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OBG MANAGEMENT

Depression: Tailoring treatment to life stage

One in 4 women experiences at least 1 major depressive episode in her lifetime—almost invariably during the reproductive years. A psychiatrist and Ob/Gyn surveys the characteristic symptoms and appropriate treatment strategies specific to each age.

Most of us have heard the statistic: The rate of depression is twice as high in women as in men.

A closer look reveals that the higher rate in women occurs during the reproductive years, when the Ob/Gyn is often the primary caregiver.[1] Because Ob/Gyns are called upon to provide a wide range of general medical care, it is important that we know how to recognize and treat depression in our patients.

Depressive disorders in women often occur in relation to estrogen levels, although nonhormonal factors also pose risks for depressive illness (**TABLE 1**).

Presenting symptoms in women

Sleep disturbances (hypersomnia, insomnia), weight gain or loss, and low energy (excessive tiredness, lack of energy, reduced activities) are common presenting complaints; however, some depressed women complain of symptoms such as pain (chronic pelvic pain, headaches, low back pain) or sexual problems (decreased interest in sex, decreased sexual pleasure).

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Hormone-related depression

Assessing adolescents. Beginning with puberty, the incidence of depression increases markedly. No evaluation of an adolescent female is complete until she is asked about mood symptoms. This is especially important for adolescents seeking oral contraceptives. Birth control pills may cause depressive symptoms or worsen symptoms in those who are already depressed.

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KEY POINTS

- A woman is most biologically vulnerable to psychiatric illness during the postpartum period.
- Antidepressant medications are not teratogenic.
- Risks associated with untreated postpartum depression have the greatest short- and long-term ramifications for both the patient and her offspring.
- Women may seek treatment only for premenstrual worsening of symptoms because they fail to recognize their ever-present depression.
- Women with premenstrual exacerbation of underlying depression may be at elevated risk of suicide.

TABLE 1

Risk factors for depressive disorders in women

- Personal history of depression or bipolar disorder
- Family history of depression, bipolar disorder, suicide
- Childhood sexual abuse
- Lack of safe environment
- Substance abuse
- Recent stressful life events
- Concurrent medical illness
- Pregnancy or recent delivery

Note that a depressed adolescent often appears "mad" rather than "sad."

Premenstrual exacerbation of underlying depression. Symptoms of depressive disorder almost always worsen premenstrually. Fortunately, premenstrual syndrome (PMS) carries less stigma than it used to, so women today are more likely to mention their symptoms. They may not realize, however, that their symptoms persist throughout the month, and only worsen in the days leading up to menstruation.

Women with dysthymia, for example, often seek treatment only for premenstrual worsening of their symptoms because they fail to recognize their ever-present depression. Patients with other depressive disorders may make the same error. It is essential that the patient keep a daily symptom diary to detect premenstrual exacerbation of underlying depression, since women with this symptom pattern may be at elevated risk of suicide.

Pregnancy. Pregnancy offers no protection against depressive illness. About 10% to 16% of pregnant women meet the criteria for a major depressive episode.[2] Although these rates are equivalent to those in nonpregnant women, the risk of untreated depressive illness is likely to be greater during gestation.

Depression in pregnant women may be associated with poor self-care, poor weight gain, and "self-medication" with alcohol, tobacco, or illicit drugs. Patients reporting such issues should be questioned about their mood.

Postpartum period. Women are more biologically vulnerable to psychiatric illness during the postpartum period than at any other time in life; further, the risks associated with untreated postpartum depression have the greatest short- and long-term ramifications for both the patient and her offspring.[3] It is well documented that untreated postpartum depression is associated with a disturbed maternal-infant relationship, later psychiatric morbidity in children, marital tension, and suicide/infanticide.

Perimenopause. Depressive symptoms commonly recur during the perimenopausal years, although new-onset depression is unlikely in this age group.

