

# Mood Disorders

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## PRINCIPLES

Mood is a subjective emotional state. It is normal human experience to have fluctuations in mood in response to occurrences in everyday life. A change in mood becomes a “mood disorder” when it significantly impairs functioning. In the emergency department (ED), patients with mood disorders often present grossly debilitated, with thoughts of suicide, homicide, or profound self-neglect. These patients frequently present in emotional crisis, but this may not be their presenting complaint. Approximately, one-fourth to one-third of ED patients screen positive for mood disorders.

The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), divides mood disorders into two broad categories: depressive disorders and bipolar disorders.<sup>1</sup> Mood disorders may also be due to a general medical condition or substance-induced mood disorders. Because the specific pathophysiologic mechanisms of these disorders are not fully understood, they are categorized by groupings of symptoms that persist for defined lengths of time.

## EPIDEMIOLOGY

Mental health patients are the fastest growing group of patients presenting to the ED. In 2007, 13% of the 94 million ED visits in the United States were for psychiatric reasons, which was an increase from 5% in 2000.<sup>2</sup> This increase is nearly double what would have been expected by population growth alone.<sup>3</sup> Up to 50% of Americans will meet the criteria for a DSM-5 disorder sometime in their life, with an estimated 21% having a mood disorder.

The World Health Organization (WHO) ranks major depressive disorder as one of the most prevalent and disabling diseases in the world. The 12-month prevalence for major depressive disorder is 5% and the lifetime prevalence is 13%. Patients with major depressive disorder frequently have other comorbid mental health issues, including anxiety disorders, personality disorders, and substance use disorders.

The lifetime prevalence of bipolar spectrum disorders is approximately 4%. Both severe depression and mania are serious and potentially life-threatening. Up to 80% of patients with bipolar disorder will exhibit suicidal behavior, and half will attempt suicide. Suicidal behavior can occur during all phases of bipolar disorder, but patients experiencing a depressed or a mixed episode are at higher risk, especially those with severe depressive symptoms and a sense of hopelessness.

## PATHOPHYSIOLOGY

The pathophysiology of the mood disorders is not well established, but much is known about the neurophysiology, genetics, and psychosocial aspects of the disorders.<sup>4</sup>

## Neurophysiology

Antidepressants work by increasing the availability and activity of serotonin and norepinephrine at the synapse to stimulate the

postsynaptic neuron. This is done by direct binding to the presynaptic and postsynaptic receptors, blocking reuptake of the neurotransmitter or inhibiting the enzymatic breakdown of the neurotransmitter. Because norepinephrine and serotonin systems traverse large portions of the brain, monoamine deficiency is hypothesized as a cause of depression. Depletion of oral tryptophan and tyrosine, amino acids essential for the production of serotonin and norepinephrine, respectively, can induce a depressive episode in subjects with a history of depression but not in healthy controls. Monoamine metabolite levels in cerebrospinal fluid, plasma, urine, and postmortem brains of patients with depression have not been reliably found to be deficient, indicating that there could be downstream effects involving second-messenger systems, such as cyclic adenosine monophosphate and phosphatidylinositol.

Other neurotransmitter systems may play a role in the development of depression. Decreased levels of both glutamate and  $\gamma$ -aminobutyric acid have been found in the prefrontal cortex of depressed subjects. Intravenous ketamine, an *N*-methyl-d-aspartate (NMDA) antagonist, induces a rapid antidepressant effect and suggests a role for glutamate in the pathophysiologic process of depression. The brain relies on the actions of protective and regenerative cytokines, such as brain-derived neurotrophic factor (BDNF). All known antidepressants raise levels of BDNF and subsequently result in neurogenesis of certain brain regions, such as the hippocampus. Other theories include the melatonergic system and related abnormalities in circadian rhythm, decreased neurosteroid synthesis, impaired endogenous opioid functioning, monoamine-acetylcholine imbalance, inflammatory effects of cytokines, and dysfunction of specific brain structures and circuits.

The neurophysiology of bipolar disorder is less well understood than unipolar depression, in part because of the fluctuating mood states and the heterogeneity of the disorder. Bipolar disorder may in part arise from abnormalities in the connections within and between structures in the brain.<sup>5</sup> Specifically implicated are circuits interconnecting the amygdala, hypothalamus, striatum, and subdivisions of the frontal cortex, all of which are involved in both the generation and regulation of emotion.<sup>5</sup>

## Neuroanatomy

Neuroimaging studies of the brain suggest that abnormalities in certain areas and the interconnections between those areas may be involved mood disorders. A common magnetic resonance imaging (MRI) finding in patients with mood disorders, especially bipolar disorder, is an increased occurrence of subcortical hyperintensities in the periventricular areas, basal ganglia, and thalamus. High-resolution MRI demonstrates reduced volumes in the hippocampus, orbital cortex, and anterior cingulate. These findings are associated with more severe illness, bipolar disorder, and increased cortisol levels. Volume reduction in the hippocampus is associated with high illness chronicity.

