Clinical Diagnosis of Mood Disorders
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The history of syndrome-based diagnosis is reviewed. Recent criteria for the mood disorders according to the American Psychiatric Association are presented. Issues in the differential diagnosis of the mood disorders are discussed. Finally, commonly encountered pitfalls in clinical descriptive diagnosis and their potential remedies are summarized.

Purpose of Diagnosis

In the 17th century, Sydenham pioneered the clinical, descriptive approach that has led to diagnostic classification by signs, symptoms, and clinical course. The term "syndrome" refers to a constellation of signs (what the examiner sees) and symptoms (what the patient reports) that regularly recur in clinical practice. A syndrome does not imply either a specific etiology or a common response to treatment. Diagnosis of a disease entity or specific disorder replaces syndrome diagnosis when a distinct pathological process is known or suggested, and, by implication, treatment selection is more specific.

A diagnosis is an hypothesis, the clinician’s best judgment about the nature of an ailment. Many medical diagnoses include an hypothesis about what the phenomenon is and how it might be explained. Thus, medical diagnoses often involve both a classification and an explanation. In psychiatry, our knowledge is still too limited to specify particular pathophysiological processes. Therefore, psychiatrists render syndrome diagnoses with the knowledge that multiple causes are likely for each syndrome.

One purpose in diagnosis is to improve the match of available treatments with the problems presented by the patient. A second purpose is prognosis—to help patients, relatives, and society to judge the likely outcome of a particular medical problem. Prognosis derives from recognition of a particular syndrome or illness and from careful study of its ultimate course and response to treatments. Diagnoses serve other practical needs as well: (a) the need to communicate succinctly between professionals; and (b) the need to refine clinical research.

Historical Perspective

Depressions have been described since mankind has kept a written history. Deranged behaviors were typically considered curses from the gods by the Ancients or as a sign of moral and personal weakness. Hippocrates was the first clinician to describe depression carefully. He argued that psychiatric problems originated from natural rather than supernatural causes. He emphasized the critical role of the brain in the development of these disorders (1).

Aretaeus of Cappadocia (A.D. 120–180) first recognized organic (more recently called endogenous) and external (situational) depressions as two separate illnesses. He described both manic and depressive episodes, noting that some disorders included only recurrent episodes of depression (now called "unipolar major depressions"), whereas others involved episodes of both depression and mania (now called "bipolar disorder").

During the Dark Ages, Western civilization returned to the beliefs in possession and supernatural forces as explanations for psychiatric disorders. The Renaissance witnessed a return to enlightened empiricism, observation, and reasoned thought. Johann Weyer (1515–1588), at St. Bartholomew’s Hospital in London, first recognized suicide as a manifestation of despair. In his Anatomy of Melancholy (1630), Robert Burton summarized the existing theories and depicted the range of depressions as extending from natural grief at death or separation to depressive disorders.

A wider recognition of specific psychiatric disorders, as well as a tendency toward humane and enlightened treatments, ensued in the 18th and 19th centuries. By the early 20th century, European clinicians focused their attention on both descriptive diagnosis (diagnosis based on the recognition of specific signs and symptoms) and on unconscious factors.

Emil Kraepelin (1856–1926) distinguished manic–depressive insanity, an episodic nondeteriorating disorder, from dementia praecox—later called "schizophrenia"—a more progressive, deteriorating disorder. Eugen Bleuler (1857–1939), a Swiss neurologist, further differentiated the concept of manic–depressive insanity. He coined the term "affective disorders," in which he included manic–depressive insanity, psychoneurotic depressive reactions, and involutional melancholia. He was, however, unable to clearly subdivide depressions further—a problem that persists even today.

Early psychoanalytic thinkers did not recognize different types of depressions and often did not distinguish between normal feelings of sadness and specific depressive disorders. Those who followed, however, began to recognize that these distinctions were critical to further understanding of depression. In other words, all depressions are not explained by "anger turned inward" or by "loss of self-esteem." Perhaps certain depressions are more likely than others to be accounted for by one or more of these hypothetical mechanisms (2).

Advances in treatment gave further impetus to the need for accurate diagnosis. In 1983, von Meduna, a Hungarian psychiatrist, tried to treat schizophrenia by inducing convulsions with inhaled camphor. In 1983, Cerletti and Bini, two Italian physicians, induced convulsions by passing an electrical current between electrodes placed on the forehead. Electroconvulsive therapy (ECT) is now recognized as an effective treatment for severe unipolar and bipolar depressions.

