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409 12th Street, SW
Washington, DC 20090-6920

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ISSN: 1536-3619
ISBN: 978-1-934984-68-0

12345/10987

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- *Vision Disorders* [Update March 2015]
## Contents

**CONTINUING MEDICAL EDUCATION** vii  
**FOREWORD** viii  

**Basic Science Update** 2  
Mood Disorders 3  
Anxiety Disorders 3  

**Mood Disorders** 4  
Major Depressive Disorder 5  
Bipolar I Disorder and Bipolar II Disorder 6  

**Anxiety and Related Disorders** 8  
Generalized Anxiety Disorder 9  
Panic Disorder 10  
Social Anxiety Disorder 10  
Obsessive–Compulsive Disorder 11  
Posttraumatic Stress Disorder 12  

**Screening** 13  

**Treatment** 17  
Lifestyle Changes 17  
Complementary and Alternative Medicine 18  
Psychotherapy 18  
Pharmacotherapy 18  
Electroconvulsive Therapy and Transcranial Magnetic Stimulation 33  

**Reproductive Considerations** 33  
Reproductive Cycle Mood Symptoms 33  
Pregnancy 37  
Psychiatric Medication Use in Pregnancy 39  
Postpartum Mood Disorders 46  
Perimenopausal Concerns 53  

**Psychiatric Medication Guidelines in Specific Settings** 56  
Contraception and Psychiatric Drug Interactions 56  
Contraception and Psychiatric Illness 56  
Tamoxifen and Psychiatric Drug Interactions 58  
Management of Pelvic Pain in the Setting of Depression and Anxiety 59  

**Referral Guidelines** 60  

**Key Points** 61  

**REFERENCES** 66
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— American Psychiatric Association
  www.psychiatry.org

— American Psychological Association
  www.apa.org

— National Alliance of Mental Illness
  www.nami.org

— National Institute of Mental Health
  www.nimh.nih.gov

— North American Society for Psychosocial Obstetrics and Gynecology
  www.naspog.org

— Postpartum Support International
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This monograph is designed to enable the obstetrician–gynecologist to do the following:

- Understand the biochemical basis of mood and anxiety disorders
- Monitor risk factors for these disorders across the lifespan of women
- Screen and diagnose patients with mood and anxiety disorders
- Evaluate patients with mood and anxiety disorders and initiate a management plan
- Treat patients with uncomplicated illness and make appropriate referrals of more complicated cases

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See page vi for submission of CME credits.
Obstetrician–gynecologists encounter many patients in their practices affected by mood and anxiety disorders. These disorders can have a profound effect on women’s quality of life as well as their response to other conditions that obstetrician–gynecologists may be managing. The treatment of these psychiatric issues is not only complex but also can be complicated by hormonal changes related to the menstrual cycle, menopause, and use of hormonal contraception. The original monograph, entitled “Depression in Women,” was published in 2002 and revised in 2008 to include anxiety disorders. Those publications served as particularly useful guides to practicing clinicians, but the editorial board recognized that a new monograph was needed to reflect emerging therapies and new pharmacotherapy.

The authors are both practicing psychiatrists and academicians who manage a specialized center for women’s mood disorders at The Johns Hopkins Hospital. This monograph will guide obstetrician–gynecologists in the recognition, diagnosis, and individualized therapy for the spectrum of mood and anxiety disorders with emphasis on how therapy is affected by hormonal changes, the reproductive cycle, and pregnancy.

Russell R. Snyder, MD
Editor
ABSTRACT: The management of psychiatric disorders in women is complicated by reproductive life cycle events. Psychiatric disorders can be initiated or exacerbated during times of hormonal change (such as menarche, the premenstrual period, the postpartum period, and perimenopause), and during the childbearing years, treatment is complicated by pregnancy and breastfeeding. These issues make determining the appropriate psychiatric medications to use in the treatment of mood and anxiety disorders in women complex. This monograph addresses practical approaches in the provision of thorough and individualized care for women with mood or anxiety disorders.

One of the most difficult aspects in the treatment of women with mood or anxiety disorders is the paucity of defined treatment parameters; every case needs to be considered individually, symptoms vary from woman to woman, and the evidence to support various treatment methods is limited. For example, continuation of psychiatric medications during pregnancy may be essential in one case and unnecessary in another, depending on factors, such as severity of illness, adverse effects of specific medications, and a history of illness during and after previous pregnancies. Obstetrician–gynecologists frequently find themselves on the front line in the provision of care for women with mental illness. Thus, a good understanding of the detection and treatment of mood and anxiety disorders throughout the woman’s life cycle, including during and after pregnancy, is essential. It is also important to understand that the treatment of mood and anxiety disorders, particularly in cases triggered by hormonal changes, is an evolving field. Much research is needed, and consequently, many of the recommendations in this monograph are based on clinical experience. However, it is also important not to become constrained by the lack of data and err on the side of not treating. Untreated mood and anxiety disorders are devastating, not only to the individuals who experience them directly but also to the patients’ families and associates.

As with any illness, the health care provider must distinguish a normal presentation from a pathological presentation, including the differences between symptoms and syndromes. Mood and anxiety symptoms can be considered normal whereas mood and anxiety syndromes involve pathology. For example, it is normal to feel sad or anxious after an upsetting event (eg, after the death of loved one or a breakup of a relationship). These symptoms usually resolve spontaneously and do not interfere with the patient’s ability to function over a long period. Similarly, many women experience mood symptoms at times of hormonal change, such as during the premenstrual period. In contrast, psychiatric mood syndromes meet severity and length of time criteria for mental disorders as discussed in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (1). For example, major depressive disorder has specific criteria that require the
patient’s mood to be low every day, most of the day, for at least 2 weeks; patients also must exhibit five or more symptoms of depression (1). Psychiatric syndromes also must interfere with the functioning of the patient. Functioning can be affected in one or more areas, including work, family and home life, personal care, and social life. A woman who reports sad mood but is performing as usual at home and at work does not have syndromal depression. These distinctions often are straightforward in healthy women but can be more difficult to parse in women who have an underlying mood or anxiety disorder.

In women in whom a mood or anxiety disorder has been diagnosed, it is important to distinguish between symptoms that are normal responses to life circumstances and those that are precursors of an episode of illness. Symptoms that are severe; those that are present longer than they would be in healthy individuals; those that are associated with serious psychiatric symptoms, such as suicidal ideation or psychosis; and those that impair functioning are clues that treatment should be initiated or altered.

CASE NO. 1. A 38-year-old woman with a history of severe depression and anxiety necessitating hospitalization presents to her obstetrician–gynecologist for a well-woman visit. She confides that she and her husband are having significant marital strain. She reports insomnia, anxiety, decreased appetite, and tearfulness and is concerned that her depression and anxiety are returning despite adherence to her antidepressant regimen. She has continued to function at work and home and enjoys spending time with her children and friends. The obstetrician–gynecologist administers the Quick Inventory of Depressive Symptoms questionnaire and notes a score of 10, indicating mild depression.

Although this patient has a mildly elevated score on the Quick Inventory of Depressive Symptoms questionnaire, her functioning is not impaired and she continues to enjoy interactions with others. If both the patient and the health care provider are unsure whether a patient’s symptoms are due to circumstances or due to a mood disorder, watchful waiting may be the best course of action. The health care provider should see the patient more frequently to provide extra support during a difficult time and to assess for the need of other interventions, such as pharmacologic management.

Basic Science Update

Despite ongoing clinical and basic science research, the pathophysiology underlying mood and anxiety disorders remains poorly understood. Depression and anxiety are highly comorbid, and recent research indicates that this high comorbidity may represent a common etiology of both genetic and environmental risk factors (2). The new Research Domain Criteria published by the National Institute of Mental Health encourage scientists to explore common pathways that lead to symptom expression, regardless of the DSM-5 diagnosis the patient may have received (3, 4). Nevertheless, because most published research is still organized by individual disorders, the following discussion is organized by clinical diagnoses.
**Mood Disorders**

The underlying pathophysiology of mood disorders (ie, major depressive disorder and bipolar disorder) likely is a combination of biologic and environmental risk factors. Both major depressive disorder and bipolar disorder appear to have genetic components. The genetic involvement in patients with major depressive disorder is approximately 30–40% (5), whereas it is approximately 70% in patients with bipolar disorder (6). However, the genetic basis for both types of mood disorders appears to be complex and likely polygenic. Genome-wide association studies have indicated that many genes are involved in major depressive disorders with small effects (7), and these studies also have identified several genes that are likely to be involved in bipolar disorder but also may play a role in other psychiatric illnesses, including schizophrenia (8).

Environmental factors that play a role in the development of mood disorders generally result in increased stress, including stressful life events, sexual abuse, and other forms of trauma. Gender differences in stress sensitivity (eg, men are more likely than women to develop depression after divorce) as well as exposure (eg, women are more likely than men to be exposed to sexual abuse) have been observed and support gender-sensitive psychosocial interventions (5).

Other areas of interest that are actively being studied in the search for the underlying biological mechanisms that result in mood disorders include the role of inflammation, cytokines, stress hormones, neurotrophic factors, and circadian rhythms. Multiple neurotransmitter systems, including the monoamine systems (serotonin, noradrenaline, and dopamine) in major depressive disorder and the glutamatergic system in bipolar disorder, have been studied. Although it has been determined that psychiatric medications target and influence these systems, the exact “defect” remains unclear in either set of mood disorders. Given the fact that multiple abnormalities, which were not pathognomonic, have been found in the brains of patients with mood disorders, and the fact that different patients respond to different medications and some do not respond to any, it is likely that both mood disorder types are groups of conditions with similar clinical presentations and different underlying biologic processes. It is hoped that ongoing research will allow scientists to disentangle the different pathophysiologic mechanisms that underlie mood disorders and will ultimately allow a personalized management approach that will improve outcomes for patients.

**Anxiety Disorders**

Both the mechanisms of overall anxiety and the biological factors that determine particular disorders are poorly understood. Current research indicates that all anxiety disorders are associated with dysfunction in the brain’s fear and defense circuit (9). The *DSM-5* has classified the stress-related disorders (posttraumatic stress disorder [PTSD] and related disorders) and the compulsive disorders (obsessive–compulsive disorder [OCD] and related disorders) into categories separate from anxiety; however, clinically, these
entities often occur together (and will be considered together in this monograph). For all mental disorders, research is increasingly showing the importance of circuits, i.e., a pattern of dysfunction across the connections among different brain regions rather than dysfunction in a particular brain region. The most important circuit for pathologic anxiety is in the limbic brain, which involves connections from the amygdala to the hypothalamus and brainstem. This circuit controls the startle response and exaggerated responses to fear; individuals with anxiety are prone to startle and to perceive threat in situations in which those without anxiety would not. This is a strong relationship in patients with phobias, whereas those with generalized anxiety disorder are less likely to have this response. Patients who have experienced one significant trauma have an excessive startle reflex, but those with chronic trauma are more likely to display negative affectivity (10). Negative affectivity is similar to depression, and individuals on this end of the anxiety spectrum have dysfunction in the connectivity between the amygdala, the insula, the anterior cingulate cortex, the medial prefrontal cortex, and the nucleus accumbens (11). Research has proposed biotypes of dysfunction within this circuit, which, depending on the type of dysfunction, may lead to negative bias or threat dysregulation, both of which play a role in anxiety symptoms (12).

Numerous family and twin studies have established a strong heritability for the anxiety disorders. The exact numbers vary across disorders, but for the most part, research has established that individuals who have first-degree relatives with an anxiety disorder have odds ratios (ORs) of 4–6 for having anxiety themselves (13). Similarly, twin studies have established heritability of 30–50% for the various anxiety disorders (14). As is true with most complex, nonmendelian disorders, linkage and association studies have not yielded consistent results. The most widely studied candidate genes are those related to neurotransmitters and those related to the stress response. Panic disorder is the most commonly studied disorder in association studies, with the serotonin transporter, brain-derived neurotrophic factor, and catechol-O-methyltransferase genes most often examined; however, the studies yielded few consistent results. Ongoing genome-wide association studies have yielded few useful results thus far because of the combination of small sample sizes and phenotypic heterogeneity; the same limitations apply to gene–environment interaction studies and epigenetic studies. Epigenetic studies have identified methylation changes in candidate genes as well as genome wide, making them worthy of further exploration.

Mood Disorders

Although the DSM-5 lists various types of mood disorders, the term “mood disorders” generally includes major depressive disorder and bipolar disorder. A complete discussion of all types of mood disorders is beyond the scope of this monograph. This overview will be devoted to the principal differences between major depressive disorder and the two major types of bipolar disorders, establishing a diagnosis, and basic treatment strategies.
Mood can be defined as the degree of well-being that one experiences at any point in time. Mood varies not only with one’s experiences but also with one’s temperament or personality. For example, some individuals are almost always in a good mood, and others are unpleasant much of the time.

Generally, mood disorders are characterized by recurrent disturbances in mood, thought process, and energy that must meet specific criteria for length of time, severity, and disturbance in an individual’s function. Mood disorders also are characterized by disturbances in the individual’s sleep, eating, cognition, and interests. Major depressive disorder is characterized by recurrent major depressive episodes during which the patient’s mood is generally low or sad and energy is low. Bipolar disorder also is characterized by recurrent major depressive episodes, but in addition, the patient has hypomanic or manic episodes, during which the mood is generally elated but also can be irritable while at the same time energy is high. Thus, the mood cycles between various mood states, including depressed, neutral, and high.

The mortality associated with mood disorders has been estimated to be as high as 10–15% in those with severe illness and approximately 6% across the spectrum of severity (15, 16). In addition, the risk of death from any cause is at least twice (and possibly as high as three times) that of the general population (17). Mood disorders also are associated with substance abuse and other unhealthy habits, such as smoking, not exercising, and eating improperly. Thus, mood disorders are a significant cause of disability, with major depressive disorder being the second leading cause of disability worldwide (18).

The average age of onset of mood disorders is in the late teens and early twenties. Onset of severe illness can disrupt the normal process of developing relationships, finishing education, and obtaining employment. Onset, particularly that of major depressive disorder, also can occur later in life. Later onset, particularly after the age of 40 years, should prompt a workup for potential contributing medical illness, including cerebrovascular and cardiovascular disease.

**Major Depressive Disorder**

Major depressive disorder is the psychiatric illness in which patients experience one or more major depressive episodes. The DSM-5 uses length of time criteria along with various symptoms to establish the diagnosis of a major depressive episode (1). The length of time requirement, namely 2 weeks or longer; the number of symptoms required (five or more) as well as the requirement of functional impairment help to ensure that depressive symptoms in response to life events do not meet criteria for a major depressive episode. Symptoms of a major depressive episode include the following (1):

- Depressed mood (irritability in young adults)
- Diminished interest or pleasure (anhedonia)
- Changes in weight related to changes in appetite
Mood and Anxiety Disorders

- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue
- Feelings of worthlessness or guilt
- Poor concentration
- Thoughts of death or suicide

Major depressive disorder is twice as common in women as in men (19). Before adolescence, the risk is equivalent in girls and boys. At adolescence, the risk for women increases to twice the risk for men and continues to be increased throughout the reproductive years until approximately menopause, when the risks for men and women begin to approach equivalent rates once again (19).

Bipolar I Disorder and Bipolar II Disorder

There are two types of bipolar disorder: bipolar I disorder is characterized by recurrent major depressive episodes and a history of at least one manic episode, and bipolar II disorder is characterized by recurrent major depressive episodes and a history of at least one hypomanic episode (1). In rare cases, the patient experiences only manic or hypomanic episodes without depression, and these episodes are still diagnosed as bipolar I disorder or bipolar II disorder.

Manic episodes are characterized by an elevated mood, which can be either elated or irritable; inflated self-esteem; excessive energy; and rapid thought processes. Manic episodes also are accompanied by one of the following three characteristics: 1) psychotic symptoms (hallucinations or delusions), 2) need for hospitalization due to dangerous behavior, or 3) symptoms or behavior that are disturbed enough to cause significant problems for the patient (for example, spending enough money to lead to bankruptcy). Hypomanic episodes are similar in quality to manic episodes but do not have any of the previously listed characteristics. In addition, the DSM-5 length of time criteria differ for manic and hypomanic episodes with manic episodes lasting at least 1 week and hypomanic episodes lasting at least 4 days. The length of time criterion often is difficult to determine because many patients with bipolar disorder have limited insight into when their elevated mood began; thus, an outside observer often is needed to determine the duration of manic and hypomanic states.

Many experts consider bipolar II disorder to be a “less severe” form of bipolar illness because it is characterized by the less severe hypomanic episodes as opposed to manic episodes. However, it is the course of illness and response to treatment that determines functional impairment. For example, a woman with bipolar II disorder who responds minimally to medications and spends much of her life alternating between depression and hypomania may be more functionally impaired than a woman with bipolar I who responds well to medication and has few discrete episodes of illness.
In contrast to major depressive disorder, bipolar I disorder is equally prevalent in the sexes, with approximately 1% of the population meeting the diagnostic criteria (20). However, bipolar II disorder appears to be more common in women than in men (21).

Sometimes it is difficult to determine if a patient has major depressive disorder or bipolar disorder, especially bipolar II disorder. Most patients with bipolar disorder, particularly those with milder hypomania, present to an outpatient setting with a major depressive episode. Thus, the clinician must obtain a detailed medical history and specifically ask about hypomaniac and manic symptoms. Notably, at least 35–45% of patients with bipolar disorder initially receive an erroneous diagnosis of major depressive disorder (22).

Although most obstetrician–gynecologists rarely will have time to obtain a detailed psychiatric history, there are a few key elements that can help a busy clinician make the distinction. A mental status examination (including an assessment of appearance; speech; mood; suicidal thoughts; current hallucinations; delusions; obsessions; compulsions; phobias; and orientation to place, time and person) takes little time and can guide the clinician’s assessment. Although a detailed family history may not be possible, simply asking whether anyone in the family has a history of bipolar disorder or suicide can have a significant effect on treatment decisions. Because bipolar disorder has a strong genetic component (8), asking whether anyone in the family has been treated for bipolar disorder is an important way to determine if antidepressants can be started or if a referral to psychiatry for a more in-depth interview is necessary. Similarly, a family history of completed suicide increases the risk that a patient with suicidal thoughts will act on them. Suspicion of bipolar disorder based on either family history or personal history should prompt a referral to psychiatry for further evaluation. A medical history can reveal factors, such as hypothyroidism or increased liver enzyme levels, which can manifest with psychiatric symptoms. Also, it is important to ask specifically about a personal history of manic and hypomanic episodes and to determine whether the patient’s current difficulties include any symptoms of mania or hypomania. A number of associated clinical factors can serve as clues that a patient may have an underlying bipolar disorder, even when the patient is presenting with (and reporting) only depression (Box 1) (23). These clues alone are not sufficient to establish a diagnosis. However, their presence should be noted and considered when formulating the case.

