HETEROGENEITY OF MOOD DISORDERS

Terminology Mood disorders are characterized by pervasive dysregulation of mood and psychomotor activity and by related biorhythmic and cognitive disturbances. The rubric of “affective disorder,” which in some European classifications also subsumes morbid anxiety states, is increasingly being replaced by the nosologically more delimited concept of “mood disorder.” Thus mood disorder is now the preferred term in both the World Health Organization's (WHO's) 10th revision of International Statistical Classification of Diseases and Related Health Problems (ICD-10) and the American Psychiatric Association's (APA's) fourth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Official mood disorder categories in current use include bipolar disorders (with manic or hypomanic, depressive, or mixed episodes) and major depressive disorders and their respective attenuated variants known as cyclothymic and dysthymic disorders. Conditions that in earlier editions of these manuals were categorized as “endogenous depression,” “involutional melancholia,” and “psychotic depressive reaction” have been incorporated into major depressive disorder, whereas “depressive neurosis” has been largely absorbed by dysthymic disorder. Although the neurotic-endogenous distinction has been officially deleted, the term “melancholic features” is now used to qualify major depressive disorders in which biological concomitants predominate. While both the American and international classifications recognize the common occurrence of mixed anxiety-depressions, whether they should be classified with mood disorders or with anxiety disorders remains unresolved. It is equally uncertain how to classify the classic neurasthenic conditions, which have recently reemerged and overlap to some extent with the so-called chronic fatigue syndrome.

Destigmatization The reshuffling and reclassification of various affective conditions into the mood disorders chapter of the third edition of DSM (DSM-III) and DSM-IV has, on balance, considerably broadened their boundaries. This change reflects, in part, new developments in pharmacotherapy that have resulted in considerable alleviation of suffering for persons whose illnesses fall short of and sometimes beyond the boundaries of classic mood disorders. As a result, many persons with recurrent mood disorders who would have been disabled can now lead productive lives. Such gratifying results have, in turn, helped to destigmatize this group of disorders. Destigmatization has been further facilitated by published self-revelations of famous persons with depressive and bipolar disorders.
Spectrum of Mood Disorders As often happens when new therapeutic interventions prove successful, the past two decades have witnessed an increased readiness to diagnose mood disorders and their variants. These developments should not be dismissed as mere therapeutic fad, however. External validating strategies, such as familial-genetic studies and prospective follow-up, can now be used to buttress the broadened concept of mood disorders. New research comparing monozygotic and dizygotic twins has demonstrated that the genetic propensity to mood disorders embraces entities that extend beyond endogenous depression (melancholia in DSM-IV) to subsume a larger variety of depressions, including some encountered in persons in the community who have never received psychiatric treatment. Although such data might seem counterintuitive to those who would restrict depression to a core primary biological disease, they suggest that the constitutional predisposition for affective dysregulation occurs in as many as one of every three persons. That ratio is similar to the proportion of those who progress to a full depressive syndrome following bereavement, of rhesus monkeys developing depressive-like behavior following a separation paradigm, and of dogs who develop learned helplessness after inescapable shock. The fact that these rates are considerably higher than one observes in clinical populations suggests that many subjects possess protective factors against major depressive episodes; alternatively, the data suggest that other factors determine which person with emotional distress will become a clinical case. A great deal might therefore be revealed about the nature of pathological affective processes through study of self-limiting affective conditions on the border of mood disorders.

The suffering and dysfunction resulting from mood disorders are among the most common reasons for consulting psychiatrists and other physicians. In fully developed cases, all activity stops—including creative powers—and life is grim and in total disarray (as portrayed in Dürer's masterpiece, Fig. 14.6-1).

FIGURE 14.6-1 Melancholia (1514) by Albrecht Dürer.

All great physicians of the past, beginning with Hippocrates, have devoted considerable space in their general medical texts to the clinical characterization of melancholic and manic states, as well as alternations in the same patient. Greco-Roman medicine recognized a broad spectrum of affective disturbances, ranging from the relatively mild temperamental variants (represented in the official nosology by dysthymic and cyclothymic disorders) to their severest forms (including what today is considered mood disorder with mood-congruent and mood-incongruent psychotic features). The ancients also recognized the intimate relation of morbid states of fear to melancholia. Furthermore, they noted that melancholia and certain physical diseases shared seasonal incidence and described the common occurrence of alcohol indulgence, especially in those prone to mania.

Boundaries The boundaries between temperament (personality) and mood disorder, grief and melancholia, anxiety and depressive states, depressive and bipolar disorders, mood-congruent and mood-incongruent psychotic features, and other (schizophrenic) psychotic conditions remain unresolved. Mood disorders have long been known to be highly comorbid with alcohol use and somatic disease; these trends continue today, with the addition of substance use disorders.

AFFECTS, MOODS, TEMPERAMENTS, AND MORBID MOOD STATES
Ethological Considerations Affects and moods refer to different aspects of emotion. Affect is communicated through facial expression, vocal inflection, gestures, and posture and (according to current ethological research) is intended to move human beings and other primates to appraise whether a person is satisfied, distressed, disgusted, or in danger. Thus joy, sadness, anger, and fear are basic affects that serve a communicative function in primates as well as many other mammalian species.

Affects tend to be short-lived expressions, reflecting momentary emotional contingencies. Moods convey sustained emotions; their more-enduring nature means that they are experienced long enough to be felt inwardly. Moods are also manifested in subtle ways, and their accurate assessment often requires empathic understanding by the interviewer. The words that subjects use to describe their inner emotions may or may not coincide with the technical terms used by researchers or clinicians and often vary from one culture to another. Furthermore, the inward emotion and the prevailing affective tone may be discordant. This conflict could be due to deliberate simulation (i.e., the subject does not wish to reveal his or her inner emotion) or it could result from a pathological lesion or process that has altered the emotions and their neural substrates. Thus, evaluating moods and affective expression requires considerable clinical experience.

Sadness and Joy The normal emotions of sadness and joy are part of everyday life and should be differentiated from major depressive disorder and mania. Sadness, or normal depression, is a universal human response to defeat, disappointment, or other adversities. The response may be adaptive, in an evolutionary sense, by permitting withdrawal to conserve inner resources, or it might signal the need for support from significant others. Transient depressive periods also occur as reactions to certain holidays or anniversaries, as well as during the premenstrual phase and the first week postpartum. Termed, respectively, “holiday blues,” “anniversary reactions,” “premenstrual tension disorder” and “maternity blues,” they are not psychopathological per se, but those predisposed to mood disorder may develop clinical depression during such times.

Premenstrual Dysphoric Mood Changes In view of the higher prevalence of depressive disorders in women, premenstrual affective changes—dysphoria, tension, irritability, hostility, and labile mood—have received both clinical and research attention. The attempt to establish a specific premenstrual dysphoric disorder has neglected the not uncommon occurrence of premenstrual euphoria, increased energy, and sexual drive. The not uncommon occurrence of these positive emotions, along with the labile mixed affective manifestations, tend to point toward a “bipolar” phenomenon. Although women with severe premenstrual complaints appear to have higher rates of lifetime major mood disorders, a recent twin study found that genetic and environmental factors contributing to premenstrual depression and major depressive disorders are largely distinct. Furthermore, events such as migraine, epileptic attacks, and panic states may, in some instances, be associated with the premenstrual phase. The foregoing considerations suggest the hypothesis that premenstrual psychobiological changes exacerbate different neuropsychiatric disorders to which women are otherwise predisposed. Whether the exaggerated premenstrual variability in emotional equilibrium constitutes a variant of mood disorder must await more definitive studies.

Grief Normal bereavement or grief, considered the prototype of reactive depression, occurs in response to significant separations and losses such as death, divorce, romantic disappointment, leaving familiar environments, forced emigration, or civilian catastrophes. DSM-IV tends to limit the concept of normal grief to loss due to death. However, the work of Elie Karam and colleagues showed that losses associated with the civil war in Lebanon served as potent forces in depression formation. In addition to depressed affect appropriate to the loss, bereavement reactions are characterized by the prominence of sympathetic arousal and restlessness, believed to represent (from an evolutionary perspective) physiological and behavioral mechanisms to facilitate the search for the lost object. Like other adversities, bereavement and loss do not generally seem to cause depressive disorder, except in those
predisposed to mood disorder.

**Elation** The positive emotion of elation is popularly linked to success and achievement. However, paradoxical depressions may also follow such positive events, possibly because of the increased responsibilities that often have to be faced alone. Elation is conceptualized psychodynamically as a defense against depression or as a denial of the pain of loss, as exemplified by the so-called maniacal grief, a rare form of bereavement reaction in which elated hyperactivity may replace the expected grief.

Other pseudomanic states include the brief energetic and unusually lucid periods encountered in dying patients or in those who need to take superhuman action in the face of unusual duress, both of which have been conceptualized as “flight into health.” In predisposed persons such reactions might be the prelude to a genuine manic episode. Sleep deprivation, which commonly accompanies major stressors, might represent one of the intermediary mechanisms between stressor and adverse clinical outcome.

**Affective Temperaments** Another mediating factor between normal and pathological moods is temperament. Most persons have a characteristic pattern of basal affective oscillations that defines their temperament. For instance, some are easily moved to tears by sad or happy circumstances, whereas others tend to remain placid. Normally oscillations in affective tone are relatively minor, tend to resonate with day-to-day events, and do not interfere with functioning. Some exhibit greater variability of emotional responses whereby, with no obvious provocation, the person alternates between normal mood and sadness or elation, or both. Temperaments tend to cluster into basic types, four of which are of the greatest relevance to mood disorders. The depressive temperament, in which the person easily swings into the sad direction, occurs in 3 to 6 percent of the general population; the hyperthymic temperament, in which the person is naturally inclined toward cheerful moods has been reported in 4 to 8 percent and the cyclothymic temperament swinging between cheerful and sad moods characterizes 4 to 6 percent of young adults. All three types have an early insidious onset and tend to persist throughout adult life. An irritable-explosive type occurs in 2 to 3 percent of young subjects and tends to attenuate by middle age.

An examination of the traits associated with these temperaments can provide the rationale for Ernst Kretschmer's hypothesis about the social functions they served. Thus, the person with a depressive temperament is hard working, dependable, and suitable for jobs that require long periods of devotion to meticulous detail (**Table 14.6-1**). Such persons shoulder the burdens of existence without experiencing its pleasures. A person with the hyperthymic temperament, endowed with high levels of energy, extroversion, and humor (**Table 14.6-1**), will assume leadership positions in society or excel in the performing arts or entertainment. In talented persons the cyclothymic temperament, which alternates between sadness and elation, could provide the inspiration and the intensity needed for composing music, painting, or writing poetry. One with the irritable temperament, probably a variant of the cyclothymic type, might be best suited for a military career or even revolutionary action. The danger with such temperaments is that they could swing too far in one or the other direction, or in both directions (i.e., major depressive, manic, or mixed episodes). Use of such substances as alcohol, caffeine, and other stimulants might further destabilize affective regulation in persons with those attributes. Some adolescent girls with the irritable temperament might develop the extreme emotional disequilibrium that in contemporary psychiatry is considered borderline personality disorder.

**Table 14.6-1** Attributes, Assets and Liabilities of Depressive and Hyperthymic Temperaments
Morbid Mood States  Mood disorders represent abnormal or extreme variations of mood and associated manifestations and are characterized by the following features.

Pathological Mood Change  Pathological moods are distinguished from their normal counterparts by being out of proportion to any concurrent stressor or situation; being unresponsive to reassurance; being sustained for weeks, months, and sometimes years; and having a pervasive effect on the person, such that judgment is seriously influenced by the mood.

Endoreactive Moods  Depression and mania are diagnosed, respectively, when sadness or elation is overly intense and continues beyond the expected impact of a stressful life event. Indeed the morbid mood might arise without apparent or significant life stress. The pathological process in mood disorders is thus partly defined by the ease with which an intense emotional state is released and especially by its tendency to persist autonomously even when the offending stressor is no longer operative. Rather than being endogenous (i.e., occurring in the absence of precipitants), mood disorders are best conceptualized as endoreactive (i.e., once released, they tend to persist autonomously). The homeostatic dyscontrol of mood, which is part of a more pervasive mood dysregulation, resists reversal to the habitual baseline affective tone. DSM-IV, which tends to disparage theory and adhere to a descriptive level of operationalization, gives insufficient weight to this fundamental characteristic of mood disorders.

Recurrence  In a more descriptive vein, what sets mood disorders apart from their normal emotional counterparts is the clustering of signs and symptoms into discrete syndromes that typically recur on an episodic basis or pursue an intermittent, subthreshold course over the span of many years, if not a lifetime. Cyclic course and in some cases regular recurrence, or periodicity, are other signs of mood dysregulation particularly relevant to bipolar disorder.

Impairment  Normative reactions to adversity and stress, including biological stress, typically consist of transient admixtures of anxiety and dysphoria that are best captured under the DSM-IV rubric of adjustment disorder with mixed emotional features. That is, the self-limiting reactions are best qualified broadly as normal affective states that produce little, if any, impairment in the main areas of functioning.

Although anxiety, irritability, and anger do occur in various types of mood disorders, pathologically sustained mood states of depression and elation characterize those disorders. Morbid mood states (mood disorders) then consist of protracted emotional reactions that deepen or escalate, respectively, into clinical depression or mania, with a tendency to recur or evolve into unremitting chronicity in 15 to 20 percent of cases. The contribution of temperamental peculiarities to such outcomes should be apparent. The impaired functioning characteristic of mood disorders is thus based on a combination of factors, including severity, autonomy, recurrence, and chronicity of the clinical features.

To recapitulate, dysregulation in mood disorders can take different forms. It could be expressed as a single severe episode that persists autonomously for many months and sometimes years or it might recur with episodes of varying severity, years apart or in rapid succession, with or without interepisodic
remission. In general, the earlier the age at onset, the more likely are recurrences, especially those of bipolar nature. Thus, depending on the course of the illness, impairment could be state dependent and occur during an episode or it could extend into the interepisodic period. According to National Institute of Mental Health (NIMH) estimates, on average, a woman with bipolar disorder spends 12 years in florid episodes (often hospitalized), loses 14 years from a productive career and motherhood, and has her life curtailed by 9 years.

Recent observations have also revealed another pattern of impairment. In dysthymic and cyclothymic disorders, which represent an intensification of temperamental instability, impairment is not due to the severity of the mood disturbance per se, but to the cumulative impact of the dysregulation beginning in the juvenile or early adult years and continuing unabated or intermittently over long periods; hence the frequent confusion with character pathology. Here the impairment is more subtle but nonetheless pervasive. Persons with cyclothymic disorder tend to be dilettantes, whereas those with dysthymic disorder often lead morose and colorless lives.

**PSYCHOPATHOLOGY**

**Depressive Syndrome** Like other illnesses, depressive disorder clusters into signs and symptoms that constitute what DSM-IV and ICD-10 term major depressive episode (Tables 14.6-2). These criteria attempt to set an operational threshold for depressive disorder based on a specified number of items and their temporal patterns. The diagnosis of clinical depression cannot be accomplished by a checklist: The DSM-IV diagnostic criteria for major depressive disorder provide only a general guide. Only after an in-depth phenomenological approach can a clinician ascertain diagnosis of a depressive disorder. Disturbances in all four spheres (mood, psychomotor activity, cognitive, and vegetative) should be ordinarily present for a definitive diagnosis of major depressive disorder, although that is not specified in DSM-IV.

**Table 14.6-2 DSM-IV Criteria for Major Depressive Episode**

**Mood Disturbances** Mood change, usually considered the sine qua non of morbid depression, appears in a variety of disturbances, including (1) painful arousal, (2) hypersensitivity to unpleasant events, (3) insensitivity to pleasant events, (4) insensitivity to unpleasant events, (5) reduced anticipatory pleasure, (6) anhedonia or reduced consummatory pleasure, (7) affective blunting, and (8) apathy. The phenomenology and psychometric properties of this broad range of mood disturbances are under investigation at the Salpêtrière Hospital in Paris. Our focus here is primarily on painfully aroused mood (depression) and diminished capacity for pleasure (anhedonia), two mood disturbances given selective weight in DSM-IV and ICD-10.

**DEPRESSED MOOD** The term “depressed mood” refers to negative affective arousal, variously described as depressed, anguished, mournful, irritable, or anxious. These terms tend to trivialize a morbidly painful emotion, typically experienced as worse than the severest physical pain. Thus depressed mood has a somatic quality that in the extreme is indescribably painful. Even when not so
severe, depressive suffering is qualitatively distinct from its neurotic counterparts, taking the form of
groundless apprehensions with severe inner turmoil and torment. This description is particularly apt for
middle-aged and elderly persons, who were once considered to be suffering from “involutional
melancholia.” The sustained nature of the mood permits no respite, although it tends to lift somewhat in
the evening. Suicide may represent an attempt to find deliverance from such unrelenting psychic
torment; death can be experienced as comforting (Fig. 14.6-2).

 Patients with a milder form of the malady typically seen in primary care settings might deny
experiencing mournful moods and instead complain of physical agony from headache (Fig. 14.6-3),
epigastric pain, precordial distress, and so on, in the absence of any evidence of diagnosable physical
illness. Such conditions have been described as “depressio sine depressione,” or “masked depression.”
In such cases, commonly observed in older patients, the physician should corroborate the presence of
mood disturbance by the depressed affect in the patient's facial expression, voice, and overall
appearance.

 ANHEDONIA AND LOSS OF INTEREST Paradoxically, the heightened perception of pain in many
persons with depressive disorder is accompanied by an inability to experience normal emotions. Patients
exhibiting the disturbance may lose the capacity to cry, a deficit that is reversed as the depression is
lifting.

 In evaluating anhedonia inquiring whether the patient has lost the sense of pleasure is not enough; the
clinician must document that the patient has actually given up previously enjoyed pastimes. When mild,
ahedonia evidences with decreased interest in life. Later, patients complain that they have lost all
interest in things. This is best illustrated by William Shakespeare in Hamlet's disgust: “How weary,
stale, flat, and unprofitable seem to me all the uses of the world” (Act I, Scene II). In the extreme,
patients lose their feelings for their children or spouses, who once were a source of joy. Thus the
hedonic deficit in clinical depression might represent a special instance of a more pervasive inability to
experience emotions.

