Mood Disorders in Women

Focus on the Postpartum

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Postpartum mood disturbances are common in women. Parents should be educated to expect postpartum blues, which typically subside without treatment. Postpartum depression, however, is debilitating and can impair the mother's ability to respond to her infant, affecting the baby's cognitive and emotional development. If untreated, it can lead to chronic depression or suicide in the mother. Postpartum psychosis is widely considered to be a manifestation of bipolar disorder, and it carries a risk of infanticide. Here Dr. Burt reviews the risk factors, clinical presentation, and treatment of postpartum mood disorders and considers the question of breastfeeding during treatment with psychotropic medication.

In the weeks and months following delivery, many new mothers experience mood instability, depression, anxiety, and feelings of incompetence and doubt. Many women, especially those with a history of psychiatric conditions, are vulnerable to mood disorders during the first six months following childbirth.[1] In this article, three postpartum conditions involving mood instability will be addressed: postpartum blues, postpartum depression, and postpartum psychosis. Although there is some controversy about whether these three conditions represent a continuum of mood syndromes or are unrelated, it is clear that they can have negative effects on family stability, may result in impaired infant development, cause great suffering for the mother, and increase her risk for future mood disorders.[2]

POSTPARTUM BLUES

Because postpartum blues occur in up to 85% of all new mothers,[3] symptoms should be expected following childbirth. The condition typically begins within two to four days after delivery, peaks between postpartum days 5 and 7, and resolves by 12 to 14 days postpartum.[4] Symptoms include mood lability, emotional hypersensitivity, and irritability. Although the etiology of postpartum blues is unknown, it has been hypothesized that the condition is a reaction to the abrupt withdrawal of estrogen[5] and/or progesterone or its anxiolytic metabolite, allopregnanolone, or to an impaired response to oxytocin-induced stimulation of maternal-infant attachment.[6]

Obstetric complications do not appear to increase the risk for postpartum blues, but for women who have a history of depression, a family history of depression, depressive symptoms during pregnancy, or premenstrual dysphoria, the blues may be more likely to evolve into a more protracted and severe depression.[7] Most cases of postpartum blues resolve by day 12 without any long-term difficulties. Nevertheless, in about 20% of cases, the condition evolves into postpartum depression.[4]

Couples who experience postpartum blues generally respond to support and reassurance that this is an expected condition that tends to resolve over several days. It is important that women and their partners be educated about this condition prior to delivery, since new mothers are often discharged from the hospital prior to the onset or full evolution of this relatively common condition.

POSTPARTUM DEPRESSION

Postpartum depression tends to begin later than postpartum blues. Although the rate of postpartum depression (12% to 13%) equals the rate of depression in the general female population, postpartum women have higher rates of subclinical depressive symptoms that are troubling and debilitating but which may not meet criteria for major depression.[8] In cases of major depression arising in the postpartum period, new mothers are at risk for suicide. Furthermore, because postpartum depressive symptoms cause great distress for the patient

