ABSTRACT

World health experts encourage women to breastfeed, but many primary care physicians, obstetricians, and psychiatrists are hesitant to encourage new mothers who are taking psychiatric medications to do so. Unfortunately, there are only a few case-controlled studies on the safety of psychotropics in breastfeeding. This article outlines the benefits of breastfeeding, both for the infant and for the mother; postpartum illness and its effect on the mother and infant; and the existing data on the most commonly used psychotropics. The effect of psychotropics on the nursing infant is examined and summarized.

INTRODUCTION

Many new mothers who need to take medications for psychiatric illness would like to breastfeed but are hesitant, as they are uncertain about the safety of these medications for their infant. There are currently very few, and no large, case-controlled studies on the safety of psychotropics in lactation. Prospective, randomized, double-blind, placebo-controlled trials cannot be conducted for obvious ethical reasons. Consequently, most of the current information available is compiled from case series and case reports and remains limited in quality and quantity. Drugs that have been on the market for some time (selective serotonin reuptake inhibitors [SSRIs], some mood stabilizers, benzodiazepines, typical antipsychotics) have accumulated relatively large or stable data. Newer drugs (dual-action antidepressants, atypical antipsychotics) have only scarce data. As a result of the lack of controlled studies, physicians are often confronted with a dilemma as to whether or not to prescribe medications for women who want to breastfeed.

In cases in which medication is felt to be necessary, consultation between the mother’s physician (primary care physician [PCP], obstetrician, and/or psychiatrist) and the pediatrician is recommended for choosing the safest options. The potential benefits of breastfeeding should always be weighed against the risks to the neonate. This should be fully discussed with the patient. The treating physician should review with the patient the available information about the risks and benefits. Discussion of risks and benefits of breastfeeding for a mother using psychiatric medications should be documented. Mothers should be made aware that the use of psychiatric medication may have other adverse consequences on the infant that are not known, as our knowledge is based on the limited data we have available at this time. If the patient decides to continue breastfeeding while using psychiatric medication, the infant should be monitored by the pediatrician for possible side effects.

This article first reviews the benefits of breastfeeding both for the infant and the mother. It discusses postpartum psychiatric illness that requires psychotropic medication. It then provides an update on the current data published about the most commonly used psychotropic agents and their safety in breastfeeding.
A closer look into this topic has become timely with the recent (May 2008) public announcement of the Food and Drug Administration’s proposed final rule on pregnancy and lactation labeling. The letter system, which categorizes drugs into risk categories A, B, C, D, and X, will be eliminated. This system is outdated and does not account for new information about drug safety and risk profiles in pregnancy and lactation. Additionally, it is over-simplified, leading to imbalanced counseling of clients by healthcare providers. The new labeling system will have separate sections for pregnancy and for lactation, and each section will have three main components: risk summary, clinical considerations, and analysis of data (animal vs. human). Some of the information proposed for inclusion in the new labeling for lactation are discussed in this article, namely, compatibility of a specific drug with breast-feeding; amount of drug passed on to the infant from breast milk; possible effects of the drug on the breastfeeding infant; recommendations for monitoring these effects; and a review of the available data addressing these issues.1

THE BENEFITS OF BREASTFEEDING

The World Health Organization, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists recommend breast milk exclusively for at least the first 6 months of life,2,6 and continued breast milk with food through 6–12 months of age.7 There is evidence for significant health-related, nutritional, immunologic, developmental, psychologic, social, economic, and environmental advantages for breastfeeding.5-8

Breastfeeding is associated with a reduction in infant mortality rates.3,7,9-11 Other associated benefits include a reduction in the risk of infectious diseases (meningitis),12,13 gastrointestinal infection,14,15 deaths due to diarrhea,16 necrotizing enterocolitis,17 otitis media,18,19 respiratory infections,15,16,20,21 urinary tract infections,22,23 and sepsis.13 Breast-fed infants have reduced rates of sudden infant death syndrome.7,10 Other positive outcomes include a lower incidence of pediatric cancers,24,25 including lymphoma, leukemia, and Hodgkin’s disease. Reports also include a lower incidence of diabetes,26 obesity,27-31 and asthma22,32-35 in children and adults who were breastfed as infants. Increased analgesia during painful procedures for infants has also been reported in breastfed infants.36,37

Some research has also suggested a possible increase in cognitive development in infants who were breastfed.7,38 However, other more recent studies have found that this association with increased cognitive function is weaker than previously thought39 and possibly most significant for babies of small gestational size.40,41 or attributable to factors other than breast milk.42 This area is still controversial and requires further study.