 Patients with severe depression may complain of being emotionally cut off from others and experience
depersonalization and a world that seems strange to them (derealization). The impact of the loss of emotional resonance can be so pervasive that patients may denounce values and beliefs that had previously given meaning to their lives. For instance, members of the clergy might present with the complaint that they no longer believe in the Church, that they have lost God. The inability of the person with depressive disorder to experience normal emotions (commonly observed among young depressed patients) differs from the schizophrenic patient's flat affect in that the loss of emotions is itself experienced as painful; that is, the patient suffers immensely from the inability to experience emotions.

Psychomotor Disturbances In depression psychomotor changes consist of abnormalities in the motor expression of mental and emotional activity. In severe cases, these changes manifest in specific facial features (Fig. 14.6-4).

FIGURE 14.6-4 The Swiss neuropsychiatrist Otto Veraguth described a peculiar triangle-shaped fold in the nasal corner of the upper eyelid. The fold, often associated with depression, is referred to as Veraguth's fold. The photograph illustrates this physiognomic feature in a 50-year-old man during a major depressive episode. Veraguth's fold may also be seen in persons who are not clinically depressed, usually while they are harboring a mild depressive affect. Distinct changes in the tone of the corrugator and zygomatic facial muscles accompany depression, as shown on electromyograms. (Courtesy of Heinz E. Lehmann, M.D.)

PSYCHOMOTOR AGITATION Although agitation (pressured speech, restlessness, hand wringing, and hair pulling) is the more readily observed abnormality, it appears to be less specific to the illness than retardation (slowing of psychomotor activity). Psychophysiological studies have documented that such slowing often coexists with agitation.

PSYCHOMOTOR RETARDATION Underlying many of the deficits seen in clinical depression, some authorities believe psychomotor retardation to be the core, or primary, pathology in mood disorders. Morbid depression—what patients describe as being “down”—can be understood in terms of moderate-to-extreme psychomotor slowing. The patient experiences inertia, being unable to act physically and mentally. Recent brain imaging research that has revealed subcortical (extrapyramidal system) disturbances in mood disorders tends to support the centrality of psychomotor dysfunction in these disorders.

Long neglected in psychopathological research, psychomotor retardation, can be measured with precision. The Salpêtrière Retardation Scale developed by Daniel Widlöcher and colleagues places special emphasis on the following disturbances: (1) paucity of spontaneous movements; (2) slumped posture with downcast gaze (Fig. 14.6-5); (3) overwhelming fatigue (patients complain that everything is an effort’); (4) reduced flow and amplitude of speech and increased latency of responses, often giving rise to monosyllabic speech; (5) a subjective feeling that time is passing slowly or has stopped; (6) poor concentration and forgetfulness; (7) painful rumination—thinking that dwells on a few (usually unpleasant) topics; and (8) indecisiveness, or an inability to make simple decisions.

FIGURE 14.6-5 A 38-year-old woman during a state of deep retarded depression (A) and 2 months later, after recovery (B). Note the turned-
down corners of her mouth, her stooped posture, her drab clothing, and her hairdo during the depressed episode. (Courtesy of Heinz E. Lehmann, M.D.)

DSM-IV places greater emphasis on the more easily observable objective or physical aspects of retardation. For the patient, however, the subjective sense of slowing is as pervasive and disabling. This more psychological dimension of retardation is most reliably elicited from depressed persons with good verbal skills.

Ms. A, a 34-year-old literature professor, presented to a mood clinic with the following complaint: "I am in a daze, confused, disoriented, staring. My thoughts do not flow, my mind is arrested... I seem to lack any sense of direction, purpose... I have such an inertia, I cannot assert myself. I cannot fight, I have no will."

Less linguistically sophisticated patients would simply complain of an inability to perform household chores or difficulty in concentrating on their studies. Such psychomotor deficits in turn underlie depressed patients' diminished efficiency or their inability to work.

**PSEUDODEMENTIA** The slowing of mental functions can be so pronounced in elderly persons that they experience memory difficulties, disorientation, and confusion.

**STUPOR** Psychomotor slowing in young persons is sometimes so extreme that patients might slide into a stupor, unable to participate even in such basic biological functions as feeding themselves. Such an episode is often the precursor of bipolar disorder, which later declares itself in a manic episode. Today depressive disorder is diagnosed in its earlier stages, and subtle stupor is much more likely to be encountered clinically.

A 20-year-old male college student seen in the emergency room spoke of "being stuck—as if I have fallen into a black hole and can't get out." Further evaluation revealed that the patient was metaphorically describing his total loss of initiative and drive and was engulfed by the disease process. A clinician without the requisite phenomenological training, might consider such a patient bizarre and perhaps even psychotic. Yet the patient responded dramatically to fluoxetine (Prozac) and in 2 weeks was back in school.

**Cognitive Disturbances** The cognitive view of depression considers negative evaluations of the self, the world, and the future (the negative triad) central to understanding depressed mood and behavior, but it is equally likely that the depressed mood colors perceptions of the self and others or that disturbed psychomotor activity leads to negative self-evaluations. Therefore, instead of being considered causal, the cognitive triad in depression is best approached empirically as a psychopathological manifestation of depression. Those faulty thinking patterns are clinically expressed as (1) ideas of deprivation and loss; (2) low self-esteem and self-confidence; (3) self-reproach and pathological guilt; (4) helplessness, hopelessness, and pessimism; and (5) recurrent thoughts of death and suicide.

The essential characteristic of depressive thinking is that the sufferer views everything in an extremely negative light. The self-accusations are typically unjustified or are blown out of proportion, as in the
case of a middle-aged woman who was tormented by guilt because as a child she had not repaid 5 cents she had borrowed from a classmate. Some of the thoughts may verge on the delusional. For instance, an internationally renowned scientist complained that he was “nothing.” Self-evaluations that indicate an extremely low image of self might nonetheless reflect an accurate perception of one's impairment from psychomotor retardation.

**MOOD-Congruent Psychotic Features** In depressive disorder with psychotic features (Table 14.6-3), negative thinking acquires grossly delusional proportions and is maintained with such conviction that the thoughts are not amenable to change by evidence to the contrary. According to Kurt Schneider, delusional thinking in depression derives from humankind's four basic insecurities, those regarding health, financial status, moral worth, and relationship to others. Thus, severely depressed patients may have delusions of worthlessness and sinfulness, reference, and persecution: They believe they are being singled out for their past mistakes and that everyone is aware of their errors. Persecutory ideation in depression is often persecutory in that it derives from the belief that the person deserves punishment for such transgressions. A severely depressed man may feel so incompetent in all areas of functioning, including the sexual sphere, that he may suspect his wife of having an affair (delusion of infidelity).

**Table 14.6-3 DSM-IV Criteria for Severity/Psychotic/Remission Specifiers for Current (or Most Recent) Major Depressive Episode**

Other depressed persons believe that they have mismanaged their finances and their children will starve (delusions of poverty) or that they harbor an occult illness, such as cancer or the acquired immune deficiency syndrome (AIDS) (delusions of ill health) or that parts of their bodies are missing (nihilistic delusions). In more severe illness the patient might feel that the world has changed and that calamity and destruction await everyone. In rare instances a parent with such delusions might kill his or her young children to save them from moral or physical decay and then commit suicide. Finally, a minority of depressed persons have fleeting auditory or visual hallucinations with extremely unpleasant content along the lines of their delusions (e.g., hearing accusatory voices or seeing themselves in coffins or graveyards). All of these psychotic experiences are genuine affective delusions or hallucinations. They are mood congruent in the sense that they are phenomenologically understandable in light of the prevailing pathological mood.

**MOOD-Incongruent Psychotic Features** Sometimes so-called first-rank or schneiderian-type symptoms can arise in the setting of a major depressive episode.

A 42-year-old civil servant said she was so paralyzed by depression that she felt that she had no personal initiative and volition left; she believed some malignant force had taken over her actions, and it would comment on every action that she would undertake. The patient recovered fully with thymoleptic medication. There is no reason to believe that in this patient the feelings of somatic passivity and running commentary indicated a schizophrenic process.

Thus, with proper phenomenological probing, certain classes of apparently mood-incongruent psychotic
experiences listed in DSM-IV can be understood as arising from the pathological mood and the profound changes in psychomotor activity that accompany them. (In other instances, the clinician must seek a history of alcohol or substance use disorder or withdrawal as a putative explanation for mood incongruence in psychotic depression.) In brief, incidental schneiderian first-rank symptoms should not distract from the diagnosis of an affective disorder if otherwise typical signs and symptoms are present.

**HOPELESSNESS AND SUICIDE**

Given that most, if not all, clinically depressed patients find themselves locked in the private hell of their negative thoughts, it is not surprising that up to 15 percent of untreated or inadequately treated patients give up hope of ever recovering and kill themselves. The suicide attempt is not, however, undertaken in the depth of melancholia. One severely depressed patient asked if she had any suicide plans, replied, “Doctor, I don't exist— I am already dead.”

Thus the risk of suicide is less pronounced during acute severe depression. Emil Kraepelin observed that it is when psychomotor activity is improving, and yet mood and thinking are still dark, that the patient is most likely to muster the requisite energy to commit the suicidal act. Hopelessness on mental status evaluation in a patient recovering from depression should alert the clinician to the possibility of such an outcome.

There is no basis for the common belief that inquiring about suicide provokes such behavior. On the contrary, patients are often relieved that the physician appreciates the magnitude of their suffering. Suicidal ideation is commonly expressed indirectly (e.g., in a wish not to wake up or to die from a malignant disease). Some depressed persons are tormented with suicidal obsessions and are constantly resisting unwanted urges or impulses to destroy themselves. Others might yield to such urges passively (e.g., by careless driving or by walking into high-speed traffic). A third group harbors elaborate plans, carefully preparing a will and taking out insurance. Deliberate planning indicates a very high suicidal risk. The foregoing examples are not exhaustive; they are meant to remind clinicians in charge of depressed patients to be always alert to the possibility of suicide.

**Vegetative Disturbances**

The Greeks considered depression a somatic illness and ascribed it to black bile; hence the term “melancholia.” The mood change in depressive disorder is accompanied by measurable alterations of biorhythms that implicate midbrain dysfunction. Once the changes occur, they tend to be independent of the environment throughout much of the episode, and as a consequence, they do not respond to interpersonal feedback of a pleasant and upbeat nature. The biological concomitants of melancholia include profound reductions in appetite, sleep, and sexual functioning as well as alterations in other circadian rhythms, especially matinal worsening of mood and psychomotor performances. These disturbances are central to the DSM-IV concept of melancholia (Table 14.6-4), a form of depression in which such biological concomitants predominate. A smaller subgroup of depressed persons exhibits a reversal of the vegetative and circadian functions, with increases in appetite and sleep—and sometimes in sexual functioning—and an evening worsening of mood; in this atypical pattern (Table 14.6-5), patients characteristically exhibit mood reactivity and sensitivity to rejection.

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<th><strong>Table 14.6-4 DSM-IV Criteria for Melancholic Features Specifiers</strong></th>
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<td><strong>A.</strong> Either of the following, occurring during the most severe period of the current episode:</td>
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<td>(1) a quality of depressed mood i.e., the depressed mood is perceived as distinctly different from the kind of feeling experienced after the death of a loved one</td>
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<td>(2) lack of reactivity to usually pleasurable stimuli does not feel much better, even temporarily, when something good happens</td>
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<td><strong>B.</strong> Three or more of the following:</td>
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<tr>
<td>(1) sleep disturbance</td>
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<td>(2) appetite disturbance</td>
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<td>(3) psychomotor retardation or agitation</td>
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<tr>
<td>(4) marked psychomotor retardation or agitation</td>
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<tr>
<td>(5) significant anorexia or weight loss</td>
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<td>(6) excessive or inappropriate guilt</td>
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ANOREXIA AND WEIGHT LOSS The most reliable somatic indicators of depressive disorder include anorexia and weight loss. In addition to the presumed hypothalamic disturbance of depression, anorexia might be secondary to blunted olfactory or taste sensations or a decreased enjoyment of food, or (rarely) it might result from a delusional belief that the food has been poisoned.

If weight loss is severe, especially after the age of 40, the psychiatrist should first use appropriate medical consultation to rule out the likelihood of an occult malignancy. Inanition, especially in elderly persons, can lead to malnutrition and electrolyte disturbances that represent medical emergencies.

WEIGHT GAIN Overeating, decreased activity, or both may result in weight gain. In middle-aged patients it may aggravate preexisting diabetes mellitus, hypertension, or coronary artery disease. In younger patients, especially women, weight problems may conform to a bulimic pattern that is sometimes the expression of the depressive phase of a bipolar disorder with infrequent hypomanic periods (bipolar II disorder).

INSOMNIA Sleep disturbance, a cardinal sign of depression, often is characterized by multiple awakenings, especially in the early hours of the morning, rather than by difficulty falling asleep. The light sleep of a depressed person, in part a reflection of the painful arousal of the disorder, tends to prolong the depressive agony over 24 hours. Thus, deep stages of sleep (3 and 4) are either decreased or deficient. The attempt to overcome the problem by drinking alcohol may initially succeed but ultimately aggravates the sleep patterns and insomnia. This is also true for sedative-hypnotic agents, which are often prescribed by the busy general practitioner who has not spent enough time diagnosing the depressive condition. Although sedatives (including alcohol) effectively reduce the number of awakenings in the short term, they are not effective in the long run because they further diminish stage 3 and stage 4 sleep. They are not antidepressants, and they tend to prolong the depression.

HYPERSONMIA Young depressed patients, especially those with bipolar tendencies, often exhibit excessive sleep and have difficulty getting up in the morning.

Kevin, a 15-year-old boy, was referred to a sleep center to rule out narcolepsy. His main complaints were fatigue, boredom, and a need to sleep all the time. Although he had always started the day somewhat slowly, he now could not get out of bed to go to school. That alarmed his mother, prompting sleep consultation. Formerly a B student, he had been failing most of his courses in the 6 months before referral. Psychological counseling, predicated on the premise that his family's recent move from another city had led to Kevin's isolation, had not been beneficial. Extensive neurological and general medical workup had also proven negative. He slept 12 to 15 hours a day but denied cataplexy, sleep paralysis, and hypnagogic hallucinations. During psychiatric interview he denied being depressed but admitted that he had lost interest in everything except his dog. He had no drive, participated in no activities, and had gained 30...
pounds in 6 months. He believed he was “brain damaged” and wondered whether it was worth living like that. The question of suicide disturbed him as it was contrary to his religious beliefs. These findings led to the prescription of desipramine (Norpramin) in a dosage that was gradually increased to 200 mg a day over 3 weeks. Not only did desipramine reverse the presenting complaints, but it also pushed him to the brink of a manic episode.

The affective nature of the disorder in such patients is often unrecognized, and their behavior is attributed to “laziness.” The vignette also illustrates the emergence of manic behavior during antidepressant treatment. Such shifts in polarity are common in major depressive disorder and necessitate revising the diagnosis to a bipolar disorder (contrary to the admonitions of DSM-IV).

CIRCADIAN DYSREGULATION Many circadian functions, such as temperature regulation and cortisol rhythms, are disrupted in major depressive disorder. Disturbances of sleep rhythms, however, have received the greatest research focus. These include deficits in stage 4 or delta sleep, as well as more intense rapid eye movement (REM) activity in the first third of the night. More specific to depressive disorders—and whether suffering from insomnia or hypersomnia—nearly two-thirds of patients exhibit a marked shortening of REM latency, the period from the onset of sleep to the first REM period. This abnormality is observed throughout the depressive episode and may also be seen during relatively euthymic periods in persons with recurrent depression. The occurrence of short REM latency in the younger “well” relatives of the affectively ill suggests that neurophysiological abnormalities might precede the overt psychopathological manifestations of the illness; upon closer scrutiny, these well relatives will often be found to meet criteria for subthreshold mood conditions such as dysthymic disorder, intermittent depression or labile temperament.

Few data exist on the consistency of sleep electroencephalographic (EEG) abnormalities in patients from episode to episode. However, clinical experience suggests that a patient observed over time (even during the same episode) may exhibit insomnia and morning worsening of mood and activity during one period of the disorder and hypersomnia extending to late morning hours during another period. In either case, persons with depressive disorder are characteristically tired in the morning, which means that even prolonged sleep is not refreshing for them. The propensity to exhibit such divergent patterns of sleep disturbance is more likely in bipolar disorders. Patients with major depressive disorder tend to exhibit insomnia more stereotypically episode after episode; despite extreme fatigue, they rarely oversleep. Such fatigue coexisting with negative affective arousal is even more exhausting.

SEASONALITY Another classic biorhythmic disturbance in mood disorders is seasonal (especially autumn-winter) accentuation or precipitation of depression. Most of those patients experience increased energy and activation, if not frank hypomania, in the spring. In the fall and winter, they complain of fatigue, tend to crave sugars, and overeat and oversleep. The hypersomnia in some of these patients is associated with delayed (rather than short) REM latencies. These data suggest dysregulation of circadian rhythms in depressive disorders rather than mere phase advance. Although autumnal-winter depression has received the greatest attention, there also exist summer depressions; the former appear related to reduction of daylight (photoperiods), and the latter to increased temperature. The DSM-IV criteria for seasonal pattern specifiers are listed in Table 14.6-6.

Table 14.6-6 DSM-IV Criteria for Seasonal Pattern Specifier
SEXUAL DYSFUNCTION  Decreased sexual desire is seen in both depressed men and women. In addition, some women experience temporary interruption of their menses. Depressed women are typically unresponsive to lovemaking or are disinclined to participate in it, a situation that could lead to marital conflict. Psychotherapists might mistakenly ascribe the depression to the marital conflict and devote unnecessarily zealous psychotherapeutic attention to conjugal issues. Decreased or lost libido in men often results in erectile failure, which may prompt endocrinological or urological consultation. Again, depression may be ascribed to the sexual dysfunction rather than the reverse, and definitive treatment may be delayed by the physician's focus on the sexual complaint. Tragically, some men with depressive disorder have been subjected to permanent penile implants before receiving more definitive treatment for their depression. This is less likely to occur in the sildenafil (Viagra) era, but even treatment with such agents would not necessarily resolve the impotence in clinically depressed patients without competent treatment of the mood disorder.

