Depressive Disorders

Depressive disorders include disruptive mood dysregulation disorder, major depressive disorder (including major depressive episode), persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder, and unspecified depressive disorder. Unlike in DSM-IV, this chapter "Depressive Disorders" has been separated from the previous chapter "Bipolar and Related Disorders." The common feature of all of these disorders is the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function. What differs among them are issues of duration, timing, or presumed etiology.

In order to address concerns about the potential for the overdiagnosis of and treatment for bipolar disorder in children, a new diagnosis, disruptive mood dysregulation disorder, referring to the presentation of children with persistent irritability and frequent episodes of extreme behavioral dyscontrol, is added to the depressive disorders for children up to 12 years of age. Its placement in this chapter reflects the finding that children with this symptom pattern typically develop unipolar depressive disorders or anxiety disorders, rather than bipolar disorders, as they mature into adolescence and adulthood.

Major depressive disorder represents the classic condition in this group of disorders. It is characterized by discrete episodes of at least 2 weeks' duration (although most episodes last considerably longer) involving clear-cut changes in affect, cognition, and neurovegetative functions and inter-episode remissions. A diagnosis based on a single episode is possible, although the disorder is a recurrent one in the majority of cases. Careful consideration is given to the delineation of normal sadness and grief from a major depressive episode. Bereavement may induce great suffering, but it does not typically induce an episode of major depressive disorder. When they do occur together, the depressive symptoms and functional impairment tend to be more severe and the prognosis is worse compared with bereavement that is not accompanied by major depressive disorder. Bereavement-related depression tends to occur in persons with other vulnerabilities to depressive disorders, and recovery may be facilitated by antidepressant treatment.

A more chronic form of depression, persistent depressive disorder (dysthymia), can be diagnosed when the mood disturbance continues for at least 2 years in adults or 1 year in children. This diagnosis, new in DSM-5, includes both the DSM-IV diagnostic categories of chronic major depression and dysthymia.

After careful scientific review of the evidence, premenstrual dysphoric disorder has been moved from an appendix of DSM-IV ("Criteria Sets and Axes Provided for Further Study") to Section II of DSM-5. Almost 20 years of additional of research on this condition has confirmed a specific and treatment-responsive form of depressive disorder that begins sometime following ovulation and remits within a few days of menses and has a marked impact on functioning.

A large number of substances of abuse, some prescribed medications, and several medical conditions can be associated with depression-like phenomena. This fact is recognized in the diagnoses of substance/medication-induced depressive disorder and depressive disorder due to another medical condition.

Disruptive Mood Dysregulation Disorder

Diagnostic Criteria **296.99 (F34.8)**

A. Severe recurrent temper outbursts manifested verbally (e.g., verbal rages) and/or behaviorally (e.g., physical aggression toward people or property) that are grossly out of proportion in intensity or duration to the situation or provocation.

B. The temper outbursts are inconsistent with developmental level.

C. The temper outbursts occur, on average, three or more times per week.

D. The mood between temper outbursts is persistently irritable or angry most of the day, nearly every day, and is observable by others (e.g., parents, teachers, peers).

E. Criteria A–D have been present for 12 or more months. Throughout that time, the individual has not had a period lasting 3 or more consecutive months without all of the symptoms in Criteria A–D.

F. Criteria A and D are present in at least two of three settings (i.e., at home, at school, with peers) and are severe in at least one of these.

G. The diagnosis should not be made for the first time before age 6 years or after age 18 years.

H. By history or observation, the age at onset of Criteria A–E is before 10 years.

I. There has never been a distinct period lasting more than 1 day during which the full symptom criteria, except duration, for a manic or hypomanic episode have been met.

Note: Developmentally appropriate mood elevation, such as occurs in the context of a highly positive event or its anticipation, should not be considered as a symptom of mania or hypomania.

J. The behaviors do not occur exclusively during an episode of major depressive disorder and are not better explained by another mental disorder (e.g., autism spectrum disorder, posttraumatic stress disorder, separation anxiety disorder, persistent depressive disorder [dysthymia]).

Note: This diagnosis cannot coexist with oppositional defiant disorder, intermittent explosive disorder, or bipolar disorder, though it can coexist with others, including major depressive disorder, attention-deficit/hyperactivity disorder, conduct disorder, and substance use disorders. Individuals whose symptoms meet criteria for both disruptive mood dysregulation disorder and oppositional defiant disorder should only be given the diagnosis of disruptive mood dysregulation disorder. If an individual has ever experienced a manic or hypomanic episode, the diagnosis of disruptive mood dysregulation disorder should not be assigned.

K. The symptoms are not attributable to the physiological effects of a substance or to another medical or neurological condition.

