. Somogyi A, Gugler R. Cimetidine excretion into breast milk. *Br J Clin Pharmacol*. 1979;7:627–629
196. Oo CY, Kuhn RJ, Desai N, McNamara PJ. Active transport of cimetidine into human milk. *Clin Pharmacol Ther*. 1995;58:548–555
197. Gardner DK, Gabbe SG, Harter C. Simultaneous concentrations of ciprofloxacin in breast milk and in serum in mother and breast-fed infant. *Clin Pharm*. 1992;11:352–354
198. Giamarellou H, Kolokythas E, Petrikkos G, Gazis J, Aravantinos D, Sfikakis P. Pharmacokinetics of three newer quinolones in pregnant and lactating women. *Am J Med*. 1989;87(suppl):49S–51S
199. Hofmeyr GJ, Sonnendecker EW. Secretion of the gastrokinetic agent cisapride in human milk. *Eur J Clin Pharmacol*. 1986;30:735–736
200. Smith JA, Morgan JR, Rachlis AR, Papsin FR. Clindamycin in human breast milk [letter]. *Can Med Assoc J*. 1975;112:806
201. Zacharias S, Aguilera E, Assenzo JR, Zanartu J. Effects of hormonal and nonhormonal contraceptives on lactation and incidence of pregnancy. *Contraception*. 1986;33:203–213
202. Meny RG, Naumburg EG, Alger LS, Brill-Miller JL, Brown S. Codeine and the breastfed neonate. *J Hum Lact*. 1993;9:237–240
203. Milunsky JM. Breast-feeding during colchicine therapy for familial Mediterranean fever [letter]. *J Pediatr*. 1991;119:164
204. Ben-Chetrit E, Scherrmann J-M, Levy M. Colchicine in breast milk of patients with familial Mediterranean fever. *Arthritis Rheum*. 1996;39:1213–1217
205. Guillonneau M, Aigrain EJ, Galliot M, Binet MH, Darbois Y. Colchicine is excreted at high concentrations in human breast milk. *Eur J Obstet Gynecol Reprod Biol*. 1995;61:177–178
206. Nilsson S, Mellbin T, Hofvander Y, Sundelin C, Valentin J, Nygren KG. Long-term follow-up of children breast-fed by mothers using oral contraceptives. *Contraception*. 1986;34:443–457
207. Nilsson S, Nygren KG. Transfer of contraceptive steroids to human milk. *Res Reprod*. 1979;11:1–2
208. American Academy of Pediatrics, Committee on Drugs. Breast-feeding and contraception. *Pediatrics*. 1981;68:138–140
209. Barsivala VM, Virkar KD. The effect of oral contraceptives on concentration of various components of human milk. *Contraception*. 1973;7:307–312
210. Borglin NE, Sandholm LE. Effect of oral contraceptives on lactation. *Fertil Steril*. 1971;22:39–41
211. Curtis EM. Oral-contraceptive feminization of a normal male infant: report of a case. *Obstet Gynecol*. 1964;23:295–296
212. Kora SJ. Effect of oral contraceptives on lactation. *Fertil Steril*. 1969;20:419–423
213. Toaff R, Ashkenazi H, Schwartz A, Herzberg M. Effects of oestrogen and progestagen on the composition of human milk. *J Reprod Fertil*. 1969;19:475–482
214. Snider DE Jr, Powell KE. Should women taking antituberculosis drugs breast-feed? *Arch Intern Med*. 1984;144:589–590
215. Cancela L, Le Boulch N, Miravet L. Relationship between the vitamin D content of maternal milk and the vitamin D status of nursing women and breast-fed infants. *J Endocrinol*. 1986;110:43–50
216. Rothberg AD, Pettifor JM, Cohen DF, Sonnendecker EW, Ross FP. Maternal-infant vitamin D relationships during breast-feeding. *J Pediatr*. 1982;101:500–503
217. Greer FR, Hollis BW, Napoli JL. High concentrations of vitamin D2 in human milk associated with pharmacologic doses of vitamin D2. *J Pediatr*. 1984;105:61–64
218. Greenhalf JO, Leonard HS. Laxatives in the treatment of constipation in pregnant and breast-feeding mothers. *Practitioner*. 1973;210:259–263
219. Dreisbach JA. Sulphone levels in breast milk of mothers on sulphone therapy. *Lepr Rev*. 1952;23:101–106
220. Mortimer EA Jr. Drug toxicity from breast milk [letter]? *Pediatrics*. 1977;60:780–781
221. FitzJohn TP, Williams DG, Laker MF, Owen JP. Intravenous urography during lactation. *Br J Radiol*. 1982;55:603–605
222. Loughnan PM. Digoxin excretion in human breast milk. *J Pediatr*. 1978;92:1019–1020
223. Levy M, Granit L, Laufer N. Excretion of drugs in human milk. *N Engl J Med*. 1977;297:789
224. Okada M, Inoue H, Nakamura Y, Kishimoto M, Suzuki T. Excretion of diltiazem in human milk [letter]. *N Engl J Med*. 1985;312:992–993
225. Zylber-Katz E, Linder N, Granit L, Levy M. Excretion of dipyrone metabolites in human breast milk. *Eur J Clin Pharmacol*. 1986;30:359–361
226. MacKintosh D, Buchanan N. Excretion of disopyramide in human breast milk [letter]. *Br J Clin Pharmacol*. 1985;19:856–857
227. Hoppu K, Neuvonen PJ, Korte T. Disopyramide and breast feeding [letter]. *Br J Clin Pharmacol*. 1986;21:553
228. Hofmeyr GJ, van Idlekinge B. Domperidone and lactation [letter]. *Lancet*. 1983;1:647
229. Jorboe CH, Cook LN, Malesic I, Fleischaker J. Dyphylline elimination kinetics in lactating women: blood to milk transfer. *J Clin Pharmacol*. 1981;21:405–410
230. Redman CW, Kelly JG, Cooper WD. The excretion of enalapril and enalaprilat in human breast milk. *Eur J Clin Pharmacol*. 1990;38:99
231. Matsuda S. Transfer of antibiotics into maternal milk. *Biol Res Pregnancy Perinatol*. 1984;5:57–60
232. Nilsson S, Nygren KG, Johansson ED. Transfer of estradiol to human milk. *Am J Obstet Gynecol*. 1978;132:653–657
233. Koup JR, Rose JQ, Cohen ME. Ethosuximide pharmacokinetics in a pregnant patient and her newborn. *Epilepsia*. 1978;19:535–539
234. Steer PL, Biddle CJ, Marley WS, Lantz RK, Sulik PL. Concentration of fentanyl in colostrum after an analgesic dose. *Can J Anaesth*. 1992;39:231–235
235. Lucas BD Jr, Purdy CY, Scarim SK, Benjamin S, Abel SR, Hilleman DE. Terfenadine pharmacokinetics in breast milk in lactating women. *Clin Pharmacol Ther*. 1995;57:398–402
236. McQuinn RL, Pisani A, Wafa S, et al. Flecainide excretion in human breast milk. *Clin Pharmacol Ther*. 1990;48:262–267
237. Wagner X, Jouglard J, Moulin M, Miller AM, Petitjean J, Pisapia A. Coadministration of flecainide acetate and sotalol during pregnancy: lack of teratogenic effects, passage across the placenta, and excretion in human breast milk. *Am Heart J*. 1990;119:700–702
238. Dan M, Weidekamm E, Sagiv R, Portmann R, Zakut H. Penetration of fleroxacin into breast milk and pharmacokinetics in lactating women. *Antimicrob Agents Chemother*. 1993;37:293–296
239. Force RW. Fluconazole concentrations in breast milk. *Pediatr Infect Dis J*. 1995;14:235–236
240. Buchanan RA, Eaton CJ, Koeff ST, Kinkel AW. The breast milk excretion of flufenamic acid. *Curr Ther Res Clin Exp*. 1969;11:533–538
241. Mattern J, Mayer PR. Excretion of fluorescein into breast milk. *Am J Ophthalmol*. 1990;109:598–599
242. Retief FP, Heyns AD, Oosthuizen M, Oelofse R, van Reenen OR. Aspects of folate metabolism in lactating women studied after ingestion of 14C-methylfolate. *Am J Med Sci*. 1979;277:281–288
243. Rofsky NM, Weinreb JC, Litt AW. Quantitative analysis of gadopentetate dimeglumine excreted in breast milk. *J Magn Reson Imaging*. 1993;3:131–132
244. Celiloglu M, Celiker S, Guven H, Tuncok Y, Demir N, Erten O. Gentamicin excretion and uptake from breast milk by nursing infants. *Obstet Gynecol*. 1994;84:263–265
245. Bell RA, Dale IM. Gold secretion in maternal milk [letter]. *Arthritis Rheum*. 1976;19:1374
246. Blau SP. Letter: metabolism of gold during lactation. *Arthritis Rheum*. 1973;16:777–778
247. Gottlieb NL. Suggested errata. *Arthritis Rheum*. 1974;17:1057

