case, other physical manifestations generally are thought to be present. Subtle adrenocortical dysfunction occurs with depressive disorders but is most likely implicated in the pathophysiology, rather than the etiology, of depressive illness.

Substance Abuse

Alcohol is far and away the most common agent implicated in causing depression in this category. Other agents, such as marijuana, opiates, and cocaine, also can produce depression.

Medications

Among medications, steroids are a frequent cause of depression (as well as mania). Beta-blockers such as propanolol have been implicated in cases of depression, but recent meta-analyses of the medical literature suggest that their impact on depression risk in general is rather low. Neuroleptics, including some antiemetics such as promethazine, can induce depression. Antiepileptics and benzodiazepines, particularly clonazepam, are sometimes implicated. Antiandrenergics, such as clonidine, and antihistamines, such as cimetidine, also can trigger depressive syndromes. Some antibiotics, such as tetracycline, and antihypertensives, such as calcium channel blockers, also have been associated with depression. Recently, depression has occurred regularly with some anti-hepatitis C treatments, such as interferon, and some anti-HIV treatments.

Bipolar Disorder

Essential Concepts

- Manic episodes can be either pure or mixed.
- Only a single spontaneous manic episode at any time is required to diagnose bipolar disorder type I.
- Bipolar disorder type II is characterized by recurrent hypomania and major depression.
- Do not limit the diagnosis of mania to euphoria. Many manic episodes are characterized by irritable or depressed mood.
- Unipolar major depressive disorder is a diagnosis of exclusion. A single spontaneous manic episode at any time establishes the diagnosis of bipolar disorder type I.
- The key difference between hypomania and mania is the absence of significant social or occupational dysfunction in hypomania. Thus the diagnosis of type II bipolar disorder implies the absence of any notable dysfunction occurring with manic-like symptoms.
- In differentiating borderline personality disorder and bipolar II disorder, focus on DIGFAST criteria to diagnose bipolar disorder type II, and focus on the typical profile (the *prototype*) in diagnosing borderline personality disorder.

In the bipolar spectrum, we are concerned with mania, hypomania, or signs of bipolarity. If either hypomania or mania is identified and meets DSM-IV criteria, then the diagnosis of bipolar disorder type I or type II (hypomania with concurrent major depression) can be made. In addition, the bipolar spectrum includes patients who are not diagnosable with either bipolar type I or type II disorders but who are also not diagnosable along the unipolar spectrum. In current DSM nosology, these patients would be diagnosed with bipolar disorder not otherwise specified (NOS). By and large, they experience

major depression but also show evidence of signs of bipolarity, short of hypomania or mania. I mentioned these signs of bipolarity in Chapter 1, and I will elaborate on them in Chapter 4.

MANIA

The sine qua non of the diagnosis of bipolar disorder in the current nosology is the presence of manic symptoms. (Remember that while having mania is diagnostic of bipolar disorder, not having mania does not rule out bipolar spectrum illness.) Mania, as defined in Chapter 1, occurs in two main forms: pure and mixed.

Pure mania consists of euphoric mood with three of seven DIGFAST manic criteria or irritable mood with four of seven DIGFAST criteria. Mixed mania consists of depressed mood with four of seven DIGFAST criteria and four of eight depressive SIGECAPS criteria. The duration of all these syndromes is 1 week at minimum, and they all also require significant social or occupational dysfunction to be present. If any patient experiences a single pure or mixed manic episode at any time, that patient should be diagnosed with bipolar disorder type I. Exclusions exist for secondary mania, that is, a single manic episode owing directly to a clear medical cause, such hyperthyroidism or use of an antidepressant.

TIP

Many, though not all, patients with antidepressant-induced mania also have a history of spontaneous manic or hypomanic episodes. If you encounter someone with antidepressant-induced mania, search very carefully for evidence of spontaneous episodes.

A number of factors stand out in the diagnostic relevance of manic episodes. First, note that euphoric mood is present in only one subtype of mania. As many, or more, manic episodes involve either irritable or depressed mood.

TIP

Do not limit the diagnosis of mania to euphoria. Many manic episodes are characterized by irritable or depressed mood.

Second, since depressed mood occurs with mixed episodes, any patient with clinical depression also needs to be assessed for manic symptoms. Otherwise, a mixed episode might be misdiagnosed as pure depression, and thus a patient with bipolar disorder type I would be misdiagnosed as having unipolar depression. Mixed episodes, as defined in DSM-IV, require that a patient experience the full criteria for a major depression (except 1-week minimum duration instead of 2 weeks) and mania at the same time.

