



## DEPRESSION

Mood disorders are emotional disturbances consisting of prolonged periods of excessive sadness, excessive joyousness, or both. Mood disorders are categorized as depressive or bipolar. Anxiety and related disorders also affect mood.

Sadness and joy (elation) are part of everyday life. Sadness is a universal response to defeat, disappointment, and other discouraging situations. Joy is a universal response to success, achievement, and other encouraging situations. Grief, a form of sadness, is considered a normal emotional response to a loss. Bereavement refers specifically to the emotional response to death of a loved one.

A mood disorder is diagnosed when sadness or elation is overly intense, continues longer than expected for a causative event, or occurs without cause; function must also be impaired. In such cases, intense sadness is termed depression, and intense elation is termed mania. Depressive disorders are characterized by depression; bipolar disorders are characterized by varying combinations of depression and mania. However, certain features of depressive and bipolar disorders can overlap, especially when they first occur.

Lifetime risk of suicide for people with a depressive disorder is 2 to 15%, depending on severity of the disorder. Risk is highest initially after hospital discharge, when treatment has been initiated and psychomotor activity is returning to normal but mood is still dark; risk remains high for 1 yr after discharge. Risk is also increased during mixed bipolar states, the premenstrual state, and personally significant anniversaries. Alcohol and substance use increases risk.

Other complications include disability ranging from mild to complete inability to function, maintain social interaction, and participate in routine activities; impaired food intake; and alcoholism and other drug dependencies.

### **Bipolar disorders**

Bipolar disorders are characterized by mania and depression, which usually alternate. Exact cause is unknown, but heredity, changes in the level of brain neurotransmitters, and psychosocial factors may be involved. Diagnosis is based on history. Treatment consists of drugs, sometimes with psychotherapy.

Bipolar disorders usually begin in the teens, 20s, or 30s. Lifetime prevalence is about 1%. Rates are about equal for men and women.

Bipolar disorders are classified partly based on long-term patterns of episodes of more intense symptoms as bipolar I disorder, bipolar II disorder, or bipolar disorder not otherwise specified (NOS). Forms associated with a disorder or drug use are classified as bipolar disorder due to their general physical condition or substance-induced bipolar disorder.

### ***Etiology***

Exact cause is unknown. Heredity plays some role. There is also evidence of dysregulation of serotonin and norepinephrine. Psychosocial factors may also be involved. Stressful life events are often associated with initial development of symptoms and later exacerbations, although cause and effect have not been established.



Bipolar disorders or symptoms of bipolar disorders can occur with several physical disorders, as adverse effects of many drugs, or as part of several other mental disorders.

### *Symptoms and Signs*

Bipolar disorder begins with an acute phase of symptoms and is followed by a repeating course of relapse and remission. Relapses are episodes marked by more intense symptoms, lasting about 3 to 6 mo. Episodes are manic, depressive, hypomanic, or a mixture (of depressive and manic features). Cycles—time from onset of one episode to that of the next—vary in length. Cyclicity is particularly accentuated in rapid-cycling forms of bipolar disorder (usually defined as  $\geq 4$  episodes/yr). Disruption of developmental and social functioning is common, especially when onset occurs between ages 13 and 18.

Psychotic symptoms may be present. In full-blown manic psychosis, the mood is usually elation, but irritability and frank hostility with cantankerousness are not uncommon.

**Bipolar I disorder** is defined by alternation of full-fledged manic and major depressive episodes. It commonly begins with depression. Depression can occur immediately before or after mania, or depression and mania can be separated by months or years.

**Bipolar II disorder** is defined by a history of at least one major depressive episode and at least one hypomanic episode. Depressive episodes alternate with hypomania. During the hypomanic period, mood brightens, the need for sleep decreases, and psychomotor activity accelerates. Often, the switch follows circadian factors (eg, going to bed depressed and waking early in the morning in a hypomanic state). Hypersomnia and overeating are characteristic and may recur seasonally (eg, in autumn or winter); insomnia and poor appetite occur during the depressive phase. For some patients, hypomanic periods are adaptive because they produce high energy, confidence, and supernormal social functioning.

**Bipolar disorder NOS** refers to disorders with clear bipolar features that do not meet the specific criteria for other bipolar disorders.