It is equally important for the physician to know how to rule out a diagnosis of bipolar disorder. Many patients with histories of irritability, social chaos, or substance abuse have received a diagnosis of bipolar disorder, but it is important to remember that, in most cases, only a personal or family history of manic or hypomanic episodes will be sufficient reason to withhold antidepressant treatment. It is helpful to interview an outside observer whenever possible. Many patients consider their hypomanic periods to be their “normal selves,” but outside observation by a family member can reveal further information that suggests that the patient actually has bipolar disorder. For example, the observation that a patient goes through periods where she sleeps less than usual, accomplishes
more, and talks fast is consistent with a hypomania, particularly if a family member has noticed these periods as different from the patient’s usual self.

If the diagnosis remains unclear, options include monitoring the patient closely while prescribing an antidepressant, instructing family members regarding the recognition of hypomanic symptoms, or initiating a mood stabilizing agent. Alternatively, the patient should be referred to psychiatry before treatment initiation, if at all possible.

CASE NO. 2. A 24-year-old woman presents with a 3-month history of difficulty getting out of bed, tearfulness, poor concentration, and weight loss of 4.5 kg (10 lb) because of poor appetite. She admits to a passive death wish but denies suicidal ideation. She has no past psychiatric history, but her father and one sister have a history of bipolar disorder.

Her obstetrician–gynecologist administered the Mood Disorder Questionnaire, which yielded a negative result for symptoms consistent with bipolar disorder. For this patient, the clinician administered an antidepressant, provided education about hypomanic symptoms, and scheduled a follow-up visit in 2 weeks. Education about hypomanic symptoms and close follow-up increase the chance that induction of hypomania caused by the antidepressant will be caught early if the patient actually has unidentified bipolar disorder.

Anxiety and Related Disorders

Anxiety disorders are among the most common psychiatric conditions, with about 10–15% of primary care patients experiencing some form of anxiety (24). One in three women will experience an anxiety disorder across her lifetime (25, 26). Women, younger
individuals, those with minimal social support, those with a family history of anxiety, and those with stressful life events have an increased probability of anxiety, and Caucasians have higher rates than African Americans (27). Individuals with anxiety are overwhelmingly likely to have other psychiatric disorders, physical health problems, and substance use problems.

Patients who have anxiety and related disorders exhibit both fear (the emotional response to a real or perceived threat) and anxiety (anticipation of future threat). These are related but distinct emotions that result in different psychologic and physical manifestations—the “fight or flight” autonomic response is associated with fear, whereas vigilance and avoidance are associated with anxiety.

In a primary care setting, most patients with anxiety disorder will report physical symptoms. Headache, fatigue, muscle tension, gastrointestinal (GI) distress, chest pain, and palpitations are frequent symptoms of anxiety; and many patients with unexplained physical symptoms will have an anxiety disorder (28). These physical symptoms also may be caused by a medical disorder; therefore, a medical workup is in order before concluding that a patient has anxiety.

Some anxiety disorders are segmented by specific triggers of anxiety, for example, separation anxiety, specific phobia, agoraphobia, or substance-induced anxiety disorder. The most commonly encountered diagnoses in a primary care setting are panic disorder, generalized anxiety disorder, and social anxiety disorder. Furthermore, OCD and PTSD, although no longer classified as anxiety disorders by the DSM-5, are closely related and commonly seen. These frequently diagnosed anxiety disorders are discussed briefly in the following sections.

**Generalized Anxiety Disorder**

Generalized anxiety disorder is the most common type of anxiety disorder, affecting up to 9% of adults across their lifetimes, with approximately two thirds of patients being women (26, 29). The key feature of generalized anxiety disorder is persistent and excessive worry across many different facets of life that the individual is unable to control. Physical symptoms, such as restlessness or agitation, muscle tension, and difficulty concentrating, are common. Although anxiety and worry are common occurrences for everyone, those with generalized anxiety disorder worry so much that it interferes with daily functioning. Often, these worries are accompanied by physical symptoms and are distressing to the patients. Although comorbidity with other psychiatric diagnoses is common, a gender split exists. Women are more likely to have depression or other anxiety disorders and men are more likely to have substance use disorders (30, 31). Most individuals with generalized anxiety disorder experience some symptoms early in life but rarely meet criteria for the diagnosis until adulthood, with the median onset in the reproductive years.
CASE NO. 3. A 26-year-old woman reports that her worries are “getting the best of her.” She admits to always being a perfectionist and remembers getting stomachaches at school as a child that would result in her being sent home. Currently, she has heart palpitations, her palms are sweaty, and she has difficulty sleeping because she worries about different situations both at home and at work. A Beck Anxiety Scale is administered. The patient receives the score of 47, indicating a significant amount of anxiety.

The physician diagnoses generalized anxiety disorder, based on her description of the symptoms. Treatment with a selective serotonin reuptake inhibitor (SSRI), which generally is well tolerated and effective for both patients with depression and those with anxiety, is begun, and the patient is referred to a therapist for cognitive–behavioral therapy, which is known to be effective for the treatment of anxiety disorders.

Panic Disorder

Patients often use the term “panic attack” to refer to increasingly bad anxiety about a known worry that builds all day and then reaches an emotional climax. However, this episode of anxiety as described is not a panic attack. A panic attack is a sudden surge of fear that peaks within minutes; it is accompanied by physical symptoms, such as sweating, palpitations, chest pain, or shortness of breath. Panic attacks can arise in response to a known trigger or can occur unexpectedly.

Panic attacks can occur in the setting of any anxiety or mood disorder and increase the severity of that disorder (with higher rates of suicidal ideation in those with panic attacks [27]). Some individuals have repeated unexpected panic attacks; such individuals have panic disorder, a diagnosis with a prevalence of approximately 2–3% in the United States (32). Caucasians have a higher rate of panic disorder than Latinos, African Americans, and Asian Americans, and women are twice as likely as men to have panic disorder (33). Typically, the onset of panic disorder is during the reproductive years, and childhood physical and sexual abuse is an important risk factor (34).

Individuals with panic disorder experience repeated and unexpected panic attacks, live in fear of the next panic attack, and often change their behavior (staying away from certain places or situations) in an effort to stave off panic attacks. The frequency and severity of attacks vary widely. Some individuals experience attacks relatively rarely (weekly or less often) whereas others experience short bursts of frequent attacks over many years. The disorder is associated with considerable disruption to emotional and occupational functioning, with high rates of unemployment and high rates of visits to medical professionals.

Social Anxiety Disorder

Social anxiety disorder is characterized by substantial fear or anxiety associated with social situations during which an individual may be subject to scrutiny by other people.
This can take the form of many different situations; for example, in conversations, when being observed, or when speaking in front of others. Individuals may worry that others will judge them or criticize them; they may worry about exhibiting anxiety symptoms in front of others (for example, blushing or stammering); or they may worry about offending others. Many individuals feel anxious in new social situations and will endure the situations with intense distress or will go out of the way to avoid the situations. To establish a diagnosis, anxiety must cause significant impairment in functioning and be present for at least 6 months to meet the criteria for social anxiety disorder. In the United States, the 12-month prevalence is approximately 7%, with women 1.5–2 times as likely as men to develop the disorder (26, 29). Native Americans have the highest rate of social anxiety disorder in the United States, followed closely by Caucasians (33). Some individuals with social anxiety disorder will self-medicate with alcohol or other substances to overcome their inhibition associated with social interactions.

**Obsessive–Compulsive Disorder**

There is a common misconception that individuals with OCD are perfectionists or care excessively about order. In fact, these are personality characteristics that some individuals (including those with obsessive–compulsive personality disorder may have, but they do not have much in common with OCD. Obsessive–compulsive personality disorder is characterized by rigidity and perfectionistic ideas, such as strong preferences regarding order or ways to complete tasks, that make perfect sense to the person with these vulnerabilities, and it is managed primarily with psychotherapy. However, OCD is characterized by the presence of obsessions, compulsions, or both that generally are ego-dystonic (ie, they do not make sense to the person with OCD). Obsessions are repetitive, intrusive thoughts, images, or urges over which an individual has no control and generally recognizes them as not realistic. They are unwanted, unpleasant, and may cause considerable distress. Examples include thoughts about contamination; images of violent or sexual or religious scenes; and urges to harm someone else. Individuals who experience obsessions will attempt to ignore them or suppress them and often will develop other behavior or mental acts in response to the obsessions. These types of behavior, which the individual often feels compelled to perform, are compulsions. Patients engage in compulsions to reduce the distress over obsessions, but such actions often are not realistic; for example, an individual concerned about contamination from the use of public transportation might shower for hours a day or an individual consumed with violent images might repeatedly count objects in order to prevent harm from coming to a loved one.

Although any individual may, on occasion, have an intrusive thought or double-check that the stove is turned off, individuals with OCD have such thoughts for at least 1 hour per day and have significant distress and impairment as a result. In order to meet the diagnostic criteria, a patient need only have either obsessions or compulsions, but most patients with OCD will experience both.
The 12-month prevalence of OCD is approximately 1.2% in the general population, with age of onset during the reproductive years and a higher rate in women than in men (although an earlier age of onset and higher rate during childhood occur in men) (26). Many individuals with OCD also have a tic disorder (30%), a mood disorder (63%), or an anxiety disorder (76%), and rates are increased in individuals with eating disorders (35).

CASE NO. 4. A 59-year-old woman is more than 1 hour late for her initial visit with her new obstetrician–gynecologist. The patient then spends nearly 40 minutes in the bathroom to give a urine sample. During the course of the interview and examination, the obstetrician–gynecologist observes that the patient shakes hands but uses a sanitizing wipe on her hands immediately afterward. Eventually, the patient confides that she experiences obsessive thoughts about germ contamination that she realizes are exaggerated, has trouble using public restrooms, and has elaborate cleaning rituals that help her with the anxiety. Based on the patient’s symptoms, the clinician establishes the diagnosis of OCD and begins treatment with an SSRI. The patient also is referred to a therapist for cognitive–behavioral therapy specifically focused on the treatment of OCD.

Posttraumatic Stress Disorder

Posttraumatic stress disorder is another commonly misunderstood psychiatric diagnosis. To meet the diagnostic criteria, an individual must be exposed to actual or threatened death, serious injury, or sexual violence and also must have both an emotional response to this exposure as well as avoidance of triggers and intrusion symptoms. Patients who have symptoms of depression or anxiety after a difficult childhood do not have PTSD. If they are children, they may have another stress-related disorder, such as reactive attachment disorder or disinhibited social engagement disorder. If they are adults, they may have depression or anxiety. Patients who have stress-related reactions to a recent trauma (less than 1 month), such as a traumatic childbirth, also do not have PTSD, but technically have an acute stress syndrome that may or may not develop into PTSD. These are important distinctions because the treatment of PTSD is different from that of anxiety, depression, and other disorders.

The traumatic event can be, among others, war, threatened or actual physical assault or sexual violence, torture, kidnapping, natural disasters, or witnessing any such event. The individual will re-experience the trauma—often in the form of nightmares or flashbacks—and has intense distress when exposed to a trigger. The individual may be especially reactive, easily startled, and prone to avoiding anything that reminds her of the trauma. The individual may have a persistent negative mood state or may engage in aggressive verbal or physical behavior.

The lifetime prevalence of PTSD in the United States is 8.7% (26, 29). Initial symptoms may emerge immediately after the trauma, but it may take months or years for an individual to meet full criteria for the diagnosis. The natural course of the disorder
is quite varied, with some individuals recovering within a few years and others exper-
encing a lifelong disorder (36). Women and those at a young age at the time of the trauma
have an increased risk of developing the disorder. In addition, women are more likely
than men to be exposed to traumatic events, particularly rape and interpersonal violence;
notably, when such differences are accounted for, the male–female differences virtually
vanish (26, 29).

**Screening**

The most salient point regarding screening for mood and anxiety disorders is the fact
that the screening is offered; the choice of the screening test is secondary. The common
screening tools are listed in Table 1. A screening and treatment algorithm for mood
disorders is presented in Figure 1 and a screening and treatment algorithm for anxiety
disorders is presented in Figure 2. Screening tools can alert the obstetrician–gynecologist
to the possible presence of a mood or anxiety disorder, but they are not diagnostic tools
and should be followed by a diagnostic interview.

### Table 1. Screening Tools for Depression, Bipolar Disorder, and Anxiety

<table>
<thead>
<tr>
<th>Tool</th>
<th>Purpose</th>
<th>Target Population</th>
<th>Number of Items</th>
<th>Scoring</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edinburgh Postnatal Depression Scale</td>
<td>Peripartum depression</td>
<td>SR</td>
<td>10</td>
<td>Depression: 13 or more points</td>
<td>Validated for antepartum and postpartum women</td>
</tr>
</tbody>
</table>
| Quick Inventory of Depressive Symptomatology (QIDS) | Depression | SR                | 16              | Mild: 8–12 points
Moderate: 13–16 points
Moderate–severe: 17–20 points
Severe: 21 points |
| Montgomery Asberg Depression Scale | Depression                     | CI                | 10              | Mild: 7–19 points
Moderate: 20–34 points
Severe: greater than 34 points |
| Patient Health Questionnaire (PHQ)  | Depression                     | SR                | 2 or 9          | Mild: 5–9 points
Moderate: 10–14 points
Moderately severe: 15–19 points
Severe: 20–27 points |
| Geriatric Depression Scale         | Depression                     | CI and SR         | Long form: 30
Short form: 15 | Long form: Normal: 0–9 points
Mild: 10–19 points
Severe: 20–30 points
Short form: Normal: 0–5 points
Depression: greater than 5 points |

(continued)
Table 1. Screening Tools for Depression, Bipolar Disorder, and Anxiety (continued)

<table>
<thead>
<tr>
<th>Tool</th>
<th>Purpose</th>
<th>Self-Rated (SR) or Clinician Interview (CI)</th>
<th>Target Population</th>
<th>Number of Items</th>
<th>Scoring</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cornell Scale for Depression in Dementia</td>
<td>Depression</td>
<td>CI</td>
<td>Geriatric population with cognitive impairment</td>
<td>19</td>
<td>Higher scores greater need for psychiatric assessment</td>
<td></td>
</tr>
<tr>
<td>The Mood Disorder Questionnaire</td>
<td>Bipolar disorder</td>
<td>SR</td>
<td>General</td>
<td>17</td>
<td>Positive screening result requires the following answers:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Item 1: “Yes” to seven or more questions</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Item 2: “Yes” to item 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Item 3: “Moderate” or “Serious”</td>
<td></td>
</tr>
<tr>
<td>Young Mania Rating Scale</td>
<td>Manic symptoms</td>
<td>CI</td>
<td>General</td>
<td>11</td>
<td>Potential mania or hypomania: greater than 13 points</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Probable mania or hypomania: greater than 21 points</td>
<td></td>
</tr>
<tr>
<td>Daily Record of Severity of Symptoms</td>
<td>Premenstrual mood symptoms</td>
<td>SR</td>
<td>Women with premenstrual symptoms</td>
<td>Rated each day of the month (Day 1 should be the beginning of the menstrual period)</td>
<td>Each symptom is given a score of 1 through 6 based on increasing severity for clinician review</td>
<td></td>
</tr>
<tr>
<td>Generalized Anxiety Disorder 7-item Scale (GAD-7)</td>
<td>Generalized anxiety</td>
<td>SR</td>
<td>General</td>
<td>7</td>
<td>Possible generalized anxiety: greater than 10 points</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Severe generalized anxiety: 15 points and greater</td>
<td></td>
</tr>
<tr>
<td>Edinburgh Postnatal Depression Scale-A (EPDS-A)</td>
<td>Perinatal anxiety</td>
<td>SR</td>
<td>Perinatal women</td>
<td>3</td>
<td>Moderate: 4–6 points</td>
<td>Use questions 3, 4, and 5 of the form as a minimal anxiety screening tool</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Severe: 7 points and greater</td>
<td></td>
</tr>
<tr>
<td>Beck Anxiety Inventory (BAI)</td>
<td>Generalized anxiety</td>
<td>SR</td>
<td>General</td>
<td>21</td>
<td>Moderate: 22–35 points</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Concerning: 36 points</td>
<td></td>
</tr>
<tr>
<td>Hospital Anxiety and Depression Scale</td>
<td>Depression and anxiety</td>
<td>SR</td>
<td>General</td>
<td>14</td>
<td>Borderline: 8–10 points for either question A or question D Abnormal: 11 points and greater</td>
<td></td>
</tr>
<tr>
<td>Posttraumatic Stress Disorder Checklist (PCL-5)</td>
<td>Posttraumatic stress disorder</td>
<td>SR</td>
<td>General</td>
<td>20</td>
<td>Likely: greater than 33 points</td>
<td>The most frequently used instrument for posttraumatic stress disorder screening</td>
</tr>
<tr>
<td>Trauma Screening Questionnaire (TSQ)</td>
<td>Posttraumatic stress disorder</td>
<td>SR</td>
<td>General</td>
<td>10</td>
<td>Likely: 6 points or greater</td>
<td>Most useful for recent trauma</td>
</tr>
<tr>
<td>Obsessive–Compulsive Inventory-Revised (OCI-R) Instrument</td>
<td>Obsessive–compulsive disorder</td>
<td>SR</td>
<td>General</td>
<td>18</td>
<td>Likely: greater than 21 points</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1. Screening for mood disorders. Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; PHQ-9, Patient Health Questionnaire-9. 

Test score
EPDS: less than 9
PHQ-9: less than 5

Mood disorder unlikely
Counsel the patient:
“Things seem to be going well for you, but I always like to check in about stress in patients’ lives. Do you have any concerns about your mood?”

Provide general mental health information and offer information about support groups and other community resources

Test score
EPDS: 9–12
PHQ-9: 5–9

Mild depression likely
Counsel the patient:
“From your screening test result, it appears that you may be having a tough time. Depression and mood disorders are very common, and it looks as though you are experiencing some anxiety. I would like to follow up with some additional questions.”

Obtain psychiatric history and administer the Mood Disorder Questionnaire to screen for bipolar disorder. If the screening test result is negative, refer the patient to psychotherapy; if the screening test result is positive, refer the patient to psychiatry.

Obtain psychiatric history and administer the Mood Disorder Questionnaire to screen for bipolar disorder. Consider starting an antidepressant if the screening test result is negative and refer to psychiatry for severe symptoms, complicated history, or in the case of positive results of the bipolar disorder screening test.

Test score
EPDS: greater than 12
PHQ-9: greater than 9

Moderate to severe depression likely
Counsel the patient:
“From your screening test result, it appears that you have quite a bit of depression. Depression and mood disorders are common. I would like to ask you some more questions to make sure we get you the right kind of help.”
Screening for anxiety as part of a well-woman visit (screen first with GAD-7 or EPDS-A)

**Test score**
- **GAD-7**: less than 5
- **EPDS-A**: less than 4

Anxiety disorder unlikely
- Counsel the patient: “Things seem to be going well for you, but I always like to check in about stress in patients' lives. Do you have any concerns?”

Provide general mental health information and offer information about support groups and other community resources

**Test score**
- **GAD-7**: 5–9
- **EPDS-A**: 4–5

Mild anxiety likely
- Counsel the patient: “From our screening test result, it appears that you may be having a tough time. Worry and anxiety are common, and it looks as though you are experiencing some anxiety. I would like to follow up with some additional questions.”

