Review

Postpartum Mood Disorders: Clinical Perspectives

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ABSTRACT

Mood disorders are common in women. A prepregnancy personal history of mood disorder (bipolar or major depression), premenstrual syndrome, or (possibly) postpartum blues places a woman at high risk for a postpartum exacerbation of symptoms. Untreated or unrecognized postpartum mood disorders can lead to serious psychologic and social consequences, in some cases even leading to suicide or infanticide. Women at risk for postpartum mood disorders need to be referred for psychiatric consultation before pregnancy and parturition. Informed, professional collaboration offers the best opportunities for prevention, as well as the earliest recognition and treatment of emergent symptoms.

Since Hippocrates' description of postpartum psychosis over 2000 years ago, the understanding of postpartum psychiatric disorders has evolved. Today, there is far more information about psychiatric disorders in general and postpartum mood disorders in particular.

Women are twice as likely as men to experience depressive illness, and their lifetime prevalence of major depression is approximately 21%. Bell et al. found that the majority of women admitted to a mother and baby unit in the United Kingdom had major depression. Estimates suggest that between 13% and 23% of women with postpartum disorders have a past history of psychiatric illness. A history of mood disorder is a significant predictor of subsequent postpartum mood disorder. Among women in the United Kingdom (who were hospitalized in a mother and baby unit of a psychiatric hospital within 6 months postpartum), those with pure puerperal psychiatric illness appeared to have a better prognosis than those with a past history of nonpuerperal psychiatric illness. Unfortunately, 38.9% of the women with pure puerperal psychiatric illnesses went on to experience subsequent nonpuerperal relapses. This finding suggests that puerperal psychiatric illness may not be distinct from nonpuerperal psychiatric illness.

Postpartum mood disorders are associated with significant morbidity and mortality. In severe cases, patients may require hospitalization. At the extreme, postpartum mood disor-
orders may be associated with suicide, infanticide, or both. Many postpartum psychiatric episodes can be anticipated and prevented with early prenatal assessment and appropriate preventive and treatment measures.

**CATEGORIES OF POSTPARTUM MOOD DISORDERS: RELATIONSHIP TO TRADITIONAL DIAGNOSES**

Terminology for postpartum mood syndromes varies. However, the following terms are widely used and are defined below: postpartum blues, postpartum depression, postpartum mania, and postpartum psychosis.

Although these disorders are identified as occurring in the postpartum period, their symptoms and treatment (except for postpartum blues, which does not require medical treatment) generally are not significantly different from similar presentations at other points in a woman's life cycle. The exception is related to issues of breast feeding and the unique psychosocial issues facing a new mother and her family in this context.

In terms of psychiatric nosology, the traditional mood disorder diagnoses apply to the postpartum period with the use of a modifier. According to the American Psychiatric Association's 1994 edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), "The specifier With Postpartum Onset can be applied to the current (or most recent) Major Depressive, Manic, or Mixed Episode of Major Depressive Disorder, Bipolar I Disorder, or Bipolar II disorder or to Brief Psychotic Disorder if onset is within 4 weeks after the delivery of a child." Some suggest that the postpartum modifier should extend to 3 months from parturition.

Along the spectrum of postpartum psychiatric disorders, mood disorders are by far the most prevalent. A British study of 108 women admitted to the Royal Edinburgh Hospital within 90 days of childbirth between 1971 and 1980 reported on frequency of psychiatric diagnosis using Research Diagnostic Criteria (RDC). The three most common diagnoses were major depressive disorder (42%), minor depressive disorder (17%), and manic disorder (14%). Delusions were definitely present in 45% of patients, and hallucinations were definitely present in 22% of patients. This study suggests that psychotic features are common among women hospitalized with postpartum psychiatric disturbances and reflects their severity but not necessarily a diagnosis of schizophrenia.

Wisner et al. reported that major depression (DSM-III) was the most commonly encountered diagnosis among 168 women with Child Bearing Related Onset Illnesses (CBROI) who were evaluated at a university psychiatric hospital. CBROI include those occurring during pregnancy (27%), postpartum (49%), and post-pregnant (i.e., a woman stated that she had been pregnant within 3 months before the onset of her illness, but the pregnancy was spontaneously or intentionally terminated [24%]).

**POSTPARTUM BLUES**

Approximately 30% or more new mothers will experience maternal blues. Postpartum blues is a "mild syndrome typically experienced by women with the first week to ten days after delivery." In the contemporary practice of obstetrics, women are frequently discharged from the hospital within 24–48 h after delivery. For this reason, it is important to educate mothers of newborns to be alert for symptoms of postpartum blues or major depression immediately postpartum. Symptoms of postpartum blues can include dysphoria, mood lability, crying, anxiety, insomnia, poor appetite, and irritability. Traditional doctrine suggests that anticipation and support are all that is required for management of postpartum blues. When the symptoms of depression or blues are intense, associated with suicidal ideation, or persist for more than 5–7 days (suggesting a diagnosis of major depression and requiring more aggressive medical and psychologic management), consultation with the obstetrician or a psychiatrist should follow.

