Comprehensive Textbook of Psychiatry/III

VOLUME 2

THIRD EDITION

Harold I. Kaplan, M.D.

Professor of Psychiatry, New York University School of Medicine;
Attending Psychiatrist, University Hospital of the New York University Medical Center;
Attending Psychiatrist, Bellevue Hospital, New York, New York

Alfred M. Freedman, M.D.

Professor of Psychiatry and Chairman,
Department of Psychiatry, New York Medical College;
Chairman, Department of Psychiatry, Psychiatric Institute,
Westchester Medical Center, Valhalla, New York;
Chairman, Department of Psychiatry, Metropolitan Hospital and
Bird S. Coler Memorial Hospital and Home, New York, New York

Benjamin J. Sadock, M.D.

Professor of Psychiatry, New York University School of Medicine;
Attending Psychiatrist, University Hospital of the New York University Medical Center;
Attending Psychiatrist, Bellevue Hospital, New York, New York

WILLIAMS & WILKINS
Baltimore/London

NOTICE

The Editors and the Publisher of this work have made every effort to ensure that the drug dosage schedules herein are accurate and in accord with the standards accepted at the time of publication. The reader is strongly advised, however, to check the product information sheet included in the package of each drug he or she plans to administer to be certain that changes have not been made in the recommended dose or in the contraindications for administration.

Made in the United States of America.

Library of Congress Cataloging in Publication Data.

Kaplan, Harold I.
Comprehensive Textbook of Psychiatry.
Includes bibliographies.
1. Psychiatry. I. Freedman, Alfred M., joint author. II. Sadock, Benjamin J., joint author. III. Title [DNLM: 1. Mental disorders. 2. Psychiatry. 3. Psychiatry—History. WM100 F855c]
RC454.F74 1975 616.8'9 74-20808
ISBN 0-683-03357-3

Composed and Printed at the Waverly Press, Inc.
Mount Royal and Guilford Avenues
Baltimore, Maryland, 21202, USA.

chapter

17

Schizoaffective Disorders

SAMUEL B. GUZE, M.D.

Introduction

The third edition of the American Psychiatric Association's (1980) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) does not define or give diagnostic criteria for schizoaffective disorders. Instead, the diagnosis is included among Psychotic Disorders Not Elsewhere Classified to indicate strong reservations about its validity as a separate disorder. Nevertheless, experienced clinicians have long recognized that certain patients, especially early in the course of their illnesses, present with a mixture of affective and psychotic features that suggest either schizophrenia or a major affective disorder, but for whom a confident differential diagnosis is not possible. In the past, many of these patients would have been diagnosed as suffering from a brief reactive psychosis, schizophreniform disorder, major affective disorder demonstrating mood-congruent or mood-incongruent psychotic symptomatology, or schizophrenia with an atypical affective disorder. In time, the clinical course permits a diagnosis of schizophrenia or affective disorder in most of these patients, but when they are first seen a diagnosis of schizoaffective disorder is frequently made to indicate uncertainty while defining the diagnostic problem.

Although many patients with schizophrenia experience depression, the significance of such affective features is uncertain. It is not clear when such depressions—because of their timing, clinical features, or severity—are to be viewed as merely intercurrent complications of the underlying schizophrenia and when they ought to be considered as intrinsic features of the disorder, thus raising questions as to whether the basic disorder is, in fact, schizophrenia. Similarly, although many patients with depression or mania experience delusions and hallucinations, it is not always clear when such psychotic features should raise questions about the underlying disorder.

Implicit in any effort to distinguish among schizophrenic, affective, and schizoaffective disorders is the assumption that the distinction has validity—that is, that the classification is associated with some significant differences in clinical course, response to treatment, outcome, familial illness patterns, cause or pathogenesis for the different disorders (Robins and Guze, 1970).

History and Definition

Since the time of Kraepelin (1919), there has been a continuing debate about the definition of schizophrenia. For some, who follow Kraepelin's views, the diagnosis of schizophrenia should be reserved for a relatively narrow group of psychotic patients whose general prognosis—both clinical and social—is poor, even though, as Kraepelin noted, about 10 to 15 per cent do recover completely. For others, who follow Bleuler's (1950) views, the diagnosis of schizophrenia may be used for a wide range of psychotic patients with variable prognoses, although, somewhat paradoxically, Bleuler insisted that none ever returned fully to his premorbid state.

Thus, psychiatrists influenced by Kraepelin have sought to identify diagnostic criteria that are associated with a generally poor prognosis and have defined schizophrenia accordingly. They have emphasized the insidious onset of the disorder, the schizoid prepsychotic personality, the absence of obvious precipitating life events, the restricted affect, the tendency to a celibate life, the inability to establish oneself in a career, and the increased familial prevalence of similar illnesses.

Psychiatrists influenced by Bleuler have generally adopted a much less constricted view of schizophrenia. They have usually been willing to diagnose schizophrenia whenever patients showed a functional psychotic illness. Bleuler emphasized certain primary symptoms—autistic thinking, ambivalence, certain affective disturbances—that he believed were always present in schizophrenic patients. By assigning delusions and hallucinations to a secondary role, he led the way to making the diagnosis in patients who show few if any unequivocal psychotic features.

Psychoanalytic theory carried this tendency even further. By emphasizing a defective ego as the hallmark of schizophrenia, psychoanalysts have included a broad range of psychopathology in the diagnosis.

It is not surprising, therefore, that major international differences have been noted in the diagnosis of schizophrenia. Most Western European authorities have used a narrow definition, in keeping with Kraepelinian views, and most Americans have used a broad definition, in keeping with the Bleulerian and psychoanalytic views.

Many useful attempts have been made to clarify these opposing views during the past 30 years, beginning in 1939 with the work of Langfeldt (1956), who tried to characterize patients who may have resembled more narrowly defined schizophrenics but whose long-term course and prognosis suggested that they were not typical Kraepelinian schizophrenics. He referred to such disorders as schizophreniform and emphasized their relatively good prognosis and response to treatment. Since then, many investigators (Astrup et al., 1962; Astrup and Noreik, 1966; Fowler, 1978; Pope and Lipinski, 1978; Strauss and Carpenter, 1978; Vaillant, 1978) have continued to work on the classification of psychotic patients according to their long-term course and prognosis. Nondemented psychotic patients may be usefully divided into two broad groups, one with a relatively poor prognosis and the other with a relatively good prognosis. Diagnostic terms such as chronic schizophrenia, nuclear schizophrenia, process schizophrenia, and nonremitting schizophrenia have been applied to those with a relatively poor prognosis, and terms like acute schizophrenia, reactive schizophrenia, remitting schizophrenia, schizophreniform disorders, and schizoaffective disorders have been applied to those with a relatively good prognosis. Some have argued that these prognostic differences, although valid, do not represent fundamentally different disorders (Vaillant, 1978); others have concluded that the differences reflect different basic conditions (Taylor and Abrams, 1975; Fowler, 1978).

Affective syndromes may develop in patients suffering from long-established schizophrenia but such patients are excluded here from the category of schizoaffective disorders, because such affective disturbances do not appear to have the same significance as affective symptoms that precede or develop concurrently with a psychotic syndrome.

Schizoaffective disorders are defined here as a syndrome of depressive or manic features that develop before or concurrently with certain psychotic symptoms, such as a preoccupation with a mood-incongruent delusion or hallucination. The psychotic symptoms are such as to be considered unusual in an uncomplicated affective disorder. The diagnosis of schizoaffective illness is not made if the illness is due to any organic mental disorder.

Two kinds of psychotic symptoms define schizoaffective disorders. The first kind includes those that are part of the criterion list for schizophrenia, such as delusions of control and certain types of auditory hallucinations, and that would suggest schizophrenia, if there were no accompanying affective syndrome. The second kind includes those that arise in the context of an affective syndrome without an apparent relationship to depression or elation. Otherwise, the clinical features consist of various mixtures of affective and schizophrenia-like symptoms.

Epidemiology

Few data are available concerning the prevalence and epidemiological distribution of schizoaffective disorders. Most population surveys of the incidence or prevalence of psychotic disorders have ignored the distinctions discussed here and have tended to assign nondemented psychotic patients to the schizophrenia category. Furthermore, investigators who have included some psychotic persons in the affective disorder (manic-depressive) category have generally done so on the basis of unspecified clinical judgment, rather than on the basis of explicit criteria.

Nevertheless, certain observations are pertinent and permit some conclusions. Most patients with depression who consult psychiatrists do not report psychotic symptoms. Probably no more than a quarter to a third of depressed patients experience delusions, hallucinations, or prominent ideas of reference (Guze et al., 1975). The presence of such psychotic features probably increases the likelihood of consulting a psychiatrist, so that the percentage of depressed persons with psychotic features among all depressed persons is probably significantly less than the percentage seen by psychiatrists. At most, an estimated 5 to 10 per cent among those who seek any professional help have both depressive and psychotic symptoms. The percentage is probably even lower, perhaps between 2 and 5 per cent, among those who never seek professional help, because this group includes many with mild and brief depressions.

The lifetime general population prevalence of depression has been estimated to be between 5 and 20 per cent, depending on the diagnostic criteria and sampling methods (Weissman et al., 1978). Using the above estimates for the frequency of psychotic features in depression, one may conclude that a maximum of somewhere between 0.1 per cent and 1.0 per cent of the population experience a depression with psychotic features.

Combining the estimated prevalence of manic disorders—0.2 per cent, according to Weissman et al. (1978)—with the estimated percentage of manic patients who show psychotic features—about 50 to 70 per cent—the prevalence of mania with psychosis may be estimated at about 0.1 per cent.

Most population studies place the prevalence of schizophrenia at a little under 1 per cent. Most schizophrenics experience affective syndromes sometime during the course of illness (Planansky and Johnston, 1978), so that an estimate of the association of schizophrenia and affective syndromes, usually depressive, is about 0.5 per cent of the population.

If the estimated frequencies of depression with psychotic features, mania with psychotic features, and schizophrenia with affective syndromes are combined, the sum is a total estimated frequency of between 0.7 and 1.6 per cent. The estimate of 1.6 per cent may be taken as an approximate maximum frequency of schizoaffective conditions. However, the frequency of schizoaffective illness as defined in DSM-III is considerably less, because intercurrent affective episodes during the course of schizophrenia are excluded, as are many patients whose psychotic features seem clearly part of an affective illness. So, finally, a reasonable estimate of the prevalence of schizoaffective disorders, as defined here, may be no more than 1 per cent.

One of the major justifications for discriminating schizoaffective disorders from schizophrenia is the difference in the familial patterns. Close relatives of patients with schizoaffective disorders show a lower prevalence of schizophrenia than is seen in relatives of schizophrenics; instead, the relatives of patients with schizoaffective disorders show an increased frequency of affective illness, a frequency similar to that seen in the relatives of patients with affective disorders (Fowler, 1978).

Differential patterns of psychiatric illness in close relatives are one of the most important parameters for validating diagnostic categories (Robins and Guze, 1970). Regardless of the causative importance of genetic and environmental factors, nearly all psychiatric disorders have been found to be familial. Thus, finding an increased prevalence among close relatives provides strong support for any particular diagnosis.

Most of the ill relatives of schizoaffective patients suffer from uncomplicated, straightforward affective illnesses. At the same time, an increased frequency of schizoaffective conditions may be seen among the relatives. Some authors have reported finding such increases and have argued, in fact, that this finding justifies considering schizoaffective disorders as a third functional psychosis, in addition to affective psychosis and schizophrenia (Leonhard, 1961; Mitsuda, 1967; McCabe and Strömgren, 1975; McCabe, 1976). Others (Robins and Guze, 1970; Fowler, 1978) have preferred to consider patients with schizoaffective disorders as a heterogeneous group with varying proportions of depression, mania, and schizophrenia, depending on the method of selecting the samples, with the question of a possible third psychosis left unresolved.

No striking sex differences in the frequency of schizoaffective disorders have been reported.

Causes

Little is known concerning the causes of all functional psychoses, including schizoaffective disorders. Evidence for some genetic predisposition to schizophrenic and affective disorders has been obtained from a wide range of twin and adoption studies, but relatively little attention has been given thus far to separating out schizoaffective conditions (see above).

Most speculation, whether biological or psychodynamic, concerning schizophrenic, depressive, and manic psychopathology has also been applied to schizoaffective conditions. This is hardly surprising, because the evidence for considering schizoaffective disorders as basically distinct from straightforward schizophrenic and affective disorders is still modest.

Clinical Features

All patients present with a mixture of affective features, depressive or manic, and one or more clearly evident hallucinations or delusions that are considered characteristic of schizophrenia or, because they have no apparent relation to the disordered mood, that are unusual in uncomplicated affective disorders.

Typically, the psychosis begins abruptly, either coincident

with an affective disturbance or after an affective syndrome has been evident for some days or weeks. It is often difficult to be sure which feature began first. The affective and psychotic components of the illness may parallel each other in intensity throughout, or one may wax and wane while the other holds steady.

A common sequence is for the affective and the psychotic features to begin more or less simultaneously; then the delusions or hallucinations subside, leaving the patient with a typical depression or mania. The psychotic features are usually dramatic and overt, creating disturbances for relatives, friends, and neighbors.

Such episodes may last very briefly, but they usually run a course of weeks to months. Some patients experience repeated episodes, separated by months or years of apparently normal psychological functioning. Others have several similar episodes that are then followed by other episodes of typical depression or mania. In yet others the episodes are supplanted by a persistent illness that is indistinguishable from typical chronic schizophrenia, with or without associated periods of disturbed mood.

Suicidal thinking and completed suicide are common in these patients. In this way they are similar to those with straightforward affective disorders. One of the as yet unanswered questions is the proportion among young schizophrenics who commit suicide of those suffering from schizoaffective disorders, rather than from uncomplicated schizophrenia. The suicide risk, like the familial illness pattern, has lent support to the view that many, if not most, schizoaffective illnesses are, in fact, atypical cases of depression or mania, rather than cases of schizophrenia.

Course and Prognosis

The long-term course and outcome of schizoaffective disorders cannot be discussed separately from the course and outcome of schizophrenia itself. The course of schizoaffective disorders may be quite variable, but it seems on average to be significantly better than the course of schizophrenia. Stephens (1978) summarized 38 long-term follow-up studies of hospitalized schizophrenics and concluded that unspecified or Kraepelinian-type schizophrenia has a much worse prognosis than does atypical schizophrenia, schizoaffective psychoses, or reactive psychosis. The better prognosis applies to the clinical course of the illness and to the social adjustment and is true for untreated patients, as well as treated patients.

Typically, the psychotic features develop acutely, and the patient is brought for professional help within weeks of their onset, because the patient's family or the patient himself recognizes that a significant change in functioning has taken place. The relatively acute onset of the psychotic features has long been recognized as an important favorable prognostic factor (Stephens, 1978). During the psychotic period, it may be difficult to assess the patient's affective state adequately, although the patient usually discusses his or her mood freely. Sometimes the patient is severely catatonic and is, therefore, inaccessible, but usually such periods are brief, and the patient communicates more freely afterward. Catatonic features may be as evident in schizoaffective disorders as in schizophrenic states (Taylor and Abrams, 1977).

Diagnosis

The diagnosis of schizoaffective disorders follows directly from their definition and the clinical picture.

PSYCHIATRIC EXAMINATION

The findings on psychiatric examination may be quite variable. In one patient the psychotic features may be more prominent than the affective features; in another patient the situation may be reversed. In any single patient, these two types of features may fluctuate together or independently. Generally, however, the delusions or hallucinations are quite striking and present no problems in recognition. Patients are disturbed and create considerable difficulty for their families and friends. In general, the more floridly disturbed the patient, the more likely is the illness to be schizoaffective, rather than schizophrenic. The affective features are similar to those seen in uncomplicated depression and mania.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis should cover affective disorders, schizophrenia, organic mental disorders, and certain substance-use disorders, particularly those associated with the abuse of amphetamines, lysergic acid diethylamide (LSD), and other hallucinogens.

Substance abuse should always be considered when confronted by an acutely psychotic patient, including one with striking affective symptoms. Outside history, blood and urine screening for appropriate metabolites, and careful observation usually permit the correct diagnosis. The great majority of substance-abuse illnesses subside within a few days after discontinuation of the drug and very rarely last more than 10 to 12 days after discontinuation.

Because some schizoaffective patients show some clouding of consciousness early in the course of an episode, an organic mental disorder must frequently be seriously considered. Most of the time, however, the confusion and bewilderment are short-lived and leave the patient with a clear sensorium, despite the continuation of other symptoms. Occasionally, though, the mild confusion or disorientation are present throughout the illness. In such cases, it may be simply a matter of policy whether the patient receives a diagnosis of schizoaffective disorder or a diagnosis of organic mental disorder.

The major differential diagnostic problems relate to schizophrenia and affective disorders. The history of the concept and the definition of schizoaffective disorders suggest that patients with these disorders are a heterogeneous group suffering from schizophrenia, affective disorders, and possibly a third functional psychosis. The relative proportion of the mixture probably varies with different circumstances and different diagnostic methods. In addition, there is still disagreement as to whether remitting or good-prognosis cases of schizophrenia should be classified as schizophrenia or as affective disorders (Fowler, 1978; Vaillant, 1978). To some extent, differential diagnosis is a matter of convention.

However, patients with these disorders do vary considerably with regard to their course and outcome. A major concern when such a patient is first seen is to estimate his or her prognosis. Efforts to separate patients prospectively into those with a relatively good prognosis and a remitting course and those with a relatively poor outcome and a chronic course have achieved varied success (Robins and Guze, 1970; Stephens, 1978; Strauss and Carpenter, 1978).

In general, successful efforts to discriminate good-prognosis and poor-prognosis cases have relied on the course of the illness up to the time of study as much as, if not more than, the clinical picture (Fowler, 1978). A poor prepsychotic life adjustment—manifested by a schizoid personality, few friends, a

limited or absent sex life, and an insidious onset of illness, so that it is difficult to tell when it began—is the characteristic prognostic feature in poor-prognosis cases. A history without schizoid personality features or life style of an acutely developing psychosis (often seemingly precipitated by some life event), usually accompanied by prominent affective symptoms, is the important prognostic feature in good-prognosis cases.

Efforts that have emphasized the clinical picture, rather than the previous history, have been less successful (Strauss and Carpenter, 1978). Prominent affective symptoms may be significant in predicting a remitting course only when seen in the context of an acute psychosis with a good premorbid life history. In the past, when interest in psychiatric diagnosis was limited, little effort was made, particularly in the United States, to distinguish affective disorders from schizophrenia, so that any patient with psychotic features was simply called schizophrenic. However, as interest in this differential diagnosis has grown, patients have been less likely to be labeled schizophrenic simply because of psychotic features. Most affective disorders with psychotic features are recognized as affective illness, and the presence of affective features alone in the remaining cases may not be as significant in differential diagnosis.

PSYCHOLOGICAL TESTS

Psychological test results, not surprisingly, show a mixture of features associated with both schizophrenia and affective disorders. Few studies have taken schizoaffective disorders as a separate classification into consideration.

Treatment

Most patients with schizoaffective disorders require hospitalization because of their psychotic features, affective disturbances, or risk of suicide. Antipsychotic agents (such as the phenothiazines and butyrophenones), tricyclic antidepressants, antimanic drugs (such as lithium and the phenothiazines), and electroconvulsive therapy are the mainstays of treatment.

The choice of drug or combination of drugs usually depends on the mixture of clinical features and the relative severity of the various clinical elements. In general, patients do not seem to respond as well to tricyclic antidepressants alone as they do to antipsychotic drugs, with or without tricyclic antidepressants, although some patients do well on the antidepressants alone. Similarly, lithium alone is sometimes effective but usually seems less satisfactory than antipsychotic drugs, with or without lithium. Many patients do quite well with pharmacological treatment, but a significant number respond so poorly or so slowly that electroconvulsive therapy is indicated.

Most patients respond well to a course of electroconvulsive therapy. It is not yet clear whether such patients are affected by concomitant drug administration, but many experienced clinicians believe that patients do better if the antipsychotic or antimood agent is continued after the electroconvulsive therapy.

Most patients are helped by the available treatments. For many, drugs or electroconvulsive therapy or a combination results in prompt recovery and the ability to return to work or school. To what extent the continuation of an antipsychotic or antimood drug prevents relapse is not clear, but some evidence indicates that such a prophylactic effort is helpful, at least in some cases. Unfortunately, some patients relapse after only a brief remission and must be treated vigorously to achieve a more lasting remission. A minority of patients show very little improvement, despite the application of all treatments, and they progress to a chronic state of illness.

Suggested Cross References

The schizophrenic disorders are discussed in Chapter 15, and the affective disorders are discussed in Chapters 18 and 19. Drug dependence is discussed in Chapter 23. Examination of the psychiatric patient is discussed in Chapter 12. The organic therapies are discussed in Chapter 31.

REFERENCES

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders,* ed. 3. American Psychiatric Association, Washington, D.C., 1980.

Astrup, C., Fossum, E., and Holmboe, R. *Prognosis and Functional Psychoses.* Charles C Thomas, Springfield, Ill., 1962.

Astrup, C., and Noreik, K. *Functional Psychoses: Diagnostic and Prognostic Models.* Charles C Thomas, Springfield, Ill., 1966.

Bleuler, E. *Dementia Praecox or the Group of Schizophrenias.* International Universities Press, New York, 1950.

* Fowler, R. C. Remitting schizophrenia as a variant of affective disorder. Schizophr. Bull., *4:* 68, 1978.

* Guze, S. B., Clayton, P. J., and Woodruff, R. A., Jr. The significance of psychotic affective disorders. Arch. Gen. Psychiatry, *32:* 1147, 1975.