248. Ostensen M, Skavdal K, Myklebust G, Tomassen Y, Aarbakke J. Excretion of gold into human breast milk. *Eur J Clin Pharmacol*. 1986;31:251–252
249. Bennett PN, Humphries SJ, Osborne JP, Clarke AK, Taylor A. Use of sodium aurothiomalate during lactation. *Br J Clin Pharmacol*. 1990;29:777–779
250. Cote CJ, Kenepp NB, Reed SB, Strobel GE. Trace concentrations of halothane in human breast milk. *Br J Anaesth*. 1976;48:541–543
251. Liedholm H, Wahlin-Boll E, Hanson A, Ingemarsson I, Melander A. Transplacental passage and breast milk concentrations of hydralazine. *Eur J Clin Pharmacol*. 1982;21:417–419
252. Ostensen M, Brown ND, Chiang PK, Aarbakke J. Hydroxychloroquine in human breast milk. *Eur J Clin Pharmacol*. 1985;28:357
253. Nation RL, Hackett LP, Dusci LJ, Ilett KF. Excretion of hydroxychloroquine in human milk. *Br J Clin Pharmacol*. 1984;17:368–369
254. Townsend RJ, Benedetti T, Erickson SH, Gillespie WR, Albert KS. A study to evaluate the passage of ibuprofen into breast-milk. *Drug Intell Clin Pharm*. 1982;16:482–483
255. Townsend RJ, Benedetti TJ, Erickson SH, et al. Excretion of ibuprofen into breast milk. *Am J Obstet Gynecol*. 1984;149:184–186
256. Eeg-Olofsson O, Malmros I, Elwin CE, Steen B. Convulsions in a breast-fed infant after maternal indomethacin [letter]. *Lancet*. 1978;2:215
257. Fairhead FW. Convulsions in a breast-fed infant after maternal indomethacin [letter]. *Lancet*. 1978;2:576
258. Lebedevs TH, Wojnar-Horton RE, Yapp P, et al. Excretion of indomethacin in breast milk. *Br J Clin Pharmacol*. 1991;32:751–754
259. Postellon DC, Aronow R. Iodine in mother's milk [letter]. *JAMA*. 1982;247:463
260. Holmdahl KH. Cholecystography during lactation. *Acta Radiol*. 1955;45:305–307
261. Berlin CM, Lee C. Isoniazid and acetylisoniazid disposition in human milk, saliva and plasma [abstr]. *Fed Proc*. 1979;38:426
262. Kumar AR, Hale TW, Mock RE. Transfer of interferon alfa into human breast milk. *J Hum Lact*. 2000;16:226–228
263. Ogbuokiri JE, Ozumba BC, Okonkwo PO. Ivermectin levels in human breast milk. *Eur J Clin Pharmacol*. 1993;45:389–390
264. Ogbuokiri JE, Ozumba BC, Okonkwo PO. Ivermectin levels in human breast milk. *Eur J Clin Pharmacol*. 1994;46:89–90
265. Dyggve HV, Dam H, Sondergaard E. Influence on the prothrombin time of breast-fed newborn babies of one single dose of vitamin K1 or synkavit given to the mother within 2 hours after birth. *Acta Obstet Gynecol Scand*. 1956;35:440–444
266. Von Kries R, Shearer M, McCarthy PT, Haug M, Harzer G, Goebel U. Vitamin K-1 content of maternal milk: Influence of the stage of lactation, lipid composition, and vitamin K-1 supplements given to the mother. *Pediatr Res*. 1987;22:513–517
267. Moretti ME, Ito S, Koren G. Disposition of maternal ketoconazole in breast milk. *Am J Obstet Gynecol*. 1995;173:1625–1626
268. Wischnik A, Manth SM, Lloyd J, Bullingham R, Thompson JS. The excretion of ketorolac tromethamine into breast milk after multiple oral dosing. *Eur J Clin Pharmacol*. 1989;36:521–524
269. Lunell HO, Kulas J, Rane A. Transfer of labetalol into amniotic fluid and breast milk in lactating women. *Eur J Clin Pharmacol*. 1985;28:597–599
270. Atkinson H, Begg EJ. Concentration of beta-blocking drugs in human milk [letter]. *J Pediatr*. 1990;116:156
271. Diaz S, Herreros C, Juez G, et al. Fertility regulation in nursing women: VII. Influence of Norplant levonorgestrel implants upon lactation and infant growth. *Contraception*. 1985;32:53–74
272. Shaaban MM, Odlind V, Salem HT, et al. Levonorgestrel concentrations in maternal and infant serum during use of subdermal levonorgestrel contraceptive implants, Norplant by nursing mothers. *Contraception*. 1986;33:357–363
273. Shikary ZK, Betrabet SS, Patel ZM, et al. ICMR task force study on hormonal contraception. Transfer of levonorgestrel (LNG) administered through different drug delivery systems from the maternal circulation into the newborn infant's circulation via breast milk. *Contraception*. 1987;35:477–486
274. McCann MF, Moggia AV, Higgins JE, Potts M, Becker C. The effects of a progestin-only oral contraceptive (levonorgestrel 0.03 mg) on breastfeeding. *Contraception*. 1989;40:635–648
275. Mizuta H, Amino N, Ichihara K, et al. Thyroid hormones in human milk and their influence on thyroid function of breast-fed babies. *Pediatr Res*. 1983;17:468–471
276. Zeisler JA, Gaarder TD, De Mesquita SA. Lidocaine excretion in breast milk. *Drug Intell Clin Pharm*. 1986;20:691–693
277. Nikodem VC, Hofmeyr GJ. Secretion of the antidiarrhoeal agent loperamide oxide in breast milk. *Eur J Clin Pharmacol*. 1992;42:695–696
278. Hilbert J, Radwanski E, Affrime MB, Perentesis G, Symchowicz S, Zampaglione N. Excretion of loratadine in human breast milk. *J Clin Pharmacol*. 1988;28:234–239
279. Cruikshank DP, Varner MW, Pitkin RM. Breast milk magnesium and calcium concentrations following magnesium sulfate treatment. *Am J Obstet Gynecol*. 1982;143:685
280. Hannon PR, Duggan AK, Serwint JR, Vogelhut JW, Witter F, DeAngelis C. The influence of medroxyprogesterone on the duration of breast-feeding in mothers in an urban community. *Arch Pediatr Adolesc Med*. 1997;151:490–496
281. Buchanan RA, Eaton CJ, Koeff ST, Kinkel AW. The breast milk excretion of mefenamic acid. *Curr Ther Res Clin Exp*. 1968;10:592–597
282. Wittels B, Scott DT, Sinatra RS. Exogenous opioids in human breast milk and acute neonatal neurobehavior: a preliminary study. *Anesthesiology*. 1990;73:864–869
283. Blinick G, Inturrisi CE, Jerez E, Wallach RC. Methadone assays in pregnant women and progeny. *Am J Obstet Gynecol*. 1975;121:617–621
284. Blinick G, Wallach RC, Jerez E, Ackerman BD. Drug addiction in pregnancy and the neonate. *Am J Obstet Gynecol*. 1976;125:135–142
285. Wojnar-Horton RE, Kristensen JH, Yapp P, Ilett KF, Dusci LJ, Hackett LP. Methadone distribution and excretion into breast milk of clients in a methadone maintenance programme. *Br J Clin Pharmacol*. 1997;44:543–547
286. Geraghty B, Graham EA, Logan B, Weiss EL. Methadone levels in breast milk. *J Hum Lact*. 1997;13:227–230
287. McCarthy JJ, Posey BL. Methadone levels in human milk. *J Hum Lact*. 2000;16:115–120
288. Cooper DS, Bode HH, Nath B, Saxe V, Maloof F, Ridgway EC. Methimazole pharmacology in man: studies using or newly developed radioimmunoassay for methimazole. *J Clin Endocrinol Metab*. 1984;58:473–479
289. Azizi F. Effect of methimazole treatment of maternal thyrotoxicosis on thyroid function in breast-feeding infants. *J Pediatr*. 1996;128:855–858
290. White WB, Andreoli JW, Cohn RD. Alpha-methyldopa disposition in mothers with hypertension and in their breast-fed infants. *Clin Pharmacol Ther*. 1985;37:387–390
291. Shore MF. Drugs can be dangerous during pregnancy and lactations. *Can Pharm J*. 1970;103:358
292. Ilett KF, Hackett LP, Paterson JW, McCormick CC. Excretion of metrizamide in milk. *Br J Radiol*. 1981;54:537–538
293. Lownes HE, Ives TJ. Mexiletine use in pregnancy and lactation. *Am J Obstet Gynecol*. 1987;157:446–447
294. Lewis AM, Patel L, Johnston A, Turner P. Mexiletine in human blood and breast milk. *Postgrad Med J*. 1981;57:546–547
295. Valdivieso A, Valdes G, Spiro TE, Westerman RL. Minoxidil in breast milk [letter]. *Ann Intern Med*. 1985;102:135
296. Terwilliger WG, Hatcher RA. The elimination of morphine and quinine in human milk. *Surg Gynecol Obstet*. 1934;58:823–826
297. Robieux I, Koren G, Vandenbergh H, Schneiderman J. Morphine excretion in breast milk and resultant exposure of a nursing infant. *J Toxicol Clin Toxicol*. 1990;28:365–370
298. Oberlander TF, Robeson P, Ward V, et al. Prenatal and breast milk morphine exposure following maternal intrathecal morphine treatment. *J Hum Lact*. 2000;16:137–142
299. Miller RD, Keegan KA, Thrupp LD, Brann J. Human breast milk concentration of moxalactam. *Am J Obstet Gynecol*. 1984;148:348–349
300. Devlin RG, Duchin KL, Fleiss PM. Nadolol in human serum and breast milk. *Br J Clin Pharmacol*. 1981;12:393–396
301. Belton EM, Jones RV. Haemolytic anaemia due to nalidixic acid. *Lancet*. 1965;2:691
302. Jamali F, Stevens DR. Naproxen excretion in milk and its uptake by the infant. *Drug Intell Clin Pharm*. 1983;17:910–911
303. Liu DT, Savage JM, Donnell D. Nefopam excretion in human milk. *Br J Clin Pharmacol*. 1987;23:99–101
304. Ehrenkranz RA, Ackerman BA, Hulse JD. Nifedipine transfer into human milk. *J Pediatr*. 1989;114:478–480
305. Varsano I, Fischl J, Shochet SB. The excretion of orally ingested nitrofurantoin in human milk. *J Pediatr*. 1973;82:886–887
306. Laumas KR, Malkani PK, Bhatnagar S, Laumas V. Radioactivity in the breast milk of lactating women after oral administration of 3H-norethynodrel. *Am J Obstet Gynecol*. 1967;98:411–413
307. Pincus G, Bialy G, Layne DS, Paniagua M, Williams KI. Radioactivity in the milk of subjects receiving radioactive 19-norsteroids. *Nature*. 1966;212:924–925
308. Olsson B, Bolme P, Dahlstrom B, Marcus C. Excretion of noscapine in human breast milk. *Eur J Clin Pharmacol*. 1986;30:213–215