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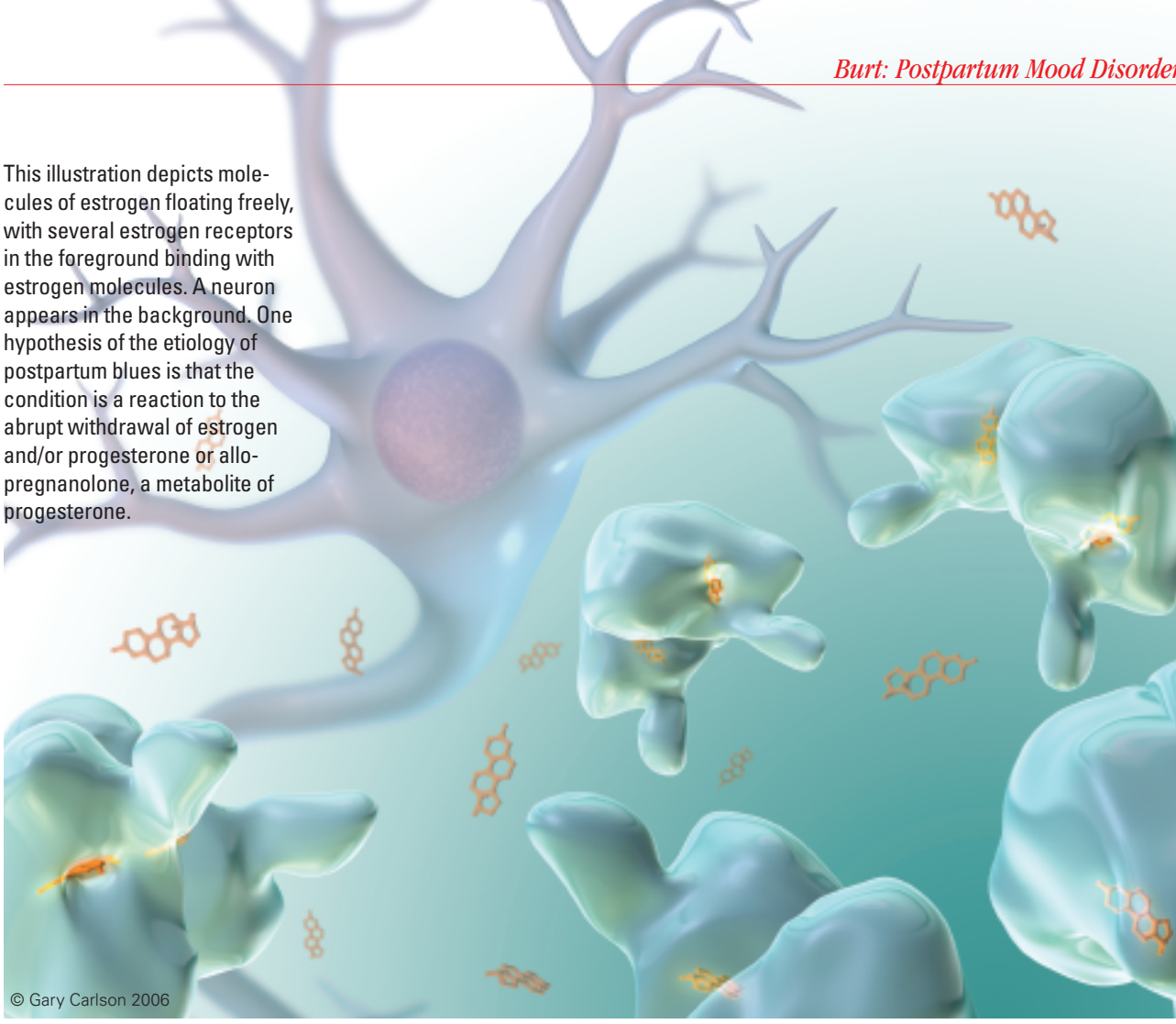

This illustration depicts molecules of estrogen floating freely, with several estrogen receptors in the foreground binding with estrogen molecules. A neuron appears in the background. One hypothesis of the etiology of postpartum blues is that the condition is a reaction to the abrupt withdrawal of estrogen and/or progesterone or allopregnanolone, a metabolite of progesterone.

PRIMARY POINTS

Identifying Postpartum Mood Disorders

- While many new mothers experience mood instability after delivery, those with a history of psychiatric conditions are particularly vulnerable to mood disorders during the first six months following childbirth.
- *Postpartum blues*—including mood lability, emotional hypersensitivity, and irritability—begin within a few days of delivery in 85% of new mothers and usually resolves within two weeks.
- *Postpartum depression* begins about four weeks after delivery but may be overlooked for several months. Screening and treatment are critical to reduce risks to children and protect the mental health of the mother.
- *Postpartum psychosis* begins within days of delivery, is a particular risk for women with a history of bipolar disorder, and is associated with child neglect, child abuse, and infanticide.
- The decision to breast-feed while taking psychotropic medication should be made after evaluating the known benefits of breast-feeding, the mother's wishes, and the risk of infant exposure to the proposed medication.

and her family and tend to be long-lasting,[9] and also because evidence suggests that postpartum depression has an adverse impact on the emotional and cognitive development of an infant, it is important to screen for, diagnose, and fully treat this disorder.

In 1994, *DSM-IV* officially recognized postpartum depression as a subcategory known as *major depression with postpartum onset*.[10] Although *DSM-IV* describes this condition as major depression arising within four weeks of childbirth, women often do not present for treatment until after the third postpartum month, probably because of increased focus on the new baby and reduced attention to the mother's needs, ignorance about what to expect following delivery, a sense of shame about being depressed, or an assumption that the symptoms represent simply a prolonged episode of postpartum blues.