A small subgroup of persons with depressive disorder may exhibit increased sexual drive or activity of a “compulsive” nature. These patients tend to have other atypical features as well; hence the increased sexual drive can be considered the “fifth reverse vegetative sign” (after evening or morning worsening of mood, initial insomnia, hypersomnia, and weight gain). In these depressed persons, increased sexual drive may indicate a mixed episode of bipolar disorder. Further scrutiny in such cases will often reveal a premorbid cyclothymic or hypomanic temperament.

Manic Syndrome  As with clinical depression, the psychopathology of mania (Table 14.6-7) can be conveniently discussed under mood, psychomotor, circadian, and cognitive disturbances. The clinical features of mania are generally the opposite of those of depression. Thus, instead of lowered mood, thinking, activity, and self-esteem, there is elevated mood, a rush of ideas, psychomotor acceleration, and grandiosity. Despite those contrasts, the two disorders share such symptoms as irritability, anger, insomnia, and agitation. Actually, an excess of such symptoms of escalating intensity suggests a mixed phase or mixed episode (Table 14.6-8) of mania and depression occurring simultaneously. Manic and mixed episodes represent the hallmark of what was once termed manic-depressive psychosis and is currently termed bipolar I disorder.

Table 14.6-7 DSM-IV Criteria for Manic Episode
Although milder mania (hypomania [Table 14.6-9]) can contribute to success in business, leadership roles, and the arts, recurrences of even mild manic symptomatology are typically disruptive. The elated mood tends to produce overoptimism concerning one's abilities, which coupled with the impulsivity characteristic of mania, often leads to disaster. Thus, accurate and early diagnosis is paramount.

Classic mania as formulated in the DSM-IV operationalization of manic episode (Table 14.6-7) is relatively easy to recognize. Misdiagnosis was once rampant in North American practice as clinicians confused severe mania with schizophrenia, and its milder variants with normality or with narcissistic and sociopathic personality disorders. Like the misdiagnosis of depressive conditions, such errors of clinical judgment are due to a lack of familiarity with the phenomenology of the classic illness. Again, DSM-IV criteria provide only a guideline. The actual diagnosis requires careful history and phenomenologic understanding. The manic patient lifts the observer's mood, makes the examiner smile and even laugh, and can often be irritating. The patient's speech is fast and may even appear “loose,” but it also can often be witty. Finally, the behavior is typically dramatic, expansive, and jesting. For the experienced clinician, the overall gestalt experienced in the presence of such patients is emotionally and qualitatively distinct from that of persons with schizophrenia or frontal lobe diseases; the latter conditions tend to leave the examiner “cold.” These considerations become clearer when the clinical observer systematically examines the psychopathology of mania in the areas of mood, behavior, and thinking.

**Mood Disturbance** Mood disturbance in mania represents a contrast to that observed in depression, but not entirely.

**MOOD ELEVATION** The mood in mania is classically one of elation, euphoria, and jubilation, typically associated with laughing, punning, and gesturing.

**LABILITY AND IRRITABILITY** The prevailing positive mood in mania is not stable, and momentary crying or bursting into tears is common. Also, the high is so excessive that many patients experience it as intense nervousness. When crossed, patients can become extremely irritable and hostile. Thus, lability and irritable hostility are as much features of the manic mood as is elation.
Psychomotor Acceleration Accelerated psychomotor activity, the hallmark of mania, is characterized by overabundant energy and activity and rapid, pressured speech. Subjectively, the patient experiences an unusual sense of physical well-being (eutonia).

FLIGHT OF IDEAS Thinking processes are accelerated, experienced as flight of ideas, and thinking and perception are unusually sharp. The patient may speak with such pressure that associations are difficult to follow; such clang associations are often based on rhyming or chance perceptions and can be lightning fast. The pressure to speak may continue despite development of hoarseness.

IMPULSIVE BEHAVIOR Manic patients are typically impulsive, disinhibited, and meddlesome. They are intrusive in their increased involvement with others, leading to friction with family members, friends, and colleagues. They are distractible and move quickly, not only from one thought to another, but also from one person to another, showing heightened interest in every new activity that strikes their fancy. They are indefatigable and engage in various activities in which they usually display poor social judgment. Examples include preaching or dancing in the street; abuse of long distance calling; buying new cars, hundreds of records, expensive jewelry, or other unnecessary items; paying the bills of total strangers in bars; giving away furniture; impulsive marriages; engaging in risky business ventures; gambling; and sudden trips. Such pursuits can lead to personal and financial ruin.

DELIRIOUS MANIA An extremely severe expression of mania (once known as “Bell's mania”), delirious mania involves frenzied physical activity that continues unabated and leads to a life-threatening medical emergency. This complication, the manic counterpart of stupor, is rare today. (There is no need to invoke here the concept of catatonic features as advocated by DSM-IV (Table 14.6-10). The DSM-IV position is terminologically confusing and phenomenologically imprecise).

Table 14.6-10 DSM-IV Criteria for Catatonic Features Specifier

<table>
<thead>
<tr>
<th>Vegetative Disturbances</th>
<th>Vegetative disturbances are more difficult to evaluate in mania than in depression.</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPOSOMNIA</td>
<td>The cardinal sign is decreased need for sleep—the patient sleeps only a few hours but feels energetic on awakening. Some patients may actually go sleepless for several days. This practice could lead to dangerous escalation of manic activity, which might continue despite signs of physical exhaustion.</td>
</tr>
<tr>
<td>INATTENTION TO NUTRITION</td>
<td>There does not seem to be a clinically significant level of appetite disturbance as such, but weight loss may occur because of increased activity and neglect of nutritional needs.</td>
</tr>
<tr>
<td>SEXUAL EXCESSES</td>
<td>The sexual appetite is typically increased and may lead to sexual indiscretion. Married women with previously unblemished sexual lives may associate with men below their social status. Men typically overindulge in alcohol, frequent bars, and squander their savings on prostitutes.</td>
</tr>
</tbody>
</table>
The sexual misadventures of manic patients result in marital disasters and hence the multiple separations or divorces that are almost pathognomonic of the disorder. Such sexual impulsivity is even more problematic now, in view of the specter of AIDS.

Cognitive Distortions Manic thinking is overly positive, optimistic, and expansive.

GRANDIOSITY, LACK OF INSIGHT, AND DELUSION FORMATION The patient exhibits inflated self-esteem and a grandiose sense of confidence and achievements. Behind that facade, however, may be a vague and painful recognition that the positive self-concepts do not represent reality. However, such insight (if present at all) is transient, and manic patients are notoriously refractory to self-examination and insight. Denial and lack of insight, cardinal psychological derangements of mania, are not listed in the DSM-IV criteria for manic episode or bipolar disorders. This is a serious omission because this lack of insight leads manic patients to engage in activities that harm themselves and their loved ones. It also explains, in part, their noncompliance with medication regimens during the manic phase. Finally, because of their lack of insight, mania nearly always reaches delusional proportions, including delusions of exceptional mental and physical fitness and exceptional talent; delusions of wealth, aristocratic ancestry, or other grandiose identity; delusions of assistance (i.e., well-placed persons or supernatural powers are assisting their endeavors); or delusions of reference and persecution, based on the belief that enemies are observing or following them out of jealousy at their special abilities. At the height of mania patients may even see visions or hear voices congruent with their euphoric mood and grandiose self-image (e.g., they might see images of heaven or hear cherubs chanting songs to praise them). The denial characteristic of mania—and the frequently psychotic nature of episodes—means that clinicians must routinely obtain diagnostic information about past episodes from significant others. (Lack of insight also unfortunately means that hospitalization must usually be arranged on an involuntary basis).

MOOD-INCONGRUENT PSYCHOSIS Psychosis in the setting of mania and mixed manic episodes is typically mood congruent. The sense of physical well-being and mental alacrity is so extraordinary that it is understandable why manic patients believe that they possess superior powers or perhaps are great scientists or famous reformers. Moreover, their senses are so vivid that reality appears richer and more exotic, and can be easily transformed into a vision. Likewise, their thoughts are so rapid and vibrant that they feel they can hear them. Thus, certain first-rank schneiderian-type symptoms that have been traditionally considered mood incongruent can be understood phenomenologically to arise from the powerful mental experiences of mania.

A 37-year-old engineer, had experienced three manic episodes for which he had been hospitalized; all three episodes were preceded by several weeks of moderate psychomotor retardation. Although he had responded to lithium (Eskallith, Lithobid) each time, once outside the hospital he had been reluctant to take it and eventually refused to do so. Now that he was euthymic, following his third and most disruptive episode during which he had badly beaten his wife, he could more accurately explain how he felt when manic. Mania, he felt, was “like God implanted in him,” so he could serve as “testimony to man's communication with God.” He elaborated as follows: “Ordinary mortals will never, never understand the supreme manic state which I'm privileged to experience every few years. It is so vivid, so intense, so compelling. When I feel that way, there can be no other explanation: To be manic is, ultimately, to be God. God himself must be supermanic: I can feel it, when mania enters through my left brain like laser beams, transforming my sluggish thoughts, recharging them, galvanizing them. My thoughts acquire such momentum, they rush out of my head, to disseminate knowledge about the true nature of mania to psychiatrists and all others concerned. That's why I will never accept lithium again—to do so is to obstruct the divinity in me.” Although he was on the brink of divorce, he would not yield to his wife's plea to go back
The vignette illustrates the possibility that even some of the most psychotic manifestations of mania represent explanatory delusions, the patient's attempt to make sense of the experience of mania. The DSM-IV criteria for severity/psychotic specifiers for manic and mixed episode (Table 14.6-11 and Table 14.6-12) are more concerned with operational rigor than with the phenomenological sophistication needed to understand such core manic experiences. (Many manic patients abuse alcohol and stimulants to enhance their mental state; mood incongruence can sometimes be explained on that basis).

**Table 14.6-11 DSM-IV Criteria for Severity/Psychotic/Remission Specifiers for Current (or Most Recent) Manic Episode**

| Note: Can be applied to a manic episode in bipolar I disorder only if in the acute manic or mixed episode. Add: Minimum symptom criteria are not met for a manic episode.删除: With psychotic features, delusions or hallucinations, if present, are brief and are not predominant. Some patients, particularly those with a history of severe mania, may develop delusions or hallucinations as a result of drug side effects or may develop delusions or hallucinations which are not regarded as having a psychiatric etiology. An apparent or genuine conversion from delusions or hallucinations to other psychotic features (behaviors or hallucinations) is not a basis for making this diagnosis. Differentiation from the delusional disorders and the schizophrenia spectrum disorders may not be possible in some cases. | Unspecified |

**Table 14.6-12 DSM-IV Criteria for Severity/Psychotic/Remission Specifiers for Current (or Most Recent) Mixed Episode**

| Note: Can be applied to a mixed episode in bipolar I disorder only if it is the acute mixed episode. Add: Minimum symptom criteria are not met for a manic or depressive episode.删除: With psychotic features, delusions or hallucinations, if present, are brief and are not predominant. Some patients, particularly those with a history of severe mania, may develop delusions or hallucinations as a result of drug side effects or may develop delusions or hallucinations which are not regarded as having a psychiatric etiology. An apparent or genuine conversion from delusions or hallucinations to other psychotic features (behaviors or hallucinations) is not a basis for making this diagnosis. Differentiation from the delusional disorders and the schizophrenia spectrum disorders may not be possible in some cases. | Unspecified |

**MANIA VERSUS HYPOMANIA** Nonpsychotic and nondisruptive variants of mania are much more common and are recognized by DSM-IV as hypomanic episodes. Diagnostically, history of a partial manic syndrome is preferably obtained from significant others who have observed the patient; the experience is often pleasant, and the subject may either be unaware of it or tend to deny it. DSM-IV stipulates a minimum duration of 4 days for hypomania; however, the Memphis and Zurich studies found a modal duration of 2 days. Finally, although DSM-IV states that treatment-emergent hypomania in a depressed patient does not count toward a diagnosis of bipolarity, prospective observations show that nearly all such episodes are followed eventually by spontaneous hypomania (or mania).

**DIAGNOSTIC CLASSIFICATION**

The classification of mood disorders in DSM-IV subsumes a large variety of patients seen in private and public, ambulatory and inpatient settings. The main demarcation in that large clinical terrain is between bipolar and depressive (unipolar) disorders. Thus, bipolar disorders range from the classic manic and depressive episodes of psychotic intensity (bipolar I disorder) through recurrent major depressive episodes, alternating with hypomanic episodes (bipolar II disorder), and cyclothymic mood swings. Likewise, depressive disorders include those with psychotic severity, melancholia, atypical features, and dysthymic variants.

Major and specific attenuated subtypes are distinguished on the basis of severity and duration. In dysthymic and cyclothymic disorders a partial mood syndrome—consisting of such subthreshold
features as subdepressive and hypomanic periods—is maintained, intermittently or continuously, for at least 2 years. Subdepressive periods dominate in dysthymia; in cyclothymia, they alternate with hypomania. The onset is typically in adolescence or childhood, and most persons with these diagnoses seen in young adulthood have had low-grade mood symptoms for 5 to 10 years. Major mood disorders, which generally begin much later in life, require the presence of either a full manic episode or a full depressive episode—sustained for at least 1 or 2 weeks, respectively—and an episodic course, typically permitting recovery or remission from episodes. DSM-IV recognizes that a significant minority of persons with major depressive disorders fails to achieve full symptomatic recovery and should thus be qualified as chronic or in partial remission. They are no longer considered dysthymic (the misleading convention in DSM-III).

**Dichotomy or Continuum?** Although, in the extreme, bipolar and depressive (unipolar) disorders can be discriminated clinically and therapeutically (Table 14.6-13), clinical observations testify to a vast overlap between those extremes. Thus the distinctions between the various affective subtypes are not as hard and fast as DSM-IV attempts to portray. For instance, full-blown bipolar disorder can be superimposed on cyclothymic disorder that tends to persist after the resolution of manic or major depressive episodes. Even more common is major depressive disorder complicating cyclothymic disorder, which should be reclassified as an important course variant of bipolar II disorder. Likewise, recent evidence indicates that dysthymic disorder may precede major depressive disorder in as many as a third of cases. Moreover, one in four persons with major depressive disorder subsequently develops hypomanic or manic episodes and so should be reclassified as having bipolar disorder. Finally, unexpected crossing from dysthymic disorder to hypomanic or manic episodes has also been described, suggesting that some forms of dysthymic disorder are subaffective precursors of bipolar disorder. Such observations are in line with Kraepelin's historic attempt to bring all mood disorders under one rubric. Epidemiological studies in the community have also shown much fluidity between various subthreshold and major mood disorders.

| Table 14.6-13 Differentiating Characteristics of Bipolar and Unipolar Depressions |
|---------------------------------|-----------------|
| Bipolar                         | Unipolar        |
| History of mania or hypomania   | No              |
| Hypomanic or hyperthymic traits | Yes             |
| Sex ratio                       | Equal           |
| Age of onset                    | Equal           |
| Posthemorrhagic episodes         | Equal           |
| Course of episode               | Equal           |
| Number of episodes              | Equal           |
| Psychometric agitation           | Equal           |
| Sleep                           | Two thirds     |
| Family history                  | Yes             |
| Bipolar relatives               | Yes             |
| Antecedents                     | Yes             |
| Pharmacological                            | Yes             |
| Culture                          | Yes             |
| Mania                            | Yes             |
| Dysthymia                       | No              |
| Cyclic                            | No              |
| Antidepressant                   | Yes             |
| Antidepressant effective         | No              |

Heterogeneity undoubtedly exists among mood disorders; however, the foregoing observations suggest that much of the unipolar terrain might be “pseudo-unipolar” (i.e., soft bipolar). The clinical significance of these considerations lies in the fact that many DSM-IV subtypes of mood disorders are not pure entities, and considerable overlap and switches in polarity take place. They also provide some rationale, for instance, for why lithium (or lithium augmentation) may be effective in some apparently unipolar depressions; such patients do not experience spontaneous hypomanic episodes, but instead often exhibit a high baseline level of hyperthymic traits. Finally, several studies have shown that bipolar patients with cyclothymic premorbid adjustment and interepisodic adjustment are at considerable risk for antidepressant-induced rapid cycling, defined as a rapid succession of major episodes with few or no intervals of freedom.

Such considerations further testify to the wisdom of supplementing major mood diagnoses with temperamental attributes. DSM-IV only makes subtle or oblique hints concerning this, and instead
provides the practitioner with an unwieldy, if not useless, array of episode and course specifiers. The DSM-IV criteria for longitudinal course specifiers are given in Table 14.6-14.

| Table 14.6-14 DSM-IV Criteria for Longitudinal Course Specifiers |
|--------------------------|--------------------------|
| Specify if can be applied to recurrent major depressive disorder or bipolar I or II disorder: |
| With full interepisode recovery: if full remission is attained between the two most recent mood episodes |
| Without full interepisode recovery: if full remission is not attained between the two most recent mood episodes |

As Krouplein illustrated in his monograph, course is best captured graphically. DSM-IV only provides examples of this for depressive disorders (Fig. 14.6-6) and limits itself to four patterns. Krouplein, after diagramming 18 illustrative patterns for the entire spectrum of manic-depressive illness, declared that the illness pursued an indefinite number of courses.

**FIGURE 14.6-6** Graphs depicting prototypical courses. A, Course of major depressive disorder, recurrent, with no antecedent dysthymic disorder and a period of full remission between the episodes. This pattern predicts the best future prognosis. B, Course of major depressive disorder, recurrent, with no antecedent dysthymic disorder but with prominent symptoms persisting between the two most recent episodes (i.e., partial remission is attained). C, Rare pattern (present in fewer than 3 percent of persons with major depressive disorder) of major depressive disorder, recurrent with antecedent dysthymic disorder but with full interepisode recovery between the two most recent episodes. D, Course of major depressive disorder, recurrent, with antecedent dysthymic disorder and no period of full remission between the two most recent episodes. This pattern, commonly referred to as double depression, is seen in about 20 to 25 percent of persons with major depressive disorder. (Reprinted with permission from American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Copyright, American Psychiatric Association, Washington, DC, 1994.)

**DEPRESSIVE DISORDERS**

The broad category of depressive disorders includes major depressive disorder, dysthymic disorder, and depressive disorder not otherwise specified.