309. Sioufi A, Hillion D, Lumbroso P, et al. Oxprenolol placental transfer, plasma concentrations in newborns and passage into breast milk. *Br J Clin Pharmacol*. 1984;18:453–456
310. Fidler J, Smith V, De Swiet M. Excretion of oxprenolol and timolol in breast milk. *Br J Obstet Gynaecol*. 1983;90:961–965
311. Leuxner E, Pulver R. Verabreichung von irgapyrin bei schwangeren und wochnerinnen. *MMW Munch Med Wochenschr*. 1956;98:84–86
312. Mirkin B. Diphenylhydantoin: placental transport, fetal localization, neonatal metabolism, and possible teratogenic effects. *J Pediatr*. 1971; 78:329–337
313. Ostensen M. Piroxicam in human breast milk. *Eur J Clin Pharmacol*. 1983;25:829–830
314. McKenzie SA, Selley JA, Agnew JE. Secretion of prednisolone into breast milk. *Arch Dis Child*. 1975;50:894–896
315. Greenberger PA, Odeh YK, Frederiksen MC, Atkinson AJ Jr. Pharmacokinetics of prednisolone transfer to breast milk. *Clin Pharmacol Ther*. 1993;53:324–328
316. Katz FH, Duncan BR. Entry of prednisone into human milk. *N Engl J Med*. 1975;293:1154
317. Pittard WB III, Glazier H. Procainamide excretion in human milk. *J Pediatr*. 1983;102:631–633
318. Diaz S, Jackanicz TM, Herreros C, et al. Fertility regulation in nursing women: VIII. Progesterone plasma levels and contraceptive efficacy of a progesterone-releasing vaginal ring. *Contraception*. 1985;32:603–622
319. Kunka RL, Venkataramanan R, Stern RM, Ladik CF. Excretion of propoxyphene and norpropoxyphene in breast milk. *Clin Pharmacol Ther*. 1984;35:675–680
320. Levitan AA, Manion JC. Propranolol therapy during pregnancy and lactation. *Am J Cardiol*. 1973;32:247
321. Karlberg B, Lundberg D, Aberg H. Letter: excretion of propranolol in human breast milk. *Acta Pharmacol Toxicol (Copenh)*. 1974;34:222–224
322. Bauer JH, Pape B, Zajicek J, Groshong T. Propranolol in human plasma and breast milk. *Am J Cardiol*. 1979;43:860–862
323. Kampmann JP, Johansen K, Hansen JM, Helweg J. Propylthiouracil in human milk: revision of a dogma. *Lancet*. 1980;1:736–737
324. Findlay JW, Butz RF, Sailstad JM, Warren JT, Welch RM. Pseudoephedrine and triprolidine in plasma and breast milk of nursing mothers. *Br J Clin Pharmacol*. 1984;18:901–906
325. Hardell LI, Lindstrom B, Lonnerholm G, Osterman PO. Pyridostigmine in human breast milk. *Br J Clin Pharmacol*. 1982;14:565–567
326. Clyde DF, Shute GT, Press J. Transfer of pyrimethamine in human milk. *J Trop Med Hyg*. 1956;59:277
327. Hill LM, Malkasian GD Jr. The use of quinidine sulfate throughout pregnancy. *Obstet Gynecol*. 1979;54:366–368
328. Horning MG, Stillwell WG, Nowlin J, Lertratanangkoon K, Stillwell RN, Hill RM. Identification and quantification of drugs and drug metabolites in human breast milk using gas chromatography mass spectrometry computer methods. *Mod Probl Paediatr*. 1975;15:73–79
329. Werthmann MW JR, Krees SV. Quantitative excretion of Senokot in human breast milk. *Med Ann Dist Columbia*. 1973;42:4–5
330. Hackett LP, Wojnar-Horton RE, Dusci LJ, Ilett KF, Roberts MJ. Excretion of sotalol in breast milk. *Br J Clin Pharmacol*. 1990;29:277–278
331. Phelps DL, Karim Z. Spironolactone: relationship between concentrations of dethioacetylated metabolite in human serum milk. *J Pharm Sci*. 1977;66:1203
332. Foulds G, Miller RD, Knirsch AK, Thrupp LD. Sulbactam kinetics and excretion into breast milk in postpartum women. *Clin Pharmacol Ther*. 1985;38:692–696
333. Jarnerot G, Into-Malmberg MB. Sulphasalazine treatment during breast feeding. *Scand J Gastroenterol*. 1979;14:869–871
334. Berlin CM Jr, Yaffe SJ. Disposition of salicylazosulfapyridine (Azulfidine) and metabolites in human breast milk. *Dev Pharmacol Ther*. 1980;1:31–39
335. Kauffman RE, O'Brien C, Gilford P. Sulfisoxazole secretion into human milk. *J Pediatr*. 1980;97:839–841
336. Wojnar-Horton RE, Hackett LP, Yapp P, Dusci LJ, Paech M, Ilett KF. Distribution and excretion of sumatriptan in human milk. *Br J Clin Pharmacol*. 1996;41:217–221
337. Chaiken P, Chasin M, Kennedy B, Silverman BK. Suprofen concentrations in human breast milk. *J Clin Pharmacol*. 1983;23:385–390
338. Lindberberg C, Boreus LO, de Chateau P, Lindstrom B, Lonnerholm G, Nyberg L. Transfer of terbutaline into breast milk. *Eur J Respir Dis Suppl*. 1984;134:87–91
339. Tetracycline in breast milk. *Br Med J*. 1969;4:791
340. Posner AC, Prigot A, Konicoff NG. Further observations on the use of tetracycline hydrochloride in prophylaxis and treatment of obstetric infections. In: Welch H, Marti-Ibanez F, eds. *Antibiotics Annual 1954–1955.* New York, NY: Medical Encyclopedia Inc; 1955:594