The amygdala is a clustering of nuclei that process emotional stimuli, especially fear, anger, and sadness. Functional neuroimaging suggests that amygdala activity is increased when the subject

is exposed to emotionally relevant stimuli. The amygdala has connections throughout the brain. A decreased amygdala volume has been associated with unipolar depression.

## Endocrine System

Physiologic changes such as increased alertness, decreased appetite, increased heart rate, and activation of the hypothalamic-pituitary-adrenal (HPA) axis occur when a person is stressed. The HPA axis may play a role in depression, especially in cases of early childhood and chronic stress.<sup>4</sup> Activation of the HPA axis releases corticotropin-releasing hormone (CRH) from the hypothalamus. Although not specific, patients with depression may have increased levels of free cortisol in the plasma, cerebrospinal fluid, and urine. Increased CRH has been demonstrated in cerebrospinal fluid, and increased levels of CRH messenger RNA and protein have been demonstrated in limbic brain regions. Although none of these measures is reliable as a diagnostic tool, successful treatment to remission has been shown to reverse some of these abnormalities.

## Genetics

Genetic vulnerability to mood disorders has not been traced to a single gene. It is likely to be due to the additive effects of many genes and environmental influences on how these genes are expressed. Family, twin, and adoption studies provide evidence that major depressive disorder is a familial disorder but is less heritable than bipolar disorder. Bipolar disorder is one of the most heritable medical illnesses with a heritability of 80% to 85% and a monozygotic twin concordance of about 40%.

## Psychosocial Factors

The etiology of most psychiatric problems, including mood disorders, involves complex interactions between both biologic and psychosocial factors.<sup>4</sup> The complex neural mechanism that regulates mood responds to and is modified by each person's experience, including events in early childhood, such as childhood sexual abuse, reward and punishment during growth and development, other lifetime trauma, marital problems, low social support, and various kinds of loss. Psychosocial theories of mood disorder form the basis for psychotherapy.<sup>4</sup>

## CLINICAL FEATURES

### Major Depressive Disorder

Major depressive disorder is characterized by one or more major depressive episodes, as defined by DSM-5 criteria (Boxes 101.1 and 101.2).<sup>1</sup> A major depressive episode is characterized by disturbances in four major areas: mood, psychomotor activity, cognition, and vegetative function. The patient must have at least five symptoms for a minimum of 2 weeks and one of the five must be depressed mood or anhedonia (decreased interest or pleasure).<sup>1</sup>

### Mood Disturbances

Patients in a depressed state often feel profoundly hopeless and helpless. There are many words and phrases that can be used to describe feeling depressed; some patients will not recognize that they are "depressed" but rather they may describe the feeling in some other manner. Someone feeling no emotion (profoundly depressed) may answer "no" when asked about depressed mood.

On the other hand, a person may meet criteria for a major depressive episode and not be experiencing a depressed mood. Depression can also be manifested as a decreased capacity to

### BOX 101.1

#### Summary of *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, Criteria for a Major Depressive Episode

- A. Five or more of the following symptoms have been present almost every day during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. *Note:* Do not include symptoms caused by a general medical condition.
  1. Depressed mood (can be irritable mood in children and adolescents)
  2. Loss of interest or pleasure in activities
  3. Significant weight loss when not dieting or weight gain, or decrease or increase in appetite
  4. Insomnia or hypersomnia
  5. Psychomotor agitation or retardation
  6. Fatigue or loss of energy
  7. Feelings of worthlessness, or excessive or inappropriate guilt
  8. Diminished ability to think or concentrate, or indecisiveness
  9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation, or a suicide plan or attempt
- B. Symptoms cause clinically significant distress or impairment in social, occupational, or other functioning.
- C. Symptoms are not caused by direct physiologic effects of a substance (eg, drug of abuse, medication) or a general medical condition (eg, hypothyroidism).
- D. Symptoms are not better explained by another mental health disorder.
- E. There has never been a manic or hypomanic episode.

Modified from American Psychiatric Association: *Diagnostic and statistical manual of mental disorders*, ed 5, Arlington, VA, 2013, American Psychiatric Association.

### BOX 101.2

#### Mnemonics for the Symptoms of Depression and Mania

##### MNEMONIC FOR THE SYMPTOMS OF DEPRESSION

###### Sig E Caps

Sleep amount increased or decreased  
 Interest (anhedonia)  
 Guilt  
 Energy level decreased  
 Concentration decreased  
 Appetite increased or decreased  
 Psychomotor activity increased or decreased  
 Suicidal ideation

##### MNEMONIC FOR THE SYMPTOMS OF MANIA

###### Dig Fast

Distractibility  
 Irritability  
 Grandiosity  
 Flight of ideas  
 Activity increased  
 Sleeplessness  
 Thoughtlessness (impulsivity, increased risk taking)

experience pleasure or interest in otherwise pleasurable activities. This loss of interest is known as *anhedonia*.