Diagnostic Features

The core feature of disruptive mood dysregulation disorder is chronic, severe persistent irritability. This severe irritability has two prominent clinical manifestations, the first of which is frequent temper outbursts. These outbursts typically occur in response to frustration and can be verbal or behavioral (the latter in the form of aggression against property, self, or others). They must occur frequently (i.e., on average, three or more times per week) (Criterion C) over at least 1 year in at least two settings (Criteria E and F), such as in the home and at school, and they must be developmentally inappropriate (Criterion B). The second manifestation of severe irritability consists of chronic, persistently irritable or angry mood that is present between the severe temper outbursts. This irritable or angry mood must be characteristic of the child, being present most of the day, nearly every day, and noticeable by others in the child's environment (Criterion D).

The clinical presentation of disruptive mood dysregulation disorder must be carefully distinguished from presentations of other, related conditions, particularly pediatric bipolar disorder. In fact, disruptive mood dysregulation disorder was added to DSM-5 to address the considerable concern about the appropriate classification and treatment of children who present with chronic, persistent irritability relative to children who present with classic (i.e., episodic) bipolar disorder.

Some researchers view severe, non-episodic irritability as characteristic of bipolar disorder in children, although both DSM-IV and DSM-5 require that both children and adults have distinct episodes of mania or hypomania to qualify for the diagnosis of bipolar I disorder. During the latter decades of the 20th century, this contention by researchers that severe, nonepisodic irritability is a manifestation of pediatric mania coincided with an upsurge in the rates at which clinicians assigned the diagnosis of bipolar disorder to their pediatric patients. This sharp increase in rates appears to be attributable to clinicians combining at least two clinical presentations into a single category. That is, both classic, episodic presentations of mania and non-episodic presentations of severe irritability have been labeled as bipolar disorder in children. In DSM-5, the term *bipolar disorder* is explicitly reserved for episodic presentations of bipolar symptoms. DSM-IV did not include a diagnosis designed to capture youths whose hallmark symptoms consisted of very severe, nonepisodic irritability, whereas DSM-5, with the inclusion of disruptive mood dysregulation disorder, provides a distinct category for such presentations.

Prevalence

Disruptive mood dysregulation disorder is common among children presenting to pediatric mental health clinics. Prevalence estimates of the disorder in the community are unclear. Based on rates of chronic and severe persistent irritability, which is the core feature of the disorder, the overall 6-month to 1-year period-prevalence of disruptive mood dysregulation disorder among children and adolescents probably falls in the 2%–5% range. However, rates are expected to be higher in males and school-age children than in females and adolescents.

Development and Course

The onset of disruptive mood dysregulation disorder must be before age 10 years, and the diagnosis should not be applied to children with a developmental age of less than 6 years. It is unknown whether the condition presents only in this age-delimited fashion. Because the symptoms of disruptive mood dysregulation disorder are likely to change as children mature, use of the diagnosis should be restricted to age groups similar to those in which validity has been established (7–18 years). Approximately half of children with severe, chronic irritability will have a presentation that continues to meet criteria for the condition 1 year later. Rates of conversion from severe, nonepisodic irritability to bipolar disorder are very low. Instead, children with chronic irritability are at risk to develop unipolar depressive and/or anxiety disorders in adulthood.

Age-related variations also differentiate classic bipolar disorder and disruptive mood dysregulation disorder. Rates of bipolar disorder generally are very low prior to adolescence (<1%), with a steady increase into early adulthood (1%–2% prevalence). Disruptive mood dysregulation disorder is more common than bipolar disorder prior to adolescence, and symptoms of the condition generally become less common as children transition into adulthood.

Risk and Prognostic Factors

Temperamental. Children with chronic irritability typically exhibit complicated psychiatric histories. In such children, a relatively extensive history of chronic irritability is

common, typically manifesting before full criteria for the syndrome are met. Such prediagnostic presentations may have qualified for a diagnosis of oppositional defiant disorder. Many children with disruptive mood dysregulation disorder have symptoms that also meet criteria for attention-deficit/hyperactivity disorder (ADHD) and for an anxiety disorder, with such diagnoses often being present from a relatively early age. For some children, the criteria for major depressive disorder may also be met.

Genetic and physiological. In terms of familial aggregation and genetics, it has been suggested that children presenting with chronic, non-episodic irritability can be differentiated from children with bipolar disorder in their family-based risk. However, these two groups do not differ in familial rates of anxiety disorders, unipolar depressive disorders, or substance abuse. Compared with children with pediatric bipolar disorder or other mental illnesses, those with disruptive mood dysregulation disorder exhibit both commonalities and differences in information-processing deficits. For example, face-emotion labeling deficits, as well as perturbed decision making and cognitive control, are present in children with bipolar disorder and chronically irritable children, as well as in children with some other psychiatric conditions. There is also evidence for disorder-specific dysfunction, such as during tasks assessing attention deployment in response to emotional stimuli, which has demonstrated unique signs of dysfunction in children with chronic irritability.

Gender-Related Diagnostic Issues

Children presenting to clinics with features of disruptive mood dysregulation disorder are predominantly male. Among community samples, a male preponderance appears to be supported. This difference in prevalence between males and females differentiates disruptive mood dysregulation disorder from bipolar disorder, in which there is an equal gender prevalence.