The etiology of postpartum depression remains unclear. Despite the fact that there is no direct evidence supporting hormonal imbalance as a cause of postpartum depression, exogenous hormone administration followed by rapid discontinuation has been shown to result in depression in women with a history of postpartum depression.[11]

The increased risk of postpartum depression in women who have experienced mood instability during other times of hormonal change, as with premenstrual dysphoric disorder, suggests that depression after delivery may occur in women who are particularly sensitive to rapid hormonal changes. It has been hypothesized that some women have a genetically determined predisposition to reproductive-related disorders. Such women may be both hypersensitive to changes in gonadal and other steroid hormones and susceptible to dysregulation of central nervous system and adaptive functioning.[12]

TABLE 1. POSTPARTUM DEPRESSION RISK FACTORS

- Depressive symptoms in pregnancy
- Personal history of depression or bipolar disorder
- Personal history of postpartum depression
- Family history of affective disorders
- Lack of partner support
- Unplanned pregnancy

Adapted from Burt and Hendrick[1] and Bloch et al.[7]

Postpartum depression increases the risk of negative parenting behaviors and places children at increased risk for delayed and abnormal social, emotional, and behavioral development.[13,14] When untreated, postpartum depression may evolve into a prolonged, chronic maternal depression, which negatively impacts children. Thus, compared to children of nondepressed mothers, children of depressed mothers have an impaired ability to regulate their emotions, are more likely to be aggressive toward parents and peers, and tend to show signs of helplessness and impaired social competence.[15,16] Breast-feeding infants of depressed mothers tend to gain less weight compared to nurslings of nondepressed mothers, possibly because maternal depression may have an adverse impact on a woman's diet, ability to breast-feed, or ability to sensitively respond to her infant's hunger signals.[17] Evidence suggests that prompt treatment of maternal depression can address adverse childhood behavioral, cognitive, and emotional difficulties.[18,19]

Risk Factors for Postpartum Depression

It has been estimated that having a history of major depression incurs a 24% risk of postpartum depression, while being depressed during the index pregnancy further increases the risk for postpartum depression to 35%.[8] Of special concern is the woman who has had a prior episode of postpartum depression, for such a history raises the risk of a recurrence to 50%.[8] Other factors that increase the likelihood of a postpartum depression include a history of premenstrual dysphoric disorders, a history of oral contraceptive–associated dysphoria, a family history of mood disorders, experiencing psychosocial stress, being in a dysfunctional marital relationship, having inadequate social supports, and having experienced stressful life events during the pregnancy (Table 1).[1,7] In cases of apparent postpartum depression, thyroid function should always be tested, as postpartum thyroid disease is common and may present with mood symptoms.[20]

Clinical Presentation

Women with postpartum depression often experience severe anxiety and tend to ruminate over their babies' health and well-being. Other symptoms include feeling incompetent as a mother, having a poor appetite, and being unable to concentrate. Of particular note, women with postpartum depression tend to complain

TABLE 2. POSTPARTUM DEPRESSION TREATMENT OPTIONS

- Education, reassurance, support
- Psychotherapy
  - Individual (cognitive, supportive)
  - Group
- Psychosocial assistance to reduce stressors
- Antidepressants (five studies, all small, none controlled)
- Hospitalization
- Electroconvulsive therapy

Adapted from Burt and Hendrick.[1]

about being physically and emotionally exhausted both during the day and at night but are unable to sleep, even when given the opportunity to do so (ie, even when nursing care is secured for their babies). Women with postpartum depression in its most severe form are unable to care for themselves, their infants, other children, or their families, and are at risk for suicide. Unlike women with postpartum psychosis, who clearly are at risk for infanticide, nonpsychotic postpartum depressed women may have suicidal ideation, but they are not likely to harm their babies.[21]

Treatment

In addition to antidepressant medication, treatment of postpartum depression includes education, psychotherapy, group support, and referrals to self-help and national organizations. Couples counseling may be called for in cases where marital discord is a factor in the depression and is an obstacle to providing the support needed to fully treat the depression (Table 2).[1] Group therapy, led by a professional trained in postpartum mood disorders, is also helpful. This provides an opportunity for ongoing support as well as frequent monitoring by a therapist, who can contact a psychiatrist should the condition of a patient with postpartum depression worsen, with the patient becoming unstable or unsafe. Psychotherapies that have been implemented include interpersonal psychotherapy, in which the treatment addresses resolution of marital disputes and role transitions that often occur during the postpartum, and cognitive behavioral approaches, which use techniques directed at correcting negative cognitive distortions and developing helpful behaviors. A recent review has concluded that well-designed studies that test the efficacy of psychotherapy specifically for the treatment of postpartum depression are lacking. However, these therapies have been widely used and are found to be effective in the treatment of general major depression.[22]

