

Postpartum depression: What to tell patients who breast-feed

Evidence suggests most—but not all—SSRIs, tricyclics are reasonable choices

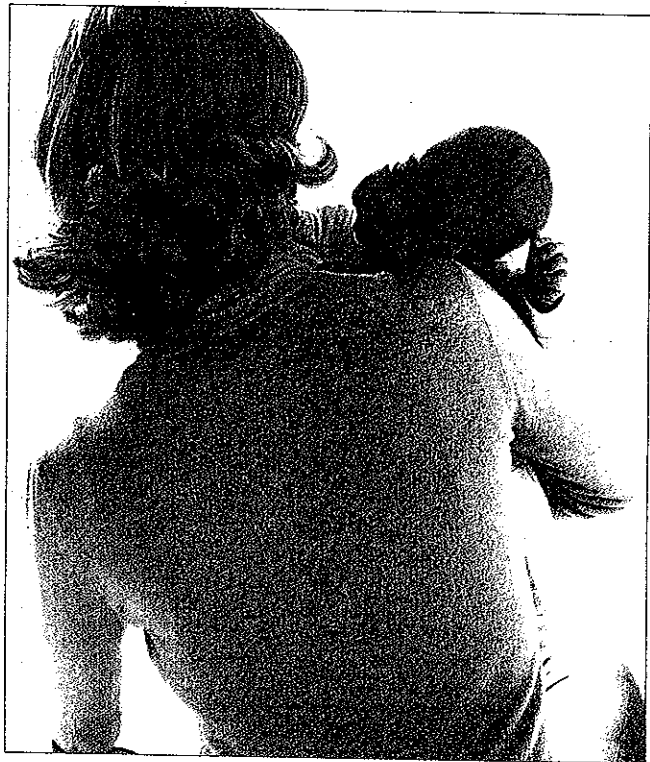
Whether you encounter postpartum depression (PPD) in a patient you have been treating or in one referred by her obstetrician, early, aggressive treatment is essential. Although PPD shares some symptoms with major depressive disorder (MDD)—and may be a subtype of that disorder—it also has distinguishing characteristics, such as timing of symptom onset (*Box 1, page 88*).^{1,2} Two screening tools facilitate diagnosis (*Box 2, page 93*).^{2,4}

Women with PPD usually respond to pharmacotherapy, but antidepressants' potential effects on a nursing mother's newborn are important to consider.

HPA axis dysregulation

Although the precise cause of PPD remains unclear, a better understanding is emerging of the complicated interplay of estrogen and progesterone with the hypothalamic-pituitary-adrenal (HPA) axis and other neuroregulatory systems associated with depressive illness. Two lines of evidence implicate hormonal dysregulation:

- Despite normal reproductive hormone levels, women with PPD may have an abnormal response to changes in these levels.⁵
- Abnormalities in HPA axis activity appear to be associated with reproductive endocrine-related mood disorders in vulnerable women, particularly during the transition from childbirth to the immediate postpartum period.



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Postpartum depression

Clinical Point

Understanding HPA axis reactivity in women with PPD could improve early identification and treatment

Box 1

Not just 'baby blues': Clues to postpartum depression

Most women will have mild mood and anxiety symptoms in the first few days to weeks postpartum—often referred to as the 'baby blues'—but these symptoms usually resolve spontaneously. More severe and persistent depressed mood and anxiety should arouse suspicion of postpartum depression (PPD).

Although not categorized as a distinct disorder in the DSM-IV-TR, PPD is diagnosed using DSM-IV-TR criteria for a major depressive episode, including feelings of being overwhelmed, guilt or worthlessness, tearfulness, appetite

change, difficulty sleeping (even when the baby is sleeping), difficulty concentrating, and loss of interest or pleasure in activities.²

PPD symptoms differ, however, in some important ways from those of nonpuerperal depression. Distinguishing characteristics of PPD are:

- severe worry, anxiety, and/or agitation
- fears of hurting the baby or oneself
- not having any interest in the baby.²

PPD usually begins within the first month postpartum but may occur later; the first 3 months appear to be the most vulnerable period.³

A radical transition. Dramatic hormonal changes occur in the transition from pregnancy to postpartum.⁶ The third trimester of pregnancy is characterized by:

- high estrogen and progesterone levels
- a hyperactive HPA axis (normal during pregnancy)
- high plasma cortisol level, stimulated in part by high levels of estrogen and progesterone.^{7,8}

Estrogen and progesterone rapidly decline as a woman transitions to the postpartum period, and HPA axis activity is blunted because of suppressed hypothalamic corticotrophin-releasing hormone (CRH) secretion.⁹

