Update on Depression in Pregnancy

Sabrina J. Khan, MD; Shari I. Lusskin, MD

For most women, pregnancy is an exciting and joyful time. But for others it can be emotionally trying, especially for those with a history of depression or other psychiatric disorders. The implications of untreated depression in pregnancy are serious and include a higher risk for postpartum depression. This article offers an update on the diagnosis and treatment of depression during pregnancy, including the use of antidepressants during pregnancy and lactation.

Depression affects 14.5% of pregnant women, with many going undiagnosed or undertreated.1 Pregnant women who are depressed often feel ashamed about not being happy while others around them are excited about the baby. They may not reveal their symptoms to their obstetricians, and by the time they do, they are often quite ill.

Untreated depression can result in poor self-care (eg, inadequate nutrition, noncompliance with prenatal care), self-medication with drugs, alcohol, or tobacco, poor bonding with the baby, postpartum depression, and suicide.2 It has also been associated with preterm birth, small-for-gestational-age babies, low-birth-weight babies, and effects on child development.3 If postpartum depression develops and is not treated, it can become a chronic or relapsing illness.

DIAGNOSIS
Obstetricians should inquire about their patients’ mood and stress level at each visit. The 10-item self-rated Edinburgh Postnatal Depression Scale can also be used to screen for antenatal depression.

The core symptoms of major depression are depressed mood and/or anhedonia for at least 2 weeks.4 Depression-related changes in sleep, energy, and appetite are often mistaken for the normal changes of pregnancy. Patients should be asked about subjective symptoms of depression: feelings of sadness, hopelessness, helplessness, guilt, or worthlessness, difficulty concentrating or making decisions, and suicidal ideation. Sleep and appetite disturbances are beyond what might be expected. The differential diagnosis should include bipolar depression. The distinction between unipolar and bipolar depression is important, since antidepressant pharmacotherapy may exacerbate mood cycling in bipolar disorder.

Anxiety is a frequent complaint in depressed patients, and comorbid anxiety disorders should be ruled out.5 Generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder are the most prevalent. Depressed women may experience disturbing obsessive thoughts about harming their baby. These patients recognize the thoughts as illogical and intrusive and may go to great lengths to avoid acting on them. In contrast, a patient with psychosis believes the thoughts are real and may harm the baby in response. It is unusual for the pregnant or postpartum woman with obsessional thoughts to become psychotic. To elicit these symptoms, the obstetrician may ask the patient whether she has had any...
RISK FACTORS
Risk factors for depression in pregnancy include a prior history of depression, especially postpartum depression, a family history of depression or bipolar disorder, and discontinuation of antidepressants. One study found that women with a history of recurrent major depression who were euthymic at conception had a 68% risk of relapse after discontinuation of their antidepressant just before or during pregnancy, compared to a 26% relapse rate among those who continued medication. The relatively high rates in both groups underscore the importance of close monitoring throughout pregnancy. Additional risk factors include medical or obstetrical complications, history of substance abuse, history of trauma including intimate partner violence, major stressful life events, financial difficulties, limited social or family support, relationship problems, and unplanned or unwanted pregnancy.

TREATMENT
Ideally, the obstetrician will identify high-risk patients prior to conception and outline an appropriate treatment plan. It is just as important that all patients be advised of the risk for depression in pregnancy and postpartum, because the low-risk patient is often missed.

Consultation with a psychiatrist is recommended if the obstetrician does not feel comfortable managing the psychiatric care, if the patient does not achieve full remission, and/or if the patient requests it. Reproductive psychiatrists, when available, may provide specialty consultations.

The severity of illness will determine the treatment approach. For cases of mild depression, psychotherapy using interpersonal or cognitive behavioral techniques may be effective. While psychotherapy is an integral part of treatment in any episode of depression, moderate to severe episodes often require combined treatment with medication.