**Major Depressive Disorder** Episodes usually begin over a prodromal period of weeks to months. The DSM-IV diagnosis of major depressive disorder requires (1) dysphoric mood or decreased interest in usual activities and (2) at least four additional classic depressive signs and symptoms, (3) which must be sustained for at least 2 weeks, and (4) cannot be explained by another process known to cause depressive symptoms, such as normal bereavement, certain physical conditions commonly associated with depression, or another mental disorder. It can be single and, more commonly, recurrent. (Table 14.6-15 and Table 14.6-16).
Comorbid Physical Disease Those considerations raise the question whether major depressive disorder should be limited to depressions of unknown etiology (i.e., those without documented physical causes). The DSM-IV approach has basically been that when the cause is known, the condition should be diagnosed as mood disorder due to a general medical condition (Table 14.6-17) which must be specified, or substance-induced mood disorder (Table 14.6-18). The problem with this approach is that many common medical factors historically associated with depression (e.g., use of certain antihypertensive agents) do not seem to be causative in the etiological sense, but rather are triggering agents in otherwise predisposed persons. This is analogous to the situation with life events, which no longer are used in making distinctions between reactive and endogenous subtypes of depression. A more troubling implication is that major depressive disorders without demonstrable physical disease are not medical or otherwise biological. More importantly there appears to be no reliable or valid way for a clinician to decide that a depressive condition is due to a specified medical condition. For this reason it is generally more practical to diagnose the depressive disorder on Axis I and specify the contributing physical condition on Axis III. In brief, the designation “due to a general medical condition” is both cumbersome and redundant. The author considers major depressive disorder to represent the final common pathway of multifactorial interacting factors—both physical and psychological—a syndrome that should be diagnosed irrespective of presumed cause.

Table 14.6-15 DSM-IV Diagnostic Criteria for Major Depressive Disorder, Single Episode

Table 14.6-16 DSM-IV Diagnostic Criteria for Major Depressive Disorder, Recurrent

Table 14.6-17 DSM-IV Diagnostic Criteria for Mood Disorder Due to a General Medical Condition

Table 14.6-18 DSM-IV Diagnostic Criteria for Substance-Induced
Mood Disorder

Diagnostic Threshold Another question concerning the DSM-IV definition of major depressive disorders relates to the threshold at which a constellation of depressive features becomes a condition distinct from the ordinary blues. According to the current definition, a person who responds to a setback with lowered spirits and self-doubt, difficulty in sleeping and concentration, and decreased sexual interest for 14 days qualifies for a diagnosis of a major depressive disorder of mild intensity. Many clinicians would consider such a condition a relatively minor departure from normality, probably no more than an adjustment disorder. Obviously, criteria other than signs, symptoms, and duration are necessary to differentiate a depressive disorder from adjustment reactions to life situations. The presence of the following characteristics might assist in such a differentiation.

- By definition, a major depressive disorder should be incapacitating. Previously, much attention was paid to the interpersonal consequences of depression. Recent evidence indicates that measurable deficits in work performance are often early manifestations. Afflicted persons also do not benefit from taking leisure time, and hence prescribing vacations is futile.
- Depressive disorder is usually perceived as a break from a person's usual or premorbid self, which can be so striking that sufferers may feel as though they are losing their minds. The important point is that both the patient and significant others can usually relate the onset of the illness to a given month or quarter of a year, which is not true, for instance, for dysthymic disorder.
- Depressive disorder is often experienced by the sufferer as qualitatively distinct from grief or other understandable reactions to loss or adversity. William James described it as follows:

There is a pitch of unhappiness so great that the goods of nature may be entirely forgotten, and all sentiment of their existence vanish from the mental field. For this extremity of passion to be reached, something more is needed than adversity; the individual must in his own person become the prey of pathological melancholy. Such sensitiveness and susceptibility of mental pain is a rare occurrence where the nervous constitution is entirely normal: one seldom finds it in a healthy subject even where he is the victim of the most atrocious cruelties of outward fortune; it is an active anguish, a sort of psychical neuraglia wholly unknown to healthy life.

Two additional features, when present, would further validate the diagnosis of major depressive disorder.

- History of past episodes.
- Consecutive-generation family history of mood disorder—especially when a large number of family members are afflicted with depression or mood disorder—is characteristic of clinical depression. For instance, one study that prospectively followed persons with minor or neurotic depression found that such pedigrees predicted the development of future major episodes. DSM-IV makes no provision for considering such familial factors in diagnostic decisions. In clinical practice these factors often strongly influence whether depression is taken seriously.

Single Episode and Recurrent Subtypes About a third of all major depressive episodes do not recur
Such patients tend to be older and less likely to have a positive family history for mood disorders, and have a more protracted (1 to 2 years) course of the disorder. Patients with major depressive disorder, single episode should be distinguished from those experiencing their first episodes of major depressive disorder, recurrent. The latter group tends to be younger, and the disorder is more likely to have been preceded by a depressive temperament or dysthymic disorder.

Research has established that recurrent major depressive disorders are more familial than their single-episode counterparts. The average length of episodes is 6 months, whereas the mean interval between episodes tends to vary (typically years). The mean number of major episodes over a lifetime, according to retrospective and prospective studies, is five to six, in contrast to an average of eight to nine major episodes in bipolar disorder.

Melancholic Features In DSM-III the neurotic-endogenous distinction was deleted. Neurotic depression was largely absorbed by dysthymic disorder and the major depressive disorders that complicate it; endogenous depression became “melancholic features,” a qualifying phrase for major depressive disorders in which anhedonia, guilt, and psychomotor-vegetative disturbances dominate the clinical picture. DSM-IV retains these conventions.

Although the foregoing conventions have received much criticism, they are based on solid data from independent studies in the United States and Germany. Thus neurotic depression, defined as a reactive (i.e., precipitated) nonpsychotic depression of mild to moderate intensity with predominant anxiety and characterologic pathology, does not seem to constitute a distinct nosological entity. Although such a presentation is common in clinical practice, well-conducted studies in the United States and Europe have shown that the prospective follow-up course of those patients is heterogeneous, including melancholic and even psychotic depressions and, in some instances, bipolar transformation. The progression of a precipitated, relatively mild depression (reactive illness) to severe psychotic depression—or one with melancholic autonomy—during prospective observation suggests that so-called endogenous depressions may have their onset in milder depressions, that neurotic and psychotic depressions do not necessarily refer to distinct disorders but to disorders that differ in severity, and that the presence of precipitating stress carries little diagnostic weight in differentiating subtypes of depression (although the absence of such stress might be used to support a melancholic level of major depressive disorder).

At the heart of the concept of morbid depression is its autonomy from stresses that may have precipitated it and its general unresponsiveness to other environmental input. This is embodied in Donald Klein's concept of endogenomorphic depression, which could be precipitated and mild (endoreactive) while exhibiting disturbances of hedonic mechanisms refractory to current interpersonal contexts. Many authorities believe that such features dictate the need to use somatic approaches to reverse the maladaptive autonomy and restore response to interpersonal feedback; that is, psychotherapeutic approaches are deemed largely ineffective until the autonomy is somatically lysed.

Given the somatic connotation of the ancient concept of melancholia, the APA classification has officially adopted it as the preferred nosological term for the revised concept of endogeneity; hence the prominence of the vegetative and biorhythmic features accorded to it in both DSM-III and DSM-IV. However, the APA diagnostic schema risks confusing endogeneity with another classic concept of mood disorder, that of “involutional melancholia.”

Psychotic Features About 15 percent of major depressive disorders, usually from the rank of those with melancholic features, develop into delusional depressions. In young persons they tend to be retarded, even stuporous, and are best considered initial episodes of a bipolar disorder. More typically, psychotic depression that develops for the first time after the age of 50 often presents with severe agitation, delusional guilt, hypochondriacal preoccupations, early-morning awakening, and weight loss. The
premorbid adjustment of such patients is classically characterized as “obsessoid.” Their mournful-anxious mood and agitation are autonomous, being refractory to psychological interventions, and they endure great psychic suffering. Except for the fact that generally one to two episodes occur in late-onset (so-called involutional) depressions, they represent a severe variant of DSM-IV melancholia. Kraepelin's postulation of a cerebrovascular basis for such cases makes the ventricular enlargement and white matter opacities reported in psychotic depressions of some interest. Their etiological specificity for persons with late-onset psychotic depression has been controversial, however, since younger (more bipolar) persons with psychotic depression exhibit similar findings. Brain imaging findings tend to be correlated with the neurocognitive deficits observed in psychotic depressions. Those features do not seem to define a distinct depressive subtype, but one of greater severity. Finally, despite attempts to suggest a neurochemical uniqueness based largely on the need for antipsychotic treatment in the acute phase of many of those patients, familial and other external validators have failed to support psychotic depression as a separate entity; hence the decision in DSM-IV to use psychotic features merely as a specifier for major depressive episode (Table 14.6-3). Emerging data, nonetheless, might eventually force a change in this convention. For instance, William Coryell and collaborators in the NIMH collaborative study of depression have shown psychotic depression to be the most consistent unipolar subtype across episodes. Alan Schatzberg's work, originally conducted at Harvard, likewise underscores the uniqueness of psychotic depression based on neuroendocrine and putative neurochemical considerations.

**Chronic Depression** The DSM-IV criteria for chronic specifier appear in Table 14.6-19. The clinical situation, however, is much more complex than these conventions. For instance, the symptom profile in chronic depressions usually displays low-grade intensity rather than severe syndromal chronicity. Severe depressive disorder in its psychotic forms is so agonizing that the sufferer is at risk of committing suicide before the disorder has a chance to become chronic. More commonly, the psychotic symptoms respond to medication or to electroconvulsive therapy (ECT), but residual depressive symptoms may linger for a long time. In other persons with chronic depressions the chronicity arises from more mundane (nonpsychotic) major depressive episodes, depressive residua following one or several clinical episodes that fail to remit fully. Instead of the customary remission within a year, the patients are ill for years. The level of depression varies, fluctuating between syndromal illness and milder symptoms. The patients often show a sense of resignation, generalized fear of an inability to cope, adherence to rigid routines, and inhibited communication.

| Table 14.6-19 DSM-IV Diagnostic Criteria for Chronic Specifier |
|-----------------|-----------------|
| Chronic: The current major depressive episode is accompanied by psychotic features. |
| Specify if: Chronic can be applied to the current or most recent major depressive episode. |
| Full criteria for a major depressive episode have been met continuously for at least 2 years. |

Rather than exhibiting a frankly depressive mood, many persons with chronic depression suffer from deficits in their ability to enjoy leisure and display an attitude of irritable moroseness. The leisure deficits and irritable humor tend to affect their conjugal lives: their marriages are typically in a state of chronic deadlock, leading neither to divorce nor to reconciliation. In other patients the residual phase is dominated by somatic features, such as sleep and other vegetative or autonomic irregularities. Thus, self-treatment with ethanol or iatrogenic benzodiazepine dependence is common. That these interpersonal, conjugal, and autonomic manifestations represent unresolved depression is shown by persistent sleep EEG (especially REM and delta phase) abnormalities that are indistinguishable from their acute counterparts.
Failure to recover from major depressive disorder is associated with increased familial loading for depression, disabled spouses, deaths of immediate family members, concurrent disabling medical disease, use of depressant pharmacologic agents, and excessive use of alcohol and sedative-hypnotic agents. Social support is often eroded in persons with residual depression, through either the death or illness of significant others. Therefore, a thorough medical evaluation and socially supportive interventions should be essential ingredients of the overall approach to those patients.

Interpersonal disturbances in such patients are usually secondary to the distortions produced by long-standing depression. Therefore, observed pathological characterological changes—clinging or hostile dependence, demandingness, touchiness, pessimism, and low self-esteem—are best considered as “postdepressive personality” changes. A dangerous stereotypical thinking holds that because a patient has not responded adequately to standard treatments (the illness has become chronic), the disorder must have a characterological substrate. The long duration of the disorder often leads the patient to identify with the failing functions of depression, producing the self-image of being a depressed person. This self-image itself represents a malignant cognitive manifestation of the depressive disorder and dictates vigorous treatment targeted at the mood disorder.

**Dysthymic Disorder** Dysthymic disorder (Table 14.6-20) is distinguished from chronic depressive disorder by the fact that it is not a sequel to well-defined major depressive episodes. Instead, in the most typical cases, patients complain that they have always been depressed. Thus, most cases are of early onset, beginning in childhood or adolescence and certainly by the time patients reach their 20s. A late-onset subtype, much less prevalent and not well characterized clinically, has been identified among middle-aged and geriatric populations, largely through epidemiological studies in the community.

**Table 14.6-20 DSM-IV Diagnostic Criteria for Dysthymic Disorder**

Although the dysthymic disorder category in DSM-IV can occur as a secondary complication of other psychiatric disorders, the core concept of dysthymic disorder refers to a subaffective disorder with (1) low-grade chronicity for at least 2 years, (2) insidious onset with origin often in childhood or adolescence, and (3) persistent or intermittent course. Although not part of the formal definition of dysthymic disorder, the family history is typically replete with both depressive and bipolar disorders, which is one of the more robust findings supporting its link to primary mood disorder.

**Social Adjustment** Dysthymic disorder is typically an ambulatory disorder compatible with relatively stable social functioning. However, the stability is precarious; recent data document that many patients invest whatever energy they have in work, leaving none for leisure and family or social activities, which results in marital friction. These empirical findings on the work orientation of persons with dysthymic disorder echo earlier formulations in the German and Japanese literature. For instance, Kraepelin described such persons as follows: “Life with its activity is a burden which they habitually bear with dutiful self-denial without being compensated by the pleasure(s) of existence.”

The dedication of persons with dysthymic disorder to work has been suggested to be an

overcompensation and a defense against their battle with depressive disorganization and inertia. Nevertheless, Kretschmer suggested that such persons are the “backbone of society,” dedicating their lives to jobs that require dependability and great attention to detail. Epidemiological studies have demonstrated that some persons with protracted dysthymic complaints, extending over many years, have never experienced clear-cut depressive episodes. Some of them may seek outpatient counseling and psychotherapy for what some clinicians might consider “existential depression,” with feelings of being empty and lacking any joy in life outside their work. Such persons have been described as leading monocategorical existences. Others present clinically because their low-grade dysphoria has intensified into a major depression disorder.

**Course** An insidious onset of depression dating back to late childhood or the teens, preceding any superimposed major depressive episodes by years or even decades, represents the most typical developmental background of dysthymic disorder. A return to the low-grade depressive pattern is the rule following recovery from superimposed major depressive episodes, if any; hence the designation “double depression” as a prominent course pattern illustrated in DSM-IV for depressive illness ([Fig. 14.6-6](#)). This pattern, commonly seen in clinical practice, consists of the baseline dysthymic disorder fluctuating in and out of depressive episodes. The more prototypical patients with dysthymic disorder often complain of having been depressed since birth or of feeling depressed all the time. They seem, in the apt words of Kurt Schneider, to view themselves as belonging to an “aristocracy of suffering.” Such descriptions of chronic gloominess in the absence of more objective signs of depression earn such patients the label of “characterological depression.” The description is further reinforced by the fluctuating depressive picture that merges imperceptibly with the patient's habitual self and thus raises uncertainty as to whether dysthymic disorder belongs in Axis I or Axis II.

**Clinical Picture** The profile of dysthymic disorder overlaps with that of major depressive disorder but differs from it in that symptoms tend to outnumber signs (more subjective than objective depression). This means that marked disturbances in appetite and libido are uncharacteristic, and psychomotor agitation or retardation is not observed. This all translates into a depression with attenuated symptomatology. However, subtle endogenous features are not uncommonly observed: inertia, lethargy, and anhedonia that are characteristically worse in the morning. Because patients presenting clinically often fluctuate in and out of a major depression, the core DSM-IV criteria for dysthymic disorder tend to emphasize vegetative dysfunction, whereas the alternative criterion B for dysthymic disorder ([Table 14.6-21](#)) in a DSM-IV appendix lists cognitive symptoms.

![Table 14.6-21 DSM-IV Alternative Research Criterion B for Dysthymic Disorder](#)

Although dysthymic disorder represents a more restricted concept than its parent, neurotic depression, it is still quite heterogeneous. Anxiety is not a necessary part of its clinical picture, yet dysthymic disorder is often diagnosed in patients with anxiety and neurotic disorders. That clinical situation is perhaps to be regarded as a secondary or “anxious dysthymia” or, in the framework of Peter Tyrer, as part of a “general neurotic syndrome.” For greater operational clarity it is best to restrict dysthymic disorder to a primary disorder, one that cannot be explained by another psychiatric disorder. The essential features of
such primary dysthymic disorder include habitual gloom, brooding, lack of joy in life, and preoccupation with inadequacy. Dysthymic disorder then is best characterized as long-standing fluctuating low-grade depression, experienced as part of the habitual self and representing an accentuation of traits observed in the depressive temperament (Table 14.6). Dysthymia then can be viewed as a more symptomatic form of that temperament (introduced in a DSM-IV appendix as a depressive personality disorder). Sleep EEG data indicate that many persons with dysthymic disorder at baseline exhibit the sleep patterns of those with acute major depressive disorder, providing support for the constitutional nature of the disorder. Further evidence for that position comes from studies demonstrating high rates of familial affective disorder in dysthymic disorder, depressive temperament, or both.

The clinical picture of dysthymic disorder that emerges from the foregoing description is quite varied, with some patients proceeding to major depression, while others manifest the pathology largely at the personality level. The foregoing considerations suggest that a clinically satisfactory operationalization of dysthymia must include symptomatic, cognitive, and trait characteristics.

A 27-year-old, male, grade-school teacher presented with the chief complaint that life was a painful duty that had always lacked luster for him. He said he felt enveloped by a sense of gloom that was nearly always with him. Although he was respected by his peers, he felt “like a grotesque failure, a self-concept I have had since childhood.” He stated that he merely performed his responsibilities as a teacher and that he had never derived any pleasure from anything he had done in life. He said he had never had any romantic feelings; sexual activity, in which he had engaged with two different women, had involved pleasureless orgasm. He said he felt empty, going through life without any sense of direction, ambition, or passion, a realization that itself was tormenting. He had bought a pistol to put an end to what he called his “useless existence” but did not carry out suicide, believing that it would hurt his students and the small community in which he lived.