As noted previously, the patient must exhibit a depressed mood or anhedonia to meet DSM-5 criteria for a diagnosis of a major depressive episode.<sup>1</sup>

## Disturbances in Psychomotor Activity

Physical activity in depression can be either increased or decreased. Psychomotor retardation is a significant slowing of physical activity. When suffering from psychomotor retardation, thinking and speaking can be slow, causing delayed responses to answers. Depressed patients often describe feeling fatigued with a general lack of energy and motivation. Conversely, patients may display psychomotor agitation, which can be manifested as fidgeting, pacing, hand wringing, or restlessness.

## Vegetative Disturbances

Vegetative symptoms include disturbances in three major areas: sleep, appetite, and sexual function. Depressed patients may complain of insomnia or hypersomnia. Insomnia may be manifested as difficulty in falling asleep, frequent awakenings throughout the night, or early-morning wakening. Depressed patients with hypersomnia may report sleeping 12 to 14 hours or more a day. Alterations in appetite and eating patterns can also occur, resulting in significant weight gain or loss during a short time. Loss of interest in sexual activity and impaired sexual functioning may also accompany depression, although this is not listed as a DSM-5 criterion.

## Thought Process and Content

Depressed patients often describe impaired concentration and forgetfulness. Executive functioning can also be impaired. In severe cases, this results in a decreased ability to perform basic activities of daily living.

Thought content tends to be negatively biased, such as recurrent thoughts of guilt, failure, worthlessness, and self-criticism. Patients in a depressed episode are at increased risk for suicide. Suicidal thoughts may range from vague notions that life is not worth living (passive) to fully envisioned suicide plans with definitive intent to kill themselves (active). All depressed patients must be questioned about suicidal thoughts. Because patients are not often forthcoming with their thoughts on suicide, a thorough review of risk factors and protective factors needs to form the basis of clinical decisions for providing the necessary level of care.

Patients with severe depression may have psychotic symptoms. The hallucinations and delusions that accompany depression are usually mood congruent, meaning that the themes of the psychotic content are consistent with the depressed mood.

## Masked Depression

Mood disorders may not be clear at presentation. The depressed patient may have only vague somatic symptoms. Common complaints include weakness, fatigue, headache, and abdominal pain with medical evaluations occurring in response. Patients may not be aware of their depression and are often heavy users of medical care. Over half of patients with major depressive disorder initially present with somatic symptoms only which can mask a hidden depression. Clues that suggest a mood disturbance include the recent onset of a set of unusual behaviors, significant social disturbance, such as job loss, financial stress and marital difficulties, and self-destructive behavior (eg, substance abuse, sexual promiscuity).

## Special Considerations

**Children and Adolescents.** Criteria for depression in children and adolescents are the same as for depression in adults. Depression in these age groups can, however, present differently.

Prepubertal children are more likely to have somatic complaints, psychomotor agitation, and mood-congruent hallucinations and less likely to have disturbances in sleep and appetite. Some children are misdiagnosed as having attention deficit disorder, especially if symptoms involve poor concentration, listlessness, agitation, and withdrawal from daily activities.

Adolescents with depression may show increased irritability, oppositional behavior, and substance abuse. Other characteristics are social withdrawal, increased rejection sensitivity, and decline in school performance. Some adolescents may be first diagnosed with depression on receiving treatment for drug and alcohol problems.

**Disruptive Mood Dysregulation Disorder.** A newly described phenomenon for children who may have been previously diagnosed with depression or bipolar disorder is disruptive mood dysregulation disorder. Children and adolescents given this diagnosis display severe, recurrent outbursts that are out of proportion for the situation and are inconsistent with developmental level. The outbursts must occur three or more times a week, and the mood in between outbursts is irritable or angry most days. There are duration criteria of 12 months with no periods of three or more consecutive months not meeting criteria. Symptoms must occur prior to age 10.<sup>1</sup>

**Geriatric Patients.** Depression is more common in elders because of more frequent occurrences of loss, comorbid health issues, and loss of autonomy. The elderly have a tendency to report more somatic complaints when depressed. They are also more vulnerable to development of melancholic depression, which is characterized by early morning awakening, diurnal variation in mood, low self-esteem, and low mood reactivity. Older depressed patients can also present with symptoms involving memory loss, inattention, withdrawal from daily activities, and lapses in personal and social hygiene that suggest dementia rather than depression. When such symptoms are from depression, the condition is called *pseudodementia*. Serious depression in elders is a highly treatable, reversible condition.

## Other Depressive Disorders

### Postpartum Depression

Postpartum depression is a depressive disorder that occurs during pregnancy or within 4 weeks of delivery and would allow for the specifier “with peripartum onset.” Symptoms of depression are common in the perinatal period. As noted in the DSM-5, between 3% and 6% of women will experience the onset of major depression during pregnancy or within the following weeks to months.<sup>1</sup> Similarly, but less severe, up to 65% of mothers report some depressed mood after childbirth, often called *postpartum blues*. Symptoms are generally mild and transient; although in 10% of mothers, it may lead to a full-fledged episode of major depression.