Postmenopause. Depressive symptoms tend to decrease after menopause, even in women with a history of depression.[4]

Spectrum of depressive disorders

TABLE 2 lists the symptoms used in the diagnosis of depressive disorders, and displays them with a popular mnemonic, SIG E CAPS.

The diagnosis of a major depressive episode requires that a patient have 5 or more symptoms that cause significant impairment and have persisted for a minimum of 2 weeks. At least 1 of the symptoms must be sadness or a loss of interest.[5]

Major depressive disorder falls within a spectrum of depressive disorders:

- Major depressive episode: 5 or more symptoms from **TABLE 2**.
- Minor depressive disorder (also called "subsyndromal" depression): At least 2 symptoms in **TABLE 2**. Recent research indicates that minor depression can increase the likelihood of recurrent depressive episodes.[6]
- Dysthymia: Low-grade depressive symptoms persisting over at least 2 years. As dis-

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cussed, women with dysthymia often fail to recognize their depression, seeking treatment only for premenstrual worsening of symptoms. In addition, perhaps because of its long duration, dysthymia can be quite resistant to treatment.

- Adjustment disorder with depressed mood: Depressive symptoms in response to an identifiable stressor. Women with adjustment disorders can progress to more severe symptoms and become suicidal.
- Depressive disorder not otherwise specified, such as premenstrual dysphoric disorder.

TABLE 2

Mnemonic for major depression: SIG E CAPS(S)

S	Sadness: Depressed mood (adolescent more mad than sad)
I	Interest: Decreased
G	Guilt: Inappropriate guilt, feelings of worthlessness
E	Energy: Decreased, fatigue
C	Concentration: Decreased, can't think, can't make decisions
A	Appetite: Decreased or increased; weight change without trying
P	Psychomotor activity: Decreased or increased
S	Sleep: Decreased or increased
S	Suicidal ideation or attempt

Concomitant depression and anxiety. Depression accompanied by anxiety is common in women. The relationship between the two can be complex but does not usually alter choice of drug therapy, since the most commonly used agents are effective for both conditions.

Management strategy

The principles for managing depression are the same regardless of whether a patient has a major depressive episode or another depressive disorder. Treatment usually begins during the acute phase of an episode and varies with symptom severity.

Assessing symptom severity. This can be judged by the degree to which symptoms interfere with the patient's usual activities:

- **Mild** symptoms cause some difficulty functioning in social, occupational, or school settings, but the patient is generally doing well.
- **Moderate** symptoms make daily tasks more arduous.
- **Severe** symptoms cause dysfunction in 1 or more areas of normal activities (social, occupational, or school), and the patient may have suicidal ideation. Suicidal or homicidal ideation always indicates severe depression, regardless of ability to function.[5]

Managing mild to moderate symptoms.

- Psychotherapy and antidepressant medications are equally effective for women with mild to moderate symptoms. Therefore, patient preference should be the determinant.
- Women with mild to moderate seasonal symptoms concentrated in the winter months may need only bright-light therapy.[7]
- Exercise alleviates a broad spectrum of depressive illnesses, so treatment plans should always include initiating or increasing physical activity.[8]

Managing moderate to severe symptoms.

- Psychotherapy alone is inadequate; antidepressant medication must be included at the start of treatment.
- Concurrent use of psychotherapy may be helpful.
- Exercise also is beneficial, though many women with low motivation and low energy cannot initiate physical activity until some improvement occurs.

When to refer for psychiatric care

Since the treatment of depressive disorders must be based on accurate diagnosis, the Ob/Gyn should consider referral to a mental health professional when the diagnosis is uncertain or response to initial treatment is inadequate.

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Comorbid mental illness, such as posttraumatic stress disorder (PTSD) or personality disorder, can cause both diagnostic confusion and treatment resistance. Consultation with a psychiatrist therefore may be necessary. Patients with PTSD probably account for most of the "treatment failures" seen by generalists (**TABLE 3**).[9] These women will benefit from antidepressant therapy initiated by their Ob/Gyns, but also need treatment by psychotherapists with experience managing PTSD.