In their prospective study, O'Hara et al. found that women with postpartum blues were more likely to develop postpartum depression than women who did not experience postpartum blues. They also found that women who met the criteria for postpartum blues were
more likely to have been depressed before pregnancy and to have had premenstrual depression.\textsuperscript{10} This study found that approximately 25\% of women meeting criteria for postpartum blues went on to have a postpartum depression.\textsuperscript{10} O’Hara et al.\textsuperscript{10} also reported that predictors of the postpartum blues included personal and family history of major depression, difficult social adjustments, and stressful life events. Pop et al.,\textsuperscript{11} in a prospective study of 303 women in the Netherlands, found that having postpartum blues was significantly correlated with the occurrence of postpartum minor depression between 4 and 10 weeks after delivery.

Harris et al.\textsuperscript{9} found that high postpartum scores for postpartum blues were associated with high antenatal progesterone concentrations on the day before delivery. Progesterone concentrations decreased from the day of delivery until the day of peak blues score. These authors suggest that it may be possible to attenuate maternal blues with progesterone treatment.\textsuperscript{9} Clearly, more data are necessary to assess whether this approach has clinical merit. In some women, progesterone therapy has been associated with depressive symptoms.

\textbf{POSTPARTUM DEPRESSION}

Evidence in the medical literature indicates that postpartum depression is clinically similar to nonpostpartum depression.\textsuperscript{12,13} As Wisner’s group noted, among women with CBROI, most have the onset of illness during the postpartum period compared with during pregnancy or after pregnancy loss.\textsuperscript{7} The diagnostic criteria for major depression are the same as for major depression occurring postpartum. As noted earlier, a modifier, \textit{with postpartum onset} (denoting the postpartum nature of the episode), can be used provided the episode occurs within 4 weeks after delivery.\textsuperscript{6} The DSM-IV criteria for major depression must include at least five symptoms present over the same 2-week period, representing a change in function, with at least one of the symptoms being either depressed mood or loss of interest or pleasure.\textsuperscript{6} Other symptoms can include significant weight loss or gain, insomnia or hypersomnia nearly every day, psychomotor agitation or retardation, fatigue, feelings of worthlessness, diminished ability to think or concentrate, or recurrent thoughts of death or suicide.\textsuperscript{6}

Using RDC for depression in a study of 293 women, Pop et al.\textsuperscript{11} found that the incidence of postpartum depression during their assessment was 20.8\%, with 6.8\% of women meeting criteria for major depression and 13.9\% for minor depression. The peak prevalence occurred at 10 weeks postpartum. The mean point prevalence was 9.7\%, with a range between 8\% and 14\%. This report also confirmed a relationship between postpartum blues and depression early in the postpartum period (between 4 and 10 weeks).\textsuperscript{11}

Two important factors that increase the likelihood that a woman will experience postpartum depression are a positive family history for depression and a personal history of mood disorder.\textsuperscript{4} In spite of this, postpartum depression represents the first episode of depression in 50\% of cases.\textsuperscript{4}

Women with postpartum depression often have recurrences. Among the women that Bell et al.\textsuperscript{1} followed (5–14 years) after admission to their mother and baby unit, relapse was common. The majority of these women experienced major depression.\textsuperscript{1} Using rereferral as a relapse indicator, the authors found that 58\% of the women required further psychiatric intervention and just under 10\% experienced puerperal relapses exclusively.\textsuperscript{1} Bell et al. also found that women with any psychiatric illness up to 6 months postpartum, who did not have a previous psychiatric history or only had a history of puerperal illness, had significantly better prognoses than those with past histories of nonpostpartum illness. Davidson and Robertson\textsuperscript{14} found that women with postpartum unipolar (nonbipolar) depression had a 40\% likelihood of developing subsequent nonpuerperal depression and a likelihood of future puerperal depression in one of four pregnancies.

Life stressors may increase the risk of postpartum depression. Marks et al.\textsuperscript{15} found that postpartum psychiatric illnesses categorized as nonpsychotic (mostly major depression) were associated with a greater likelihood of the woman’s having experienced at least one se-
vere life event. Of the women they studied who had nonpsychotic postpartum illness, 62% had a preceding event compared with 22% of all women who were not ill.15

Among medical comorbid factors that may be associated with postpartum depressive symptoms, thyroid dysfunction is notable. Harris et al.16 found an excess of depressive symptoms and cases of depression (not major depression) in women with antithyroid antibodies in the 8 months after delivery. The authors noted that approximately 12% of postpartum women were antibody positive, of which approximately half would develop features of a depressive syndrome. Harris et al. suggest that approximately two thirds of thyroid antibody-positive childbearing women with depressive symptoms will have a probable basis in autoimmune thyroid disease.16

