

# Postpartum depression or medical problem?

Watch for fatigue, weight change, other physical signs



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**M**any medical conditions common among new mothers can cause depressed mood, fatigue, and other symptoms that suggest postpartum depression. To help you quickly pinpoint the source of a new mother's depressive symptoms and plan treatment, this article reviews:

- new-onset or pre-existing neurologic, cardiovascular, thyroid, and other conditions that mimic postpartum depression
- risk factors and clinical features that distinguish postpartum depression from other psychiatric disorders
- laboratory tests that confirm or rule out medical problems.

### CASE: 'I CAN'T SLEEP'

Mrs. A, age 40, sleeps 2 hours nightly at most. Awakened by her 3-month-old daughter's overnight crying, she lies awake and ruminates over the day's events. Throughout the day, she fears she cannot care

Table 1

### Possible tests if postpartum patient is constantly fatigued

Laboratory test	Confirms or rules out	Order if patient also presents with:
Acetylcholine receptor antibodies	Myasthenia gravis	Double vision, droopy eyelids, muscle weakness
Alkaline phosphatase	Primary biliary cirrhosis	Jaundice, pruritus
Antimitochondrial antibody	Primary biliary cirrhosis	Jaundice, pruritus
Antinuclear antibody	Systemic lupus erythematosus	'Butterfly' facial rash, joint pain, morning stiffness
CBC	Microcytic anemia, megaloblastic anemia	Pallor, low energy, peripheral neuropathy, shortness of breath
Electrolytes	Adrenal insufficiency, renal disease	Low blood pressure, seizures, skin pigmentation
Glucose (fasting or glucose tolerance)	Type 1 or 2 diabetes mellitus	Blurred vision, excessive thirst/hunger, headaches, frequent urination, unexplainable weight loss
HIV	HIV infection/AIDS	Anorexia, recurrent infections, weight loss
Liver function tests	Alcohol abuse, hepatitis, primary biliary cirrhosis	Asterixis (flapping tremor), easy bruising, jaundice, pruritus, spider telangiectasias
Lumbar puncture	Multiple sclerosis	Bladder dysfunction, gait ataxia, ocular signs, sensory loss, spasticity

for her baby and 2-year-old son, and she depends on a family member to stay home with her. Financial concerns force her back to work 3 months after giving birth, but she is so despondent that she can barely function.

Mrs. A's primary care physician diagnoses primary insomnia and prescribes mirtazapine and zolpidem, 15 and 10 mg each night, respectively, but her sleep disturbance persists after 6 weeks. The physician adds the hypnotic temazepam, 15 mg at night, and the sedating anticonvulsant gabapentin, 300 mg at bedtime. Both are titrated over 6 months to 45 mg and 1,800 mg at bedtime, respectively, but Mrs. A continues to lose sleep.

After 6 months, the doctor stops mirtazapine

because Mrs. A has gained 20 lb. A switch to sertraline, 25 mg/d, has no effect.

Eighteen months after symptom onset, Mrs. A still sleeps poorly, even though her daughter—now age 2—sleeps through the night. Her depressed mood—undiagnosed by the physician—continues to worsen. She sees a psychiatrist after routine blood tests and a sleep study reveal no medical cause for her insomnia.

### IS IT POSTPARTUM DEPRESSION?

Mrs. A's despondent mood, sleep disturbances, feelings of inadequacy as a parent, and impaired concentration suggest postpartum depression. Ego-dystonic obsessive thoughts of harming the

Table 2

## Possible tests if postpartum patient has lost or gained weight

Laboratory test	Confirms or rules out	Order if patient also presents with:
Antithyroid antibody	Postpartum thyroiditis	Constipation, dry skin, hair loss, lethargy, memory loss
Glucose (fasting or glucose tolerance)	Type 1 or 2 diabetes mellitus	Blurred vision, excessive thirst/hunger, fatigue, frequent urination, headaches
HIV	HIV infection/AIDS	Anorexia, fatigue, recurrent infections
TSH ± thyroid panel	Hypothyroidism	Constipation, dry skin, hair loss, lethargy
TSH ± thyroid panel	Hyperthyroidism	Agitation, anxiety, heat intolerance, palpitations

infant might emerge, although nonpsychotic patients rarely act upon them.<sup>1</sup>