Suicide Risk

In general, evidence documenting suicidal behavior and aggression, as well as other severe functional consequences, in disruptive mood dysregulation disorder should be noted when evaluating children with chronic irritability.

Functional Consequences of Disruptive Mood Dysregulation Disorder

Chronic, severe irritability, such as is seen in disruptive mood dysregulation disorder, is associated with marked disruption in a child's family and peer relationships, as well as in school performance. Because of their extremely low frustration tolerance, such children generally have difficulty succeeding in school; they are often unable to participate in the activities typically enjoyed by healthy children; their family life is severely disrupted by their outbursts and irritability; and they have trouble initiating or sustaining friendships. Levels of dysfunction in children with bipolar disorder and disruptive mood dysregulation disorder are generally comparable. Both conditions cause severe disruption in the lives of the affected individual and their families. In both disruptive mood dysregulation disorder and pediatric bipolar disorder, dangerous behavior, suicidal ideation or suicide attempts, severe aggression, and psychiatric hospitalization are common.

Differential Diagnosis

Because chronically irritable children and adolescents typically present with complex histories, the diagnosis of disruptive mood dysregulation disorder must be made while considering the presence or absence of multiple other conditions. Despite the need to consider

many other syndromes, differentiation of disruptive mood dysregulation disorder from bipolar disorder and oppositional defiant disorder requires particularly careful assessment.

Bipolar disorders. The central feature differentiating disruptive mood dysregulation disorder and bipolar disorders in children involves the longitudinal course of the core symptoms. In children, as in adults, bipolar I disorder and bipolar II disorder manifest as an episodic illness with discrete episodes of mood perturbation that can be differentiated from the child's typical presentation. The mood perturbation that occurs during a manic episode is distinctly different from the child's usual mood. In addition, during a manic episode, the change in mood must be accompanied by the onset, or worsening, of associated cognitive, behavioral, and physical symptoms (e.g., distractibility, increased goal-directed activity), which are also present to a degree that is distinctly different from the child's usual baseline. Thus, in the case of a manic episode, parents (and, depending on developmental level, children) should be able to identify a distinct time period during which the child's mood and behavior were markedly different from usual. In contrast, the irritability of disruptive mood dysregulation disorder is persistent and is present over many months; while it may wax and wane to a certain degree, severe irritability is characteristic of the child with disruptive mood dysregulation disorder. Thus, while bipolar disorders are episodic conditions, disruptive mood dysregulation disorder is not. In fact, the diagnosis of disruptive mood dysregulation disorder cannot be assigned to a child who has ever experienced a full-duration hypomanic or manic episode (irritable or euphoric) or who has ever had a manic or hypomanic episode lasting more than 1 day. Another central differentiating feature between bipolar disorders and disruptive mood dysregulation disorder is the presence of elevated or expansive mood and grandiosity. These symptoms are common features of mania but are not characteristic of disruptive mood dysregulation disorder.

Oppositional defiant disorder. While symptoms of oppositional defiant disorder typically do occur in children with disruptive mood dysregulation disorder, mood symptoms of disruptive mood dysregulation disorder are relatively rare in children with oppositional defiant disorder. The key features that warrant the diagnosis of disruptive mood dysregulation disorder in children whose symptoms also meet criteria for oppositional defiant disorder are the presence of severe and frequently recurrent outbursts and a persistent disruption in mood between outbursts. In addition, the diagnosis of disruptive mood dysregulation disorder requires severe impairment in at least one setting (i.e., home, school, or among peers) and mild to moderate impairment in a second setting. For this reason, while most children whose symptoms meet criteria for disruptive mood dysregulation disorder will also have a presentation that meets criteria for oppositional defiant disorder, the reverse is not the case. That is, in only approximately 15% of individuals with oppositional defiant disorder would criteria for disruptive mood dysregulation disorder be met. Moreover, even for children in whom criteria for both disorders are met, only the diagnosis of disruptive mood dysregulation disorder should be made. Finally, both the prominent mood symptoms in disruptive mood dysregulation disorder and the high risk for depressive and anxiety disorders in follow-up studies justify placement of disruptive mood dysregulation disorder among the depressive disorders in DSM-5. (Oppositional defiant disorder is included in the chapter "Disruptive, Impulse-Control, and Conduct Disorders.") This reflects the more prominent mood component among individuals with disruptive mood dysregulation disorder, as compared with individuals with oppositional defiant disorder. Nevertheless, it also should be noted that disruptive mood dysregulation disorder appears to carry a high risk for behavioral problems as well as mood problems.