Suicide

Depressed patients frequently experience suicidal ideation, and approximately 15% of patients with depression will end their lives by suicide.17 Yet, according to one British study, in the first postnatal year, women have a low risk of suicide despite their high rate of psychiatric morbidity.18 Appleby18 found that the standardized mortality ratio for postnatal suicide was 0.17—one sixth of that expected. Sixty-three percent of the suicides in this report occurred in women who had a past or current history of psychiatric disorder.18 Appleby found a higher suicide rate among women who experienced stillbirths (associated with a rate six times that in all women after childbirth). Each of the four suicides following stillbirths occurred following first pregnancies.18 The study suggests that having living children offers some protection from postpartum suicide. Higher suicide rates were noted among teenage and unmarried mothers. Women tended to commit suicide during the first postpartum month and to use violent methods.18

In spite of the apparent protective effect that surviving the first postpartum year offers, women do commit suicide. Good preventive medicine requires that clinicians be alert and question women about their depression. For example, one of the authors (SFP) was asked to serve as a defense expert in a malpractice case involving a postpartum depression that led to suicide. In that instance, the patient had expressed concerns about anxiety and depression to her obstetrician. A prescription was telephoned in for a benzodiazepine, and the patient was referred to a mental health professional in the event that her symptoms persisted. In the end, the plaintiff’s case was supported by both the possibility that the anxiety agent may have reduced the patient’s judgment, increasing her risk of suicide, and that the obstetrician’s intervention was not sufficiently aggressive. It is the clinician’s responsibility to inquire about suicidal ideation. When suicidal ideation is an issue, emergent psychiatric consultation is warranted.

Treatment issues

Goals of treatment should include resolution of neurovegetative symptoms of depression and positive interpersonal interactions. In addition to the clinical benefits of treatment for a woman with postpartum depression, improved maternal-child interaction may also result. Stein et al.19 reported on an index group of 49 mothers who had depressive disorders in their postpartum year compared with 49 women controls who had been free of psychiatric disorders since delivery. These authors determined that there was a significant association between maternal depression in the postpartum year and reduced quality of mother-child interaction 19 months after delivery. They also found that this association held (though less strongly) for mothers who were depressed at 19 months postpartum as well as those who had recovered from depression by then.19 This information suggests the value of inquiring about maternal-child interaction among women with past or present postpartum depression and, ideally, observing the interaction. When there is evidence of mother-infant issues, appropriate medical and psychosocial intervention is indicated.

Altschuler et al.20 thoroughly reviewed the literature (1966–1995) regarding the use of psychotropic medication during pregnancy. Psychotropic medication crosses the placenta. Fetal psychotropic drug exposure may lead to
organ malformation (teratogenicity), neonatal toxicity, and behavioral sequelae.\textsuperscript{20} Treating clinicians should be current with knowledge about fetal risks when prescribing for the pregnant patient. Although it may appear to be ideal to discontinue psychotropics before pregnancy, it is not always possible because of concerns about symptom activation and recurrence.

Antidepressant use in pregnancy

Women with significant depression during pregnancy can benefit from antidepressant treatment. Concerns about teratogenesis and behavioral changes in neonates complicate treatment issues. Today, the serotonin-specific reuptake inhibitor antidepressants (SSRIs) (e.g., fluoxetine, sertraline, and paroxetine) are commonly used as first-line agents in the treatment of major depression. Their popularity is related to their relative safety in cases of overdose and their lack of cardiac toxicity and of anticholinergic side effects. These agents have not been studied to the same extent as the older tricyclic antidepressants (TCAs, e.g., imipramine, nortriptyline, and desipramine) in pregnancy. However, because of their safety in comparison with TCAs, SSRIs are commonly used during pregnancy.

Fluoxetine has been studied in pregnancy. In a prospective study of 128 pregnant women exposed to fluoxetine, TCAs, or nonteratogens, Pastuszak et al.\textsuperscript{21} found no differences between the groups in rates of malformations. Women treated with fluoxetine and TCAs tended to report “higher rates of miscarriage.” The authors recommend further studies to “confirm this observation and to separate the effects of the psychiatric condition from the associated drugs.”\textsuperscript{21} Chambers et al.\textsuperscript{22} reported that women taking fluoxetine in the first trimester of pregnancy were at greater risk of three or more minor (not specified) malformations (30\% were taking other psychotropic agents, e.g., benzodiazepines). These minor malformations were found in 15.5\% of offspring exposed during the first trimester compared with 6.5\% in the unexposed group.\textsuperscript{22} These authors found no increase in the risk of major congenital malformations.\textsuperscript{22} Infants exposed to fluoxetine in the third trimester were found to be at increased risk for premature delivery, lower birth weight, and admission to special care nurseries. The SSRIs are not considered to be major teratogens. Nulman et al.\textsuperscript{23} found no evidence that fluoxetine or TCA exposure during pregnancy affects either global IQ, language development, or behavioral development in preschool children.