Postpartum mood episodes with psychotic features can be particularly dangerous. Infanticide is most often associated with command hallucinations to kill the infant or associated delusions. The risk for this is most closely related to a past history of postpartum episodes with psychosis, a history of depression or bipolar disorder, or a family history of bipolar disorder.

### Persistent Depressive Disorder

Persistent depressive disorder is a new diagnosis that combines two former diagnoses: chronic major depressive disorder and dysthymic disorder. Specific criteria include the following: depressed mood most of the day, most days for at least 2 years;

two or more of the following: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness; never more than 2 months of the 2 years without symptoms; and must cause significant distress or impairment in functioning. Exclusion criteria include a history of hypomania or mania and a history of psychotic illness. Also, it cannot be due to a substance or medical condition.<sup>1</sup> There are multiple specifiers that can be applied to this diagnosis.

### Premenstrual Dysphoric Disorder

Premenstrual dysphoric syndrome is a new diagnosis included in the DSM-5. At least five of the listed symptoms must be present in the final week before the onset of menses and start to improve within a few days after the onset of menses and be absent or minimal in the week post menses. These symptoms must be present for most cycles over the preceding year. The onset can occur at any point after menarche. Risks for development include stress, history of interpersonal trauma, seasonal changes, and sociocultural aspects of female sexual behavior.

### Seasonal Affective Disorder

Seasonal affective disorder is not a separate mood disorder, but rather, a specifier of major depressive disorder. An example of the use of a specifier is “major depressive disorder, recurrent, moderate, with seasonal pattern.” This specifier can only be used with a recurrent major depressive disorder. The criteria for this include the following: a regular temporal relationship between onset of depressive episode and a particular time of year, full remissions at a specific time of year, two depressive episodes within 2 years that demonstrate a temporal relationship, no nonseasonal episodes within the same period, and substantially more seasonal depressive episodes than nonseasonal episodes over the person’s lifetime.<sup>1</sup> Melatonin, a hormone secreted in the brain and produced at high levels in the dark, has been implicated in the etiology of this disorder. Phototherapy is an effective and safe treatment of seasonal depression. Light exposure to the eyes seems to be essential, but the exact mechanism of action is still unknown.

### Bipolar Disorders

Bipolar disorder is lifelong, with episodic exacerbation of symptoms and deterioration of function characterized by extreme mood episodes. Patients with bipolar disorder may require different forms and intensities of treatment at different stages of the illness. *Bipolar I disorder* includes at least one manic episode, and patients have typically had one or more major depressive episodes, although a depressive episode is not necessary for diagnosis. *Bipolar II disorder* involves a hypomanic episode and at least one major depressive episode. A hypomanic episode includes the features of a manic episode without psychosis, marked impairment of function, or the need for hospitalization.

### Manic Episode

During a manic episode (Boxes 101.2 and 101.3), the disturbance in mood must be severe enough to include psychosis, the need for hospitalization, or marked impairment in functioning. Bipolar disorders are much less common than major depressive disorder. The overall prevalence of a manic episode is about 2% in both women and men.

In many cases, manic patients are brought to the ED by someone else (eg, family, police, or emergency medical services). Patients who are experiencing a manic episode may present

#### BOX 101.3

### Summary of *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, Criteria for a Manic Episode

- A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood, and abnormally and persistently increased goal-directed activity or energy lasting at least 1 week (or any duration if hospitalization is necessary).
- B. During the period of mood disturbance and increased energy or activity, three or more of the following symptoms have persisted (four, if the mood is only irritable) and have been present to a significant degree:
  1. Inflated self-esteem or grandiosity
  2. Decreased need for sleep (eg, feels rested after only 3 hours of sleep)
  3. More talkative than usual or pressure to keep talking
  4. Flight of ideas or subjective experience that thoughts are racing
  5. Distractibility (ie, attention too easily drawn to unimportant or irrelevant external stimuli)
  6. Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  7. Excessive involvement in pleasurable activities that have a high potential for painful consequences (eg, buying sprees, sexual indiscretions, foolish investments)
- C. Mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or social activities or to necessitate hospitalization to prevent harm to self or others, or psychotic features are present.
- D. Symptoms are not caused by direct physiologic effects of a substance (eg, drug of abuse, medication) or a general medical condition (eg, hyperthyroidism).

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as gregarious, humorous, and engaging, which may suddenly alternate with belligerence and irritability. Patients may display pressured speech, in which they keep talking, often rapidly and loudly without pauses between thoughts or sentences, and are difficult to interrupt. The thought process in mania is characterized by illogical associations and flight of ideas. An inflated self-esteem and grandiose delusions may lead them to also be argumentative, impatient, and condescending. Grandiosity often centers on very broad dramatic or universal themes, such as religion or politics. The patient may describe a massive undertaking, such as “uniting the world’s churches” or “solving world poverty.” These severe symptoms are usually accompanied by a profound lack of insight. Despite obvious altered behavior, impaired judgment, and poor impulse control, the patient may insist that there is nothing wrong or blame problems on others.