Attention-deficit/hyperactivity disorder, major depressive disorder, anxiety disorders, and autism spectrum disorder. Unlike children diagnosed with bipolar disorder or oppositional defiant disorder, a child whose symptoms meet criteria for disruptive mood dysregulation disorder also can receive a comorbid diagnosis of ADHD, major depressive disorder, and/or anxiety disorder. However, children whose irritability is present only in the context of a major depressive episode or persistent depressive disorder (dysthymia)

should receive one of those diagnoses rather than disruptive mood dysregulation disorder. Children with disruptive mood dysregulation disorder may have symptoms that also meet criteria for an anxiety disorder and can receive both diagnoses, but children whose irritability is manifest only in the context of exacerbation of an anxiety disorder should receive the relevant anxiety disorder diagnosis rather than disruptive mood dysregulation disorder. In addition, children with autism spectrum disorders frequently present with temper outbursts when, for example, their routines are disturbed. In that instance, the temper outbursts would be considered secondary to the autism spectrum disorder, and the child should not receive the diagnosis of disruptive mood dysregulation disorder.

Intermittent explosive disorder. Children with symptoms suggestive of intermittent explosive disorder present with instances of severe temper outbursts, much like children with disruptive mood dysregulation disorder. However, unlike disruptive mood dysregulation disorder, intermittent explosive disorder does not require persistent disruption in mood between outbursts. In addition, intermittent explosive disorder requires only 3 months of active symptoms, in contrast to the 12-month requirement for disruptive mood dysregulation disorder. Thus, these two diagnoses should not be made in the same child. For children with outbursts and intercurrent, persistent irritability, only the diagnosis of disruptive mood dysregulation disorder should be made.

Comorbidity

Rates of comorbidity in disruptive mood dysregulation disorder are extremely high. It is rare to find individuals whose symptoms meet criteria for disruptive mood dysregulation disorder alone. Comorbidity between disruptive mood dysregulation disorder and other DSM-defined syndromes appears higher than for many other pediatric mental illnesses; the strongest overlap is with oppositional defiant disorder. Not only is the overall rate of comorbidity high in disruptive mood dysregulation disorder, but also the range of comorbid illnesses appears particularly diverse. These children typically present to the clinic with a wide range of disruptive behavior, mood, anxiety, and even autism spectrum symptoms and diagnoses. However, children with disruptive mood dysregulation disorder should not have symptoms that meet criteria for bipolar disorder, as in that context, only the bipolar disorder diagnosis should be made. If children have symptoms that meet criteria for oppositional defiant disorder or intermittent explosive disorder *and* disruptive mood dysregulation disorder, only the diagnosis of disruptive mood dysregulation disorder should be assigned. Also, as noted earlier, the diagnosis of disruptive mood dysregulation disorder should not be assigned if the symptoms occur only in an anxiety-provoking context, when the routines of a child with autism spectrum disorder or obsessive-compulsive disorder are disturbed, or in the context of a major depressive episode.

Major Depressive Disorder

Diagnostic Criteria

A. Five (or more) of the following symptoms have been present 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 that are clearly attributable to another medical condition.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observation made by others (e.g., appears tearful). (**Note:** In children and adolescents, can be irritable mood.)
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).

3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. (**Note:** In children, consider failure to make expected weight gain.)
4. Insomnia or hypersomnia nearly every day.
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. Fatigue or loss of energy nearly every day.
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the physiological effects of a substance or to another medical condition.

Note: Criteria A–C represent a major depressive episode.

Note: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgment based on the individual's history and the cultural norms for the expression of distress in the context of loss.[1]

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic episode or a hypomanic episode.

Note: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

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[1] In distinguishing grief from a major depressive episode (MDE), it is useful to consider that in grief the predominant affect is feelings of emptiness and loss, while in MDE it is persistent depressed mood and the inability to anticipate happiness or pleasure. The dysphoria in grief is likely to decrease in intensity over days to weeks and occurs in waves, the so-called pangs of grief. These waves tend to be associated with thoughts or reminders of the deceased. The depressed mood of MDE is more persistent and not tied to specific thoughts or preoccupations. The pain of grief may be accompanied by positive emotions and humor that are uncharacteristic of the pervasive unhappiness and misery characteristic of MDE. The thought content associated with grief generally features a preoccupation with thoughts and memories of the deceased, rather than the self-critical or pessimistic ruminations seen in MDE. In grief, self-esteem is generally preserved, whereas in MDE feelings of worthlessness and self-loathing are common. If self-derogatory ideation is present in grief, it typically involves perceived failings vis-à-vis the deceased (e.g., not visiting frequently enough, not telling the deceased how much he or she was loved). If a bereaved individual thinks about death and dying, such thoughts are generally focused on the deceased and possibly about "joining" the deceased, whereas in MDE such thoughts are focused on ending one's own life because of feeling worthless, undeserving of life, or unable to cope with the pain of depression.