**Dysthymic Variants** Dysthymia is not uncommon in patients with chronically disabling physical disorders, particularly among elderly adults. Dysthymia-like clinically significant subthreshold depression lasting 6 or more months has also been described in neurological conditions, including stroke. According to a recent WHO conference, this condition aggravates the prognosis of the underlying neurological disease and, therefore, deserves pharmacotherapy. Ongoing studies should provide more explicit clinical recommendations on this topic.

Prospective studies on children have revealed an episodic course of dysthymia with remissions, exacerbations, and eventual complications by major depressive episodes, 15 to 20 percent of which might even progress to hypomanic, manic, or mixed episodes postpuberty. Persons with dysthymic disorder presenting clinically as adults tend to pursue a chronic unipolar course that may or may not be complicated by major depression. They rarely develop spontaneous hypomania or mania. However, when treated with antidepressants, some of them may develop brief hypomanic switches that typically disappear when the antidepressant dose is decreased. Although DSM-IV would not allow the occurrence of such switches in dysthymia, systematic clinical observation has verified their occurrence in as many as a third of dysthymic patients. In this special subgroup of persons with dysthymic disorder, the family histories are often positive for bipolar disorder. Such patients represent a clinical bridge between depressive disorder and bipolar II disorders.

**Depressive Disorder Not Otherwise Specified** The DSM-IV criteria for depressive disorder not otherwise specified, are presented in Table 14.6. What follows are descriptions of conditions that are commonly used in the epidemiological, clinical, or pharmacological literature but do not easily fit into
the official nosology of depressive disorders. Some represent complex interweaving of depression with personality constructs. For instance, community studies have revealed a prevalent pattern of intermittent depressive manifestations with brief episodes, below the 2-week duration threshold for major depressive disorder. In so-called minor depressive disorder (Table 14.6-23), observed in primary care settings, the depression is subthreshold, milder than major depression and yet not protracted enough to be considered dysthymic. These varied manifestations of depression argue for a continuum model (Fig. 14.6-7) as originally envisaged by Kraepelin. Lewis Judd and collaborators at the University of California at San Diego have suggested that subthreshold depressive symptoms—without necessarily meeting the criterion for mood change—might actually represent the most common expressions of a depressive diathesis. From such a subsyndromal symptomatic depressive base, individuals predisposed to depressive illness are said to fluctuate in and out of the various DSM-IV and subthreshold subtypes of depressive disorders. This viewpoint is presently most cogent for subsyndromal symptomatic depression that follows major depressive disorder, a strong predictor of subsequent frequent relapse or chronic course. There is an important message for the clinician here: treat subsyndromal symptomatic depression residual to major depressive disorder.

**Table 14.6-22** DSM-IV Diagnostic Criteria for Depressive Disorder Not Otherwise Specified

**Table 14.6-23** DSM-IV Research Criteria for Minor Depressive Disorder


**Recurrent Brief Depressive Disorder** Now in a DSM-IV appendix (Table 14.6-24), recurrent brief depressive disorder derives from British work on young adults with frequent suicide attempts and epidemiological studies conducted in a young adult cohort in Zurich. It is described as short-lived depressions that usually recur on a monthly basis but are not menstrually related. They could coexist
with major depressive disorder and dysthymic disorder. Such patients are believed to be more prevalent in primary care than in psychiatric settings. Those seen in psychiatric settings are likely to be given Axis II diagnoses such as borderline personality disorder.

### Table 14.6-24 DSM-IV Research Criteria for Recurrent Brief Depressive Disorder

| A. Criteria, except for duration, are met for a major depressive episode. |
| B. The depressive period(s) are at least 2 weeks but less than 2 months. |
| C. The episode(s) occur at least once a month or 12 consecutive months, and are not associated with the menstrual cycle. |
| D. The periods of depressed mood cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition. |
| F. There has never been a major depressive episode, and criteria are not met for dysthymic disorder. |
| G. There has never been a manic episode, a mixed episode, or a hypomanic episode, and criteria are not met for cyclothymic disorder. |
| H. Substance-induced depressive disorder, schizoaffective disorder, bipolar disorder, or psychotic disorder not otherwise specified. |


The current nosological status of those patients is uncertain, but they testify to Kraepelin's observation that many transitional forms link the depressive temperament to affective episodes:

A permanent gloomy stress in all the experiences of life usually perceptible already in youth, and may persist without essential change throughout the whole of life (or) there is actually an uninterrupted series of transitions to periodic melancholia in which the course is quite indefinite with irregular fluctuations and remissions.

**Reactive Depression**

Classically, reactive depression is defined as resulting from a specific life event. In an ideal case the depression would not have occurred without the event (e.g., love loss) to which it is a reaction. It continues as long as the event is present, and it terminates with the reversal of the event (e.g., return of the lover). Depressions exhibiting all of those features are almost never seen in clinical practice. With interpersonal support most people can face life's reverses, which explains why reactive depression tends to be self-limiting. Hence, adjustment disorder is the more appropriate diagnosis for most cases of reactive depression.

Conceptually, however, one can envision chronically unsatisfactory life situations that might lead to chronic demoralization. However, such a condition, which could warrant the designation of chronic reactive depression, is a contradiction in terms. The question often raised is why a person would continue to stay in the situation. Sometimes psychodynamic authors invoke the concept of masochism to explain why certain persons cannot rid themselves of painful life situations, implying that they somehow contribute to their maintenance. Current thinking is that some of those presumed self-defeating traits are more situation specific than previously believed and might resolve with the elimination of the situation. So-called self-defeating features then are best considered psychodynamic mechanisms rather than indicators of a specific personality. At the present stage of knowledge, they do not deserve to be raised to the level of a nosological entity (hence, their disappearance from DSM-IV). Chronic adjustment disorder might describe the chronic demoralization observed among some individuals stuck in chronically unsatisfactory life situations. Many more might fulfill the criteria for dysthymia.

**Neurasthenia**

A century-old term developed by the American neuropsychiatrist George Beard, neurasthenia refers to a more chronic stage of anxious-depressive symptomatology. The anxiety generated by overstimulation is so excessive that it is replaced by a chronic disposition to irritability, fatigue (especially mental fatigue), lethargy, and exhaustion. It is as if the sufferer's mind refuses to take on new stresses. The clinical picture described by Beard suggests that anxious manifestations were preeminent in his time. They included headache, scalp tenderness, backache, heavy limbs, vague neuralgias, yawning, dyspepsia, palpitations, sweating hands and feet, chills, flushing, sensitivity to...
weather changes, insomnia, nightmares, pantaphobia, asthenopia, and tinnitus.

Although the diagnosis of neurasthenia is now used more in China than in the rest of the world, the recent worldwide popularity of the concept of chronic fatigue syndrome attests to the clinical acumen of classic physicians. Despite much energy invested in finding a viral or immunological cause, current descriptions tend to suggest an anxiety or mood disorder basis for some (but not all) of those with the syndrome. However, what circumstances would lead anxiety or depression to manifest primarily in fatigue is as elusive as it was 100 years ago. Like many other patients presenting to primary care settings with somatic complaints, those with chronic fatigue tend to denounce psychiatric diagnoses as inadequate explanations for their ills.

**Postpsychotic Depressive Disorder of Schizophrenia** DSM-IV describes postpsychotic depressive disorder of schizophrenia as follows:

> The essential feature is a Major Depressive Episode that is superimposed on, and occurs only during, the residual phase of Schizophrenia. The residual phase of Schizophrenia follows the active phase (i.e., symptoms meeting Criterion A) of Schizophrenia. It is characterized by the persistence of negative symptoms or of active-phase symptoms that are in an attenuated form (e.g., odd beliefs, unusual perceptual experiences). The superimposed Major Depressive Episode must include depressed mood (i.e., loss of interest or pleasure cannot serve as an alternate for sad or depressed mood). Most typically, the Major Depressive Episode follows immediately after remission of the active-phase symptoms of the psychotic episode. Sometimes it may follow after a short or extended interval during which there are no psychotic symptoms. Mood symptoms due to the direct physiological effects of a drug of abuse, a medication, or a general medical condition are not counted toward postpsychotic depressive disorder of Schizophrenia.

According to DSM-IV, persons whose presentation meets those research criteria would be diagnosed as having depressive disorder not otherwise specified. As already pointed out, mood or depressive disorder not otherwise specified represents such a hodgepodge of clinical situations that the designation not otherwise specified is at best meaningless and at worst countertherapeutic. In all postpsychotic depressions, one must first exclude a missed bipolar diagnosis. Negative symptoms due to classic antipsychotics—especially depot phenothiazines and those due to the residuum of schizophrenia once positive symptoms are brought under control—should be distinguished from the depressive episodes that complicate the course of schizophrenia in young, intelligent patients.

<table>
<thead>
<tr>
<th>Table 14.6-25 DSM-IV Research Criteria for Postpsychotic Depressive Disorder of Schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Criteria met for a major depressive episode.</strong> Note: The major depressive episode must include criteria A1: depressed mood. Do not include symptoms that are better accounted for as medication side effects or negative symptoms of schizophrenia.</td>
</tr>
<tr>
<td><strong>B. The major depressive episode is superimposed on and occurs only during the residual phase of schizophrenia.</strong></td>
</tr>
<tr>
<td><strong>C. The major depressive episode is not due to the direct physiological effects of a substance or a general medical condition.</strong></td>
</tr>
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</table>

**BIPOLAR DISORDERS**

Four bipolar disorders are included in DSM-IV: bipolar I disorder, bipolar II disorder, cyclothymic disorder, and bipolar disorder not otherwise specified.
Bipolar I Disorder  Typically beginning in the teenage years, the 20s, or the 30s, the first episode could be manic, depressive, or mixed. One common mode of onset is mild retarded depression, or hypersomnia, for a few weeks or months, which then switches into a manic episode. Others begin with a severely psychotic manic episode with schizophreniform features; only when a more classic manic episode occurs is the affective nature of the disorder clarified. In a third group several depressive episodes take place before the first manic episode. A careful history taken from significant others often reveals dysthymic or cyclothymic traits that antedated the frank onset of manic episodes by several years.

According to DSM-IV, bipolar I disorder, single manic episode (Table 14.6-26) describes patients having a first episode of mania (most such patients eventually develop depressive episodes). The remaining subcategorization is used to specify the nature of the current or most recent episode in patients who have had recurrent mood episodes (Table 14.6-27, Table 14.6-28, Table 14.6-29, Table 14.6-30 and Table 14.6-31. For clinicians and researchers alike it is more meaningful to chart a patient's course in color over time—for example using red rectangles for manic, blue for depressive, and violet for mixed episodes, with hypomanic, dysthymic, and cyclothymic periods drawn in the appropriate colors on a smaller scale between the major episodes. Life events, biologic stressors, and treatment can be indicated by arrows on the time axis. This approach, originally championed by Kraepelin, is routinely used in mood clinics. Robert Post at the NIMH has developed this approach into systematic clinical science.

Table 14.6-26 DSM-IV Diagnostic Criteria for Bipolar I Disorder, Single Manic Episode

<table>
<thead>
<tr>
<th>A. Presence of only one manic episode and no past major depressive episodes. Note: Recurrence is defined as either a change in polarity from depression or an interval of at least 2 months without manic symptoms.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. The manic episode is not better accounted for by schizoaffective disorder, and is not superimposed on schizophrenia, schizoaffective disorder, delusional disorder, or psychotic disorder not otherwise specified. Specify if: Mixed: if symptoms meet criteria for a mixed episode.</td>
</tr>
</tbody>
</table>

Table 14.6-27 DSM-IV Diagnostic Criteria for Bipolar I Disorder, Most Recent Episode Manic

| A. Currently (or most recently) in a manic episode. |
| B. There has previously been at least one major depressive episode, manic episode, or mixed episode. |
| C. The mood episodes in criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizoaffective disorder, delusional disorder, or psychotic disorder not otherwise specified. Specify if: Current (or most recent episode): |
| Longitudinal course specifier (with and without interepisode remission). With seasonal pattern (applies only to the pattern of major depressive episodes). With rapid cycling. |

Table 14.6-28 DSM-IV Diagnostic Criteria for Bipolar I Disorder, Most Recent Episode Hypomanic

| A. Currently (or most recently) in a hypomanic episode. |
| B. There has previously been at least one manic episode or mixed episode. |
| C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. |
| D. The mood episodes in criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizoaffective disorder, delusional disorder, or psychotic disorder not otherwise specified. Specify: |
| Longitudinal course specifier (with and without interepisode remission). With seasonal pattern (applies only to the pattern of major depressive episodes). With rapid cycling. |

On average, manic episodes predominate in youth, and depressive episodes in later years. Although the overall sex ratio is about one to one, men on average undergo more manic episodes and women experience more mixed and depressive episodes. Bipolar I disorder in children is not as rare as previously thought; however, most reported cases are in boys, and mixed-manic (dysphoric-explosive) presentations are the mode. Childhood-onset depression must also be considered a major risk for ultimate bipolar transformation. This is based on the following characteristics: (1) early age of onset; (2) even sex ratio; (3) prominence of irritability, labile moods, and explosive anger, suggesting mixed episodes; (4) questionable response to antidepressants, hypomanic switches, or both; (5) high recurrence rate after depression; and (6) familial affective loading. Mania can also first appear after age 65, though a diligent search often reveals a past mild, forgotten, or untreated depressive episode in earlier years.

**Acute Mania** Mania typically escalates over a period of 1 to 2 weeks; more-sudden onsets have also been described. The DSM-IV criteria (Table 14.6-7) stipulate (1) a distinct period that represents a break from premorbid functioning, (2) a duration of at least 1 week, (3) an elevated or irritable mood, (4) at least three to four classic manic signs and symptoms, and (5) the absence of any physical factors that could account for the clinical picture. The irritable mood in mania can deteriorate to cantankerous behavior, especially when the person is rebuffed. Such patients are among the most aggressive seen in the emergency room. Florid grandiose psychosis with paranoid features, a common presentation of mania, further contributes to the aggression. Alcohol use, observed in at least 50 percent of bipolar I
patients (often during the manic phase), further disinhibits the patient and might lead to a dangerous frenzy. Such patients may attack loved ones and hurt them physically. So-called crimes of passion have been committed by patients harboring delusions of infidelity on the part of spouses or lovers, usually when under the influence of alcohol.

The genesis of delusional, hallucinatory, even first-rank, psychotic experiences in mania has been described. Recent research has documented that most types of formal thought disorders are common to both schizophrenic and mood psychoses; only poverty of speech content (vagueness) emerges as significantly more common in schizophrenia. Finally, posturing and negativism occur in mania (and, in the author's view, do not warrant the designation of catatonic features as advocated by DSM-IV). Although not specifically mentioned in the DSM-IV definition, confusion, even pseudodemented presentations, can occur in mania. Mania is most commonly expressed as a phase of bipolar type I disorder, which has strong genetic determinants. Available evidence does not permit separating recurrent mania without depressive episodes from that type as a distinct nosological entity.

**Secondary Mania** Although there is some suggestion that postpartum mania without depression is distinct from familial bipolar I disorder (in which depressive, manic, and especially mixed manic episodes occur in the postpartum period), the evidence for a distinct puerperal mania is not compelling at this time (hence the decision in DSM-IV to include the postpartum-onset specifier [see Table 13.4-3], rather than a separate mood disorder diagnosis). Mania without prior bipolarity can arise in the setting of such somatic illnesses as thyrotoxicosis, systemic lupus erythematosus or its treatment with steroids, rheumatic chorea, multiple sclerosis, Huntington's disease, cerebrovascular disorder, diencephalic and third ventricular tumors, head trauma, complex partial seizures, syphilis, and (most recently) AIDS. The family history is reportedly low in such cases, suggesting a relatively low genetic predisposition and thus a lower risk of recurrence. These patients do not easily fit into the DSM-IV category of mood disorder due to a general medical condition (Table 14.6-17) because most of the conditions appear to be cerebral. Such factors must always be diligently sought in manias of late life.

Less well defined forms of mania are the so-called reactive manias. Personal loss and bereavement are hypothesized to be triggering factors, and the reaction is conceptualized psychodynamically as a denial of loss. Although such explanations may be plausible in individual cases, no systematic data suggest that these patients differ in family history from persons with other manias. The same is generally true for depressed patients who switch to hypomania or mania after abuse of stimulant drugs, treatment with antidepressants, or sleep deprivation. In all of these situations a bipolar diathesis is usually manifest either in a family history of mania or in spontaneous excited episodes during prospective observation. First-onset manic episodes can also occur in persons who abruptly abstain from alcohol after one or more decades of chronic use and then develop classic bipolar I disorder.

**Chronic Mania** DSM-IV does not specifically address the diagnostic questions posed by the 5 percent of bipolar I patients who have a chronic manic course. These cases commonly represent deterioration of course dominated by recurrent manic episodes grafted on a hyperthymic baseline. Noncompliance with pharmacological treatment is the rule. Recurrent excitement is personally reinforcing, subjective distress is minimal, and insight is seriously impaired. Thus the patient sees no reason to adhere to treatment. Episodic or chronic alcohol abuse, prevalent in such patients, has been suggested as a contributory cause of the chronicity. Some authorities further consider comorbid cerebral pathology responsible for nonrecovery (and increased mortality) from manic excitement occurring in late life.

Grandiose delusions (e.g., delusions of inventive genius or aristocratic birth) are not uncommon in chronic mania and may lead to the mistaken diagnosis of paranoid schizophrenia. Because of their social deterioration, Kraepelin subsumed such patients under the category “manic dementia.” Organic factors such as head trauma and chronic alcohol abuse may contribute to the deterioration. Nonschizoid
premorbid adjustment, a family history of bipolar I disorder, and the absence of flagrant formal thought disorder can be marshaled in establishing the affective basis of these poor-prognosis manic states.

**Bipolar Mixed Phase** Momentary tearfulness and even depressed mood are commonly observed at the height of mania or during the transition from mania to retarded depression. These transient labile periods, which occur in most bipolar I disorder patients, must be contrasted with mixed episodes proper.