Manic patients have decreased or no need for sleep and typically report being awake for days. They may be involved in a massive project (eg, writing a novel), may completely disregard consequences of actions, may have difficulty with spending (eg, credit cards revoked), and may engage in risky behavior (eg, sexual liaisons with strangers, risky driving). Whenever possible, a corroborating history should also be obtained from family or others who know of the patient’s behavior.

Manic patients may present as trauma patients, injured by an action reflecting the patient’s grandiosity (eg, attempting to fly), impulsivity, or belligerence (eg, fighting, resisting arrest). A manic episode may be punctuated by abrupt periods of tearfulness and profound depression, including suicidal ideation. When

depressive and manic features occur concurrently in such a manner, the disorder is termed *mixed* or *bipolar, mixed phase*.

### Cyclothymic Disorder

Cyclothymic disorder is characterized by chronic mood swings that do not meet criteria for a hypomanic or depressive episode. The mood episodes must occur over at least 2 years, present for at least half the time, and the individual cannot be symptom free for more than 2 months at a time.<sup>1</sup>

### Mood Disorders Caused by a General Medical Condition

This diagnosis requires a prominent and persistent period of depressed mood or anhedonia that predominates the clinical picture, with evidence that the disturbance is the direct pathophysiological consequence of a medical condition, and not better explained by another mental disorder or occurring during the course of delirium.<sup>1</sup> Bipolar disorder requires a prominent and persistent period of abnormally elevated, expansive, or irritable mood; and abnormally increased activity or energy that predominates the clinical picture, with evidence of direct pathophysiological consequence of another medical condition, and it is not better explained by another mental disorder or occurs during the course of delirium.<sup>1</sup>

Certain medical illnesses have a well-known association with mood disorder. In Parkinson's disease, electrical stimulation to a certain area of the substantia nigra alleviates symptoms of depression. Stimulation of an area only 2 mm away can cause acute reversible symptoms of depression, such as crying, not wanting to live, and hopelessness. Parkinson's disease has a well-known association with depression, with up to 40% of patients demonstrating major depression.

Certain malignant neoplasms have a well-known association with depression, including pancreatic carcinoma, brain neoplasm, and disseminated malignant disease (eg, lymphoma). Coronary artery disease, myocardial infarction, stroke, end-stage renal disease, acquired immunodeficiency syndrome, several endocrine diseases, and connective tissue disease are also associated with major depressive disorder. After a myocardial infarction, patients with depression have a 3.5-fold increase in cardiovascular mortality compared with nondepressed patients. The development of stroke, diabetes, and osteoporosis is more likely in patients with depression than in those who are not depressed.

Depression related to medical conditions may be different in some respects from primary depression and responds less favorably than primary depression to antidepressant medication.

### Mood Disorders Caused by Medications or Other Substances

These are very similar to mood disorders caused by medical conditions, with the exception of that the symptoms must develop during or soon after substance intoxication or withdrawal, or after exposure to a medication capable of producing the symptoms.<sup>1</sup>

Many medications are associated with symptoms of mood disorders. Multiple antihypertensives, anticonvulsants, and hormones have been associated with depressive symptoms, and certain antibiotics and steroids are associated with manic symptoms. Intoxication with or chronic heavy use of alcohol, sedatives, hypnotics, anxiolytics, narcotics, and other depressants can cause symptoms of a major depressive episode. Stimulants such as cocaine, phencyclidine, hallucinogens, and amphetamines can cause symptoms of a manic episode. Mood disorder symptoms can also develop during withdrawal. To qualify for this diagnosis, the symptoms must not occur exclusively during a course of

delirium, must cause significant distress or impairment of functioning, and must develop within a month of either substance intoxication or withdrawal. When the mood disorder predates the period of substance abuse or lasts longer than 1 month after the period of abuse, the diagnosis may be an underlying mood disorder, such as a major depressive disorder or bipolar disorder, with a comorbid substance abuse or dependence diagnosis.

## DIFFERENTIAL DIAGNOSIS

### Medical Disorders, Medications, and Substance Abuse or Withdrawal

Medical disorders, medications, and substance abuse or withdrawal can either cause or mimic mood disorders. The patient with symptoms and signs of depression may have an unrecognized malignant neoplasm or sedative intoxication. Differential diagnostic considerations for manic symptoms include stimulant abuse (eg, cocaine, amphetamines), hallucinogen abuse, alcohol or sedative withdrawal, delirium, hyperthyroidism, and other medical conditions causing agitation. See the previous section for further information. Patients may be treated with antidepressant medication for a variety of disorders other than depression, such as anxiety, obsessive-compulsive disorder, post-traumatic stress disorder, pain syndromes, smoking cessation, and vasodepressor syncope.