Maternal benefits of breastfeeding include decreased postpartum bleeding, more rapid uterine involution,43 and faster weight loss to pre-pregnancy weight.44,45 Studies have also shown a reduced risk of breast cancer46-51 and ovarian cancer,52-54 and possibly a lower prevalence of the metabolic syndrome.55

Other benefits of breastfeeding include lower overall healthcare costs for less infant illness.56 Breastfeeding is much more economical than buying formula. Environmental benefits include less waste generated by disposal of formula packaging.7 However, for women who are unable or disinclined to breastfeed, formula is a reasonable alternative to breastfeeding.

WHEN BREASTFEEDING IS CONTRAINDED 

Some women should not breastfeed because of certain health risks it may pose to the baby. Breastfeeding is not recommended for mothers receiving certain chemotherapeutic agents or radioactive isotopes and selected other medications rated to be unsafe by the American Academy of Pediatrics. Mothers with herpes simplex lesions on the breast, HIV, or active tuberculosis, or those abusing drugs should also not breastfeed.7 Infants with galactosemia, premature children, and children with inherited disturbances in metabolism may be particularly vulnerable to the effects of psychotropics during breastfeeding.27

Another reason a woman may choose not to breastfeed includes mental illness where the risk of sleep disruption could worsen the condition, such as bipolar disorder. In some instances, women may opt to bottle feed, as the burden of frequent night feedings and prolonged sleep deprivation may be shared with another caregiver.

There is a high rate of psychiatric illness after childbirth. This may be attributable to hormonal factors, but also can be associated with psychological stress and previous psychiatric illness in the mother.58,59 Given the high rate of psychiatric illness during and after pregnancy, the healthcare practitioner should carefully and thoroughly evaluate the postpartum patient who is at risk for psychiatric illness to determine whether medication is necessary. They should understand the risks associated with psychiatric medications, and carefully assess the need for medication in the nursing mother.

Postpartum blues is a temporary and common condition affecting up to 85% of new mothers. This condition is characterized by tearfulness, mood lability, irritability, and anxiety. Symptoms usually begin around postpartum days 2–4 and resolve spontaneously, usually in ~2 weeks. Symptoms are generally transient and require no medication treatment. However, women with postpartum blues may be at increased risk for the subsequent development of postpartum depression.49

The highest rates of major depressive disorder (MDD) occur in women during the childbearing years, between 25–44 years of age.2,61 Postpartum depression is common, and occurs in up to 5% to 20% of women.57 Symptoms of postpartum depres-
sion are the same as for depression at other times and include depressed mood, insomnia, anhedonia, and suicidal ideation. The criteria of “postpartum onset” specifier in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition–Text Revision,62 is applied to the first 4 weeks after childbirth. The International Statistical Classification of Diseases and Health Related Problems, Tenth Revision,63 coding permits classifications of postpartum mental disorders 6 weeks after childbirth. In reality, many clinicians would consider depressive symptoms to be “postpartum depression” for a much longer period than this. Proposals for revisions of classifications include a specifier for onset within 3 months postpartum.64 The Edinburgh Postnatal Depression Scale is recommended for screening in women at risk for postpartum depression.