Because a lack of social support is often associated with postpartum depression, efforts should be directed at harnessing resources to provide help around the home in order to ensure that the depressed mother is able to obtain adequate rest and care for herself. Referrals to self-help groups and national organizations, such as Postpartum Support International, may further enhance access to additional resources for women with postpartum depression (Table 3).

Although antidepressant medications have been widely used to treat major depression in general and are considered an important modality in the treatment of major depression arising in the postpartum period, published studies of the use of medications to treat this condition tend to be small and are often poorly controlled, or not controlled at all.[23-27] Nevertheless, clinical experience suggests that an approach involving antidepressants, psychotherapy, and psychosocial support provides effective treatment of postpartum de-

TABLE 3. RESOURCES FOR WOMEN WITH POSTPARTUM DISORDERS

Postpartum Support International

927 N Kellogg Avenue
Santa Barbara, CA 93111-1022
(805) 967-7636

www.postpartum.net

Provides referrals for group support, individual therapists, and psychiatrists.

Motherisk

(416) 813-6780

www.motherisk.org

Canadian-based program that provides information on safety or risks of drugs in pregnancy and lactation.

Massachusetts General Hospital Center for Women's Mental Health

www.womensmentalhealth.org

Web site of the Massachusetts General Hospital Reproductive Psychiatry Resource and Information Center. Provides information on pregnancy, postpartum, and psychiatric disorders.

pression. In any case, the decision to use medications should include careful consideration of whether the mother is breast-feeding (see page 21). Mothers and their partners (and any other involved family member) should be included in the development of a treatment approach, as support is essential for enhancing the effective treatment of postpartum depression.

As with any serious depressive episode, untreated episodes of postpartum depression may become more severe and difficult to treat. For this reason, treatment should begin early, and patients should be carefully monitored to ensure progressive improvement.

As has been mentioned earlier, women with a history of postpartum depression are at increased risk for developing a subsequent postpartum depressive episode. Although the evidence is conflicting, it has been suggested that beginning antidepressant treatment during the first one to two days following delivery may reduce the risk of a recurrence of postpartum depression.[28-30]

Two studies have addressed the possibility that estrogen may be effective in treating postpartum depression.[31,32] However, both studies have been limited by small numbers of subjects and inadequate controls. Furthermore, estrogen therapy in the postpartum period may reduce breast milk supply, increase the risk for endometrial hyperplasia, and increase the risk for thromboembolism. Therefore, at this time, the use of exogenous estrogen to treat postpartum depression is not warranted. The use of natural progesterone (which is converted to a GABAergic anxiolytic metabolite, allopregnanolone) to treat postpartum depression has yet to be evaluated in a clinical trial. Synthetic progestins, which are not metabolized into GABAergic anxiolytic agents, do not ameliorate postpartum depression and may exacerbate depressive symptoms.[33]

As with any serious depressive episode, untreated episodes of postpartum depression may become more severe and difficult to treat. For this reason, treatment should begin early, and patients should be carefully monitored to ensure progressive response and improvement, and ultimately, remission and a return to full and normal functioning. For women who have marked anxiety that complicates the depression, short-term use of benzodiazepines may be considered. With the exception of an occasional low-dose of a short-acting benzodiazepine agent such as oxazepam, this is generally not recommended if the patient is breast-feeding. If a response does not occur, or if symptoms worsen, hospitalization may be necessary. Electroconvulsive therapy (ECT) should be considered for severe cases that are marked by suicidal ideation or psychosis, or in cases where maternal or infant health is compromised.[4]

TABLE 4. POSTPARTUM PSYCHOSIS OVERVIEW

Frequency

1–2 cases per 1,000 births

Risk factors

Bipolar disorder
Prior postpartum psychosis
Family history of bipolar disorder
Family history of postpartum psychosis
Psychosocial stressors

Adapted from Burt and Hendrick.[1]

POSTPARTUM PSYCHOSIS

Postpartum psychosis is a severe psychiatric illness that affects one to two women per thousand births.[3] Onset of symptoms is early and rapid, generally within the first two to three days postpartum. There is a risk of infanticide, estimated at about one in 50,000.