Coding and Recording Procedures

The diagnostic code for major depressive disorder is based on whether this is a single or recurrent episode, current severity, presence of psychotic features, and remission status. Current severity and psychotic features are only indicated if full criteria are currently met for a major depressive episode. Remission specifiers are only indicated if the full criteria are not currently met for a major depressive episode. Codes are as follows:

Severity/course specifier	Single episode	Recurrent episode*
Mild (p. 188)	296.21 (F32.0)	296.31 (F33.0)
Moderate (p. 188)	296.22 (F32.1)	296.32 (F33.1)
Severe (p. 188)	296.23 (F32.2)	296.33 (F33.2)
With psychotic features** (p. 186)	296.24 (F32.3)	296.34 (F33.3)
In partial remission (p. 188)	296.25 (F32.4)	296.35 (F33.41)
In full remission (p. 188)	296.26 (F32.5)	296.36 (F33.42)
Unspecified	296.20 (F32.9)	296.30 (F33.9)

*For an episode to be considered recurrent, there must be an interval of at least 2 consecutive months between separate episodes in which criteria are not met for a major depressive episode. The definitions of specifiers are found on the indicated pages.

**If psychotic features are present, code the "with psychotic features" specifier irrespective of episode severity.

In recording the name of a diagnosis, terms should be listed in the following order: major depressive disorder, single or recurrent episode, severity/psychotic/remission specifiers, followed by as many of the following specifiers without codes that apply to the current episode.

Specify:

With anxious distress (p. 184)
With mixed features (pp. 184–185)
With melancholic features (p. 185)
With atypical features (pp. 185–186)
With mood-congruent psychotic features (p. 186)
With mood-incongruent psychotic features (p. 186)
With catatonia (p. 186). **Coding note:** Use additional code 293.89 (F06.1).
With peripartum onset (pp. 186–187)
With seasonal pattern (recurrent episode only) (pp. 187–188)

Diagnostic Features

The criterion symptoms for major depressive disorder must be present nearly every day to be considered present, with the exception of weight change and suicidal ideation. Depressed mood must be present for most of the day, in addition to being present nearly every day. Often insomnia or fatigue is the presenting complaint, and failure to probe for accompanying depressive symptoms will result in underdiagnosis. Sadness may be denied at first but may be elicited through interview or inferred from facial expression and demeanor. With individuals who focus on a somatic complaint, clinicians should determine whether the distress from that complaint is associated with specific depressive symptoms. Fatigue and sleep disturbance are present in a high proportion of cases; psychomotor disturbances are much less common but are indicative of greater overall severity, as is the presence of delusional or near-delusional guilt.

The essential feature of a major depressive episode is a period of at least 2 weeks during which there is either depressed mood or the loss of interest or pleasure in nearly all activities (Criterion A). In children and adolescents, the mood may be irritable rather than sad. The individual must also experience at least four additional symptoms drawn from a list that includes changes in appetite or weight, sleep, and psychomotor activity; decreased energy; feelings of worthlessness or guilt; difficulty thinking, concentrating, or making decisions; or recurrent thoughts of death or suicidal ideation or suicide plans or attempts. To count toward a major depressive episode, a symptom must either be newly present or must have clearly worsened compared with the person's pre-episode status. The symptoms must persist for most of the day, nearly every day, for at least 2 consecutive weeks. The episode must be accompanied by clinically significant distress or impairment in social, occupational, or other important areas of functioning. For some individuals with milder episodes, functioning may appear to be normal but requires markedly increased effort.

The mood in a major depressive episode is often described by the person as depressed, sad, hopeless, discouraged, or "down in the dumps" (Criterion A1). In some cases, sadness may be denied at first but may subsequently be elicited by interview (e.g., by pointing out that the individual looks as if he or she is about to cry). In some individuals who complain of feeling "blah," having no feelings, or feeling anxious, the presence of a depressed mood can be inferred from the person's facial expression and demeanor. Some individuals emphasize somatic complaints (e.g., bodily aches and pains) rather than reporting feelings of sadness. Many individuals report or exhibit increased irritability (e.g., persistent anger, a tendency to respond to events with angry outbursts or blaming others, an exaggerated sense of frustration over minor matters). In children and adolescents, an irritable or cranky mood may develop rather than a sad or dejected mood. This presentation should be differentiated from a pattern of irritability when frustrated.

Loss of interest or pleasure is nearly always present, at least to some degree. Individuals may report feeling less interested in hobbies, "not caring anymore," or not feeling any enjoyment in activities that were previously considered pleasurable (Criterion A2). Family members often notice social withdrawal or neglect of pleasurable avocations (e.g., a formerly avid golfer no longer plays, a child who used to enjoy soccer finds excuses not to practice). In some individuals, there is a significant reduction from previous levels of sexual interest or desire.

Appetite change may involve either a reduction or increase. Some depressed individuals report that they have to force themselves to eat. Others may eat more and may crave specific foods (e.g., sweets or other carbohydrates). When appetite changes are severe (in either direction), there may be a significant loss or gain in weight, or, in children, a failure to make expected weight gains may be noted (Criterion A3).

Sleep disturbance may take the form of either difficulty sleeping or sleeping excessively (Criterion A4). When insomnia is present, it typically takes the form of middle insomnia (i.e., waking up during the night and then having difficulty returning to sleep) or terminal insomnia (i.e., waking too early and being unable to return to sleep). Initial insomnia (i.e., difficulty falling asleep) may also occur. Individuals who present with oversleeping (hypersomnia) may experience prolonged sleep episodes at night or increased daytime sleep. Sometimes the reason that the individual seeks treatment is for the disturbed sleep.