Women with a history of depression, postpartum depression, or previous psychiatric disorder are at an increased risk for postpartum depression.57,65-67 Social isolation, high parity, and psychological distress in late pregnancy are associated with postpartum depression.65 During pregnancy there is a high rate of relapse in patients with a history of MDD. A recent study68 of pregnant women with moderate-to-severe recurrent depression, who were taking antidepressants before conception and who then chose to discontinue medication, showed a 68% relapse rate of depression during their pregnancies. This was compared with a 25% relapse rate for those women who chose to continue antidepressants throughout their pregnancies.68

Postpartum psychosis is much less common, affecting ~0.1% to 0.2% of all women.69 It is characterized by mood lability, agitation, confusion, thought disorganization, hallucinations, and disturbed sleep. Postpartum psychosis has been associated with an increased risk of suicide, infant neglect, and infanticide,67,70 and is considered an emergency. Although relatively rare in the general population, the risk of postpartum psychosis in mothers with a history of previous inpatient psychiatric hospitalization is increased significantly compared to those without.71,72 There is also a very high risk of postpartum psychosis in mothers with bipolar depression, reported as high as 46%.2,58,59 Women who have had an episode of postpartum psychosis are at risk for developing bipolar affective disorder, suggesting that this could be a subcategory of bipolar disorder.67 Rates of relapse of bipolar disorder after pregnancy are high, ranging from 20% to 35%.67

Anxiety disorders are also very common, especially in the postpartum period. Postpartum panic disorder has been the most frequently reported anxiety condition.2,67 Rates of obsessive-compulsive disorder (OCD) have been reported to be higher postpartum than during pregnancy. Both OCD and generalized anxiety disorder (GAD) have been found to have higher rates in the postpartum population than in the general population.73

Although the DSM-IV-TR does not specifically identify childbirth as an example of a traumatic event, childbirth can be recognized as a stressful medical/surgical procedure that involves intense pain and invasive procedures, suggesting that it is relevant to consider it as a stressor. Posttraumatic stress disorder (PTSD) is also now being recognized in postpartum period.73 Stressful life events as well as depression during pregnancy and GAD have been identified as being related to PTSD symptoms.73-75 Anxiety late in pregnancy also was found to be predictive of PTSD.76

Schizophrenia in pregnancy has been associated with an increased risk of stillbirths, infant death, preterm delivery, and low birth weight.77,78 Postpartum schizophrenia and psychosis, particularly if left untreated, can lead to increased rates of refusal of care, maternal self-mutilation, postnatal death, and poor perinatal outcomes.7,70,78

**UNTREATED MATERNAL PSYCHIATRIC ILLNESS**

Psychiatric illness has been known to negatively influence mother-child interactions. Maternal depression is associated with an increase in premature births, low birthweight infants, fetal growth restriction, and postnatal complications.2 Infants of mothers with untreated depression have been shown to cry more and are more difficult to console.79 There is evidence that having a maternal psychiatric disorder also increases the risk of childhood behavioral problems.80

Maternal depression may also result in poor compliance with care and increased exposure to additional medications, illicit drugs, herbal remedies, alcohol, and tobacco. Untreated psychiatric illness has also been associated with difficulties with maternal-infant bonding.2 Studies81 also show that mothers with depression have a poor pattern of infant healthcare utilization, including an increased use of acute care and emergency room visits as well as decreased utilization of preventative services such as well-care visits and up-to-date vaccinations. Depressed mothers are also less likely to continue to breastfeed82 and less likely to promote childhood development by playing and talking to their baby and following predictable routines.83,84 Maternal depression has been shown to increase the risk of subsequent childhood psychopathology, including disruptive behaviors, anxiety disorders, and depression.85-88 On the other hand, remissions in maternal depression positively affect both mother and child, resulting in a significantly lower rate of children’s psychiatric symptoms and diagnoses.89

There is a high risk of relapse of psychiatric illness during and after pregnancy, and there is much evidence that untreated maternal illness may be harmful to both mother and baby. Psychotherapy should always be considered as part of the treatment choices. However, there are often instances when medications are helpful and in many cases necessary. With this in mind, the risks of fetal exposure to medication must be carefully weighed against the risk of the untreated psychiatric illness.
PSYCHOTROPIC MEDICATIONS AND BREASTFEEDING