**Mania:** A manic episode is defined as  $\geq 1$  wk of a persistently elevated, expansive, or irritable mood, accompanied by  $\geq 3$  additional symptoms: inflated self-esteem or grandiosity, decreased need for sleep, greater talkativeness than usual, persistent elevation of mood, flight of ideas or racing of thoughts, distractibility, increased goal-directed activity, and excessive involvement in pleasurable activities with a higher risk of undesirable consequences (eg, injury, loss of money). Symptoms impair functioning.

Typically, patients in a manic episode are exuberant and flamboyantly or colorfully dressed; they have an authoritative manner with a rapid, unstoppable flow of speech. Patients make clang associations: New thoughts are triggered by word sounds rather than meaning. Easily distracted, patients may constantly shift from one theme or endeavor to another. However, they tend to believe they are in their best mental state. Lack of insight and an increased capacity for activity often lead to intrusive behavior and can be a dangerous combination. Interpersonal friction results and may lead to paranoid delusions that they are being unjustly treated or persecuted. Accelerated mental activity is experienced as racing thoughts by patients, is observed as flights of ideas by the physician, and, in its extreme form, is difficult to distinguish from the loose associations of schizophrenia. Psychotic symptoms develop in some patients with bipolar I disorder. Need for sleep is decreased. Manic patients are inexhaustibly, excessively, and impulsively involved in various activities without recognizing the inherent social dangers.



**Hypomania:** A hypomanic episode is a distinct episode of  $\geq 4$  days that is distinctly different from the patient's usual nondepressed mood. The episode is marked by  $\geq 4$  symptoms that occur during a manic episode, but the symptoms are relatively less intense, so that functioning is not markedly impaired.

**Mixed state:** A mixed episode blends depressive and manic or hypomanic features. The most typical examples are momentary switches to tearfulness during the height of mania or racing thoughts during a depressive period. In at least  $\frac{1}{3}$  of people with bipolar disorder, the entire episode is mixed. A common presentation consists of a dysphorically excited mood, crying, curtailed sleep, racing thoughts, grandiosity, psychomotor restlessness, suicidal ideation, persecutory delusions, auditory hallucinations, indecisiveness, and confusion. This presentation is called dysphoric mania (ie, prominent depressive symptoms superimposed on manic psychosis).

### **Diagnosis**

Some patients who experience hypomania or mania do not report it unless they are specifically questioned. Skillful questioning may reveal morbid signs (eg, excesses in spending, impulsive sexual escapades, stimulant drug abuse). Such information is more likely to be provided by relatives. Diagnosis is based on the symptoms and signs described above. All patients must be asked gently but directly about suicidal ideation, plans, or activity.

A review of substance (especially amphetamines, particularly methamphetamine—see [Drug Use and Dependence: Amphetamines](#)) and prescription drug use and of body systems is needed to exclude drugs and physical disorders. Although no laboratory findings are pathognomonic for bipolar disorders, routine blood tests should be done to screen for physical disorders; thyroid-stimulating hormone (TSH) excludes hyperthyroidism. Other physical disorders (eg, pheochromocytoma) occasionally confuse the diagnosis. Anxiety disorders (eg, social phobia, panic attacks, obsessive-compulsive disorders) may also confuse the diagnosis.

### **Prognosis and Treatment**

Most patients with hypomania can be treated as outpatients. Acute mania usually requires inpatient management. Typically, mood stabilizers are used to induce remission in patients with acute mania or hypomania.

**Prevention of rapid cycling:** Antidepressants, even when given with a mood stabilizer, can induce rapid cycling in some patients (eg, patients with bipolar II disorder). Antidepressants should not be used prophylactically unless previous depressive episodes have been severe and, if used, should be given for only 4 to 12 wk. When disruptive psychomotor acceleration or mixed states supervene, adding 2nd-generation antipsychotics

**Education and psychotherapy:** Enlisting the support of loved ones is crucial to preventing major episodes. Group therapy is often recommended for patients and their partner; there, they learn about bipolar disorder, its social sequelae, and the central role of mood stabilizers in treatment. Individual psychotherapy may help patients better cope with problems of daily living and adjust to a new way of identifying themselves.

Patients, particularly those with bipolar II disorder, may not comply with mood-stabilizer regimens because they believe that these drugs make them less alert and creative. The physician can explain that decreased creativity is relatively uncommon because mood stabilizers usually provide



opportunity for a more even performance in interpersonal, scholastic, professional, and artistic pursuits.