Finding risk factors for postpartum depression can clarify the diagnosis. Ask the patient:

- **When did you first notice symptoms?** DSM-IV-TR says postpartum depression usually begins within 4 weeks of giving birth,<sup>2</sup> but most researchers define the postpartum period as ≤ 6 months after delivery.<sup>1,3</sup> Mrs. A's depression and insomnia started 3 months after childbirth.

- **Have you been depressed before?** Women with past postpartum or other depressive episodes face a high risk of recurrence after subsequent pregnancies.<sup>1,3</sup> Active eating disorder during pregnancy<sup>4</sup> and past premenstrual dysphoric disorder also are risk factors.<sup>1,3</sup>

- **Has anyone in your family had depression?** This increases postpartum depression risk.<sup>5</sup>

- **Who is helping you?** Psychosocial stress and lack of social support can fuel postpartum depression.<sup>1,3</sup> Mrs. A gets practical help from family members, but life's pressures are taking their toll.

## IS IT ANOTHER MENTAL ILLNESS?

Screen women with postpartum depressive symptoms for anxiety, which is highly comorbid with depression.<sup>6</sup>

Include bipolar disorder in the differential diagnosis. Ask new mothers with depressive symptoms if they feel inexplicably happy, irritable, or unusually energetic at times. Also screen for postpartum psychosis, which can progress to bipolar disorder<sup>7</sup> and—worse—greatly increase the risk of infanticide.

The Edinburgh Postnatal Depression Scale,<sup>8</sup> a 10-item self-report screening tool that takes about 5 minutes to complete, can help identify postpartum depression (see Related resources).

## CASE CONTINUED: A POSTPARTUM HEADACHE

During our initial interview, Mrs. A denies thoughts of harming herself or her children, and psychotic symptoms are not apparent. She reports no past depressive or anxiety episodes and does not use alcohol or illicit drugs. Her sister has a history of depression (not postpartum).

During review of systems, Mrs. A complains of persistent headaches. Brain MRI reveals a 4.5 x 5 mm microadenoma in the pituitary gland. We refer her to an endocrinologist, who obtains prolactin readings of 92 and 122.4 ng/mL (normal range, 2.8 to 29.2 ng/mL).

**Discussion.** Mrs. A had few predictive factors for postpartum depression, an atypical presentation

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Table 3

**Possible tests if postpartum patient has other physical symptoms**

Laboratory test	Confirms or rules out	Order if patient presents with:
Blood urea nitrogen/creatinine	Renal disease, dehydration	Back pain, frequent urination or oliguria, low blood pressure
Brain MRI	Brain tumors, white matter disease	Focal deficits, headaches, seizures, vision problems, vomiting
C-reactive protein	Rheumatoid arthritis	Joint pain, morning stiffness
ECG	Cardiomyopathy	Extremity swelling, palpitations, shortness of breath at night and with exertion
Erythrocyte sedimentation rate	Rheumatoid arthritis, SLE	'Butterfly' facial rash, joint pain
Folate	Folate deficiency	Ataxia, loss of vibration and position sense, peripheral neuropathy, weakness
Prolactin	Prolactinoma, hypopituitarism	Amenorrhea/galactorrhea, headache, visual field loss
Rapid plasma reagin	Syphilis	Ataxic wide-based gait, loss of position, deep pain and temperature sensation, palmar/plantar rash
Rheumatoid factor	Rheumatoid arthritis	Morning stiffness, symmetric joint pain
Urinalysis	Urinary infection, diabetes, renal disease	Burning or difficulty with voiding, dark-colored urine, frequent urination
Urine drug screen	Substance abuse disorder	Erratic behavior, irritability or aggression; violence, mental status changes
Vitamin B12	Anemia, malnutrition, inflammatory bowel disease	Loss of position or vibratory sensation, mood and cognitive changes, tingling and numbness in hands and feet

SLE: Systemic lupus erythematosus

with insomnia as the main symptom, and incomplete response after 18 months of treatment. These findings—plus her elevated prolactin and brain MRI results—suggest a medical cause.