All psychiatric drugs pass into breast milk. Most psychiatric drugs are lipid soluble and pass easily into breast milk through passive diffusion across cell membranes. The most reliable method for measuring infant drug exposure is by measuring the drug level in the infant’s serum. The relative infant dose is one way of quantifying infant drug exposure, and is defined as the percentage of the maternal plasma level, in mg/kg, received by the infant in a 24-hour period. This is the infant plasma drug level divided by the average maternal plasma drug level. Most medications are considered safe when the infant dose is <10%. Breast milk levels also are measured and used to gauge potential for infant drug exposure. The American Academy of Pediatrics (AAP) has rated the compatibility of drugs during lactation. This rating is based on the reports found in the literature and is intended to assist the physician in counseling the mother regarding breastfeeding while taking medication (Table 1).

ANTIDEPRESSANTS

The AAP Committee on Drug Safety rates all antidepressants as effects “unknown” and may be “of concern” in breastfeeding. However, a pooled analysis of antidepressant levels in lactating mothers suggests that it is probably safe to use antidepressants during lactation.

SSRIs

The growing evidence is generally reassuring concerning safety of using SSRIs in breastfeeding mothers. There are few reports of adverse effects on exposed infants to these medications. The excretion of SSRIs into breast milk ranges from relatively low to undetectable. Long-term effects of infant exposure to SSRIs have been less well studied.

Fluoxetine

Fluoxetine 20–40 mg results in relatively low infant plasma levels. A PubMed search identified a total of 67 cases of exposure. Norfluoxetine, the active metabolite of fluoxetine, has a very long half-life; it may likely be responsible for higher levels than the other SSRIs and accumulation in infants. There have been several reports of tremulousness, excessive crying, colic, poor feeding, and in one case lethargy in infants exposed to fluoxetine through breast milk. However, in most studies, no adverse effects were seen in infants up to 1 year of age.

Sertraline

Sertraline has been relatively well studied. Ninety-five cases were identified looking at breastfeeding level and effects on infants. Levels in nursing infants have been reported as low to undetectable in infant serum and low in breast milk. No adverse effects have been reported in the exposed infants. No significant change in serotonin transport in the infants were found in exposed infants.

Citalopram

Citalopram exposure through breast milk produced relatively higher infant levels than the other SSRIs. Nevertheless, infant levels are still found to be low to undetectable in most studies. One study reported poor sleep in an exposed infant, but symptoms resolved after the dose was reduced. Fifty-three cases were identified in the literature. Most studies did not report adverse events in infants who were breastfed while their mothers were taking citalopram, including a small case-controlled study of 31 women-infant pairs.

Escitalopram

Few cases have been published to date on the safety of the use of escitalopram in nursing. In a total of nine mother-infant pairs, infant levels were found to be low to undetectable and no adverse effects were seen in infants who had normal developmental milestones. Another study with two mother-infant pairs showed breast milk levels as similar to levels found with citalopram, and infants showed no adverse effects.

Fluvoxamine

In the 10 case reports found on PubMed on fluvoxamine, the drug has shown to produce variable but relatively low levels in exposed infants with no adverse effects reported and no adverse effects after 2–3 years.

TABLE 1

<table>
<thead>
<tr>
<th>Medication</th>
<th>American Academy of Pediatrics Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI and TCA</td>
<td>Effects unknown but may be of concern</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Effects unknown but may be of concern</td>
</tr>
<tr>
<td>Lithium</td>
<td>Use with caution</td>
</tr>
<tr>
<td>Carbamazepine and VPA</td>
<td>Compatible with breastfeeding</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Effects unknown but may be of concern</td>
</tr>
<tr>
<td>Typical antipsychotics (most)</td>
<td>Effects unknown but may be of concern</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Effects unknown but may be of concern</td>
</tr>
<tr>
<td>Other atypical antipsychotics</td>
<td>Not Rated</td>
</tr>
</tbody>
</table>

AAP=American Academy of Pediatrics; SSRI=selective serotonin reuptake inhibitor; TCA=tricyclic antidepressant; VPA=valproic acid.