Screen for:
- **PTSD**: Ask about previous trauma, nightmares, flashbacks, or easy startling
- **OCD**: Ask about obsessions (ie, intrusive repetitive thoughts, often violent or sexual) and compulsions (ritualized behavior to reduce distress)
- **Panic disorder**: Ask about physical symptoms (eg, chest tightness or palpitations) and feelings of impending doom

Screening result positive? No Yes
- Refer to psychotherapy
- Administer a more thorough diagnostic tool (TSQ or OCI-R) and refer to psychiatry

**Test score**
- **GAD-7**: 10 or greater
- **EPDS-A**: 6 or greater

Moderate to severe anxiety likely
- Counsel the patient: “From your screening test result, it appears that you have quite a bit of anxiety. Anxiety is common, and I would like to ask some more questions to make sure we get you the right kind of help.”

Screen for bipolar disorder and then begin an SSRI; if “bridging” medication is needed, try gabapentin before benzodiazepines

Screen for bipolar disorder and then begin an SSRI; if “bridging” medication is needed, try gabapentin before benzodiazepines

Screening result positive? No Yes
- Refer to psychotherapy
- Administer a more thorough diagnostic tool (TSQ or OCI-R) and refer to psychiatry

**Figure 2.** Screening for anxiety. Abbreviations: EPDS-A, Edinburgh Postnatal Depression Scale-A; GAD-7, generalized anxiety disorder-7; OCD, obsessive compulsive disorder; OCI-R, Obsessive–Compulsive Inventory-Revised; PTSD, posttraumatic stress disorder; SSRI, selective serotonin reuptake inhibitor; TSQ, Trauma Screening Questionnaire. ☚
Treatment

Approaches to treating mood and anxiety disorders have many overlapping features; for example, antidepressant medications typically are effective in both types of conditions. Comorbidity in patients with mood and anxiety disorders is high and many psychotherapeutic interventions and medications are effective in patients with both types of disorders. This section addresses various types of treatment approaches, including lifestyle changes, complementary and alternative medicine, psychotherapy, and pharmacotherapy.

Lifestyle Changes

Although lifestyle changes generally are not effective alone for moderate-to-severe psychiatric illness, it is always important to examine the patient’s lifestyle and health habits as contributing factors to presenting symptoms. Inadequate sleep and excessive use of (or withdrawal from) alcohol, nicotine, stimulants, or other substances can induce mood and anxiety symptoms. Interventions that increase quality of sleep, decrease abuse of substances, and reduce stress are helpful for coping with anxiety and depressive symptoms. Exercise, in general, and yoga, in particular, have been associated with improvement in anxiety and mood symptoms, and a meta-analysis confirmed the efficacy of exercise both as a standalone modality and as an adjunct to medication in patients with major depressive disorder (37). Although no studies support a specific exercise regimen over another, a regular routine of aerobic exercise at least 20 minutes per day four times weekly can be recommended. Particularly for women with mood disorders, instituting a morning exercise regimen can be helpful in terms of increasing energy throughout the day, although any time a woman can fit regular exercise into her schedule is preferable to not exercising at all. Interventions that reduce stress, such as meditation, yoga, music, journal writing, and massage therapy also can be helpful. Examples of helpful lifestyle interventions are listed in Box 2.

Box 2. Lifestyle Changes for Mood and Anxiety Disorders

- Exercise
- Elimination or limitation of caffeine intake
- Smoking cessation
- Elimination or limitation of alcohol intake
- Healthy sleep habits
- Meditation
- Biofeedback
- Relaxation training
- Yoga
- Acupuncture
- Psychotherapy—supportive, interpersonal, cognitive–behavioral therapy, dialectical behavioral therapy, or mindfulness-based therapy
Complementary and alternative remedies, such as Kava root extract (for depression) and St. John’s Wort (for anxiety), have been found to be beneficial (38–41). However, use of both is associated with significant adverse effects (potential hepatotoxicity for Kava and cytochrome P450 interactions for St. John’s Wort).

Acupuncture also has some benefit, particularly for anxiety in special populations (42). In pregnant women with gestational diabetes mellitus, a substantial difference, both clinically and statistically significant, was found in anxiety scores after an acupuncture intervention (42), and several studies have found statistically significant improvement in depression in women (43). However, systematic reviews have pointed out that evidence across all populations is still weak (44–46).

Light therapy, although an excellent evidence-based treatment for depression, is not recommended for individuals with anxiety disorders because it can increase anxiety and jitters. In contrast, it has been demonstrated to be effective for seasonal depression, depression without a seasonal component, and antenatal depression (47).

Psychotherapy
A significant body of evidence supports the use of psychotherapy, particularly cognitive–behavioral therapy, in patients with mood and anxiety disorders. For those with generalized anxiety disorder and panic disorder, cognitive–behavioral therapy tends to focus on recognizing cognitive distortions and anxiety triggers and learning coping skills. For those with social anxiety disorder, exposure therapy (a subtype of cognitive–behavioral therapy) enables patients to confront the feared situations and challenge their distorted thinking. For those with OCD, exposure and response therapy helps them confront their fears (obsessions) and prevents them from engaging in their usual responses (compulsions) (48). For patients with PTSD, evidence is not yet clear on which psychotherapeutic techniques may be most beneficial, although numerous approaches are used, including prolonged exposure, rapid-eye-movement desensitization, hypnosis, and cognitive processing (49). Although many psychotherapeutic techniques have some evidence of efficacy in patients with any anxiety disorder, a 2015 meta-analysis found that all types of psychotherapy alone were less effective than pharmacotherapy; however, cognitive–behavioral therapy when combined with a medication was the third most effective management strategy (after use of antidepressants and benzodiazepines) (50).

Pharmacotherapy
Medications typically used for mood and anxiety disorders include antidepressants, anti-anxiety agents, mood stabilizers, and antipsychotics. As with any chronic medical condition, health care providers must weigh the risks and benefits of medications and try to minimize adverse effects while maximizing outcomes. Because psychiatric illnesses are
usually chronic and often serious, adverse effects may need to be tolerated in order for the patient to function. In addition, because there is no laboratory test to determine the type of psychiatric illness or which medication would be most effective in the treatment of illness (although genotype testing for enzyme metabolism is increasingly common and may help determine medication selection in the future), patients and their health care providers often undergo a process of trial and error with psychiatric medications to find the medication or combination of medications that produces the greatest stability in psychiatric symptoms and minimizes the adverse effects. Table 2 provides a full listing of common psychiatric medications, starting dosages, and dosage ranges, and Table 3 lists medications specifically used in patients with anxiety disorders.

<table>
<thead>
<tr>
<th>Table 2. Typical Dosages of Psychiatric Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychiatric Medication</strong></td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors</strong></td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
</tr>
<tr>
<td>Fluoxetine (Prozac, Prozac Weekly, Selfemra, and Sarafem)</td>
</tr>
<tr>
<td>Fluvoxamine (Faverin, Luvox, and Luvox CR)</td>
</tr>
<tr>
<td>Paroxetine (Paxil, Paxil CR, and Pexeva)</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
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</tbody>
</table>

(continued)
### Table 2. Typical Dosages of Psychiatric Medications (continued)

<table>
<thead>
<tr>
<th>Psychiatric Medication</th>
<th>Starting Dosage</th>
<th>Typical Dosage Range</th>
<th>Dosage Comments</th>
<th>Pregnancy and Lactation Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serotonin–Norepinephrine Reuptake Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>50 mg/d</td>
<td>50–100 mg/d, but dosages up to 400 mg/d have been used</td>
<td>More studies of patients with depression than with anxiety</td>
<td>No systematic studies in human pregnancy; animal data reveal no known teratogenicity</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>20–30 mg/d</td>
<td>30–120 mg/d</td>
<td>Generally used at higher doses for anxiety than for other mood disorders, but evidence is limited</td>
<td>Limited human data available; no known teratogenicity</td>
</tr>
<tr>
<td>Venlafaxine (Effexor)</td>
<td>37.5–75 mg/d</td>
<td>75–350 mg/d</td>
<td>Especially effective for patients with anxiety with FDA approval for the treatment of generalized anxiety disorder, social phobia, and panic disorder; to be used at higher dosages (more than 225 mg/d) for dual serotonin–norepinephrine action</td>
<td>Limited data, mostly animal; case studies have shown decreased weight gain in breastfeeding infants</td>
</tr>
<tr>
<td><strong>Other Antidepressants</strong></td>
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</tr>
<tr>
<td>Buproprion (Wellbutrin SR or Wellbutrin XL)*</td>
<td>150 mg/ (XL) 100 mg/d (SR)</td>
<td>300–450 mg/d (XL) 200–450 mg/d (SR)</td>
<td>Can increase anxiety; used almost exclusively for depression; no sexual adverse effects and little weight gain</td>
<td>No increase in congenital defects in animal studies; limited human data, mostly registry; can be useful for smoking cessation; associated with fewer sexual adverse effects and less weight gain than other antidepressants; decreases seizure threshold; contraindicated in patients with preeclampsia; theoretical risk of seizure in fetus or infant, but no data</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>10–15 mg/d</td>
<td>15–60 mg/d†</td>
<td>Actions on anxiety can begin shortly after administration</td>
<td>No known congenital defects from animal studies; human data are limited to case reports; fewer sexual adverse effects than other antidepressants; can be helpful with nausea, vomiting, and weight restoration; used in patients with hyperemesis gravidarum although few supporting data exist</td>
</tr>
<tr>
<td>Trazodone (Desyrel)</td>
<td>25–50 mg/d</td>
<td>50–200 mg/d in patients with sleep disorders 150–400 mg/d in patients with major depressive disorder</td>
<td>Rarely used for anxiety or depression, primarily for insomnia</td>
<td>Limited data; no known teratogenicity in animal studies but no systematic human data exist</td>
</tr>
<tr>
<td>Viibryd (Vilazodone)</td>
<td>10 mg/d</td>
<td>10–40 mg/d</td>
<td></td>
<td>No data in pregnant women</td>
</tr>
<tr>
<td>Vortioxetine (Brintellix)</td>
<td>10 mg/d</td>
<td>10–20 mg/d</td>
<td></td>
<td>No data in pregnant women</td>
</tr>
<tr>
<td><strong>Tricyclic Antidepressants</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>25 mg/d at bedtime</td>
<td>75–300 mg/d; may be increased by 25 mg every 3–7 days; plasma levels should be monitored</td>
<td>Used more often for depression than anxiety</td>
<td>Adverse effects can be burdensome in pregnant women; may cause orthostatic hypotension; pharmacokinetic changes of pregnancy increase the likelihood of increasing the dosage; no known teratogenicity based on human and animal data</td>
</tr>
<tr>
<td>Psychiatric Medication</td>
<td>Starting Dosage</td>
<td>Typical Dosage Range</td>
<td>Dosage Comments</td>
<td>Pregnancy and Lactation Comments</td>
</tr>
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<td>--------------------------------</td>
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<tr>
<td><strong>Tricyclic Antidepressants</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Clomipramine (Anafranil)</td>
<td>25 mg/d at bedtime</td>
<td>150–250 mg/d; may be increased by 25 mg every 3–7 days; plasma levels should be monitored</td>
<td>Especially effective in patients with OCD; requires dosages at higher end for the management of OCD (200–250 mg/d); dosages of 300 mg/d or higher have unacceptable seizure risk; patients should be monitored for possible p450 interactions with other antidepressants</td>
<td>Adverse effects can be burdensome in pregnant patients; may cause orthostatic hypotension; pharmacokinetic changes of pregnancy increase the likelihood of increasing the dosage; no known teratogenicity based on animal data; human data show possible risk of cardiac malformations but confounded by indication and not replicated</td>
</tr>
<tr>
<td>Desipramine (Norpramin)</td>
<td>25 mg/d at bedtime</td>
<td>150–300 mg/d; may be increased by 25 mg every 3–7 days; plasma levels should be monitored</td>
<td>Adverse effects can be burdensome in pregnant patients; may cause orthostatic hypotension; pharmacokinetic changes of pregnancy increase the likelihood of increasing the dosage; no known teratogenicity based on animal and human data (studies mostly involved imipramine, a closely related agent)</td>
<td></td>
</tr>
<tr>
<td>Doxepin (Sinequan)</td>
<td>25 mg/d at bedtime</td>
<td>75–150 mg/d; 3–6 mg/d for insomnia; plasma levels should be monitored</td>
<td>May have immediate effects in treating anxiety or insomnia; strong antihistamine properties at low doses</td>
<td>Adverse effects can be burdensome in pregnant patients; may cause orthostatic hypotension; pharmacokinetic changes in pregnancy may increase the likelihood of increasing the dosage; no known teratogenicity based on animal data, human data limited to a few reports (not systematic)</td>
</tr>
<tr>
<td>Imipramine (Tofranil)</td>
<td>25 mg/d at bedtime</td>
<td>150–300 mg/d; may be increased by 25 mg every 3–7 days; plasma levels should be monitored</td>
<td>May have immediate effects in treating anxiety</td>
<td>Adverse effects can be burdensome in pregnant patients; may cause orthostatic hypotension; pharmacokinetic changes in pregnancy increase the likelihood of increasing the dosage; no known teratogenicity based on human and animal data</td>
</tr>
<tr>
<td>Nortriptyline (Pamelor)</td>
<td>10–25 mg/d at bedtime</td>
<td>75–150 mg/d; may be increased by 25 mg every 3–7 days; plasma levels should be monitored</td>
<td>May have immediate effects in treating anxiety</td>
<td>More tolerable adverse effect profile than other tricyclic antidepressants and greater volume of safety data; no known teratogenicity; good evidence with neurobehavioral data in children; no known adverse effects in breastfeeding; the preferred tricyclic antidepressant in pregnancy because of the quantity of data</td>
</tr>
</tbody>
</table>

*Table 2. Typical Dosages of Psychiatric Medications (continued)*
<table>
<thead>
<tr>
<th>Psychiatric Medication</th>
<th>Starting Dosage</th>
<th>Typical Dosage Range</th>
<th>Dosage Comments</th>
<th>Pregnancy and Lactation Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood Stabilizers and Antiepileptics</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>300 mg/d</td>
<td>900–1,200 mg/d for maintenance; 1,800 mg/d for treatment of an acute episode</td>
<td>Dosage is based on therapeutic blood levels generally accepted to be 0.8–1.2 mEq/L (0.8–1.2 mmol/L). Lower blood levels, 0.5–0.7 mEq/L (0.5–0.7 mmol/L), may be clinically efficacious in some cases. Lithium levels can decrease as pregnancy progresses and should be monitored.</td>
<td>Risk of Ebstein anomaly approximately 1%; thyroid function should be monitored throughout pregnancy; small risk of infant diabetes insipidus leading to polyhydramnios; rarely newborn may have decreased muscle tone and difficulty breathing and feeding, which resolve over a few days; lithium should be withheld before planned delivery or at first sign of labor and restarted at pre-pregnancy dosage after delivery to prevent increased or toxic lithium levels; breastfeeding is complicated by risk of lithium toxicity in dehydrated infants but can be managed with vigilance and guidance of the pediatrician</td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>200 mg BID</td>
<td>400–1,200 mg BID</td>
<td>The patient should be monitored for interactions with P450 agents and oral contraceptives; dosage is based on therapeutic blood levels generally accepted to be 4–12 mg/L.</td>
<td>Risk of neural tube defects; some studies show craniofacial abnormalities and developmental delay; if used in pregnancy, high-dose folate supplementation (4–5 mg) should be provided; limited evidence supports vitamin K supplementation near delivery to prevent neonatal bleeding; no contraindication to breastfeeding</td>
</tr>
<tr>
<td>Gabapentin (Neurontin)</td>
<td>300 mg/d; should be increased to 300 BID over 3 days</td>
<td>1,200–3,600 mg in 2–3 divided doses per day</td>
<td>Can be useful in patients with anxiety, particularly as bridging agent before an SSRI becomes effective</td>
<td>Limited evidence; animal studies show evidence of fetal growth impairment and developmental delay; few small controlled studies in humans do not suggest increased malformations; no contraindication to breastfeeding</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>25 mg/d for 2 weeks, then 50 mg/d for 2 weeks, then 100 mg/d</td>
<td>100–400 mg/d</td>
<td>Caution is required because valproate can double lamotrigine levels; patient should be monitored for interactions with oral contraceptives; lamotrigine levels can decrease as pregnancy progresses and the patient should be monitored.</td>
<td>Older data reporting oral cleft defects have not been confirmed, and data do not show any other risk of malformation; must titrate slowly because of Steven–Johnson syndrome risk (not a good choice for acute symptoms); no contraindication to breastfeeding, but infants display high serum levels and should be monitored carefully for adverse effects, especially rash; recommendations for high-dose folate supplementation have recently been revised down to typical 1 mg/d</td>
</tr>
<tr>
<td>Oxycarbazepine (Trileptal)</td>
<td>300 mg BID</td>
<td>1,200–2,400 mg/d in divided doses</td>
<td>Patients should be monitored for interactions with P450 agents and oral contraceptives</td>
<td>No human data; animal data suggest same risks as closely-related carbamazepine</td>
</tr>
<tr>
<td>Topiramate (Topamax)</td>
<td>25 mg/d</td>
<td>50–300 mg/d</td>
<td>Developmental toxicity in animal studies; limited human studies show an association with oral cleft defects; limited evidence of efficacy in patients with bipolar disorder</td>
<td>(continued)</td>
</tr>
</tbody>
</table>
### Table 2. Typical Dosages of Psychiatric Medications (continued)

