TIP

You do not need to have *classic* manic symptoms of dysfunction, such as sexual indiscretions or spending sprees, to be diagnosed with mania; *any* kind of significant social or occupational dysfunction is sufficient.

2 The Unipolar Depressive Spectrum

Essential Concepts

- The three major types of unipolar mood disorders are dysthymia, chronic depression, and recurrent major depressive disorder.
- Single-episode major depressive conditions are common.
- Depressive symptoms can occur in other conditions, such as bipolar disorder, posttraumatic stress disorder, anxiety disorders, and schizophrenia.
- Secondary depression always should be ruled out, the most common causes being substance abuse and neurologic conditions.

DYSTHYMIA

Dysthymia is a condition of chronic mild depressive symptoms. Historically, the category of dysthymia was included in DSM-III owing to a conflict between some members of the DSM-III task force, who wanted simply to have a category for major depression, and many practitioners, who did not feel that the category of major depression adequately captured persons with mild depressive symptoms, previously termed *neurotic depression.* Officially, in DSM-IV, *dysthymia* is defined as possessing at least two mild depressive criteria, as shown in the mnemonic *CHASE-E* (Table 2.1).

This means that the individual must have some depressive symptoms but not enough to meet the full criteria for a single episode of major depression. Further, these depressive symptoms must be chronic and frequent; the DSM terminology calls for the symptoms being present more often than not without any period of euthymia lasting 1 month or longer in a 2-year period. Thus you must assess a 2-year period. Depressive symptoms must be present more than 50% of the time ("more often than not"), and there must not be any stretches of less than this level of depression (basically *euthymia*) lasting more than a month.

Now this is in fact an exacting standard. Yet I frequently observe my colleagues making the diagnosis of dysthymia in

TABLE 2.1. Mnemonic of DSM-IV Criteria for Dysthymia

Concentration is poor.
Hopelessness feelings are present.
Appetite is low or high.
Sleep is low or high.
Energy is low.
Esteem is low

our psychopharmacology clinic. In research studies of pure dysthymia, where these diagnostic standards must be assessed carefully, my experience has been that it is very difficult to find apparently dysthymic patients who have not also had major depressive episodes in their past. In other words, dysthymia and episodic major depression seem to overlap. Thus, while an individual may have a 2-year or longer period of dysthymia in his or her life, that person also likely will have experienced 2 weeks or more of full major depressive symptoms at some point in his or her life. This combination of major depression alternating with dysthymia is colloquially called *double depression.*

TIP

Most cases of dysthymia represent *double depression* rather than pure dysthymia.

Another factor to keep in mind is that dysthymic criteria overlap greatly with criteria for generalized anxiety disorder (GAD). It is worth remembering that most of these patients used to be diagnosed with *neurotic depression* in the pre-DSM-III days and that these categories of dysthymia and GAD are really meant to capture that class of mildly depressed and anxious individuals frequently seen in ambulatory treatment settings.

For the purpose of comparison, let's look at the DSM-IV criteria for GAD, summarized in the mnemonic *MERCI-S* (Table 2.2). For GAD, these symptoms need to be present for at least 6 months, associated with multiple excessive worries. Note that GAD essentially reflects chronic anxious mood with a set of associated symptoms that are quite similar to dysthymia. Thus the main difference between dysthymia and GAD in the current DSM-IV nosology is between chronic anxious mood (in GAD) and chronic depressed mood (in

TABLE 2.2. Mnemonic of DSM-IV Criteria for Generalized Anxiety Disorder

Muscle tension is present.
Energy is low.
Restlessness or feeling keyed up or on edge is present.
Concentration is impaired.
Irritability is present.
Sleep is disturbed.

dysthymia), all, of course, in the absence of major depression. This is probably a distinction without a difference, reflecting more the wish of the organizers of DSM-IV to categorize something difficult to separate in practice. Many of these patients have chronic depressed and anxious mood and thus would have to be diagnosed with both dysthymia and GAD, which, in my opinion, primarily reflects the immense crossover of symptoms in the two definitions.

TIP

Dysthymia and GAD are often diagnosable in the same person because mild chronic depression and anxiety often go together.