Primary Psychiatry

M.A. Becker, G.F. Mayor, E.J.S. Kunkel

© MBL Communications March 2009

46

Paroxetine

Infants exposed to paroxetine through breastfeeding have been found to have low to undetectable serum levels. A total of 88 mother-infant pairs were examined. All of these cases reported no significant adverse side effects in the exposed infants observed\(^{100,120-122}\) and did not appear to affect weight gain or developmental milestones.\(^{123}\)

Summary of SSRI Data

Low infant plasma levels have been found with all the SSRIs, but higher concentrations have been reported for fluoxetine\(^ {98,99}\) and citalopram.\(^ {91}\) Sertraline and paroxetine usually produced undetectable infant levels.\(^ {91,92}\) The reviewed literature suggests that sertraline and paroxetine should be considered first-line choices in breast-feeding mothers who need to take SSRIs.\(^ {61}\) However, the risk of relapse should always be considered; if a woman has been stable on another antidepressant throughout her pregnancy, one should not necessarily change medication, as the evidence suggests that most SSRI levels have been found to be quite low in the infant. However, fluoxetine and citalopram should not be first choices, and if needed for their effectiveness in individual women, they should be used with caution. An alternative is the decision not to breastfeed. This should be considered and discussed with the patient.

Tricyclic Antidepressants

The AAP rates the effects of tricyclic antidepressants (TCAs) as “unknown but may be of concern.” The levels of TCAs ingested by nursing infants was found to be low (<1% of maternal dose).\(^ {124}\) Most reports show no adverse effects in the nursing infant.\(^ {57,125}\) In most cases, there have been no adverse effects found with exposure to nortriptyline, imipramine, desipramine, or clomipramine.\(^ {2,57,124}\)

Doxepin

Doxepin has a long half-life and can accumulate in exposed infants. Despite low transfer into breast milk and infant plasma, two cases\(^ {126,127}\) of infants exposed to doxepin through breast milk were associated with sedation and respiratory depression, likely due to accumulation in the infant. Because of this limited data it has been suggested that doxepin should be avoided during breastfeeding.\(^ {57}\) However, with such a small number of cases it is difficult to draw any conclusions regarding the safety of doxepin in lactation.

Nortriptyline

Nortriptyline levels have been shown to be low to undetectable in infant serum, and no adverse effects were noted in the exposed infants.\(^ {91,128,129}\)

Monoamine Oxidase Inhibitors

No current data was found regarding monoamine oxidase inhibitors.

Serotonin-Norepinephrine Reuptake Inhibitors

Venlafaxine

There are very few case reports published on the safety of venlafaxine in nursing. These show low to variable infant plasma levels in breast-fed infants. The mean infant dose ranged from 4.7% to 9.2%, which is relatively high compared with data published for other antidepressants.\(^ {130}\) None of the cases of exposure to venlafaxine showed any adverse effects to the exposed infants.\(^ {57,130-132}\)

Duloxetine

No data is currently available for duloxetine.

Dopamine Reuptake Inhibitors

Bupropion

There are no studies and only a few case reports on the safety of bupropion in breastfed infants. Low infant serum levels were found.\(^ {133,134}\) No adverse effects in two exposed infants were found.\(^ {133}\) One study\(^ {135}\) reported a seizure in a 6-month-old infant, which was possibly attributable to the use of bupropion during breastfeeding.

Other Antidepressants

Trazadone

There is very little data on trazadone. In the few cases examined, levels in breast milk have been found to be low.\(^ {136}\)

Mirtazapine

There are few studies looking at mirtazapine—a total of six cases of infant exposure in the literature. In these cases, infant levels were low to undetectable. No adverse effects were seen in the exposed infants, including no sedation or weight gain.\(^ {137-139}\)