<table>
<thead>
<tr>
<th>Psychiatric Medication</th>
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<tbody>
<tr>
<td><strong>Mood Stabilizers and Antiepileptics (continued)</strong></td>
<td></td>
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</tr>
<tr>
<td>Valproic acid (Depakote)</td>
<td>250–500 mg/d</td>
<td>1,200–1,500 mg/d in patients with mania</td>
<td>Dosage based on therapeutic blood levels generally accepted to be 50–125 micrograms per milliliter; patients should be monitored for serum levels and interactions with lamotrigine and carbamazepine.</td>
<td>Should be discontinued in pregnancy if at all possible; 1–2% risk of lumbar meningomyelocele; risk of other neural tube defects likely higher than with other anticonvulsants; also decreased IQ and increased cognitive defects; if used in pregnancy, high-dose folic acid supplementation (4–5 mg/d) is required.</td>
</tr>
<tr>
<td><strong>Antianxiety Medications</strong></td>
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</tr>
<tr>
<td>Alprazolam (Xanax)</td>
<td>0.75–1.5 mg/d in divided doses</td>
<td>1–4 mg/d (immediate release) for anxiety 5–6 mg/d (immediate release) for panic disorder 3–6 mg/d (extended release) for panic disorder</td>
<td>Generally administered at approximately twice the dosage of clonazepam; is associated with a high likelihood of tolerance, dependence, or both; the extended-release formulation has a longer half-life than clonazepam.</td>
<td>No known teratogenicity in animals; limited human data; withdrawal effects possible in fetus.</td>
</tr>
<tr>
<td>Buspirone (Buspar)</td>
<td>10 mg BID</td>
<td>15–60 mg daily in divided doses</td>
<td>Generally takes 2–4 weeks to achieve efficacy; 2–3-times daily dosage required for full effect.</td>
<td>Limited data, no controlled studies in humans; animal data reveal no known teratogenicity; limited data in breastfeeding; low serum levels for infants, but not systematically studied.</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.5–1 mg/d in divided doses</td>
<td>0.5–2 mg/d in divided doses</td>
<td>Periodic complete blood count and liver function tests should be performed in medically ill patients; half the dosage of alprazolam is typical; longer half-life than other benzodiazepines (30–40 hours) makes it preferable for long-term use.</td>
<td>No known teratogenicity in animal or human studies; withdrawal effects possible in the fetus; other agents preferred in breastfeeding women because infant sedation has been observed (long half-life).</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>2–10 mg/d in divided doses</td>
<td>4–40 mg/d in divided doses</td>
<td>Periodic complete blood count and liver function tests should be performed in medically ill patients; available in injectable formulations; less frequently used in patients with anxiety than other benzodiazepines.</td>
<td>Oral cleft defects in mice; no known teratogenicity in humans, but data are limited; withdrawal effects possible in the fetus; more likely than some other benzodiazepines to accumulate in the fetus (not preferred in pregnancy); other agents preferred in breastfeeding women because of long half-life.</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>0.5–1.5 mg/d in divided doses</td>
<td>2–6 mg/d in divided doses</td>
<td>Periodic complete blood count and liver function tests in medically ill patients; available in injectable formulations; intermediate half-life (10–20 hours); paradoxical reaction possible.</td>
<td>No increase in congenital anomalies in animal or human data; may cause sedation or hypotonia in newborns when used near delivery (if possible, dosage should be decreased near delivery); low levels in infant serum during breastfeeding, no reports of adverse effects, and shorter half-life make this the preferred benzodiazepine in breastfeeding.</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>15 mg/d at bedtime</td>
<td>15–30 mg/d at bedtime</td>
<td>Periodic complete blood count and liver function tests in medically ill patients; intermediate half-life (8–15 hours); used for insomnia, not anxiety.</td>
<td>Animal studies show no increase in congenital malformations; no systematic human studies, but one case report of fetal death when temazepam was combined with diphenhydramine; low levels in serum of breastfed infants and no contraindications.</td>
</tr>
</tbody>
</table>

(continued)
Table 2. Typical Dosages of Psychiatric Medications (continued)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Atypical Antipsychotics</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Aripiprazole (Abilify)</td>
<td>2–5 mg/d as augmentation for depression or anxiety, 5–10 mg/d for mood stabilization, and 10–15 mg/d for psychosis</td>
<td>5–10 mg/d as augmentation for depression or, anxiety 10–20 mg/d for mood stabilization, and 15–30 mg/d for psychosis</td>
<td>Limited data during pregnancy; recent registry data indicate no increased incidence of birth defects; patients should be monitored for macrosomia; limited data during breastfeeding; but may be associated with hyperprolactinemia</td>
<td></td>
</tr>
<tr>
<td>Lurasidone (Latuda)</td>
<td>20–40 mg/d</td>
<td>40–120 mg/d</td>
<td>Animal data indicate no increase in congenital anomalies; no human data for pregnancy or breastfeeding are available</td>
<td></td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>2.5–5 mg/d as augmentation for depression and 5–10 mg/d for mood stabilization or psychosis</td>
<td>10–15 mg/d for mood stabilization and 20–30 mg/d for acute psychosis</td>
<td>Experimental animal data and some human data, including recent registry data, indicate no increased incidence of birth defects; patients should be monitored for macrosomia; more data are available during breastfeeding (no adverse effects reported, including developmental data in infants—the preferred atypical agent in lactation); infants should be monitored for sedation; may be associated with hyperprolactinemia</td>
<td></td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>25 mg BID, increase by 25–50 mg/d until effective dosage</td>
<td>200–300 mg/d for bipolar disorder; 100–400 mg/d for mood stabilization, and 400–800 mg/d for acute mania or psychosis</td>
<td>Animal and human data indicate no increase in malformations; recent registry data indicate no increased incidence of birth defects; patients should be monitored for macrosomia; may be associated with hyperprolactinemia; in breastfeeding, low levels in infant serum and no reports of adverse effects in infants</td>
<td></td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>1 mg/d in divided doses</td>
<td>2–8 mg/d for acute mania or psychosis; not generally used as augmentation for depression or anxiety or as a primary mood stabilizer</td>
<td>Higher risk of extrapyramidal effects than with other atypical agents; dose-dependent</td>
<td>Limited data; recent registry data, animal studies, and other human experience indicate no increased incidence of birth defects; patients should be monitored for macrosomia; relatively high passage into breast milk make this a second-line agent in breastfeeding patients; may be associated with hyperprolactinemia (higher incidence than with other atypical agents)</td>
</tr>
<tr>
<td><strong>Biologically Based Therapies</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Melatonin</td>
<td>0.5 mg/d at bedtime</td>
<td>1–3 mg/d at bedtime</td>
<td>Used for sleep and circadian rhythm disorders, so time of administration is important; not regulated by FDA—different brands may offer different preparations</td>
<td>Limited data on the administration of exogenous melatonin in pregnancy and lactation; no known teratogenicity</td>
</tr>
<tr>
<td>Phytoestrogens and soy</td>
<td>Varies by preparation</td>
<td>Varies by preparation</td>
<td>Limited data indicate that consumption of isoflavones in food is not expected to increase congenital anomalies</td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Typical Dosages of Psychiatric Medications (continued)

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>St. John’s wort</td>
<td>Varies, but 300 mg three times per day is frequently used; dosages may start as low as 20 mg/d</td>
<td>For anxiety, 900 mg BID; for depression, 20–1,800 mg BID</td>
<td>May reduce the efficacy of oral contraceptives; not regulated by FDA—different brands may offer different preparations</td>
<td>Animal data show no known increase in malformations; little human data in pregnancy; one lactation study shows some increase in colic and lethargy, but others do not</td>
</tr>
<tr>
<td>Vitex agnus castus (Chasteberry)</td>
<td>Begin at usual dosage (varies by preparation)</td>
<td>35–60 mg of dried supplement in divided doses or 40 drops of liquid extract in the morning</td>
<td>Used for premenstrual syndrome and perimenopausal symptoms; evidence is limited; not regulated by FDA—different brands may offer different preparations</td>
<td>Limited data indicate no increase in malformations but should be avoided in pregnancy because it is a uterine stimulant; no data on use in breastfeeding</td>
</tr>
<tr>
<td>Black cohosh</td>
<td>Begin at usual dosage (varies by preparation)</td>
<td>20–40 mg BID</td>
<td>Used for premenstrual syndrome and perimenopausal symptoms; evidence is limited; not regulated by FDA—different brands may have very different preparations</td>
<td>No animal or human data in pregnancy and breastfeeding</td>
</tr>
</tbody>
</table>

*An immediate-release formulation (Wellbutrin [R]) also exists but is not often used and is associated with an increased seizure risk and three-times-a-day dosage.
†Lower dosages cause more sedation.

Abbreviations: BID, twice per day; FDA, U.S. Food and Drug Administration; OCD, obsessive–compulsive disorder; SSRIs, selective serotonin reuptake inhibitors.


### Table 3. Medications Used for Anxiety Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Approved by the U.S. Food and Drug Administration</th>
<th>Other Agents With Evidence of Efficacy</th>
<th>Evidence</th>
<th>Dosage Tips</th>
<th>Augmentation Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Generalized anxiety disorder</td>
<td>• Escitalopram • Paroxetine • Venlafaxine XR • Duloxetine</td>
<td>• Imipramine • Sertraline • Buspirone • Mirtazapine • Pregabalin • Riluzole</td>
<td>Up to 70% of patients with generalized anxiety disorder will respond to a benzodiazepine in the short term, but they are not effective long-term agents because of tolerance. Evidence is mixed on efficacy of buspirone. Venlafaxine XR has good evidence of both short-term and long-term efficacy</td>
<td>Benzodiazepines may be more effective for arousal symptoms and less effective for psychiatric symptoms than other agents; the reverse is true for the antidepressants.</td>
<td>An antidepressant should be combined with a benzodiazepine for short-term treatment (for bridging) or with gabapentin or pregabalin for long-term treatment.</td>
</tr>
<tr>
<td>Disorder</td>
<td>Approved by the U.S. Food and Drug Administration</td>
<td>Other Agents With Evidence of Efficacy</td>
<td>Evidence</td>
<td>Dosage Tips</td>
<td>Augmentation Strategies</td>
</tr>
<tr>
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</tr>
<tr>
<td>Panic disorder</td>
<td>• Fluoxetine • Paroxetine • Sertraline • Venlafaxine XR • Alprazolam • Alprazolam XR</td>
<td>• Citalopram • Escitalopram • Clomipramine • Mirtazapine • Reboxetine • Imipramine • Clonazepam</td>
<td>Tricyclic antidepressants and monoamine oxidase inhibitors showed robust efficacy in 1990s. It is now known that SSRIs are at least as effective, and there is good evidence for efficacy of venlafaxine XR. Alprazolam was first approved for panic disorder but now is second line because of abuse potential and issues with sedation and discontinuation. Clonazepam has decreased efficacy in the treatment of panic attack but is effective for other elements of panic disorder.</td>
<td>Patients with panic disorder are sensitive to activating effects of antidepressants and will be inclined to discontinue the medication if not warned. It should be started with a low dosage and increased slowly using a bridging agent. Improvement is evident if administered over a long period (evidence for 4 years). Benzodiazepines should be avoided in the elderly population.</td>
<td>A long-acting benzodiazepine (clonazepam) should be combined with an antidepressant to combat adverse effects and act as a bridge.</td>
</tr>
<tr>
<td>Social anxiety disorder</td>
<td>• Paroxetine • Sertraline • Venlafaxine XR • Alprazolam • Clonazepam • Bromazepam • Gabapentin • Pregabalin • Beta-blockers</td>
<td>• Fluvoxamine • Fluvoxamine CR • Escitalopram</td>
<td>Fluvoxamine is extensively studied; no placebo-controlled trials of citalopram; fluoxetine and nefazodone failed to show higher efficacy than placebo in more than one study. Efficacy was shown for the three benzodiazepines studied (others not studied). Effective at a range of dosages; response rates higher than placebo; intuitively appealing but found effective only for performance anxiety Some limited evidence also for clonazepam and ondansetron</td>
<td>If a benzodiazepine is needed, a long-acting agent should be chosen. Treatment is most effective if given over years; this is a chronic condition</td>
<td>Long-acting benzodiazepine plus antidepressant can be helpful.</td>
</tr>
</tbody>
</table>
| Obsessive–compulsive disorder| • Fluvoxamine • Fluoxetine • Sertraline • Paroxetine • Clomipramine | • Escitalopram | Clomipramine was the first drug approved for obsessive–compulsive disorder in the early 1990s. In the mid 1990s, SSRIs were found equally effective. Serotonin–norepinephrine reuptake inhibitors or tricyclic antidepressants with more norepinephrine are not effective. | High doses are needed—recent evidence has shown effect for sertraline at up to 400 mg. | Clomipramine plus fluvoxamine Antipsychotics Combination of pharmacologic therapy and behavioral therapy | (continued)
Table 3. Medications Used for Anxiety Disorders (continued)

<table>
<thead>
<tr>
<th>Disorder</th>
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<th>Evidence</th>
<th>Dosage Tips</th>
<th>Augmentation Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posttraumatic stress disorder</td>
<td>Sertraline, Paroxetine</td>
<td>Amitriptyline, Imipramine, Phenelzine, Moclobemide, Fluoxetine, Fluvoxamine, Venlafaxine XR, Mirtazapine, Nefazodone, Carbamazepine, Valproate, Prazosin</td>
<td>Tricyclic antidepressants and monoamine oxidase inhibitors were studied first, but SSRIs and serotonin–norepinephrine reuptake inhibitors are now known to have equal efficacy. Long-term treatment is most efficacious. Some encouraging evidence with anticonvulsants; no evidence for antipsychotics Two trials show efficacy of prazosin in patients with nightmares. There is no evidence to support the use of benzodiazepines in patients with posttraumatic stress disorder.</td>
<td>An antidepressant should be used for long-term treatment with prazosin for nightmares.</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SSRI indicates selective serotonin reuptake inhibitor.


Antidepressants

Currently available antidepressants can be classified into the following five groups:

1. Selective serotonin reuptake inhibitors
2. Serotonin–norepinephrine reuptake inhibitors (SNRIs)
3. Tricyclic antidepressants
4. Monoamine oxidase inhibitors (MAOIs)
5. Other, ie, a group of medications with unique mechanisms of action that do not fit into the other drug categories

It is important to counsel the patient regarding adverse effects, especially coping with the adverse effects and the need to adhere to the regimen long enough for it to work (at least 6–8 weeks at therapeutic doses). Box 3 lists counseling points for initiating treatment with antidepressants.

Selective serotonin reuptake inhibitors generally are considered first-line treatment for patients with mood and anxiety disorders not because they are necessarily more effective than other agents, but because they are effective and have the fewest adverse effects. Approval by the U.S. Food and Drug Administration (FDA) varies across the types of mood and anxiety disorders, but clinically all six of the standard SSRIs are considered effective for the management of anxiety disorders as well as major depressive disorder (Table 2). Adverse effects can include nausea, weight gain, headaches, jitteriness, dizziness, and sexual adverse effects, but most patients tolerate these medications well (Box 4).
The patient should be instructed to do the following when initiating antidepressant treatment:

- Contact the physician if symptoms worsen or if the patient develops suicidal thoughts
- Contact the physician if the patient experiences significant adverse effects but try to continue taking the medication
- Contact the physician if the patient cannot sleep, becomes energized, or feels elated
- Expect many adverse effects to improve as the depression improves
- Take your medication at the same time each day

The following points also should be emphasized:

- It may take 4–8 weeks for the patient to begin to feel better, but some patients feel better sooner.
- Several different medications may have to be tried depending on the patient’s response and adverse effects.
- The dosage may have to be increased.
- It is important to continue taking the medication even after the patient begins to feel better.
- Antidepressant therapy is recommended for 6 months after the first episode of depression, 12 months after the second episode, and lifelong after the third episode.

**Box 4. Common Adverse Effects of Selective Serotonin Reuptake Inhibitors**

- Drowsiness
- Nausea
- Dry mouth
- Insomnia
- Diarrhea
- Nervousness, agitation, or restlessness
- Dizziness
- Sexual problems, such as reduced sexual desire or difficulty reaching orgasm
- Headache
- Blurred vision
- Bruxism
The key to managing adverse effects is to start with a low dosage, increase the dosage slowly, and encourage patients to endure the adverse effects for several days to see if they diminish.

Serotonin-norepinephrine reuptake inhibitors, with a similar profile of adverse effects as the SSRIs, are equally effective in the management of anxiety and depression, with venlafaxine studied most rigorously in patients with anxiety. Additionally, the SNRIs are effective in the management of many types of pain, unlike the SSRIs.

Tricyclic antidepressants are highly effective in the treatment of depression, anxiety, and particularly OCD. However, these drugs are associated with an increased risk of adverse effects; therefore, generally they are tried only after other antidepressants have failed. Adverse effects include dry mouth, constipation, sedation, orthostatic hypotension, sexual adverse effects and, rarely, QTc prolongation. One advantage of the tricyclic antidepressants is that most have clear therapeutic blood levels, which simplifies treatment in pregnancy (blood levels of antidepressants generally decrease during pregnancy and may require dose increases to maintain the clinical effect).

Monoamine oxidase inhibitors also are effective, but the risk of hypertensive crisis, the need for a washout period from other antidepressants before MAOI use, and the special diet requirements (eliminating all foods containing tyramine), indicate they should be used as a last resort and should be administered only by a specialist. For that reason, they are not included in the tables of medications in this monograph.

The antidepressants labeled as “other” in this monograph include antidepressant medications that have mechanisms of action that do not fit neatly into one of the other categories. The two newest antidepressants (vilazodone [Viibryd] and vortioxetine [Trintellix]) also primarily affect serotonin levels, but through a different mechanism of action than the classic SSRIs. They have been approved by the FDA only for the management of major depressive disorder and have not been in use long enough to yield any clinical information about their efficacy in patients with anxiety disorders. Buspirone is primarily used for chronic anxiety. It acts as a partial agonist to the 5-HT1A receptor, is well-tolerated, and has a low potential for dependence, but it takes 2–3 weeks to become effective. Mirtazapine generally is sedating and increases appetite but has good efficacy in patients with major depressive disorder and anxiety disorders. It almost always causes weight gain and can be useful in patients who have lost weight because of their illness. Also, it is an effective antinausea agent and, therefore, may be an appropriate agent for patients with both depression and severe nausea (for example, hyperemesis gravidarum) (51). Bupropion is a unique antidepressant that generally improves energy and cognition. It can be stimulating for some patients with anxiety but is generally appropriate for patients who are fatigued and have poor concentration. It should not be prescribed to patients with a seizure disorder, an eating disorder, or other medical potential for seizure because it decreases the seizure threshold.
Most antidepressants can cause discontinuation syndrome if they are stopped precipitously, sometimes even when tapered slowly, although the symptoms are thought to be more common with SNRIs than with other antidepressants (Box 5) (52). Box 6 lists common symptoms of antidepressant discontinuation syndrome. One approach for patients who are having trouble discontinuing an antidepressant is to switch them to a low dose of fluoxetine for a week (for example, 20 mg), taper to 10 mg for a week, and

### Box 5. Tapering off Psychiatric Medications
- Decrease the total dose by the smallest or next to the smallest dose (eg, lithium can be decreased by 300 mg, sertraline by 50 mg, and escitalopram by 5 mg)
- Decrease every 3–5 days
- Tapering off may have to progress more slowly (every 7–14 days) in patients who experience antidepressant discontinuation syndrome

### Box 6. Antidepressant Discontinuation Syndrome

**Common General Symptoms**
- Dizziness
- Lightheadedness
- Sweating
- Headache or brain zap
- Insomnia
- Body aches

**Psychiatric Symptoms**
- Anxiety
- Agitation
- Hallucinations (rare)
- Confusion
- Mood changes

**Neurologic Symptoms**
- Parasthesia
- Numbness
- Visual disturbances

**Gastrointestinal Symptom**
- Nausea

then discontinue. Its long half-life makes it easier to discontinue because it essentially self-tapers.

Generally, antidepressants should not be prescribed alone without a mood stabilizing medication to patients with suspected bipolar disorder because they may not be effective and may carry the theoretical risk of precipitating a manic or hypomanic episode. Such patients should be referred for a psychiatric evaluation.

Nonspecialists tend to prescribe these drugs at lower doses than specialists, often rendering the regimens ineffective. Although it is necessary to “start low and go slow,” it is also important to remember that most antidepressants can be titrated up every 5–7 days, and that it is not advisable to discontinue a drug until a therapeutic dose has been reached. The therapeutic range for most anxiety disorders is higher than for major depressive disorder, and the range for OCD is higher still. A frequent clinical scenario in a psychiatrist’s office is the patient who presents with generalized anxiety disorder, and has been taking 25 mg or 50 mg of sertraline for 6 months with little effect. If the patient has been tolerating this dose for some time, there is no reason to continue at this dose. The medication should be titrated up rapidly to at least 150 mg; many patients will need 200 mg or 250 mg. If there is still no effect after 4–6 weeks of this dose, it is time to move on to a different drug.