341. Yurchak AM, Jusko WJ. Theophylline secretion into breast milk. *Pediatrics*. 1976;57:518–520
342. Andersen LW, Qvist T, Hertz J, Mogensen F. Concentrations of thiopentone in mature breast milk and colostrum following an induction dose. *Acta Anaesthesiol Scand*. 1987;31:30–32
343. Williams RH, Kay GA, Jandorf BJ. Thiouracil: its absorption, distribution, and excretion. *J Clin Invest*. 1944;23:613–627
344. von Kobyletzki D, Dalhoff A, Lindemeyer H, Primavesi CA. Ticarcillin serum and tissue concentrations in gynecology and obstetrics. *Infection*. 1983;11:144–149
345. Moiel RH, Ryan JR. Tolbutamide orinase in human breast milk. *Clin Pediatr*. 1967;6:480
346. Sagranes R, Waller ES, Goehrs HR. Tolmetin in breast milk. *Drug Intell Clin Pharm*. 1985;19:55–56
347. Arnauld R. Etude du passage de la trimethoprime dans le lait maternel. *Ouest Med*. 1972;25:959
348. Miller RD, Salter AJ. The passage of trimethoprim/sulphamethoxazole into breast milk and its significance. Proceedings of the 8th International Congress of Chemotherapy, Athens. *Hellenic Soc Chemother*. 1974;1:687
349. Alexander FW. Sodium valproate and pregnancy. *Arch Dis Child*. 1979;54:240
350. von Unruh GE, Froescher W, Hoffman F, Niesen M. Valproic acid in breast milk: how much is really there? *Ther Drug Monit*. 1984;6:272–276
351. Anderson P, Bondesson U, Mattiasson I, Johansson BW. Verapamil and norverapamil in plasma and breast milk during breast feeding. *Eur J Clin Pharmacol*. 1987;31:625–627
352. Orme ML, Lewis PJ, de Swiet M, et al. May mothers given warfarin breast-feed their infants? *Br Med J*. 1977;1:1564–1565
353. Pons G, Francoual C, Guillet P, et al. Zolpidem excretion in breast milk. *Eur J Clin Pharmacol*. 1989;37:245–248
354. Wild CP, Pionneau FA, Montesano R, Mutiro CF, Chetsanga CJ. Aflatoxin detected in human breast milk by immunoassay. *Int J Cancer*. 1987;40:328–333
355. Maxwell SM, Apeagyei F, de Vries HR, et al. Aflatoxins in breast milk, neonatal cord blood and sera of pregnant women. *J Toxicol Toxin Rev*. 1989;8:19–29
356. Zarba A, Wild CP, Hall AJ, et al. Aflatoxin M1 in human breast milk from The Gambia, west Africa, quantified by combined monoclonal antibody immunoaffinity chromatography HPLC. *Carcinogenesis*. 1992; 13:891–894
357. Stegink LD, Filer LJ Jr, Baker GL. Plasma, erythrocyte human milk levels of free amino acids in lactating women administered aspartame or lactose. *J Nutr*. 1979;109:2173–2181
358. Mangurten HH, Kaye CI. Neonatal bromism secondary to maternal exposure in a photographic laboratory. *J Pediatr*. 1982;100:596–598
359. Radisch B, Luck W, Nau H. Cadmium concentrations in milk and blood of smoking mothers. *Toxicol Lett*. 1987;36:147–152
360. Miyazaki T, Akiyama K, Kaneko S, Horii S, Yamagishi T. Chlordane residues in human milk. *Bull Environ Contam Toxicol*. 1980;25:518–523
361. Resman BH, Blumenthal P, Jusko WJ. Breast milk distribution of theobromine from chocolate. *J Pediatr*. 1977;91:477–480
362. Wolff MS. Occupationally derived chemicals in breast milk. *Am J Ind Med*. 1983;4:259–281
363. Egan H, Goulding R, Roburn J, Tatton JO. Organo-chlorine pesticide residues in human fat and human milk. *Br Med J*. 1965;2:66–69
364. Quinby GE, Armstrong JF, Durham WF. DDT in human milk. *Nature*. 1965;207:726–728
365. Bakken AF, Seip M. Insecticides in human breast milk. *Acta Paediatr Scand*. 1976;65:535–539
366. Adamovic VM, Sokic B, Smiljanski MJ. Some observations concerning the ratio of the intake of organochlorine insecticides through food and amounts excreted in the milk of breast-feeding mothers. *Bull Environ Contam Toxicol*. 1978;20:280–285
367. Savage EP, Keefe TJ, Tessari JD, et al. National study of chlorinated hydrocarbon insecticide residues in human milk, USA. I. Geographic distribution of dieldrin, heptachlor, heptachlor epoxide, chlordane, oxychlordane, and mirex. *Am J Epidemiol*. 1981;113:413–422
368. Wilson DJ, Locker DJ, Ritzen CA, Watson JT, Schaffner W. DDT concentrations in human milk. *Am J Dis Child*. 1973;125:814–817
369. Bouwman H, Becker PJ, Cooppan RM, Reinecke AJ. Transfer of DDT used in malaria control to infants via breast milk. *Bull World Health Organ*. 1992;70:241–250
370. Stevens MF, Ebell GF, Psaila-Savona P. Organochlorine pesticides in Western Australian nursing mothers. *Med J Aust*. 1993;158:238–241
371. Emanuel B, Schoenfeld A. Favism in a nursing infant. *J Pediatr*. 1961; 58:263–266