Kraepelin, E. *Dementia Praecox and Paraphrenia.* E and S Livingstone, Edinburgh, 1919.

Langfeldt, G. The prognosis in schizophrenia. Acta Psychiatr. Neurol. Scand. (Suppl.), 110, 1956.

Leonhard, K. Cycloid psychoses: Endogenous psychoses which are neither schizophrenic nor manic depressive. J. Ment. Sci., *107:* 633, 1961.

McCabe, M. S. Reactive psychoses and schizophrenia with good prognosis. Arch. Gen. Psychiatry, *33:* 571, 1976.

McCabe, M. S., and Strömgren, E. Reactive psychoses: A family study. Arch. Gen. Psychiatry, *32:* 447, 1975.

Mitsuda, H. The concept of "atypical psychosis" from the aspect of clinical genetics. In *Clinical Genetics in Psychiatry,* H. Mitsuda, editor, p. 34. Bunkosha, Kyoto, 1967.

Planansky, K., and Johnston, R. Depressive syndrome in schizophrenia. Acta Psychiatr. Scand., *57:* 207, 1978.

* Pope, H. G., Jr., and Lipinski, J. F., Jr. Diagnosis in schizophrenia and manic depressive illness. Arch. Gen. Psychiatry, *35:* 811, 1978.

* Robins, E., and Guze, S. B. Establishment of diagnostic validity in psychiatric illness: Its application to schizophrenia. Am. J. Psychiatry, *126:* 983, 1970.

Stephens, J. H. Long-term prognosis and follow-up in schizophrenia. Schizophr. Bull., *4:* 25, 1978.

Strauss, J. S., and Carpenter, W. T., Jr. The prognosis of schizophrenia: Rationale for a multidimensional concept. Schizophr. Bull., *4:* 56, 1978.

* Taylor, M. A., and Abrams, R. Manic depressive illness in good prognosis schizophrenia. Am. J. Psychiatry, *132:* 741, 1975.

Taylor, M. A., and Abrams, R. Catatonia. Arch. Gen. Psychiatry, *34:* 1223, 1977.

Vaillant, G. E. A ten-year followup of remitting schizophrenics. Schizophr. Bull., *4:* 78, 1978.

Weissman, M. M., Myers, J. K., and Harding, P. S. Psychiatric disorders in a U.S. urban community: 1975–76. Am. J. Psychiatry, *135:* 459, 1978.

chapter

18

Affective Disorders

18.1 Overview of Affective Disorders

GERALD L. KLERMAN, M.D.

Introduction

The term "affective disorders" groups together a number of clinical conditions whose common and essential feature is a disturbance of mood accompanied by related cognitive, psychomotor, psychophysiological, and interpersonal difficulties.

Mood usually refers to sustained emotional states that color the whole personality and psychic life. Affect sometimes refers to the subjective aspect of emotion, apart from its bodily component; mood refers to the pervasive or prevailing emotion. Therefore, some authorities have suggested that the term "mood disorders" would be the more precise designation. In the clinical disorders under consideration, the emotional changes are pervasive and sustained, meeting the definition of mood. However, since historical continuity and clinical usage have preferred "affective disorders," that term is used in the third edition of the American Psychiatric Association's (1980) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) and here. Although human experience includes a variety of emotions—such as fear, anger, pleasure, and surprise—the clinical conditions considered under the affective disorders involve depression and mania.

Grouping the affective disorders according to the patient's predominant symptoms represents less than the ideal basis for nosology. An ideal nosology would base classification on causes—genetic, psychodynamic, and biological factors. Those and other factors have been proposed as causal for the affective disorders, and investigations are underway to establish their precise roles. It is probable that the conditions grouped together as affective disorders are heterogeneous as to cause; some or most are probably multifactorial in causation, involving complex interactions of genetic, biochemical, developmental, and environmental factors. However, in view of the limited extent of the current knowledge about the causes of most mental disorders, classification by type of psychological impairment has had great heuristic value. Since the late 19th century, mental disorders have been classified by the psychological faculty manifestly most impaired: intelligence (mental retardation), thinking and cognition (the dementias, the deliriums, the schizophrenias), social behavior (character and personality disorders), and mood (affective disorders). That approach to the classification of mental disorders parallels the classification of internal medicine disorders by organ (heart, kidney, and so on), the faculties of the mind assuming the place of mental structures equivalent to body organs in providing a basis for classification when a causal classification is not yet sufficiently substantiated by research or clinical experience.

The DSM-III category of affective disorders groups all the affective disorders together, regardless of the presence or absence of psychotic features or association with precipitating life experiences (see Table I). Within that group, the subcategory "major affective disorders" includes bipolar disorder—mixed, manic, or depressed—and major depression—single episode or recurrent. Under "affective disorders" there are two additional subcategories: "other specific affective disorders"—including cyclothymic disorder and dysthymic disorder—and "atypical affective disorders"—including atypical bipolar disorder and atypical depression.

The classification system for DSM-III has undergone successive modification and refinement, and some terms used previously for a variety of affective disorders have been changed. For example, involutional melancholia is now classified as major depression, single episode, with melancholia or with mood-congruent psychotic features. Manic-depressive illness, manic type, is now classified as bipolar disorder, manic type; manic-depressive illness, depressed type, as major depression, single episode or recurrent; and manic-depressive illness, circular type, as bipolar disorder—manic, depressed, or mixed. Depressive neurosis is now classified as either major depression—single episode or recurrent, without melancholia—dysthymic disorder, or adjustment disorder with depressed mood. Furthermore, DSM-III accepts the evidence pointing to the importance of the distinction between unipolar and bipolar forms of affective disorders.

Before the individual clinical disorders are discussed, certain general considerations are warranted to provide an overview. Those considerations include the nature of human emotions, the relationship of normal emotional states to clinical disorders, and a summary of major causal factors.

History

Literary and clinical descriptions of depression—the mental, bodily, and spiritual state that in previous eras was called melancholia—and mania date back to antiquity, as do speculations about the relation of those emotional states to health and illness and to the human condition. Scientific investigations of affective disorders, however, are only a century or two old, and, although major advances in treatment have

TABLE I
*DSM-III Classification of Affective Disorders**

Major affective disorders
Code depressed episode in fifth digit: 6 = in remission, 4 = with psychotic features (the non-ICD-9-CM fifth digit 7 may be used to indicate that the psychotic features are mood-incongruent), 3 = with melancholia, 2 = without melancholia, 0 = unspecified.

Code manic episode in fifth digit: 6 = in remission, 4 = with psychotic features (the non-ICD-9-CM fifth digit 7 may be used to indicate that the psychotic features are mood-incongruent), 2 = without psychotic features, 0 = unspecified.

Bipolar disorder
296.6x mixed, _____
296.4x manic, _____
296.5x depressed, _____

Major depression
296.2x single episode, _____
296.3x recurrent, _____

Other specific affective disorders
301.13 Cyclothymic disorder
300.40 Dysthymic disorder (Depressive neurosis)

Atypical affective disorders
296.70 Atypical bipolar disorder
296.82 Atypical depression

* From American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, ed. 3. American Psychiatric Association, Washington, D.C., 1980.

been developed, research has yet to clarify fully the nature and the causes of that complex group of disorders.

Within the past 3 decades, there has been a noticeable increase in the attention given to depression and other affective disorders. That attention has been increasing among both mental health professionals and the public, especially in North American and Western Europe. The shifts in professional attention and public interest possibly reflect a historical trend, the emergence of a new age of melancholia, in contrast to the age of anxiety that followed World War II. Precipitated in part by recent adverse global events and consequent doomsday prophecies concerning nuclear warfare, overpopulation, and ecological destruction, public attention to and acknowledgment of depressions and other affective states have increased during the 1970's. Coverage of mental illness by the mass media has reduced the stigma attached to depression, and a number of political leaders, astronauts, and figures in the arts and entertainment fields have publicly acknowledged that they have suffered from depression.

There have been other ages of melancholia in Western society. Robert Burton (1927) described the widespread despair of 17th century England in his classic, *The Anatomy of Melancholy*. The poets, novelists, and philosophers of the romantic movement documented the *weltschmertz* of the early 19th century. In the post-Civil War period, the American physician George M. Beard (1880) described neurasthenia as prevalent in America, calling that malaise the "most frequent, most interesting, and most neglected nervous disease" of modern times.

The current age of melancholia seems to be generated not so much by absolute levels of human misery as by the relative gap between rising hopes and the actual fulfillment of expectations. The earth's resources are limited, the human population is expanding uncontrollably, and recent sociopolitical movements have proved themselves incapable of creating the utopian futures promised by their ideologies. Those historical changes seem to be associated with an apparent increase in the incidence of affective disorders, particularly depression, manifested by a rise in suicide attempts and by increased numbers of patients seeking medical-psychiatric help for symptoms of depression.

Those changes in the epidemiology of affective disorders have coincided with the development of new treatments, enhanced professional confidence, and new theoretical and research approaches. Impressive progress has been made in the quality and the quantity of research, both in clinical disciplines and in the laboratory sciences. Animal studies, particularly those involving primates, have established the validity of behavioral models related to separation and loss, which provide a long-needed bridge between clinical observation and experimental psychology. The most dramatic advance has been the success of drug therapy. The neuroleptics, the tricyclic antidepressants, the monoamine oxidase inhibitors, and lithium have entered the psychiatrist's armamentarium. Also, there are new forms of psychotherapy—interpersonal, group, family, behavioral, and cognitive. When a field develops new therapeutic technology, a phase of optimism and intellectual activity is often initiated. That seems to be true today in the area of depression and the affective disorders. The efficacy of the new treatments has greatly improved the prognosis of patients with affective disorders and has contributed to the rapid expansion of the scope, diversity, and availability of community-based mental health services, both private and public, in North America and Western Europe.

Scope of Affective Disorders

Epidemiological studies of affective disorders—hindered by problems of diagnosis, classification, and methodology (Turns, 1978)—have yielded varying estimates of prevalence and incidence. However, it is recognized that affective disorders, particularly depression, are the most common type of mental disorders among adults.

Epidemiological studies in Scandinavia (Essen-Möller and Hagnell, 1961; Hagnell, 1966), the United Kingdom (Brown et al., 1975), New Haven (Weissman and Myers, 1978), and New York (Srole et al., 1962) indicated that perhaps 15 to 30 per cent of adults experience clinical depressive episodes, often of moderate severity, at some point in their lives. However, only 25 per cent of persons with depressive symptoms seek mental health professional attention. Most depressives are in the general health care system, often misdiagnosed and inappropriately treated. Thus, a vast reservoir of clinically distressed persons exists, but—because of inability to gain access to treatment, financial disadvantage, stigma and shame, or other reasons—most of them do not receive psychiatric treatment for their depression. That group poses a challenge to the mental health professions and an opportunity for clinical psychiatry.

Depression as a Normal Human Emotion

Although the major focus of this chapter is on the affective disorders as clinical conditions, an understanding of their psychopathology and treatment is greatly enhanced by viewing the clinical states within the range of human experience and behavior. Depression serves as a useful illustration, since it refers to a normal human emotion, to a clinical symptom, and to a group of syndromes or disorders.

Before those aspects of depression are reviewed in detail, it is important to identify a major source of confusion that arises because the term "depression" has different meanings in various scientific fields, such as neurophysiology, pharmacology, psychology, and psychiatry. For the neurophysiologist, depression refers to any decrease in electrophysiological activity—for example, cortical depression. For the pharmacologist, depression refers to the effect of drugs that decrease the activity of

the target organ. Thus, the central nervous system depressants include drugs, such as the barbiturates and the anesthetics, that decrease responsiveness to stimuli by producing sleep or coma. For the psychologist, depression refers to any decrement in optimal cognitive, perceptual, or motor performance. For the clinical psychiatrist, however, depression covers a wide range of changes in emotional states, ranging in severity from the normal mood fluctuations of everyday life to severe psychotic episodes.

The use of the term "depression" in a number of scientific fields has tended to lend support to the view or, perhaps more accurately, the wish that common mechanisms underlie the neurophysiological, pharmacological, psychological, and clinical phenomena. As a result, many clinicians and investigators have postulated that clinical depressive symptoms are the result of a reduction of some generalized or specific central nervous system function and, therefore, are treated best with a drug that has a countereffect—that is, a stimulant drug. That view, the stimulant-depressant continuum, had been the classic model for the neuropharmacology and pathophysiology of affective states (Klerman, 1966). In that model, clinical states were ordered on the continuum according to the polarity and the intensity of the alterations in psychomotor activity—for example, manic excitements are presumably due to excessive central nervous system excitation. The therapy also made use of the stimulant-depressant classification of drugs that was accepted before 1952, when the amphetamines and the barbiturates were the major central nervous system drugs. The early version of the catecholamine hypothesis implied a similar concept, postulating that excessive catecholamines would produce mania and that deficient catecholamines would produce depression. The complexity of actions of the new psychotropic agents—particularly the phenothiazines, the tricyclic antidepressants, and lithium—makes the traditional stimulant-depressant continuum obsolete and overly simplistic. Similar concepts of a bipolar continuum of emotional states were correlated with Pavlovian conditioning theory (Eysenck, 1961) and psychoanalytic libido theory (Ostow, 1962). Until the new theories of the psychobiology of affective disorders are validated, the term "depression" is best restricted to emotional phenomena without presumption of any underlying causation, whether located in the central nervous system or in the psyche.

As a mood, affect, feeling state, or emotion—those terms are used interchangeably for the purposes of this section—depression is a pervasive feature of normal human experience. Feelings of sadness, disappointment, frustration, discouragement, and related emotions are frequent concomitants of the vicissitudes of the human condition.

The normality of depression poses multiple problems for clinical practice and theory. For clinical practice, criteria are needed to specify the boundaries between the normal mood state and those abnormal states that merit clinical intervention. For theory, it is necessary to understand the nature and the function of depression as a normal emotion and to elucidate which aspects of depression are common to both normal and pathological states, as distinguished from those features that are unique to the abnormal states.

The most important insights concerning normal depressive affect derive from the ideas of Darwin, particularly those related to adaptation. According to the strictest criterion of evolutionary theory, a trait or behavior is adaptive from the phylogenetic viewpoint if it promotes the survival of the species. Moreover, from the ontogenetic view, a trait is adaptive if it promotes the growth and survival of the individual members of the species. Darwin himself pioneered in the application of the evolutionary approach to behavior and, especially, to emotional responses. Darwin's theory of evolution postulated that there exists an evolution not only of morphological structures but also of mental and expressive capacities. Darwin (1965) collected material to document the phylogenetic continuity of emotional expressions in animals, particularly in primates and human beings, but most of his observations and theory lay dormant for many decades. Since World War II, however, there has been a remarkable upsurge of interest in the comparative biology of emotional states. From studies of mammalian behavior, specifically of mother-child development in primates, a significant convergence of findings from neurobiology, ethology, and comparative psychology has emerged.

At the same time, studies of human infant development, particularly those studies using psychodynamic theory, have paralleled the animal researches. Bowlby (1969) and others have demonstrated that the genesis of emotion in the child is related to the vicissitudes of the child's attachment bond to mothering figures. Because of their prolonged state of dependence, human infants are highly vulnerable to the effects of separation and subsequent feelings of helplessness. The infant's depressive behaviors serve to alert the social group, usually the family, to his or her need for nurturing, assistance, and succor.

That generalization is true for the child, but what of the adult living in a modern industrial society? Is civilized man's or woman's depression merely the automatic perpetuation of previously developed evolutionary responses? If so, is the clinical depression of adults an adaptive response, or is it a maladaptive recurrence of behaviors adaptive in an earlier developmental state? The investigations into those questions involve clinical and biological research and theoretical analysis.

An adaptational approach, which this section proposes, examines possible functions of emotions, particularly depression. It inquires into the neuroanatomical structures and neurochemical mechanisms by which natural selection, genetic mutation, environmental conditioning, and social learning mediate the impact of environmental change and initiate, organize, integrate, and terminate the emotional, metabolic, and goal-directed activities of the organism, both in its normal depressive moods and in clinical depressive states.

The field studies of ethologists, the experimental studies of comparative psychologists, and clinical studies with children have yielded convergent findings that form a crucial basis for an adaptational approach (Harlow, 1959; Bowlby, 1969). When the mammal mother-infant bond is broken by separation or loss, typical behavioral patterns emerge. The initial pattern is characterized by anxiety, agitation, and protest. That pattern is followed by withdrawal, decreased social participation, and decreased motor activity. Intensive psychological studies have convinced most observers that those characteristics of animal depression are similar if not identical with normal emotional states in humans (Akiskal and McKinney, 1973). Those animal reactions to separation and loss are so similar to human sadness that few observers now doubt the essential continuity between animal and human infant experiences (Kaufman and Rosenbaum, 1967).

Thus, depression as an emotion in primates and in human beings serves a signal function. It alerts the mother or other members of the social group that one of its helpless members, the infant, is in potential danger. That is especially true during the phase of rapid central nervous system maturation and during the acquisition of cognitive, perceptual, motor, and social skills. Alerted protectors can rally resources for nurtur-

ance, support, and protection and thus promote biological survival.

ADAPTIVE FUNCTIONS

This brief discussion of the significance of separation and loss in animals and infants allows the delineation of some general aspects of the adaptive role of affects. From an adaptational view, affects can be regarded as having multiple psychobiological functions. Four adaptive functions of affects are relevant to clinical psychiatry: social communication, physiological arousal, subjective awareness, and psychodynamic defense.

Social communication. The adaptive role of depressive emotion as social communication has been elucidated by animal studies, especially in primates (Kaufman and Rosenbaum, 1967; Harlow et al., 1971; Suomi et al., 1978), and by studies of human infancy (Bowlby, 1969). The components of affective communication—crying, facial expression, posture, touch, smell—have been studied clinically and experimentally.

It is now widely accepted that all mammals inherit complex behavioral systems that promote the mother-infant attachment and facilitate the formation of other social bonds. The importance of those bonds is increased among primates, for whom the period of extrauterine growth and development is prolonged. The helplessness and the dependence of the infant primate promote those bonds and provide the opportunity for social communication, learning, and group interactions. The development of those behavioral systems has been profoundly adaptive for the species and for the individual; those systems facilitate the biological survival of infants during the long period of extrauterine development before biological self-sufficiency is achieved. Moreover, those systems encourage social learning, which is highly significant from an evolutionary standpoint. Mammals, unlike lower species, learn responses that enable them to react appropriately and adaptively to changes produced by the environment.

Perhaps of greatest significance for understanding the adult clinical depressions is the development of animal models of depression based on the separation-loss paradigm (Kaufman and Rosenbaum, 1967; Harlow et al., 1971; Suomi et al., 1978). Until recently, the nearest approximation of animal models was the amine-depleted animal induced by drugs, such as reserpine and benzoquinoline derivatives (Klerman, 1971). That model proved useful for screening new antidepressant drugs and for the investigation of the neuropharmacological actions related to biogenic amines, but it was deficient as a behavioral model. The new models, based on the separation-loss paradigm, have behavioral validity. Not only have those animal experiments replicated the clinical syndrome of anaclitic depression observed in human infants, but they have provided means of testing hypotheses about subsequent behavioral, cognitive, and social consequences of early separations—experiments that have high relevance for verifying many clinical theories relating the vulnerability of certain adults to affective disorders to their experiences in infancy and childhood.

Physiological arousal. Clinical observation and animal experimentation have established the relation of separation-loss to infant depressive affect and have clarified the role of depressive affect as a social signal. Problems arise in specifying the neuroanatomical, electrophysiological, and neurochemical mechanisms by which those affective states are initiated, perpetuated, and terminated.

Parallel problems have been investigated for anxiety-fear, an affect closely related clinically and developmentally to depression. Following on the research of Cannon (1936), scientists accept the hypothesis that anxiety-fear arouses the organism in preparation for fight or flight. That function is carried out by complex neuroendocrine systems, especially those involving hypothalamic and adrenergic structures and the release of epinephrine.

When one attempts a similar description of the mechanisms involved in depression, less agreement is evident. Impressive research, mostly based on advances in psychopharmacology, strongly implicates the central nervous system biogenic amines and neuroendocrine systems in those reactions. Although the evidence derives more from neuropharmacological studies than from direct observations in humans, the patterns and trends increasingly support a role for biogenic amines in the mediation of affective responses, especially depression (Kety and Schildkraut, 1967; Usdin et al., 1977; Barchas et al., 1978; Schildkraut, 1978).

Another hypothesis defining the physiological adaptive function of depression was offered by Engel (1962) and Schmale (1973) and their associates. They postulated that the depression involves conservation-withdrawal, with reduced psychomotor activity (Frank, 1954). That is an intriguing hypothesis for which experimental verification is required. Although the formulation may be consistent with observations of infantile states, the clinical depression in adults is associated with increased adrenal-cortical activity and with anxiety and tension, presumably due to heightened adrenergic activity—changes inconsistent with the conservation-withdrawal formulation. One explanation for the discrepancy is to assume that the clinical depressions of adults involve a failure of mechanisms operative in normal and infantile states. Also, different psychobiological changes probably distinguish the protest phase from the despair phase after loss and separation; the increased sympathetic and neuroendocrine activity is probably related to the protest phase, and the conservative-withdrawal processes come into operation later, in the despair phase (Akiskal and McKinney, 1973).

Subjective awareness. The subjective aspect of affect has been emphasized by most clinical research and theory and is probably unique to human experience. The subjective function of affect has been controversial, particularly since the James-Lange theory proposed that conscious awareness follows the physiological reaction (Tyrer, 1973). Accordingly, the conscious awareness of the affective states is regulated by epiphenomena; that is, it arises primarily from visceral and skeletal muscular sensations. The James-Lange theory contradicts the commonly held view that psychological processes initiate physiological change. Thus, there is a debate over the sequence of events relating stimulus, perception, subjective awareness of feeling, and the psychophysiological changes, whether central or peripheral.