Clinical Presentation

Clinically, the patient presents with prominent mood instability, with swings from depression to mixed depression and mania, severe agitation, confusion, disorientation, thought disorganization, hallucinations and delusions, and sleeplessness. Postpartum psychosis is widely considered to be a manifestation of bipolar disorder.[34] Women who have experienced an episode of postpartum psychosis are at risk for future nonpostpartum episodic relapses.

Risk Factors

Women with a history of bipolar disorder are at high risk for postpartum mood disorders—both depression and psychosis. It has been estimated that in women with bipolar disorder, the risk for postpartum psychosis is 100 times greater than that in postpartum women in the general population (Table 4).[35] Thus, estimates of postpartum psychosis in bipolar women have been reported to range from 26% to 35%.[1,36] Women with

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a history of both bipolar disorder and postpartum psychosis have at least a 38% to 50% risk of recurrence of postpartum psychosis.[36] Other risk factors for postpartum psychosis include a family history of postpartum psychosis, and possibly also primiparity.[3,36]

Treatment

Postpartum psychosis is associated with serious child neglect, child abuse, and infanticide. Treatment invariably requires psychiatric hospitalization. Pharmacologic treatment includes the administration of mood stabilizers, benzodiazepines for agitation and anxiety, and antipsychotics for psychosis (Table 5). Antidepressants should be used cautiously, and patients should be watched closely for secondary rapid cycling. ECT is an option that is used to treat refractory postpartum psychosis. Family participation is essential; family members must be counseled and educated about the condition. They also need reassurance that with appropriate treatment, women with the disease can recover and become functional and loving mothers. Social work assistance is also very helpful in addressing the needs of the family while the patient is in treatment.

Women with an established history of bipolar disorder should be managed with a maintenance treatment regimen that includes a mood stabilizer. An atypical neuroleptic is often included in a maintenance regimen, and occasionally an antidepressant and a benzodiazepine are also included. For women who develop postpartum psychosis in the absence of a history of bipolar disorder, a decision as to whether to continue treatment or taper medication can be made after a period of emotional stability that has resulted from effective treatment. When tapering medication, the patient should be carefully monitored for at least a year, to ensure that she does not experience decompensation. Treatment with a mood stabilizer should, however, be started immediately after a subsequent delivery in order to prevent another postpartum psychotic episode.[1,4]

In general, women with bipolar disorder should be cautioned about the risks associated with breast-feeding their infants. There is a relative paucity of data about the effect of commonly used mood stabilizers in infants who are exposed to these agents through breast milk. However, another important reason to suggest that bipolar women *not* nurse their infants is that breast-feeding requires that mothers devote many hours each day to nourishing their infants. Sleep deprivation is a difficult and risky stressor for bipolar patients, whose need for uninterrupted sleep is even greater than that in the general population or in patients with other psychiatric disorders. Thus, to minimize risk to both mother and infant, it seems appropriate to advise women with bipolar disorder who are approaching delivery or who are newly postpartum that if they do all they can to remain psychologically healthy, their ability to bond with their babies is likely to be strong even if they forgo breast-feeding.

BREAST-FEEDING AND PSYCHOTROPIC MEDICATIONS

The decision to breast-feed while taking psychotropic medication is complicated. Decisions should be made after evaluation of the known benefits of breast-feeding to infant and mother, the mother's wishes, the risk of infant exposure to the medication in question, and the possibility that a severely depressed, anxious, or even psychotic mother might decide not to be treated rather than give up breast-feeding.

It has been estimated that about 50% of new mothers breast-feed. Breast-feeding confers a number of health benefits: Breast milk contains antibodies, enzymes, hormones, growth factors, and other substances that enhance the growth and well-being of infants. Over the past two decades, the increase in the published data on the use of psychotropic medication in breast-feeding mothers has made it possible for clinicians to provide them with information about the extent of exposure and associated risks (if any) of many psychotropic medications.