**IS IT A MEDICAL PROBLEM?**

Pre-existing or new-onset postpartum medical conditions can confound the diagnosis.

- Fatigue can mimic depression's neurovegetative signs (poor energy, decreased appetite,

sleep). Common causes include sleep deprivation, thyroid disorders, anemia, cardiomyopathy, and infections (Table 1, page 63).<sup>9</sup>

- Weight change could signal a medical condition whose symptoms resemble postpartum depression—such as diabetes or human immunodeficiency virus (HIV) (Table 2, page 64).

- Other disorders—including neurologic diseases, prolactinomas, systemic lupus erythematosus, diabetes, and rheumatoid arthritis—can cause

depressive and other psychiatric symptoms (Table 3, page 67).

Recognizing the following disorders' physical signs is key to uncovering a medical cause for postpartum depressive symptoms.

**Thyroid disease.** Postpartum thyroiditis (PPT) can occur 1 to 3 months after delivery,<sup>10</sup> often recurs after subsequent pregnancies,<sup>11</sup> and can progress to permanent hypothyroidism within 5 years.<sup>10</sup> Hypothyroidism can cause cognitive slowing, depression, and psychosis, and acute mania has been reported with severe hypothyroidism secondary to PPT.<sup>12</sup>

Find out if the patient tested positive early in gestation for thyroid antibodies, as this may predict postpartum depression.

**Multiple sclerosis (MS)** can cause anxiety, mania, depression, and cognitive impairment.<sup>13</sup> Drugs used to treat MS—such as steroids or interferon—can induce depression.

Relapses are infrequent during pregnancy but increase significantly within 3 months after giving birth<sup>14</sup> in about one-third of women with active MS before pregnancy.<sup>15</sup> Gait ataxia, sensory loss, numbness, hyperactive reflexes or spasticity, bladder dysfunction, visual impairment, disordered ocular motility, and fatigue are prominent clinical signs of MS.<sup>16</sup> **Myasthenia gravis (MG).** Women who become pregnant within 1 year after diagnosis run a high risk of MG exacerbation.<sup>17</sup>

Fatigue and muscular weakness caused by MG can mimic depression, and adjusting to this debilitating illness can cause depression. Double vision, droopy eyelids, and muscle weakness alleviated by rest but worsened by activity are pathognomonic signs.<sup>16</sup>

**Other neurologic diseases.** Pre-existing seizure disorders can worsen after giving birth and cause depression.<sup>14</sup>

Subtle presentations of brain tumors include cognitive deficits, mood disturbance, and personality change. A left frontal lobe tumor can cause depression.

Ask the patient if she has had headaches, visual symptoms, vomiting, seizures, or focal neurologic deficits—any of these could signal a primary brain tumor or intracranial hemorrhage. **Prolactinomas,** the most common pituitary tumor in pregnant and postpartum women, enlarge during pregnancy and regress after delivery.<sup>14</sup> Depression, anxiety, apathy, and personality changes may stem from the pituitary tumor, its treatment, or changes in the hypothalamic-pituitary-end organ axis.<sup>18</sup> Typical amenorrhea-galactorrhea syndrome resembles postpartum physiologic changes.

Headaches are common, and compression of the optic chiasm with macroadenomas causes visual field changes.

**Systemic lupus erythematosus (SLE),** most prevalent in young women, might flare during pregnancy and within 6 weeks after giving birth.<sup>11</sup> Headaches, seizures, or cerebrovascular events with comorbid mood disorders, delirium, dementia, psychosis, or anxiety can signal SLE.<sup>13</sup>

Suspect SLE if the patient presents with fatigue, “butterfly” face rash, or joint pain. Test for renal or cardiopulmonary involvement.