The latter, variously referred to as “mixed mania” or “dysphoric mania,” are characterized by dysphorically excited moods, irritability, anger, panic attacks, pressured speech, agitation, suicidal ideation, severe insomnia, grandiosity, and hypersexuality, as well as persecutory delusions and confusion. Severely psychotic mixed states that involved hallucinations and Schneiderian symptoms risk being labeled “schizoaffective.” A correct diagnosis is mandatory because conventional antipsychotic drugs tend to exacerbate the depressive component and failure to use mood stabilizers can prolong the patient's misery.

New research data from mood centers worldwide on mixed mania suggest that dysphoric mania—mania and full-blown depression occurring simultaneously—is relatively uncommon. Two to four depressive symptoms from the list of depressed mood, helplessness, hopelessness, fatigue, anhedonia, guilt, and suicidal ideation, or impulses, or both, in the setting of a manic syndrome, appear to suffice for the diagnosis of mixed manic states, which occurs in 50 percent of patients with bipolar disorder sometime during their lives. Mixed states occur predominantly in females in whom mania is superimposed on a depressive temperament or a dysthymic baseline. These considerations suggest that the DSM-IV concept of mixed episode (Table 14.6-8) as a cross-sectional mixture of mania and depression is simplistic and phenomenologically naive. The emerging conceptualization of mixed mania is a manic state intruding upon long-term depressive traits.

**Depressive Phase** Psychomotor retardation, with or without hypersomnia, marks the uncomplicated depressive phase of bipolar I disorder. Onset and offset are often abrupt, though onset can also occur gradually over several weeks. Patients may recover into a free interval or switch directly into mania. Switching into an excited phase is particularly likely when antidepressants have been used. However, not all patients develop mania after antidepressant treatment of bipolar depression. Some develop a mixed agitated depression; indeed, patients may be stuck for many months in a severe depressive phase with some manic admixtures such as racing thoughts and sexual arousal. DSM-IV does not specifically recognize a mixed depressive phase with few manic symptoms occurring during full-blown depression. Such recognition is necessary because these patients don't need continued aggressive antidepressant therapy but mood stabilizers, ECT, or both.

Delusional and hallucinatory experiences are less common in the depressive phase of bipolar I disorder than in the manic and mixed manic phases. Stupor is the more common psychotic presentation of bipolar depression, particularly in adolescents and young adults. Pseudodemented organic presentations appear to be the counterpart of stupor in elderly adults.

**Cyclothymic Disorder** An attenuated bipolar disorder that typically begins insidiously before the age of 21, cyclothymic disorder is characterized in DSM-IV by frequent short cycles of subsyndromal depression and hypomania (Table 14.6-32). The author's research has revealed alternating patterns of moods, activity, and cognition (Table 14.6-33), which are more explicit than the DSM-IV criteria. The course of cyclothymia is continuous or intermittent, with infrequent periods of euthymia. Shifts in mood often lack adequate precipitants (e.g., sudden profound dejection with social withdrawal for a few days switching into cheerful, gregarious behavior). Circadian factors may account for some of the extremes of emotional lability, such as the person's going to sleep in good spirits and waking up early with suicidal urges. The mood changes of cyclothymia are best described as “endoreactive” in the sense that
endogenous overreactivity seems to determine the sudden shifts in mood and behavior (e.g., falling in love with a person one has just met and as quickly falling out of love).

**Table 14.6-32 DSM-IV Diagnostic Criteria for Cyclothymic Disorder**

A. For at least 2 years, the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a major depressive episode, bipolar mania, or cyclothymic disorder in children and adolescents; the duration must be at least 1 year in adults.

B. During the above 2-year period 15 or more episodes of mood swings are present (e.g., intermittent periods in which both hypomanic and depressive symptoms are present, each lasting at least a few days at a time, with recurrent euthymic periods).

C. The mood swings must be accompanied by at least 2 periods of low mood or a depressed mood or a loss of interest in activities that were previously pleasurable (either in the same or different episodes).

D. The mood swings must be sufficiently severe to cause marked distress or impair important areas of functioning.

E. The mood swings are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia.

F. The symptoms are not due to the direct physiological effects of a substance (e.g., drug of abuse, a medication) or a general medical condition.

**Table 14.6-33 Clinical Features of Cyclothymic Disorder**

Mood swings in these ambulatory patients are overshadowed by the chaos that the swings produce in their personal lives. Repeated romantic breakups or marital failures are common because of interpersonal friction and episodic promiscuous behavior. Uneven performance at school and work is also common. Persons with cyclothymic disorder are dilettantes; they show great promise in many areas, but rarely bring any of their efforts to fruition. As a result, their lives are often a string of improvident activities. Geographical instability is a characteristic feature; easily attracted to a new locale job, or love partner, they soon lose interest and leave in dissatisfaction. Polysubstance abuse which occurs in as many as 50 percent of such persons, is often an attempt at self-treatment.

**Bipolar II Disorder (and the Soft Bipolar Spectrum)** Research conducted during the past three decades showed that between the extremes of classic manic-depressive illness defined by at least one acute manic episode (bipolar I disorder) and strictly defined major depressive disorder without any personal or family history of mania (pure unipolar disorder), exists an overlapping group of intermediary forms characterized by recurrent major depressive episodes and hypomania. **Table 14.6-34** summarizes the author's observations in defining the clinical subtypes within this intermediary realm best described as “soft bipolarity.” The most accepted of the subtypes is bipolar II disorder (with spontaneous hypomania), elevated to the status of a nosological entity in DSM-IV (**Table 14.6-35**). Current data worldwide indicate that bipolar II disorder is actually more prevalent than bipolar I disorder. This certainly appears true in the outpatient setting, where 30 to 50 percent of persons with major depressive disorder have been reported to conform to the bipolar II pattern.

**Table 14.6-34 Spectrum of Bipolar Disorders Compared With Unipolar Depression**
The following self-description provided by a 34-year-old poet illustrates the pattern:

I have known melancholy periods, lasting months at a time, when I would be literally paralyzed: All mental activity comes to a screeching halt, and I cannot even utter one word. I become so dysfunctional that I was once hospitalized. Although the paralysis creeps into me insidiously—often lasting months—it typically reverses within hours. I am suddenly alive and vibrant, I cannot turn off my brain neither during the day nor at night; I usually go on celebrating like this for many weeks, needing no more than few hours of slumber each day.

This vignette is nearly identical to the autobiographical description provided by the British poet William Cowper three centuries earlier:

I have known many a lifeless and unhallowed hour ... long intervals of darkness interrupted by short returns of peace and joy ... For many succeeding weeks to rejoice day and night was all my employment. Too happy to sleep much, I thought it was lost time that was spent on slumber.

The hypomania at the end of depressive episodes in most bipolar II patients does not persist long; it is usually measured in days. The modal duration of hypomania found in Memphis and Zurich studies was 2 days. Another common form of bipolar II disorder is major depressive disorder superimposed on cyclothymic disorder, in which hypomania precedes and follows major depression, the entire interepisodic period characterized by cyclothymic mood instability. As a result, these are difficult bipolar II patients to manage in clinical practice.

Hypomania in bipolar II disorder can be defined as minimanic episodes occurring spontaneously. Bipolar II disorder—especially when major depressions are superimposed on cyclothymia—is thus best characterized as cyclical or “cyclothymic depression.”

The depressive episodes of patients with bipolar disorder often have admixtures (e.g., flight of ideas, increased drives and impulsivity in sexual and other domains). The phenomenon of lithium
augmentation is perhaps best explained by the high prevalence of pseudounipolar depressions with subtle hypomania either during or following a depressive episode, as well as the mixed simultaneous presence of depressive and hypomanic symptoms. The latter are not as severe as dysphoric mixed states, but are refractory to antidepressants nonetheless.

**Hypomania** The common denominator of the soft spectrum of bipolar disorders is the occurrence of hypomania. Hypomania (Table 14.6-9) refers to a distinct period of at least a few days of mild elevation of mood, sharpened and positive thinking, and increased energy and activity levels, typically without the impairment characteristic of manic episodes. It is not merely a milder form of mania. Hypomania occurring as part of bipolar II disorder rarely progresses to manic psychosis; distractibility is uncommon in hypomania, and insight is relatively preserved. Hypomania is distinguished from mere happiness in that it tends to recur (happiness does not) and can sometimes be mobilized by antidepressants. In cyclothymic disorder it alternates with minidepressions; in hyperthymic temperament it constitutes the person's habitual baseline. These definitions then recognize three patterns of hypomania: brief episodes heralding the termination of a retarded depressive episode (bipolar II disorder), cyclic alternation with minidepressions (cyclothymic disorder), and an elevated baseline of high mood, activity, and cognition (hyperthymic or chronic hypomanic traits).

Because hypomania is experienced either as a rebound relief from depression or as pleasant, short-lived, ego-syntonic mood state, persons with bipolar II disorder rarely report it spontaneously. Skillful questioning is thus required to make the diagnosis of soft bipolar conditions; as in mania, collateral information from family members is crucial. In interviewing the patient the following probes have been found useful to elicit hypomania: “Have you had a distinct sustained high period (1) when your thinking and perceptions were unusually vivid or rapid, (2) your mood was so intense that you felt nervous, and (3) you were endowed with such energy that others could not keep up with you?” The hypomanic manifestations for hypomania in the DSM-IV scheme basically list the signs and symptoms of mania in criterion A and B for mania (Table 14.6-9) but require fewer items and shorter duration. Clinical and epidemiological studies in the United States and Europe have revealed a richer range of manifestations including an increase in cheerfulness and jocularity; gregariousness and people seeking; greater interest in sex; talkativeness, self-confidence, and optimism; and decreased inhibitions and sleep need. The clinician must ascertain that those experiences were not due to stimulant or alcohol withdrawal. Depressive and hypomanic periods are often not easily discerned because chronic caffeinism, stimulant abuse, or both complicate the depression. In such instances, diagnosis should be based on clinical observation for 1 month after detoxification.

When in doubt, direct clinical observation of hypomania—sometimes elicited by antidepressant pharmacotherapy—provides definitive evidence for the bipolar nature of the disorder. Unfortunately DSM-IV denies bipolar status to treatment-emergent hypomanic episodes. Follow-up studies in juvenile and young adults with pharmacological hypomania have demonstrated that nearly all such individuals progress to spontaneous hypomanic (or manic) episodes. Although DSM-IV stipulates a minimum duration of 4 days for hypomania, any recurrent hypomania coupled with major depression should count toward the diagnosis of bipolar II.

**Seasonal Patterns** Seasonality is observed in many cyclic depressions, often with autumn or winter anergic depression and energetic periods in the spring. This natural propensity explains why phototherapy may provoke mild hypomanic switches. Although not specifically identified by DSM-IV, seasonal depressions conform, in large measure, to the bipolar II or III pattern. Furthermore, preliminary evidence suggests that treatment with classic antidepressants disrupts the baseline seasonality, with the depressive phase appearing in the spring and summer. The changes antidepressants induce in seasonal depressions probably represent a special variant of the rapid-cycling phenomenon.
**Temperament and Polarity of Episodes** New systematic clinical observations have revealed that bipolar II disorder (characterized predominantly by depressive attacks) arises more often from a hyperthymic or cyclothymic baseline, whereas bipolar I disorder (defined by manic attacks) not uncommonly arises from the substrate of a depressive temperament. When the hyperthymic temperament occurs in bipolar I disorder, it is usually associated with a recurrent mania, which is an uncommon bipolar course. A prospective 11-year NIMH study of major depressive disorder patients who switched to bipolar II disorder showed that “mood-labile” (cyclothymic) and “energetic-active” (hyperthymic) temperament traits were highly specific and reasonably sensitive predictors of such an outcome.

Bipolarity is conventionally defined by the alternation of manic (or hypomanic) and depressive episodes. The foregoing data on temperaments suggest that a more fundamental characteristic of bipolarity is the reversal of temperament into its “opposite” episode (in the case of the bipolar II spectrum, from cyclothymia and hyperthymia to major depression). Such findings suggest that the intrusion of cyclothymic and hyperthymic traits into a depressive episode may underlie the instability of the bipolar II subtype and could partly explain why bipolar II depression often has mixed features. These considerations may have important implications for preventing recurrence. For instance, a prospective study of the onset of bipolar disorder in the offspring or sibs of adults with the disorder found that children with depressive onsets as their first episode (and which were usually treated with antidepressants) had significantly higher rates of recurrence than those with manic or mixed onsets (treated with lithium) during a 3-year prospective observation. It appears that temperamental instability in the depressive group might have predisposed them to the cycling effect of antidepressants.

**Alcohol, Substance Abuse, and Suicide** New evidence supports the high prevalence of alcohol and substance abuse in mood disorder subtypes, especially those with interepisodic cyclothymia and hyperthymia. The relation appears particularly strong in the teenage and early adult years, when the use of such substances often represents self-medication for the mood instability. It is not just self-treatment for selected symptoms associated with the down or up phases (e.g., alcohol to alleviate the insomnia and nervousness characteristic of both phases), it also augments certain desired ends (e.g., stimulants to enhance high-energy performance and sexual behavior associated with hypomania). How many display alcohol and substance abuse secondary to an underlying bipolar diathesis remains to be determined. But in view of findings suggesting a link between polysubstance abuse and suicide in adolescents with bipolar familial backgrounds, the use of mood stabilizers in these adolescents should be strongly considered. Although alcohol and stimulant use continues into adult years in a considerable number of bipolar disorder patients, such use is often unrelated to familial alcoholism, and frequently tends to dwindle during long-term follow-up, which supports the self-medication hypothesis. To complicate matters, in a substantial minority of cases, bipolar mood swings appear for the first time after abrupt cessation of long-term alcohol use; it is not uncommon for such mood swings to escalate into full-blown bipolar syndromes.

**Rapid-Cycling Bipolar Disorder** Rapid cycling is defined as the occurrence of at least four episodes—both retarded depression and hypomania (or mania)—a year (Table 14.6-36). Thus rapid cyclers are rarely free of affective symptoms and suffer serious vocational and interpersonal incapacitation. Lithium is often only modestly helpful to those patients, as are traditional antipsychotic agents; most antidepressants readily induce excited episodes and thus aggravate the rapid-cycling pattern. A balance among mood stabilizers, antipsychotic drugs, and antidepressants may be difficult to achieve. Many such patients require frequent hospitalization because they develop explosive excitement and precipitous descent into severe psychomotor inhibition. The disorder is a roller coaster nightmare for the patient, significant others, and the treating physician. Treating these patients is an art.
As expected, rapid cycling commonly arises from a cyclothymic substrate, which means that most rapid cyclers have bipolar II disorder. Factors favoring its occurrence include (1) female gender; (2) borderline hypothyroidism; (3) menopause; (4) temporal lobe dysrhythmias; (5) alcohol, minor tranquilizer, stimulant, or caffeine abuse; and (6) long-term, aggressive use of antidepressant medications. Most clinically identified patients are bipolar II women in middle age or upper social classes. Rapid cycling is uncommon from a bipolar I base.

Leadership and Creativity Persons with hyperthymic temperament and soft bipolar conditions in general possess assets that permit them to assume leadership roles in business, the professions, civic life, and politics. Increased energy, sharp thinking, self-confidence and eloquence represent the virtues of an otherwise stormy life.

Creative achievement is relatively uncommon among those with the manic forms of the disorder, which is too severe and disorganizing to permit the necessary concentration and application. Notable artistic achievements are found among those with soft bipolar disorders, especially cyclothymic disorders.

Psychosis, including severe bipolar swings, is generally incompatible with creativity. That conclusion, based on recent systematic studies, tends to refute the romantic tendency to idolize insanity as central to the creative process. As talent is the necessary ingredient of creativity, how might soft bipolarity contribute? The simplest hypothesis is that depression might provide insights into the human condition, and the activation associated with hypomania helps in producing the artistic work. A more profound interpretation suggests that the repeated self-doubt that comes with recurrent depression might be an important ingredient of creativity, because original artistic or scientific expression is often initially rejected, and the self-confidence that accompanies repeated bouts of hypomania can help in rehearsing such ideas or expressions until they are perfected. Finally, the tempestuous object relations associated with bipolarity in the parent's or the patient's life often create the unique biographical landmarks that might be immortalized in an artistic medium.

Bipolar Disorder Not Otherwise Specified The criteria for bipolar disorder not otherwise specified are listed in Table 14.6-37.

Recurrent hypomanic episodes without intermittent depressions (example 2 in the DSM-IV criteria for
bipolar disorder not otherwise specified are almost never observed clinically.

**Recurrent Brief Hypomania** Recurrent brief depressive disorder as a transitional form between dysthymia and major depression or brief hypomanic episodes often have been missed during evaluations performed by nonclinicians. Some patients who meet the Zurich description might therefore belong in the soft bipolar spectrum. Indeed, subsequent evaluation and analyses have revealed high rates of comorbidity between recurrent brief depression and brief hypomania. Thus, some recurrent brief depressive cases appear to be variants of bipolar disorder. The subtle bipolar nature of recurrent brief depressive disorder is clinically supported by the fact that the very few such patients the author has encountered in his own practice did poorly with antidepressant monotherapy but benefited from mood stabilizers used alone or combined with antidepressants.

The recurrent hypomanic counterpart of recurrent brief depressive disorder is described under soft bipolar conditions. By DSM-IV criteria, it represents an instance of bipolar disorder not otherwise specified.

**Hysteroid Dysphoria** The category hysteroid dysphoria combines reverse vegetative signs with the following characteristics: (1) giddy responses to romantic opportunities and an avalanche of dysphoria (angry-depressive, even suicidal responses) upon romantic disappointment; (2) impaired anticipatory pleasure, yet the capability to respond with pleasure when such is provided by others (i.e., preservation of consummatory reward); (3) craving for chocolate and sweets, which contain phenylethylamine compounds and sugars believed to facilitate cellular and neuronal intake of the amino acid L-tryptophan, hypothetically leading to synthesis of endogenous antidepressants in the brain. The use of the epithet “hysteroid” was used to convey that the apparent character pathology was secondary to a biological disturbance in the substrates governing affect, drives, and reward. The intense, giddy, unstable life of the patient with hysteroid dysphoria suggests links to cyclothymic disorder or bipolar II disorder. This suggestion is further supported by the Columbia group’s tendency to subsume those patients under atypical depressions (some of which, as indicated, have bipolar affinities). Like patients with bipolar depression, they respond preferentially to monoamine oxidase inhibitors (MAOIs). In brief, hysteroid dysphoria appears to be a variant of bipolar II with cyclothymic-irritable traits. Other variants of bipolar II disorder with hyperthymic-narcissistic traits are described under soft bipolar disorder and represent instances of bipolar disorder not otherwise specified.