TABLE 5. POSTPARTUM PSYCHOSIS MANAGEMENT OPTIONS

- Hospitalization
- Mood stabilizers
- Anxiolytics
- Antidepressants (caution to avoid mania)
- Antipsychotics
- Electroconvulsive therapy
- Family counseling: support, education, psychosocial assistance

Adapted from Burt and Hendrick.[1]

TABLE 6. BREAST-FEEDING AND THE POSTPARTUM DEPRESSED PATIENT: CONSIDERATIONS

Known

Untreated maternal depression has adverse impact on infants
- Mother-infant attachment
- Cognitive and behavioral development

Nonpharmacologic and pharmacologic treatments appear to be efficacious

Increasing data show

All psychotropic drugs studied are excreted in breast milk

Infant serum concentrations are typically below standard laboratory sensitivity

There is no evidence of serious adverse effects of antidepressant exposure during breast-feeding

Unknown

Effects of neonatal medication exposure on infant development

Adapted from Burt et al.[37]

TABLE 7. TREATING THE POSTPARTUM DEPRESSED PATIENT WHO IS BREAST-FEEDING

- Conduct baseline assessment of infant
- Monitor infant's clinical status
- Understand risks with specific drugs
- Prescribe low-dose monotherapy, if possible

Adapted from Burt and Hendrick[1] and Burt et al.[37]

The choice of a medication depends on the diagnosis, medical history of the mother (and what medications were effective in the past), side-effect profile, and dose flexibility. As a general rule, breast-feeding mothers should be given the minimum dose of the medication that achieves remission of debilitating psychiatric symptoms. However, doses so low that treatment is ineffective result in needless exposure of the infant to medication.[37]

Before a patient begins breast-feeding while taking medications, a clinician should discuss with the new mother the available data on breast-feeding and psychotropic medication use, including a review of risks and benefits (Table 6). A pediatrician who is aware of the breast-feeding mother's use of a medication should monitor the infant to ensure that he or she is developing normally and that the infant is not suffering from any adverse effects (Table 7). Since infant drug clearance increases from 33% of the maternal weight-adjusted clearance at birth to 100% at six months, medication use in a new mother who is breast-feeding is thought to be somewhat riskier than that in a nursing mother who is several months into the postpartum period. Premature infants tend to have immature P450 enzymes, and therefore it may not be prudent for a premature infant to be breast-fed by a mother who is taking a psychiatric medication.

A detailed discussion of the risks and benefits of each of the different psychotropic agents in breast-feeding mothers is beyond the scope of this article. However, it should be noted that most of the data that have been published regarding the use of antidepressants in breast-feeding mothers is for SSRIs. All medications, including SSRIs, are excreted in breast milk. Nevertheless, no serious adverse events have been reported in children breast-fed by mothers who are taking any of the SSRIs. There are some data suggesting that exposure for a nursling is lowest with sertraline, fluvoxamine and paroxetine, and highest with citalopram and fluoxetine. However, since overall there are no serious adverse effects in babies exposed via breast milk to any of the SSRIs, it seems reasonable to treat breast-feeding mothers who are depressed with the medication that is most successful at achieving remission and a return to full function. There are no studies addressing long-term effects of SSRIs on child development in children exposed to these drugs via breast milk.[37,38]

In general, patients requiring ongoing treatment with other agents such as benzodiazepines, mood stabilizers, and/or antipsychotics are best advised to forgo breast-feeding. Less is known about most of the other psychotropic agents than about the SSRIs in breast-feeding mothers. Furthermore, women requiring daily treatment with mood stabilizers, antipsychotics, and benzodiazepines tend to be seriously ill. Many require very aggressive treatment, often with multiple medications. They also do best if they have the opportunity to receive uninterrupted sleep for at least seven to eight hours each night, which necessitates adjunctive care for nighttime baby feedings by a trusted family member or baby nurse. In this

way, patients will more likely be able to be treated aggressively and remain psychologically stable and in a position to mother their infants more effectively than if they were sleep-deprived and breast-feeding their babies.

CONCLUSION

The postpartum period is a time of increased risk for mood instability, particularly in women with an established history of depression, bipolar disorder, and other psychiatric conditions that occur at times of hormonal changes (eg, premenstrual dysphoric disorder). Prior episodes of postpartum psychiatric disorders and family history of mood disorders (including postpartum depression and psychosis) are also associated with increased risk. Consideration should be given to prevention with antidepressants and psychotherapy for women at high risk for postpartum mood disorders. The adverse, often lasting, consequences of postpartum disorders in the mother, the infant, and the family unit justify the need for careful screening in all women, and especially in women at risk, as they approach delivery and move through the postpartum period. Once identified, women with postpartum mood disorders should be treated promptly and followed carefully. ♀

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