There is a possibility of withdrawal symptoms in infants born of mothers taking SSRIs. One of the authors (DKG) has seen what appeared to be withdrawal from an SSRI (sertraline) in an infant whose mother was taking the drug. The infant experienced irritability and what were described as choreiform movements lasting approximately 5 days. The irritability was severe enough to require medical intervention with phenobarbital. Umbilical cord blood revealed levels of norsertraline (34 ng/ml). At 48 h following birth, the infant had nondetectable levels of sertraline and norsertraline.

Some patients will require TCA therapy during pregnancy. Wisner et al.\textsuperscript{24} reported that tricyclic dose requirements may increase during pregnancy “especially in the third trimester.”

In general, tricyclic therapeutic drug monitoring is important to increase the likelihood of antidepressant response by determining the presence of therapeutic levels and to reduce the likelihood of toxicity. However, as Wisner et al. note, dose-response curves have not been validated in pregnancy.\textsuperscript{24} In their report, the pregnant subjects responded to similar serum levels. Surveys of TCA use in pregnancy fail to demonstrate a significant increase in the incidence of congenital anomalies.\textsuperscript{23,25} Although use of TCAs appears to be relatively benign in regard to teratogenesis, there are concerns about maternal serum levels affecting the newborn. Transient withdrawal symptoms (hypotonia, tachypnea, cyanosis, irritability, and a poor sucking reflex) can be observed in neonates. These symptoms tend to be more severe with higher maternal doses. Symptoms generally resolve without treatment in 3–6 days. To minimize the possibility of tricyclic withdrawal, it is advisable to consider slowly tapering tricyclics before delivery when maternal depression is considered stable.
Hospitalization is warranted in severe, life-threatening cases of depression during pregnancy or postpartum. Electroconvulsive therapy (ECT) should be considered in these circumstances. Miller26 reviewed 300 case reports of ECT during pregnancy (1942–1991). ECT during pregnancy appears to be relatively safe provided safeguards are taken to reduce the risks. These include discontinuation of non-essential anticholinergic medication and careful use of uterine tocodynamometry, intravenous hydration, and administration of a nonparticulate antacid.26 While ECT is administered, the patient’s right hip should be elevated, and the fetus should be monitored externally. The patient should be intubated, and excessive hyperventilation should be avoided.26

Use of antidepressants postpartum

Following delivery, antidepressants can be prescribed as they would routinely be except for the issue of breast feeding. Response to any available antidepressant requires at least 4–6 weeks, assuming the patient is taking an appropriate dose. The likelihood of success in a patient who completes the first 3 weeks of treatment (initial dropout rate from side effects is approximately 15%) reportedly can reach 60%–70%.27

Patients with a first episode of major depression should be treated with antidepressants until full remission of symptoms is achieved. Following full remission of symptoms, patients with major depression (this may not necessarily apply to postpartum depression, which may be briefer, although more specific data are needed) should continue antidepressant therapy for an additional 16–20 weeks.27 Then the dose may be slowly tapered while clinically monitoring the patient. Some patients with histories of postpartum depression will do best with either prophylaxis or maintenance therapy. Wisner and Wheeler,28 in an open clinical trial, found that only 1 of the 15 (6.7%) women who had had at least one previous episode of postpartum depression suffered a recurrence if treated prophylactically with antidepressants. The initial antidepressant dose was given within 24 h of birth. In contrast, of 8 women who elected postpartum monitoring, only 5 (62.5%) suffered a recurrence.

In nonpuerperal experience, a history of three or more episodes of major depression warrants consideration of lifetime maintenance therapy to prevent recurrence.29 The value of lifetime maintenance therapy for women with exclusively postpartum depression has not been established. Given that nonpuerperal recurrence is relatively common, each case should be considered individually. Maintenance therapy is most effective when patients are treated with the full dose of antidepressants required for acute treatment.30,31

Antidepressants and breast feeding

The safety of breast feeding during maternal treatment with SSRIs has not been clearly established. The SSRIs may have an advantage in breast feeding because they are highly protein bound. This means that relatively little free drug is available to cross into breast milk. Altshuler et al.32 measured eight serial breast milk sertraline levels in one woman taking both sertraline and nortriptyline. In this case, although breast milk contained sertraline, none was detected in the infant either at 3 or 7 weeks. Nortriptyline was not detected in the infant at 3 weeks of age.32 Lester et al.33 reported on a possible association between fluoxetine in breast milk and symptoms (such as crying, sleep reduction, watery stools, and feeding problems) in a breast-fed infant that improved when the infant was switched to formula. Wisner et al.34 published a thorough and critical review of the literature regarding the use of antidepressants during breast feeding. They noted that amitriptyline, nortriptyline, desipramine, clomipramine, doxepin, and sertraline were not found in "quantifiable amounts in nurslings, and no adverse effects were reported."34

Psychotherapy in postpartum depression

Psychotherapy offers potential benefit in the treatment of postpartum depression. While waiting for drug response, support and education are extremely important for the patient. Various types of psychotherapy may be employed: cognitive therapy, interpersonal therapy, supportive psychotherapy, and conjoint
therapy to involve the new father. Stuart and O’Hara are investigating the role interpersonal psychotherapy (IPT) may play in the treatment of postpartum depression. IPT may be especially useful because women with postpartum depression often experience stressors, including disrupted interpersonal relationships, especially with their spouses or significant others. This type of psychotherapy is appealing to study because it is short term and offers consistency among therapists.