Psychomotor changes include agitation (e.g., the inability to sit still, pacing, handwringing; or pulling or rubbing of the skin, clothing, or other objects) or retardation (e.g., slowed speech, thinking, and body movements; increased pauses before answering; speech that is decreased in volume, inflection, amount, or variety of content, or muteness) (Criterion A5). The psychomotor agitation or retardation must be severe enough to be observable by others and not represent merely subjective feelings.

Decreased energy, tiredness, and fatigue are common (Criterion A6). A person may report sustained fatigue without physical exertion. Even the smallest tasks seem to require

substantial effort. The efficiency with which tasks are accomplished may be reduced. For example, an individual may complain that washing and dressing in the morning are exhausting and take twice as long as usual.

The sense of worthlessness or guilt associated with a major depressive episode may include unrealistic negative evaluations of one's worth or guilty preoccupations or ruminations over minor past failings (Criterion A7). Such individuals often misinterpret neutral or trivial day-to-day events as evidence of personal defects and have an exaggerated sense of responsibility for untoward events. The sense of worthlessness or guilt may be of delusional proportions (e.g., an individual who is convinced that he or she is personally responsible for world poverty). Blaming oneself for being sick and for failing to meet occupational or interpersonal responsibilities as a result of the depression is very common and, unless delusional, is not considered sufficient to meet this criterion.

Many individuals report impaired ability to think, concentrate, or make even minor decisions (Criterion A8). They may appear easily distracted or complain of memory difficulties. Those engaged in cognitively demanding pursuits are often unable to function. In children, a precipitous drop in grades may reflect poor concentration. In elderly individuals, memory difficulties may be the chief complaint and may be mistaken for early signs of a dementia ("pseudodementia"). When the major depressive episode is successfully treated, the memory problems often fully abate. However, in some individuals, particularly elderly persons, a major depressive episode may sometimes be the initial presentation of an irreversible dementia.

Thoughts of death, suicidal ideation, or suicide attempts (Criterion A9) are common. They may range from a passive wish not to awaken in the morning or a belief that others would be better off if the individual were dead, to transient but recurrent thoughts of committing suicide, to a specific suicide plan. More severely suicidal individuals may have put their affairs in order (e.g., updated wills, settled debts), acquired needed materials (e.g., a rope or a gun), and chosen a location and time to accomplish the suicide. Motivations for suicide may include a desire to give up in the face of perceived insurmountable obstacles, an intense wish to end what is perceived as an unending and excruciatingly painful emotional state, an inability to foresee any enjoyment in life, or the wish to not be a burden to others. The resolution of such thinking may be a more meaningful measure of diminished suicide risk than denial of further plans for suicide.

The evaluation of the symptoms of a major depressive episode is especially difficult when they occur in an individual who also has a general medical condition (e.g., cancer, stroke, myocardial infarction, diabetes, pregnancy). Some of the criterion signs and symptoms of a major depressive episode are identical to those of general medical conditions (e.g., weight loss with untreated diabetes; fatigue with cancer; hypersomnia early in pregnancy; insomnia later in pregnancy or the postpartum). Such symptoms count toward a major depressive diagnosis except when they are clearly and fully attributable to a general medical condition. Nonvegetative symptoms of dysphoria, anhedonia, guilt or worthlessness, impaired concentration or indecision, and suicidal thoughts should be assessed with particular care in such cases. Definitions of major depressive episodes that have been modified to include only these nonvegetative symptoms appear to identify nearly the same individuals as do the full criteria.

Associated Features Supporting Diagnosis

Major depressive disorder is associated with high mortality, much of which is accounted for by suicide; however, it is not the only cause. For example, depressed individuals admitted to nursing homes have a markedly increased likelihood of death in the first year. Individuals frequently present with tearfulness, irritability, brooding, obsessive rumination, anxiety, phobias, excessive worry over physical health, and complaints of pain (e.g., headaches; joint, abdominal, or other pains). In children, separation anxiety may occur.

Although an extensive literature exists describing neuroanatomical, neuroendocrinological, and neurophysiological correlates of major depressive disorder, no laboratory test has yielded results of sufficient sensitivity and specificity to be used as a diagnostic tool for this disorder. Until recently, hypothalamic-pituitary-adrenal axis hyperactivity had been the most extensively investigated abnormality associated with major depressive episodes, and it appears to be associated with melancholia, psychotic features, and risks for eventual suicide. Molecular studies have also implicated peripheral factors, including genetic variants in neurotrophic factors and pro-inflammatory cytokines. Additionally, functional magnetic resonance imaging studies provide evidence for functional abnormalities in specific neural systems supporting emotion processing, reward seeking, and emotion regulation in adults with major depression.