Whatever the ultimate outcome of that controversy, it is widely if not universally accepted that the subjective components of human emotion, whether epiphenomenal or real, conscious or unconscious, play important functions in goal setting and in the monitoring of current behavior, particularly by judging personal reality against internalized values and goals. Engel (1962) stated:

> Intrapsychically, affects provide information concerning the status of the self per se and of the self in relation to objects, and they indicate the level of drive tensions. In the adult, such intrapsychic activities are ego functions having motivational and warning properties. As signals, affects anticipate, on the basis of past experience, intrapsychic changes,

thereby permitting the ego to initiate psychic processes or behavior to maintain the psychic balance.

There is a growing convergence of, on the one hand, social-psychological studies that have explored fluctuations in self-esteem, self-image, aspirations, and interpersonal relations and, on the other hand, behavioral approaches that search for sources of reinforcement in the real-life social world of normal persons related to their mood fluctuations. Beck (1969) described cognitive dysfunctions in depressed patients, particularly their impaired capacity to judge themselves and their performances realistically, and from those observations proposed a cognitive psychotherapy of depression. The capacity of human beings to relate affective awareness to associated ideas and cognitive representations serves important self-regulating functions in maintaining self-esteem and in setting and modifying goals. That capacity depends on the species' achievement of language and rational thought, evolutionary attainments of great significance.

Psychodynamic defenses. The fourth adaptive function of depression, intrapsychic defense, is the one most discussed in clinical practice, especially by those influenced by psychoanalytic approaches; nevertheless, it represents an area of continuing debate.

Originally, Freud viewed emotions as archaic discharge syndromes. In addition to drive discharge, the specifically psychodynamic functions of affect include the initiation of defense mechanisms. After Freud's writing about anxiety in the mid-1920's, psychodynamic theorists emphasized the defensive functions of affects in the studies of ego psychology. Freud maintained a strong biological view that derived human emotional capacities from instinctual drives. He also emphasized the continuity between adult behavior and infant behavior. Thus, psychodynamic theory stimulated interest in the developmental aspects of emotions, particularly in the possible role of early childhood experiences as determinants of adult psychopathology. Psychodynamic thinking also stressed the important and perhaps crucial role of emotional experience not directly within the conscious awareness of the self but potentially recoverable by reconstruction, free association, dreams, projective tests, or hypnosis.

Although psychodynamic theory has reinterpreted its formulations regarding anxiety to incorporate Cannon's (1936) discovery of adrenergic mechanisms and Freud's concept stated in *Inhibitions, Symptoms and Anxiety* (1926) that anxiety serves as a signal to initiate ego defenses, similar formulations of depression have been slow to appear. Ego psychology approaches (Hartmann, 1958) have only recently been applied in depression (Bibring, 1953; Rapaport, 1967).

A major obstacle in developing a comprehensive ego-adaptive view of depression arises from the postulate that hostility is primary to depression. Until recently, dominant clinical teaching stressed that depression is hostility turned against itself. In many clinical settings that oversimplification became the practical distillate of the classic psychodynamic theory of depression initially proposed by Abraham (1927) and Freud during the period of 1908 to 1921. In the classical view, the clinical features of adult depression result from retroflexion onto the self of the hostility directed at the lost object. Through incorporation, the self identifies with the lost object. The self is defended against the trauma of loss and, thus, avoids its psychic consequences. In depression, predisposition to that mechanism is postulated to have been determined by libidinal fixations in the late oral or early anal stages of development. Crucial to that formulation is the central role given to aggressive drives aroused by the ambivalence and dependence characteristic of the depressed person in his or her interpersonal and object relations (Rado, 1929; Cohen et al., 1954).

Freud used a transformation or alchemy explanation for three clinical phenomena: conversion hysteria, anxiety, and depression. Freud's earliest conception of the conversion mechanism in hysteria, developed about 1895, postulated that, in the process of symptom formation, psychic energy that was not discharged was converted into a physical symptom of a hysterical nature, such as paralysis of limb or loss of vision. Freud proposed a similar transformation explanation of anxiety in his early toxicological theory; for many years he held that anxiety neurosis was one of the actual neuroses, arising from biological causes, rather than a psychoneurosis, arising from conflict. His initial formulation was that anxiety was the psychological manifestation of undischarged sexual libido, and not until 1923 did he formulate his signal theory of anxiety, in which he designated the role of anxiety as the initiator of defense processes. Freud's concept of depression as the transformation (retroflexion) of aggressive drives deriving from oral fixations persists into the present time as the dominant view in many clinical settings.

As Bibring (1953), Rapaport (1967), and Chodoff (1970) elucidated, the classical theory derives from an exclusively instinctual view of the genesis of emotions and from insufficient attention to modern views of ego functions. The classic theory of depression fails to classify depression as a primary affective disorder in its own right but, rather, relegates depression to a transmutation or transformation of another affect, hostility.

In recent years, numerous studies have directly investigated the relation between depression and hostility (Gershon et al., 1968; Klerman and Gershon, 1970; Weissman et al., 1971). The findings from those empirical studies have confirmed the independence of depression from hostility. The data show alternative patterns; both high and low intensities of manifest hostility occur, depending on the patient's personality patterns and the nature of his or her social relations. Those research projects support the desirability of rejecting the hostility-turned-against-itself mechanisms as universally necessary and primary in the pathogenesis of depression. The findings support the hypothesis that depression is a primary ego state that serves important ego-adaptive functions. That view places the psychodynamic aspects of depression closer to other approaches.

DEPRESSION AND NORMAL ADAPTATION

Viewed in the framework of biological adaptation, the capacity of human beings to react to environmental changes, especially separation and loss, is the outcome of mammalian and primate evolutionary changes. As a consequence of millions of years of evolutionary development, complex neurobiological structures and behavioral mechanisms emerged. That capacity has been profoundly adaptive for human infants, even to this day.

In adult human experience, however, the contingencies that initiate, perpetrate, and terminate depression are less evident. Overt loss and separation are one category of larger groups of life event stimuli that include economic, social, and interpersonal changes. Many attempts have been made to develop a unified, all-encompassing theory, and various theorists have focused on factors such as symbolic loss, life stress, self-esteem, helplessness and hopelessness, social role change, and reward and reinforcement. No comprehensive solution has yet emerged, but the nature of the convergences is apparent.

The Clinical States

Moving from a discussion of normal affects to clinical states requires careful consideration of the boundary issues attendant to distinguishing normal mood fluctuations from clinical psychopathological conditions meriting therapeutic attention.

DISTINGUISHING NORMAL MOOD FROM CLINICAL PSYCHOPATHOLOGY

Feelings of sadness, disappointment, and frustration are normal accompaniments of the human condition. Because clinicians and investigators do not fully agree as to the complete range of affective disorders to be diagnosed as psychopathological, the boundary between normal mood and abnormal depressions remains undefined. That situation has far-reaching consequences. In clinical practice, there are often inconsistencies in referrals and marked variations in decisions as to treatment, whether psychotherapeutic or psychopharmacological. Without validated diagnostic criteria, case finding is highly variable; epidemiological surveys are inconclusive or ungeneralizable; and it is difficult, if not impossible, to calculate accurate estimates of incidence, prevalence, and other basic rates.

The symptoms of affective disorders involve accentuations of the intensity or the duration of otherwise normal emotions. Because almost all human beings experience unhappy, sad, depressed, and discouraged states, patients' distress readily gains the empathic understanding of clinicians and family members. That very familiarity sometimes renders clinical assessment and differential diagnosis difficult. Familiarity obscures the boundary between normality and abnormality; often, family and friends tend to minimize the severity of the patient's difficulties because the manifestations are similar to the normal emotional state.

In severe forms, most affective states are readily recognized as pathological, even by laymen, by virtue of their intensity, pervasiveness, persistence, and interference with usual social and physiological functioning. The difficult problems arise in recognizing and diagnosing the mild forms. A number of features distinguish clinically ill patients from those with normal mood. In addition to disturbances of mood, the psychopathological state involves a combination of the following features: (1) impairments of body functioning, indicated by disturbances in sleep, appetite, sexual interest, and autonomic nervous system and gastrointestinal activity; (2) reduced desire and ability to perform the usual, expected social roles in the family, at work, in marriage, or in school; (3) suicidal thoughts or acts; and (4) disturbances in reality testing, manifested in delusions, hallucinations, or confusion.

An incompletely defined gradient of intensity exists between normal mood and the pathological states, but the clear demarcation has not been fully delineated. In recent years, much psychometric research has been conducted on rating scales used in diagnosing depression. Normative data have been collected for a number of standard scales—particularly the Beck (1969), Zung (1965), and Hamilton (1960) scales—so that it is now possible to identify cut-off points that distinguish the normal mood from clinical states. However, recent data from epidemiological studies (Weissman and Myers, 1978) indicate that, although many persons in the community are distressed by depressive symptoms, not all meet the criteria for affective disorders defined by the Research Diagnostic Criteria (Spitzer et al., 1978).

The presence or absence of an overt stress (precipitating life event) poses multiple dilemmas. Psychiatrists tend to think they understand emotional fluctuations occurring in relation to the precipitating event. Often, they tend to minimize the severity of depressive reactions when the life stress seems apparent, and it is desirable for the classification of clinical states to be derived independently of environmental circumstances. Whatever the duration, intensity, or presence of precipitating events, the existence of certain characteristic features—such as hallucinations, delusions, marked weight loss, and suicidal trends—indicate, according to almost all observers, that the boundary between normal and pathological has been passed and that the patient is into the range of psychopathology.

The desirability of operational definitions for the diagnostic criteria is now accepted. The diagnostic summaries that appear in textbooks and in the official nomenclature give only general guides. The most common clinical practice has been to list the number of symptoms in various categories, one or more of which may be necessary for the diagnosis. That practice embodies a Chinese-restaurant-menu approach to diagnosis. To qualify for a certain diagnosis, the patient must have a number of symptoms in each of the categories A, B, and C. That form of clinical thinking implies a necessary-and-sufficient model, with emphasis on salient symptoms derived from the clinician's experience with ideal cases. Attempts to put the necessary-and-sufficient model into operation have been developed recently. To meet the diagnosis, the patient must display symptoms that have been operationally defined and categorized, and exclusion criteria are also elaborated (Feighner et al., 1972; Spitzer et al., 1978). The application of that model to the affective disorders is embodied in DSM-III.

The necessary-and-sufficient approach, although appealing to the clinician because of its logical simplicity, has been criticized for its lack of quantitative sophistication and for its emphasis on pure forms that may be relatively infrequent. An alternative approach has used multivariate statistical methods to generate scales. Factor analysis and multiple regression have been widely used. Those techniques have been applied to the depression scales developed by Hamilton (1960), Beck (1969), Zung (1965), Raskin et al. (1970), and J. R. Wittenborn (unpublished data, 1968). Similar approaches were used in developing the D Scale of the Minnesota Multiphasic Personality Inventory (MMPI). Attempts are now underway to determine scale points characteristic of normal and depressed outpatients and hospitalized patients. That approach aims to generate scales similar to the thermometer, by which gradations of clinical severity are related to specified scale values.

A related approach derives from naturalistic studies of normal states. Prominent in that area are the excellent studies of normal mourning among widows (Parkes, 1970; Clayton et al., 1972). Those studies offer the promise of delineating the duration and the intensity of grief. In concert with the grief studies, observations of normal persons derived from systematic population surveys indicate that, although mood complaints are common, clinical states are characterized not only by mood disturbance but by associated vegetative and bodily dysfunctions and by persistent and pervasive impairments in usual social performance (Katz, 1970; Weissman et al., 1972).

Whatever the outcome of those research efforts, one can expect further use of more accurate, operationally defined criteria for diagnosis and more precise formulations of the boundaries between normal and clinical depression. Although the research has progressed rapidly to the point at which scale norms are now available for many scales and those norms are useful for research studies, they have not yet been sufficiently

validated and used to be recommended for routine clinical practice.

DEPRESSION AND MANIA AS SYMPTOMS

Depression and mania can occur as symptoms; depressive symptoms are seen more often than are manic symptoms. The symptoms seldom occur alone; usually, they are associated with bodily complaints or psychological and social impairment. Epidemiological studies using survey questions or symptom scales have found such symptoms widespread in the general population. Usually, the symptoms are mild to moderate in intensity and transient in duration, thus not meeting the criteria for a clinical disorder as specified in the Research Diagnostic Criteria or the DSM-III (Weissman and Myers, 1978).

Depressive symptoms may occur as reactions to stressful personal experience, such as in grief and bereavement, or in response to adverse social and economic circumstances, as in poverty and racial or ethnic discrimination, or as part of a reaction to medical and surgical illnesses. In those contexts, psychiatric intervention may be useful, although systematic clinical trials have not been undertaken. The concept elaborated here—that some patients with depressive symptoms are worthy of clinical attention, even though their psychopathological features do not meet the diagnostic criteria for a full syndrome—merits further research and clinical experience before specific diagnostic and therapeutic recommendations can be proposed.

PRIMARY AND SECONDARY AFFECTIVE DISORDERS

Having established that a patient's affective disturbance represents a clinical state, rather than being within the range of normal mood, the clinician is faced with issues of nosology and classification. Since affective symptoms can occur in association with many other psychiatric and medical illnesses, confusion has been evident as to the status of those affective conditions.

Robins and Guze (1972) proposed a distinction between primary and secondary affective disorders based on two criteria, chronology and the presence of associated illnesses. Primary affective disorders are the disorders in patients who have been well or whose only previous episodes of psychiatric disease were mania or depression. Secondary affective disorders occur in mentally ill persons who have had another psychiatric illness (Robins et al., 1972) or physical illness. The diagnosis is made regardless of the presence or absence of an apparent life stress, thus avoiding the knotty problems of the endogenous-reactive distinction and of severity and, therefore, avoiding the issue of psychosis (see Figure 1).

Clinical criteria that use specified symptom sets now exist for depression and for bipolar disorders. The mood symptom is one component of the syndrome, various signs or symptoms occurring in association with each other.

The nosological approach using the primary-secondary distinction operates within the traditional medical model. Depression and other affective disorders are regarded as heterogeneous clinical phenomena—like anemia, arthritis, edema, jaundice, and heart failure—not as an etiological classification. That nosological approach attempts to separate out depression and bipolar disorder that occur in the presence of disorders with known causation and then to define a residual category of primary affective disorders as a subject for more intensive investigation.

Affective disorders associated with other psychiatric disorders. Although the primary-secondary distinction is conceptually clear-cut, a number of practical problems arise in differentiating depression that occurs in association with other clinical psychiatric states. In clinical practice, the problem arises in schizophrenic and schizoaffective disorders, anxiety states, alcohol dependence, and personality disorders.

Affective disorders associated with medical diseases. Although Robins and Guze (1972) did not include medical conditions and drugs as secondary depressions, it seems logically consistent and theoretically relevant to extend the concept of secondary affective disorders to include those states.

The recognition that affective symptoms and disorders occur secondary to systemic disease, drug reactions, and central nervous system states has practical and theoretical significance. Practically, the clinician is always troubled about misdiagnosing depressions that may be associated with tumors or endocrine disorders, especially when appropriate and effective treatment of the primary medical disorder is available. Similar considerations apply to secondary mania. Moreover, the secondary affective disorders often pose difficult therapeutic problems because of the possible interactions between psychotropic drugs and medications that may be used for the systemic disease.

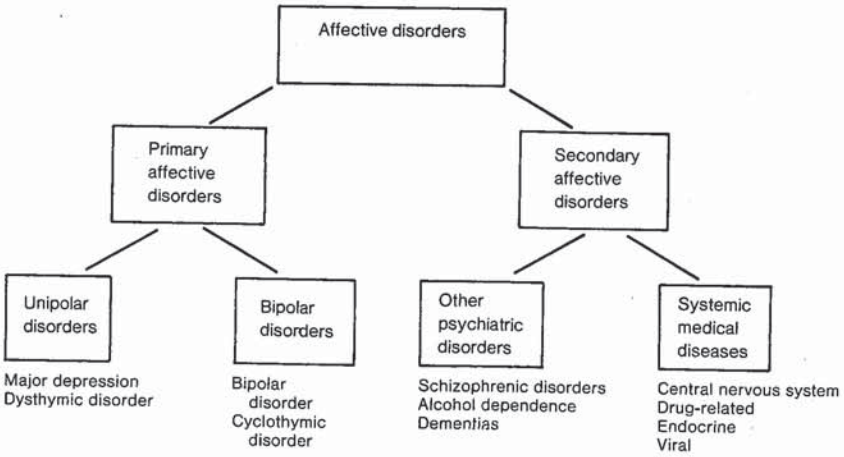

FIGURE 1. Suggested nosology of affective disorders. (Adapted from Klerman, G. L. Affective disorders. In *The Harvard Guide to Modern Psychiatry*, A. M. Nicholi, editor, p. 253. Harvard University Press, Cambridge, Mass., 1978.)

Drug-induced depressions constitute another large group of secondary depressions that have many similarities to primary affective disorders. The most significant group of patients are the hypertensives who became depressed when treated with reserpine. Similar reactions have occurred with other antihypertensive drugs, such as methyldopa (Aldomet). Rebound-depressive reactions may follow the abuse of amphetamine or other addictive substances, such as the barbiturates.

Depression may also occur secondary to a wide variety of medical illnesses—for example, viral infections, nutritional deficiencies, endocrine disorders, anemias, such central nervous system disorders as multiple sclerosis, tumors, and cerebral vascular disease. The depressions of the elderly are particularly complex because the differential diagnosis often involves organic brain damage and clinical depression. The diagnostic differentiation is complicated by the fact that persons with early signs of senile brain changes, vascular disease, or other neurological diseases associated with age may be more at risk for depressions than is the general population. In the United States there has been a tendency to overdiagnose arteriosclerosis and senility in persons over 65, without recognizing that depression may manifest itself by a slowing of psychomotor activity, a reduction of intellectual functioning, a decrease in concentrating ability, and a loss of interest in sex, hobbies, and activities—changes that may be taken as signs of brain damage.

Theoretically, those secondary depressions are of tremendous research significance, for clinical depression has been the subject of controversy and inconsistent clinical and research findings. Secondary depressions often involve endocrine disorders and an interrelationship between thyroid, adrenal, and gonadic hormones. The systematic investigation of those secondary depressions may help elucidate the role of the endocrine organs and their humoral substances. The hypertensive patients who become depressed with reserpine provide an important stimulus to the development of the catecholamine hypothesis, and similar insights will probably emerge from intensive clinical and pathophysiological studies of those secondary depressions.

Secondary mania. A similar approach has been applied recently to mania. The majority of manic disorders usually occur as a phase of bipolar disorder and can be considered primary. However, some mania occurs secondary to other conditions—medical and pharmacological—in patients with no history of affective disorder, and they should also be considered secondary. In a review of the literature, Krauthammer and Klerman (1978) found that mania occurs secondary to drugs, infections, neoplasms, epilepsy, and metabolic disturbances. The evidence that mania can result from a variety of pharmacological, structural, and metabolic disturbances suggests that mania, like depression, is a clinical syndrome with multiple causes. The diversity of causes probably involves more than one pathophysiological pathway and challenges any unitary model of causation, whether the proposed factor of causation be biochemical, psychological, genetic, or structural.

Nosology of Affective Disorders

In clinical experience the majority of affective disorders do not occur in clear association with other medical or psychiatric disorders, and it is on the primary affective disorders that the greatest attention is focused in both research and clinical practice.

Not all patients have all the classic affective symptoms; on the other hand, although there is much individual variability, the variations are not infinite—hence the need for categorization and classification to find regularities in the presence of variation (Klerman and Barrett, 1973). For example, in practice, depressed patients present with multiple symptoms, including the abnormal and persisting affective changes associated with feelings of worthlessness, guilt, helplessness and hopelessness, anxiety, crying, suicidal tendencies, loss of interest in work and other activities, impaired capacity to perform everyday social functions, and hypochondriasis, accompanied by such physical alterations as anorexia, weight change, constipation, psychomotor retardation or agitation, headache, and other bodily complaints. Even to the untrained observer, most depressive states are clearly seen as pathological by virtue of their intensity, pervasiveness, persistence, and interference with normal social and physiological functioning. Awareness of that variability has contributed to the current concern for diagnosis and classification (Kendell, 1976). That concern has relevance for theory and research and for clinical diagnosis and therapy. The traditional psychotic-neurotic distinction and endogenous-reactive continuum have been critically reexamined, and a new classificatory schema has evolved, the primary-secondary division proposed by Robins and Guze (1972). The unipolar-bipolar dichotomy, first described by Leonhard et al. (1962) and subsequently developed by Perris (1966) in Scandinavia, Winokur in the United States (Winokur et al., 1969), and Angst (1966) in Switzerland, is continually being refined. Those new systems attempt to resolve the confusions emanating from the manic-depressive classification described initially by Kraepelin (1921), modified shortly thereafter by Bleuler (1951), and further elaborated on by various researchers over the past 75 years.

After Kraepelin's (1921) delineation of manic-depressive insanity as a diagnostic entity, debates arose over the breadth of the concept; additional diagnostic labels, such as psychoneurotic-depressive reaction and involutional melancholia, were included in textbooks, official governmental classifications, and semiofficial professional nosologies. The debates were partially resolved by the creation by Bleuler (1951) of the general grouping called affective disorders. That particular grouping has had many advantages. It allowed for multiple subcategories, with possibly differing causes; it offered more theoretical flexibility than the manic-depressive entity; and it emphasized affect as a normal human faculty, thus not restricting the scope of psychiatrists' attention to insanity and other psychotic phenomena. However, many unresolved issues remain as to the scope of the affective disorders and the principles on which subcategories are to be delineated and validated.