In any case, the concept of dysthymia reflects the mildly chronically depressed (and often anxious) individual. Perhaps the old term of *neurotic depression* actually did more justice to this condition than the somewhat falsely stolid terms *GAD* and *dysthymia.* In fact, many patients with mood symptoms who seek help from health professionals (often general practitioners, but also general psychiatrists) fall into this group. These days, most such patients receive treatment with antidepressants and sometimes anxiolytics. This is basically symptom-oriented therapy because these patients usually are not diagnosable with true recurrent primary unipolar depression but rather have moderate depressive and anxiety symptoms just short of the threshold of severity needed for recurrent discrete depressive episodes. In Chapter 8, I will discuss my view on why I think antidepressants are overprescribed in this population. Here, suffice it to say that the widespread use of antidepressants in this group has a quite weak evidence base; some studies in primary-care medicine demonstrate that no treatment (spontaneous recovery)

produces as much benefit as antidepressant treatment. Other data exist that suggest benefit with supportive or other psychotherapies. My view is that the use of antidepressants in this group is driven by marketing and by convenience (as well as insurance coverage). Psychotherapies are probably as effective, and certainly safer, but are more time consuming and more expensive (and often not covered by insurance). Hence, in the real world of American medicine, patients with neurotic depression tend to get antidepressants. Strictly medically speaking, however, they likely would be better treated with psychotherapies, often without medications.

The earlier European literature tends to discuss dysthymia as a personality type. Individuals exhibiting this condition were seen as being introverted, shy, unenthusiastic about life, mildly depressed in affect, slow in thought and speech, mildly low in energy, and often requiring more than 8 hours sleep. It seems rather arbitrary to argue that dysthymia is or is not a personality state. Do pure dysthymic patients need treatment? Even though such individuals have limited depressive symptoms, there is evidence that even dysthymic (or so-called minor depressive) symptoms can impair one's ability to function in life (socially or occupationally). In other words, such individuals may not be extremely depressed or suicidal, but they will have less successful careers and less satisfying personal relationships. They may experience divorce more frequently or have difficulty establishing or maintaining romantic relationships. Often, others are more likely to notice that they are mildly depressed than the individuals with dysthymia themselves.

In many cases, such individuals will experience at least one major depressive episode, and then their "double depression" often reaches professional attention. Although there are limited studies of this group, the available research tends to suggest similarities in treatment and outcome with individuals diagnosed with chronic depression.

CLINICAL VIGNETTE

A 32-year-old man is referred for treatment by his parents. His father, a physician, reports that the patient has not been very motivated for a number of years; he did not complete graduate school, has worked only at the local bookstore part time, still lives at home, and is uninterested in getting married. His parents fear that he will not be able to support himself independently in the future. His father had prescribed

fluoxetine for 3 months, escitalopram for 4 months, alprazolam for 6 months, and sertraline for 2 months, all without benefit. On interview, the patient endorsed insomnia, anhedonia, difficulty with concentration, low self-esteem, but normal energy, appetite, and no suicidal ideation. His symptoms were chronic and did not wax and wane; no discrete episodes could be identified (confirmed by family interview). He did not have any previous manic or hypomanic episodes (also confirmed by family interview). There was no diagnosed or probable psychiatric illness in his family. After discussion, the interviewer recommended weekly individual psychotherapy and discontinuation of all medications. The patient had been reluctant to take medications and was happy to stop them, yet he also was reluctant to begin psychotherapy. The patient's physician-father was skeptical about the benefits of psychotherapy. The interviewer explained to both of them that the patient's chronic anxiety/depressive condition was not the same as recurrent unipolar depressive disorder and thus may not respond biologically in the same way. After 1 year of psychotherapy, the patient's symptoms were moderately improved.

CHRONIC DEPRESSION

Added to DSM-IV in 1994, chronic major depression reflects the scenario where someone has full major depressive criteria for 1 year or longer. The individual with chronic depression differs from the person with dysthymia on the question of whether criteria for a full major depressive episode are met or not. If met, the diagnosis is chronic depression; if not, it is dysthymia.

CLINICAL VIGNETTE

A 46-year-old woman seeks treatment as a result of a recent conflict with her husband. She describes feeling depressed most days in her mood for the past year and a half, along with decreased energy and interest, increased sleep, and increased appetite. She denies any suicidal ideation or guilt. She smiles during the interview and reports that some things, such as exercise, still give her pleasure. She continues to exercise and reports being able to work without too

much difficulty. On questioning, she reports that her sister has been diagnosed with "depression." She denies hypomanic or manic periods in the past. Her husband, reached by telephone the next day, also denies hypomanic or manic periods in the past. The interviewer diagnoses chronic unipolar major depression.