Psychotherapy may have a special role for women who choose not to take antidepressants or who experience milder depression. Issues of maternal guilt (may be related to difficulty in caring for the infant), poor self-esteem, family conflict, and stress can be addressed. Many experts believe that a combination of pharmacotherapy and psychotherapy is the best approach in the treatment of depression. More data are needed to assess the value of IPT and other forms of psychotherapy in the treatment of postpartum depression.

**POSTPARTUM MANIA**

The DSM-IV criteria for a manic episode include a distinct period during which there is an abnormally and persistently elevated, expansive, or irritable mood (lasting at least 1 week, or less if the woman is hospitalized). At least three other symptoms must come from a cluster that includes inflated self-esteem or grandiosity, decreased need for sleep, pressure of speech, flight of ideas, distractibility, increased involvement in goal-directed activities, or psychomotor agitation and excessive involvement in pleasurable activities with a high potential for painful consequences. In the case of an irritable mood, there must be at least four of the other symptoms listed. It is possible to see an admixture of depression and mania occurring concurrently, a condition referred to as a mixed manic episode.

**Risk of bipolar symptomatology during pregnancy and postpartum**

The morbidity of psychiatric illness is generally reduced during pregnancy and increased during the postpartum interval. Among women with bipolar disorder, the risk of postpartum illness is exceptionally high. The frequency of hospital admissions for bipolar disorder during pregnancy is about 0.75 the frequency during periods not related to pregnancy and delivery. In the month following delivery, the frequency of hospitalizations for bipolar women is increased eightfold. During the second to twelfth months following delivery, it is twice as high as the reference frequency.

Klompenhouwer and van Hulst studied the relationship between delivery and symptom onset in 250 women admitted to a mother-baby unit (for women with puerperal mental illness) in the Netherlands. Using RDC (operational criteria similar to the DSM-IV), they found that manics had the closest relationship between delivery and the onset of symptoms, 94% within 2 weeks and 97% within 3 weeks from delivery. All other categories had a less proximal relationship between delivery and onset of symptoms.

The increased risk of mania during the postpartum period has been attributed to psychologic factors and hormonal factors, such as estrogen and progesterone withdrawal. Wehr suggests that postpartum sleep deprivation may serve as a possible trigger. This theory may explain an interesting observation, that is, that mania following childbirth is as likely to occur in male as in female patients. Enhancing normal sleep-wake cycles with extra support may help prevent postpartum manic activation.

**Treatment issues**

A history of bipolar disorder identifies a pregnancy as being at high risk. Bipolar patients should have a psychiatric evaluation before conception, if possible. At that time, based on the history and other clinical factors, a treatment plan with follow-up throughout pregnancy and the postpartum interval should be developed. Successful treatment of bipolar disorder involves therapy with a mood stabilizer(s) and often some form of psychotherapy. Mood stabilizers include lithium carbonate and the anticonvulsants, valproic
acid (divalproex sodium) and carbamazepine. These anticonvulsants appear to be more effective than lithium in both dysphoric mania and rapid cycling bipolar patients.\textsuperscript{43-46} Swann et al.\textsuperscript{47} reported that even modest pretreatment depressive symptoms in manic patients are robust predictors of lithium nonresponse and associated with a better response to valproic acid (divalproex). Some patients will require combinations of mood stabilizers, such as lithium and valproic acid, to achieve stability. In more complicated cases, adjunctive therapy with neuroleptics (antipsychotics) and the benzodiazepine clonazepam may be necessary. Because the antimanic agents lithium and the anticonvulsants are the mainstays of treatment, they are the therapeutic focus.

**Antimanic agents and pregnancy**

First-trimester lithium use has been linked to congenital anomalies, especially cardiac anomalies, such as Ebstein’s anomaly (downward displacement of tricuspid valve into the right ventricle).\textsuperscript{20,48} According to Cohen et al.,\textsuperscript{49} the best estimate of risk of major congenital anomalies among offspring of women exposed to lithium early in pregnancy is approximately 4%-12%. Women in untreated comparison groups were found to have anomalies in 2%-4% of cases. In the past, the estimated relative risk of Ebstein’s anomaly among children whose mothers were exposed to lithium in the first trimester was estimated to be 400. However, no women who took lithium during pregnancy were found among four case-controlled studies of Ebstein’s anomaly.\textsuperscript{49} Ideally, bipolar women should have an opportunity for high-risk obstetric evaluation before conceiving. Women exposed to lithium in the first trimester of pregnancy should have early ultrasound confirmation of pregnancy dates and fetal echocardiograms at 16-18 weeks of gestation.