Much research suggests that patients can have two other varieties of mixed episodes, however. In the first, dysphoric mania, a patient meets the full criteria for mania but also experiences a few depressive symptoms. In the second, agitated depression, a patient meets the full criteria for depression but also experiences a few manic symptoms. In fact, in Kraepelin's original work, he considered agitated depression, such as classic major depression, but with a manic sign of racing thoughts, to be a mixed-manic feature. If one broadens the concept of *mixed states* to include the strict DSM-IV mixed episode, as well as dysphoric mania and agitated depression, then one greatly increases the diagnostic rate of these states. Some research studies support the validity of this broad definition, with, among other aspects, greater evidence of anticonvulsant response (as opposed to lithium) reported in dysphoric mania.

TIP

Every depressed patient should be assessed carefully for current manic symptoms to rule out a mixed episode. Broader definitions of mixed states include dysphoric mania and agitated depression.

CLINICAL VIGNETTE

Thomas is a 38-year-old man who presents for a consultation for refractory depression. He reports having had depression "all my life," but most antidepressants are reportedly "ineffective." Careful assessment of treatment history reveals that he has indeed been treated with adequate doses and durations of treatment with multiple antidepressants from different classes. Electroconvulsive therapy (ECT) also has been ineffective. On further questioning, it becomes apparent that Thomas experiences at least two different kinds of depression. The first kind

is associated with depressed mood, decreased energy, increased sleep and appetite, and impaired concentration, along with marked anhedonia. These pure major depressive episodes usually last about 6 months and get neither better nor worse with antidepressants. The second kind is associated with depressed and irritable mood, increased "nervous" energy, decreased sleep and appetite, distractibility, a near-normal level of activities compared with euthymia, racing thoughts, rapid speech, increased guilt, marked psychomotor agitation, and marked suicidal ideation. These mixed episodes also usually last about 6 months and are worsened by antidepressants. The patient is treated with divalproex in the absence of antidepressants with marked improvement.

It is also notable that all forms of mania, whether pure or mixed, require significant social or occupational dysfunction as part of their diagnostic criteria. This means no more and no less. A patient should not be diagnosed with mania unless that patient is experiencing significant life problems owing to those manic symptoms. Conversely, a patient *only* needs to experience any kind of significant life problems with manic symptoms to be diagnosable with mania (as opposed to hypomania). It is not necessary for patients to be classically manic (e.g., spending sprees, religious delusions, sexual indiscretions) to have significant social or occupational dysfunction. It can be sufficient simply to have major conflict at work with one's coworkers and boss or at home with one's spouse and other relatives.

Spontaneous manic episodes almost always recur. Unlike depression, there are a small proportion of single-episode outcomes. Sometimes, with purely antidepressant-induced mania, a single episode might occur without future recurrence, especially if antidepressants are avoided. However, it is very important to remember that a single spontaneous manic episode at any time marks the diagnosis as bipolar disorder type I and nothing else. A patient might experience 30 major depressive episodes, but a single spontaneous manic episode makes the diagnosis bipolar disorder type I, not unipolar major depression.

TIP

Remember, unipolar major depressive disorder is a diagnosis of exclusion. A single spontaneous manic episode at any time establishes the diagnosis of bipolar disorder type I.

HYPOMANIA

Hypomanic episodes are essentially the same as manic episodes, except that significant social or occupational dysfunction is absent. (They also can last a minimum of 4 days, according to DSM-IV, as opposed to 1 week for mania.) Hypomanic episodes can (and usually do) occur in bipolar disorder type I along with manic episodes. What is diagnostic of bipolar disorder type II is that hypomanic episodes occur to the exclusion of manic episodes. In other words, if one diagnoses bipolar disorder type II, one is asserting that a single spontaneous manic episode has never occurred in that patient at any time in the past. More specifically, that patient's manic symptoms have never, ever, been associated with significant social or occupational dysfunction. It is important to make this distinction because, otherwise, bipolar disorder type II would tend to be overdiagnosed to the detriment of bipolar disorder type I. As I will discuss in the treatment sections, there are important practical implications in trying to make this difficult distinction as accurately as possible.

TIP

If you diagnose bipolar disorder type II, make sure that the patient never experienced a single spontaneous manic episode, that is, never had significant social or occupational dysfunction owing to manic symptoms.

CLINICAL VIGNETTE (PART I)

Sally is a 23-year-old woman who works as a paralegal aide and has experienced recurrent depressive episodes. She and her boyfriend came to an appointment because of a recurrence of major depression in the past month. On questioning, her boyfriend was able to report a preceding change in her behavior for 3 weeks before the onset of her current depression. Over that 3-week period (about 2 months previously), he reports, she slept only 4 hours nightly, instead of her usual 6, with increased energy and increased time spent at work (60 hours per week instead of her usual 40 hours). She also had been more talkative, somewhat giddy, and had increased libido. He reports that her increased energy and libido were not a problem, and her coworkers and boss were impressed by her increased productivity at work. Neither he

nor his girlfriend thought that this increased energy and activity merited any intervention.