Traditionally, major depressive conditions have been seen as episodic. They might occur once or more than once, but they go away. They do not persist beyond the natural duration of the episode, which is 6 to 12 months in unipolar depression and 3 to 6 months in bipolar depression, according to traditional texts. Recent experience suggests that a subgroup of unipolar depressed patients suffers from longer episodes, lasting years at a time.

A number of studies with medications, particularly sertraline and nefazodone, have been conducted in chronic depression and double depression. These studies suggest a need for and support the effectiveness of standard antidepressant medications in these patients. Interestingly, certain kinds of psychotherapy, especially cognitive behavioral therapy (CBT), also have been proven useful for these individuals, especially when combined with standard antidepressant medications. It appears that patients with chronic depression need standard antidepressant medications for the long term and have additive benefit with psychotherapies also.

RECURRENT MAJOR DEPRESSION

About 50% of persons who experience a major depression also experience additional episodes in the future, usually more than two or three occurrences. Recurrent major depression seems to have very different implications than nonrecurrent major depression. In persons who have just one single major depressive episode and never another, research supports the concept that either medication or psychotherapy (particularly CBT) is equally effective. If medication is used, patients can be weaned off successfully, in general, in 6 to 12 months. In persons who have multiple major depressive episodes, that is, in recurrent depression, medications appear more effective than psychotherapies (CBT and interpersonal therapy have been studied the most) both for acute treatment of depression and for long-term prevention of relapse into

future depressive episodes. The combination of CBT and medication also may be as effective as, or even more so than, medication alone in acute severe recurrent depression. However, medication is a mainstay of treatment for recurrent depression, whereas in nonrecurrent depression it can be optional if appropriate psychotherapies are employed.

TIP

Antidepressant medications tend to be necessary to treat and prevent recurrent unipolar depression, but may be optional in single-episode nonrecurrent unipolar depression.

I have often noticed that clinicians will obtain careful histories about current depressive symptoms in individuals with major depression, but they do not always carefully assess the number of episodes that a patient has experienced in the past. This can be difficult because patients often have difficulty remembering with accuracy whether they had the specific symptoms required to diagnose past major depressive episodes. However, such history is vital to formulating an effective treatment plan. There is a huge difference between the treatments initiated for a person who has experienced 2 major depressive episodes versus a person who has experienced 22 major depressive episodes.

CLINICAL VIGNETTE

Jane is a 30-year-old white woman who makes an appointment at the outpatient clinic for depression. She reports marked feelings of sadness for the past 3 months in relation to the breakup of a relationship. She also has conflict with her boss at work and feels unfulfilled in her current job, where she has worked for 5 years. She feels unsupported by her mother, who criticizes her for the problems in her life. She reports decreased sleep, interest, and energy and poor appetite, but denies suicidal ideation. Her concentration is generally intact, and she is able to work, although somewhat less effectively than in the past. She denies ever having experienced these or similar symptoms in the past. Jane is wary about taking medications because she has heard that they might have serious side effects. She would rather avoid them if she could. The psychiatrist consults with his psychotherapist colleagues but does not identify anyone

who has been specially trained in CBT or interpersonal therapy at a training institute for those therapies. However, he finds a colleague with some experience in CBT who mixes that approach with supportive therapy, and he refers the patient to that therapist. Six months later, the patient feels better, and she discontinues her therapy 1 year later.

CLINICAL VIGNETTE

James is a 44-year-old white man who has experienced major depression for the past 6 months. During that time, he has been eating more, sleeping more, uninterested in his usual activities, and tired all the time. He feels that life is not worth living, but he does not wish to end his life by his own hand. He has trouble concentrating. He denies guilt. He denies any specific triggers, although he describes problems with his girlfriend, which he thinks might be related to his depression and associated decreased libido. On questioning, he reports first experiencing symptoms similar to these at age 21 in college and again at age 30 after losing a job. The psychiatrist recommends antidepressant medication, with or without psychotherapy. James prefers to avoid psychotherapy for now owing to cost and his inability to take much time off his current job. After 2 months, he is beginning to improve, and after 6 months, he is much better. The psychiatrist recommends that he maintain his current dose of medication indefinitely.