In patients with comorbid personality disorders, meanwhile, the emergence of self-harming behavior is high. These patients—and any women at high risk for self-harm—should be referred to a psychiatrist for initiation of therapy.

Likewise, patients with a history suggestive of bipolar disorder should be referred to a psychiatrist for treatment.

Initiating drug therapy

TABLE 4 lists most antidepressant medications prescribed by generalists. It is normally unnecessary to change to a different drug class if an antidepressant fails, or if depressive symptoms recur. Unlike antibiotic treatment, in which failure with 1 agent predicts failure with other drugs in the same class, there is considerable variation within classes of antidepressants. Thus, changing to another drug in the same class is likely to be successful.

Side effects. Medications vary in their side-effect profiles. Nefazodone and buproprion are less likely than other agents to cause sexual side effects. Fluoxetine and sertraline, meanwhile, are less likely to cause weight gain in the first few months of treatment (although long-term data are less reassuring). Buproprion has not been associated with weight gain.

Specific subsets of patients. **TABLE 5** lists some factors to consider when selecting antidepressant medications for women of reproductive age; women who have and who have not previously taken antidepressants; and women with premenstrual symptom exacerbation, obsessive-compulsive symptoms, an eating disorder, or specific symptom patterns (such as sleep disturbance, anger, low energy, or poor concentration).

In a patient with prominent anxiety symptoms, the prescribed medication should be initiated at half the usual starting dose, with gradually increasing doses. All selective serotonin reuptake inhibitors and serotonin/norepinephrine reuptake inhibitors are effective treatments for anxiety disorders. Because these women are less likely to tolerate buproprion than other agents, starting at a low dose and advancing therapy slowly is especially important with this treatment.

For perimenopausal women, consider concomitant therapy with estrogen and an antidepressant to maximize treatment response. Patients with prominent menopausal symptoms and no history of depression should be started on hormones prior to the initiation of antidepressant agents. Women with a history of depressive symptoms or treatment for depression, on the other hand, might respond better if started on the antidepressant first; hormonal therapy can be added as indicated.

TABLE 3

Traumatic events and risk for posttraumatic stress disorder*

Rape	49.0%
Severe beating	31.9%
Other sexual assault	23.7%
Serious accident or injury	16.8%
Shooting or stabbing	15.4%
Child's life-threatening illness	14.3%
Sudden unexpected death of a close friend or relative	10.4%
Witness killing or serious injury	7.3%
Natural disaster	3.8%

*Age 15-45 years

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TABLE 4

Common medications for major depression

AGENT	TRADE NAME	CLASS	NEUROTRANSMITTER, INITIAL SIDE EFFECTS
Selective serotonin reuptake inhibitors			
Citalopram/escitalopram	Celexa, Lexapro	C	Serotonin, activating
Fluoxetine	Prozac,* Sarafem, Prozac Weekly	C	Serotonin, activating
Fluvoxamine	Luvox	C	Serotonin, sedating
Paroxetine	Paxil Paxil-CR	C	Serotonin, sedating
Sertraline	Zoloft	C	Serotonin, activating
Other antidepressants			
Buproprion	Wellbutrin* Wellbutrin-SR	B	Dopamine, activating
Mirtazapine	Remeron Remeron SolTab	C	Complex, sedating
Nefazodone	Serzone	C	Serotonin, mildly sedating
Venlafaxine	Effexor Effexor-XR	C	Serotonin, norepinephrine, mildly sedating

*Generic available

Base treatment duration on episode pattern

Depression is usually a chronic condition marked by recurrent episodes. Thus, the duration of treatment is related to the number of recurrences the patient has experienced, and the aim of therapy is to prevent further episodes. If treatment has been incomplete, depressive symptoms often recur in the first few weeks following discontinuation.