**Bipolar III Disorder** In bipolar III disorder (which is not an official nosological term but can be subsumed under bipolar disorder not otherwise specified) evidence of bipolarity is softer, such as a single brief episode of an antidepressant-mobilized switch. In a related subgroup of cryptic bipolar disorders, strong evidence for familial bipolarity raises the possibility that some phenotypically “unipolar” depressed patients are nonetheless constitutionally bipolar; in such cases, history for hypomania occurring in discrete episodes is not obtained; instead the patient's habitual temperamental baseline is sunny, overenergetic, and overoptimistic (hyperthymic).

Depending on the threshold of traits used in determining the presence of hyperthymia, bipolar III patients may constitute 10 to 20 percent of those with major depressive disorder. Thus, many patients with so-called unipolar depression are actually “pseudounipolar.” The presence of marked narcissistic traits is a helpful clinical clue that a clinically depressed patient might belong to the group of those with hyperthymic depressions.

**MOOD DISORDERS NOT OTHERWISE SPECIFIED**

After all diagnostic information has been obtained, some depressed and bipolar or otherwise affective
patients do not meet the specific criteria for the mood conditions described thus far. Mood disorders not otherwise specified is a statistical concept for filing purposes and not a clinical description. The author prefers to consider such cases as undiagnosed mood disorders rather than using the DSM-IV categories of depression disorder not otherwise specified, bipolar disorder not otherwise specified or mood disorder not otherwise specified.

What follows are descriptions of conditions that commonly appear in the psychiatric literature but do not easily fit into the official nosology of mood disorders. They represent hybrids between mood and anxiety disorders.

**Mixed Anxiety-Depressive Disorder** The inclusion of anxious depressive states in a DSM-IV appendix acknowledges the simultaneous occurrence of anxious (e.g., the threat loss represents) and depressive (e.g., the despair of loss) cognition in a person confronted with a major aversive life situation. The admixture implies that the psychopathology progresses from anxiety to depression, that the patient's mental state is still in flux, and that the ongoing dynamics partly explains the subacute or chronic nature of the disorder. Anxious depression serves to point to the common presence of anxiety in depressive states, especially its greater visibility when the depression is less prominent. Patients with the latter presentation are reportedly most prevalent in general medical settings. This should not come as a surprise, because depressive symptoms that motivate medical consultation commonly complicate generalized anxiety states with a subthreshold level of symptomatology. Some authorities argue that neurotic depressions arise as maladaptive responses to anxiety and on that basis suggest retaining the “neurotic depression” rubric. Recent preliminary genetic data indirectly support the contention that certain (unipolar) depressive and (generalized) anxiety states are related. However, more research is needed before such an entity can be unequivocally accepted as an official nosological category. The difficulty is that as currently defined, anxious depressions are heterogeneous. In patients refractory to anxiolytic or antidepressant treatment or both, practitioners must entertain the diagnosis of a complex bipolar II disorder with mixed features. Indeed, recent genetic investigations suggest that bipolar II disorder with panic attacks might represent a special form of bipolar disorder.

**Atypical Depression** Although a delimited version of atypical depression was incorporated into DSM-IV as “atypical features (Table 14.6-5) to qualify the cross-sectional picture of depressive disorders, this construct is much broader in the clinical research literature. Originally developed in England and currently under investigation at Columbia University in New York, atypical depression refers to fatigue superimposed on a history of somatic anxiety and phobias, together with reverse vegetative signs (mood worse in the evening, insomnia, tendency to oversleep and overeat). Sleep is disturbed in the first half of the night in many persons with atypical depressive disorder, so irritability, hypersomnolence, and daytime fatigue would be expected. The temperaments of these patients are characterized by inhibited-sensitive traits. The MAOIs and serotonergic antidepressants seem to show some specificity for such patients, which is the main reason that atypical depression is taken seriously.

Other research suggests that reverse vegetative signs can be classified as either (1) the anxious type just described or (2) a subtle bipolar subtype with protracted hyperphagic-hypersomnic-retarded dysthymic disorder with occasional brief extroverted hypomanic-type behavior, often elicited by antidepressants. Increasing evidence indicates considerable affinity between atypical depression and bipolar II and III disorders. Furthermore, many patients with dysthymic disorder exhibit atypical features at various times. Actually, atypical depression might be an artifact of the DSM-IV definition of hypomania of 4 or more days. Recent Italian research suggests that many patients with atypical depressive meet criteria for brief hypomania or cyclothymic disorder.

The categories of not otherwise specified in the DSM-IV mood disorders schema largely reflect inadequacies of the operational approach to capture patients whose symptomatology falls between or on
the boundaries of more classic diagnoses.

DIFFERENTIAL DIAGNOSIS

A missed mood disorder diagnosis means that the disorder does not receive specific treatment, which has serious consequences. Many such persons drop out of school or college, lose their jobs, get divorced, or may commit suicide. Those with unexplained somatic symptoms are frequent users of the general health system. Others are unwell despite interminable psychotherapy. Some, treated with dopamine receptor antagonists develop tardive dyskinesia unnecessarily. As with other medical disorders for which specific treatments are available, accurate diagnosis and early treatment are within the purview of all physicians and mental health professionals. Psychiatrists, in particular, should develop the competence to detect the entire spectrum of mood disorders. Despite massive educational efforts, underdiagnosis and undertreatment of mood disorders remain serious problems worldwide.

Although much enthusiasm was generated a decade ago about the potential use of certain biologic markers (e.g., REM latency, dexamethasone (Decadron) suppression test, and the thyrotropin-releasing-hormone test) to corroborate the differentiation of mood disorder from adjacent disorders, no definitive progress justifies their routine use in clinical practice. Faced with unusual or confusing presentations, a systematic clinical approach is still the best method in differential diagnosis (1) to detail all clinical features of the current episode, (2) to elicit a history of more typical major mood episodes in the past, (3) to assess whether the presenting complaints recur periodically or cyclically, (4) to substantiate adequate social functioning between periods of illness, (5) to obtain a positive family history for classic mood disorder and to construct a family pedigree, and (6) to document a history of unequivocal therapeutic response to thymoleptic medication or ECT in either the patient or the family.

Using the foregoing validating approach, one can examine the affective links of many DSM-IV disorders currently listed under mood disorders not otherwise specified, as well as controversial nosological entities currently categorized as nonmood disorders. The latter include conduct disorders; borderline personality disorder; impulse-control disorders; polysubstance abuse; psychotic disorder not otherwise specified; pain disorder; hypochondriasis; hypoactive sexual desire disorder; circadian rhythm sleep disorder, delayed sleep phase type; bulimia nervosa; and adjustment disorder (with work inhibition). These conditions place special emphasis on selected affective features, such as disinhibited behavior, temperamentality, mood lability, vegetative disturbances, and psychomotor anergia. What follows is a systematic examination of the differential diagnosis of mood disorders with their more classic boundaries.

Alcohol and Substance Use Disorders The high comorbidity of alcohol and substance use disorders with mood disorders cannot be explained as merely the chance occurrence of two prevalent disorders. Self-medication for mood disorders is insufficiently appreciated by both psychiatrists and other professionals who deal with addiction. Given the clinical dangers of missing an otherwise treatable disorder, mood disorder should be seriously considered as the primary diagnosis if marked affective manifestations persist or escalate after detoxification (e.g. 1 month). This consideration also pertains to cyclothymic disorder and dysthymic disorder, which appear particularly likely to invite self-medication. The clinical validating strategies listed above can further buttress a mood disorder diagnosis.

The DSM-IV category of substance-induced mood disorder (Table 14.6-18) is difficult to validate clinically because in the absence of an affective diathesis, detoxification should, in principle, rapidly clear affective disturbances in persons whose primary problem is that of substance abuse. In the author's view, a dual diagnosis of both a mood disorder and a substance use disorder is a more realistic clinical approach to this group of patients. Bipolarity, particularly bipolar II disorder, should be sought in the
interface of mood and substance use disorders.

A 27-year-old married businessman employed in an international family venture owned by his father presented with a court-ordered request for psychiatric treatment. He had been found “bringing” cocaine across the U.S.-Mexican border and was briefly jailed. He had used stimulants since his late teens to enhance his already high level of energy. His family was rich, and he had no difficulty affording cocaine. During the previous year, he had needed more cocaine because of greater moodiness and fleeting suicidal ideation, which he linked to increasing tensions between him and his father: “My father was never satisfied with me and demanded greater and greater performance from me.” His arrest by police was a major embarrassment for him and his family and motivated his compliance with psychiatric hospitalization to detoxify him. He had not had cocaine for 10 days, exhibited marked lability of mood, and gradually sank into a severe hypersomnic-retarded depression of stuporous proportions. He was treated with tranylcypromine (Parnate) 20 mg twice a day, and within 10 days he switched into hypomania, his mind “exploding with creativity and confidence,” marked jocularity and witticisms that entertained other patients, and marked seductiveness toward the nurses. His wife recalled that the patient previously had had several such periods naturally (i.e., “off cocaine”), which had strained their marriage due to “brief sexual liaisons.” Reducing the tranylcypromine dosage by 50 percent did not eliminate the hypomanic behavior and lithium 900 mg a day was added. He has since been maintained on a combination of tranylcypromine and lithium for 4 years; he has not relapsed into cocaine use, and following few psychoeducational sessions involving father and spouse, relationships with family and spouse have been less tempestuous. (Since consultation was sought by the patient's 60-year-old mother, an attractive, sophisticated woman, who confessed that for years she had been engaging in “love relationships” with young artists, with apparently her husband's “silent consent”; since at least her mid-20s, she by history would meet the criteria for bipolar II, only treated “on the couch,” and both her sister and brother had received treatment for “alcohol excesses.”) Patient states that pharmacotherapy—which did require adjustment now and then—has helped in balancing the “rough edges” of his “high-nervous temperament” and his “periodic lapse into paralyzing fatigue states that occurred at stressful times.”

If clinicians had assumed that primarily due to cocaine withdrawal, they would have never treated the patient's bipolar II disorder. DSM-IV conventions in this regard unfortunately bias diagnosis in favor of substance use disorders and, more tragically, against the realistic chance of cure from substances.

There is emerging interest in treating dually diagnosed patients with mood stabilizers, especially anticonvulsants. The intention is to attenuate any withdrawal phenomena from substances of abuse, while treating any underlying or emerging soft bipolar disorders.

**Personality Disorders** The state dependency of most personality measures is well documented. Accordingly, as exhorted by DSM-IV, clinicians should refrain from using personality disorder labels in describing patients with active affective illness and should focus instead on competent treatment of the mood disorder. Even in those with chronic or subthreshold mood disorders, personality maladjustment is best considered postaffective, arising from the distortions and conflicts that affective disturbances produce in the life of the sufferer. The most problematic of the personality labels used in those with mood disorders is borderline personality disorder, usually applied to teenage and young adult females. The DSM-IV diagnostic criteria for the disorder indicate a liberal mélange of low-grade affective symptoms and behavior. Table 14.6-38 shows that the overlap between borderline personality and mood disorders is extensive, so that giving a “borderline” diagnosis to a person with mood disorder is redundant. Use of personality disorder diagnoses may lead to neglect of the mood disorder or perhaps...
half-hearted treatment of the mood disorder; failure to respond would then be blamed on the patient's “self-defeating character” or “resistance to getting well,” thus exculpating the clinician.

Table 14.6-38 Overlap of Borderline Personality Disorder and Mood Disorders

Although more-systematic research is needed on the complex interface of personality and mood disorders, clinically they are often inseparable. As with alcohol and substance use disorders, it is generally preferable to diagnose mood disorders at the expense of personality disorders, which should not be difficult to justify in most cases that satisfy the validating strategies outlined above. When features of personality and mood disorders coexist, it is good practice to defer Axis II diagnoses and embark upon competent treatment of the concurrent mood disorder. Although not all personality disturbances recede with the competent treatment of mood disorders, so many experienced clinicians have seen such disturbances melt away with the successful resolution of the mood disorder that erring in favor of mood disorders is justified.

A 19-year-old single woman presented with the chief complaint that “all men are bastards.” Since her early teens, with the onset of her menses, she had complained of extreme variability in her moods on a nearly daily basis; irritability with hostile outbursts was her main affect, though more protracted hypersomnic depressions with multiple overdoses and wrist slashings had led to at least three hospitalizations. She also suffered from migrainous headaches that, according to the mother, had motivated at least one of those overdoses. Despite her tempestuous and suicidal moods that led to these hospitalizations, she complained of “inner emptiness and a bottomless void.” She had used heroin, alcohol, and stimulants to overcome this troubling symptom. She also gave history of ice-cream craving and frequent purging. She was talented in English and wrote much-acclaimed papers on the American confessional poet, Anne Sexton. She said she was mentally disturbed because of a series of stepfathers who had all forced “oral rape” between the ages of 11 and 15. She subsequently gave herself sexually to any man she met in bars, no longer knowing whether she was a “prostitute” or a “nice little girl.” On two occasions she had inflicted cigarette burns on her vagina “to feel something.” She had also engaged in a “brief lesbian relationship” that ultimately left her “emptier” and guilt-ridden; nonetheless, she now believed that she should burn in hell, because she could not get rid of “obsessing” about the excitement of mutual cunnilingus with her much older female partner. The patient's mother, who owned an art gallery, had been married five times and gave history of unmistakable hypomanic episodes; a maternal uncle had died from alcohol-induced cirrhosis. The patient's father, a well-known lawyer known for his “temper and wit,” had committed suicide. The patient was given phenelzine (Nardil), eventually raised to 75 mg a day, at which point the mother described her as “the sweet daughter she was before age 13.” At her next premenstrual phase, patient developed insomnia, ran away from home at night, started “dancing like a go-go girl,” met an “incredibly handsome man” of 45 years (actually, a pornography shop owner) and got married. Lithium augmentation controlled this excited episode. After many dosage adjustments, she is maintained on a combination of lithium (900 mg a day) and divalproex (Depakote) (750 mg a day). The patient now attends college and has completed four semesters in art history. In addition to control of her irritable and suicidal
moods, bulimic and migraine attacks have abated considerably. Her marriage has been annulled on the basis that she was not mentally competent at the time of the wedding. She is no longer sexually and now expresses fear of intimacy with men she is attracted to. She is receiving individual psychotherapy for this problem.

The author often hears the complaint that even when a mood disorder is diagnosed in a “borderline” patient, response to antidepressants is disappointing. The problem is that affective disorders in these patients usually conform to bipolar II disorder—often complicated by ultrarapid cycling—and many clinicians, including some with biological orientation, may lack sufficient experience in the art of pharmacologically managing patients who markedly deviate from classic bipolar I disorder.

The interface of mood disorders and behavioral disturbances (conduct and attention-deficit/hyperactivity disturbances) in children is even more problematic than in adult psychiatry. Nonetheless, progress has occurred in clinically recognizing certain behavioral manifestations as possible signs of depression in juvenile subjects, including periodic marked decline in school performance; restlessness and pulling or rubbing hair, n, or clothing; outbursts of complaining, shouting, or crying; and aggressive or antisocial acts (such as kicking the mother, shoplifting) out of character to the child; as well as other acute personality changes ranging from defiant attitudes to negativism and avoidant behavior. Examined carefully, children and pubescent youth with these characteristics often meet the specific criteria for the diagnosis of major depressive disorder or dysthymic disorder. However, most children do not complain of subjective dysphoria; instead, the clinician can observe the depressed affect in the child's facial expressions or overall demeanor. After much resistance, many child clinicians now accept the existence of childhood mood disorders.

Table 14.6-39 lists those and related conditions often confused with bipolar disorders in juvenile patients. Many children express bipolar disorder in explosive outbursts of irritable mood and behavior (i.e., as a mixed or dysphoric manic state); another pattern is intermittent hypomania and cyclothymia. Children with bipolar disorder are distinguished from those with so-called externalizing disorders by the fact that they are often, though not always, considered charming and likeable, yet overconfident or delusionally grandiose, and may exhibit age-inappropriate sexual behavior, such as lecherous advances toward adult women (e.g., their elementary school teachers): Moreover, they often get worse on stimulant medication. Correct diagnosis depends on the index of suspicion of a clinician who is convinced that

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Bipolar disorder in children, even in adolescents, is still grossly underdiagnosed at the expense of so-called externalizing disorders. Table 14.6-39 lists those and related conditions often confused with bipolar disorders in juvenile patients. Many children express bipolar disorder in explosive outbursts of irritable mood and behavior (i.e., as a mixed or dysphoric manic state); another pattern is intermittent hypomania and cyclothymia. Children with bipolar disorder are distinguished from those with so-called externalizing disorders by the fact that they are often, though not always, considered charming and likeable, yet overconfident or delusionally grandiose, and may exhibit age-inappropriate sexual behavior, such as lecherous advances toward adult women (e.g., their elementary school teachers): Moreover, they often get worse on stimulant medication. Correct diagnosis depends on the index of suspicion of a clinician who is convinced that bipolarity exists in juvenile subjects. Depression with first onset before age 18 has an extremely high rate of switching into both bipolar I and bipolar II disorders.

Table 14.6-39 Misdiagnosis in the Affectively Ill Juvenile Kin of Adults With Bipolar Disorder

Normal Bereavement Bereaved persons exhibit many depressive symptoms during the first 1 to 2 years after their loss, so how can the 5 percent of bereaved persons who have progressed to a depressive disorder be identified?

- Grieving persons and their relatives perceive bereavement as a normal reaction, while those with depressive disorder often view themselves as sick and may actually believe they are losing their minds.
- Unlike the melancholic person, the grieving person reacts to the environment and tends to show a range of positive affects.
- Marked psychomotor retardation is not observed in normal grief.
- Although bereaved persons often feel guilty about not having done certain things that might have saved the life of the deceased loved one (guilt of omission), they typically do not experience guilt of commission.
- Delusions of worthlessness or sin and psychotic experiences in general point toward mood disorder.
- Active suicidal ideation is rare in grief but common in major depressive disorder.
- Mummification (i.e., keeping the belongings of the deceased person exactly as they were before his or her death) indicates serious psychopathology.
- Severe anniversary reactions should alert the clinician to the possibility of psychopathology.