372. Simpson WJ, Tuba J. An investigation of fluoride concentration in the milk of nursing mothers. *J Oral Med*. 1968;23:104–106
373. Esala S, Vuori E, Helle A. Effect of maternal fluorine intake on breast milk fluorine content. *Br J Nutr*. 1982;48:201–204
374. Dreyfus-See G. Le passage dans le lait des aliments ou medicaments absorbes par denourrices. *Rev Med Interne*. 1934;51:198
375. Ando M, Hirano S, Itoh Y. Transfer of hexachlorobenzene (HCB) from mother to newborn baby through placenta and milk. *Arch Toxicol*. 1985;56:195–200
376. West RW, Wilson DJ, Schaffner W. Hexachlorophene concentrations in human milk. *Bull Environ Contam Toxicol*. 1975;13:167–169
377. Rabinowitz M, Leviton A, Needelman H. Lead in milk and infant blood: a dose-response model. *Arch Environ Health*. 1985;40:283–286
378. Sternowsky JH, Wessolowski R. Lead and cadmium in breast milk. Higher levels in urban vs rural mothers during the first 3 months of lactation. *Arch Toxicol*. 1985;57:41–45
379. Namihira D, Saldivar L, Pustilnik N, Carreon GJ, Salinas ME. Lead in human blood and milk from nursing women living near a smelter in Mexico City. *J Toxicol Environ Health*. 1993;38:225–232
380. Baum CR, Shannon MW. Lead in breast milk. *Pediatrics*. 1996;97:932
381. Koos BJ, Longo LD. Mercury toxicity in the pregnant woman, fetus, and newborn infant. A review. *Am J Obstet Gynecol*. 1976;126:390–409
382. Amin-Zaki L, Elhassani S, Majeed MA, Clarkson TW, Doherty RA, Greenwood MR. Studies of infants postnatally exposed to methylmercury. *J Pediatr*. 1974;85:81–84
383. Pitkin RM, Bahns JA, Filer LJ Jr, Reynolds WA. Mercury in human maternal and cord blood, placenta, and milk. *Proc Soc Exp Biol Med*. 1976;151:565–567
384. Hersh J, Bono JV, Padgett DE, Mancuso CA. Methyl methacrylate levels in the breast milk of a patient after total hip arthroplasty. *J Arthroplasty*. 1995;10:91–92
385. Stegink LD, Filer LJ Jr, Baker GL. Monosodium glutamate: effect on plasma and breast milk amino acid levels in lactating women. *Proc Soc Exp Biol Med*. 1972;140:836–841
386. Miller RW. Pollutants in breast milk: PCBs and cola-colored babies [editorial]. *J Pediatr*. 1977;90:510–511
387. Rogan WJ, Bagniewska A, Damstra T. Pollutants in breast milk. *N Engl J Med*. 1980;302:1450–1453
388. Wickizer TM, Brilliant LB, Copeland R, Tilden R. Polychlorinated biphenyl contamination of nursing mothers' milk in Michigan. *Am J Public Health*. 1981;71:132–137
389. Brilliant LB, Van Amburg G, Isbister J, Bloomer AW, Humphrey H, Price H. Breast-milk monitoring to measure Michigan's contamination with polybrominated biphenyls. *Lancet*. 1978;2:643–646
390. Wickizer TM, Brilliant LB. Testing for polychlorinated biphenyls in human milk. *Pediatrics*. 1981;68:411–415
391. Bagnell PC, Ellenberg HA. Obstructive jaundice due to a chlorinated hydrocarbon in breast milk. *Can Med Assoc J*. 1977;117:1047–1048
392. Higginbottom MC, Sweetman L, Nyhan WL. A syndrome of methylmalonic aciduria, homocystinuria, megaloblastic anemia neurologic abnormalities in a vitamin B12-deficient breast-fed infant of a strict vegetarian. *N Engl J Med*. 1978;299:317–323