ANTIDEPRESSANTS IN PREGNANCY
Teratogenicity
Various studies have evaluated the risk for congenital malformations with first-trimester exposure to selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs). The majority have shown no increased risk of birth defects following first-trimester exposure. However, a controversy about paroxetine developed when an increased incidence of septal heart defects was found in a large insurance database study. Many patients consequently discontinued paroxetine before or during pregnancy and relapsed. Subsequent studies found no association with cardiovascular malformations, including a 2009 analysis of 3,235 paroxetine exposures in the first trimester.

In 2007, two large case-control studies examined the teratogenicity of SSRIs. Both concluded that there was no association between congenital heart defects or other anomalies and first trimester use of SSRIs overall. Secondary analyses of each data set suggested very small associations between individual SSRIs and rare birth defects. Of note, the 2 studies produced conflicting results. Limitations of both studies include the small number of exposed infants, the use of multiple comparisons, failure to control for maternal illness and substance abuse (including tobacco), and lack of confirmation of drug exposure. A recent population-based cohort study also found no increased risk for major malformations when all SSRIs were combined, although individually sertraline and citalopram, but not paroxetine, were associated with an increased incidence of septal heart defects (1.5% and 1.1%, respectively, vs 0.5% in the control group). Limitations were similar to the 2007 studies.

In the September 2009 guidelines on the treatment of depression in pregnancy issued by the American Psychiatric Association and

News Update: For the most recent ACOG committee opinion on screening for depression in pregnancy, see the February 2010 issue of the green journal (ACOG Committee on Obstetric Practice. Committee opinion no. 453: Screening for depression during and after pregnancy. Obstet Gynecol. 2010;115[2 Pt 1]:394-395.) The opinion lists suggested screening tools and provides coding information.
ACOG, the expert panel concluded that “the current data on SSRI exposure show no consistent information to support specific morphological teratogenic risks.” This report also addressed the use of TCAs and the newer antidepressants. Though the TCAs are less often used (given their side-effect profile), studies have not shown an association with malformations. Compared with SSRIs, there are fewer data on bupropion and venlafaxine in pregnancy, but no studies have found an increased risk for congenital anomalies with these newer medications. Sertraline is now considered the first-line antidepressant in pregnancy, but treatment must be individualized.

**Neonatal Complications**

Symptoms including respiratory distress, hypoglycemia, jitteriness, lethargy, weak crying, irritability, tremor, feeding difficulties, and (rarely) hypotonia and convulsions have been reported with TCAs, SSRIs, and SNRIs. “Poor neonatal adaptation” is a preferred term for these symptoms that are typically transient, resolve within 2 weeks (usually within the first 2 days), and require only supportive (if any) care.

In one population-based study that attempted to control for maternal mental illness, the rate of neonatal complications appeared to be elevated in babies exposed to SSRIs. However, a prospective cohort study found no association between antidepressant exposure and poor neonatal adaptation. A major limitation of each study was not controlling for tobacco use; neonatal signs such as jitteriness and res-

### Coding for Depression in Pregnancy

Many of the symptoms mentioned in this article do not have associated ICD-9 codes, but there are several that could be used to document the diagnosis.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>290.0</td>
<td>Bipolar I disorder, single manic episode&lt;br&gt;Puerperal, single episode or unspecified</td>
</tr>
<tr>
<td>296.2</td>
<td>Major depressive disorder, single episode</td>
</tr>
<tr>
<td>296.3</td>
<td>Major depressive disorder, recurrent episode</td>
</tr>
<tr>
<td>296.9</td>
<td>Other and unspecified episodic mood disorder</td>
</tr>
</tbody>
</table>

You must use a fifth digit with the 296.0–296.3 categories:

- **0**: Unspecified
- **1**: Mild
- **2**: Moderate
- **3**: Severe, without mention of psychotic behavior
- **4**: Severe, specified as with psychotic behavior
- **5**: In partial or unspecified remission
- **6**: In full remission

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>300.0</td>
<td>Anxiety states</td>
</tr>
<tr>
<td>300.00</td>
<td>Anxiety state, unspecified</td>
</tr>
<tr>
<td>300.01</td>
<td>Panic attack</td>
</tr>
<tr>
<td>300.3</td>
<td>Obsessive-compulsive disorders</td>
</tr>
<tr>
<td>300.4</td>
<td>Anxiety depression&lt;br&gt;Depression with anxiety</td>
</tr>
<tr>
<td>300.9</td>
<td>Unspecified nonpsychotic mental disorder&lt;br&gt;Suicidal tendencies&lt;br&gt;Self-mutilation</td>
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If the clinician needs to meet with the patient to discuss the condition, the appropriate E & M code should be utilized based on time.