**Antianxiety Agents**

Although the antidepressants are first-line treatment for chronic anxiety, they do not work right away, and patients often will need a “bridging” drug to manage immediate symptoms until the antidepressant begins to work. The benzodiazepines, which act on the gamma-aminobutyric acid-A (GABA_A) receptor and produce muscle relaxation, sedation, and calmness, and are rapid, effective, and well tolerated. They are effective in the treatment of acute anxiety symptoms but are less appropriate for long-term use because of the potential for tolerance and dependence (53). The shorter-acting agents have a high potential for abuse and should be prescribed with extreme caution. Clonazepam, with a half-life of 50 hours, is the preferred bridging agent for patients with anxiety disorders because of its lower potential for abuse. The shorter-acting agents can be useful for specific phobias. For example, prescribing a few pills of alprazolam or lorazepam for a patient with a fear of flying is an appropriate use of these drugs.

Three other medications deserve mention in this category: 1) gabapentin, 2) pregabalin, and 3) quetiapine. Gabapentin is a useful anxiolytic and is well tolerated by many patients even at high dosages (up to 1,200 mg three times per day) (54). Pregabalin acts in a similar way to gabapentin and has been used in patients with pain conditions, including neuropathy and fibromyalgia. Also, it may decrease anxiety and can be used effectively in patients with both pain and anxiety. Quetiapine, an atypical antipsychotic, has been found to be effective as monotherapy for patients with generalized anxiety disorder (55).
Mood Stabilizers

The mainstay of treatment for bipolar disorder is the use of mood stabilizers. The classic mood stabilizers include lithium and several antiepileptic agents, including valproic acid, carbamazepine, oxcarbazepine, and lamotrigine. Atypical antipsychotics (described in the section “Antipsychotic Medications”) also can be used as mood-stabilizing agents and are reasonable medications for a generalist to prescribe in patients with suspected bipolar disorder who are in need of a psychiatric consultation that cannot be arranged immediately. Generally, the classic mood stabilizers should be prescribed by a psychiatric treatment provider, given both the subtleties of treating bipolar disorder and the need for monitoring blood levels and medical adverse effects. Important medical adverse effects for obstetrician–gynecologists to be aware of are also listed in Table 4.

Antipsychotic Medications

Antipsychotic medications are used not just for psychotic symptoms and disorders but for a wide range of psychiatric indications, including as augmentation agents for patients with major depressive disorder, mood stabilizing agents for patients with bipolar disorder, and as primary treatments for patients with bipolar depression, anxiety, and agitation. Most patients who take antipsychotic medications should be treated by a psychiatrist, given the potential of these drugs for long-term adverse effects, including extrapyramidal symptoms and tardive dyskinesia. Furthermore, a psychiatric referral is necessary in these patients because most patients who require antipsychotic medications generally have severe illness. However, antipsychotic medications can be prescribed for patients who are thought to possibly have bipolar disorder or psychosis who are not ill

Table 4. Medical Monitoring for Mood Stabilizing Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>Before starting, during dosage adjustment, and every 6–12 months: CBC, thyroid function testing, and kidney function testing</td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>Complete blood count before starting and every 2–4 weeks for 2 months; every 3–6 months thereafter</td>
</tr>
<tr>
<td></td>
<td>Liver, thyroid, and kidney function tests before starting and every 6–12 months thereafter</td>
</tr>
<tr>
<td>Gabapentin (Neurontin)</td>
<td>None</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>None</td>
</tr>
<tr>
<td>Oxycarbazepine (Trileptal)</td>
<td>Complete blood count, liver function tests, and electrolyte tests before starting and every 6–12 months thereafter</td>
</tr>
<tr>
<td></td>
<td>Sodium level measurement in the first 3 months</td>
</tr>
<tr>
<td>Topiramate (Topamax)</td>
<td>Baseline and periodic serum bicarbonate test</td>
</tr>
<tr>
<td>Valproic acid (Depakote)</td>
<td>Before starting, during dose adjustment, and annually: platelet test and liver function tests</td>
</tr>
<tr>
<td>Atypical antipsychotics</td>
<td>Body mass index before starting and at least quarterly thereafter; blood pressure and fasting glucose and lipid tests at least annually Monitoring for signs of hyperprolactinemia</td>
</tr>
</tbody>
</table>

Abreviation: CBC indicates complete blood count.
enough to be hospitalized but are waiting for a psychiatric evaluation. Also, they can be prescribed on a short-term basis in the hospital setting for suspected cases of postpartum psychosis. Table 2 lists dosage information.

**Electroconvulsive Therapy and Transcranial Magnetic Stimulation**

Electroconvulsive therapy (ECT) is a treatment during which a patient is briefly placed under general anesthesia, and electrical current is used to induce a seizure while the patient’s muscles are paralyzed; thus, no convulsions are experienced (56). Electroconvulsive therapy can be performed on either an inpatient or an outpatient basis, but referral to a center that conducts ECT is necessary. Typically, treatments are provided three times weekly, and each treatment requires preparation similar to having outpatient surgery, including not eating after midnight and, in the case of outpatient ECT, a companion to drive the patient home afterward. Adverse effects can include short-term memory loss, headache, and mild-to-severe delirium as well as the risks associated with general anesthesia. Patients receiving ECT are asked not to drive during the course of ECT and for 2–4 weeks after the last treatment. Indications for ECT include severe cases of depression (associated with major depressive disorder or bipolar disorder), particularly when one or more medication trials have been unsuccessful. Generally, ECT is not indicated for primary psychotic disorders, such as schizophrenia, or for primary anxiety disorders without accompanying mood disturbance. Electroconvulsive therapy also has been used successfully and safely during pregnancy (57).

Transcranial magnetic stimulation is a relatively new treatment modality that involves using magnets to stimulate parts of the brain (56). It is primarily indicated for treatment-resistant depression and requires referral to a psychiatrist or a center with the required equipment and expertise to conduct the treatment. The most common adverse effect is headache, although rare seizures have occurred. Initial treatments are required 5 times per week, and the frequency can be decreased after clinical response is achieved. Referral to a center that conducts transcranial magnetic stimulation can be undertaken when at least one adequate trial of an antidepressant has been unsuccessful, and the patient is willing to receive daily weekday treatments for 4–6 weeks. The one open-label pilot study of transcranial magnetic stimulation in pregnancy to date involved 10 pregnant women with major depressive disorder and demonstrated no adverse pregnancy or fetal outcomes (58).

**Reproductive Considerations**

**Reproductive Cycle Mood Symptoms**

Many women experience reproductive cycle mood symptoms at times of hormonal change (59). These symptoms include premenstrual mood symptoms (PMS), postpartum “blues,” and perimenopausal mood symptoms, which are common in the general population. These mood symptoms often are complicated by anxiety symptoms and are generally mild and short lived. They may be a nuisance, but they do not affect functioning.
Generally, they can be viewed as a spectrum of mood symptoms in response to times of hormonal change, with most women experiencing mild reproductive cycle mood symptoms at some point during their reproductive lifetime. The obstetrician–gynecologist must determine if a woman who presents with such symptoms is experiencing normal reproductive cycle mood symptoms or if she meets criteria for a mood syndrome associated with the reproductive cycle, such as premenstrual dysphoric disorder or postpartum depression or for a mood disorder outside of the reproductive cycle, such as major depressive disorder or bipolar disorder.

Figure 3 illustrates a diagnostic and management algorithm for women with PMS. Although Figure 3 applies specifically to PMS, many of the same concepts apply to all reproductive mood symptoms. If a woman reports reproductive mood symptoms, the first step is to determine if the woman meets criteria for a mood disorder outside of the reproductive cycle and whether this mood disorder is being adequately treated. This is best accomplished by obtaining a psychiatric history and asking the patient about mood or anxiety episodes that have occurred unrelated to the reproductive cycle in the past or if symptoms are occurring outside of what would be expected for a reproductive mood syndrome. In contrast, many patients report PMS, but upon questioning they will admit that their mood is low almost all of the time, regardless of the stage of their menstrual cycle, and that the symptoms worsen premenstrually. In this case, the patient is more likely experiencing major depressive disorder and will need treatment for mood disorder and not necessarily an approach specific to PMS. Similarly, many women with already diagnosed mood disorders will report premenstrual or perimenopausal mood symptoms,

**Figure 3.** Diagnostic and management algorithm for women with reproductive cycle mood symptoms.
but upon closer examination it becomes clear that their underlying mood disorder is inadequately treated. If it is determined that the patient has a mood disorder, treatment should be initiated for the mood disorder first (Fig. 1). Nonpharmacologic and lifestyle changes for reproductive cycle mood symptoms also can be instituted (Box 7). Table 5 describes the current data supporting the use of various vitamins and herbal remedies in patients with reproductive cycle mood symptoms and mood syndrome associated with the reproductive cycle that can be helpful in women who do not want prescription pharmacologic interventions. Once the mood disorder has been adequately treated, if the patient continues to have reproductive cycle mood symptoms, other pharmacologic approaches can be attempted in appropriate cases. Once an underlying or undertreated mood disorder has been ruled out, the next step is to determine whether the patient

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**Box 7. Lifestyle Modifications For Reproductive Cycle Mood Symptoms**

- Exercise
- Limitation or elimination of caffeine intake
- Smoking cessation
- Limitation or elimination of sugar intake
- Calcium supplementation, 600 mg twice daily
- Stress reduction
- Cognitive–behavioral therapy

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**Table 5. Biologically Based Therapies That are Potentially Helpful in Patients With Premenstrual and Perimenopausal Mood and Anxiety Symptoms**

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black cohosh (for hot flushes)</td>
<td>One RCT with positive evidence; six with negative evidence</td>
</tr>
<tr>
<td>Calcium (600 mg twice per day)</td>
<td>Two RCTs with positive evidence</td>
</tr>
<tr>
<td>Chasteberry (Vitex agnus castus fruit extract)</td>
<td>Eight RCTs with positive evidence, two with negative evidence</td>
</tr>
<tr>
<td>Evening primrose oil</td>
<td>Two RCTs with negative evidence</td>
</tr>
<tr>
<td>Ginkgo biloba</td>
<td>One RCT with positive evidence</td>
</tr>
<tr>
<td>Magnesium (400 mg/d)</td>
<td>Two RCTs using magnesium oxide with negative evidence, one RCT using magnesium pyrrolidone carboxylic acid with positive evidence</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Two RCTs with negative evidence</td>
</tr>
<tr>
<td>Vitamin B&lt;sub&gt;6&lt;/sub&gt; (50–100 mg/d)</td>
<td>Six RCTs with negative evidence; six RCTs with positive evidence</td>
</tr>
<tr>
<td>Vitamin E (400 international units per day)</td>
<td>One RCT with negative evidence; one RCT with positive evidence</td>
</tr>
</tbody>
</table>

Abbreviation: RCT, randomized controlled trial.

meets criteria for a reproductive cycle-associated syndrome. A number of tools exist that can be helpful in distinguishing between an undertreated mood disorder and reproductive cycle mood symptoms (Table 1). Although these tools offer the health care provider a rich source of data on symptoms, they can be burdensome for patients. Often, it is just as simple to have the patient get a monthly calendar and rate her mood on a scale from 0 (depressed) to 10 (extremely happy; manic in the patient with bipolar disorder), with 5 being neutral (what most individuals experience on an average day) and to also note the start of menses, any medication changes, and hours of sleep. Sleep information is useful, particularly for the patient with bipolar disorder because regular patterns may be observed between decreased sleep and mood cycling that can mimic PMS but actually necessitate a sleep intervention in order to improve symptoms.

The term PMS was coined in the 1950s and is used to describe the symptoms that most women experience during the premenstrual period. These symptoms include both mood changes (usually irritability or depressed mood) and physical symptoms, such as fluid retention, breast tenderness, and headache. Symptoms remit entirely once menstruation begins and, generally, begin again 1–2 weeks before the next menstrual period. The symptoms usually are mild and manageable and do not significantly impair functioning. This differentiates PMS from premenstrual dysphoric disorder in which the symptoms are severe enough that they negatively affect the patient’s functioning in one or more areas of life. Notably, the effect of premenstrual dysphoric disorder on quality of life is similar to that of major depressive disorder (60), and premenstrual dysphoric disorder can thus be considered a disorder that involves major depressive episodes that occur regularly during the premenstrual period.

Although prevalence estimates vary, most women experience at least mild symptoms premenstrually at some point during their lifetime, most typically in their 20s and 30s (61–63). For instance, in one study of 1,194 women, 84% of women interviewed reported at least moderate symptoms of PMS, whereas only 4.7% met DSM-5 criteria for premenstrual dysphoric disorder (63).

Evidence from trials on premenstrual dysphoric disorder reveals that SSRIs and SNRIs are effective within the first menstrual cycle and also are effective with intermittent luteal-phase treatment (64–71). This contrasts with the minimum of 4–8 weeks required for the treatment of major depressive disorder (72, 73). Furthermore, SSRIs and SNRIs are effective for premenstrual dysphoric disorder, whereas nonserotonergic antidepressants are not effective in the management of premenstrual dysphoric disorder. In contrast, nonreproductive depression can be treated effectively with SSRIs, SNRIs, and nonserotonergic antidepressants. These observations suggest a specific mechanism, which involves serotonergic pathways that underlie the pathophysiology of premenstrual dysphoric disorder, that is distinct from the mechanisms that underlie nonreproductive cycle-related major depressive disorder.
Oral contraceptive pills (OCPs)—both those containing a combination of estrogen and progesterone and those containing progesterone alone—also have been used to treat premenstrual mood disturbances (74). Studies have reported the benefit of OCP use, especially those formulated with the novel progestin, drospirenone, in women with PMS and premenstrual dysphoric disorder. Benefits are seen both as singular therapy in patients with PMS and premenstrual dysphoric disorder (75, 76) as well as an adjunctive treatment in premenopausal women with treated major depressive disorder and premenstrual relapse (77, 78). It is unknown whether these benefits are specific to the OCP containing drospirenone. A comprehensive review suggests that drospirenone may play an important role because use of progesterone-only and combination oral contraceptives with other progestins failed to show a clear benefit (79), consistent with earlier evidence that older progesterone preparations are ineffective in women with PMS and premenstrual dysphoric disorder (80). Other studies have found that suppression of ovulation with the gonadotropin-releasing hormone agonist leuprolide also appears to improve symptoms of premenstrual depressive symptoms (81).

Several studies using estrogen therapy alone for severe premenstrual mood symptoms in young women have been conducted. Continuous use of estrogen therapy throughout the menstrual cycle (82–84) reduced premenstrual dysphoria; however, this was not the case with estradiol therapy used only during the luteal phase (85). The continuous use of unopposed estrogen is not an option in most women with a uterus, but such studies do point toward the possible mood improving benefits of such treatment.

**Pregnancy**

In the past, pregnancy was considered to be protective against psychiatric illness, particularly depression (86). However, for women with preexisting psychiatric conditions, pregnancy and the postpartum period are periods when psychiatric illness may worsen or relapse. Approximately 15% of all pregnant women have a psychiatric illness and as many as 10% of pregnant women in the general population take a psychotropic medication, thus exposing fetuses to these agents (87, 88).

**Mood Disorders in the Perinatal Period**

Research has shown that pregnancy is not protective but poses a neutral risk of development of mood episodes. For example, a study conducted as part of the 2002 National Epidemiologic Survey on Alcohol and Related Conditions interviewed 14,549 women with a known past-year pregnancy and compared rates of major psychiatric illness in pregnant women, in postpartum patients, and in the nonpregnant female population (89). In the study, the risk for major depressive disorder and bipolar disorder during pregnancy was approximately equivalent to the risk for women who were not pregnant; however, the risk in the immediate postpartum period was clearly increased in patients with major depressive disorder, with an adjusted OR of 1.52 (CI; 1.07–2.15). The OR for bipolar
disorder for patients in the immediate postpartum period was nonsignificant, but the sample was small. Although pregnancy poses a neutral risk, many women with psychiatric disorders experience relapse during pregnancy whether they take medication or not. In one study, approximately 50% of women with a mood disorder reported significant mood symptoms during pregnancy, after pregnancy, or both (59). Furthermore, the risk of relapse during pregnancy increases in the setting of medication discontinuation. One study demonstrated a 68% relapse rate in women with major depressive disorder who discontinued their medication during the first trimester (90). Among women with bipolar disorder, pregnant women who discontinued mood stabilizer treatment had a recurrence risk of 81–85.5%, whereas women who continued mood stabilizer treatment had a lower recurrence risk of 29–37% (91, 92). Another study compared a group of pregnant women who discontinued mood stabilizers with a group of pregnant women who continued the anticonvulsant lamotrigine (93). The recurrence risk of bipolar disorder was 100% in the group of women who discontinued all mood stabilizing medications. Such findings suggest that treatment during pregnancy is necessary to prevent recurrence in many patients.

ANXIETY AND RELATED DISORDERS IN THE PERINATAL PERIOD

During pregnancy and the postpartum period, anxiety and related disorders are common and underrecognized (94). When screening for mental health concerns is performed during the perinatal period, it is usually focused on depression rather than anxiety (95). Depression and anxiety are highly co-morbid, but many women exhibit clinically significant anxiety symptoms without depressive symptoms, and, thus, are missed in traditional screening. However, current research indicates that these disorders are common in the perinatal period and may even have their onset at this time (96).

Clinical features of anxiety in the perinatal period can be similar to those at other times, but some research indicates distinctive patterns. Specific phobias and generalized anxiety disorders are the most common disorders, with almost 11% of women in one sample meeting criteria for generalized anxiety disorder and up to 27% in another sample having some form of anxiety (97). Furthermore, pregnancy-specific anxiety is experienced by approximately 14% of women and consists of specific worries about the fetus or the pregnancy. The burden of anxiety symptoms appears to be higher than the burden of diagnosable anxiety symptoms. In a 2014 chart review, Brown University researchers found that, among patients in a peripartum day hospital, 63% reported generalized anxiety symptoms but only 1.5% met criteria for generalized anxiety disorder. Furthermore, 30% of patients reported having obsessions (although only 3.9% met criteria for OCD) and 58.1% reported at least one panic attack (although only 4.2% had a panic disorder) (98).

CASE NO. 5. A 33-year-old woman presents for her first prenatal visit with her obstetrician–gynecologist and reports left-sided numbness and tingling in her arm, abdomen, and leg. She also had intrusive thoughts that her diet and exposure to environmental factors, such as paint fumes, would
harm the baby. She had a history of anxiety treated successfully with an SSRI that she discontinued in anticipation of pregnancy. A neurologic examination and workup results were within normal limits. This case illustrates pregnancy-specific worries that focus on the health and safety of the fetus. The clinician referred the patient to a therapist for supportive psychotherapy and cognitive–behavioral therapy and recommended re-starting the SSRI that had previously resolved the patient’s anxiety symptoms.