Benzodiazepines

The AAP Committee on Drug Safety considers effects of benzodiazepines as “unknown, but may be of concern” in breastfeeding. Generally, the evidence shows that benzodiazepines have lower infant milk/plasma ratios than other psychotropic medications. Benzodiazepines with shorter half-lives (ie, lorazepam, alprazolam, and oxazepam) have been found to be very low in breast milk. No adverse effects were found in most exposed infants.\(^ {2,57,140-144}\)

Diazepam

Diazepam levels are very low in breast milk.\(^ {143,145,146}\) Generally, infants have not shown any adverse effects, although there have been two cases\(^ {147,148}\) reported where exposed infants became lethargic. These effects resolved after cessation of breastfeeding. Because of the longer half-life of
diazepam, however, woman taking high doses or having long-term treatment should probably not breastfeed.\textsuperscript{57}

**NON-BENZODIAZEPINES/HYPNOTICS**

**Zolpidem**

There is very limited data on zolpidem at this time, but in cases of five nursing women the drug was excreted in very low levels in breast milk.\textsuperscript{149}

**MOOD STABILIZERS**

**Lithium**

The AAP Committee on Drug Safety considers lithium to be associated “with significant effects on some nursing infants and should be given to nursing mothers with caution.”\textsuperscript{790} Breast milk levels have been found to be high, at \(-50\% of maternal serum levels.\textsuperscript{150-152} Infant levels have been reported as variable, but higher than many other medications; from 33\% to 55\% of maternal levels.\textsuperscript{151} In the few case reports,\textsuperscript{153,154} adverse infant effects reported have included cyanosis, hypotonia, heart murmur, electrocardiogram changes, lethargy, and hypothermia. A more recent case study\textsuperscript{152} of 10 mother-infant pairs found that infant serum levels are probably only 25\% of mother’s serum level, which is somewhat lower than previously thought. Occasional and transient lab abnormalities of elevated blood urea nitrogen (BUN), creatine, and thyroid stimulating hormone were observed in the sample of infants studied. Another recent study\textsuperscript{155} found considerable variability (0\% to 30\% of maternal dose) in infant serum levels of lithium, but again, lower than previously thought.

Infants may be more susceptible to both dehydration and lithium toxicity due to their immature kidney function and the potential for rapid dehydration. Therefore, the hydration status, BUN and creatine, lithium level, and thyroid levels should be carefully monitored in both mother and baby if it is necessary to use lithium in nursing.

**Valproic Acid**

The AAP Committee on Drug Safety considers valproic acid to be “compatible” with breastfeeding. Levels have been found to be very low in breast milk\textsuperscript{156} and very low in infant serum (0.9\% to 7.6\%).\textsuperscript{157-159} Only one adverse event of thrombocytopenia and anemia in an exposed infant was reported.\textsuperscript{160}

**Carbamazepine**

The AAP Committee on Drug Safety considers carbamazepine to be “compatible” with breastfeeding. Levels reported in infant serum were highly variable, from 15\% to 65\% of maternal levels.\textsuperscript{158,161} However, in case reports,\textsuperscript{162-164} carbamazepine was associated with infant hepatotoxicity. Exposed infants should be monitored by serum levels and liver function tests.

**Lamotrigine**

The effects of lamotrigine are classified by the AAP as “unknown, but may be of concern.” Lamotrigine is excreted in relatively high levels in breast milk. Infant serum levels were \(-30\% of maternal levels, likely due to a slow immature elimination in infants. However, none of the case reports found adverse effects in the infants.\textsuperscript{165-169} There have been no reported cases of Stevens-Johnson syndrome in nursing infants to date. Because of this concern, however, infants should be closely monitored.\textsuperscript{167}

**Summary of Mood Stabilizers**

Carbamazepine and valproic acid are more compatible with breast feeding than lithium. Lamotrigine is not recommended while breastfeeding.\textsuperscript{57}

The physician, however, always needs to give careful consideration to the need of keeping the mother on the medication that has kept her stable in the past (or during the pregnancy), rather than to risk relapse.