Prevalence

Twelve-month prevalence of major depressive disorder in the United States is approximately 7%, with marked differences by age group such that the prevalence in 18- to 29-year-old individuals is threefold higher than the prevalence in individuals age 60 years or older. Females experience 1.5- to 3-fold higher rates than males beginning in early adolescence.

Development and Course

Major depressive disorder may first appear at any age, but the likelihood of onset increases markedly with puberty. In the United States, incidence appears to peak in the 20s; however, first onset in late life is not uncommon.

The course of major depressive disorder is quite variable, such that some individuals rarely, if ever, experience remission (a period of 2 or more months with no symptoms, or only one or two symptoms to no more than a mild degree), while others experience many years with few or no symptoms between discrete episodes. It is important to distinguish individuals who present for treatment during an exacerbation of a chronic depressive illness from those whose symptoms developed recently. Chronicity of depressive symptoms substantially increases the likelihood of underlying personality, anxiety, and substance use disorders and decreases the likelihood that treatment will be followed by full symptom resolution. It is therefore useful to ask individuals presenting with depressive symptoms to identify the last period of at least 2 months during which they were entirely free of depressive symptoms.

Recovery typically begins within 3 months of onset for two in five individuals with major depression and within 1 year for four in five individuals. Recency of onset is a strong determinant of the likelihood of near-term recovery, and many individuals who have been depressed only for several months can be expected to recover spontaneously. Features associated with lower recovery rates, other than current episode duration, include psychotic features, prominent anxiety, personality disorders, and symptom severity.

The risk of recurrence becomes progessively lower over time as the duration of remission increases. The risk is higher in individuals whose preceding episode was severe, in younger individuals, and in individuals who have already experienced multiple episodes. The persistence of even mild depressive symptoms during remission is a powerful predictor of recurrence.

Many bipolar illnesses begin with one or more depressive episodes, and a substantial proportion of individuals who initially appear to have major depressive disorder will prove, in time, to instead have a bipolar disorder. This is more likely in individuals with onset of the illness in adolescence, those with psychotic features, and those with a family history of bipolar illness. The presence of a "with mixed features" specifier also increases the risk for future manic or hypomanic diagnosis. Major depressive disorder, particularly with psychotic features, may also transition into schizophrenia, a change that is much more frequent than the reverse.

Despite consistent differences between genders in prevalence rates for depressive disorders, there appear to be no clear differences by gender in phenomenology, course, or treatment response. Similarly, there are no clear effects of current age on the course or treatment response of major depressive disorder. Some symptom differences exist, though, such that hypersomnia and hyperphagia are more likely in younger individuals, and melancholic symptoms, particularly psychomotor disturbances, are more common in older individuals. The likelihood of suicide attempts lessens in middle and late life, although the risk of completed suicide does not. Depressions with earlier ages at onset are more familial and more likely to involve personality disturbances. The course of major depressive disorder within individuals does not generally change with aging. Mean times to recovery appear to be stable over long periods, and the likelihood of being in an episode does not generally increase or decrease with time.

Risk and Prognostic Factors

Temperamental. Neuroticism (negative affectivity) is a well-established risk factor for the onset of major depressive disorder, and high levels appear to render individuals more likely to develop depressive episodes in response to stressful life events.

Environmental. Adverse childhood experiences, particularly when there are multiple experiences of diverse types, constitute a set of potent risk factors for major depressive disorder. Stressful life events are well recognized as precipitants of major depressive episodes, but the presence or absence of adverse life events near the onset of episodes does not appear to provide a useful guide to prognosis or treatment selection.

Genetic and physiological. First-degree family members of individuals with major depressive disorder have a risk for major depressive disorder two- to fourfold higher than that of the general population. Relative risks appear to be higher for early-onset and recurrent forms. Heritability is approximately 40%, and the personality trait neuroticism accounts for a substantial portion of this genetic liability.

Course modifiers. Essentially all major nonmood disorders increase the risk of an individual developing depression. Major depressive episodes that develop against the background of another disorder often follow a more refractory course. Substance use, anxiety, and borderline personality disorders are among the most common of these, and the presenting depressive symptoms may obscure and delay their recognition. However, sustained clinical improvement in depressive symptoms may depend on the appropriate treatment of underlying illnesses. Chronic or disabling medical conditions also increase risks for major depressive episodes. Such prevalent illnesses as diabetes, morbid obesity, and cardiovascular disease are often complicated by depressive episodes, and these episodes are more likely to become chronic than are depressive episodes in medically healthy individuals.

Cuiture-Related Diagnostlc Issues

Surveys of major depressive disorder across diverse cultures have shown sevenfold differences in 12-month prevalence rates but much more consistency in female-to-male ratio, mean ages at onset, and the degree to which presence of the disorder raises the likelihood of comorbid substance abuse. While these findings suggest substantial cultural differences in the expression of major depressive disorder, they do not permit simple linkages between particular cultures and the likelihood of specific symptoms. Rather, clinicians should be aware that in most countries the majority of cases of depression go unrecognized in primary care settings and that in many cultures, somatic symptoms are very likely to constitute the presenting complaint. Among the Criterion A symptoms, insomnia and loss of energy are the most uniformly reported.