Kraepelin's textbooks attempted a causal basis for the classification of mental disorders. Based on the 19th-century medical illness model, disease entities were delineated by the methods of syndromal description and then correlated with pathology, histology, bacteriology, and natural history. Applied to mental illnesses, those approaches proved successful, especially for the infectious disorders, such as general paresis caused by central nervous system syphilis, and for nutritional disease like pellagra. Early in the 20th century, however, doubts arose about the adequacy of the approach for the group of functional disorders, those psychiatric syndromes for which no apparent structural or organic pathology could be demonstrated by the then-available methods.

Among the functional disorders, the affective disorders in particular generated continued controversy. Kraepelin's concept of manic-depressive illness brought together a large number of clinical states—including mania, melancholia, and cyclic psychoses—and clarified many issues to create a brief period of unity. During the middle decades of the 20th century, however, the apparent unity achieved by Kraepelin's manic-depressive illness concept gave way to the proliferation of multiple new categories.

The endogenous-reactive and the neurotic-psychotic distinctions were proposed as new subcategories. Debates arose over the validity of the vaguely defined psychotic depressive reaction. To add to the controversies, Kasanin's (1933) description of the schizoaffective psychoses created a nosological bridge between schizophrenia and the manic-depressive disorders. In the 1940's and 1950's borderline states and pseudoneurotic schizophrenia were described for patients in whom depression and other mood swings were prominent, creating yet another bridge between psychotic states and neurotic reactions—in that instance, between schizophrenia and depression.

In retrospect, the confusion was the consequence of multiple factors. As psychiatric services expanded outside the mental institutions and into general hospitals, outpatient clinics, social agencies, and private practice, increasing numbers of nonpsychotic and noninstitutionalized patients came to the attention of psychiatrists. Today, the preponderance of patients with affective disorders are neither hospitalized nor psychotic, and they manifest behaviors and symptom patterns differing in many respects from the classic syndromes formulated in the late 19th century.

Today, patients with affective symptoms deviate markedly from expectations derived from the descriptions of classic manic-depressive illness. That trend is clearly evident in the increase in the frequency of the nonpsychotic forms of depressions, variously called over the years neurotic depression, depressive characters, personality disorders with depression, and mixed anxiety-depression states. Similar deviations are also recognizable in the manic states, particularly those without psychotic features, which may not reach the attention of psychiatrists because they are pleasurable, ego-syntonic, and socially adaptive for the patient. The characteristics of persons with those manias merge gradually with those having cyclothymic disorder, whose mood swings may cause them and their families minor distress but who are usually not so socially disruptive as to require hospitalization. Today, however, their behavior may be considered suitable for treatment with lithium. Thus, any contemporary classification system must be broad enough to encompass the wide range of ambulatory, personally distressed, yet socially functioning forms of affective disorders.

Not all the new nosological proposals have yet been incorporated into the official diagnostic nomenclatures of the World Health Organization (WHO), the ninth revision of the *International Classification of Diseases* (ICD-9-CM), or DSM-III. As further research on the reliability and the validity of diagnosis progresses, the findings will certainly influence future official classifications—DSM-IV and ICD-10.

BIPOLAR-UNIPOLAR DISTINCTION

Leonhard et al. (1962) originally proposed the separation of depressed patients with a history of manic episodes (the bipolar group) from those patients who have had only recurrent episodes of depression (the unipolar group). Among the newer approaches, the bipolar-unipolar distinction has achieved considerable rapid acceptance. DSM-III accepts the evidence pointing to the importance of the distinction between unipolar and bipolar forms of affective disorder.

Considerable evidence of possible genetic, familial, personality, biochemical, physiological, and pharmacological differences between bipolar and unipolar affective disorders has been presented. When the possible genetic factors were studied carefully, patients with bipolar disorder showed a far higher frequency of positive family history than did patients with only depression (Gershon, 1978; Winokur, 1978). Psychopharmacological studies have also indicated differences in the response of bipolar and depressed patients to psychoactive drugs, especially lithium. Patients with bipolar disorder are more likely to develop hypomanic responses to dopa or to imipramine and other tricyclics than are patients with depression.

Although the concept of bipolar disorder is well defined and amply substantiated by research and by clinical experience, the status of unipolar disorder (depression) is still uncertain. The criterion for bipolar disorder is clear—evidence of a current or past manic episode. Since virtually all individuals with manic episodes eventually develop depressive episodes, most investigators now conceptualize manic episodes as being subsumed under bipolar disorder. Therefore, in DSM-III, the diagnosis of bipolar disorder is made when there is a manic episode, whether or not there has been a depressive episode. It is unclear, however, if all episodes of depression are to be regarded as unipolar. In some studies, psychosis has been a necessary criterion; in other reports, all depressions, whether psychotic or not, have been included. Some investigators require evidence for psychotic forms of depression and for frequent recurrences. Perris (1968) specified three recurrences, and Schou (1968) specified two recurrences within a 1-year or 2-year period.

PSYCHOTIC DEPRESSIONS

In the late 19th century and the first decades of the 20th century, psychotic meant disturbance of high-level mental functions—memory, language, orientation, perception, and thinking. Freud and other psychoanalysts postulated that psychoses involved the loss of reality testing, one of the major functions of the ego. Although the traditional meaning of the term "psychotic" emphasized loss of reality testing and impairment of mental functioning—manifested by delusions, hallucinations, confusion, and impaired memory—two other meanings have evolved during the past 50 years. In the most common American usage of the term, psychotic became synonymous with severe impairment of social and personal functioning, manifested by social withdrawal and inability to perform the usual household and occupational roles. The other use of the term is derived from psychoanalytic theory and specifies degree of ego regression—as formulated by Fenichel (1945) in his influential work, *The Psychoanalytic Theory of Neurosis*—as the criterion for psychotic illness. As a consequence of those multiple meanings, in current clinical and research practice the term has lost its precision. Attempts to separate psychotic and neurotic patients into distinct, statistically verifiable nosological groups have been unsuccessful. Current evidence indicates that the psychotic-neurotic distinction is better regarded as a continuum along which patients can be placed (Kendell, 1976). In DSM-III, the category of affective disorders groups all the affective disorders together, regardless of the presence or absence of psychotic features.

By any criteria, psychotic depressions are relatively infrequent in current clinical practice. Only 10 per cent of large samples show delusions, hallucinations, confusion, and other manifestations of impaired reality testing. With better diagnostic criteria, more mental health facilities, greater willingness of patients to seek psychiatric help, and new psychopharmacological agents, treatment is being initiated early in the clinical course, before psychotic stages develop.

Causal assumptions have also confused the usage of the terms. Biological causes and disturbances of brain function are presumed to account for psychotic forms of depression. Neurotic forms, on the other hand, have been ascribed to social

and psychological causes that lead to an impairment of personality function. Evidence for those presumed causal correlations is minimal at best.

Moreover, in clinical practice the endogenous-reactive dichotomy has, unfortunately, been used interchangeably with the psychotic-neurotic distinction. That interchangeability is not valid, since psychotic states may also often follow reactions to life stress, such as loss and grief. Furthermore, persons with endogenous features, particularly sleep disturbance and weight loss, usually do not have psychotic symptoms, such as delusions and hallucinations.

For clinical description, the term "psychotic" does have some limited clinical usefulness. The description of a psychotic depression implies severe impairment, high suicidal risk, and possibly the need for hospitalization. Moreover, research indicates that patients with psychotic depressions do not respond to tricyclic antidepressants alone and may require combined tricyclic and phenothiazine treatment or electroconvulsive therapy (Glassman et al., 1975). Until further research findings are available, the psychotic-neurotic distinction should be regarded as a descriptive term used to place patients on a continuum with some clinical value, rather than as a basis for distinguishing clear-cut nosological groupings with established causal differences.

NEUROTIC DEPRESSIONS

So many theoretical and clinical inconsistencies surround the concept of neurotic depression that a number of investigators have recommended that it be dropped as a nosological entity (Akiskal et al., 1978; Klerman et al., 1979). Formerly classified as depressive neurosis in DSM-II, this term is not included in DSM-III. Depressive neuroses, or neurotic depressions, are now distributed among other classifications, each defined by shared symptoms or other descriptive characteristics. The appropriate classes include major depression, single episode or recurrent, without melancholia; dysthymic disorder; and adjustment disorder, with depressed mood.

Most often, neurotic depressions refer to nonpsychotic forms of depression. Although little evidence exists that precipitating events have a high correlation with nonpsychotic symptom states, in many instances the term "neurotic depression" is used synonymously with "reactive depression." Some clinicians use the term "neurotic" to refer to those depressions that arise in people with long-standing character problems or chronic maladaptive personality patterns. Reviewing divergencies in diagnostic practice and treatment recommendations has led to the identification of a number of different meanings for neurotic depression (Klerman et al., 1979):

1. Neurotic depressions are nonpsychotic. In this usage, neurotic depression is a residual category for those patients not showing psychotic features and is contrasted with a psychotic depression; the patient is considered to have a neurotic depression if there is an absence of hallucinations, delusions, confusion, memory impairment, or other signs of impairment of reality testing and intactness of high mental functions.
2. Neurotic depressions are less socially incapacitating than psychotic depressions. This usage is synonymous with a judgment of mild severity of social dysfunction. Thus, neurotic depressed patients usually continue their social functioning, although they may experience personal distress and inner conflict.
3. Neurotic depressions do not manifest endogenous symptoms. This usage defines a clinical picture without endogenous symptoms—that is, early morning awakening, weight loss, psychomotor retardation, guilt.
4. Several observers have proposed that in some neurotic depressions there is not only the absence of the endogenous symptom pattern but also the presence of a characteristic constellation of symptoms of its own, with self-pity, irritability, reactivity, and fluctuating symptoms (labeled the self-pitying constellation) (Rosenthal and Gudeman, 1967).
5. Neurotic depressions follow a stressful event that is usually but not exclusively psychosocial in nature. This usage is synonymous with situational depression and reactive depression. It is presumed that the stressor is the immediate proximate or contributing cause and has temporarily overwhelmed a previously normal person's capacity to cope and adapt. Such depressions are seen as extensions of normal states, quantitatively rather than qualitatively different from the normal reactions of loss, separation, disappointment, and other precipitants of a normal mood shift.
6. Neurotic depressions are the consequences of a long-standing maladaptive personality pattern. The depressions represent merely the latest ripple on a long-standing wave of personality inadequacies and social maladaptations. This type of depression is sometimes called "characterological depression" (Schildkraut, 1972) or "depressive personality." This concept emphasizes predisposition, in terms of the patient's long-standing preexisting personality structure and character pathology.
7. Neurotic depressions are the result of unconscious psychodynamic conflicts. According to psychoanalytic theory, these depressions result from four factors: (a) mood changes after interpersonal loss, disappointment, or deprivation; (b) a fall in self-esteem; (c) conflicts over the aggressive drive; and (d) a premorbid personality involving narcissism, dependency, and ambivalence (Nemiah, 1975).

Many official classifications and textbooks once separated neurotic depressions from other forms of affective disorders, particularly psychotic types. Those affective disorders were treated as psychoses, often together with schizophrenia, whereas neurotic depressions were grouped in some other category. This chapter examines all forms of affective disorders, independent of whether they have previously been categorized as neurotic or psychotic and without limitation due to specific symptoms, degree of severity, or impairment of social functioning.

ENDOGENOUS DEPRESSIVE SYMPTOM PATTERN

Interest has also revived in the endogenous-reactive continuum as another means of subdividing depressions, particularly those responsive to drug treatment. The concept has at least four component hypotheses: (1) There is a co-variation of symptoms, so that a central group of symptoms—including retardation, early morning awakening, weight loss, guilt, and unreactivity—occur together. (2) There is a correlation with life stress related to low frequency and relative difficulty in soliciting a history of recent life events and precipitating events. Hence, there has developed the concept of the reactive depressions, which occur in response to recent loss, disappointment, stress, and other external events. The implication is that those depressions without a recent history of external stress result from some intrinsic biological process; hence, they have acquired the label "endogenous." (3) There is a correlation with age; old patients are more likely to be endogenous, and young patients are more likely to be reactive. (4) There is a correlation with personality; the endogenous patients show a more stable nonneurotic form of premorbid personality than do the reactives.

Recent research has produced data to partially verify each of those four hypotheses. However, there is only a low level of correlation among the four components, particularly between

the symptom complex and the presence or absence of precipitating life events.

Moreover, there is a shift away from the endogenous-reactive continuum. The criteria for the endogenous diagnosis are variable. Some clinicians require the symptom-cluster criteria and minimize the role of life events; others emphasize the history of life events, even if the characteristic symptom complex does not occur. Some require both criteria, and others are flexible in shifting criteria between symptom pattern and reactive events in accordance with clinical judgment. To add further to the confusion, psychiatrists of Meyerian persuasion insist that all depressions are reactive.

However, when attempts have been made to separate groups on the basis of the distribution of patients in a multidimensional statistical space in order to search for separations, those efforts have failed. Although factors do form suitable dimensions on which to score persons, whenever efforts have been made to examine the distribution of those factor scores to determine bimodality of distribution or to find visual clustering that may identify subgroups, inconsistent results have emerged. The endogenous-reactive dichotomy represents a continuum, rather than a means of dividing patients into relatively clear-cut groups. Most patients appear to lie intermediate on the continuum; few are at the extremes.

In view of those developments, the solutions embodied in the Research Diagnostic Criteria (RDC) (Spitzer et al., 1978) and DSM-III seem prudent. Separating the endogenous symptom complex—sleep difficulty, anorexia, weight loss, retardation—from the presence of life events as a precipitation allows independent concurrent judgment of endogenous and situational or reactive types of depression. Research has shown that a moderate proportion of patients with the endogenous symptom pattern have clear precipitants (Katz and Hirschfeld, 1978).

Furthermore, the endogenous symptom pattern does predict response to treatment with electroconvulsive therapy and tricyclic antidepressants and, therefore, has clinical usefulness. The term "endogenous" is unfortunate because it implies a causal locus within the organism. However, if its use as a descriptive term can be refined and circumscribed, it can continue to have research and clinical value.

WINOKUR'S SCHEMA

Winokur and his colleagues (1978) presented a system of diagnosis in unipolar depression that is based on the use of specific familial backgrounds. Patients with primary depression are assigned to one of several distinctive subgroups that may be identified by different familial constellations of illness. Depression spectrum disease has been defined as an illness in which a first-degree family member has alcoholism or an antisocial personality or both. Pure depressive disease patients have family histories of depression, including a depressed first-degree family member.

Although few differences were found between the two groups in either the presenting clinical pictures or the precipitating factors, evidence indicated differences in the areas of personal problems and personality, as well as the course of illness (VanValkenburg et al., 1977; Winokur, 1979). The depression spectrum patients were less likely to experience loss of interest in usual activities as a symptom than were pure depressive disease patients and were more likely to have had a history of sexual problems, to have been divorced or separated, to have been described as irritable, and to report prior episodes of depression. They were also found to be more likely to recover completely than were the pure depressive disease patients (VanValkenburg et al., 1977).

Epidemiology

Interest in the epidemiology of the affective disorders has grown in recent years. Investigation in this area focuses on the incidence and the prevalence of the disorders in total populations and in subgroups defined by sociodemographic factors, such as age, sex, and social class.

INCIDENCE AND PREVALENCE

The affective disorders, particularly depression, are among the most frequently occurring or prevalent psychiatric disorders in adults. The meaning of such statements can vary, however, and statistics and reports of the frequency of occurrence are derived from a variety of measures.

Incidence (new cases a year) and prevalence (total cases a year) are the basic epidemiological rates. Attaining the most complete information on those rates, however, requires community surveys (Weissman and Myers, 1978). Although the cases under treatment (treated prevalence) indirectly reflect true incidence and prevalence, in addition to providing information on the use of mental health facilities, only a minority of persons with affective disorders seek or receive medical or psychiatric attention—that is, become patients and part of treated prevalence.

Prevalence and incidence rates do, of necessity, vary with the individual country's mortality rate—both the general mortality and the mortality specifically associated with affective disorders. However, the lifetime expectancy measure allows for an age-corrected expression of morbidity, independent of the mortality rate. That measure is, therefore, useful for international and historical comparisons.

The lifetime expectancy of developing an affective disorder of any type ranges from 8 per cent to 20 per cent. For Western nations, if attention is limited to bipolar disorder, lifetime expectancy is about 1 to 2 per cent. If broadly defined neurotic depressions are included, however, lifetime expectancy rates increase markedly, going as high as 20 to 30 per cent in some estimates (Essen-Möller and Hagnell, 1961). Those higher rates are determined not only by broadened diagnostic criteria but also by contemporary social forces—the public's expanding expectation of relief from distressing symptoms, such as anxiety, tension, and depression; the weakening of traditional psychosocial supports, such as the extended family, the neighborhood, and religious institutions; and the expectation that the health system, especially psychiatry, can, should, and will respond to those forms of distress.

A wide variety of data about the incidence and the prevalence of affective disorders comes from studies of admissions to psychiatric facilities, usually public mental hospitals. Figures for affective disorders, expressed as annual admission rate per 1 million population, range from 30 to 40 per cent. The reported rates show wide variations because admissions are influenced by a number of factors—differences in the availability of mental hospitals, the presence of other facilities for the care of the mentally ill, changes in diagnostic practices, the severity of the patient's illness, demographic characteristics of the communities from which patients are drawn and to which they return, and attitudes of the patient's family and the community toward the mentally ill.

A considerable proportion of persons with depression never see a physician. In all categories of depression only 20 to 25

per cent of depressed people receive treatment. Reported prevalence and incidence figures, however, particularly those based on hospital admissions, must be viewed as minimum estimates (Klerman and Barrett, 1973). Mild cases are now being treated, further reducing the duration of treatment reported for the incidence and the improvement rates of acute cases.

SEX

An almost universal trend, independent of country, is the greater prevalence of depression among women than among men (Weissman and Klerman, 1977). Regardless of the measure used—annual incidence, hospitalization rate, point prevalence, or lifetime expectancy—there is a fairly consistent female-to-male ratio of two to one when all types of depression are considered. The sex difference is less marked for bipolar disorder, in which the ratio of females to males is one and a half to one or two to one. Silverman (1968) summed up the sex role difference in this way:

> There appear to be no exceptions to the generalization that depression is more common in women than in men, whether it is the feeling of depression, neurotic depression, or depressive psychosis.

SOCIAL CLASS

Social class, occupation, and education are related to type, duration, and treatment of psychiatric illnesses. An almost universal finding, for example, is the increased incidence and prevalence of schizophrenic disorder in lower-class groups. In contrast, affective disorders were first reported to be disorders of the upper and middle classes by Faris and Dunham (1939) on the basis of data from public mental hospitals alone. Subsequent investigators, however, have found no clear relationship between social class and affective disorders.

MARITAL STATUS

Marital status is another social variable related to the prevalence of certain mental disorders, especially to schizophrenic disorders, with a much higher rate of disorder among people who are single, widowed, and divorced than among the married. With affective disorders, that relationship either does not exist or is very weak. Hospital admission rates for affective disorders are practically the same in single and married groups. Although researchers (Gove, 1972; Pearlin and Johnson, 1977) reported increased incidence rates of depressive neuroses and reactive or situational depressions among separated and divorced persons than among married and single persons, they conclude that marital status shows a much less significant relationship to the broad spectrum of depressive disorders than it does to schizophrenic disorders and that the relationship is negligible for affective disorders alone. Even though schizophrenics are less apt to marry than is the general population and even though persons with affective disorders marry at the same rate as their healthy, age-matched peers, the relationship between marriage and affective disorders remains insignificant.

Causes

GENETIC FACTORS

The possibility of genetic factors in the causes of affective disorders has been investigated in Scandinavia, Germany, the United Kingdom, and, recently, the United States. Four basic techniques of genetic investigation are used: (1) familial aggregation studies, comparing illness rates within and between generations of a particular family; (2) twin studies, comparing illness rates in monozygotic and dizygotic twins; (3) general population surveys, comparing illness rates of relatives of depressed patients with those of the general population; and (4) linkage studies, using known genetic markers, such as blood type or color-blindness.

Evidence from such investigations supporting genetic transmission includes an increased frequency of the illness in relatives of the proband (patient) compared with the general population, a greater concordance rate for the disease in monozygotic twins than in dizygotic twins, an increased frequency of psychiatric abnormalities in relatives of the affective disorder proband than in the general population, and onset of the illness at a characteristic age without any evidence of a precipitating event. Good evidence exists for a genetic factor in affective disorders. Furthermore, the genetic evidence supports the use of bipolar-unipolar classification of patients with affective disorders.

OTHER BIOLOGICAL FACTORS

In addition to genetic transmission, other biological factors may be significant in the cause and pathogenesis of affective disorders. Those factors include electrolyte disturbances, especially of sodium and potassium; neurophysiological alterations based on findings from electrophysiological studies using electroencephalography and evoked potential methods; dysfunction and faulty regulation of autonomic nervous system activity; neuroendocrine abnormalities, including hypothalamic, pituitary, adrenal cortical, thyroid, and gonadal changes; and neurochemical alterations in the neurotransmitters, especially in the biogenic amines, which serve as central nervous system and peripheral neurotransmitters, including norepinephrine, serotonin, dopamine, and acetylcholine.

The research in support of those hypotheses has been extensive and of high quality. Neurochemical hypotheses, particularly those involving the catecholamines, have received the greatest attention, because of the function of those amines as neurotransmitters involved in the actions of psychoactive drugs.