Differences in HPA reactivity. In a normal HPA axis, the delivery of CRH from the paraventricular nucleus of the hypothalamus triggers the stimulation of adrenocorticotrophic hormone (ACTH) from the anterior pituitary and, consequently, cortisol from the adrenal cortex. This hormonal system is regulated by negative feedback mediated by cortisol receptors on the anterior pituitary, hypothalamus, and hippocampus, as well as ACTH receptors in the anterior pituitary and CRH autoreceptors in the hypothalamus.¹⁰

A hallmark feature of the HPA axis in depression is altered response to stress and inability to maintain regulation:

- In MDD, HPA axis hyperactivity is one of the most robust biological findings.¹¹

In general, women with MDD exhibit high baseline cortisol and an exaggerated response to the dexamethasone/corticotropin releasing hormone test.

- In contrast, women with PPD experience a more blunted ACTH response to CRH, which may reflect a hyporeactive HPA axis.⁹

Nonetheless, Bloch et al¹² observed an increased cortisol response to CRH in women with a history of PPD during high-dose gonadal steroid administration, which suggests either a trait vulnerability related to PPD onset or a consequence of an earlier depression.

It has been hypothesized that both increased cortisol and decreased cortisol (observed under conditions of sustained elevated gonadal steroid levels or withdrawal of gonadal steroids) may result in insufficient glucocorticoid signaling.¹³ Impaired glucocorticoid signaling may be the "final common pathway" leading to psychiatric disturbance in MDD and PPD.

Understanding the characteristics of HPA axis reactivity in women with PPD could improve early identification and, theoretically, prevention or immediate treatment for at-risk women. In addition to HPA axis dysregulation, disturbances in other endocrine systems may play a role in PPD. Women with antenatal total and free thyroxine concentrations in the lower euthyroid range may be at increased risk of developing postpartum depressive symptoms.¹⁴



2 tools for rapid postpartum depression screening

Two well-validated, simple-to-administer postpartum depression (PPD) screening instruments are useful during the postnatal period:

- the Edinburgh Postnatal Depression Scale (EPDS),³ a 10-item self-report questionnaire that asks about mood, anxiety, guilt, and suicide ideation
- the Postpartum Depression Screening Scale (PDSS),⁴ a 35-item self-report questionnaire that asks about sleeping/eating disturbances, anxiety/insecurity,

emotional lability, mental confusion, loss of self, guilt/shame, and suicide ideation.

If screening indicates a patient has PPD, her psychiatric history will influence your treatment selection. Pay particular attention to:

- past episodes of depression, hypomania, or mania
- severity and timing of those episodes
- treatment history, including documentation of response to antidepressants.²

Risks with or without treatment

PPD has potentially serious adverse consequences and needs to be aggressively treated. Ethical and practical challenges have hindered PPD research, however, and evidence to guide treatment is limited.¹⁵

Approximately 70% of mothers in the United States breast-feed their infants at least for the first 3 months.¹⁶ With any patient with PPD who is breast-feeding, carefully discuss the risk of antidepressant side effects for the mother and child.¹⁷

Also discuss potential risks and benefits of treatment vs no treatment.¹⁷ Potential risks of untreated depression include:

- impaired mother/child bonding because of ongoing maternal depressive illness
- impaired cognitive, emotional, and social development in the child.¹⁸

A collaborative, multidisciplinary treatment approach that includes the patient's psychiatrist, obstetrician, and pediatrician is important to:

- educate the patient about potential antidepressant side effects for mother and baby
- avoid communicating "mixed messages" to the patient about the risk and benefits of treatment
- ensure the health of mother and baby.¹⁷

Advise mothers who take antidepressants that they can minimize their babies' exposure to peak drug concentrations by taking the antidepressant immediately after breast-feeding and before the infant sleeps.¹⁷

Also discuss strategies for balancing the need for sleep with the demands of breast-feeding. Reassure patients that although this is not easy, it can be accomplished with thoughtful planning and good partner support.