Lithium use during pregnancy at or near term may cause severe, usually reversible, toxicity in the newborn.\textsuperscript{20,49} Lithium toxicity in the fetus and newborn has been linked to cyanosis, hypotonia, bradycardia, thyroid depression with goiter, atrial flutter, hepatomegaly, electrocardiographic abnormalities (T wave inversion), cardiomegaly, gastrointestinal bleeding, diabetes insipidus, polyhydramnios, seizures, and shock.\textsuperscript{49} Neonatal recovery from lithium toxicity may require several weeks or more. Lithium half-life is prolonged in the newborn (68-96 h) compared with the healthy adult (10-20 h).\textsuperscript{49} Women who take lithium throughout pregnancy should optimally be tapered or discontinued from the lithium approximately 48 h before delivery. During pregnancy, regular determination of lithium levels is advisable. Renal lithium clearance rises during pregnancy and returns to prepregnancy levels after delivery.

Studies in women with psychiatric illness to assess rates of teratogenesis of anticonvulsants in pregnancy are lacking, in contrast to many studies done with women who have seizure disorders.\textsuperscript{20} Women with seizure disorders appear to have higher rates of malformations in their infants than do women who do not suffer seizures.\textsuperscript{20} Even when the risk of anticonvulsant-linked malformations is factored out, the anticonvulsants still appear to be possible teratogens.\textsuperscript{20}

Carbamazepine traverses the placenta, producing highest levels in the fetal liver and kidney.\textsuperscript{48} Fetal levels represent between 50% and 80% of maternal serum levels.\textsuperscript{48} Carbamazepine’s teratogenic risks include neural tube defects (approximately 0.5%-1%), craniofacial defects, development delays, and fingernail hypoplasia.\textsuperscript{20,48}

Valproic acid and its salt, sodium valproate, readily cross the placenta.\textsuperscript{48} Fetal/newborn consequences of valproic acid use during pregnancy are reported to include major and minor congenital abnormalities (spina bifida 1%-5%, and minor facial defects), hyperbilirubinemia, hepatotoxicity, transient hyperglycemia, afinitynogenemia, and fetal/neonatal distress.\textsuperscript{20,48} Because pregnant women taking valproic acid have the potential for decreased maternal fibrinogen levels, maternal vitamin K administration should be a consideration.\textsuperscript{48} There may be greater risk of malformations in women who are taking multiple anticonvulsants in the first trimester.\textsuperscript{20,48}

Among well-functioning bipolar women, drug treatment should not be given during the first trimester to avoid teratogenesis. Even when drug treatment is not used during preg-
Postpartum Mood Disorders

nancy, very careful psychiatric monitoring should be carried out. If the patient becomes symptomatic, treatment can be carefully instituted. In that case, medication management can be offered, with careful attention to the multiple challenges pregnancy brings to the use of mood stabilizers.

**Antimanic agents and breast feeding**

Lithium is excreted into human breast milk.\(^{50}\) Human milk levels are approximately 33%–50% of maternal serum lithium levels.\(^{48,50}\) Dehydration in infants or neonates born to mothers taking lithium can be a concern. Lithium can accumulate to toxic levels when its renal elimination is impaired as a result of dehydration. The American Academy of Pediatrics Committee on Drugs views breast feeding as contraindicated when mothers are taking lithium.\(^{50}\) According to the American Academy of Pediatrics, both valproic acid and carbamazepine are compatible with breast feeding.\(^{50}\)

**Antimanic agents postpartum**

Following delivery, bipolar women should restart mood-stabilizing therapy (provided they are not taking lithium and planning to breastfeed). In one report of 15 bipolar women, there was evidence of significant relapse reduction among medicated patients (27% of medicated patients relapsed postpartum versus 60% of untreated patients).\(^{51}\) Cohen et al.\(^{52}\) in a retrospective cohort study, described the course of 27 bipolar women who were followed clinically during pregnancy and the postpartum period. In their study, only 1 in 14 patients on prophylactic agents during the acute puerperium was noted to relapse in the first 3 months postpartum.\(^{52}\) Eight of 13 women who were not treated prophylactically showed evidence of "recurrent affective instability during the comparable period of time."\(^{52}\) Evidence suggests that such an approach will dramatically reduce the likelihood of symptom exacerbation. Carbamazepine (but not divalproex sodium) can increase the hormonal clearance of oral contraceptives, making them unreliable.\(^{48}\)

**Psychotherapy in postpartum bipolar disorder**

Psychotherapy for the very manic patient has limited value. However, it can play an important role for the relatively stable bipolar woman before conception, during pregnancy, and postpartum. Psychotherapy may augment the efficacy of outpatient pharmacotherapy.\(^{53}\) Specific goals can include "modifying social risk factors, enhancing medication adherence, increasing the patient's and family's willingness to accept the reality of this disorder, and reducing suicidal risk."\(^{54}\) Bipolar disorders can lead to chaotic interpersonal and work relationships. The patients may resist treatment because they do not want to give up their manic experiences. This can lead to anger and resentment among family members. Even the treating psychiatrist may experience negative transference from the patient because the patient lacks insight into the need for treatment. In our experience, when the patient has a significant relationship (marital or otherwise), conjoint or family therapy may be quite beneficial.