If the clinician decides to request a consultation from a psychiatrist, it is recommended that this request be documented in the patient’s medical record.

**Philip N. Eskew Jr, MD**, is past member, Current Procedural Terminology (CPT) Editorial Panel; past member, CPT Advisory Committee; past chair, ACOG Coding and Nomenclature Committee; and instructor, CPT coding and documentation courses and seminars.
piratory difficulties may be related to nicotine withdrawal.\textsuperscript{16} SSRI exposure has been linked to preterm birth and low birth weight.\textsuperscript{3} However, a recent prospective observational study analyzing neonatal outcomes showed no increased risk for low birth weight, respiratory difficulties, or neonatal ICU admissions with SSRI exposure.\textsuperscript{17} In this study, the risk for preterm birth was 20\% both for babies exposed to SSRIs and for babies exposed to depression but not SSRIs. This suggests that the increased risk may be secondary to depression.

In a retrospective case-control study, an increased risk for persistent pulmonary hypertension (PPHN) with SSRI exposure after 20 weeks of pregnancy was found, with an odds ratio of 6.1 (resulting in an incidence of 6 to 12 per 1,000).\textsuperscript{18} In contrast, other research has found no association between SSRI use in late pregnancy and PPHN.\textsuperscript{19}

**Neurobehavioral Teratogenicity**

Though studies are limited, no association has been found between SSRI or TCA exposure in utero and impaired neurodevelopment, including IQ, language, and behavior.\textsuperscript{20-22} Each study did show that variations from the norm within both exposed and unexposed control groups were correlated with maternal postpartum depression.

**Dosing**

Women on antidepressants are often advised to lower their antidepressant doses prior to or during pregnancy. Unfortunately, this increases the risk for relapse.\textsuperscript{6} In fact, patients often require increasing doses of antidepressants as the pregnancy progresses to maintain a therapeutic effect. This is due to alterations in pharmacokinetics secondary to decreased gastric motility, increased total body water, decreased albumin concentration, and altered hepatic drug metabolism.\textsuperscript{23}

**BREASTFEEDING**

Postpartum depression affects more than 10\% of women.\textsuperscript{1} Switching or discontinuing the antidepressant postpartum is not recommended; exposure during breastfeeding is lower than during pregnancy, rates of infant complications are low, and discontinuation would increase the risk of relapse. The mother, in conjunction with the pediatrician, can monitor the baby for side effects.\textsuperscript{24} The largest body of data exists for fluoxetine, sertraline, and paroxetine. Sertraline is also now considered first line during lactation.

**CONCLUSION**

The sooner a pregnant woman with depression is diagnosed, the sooner she can be treated to remission. There is no “one-size-fits-all” approach to management. While some patients may benefit from a trial of psychotherapy, others will require medication, and a combination of treatments is often needed. If a trial of pharmacotherapy is indicated, treatment must be individualized so that the patient is on the medication that works best for her.

It is essential that the patient (and her partner, whenever possible) make an informed decision about treatment of depression during pregnancy. This is accomplished by having a thorough discussion regarding the risks and benefits of treatment, including but not limited to the risks of teratogenicity, neonatal complications, and neurobehavioral abnormalities. It is also critical to review the risks of no treatment. There is no such thing as “nonexposure”: The baby will be exposed to the illness or the medications, or to both. Close monitoring, and coordination of care between the obstetrician, the psychiatrist, and the pediatrician, will help ensure the best outcome for the mother, baby, and family.

The authors report no actual or potential conflicts of interests in relation to this article.

**REFERENCES**

6. Cohen LS, Altshuler LL, Harlow BL, et al. Relapse of major depression during pregnancy in women who maintain or...