An Australian psychiatrist, John Cade, reported lithium to be effective in the treatment of mania in 1949. In the 1950s, the antidepressant qualities of monoamine oxidase inhibitors were discovered. In 1957, the so-called tricyclic antidepressants were found, and in the 1970s new classes of antidepressants (e.g., tetracyclic compounds) were introduced.

The last decade has also witnessed the development of short-term psychotherapeutic methods specifically designed for the treatment of depression (3). These psychotherapies...
may help in the treatment of some depressions that respond poorly to currently available medications.

In summary, then, depression is a syndrome with multiple causes. Depressions therefore represent a heterogeneous group of disorders, probably including a number of distinct pathophysiological conditions.

Accuracy of Diagnosis

As already noted, diagnosis should serve the purposes of treatment selection, prognostication, and communication. Clinicians, however, have somewhat different needs than researchers with regard to diagnosis (4).

For clinicians, diagnosis mainly serves the needs of patient care. A diagnosis should be a useful statement about the patient’s problems. Because practitioners see a broad variety of patients, broad diagnostic classes to encompass these patients may be of value. Conversely, as more specific treatments become available, and as more specific diagnoses are demanded, more restrictive diagnostic groupings may be needed.

The researcher, on the other hand, often prefers more narrowly defined categories so that "pure" or more homogeneous groups can be identified for further biological or psychological studies. Furthermore, such narrow groupings also facilitate clear communication and replicability of investigations.

Recently, the development of specific criteria for different psychiatric syndromes has dramatically improved clinical diagnostic practice. The third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (5) and its recent revision, DSM-III-R (6), incorporates these more specific criteria. Further, it employs a multiaxial system so that personality (Axis II) is separated from syndrome (Axis I) and from psychosocial stressors (Axis IV). These changes have significantly improved the reliability of syndrome diagnosis.

Spitzer et al. (7) identified several sources of variance that can reduce the reliability of diagnosis. Subject variance can result from specific patients having different diagnoses at different times, which leads observers to classify them differently. For instance, a schizophrenic patient with personality delusions may be diagnosed as paranoid; later, this patient’s symptoms may have a strong affective component and may lead to the diagnosis of schizoaffective disorder.

Occasion variance occurs when patients with the same underlying condition display different symptoms because they are interviewed on different occasions. For example, the alcohol-dependent patient may be acutely intoxicated on one occasion and in delirium tremens at another time. Information variance occurs when observers gather their information from two different sources or ask different questions of the same information source. For example, an angry wife may stress her husband’s drinking habits and behavioral disturbances as primary problems, whereas the patient may emphasize his disturbed mood and insomnia. Observer variance occurs when two clinicians observe the same information or data differently. For example, one practitioner may put more weight on symptoms suggestive of a formal thought disorder, while another clinician will focus on symptoms of an affective disturbance. Criterion variance occurs when two clinicians gather the same data, but render different diagnoses because they use different criteria. For example, Americans may diagnose schizophrenia more frequently than their British counterparts because they have a different concept of schizophrenia (4).

What can clinicians do about these sources of variance? Information variance can be reduced by the use of structured interviews and by standardizing information sources. Interviewing both the patient and a close relative is particularly helpful in improving the reliability of descriptive diagnosis. Observer variance may also be decreased by the use of structured interviews and by interviewing the patient on more than one occasion. Two diagnostic interviews separated by several days will help decrease occasion variance. Reliance on criteria that are widely accepted and have definition of terms will minimize criterion variance.

The Present State Examination (PSE) (8) and the Schedule for Affective Disorders and Schizophrenia (SADS) (9) are examples of structured interviews that were developed recently for research purposes. Each contains specific questions designed to elicit information about particular symptomatology, and each defines ambiguous terms such as “formal thought disorder.” The PSE focuses exclusively on current symptomatology, while the SADS evaluates both current and past symptoms—thus allowing for both current and lifetime diagnoses. Neither system, however, covers organic brain or personality disorders in detail (4).

As noted above, diagnostic nomenclature has moved from general narrative descriptions of diagnostic entities as in DSM-II (10) to specific criteria to operationalize the diagnostic process (5–6). In addition to DSM-III and DSM-III-R, the “St. Louis Criteria” (11) and the Research Diagnostic Criteria (RDC) (7) are widely used by clinical researchers. Any of these operationalized criteria will significantly improve the reliability of diagnosis. Reliability is assessed by either the degree of agreement between raters (inter-rater reliability) or by the degree of agreement on two different occasions (test–retest reliability). Both observer variance and criterion variance affect inter-rater reliability, while test–retest reliability is also affected by occasion variance. Thus, test–retest reliability is likely to be lower than inter-rater reliability (4).