Jane could just as well have taken medication for 6 months, and James also might have accepted psychotherapy with perhaps faster or more pronounced improvement, but the preceding scenarios are acceptable clinical ways of treating nonrecurrent and recurrent depression, respectively.

One of the important aspects of recurrent major depression, besides its need for pharmacotherapy, is that it often is associated with bipolar rather than unipolar depression (see Chapter 3). Further, recurrent major depression is frequently more severe than nonrecurrent depression and thus may be associated with hospitalization and increased suicide risk. Thus it is quite important to enumerate and identify recurrent major depressive episodes. In some persons, recurrent episodes are extremely frequent and brief (e.g., 2 weeks to 3 months), another possible sign of bipolarity.

DEPRESSION IN OTHER PSYCHIATRIC SYNDROMES

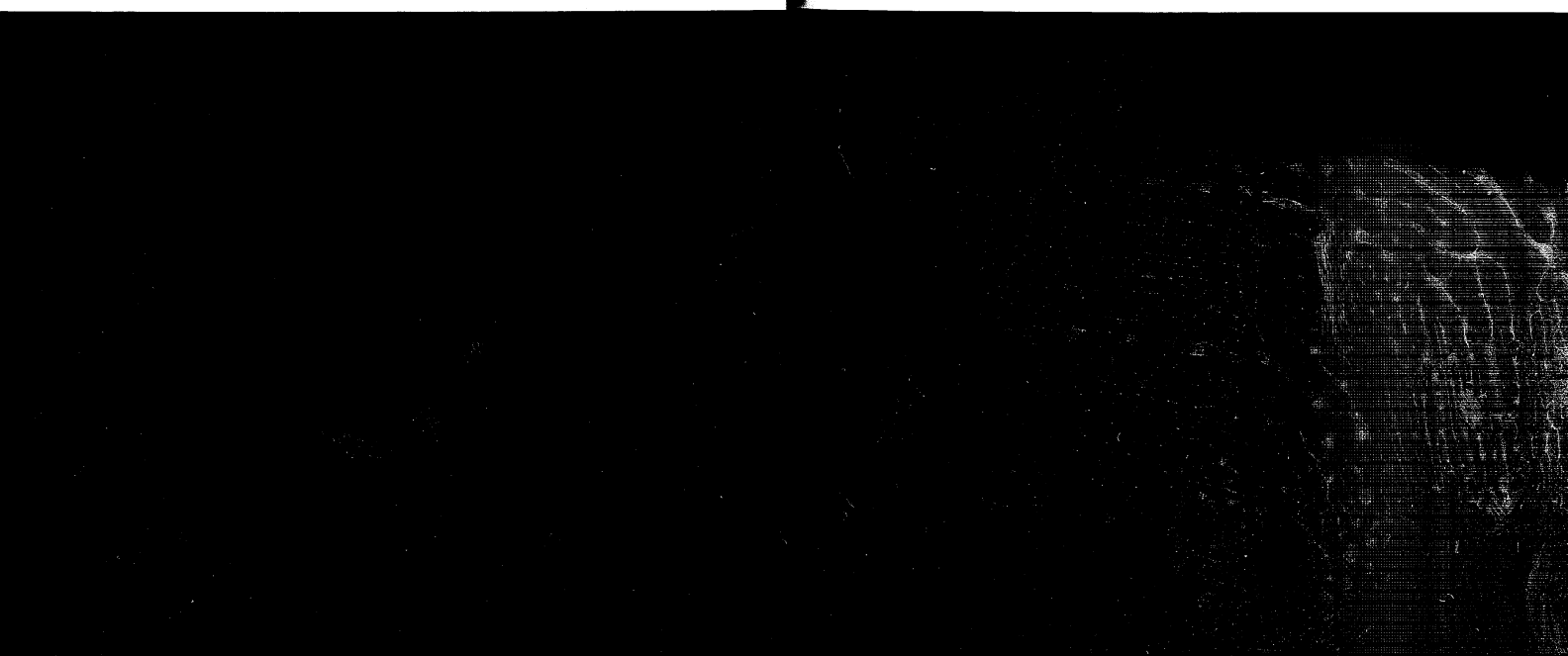
Depression also can occur in relation to panic disorder, posttraumatic stress disorder (PTSD), and schizophrenia. With panic disorder, depression sometimes seems to precede panic attacks and appears clinically primary. In such cases, treatment that focuses on treating the depression with antidepressant medication also will lead to resolution of panic attack symptoms. In other cases, although depression is not present initially, once the panic attacks are treated with benzodiazepines, depressive symptoms emerge. In such situations, one could interpret events in two ways: Either benzodiazepines caused the depression, or treating the panic disorder led to the *unmasking* of an underlying or associated depression. One then also needs to treat the depression with an antidepressant medication. My hunch, though difficult to prove, is that anxiety and depression co-occur so frequently that the unmasking hypothesis makes the most sense.