Antidepressants. In general, women with PPD respond well to antidepressant therapy. They may be hesitant to take any medication while breast-feeding because of possible harmful effects to their babies, but most studies examining antidepressant use by lactating women found low rates of adverse events in infants exposed to antidepressants (*Table, page 94*).¹⁹⁻²⁴ Potential adverse effects include:

- sedation
- changes in sleep or feeding
- irritability.¹⁷

Selective serotonin reuptake inhibitors (SSRIs) and tricyclics (except doxepin) are commonly used to treat PPD.²⁵ Neither class has been proven superior.¹⁷ Monoamine oxidase inhibitors are not recommended because they can exacerbate hypertension and interact with food and other medications.²⁵

SSRIs. Few adverse events have been reported with sertraline, paroxetine, and



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Most studies of antidepressant use in lactating women found low rates of adverse events in infants



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Use fluoxetine or citalopram only in women who responded to them during a previous pregnancy or depressive episode

Table

Antidepressants for postpartum depression

Medication	Starting dosage	Maximum dosage during lactation	Potential adverse event(s)
Selective serotonin reuptake inhibitors			
Citalopram	10 mg	60 mg	High milk/plasma concentration at higher doses ²⁰
Escitalopram	10 mg	20 mg	Very limited data to date show lower milk/plasma concentrations compared with citalopram ²¹
Fluoxetine	10 mg	60 mg	Long half-life can increase the potential for accumulation ²⁰
Paroxetine	10 mg	50 mg	Minimal detection of drug in infants' serum ^{19,20}
Sertraline	25 mg	150 to 200 mg	Minimal detection of drug in infants' serum ^{19,20}
Tricyclics			
Desipramine	25 mg	200 mg	Minimal detection of drug in infants' serum ^{19,22}
Imipramine	25 mg	200 mg	Minimal detection of drug in infants' serum ^{19,22}
Nortriptyline	25 mg	125 to 150 mg	Minimal detection of drug in infants' serum ^{19,22}
Others			
Bupropion	75 to 150 mg	300 mg	Limited data available. Small increased risk of infant seizure (case report) ²⁴
Mirtazapine	7.5 mg	45 mg	Limited data available. Well tolerated in a small study. ²³ Always monitor for changes in sleep (sedation and activation) and eating behaviors

Note: Clinical monitoring of the infant for adverse effects—including sedation, changes in sleep or feeding, and irritability—should be part of routine care.

fluvoxamine during lactation.²⁰ However, paroxetine may be associated with increased risk of cardiac abnormalities in infants exposed during the first trimester of pregnancy.²⁶ Two agents in this class may be less desirable:

- fluoxetine, because it has a long half-life
- citalopram, because of potentially high breast milk concentration.²⁰

Use fluoxetine or citalopram only in patients who had a good response to them during pregnancy or a previous depressive episode. For women who took an antidepressant during pregnancy, continue the same medication postpartum to prevent exposing the infant to another drug.

Tricyclics might be indicated for patients who responded to them previously or who have not responded to SSRIs. No adverse effects have been reported in breast-feeding infants receiving amitriptyline, clomipramine, desipramine, imipramine,

or nortriptyline.²⁵ Avoid doxepin, however, because it has the longest half-life among tricyclics, and adverse effects in infants—including respiratory distress, drowsiness, and vomiting—have been reported.

Other antidepressants. Venlafaxine and duloxetine are not recommended because of limited data about use of these agents during lactation. Bupropion poses a small increased risk of seizures in newborns but is not absolutely contraindicated.²⁴ Trazodone also has limited data, but in clinical practice it has been used safely at low doses for many years.²⁰

Psychotherapeutic techniques—including individual or group therapy—also can effectively reduce depressive symptoms in women with PPD.²⁷

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Related Resources

Clinician resource

- Cuijpers P, Brännmark JG, van Straten A. Psychological treatment of postpartum depression: a meta-analysis. *J Clin Psychol* 2008;64(1):103-18.

Patient resource

- American Psychiatric Association. Postpartum depression. www.healthyminds.org/postpartumdepression.cfm.

Drug Brand Names

Amitriptyline • Elavil, Endep	Fluvoxamine • Luvox
Bupropion • Wellbutrin	Imipramine • Tofranil
Citalopram • Celexa	Mirtazapine • Remeron
Clomipramine • Anafranil	Nortriptyline • Aventyl
Desipramine • Norpramin	Paroxetine • Paxil
Doxepin • Sinequan	Sertraline • Zoloft
Duloxetine • Cymbalta	Trazodone • Desyrel
Escitalopram • Lexapro	Venlafaxine • Effexor
Fluoxetine • Prozac	

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Avoid doxepin because adverse effects have been reported in infants exposed to it via breast milk

Bottom Line

Carefully discuss antidepressant use during lactation with any breast-feeding woman diagnosed with postpartum depression (PPD). The risks and benefits of not treating PPD with antidepressants vs antidepressant exposure during lactation must be considered on an individual basis. Despite infants' exposure to medications in breast milk, selective serotonin reuptake inhibitors and tricyclic antidepressants appear to be well tolerated by nursing mothers and their infants, with low adverse events rates.