Screening for Perinatal Mood and Anxiety Disorders

The American College of Obstetricians and Gynecologists recommends screening at least once during the perinatal period for depression and anxiety using a standardized, validated tool (Table 1) and also recommends close evaluation and monitoring of women with risk factors, including current symptoms, a past psychiatric history, or a history of perinatal psychiatric disorders (99). Obstetrician–gynecologists can then initiate treatment and, when appropriate (see Box 8), refer patients for psychiatric care.

Psychiatric Medication Use in Pregnancy

Controversies and Limitations of the Literature

The treatment of psychiatric disorders during pregnancy is complicated by the fact that few studies have been conducted to determine which medications are efficacious, how changes in body weight and metabolism may affect dosages, and what alternatives to medications are available that successfully manage psychiatric illness during pregnancy. Thus, treatment decisions rely on little evidence. To further complicate the treatment decision process, abrupt discontinuation of psychotropic medication can result in discontinuation symptoms (Box 6) and relapse of psychiatric illness. Multiple studies have demonstrated that exposure to psychiatric illness in utero results in poor outcomes for both the woman and the infant (100–104).

Box 8. Referral to Psychiatry

An obstetrician–gynecologist should refer a patient to psychiatry when the following factors are present:

• Failure to respond to one or two trials of an antidepressant
• Concern for a bipolar disorder
• Complicated presentation, including personality vulnerabilities, trauma, substance abuse, and significant anxiety
• Any suspicion of psychotic symptoms
• Eating disorder
• Complicated life stressors
• Thoughts of suicide or self-injury
It is important to understand that the use of psychotropic medications during pregnancy is essentially a marker for a population of women with different risk factors than the general population of pregnant women. These risk factors, including health-related behavior, associated illnesses, and other characteristics, may influence the outcomes of studies attempting to examine the risks of in-utero exposure to psychotropic medication. For example, diabetes mellitus, obesity, smoking, and substance use are more common in patients with psychiatric illness than in the general population (105). Studies that have not controlled for the underlying psychiatric illness and its confounding behavior and characteristics may find associations between psychotropic medications and outcomes that are not caused directly by exposure to the medication itself but by characteristics that are prevalent in the population of patients who take psychotropic medications during pregnancy.

The reports about in-utero antidepressant exposure and infant cardiac defects are a good example of the importance of controlling for confounding factors in psychiatric clinical research. Some but not all previous studies demonstrated a possible association between in-utero antidepressant exposure (particularly SSRIs) and heart defects (106). However, most of these studies were “confounded by indication” and compared outcomes of the psychiatric population with those of the general population instead of comparing women with major depressive disorder who took antidepressants with women with major depressive disorder who did not take antidepressants in pregnancy. More recent, better designed studies have not found an association between antidepressant exposure and heart defects. For example, one study with a sample size of more than 900,000 women did not find an association between first-trimester antidepressant exposure and cardiac malformations when the statistical analyses controlled for major depressive disorder by comparing the outcomes of women with depression who took antidepressants with those of women with depression who did not take antidepressants in the first trimester (107). A meta-analysis of prospective cohort studies found no association between SSRI use in the first trimester and heart defects when comparing women with depression who took SSRIs in the first trimester and women with depression who did not take antidepressants in pregnancy (108). Thus, the previously identified association between in-utero antidepressant exposure and heart defects appears most likely to be associated with other risk factors and behavior that are prevalent in the population of women taking antidepressants in pregnancy.

A similar event has unfolded for the possible association between in-utero antidepressant exposure and persistent pulmonary hypertension in the newborn. An association between SSRI exposure and persistent pulmonary hypertension was first noted in 2006 and led to an FDA alert regarding the possible association of SSRIs and persistent pulmonary hypertension (109). Since this first study, six additional studies have been conducted—three found no association between SSRI exposure and persistent pulmonary hypertension (110–112) and two found an association (113, 114), although with lower ORs than the first study. The sixth and most recent study (115) analyzed close to
3.8 million pregnant women and found an OR of 1.51 (CI, 1.35–1.69) for an association between SSRI exposure and persistent pulmonary hypertension in the unadjusted analysis. However, when the analyses were adjusted for potential confounders associated with major depressive disorder, the OR became insignificant (OR, 1.1; CI, 0.94–1.29), although a statistical association remained when the analyses were limited to cases of primary persistent pulmonary hypertension in full-term infants (OR, 1.28; CI, 1.01–1.64).

Over the years, in addition to cardiac defects and persistent pulmonary hypertension, in-utero antidepressant exposure has been associated with low birth weight, premature birth, spontaneous abortion, and most recently, autism (106). However, studies that control for underlying confounders associated with psychiatric illness, generally yield negative results. For example, a meta-analysis examined neonatal outcomes in women with depression receiving no treatment and compared them with outcomes in women without depression (116). This study found that untreated depression was associated with significantly increased risks of preterm birth and low birth weight, indicating that having major depressive disorder affected infant outcomes. Although it remains to be seen whether there are associations between antidepressant exposure and poor infant outcomes, it is clear that the psychiatric illness itself, and its associated risk factors, are associated with significant effects on infant outcomes. Future studies will need to control clearly for confounding behavior, risks, and illnesses to legitimately determine if antidepressant exposure is directly linked to poor infant outcomes.

**Poor Neonatal Adaptation Syndrome**

One outcome that is most likely associated with in-utero antidepressant exposure is poor neonatal adaptation syndrome. The first report of withdrawal symptoms in infants exposed to antidepressants was published in 1973 (117). It is unclear if neonatal withdrawal syndrome is actually a result of withdrawal from the antidepressant or is caused by toxicity. Thus, the alternative term “poor neonatal adaptation syndrome” may be a better description. There are a number of limitations in the available literature, including inconsistent definitions, no measurement tool, a lack of blinded ratings, and a lack of studies investigating treatment or prevention of the syndrome. Regardless, the FDA instituted a class labeling change in 2004 for both SSRI and SNRI antidepressants warning that third trimester exposure to these drugs may be associated with poor neonatal adaptation syndrome. According to the label change, “reported clinical findings have included respiratory distress, cyanosis, apnea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, hypotonia, hypertonia, hyperreflexia, tremor, jitteriness, irritability, and constant crying” (118). Subsequently, many practitioners have recommended tapering antidepressants before delivery although it remains unclear if this approach decreases the risk of poor neonatal adaptation syndrome and is safe for the woman (Box 5). Most cases of the poor neonatal adaptation syndrome appear to be mild and self-limited and are not associated with lasting repercussions (119). Available data suggest that approximately one third of exposed infants will have at least mild symptoms...
consistent with the syndrome and this risk increases when multiple agents, particularly benzodiazepines, are used (120). Clearly, larger, more rigorous studies of the syndrome as well as strategies to minimize the rate of the syndrome are needed. At this time, evidence is lacking from a safety perspective to recommend tapering of antidepressants in the third trimester, particularly in cases of moderate-to-severe maternal mental illness. Actually, many women may need higher doses of medication in the third trimester because pharmacokinetic changes and an increased volume of distribution can lead to decreased drug concentrations and a reemergence of symptoms.

**U.S. Food and Drug Administration Pregnancy Categories and the Pregnancy and Lactation Labeling Rule**

In 2014, the FDA published the final version of the “Pregnancy and Lactation Labeling (Drugs) Final Rule” mandating changes to the content and format of prescription drug labeling as they pertain to use during pregnancy and lactation (121). The labeling changes went into effect in 2015 for all products submitted for FDA approval and will be phased in over time for other medications and products. The labeling will attempt to summarize all currently available information to help the clinician weigh the risks and benefits of prescribing a drug during pregnancy (122).

Because the rule will be phased in over time and initially will not apply to medication approved before 2001, it is still important to understand the meaning of the former FDA categories. Categories include A, B, C, D, and X, and this classification is based on the amount of evidence for safety in animal and human studies. Many clinicians assume that there is an increasing level of risk from category A to X, which is inaccurate. For example, drugs that have been classified as category B have not been studied adequately in humans to warrant placing them in category A as safe (or in C, D, or X depending on the level of risk in humans); therefore, most medication new to the market will be classified as Category B. Many prescribers may err by prescribing a medication classified as category B over an older medication classified as category C or D, thinking it is safer, although evidence is lacking about its safety during pregnancy. It is hoped that by providing more information through the “new rule,” clinicians will make more informed choices when prescribing medication during pregnancy.

**Prepregnancy Planning**

It is important to assume that every woman of childbearing age will get pregnant. Ideally, medication use during pregnancy and use of birth control measures should be discussed as part of the woman’s ongoing treatment before pregnancy occurs (Box 9). If a woman is taking a medication that generally should not be used during pregnancy unless absolutely necessary, such as valproic acid, a scenario of unplanned pregnancy should be discussed with the woman and, if possible, her sexual partner. As many as 50% of pregnancies are unplanned in the United States; thus, prior discussion of prepregnancy planning and contingency plans for an unplanned pregnancy will minimize the chance
that psychiatric medications will be abruptly discontinued and the illness will relapse (123, 124).

The following four factors should be considered during prepregnancy planning:
1. The patient’s past psychiatric history
2. Severity of illness
3. The patient’s past history of medication response
4. The patient’s and, if possible, the partner’s wishes for treatment during pregnancy

Every case should be considered individually, weighing the risks and benefits of the various options.

Individual differences in history of response to medications and severity of illness will frequently dictate clinical care during pregnancy. For example, although fluoxetine and

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**Box 9. Useful Tips for Pregnancy Planning In Women With Mood Disorders**

- Patients should be encouraged to have psychiatric care during and after pregnancy
- All medication changes should be completed before pregnancy, if possible.
- Ideally the patient should be stable psychiatrically before attempting pregnancy.
- Medications with well-established profiles should be used. “Older is usually (but not always) better.”
- Fetal exposure to harmful factors should be minimized, including exposure to psychiatric illness.
- Breastfeeding should be considered when planning for pregnancy.
- If the fetus was exposed to a medication during pregnancy, it may not be reasonable to discontinue that medication during breastfeeding (or avoid breastfeeding).
- A team approach should be used, including frequent communication with the relatives of the patient and other involved physicians.
- Support should be given even if the patient does not accept the physician’s recommendations.
- The classification of the drug by U.S. Food and Drug Administration as Category B means that adequate data in pregnant women are not available; a Category B drug is not necessarily safer than a Category C or a Category D drug.
sertraline can be considered appropriate antidepressant choices during pregnancy, if a woman has a history of not responding to either of these medications, they cannot be part of the treatment plan.

Severity of illness also is important to consider. If the symptoms of depression were mild in a patient, she responded well to medication, and the illness did not recur, discontinuation of the medication before pregnancy could be considered in that patient. In contrast, if depression was severe, dangerous, and required hospitalization several times, such a patient would not be a candidate for medication discontinuation.

The patient and her partner’s wishes regarding medication use during pregnancy should be considered when designing a treatment plan. If one or the other is strongly against medication use during pregnancy, it is best for the health care provider to make sure they both understand the risks of no treatment to both the pregnant woman and the fetus and the rates of relapse and to outline a course of close follow-up during and after pregnancy. Ultimately, the patient must make the final decision regarding medication use during her pregnancy. A partnership and good communication with the patient and her partner are important, so that if there is a relapse of illness, the patient will remain safe and is likely to seek care and treatment. The primary goal of treatment in pregnancy is to minimize exposure to medication while controlling the psychiatric illness. If a woman is planning pregnancy well in advance and she uses a newer, less-studied psychiatric medication, there is enough time to attempt to switch to a medication that has more safety data, but only if she does not have a history of nonresponse to that medication.

CASE NO. 6. A 30-year-old woman has been using vilazodone for 2 years after experiencing a recurrent episode of severe major depressive disorder. She presents to her obstetrician–gynecologist for a prepregnancy evaluation and counseling. Vilazodone is a newer antidepressant and less is known about its safety profile than some older antidepressants. Therefore, the obstetrician–gynecologist gives the patient the choice of attempting to switch to an older antidepressant with a known safety profile or continuing to take the vilazodone.

UNPLANNED PREGNANCY IN WOMEN WITH MOOD DISORDERS

Although health care providers may have the option of advanced planning for medication use in pregnancy with some patients, that will not match the reality for many patients. Fifty percent of pregnancies are unplanned in the United States (123, 124). Therefore, most practitioners will encounter a patient with unexpected pregnancy who uses psychiatric medication.

The principles outlined for prepregnancy planning (Box 9) also apply in the case of an unplanned pregnancy. Box 10 offers a management approach for unexpected pregnancy in women with mood disorders. The most important principle is to avoid immediate discontinuation of all psychiatric medication. Sudden discontinuation of psychiatric
medication can cause great stress and anxiety for the patient, precipitate withdrawal, and precipitate a relapse of mental illness (125). The best approach is to review the medication list based on the principles for prepregnancy planning. Stopping some medications may minimize the effect on the fetus, but doing so in a controlled and logical fashion is ideal. One common scenario (described in Case No. 7) is for a pregnant woman taking a newer antidepressant to be switched to an older medication that has more evidence for safety during pregnancy. Although this might have been a reasonable approach before pregnancy, in the case of unintended pregnancy this plan would actually increase fetal exposure significantly. The fetus has already been exposed to the newer antidepressant and switching to an older medication would expose the fetus a second time. Furthermore, the likelihood that the illness would relapse while switching is high, thus exposing the fetus to risks associated with maternal mood disorder (third exposure). Also, the second drug may not be effective, necessitating fetal exposure a fourth time to another medication.

CASE NO. 7. A 30-year-old woman has used vilazodone for 2 years after experiencing a recurrent episode of severe major depressive disorder. This patient comes to her obstetrician–gynecologist for a prepregnancy evaluation and counseling; however, her pregnancy test result indicates that she is already pregnant. Vilazodone is a newer antidepressant and less is known about it than some older antidepressants. Because the patient is already pregnant, the fetus has been exposed to an antidepressant. Therefore, the obstetrician–gynecologist recommends continuing the vilazodone. Switching to another medication at this point would expose the fetus not only to the vilazodone and the second antidepressant but to a relapse of maternal mental illness. 

### Box 10. Management Approach for an Unplanned Pregnancy In Women With Mood Disorders

- See the patient or talk to her as soon as possible.
- Do not stop all psychiatric medications immediately; most can be continued.
- If a decision is made to discontinue a medication, taper whenever possible.
- Consider stopping medications that are known to be teratogenic.
- As in prepregnancy planning, try to minimize the number of medications the patient is taking. However, it is important to take the patient’s history into account because exposure to maternal psychiatric illness affects the child.
- If the patient is psychiatrically ill, make a plan that includes treating the illness.
Despite evidence of safety, many patients will decide not to use psychiatric medications during pregnancy, breastfeeding, or both. Many women may feel guilty if they take any medication during pregnancy, and most women underestimate the risks of untreated mood disorder during pregnancy. Also, many women are pressured by significant others, friends, or family members, and even other health care providers to discontinue medication during pregnancy and breastfeeding. Using a team approach often will help avoid disagreements, and providing information regarding the risks of untreated mood disorder during pregnancy also can be helpful. In addition to talking directly to relatives and other health care providers, it is appropriate to offer close follow-up care, so that any relapse is caught early and treatment is offered. This care should include counseling regarding the risks and benefits of treatment, the risks of untreated psychiatric illness to both the patient and the fetus, as well as signs and symptoms of relapse. The patient and her family must feel comfortable with the treatment used during pregnancy to avoid regret about the decisions later.

If a decision is made to stop a medication, it should be tapered, if at all possible (Box 5). This will eliminate the risk of withdrawal, thus maximizing outcomes for both the woman and the fetus. It is also important to make a plan for treatment if the patient has psychiatric illness. This seems obvious, but many patients and practitioners overlook the fact that the patient may need more treatment, not less, in the excitement of an unplanned pregnancy. As mentioned earlier in this section, exposure to untreated maternal psychiatric illness in the pregnant patient presents risks for the fetus.

Postpartum Mood Disorders

Definitions

There are three types of postpartum mood disorders: 1) postpartum blues, 2) postpartum depression, and 3) postpartum psychosis. Postpartum blues is a relatively common phenomenon occurring in up to 80% of women, generally within a few days of labor and delivery (126). It is usually a self-limited process, resolving over the course of several days. Symptoms include tearfulness, mood lability, and feeling overwhelmed but also can include positive feelings of happiness or elation (126). Postpartum blues generally begin within a few days after labor and delivery and generally last from 2 to 3 days to less than 2 weeks. If such symptoms are lasting for as long as 2 weeks, serious consideration should be given to the diagnosis of postpartum depression. Postpartum blues are thought to be related to the hormonal changes that women experience after giving birth and are generally self-limited with no intervention other than emotional and social support.

Postpartum depression, is less common than postpartum blues, occurring in 10–20% of the general population. According to DSM-5 criteria, it is classified as a major depressive episode and as such, lasts at least 2 weeks (127). The risk of postpartum depression is increased in women with a history of major depressive disorder (128), bipolar disorder (59), or postpartum depression after previous pregnancies (129). Although the etiology
of postpartum depression is not known, it is likely to be multifactorial with psychologic factors; biologic factors, including hormonal changes; and social factors all playing a role.

Postpartum psychosis is a rare phenomenon, occurring in approximately 0.1% of all births (130). It is common in women with bipolar I disorder, occurring in up to 30% of those who have children (131). Postpartum psychosis is considered a psychiatric emergency and resembles a manic or mixed episode with decreased sleep, psychosis, and agitation. Any woman with suspected postpartum psychosis should seek emergency treatment and will almost always require hospitalization.

**Effects of Postpartum Psychiatric Illness on Children**

Postpartum depression has been shown to have deleterious consequences for infants and children, although the effects of exposure to recurrent depression on child development are a confounding factor (132). Impaired bonding during this critical time has been linked to attachment insecurity in the child (133). Other studies showed impaired emotional development, language development, attention, and cognitive skills. Offspring of women with depression also are more likely to develop long-term behavioral problems. Postpartum depression has been associated with significantly increased rates of infantile colic and impaired maternal–infant bonding (134). Postpartum depression is associated with impaired parenting behavior, such as decreased rates of infant safety and healthy child development practices (135), and increased use of harsh discipline practices (136).

Postpartum psychosis is rare, and few studies have been conducted of the specific effects of postpartum psychosis on children. However, given the severity of the illness, which often results in hospitalization for the woman, one can assume similar outcomes for children as with postpartum depression.

Exposure of the child to postpartum depression or postpartum psychosis should be considered a risk of exposure in the same way as breastfeeding while taking an antidepressant presents a risk of exposure for an infant. To date, the risks of exposure to postpartum depression appear to outweigh at least the short-term risks of exposure to antidepressants during breastfeeding, although additional, particularly long-term, studies need to be completed to firmly support this statement. Identification, treatment, and prevention of postpartum depression and postpartum psychosis are of paramount importance for the wellbeing of the infants as well as the women.