**Rheumatoid arthritis (RA).** Because inflammatory activity is heightened after childbirth, postpartum women—particularly after bearing a first child—face a five-fold risk of RA compared with other women.<sup>11</sup> Breast-feeding might worsen RA, presumably by increasing prolactin production.

Physical limitations caused by RA can cause depression. Symmetric joint pain associated with morning stiffness—especially in the fingers, hands, or knees—might signal RA.

Did the patient test positive early in gestation for thyroid antibodies?

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Table 4

Findings that signal a possible postpartum medical problem

Laboratory finding	Could signal ...
Low hemoglobin, hematocrit and mean cell volume (MCV) values	Microcytic anemia
MCV > 100 mm <sup>3</sup>	Megaloblastic anemia
Positive anticardiolipin or antinuclear antibody	Systemic lupus erythematosus
Blood urea nitrogen > 20 mg/dL, creatinine > 1.5 mg/dL	Acute or chronic renal failure
Low specific gravity on urinalysis	Diabetes insipidus or renal tubular abnormalities
Proteinuria with glycosuria	Diabetes mellitus
Proteinuria with protein or cellular casts	Systemic lupus erythematosus
Hyponatremia and hyperkalemia	Adrenocortical insufficiency
Hypo/hyponatremia	Seizures
Albumin < 3 g/dL	Malnutrition
SGOT/SGPT > 35 u/L (each)	Alcohol abuse disorder, hepatitis, hepatic encephalopathy
Alkaline phosphatase > 120 u/L, positive antimitochondrial antibody	Primary biliary cirrhosis
Erythrocyte sedimentation rate > 20 mm/hr	Systemic lupus erythematosus, rheumatoid arthritis
Positive rheumatoid factor	Rheumatoid arthritis
Prolactin > 24 ng/mL	Prolactinoma
TSH > 5 µu/mL	Hypothyroidism
TSH < 0.35 µu/mL	Hyperthyroidism
IgG > 1.4 mg/dL, oligoclonal bands, myelin basic protein in CSF	Multiple sclerosis
White matter hyperintensities in brain MRI	Multiple sclerosis, CNS vasculitis, tumors

Source: Reference 5

**Anemia.** Increased need for iron and folic acid during pregnancy can lead to anemia. Neuropsychiatric manifestations of folate deficiency range from mild irritability to severe depression, dementia, psychosis, and confusion.<sup>19</sup> Vitamin B12 deficiency can lead to megaloblastic

anemia or neurologic problems such as peripheral neuropathy, as well as depression, delirium, or dementia.<sup>19</sup>

Ask the patient about:

- alcohol dependence, malnourishment, chronic illness, inflammatory bowel disease, gas-



tric bypass or other gastric surgery, which can impair vitamin B12 absorption

- use of anticonvulsants such as carbamazepine or valproic acid, which can decrease folate.

**Hypotension** mimics anergia. Postpartum hypotension can cause partial or total necrosis of the anterior pituitary gland. This leads to panhypopituitarism (Sheehan's syndrome)—a rare complication characterized by failure to lactate, amenorrhea, hypothyroidism, and adrenal insufficiency.

When not in hypotensive circulatory shock, patients with adrenal insufficiency might present with depression, delirium, or psychosis.<sup>13</sup> Ask the patient if she is having lactation problems and irregular periods, which could signal a pituitary problem.

**Peripartum cardiomyopathy**—an acute dilated cardiomyopathy—appears  $\leq 6$  months after delivery and may cause fatigue.<sup>10,20</sup> Check for shortness of breath at night and with exertion, palpitations, and extremity swelling.

**Gestational diabetes.** Pregnancy-induced insulin resistance leads to gestational diabetes mellitus. Women with gestational diabetes can develop type 2 diabetes after giving birth.<sup>10</sup>

Blood sugar fluctuations can cause depression, irritability, or memory problems. Depression can sabotage adherence to diet and treatment, leading to poor glycemic control.

Ask the patient if she was diagnosed with gestational diabetes and if she is experiencing fatigue, excessive thirst, frequent urination, blurred vision, headaches, excessive hunger, or unexplainable weight loss.