Patients should be counseled to avoid stimulant drugs and alcohol, to minimize sleep deprivation, and to recognize early signs of relapse. If patients tend to be financially extravagant, finances should be turned over to a trusted family member. Patients with a tendency to sexual excesses should be given information about conjugal consequences (eg, divorce) and infectious risks of promiscuity, particularly AIDS.

### **Cyclothymic disorder**

Cyclothymic disorder is characterized by hypomanic and mini-depressive periods that last a few days, follow an irregular course, and are less severe than in bipolar disorder. Diagnosis is clinical and based on history. Management consists primarily of education, although some patients with functional impairment require drug therapy.

Cyclothymic disorder is commonly a precursor of bipolar II disorder. However, it can also occur as extreme moodiness without becoming a major mood disorder. In chronic hypomania, a form rarely seen clinically, elated periods predominate, with habitual reduction of sleep to < 6 h. People with this form are constantly overcheerful, self-assured, overenergetic, full of plans, improvident, overinvolved, and meddlesome; they rush off with restless impulses and accost people.

For some people, cyclothymic and chronic hypomanic dispositions contribute to success in business, leadership, achievement, and artistic creativity; however, they more often have serious detrimental interpersonal and social results. Results often include instability with an uneven work and schooling history, impulsive and frequent changes of residence, repeated romantic or marital breakups, and an episodic abuse of alcohol and drugs.

### ***Treatment***

Patients should be taught how to live with the extremes of their temperamental inclinations; however, living with cyclothymic disorder is not easy because interpersonal relationships are often stormy. Jobs with flexible hours are advised. Patients with artistic inclinations should be encouraged to pursue careers in the arts because the excesses and fragility of cyclothymia may be better tolerated there.

The decision to use a mood stabilizer depends on the balance between functional impairment and the social benefits or creative spurts that patients may experience.

### **Depressive disorders**

Depressive disorders are characterized by sadness severe enough or persistent enough to interfere with function and sometimes by decreased interest or pleasure in activities. Exact cause is unknown but probably involves heredity, changes in neurotransmitter levels, altered neuroendocrine function, and psychosocial factors. Diagnosis is based on history. Treatment usually consists of drugs, psychotherapy, or both, and sometimes electroconvulsive therapy.

The term depression is often used to refer to any of several depressive disorders. Three are classified in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) by specific symptoms: major depressive disorder (often called major depression), dysthymia, and depressive disorder not otherwise specified. Two others are classified by etiology: depressive disorder due to a general physical condition and substance-induced depressive disorder. Depressive



disorders occur at any age but typically develop during the mid teens, 20s, or 30s. In primary care settings, as many as 30% of patients report depressive symptoms, but < 10% have major depression. The term depression is often used to describe the low or discouraged mood that results from disappointments or losses. However, a better term for such a mood is demoralization. The negative feelings of demoralization, unlike those of depression, resolve when circumstances or events improve; the low mood usually lasts days rather than weeks or months, and suicidal thoughts and prolonged loss of function are much less likely.

### ***Etiology***

Exact cause is unknown. Heredity has an uncertain role; depression is more common among 1st-degree relatives of depressed patients, and concordance between identical twins is high. Hereditary genetic polymorphisms for the serotonin transporter active in the brain may be triggered by stress. People who have a history of child abuse or other major life stresses and have the short allele for this transporter are about twice as likely to develop depression as those who have the long allele. Other theories focus on changes in neurotransmitter levels, including abnormal regulation of cholinergic, catecholaminergic (noradrenergic or dopaminergic), and serotonergic (5-hydroxytryptamine) neurotransmission. Neuroendocrine deregulation may be a factor, with particular emphasis on 3 axes: hypothalamic-pituitary-adrenal, hypothalamic-pituitary-thyroid, and growth hormone.

Psychosocial factors also seem involved. Major life stresses, especially separations and losses, commonly precede episodes of major depression; however, such events do not usually cause lasting, severe depression except in people predisposed to a mood disorder.

People who have had an episode of major depression are at higher risk of subsequent episodes. People who are introverted and who have anxious tendencies may be more likely to develop a depressive disorder. Such people often lack the social skills to adjust to life pressures. Depression may also develop in people with other mental disorders.