LIFE EVENTS AND ENVIRONMENTAL STRESS

Most American clinicians and investigators have long been convinced that a relationship exists between stressful life events and clinical depression. Clinical case discussions often include statements relating stress, especially from life events, to the onset of depressive episodes. In such discussions, life events are thought to play an important role in the causation of depression, at least its precipitation, as evidenced by such statements as "The depression arose in relation to ...." and "The depression was precipitated by. ...." Some clinicians even believe that life events play the primary or major role in depressions; others are more conservative, limiting the role of life events to contributing to the onset and timing of the acute episode.

The theory of an environmental cause of affective disorders has multiple sources: Meyer's (1957) general psychobiological approach, psychological observations on reactions to loss, and psychopathological studies relating the presence or absence of precipitating events to the assignment of patients along the endogenous-reactive continuum.

In general, the research confirms the relationship between life events and depression. Recently, the refined hypothesis

that particular events or classes of events may be associated with the onset of depression has been studied. For example, the New Haven group characterized life events as either exits from or entrances into the social field and found that exits, such as deaths and losses, are frequently associated with depression. In addition, when life events are classified as desirable or undesirable, a great number of undesirable events are associated with depression (Paykel, 1974).

In any review of the evidence, a few cautionary notes are in order. Specific events can contribute only partially to the onset or the development of depression. Wender (1967) noted that, when the incidence of a single event to account for the disease is low, as with affective disorders, the power of a single event to account for the disease is relatively limited. Thus, in an analysis of loss in relation to depression, exits from the social field occurred in 25 per cent of depressives and 5 per cent of controls. Exits preceded depression in only a small, though substantial, number of depressive cases. Furthermore, less than 20 per cent of the population experiencing exits became clinically depressed. That evidence suggests that a significant factor in the depression must be some predisposition, whether genetic, psychosocial, or characterological.

PERSONALITY AND PSYCHODYNAMIC FACTORS

Clinicians since the time of Hippocrates have noted that certain temperaments are related to depressions and elations, but only in the 20th century—after the observations of Abraham (1927), Rado (1929), Bibring (1953), Freud (1957), and other psychoanalysts—have those relationships been explored in depth. It is widely believed that persons prone to depression are characterized by low self-esteem, strong superego, clinging and dependent interpersonal relations, and limited capacity for mature and enduring object relations. Although those traits are common among depressives, no single personality trait, constellation, or type has been established as uniquely predisposed to depression. All humans, of whatever personality pattern, can and do become depressed under appropriate circumstances, although certain personality types—the oral-dependent, the obsessive-compulsive, and the hysterical—may be at greater risk for depression than the antisocial, the paranoid, and certain other types who use projection and other externalizing modes of defense.

Similarly, efforts have been made to identify a single psychodynamic factor or mechanism, such as loss or hostility turned against the self, as central and unique to the psychogenesis of depression. Although those factors have gained wide clinical emphasis, especially in guiding psychotherapy, the research evidence supporting their causal basis is still being developed.

Psychodynamic formulations are concerned not only with ongoing dynamic conflicts—evident in guilt, reactions to loss, and hostility turned against the self—that may be involved in the manifest depressive episode but also with features that may antedate the acute depressive episode and, therefore, may be regarded as causal. Some of those features are rooted in personality, since a major psychodynamic hypothesis focuses on the predisposition of certain personality types to depression.

More basic in psychodynamic thinking is the belief that the most crucial causal forces are those that operate in childhood. In regard to depression and mania, emphasis on infancy and early childhood has focused on possible impairments of ego function and sensitivities to separation and loss that arise from the vicissitudes of the early mother-child relationship. Attempts to test that hypothesis have relied on direct observations of infants and young children, particularly those in institutions who developed the anaclitic depressions described by Spitz (1946) and Bowlby (1969). Another line of investigation has focused on the frequency of parental loss and other kinds of psychic trauma in the childhood of depressives. Although those studies indicate that, as a group, depressives seem to experience more parental loss from death, separation, and other causes than do normal and other diagnostic groups, that factor alone does not seem sufficiently universal to account for all forms of depression. At the present time, the psychodynamic hypotheses are primarily of great heuristic value, contributing to case formulation, guidance of psychotherapeutic practice, and the design of future research.

Conclusion

The trend of all clinical experience and research studies supports the view that adult clinical states of affective disorders occur in relation to the balance between stresses on the person and vulnerability or predisposition. Although it is often difficult to gauge the relative importance of those two factors, environmental stress seems to play a role mainly in the timing and precipitation of the acute episode, but a purely environmentalistic view is incomplete. A major if not the most significant factor accounting for adult affective disorders lies in the person's predisposition or vulnerability. A number of alternative explanations have been proposed to account for those vulnerabilities. The explanations include genetically determined, hereditary predisposition, as embodied by the bipolar concept; early life experiences predisposing the person to sensitivity and loss, as proposed in a developmental psychodynamic model; and more recent behaviorist attempts to interpret depressive symptoms as failures of coping and rewards for self-esteem and hopelessness.

Although the depressive and manic affects are clearly a part of human adaptation, if not all mammalian adaptation, psychiatrists dealing with adults often see the maladaptive response, rather than the successful one. Therapeutic efforts, therefore, are often directed at altering that balance by providing for increased capacity for persons to cope, whether with drugs or psychotherapeutic techniques or environmental manipulations, or by attempting to modify the impact of various stresses. The affective disorders, then, seem to be a heterogeneous group of syndromes, with multiple causations. Until further research has demonstrated fully the various causative pathways, an open-minded approach is called for.

Suggested Cross References

Affective disorders are discussed in this chapter and in Chapter 19. Schizophrenic disorders are discussed in Chapter 15 and schizoaffective disorders in Chapter 17. Anxiety neurosis is discussed in Section 21.1a. Suicide is discussed in Section 29.1. Maternal deprivation is discussed in Section 43.1, and affective disorders in children are discussed in Section 43.15. Harlow discusses ethology in Section 4.6. Classification of mental disorders and DSM-III are discussed in Section 14.1. Epidemiology is discussed in Section 6.1. Alcoholism is discussed in Section 23.3, personality disorders in Chapter 22, and geriatic psychiatry in Chapter 53. Organic therapies are discussed in Chapter 31. Freud's theories are discussed in Chapter 8 and Adolf Meyer's theories in Section 10.2.

REFERENCES

Abraham, K. *Selected Papers of Karl Abraham, M.D.* Hogarth Press, London, 1927.

* Akiskal, H. S., Bitar, A. H., Puzantian, V. R., Rosenthal, T. L., and Walker, P. W. The nosological status of neurotic depression. Arch. Gen. Psychiatry, *35:* 756, 1978.

Akiskal, H. S., and McKinney, W. T. Depressive disorders: Toward a unified hypothesis. Science, *182:* 20, 1973.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, ed. 3. American Psychiatric Association, Washington, D.C., 1980.

Angst, J. Etiological and nosological considerations in endogenous depressive psychosis. In *Monographien aus dem Gesantgebiete der Neurologie und Psychiatrie.* Springer, Berlin, 1966.

Barchas, J. D., Akil, H., Elliott, G. R., Holman, R. B., and Watson, S. J. Behavioral neurochemistry: Neuroregulators and behavioral states. Science, *200:* 964, 1978.

Beard, G. M. *A Practical Treatise on Nervous Exhaustion (Neurasthenia).* William Wood, New York, 1880.

Beck, A. T. Cognition and psychopathology. In *Depression: Clinical, Experimental, and Theoretical Aspects*, A. T. Beck, editor, p. 253. Harper & Row, New York, 1969.

* Bibring, E. Mechanism of depression. In *Affective Disorders*, P. Greenacre, editor, p. 13. International Universities Press, New York, 1953.

Bleuler, E. *Textbook of Psychiatry.* Dover, New York, 1951.

Bowlby, J. *Attatchment.* Basic Books, New York, 1969.

Brown, G., Bhrolchain, M., and Harris, T. Social class and psychiatric disturbance among women in an urban population. Sociology, *9:* 225, 1975.

Burton, R. *The Anatomy of Melancholy.* Tudor, New York, 1927.

Cannon, W. B. *The Wisdom of the Body.* W. W. Norton, New York, 1936.

Chodoff, P. The core problem in depression: Interpersonal aspects. In *Science and Psychoanalysis*, J. Masserman, editor, vol. 17, p. 56. Grune & Stratton, New York, 1970.

Clayton, P. J., Halikas, J. A., and Maurice, W. I. The depression of widowhood. Br. J. Psychiatry, *120:* 71, 1972.

Cohen, M. B., Baker, G., Cohen, R. A. Fromm-Reichmann, G., and Weigert, E. An intensive study of 12 cases of manic-depressive psychosis. Psychiatry, *17:* 103, 1954.

Darwin, C. *The Expression of the Emotions in Man and Animals.* University of Chicago Press, Chicago, 1965.

Engel, G. *Psychological Development in Health and Disease.* W. B. Saunders, Philadelphia, 1962.

Essen-Möller, E., and Hagnell, O. The frequency and risk of depression within a rural population group in Scandinavia. Acta. Psychiatr. Scand., *37* (Suppl.): 28, 1961.

Eysenck, H. J. *Experiments with Drugs.* Pergamon Press, London, 1961.

Faris, R. E., and Dunham, H. W. *Mental Disorders in Urban Areas.* University of Chicago Press, Chicago, 1939.

Feighner, J. P., Robins, E., Guze, S. B., Woodruff, R. A., Winokur, G., and Muñoz, R. Diagnostic criteria for use in psychiatric research. Arch. Gen. Psychiatry, *26:* 57, 1972.

Fenichel, O. *The Psychoanalytic Theory of Neurosis.* W. W. Norton, New York, 1945.

Frank, R. The organized adaptive aspect of the depression-elation response. In *Depression: Proceedings of Forty-Second Annual American Psychopathological Association*, p. 51. Grune & Stratton, New York, 1954.

* Freud, S. Mourning and melancholia. In *Standard Edition of the Complete Psychological Works of Sigmund Freud*, vol. 14, p. 243. Hogarth Press, London, 1957.

Gershon, E. S. The search for genetic markers in affective disorders. In *Psychopharmacology: A Generation of Progress*, M. A. Lipton, A. DiMascio, and K. F. Killam, editors, p. 1197. Raven Press, New York, 1978.

Gershon, E. S., Cromer, M., and Klerman, G. L. Hostility and depression. Psychiatry, *31:* 224, 1968.

Glassman, A. H., Kantor, S. J., and Shostak, M. Depression, delusions, and drug response. Am. J. Psychiatry, *132:* 716, 1975.

Gove, W. R. The relationship between sex roles, marital and mental illness. Soc. Forces, *51:* 34, 1972.

Hagnell, O. *A Prospective Study of the Incidence of Mental Disorder.* Scandinavian University Books, Stockholm, 1966.

Hamilton, M. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry, *23:* 56, 1960.

Harlow, H. F. Love in infant monkeys. Sci. Am., *200:* 68, 1959.

Harlow, H. F., Harlow, M. K., and Suomi, S. J. From thought to therapy: Lessons from a primate laboratory. Am. Sci., *59:* 538, 1971.

Hartmann, E. *Ego Psychology and the Problem of Adaptation.* International Universities Press, New York, 1958.

Kasanin, J. Acute schizo-affective psychoses. Am. J. Psychiatry, *90:* 97, 1933.

* Katz, M. M. On the classification of depression: Normal, clinical, and ethnocultural variations. In *Depression in the 1970's*, R. Fieve, editor, p. 31. Excerpta Medica, Amsterdam, 1970.

Katz, M. M., and Hirschfeld, R. M. A. Phenomenology and classification of depression. In *Psychopharmacology: A Generation of Progress*, M. A. Lipton, A. DiMascio, and K. F. Killam, editors, p. 1185. Raven Press, New York, 1978.

Kaufman, J. C., and Rosenbaum, L. A. The reaction to separation in infant monkeys: Anaclitic depression and conservation-withdrawal. Psychosom. Med., *29:* 648, 1967.

Kendell, R. E. The classification of depressions: A review of contemporary confusion. Br. J. Psychiatry, *129:* 15, 1976.

Kety, S., and Schildkraut, J. J. Biogenic amines and emotion. Science, *156:* 21, 1967.

Klerman, G. L. Modes of action of antidepressant drugs. In *Pharmacotherapy of Depression*, J. Cole and J. R. Wittenborn, editors, p. 134. Charles C Thomas, Springfield, Ill., 1966.

Klerman, G. L. Clinical research in depression. Am. J. Psychiatry, *24:* 305, 1971.

Klerman, G. L. Affective disorders. In *The Harvard Guide to Modern Psychiatry*, A. M. Nicholi, editor, p. 253. Harvard University Press, Cambridge, Mass., 1978.

Klerman, G. L., and Barrett, J. E. The affective disorders: Clinical and epidemiological aspects. In *Lithium: Its Role in Psychiatric Research and Treatment*, S. Gershon and B. Shopsin, editors, p. 201. Plenum Publishing Corp., New York, 1973.

Klerman, G. L., Endicott, J., Spitzer, R., and Hirschfeld, R. M. A. Neurotic depressions: A systematic analysis of multiple criteria and meanings. Am. J. Psychiatry, *136:* 57, 1979.

Klerman, G. L., and Gershon, E. S. Imipramine effects upon hostility in depression. J. Nerv. Ment. Dis., *150:* 127, 1970.

Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* E. and S. Livingstone, Edinburgh, 1921.

Krauthammer, C., and Klerman, G. L. Secondary mania: Manic syndromes associated with antecedent physical illness or drugs. Arch. Gen. Psychiatry, *35:* 1333, 1978.

Krauthammer, C., and Klerman, G. L. The epidemiology of mania. In *Manic Disease*, B. Shopsin, editor, p. 11. Raven Press, New York, 1979.

Leonhard, K., Korff, I., and Schulz, H. Temperament in families with monopolar and bipolar phasic psychoses. Psychiatr. Neurol., *143:* 416, 1962.

Meyer, A. *Psychobiology: A Science of Man.* Charles C Thomas, Springfield, Ill., 1957.

Nemiah, J. C. Depressive neurosis. In *Comprehensive Textbook of Psychiatry*, A. M. Freedman, H. I. Kaplan, and B. J. Sadock, editors, ed. 2, p. 1255. Williams & Wilkins, Baltimore, 1975.

Ostow, M. *Drugs in Psychoanalysis and Psychotherapy.* Basic Books, New York, 1962.

Parkes, C. M. The first year of bereavement: A longitudinal study of the reaction of London widows to the death of their husbands. Psychiatry, *33:* 444, 1970.

Paykel, E. A. Recent life events and clinical depression. In *Life Stress and Illness*, E. K. Gunderson and R. H. Rahe, editors. Charles C Thomas, Springfield, Ill., 1974.

Pearlin, L. I., and Johnson, J. S. Marital status, life-strains, and depression. Am. Soc. Rev., *42:* 704, 1977.

Perris, C. A study of bipolar (manic-depressive) and unipolar recurrent depressive psychoses. Acta Psychiatr. Scand., *194* (Suppl.): 1, 1966.

Perris, C. The course of depressive psychoses. Acta Psychiatr. Scand., *44:* 238, 1968.

Rado, S. The problem of melancholia. Int. J. Psychoanal., *9:* 420, 1929.

Rapaport, D. Edward Bibring's theory of depression. In *Collected Papers of David Rapaport*, M. Gill, editor, p. 758. Basic Books, New York, 1967.

Raskin, A., Schulterbrandt, J. G., Reatig, N., and McKeon, J. J. Differential response to chlorpromazine, imipramine, and placebo. Arch. Gen. Psychiatry, *23:* 164, 1970.

Robins, E., and Guze, S. B. Classification of affective disorders. In *Recent Advances in the Psychobiology of the Depressive Illnesses*, T. A. Williams, M. M. Katz, and J. A. Shield, Jr., editors, p. 283. United States Government Printing Office, Washington, D.C., 1972.

Robins, E., Muñoz, R. A., Martin, S., and Gentry, K. A. Primary and secondary affective disorders. In *Disorders of Mood*, J. Zubin and F. A. Freyhan, editors. Johns Hopkins University Press, Baltimore, 1972.

Rosenthal, S., and Gudeman, J. E. The self-pitying constellation in depression. Br. J. Psychiatry, *113:* 485, 1967.

Schildkraut, J. J. *Neuropharmacology and the Affective Disorders.* Little, Brown, and Co., Boston, 1972.

Schildkraut, J. J. Current status of the catecholamine hypothesis of affective disorders. In *Psychopharmacology: A Generation of Progress*, M. A. Lipton, A. DiMascio, and K. F. Killam, editors, p. 1223. Raven Press, New York, 1978.

Schmale, A. The adaptive role of depression in health and disease. In *Separation and Depression*, J. P. Scott and E. C. Senay, editors, p. 187. King, Baltimore, 1973.

Schou, M. Lithium in psychiatric therapy and prophylaxis. J. Psychiatr. Res., *6:* 67, 1968.

Silverman, C. *The Epidemiology of Depression.* Johns Hopkins University Press, Baltimore, 1968.

Spitz, R. A. *Anaclitic Depression: The Psychoanalytic Study of the Child*, vol. 2. International Universities Press, New York, 1946.

* Spitzer, R. L., Endicott, J., and Robins, E. Research diagnostic criteria: Rationale and reliability. Arch. Gen. Psychiatry, *35:* 773, 1978.

Srole, L., Langer, T. S., Michael, S. T., Opler, M. K., and Rennie, T. A. *Mental Health in the Metropolis.* McGraw-Hill, New York, 1962.

Suomi, S. J., Seaman, S. F., Lewis, J. K., DeLizio, R. D., and McKinney, W. T. Effects of imipramine treatment of separation-induced social disorders in rhesus monkeys. Arch. Gen. Psychiatry, *35:* 321, 1978.

Turns, D. The epidemiology of major affective disorders. Am. J. Psycother., *32:* 5, 1978.

Tyrer, P. Relevance of bodily feelings in emotion. Lancet, *1:* 915, 1973.

Usdin, E., Hamburg, D. A., and Barchas, J. D. *Neuroregulators and Psychiatric*

Disorders. Oxford University Press, New York, 1977.
VanValkenburg, C., Lowry, M., Winokur, G., and Cadoret, R. Depression spectrum disease versus pure depressive disease. J. Nerv. Ment. Dis., *165:* 341, 1977.
Weissman, M. M., and Klerman, G. L. Sex differences and the epidemiology of depression. Arch. Gen. Psychiatry, *34:* 98, 1977.
Weissman, M. M., Klerman, G. L., and Paykel, E. S. Clinical evaluation of hostility in depression. Am. J. Psychiatry, *128:* 261, 1971.
• Weissman, M. M., and Myers, J. K. Affective disorders in a U. S. urban community: The use of research diagnostic criteria in an epidemiologic survey. Arch. Gen. Psychiatry, *35:* 1304, 1978.
Weissman, M. M., Prusoff, B. A., and Paykel, E. S., Checklist quantification of a psychological therapy: Pilot studies of reliability and utility. J. Nerv. Ment. Dis., *154:* 125, 1972.
Wender, P. H. On necessary and sufficient conditions in psychiatric exploration. Arch. Gen. Psychiatry, *16:* 41, 1967.
Winokur, G. Mania and depression: Family studies and genetics in relation to treatment. In *Psychopharmacology: A Generation of Progress*, M. A. Lipton, A. Dimascio, and K. F. Killam, editors, p. 1213. Raven Press, New York, 1978.
Winokur, G. Unipolar depression: Is it divisible into autonomous subtypes? Arch. Gen. Psychiatry, *36:* 47, 1979.
Winokur, G., Behar, D., VanValkenburg, C., and Lowry, M. Is a familial definition of depression both feasible and valid? J. Nerv. Ment. Dis., *166:* 764, 1978.
Winokur, G., Clayton, P., and Reich, T. *Manic Depressive Illness.* C. V. Mosby, St. Louis, 1969.
Zung, W. W. K. A self-rating depression scale. Arch. Gen. Psychiatry, *12:* 63, 1965.

18.2 Major Affective Disorders

EDWARD A. WOLPERT, M.D., Ph.D.

Introduction

Major affective disorders are characterized by one or more episodes of major illness involving a prominent and persistent disturbance in mood, either manic or depressed, clearly distinguished from prior functioning. The essential feature of a manic episode is an elevated, expansive, or irritable mood associated with such symptoms as hyperactivity, excessive involvement in activities without use of judgment, pressured speech, inflated self-esteem, distractibility, flight of ideas, and decreased need for sleep. The essential feature of a depressed episode is a depressive mood or pervasive loss of interest or pleasure associated with symptoms of sleep and appetite disturbance, change in weight, psychomotor agitation or retardation, decrease in energy, a feeling of guilt or worthlessness, and thoughts of suicide. Any given episode may be characterized as manic, depressed, or mixed in symptomatology, and with or without psychosis in intensity. When the symptoms disappear, the resulting picture is one said to be in remission.

The major affective disorders present with a clear and precise point of onset, and the period of illness is clearly circumscribed from the preillness and postillness functioning of the patient. A major affective disorder is clearly distinguishable from a chronic minor affective disorder in that in the chronic minor affective disorder the disturbance of affect is long lasting (usually more than 2 years), and there seems to be a gradual and unclear point of onset of the illness. A patient with a chronic minor affective disorder may have a superimposed major affective disorder.

The diagnosis of a major affective disorder is not made if the affective state is secondary to a known organic disorder, such as a hypomanic or manic response to steroids, or if the affective state accompanies a primary thought disorder, such as schizophrenia. However, recent work suggests that some organic conditions release an affective illness previously not expressed and that the patient may have both an affective disorder and a thought disorder simultaneously.