Since patients change significantly between evaluations, test–retest reliability is also affected. Thus, test–retest reliability may reflect the inherent variability in clinical populations as much as it does the reliability of the diagnostic system itself (4).

Recently, computerized approaches to diagnosis have been proposed. In most computerized diagnostic systems, such as CATEGO and DIAGNO, a logical decision-tree approach is used (13–16). Such an approach closely approximates what occurs in actual clinical practice, because it is based on a hierarchical conceptualization of diagnoses. Both DIAGNO and CATEGO have modest-to-good agreement with clinical judgments, limited by their inherent rigidity. Computers do not conceptualize, perceive novel or unexpected relationships, or modify and redesign the problem-solving process as unanticipated difficulties arise. Thus, computerized approaches to diagnosis are likely to have only limited applications and will not replace traditional clinical diagnostic methods, even for research purposes (4).

Let us now turn to the issue of validity. Reliability is easier to establish in a diagnostic system than is validity. Conventionally, there are four types of validity: face validity, content validity, construct validity, and criterion validity. Face validity refers to whether or not the diagnostic category makes sense clinically and appears to describe a clinical condition that actually occurs. Content validity is assessed by determining whether or not patients actually fit the various diagnostic categories and whether or not all

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patients can be classified by the system. Construct validity refers to whether or not the diagnostic system is consistent with an underlying theory or construct as, for example, the genetic theory of manic-depressive illness. Criterion validity, the most important type of validity for the clinician, refers to whether or not a particular diagnosis is useful in making predictions about some future behavior, such as response to treatment, clinical course, or prognosis. External aids such as laboratory tests may be valuable in validating diagnostic categories. Much clinical research is currently aimed at evaluating the extent to which various laboratory tests may assist in the diagnostic process. However, these laboratory investigations depend entirely on whether diagnosticians can delineate homogeneous and internally consistent diagnostic groupings for study.

In addition to laboratory tests, other clinical correlates, such as family history, response to treatment, and prognosis or course have been used to validate various diagnostic categories. Only rarely have these clinical correlates provided clear-cut validation of new nosological entities.

In DSM-III-R (6) a multiaxial system is used in an attempt to gain from both typological and dimensional approaches to diagnosis.

The typological approach is based on the medical model and perceives classification systems as consisting of more or less discrete and independent categories of disease. Clinicians working typologically tend to think in terms of placing the patient's signs and symptoms into a single diagnostic category, recognizing, of course, that some patients may present with multiple disorders.

The dimensional approach characterizes each patient by several dimensions or variables, so each patient is assigned a unique place utilizing multiple dimensions.

The typological approach has the virtue of simplicity. The dimensional approach can be extremely complex. However, the latter offers maximum flexibility. Some investigations have shown that the dimensional approach can predict outcome when multiple regression and statistical methods are used. The majority of research so far, however, finds that the validity of a typological classification system is at least as good as or better than that based on the dimensional approach.

The multiaxial system of DSM-III-R (Table 1) separates syndrome (Axis I) from personality (Axis II; the patient's usual behavioral pattern when the syndrome is not present). Co-existent medical and surgical disorders are described in Axis III. Environmental stressors are construed as independent variables (Axis IV), which do not determine diagnosis. Thus, the term "reactive depression," referring to depressed states precipitated by recent psychosocial stressors, is no longer used. The presence of psychosocial stressors on Axis IV does not contribute to the Axis I diagnosis of the syndrome of depression.

### Basis for Diagnosis

Several bases for diagnosis have been proposed, including etiology, symptomatology, course, pathogenesis, and response to various treatments. If a predictable relationship is found between the factors of etiology, clinical symptom picture, and course, then a nosological entity has been established. Such a disorder is likely to take a particular course and to be caused by a particular etiological constellation. Such a nosological entity is a rarity, if not a fiction, in present-day psychiatry. In our current state of knowledge, psychiatric syndromes are etiologically nonspecific. Similar or dissimilar precipitants, stressors, or other "causes" may provoke the same or different pathological reactions. For the mood disorders, the field is replete with ideas, but no current model is specific enough for us fully to understand the etiology or pathogenetic mechanisms in any given case.