TIP

With panic disorder and depression, ask yourself the following questions: Which came first? Which seems to be the main problem? If panic disorder occurred first, and depression appeared after panic symptoms subsided, do not assume automatically that the antianxiety treatment caused the depression. Depression and anxiety often go together.

Depression can occur in PTSD. Frequently, these individuals have experienced trauma so severe—whether sexual, physical, or military—that they are markedly impaired in their lives and become dejected about their circumstances. Antidepressants are used frequently for, and somewhat effective in, PTSD and are more necessary if depressive symptoms are present. In my opinion, manic or bipolar symptoms are not likely part of the PTSD complex but more likely reflect separate comorbid bipolar disorder that needs to be treated separately with mood stabilizers.

Depression in schizophrenia is an issue of some complexity. The key diagnostic question is whether and how to distinguish schizophrenia with comorbid major depression from schizoaffective disorder, depressed type. The key difference may be a matter of degree. In schizophrenia with comorbid



major depression, only one or a few major depressive episodes occur, and they are brief. In schizoaffective disorder, depressed type, many (more than three) recurrent major depressive episodes occur, and they are of substantial duration (more than a few weeks). In either case, antidepressants need to be added to antipsychotic agents, but in comorbid schizophrenia and major depression, long-term antidepressant treatment may not be necessary (unlike schizoaffective disorder, depressed type).

SECONDARY DEPRESSION

It is customary to provide a long list of medical syndromes that have been associated with depression, but this is not clinically useful for a handbook. If one looks at practically every drug's package insert, depression is listed as a potential side effect. It is more important to have a "big picture" sense of the kinds of conditions and substances that frequently cause depression.

KEY POINT

The three main medical classes of conditions that frequently cause depression are cardiac, endocrinologic, and neurologic conditions.

KEY POINT

Besides medical illness, the main causes of secondary depression are substance abuse and prescribed medications.

As mentioned earlier, most medications are associated with depression, but the biggest culprits are steroids, which can cause depression or mania.

TIP

Steroids are probably the most common class of medications that frequently cause depression.

Let's discuss these different causes of secondary depression one by one.

Cardiac Illness

Depression can be both a risk factor and an end result of cardiac illness. Studies show that depressive symptoms are an independent risk factor for cardiac disease, even when the depressive symptoms do not meet full DSM-IV criteria for a major depressive episode. It is possible that some of the secondary physiologic manifestations of depression, such as increased adrenocortical activity, may increase the risk of heart disease. It is also often stated that increased depression after the onset or worsening of cardiac illness bodes especially ill for the long-term outcome.

Neurologic Illnesses

The most common neurologic disorders associated with depression are multiple sclerosis, Alzheimer's dementia, Parkinson's disease, stroke, and epilepsy. Of these, the most common presentation of depression may occur in epilepsy, where depression is sometimes part of the ictal phenomena of temporal lobe epilepsy. Depressive symptoms frequently also can occur interictally. In Alzheimer's disease, depression is often an early manifestation of dementia, and it is sometimes quite difficult to distinguish this scenario for simple major depression with marked cognitive impairment (*depressive pseudodementia*). Depression associated with Parkinson's disease may be related to decreased dopaminergic activity, and depression with stroke and with multiple sclerosis can be related either to the effects of specific lesions or to the psychological impact of chronic disability. Classically, the most common location for stroke-related depression is said to involve a left frontal lobe lesion.

Endocrinologic Illnesses

Hypothyroidism is perhaps the classic endocrinologic disease associated with depression. It is important to note that even mild hypothyroidism can lead to depression in a susceptible individual, and thus depression can be an early sign of hypothyroidism. In most cases of hypothyroidism, the classic physical features (such as thickening of the skin) are later manifestations. Thus thyroid function should be checked in any depressed individual. Cushing's disease, reflecting adrenocortical hypofunction, is also associated with depression, but in this

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