Definition and History

The third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) of the American Psychiatric Association (1980) separates the major affective disorders into two subgroups—major depression and bipolar disorder—based on whether or not both manic and depressive episodes are involved longitudinally. In such a scheme, recurrent depressive illness, as well as solitary depressive illness, such as involutional melancholia, are considered subgroups of major depression. Bipolar disorder is subdivided according to the symptomatology of the current episode: manic, depressed, or mixed.

Throughout recorded history, affective disorders have been described in both medical and poetic literature. Greek and Roman physicians early recognized the connection between psychic loss and depressed states, and their treatment was along humanitarian lines appropriate to the illness—rest, refreshment, the forging of new emotional connections. Anticipating later discoveries, Roman physicians recognized the soothing nature of the waters of certain spas in the north of Italy and sent agitated or euphoric patients to drink of the waters, discovered 2,000 years later to be rich in lithium salts.

With the collapse of the Roman Empire, much of the treatment of the mentally ill became the control of the demoniacally possessed. It was not until the end of the 18th century that Pinel, by freeing his patients from chains, symbolically inaugurated Western civilization's commitment to the scientific study of psychological illness.

Falret, in 1854, recognized that some depressed patients became elated and again depressed and described *la folie circulaire.* Baillarger published a description of *folie à double forme,* remarkably similar to Falret's observation. In 1879 Falret's son noted the hereditary nature of *la folie circulaire,* and in 1882 Kahlbaum described mania and melancholia as stages in a single disease process, a milder form of which he titled "cyclothymia."

The apogee of descriptive phenomenology came with the work of Emil Kraepelin (1856–1926), who attempted to integrate the findings of the infant experimental psychology founded by his revered teacher Wilhelm Wundt with his own painstaking clinical observation of patients over a period of many years. Kraepelin early recorded clear, precise descriptions of a variety of affective disorders, differentiating mania, hypomania, circular insanity, recurrent depression, melancholia, and mild affective mood swings. In 1921 Kraepelin postulated that because each variety of affective illness seemed identical in certain fundamental features, seemed to be mutually replaceable, and had a favorable prognosis, each must be an alternate manifestation of an underlying disease entity. He called that hypothetical underlying disease entity "manic-depressive illness," which DSM-III recognizes as "major affective disorder."

Kraepelin's nosological views have had an immense effect on psychiatry. Abraham, the first psychoanalyst to study manic-depressive illness, used as his case material a variety of phenomenologically different patients similar only in that their disorders were disorders of affect. The psychodynamics he derived from his study were to be applicable to all patients with affective disorders, whatever the surface phenomenology. Although Freud expressed some reservations, most psychoanalytic writers have followed Abraham. The validity of Kraepelin's view of a uniform affective disease entity has been questioned by recent empirical findings in a variety of areas. Leonhard in 1957 proposed differentiating patients with episodic affective disorders into

a bipolar group (those patients with both depressed and manic phases) and a unipolar group (those patients with depressed phases only). Empirical evidence indicates that there are considerable genetic, familial, biochemical, physiological, and pharmacological differences between bipolar and unipolar patients—that is, patients with bipolar affective disorder and with major depression in the present nomenclature. Furthermore, true cases of unipolar manic disorder without depressive episodes are hard to find and, when noted, often represent the first episode of a long bipolar affective process. DSM-III in effect accepts the differentiation between unipolar and bipolar illness, but unfortunately does not use this nomenclature.

Epidemiology

A large body of data on the epidemiology of affective disorder has accumulated in recent years. Unfortunately, the data are not easy to interpret, because there are great variations in the classification systems used, in the measures used, in the control variables studied, and in the reliability of the diagnostic categories. Nevertheless, Berger (1978), in summarizing the data available from the United States, thought that the incidence of bipolar illness is about 300 per 100,000, or 0.3 per cent, and that about 600,000 bipolar patients are identified and treated each year. Unipolar illness is more prevalent than bipolar illness. Although some 1.5 million people are treated for unipolar illness each year in the United States, Berger estimated that 4.5 to 7.5 million people with unipolar illness go untreated. British and American statistics suggest that as many as 15 per cent of the population will have at least one severe depression during their lifetimes.

The reported lifetime expectancy for developing any type of affective illness ranges from 1.2 to 1.8 per cent in Norway and from 8.5 to 17.7 per cent in Sweden. If one limits the expectancy to manic-depressive illness, the figures drop to from 0.6 to 1.4 per cent in the United States and to 2.09 per cent in Iceland (Klerman and Barrett, 1975). Estimates of the percentages of ill patients receiving treatment range from 20 to 33 per cent world-wide (Berger, 1978).

There is a widely held but incorrect belief that, although schizophrenia is a disease of early onset—beginning during late childhood and adolescence—manic-depressive or major affective disorder manifests itself during early to middle adulthood. Kraepelin (1921) noted that in his case material

> the greatest frequency of first attacks fall ... in the period of development with its increased emotional excitability between the 15th and 20th year.

Bipolar illness typically begins before age 30, but major depression seems to begin evenly throughout adult life. One-third of Winokur et al.'s (1969) bipolar manic-depressive patients demonstrated onset before 20 years of age, 40 per cent of Perris's (1968) patients demonstrated onset between ages 15 and 25, and 20 per cent of Wertham's (1929) 2,000 manic patients had their first attacks before age 20. Although rare, cases of bipolar illness have been reported in childhood (Feinstein and Wolpert, 1973).

Major depressive illness is more common in women than in men. It has been estimated that 18 to 23 per cent of all women and 8 to 11 per cent of all men have depressive episodes at some time; 6 per cent of those women and 3 per cent of those men at some time require hospitalization. Although bipolar affective disorder is far less common than unipolar depressive illness, 0.4 to 1.2 per cent of the adult population are estimated to have the syndrome. It is apparently as common in women as in men.

Ever since Kraepelin's time, it has been known that the risk of affective disorder in the families of patients with known affective disorder is greater than in the general population at large. In addition, the risk of affective disorder in the families of patients ill with affective disorder is greater than the risk of schizophrenia in the families of patients ill with schizophrenia. Relatives of unipolar patients have a significantly greater risk for unipolar illness than for bipolar illness, and relatives of bipolar patients have a significantly greater risk for bipolar than for unipolar illness.

Causes

Any discussion of the causes of the major affective disorders must take into account work on hereditary, constitutional, biological, psychological, and social factors involved in the disease process. The early work in the field is well summarized in Bellak's classic 1952 monograph. Much of the work reported therein is speculative and not supported by attempted replication. After a survey of the state of present knowledge, an attempt is made here to present a unified theory of the illnesses.

HEREDITARY FACTORS

For many years the tremendous loading of affectively ill family members in patients with affective illness has been noted and commented on. The loading is far greater than that found in the families of schizophrenics (Slater and Cowie, 1971). After Leonhard's (1957) separation of affective disorder into monopolar and bipolar subtypes, genetic researchers studied possible genetic differences between those two phenomenologically separate illnesses.

Three independent family studies carried out by Perris (1966) in Sweden, Angst (1966) in Switzerland, and Winokur and Clayton (1967, 1969) in the United States found relatives of bipolar patients to have a significantly higher risk for bipolar than for unipolar illness, but relatives of unipolar patients were more at risk for unipolar than bipolar illness. Twin studies indicate significantly greater risk in monozygotic twins than in dizygotic twins for similar affective disease processes (Slater and Cowie, 1971).

Studies showing increased risk for illness in the family of ill manic-depressives do not demonstrate unequivocally the genetic nature of the illness, because the argument could be made that what is expressed is the consequence of a certain powerful psychological milieu, rather than a genetic predisposition. Indeed, work from the interpersonal point of view suggests a powerful specific family dynamic in the causes of manic-depressive illness. However, the direct study of X-linked markers, such as Deutan color-blindness (Reich et al., 1969) and the XG_a blood group (Winokur and Tanna, 1969), provided more compelling evidence that bipolar affective disorder is transmitted by an X-linked dominant gene. Although the original findings have been replicated by other workers, doubt is thrown on the significance of those findings by repeated reports of contradicting group data, especially the findings of sick father-son pairs, a finding directly contradicting the hypothesis. Recent work (Ostrow et al., 1978) demonstrates father-to-son transmission of membrane lithium transport abnormalities in red blood corpuscles. Two genetic subgroups of bipolar disease may exist: a classical early-onset group (mean age of onset, 25 years) and a late-onset group (mean age, 39 years). Those in the first group show positive family histories, but those in the second group do not (Mendlewicz et al., 1972).

Thus, bipolar affective disorder seems to be under different genetic controls in different patients. In some patients it behaves like an X-linked genetically controlled illness; in other patients it behaves as if it is transmitted in a pattern of autosomal dominant inheritance with variable expressivity; and in still other patients it behaves as if it is not genetically controlled.

Among patients with major depression, no genetic markers have yet been found. Winokur (1973) differentiated two subgroups of major depression patients—early-onset females (onset before age 40) and late-onset males (onset after age 40). Those subgroups demonstrate family members with very different illnesses. In the families of late-onset male probands, one finds depression as often in the males as in the females, and one finds little alcoholism or sociopathy in male relatives. In the families of early-onset female probands, on the other hand, one finds more depression in female relatives than in male relatives, and one finds more alcoholism and sociopathy in male relatives than in the other families. Those findings have been generalized to form two prototypic subgroups; depression spectrum disease (early-onset females) and pure depressive disease (late-onset males). Those findings require further confirmation.

CONSTITUTIONAL FACTORS

The association of temperament with physical appearance has a long history in both poetic and scientific literature. In the 20th century two workers—Kretschmer (1921) and Sheldon (Sheldon et al., 1940; Sheldon and Stevens, 1942)—sought to correlate body types with personality characteristics. Although such correlation had a certain vogue in the first quarter of the century, those notions have receded from importance as more basic, cellular discoveries have suggested a physiological cause of the major affective disorders.

BIOLOGICAL FACTORS

Biological rhythms. Kraepelin (1921) in his final formulation thought that his manic-depressive illness, equivalent to the DSM-III over-all category of major affective disorders, was due to unspecified inner structural changes and was not related to psychological factors of any sort. He pointed out that psychological precipitants may be present or not in a given case, and hence he considered them as fortuitous circumstances, not as necessary causes of illness episodes. He believed that the psychophysiological slowing in depression and speeding in mania was under physiological control, but the nature of that control was not possible to determine in his lifetime.

Bunney (1977) and his colleagues in the United States and Jovanovic (1977) in Germany independently arrived at a conceptualization in which manic-depressive illness is seen as a disorder of the kinetics of bodily functioning. According to that conceptualization, in Wehr's (1977) language, there is

> an underlying process that is continuous over time, where change occurs daily, and where remission as well as relapses are expressions of the illness.

Such a conceptualization continued where Kraepelin left off. The inner structural changes Kraepelin postulated were asserted to be a disturbance of the biological clock, so that various self-sustained rhythms of 24-hour periodicity (circadian activity cycle) are alternately speeded or slowed, thereby putting the person's most effective functioning period out of synchrony with the environment. In such a formulation, psychogenic factors are fortuitous in occurrence.

Circadian activity cycles described to date include diurnal variations in mood, the rest-activity cycle, diurnal electroencephalographic patterns, variation in the neuroendocrine pattern of secretion of thyroid-stimulating hormone, growth hormone, adrenocorticotropic hormone, melantonin, testosterone prolactin, cortisol and its metabolites, and 17-ketosteroids. Malfunction of the circadian rhythm explains a variety of clinical findings: difficulty in falling asleep, hypersomnia, early morning arising, increased rapid eye movement (REM) pressure in depression, decreased REM pressure in mania, variation in diurnal rest-activity cycles. In each case in which opposite valence abnormalities are found in mania and depression, the rhythm of activity is advanced in depression and delayed in mania.

Over the years a number of clinicians have remarked on an interesting phenomenon often found to presage a change of activity level. The phenomenon, first described by Lange in 1928 in Germany, has been called the hypomanic alert by J. Jacobson (1965), the prodromal symptom state by Wolpert (1975), and the switch by Bunney (1977). Patients, often at night, perhaps while dreaming, enter a state best described as activated. In that state, dreams are unusually vivid; they are dreams of pure sensation, or they represent symbolically the overthrow of psychic controlling structures by untamed primitive energies. If found during waking, the state is one of panhyperacusis. A particularly interesting example was described by Wolpert in 1977b. Isolation of prodromal symptom states allows the therapist to treat the illness rapidly, because variation in activity level is predicted and episodes of illness can be aborted.

Antimanic agents like lithium and ethanol slow the rhythm of the intrinsic pacemaker in experimental animals, thereby lengthening the circadian activity rhythm. Estrogen accelerates the intrinsic pacemaker, thereby shortening the circadian activity rhythm. Tricyclic antidepressants have been shown to accelerate the reestablishment of normal circadian rhythms in experimental animals. Thus, known antimanic agents and some known antidepressants have opposite effects on the biological clock.

It seems well established that the various circadian activity cycles are driven by an endogenous, self-sustained clock-like mechanism persisting in the absence of environmental input. In some animals, possibly including humans, the daily activity cycles may be controlled by a central pacemaker (the anatomical biological clock) located in the suprachiasmatic nucleus of the hypothalamus. That regulatory mechanism may process environmental cues to allow for adjustments to be made with the external 24-hour day-night cycle. Malfunction of the regulatory clock on a daily basis leads to the cyclic phenomenon in a given episode of illness; the malfunctioning of the regulatory clock in reaction to normal long-term biological rhythms (menstrual cycle, seasonal cycle) leads to the cyclicity seen in some patients. Alternatively, the illness is cyclic itself and not attached to brain biological rhythms.

Transmission of the nervous impulse. In the past 25 years various research findings have suggested the general hypothesis that affective disorders represent a disturbance in the transmission of the nervous impulse across the synaptic cleft by chemical neurotransmitters. Two divergent disorders of neurotransmitter substances have been suggested—catecholamine (norepinephrine) deficiency (Schildkrout and Kety, 1967) and indoleamine (serotonin) deficiency. The work of Maas (1975) and others suggests the existence of two chemically discrimin-

able subtypes of unipolar depression. The first subtype is characterized by decreased cerebrospinal fluid 5-hydroxyindolacetic acid, normal or high urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) (a metabolite of norepinephrine), a normal growth hormone response to insulin, and a better response to amitriptyline treatment than to imipramine treatment. The second subtype of unipolar depression is characterized by normal cerebrospinal fluid 5-hydroxyindolacetic acid, low urinary MHPG, low growth hormone response to insulin, and a better response to imipramine treatment than to amitryptyline treatment. However, there is as yet no good way to predict clinically or epidemiologically which untreated patient will respond better to which of the two drug treatments. A patient's previous response to one or the other drug treatment may be helpful in determining which treatment is likely to be more effective. To date, there have been no reports of a successful correlation of a given form of treatment with either of the subtypes.

Data from a variety of studies seem consistent in implicating diminished norepinephrine as a major factor in depression. Mania, on the other hand, seems to be more complicated than being the simple result of excess norepinephrine, as was thought at first. Although a multitude of mechanisms have been proposed, at present it is believed that mania results from the relative predominance of dopamine function, either through actual excess or as a result of cholinergic deficiencies.

How the biological rhythms are related to the events at the cellular level has not yet been determined.

PSYCHOLOGICAL FACTORS

Karl Abraham (1877–1925) was the first writer to attempt to understand affective disorders from a psychodynamic point of view. Accepting Kraepelin's assertion that all affective disorders are one, Abraham presented a psychodynamic formulation based on analyses of six patients with divergent disease pictures. He thought that episodes of manifest illness are precipitated by the loss of a libidinal object, eventuating in a regressive process in which the ego retreats from its mature functioning state to one in which the infantile trauma of the oral-sadistic stage of libidinal development dominates because of a fixation process in earliest childhood. Between periods of gross illness, the patient typically demonstrates a compulsive character, differing from the true compulsive in that the process of regression eventuates in abandonment of the object, instead of retaining it in altered form.

In Freud's structural theory, the introjection of the lost object into the ego leads to the typical depressive symptoms diagnostic of a lack of energy available to the ego. The superego, unable to retaliate against the lost object externally, flails out at the psychic representation of the lost object, now internalized in the ego as an introject. When the ego overcomes or merges with the superego, there is a release of energy that was previously bound in the depressive symptoms, and a mania supervenes with the typical symptoms of excess. Freud also noted that there seem to be two types of illness episodes—spontaneous and psychogenic. He further stated that in some cases the illness seems to be more somatic than psychogenic. Those inferences, based on careful clinical consideration, fit well with the biological facts. Later, an attempt is made to use both biological and psychological parameters to form a unitary theory.

Later analytic writers have elaborated the basic Abraham-Freud conceptualization in various ways. Although most analytic writers pay lip service to the concept that the disease has an underlying neurophysiological substrate, few attempt to conceptualize that state in any but psychological terms. Indeed, Pao—writing in 1968, when lithium carbonate was beginning to be used in American psychiatry—conceived elation to be a normal response to either the joy of reunion with a temporarily lost object or pleasure at a successful work performance. In concluding the report of a case treated analytically, Pao (1968) stated:

> that even if the validity of the catecholamine hypothesis were beyond doubt, the psychological factors in this case played the key role in bringing about the various physiological changes.

Heinz Kohut (1971) made significant contributions to the psychology of the self and the treatment of narcissistic personality disorders. Narcissistic personality disorder is one of the frequent differential diagnostic considerations in manic-depressive patients because patients with that personality disorder frequently demonstrate transient periods of elation and depression, often with grandiosity and euphoria in one phase and self-depreciation in a succeeding phase, just as is seen in classical manic-depressive disorder. To Kohut the distinction is made clear by the longitudinal history of the patient; periods of euphoria on the one hand and depression on the other are in the narcissistic character clearly responsive to a loss of the feeling of empathy with the therapist or a significant other and are amenable to interpretation. In the manic-depressive, on the other hand, the psychic structure is poorly integrated and disintegrates in the presence of stress, and interpretation does not relieve the clinical picture. Particularly persuasive examples of the differentiation are reported by Feinstein and Wolpert (1973) in a child and by Preodor and Wolpert (1979) in several hospitalized adolescents.

On a metapsychological level the two clinical entities are distinguishable by the relative cohesiveness of two important narcissistic structures—the grandiose self and the idealized parent imago. The patient with a narcissistic personality disorder has stable narcissistic structures, and stress does not completely fragment those structures. In the true manic-depressive, the narcissistic structures are weakly held together and fragment easily under the stress of the affective storm.

SOCIOLOGICAL AND INTERPERSONAL FACTORS

Freida Fromm-Reichmann and her colleagues (Cohen et al., 1954) approached the study of manic-depressive illness by attending carefully to the psychological, cultural, and social histories of 12 patients in intensive psychotherapy in a private, middle to upper-class social setting. The authors offered a conceptualization of the illness in which the family of the manic-depressive-to-be was found to be upward-striving socially, culturally, and economically but isolated within the geographic community. One parent, usually the mother, was seen as the ultimate authority but cold and unloving; the other parent, usually the father, was warmer but ineffectual. The child in that situation became the instrument to validate the family and was expected to conform to high standards of conduct and success. In the family, discipline was inconsistent and contradictory. There was little chance for the child to feel valued for himself or to have feelings that he or she was intrinsically worthwhile. Such a familial constellation was said to predispose to manic-depressive illness. Other authors, in particular Arieti (1959), have written similarly.

Gibson et al. (1959) did a validation study in which 27 manic-depressive patients and 17 schizophrenic patients were treated in a large public hospital with intensive psychotherapy that confirmed and expanded the results of the earlier study. Inasmuch as the settings of the two studies were different and the findings were consistent, any explanation of the illness must take social factors into account.

A UNIFIED THEORY

Any attempt to understand the major affective disorders must take into account the genetic, biological, psychological, and sociological studies cited. Robert Cohen (1975), one of Fromm-Reichmann's co-workers, writing in an earlier edition of this textbook, asserted:

> In the writer's opinion, investigators in each of the etiological areas described in the foregoing pages have adduced sufficient evidence to indicate that various factors play some role in the development of the manic-depressive reaction. What does not yet exist is a way of weighing each factor with accuracy and precision. It seems reasonable to expect that, with further research, we will be able to define groups of patients characterized by certain patterns of factors. This point of view is well described by Bellak (1952) in his multiple-factor psychosomatic theory of manic-depressive psychosis.

Today, it seems fruitful to conceive of the major affective disorders as genetically controlled disorders in which spontaneous shifts of activity cycles cause typical symptoms of the disorder. Alternately, specific psychogenic factors meaning "loss" act as triggers and can precipitate an episode, either manic or depressed. Once started, the episode does not respond to interpretation, and in appropriate subgroups one or another chemical treatment is indicated. Once the episode is controlled chemically, psychological treatment may be necessary to help the patient deal with secondary consequences of his illness, to help remove the effects of specific psychogenic triggers, or to deal with psychological problems diagnostic of a second disorder. Hence, the present author views major affective disorders as an actual neurosis in Freud's sense of the term (the direct result of a physiological disorder), not as a psychogenic disorder (the result of a conflict between hypothesized psychological structures), and readily conceives of some patients' being subject to two illnesses—one psychological and one physiological. Thus, in the author's experience some patients with bipolar illness need lithium carbonate only, some need lithium carbonate and psychological help with handling psychological losses, and some need lithium carbonate and psychological treatment of a coexisting narcissistic or other personality disorder.

Clinical Features

The essential feature of each type of major affective disorder is a distinctive psychophysiological state, together with certain but inconstant laboratory findings. At times it is even possible to differentiate recurrent depressive episodes of major depression from depressive episodes of bipolar disorder by these laboratory findings. Associated features sometimes present are not consistent in appearance or diagnostic of the state (see Table I).