When diagnoses are based on signs and symptoms alone, one must take into account the fact that sex, age, and the patient's personality, as well as a host of other variables, may affect the presentation of a particular syndrome. When one turns to diagnosis based on course, naturalistic studies of depressed patients are rare, and most are confounded by concurrent therapeutic interventions that may range from psychoanalysis or short-term psychotherapies to antidepressant medications or electroconvulsive therapy. While diagnosis based on treatment response may be of particular value for researchers, it does not allow the physician to select treatment for an individual patient.

In light of these problems, DSM-III-R diagnoses are simply based on the apparent phenomenology (the particular signs and symptoms) and do not imply a specific etiology.

### Diagnostic Criteria

It is not possible to describe in detail all the criteria used for the diagnosis of nine different forms of affective disorders as listed in DSM-III-R. However, Tables 2 through 5 list the criteria for major depression, dysthymia, mania, and cyclothymia, according to DSM-III-R. Patients with major depression who present with only recurrent depressive episodes are diagnosed as having unipolar depression, whereas those who present with both major depressive and manic episodes or with manic episodes alone are classified as bipolar disorder. Some patients evidence major depression and only hypomanic episodes. In these instances, a diagnosis of atypical bipolar disorder is made.

Patients having a simultaneous mixture of both manic and depressive symptomatology pose a significant diagnostic problem. Their symptoms are likely to be confused with

### Table 1. Multiaxial System

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<th>Axis</th>
<th>Description</th>
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<tr>
<td>Axis I</td>
<td>Clinical syndrome</td>
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<tr>
<td>Axis II</td>
<td>Personality disorders (developmental disorders)</td>
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<tr>
<td>Axis III</td>
<td>Physical disorders</td>
</tr>
<tr>
<td>Axis IV</td>
<td>Psychosocial stressors</td>
</tr>
<tr>
<td>Axis V</td>
<td>Highest adaptive functioning within past year</td>
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### Table 2. Major Depressive Episode

A. At least five of the following, present for at least two weeks, and are a change from previous functioning and must include either (1) or (2)

1. Depressed mood (irritable for children/adolescents), nearly every day
2. Diminished interest/pleasure
3. Significant weight loss/gain (5% of body weight in one month) or appetite increase/decrease
4. Insomnia/hypersomnia
5. Observed psychomotor agitation/retardation
6. Fatigue or loss of energy
7. Feelings of worthlessness/guilt
8. Decreased concentration/decision-making
9. Thoughts of death/suicide

B. No organic factor; not grief
C. Delusions/hallucinations do not occur without mood symptoms
D. Not superimposed on other psychotic disorders
those of schizoaffective disorder, schizophrenia, or psychotic depressions. Proper diagnosis as mixed-phase bipolar patients is important, because the treatment to be instituted often includes both antidepressant medication and lithium.

Major depression is subdivided by a number of categories. "Chronic" refers to an episode that lasts for more than two years. "Seasonal" major depression or bipolar disorder refers to those patients whose onset and offset of the episode of depression or mania has a reasonably tight association with the time of year. Classically, in such cases, the onset of depression occurs in the fall, while the offset occurs in the spring. Whether these patients have a different response to tricyclic antidepressants or psychotherapy is unclear, although therapy with light (extending the light period of each day with artificial illumination) appears helpful.

A third subdivision—melancholia—is intended to identify those patients who are particularly likely to respond to antidepressant medication or electroconvulsive therapy (see Table 6).

Finally, a fifth digit is used in DSM-III-R to designate the severity of illness (Table 7). It appears from studies by Glassman et al. (26) and others that psychotic depressions will fare better on a combination of tricyclic and neuroleptic medications than on tricyclics alone. Also, electroconvulsive therapy is more likely to be called for in melancholic or psychotic depressions.

Differential Diagnosis of Dyshoria

Figure 1 shows the differential diagnosis of patients complaining of dyshoria. Dyshoria may be described by

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Table 3. Dysthymic Disorder
A. Depressed mood (or irritable for children and adolescents) for most of the day, more days than not, for at least two years
B. While depressed, at least two of the following:
   (1) Poor appetite/appetite
   (2) Insomnia/hypersomnia
   (3) Low energy/fatigue
   (4) Low self-esteem
   (5) Poor concentration/difficulty making decisions
   (6) Feelings of hopelessness
C. Never without (A.) for more than two months in the two-year period
D. No major depressive episode in the first two years of the disorder
E. No manic episodes
F. Not superimposed on any psychotic disorder
G. No organic factor