### Grief and Bereavement

Grief and bereavement are normal human reactions to the acute loss of another person, health, social position, or job. The period of mourning is characterized by sadness, diminished sense of well-being (somatic complaints), sleeplessness, and sadness triggered by thoughts of the loss. Normal grief, however, does not include guilt, loss of self-esteem, feelings of worthlessness, suicidal intent, psychomotor retardation, or occupational dysfunction. The duration of normal grief and bereavement differs among cultures and among individuals within cultures, but severe symptoms normally resolve within 6 to 12 months.

### Adjustment Disorders

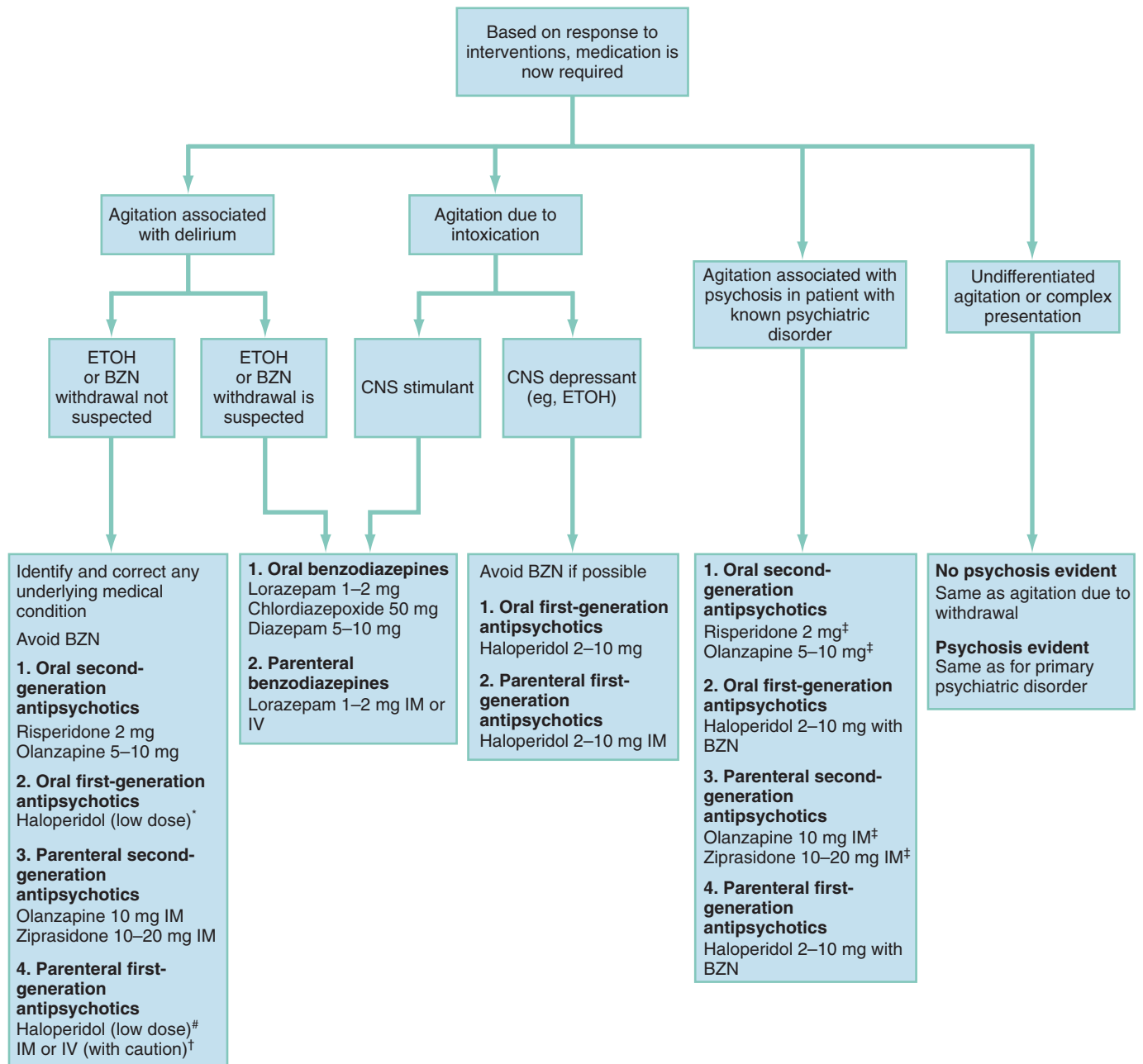
Adjustment disorders are behavioral or emotional disorders that occur in response to an identifiable stress or stressors, with marked distress that is out of proportion to the severity of the stressor. The emotional component can involve sadness, low self-esteem, suicidal behavior, hopelessness, helplessness, or other self-threatening behavior. Acute adjustment disorder occurs within 3 months of the stressor and does not last longer than 6 months.<sup>1</sup> The stressors are typically not as severe as those precipitating bereavement reaction, and the responses are often more maladaptive.