Women are at higher risk, but no theory explains why. Possible factors include greater exposure to or heightened response to daily stresses, higher levels of monoamine oxidase (the enzyme that degrades neurotransmitters considered important for mood), and endocrine changes that occur with menstruation and at menopause. In postpartum depression, symptoms develop within 4 wk after delivery; endocrine changes have been implicated, but the specific cause is unknown. Also, thyroid function is more commonly dysregulated in women.

In seasonal affective disorder, symptoms develop in a seasonal pattern, typically during autumn or winter; the disorder tends to occur in climates with long or severe winters. Depressive symptoms or disorders may occur with various physical disorders, including thyroid and adrenal gland disorders, benign and malignant brain tumors, stroke, AIDS, Parkinson's disease, and multiple sclerosis. Certain drugs, such as corticosteroids, some  $\beta$ -blockers, antipsychotics (especially in the elderly), and reserpine, can also result in depressive disorders. Abuse of some recreational drugs (eg, alcohol, amphetamines) can lead to or accompany depression. Toxic effects or withdrawal of drugs may cause transient depressive symptoms.

### ***Symptoms and Signs***

Depression causes cognitive, psychomotor, and other types of dysfunction (eg, poor concentration, fatigue, loss of sexual desire, menstrual abnormalities) as well as a depressed mood. Other mental



symptoms or disorders (eg, anxiety and panic attacks) commonly coexist, sometimes complicating diagnosis and treatment. Patients with all forms of depression are more likely to abuse alcohol or other recreational drugs in an attempt to self-treat sleep disturbances or anxiety symptoms; however, depression is a less common cause of alcoholism and drug abuse than was once thought. Patients are also more likely to become heavy smokers and to neglect their health, increasing their risk of development or progression of other disorders (eg, COPD). Depression may reduce protective immune responses. Depression increases risk of MIs and stroke because cytokines and factors that increase blood clotting are released during depression.

**Major depression (unipolar disorder):** Periods (episodes) that include  $\geq 5$  mental or physical symptoms and last  $\geq 2$  wk are classified as major depression. Symptoms must include sadness deep enough to be described as despondency or despair (often called depressed mood) or loss of interest or pleasure in usual activities (anhedonia). Other mental symptoms include feelings of worthlessness or guilt, recurrent thoughts of death or suicide, reduced ability to concentrate, and occasionally agitation. Physical symptoms include changes in weight or appetite, loss of energy, fatigue, psychomotor retardation or agitation, and sleep disorders (insomnia, hypersomnia, early morning awakening). Patients may appear miserable, with tearful eyes, furrowed brows, downturned corners of the mouth, slumped posture, poor eye contact, lack of facial expression, little body movement, and speech changes (eg, soft voice, lack of prosody, use of monosyllabic words). The appearance may be confused with Parkinson's disease. In some patients, depressed mood is so deep that tears dry up; they report that they are unable to experience usual emotions and feel that the world has become colorless and lifeless. Nutrition may be severely impaired, requiring immediate intervention. Some depressed patients neglect personal hygiene or even their children, other loved ones, or pets.

Major depression is often divided into subgroups. The psychotic subgroup is characterized by delusions, often of having committed unpardonable sins or crimes, harboring incurable or shameful disorders, or of being persecuted. Patients may have auditory or visual hallucinations (eg, accusatory or condemning voices). The catatonic subgroup is characterized by severe psychomotor retardation or excessive purposeless activity, withdrawal, and, in some patients, grimacing and mimicry of speech (echolalia) or movement (echopraxia). The melancholic subgroup is characterized by loss of pleasure in nearly all activities, inability to respond to pleasurable stimuli, unchanging emotional expression, excessive or inappropriate guilt, early morning awakening, marked psychomotor retardation or agitation, and significant anorexia or weight loss. The atypical subgroup is characterized by a brightened mood in response to positive events and rejection sensitivity, resulting in depressed overreaction to perceived criticism or rejection, feelings of leaden paralysis or anergy, weight gain or increased appetite, and hypersomnia.

**Dysthymia:** Low-level or subthreshold depressive symptoms are classified as dysthymia. Symptoms typically begin insidiously during adolescence and follow a low-grade course over many years or decades (diagnosis requires a course of  $\geq 2$  yr); dysthymia may intermittently be complicated by episodes of major depression. Affected patients are habitually gloomy, pessimistic, humorless, passive, lethargic, introverted, hypercritical of self and others, and complaining.