Table 4. Manic Episode
A. Mood (elevated, expansive, irritable)
B. At least three (or four if irritable) of the following:
   (1) Inflated self-esteem/grandiosity
   (2) Decreased need for sleep
   (3) Pressured speech
   (4) Racing thoughts or flight of ideas
   (5) Distraction
   (6) Increase in goal-directed activity or psychomotor agitation
   (7) Excessive involvement in pleasurable activities with high potential for painful consequences
C. Marked impairment of occupational, social, or interpersonal function, or hospitalization to prevent harm to self or others
D. No delusions or hallucinations for as long as two weeks without mood symptoms
E. Not superimposed on another psychotic disorder
F. No organic etiological factor

Table 5. Cyclothymic Disorder
A. At least two years (one year for children and adolescents), numerous hypomanic episodes, and numerous periods of depressed mood or loss of interest/pleasure that are not a major depressive episode
B. During the two-year period, never without symptoms for greater than two months
C. No clear evidence of major depressive episode or manic episode during first two years (one year for children and adolescents) of disorder
D. Not superimposed on any psychotic disorder
E. No organic factor

Table 6. Major Depressive Episode—Melancholic Type
At least five of the following:
(1) Loss of interest/pleasure in almost all activity
(2) Unreactive mood
(3) Mood regularly worse in the morning
(4) Early morning awakenings (2 h)
(5) Psychomotor agitation/retardation
(6) Significant anorexia/weight loss
(7) No personality disturbance before initial major depressive episode
(8) Complete recovery from a previous major depressive episode
(9) Good previous response to a specific biological treatment

Table 7. Major Depressive Episode—Fifth Digit
1—Mild
2—Moderate
3—Severe without psychotic features
4—With psychotic features
   a. Mood congruent
   b. Mood incongruent
   5—in partial remission
   6—in full remission
   0—Unspecified

A third subdivision—melancholia—is intended to identify those patients who are particularly likely to respond to antidepressant medication or electroconvulsive therapy (see Table 6).
patients as sadness, anxiety, irritability, or a combination of these dysphoric effects. Most dysphoria encountered in everyday life is not tied to a psychiatric or medical diagnosis. These dysphorias are normal affective responses to daily life events. Such normal dysphorias are typically brief and lead neither to functional impairment nor to help-seeking behavior from psychiatric or other medical professionals.

Conversely, symptoms of many medical disorders (see Table 8) may be associated with dysphoria. Organic affective disorders can present as dysphoria, dysthymia, or even major depression, as well as mania, hypomania, or cyclothymic disorder. In addition, grief or bereavement is typified by dysphoria, but grief is by definition a state that occurs in relation to the loss of a particularly important other person, and is time-limited. If the symptomatology of a grieving patient persists for more than six months after the loss, major depression is diagnosed. Adjustment reactions may be associated with dysphoria, but they do not meet the criteria for major depression or dysthymia. Once organic affective disorders, grief or bereavement, adjustment reactions, and medical illnesses associated with dysphoria have been eliminated, one is left with the psychiatric affective disorders.

Organic Affective Disorders

With regard to organic affective disorders, Table 8 enumerates many of the medical disorders that may be associated with depression and Table 9 lists medical causes for mania or hypomania. Table 10 lists medications that may be associated with either major depression or dysthymia.

Our experience over the past few years at the Mood Disorders Outpatient Clinic at the University of Texas Southwestern Medical Center suggests that 10% to 20% of patients who meet descriptive criteria for major depression or dysthymia actually have an undiagnosed medical disorder or are taking medications that can cause symptoms of depression. We speculate that, when a patient presents with dysphoria, the practitioner often interviews the patient to determine whether his or her life circumstances might account for the dysphoric response. If the judgment is positive, patients are referred for psychiatric treatment, often without a thorough neurological, medical, historical, physical, or laboratory evaluation to detect iatrogenic or medical causes.

A word of caution is therefore in order. Most of us have a proclivity to explain our internal mood by external circumstances and the personal meaning we attribute to them. Patients, too, generalize from their usual day-to-day experiences that dysphorias are explainable by life events. Moreover, major depressions, dysthyrias, or organic affective disorders are all likely to be associated with cognitive changes. What this means is that recall of recent and past events can be biased in a negative direction. As a result, patients are very likely to recall selectively one or more negative events in an attempt to explain their dysphoria. The events themselves may not have happened at all, not have happened at the recalled time, or not have been as negatively experienced then as now. Thus, patients—like the rest of us—can search their lives for significant current stresses to explain their affective or mood state. This is an incorrect attribution of cause. Neurochemical events are obviously beyond individual awareness.