**Bipolar disorder summary guidelines**

Because bipolar disorder is so commonly associated with problems, bipolar women should be seen and followed carefully by both a psychiatrist and the obstetrician-gynecologist during pregnancy, immediately postpartum, and beyond. Because of the very high risk of recurrent depression and mania in bipolar patients, lifetime psychiatric follow-up and maintenance therapy are generally the standard of care.\(^{42}\) Suggestions for optimal treatment of the bipolar patient who is facing pregnancy or is pregnant include the following.

1. Discuss and provide education (document this) for the patient and, ideally, her partner about the potential teratogenesis of antimanic agents as well as the likelihood of postpartum illness activation.
2. When prescribing mood stabilizers for women at risk for pregnancy, encourage careful contraceptive practice (carbamazepine can reduce the efficacy of oral contraceptives).
3. In ideal circumstances, consider discontinu-
430 PARISER ET AL.

ation of mood-stabilizing medication before pregnancy and during the first trimester.
4. Women requiring antimanic treatment during pregnancy should have regular determination of the prescribed agent’s serum levels.
5. Consider reduction or cessation of antimanic agent(s) as delivery approaches.
6. Carefully observe (in a neonatal care unit) the neonates born of bipolar women who were treated with psychotropic agents during the final weeks of pregnancy. Monitor the infant’s serum levels of the maternal prescribed antimanic medication in relation to clinical symptomatology.
7. Restart mood stabilizers immediately after delivery (if they have been discontinued during pregnancy). Lithium is contraindicated during breast feeding; valproic acid and carbamazepine are not.
8. Carefully follow the mother during the postpartum year to detect the earliest signs of mania or depression. Initiate or modify treatment to address the clinical picture.

POSTPARTUM PSYCHOSIS

Postpartum psychosis is a terrible experience for a new mother. It usually leads to psychiatric hospitalization. In the most severe cases, it can lead to infanticide or maternal suicide. Although schizophrenia may emerge postpartum with either new symptoms or an exacerbation, most postpartum psychoses are severe mood disorders.55

Psychosis is a term that carries different connotations, none of which is universally accepted.6 Psychosis, narrowly, may refer to the specific presence of hallucinations or delusions occurring in the absence of insight into their pathology.6 However, psychosis may also refer to schizophrenia (positive symptoms), such as disorganized speech and thoughts and bizarre or catatonic behavior.6 In addition, psychosis may refer to a psychiatric illness with severe functional impairment, or it may conceptually refer to loss of ego boundaries.6 Because of a lack of definition agreement, the term “postpartum psychosis” carries different connotations. Often, the literature refers to postpartum psychosis when implying that hallucinations or delusions are present (which may be the case in psychotic mood disorders or schizophrenia) or to the fact that the mood disorder or schizophrenia causes very severe limitation in the ability to function. In any case, psychosis is highly serious and potentially lethal when it occurs postpartum.

According to the DSM-IV, a specifier (with Psychotic Features) can be added to either major depressive or bipolar diagnoses.6 The psychotic feature modifier indicates the presence of either delusions or hallucinations (typically auditory).6 The content of either delusions or hallucinations is usually mood congruent, that is, consistent with either depressive or manic themes.

Videbech and Gouliaev,56 using the Danish Psychiatric Central Register and the Danish Medical Birth Center, found that 1 of 1000 women was admitted to a psychiatric department within 1 year with first-episode psychosis. The index episodes were manic-depressive psychosis in approximately 50% of the cases. Twenty percent had mania, 60% had severe depression, and none had schizophrenia.56 Rohde and Marenos57 found that among 86 women who suffered from a psychotic disorder for the first time in their lives within 6 weeks after delivery, the majority became sick after the first (75%) full-term normal (63%) delivery and within the first 2 weeks after delivery (78%). These authors found that there was a 1:4 recurrence following additional pregnancies.57

Women with postpartum psychosis may have symptoms even more striking than non-postpartum women with psychosis. Wisner et al.58 studied women with CBROI and found that those who were psychotic demonstrated “prominent symptoms related to cognitive impairment and bizarre behavior,” as compared to women with non-CBROI psychoses.

Treatment issues

The management approach for postpartum psychosis includes hospitalization and the appropriate medical therapy (antidepressants, mood stabilizers, antipsychotics, or ECT). When antipsychotics are prescribed, their uses
should be limited to the minimal dose and duration necessary to avoid tardive dyskinesia. Neuroleptic treatment is associated with a risk of tardive dyskinesia (women are more at risk than men). In many cases, mood stabilizers or antidepressants will reduce psychotic symptoms, with only periodic need for antipsychotics.