The Transfer of Drugs and Other Chemicals Into Human Milk

Committee on Drugs

Pediatrics 2001;108;776
DOI: 10.1542/peds.108.3.776

AMERICAN ACADEMY OF PEDIATRICS

Committee on Child Health Financing and Committee on Substance Abuse

Improving Substance Abuse Prevention, Assessment, and Treatment Financing for Children and Adolescents

ABSTRACT. The numbers of children, adolescents, and families affected by substance abuse have sharply increased since the early 1990s. The American Academy of Pediatrics recognizes the scope and urgency of this problem and has developed this policy statement for consideration by Congress, federal and state agencies, employers, national organizations, health care professionals, health insurers, managed care organizations, advocacy groups, and families.

ABBREVIATIONS. SCHIP, State Children's Health Insurance Program; LSD, lysergic acid diethylamide; PCP, phencyclidine hydrochloride; ADHD, attention-deficit/hyperactivity disorder.

INTRODUCTION

Leading the list of Americans' concerns for children is drug abuse, according to a 1997 Harvard study.[1] The numbers of children, adolescents, and families affected by substance abuse have sharply increased since the early 1990s.[2] Unfortunately, the availability of and financing for substance abuse prevention, assessment, and treatment have not kept pace with the needs of young people. Access to substance abuse services has decreased during the past decade because of inadequate insurance coverage, managed care controls, and low reimbursement rates. Although there are no national estimates of unmet need for substance abuse services for children, the surgeon general estimated that as many as 75% to 80% of children who are in need of mental health treatment fail to receive it.[3] The consequences of failing to intervene early and not providing age-appropriate substance abuse and mental health treatment are substantial and long-term.

This policy statement includes a summary of the prevalence of substance abuse among children and adolescents along with a review of financing problems experienced by those who are insured through private health insurance, Medicaid, and the State Children's Health Insurance Program (SCHIP), and those who are uninsured. The statement concludes with specific recommendations for financing substance abuse prevention, assessment, and treatment for children and adolescents. By necessity, these recommendations incorporate mental health problems and interventions because of the high prevalence of comorbid psychiatric disorders among children with substance abuse problems.

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

PEDIATRICS (ISSN 0031 4005).

PREVALENCE AND IMPACT OF SUBSTANCE ABUSE AMONG CHILDREN AND ADOLESCENTS

Substance abuse by young people has increased in the past decade, and it is occurring at younger ages. According to results from the *Monitoring the Future Study* conducted in 1999 at the University of Michigan Institute for Social Research, 33% of 12th graders and 9% of eighth graders reported being drunk 1 or more times during the last 30 days.[2] As many as 23% of high school seniors and 10% of eighth graders reported using marijuana in the last 30 days, up from 14% and 3%, respectively, in 1991. The percentage of adolescents who reported using hallucinogens, lysergic acid diethylamide (LSD), phencyclidine hydrochloride (PCP), cocaine and crack cocaine, heroin, amphetamines, methamphetamines, barbiturates, and tranquilizers also increased between 1991 and 1999. In addition, cigarette use among adolescents, which is a risk factor for use of marijuana and other illicit drugs, also markedly increased during this decade. In 1999, 35% of 12th graders reported smoking cigarettes during the last 30 days, up from 28% in 1991. Among eighth graders, the reported 30-day cigarette use rate increased from 14% to 18%.

Epidemiologic data revealed that 9% of adolescent females and 20% of adolescent males meet adult diagnostic criteria for an alcohol use disorder.[4] Among adolescents and young adults with a substance abuse disorder, 41% to 65% also have a mental health disorder.[3] The most common of these are depression, conduct disorder, and attention-deficit/hyperactivity disorder (ADHD) in combination with conduct disorder. ADHD and learning disorders in combination with depression and anxiety disorders also carry a high risk of substance abuse. If the significant number of drug-exposed infants and the 1 in 6 children exposed to substance abuse within their families are added to these estimates, the size of the population affected by substance abuse and, therefore, potentially needing assistance dramatically increases.[5]

Obtaining accurate estimates of the prevalence of substance abuse among children and adolescents is very difficult. Most national studies survey only students, but many high-risk youth do not regularly attend school and, thus, are not included in these estimates. Other difficulties in obtaining reliable estimates are the results of coverage and reimbursement problems. Rather than using a substance abuse

diagnosis, health care professionals may be using procedure codes for treating associated symptoms of substance abuse, such as fatigue, irritability, weight loss, headache, abdominal pain, or depression. The lack of use of substance abuse codes may also reflect health care professionals' attempt to avoid stigmatizing a child. Consequently, existing prevalence data likely underestimate the scope of the problem.

Data specific to adolescents are limited, but there is growing evidence that successful early intervention and treatment carries significant benefit for the individual and society.[6] The most appropriate assessment of costs and benefits of treatment are based on broader outcome measures rather than abstinence alone. Despite the fact that there is no single treatment approach that works for all patients, standard treatments have been shown to produce significant decreases in drug use and in drug-related problems of crime, family violence, unemployment, welfare dependence, underachievement, and other antisocial behaviors.[7]

EXTENT OF FINANCING PROBLEMS FOR SUBSTANCE ABUSE SERVICES

Although most families whose children require substance abuse services experience financial difficulties related to high out-of-pocket expenses, those who are uninsured are at the greatest disadvantage. An estimated 14 million or 15.9% of children younger than 22 years had no health insurance coverage in 1999.[8] These families must rely exclusively on publicly funded services through their state's substance abuse and mental health agencies or must pay for care themselves. Often, uninsured youth receive uncompensated hospital and emergency care for acute symptoms only, which is seldom coordinated with primary care and behavioral health services. Unfortunately, publicly supported substance abuse and mental health services are underfunded and are typically available only for youth with serious emotional disturbances whose families meet a certain income threshold. Many young people, particularly those who are just beginning to abuse alcohol and other drugs, do not have serious emotional disturbances and, therefore, do not qualify for state-funded services. Moreover, children who are privately insured but without adequate substance abuse and mental health benefits are seldom eligible for state-funded services.