Differential Diagnosis of Mood Disorders

Table 11 outlines several other psychiatric syndromes that may confound the diagnosis of depression or mania. Perhaps the most common in this regard are the symptoms of anxiety. Anxiety disorders have specific criteria, as enumerated in DSM-III-R. However, patients with major depression may also present with episodes of panic, with specific phobias, or even with agoraphobia.
This differential diagnosis is critical: anxiolytic agents are correctly prescribed if the diagnosis of an anxiety disorder is made, but antidepressant medications are the appropriate choice in major depression, even though patients may report panic episodes or agoraphobia in association with the depressive episodes.

Obsessive–compulsive personality or other personality styles may be magnified by the presence of a mood disorder. Thus, patients with major depression may present with a chief complaint of recurrent obsessions, or with compulsions. In such circumstances, again, treatment should generally be aimed primarily at the depressive disorder, rather than at the obsessive–compulsive symptomatology.

Disturbances in sleep and (or) daytime drowsiness are found in various sleep disorders (e.g., narcolepsy or sleep apnea). Differentiating these disorders from depression is critical. Depressed patients often complain of difficulty in sleep and daytime fatigue, but do not complain of drowsiness. Rarely, if ever, does a depressed patient report the acute, irresistible onset of sleep during the day. Other criteria for narcolepsy should be searched for, including cataplexy, and hypnogogic and hypnopompic hallucinations (27). Sleep apnea can be detected by a history of snoring and profound daytime drowsiness, but without the profound disturbance in appetite, weight, or the capacity for enjoyment seen in most patients with depression. In some instances, a sleep-laboratory evaluation is useful to identify suspected sleep disorders.

Patients may present with symptoms suggestive of an affective disorder in association with symptoms of formal thought disorder. The latter include thought broadcasting, thought withdrawal, thought insertion, and similar disorders (see DSM-III-R). In these cases, a diagnosis of schizoaffective symptoms rather than schizophrenia is made. Treatment typically includes, but may not be limited to, antidepressant medication, neuroleptics, lithium, or electroconvulsive therapy.

Some patients show profound disturbances in weight, appetite, and eating patterns. Anorexia nervosa, as well as bulimia, must then be considered in the differential diagnosis. We have seen a number of patients with major depression who also had symptoms of bulimia, a compulsion to eat plus a tendency to self-induced vomiting (28). In some cases, treatment aimed at the major depression will relieve both the bulimic and affective symptomatology.

At times, the clinical presentation may be largely dominated by vague somatic complaints. Pain is particularly common in patients with major depression, with some 70% reporting headaches and 40% reporting abdominal or chest pain. Joint pains, muscle aches, and backaches are also common. Patients may attribute other symptomatology such as sleep difficulties, poor appetite, and weight loss to the presence of the pain and its analgesic treatment. Regardless of whether these symptoms are attributed to the pain by the patient or by the clinician, they should be counted as present when one is determining whether the descriptive criteria for major depression are met. The same holds true when dysphoria is present, even if it is attributed by the patient to the pain or to frustration in the pursuit of relief. Clinicians sometimes label these cases “masked depression” when patients deny dysphoria, but do report sleep and appetite disturbances and other symptoms of the depressive syndrome. Treatment with antidepressant medication is often helpful here. Some therapists advocate the use of monoamine oxidase inhibitors alone or in combination with small doses of antipsychotic medication for these patients (29).

Patients over the age of 50, and especially those over 65, may initially complain chiefly of troubles with concentration, decision-making, or short-term memory recall of events. A number of these patients, if carefully interviewed, will be found to meet criteria for major depression. That is, some patients (up to 30% or more) with dementia of the Alzheimer’s type may also suffer from depression (30). Conversely, some investigators suggest the term “pseudodementia” for patients who appear with prominent symptoms suggestive of dementia, but who ultimately respond completely to antidepressant medication. That is, their apparent dementia is actually a depression. Differential diagnosis of true dementia, pseudodementia, and dementia with depression is often difficult. Clinicians are best advised to supplement the patient’s history that is obtained from an important other person who is familiar with the patient’s current or previous levels of functioning. Psychological or neurological evaluation can also be helpful, but in some cases a trial of antidepressant medication may be the only definite method to differentiate pseudodementia from true dementia.