Gender-Related Diagnostic Issues

Although the most reproducible finding in the epidemiology of major depressive disorder has been a higher prevalence in females, there are no clear differences between genders in symptoms, course, treatment response, or functional consequences. In women, the risk for suicide attempts is higher, and the risk for suicide completion is lower. The disparity in suicide rate by gender is not as great among those with depressive disorders as it is in the population as a whole.

Suicide Risk

The possibility of suicidal behavior exists at all times during major depressive episodes. The most consistently described risk factor is a past history of suicide attempts or threats, but it should be remembered that most completed suicides are not preceded by unsuccessful attempts. Other features associated with an increased risk for completed suicide include male sex, being single or living alone, and having prominent feelings of hopelessness. The presence of borderline personality disorder markedly increases risk for future suicide attempts.

Functional Consequences of Major Depressive Disorder

Many of the functional consequences of major depressive disorder derive from individual symptoms. Impairment can be very mild, such that many of those who interact with the affected individual are unaware of depressive symptoms. Impairment may, however, range to complete incapacity such that the depressed individual is unable to attend to basic self-care needs or is mute or catatonic. Among individuals seen in general medical settings, those with major depressive disorder have more pain and physical illness and greater decreases in physical, social, and role functioning.

Differential Diagnosis

Manic episodes with irritable mood or mixed episodes. Major depressive episodes with prominent irritable mood may be difficult to distinguish from manic episodes with irritable mood or from mixed episodes. This distinction requires a careful clinical evaluation of the presence of manic symptoms.

Mood disorder due to another medical condition. A major depressive episode is the appropriate diagnosis if the mood disturbance is not judged, based on individual history, physical examination, and laboratory findings, to be the direct pathophysiological consequence of a specific medical condition (e.g., multiple sclerosis, stroke, hypothyroidism).

Substance/medication-induced depressive or bipolar disorder. This disorder is distinguished from major depressive disorder by the fact that a substance (e.g., a drug of abuse, a medication, a toxin) appears to be etiologically related to the mood disturbance. For example, depressed mood that occurs only in the context of withdrawal from cocaine would be diagnosed as cocaine-induced depressive disorder.

Attention-deficit/hyperactivity disorder. Distractibility and low frustration tolerance can occur in both attention-deficit/ hyperactivity disorder and a major depressive episode; if the criteria are met for both, attention-deficit/hyperactivity disorder may be diagnosed in addition to the mood disorder. However, the clinician must be cautious not to overdiagnose a major depressive episode in children with attention-deficit/hyperactivity disorder whose disturbance in mood is characterized by irritability rather than by sadness or loss of interest.

Adjustment disorder with depressed mood. A major depressive episode that occurs in response to a psychosocial stressor is distinguished from adjustment disorder with depressed mood by the fact that the full criteria for a major depressive episode are not met in adjustment disorder.

Sadness. Finally, periods of sadness are inherent aspects of the human experience. These periods should not be diagnosed as a major depressive episode unless criteria are met for severity (i.e., five out of nine symptoms), duration (i.e., most of the day, nearly every day for at least 2 weeks), and clinically significant distress or impairment. The diagnosis other specified depressive disorder may be appropriate for presentations of depressed mood with clinically significant impairment that do not meet criteria for duration or severity.

Comorbidity

Other disorders with which major depressive disorder frequently co-occurs are substance-related disorders, panic disorder, obsessive-compulsive disorder, anorexia nervosa, bulimia nervosa, and borderline personality disorder.

Persistent Depressive Disorder (Dysthymia)

Diagnostic Criteria **300.4 (F34.1)**

This disorder represents a consolidation of DSM-IV-defined chronic major depressive disorder and dysthymic disorder.

A. Depressed mood for most of the day, for more days than not, as indicated by either subjective account or observation by others, for at least 2 years.

   Note: In children and adolescents, mood can be irritable and duration must be at least 1 year.

B. Presence, while depressed, of two (or more) of the following:

   1. Poor appetite or overeating.
   2. Insomnia or hypersomnia.
   3. Low energy or fatigue.
   4. Low self-esteem.
   5. Poor concentration or difficulty making decisions.
   6. Feelings of hopelessness.

C. During the 2-year period (1 year for children or adolescents) of the disturbance, the individual has never been without the symptoms in Criteria A and B for more than 2 months at a time.

D. Criteria for a major depressive disorder may be continuously present for 2 years.

E. There has never been a manic episode or a hypomanic episode, and criteria have never been met for cyclothymic disorder.

F. The disturbance is not better explained by a persistent schizoaffective disorder, schizophrenia, delusional disorder, or other specified or unspecified schizophrenia spectrum and other psychotic disorder.

G. The symptoms are not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g. hypothyroidism).

H. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: Because the criteria for a major depressive episode include four symptoms that are absent from the symptom list for persistent depressive disorder (dysthymia), a very limited