**ANTIPSYCHOTICS**

**Typical Antipsychotics**

The AAP Committee on Drug Safety rates the effects of haloperidol, chlorpromazine, thiothixene, mesoridazine, and trifluoperazine as “unknown and may be of concern” to nursing infants. Haloperidol is excreted in relatively high amounts in breast milk, but also has been shown to have no adverse effects on the infant.\textsuperscript{170,171} Chlorpromazine exposure has been associated with drowsiness and lethargy in one infant.\textsuperscript{172} In one study of seven infants with exposure to chlorpromazine through breast milk, there were no adverse effects reported at 16-month and 5-year follow-up evaluations.\textsuperscript{173} One study\textsuperscript{174} showed that infants exposed to haloperidol and chlorpromazine through breast milk exhibited developmental delays at 12–18 months of age. It is unclear if these delays were due to medication exposure or other factors.
Atypical Antipsychotics

**Risperidone**
Risperidone has not been rated by the AAP Committee on Drug Safety. There are only three case reports published to date on the safety of risperidone in lactation. Infant serum levels have been found to be low to undetectable in samples of nursing infants of women taking risperidone. No adverse effects in any of the exposed infants were reported.

**Olanzapine**
Olanzapine has not yet been rated for safety in breastfeeding, and there are few case reports at this time. Serum levels were low to undetectable in the small number studied. Most infants showed no adverse effects. In one infant exposed, there was a report of cardiomegaly, jaundice, and sedation. However, it is unclear whether this is accounted for by breastfeeding or in utero exposure.

**Quetiapine**
Quetiapine has not yet been rated on safety in breastfeeding. There are only two case reports to date on this medication. Breast milk levels were found to be low and there were no reported adverse effects in the exposed infants.

**Clozapine**
There are very few studies published on the safety of clozapine. The AAP rates effects as "unknown and of concern" in breastfeeding. It has been found in one case of a relatively high accumulation in breast milk. There has been a case published possibly attributing delayed speech acquisition to clozapine, in an infant after the mother was treated with clozapine both prenatally and during breastfeeding. Although no cases have been reported of agranulocytosis in nursing infants, it is a theoretical risk.

**Ziprasidone**
Ziprasidone has not yet been rated. There are no studies published on its safety in breastfeeding.

**Aripiprazole**
There are no cases or studies published on safety of aripiprazole during lactation.

**Summary of Antipsychotics**
With limited data, if women breastfeed while taking antipsychotics, infants should be monitored closely for possible adverse effects. It is recommended that clozapine should not be used, as there is a theoretical risk of agranulocytosis in the infant.

Table 2 summarizes the safety data of the major psychotropic medications when used during lactation.

### Table 2
**SUMMARY DATA OF PSYCHOTROPIC MEDICATION USE IN BREASTFEEDING**

| SSAIs | • Well-studied, reassuring safety data, low BML, few AE in infants
| TCAs | • Low IL mostly no AE
| MAOIs | • No data
| Newer Antidepressants | • Venlafaxine, bupropion, trazadone, and mirtazapine; low BML or IL, no AE
| | • Bupropion: possible seizure in infant
| | • Nortriptyline: low IL, no AE
| | • Nortriptyline, imipramine, desipramine, and clomipramine: no AE in most cases
| Benzodiazepines | • Ones with shorter half-lives have low BML and AE
| | • Diazepam: low BML, report of lethargy in infant
| Zolpidem | • Low BML in five case reports
| Lithium | • High BML, high IL, known AE, including toxicity in infant
| Carbamazepine | • Low IL, AE reported
| Valproic Acid | • Low BML and IL
| Lamotrigine | • High BML but no AE reported
| | • High BML, no IL
| TCA Antipsychotics | • Haloperidol: high BML but no AE
| | • Chlorpromazine: AE reported in one infant, no AE at 16 months or 5 years of age
| | • Chlorpromazine: AE reported
| | • Ziprasidone and aripiprazole: no data

SSRIs=selective serotonin reuptake inhibitors; BML=breast milk levels; AE=adverse events in infants exposed reported; IL=infant levels; TCAs=tricyclic antidepressants; MAOIs=monoamine oxidase inhibitors.
REFERENCES