MAJOR DEPRESSION

The essential feature of major depression is a distinct period of decreased psychophysiological activation. In that state the predominant mood is depressed, or the patient shows a pervasive loss of interest or pleasure. The patient is frequently not aware of or does not complain of the mood disturbance, and what is evident is a withdrawal from usual activities. Symptoms that may be present include sleep disturbance (usually early morning awakening), loss of appetite, cognitive disturbance (including inability to concentrate or to make decisions), slowed thinking, decreased energy, feelings of worthlessness

TABLE I
Clinical Features of Major Affective Episodes

	Manic Episode	Depressive Episode in Major Depression	Depressive Episode in Bipolar Disorder
Essential features	Predominant mood elevated, expansive, or irritable	Depressive mood or pervasive loss of interest or pleasure	A history of alternating episodes of mania and major depression
Symptoms	Hyperactivity, excessive involvement in activities, poor judgment, pressure of speech, flight of ideas, loosened associations, inflated self-esteem, decreased need for sleep, distractibility, hypersexuality	Loss of interest or pleasure, sleep disturbance, appetite disturbance, change in weight, psychomotor agitation or retardation, cognitive disturbance, decreased energy, feelings of worthlessness or guilt, thoughts of death or suicide	As in depressive episode in major depression
Laboratory findings (inconstant)	Nocturnal EEG: decreased total sleep time, decreased percentage of dream time, increased REM latency (decreased pressure to dream)	Nocturnal EEG*: decreased total sleep time and increased percentage of dream time, decreased REM latency (increased pressure to dream), first REM period very long	Nocturnal EEG*: depressed phase-normal total sleep time and increased percentage of dream time, decreased REM latency; manic phase as in mania
Associated features	Lability of mood, depression within mania, hallucinations, delusions related with mood	Depressed facies, tearfulness, anxiety, irritability, fearfulness, brooding, phobic attacks, paranoid symptoms, delusions of poverty	As in mania and major depression in different episodes of illness

* Nocturnal electroencephalogram differentiates unipolar from bipolar depressed patients according to Hartman (1968).

and guilt, and thoughts of suicide and death. Sexual interest is greatly diminished.

When the depression is mild, environmental changes may lead to some amelioration of the condition; but, when the depression is severe, no such effect is found.

A 54-year-old woman was referred to the writer in 1968 for consideration of the institution of lithium carbonate treatment under a federally approved research protocol. The referring physician thought her illness was recurring unipolar depression but believed that the relatively normal interepisode periods could be considered mild manias. He noted that she had been recurrently depressed since age 18, and treatment with psychotherapy—both supportive and uncovering—electroshock therapy, and drugs had had only temporary success.

Her medical history revealed a very deprived childhood. The youngest of two children born to poor immigrants, the patient vividly remembered being left alone with her brother early in the morning, when both parents went to work at a job in a fruit market. She anxiously stayed at the window most of the day, waiting for her parents to return. She often went to bed hungry and was the butt of other children's taunts because of her "funny" clothes.

As adolescence approached, she made friends with wealthier girls her age. Although she was popular and invited out frequently, she always felt unliked and thought that the other girls were talking behind her back. At age 18 she developed a psychotic depressive reaction, with the delusion that her father was poisoning her orange juice and that her body was rotting away, and she was hospitalized privately. The remainder of her hospital history is reported in Table II, from which it can be seen that she had a total of 15 hospitalizations from ages 18 to 54. Some of the episodes of depression seemed precipitated by external events; some seemed spontaneous.

On admission to the hospital, the patient was depressed and anxious. She wrung her hands and repeated over and over that she was lost, she would never get well, God was punishing her for her sins. She was disoriented for time but not for person and place. Her fund of information was within normal limits for her age and station, but she answered questions haltingly. She evidenced some delusional material concerning her husband and her body. She demonstrated a typical sighing depression. Imipramine (Tofranil), 150 mg. a day, was started, and, as the psychiatrist began a lengthy year-by-year medical history, the patient gradually became less depressed. By the time she was discharged, the imipramine had been raised to 300 mg. a day.

At discharge, both the patient and her husband reported that she had never appeared so well and that they felt a whole new life was open to them. Since then, the patient has been seen at least once a month and has experienced the fatal illness and death of her husband and severe illness in her brother without any severe depressive episodes. Whenever an attempt was made to reduce the imipramine, a mild depression ensued; the depression remitted when the imipramine was raised back to its standard level of 300 mg. a day. In the 11 years of that treatment, the results of liver function tests, electrocardiograms, blood urea nitrogen tests, creatinine tests, and complete blood counts have all remained normal.

The case is a good example of recurrent major depression and its vicissitudes. Despite acute treatment by electroshock therapy, Metrazol shock therapy, and psychotherapy, recurrent depressive episodes continued until a tricyclic, imipramine, was used for prophylaxis. The results were spectacular—for the first time since her first hospitalization at age 18, the patient has been free of severe illness for 11 years. It is critical to note that any one of her depressive episodes would qualify, if found alone in a longitudinal history, as a solitary episode of major depression.

TABLE II
*History of Treatment of a Woman with Major Depression, Recurrent**

Episode	Age	Hospital Stay	Modality Used
1	18	2 months	14 Metrazol shock treatments
2	24	10 days	Supportive psychotherapy
3	27	1 month	Supportive psychotherapy
4	33	1 month	5 electroshock treatments
5	34	1 month	5 electroshock treatments
6	41	1 month	4 electroshock treatments
7	43	1 month	6 electroshock treatments
8	45	1 month	9 electroshock treatments
9	47	2 months	Supportive psychotherapy
10	48	2 months	Supportive psychotherapy
11	48	1 month	5 electroshock treatments
12	50	2 weeks	Supportive psychotherapy
13	50	10 days	Supportive psychotherapy
14	51–53	15 months	Uncovering psychotherapy
15	54	2 months	Tricyclic antidepressants and psychotherapy

* No hospitalizations from age 54 to age 65 (current age).

There are certain age-associated features of major depression. In early childhood, separation anxiety may lead to clinging behavior and school phobia. In latency and early-adolescent boys especially, negative and antisocial behavior may occur (depressive equivalents). Sexual acting out, truancy, and running away are seen in older boys and girls. In the elderly, pseudodementia—that is, depression presenting primarily as a loss of intellectual functioning—must be carefully differentiated from true dementia caused by organic mental disorder.

Laboratory findings may differentiate depressed unipolar patients from depressed bipolar patients. In unipolar depressed patients rapid eye movement (REM) latency is decreased, and the first REM period may be unusually long, but total sleep time and the percentage of dream time are decreased. In bipolar depressed patients, total sleep time is normal, dream time and the percentage of dream time is normal or increased, and REM latency is decreased.

BIPOLAR DISORDER

In bipolar affective disorder the patient's history is one of recurrent discrete periods of illness in which episodes of mania and of major depression alternate with each other.

The essential feature of a manic episode is a distinct period of intense psychophysiological activation. In that state the predominant mood is either elevated or irritable, accompanied by one or more of the following symptoms: hyperactivity, the undertaking of too many activities, lack of judgment of the consequences of actions, pressure of speech, flight of ideas, distractibility, inflated self-esteem, and hypersexuality.

The elevated mood is euphoric and often infectious in nature. The author finds that, whenever he meets a patient whose discourse quickly leads to mirth, the diagnosis is almost certain. Although uninvolved people may not recognize the unusual nature of the patient's mood, those who know the patient recognize it as not usual for the patient, or it is characteristic of the patient when high. Alternatively, the mood may be irritable, especially when the patient's activities are thwarted. Often, a patient who suffers from recurring manic episodes exhibits a change of predominant mood from euphoria early in the course of the illness to irritability later in the process.

A 54-year-old man was referred by a court for outpatient lithium treatment. He was in the midst of his fourth manic episode. His despairing wife detailed a history of increasingly severe manias that became more frequent and more intense as the patient aged. The first

manic episode occurred at age 26. At its most severe point he was only slightly high and was able to function without trouble. A decreased need for sleep—only 4 to 5 hours—and increased libido—intercourse once or twice every night—were the main symptoms observable to the wife, and they did not interfere with his business, social, or marital life. His predominant mood was euphoric, with an infectious hilarity. He remitted spontaneously in 3 to 4 weeks. No obvious precipitant could be found in his external life, and he was not known to have suffered a rebound depression afterward.

The patient remained illness free until at age 44 he suffered a mild heart attack. After a successful and uneventful convalesence, he became hypomanic 6 months after leaving the medical hospital. He became euphoric, needed only 3 or 4 hours' sleep a night, and was after his wife at all times of the day and night for intercourse, which she usually refused. He was admitted to a private psychiatric hospital, where pressure of speech was noted, without evidence of flight of ideas. His self-esteem was thought to be inflated, and increased psychomotor activity was noted, without its being considered agitation. He responded quickly to the use of phenothiazines and was discharged from the hospital within 3 weeks of admission. The patient discontinued his phenothiazines without any observable ill effects. No rebound depression was noted.

At age 52, after being illness free for 8 years, he was examined by a consulting cardiologist and advised to have a cardiac surgical procedure. The night of his examination he was sleepless and over the next 3 days gradually developed a mania characterized by sleeplessness, irritable mood, hyperactivity, and many activities showing a lack of judgment—objectionable flirtation with strangers, spending sprees, involvement in many new projects. He was admitted to a private psychiatric hospital and given eight electroshock treatments, and the mania resolved. He was discharged 1 month after admission. None of his manic activities threatened his business, social, or marital position.

The situation was very different with his most recent manic episode at age 54. Between the third and fourth episodes of mania, he had undergone the recommended cardiac surgery without any obvious psychological reaction to the procedure. The fourth manic episode developed insidiously, without obvious precipitant, and was characterized by hypersexuality, sleeplessness, loosened associations, bizarre behavior, and apparently boundless energy but involvement in poorly conceived financial projects that were to have serious consequences after the mania remitted. He refused to see a psychiatrist, let alone be admitted to a psychiatric hospital. His wife sought legal counsel, and he was admitted to a state hospital by court order under police escort. At the time of admission, he was found to be hyperactive, with pressure of speech and flight of ideas to the degree that his speech was incoherent. He was sleepless and could not sit still. Lithium carbonate and haloperidol (Haldol) were started. By the time of his court hearing, 5 working days after his admission to the hospital, his mania was in partial control, and he persuaded the judge to discharge him with the stipulation that he obtain private follow-up care and that the private psychiatrist report his progress to the court every 30 days for 3 months.

When first seen by the writer, he was irritable, paranoid, and bombastic and would not sit still. His associations were illogical, and he felt that he was persecuted by the court and his wife, he did not agree to a hospitalization, and he walked out of the office, stating that he was going to France to recoup his finances. While in France he continued to take the lithium carbonate prescribed by the state hospital (300 mg. three times a day, with blood level of 0.4 meq./L.). He developed some insight into his condition after a business acquaintance pointed out a gross error in an order, and he returned to Chicago for private hospitalization.

In the hospital he was verbally abusive, irritable, sleepless, and disordered in thought. The lithium carbonate was increased to 600 mg. four times a day, reaching a blood level of 1.4 meq./L. on the fourth day. By the sixth day he was settled down, and within 2 weeks 300 mg. of lithium carbonate four times a day assured a blood level of 0.9 meq./L. He felt much better, and his irritability and the other symptoms of the mania were absent.

After discharge the patient allowed a follow-up and agreed to lithium prophylaxis. He had many business difficulties to deal with—almost all the result of injudicious projects begun during his mania. In addition, he began to complain of symptoms of depression and, under close questioning, revealed that each of his manic episodes had been followed by a period of depression, which he had always neglected to tell his physician about when manic.

The above case illustrates well the frequent presenting symptoms of the manic patient and the change in symptom presentation often seen during the course of the illness over a lifetime. Early, the picture was predominantly one of euphoria, with few adverse social complications. Later, the picture was one of irritability, paranoia, and many social complications because of the destructive nature of the illness. Although each episode of illness was clearly a mania and the patient and his wife presented his history as recurring mania, working with the patient proved that he really had a bipolar process, not a unipolar recurring manic process, as he had stated initially. Indeed, each patient the author has seen who claimed to have had recurring mania without depression was found on closer inspection or on long-term follow-up to exhibit depression recurrently, as well as mania. Of further interest, in the above patient the first episode seemed to be spontaneous, the third episode seemed to be psychogenic, and the second and fourth episodes could be interpreted as either spontaneous or psychogenic.

In addition to mood disturbance, speech is often disturbed. As the mania gets more intense, formal and logical speech considerations are overthrown, and speech becomes loud, rapid, and difficult to interpret. As the activated state increases, speech becomes full of puns, jokes, plays on words, and irrelevancies that are at first amusing; but, as the activity level increases still more, associations become loosened. Increasing distractibility leads to flight of ideas, word salads, and neologisms. In acute manic excitement, speech may be totally incoherent and indistinguishable from that of a schizophrenic in acute catatonic excitement.

Self-esteem is inflated during a manic episode, and, as the activity level increases, the feelings about the self become increasingly disturbed. Delusional grandiose symptoms are in evidence, and the patient is willing to undertake any project possible.

A 75-year-old retired engineer with bilateral cataracts was admitted to a hospital when his resolve to drive from Chicago to Montreal alone, despite his inability to see the road signs, frightened his wife and son. He wished to attend a world congress of petroleum chemists, a field he had never worked in, because he claimed he had the answer to the gasoline shortage. On admission, he demonstrated pages devoid of writing on which his formulae, he said, were inscribed.

Nocturnal electroencephalographic findings in mania are of a decreased total sleep time and a decreased percentage of dream time, as well as an increased dream latency. Those findings may be interpreted as supportive of the hypothesis that circadian rhythm activities are delayed in mania because of an increase in the activity of the intrinsic pacemaker.

Associated features found in mania include lability of mood, with rapid shifts to brief depression. Such a finding accounts for those patients who present loosened associations and alternately laugh and cry. In addition, hallucinations of any type, ideas of reference, and frank delusions may be present. Unlike the delusions seen in schizophrenia, those seen in mania are

often fleeting and related to the level of activity of the mood, rather than to long-lasting psychological conflict.

A 24-year-old man was admitted to a hospital with the delusion that his father was trying to steal his inheritance from his dead grandfather. In addition, he heard the voice of his grandfather warning him of danger.

At age 18 the diagnosis of manic-depressive illness had been made and lithium carbonate started. He had done well under frequent medical supervision in twice-weekly psychotherapy but had discontinued therapy to move to a distant city for an attractive job. Once in the distant city he began to vary the dosage of lithium to get more energy when business crises occurred.

On admission to the hospital, he admitted he had taken little of the prescribed lithium carbonate; his blood level was 0.2 meq./L. Lithium carbonate, 1,500 mg. a day, was started. The delusion and the hallucinations remitted after 4 days, when his blood level reached 0.9 meq/L.

Often the first episode in bipolar disorder is a severe depression. If a sudden switch to mania is noted, the correct diagnosis—as in the following case—is easily made.

A 17-year-old college student was admitted to a hospital because of a progressively severe depression of 1½ months' duration. During the course of his illness, he lost all interest in the outside world, had difficulty in sleeping (trouble falling asleep and early morning awakening), and lost interest in sex, rock music, his many artistic endeavors, and the sports he loved. He felt that people hated him, as did God, and for 48 hours before admission his stepfather stayed in the same room with him because of his constant threats of suicide.

The patient's mother described him as a volatile child who would either be very productive or not at all productive. Because of difficulty in school after his parents' divorce, the patient had psychotherapy for his erratic behavior at age 14. However, before his depression at age 17, he had no periods of clinical depression; indeed, he did not react at all to his father's death, a death under questionable circumstances—some thought it was suicide—when he was 13. The mother's description of the father was consistent with the diagnosis of manic-depressive disorder.

During the early months of his hospitalization, the patient talked in an animated way but said that he could feel no feelings. Psychotherapy, without the use of drugs, was begun. He could do no school work or work on artistic projects. He slept a great deal of time, both during the day and at night. In the fourth month of his hospitalization, a friend committed suicide. The patient reacted quickly, and within 24 hours his depression switched to a mania. He was sleepless and full of unbounded energy, and he began and quickly completed the school work he had been unable to do. He engaged in countless artistic projects. The diagnosis of manic-depressive disorder was made, and lithium carbonate was started.

The mania was controlled within a week. A maintenance level of lithium carbonate was established, and the patient was discharged after an additional 2 months' hospitalization. Once out of the hospital, the patient demonstrated a success neurosis. He varied the dose of lithium to get extra energy for important projects but, in so doing, would sabotage his efforts. Although successful in his profession, he always just managed to miss a complete success.

That case is of additional interest because it illustrates the coexistence of two illnesses, manic-depressive disorder, an actual neurosis, and a psychological illness, so-called success neurosis, a form of hysteria. Although the manic-depressive disorder is within tolerable control, the hysterical process has not been dealt with adequately in the past 6 years.

Clinical Course and Prognosis

The classic study by Rennie (1942) of 208 patients admitted to Phipps Clinic between 1913 and 1916 provides a reliable source of data of the course and the prognosis of patients treated before the advent of electroshock therapy, antidepressant medications, and lithium carbonate. Of 17 manic patients, 14 had a second episode, and 11, 5, and 3 patients had a third, fourth, and fifth episode, respectively. Of 121 depressed patients, 93 had a second episode, 64 a third episode, and 36 and 18 patients a fourth and fifth episode, respectively. Of 49 cyclothymic patients, 2 had only one episode, 4 had two episodes, 6 had three episodes, and the remaining 37 patients had numerous recurrences. The first manic episode lasted an average of 3½ months, and the first depressive attack lasted an average of 6½ months. The shortest first episode was 3 days; the longest episode was 36 months. One case of chronic mania lasted 24 years. Although recurrences were found to be of about the same duration before age 45, after age 45 they become progressively longer. Of these 208 patients, 11 were known to have committed suicide and an additional 7 patients made serious but nonfatal attempts.

Most of the early literature confirms Rennie's findings. A minimal period of recovery from involutional melancholia was 9 months, but some patients took up to 7 years to recover from a severe episode. Kraepelin (1921) reported only 33 per cent remission in involutional melancholia. A dramatic reversal followed the introduction of electroshock therapy, antidepressants, and lithium carbonate. From 50 per cent to 80 per cent are currently reported to recover from involutional melancholia. In the author's experience, episodes of recurrent bipolar and unipolar illnesses are usually treatable within a short time. Prophylaxis against both unipolar and bipolar disorders is now possible. Davis (1976) summarized the accumulated evidence of the effectiveness of lithium carbonate prophylaxis in mania and depression (see Tables III and IV) and of tricyclics in recurring depression. From the data it seems negligent to fail

TABLE III

*Effectiveness of Lithium versus Placebo in Preventing Relapse of Patients with Recurrent Illness: Grouped Data of Nine Studies**

	Patients in Lithium Group	Patients in Placebo Group	Totals
No relapse	212	68	280
Relapse noted	117	262	379
Totals	329	330	659

* Based on Davis, J. W. Overview: Maintenance therapy in psychiatry. II. Affective disorders. Am. J. Psychiatry, *133:* 1, 1976.

TABLE IV

*Effectiveness of Lithium Prophylaxis in Unipolar and Bipolar Depressive Illness: Grouped Data of Four Studies**

	Bipolar Depression			Unipolar Depression		
	Lithium	No Lithium	Totals	Lithium	No Lithium	Totals
No relapse	121	35	156	56	20	76
Relapse noted	55	137	192	20	49	69
Totals	176	172	348	76	69	145

* Based on Davis, J. W. Overview: Maintenance therapy in psychiatry. II. Affective disorders. Am. J. Psychiatry, *133:* 1, 1976.

to offer prophylaxis to patients suffering from the major affective disorders unless the drugs are contraindicated by intercurrent physical illness. Without prophylactic treatment the usual course of recurring episodic affective disorders is gradual loss of social, economic, and psychological position in society.

Diagnosis

A diagnosis of the major affective disorders should be made only after finding the typical positive criteria defining episodes of the illness and only if the episode of manifest illness is clearly distinguishable from the patient's usual functioning. If the disturbance of affect is depressed, the depression must be sustained for at least 2 weeks; the diagnosis of manic episode requires a disturbance of affect lasting at least 1 week.

A manic episode is characterized by a change of mood from a usual normal mood to a predominantly elevated, expansive, or irritable mood. If the mood is elevated or expansive, at least four of the following seven symptoms should be present; if the mood is irritable, five symptoms are necessary: (1) increased activity socially, sexually, and at work; (2) increased talkativeness; (3) flight of ideas by objective examination or subjective report of racing thoughts; (4) grandiosity, at times to a delusional degree; (5) decreased need for sleep; (6) distractibility; and (7) poorly thought-out involvement in projects or activities.

A depressive episode is characterized by a change of mood from a usual normal mood to a predominantly dysphoric mood or by a loss of interest or pleasure in all or almost all of the patient's usual activities. At least four of the following symptoms should be present: (1) striking change of weight; (2) sleep difficulty, either measurable insomnia or measurable hypersomnia; (3) decreased energy; (4) psychomotor retardation or agitation, objectively observable; (5) decreased interest in usual activities or in sexuality; (6) excessive self-reproach or guilt; (7) decreased ability to think or concentrate; and (8) suicidal action or recurrent thoughts of suicide.

DSM-III requires the absence of organic mental disorders, schizophrenic symptoms, and schizoaffective symptoms for the diagnosis of a major affective disorder. The author is in disagreement, knowing instances in which a quiescent affective disorder was reactivated by steroid treatment of an organic medical condition and controlled by lithium carbonate and of complicated cases in which both a major affective disorder and a thought disorder coexisted (see Table V).