### Borderline Personality Disorder

Borderline personality disorder is characterized by unstable personal relationships, unstable self-image, and self-destructive behaviors. The disorder may include chronic feelings of emptiness, which may be misdiagnosed as depression, or reactivity of mood, which may be mistaken for mania or hypomania. These patients typically live lives of crisis and constant conflict.

### Dementia

Dementia can be confused with depression but is characterized by abnormal mental status, including abnormalities in tests of memory, calculation, and judgment.



**Fig. 101.1.** Protocol for treatment of agitation. *BZN*, Benzodiazepine; *CNS*, central nervous system; *ETOH*, ethyl alcohol; *IM*, intramuscular; *IV*, intravenous. \*There is strong evidence that doses above 3 mg (per day) in patients with delirium are associated with significant risk of extrapyramidal side effects (EPS), so patients receiving more than 3 mg/day should be assessed carefully for EPS. †See U.S. Food and Drug Administration (FDA) guidelines. ‡If an antipsychotic alone does not work sufficiently, add lorazepam 1 to 2 mg (oral or parenteral). (Redrawn from Wilson MP, Pepper D, Currier GW, et al: The psychopharmacology of agitation: consensus statement of the American Association for Emergency Psychiatry Project BETA Psychopharmacology Workgroup. *WJEM* 13[1]:26-34, 2012.)

## DIAGNOSTIC TESTING

History and physical examination should focus on determining if the patient has a mood disorder or the possibility that drug abuse, medications, or a general medical condition may be responsible for the patient's condition instead. It is essential to identify medical conditions that may exacerbate a psychiatric presentation. The psychiatric history should ask about current symptoms, precipitating events (eg, job loss or relationship), past psychiatric and substance history, history of self-harm or suicide attempts, and identification of support systems. Even if not suggested by the

patient, careful questioning of suicidal thoughts is necessary. If possible, history should be confirmed by speaking with the patient's regular health care providers and interviewing family, friends, or eyewitnesses to the events that precipitated the ED visit. A tentative diagnosis can be established by use of DSM-5 criteria. Laboratory tests to investigate medical conditions may be necessary based on the specifics of the clinical presentation, but no tests can confirm or exclude mood disorders. Patients with new symptoms compatible with mood disorders need a more extensive medical and psychiatric investigation than those with a known disorder.

## MANAGEMENT

Patients presenting with mood disorder symptomology are frequently in crisis, often overwhelmed, and frankly scared. The ED is a chaotic, stimulating environment that may cause or exacerbate the patients' level of agitation. Creation of a safe and stable environment for the patient is a high priority. The patient with an acute manic episode may be disruptive, refuse medical evaluation, and make repeated attempts to leave the ED. The initial step in treating such a disruptive patient is to offer assistance in reducing the agitation. A recent consensus guideline produced by the American Association for Emergency Psychiatry, noted keys to de-escalation.<sup>6</sup> One key is offering anxiolytic medication early in the patient's presentation. If de-escalation techniques and medication do not resolve the agitation, the patient may need to be placed in seclusion or restraints for his or her safety and that of others. This is a last resort after other de-escalation measures have failed. Chapter 189 discusses the use of seclusion and restraints in the ED. If a medical cause for agitation is found, treatment is aimed at the underlying cause (eg, oxygen for hypoxic delirium). Often in the ED, treatment may need to begin prior to the cause of the agitation being fully recognized.<sup>7</sup> Figure 101.1 shows a simple algorithm for approaching the agitated patient.

Treatment of depression in the ED is more controversial. Selective serotonin reuptake inhibitors (SSRIs) and serotonin norepinephrine reuptake inhibitors (SNRIs) are the main treatments for depression. For the patient who is awaiting inpatient psychiatric placement, these medications could be started in consultation with the admitting service. If the patient has a mild to moderate depression, not requiring hospitalization, they may be started on an SSRI as long as they have close follow-up arranged. SSRIs are known to have a myriad of side effects that can lead to premature discontinuation.<sup>8</sup> For the patients who are already on psychotropic medications but have discontinued them for some reason, it is reasonable to restart these medications in the ED.

A non-agitated manic patient may be able to inform the treatment team about what has worked well in the past. There are two medication choices for acute mania: antipsychotics and mood stabilizers. All of the atypical, or second generation, antipsychotics have been approved to treat acute mania as monotherapy or as an adjunctive therapy, except paliperidone and iloperidone. Lithium, valproic acid/divalproate, and carbamazepine are the most well

studied mood stabilizers. Lithium and carbamazepine need to be titrated, but valproic acid can be loaded in the ED at 20 to 30 mg/kg a day (divided dose) in a healthy person with normal liver function.