Finally, patients presenting with sexual complaints may attribute their dysphoria to these problems. Sleep disturbances, lack of interest, and self-criticism, as well as other symptoms of major and minor depression, may also be attributed to these sexual difficulties. When formerly orgasmic females become nonorgasmic, or males develop impotence or other difficulties in sexual performance, a careful interview for major depression or dysthymia is indicated. Treatment of depression, if present, will often reverse the sexual complaints.

Difficulties in the Clinical Descriptive Diagnosis of Depression

Table 11 lists various patient, medical, sociocultural, and iatrogenic factors that commonly confound the recognition and diagnosis of depression. With regard to patient factors, male patients may often deny many symptoms in an attempt to "look strong," and older patients are more likely than younger ones to manifest somatic or vegetative symptoms (such as disturbances in sleep, appetite, and weight). Socioeconomically disadvantaged patients may present with difficulties in impulse control or even trouble with the law, with their dysphoria only elicitable after careful interviewing. There is some suggestion that increased hostility and even paranoid thinking may characterize depression in members of the lower socioeconomic classes. In addition, patients in the lower socioeconomic class are more likely to
Table 12. Problems in Descriptive Diagnosis of Depression or Mania

<table>
<thead>
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<th>Patient factors</th>
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<tbody>
<tr>
<td>1. Age/sex/racial background</td>
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<tr>
<td>2. Socioeconomic class</td>
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<tr>
<td>3. Negative cognitive bias/erroneous anamnesis</td>
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<tr>
<td>4. Memory/concentration problems</td>
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<table>
<thead>
<tr>
<th>Medical factors</th>
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<tbody>
<tr>
<td>1. Taking psychotropics that modify symptom picture</td>
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<tr>
<td>2. Presence of other medical disorders or other drugs</td>
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<tr>
<td>3. Episodic nature of depression</td>
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<tr>
<td>4. Symptom picture leading to confusion between personality and syndrome</td>
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<table>
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<tr>
<th>Sociocultural factors</th>
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<tbody>
<tr>
<td>1. Stigma, denial</td>
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<td>2. Presence of life stresses that may be erroneously viewed as etiological or explanatory by patient or physician</td>
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<td>3. Presence of complications (consequences) of depression (e.g., alcoholism, trauancy, drug dependency, legal problems, marital discord)</td>
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<td>4. Patient-blaming social or religious systems that preclude seeking a diagnosis</td>
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<th>Iatrogenic factors</th>
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<td>1. Focus on one or two symptoms without eliciting the full syndrome (e.g., chronic pain, headaches, menstrual changes, gastrointestinal complaints)</td>
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<tr>
<td>2. Attribution of cause to life events, which may impede thorough descriptive psychiatric, medical, neurological examinations</td>
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<td>3. Premature symptomatic drug prescription (e.g., hypnotics) without sufficient history or observation</td>
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<td>4. Failure to interview spouse/important other for diagnostic purposes</td>
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<td>5. Over-reliance on laboratory tests as opposed to historical and status data</td>
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<td>6. Underutilization of psychiatric consultation</td>
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<tr>
<td>7. Failure to use criteria to characterize symptom picture</td>
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present with complaints of chronic pain.

Unfortunately, clinicians too often rely on the patient as the sole source of clinical diagnostic information. This practice is particularly problematic in depression, because depressed patients may negatively distort their recall of events (31) or confound history-taking by their profound problems with memory and concentration. To correct for such potential errors in recall, we routinely interview a family member or someone who knows the patient very well, in addition to the patient himself.

Next, several medical factors may present diagnostic problems. Patients who already are taking psychotropic medications commonly present themselves to the diagnostician. Because symptoms persist and motivate the patient to seek help, the presumably ineffective medications are notorious for confounding the clinical picture. Antipsychotic medications, for example, even in low doses, may decrease insomnia or increase psychomotor retardation, and may blunt the intensity of the dysphoria that may be present. Anxiolytic medications can decrease the degree of dysphoria and partially help with insomnia, thereby making the recognition of the full depressive syndrome difficult, if not impossible. Whenever clinically possible, we stop all psychotropic medications for at least seven—and preferably 10 to 14—days to unmask symptoms that, if present, allow an appropriate diagnosis to be rendered. Close telephone contact and additional appointments may be needed to assist patients through this medication-free period.

Other medications act not to obscure, but to cause some of the symptoms found in clinical depression. This is particularly the case with anti hypertensive agents. A brief period off such medication, if this is possible, will often give a clear-cut answer if there is a question of whether or not the medication is playing a causal role.