- A woman experiencing depression for the first time has a 50% likelihood of recurrence. She should continue medication for 4 to 6 months after she feels well (that is, she feels fully back to her "usual self," not just somewhat better).
- A woman with a second major depressive episode has about a 70% chance of recurrence and should remain on medication for 1 year after she feels fully well.
- A woman experiencing a third episode has more than a 90% chance of recurrence and probably should consider lifelong antidepressant therapy.
- For postpartum onset, psychiatrists often recommend a full year of antidepressant therapy even if it is the patient's first depressive episode. This is because the stress and sleeplessness associated with care of an infant undermine recovery from a depressive disorder.

Ending treatment

Clinicians should terminate antidepressant treatment with a slowly tapering regimen. Abruptly discontinuing treatment may precipitate recurrent depressive symptoms that will require further management.

A common approach is to decrease from a high dose by halving it every 5 to 7 days. Once the patient reaches a lower dose, slow the drug tapering even further. Some women may need alternate-day dosing at the end of the taper to avoid rebound or discontinuation symptoms.

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TABLE 5

Factors to consider in initiating antidepressant medications in women

IF THE PATIENT HAS...	THEN CHOOSE OR CONSIDER...	SUCH AS...
Previously used an antidepressant medication	The same medication unless it was discontinued due to inefficacy or intolerable side effects.	
Never taken antidepressant therapy, but first-degree relatives have used a therapy successfully	The same medication used by the relative	
The potential for pregnancy and lactation	An agent that can be continued during pregnancy and lactation	All antidepressant medications
Anger and irritability as primary symptoms	A serotonergic agent	Fluoxetine, sertraline, paroxetine, citalopram/ escitalopram, venlafaxine, nefazodone
Low energy and poor concentration as the primary debilitating symptoms	An energizing agent	Buproprion, fluoxetine, sertraline, citalopram/ escitalopram
Severely disturbed sleep	An agent that has sedating side effects to be used at bedtime; these effects may be less welcome once the depression remits	Fluvoxamine, mirtazapine
Prominent premenstrual syndrome or	Serotonergic agent, intermittent dosing	Fluoxetine, sertraline, paroxetine, citalopram/ escitalopram, venlafaxine, nefazodone
Premenstrual exacerbation of depressive symptoms	An agent that's not an intermittent (luteal-phase) antidepressant; continuous treatment with increased premenstrual dosing, return to basic dose with onset of menses	
Obsessive-compulsive symptoms (counting, checking, or intrusive thoughts) or an **eating disorder**	Serotonergic agents as first choice; higher doses may be needed to control symptoms	Fluoxetine, sertraline, paroxetine, citalopram/ escitalopram, venlafaxine, nefazodone

With history of PMS, taper only after menses. If a woman experienced PMS before her current depressive episode, consider using a very slow taper, decreasing doses after the onset of menses each month. Help the patient anticipate the reemergence of PMS and teach her to counter it with exercise, with calcium supplementation, and by restarting a serotonergic antidepressant, as indicated.

Taper SAD patients during their "best" season. In women with seasonal affective disorder (SAD), begin tapering antidepressants during the season in which the patient is at her healthiest, psychologically. For a woman with winter dysphoric symptoms, do not consider reducing antidepressant medication until the days are lengthening in the spring, even if she has taken the drug for the recommended length of time.

Managing serotonin discontinuation syndrome. Abrupt discontinuation of serotonergic agents may lead to a constellation of symptoms called "serotonin discontinuation syndrome" (TABLE 6).[10] Agents with a long

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half-life or multiple active metabolites (e.g., fluoxetine, sertraline) are less likely to cause discontinuation symptoms than agents with a short half-life or no active metabolites (e.g., paroxetine, venlafaxine).

Specific symptoms can be treated; for example, analgesics for headache, medication for sleep or anxiety. If the patient is experiencing dizziness or poor balance, take steps to protect her from secondary injury, such as a fall.