**Primary biliary cirrhosis** is most prevalent in women ages 35 to 60 and may cause depression.<sup>20</sup> Pruritus, fatigue, jaundice, and liver abnormalities point to this autoimmune disease, and postpartum exacerbations have been reported.<sup>21</sup>

**HIV infection** often leads to cognitive loss and depression with suicidal thoughts.<sup>13</sup> Highly active antiretroviral medications commonly cause agitation, pain, mood changes, and insomnia.

Ask the patient if she is HIV positive. Watch for weight loss, fever, anorexia, and recurrent infections.

**Substance abuse.** Intoxication, withdrawal, or long-term alcohol or drug use can contribute to depression. Women at high risk for substance abuse disorder might not adhere to psychiatric treatment and may be prone to sexually transmitted diseases. If possible, see the patient every 3 to 4 weeks during the postpartum period.

**Pain**—if not adequately controlled—can fuel depression.

Ask the patient if she has chronic pain or suffered a severe injury.

Has the patient lost weight? Does she have recurrent infections? She could be HIV positive

#### DETERMINING A MEDICAL CAUSE

Laboratory and neuroimaging findings—obtained in concert with the patient's primary care physician—will help confirm or rule out a medical problem (Table 4, page 71). Consult with a neurologist, endocrinologist or rheumatologist if indicated.

#### CASE: WILL THE TUMOR RESOLVE?

Mrs. A's endocrinologist prescribes bromocriptine to manage her hyperprolactinemia, but she refuses to start the dopamine agonist after the doctor explains that it might cause psychosis.

Working closely, the psychiatrist and endocrinologist postpone bromocriptine therapy to see if the prolactinoma will resolve without treatment. They order brain MRIs every 6 months to track the tumor.

Mrs. A starts weekly psychodynamic therapy, during which she explores her fear of failure as a mother. Within 2 months, she recognizes that she has set unrealistically high expectations for herself. Adopting a supportive approach, the therapist encourages her to go on dates with her husband

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and run errands or relax alone for 2 hours each weekend.

The psychiatrist discusses sleep hygiene and adds quetiapine, 25 mg at bedtime; reduces gabapentin over 3 months to 300 mg nightly; and titrates sertraline to 100 mg/d. The psychiatrist also weans Mrs. A off temazepam over 3 months, watching closely for withdrawal symptoms.

At the psychiatrist's suggestion, Mrs. A. resumes exercising at a gym four to five times a week. Mrs. A reduces zolpidem use—taking it only as needed for insomnia—then tapers off gabapentin. Quetiapine is discontinued.

After 4 months, psychotherapy sessions are decreased to biweekly. Prolactin is 66.6 ng/mL at 3 months, then normalizes to 23.4 ng/mL at 6 months. Six months later, brain MRI shows no change in baseline tumor size. The endocrinologist continues semiannual brain MRI and prolactin testing to see if the tumor will shrink without surgery.

Nearly 1 year after presentation, Mrs. A's depression is in remission.

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#### Related resources

- ▶ Edinburgh Postnatal Depression Scale. <http://www.drgrelling.com/Downloads.htm> (click on "Edinburgh Postnatal Depression Scale" under "Resources for professionals").
- ▶ Postpartum Support International. [www.postpartum.net](http://www.postpartum.net).

#### DRUG BRAND NAMES

Bromocriptine • Parlodel	Sertraline • Zoloft
Carbamazepine • Tegretol, others	Temazepam • Restoril
Gabapentin • Neurontin	Valproic acid • Depakene
Mirtazapine • Remeron	Zolpidem • Ambien
Quetiapine • Seroquel	

#### DISCLOSURES

Dr. Seritan reports no financial relationship with any company whose products are mentioned in this article, or with manufacturers of competing products.

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Many medical conditions common among new mothers can mimic postpartum depression. Look for weight changes and other physical signs of a medical problem. Order laboratory and neuroimaging tests based on clinical suspicion; watch for findings that warrant referral for further treatment.

BottomLine