In another form of bereavement depression, the sufferer simply pines away, unable to live without the departed person, usually a spouse. Although not necessarily pathological by the foregoing criteria, such persons do have a serious medical condition. Their immune function is often depressed, and their cardiovascular status is precarious. Death can ensue within a few months of that of a spouse, especially among elderly men. Such considerations (highlighted in the work of Sidney Zisook and his San Diego colleagues at the University of California) suggest that it would be clinically unwise to withhold antidepressants from many persons experiencing an intensely mournful form of grief.

A 75-year-old widow was brought by her daughter because of severe insomnia and total loss of interest in daily routines following her husband's death 1 year before. She had been agitated for the first 2 to 3 months and thereafter “sank into total inactivity—not wanting to get out of bed, not wanting to do anything, not wanting to go out.” According to her daughter, she was married at 21, had four children, and had been a housewife until her husband's death from a heart attack. Past
Anxiety Disorders Anxiety symptoms including panic attacks, morbid fears, and obsessions are common during depressive disorders, and depression is a common complication of anxiety states. Systematic British studies have shown that early-morning awakening, psychomotor retardation, self-reproach, hopelessness, and suicidal ideation are the strongest clinical markers of depression in that differential diagnosis. On follow-up of depressed patients, the manifestations tend to remit, whereas those with anxiety states continue to exhibit marked tension, phobias, panic attacks, vasomotor instability, feelings of unreality, and perceptual distortions as well as hypochondriacal ideas. A predominance of such anxiety features antedating the present disorder suggests the diagnosis of an anxiety disorder. Since anxiety disorders rarely first appear after the age of 40, late appearance of marked anxiety features strongly favors the diagnosis of melancholia. The clinical picture is often one of morbid groundless anxiety with somatization, hypochondriasis, and agitation. The depressive nature of the illness is further supported by a superior response to ECT.

Periodic monosymptomatic phobic and obsessional states exist that can be regarded as affective equivalents on the basis of a family history of mood disorders and their response to thymoleptic agents. Recent data from a large clinical series suggests that 15 percent of patients with obsessive-compulsive disorders develop unmistakable hypomanic symptoms; these patients are best considered to have bipolar II disorder and treated with lithium salts. Social phobias exist that usher in adolescent depression, even a bipolar disorder.

The psychopathological differentiation of anxiety and depressive states has not been entirely resolved. Cognitive factors may differentiate them best (Table 14.6-40). Although recurrent (especially retarded) major depressive disorder is a distinct disorder from anxiety states, at least some forms of depression may share a common diathesis with anxiety disorders, particularly generalized anxiety disorders. Before assigning patients to such a putative mixed anxiety-depressive group (not yet an official nosological entity), the clinician must note that anxiety that arises primarily during depressive episodes is best considered as epiphenomenal to depressive disorder. The same is generally true for anxiety symptoms that occur in a person with depressive disorder who is using alcohol or sedative-hypnotic or stimulant drugs. Finally, anxiety symptoms could be prominent features of mixed bipolar states as well as of complex partial seizures.

Table 14.6-40 Unique Cross-Sectional Profiles of Clinical Anxiety and Depression

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psychiatric history was negative; premorbid adjustment had been characterized by compulsive traits. During the interview she was dressed in black, appeared moderately slowed, and sobbed incessantly, saying “I search everywhere for him ... I don't find him.” When asked about life, she said everything I see is black.” Although she expressed no interest in food, she did not seem to have lost an appreciable amount of weight. Her dexamethasone suppression test result was 18 µg/dL. The patient declined psychiatric care, stating that she “preferred to join her husband rather than get help.” She was too religious to commit suicide but by refusing treatment she felt she would “pine away ... find relief in death and reunion.”

Anxiety symptoms including panic attacks, morbid fears, and obsessions are common during depressive disorders, and depression is a common complication of anxiety states. Systematic British studies have shown that early-morning awakening, psychomotor retardation, self-reproach, hopelessness, and suicidal ideation are the strongest clinical markers of depression in that differential diagnosis. On follow-up of depressed patients, the manifestations tend to remit, whereas those with anxiety states continue to exhibit marked tension, phobias, panic attacks, vasomotor instability, feelings of unreality, and perceptual distortions as well as hypochondriacal ideas. A predominance of such anxiety features antedating the present disorder suggests the diagnosis of an anxiety disorder. Since anxiety disorders rarely first appear after the age of 40, late appearance of marked anxiety features strongly favors the diagnosis of melancholia. The clinical picture is often one of morbid groundless anxiety with somatization, hypochondriasis, and agitation. The depressive nature of the illness is further supported by a superior response to ECT.
**Physical Disease** Somatic complaints are common in depressive disorders. Some, such as vegetative disturbances, represent the hypothalamic pathology that is believed to underlie a depressive disorder. Autonomic arousal, commonly associated with depression, could explain such symptoms as palpitations, sweating, and headache. In some instances the physical symptoms might reflect delusional experiences. The clinician must be vigilant about the likelihood that somatic complaints in depression can also reflect an underlying physical illness. Table 14.6-41 lists the most common medical conditions that have been associated with depression. When depressive symptoms occur in the setting of physical illness, it is not always easy to determine whether they constitute a genuine depressive disorder. Before diagnosing depression, psychiatrists must ensure that they are not dealing with pseudodepression: (1) functional loss due to physical illness; (2) vegetative signs, such as anorexia and weight loss, as manifestations of such an illness; (3) stress and demoralization secondary to the hospitalization; (4) pain and discomfort associated with the physical illness; and (5) medication adverse effects. On the other hand, nonpsychiatric physicians who manage such patients must consider the diagnosis of depression in the presence of persistent anhedonia; observed depressed mood with frequent crying; observed psychomotor retardation or agitation; indecisiveness; convictions of failure, worthlessness, or guilt; and suicidal ideation. The physician should also suspect clinical depression in all patients who refuse to participate in medical care.

### Table 14.6-41 Pharmacological Factors and Physical Diseases Associated with Onset of Depression

<table>
<thead>
<tr>
<th>Pharmacological</th>
<th>Physical Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrinology</td>
<td>Hypothalamic disturbances, obesity, hypothymic disturbances, endocrine disturbances, alterations in menstrual cycle, diabetic neuropathy, hypothyroidism, hypoglycemia, hypopituitarism, hyporeninemia, lymphoma, myeloma, ovarian cyst, pituitary adenoma, renal failure, pancreatic disease, peritoneal carcinomatosis, small bowel obstruction, bladder cancer, colorectal cancer, endometrial cancer, lymphoma, melanoma, ovarian cancer, pancreatic cancer, and prostate cancer.</td>
</tr>
<tr>
<td>Neurological</td>
<td>Hypertension, myocardial infarction, cerebrovascular disease, brain tumors, stroke, Parkinson’s disease, and multiple sclerosis.</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Gastritis, peptic ulcer, appendicitis, pylorospasm, and chronic constipation.</td>
</tr>
<tr>
<td>Neoplastic</td>
<td>Neoplasmic metastasis, chemical carcinogen, and anemia.</td>
</tr>
</tbody>
</table>

Diagnosing depression in medically ill elderly patients can be particularly difficult. This task should be undertaken diligently because it was recently reported that (especially in those with cardiovascular disease) mortality is accelerated by depression. Depressed elderly adults often deny being “depressed” but complain of anxiety, fatigue, and worsening memory. Hypochondriacal symptoms and pain are common. Patients may exhibit extreme negativism and querulousness when invited to participate in medical procedures; others develop poor fluid and food intake out of proportion to their physical conditions.

Another important diagnostic problem at the interface of mood disorder and physical disease is the rare development of malignancy in patients with an established mood disorder. Patients who had responded well to a given antidepressant during previous episodes now have an unsatisfactory response to the same medication. Even a small dose may cause such alarming symptoms as agitation, dizziness, depersonalization, and illusions, which might indicate an occult malignancy, perhaps in the abdomen or...
the brain. The psychiatrist should always be vigilant about the development of life-threatening physical diseases in patients with preestablished depressive disorder.

Although less common today, stupor still raises a diagnostic problem in differentiating between a mood disorder and somatic disease as well as other psychiatric disorders. Depressive stupor is relatively easy to distinguish from so-called hysterical mutism; in the latter, behavior is meaningfully directed to significant others in the patient's environment. The rubric of catatonic stupor is best reserved for a phase of schizophrenia; in such patients the schizophrenic origin of the stupor is best reserved for a phase of schizophrenia; in such patients the schizophrenic origin of the catatonia might be apparent from the patient's history. Otherwise, most acute-onset stupors are probably of affective origin. The main differential diagnosis here is from organic stupor (due to drugs or acute intracranial events); the physical and neurological examination is not always decisive in such cases, and diagnosis depends on a high index of suspicion of possible somatic factors.

Depressive Pseudodementia The geriatric equivalent of semistupor in younger persons with depressive disorder, depressive pseudodementia is distinguished from primary degenerative dementia by its acute onset without prior cognitive disturbance; a personal or family history of past affective episodes; marked psychomotor retardation with reduced social interaction; self reproach; diurnal cognitive dysfunction (worse in the morning); subjective memory dysfunction in excess of objective findings; circumscribed memory deficits that can be reversed with proper coaching; and a tendency to improve with sleep deprivation.

Chronic Fatigue Syndrome Chronic fatigue syndrome is a complex differential diagnostic problem in view of the subtle immunological disturbances presumably associated with it. The following self-report by such a patient illustrates many of the uncertainties marking the present knowledge of the interface between the syndrome and mood disorders.

I am a 39-year-old, never-married woman, trained as a social worker, but currently on disability. I have experienced extreme lethargy and fatigue for many years. I have always felt foggy headed and had trouble thinking and concentrating. My complaint is of fatigue, not of depression. My body feels like lead and aches all over. My brain feels achy and sore. I feel much worse in the morning and I can't get out of bed; I feel better at night. I feel bad every day. I ache all over, as though someone had beaten me up. Exercise has been prescribed to me, but it makes me worse. Also, I am very sensitive to hot and cold. My sexual drive is low. I have a general feeling of anhedonia. As far back as I remember—in junior high school—I was always exhausted. I always complained about fatigue, not depression, because that has been the overwhelming problem. I feel the depression is secondary to the fatigue. In high school I was a compulsive overeater and I was bulimic for a few years, but it was never severe and I was only about 10 pounds overweight. In those days I would sleep 10 or 12 hours a night on the weekend and still feel exhausted; I could not get up for school on Monday. As an adolescent, I felt inferior. I couldn't make decisions, I
While awaiting more definitive research on the etiology of chronic fatigue syndrome, the psychiatrist can cautiously consider certain patients for thymoleptic trials. That decision can be bolstered by the following considerations: the patient wakes up with fatigue and dread of facing the day; fatigue is part of a more generalized psychomotor inertia or lack of initiative; fatigue is associated with anhedonia, including sexual anhedonia; and fatigue coexists with anxious and pessimistic ruminations. Although none of the foregoing alone is pathognomonic for depression, in aggregate they point in that direction. The occurrence of hypomanic-like periods (as in the above vignette) further supports the link between some cases of chronic fatigue and mood disorder. Use of antidepressants without sedative effects, given in gradually increasing doses as tolerated, is a rational strategy; lithium and valproate, though not formally tested in such patients, are rational augmentation choices. Several recent neuroendocrine challenge studies suggest that some chronic fatigue patients might have a strong anxiety substrate and could be managed accordingly. This is not to say that chronic fatigue is largely a matter of missed affective diagnoses; yet it would be a pity to miss potentially treatable diagnoses. A family or past personal history of classic affective illness or episodes should strongly weigh in this direction. Obviously definitive data are lacking on the essential nature of chronic fatigue, and practitioners should be guided by their own clinical experience.

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**Schizophrenia**

Cross-sectionally, young patients with bipolar disorder might seem psychotic and disorganized and thus schizophrenic. Their thought processes are so rapid that they may seem loose, but, unlike those with schizophrenia, they display expansive and elated affect, which is often contagious. By contrast, the severely retarded bipolar depressive person, whose affect may superficially seem flat, almost never exhibits major fragmentation of thought. The clinician, therefore, should place greater emphasis on the pattern of symptoms than on individual symptoms in the differential diagnosis of mood and schizophrenic psychoses. No pathognomonic differentiating signs and symptoms exist. Differential diagnosis should be based on the overall clinical picture, phenomenology, family history, course, and associated features. Because the two groups of disorders entail radically different pharmacological treatments on a long-term basis, the differential diagnosis is of major clinical importance. **Table 14.6-42** summarizes the author’s clinical experience in the area and lists the most common pitfalls in diagnosis. In the past many bipolar patients, especially those with prominent manic features at onset, were labeled as having “acute schizophrenia” or “schizoaffective schizophrenia.” Such misdiagnoses (which typically led to long-term treatment with antipsychotic agents) has been costly in terms of tardive dyskinesia, vocational and social decline, and even suicide. For instance, some patients with postpsychotic depressive disorder of schizophrenia in the DSM-IV scheme (**Table 14.6-25**) have postmanic depressions that were treated with neuroleptic monotherapy without the benefit of more definitive thymoleptic agents.

**Table 14.6-42** Misdiagnosis of Mood Disorder as Schizophrenia

Modern treatments, which tend to keep many persons with schizophrenia out of the hospital, do not seem to prevent an overall downhill course. By contrast, the intermorbid periods in bipolar illness are relatively normal or even supernormal, yet over time some social impairment may result from the accumulation of divorces, financial catastrophes, and ruined careers. (Although rapid-cycling disorders, which have sharply risen during the past two decades, cause considerable social impairment, mood symptoms are so prominent that differentiation from schizophrenia is generally not difficult; also such patients usually display more classic bipolar phases before the rapid cycling).

Postpsychotic depressions in persons with established schizophrenia are sometimes due to inadequate control of schizophrenic symptomatology. In other patients, especially more intelligent young schizophrenic patients, they reflect the experience of losing one’s ego and sanity. It would be more meaningful to give such patients a diagnosis of both schizophrenia and a depressive disorder and treat the patient accordingly.

**Schizoaffective Disorder**

As the above considerations suggest, depression in the setting of a schizophrenic disorder does not necessarily constitute a distinct nosological entity. The concept of schizoaffective (or cycloid) psychosis should be restricted to recurrent psychoses with full affective and schizophrenic symptoms occurring nearly simultaneously during each episode. This diagnosis should not be considered for a mood psychosis in which mood-incongruent psychotic features (e.g., schneiderian and bleulerian symptoms) can be explained on the basis of one of the following: (1)
affective psychosis superimposed on mental retardation, giving rise to extremely hyperactive and bizarre manic behavior; (2) affective psychosis complicated by concurrent brain disease, substance abuse, or substance withdrawal, known to give rise to numerous schneiderian symptoms; or (3) mixed episodes of bipolar disorder (which are notorious for signs and symptoms of psychotic disorganization). Official diagnostic systems such as DSM-IV use the category of schizoaffective disorder broadly. Thus patients with clear-cut manic episodes receive a schizoaffective diagnosis if delusions or hallucinations occur in the interepisodic period, in the absence of prominent affective symptoms. Many psychotic symptoms in mood disorders are often explanatory (albeit delusional), whereby the patient tries to make sense of the core experiences of the affective illness. In patients with recurrent episodes, delusional thinking can be carried over into the interepisodic period. Such patients are thus delusional in the absence of prominent mood symptoms and technically (i.e., by research diagnostic or DSM-IV criteria) might be considered schizoaffective.

The author does not concur with that convention. Affective illness is typically a lifelong process, and limiting its features to discrete episodes is artificial. Although neuroleptic agents might be prescribed on an as needed basis to reduce the strong affective charge of those interepisodic delusions, they do not effectively eliminate the affect-laden experiences. Continued thymoleptic treatment (resorting to ECT, if necessary) and an empathic psychotherapeutic approach are more rewarding in the long run.

She was in effect told that her self-professed role in the international scheme was highly implausible and that someone with her superior education and high social standing could not entertain a belief, to use her own words, “as crazy as that.” She eventually broke into tears, saying that everyone in her family was so accomplished and famous that to keep up with them, she had to be involved in something grand; in effect, the international scheme, she said, was her only claim to fame: “Nobody ever gives me credit for raising two kids, and throwing parties for my husband's business colleagues. My mother is a dean, my older brother holds high political office, my sister is a medical researcher with five discoveries to her credit [all true] and who am I? Nothing. Now, do you understand why I need to be a national hero?” As she alternated, over subsequent months, between such momentary flashes of insight and delusional denial, antipsychotic medication was gradually discontinued. Maintained on lithium, she now only makes passing reference to the grand scheme. She was encouraged to pursue her career goal toward a master's degree in library science.

The vignette illustrates how phenomenological understanding, rational pharmacotherapy, and practical psychotherapeutic or vocational guidance can be fruitfully combined in the approach to patients with psychotic mood disorders. At a more fundamental level it suggests that clinical diagnoses in psychiatry cannot be based entirely on operational criteria; one's opinion of patient's illnesses is not infrequently changed by their response to treatment.

In the author's view, DSM-IV represents something good (operationalization of diagnostic criteria) carried to extreme (arbitrary precision often divorced from clinical reality).

**ICD-10**

The ICD-10 criteria for mood disorders, which are used throughout the world, are listed in Table 14.6-43. Although these criteria derive in part from DSM-III-R, they are more flexible and clinician-friendly: they do not pretend to impose arbitrary precision on the clinical universe of psychiatry.

**Table 14.6-43 ICD-10 Diagnostic Criteria for Mood [Affective] Disorders**
SUGGESTED CROSS-REFERENCES

Diagnosis and psychiatry are discussed in Chapter 7, the clinical manifestations of psychiatric disorders are covered in Chapter 8, and the classification of mental disorders is presented in Chapter 9. Schizophrenia is the subject of Chapter 12. The somatic treatment of mood disorders is discussed in Section 14.7 and Section 14.8. Psychotherapy is covered in Section 14.9. Mood disorders and suicide in children are the topic of Chapter 45. Anxiety disorders are presented in Chapter 15, and mood disorders in geriatric psychiatry are discussed in Section 51.3d. Somatoform disorder including neurasthenia and chronic fatigue syndrome is covered in Chapter 16.

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