Restarting the serotonergic agent will relieve discontinuation symptoms rapidly. The drug then can be tapered slowly to avoid further adverse effects. Of course, this approach is not an option if the medication was stopped because of an allergic reaction. In these cases, reassure the patient that discontinuation symptoms are transient and not dangerous.

If rapid discontinuation is desired, a patient on the lower end of the dosage spectrum often can simply stop the drug, taking a low dose whenever she experiences discontinuation symptoms (e.g., taking 3 or 4 doses over a 10-day period).

Medication during pregnancy

It is essential that Ob/Gyns develop a management plan that anticipates the possibility of a patient becoming pregnant while on antidepressant therapy.

Do not stop treatment reflexively if pregnancy occurs during therapy. Rather, discuss the risk-benefit ratio with the patient and her partner and establish a management plan while she is euthymic. Although no therapy is completely risk free, the goal is to limit exposure to both the illness and the treatment, and to help the patient decide which option poses the least risk. This discussion also should focus on protecting the patient's mood after she gives birth, since her history of depression increases her risk for postpartum depression.[11]

If the patient decides to continue medication during gestation (and, possibly, during lactation), continue the agent used before pregnancy. Changing medications simply increases the number of fetal exposures. If she instead opts to stop medication, rapidly tapering therapy over 3 to 5 days may decrease rebound and discontinuation symptoms.[11]

There are more data on first-trimester exposure and neurobehavioral outcome for antidepressants than almost any other drug class. For most agents, the window of risk to fetal development occurs in the first trimester (TABLE 7). It is best to avoid agents during periods of highest risk, if this will not threaten the mother's stability.[11] Note, however, that psychotropic medications (excluding anticonvulsants) have not been implicated in developmental issues with children.

Identifying and preventing postpartum depression

This syndrome occurs in 10% to 16% of adult women, and up to 26% of adolescent women.[12] Common symptoms include despondency, sleep disturbances and fatigue, irritability, anorexia, poor concentration, feelings of inadequacy, and ego-dystonic thoughts about harming the baby.

Women who develop mood symptoms during the current pregnancy, as well as those

TABLE 6

Serotonin discontinuation syndrome[10]

GENERAL	
Dizziness	Headache
Lightheadedness	Insomnia
Sweating	Nausea
PSYCHIATRIC	
Anxiety	Confusion
Agitation	Mood changes
Hallucinations	
NEUROLOGIC	
Paraesthesias	Imbalance
Numbness	Tremor
Visual disturbances	

TABLE 7

Windows and types of teratogenic risk for psychopharmacologic agents

DRUG CLASS	TERATOGENIC RISK	WINDOW OF RISK
Anticonvulsants	Neural tube Craniofacial	0-5 weeks 9-13 weeks
Benzodiazepines	Lip and palate	8-11 weeks
Lithium	Heart	4-8 weeks
Antidepressants (all classes)	None known	None known

with a prepregnancy history of depressive disorders or previous postpartum mood symptoms, are at high risk for postpartum depression.[2] These mothers and their infants will benefit from prophylactic treatment, which should be started at delivery or during late pregnancy.

Medication during lactation. All psychotropic medications cross into breast milk, but in such small quantities that most researchers believe women can continue depression therapy during lactation. No adverse effect is commonly observed in infants who are exposed to antidepressant medication through breast milk.[11]

This starkly contrasts to the potential adverse impact on both mother and infant when postpartum depression remains untreated.[13]

Alternative therapies

Botanical therapies have been widely used for mood and anxiety symptoms. Very high use is seen among the elderly and people with limited access to—or belief in—the mental health system.[14] Note that data are insufficient to support the use of alternative therapies during pregnancy and lactation.

Patients should be warned not to use kava kava due to recent reports of sometimes-fatal liver toxicity. This substance has been used as an anxiolytic.[15] ■

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