Because of the severity and likelihood of recurrence, prophylaxis should be given consideration. In one report of four women with a history of puerperal affective psychosis who were given lithium prophylactically, none of the four experienced a recurrence of their postpartum psychotic symptoms following delivery. This is significant, given that the risk of recurrence in the four patients in past pregnancies varied from 20% to 50%.

Given the propensity for recurrence, patients with histories of postpartum psychoses may well deserve prophylaxis with the appropriate psychotropic agent(s) following delivery or, at the bare minimum, intensive observation. Appearance of even mild psychiatric symptoms should strongly prompt consideration of reinstating previously effective drug therapy.

DISCUSSION

Postpartum mood disorders are common. Extensive evidence documents the recurring nature of mood disorders, including postpartum mood disorders. Awareness of the critical issues in the identification of women at high risk for recurrence is important. Such awareness affords the opportunity for patients and clinicians to recognize these syndromes early, permitting prompt treatment and reduction in morbidity and mortality. In some instances, maintenance therapy can be offered to reduce the likelihood of recurrence.

This approach requires appropriate consultation and collaboration among the treatment team (primary care physicians, obstetrician, psychiatrist, pediatrician, and nurses) and the patient and her family. A well-developed, proactive approach can protect the patient and her family from intense personal pain. It should also serve the mission of cost control, including the avoidance of preventable hospital admissions. These issues are increasingly more relevant in our contemporary managed-care environment.

It is wise to obtain a psychiatric consultation on any female patient at high risk for or with symptoms of a postpartum mood disorder. The key to ascertaining high-risk status is careful and detailed history-taking along with well-directed attention to the patient’s mood and mental status. Patients who appear to be dysphoric, anxious, or both deserve careful scrutiny. Symptoms of sleep disruption (either insomnia or hypersomnia), poor concentration, loss of interest in usual activities, tearfulness, hopelessness, or morbid ideation all point to depression. Patients who are euphoric or highly irritable and have other symptoms (such as decreased need for sleep, racing thoughts, distractibility, hyperverbal behavior with pressured speech, grandiosity, hypersexuality, and spending sprees) may be bipolar. All patients with depression should still be queried about a past history of mania or hypomania because they may have bipolar depression. Bipolar will usually be managed first with mood stabilizers. Antidepressants may be used in some cases.

Ideally, psychiatric consultation should be obtained before conception in women with positive psychiatric histories or current symptoms. This will permit the psychiatrist, the obstetrician, and the patient to design a treatment plan that is most likely to prevent catastrophic problems of severe mood disorder episodes. The prepartum psychiatric evaluation should

- Establish an accurate psychiatric diagnosis, including an assessment of psychosocial well-being, family support, and the presence or absence of comorbid variables that may interfere with effective treatment (e.g., drug or alcohol problems, spousal abuse).
- Inform the patient of the implications of her diagnosis with regard to medical and psychiatric management. Issues of fetal drug exposure and breast feeding need to be addressed and documented.
- Alert the patient to the need for prompt intervention in the presence of symptom activation or worsening, including suicidal ideation.
• Lead to communication with the obstetrician about diagnosis and treatment recommendations. It is important to maintain an open dialogue between the obstetrician and psychiatrist throughout the pregnancy and postpartum period.

Careful follow-up with the psychiatrist and other therapists during the pregnancy and in the ensuing weeks and months postpartum is also worthwhile. As a part of this process, patient education is essential to enhance the likelihood of medication adherence, reduce the guilt that may be associated with psychiatric illness, and afford the best opportunities for prophylaxis. Concerns about the postpartum patient should include the well-being of the infant’s father. A healthy, supportive relationship between the new mother and the infant’s father is valuable, especially for the woman with a postpartum mood disorder. Furthermore, enhanced rates of mental illness have been reported among spouses of women with postpartum psychiatric disorders. Spouses of women with postpartum psychiatric disorders experienced greater marital dissatisfaction and more change in household routines, recreation, and intimacy with their partners than controls. Clearly, the postpartum mood disorder patient should be understood in the context of her family and environment for optimal clinical benefit. For this reason, it is ideal to see the woman with a postpartum mood disorder along with her significant other. Women with postpartum psychiatric illness need to be followed carefully not only during subsequent pregnancies but throughout their lives for the possibility of recurrent illness. Postpartum mood disorders can be anticipated and recognized early. With prompt, humane treatment, the pain of psychiatric illness at such an important and special time for the family can be minimized.

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REFERENCES

23. Nulman I, Rovet J, Stewart DE, et al. Neurodevelopment of children exposed in utero to antidepressant drugs. N Engl J Med 1997;336:258.
35. Stuart S, O'Hara M. Treatment of postpartum depression with interpersonal therapy [Letter to the Editor]. Arch Gen Psychiatry 1995;52:75.

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