Most children under age 22 (65.4% or 57.7 million) are privately insured by plans purchased by their families individually or through their employers.[8] Often, these families rapidly exhaust their annual and even lifetime allotment of substance abuse benefits and must pay for needed services themselves or rely exclusively on self-help organizations, such as Alcoholics Anonymous and Narcotics Anonymous. Most private health insurance plans impose benefit limitations and cost-sharing requirements on substance abuse and mental health services that are greater than those imposed on general medical services.[9,10] For example, coverage of outpatient substance abuse services, when available, is typically short in duration and is often capped at an inadequate number of visits. Family therapy is often excluded. Inpatient substance abuse services are sometimes excluded altogether or covered only for acute detoxification purposes. Coverage of prevention, assessment, early intervention, relapse prevention, crisis intervention, partial hospitalization or day treatment, and residential care is seldom covered by private plans. Mental health benefits, however, are often provided somewhat more generously than are substance abuse benefits.[2,11]

In addition to benefit limitations, many private insurance plans require higher copayments or coinsurance in addition to separate deductibles for substance abuse benefits.[11] The Mental Health Parity Act of 1996 prohibits plans from imposing higher annual and lifetime out-of-pocket maximums for mental health services than for general medical services.[12] Although many states have passed mental health parity legislation, substance abuse parity is often not included. Thus, many of the gains that have been made in achieving parity only apply to mental health. This may perpetuate the pattern of physicians using procedure codes for treating associated symptoms of substance abuse rather than codes for a substance abuse diagnosis, which further distorts prevalence statistics. Also, the lack of specific data furthers the misconception that substance abuse is a consequence of mental illness rather than a primary disease, a comorbidity, or a significant precipitant of mental health problems.

Medicaid, the source of insurance for 16.4 million or 18.7% of all children younger than 22 years, has historically covered fewer adolescents than younger children.[8] Not until the enactment of SCHIP have many states taken the option to expand Medicaid to cover all adolescents from families with incomes at 100% of the federal poverty level. Unlike private coverage, Medicaid's benefits for children and adolescents are comprehensive and cover a continuum of inpatient and outpatient substance abuse and mental health services. Although Medicaid benefits are expansive, reimbursement rates have been very low and, as a result, serve as a disincentive to provide qualified pediatric and substance abuse services.

Regardless of the source of health insurance coverage, most substance abuse and mental health services are delivered by managed behavioral plans, distinct from general managed care plans and primary pediatric medical care. Although the literature shows that managed behavioral health plans have provided greater overall access to mental health services and a greater continuum of care, it also shows that as a result of tight utilization management, rates of ambulatory visits and hospitalizations have decreased.[3] Pediatricians and other referring health care providers report persistent problems in obtaining authorization for substance abuse treatment for children and adolescents. Often, utilization review criteria address the needs of adults, and children's conditions must be severe or associated with comorbidities to warrant extended counseling or hospital stays. For example, criteria such as chronicity, loss of work, and adult comorbidities—which are inappro-

priate for young people—are often used to determine whether substance abuse treatment is medically necessary. Moreover, many behavioral health plans have closed panels of mental health professionals with limited pediatric substance abuse training or experience. Seldom does coordination between primary care and behavioral health care take place effectively. Problems have also been reported in sharing medical information between behavioral health plans and primary care providers.

Compounding these difficulties is the overall shortage of ambulatory and inpatient substance abuse and mental health services for children and adolescents. Many inpatient facilities have closed during recent years. These shortages have resulted from many factors, including historically low rates of reimbursement provided to substance abuse and mental health professionals. To serve this population effectively is very labor intensive, and insurance dollars and public funds consistently fail to provide adequate reimbursement. Also contributing to payment and service gaps is the fact few insurers recognize the new *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: Primary Care Version*, which was developed jointly by the pediatric and mental health communities to encourage earlier identification and primary behavioral interventions.[13] In addition, pediatricians are seldom able to receive reimbursement for providing counseling and education services to children at high risk of developing substance abuse problems.

Serious problems exist in the availability and organization of behavioral health services for the treatment of substance abuse problems among youth. Although there are substantial problems with low payment and persistent obstacles in gaining access to needed interventions, pediatricians are in a unique role to identify and intervene with children and adolescents who have or are at risk of substance abuse problems.[14] In addition, a cadre of physicians needs to be trained in the field of pediatric addiction medicine. However, the recruitment and retention of pediatricians and other health care providers in the field of addiction medicine has been very difficult, which seriously compromises the provision of high-quality substance abuse care.[14]

FINANCING RECOMMENDATIONS

Many changes need to be made to the financing and delivery of substance abuse care to improve the availability of services for all children and adolescents. Change in this area, however, is not likely to occur without the participation of a coalition of national and state legislators, public purchasers, employers, health professionals, families, and health services researchers. The American Academy of Pediatrics, together with other participating behavioral health organizations and consumer groups, released a consensus statement on insurance coverage for mental health and substance abuse services for children and adolescents, which highlights the deterioration of mental health and substance abuse services and recommends access, coordination, and monitoring strategies for achieving service improvements.[15] That article and this policy statement on financing should serve as blueprints for Congress, federal and state policy-makers, and employers.

The American Academy of Pediatrics recommends that Congress authorize the Substance Abuse and Mental Health Services Administration to conduct a comprehensive national study of the supply, distribution, financing, and quality of substance abuse prevention, assessment, and treatment services for children and adolescents.

Additional recommendations address the needs of all children, regardless of insurance status. In addition, there are specific recommendations that apply to those with private insurance, those with Medicaid or SCHIP coverage, and those who are uninsured.

For All Children and Adolescents, Regardless of Insurance Status

1. Ensure that substance abuse and mental health benefits are sufficient in amount, duration, and scope to reasonably achieve their purpose.
2. Allow pediatricians and safety net providers trained or experienced in substance abuse prevention, assessment, evaluation, and management services to be included in panels of professionals that provide these services.
3. Create an integrated system of referral and treatment for substance abuse that is consistent with the referral and treatment process of other chronic diseases.
4. Simplify and coordinate processes for families attempting to access substance abuse and mental health services for their children across public and private insurers plans, and public programs.
5. Improve preauthorization and utilization review criteria to be consistent with national standards on the treatment of substance abuse among youth developed by the American Academy of Pediatrics,[16] the Substance Abuse and Mental Health Services Administration,[17] the National Institute on Alcohol Abuse and Alcoholism,[18] and the American Society of Addiction Medicine.[19]
6. Provide reasonable compensation and allow reimbursement of counseling, coordination, and consultation procedure codes to enable pediatricians and other primary care providers to provide primary substance abuse and mental health services.
7. Adjust capitation rates to take into account substance abuse service needs and recommended clinical guidelines for length of care for children and adolescents rather than relying on historic utilization rates to establish capitation amounts.[19]
8. Encourage payers to reimburse for individual and group counseling and risk factor reduction interventions for children at risk of substance abuse problems.
9. Establish financing mechanism for smoking cessation programs for children.
10. Create financial incentives for comanagement of substance abuse treatment between primary care and behavioral health care (eg, transferring some behavioral health dollars into primary care).