***Depression not otherwise specified (NOS):*** Clusters of symptoms that do not meet criteria for other depressive disorders are classified as depression NOS. For example, minor depressive disorder may involve  $\geq 2$  wk of any of the symptoms of major depression but fewer than the 5 required for diagnosing major depression. Brief depressive disorder involves the same symptoms required for diagnosing major depression but lasts only 2 days to 2 wk. Premenstrual dysphoric syndrome involves a depressed mood, anxiety, and decreased interest in activities but only during most menstrual cycles, beginning in the luteal phase and ending within a few days after onset of menses.

***Mixed anxiety-depression:*** Although not considered a type of depression in DSM-IV, this condition, also called anxious depression, refers to concurrent mild symptoms common to anxiety and depression. The course is usually chronically intermittent. Because depressive disorders are more serious, patients with mixed anxiety-depression should be treated for depression. Obsessions, panic, and social phobias with hypersomniac depression suggest bipolar II disorder.

### ***Diagnosis***

Diagnosis is based on identifying the symptoms and signs described above. Several brief questionnaires are available for screening. They help elicit some depressive symptoms but cannot be used alone for diagnosis. Specific close-ended questions help determine whether patients have symptoms required by DSM-IV criteria for diagnosis of major depression.

Severity is assigned by the degree of pain and disability (physical, social, and occupational); duration of symptoms also helps determine severity. The presence of suicidal risk (manifested as suicidal ideas, plans, or attempts) indicates that the disorder is severe. A physician should gently but directly ask patients about any thoughts and plans to harm themselves or others. Psychosis and catatonia indicate severe depression. Melancholic features indicate severe or moderate depression. Coexisting physical conditions, substance abuse disorders, and anxiety disorders may add to severity.

### ***Prognosis and Treatment***

With treatment, symptoms often remit. Mild depression may be treated with general support and psychotherapy. Moderate to severe depression is treated with drugs, psychotherapy, or both, and sometimes electroconvulsive therapy. Some patients require  $> 1$  drug or a combination of drugs. Improvement may require 1 to 4 wk of taking drugs as prescribed. Depression, especially in patients who have had  $> 1$  episode, is likely to recur; therefore, severe cases often warrant long-term maintenance drug therapy.

Most people with depression are treated as outpatients. Patients with significant suicidal ideation, particularly when family support is lacking, require hospitalization, as do those with psychotic symptoms or physical debilitation.

Depressive symptoms in patients with substance abuse disorders often resolve within a few months of cessation of substance use. If a physical disorder or drug toxicity could be the cause, treatment is directed first at the disorder. If the diagnosis is in doubt or if symptoms are disabling or include suicidal ideation or hopelessness, a therapeutic trial with an antidepressant or a mood-stabilizing drug may help.



*Initial support:* A physician should see patients weekly or biweekly to provide support and education and to monitor progress. Telephone calls may supplement office visits. Patients and loved ones may be worried or embarrassed about the idea of having a mental disorder. The physician can help by explaining that depression is a serious medical disorder caused by biologic disturbances and requiring specific treatment and that depression is most often self-limiting and the prognosis with treatment is good. Patients and loved ones should be reassured that depression does not reflect a character flaw (eg, laziness). Telling patients that the path to recovery often fluctuates helps them put feelings of hopelessness in perspective and improves compliance.

Encouraging patients to gradually increase simple activities (eg, taking walks, exercising regularly) and social interactions must be balanced with acknowledging their desire to avoid activities. The physician can suggest that patients avoid self-blame and explain that dark thoughts are part of the disorder and will go away.

*Psychotherapy:* Individual psychotherapy, often as cognitive-behavioral therapy (individual or group) alone is often effective for milder forms of depression. Cognitive-behavioral therapy is increasingly used to combat the inertia and self-defeating mental set of depressed patients. However, cognitive-behavioral therapy is most useful when used with antidepressants to treat moderate to severe depression. Cognitive-behavioral therapy may improve coping skills and enhance gains by providing support and guidance, by removing cognitive distortions that prevent adaptive action, and by encouraging the patient to gradually resume social and occupational roles. Couple therapy may help reduce conjugal tensions and disharmony. Long-term psychotherapy is unnecessary except for patients who have long-term interpersonal conflicts or who are unresponsive to brief therapy.