**Diagnosis of Postpartum Depression Versus Postpartum Blues**

Postpartum depression meets *DSM-5* criteria for a major depressive episode (1), including the requirement that symptoms be present for at least 2 weeks. In some cases, a woman presents with symptoms that do not meet this criterion (ie, the symptoms have been present for less than 2 weeks), and it is unclear if she is experiencing postpartum...
blues or if she is early in the course of a postpartum depression and needs to be treated. Clinical clues of postpartum depression versus postpartum blues are described in Box 11. If it remains unclear if the woman has postpartum blues or postpartum depression, watchful waiting may be in order. The clinician should discuss signs and symptoms of postpartum depression with the patient and her family and should monitor the patient closely to initiate treatment if the symptoms worsen or continue.

**Box 11. Differential Diagnosis of Postpartum Depression Versus Baby Blues**

A woman is likely to have postpartum depression rather than baby blues if the following clinical clues are present:

- **The woman has a history of a mood disorder or previous postpartum mood episodes.** This is especially true if the woman is currently not taking psychiatric medications.

- **The symptoms of postpartum depression are severe, unusual, or debilitating.** Baby blues are usually mild and transient, not severe and disabling. A woman may be tearful or emotional with baby blues, but she is generally able to function and care for the infant. Symptoms of psychomotor retardation, psychosis, or suicidal ideation should prompt treatment because they may indicate more severe postpartum mood disorders. Unusual symptoms, such as obsessions or compulsions, also require treatment.

- **The symptoms of postpartum depression are lasting longer than is typical for baby blues.** Most episodes of baby blues last 1–3 days. Symptoms that are lasting longer than 1 week (but are not quite meeting the 2-week criteria for a major depressive episode) may indicate a postpartum depression.

### Screening for Postpartum Psychosis

Symptoms of postpartum psychosis, like general psychosis often can be elicited by inference from the patient’s behavior, statements, or both. Box 12 lists general questions to ask patients to screen for psychosis. Patients with psychotic symptoms often, but not always, appear disorganized, have speech that does not flow logically, and appear distracted. Many patients with psychosis volunteer their symptoms simply by being asked what is happening to them. Initial questioning can begin by asking the patient to explain any odd behavior or statements and the clinician can then proceed to ask specific questions, such as “Are you hearing voices?”
CASE NO. 8. A 24-year-old woman with no prior psychiatric history who gave birth to her first child 2 days ago is recovering from a cesarean delivery in the hospital. Although she slept briefly the first night after the delivery, it was noted by staff that she stayed awake the second night. The next morning, she was found to be pacing her room, holding the baby distractedly, and talking to herself. When asked if she was hearing voices or if anything unusual was happening, the patient replied that she was hearing the voice of God telling her that her newborn was an angel. A psychiatrist was consulted and the patient was transferred to psychiatry for further care.

MEDICATION TRIALS IN THE PREVENTION AND TREATMENT OF POSTPARTUM DEPRESSION

Few randomized trials have examined the prevention and treatment of postpartum depression in women. Two placebo-controlled trials on the prevention of recurrent postpartum depression have been conducted, one using nortriptyline in 26 participants (137) and the other using sertraline in 14 participants, all with histories of postpartum depression (138). Nortriptyline failed to decrease the rate of postpartum depression whereas sertraline was successful, although the study of nortriptyline may have been underpowered. In a randomized trial of treatment of current postpartum depression, no difference between sertraline and nortriptyline was observed. However, the response to sertraline was significant within the first week of treatment, whereas the response to nortriptyline was not significant until the second week (139), suggesting that in women who responded to sertraline, the onset of action was more rapid. Although a 1-week difference is small, these observations suggest that postpartum depression may respond more rapidly to SSRIs that to tricyclic antidepressants, although further studies need to be performed. A double-blind study of fluoxetine versus placebo in combination with
one or six sessions of counseling for the treatment of new onset postpartum depression showed that significantly more women using fluoxetine improved compared with those who used placebo (140). There was no significant interaction with therapy. A number of open-label studies have supported the use of various antidepressants to treat postpartum depression, including sertraline (141), venlafaxine (142), and fluvoxamine (143).

Studies of nonantidepressant medications for the prevention or treatment of postpartum depression are limited. A randomized, double-blind trial of thyroxine in the prevention of postpartum depression in thyroid antibody-positive participants showed no effect of thyroxine (144). An open-label study of omega-3 fatty acids in the treatment of women with perinatal depression showed a significant response rate (145); however, a later randomized trial using omega-3 fatty acids in addition to psychotherapy did not show increased benefit over psychotherapy alone (146).

**Estrogen Treatment in Patients With Postpartum Mood Disorders**

Postpartum depression occurs in the setting of a dramatic decrease in circulating levels of estradiol and progesterone. Although depression risk is not predicted by serum levels of gonadal hormones in humans, rapid withdrawal from these hormones may be a key factor in triggering postpartum depression (147, 148). One study demonstrated that women with a history of postpartum depression developed mood symptoms in response to blinded withdrawal from supraphysiologic doses of estrogen and progesterone, whereas women without a history of postpartum depression did not (148). Several small studies have provided limited support for the idea that estrogen treatment in the postpartum period may be therapeutic for patients with postpartum depression and postpartum psychosis, although most were not randomized or controlled and some of the participants also were given antidepressants. A long-awaited pilot randomized trial studied the use of transdermal estrogen, sertraline, or placebo in the postpartum setting. However, the study was stopped after it was found that serum estrogen concentrations were lower than expected and that transdermal estrogen doses greater than 100 micrograms per day did not increase serum concentrations (149). The mean serum estrogen concentration was nonsignificantly higher in those participants who responded compared with those who did not respond to therapy. These results leave open the question of whether or not estrogen treatment for postpartum depression is a viable option. The potential medical complications of using estrogen from the thromboembolic standpoint limit the clinical usefulness of these trials (150).

**A Practical Approach to the Treatment of Postpartum Depression and Postpartum Psychosis**

It can be assumed that the treatment of postpartum depression is similar to the treatment of nonreproductive-related major depressive disorder, although additional studies should be performed. Similarly, the treatment of postpartum psychosis is similar to the treatment of a bipolar manic or mixed episode. It is important to emphasize that
the treatment of postpartum psychosis has more in common with the management of bipolar disorder than with management of primary psychotic disorders; it is an affective (mood) illness, despite its name. The treatment and prevention of postpartum depression and postpartum psychosis should be dictated by the patient’s previous history of response to medications. Additional issues to be considered include breastfeeding and previous medication use during pregnancy. In patients with postpartum depression, the use of SSRIs should be considered first unless the patient has a history of nonresponse to SSRIs, given the current evidence of a possible advantage of SSRIs over tricyclic antidepressants. Similar to treatment during pregnancy, the goal is to minimize exposure for the infant. Thus, if a woman is already taking an antidepressant medication and has relapsed, the current antidepressant regimen should be maximized rather than switching to another because the infant has already been exposed to that medication. Ideally, only one or as few medications as possible should be used, and the guidelines for treatment during pregnancy should be followed (Box 9).

Postpartum psychosis is considered a psychiatric emergency and patients with postpartum psychosis should be immediately hospitalized. Postpartum psychosis should prompt a medical evaluation. Patients generally respond to lithium, antipsychotic treatments, or both (151).

Guidelines for First Episode of Postpartum Depression

If a patient with postpartum depression has no previous psychiatric history, it is important to educate the patient about major depressive disorder, postpartum depression, bipolar disorder, and suicidal thoughts. Because the patient has never been psychiatrically ill before, it is important that she understand her illness. Women without a previous history of mood disorder presenting with a new onset postpartum depression also should be educated about the signs and symptoms of hypomania or mania because antidepressant treatment may trigger the onset of such symptoms. However, it is a rare phenomenon, occurring in approximately 8% of cases (152). Women with a family history of bipolar disorder also should be monitored closely for the development of hypomanic or manic symptoms and appropriate treatment with mood stabilizers instituted, if such symptoms emerge. Because antidepressant treatment can trigger suicidal thoughts, women should be counseled about these thoughts and instructed to call their health care providers if they develop such thoughts. It is also vitally important to inquire about (but not morally condemn) thoughts about harming the child. Some practitioners shy away from directly asking about such thoughts because they are uncomfortable. Many women with postpartum mood disorders have such thoughts—ranging from intrusive obsessive-type thoughts of harm coming to the infant (eg, What if the baby fell? What if I put dishwashing detergent in the formula?) to thoughts of actively harming the baby. In such a case, it is important to determine intent and the need for safety intervention (Box 13). The woman may be ashamed of having them, and receiving the information that such thoughts are common in postpartum depression can help relieve some of her angst.
The patient must be monitored closely, psychiatric evaluation should be arranged as soon as possible, or both. The monitoring and referral are crucial in case the patient develops adverse effects, such as GI distress, anxiety, and insomnia; suicidal thoughts; or thoughts of harming the infant; and in case hypomanic or manic symptoms emerge.

**General Recommendations for Breastfeeding**

The benefits of breastfeeding for the infant are well documented. Currently, the American Academy of Pediatrics advocates breastfeeding through the first 6 months of life (153). All psychotropic medications pass readily into breast milk, and it is not reasonable to switch a medication from one that the infant was exposed to in utero to another for breastfeeding, except in the following cases:

- The mother’s psychiatric illness relapsed and the current psychiatric medication regimen is not effective
- The mother is on a medication that has a risk of severe adverse effects with continued exposure for the infant (for example, an antipsychotic drug clozapine)
- The infant develops an adverse reaction or medical complications related to the medication exposure during breastfeeding

If the medication regimen needs to be changed during breastfeeding, the patient, her family, and her health care providers should consider whether continued breastfeeding outweighs the risks of increasing the infant’s exposure to medications.

It is important to involve the pediatrician in the decision-making process. Infants should be monitored for potential adverse effects. If the exposure to a particular medication can be monitored through blood level measurements, then a plan for an appropriate blood workup in the infant should be established. A common adverse effect for many psychiatric medications is sedation, and the infant should be monitored for excessive sleepiness and decreased appetite, particularly during the feeding after the mother takes the medication. If the infant is exposed to an antipsychotic medication, the infant should be monitored for stiffness, cogwheeling, and extrapyramidal adverse effects, although these are uncommon. Many infants are fussy and colicky or have feeding difficulties without exposure to medications during breastfeeding; therefore, at times it can be difficult to distinguish between an infant affected by medication adverse effects and simply a fussy infant. When in doubt, the wisest choice is to do what makes the parents comfortable.

**Perimenopausal Concerns**

**Perimenopausal Mood Instability**

*Perimenopausal mood instability* is defined as mood symptoms, including irritability, low mood, tearfulness, decreased energy, and poor concentration, which intermittently occur during perimenopause and which do not meet criteria for a major mood disorder, such as major depressive disorder (as in Case No. 1). The prevalence of these symptoms is approximately 40% of the general population (154); however, studies that have examined this issue are few. Many women report that mood instability, similar in quality to PMS but not necessarily tied to the menstrual cycle, occurs around the time of menopause. Perimenopause can last for years; thus, these symptoms can recur intermittently for years and generally were treated with homeopathic remedies in the past. The hallmark of perimenopausal mood instability is that the mood returns to normal between episodes of irritability, and the criteria for a major depressive episode, such as length of time, severity, or effect on functioning, are not met. One study suggests that these symptoms may be due to hormonal fluctuations that occur during perimenopause (155). Perimenopausal mood instability often can be improved with the nonpharmacologic remedies or lifestyle changes detailed in Box 7 but may at times need pharmacologic intervention.
CASE NO. 9. A 47-year-old woman with no psychiatric history reports hot flushes, interrupted sleep, fatigue, and mood swings for the past year. The mood lability has sometimes caused the patient to argue with her husband, but her work and personal life are otherwise unaffected. She describes her mood as good and denies anhedonia.

This woman has reproductive mood symptoms that do not impair functioning, and the patient’s mood does not appear to be impaired outside of hormonally triggered mood swings. Therefore, the clinician reassured the patient that her symptoms were consistent with the menopausal transition and counseled her on healthy lifestyle changes that might be helpful (Box 7).

PERIMENOPAUSAL DEPRESSION

In addition to perimenopausal mood instability, women also can experience major depressive episodes during perimenopause. The American College of Obstetricians and Gynecologists defines perimenopause as “a time span that begins with the onset of intermenstrual cycle irregularities (+/- 7 days) and/or other menopause related symptoms and extends through menopause [the final menstrual period] to 1 year after menopause” (156). Other criteria have been used, including those developed by the Stages of Reproductive Aging Workshop (157), which define menopause as 1 year of amenorrhea and perimenopause as the period leading up to menopause that is characterized by menstrual cycle irregularities. Most longitudinal studies agree that the risk of depression during the menopause transition is increased, with statistically significant ORs ranging from 1.33 to 1.79 in both women with a history of major depressive disorder and those without a history of major depressive disorder (158). Overall, the rate of major depressive disorder increases two- to threefold during perimenopause and the early postmenopausal period as defined by the Stages of Reproductive Aging Workshop criteria (158). First-line treatment for depression and anxiety in the menopausal transition remains the same as that for depression at other times, ie, antidepressants (although estrogen supplementation also can be helpful). Only antidepressants that affect serotonin have been officially studied for perimenopausal depression. The few studies that have examined antidepressants as monotherapy have found them to be effective, but small numbers and inconsistent definitions of perimenopause mean that additional research is needed (159).

CASE NO. 10. A 49-year-old woman presents for her well-woman examination and reports feeling overwhelmed and having difficulty sleeping and tearful episodes. Over the past year, her menstrual periods have become unpredictable and she’s developed hot flushes, during which she wakes up with heart palpitations. During these episodes, she becomes extremely anxious and upset and has thoughts that she is dying. The week before the office visit, she had a similar experience while shopping in a grocery store and had to leave the store without her groceries.

This patient’s medical history, signs, and symptoms indicate menopause and an increased suspicion of a perimenopausal mood disorder. Her obstetrician–gynecologist administers the Hospital Anxiety and Depression Scale and the patient receives a score of 15 points. The patient receives the diagnoses of both major depressive disorder and panic disorder, is started on an SSRI, and referred to psychiatry. ☰
**Estrogen**

A number of studies have demonstrated that menopausal estrogen therapy is effective for perimenopausal depression but not for depression in postmenopausal women (160). In studies of perimenopausal women, estradiol (at 50–100 micrograms per day) improved depressive symptoms when administered as monotherapy (161, 162) and in combination with antidepressants when hormone therapy alone was only partially effective (163–165). In contrast, a randomized placebo-controlled trial of estrogen (100 micrograms per day) in older postmenopausal women with depressive disorders but no vasomotor symptoms demonstrated no improvement in mood symptoms (166). Furthermore, results from the Heart and Estrogen/Progestin Replacement Study trial of postmenopausal hormone therapy showed that combination therapy (0.625 mg/d of estrogen plus 2.5 mg/d of progestin) improved depression symptoms in postmenopausal women only if they were experiencing vasomotor symptoms (167). It remains unclear if the result in the Heart and Estrogen/Progestin Replacement Study is due to the use of combination of estrogen and progestin or if the presence of vasomotor symptoms contributes to depressive symptoms in this population, thus allowing for improvement when vasomotor symptoms are decreased. Regardless, available data suggest that estrogen treatment during perimenopause, a time of hormonal fluctuation, may be helpful in treating depressive symptoms. In contrast, in postmenopausal women, estrogen therapy alone does not appear to improve depression unless vasomotor symptoms are present (160).

**Anxiety and Related Disorders During Perimenopause**

The evidence concerning anxiety in the perimenopausal period is sparse and mixed. As with the perinatal period, most research focuses on depression. Although the bulk of the evidence, including several national studies (Study of Women's Health Across the Nation, Penn Ovarian Aging Study, and others), indicates a relationship between mental distress and the perimenopause, some research has questioned whether there is an increase in symptoms (168). Several studies have indicated that individual differences in the reporting of symptoms (both physical and psychologic) may be related to differences in trait anxiety and anxiety sensitivity (the tendency to react to anxiety symptoms with fear) (169–171). Although no studies have focused on individual anxiety disorders in the perimenopausal period, several studies have indicated that women report increased anxiety symptoms during the menopausal transition, with 51% of women in one study reporting nervousness or irritability (172) and 23% in another study endorsing specific anxiety symptoms (173). The Study of Women's Health Across the Nation, with data from more than 3,000 women, found that those with low baseline anxiety were more likely to report anxiety symptoms in the perimenopause (ie, the menstrual irregularity over the past 12 months) than premenopause (ie, regular menstrual periods over the past 12 months) (174).

Clinical features of anxiety in the perimenopause can be similar to those at other times, including generalized anxiety symptoms, such as stress, fatigue, GI problems, and headache. Also, they may mimic the physical symptoms of medical illnesses that are
increasingly common as women age (eg, shortness of breath, racing heart, and sweating) or may be confused with vasomotor symptoms (175) (see Case No. 10). As a result, many women may not recognize their symptoms as anxiety.

As with anxiety during the perinatal period, research into the biologic causal factors is limited; some but not all studies have found a relationship between estradiol fluctuation and mood, but most have not studied the relationship of estradiol and anxiety. Newer research has proposed that alterations in the hypothalamic–pituitary–adrenal axis may induce a prolonged stress response, that vascular changes and neurodegeneration may contribute to anxiety, and that cognitive decline also may play a role (158, 176, 177).

Psychosocial risk factors are abundant in this period. Generally, the menopausal transition is a time of change in women’s lives—children are leaving home, many women are making career transitions, marital relationships may be in flux, parents are aging or dying, physical health needs may be changing, and the physical symptoms of menopause (especially hot flushes) may exacerbate anxiety and mood disorders. Psychotherapy, including cognitive–behavioral therapy, interpersonal therapy, and stress reduction approaches, can be especially helpful to address these psychosocial factors.

**Psychiatric Medication Guidelines in Specific Settings**

**Contraception and Psychiatric Drug Interactions**

A number of potential drug interactions exist between OCPs and various psychiatric medications. Some psychiatric medications can affect the efficacy of OCPs. In turn, OCPs can affect the efficacy or potency of some psychiatric medications. Table 6 lists these interactions.