Many patients will present with a concurrent significant medical illness that may not, in fact, be the cause for the depressive syndrome, but to which the clinician might erroneously attribute etiological importance. Consider the case of a 32-year-old nurse who suffered from multiple sclerosis that waxed and waned, but did not prevent her from continuing her occupational activities. Over time, however, she developed a significant major depression. The natural tendency was to regard her depression as a response to her multiple sclerosis and to recommend supportive psychotherapy. However, further intensive evaluation revealed that the patient suffered from marked hypothyroidism. When this was treated appropriately, complete remission of the depressive episode ensued.

A further complication is that depressions are typically episodic in nature. Thus, patients may come to their doctor weeks after the real nadir of their depressive episode. Present symptoms may be less than the full-blown major depression—even with melancholic features—that may have existed previously. And, finally, extensive interviewing is often required to separate the syndrome from the patient's usual personality. At times, this judgment is difficult, but by using a second source of information (e.g., husband, wife, or close friend), this complicating factor can be minimized.

Some patients and their families, unfortunately, still view psychiatric disorders as a sign of weakness. This attitude may lead them to deny significant problems such as the presence of suicidal ideation or past episodes of major depression. By having informational brochures available in patients' waiting areas and by providing patients with educational information during the interview, one can often reduce the need for such denial and associated shame.

Mention has already been made that life stresses may be erroneously viewed as etiological or fully explanatory by either the patient or physician. Even in bereavement, it is often difficult to determine whether the depressive symptomatology substantially preceded or followed the major loss. Normal grief reactions should not last longer than six months, although intermittent sadness over the loss may persist for a year or two.

In addition, the complications or consequences of depression may confound the diagnostic impression. For example, juvenile delinquency, school truancy, alcohol dependency, marital problems, occupational conflicts, and the like are common sequelae of depression, and are often presented by the patient. Unless carefully interviewed for the signs and symptoms of depression, these patients may be inappropriately shunted into treatment for a secondary problem (e.g., alcohol treatment program when the alcoholism is an attempt to self-medicate depression or mania, or therapy of couples to treat the marital discord that ensues from major depression) without appropriate focus on the underlying cause.

The fact that some social, religious, or family systems attribute the cause for dysphoria solely to individual responsibility can lead some patients to refuse to seek needed attention and appropriate diagnosis for their disorders. Even when seeking help, such patients tend to focus on a single symptom, at times distracting the physician from other, more complex sides of the clinical picture. For example, tension headaches, gastrointestinal symptoms, abdomi-

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nal pain, and even menstrual cycle changes are more common than not, in association with major depression. Premature focus on a single symptom and failure to recognize the full depressive syndrome may result in inappropriate treatment (e.g., anxiolytics) or expensive and unnecessarily complex evaluations.

Persons with complaints of pain pose a particular hazard in this regard. Expensive and time-consuming diagnostic evaluations by numerous specialists can be avoided when careful elicitation of signs and symptoms shows the chronic pain to be a part of the depressive episode. The analesgesic medications often used in such cases may obscure or distort depressive symptoms. Discontinuation, if possible, is advisable during the diagnostic evaluation. In short, a high index of suspicion for depression is required throughout every initial evaluation, and an attempt should be made to elicit all its signs and symptoms.

On the clinician's side, the premature use of psychotropic medications for symptoms (rather than for the syndrome) is a common practice. It is erroneous to prescribe sedative-hypnotic medications for the insomnia associated with depression, especially if the full depressive syndrome goes unrecognized. Antidepressants are effective for the insomnia; it is rarely necessary to utilize more than a single psychotomimetic agent to treat most depressions. Multiple medications can cloud the diagnostic picture, produce a partial response (with confusion about which drug is responsible), or cause complex drug reactions.

The recent availability of laboratory tests for depression offers a final snare for the diagnostician. As criterion-based diagnosis is a recent development, most nonpsychiatric practitioners did not learn this system in medical school. Also, some tests such as the dexamethasone suppression test, which has received considerable publicity, are easily ordered. These two developments tempt the practitioner toward an over-reliance on laboratory results as opposed to clinical information.

In conclusion, the past decade has witnessed four major advances in our ability to diagnose and treat depressions: criterion-based diagnosis (DSM-III and DSM-III-R), development of apparently effective and specific short-term psychotherapies for depression, development of new and different antidepressant compounds, and the discovery of measurable biological derangements that may ultimately assist us in diagnosis and treatment selection for some patients. With these advances, it becomes the clinician's responsibility to more accurately diagnose and to creatively treat these patients. With them also comes the promise of more effective, shorter, safer, and less-expensive treatment modes for our patients.

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