It is worth noting that hypomania itself does not often require treatment per se. However, it is almost always preceded or followed by a major depressive episode, and thus the mood cycling as a whole merits mood-stabilizing treatment. Mania, at its most subtle, can differ quite a bit from marked hypomania, and indeed, hypomania sometimes is a stage on the way toward development of a manic episode. In the preceding vignette, the smooth transition from hypomania to mania might be illustrated as follows.

CLINICAL VIGNETTE (PART II)

Two weeks later, Sally's boyfriend calls to report that her depression had resolved and was followed by another period of mildly elevated mood, decreased need for sleep, increased work activity, and increased talkativeness. However, after 1 week of these symptoms, Sally's coworkers began to be concerned that she was spending too much time on certain projects. When they tried to redirect her, she became quite irritable and acted "arrogantly," according to the coworkers, which was out of character for her. Her supervisor called her into a meeting in which he reprimanded her. She became more irritable, feeling that her coworkers did not appreciate her special skills. Her supervisor asked her to take a leave of absence.

This vignette demonstrates how very similar symptoms can occur in mania and hypomania, the difference being primarily on the effect of those symptoms in the patient's social and occupational surroundings. In other words, the symptoms themselves are not the key difference but rather the impact of those symptoms on psychosocial functioning.

In addition to never experiencing a manic episode, the patient with hypomania can be diagnosed with bipolar disorder type II only if he or she also experienced a major depressive episode. This is usually easy to establish because one of the most common clinical scenarios is when a patient presents for treatment of major depression, and the clinician discovers evidence of past hypomania during the interview. Such

retrospective diagnosis of hypomania is notoriously difficult, however, and clinicians frequently do not agree on it (low reliability) because errors can occur in two different directions. As just mentioned, mania might be missed owing to underreporting or lack of information on how much dysfunction occurred during the purported hypomanic period. Alternatively, variations of normal mood in which a person might have been elated for some reason may be misinterpreted as hypomania. In my experience, the latter problem is less frequent. When it does occur, the scenario sometimes relates to a patient reporting apparent hypomanic symptoms but only in association with the occurrence of happy life events. For instance, a patient might win the lottery and then report elated mood and some other elevated mood symptoms for several days. In my experience, the best way to deal with these scenarios is to count the number of times they occur. Someone might win the lottery once or even experience a few ecstasy-producing events, but frequent and repeated events of this variety strain common sense.

It is important to remember that the brain is a rationalizing machine and that we all create stories to explain what we experience. Almost all patients, especially early in their illness, will ascribe manic or hypomanic (and indeed depressive) episodes to external life events. It is important to listen carefully and take note of such ascriptions but not to take them at face value. Such life events can trigger mood episodes, but an underlying illness susceptibility needs to be present. In the cases where a life event alone might wholly cause a mood episode, my view is that the best sign is that such scenarios are nonrepetitive; they occur once, maybe twice in a lifetime, producing one or two mood episodes. (Most people don't win the lottery more than once in a lifetime, or to put it another way, repeated euphoric happiness is infrequent in real life!) More frequent episodes, even with apparently impressive surrounding life events, should trigger a more serious appraisal of an underlying mood illness.

TIP

Hypomania can be difficult to distinguish from normal happiness, especially retrospectively. Remember that repeated episodes usually reflect underlying mood disorder, whereas mood episodes wholly caused by life events tend to occur only once or twice in a lifetime.

It is also important to remember that some persons use the terms *manic* or *hypomanic* loosely as equivalents to *mood swings*. I think that it is important to stick with the strict definition of hypomania offered here and used in DSM-IV. "Softer" versions of bipolar symptoms can be embraced with the bipolar spectrum disorder concept (see Chapter 4). Hypomania means more than just "mood swings"; it means clear presence of manic symptoms, as outlined earlier.

Bipolar disorder type II is associated more frequently with rapid-cycling episodes than bipolar disorder type I. *Rapid cycling*, defined as four or more mood episodes (of any kind: mania, hypomania, or depression) in a year, is also associated with a higher predominance among females than males (unlike non-rapid-cycling bipolar disorder, which has equal gender prevalence). Thus a typical patient with bipolar disorder type II is a depressed female with four or more depressive or hypomanic episodes in the past year.

TIP

Rapid-cycling episodes are common in bipolar disorder type II, especially among women.