**Contraception and Psychiatric Illness**

Hormonal methods of contraception, including OCPs, patches, intrauterine devices, and medroxyprogesterone acetate injections, may exacerbate symptoms of depression, anxiety, or both, although the exact relationship is unclear (178). One study found no increased risk of depressive episodes in women with major depressive disorder or bipolar disorder who used hormonal contraception (179), but another study found an increased risk of depression associated with the use of various forms of hormonal contraception (180). When prescribing any hormonal method of contraception, obstetrician–gynecologists should mention the possibility of these interactions and instruct patients to return for follow-up if such symptoms occur. Although evidence is lacking, a woman with a history of sensitivity to hormonal interventions may be likely to decompensate with other forms of hormonal contraception. Thus, brief screening for this phenomenon is recommended before prescribing hormonal contraception.
Table 6. Drug Interactions Between Oral Contraceptive Pills and Common Psychiatric Medications

<table>
<thead>
<tr>
<th>Psychiatric Medication</th>
<th>Type of Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
<td></td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td>None</td>
</tr>
<tr>
<td>Serotonin–norepinephrine reuptake inhibitors</td>
<td>None</td>
</tr>
<tr>
<td>Other antidepressants (buproprion, mirtazapine, tradozone, and viladozone)</td>
<td>None</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Increased levels of the tricyclic antidepressant; blood levels should be monitored</td>
</tr>
<tr>
<td>Monoamine oxidase inhibitors</td>
<td>None</td>
</tr>
<tr>
<td><strong>Mood Stabilizers and Antiepileptics</strong></td>
<td></td>
</tr>
<tr>
<td>Lithium</td>
<td>None</td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>Reduced OCP efficacy</td>
</tr>
<tr>
<td>Gabapentin (Neurontin)</td>
<td>None</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>Reduced levels of lamotrigine in the blood; no effect on OCP efficacy</td>
</tr>
<tr>
<td>Oxycarbamazepine (Trileptal)</td>
<td>Reduced OCP efficacy</td>
</tr>
<tr>
<td>Topiramate (Topamax)</td>
<td>Reduced OCP efficacy</td>
</tr>
<tr>
<td>Valproic acid (Depakote)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Antianxiety Medications</strong></td>
<td></td>
</tr>
<tr>
<td>Alprazolam (Xanax)</td>
<td>Increased effect of alprazolam</td>
</tr>
<tr>
<td>Barbituates</td>
<td>Reduced OCP efficacy</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium)</td>
<td>Increased effect of chlordiazepoxide</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>Increased effect of diazepam</td>
</tr>
<tr>
<td>Fluoxetine (Dalmane)</td>
<td>Increased effect of fluoxetine</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>Decreased effect of lorazepam</td>
</tr>
<tr>
<td>Oxazepam (Serax)</td>
<td>Decreased effect of oxazepam</td>
</tr>
<tr>
<td>Temazepam (Restoril)</td>
<td>Decreased effect of temazepam</td>
</tr>
<tr>
<td>Triazolam (Halcion)</td>
<td>Increased effect of triazolam</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
</tr>
<tr>
<td>Clozapine (Clozaril)</td>
<td>Increased blood level (and adverse effects) of clozapine</td>
</tr>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>Increased blood level (and adverse effects) of chlorpromazine</td>
</tr>
<tr>
<td>Other typical and atypical antipsychotics</td>
<td>None</td>
</tr>
<tr>
<td><strong>Biologically Based Therapies</strong></td>
<td></td>
</tr>
<tr>
<td>Melatonin</td>
<td>Increased effect of melatonin</td>
</tr>
<tr>
<td>Phytoestrogens and soy</td>
<td>Theoretical increase in adverse effects of OCPs</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Reduced OCP efficacy</td>
</tr>
<tr>
<td>Vitex agnus castus</td>
<td>Reduced OCP efficacy</td>
</tr>
</tbody>
</table>

Abbreviation: OCP indicates oral contraceptive pill.
Tamoxifen and Psychiatric Drug Interactions

A number of potential drug interactions exist between tamoxifen and some psychiatric medications, primarily decreasing the effectiveness of tamoxifen or prolonging the QTc. Table 7 provides a full listing of these interactions. Tamoxifen is converted to endoxifen by the liver enzyme CYP2D6. Patients with estrogen receptor-positive breast cancer who are homozygous for the poor metabolizer CFYP2D6 genotype are more likely to experience a recurrence of cancer than those who carry an allele for the active enzyme. Many antidepressants inhibit CYP2D6 and, therefore, could affect cancer outcomes (181). Generally, when prescribing an antidepressant to a woman who uses tamoxifen, the following antidepressants should be considered because they do not inhibit CYP2D6: venlafaxine, desvenlafaxine, fluvoxamine, escitalopram, and mirtazapine. Strong CYP2D6 inhibitors that should be avoided in the setting of tamoxifen include paroxetine, fluoxetine, duloxetine, and bupropion.

Table 7. Drug Interactions Between Tamoxifen and Common Psychiatric Medications

<table>
<thead>
<tr>
<th>Psychiatric Medication</th>
<th>Type of Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selective Serotonin Reuptake Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Citalopram (Celexa)</td>
<td>None</td>
</tr>
<tr>
<td>Escitalopram (Lexapro)</td>
<td>None</td>
</tr>
<tr>
<td>Fluoxetine (Prozac, Prozac Weekly, Selfemra, and Sarafem)</td>
<td>Decreased tamoxifen activity</td>
</tr>
<tr>
<td>Fluvoxamine (Faverin, Luvox, and Luvox CR)</td>
<td>None</td>
</tr>
<tr>
<td>Paroxetine (Paxil, Paxil CR, and Pexeva)</td>
<td>Decreased tamoxifen activity</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>Decreased tamoxifen activity</td>
</tr>
<tr>
<td><strong>Serotonin–Norepinephrine Reuptake Inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>None</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>Decreased tamoxifen activity</td>
</tr>
<tr>
<td>Venlafaxine (Effexor)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Other Antidepressants</strong></td>
<td></td>
</tr>
<tr>
<td>Buproprion (Wellbutrin)</td>
<td>Decreased tamoxifen activity</td>
</tr>
<tr>
<td>Buspirone (Buspar)</td>
<td>None</td>
</tr>
<tr>
<td>Mirtazapine (Remeron)</td>
<td>None</td>
</tr>
<tr>
<td>Trazodone (Desyrel)</td>
<td>Moderate risk of prolonged QTc</td>
</tr>
<tr>
<td>Viibryd (Vilazodone)</td>
<td>Tamoxifen may increase vilazodone levels</td>
</tr>
<tr>
<td>Vortioxetine (Brintellix)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Tricyclic Antidepressants</strong></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>Moderate risk of prolonged QTc</td>
</tr>
<tr>
<td><strong>Monoamine Oxidase Inhibitors</strong></td>
<td></td>
</tr>
</tbody>
</table>
| All | None | (continued)
Management of Pelvic Pain in the Setting of Depression and Anxiety

The diagnosis and treatment of pelvic pain are beyond the scope of this monograph. However, a number of psychiatric medications are particularly useful in the management of pain, including pelvic pain. Furthermore, mood and anxiety disorders are extremely common in patients presenting with pain, and successful treatment of the psychiatric illness often leads to improved pain control and, therefore, quality of life. Women presenting with pelvic pain should be carefully screened for any psychiatric symptoms, and psychiatric medications that have antidepressant or antianxiety as well as analgesic properties can be used. Classes of psychiatric medications that are typically useful in this setting include SNRIs and tricyclic antidepressants, which affect both serotonin and norepinephrine, as well as antiepileptic medications. Box 14 lists psychiatric medications that are useful for pain conditions.
Referral Guidelines

Many obstetrician–gynecologists are comfortable initiating treatment for uncomplicated mood and anxiety disorders. However, consultation or referral may be necessary in some situations. Box 8 outlines guidelines for referral to psychiatry and Box 15 outlines guidelines for referral to the emergency room.

Box 14. Psychiatric Medications Useful for Pain Management

<table>
<thead>
<tr>
<th>Serotonin–Norepinephrine Reuptake Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Venlafaxine</td>
</tr>
<tr>
<td>• Desvenlafaxine</td>
</tr>
<tr>
<td>• Duloxetine</td>
</tr>
<tr>
<td>Tricyclic Antidepressants</td>
</tr>
<tr>
<td>• Nortriptyline</td>
</tr>
<tr>
<td>• Amitriptyline</td>
</tr>
<tr>
<td>Antiepileptic Medications</td>
</tr>
<tr>
<td>• Carbamazepine</td>
</tr>
<tr>
<td>• Gabapentin</td>
</tr>
<tr>
<td>• Oxcarbamazepine</td>
</tr>
<tr>
<td>• Pregabalin</td>
</tr>
<tr>
<td>• Topiramate</td>
</tr>
<tr>
<td>• Valproic acid</td>
</tr>
</tbody>
</table>

Referral Guidelines

An obstetrician–gynecologist should refer a patient to the emergency department under the following circumstances:

• When a patient has suicidal thoughts or plans and there is a belief she may act on the thoughts or plans
• When a patient has thoughts of hurting someone else, including her infant, and there is a belief she may act on these thoughts
• When psychotic symptoms are present
• When a patient displays disorganized behavior or thoughts
The treatment of mood and anxiety disorders by primary and preventive care providers, including obstetrician–gynecologists, is increasing. The U.S. Preventive Services Task Force now recommends screening for depression in all adults, including pregnant women and those in the postpartum period (182). A number of screening tools can be administered easily in the clinical setting for patients who present with mood and anxiety symptoms (Table 1). Treatment for most cases of mood and anxiety disorders can be undertaken by the obstetrician–gynecologist with appropriate referral of patients with complex conditions or those who do not respond to initial efforts. The reproductive lifecycle can complicate treatment of mental illness in women, but there are many safe treatment options. Also, significant risks are associated with untreated mental illness. Identification and treatment of mood and anxiety disorders is an important skill set for all obstetrician–gynecologists in their efforts to improve the health of women.

The most poignant points in the management of obstetric–gynecologic patients with mood and anxiety symptoms include the following:

• Patients presenting with symptoms consistent with a major depressive episode may have either major depressive disorder or bipolar disorder.

• Screening for bipolar disorder includes asking about a family and personal history of hypomanic or manic episodes.

• The literature on the safety of psychiatric medication use during pregnancy is complicated by poor control of confounding risks and behavior associated with the population of women with psychiatric illness.

• There are many psychiatric medications that can be used safely during pregnancy.

• Untreated psychiatric illness during pregnancy is associated with poor outcomes for the woman and the infant.

• Hormonal fluctuations associated with the premenstrual, postpartum, and perimenopausal periods are associated with changes in mood that may be limited to the period of hormonal fluctuations or may be indicative of an untreated or under-treated mood disorder.
Resources

Resources From the American College of Obstetricians and Gynecologists


The following list is for information purposes only. Referral to these sources and websites does not imply the endorsement of the American College of Obstetricians and Gynecologists. This list is not meant to be comprehensive. The exclusion of a source or website does not reflect the quality of that source or website. Please note that websites are subject to change without notice.

Resources From Other Agencies and Organizations

American Foundation for Suicide Prevention
120 Wall Street, 29th Floor
New York, NY 10005
Telephone: 212-363-3500 or 888-333-2377
Web: www.afsp.org

American Psychiatric Association
1000 Wilson Blvd, Suite 1825
Arlington, VA 22209-3901
Telephone: 888-357-7924
Web: www.psychiatry.org

American Psychological Association
750 First Street, NE
Washington, DC 20002-4242
Telephone: 202-336-5500 or 800-374-2721
Web: www.apa.org

National Alliance of Mental Illness
3803 N. Fairfax Drive, Suite 100
Arlington, VA 22203
Telephone: 703-524-7600 or 800-950-6264 (helpline)
Web: www.nami.org

National Institute of Mental Health
6001 Executive Boulevard
Room 6200, MSC 9663
Bethesda, MD 20892-9663
Telephone: 301 443-4843 or 866-615-6464
Web: www.nimh.nih.gov

(continued)
Resources (continued)

Resources From Other Agencies and Organizations (continued)

North American Society for Psychosocial Obstetrics and Gynecology
8213 Lakenheath Way
Potomac, MD 20854
Telephone: 301-983-6282
Web: www.naspog.org

Postpartum Support International
6706 SW 54th Ave
Portland, OR 97219
Telephone: 503-894-9453 or 800-944-4773
Web: www.postpartum.net

Websites

For general information about women’s mental health:
MGH Center for Women’s Mental Health
Reproductive Psychiatry Resource and Information Center
womensmentalhealth.org/?doing_wp_cron=1469720382.9335598945617675781250

For treatment guidelines and provider toolkit for perinatal mental health:
Massachusetts Child Psychiatry Access Program for Moms: promoting maternal mental health during and after pregnancy
www.mcpapformoms.org

For clinical information about medications in pregnancy:
ReproTox (subscription service)
reprotox.org

For clinical information about medications in breastfeeding:
National Library of Medicine
Drugs and lactation database: LactMed: a toxnet database
toxnet.nlm.nih.gov/newtoxnet/lactmed.htm

For evidence-based, patient-friendly fact sheets and information:
MotherToBaby: medications and more during pregnancy and breastfeeding: ask the experts
A service of the Organization of Teratology Information Specialists
mothertobaby.org

Healthy New Moms: Maryland’s Maternal Mental Health Campaign
Mental Health Association of Maryland
healthynewmoms.org

Eunice Kennedy Shriver National Institute of Child Health and Human Development
Mom’s Mental Health Matters: Depression and Anxiety Around Pregnancy
National Child and Maternal Health Education Program
Complete the answer sheet at www.clinicalupdates.org under “Test Your Clinical Skills” and receive 5 continuing medical education credits. He answers appear on page 74.

Directions: Select the one best answer or completion.

1. The genetic involvement in bipolar disorder is
   A. 10%
   B. 30%
   C. 50%
   D. 70%

2. In which stage of life is the risk of major depressive disorder for women twice that for men?
   A. Before adolescence
   B. During adolescence
   C. During reproductive years
   D. During menopause

3. The best method to determine if hypomania exists is
   A. diagnosis by primary care physician
   B. diagnosis by psychiatrist
   C. history from a family member
   D. history from the patient

4. The ethnic group in the United States with the highest rate of social anxiety disorder is
   A. African American
   B. American Indian
   C. Caucasian
   D. Asian American

5. Which of the following comorbidities is most often seen in individuals with obsessive–compulsive disorder?
   A. Anxiety disorder
   B. Eating disorder
   C. Mood disorder
   D. Tic disorder

6. What group of antidepressants is also effective in pain management?
   A. Monoamine oxidase inhibitors
   B. Serotonin–norepinephrine reuptake inhibitors
   C. Selective serotonin reuptake inhibitors
   D. Tricyclic antidepressants

7. The therapeutic range for antidepressants is highest in patients with which disorder?
   A. Bipolar disorder
   B. Generalized anxiety disorder
   C. Major depressive disorder
   D. Obsessive–compulsive disorder
8. The minimum response time of selective serotonin reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors used to treat premenstrual dysphoric disorder is
   A. 1 week
   B. 2 weeks
   C. 4 weeks
   D. 8 weeks

9. What percentage of pregnant women report pregnancy-specific anxiety?
   A. 4%
   B. 11%
   C. 14%
   D. 27%

10. Which of the following psychiatric medications is most important to discontinue before pregnancy?
    A. Fluoxetine
    B. Sertraline
    C. Valproic acid
    D. Vilazodone

11. A patient comes in for prenatal care at 11 weeks of gestation. The pregnancy was unintended and she has been taking a newer antidepressant for 1 year. According to the authors, the patient should be advised to
    A. continue the drug
    B. discontinue the drug immediately
    C. switch to an older selective serotonin reuptake inhibitor
    D. withdraw the drug slowly

12. The minimum duration of symptoms required to diagnose postpartum depression is
    A. 1 week after delivery
    B. 2 weeks after delivery
    C. 4 weeks after delivery
    D. 8 weeks after delivery

13. Menopausal estrogen therapy is of value
    A. in all women
    B. in perimenopausal women only if vasomotor symptoms are present
    C. in postmenopausal women only if vasomotor symptoms are present
    D. in no cases

14. Which of the following antidepressants is safest to prescribe to a patient who takes tamoxifen?
    A. Bupropion
    B. Escitalopram
    C. Fluoxetine
    D. Paroxetine


5. Hasler G. Pathophysiology of depression: do we have any solid evidence of interest to clinicians? World Psychiatry 2010;9:155–61. (Level III)


44. Dennis C, Dowswell T. Interventions (other than pharmacological, psychosocial or psychological) for treating antenatal depression. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD006795. (Systematic review)


68 Mood and Anxiety Disorders


54. Berlin RK, Butler PM, Perloff MD. Gabapentin therapy in psychiatric disorders: a systematic review. Prim Care Companion CNS Disord 2015;17. (Systematic review)


68. Jermain DM, Preece CK, Sykes RL, Kuehl TJ, Sulak PJ. Luteal phase sertraline treatment for premenstrual dysphoric disorder. Results of a double-blind, placebo-controlled, crossover study. Arch Fam Med 1999;8:328–32. (Level I)


79. Halbreich U, O’Brien PM, Eriksson E, Backstrom T, Yonkers KA, Freeman EW. Are there differential symptom profiles that improve in response to different pharmacological treatments of premenstrual syndrome/premenstrual dysphoric disorder? *CNS Drugs* 2006;20:523–47. (Level III) ✧


104. Field T, Diego M, Hernandez-Reif M. Prenatal depression effects and interventions: a review. Infant Behav Dev 2010;33:409–18. (Level III)  


175. Siegel AM, Mathews SB. Diagnosis and treatment of anxiety in the aging woman. *Curr Psychiatry Rep 2015;17:93,015-0636-3.* (Level III) 


Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I Evidence obtained from at least one properly designed randomized controlled trial.

II-1 Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Answers

Forthcoming and Current Titles

Each monograph in *Clinical Updates in Women’s Health Care* is an overview of a topic of importance to obstetrician–gynecologists in practice. Upcoming titles include the following:

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- Arthritis

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- Liver Disease: Reproductive Considerations (Volume XVI, No. 1, January 2017)
- Structural Heart Disease (Volume XVI, No. 2, March 2017)
- Arrhythmias (Volume XVI, No. 3, May 2017)
- Gynecologic and Obstetric Care for Breast Cancer Survivors (Volume XIV, No. 4, July 2017)

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- Anorectal Disorders (May 2015)
- Care of Aging Women (April 2015)
- Complementary and Alternative Medicine (June 2015)
- Dermatoses (April 2015)
- Eating Disorders (February 2015)
- Elder Abuse (January 2015)
- Lower Urinary Tract Disorders (May 2014)
- Multiple Sclerosis (January 2013)
- Obesity (October 2013)
- Occupational Diseases and Injuries (July 2016)
- Sleep Disorders (September 2015)
- Upper Gastrointestinal Tract, Biliary, and Pancreatic Disorders (June 2017)
- Vision Disorders (March 2015)
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Liver Disease: Reproductive Considerations (Vol. XVI, No. 1, January 2017)
Structural Heart Disease (Volume XVI, No. 2, March 2017)
Arrhythmias (Volume XVI, No. 3, May 2017)
Gynecologic and Obstetric Care for Breast Cancer Survivors (Volume XIV, No. 4, July 2017)

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Hypertension (Vol. XV, No. 1, January 2016)
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Liver Disease: General Pathophysiology, Diagnosis, and Management Supplement (Vol. XV, No. 6, November 2016)

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Metabolic Bone Disease (Vol. XIV, No. 2, April 2015)
Benign Breast Disease (Vol. XIV, No. 3, July 2015)
Hormone Therapy and Alternative Therapies for Menopause (Vol. XIV, No. 4, October 2015)
Lower Gastrointestinal Tract Disorders (Vol. XIV, No. 5, November 2015)

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Sexuality and Sexual Disorders (Vol. XIII, No. 2, April 2014)
Nutrition (Vol. XIII, No. 3, July 2014)
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Memory Loss and Dementia (Vol. XIII, No. 5, November 2014)

2013
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Addiction and Substance Abuse (Vol. XI, No. 1, January 2012)
Sleep Disorders (Vol. XI, No. 3, July 2012)
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Anorectal Disorders Supplement (Vol. IX, No. 1, January 2010)
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2007
Dermatoses (Vol. VI, No. 3, July 2007)

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