11. Create mechanisms for sharing risk among public and private payors to allow for coverage of a comprehensive set of interventions to better manage children with complex cases.
12. Establish clear delineation of responsibilities with regard to children involved with multiple state agencies and required court-ordered treatment.
13. Ensure that health plans and health care providers adopt medical record and billing procedures to protect the confidentiality of children and adolescents.

For Privately Insured Children and Adolescents

1. Extend benefits to include a broader array of substance abuse prevention, assessment, and treatment services.
2. Establish parity between medical services and substance abuse and mental health services so that coverage of the management of substance abuse and mental health disorders is the same as coverage of other chronic conditions.
3. Reduce limitations on substance abuse and mental health services and allow for substitution of mental health and substance abuse benefits and use of alternative sites of care, including schools and homes.
4. Eliminate exclusions for specific diagnostic categories, chronic disorders, and preexisting conditions.
5. Reduce cost-sharing requirements for substance abuse services to encourage their use.

For Medicaid and SCHIP Insured Children and Adolescents

1. Target outreach efforts to ensure that Medicaid- and SCHIP-eligible adolescents are covered.
2. Ensure that a continuum of substance abuse and mental health services for children and adolescents are specified in state Medicaid plans and contracts, using a variety of benefit categories, including Early and Periodic Screening, Diagnosis, and Treatment expanded services.
3. In non-Medicaid SCHIP programs, offer supplemental or wraparound benefits to allow expanded behavioral health coverage for those who meet certain risk criteria.

For Uninsured Children and Adolescents

1. Expand SCHIP income eligibility levels to the maximum possible.
2. Expand the eligibility criteria of states' substance abuse and mental health service programs to include children with all levels of substance abuse and mental health risk.
3. Increase funding of state substance abuse and mental health programs for children and adolescents on the basis of comprehensive needs assessments and behavioral risk profiles of local communities.
4. Earmark a reasonable share of state block grants for prevention, assessment, and treatment services for children and adolescents.
5. Identify new revenue sources to increase availability of substance abuse services, including tobacco settlement funds and new taxes on alcohol.

REFERENCES

1. Harvard University, The Robert Wood Johnson Foundation, and University of Maryland. *American Attitudes Toward Children's Health Care Issues*. Princeton, NJ: Harvard University School of Public Health; 1997
2. Johnston LD, O'Malley PM, Bachman JG. *The Monitoring the Future National Survey Results on Adolescent Drug Use. Overview of Key Findings, 1999*. Bethesda, MD: National Institute on Drug Abuse; 2000. Available at: http://www.monitoringthefuture.org/pubs.html. Accessed December 18, 2000
3. US Department of Health and Human Services. *Mental Health: A Report of the Surgeon General*. Rockville, MD: US Department of Health and Human Services; 1999
4. Cohen P, Cohen J, Kasen S, et al. An epidemiological study of disorders in late childhood and adolescence—I. Age- and gender-specific prevalence. *J Child Psychol Psychiatry*. 1993;34:851–867
5. Grant B. Estimates of US children exposed to alcohol abuse and dependence in the family. *Am J Public Health*. 2000;90:112–115
6. Bukowski WJ, Evans RI, eds. *Cost-Benefit/Cost-Effectiveness Research of Drug Abuse Prevention: Implications for Programming and Policy*. Rockville, MD: National Institute on Drug Abuse; 1998
7. National Institute on Drug Abuse. *Principles of Drug Addiction Treatment*. Rockville, MD: National Institute on Drug Abuse, National Institutes of Health; 1999. NIH Publ. No. 00-4180. Available at: http://www.nida.nih.gov/PODAT/PODATindex.html. Accessed February 8, 2001
8. American Academy of Pediatrics, Division of Health Policy Research. *US Children's Health Insurance Status and Public Program Participation: State Reports, 1999 and 2001 Estimates*. Elk Grove Village, IL: American Academy of Pediatrics; 2000
9. Buck JA, Teich JL, Umland B, Stein M. Behavioral health benefits in

employer-sponsored health plans, 1997. *Health Aff (Millwood)*. 1999;18: 67–78
10. Dilonardo J, Chalk M. *Employer-Sponsored Health Plans Still Limit Alcohol and Other Drug Coverage.* Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 1999
11. Buck JA, Umland B. Covering mental health and substance abuse services. *Health Aff (Millwood)*. 1997;16:120–126
12. Mental Health Parity Act of 1996. Pub L No. 104–204 (1997)
13. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: Primary Care Version*. 4th ed. Washington, DC: American Psychiatric Association; 1996
14. American Academy of Pediatrics, Committee on Substance Abuse. Tobacco, alcohol, and other drugs: the role of the pediatrician in prevention and management of substance abuse. *Pediatrics*. 1998;101:125–128
15. Academy for Eating Disorders, American Academy of Child and Adolescent Psychiatry, American Academy of Pediatrics, American Psychiatric Association, American Psychological Association, Family Voices, International Society of Psychiatric-Mental Health Nurses, and Society for Developmental and Behavioral Pediatrics. Consensus statement on insurance coverage of mental health and substance abuse services for children and adolescents. *Pediatrics*. 2000;106:860–862
16. American Academy of Pediatrics. Current AAP policy statements. Available at: http://www.aap.org/policy/pprgtoc.cfm. Accessed June 11, 2001
17. Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment. Treatment improvement protocol series. Available at: http://www.samhsa.gov/centers/csat/csat.html. Accessed June 1, 2001
18. National Institute on Alcohol Abuse and Alcoholism. Reports, manuals, and guides. Available at: http://www.niaaa.nih.gov/publications/guides.htm. Accessed June 11, 2001
19. American Society of Addiction Medicine. *Patient Placement Criteria, Second Edition.* Chevy Chase, MD: American Society of Addiction Medicine; 2000

ERRATUM

An error occurred in the policy statement "Transfer of Drugs and Other Chemicals Into Human Milk" (Pediatrics 2001;108:776–789). In the first paragraph under "Breastfeeding and Smoking," line 14, the word "acotinine" should be "cotinine."

The Transfer of Drugs and Other Chemicals Into Human Milk

Committee on Drugs

Pediatrics 2001;108;776
DOI: 10.1542/peds.108.3.776