This characteristic often leads to the differential diagnostic dilemma of borderline personality disorder versus bipolar disorder type II. In borderline personality disorder, rapid mood shifts are present. In rapid-cycling bipolar disorder, mood episodes must occur at least every 3 months (four episodes per year), but sometimes they occur monthly, weekly, or even more quickly. When such episodes occur every few days or less, they can be difficult to distinguish from the rapid mood shifts of borderline personality disorder. In my opinion, the key distinction gets back to the concept that hypomania is not simply mood swings. Hypomania involves the presence of DIGFAST symptoms in the same way as in mania. The symptoms are the same in number; it is their severity that is lessened in hypomania. In contrast, the patient with borderline personality disorder does not meet DIGFAST criteria even for a few days. Rather, patients with borderline personality disorder only have mood shifts along with other features of the personality disorder but not such diagnostic manic symptoms as decreased need for sleep for 4 days or longer or episodic increased talkativeness for 4 days or longer with a normal baseline for both features. In

fact, bipolar disorder and borderline personality disorder differ in a single major way that influences my diagnostic process: The diagnostic criteria for bipolar disorder are episodic and well validated; the diagnostic criteria for borderline personality disorder are often chronic and less well validated. Thus, in diagnosing bipolar disorder, I emphasize specifically assessing DIGFAST criteria; in diagnosing borderline personality disorder (and in fact most personality disorders), I deemphasize the specific diagnostic criteria and focus instead on the overall typical profile (the *prototype* approach to diagnosis) of the kind of patient who has that diagnosis.

In borderline personality disorder, the typical patient has a history of childhood abuse, unstable interpersonal relationships, rapid mood shifts, and all-or-nothing thinking, and often elicits aggressive countertransference feelings. If a patient has "mood swings" with the rest of that diagnostic picture and no other DIGFAST criteria, then the diagnosis of borderline personality disorder should be made. On the other hand, if someone meets the DIGFAST criteria for recurrent hypomanic episodes and has one or maybe two of the features of borderline personality disorder (not otherwise having the typical picture), then that person should be diagnosed with bipolar disorder type II. There are, of course, persons who have both conditions, and they would meet DIGFAST criteria and have a typical profile of borderline personality disorder.

TIP

In differentiating borderline personality disorder and bipolar disorder type II, focus on the DIGFAST criteria to diagnose bipolar disorder type II, and focus on the typical profile (the *prototype*) in diagnosing borderline personality disorder. Sometimes both occur.

THE REST OF THE BIPOLAR SPECTRUM

Clinicians in outpatient practice often recognize that a large proportion of patients do not meet classic criteria for unipolar major depressive disorder, nor are they diagnosable with type I or type II bipolar disorder. In the current DSM-IV nosology, they would be diagnosed with bipolar disorder

NOS. I use the phrase *bipolar spectrum* to loosely refer to these patients, as opposed to type I or type II bipolar patients. These bipolar spectrum patients mainly suffer from major depression, but they also tend to have a number of signs that are atypical for unipolar depression but typical for bipolar disorder. These features of bipolarity are described in detail in Chapter 4.

The Bipolar Spectrum

Essential Concepts

- The bipolar spectrum consists of features of bipolarity besides the classic kind found in DSM-IV in the criteria of bipolar disorder type I.
- A proposed new diagnosis, *bipolar spectrum disorder,* occurs in persons with severe major depression but not spontaneous hypomania or mania and yet with many signs of bipolarity.
- The most important signs of bipolarity are a family history of bipolar disorder in a first-degree relative and antidepressant-induced mania/hypomania.
- Other useful signs of bipolarity include brief, recurrent, atypical psychotic or postpartum major depressive episodes.
- Treatment often can begin with low-dose standard mood stabilizers (e.g., lithium or valproate), followed by novel anticonvulsants alone or in combination with the standard mood stabilizers.

The bipolar spectrum concept has been used at least three different ways in recent literature. At one level, it reflects a broad definition of any bipolar condition from classic forms of type I disorder to type II and not otherwise specified (NOS) forms. This is what Kraepelin meant with his concept of "manic-depressive illness." At another level, the bipolar spectrum can reflect any atypical form of bipolar disorder; for instance, the term may be applied to type II and NOS conditions only, excluding type I bipolar disorder. At a third level, the term may be applied to any condition that may be bipolar in some fashion but is not diagnosable or recognized by current DSM-IV criteria. This way of looking at it conceptualizes the bipolar spectrum concept as an overlap between more classic presentations of unipolar depression or bipolar disorder. Since DSM-IV recognizes type I and type II disorders with specific criteria, this last use of the term *bipolar*