The atypical antipsychotic medicines including ziprasidone, risperidone, olanzapine, aripiprazole, and quetiapine, cause fewer side effects (such as, acute dystonia) than conventional antipsychotic agents. Oral doses should be offered first, and several agents, including risperidone, olanzapine, and aripiprazole, are available in rapidly dissolving tablet form. Three are available as an intramuscular injection: ziprasidone (Geodon), olanzapine (Zyprexa), and aripiprazole (Abilify). Ziprasidone 10 mg to 20 mg is effective; however, its use is limited to 40 mg per 24 hours. Olanzapine 2.5 mg to 10 mg is effective but is associated with postural hypotension, and it is not recommended in combination with parenteral benzodiazepines because of the risk of cardiopulmonary depression. Aripiprazole is the newest agent and at doses of 9.75 mg to 15 mg seems to be the least sedating of the atypicals, but it is more likely to cause nausea and vomiting. It is valuable to obtain psychiatric consultation during the initiation of agitation treatment, because these patients will generally require significant ED treatment or psychiatric hospitalization.

## DISPOSITION

To determine the appropriate disposition for patients presenting with a mood disorder, a suicide risk assessment is required. The Substance Abuse and Mental Health Services Administration developed a practical tool referred to as the Suicide Assessment Five-Step Evaluation and Triage (SAFE-T).<sup>9</sup> Current suicidal thoughts, risk factors and protective factors should be identified, as well as past suicidal thoughts, plans, or acts. Chapter 105 provides an in-depth discussion of suicide assessment. It is only after considering this information that an appropriate intervention can be determined. With the help of social workers or a mental health worker, many patients can be safely discharged home with close follow-up. Patients receiving initial treatment in the ED, without a proper handoff to outpatient care, are at an increased risk for return. If available, it is preferred that a social worker or mental health worker connect discharged patients with outside agencies and services, rather than providing patients with a referral list.

## KEY CONCEPTS

- Patients with apparent mood disorders should be evaluated for medical disorders, medication effects, or substance abuse or withdrawal because these conditions can mimic both depression and mania.
- Mood disorders should be suspected in patients with multiple, vague, nonspecific complaints and in patients who are frequent, heavy users of medical care.
- The differentiation of depression and dementia in elders can be difficult but is important because depression often responds dramatically to treatment.
- Patients with mood disorders should be assessed for their suicide potential.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

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## CHAPTER 101: QUESTIONS &amp; ANSWERS

- 101.1. What is the lifetime suicide risk for people with major untreated depression?
- A. 5%
  - B. 10%
  - C. 15%
  - D. 20%
  - E. 25%

**Answer: C.** Patients with major depression have a high lifetime suicide risk, and although episodes of acute decompensation with even higher risk can be identified and treated, a certain number of patients succeed in committing suicide.

- 101.2. Which of the following imbalances of central nervous system neurotransmitters is seen in patients with clinical depression?
- A. Decreased hypothalamic-pituitary-adrenal (HPA) activity
  - B. Depressed serotonin levels
  - C. Elevated gamma-aminobutyric acid (GABA) levels
  - D. Elevated norepinephrine levels
  - E. Unchanged dopamine levels

**Answer: B.** The central biochemical features toward which pharmacologic management is directed are depressed levels of norepinephrine and serotonin. Data are also emerging that suggest decreased dopamine levels. The HPA axis may also be altered with elevated cortisol levels.

- 101.3. Which of the following statements regarding depression in children and elders is *true*?
- A. Children with depression rarely present with somatic complaints.
  - B. Depression in children may be manifested as attention deficit disorder (ADD).
  - C. Depression presents differently from dementia in elders.
  - D. Diagnostic criteria for depression in children are different.
  - E. Serious depression in elders is generally refractory to treatment.

**Answer: B.** Depression in children and adolescents can be manifested as ADD. Somatic complaints are a common feature of children and adolescents presenting with depression, but the diagnostic criteria are not different. Geriatric depression may be manifested in a manner similar to dementia (pseudodementia), but unlike dementia, the depression is highly treatable and reversible once it is recognized.

- 101.4. A 31-year-old attorney is brought to the emergency department (ED) by his family for a chief complaint of agitation and a behavioral change. He has no past medical history and takes no medications. The family reports decreased sleep, increased talkativeness, marked increased time and involvement at work, and an uncharacteristic buying spree. Your examination is remarkable for distractibility, gregarious and pressured speech, flight of ideas, and mild psychomotor agitation. Laboratory examination and urine drug screen results are negative. The patient is adamant that he has important things to do and needs to leave. Which of the following statements is most true?
- A. Antipsychotic agents are not effective.
  - B. Hallucinations would be atypical.
  - C. If treated, intravenous valproic acid is indicated.
  - D. Initiating treatment in the ED is not indicated.
  - E. Multiple antibiotics can cause this clinical picture.

**Answer: E.** This patient has a fairly classic presentation for acute mania with pressured speech, distractibility, grandiosity, increased involvement (in this case with work), and decreased need for sleep. Multiple drugs may precipitate this, including acyclovir, isoniazid, sulfonamides, the floxins, and chloroquine. An acute manic episode may be manifested with hallucinations and mimic an acute psychosis. ED treatment is usually indicated for this disorder. Acute stabilization is generally effective with major tranquilizers, such as haloperidol.