PSYCHIATRIC EXAMINATION

A complete psychiatric examination should be obtained in each case studied. The more behaviorally disturbed the patient is, the more important it is to obtain historical information from interested family members. Information so obtained must be regarded as biased, but it can still provide critically important data for the treating physician. When there is a history of a previous medical or psychiatric evaluation or treatment or the existence of psychological testing or medical work-up results, prudence dictates that the examining physician obtain that information for the safety of the patient and for the correctness of the diagnosis. Such material can be obtained only if the patient executes a valid request for the release of information from previous treating physicians, psychiatrists, psychologists, or institutions.

A 25-year-old male stockbroker entered treatment for anxiety and difficulty in making satisfying relationships with women. His medical history brought out a brief hospitalization some 4 years before. Failure to take a complete history and obtain previous records resulted in the treating psychiatrist's being unaware that the patient had frequently suffered from recurring depressive episodes during the autumn beginning at age 8. Also unknown to the treating psychiatrist was a long family history of depressive episodes in a number of relatives and the fact that the brief hospitalization had lasted 4 months and had been caused by a serious overdose of drugs. When the patient entered an anxiety state in the autumn of the second year of his once-a-week treatment, the therapist was unprepared for what followed.

TABLE V
*Diagnostic Criteria for Specific Major Affective Disorders**

Major depressive disorder	
296.2x:	Major depressive disorder, single episode. One depressive episode.
296.3x:	Major depressive disorder, recurrent. Has never had a manic disorder.
Bipolar affective disorder	
296.4x:	Bipolar affective disorder, manic. Has had one or more depressive episodes and is currently or was most recently in a manic episode.
296.5x:	Bipolar affective disorder, depressed. Has had one or more manic episodes and is currently or was most recently in a depressive episode.
296.6x:	Bipolar affective disorder, mixed. Current or most recent episode involves symptoms of both manic and depressive episodes, intermixed or rapidly alternating. Depressive symptoms last at least 1 day.

* Based on American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, ed. 3. American Psychiatric Association, Washington, D.C., 1980.

In addition, it is important to perform a complete mental status examination both to derive information relative to the current level of functioning and to provide a baseline to assess ongoing treatment results. Such an examination should be done at the beginning of treatment and at important points during the course of the treatment.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of the major affective disorders should cover both somatic and other psychological disorders.

Manic episodes

Somatic disease. Certain substances used to treat somatic illnesses may trigger a manic response. In those instances, the most common of which is the manic response to steroids, the disorder is coded as an organic affective syndrome. However, cases exist in which spontaneous manic and depressive episodes originated some years later in patients whose first illness episode seemed to be triggered by the steroids used to treat an organic illness. Other drugs are also known to have the potentiality for initiating a manic syndrome—for example, amphetamines and tricyclic antidepressants. Indeed, some psychiatrists regularly try to induce a hypomanic response in a depressed patient by administering tricyclics as a kind of therapeutic test of diagnosis. Although the logic is circular, the practice has some advantage for the patient.

Psychological disease. Two general groups of patients have manic and hypomanic-like reactions to be differentiated from true manic episodes: schizophrenics and patients with narcissistic personality disorders.

Although DSM-III precludes the diagnoses of schizophrenia

and manic-depressive disorder simultaneously, the writer is of the opinion that clear-cut cases exist in which the phenomena of both disorders are present simultaneously and the treatment of one disorder does not affect the other disorder. However, in DSM-III, mania is excluded if any of the following mood-incongruent psychotic features or, better said, symptoms of schizophrenia are present: (1) delusions of control from outside; (2) delusions of broadcasting thoughts; (3) delusions of insertion of thoughts into the patient's mind; (4) experience of withdrawal of thoughts from the patient's mind; (5) auditory hallucination of a commentary on the patient's behavior or thoughts or of a conversation between voices; (6) auditory hallucination not related to levels of depression or elation; (7) monoideatic delusions or hallucination other than those related to delusions of poverty, guilt, and self-depreciation; (8) persistence of delusions or hallucinations 1 month after the resolution of the affective state within which they were experienced.

Narcissistic personality disorder often presents with periods of euphoria and depression quite similar in content to the phenomena seen in the major affective disorders. In the personality disorder, however, the affective disturbance is solely initiated by a failure of empathy on the part of a significant object, it is fleeting, it is not as intense as in the major affective disorders, and it is amenable to interpretation.

Depressive episodes

Somatic disease. Depressive syndromes are known to occur after substance use—for example, reserpine-induced depression—and in organic illnesses—for example, cancers of all types and infectious diseases. In both cases the disorder is considered an organic affective syndrome secondary to the known causative agent. If a full-blown affective syndrome develops in reaction to a functional impairment secondary to a physical illness, the syndrome is a full-blown affective disorder, and the physical disorder is noted on Axis III and the psychosocial stressor on Axis IV.

Senile, presenile, and multiinfarct dementia must be differentiated from depressive episodes in the elderly. In the case of pseudodementia, the depression presents with symptoms mimicking an organic state that clears with appropriate treatment of the depression. In the dementias, treatment of the depression is not rewarding.

Psychological disease. Any psychological illness may present with symptoms of depression. As previously noted, the author believes that schizophrenia and major depressive disorder may coexist, but that is excluded by DSM-III. Chronic depressive and cyclothymic disorders may, according to DSM-III, have superimposed depressive episodes, and both diagnoses should be given if warranted. That situation may also be true of patients with alcoholism, somatization disorder, and anxiety disorders, including children with separation anxiety disorders that develop the full-blown clinical syndrome.

Uncomplicated bereavement is not considered a mental disorder, even if the full depressive syndrome develops, unless resolution of grief does not occur.

Treatment

The treatment of the major affective disorders is one of the most rewarding to the psychiatrist. Specific treatment is now available in the acute phase and to prevent the recurrence of both manic and depressive episodes. Nevertheless, it remains true that the therapist must always be on guard against the possibility of suicide, a possibility likely to occur when the patient begins to come out of a depression and has the energy available to act on the suicidal impulse he talked about when he was deeply depressed but lacked the energy to carry out. Because the prognosis for each individual episode is good, despite any negative results of initial treatment efforts, optimism is always warranted and welcomed by both patient and family.

HOSPITALIZATION

The first and most critical decision the physician must make is whether to hospitalize the patient or to attempt outpatient treatment. In this era, when hospitalization is discouraged by governmental authorities and third-party intermediaries, it is critical that the physician make his judgment on the basis of clinical considerations. In the presence of acute mania or acute depression, hospitalization is imperative. Acute manic excitements are life threatening, and immediate supportive measures must be instituted to prevent a fatal outcome. In the presence of a history of rapidly progressing symptoms and rupture of the usual support systems in the environment, hospitalization is also strongly indicated.

Mild depression or mild hypomania may be safely treated in the office if the physician evaluates the patient frequently, there are no signs of lapses of judgment or of weight loss and insomnia, and the environmental support system is considered strong and neither overinvolved with nor withdrawing from the patient. Situations between those extremes require careful and frequent evaluation. The dictum that, in the presence of the history of a previous episode, the current episode will be of the same or greater severity and duration may be misleading. Some interpret such a dictum too literally and do not evaluate the day-to-day situation as carefully as possible. In all cases, any sign of a change for the worse in symptoms, external behavior, or attitude of the environment toward the patient is sufficient to warrant a hospitalization.

SOMATOTHERAPIES

Electroconvulsive therapy. Electroconvulsive therapy (ECT) is regarded by many as a specific therapy for those retarded depressions characterized by somatic delusions and delusional guilt accompanied by a lack of interest in the world, suicidal ideation, and weight loss. It is also used in less severe depression that is resistant to antidepressant drugs. Historically, the emergence of antidepressant drugs lessened the use of ECT in depression. In many respects that was unfortunate, for, although ECT has the reputation of being barbaric and brutal, morbidity and mortality after its use have been reported to be lower than that seen in the use of antidepressants. In addition, ECT is used to terminate a mania when all other measures fail.

In experienced hands ECT is quite safe. Unilateral (D'Elia and Raotma, 1975; Squire, 1977) or bilateral shock can be given by using a variety of sources. Complications can be reduced by drying the respiratory and gastrointestinal systems (nothing by mouth after midnight, use of atropine sulfate as a premedication), paralyzing the musculature just before the shock itself (use of curare or curare-like drugs with forced oxygen breathing while the muscles of respiration are paralyzed), and providing appropriate pressure manually to keep the chemically modified convulsion under complete control. The patient to whom ECT is to be administered must be evaluated to detect cardiac, cerebral, and other abnormalities. In the presence of organic illness, a medical consultation is imperative. Severe medical illness is not necessarily a contraindication to ECT. The author once successfully gave ECT to a

depressed woman in an operating room with a cardiologist and a surgeon in attendance. The patient was depressed after a myocardial infarction, and her cardiologist considered the use of antidepressant drugs as unsafe. The ECT resulted in no complications, and the depression was alleviated.

There are no general rules as to the frequency and the strength of shocks needed to induce a remission. Some authors state that 8 to 12 treatments suffice, but often 16 to 20 are needed. Each case is different and must be carefully evaluated. In the author's experience with bilateral ECT, an appropriate end point is relief of depression, with concurrent loss of recent memory. Such a memory loss empirically signifies that the treatment will hold, and the relief of depression remains in effect for a significant period of time. When ECT is given to a depressed patient with manic potential, hypomanic or manic responses may often be seen after one, two, or three shocks.

Sleep therapy. Narcosis induced by barbiturates or other hypnotics was once nearly the treatment of choice for manic episodes. That treatment is rarely used in this age of effective antipsychotic and antimanic drug therapies, but it may play an ancillary role in acute manic excitements.

A 45-year-old woman developed an acute manic excitement after receiving word that her lover was taking a younger woman. She paced the hospital unit, sweating profusely, with widely dilated eyes and wild incoherent speech. Her clothes were sopping wet with perspiration. Her blood pressure was 220 over 140; her pulse rate was 180 or faster; her respiratory rate was 60. She was sedated with an intramuscular injection of paraldehyde, and two intravenous infusions were used to replenish the fluids and the electrolytes excreted through perspiration. The process was controlled within 6 hours, but she was amnesic for the episode. Once the episode was controlled, her blood pressure was 120 over 80, her pulse rate was 72, and her respiratory rate was 20.

Hydrotherapy. Another remnant of a past era is hydrotherapy, once used for manic and hypomanic states. Mild agitation may still yield to the gentle play of water on the body, either through frequent showers or by a steady influx of water into a tub replacing an equal amount of efflux. Such measures should not be used alone unless the case is quite mild.

Psychopharmacological agents

Antidepressant drugs. Table VI lists some of the common antidepressant drugs and their approximate daily dose range.

TABLE VI
Approximate Daily Dose Range of Antidepressant Drugs

Chemical Group	Range
	mg./day
Tricyclic antidepressants	
Amitriptyline (Endep, Elavil, Etrafon)	75 to 300
Desipramine (Pertofrane, Norpramine)	75 to 200
Doxepin (Adapin, Sinequan)	75 to 300
Imipramine (Imavate, Tofranil, Presamine)	75 to 300
Nortriptyline (Aventyl)	40 to 100
Protriptyline (Vivactil)	30 to 60
Monoamine oxidase inhibitors	
Tranylcypromine (Parnate)	20 to 30
Isocarboxazid (Marplan)	Initially 30, reduce to 5 to 30 (lowest possible)

In the case of the tricyclic antidepressants, the exact dose needed to obtain a therapeutic effect is variable and may be related to individual variations in the drug's rate of metabolism. The relationship of drug blood level and therapeutic response is under investigation in many centers. It is generally agreed that antidepressant drugs should be started at a low dose and increased gradually until a therapeutic effect is obtained, unpleasant side effects (usually attributable to anticholinergic activity) occur, or the highest recommended dose does not lead to a remission of the depression. When a therapeutic effect is obtained, the drug is decreased to about half the therapeutic level for at least 2 months. In all, the patient should be on the antidepressant medication for 6 asymptomatic months. When an antidepressant is discontinued, the dosage should be gradually reduced to avoid unpleasant side effects.

The monoamine oxidase (MAO) inhibitors are considered relatively dangerous drugs, because of their potentiation of sympathomimetic substances, such as amphetamines, dopamine, norepinephrine, tryptophan, and tyramine. The last two substances are particularly dangerous because of their occurrence in cheeses, beers, wines, chicken livers, and other foods.

A 56-year-old severely depressed woman did not respond to psychotherapy or to tricyclic antidepressant treatment or to both combined. Nine months after admission to a hospital, she was started on a MAO inhibitor and, although warned of the foods she should not eat, ate a salad that, unknown to her, had cheese in the dressing.

She responded with a hypertensive crisis, followed by shock, and she ultimately experienced renal shutdown, hepatitis, and pericarditis. When the organic complication cleared, she was still depressed but responded to a course of 12 electroconvulsive treatments.

When changing from tricyclic drugs to MAO inhibitors, the therapist should allow 7 days of a drug-free state to intervene.

Stimulant drugs, amphetamines, and the like are not recommended for deep depressions because of their addictive potential and the numerous side effects that may ensue if used in the large dosages and for the lengthy periods necessary to resolve such depressions.

The author recommends that the psychiatrist become familiar with the use of one or two tricyclics and one MAO inhibitor. Most cases presented for treatment can be handled successfully with such an armamentarium.

Antimanic drugs. Rauwolfia alkaloids were introduced in the 1950's to control agitation, but they are not presently used in manic states. Phenothiazines and butyrophenones, replacing the reliable paraldehyde of the past, are used to control severely agitated patients because the effect is immediate if the drug is given intramuscularly.

However, the treatment of choice in the acute manic episode, short of a manic excitement, is lithium carbonate. Before treatment is begun, evaluation of renal, cardiac, and organic cerebral function must be done. If any significant illness is found, the possible benefits of treatment with lithium must be weighed against the possible harm to the diseased organ system. Often, the decision to treat or not to treat with lithium is a joint decision of the psychiatrist and the patient's internist.

Control of an acute manic state with lithium is similar to the control of diabetes mellitus with insulin. Enough lithium must be given so that the manic symptoms are controlled without the development of debilitating side effects—nausea, vomiting, tremor, and diarrhea in mild cases and cardiorespiratory and central nervous system symptoms in more severe cases. Once the mania yields to lithium treatment, the dose must be reduced so that side effects do not develop. A given oral dose of lithium

that controls acute mania with serum lithium levels in a given range, without side effects, will cause side effects and an elevated serum lithium level when the mania passes. It is operationally as if the lithium were titrating a hypothetical quantity of mania in the central nervous system, and, once an equilibrium is reached, the mania is controlled, and the blood lithium rises, leading to peripheral side effects.

In practice, the usual dose of lithium carbonate needed to control a mania ranges from 1 gm. to 3 gm. for 5 to 10 days. A serum level of from 0.8 meq./L. to 1.8 meq./L. of lithium usually indicates a therapeutic dose. Levels below 0.8 meq./L. usually indicate inadequate treatment; levels above 1.8 meq./L. presage the development of toxicity. During the initiation of treatment, lithium levels should be drawn every 3 to 4 days, but day-to-day clinical observation is often more effective in detecting early signs of toxicity.

In the presence of disruptive behavior, a combination of lithium and a neuroleptic may be helpful. As violent behavior decreases, the neuroleptic may be discontinued. Earlier warnings that such a combination predisposes to organic mental disorders does not seem to be borne out by recent experiences.

Once the acute mania is controlled, prophylaxis may be undertaken. While some clinicians recommend the use of prophylaxis only if the patient has three or more hospitalizations, the author feels the practitioner must weigh possible toxic effects of the drug against possible disruption of the patient's life by recurrent illness. If prophylaxis is decided upon, the high dose of lithium used in the acute phase is lowered until an oral dose is found at which side effects are minimal or absent, symptoms are absent, and plasma lithium levels fall between 0.6 meq./L. and 1.2 meq./L. The exact amount of drug necessary to achieve that state varies from person to person and in one person from time to time. It is as if, operationally, lithium were being given to flatten out the highs and lows of an unknown psychophysiological cycle in the form of a sine wave; when the cycle starts up or down, more lithium than at other times is necessary to maintain the patient symptom free. Indeed, the presence of a prodromal symptom state (Wolpert, 1975) suggests the need to briefly increase the oral dose of lithium to control the threatened mania. The author attempts to teach his patients to recognize their unique prodromal states, because, if present, those states serve as useful indicators of an incipient change in activity level and, hence, of a need to increase lithium. The author recommends that, once on lithium, the patient be taught to expect to remain on lithium throughout his or her lifetime, as long as physical illness does not make such a regimen impractical.

Once stabilized, the patient may be checked relatively infrequently if clinical conditions warrant. The author has patients with uncomplicated illness who, once on stable prophylactic doses, are seen yearly. Other patients are seen monthly. Lithium levels are obtained as needed. Thyroid and kidney functions are checked at least yearly. At present, there is much concern that interstitial nephritis may be a late result of lithium treatment, and several centers are engaged in studying the issue. Lithium-unmasked thyroid deficiency and lithium-induced nephrogenic diabetes insipidus are frequently encountered.

Other effects of lithium treatment to be taken into account are the development of diffuse nontoxic goiter, decreased glucose tolerance, elevated white blood count, and lithium-induced delirium, especially in patients with schizoaffective illness. Although the incidence of lithium-induced birth defects is not accurately known, prudence dictates that women not in gross manic states not be on lithium during pregnancy. Breast-feeding mothers should not be on lithium because lithium is selectively excreted in breast milk.

In general, lithium is released by the Food and Drug Administration only for the treatment of acute mania and for the prevention of manic-depressive states in patients older than 12. Although the treating physician is the final judge of what is best for his patient, he must be prepared to defend any deviation from usual and customary treatment.

PSYCHOTHERAPY

In the author's experience psychotherapy is essential to at least supplement drug treatments in those cases in which the patient seems to suffer from a basically physiological form of the illness, and psychotherapy is absolutely central to the treatment of those patients who seem to have a psychological illness in addition to the physiological illness. As in the cases of the 17- and 24-year-old manic men cited earlier, some self-destructive, ambitious, early-onset manic-depressives easily manipulate their doses of lithium in an apparent attempt to increase their energy level, while actually sabotaging their work efforts. Without effective psychotherapy, those patients destroy their careers. Other patients need to isolate a loss experience, triggering an episode of illness to detoxify such experiences. Thus, psychotherapy may range from analytic procedure to supportive care. In some cases the psychiatrist's treatment of the manic-depressive with lithium resembles the internist's treatment of the diabetic with insulin.

EVALUATION OF TREATMENT

Generally, the literature indicates that severe acute depression responds well to ECT (Zung, 1968), less severe depression responds well to tricyclics (Post, 1972), and lithium or tricyclics can be useful prophylactic agents against depression (Davis, 1976). Acute mania responds to neuroleptics and lithium, and lithium is prophylactic against recurrences of mania.

Most of the evaluative studies of lithium reported have originated from lithium or other types of clinics. How good can the private practitioner expect his own results to be? Wolpert and his associates (1979) studied the use of lithium carbonate in the private practices of psychiatrists associated with the Psychosomatic and Psychiatric Institute of Michael Reese Hospital. Their data, based on 74 patients, indicated that lithium was successful in controlling acute bipolar illness in 82 per cent of all cases and was successful in 72 per cent of cases in preventing severe, hospitalized recurrences but was less successful in preventing less severe mood swings. The incidence of side effects, 65 per cent, was considerable. In an analysis of personal follow-up interviews, it became clear that treatment failures were due to the inability of individual psychiatrists to view their patients as having needs both in the physiological sphere and in the psychological sphere; treatment of one and not of the other was insufficient.

Suggested Cross References

An overview of affective disorders is found in Section 18.1. Other specific affective disorders are discussed in Section 18.3, schizoaffective disorders in Chapter 17, and other affective disorders in Chapter 19. Schizophrenic disorders are discussed in Chapter 15 and personality disorders in Chapter 22. Nosology is discussed in Section 14.1. Historical trends in psychiatry are described in Section 1.1. Freud's theories are discussed in

Chapter 8. Biological rhythms in psychiatry are covered in Section 2.6 and psychopharmacology in Chapter 31.

REFERENCES

Abraham, K. Notes on the psychoanalytical investigation and treatment of manic-depressive insanity and allied conditions (1912). In *Selected Papers of Karl Abraham,* p. 137. Hogarth Press, London, 1968a.

Abraham, K. A short study of the libido, viewed in the light of mental disorders (1924). In *Selected Papers of Karl Abraham,* p. 418. Hogarth Press, London, 1968b.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders,* ed. 3. American Psychiatric Association, Washington, D.C., 1980.

Angst, J. Zur Atiologie und Noslogy endogener depressiver. Psychosen. Monogr. Gesamtgeb. Neurol. Psychiatr., *112:* 1, 1966.

Arieti, S. Manic depressive psychosis. In *American Handbook of Psychiatry,* S. Arieti, editor, vol. 1, p. 419. Basic Books, New York, 1959.

Bellak, L., Pasquarelli, B., Parkes, E., Bellak, S. S., and Braverman, S. *Manic-Depressive Psychosis and Allied Conditions.* Grune & Stratton, New York, 1952.

Berger, P. A. Medical treatment of mental illness. Science, *200:* 974, 1978.

Bunney, W. E., Jr., moderator. The switch process in manic-depressive psychosis. Ann. Intern. Med., *87:* 319, 1977.

Bunney, W. E., Jr., Mason, J. W., Roatch, J. F., and Hamburg, D. A. A psychoendocrine study of severe psychotic depressive crises. Am. J. Psychiatry, *122:* 72, 1965.

Cohen, M. B., Baker G., Cohen, R. A., Fromm-Reichman, F., and Weigert, E. V. An intensive study of twelve cases of manic-depressive psychosis. Psychiatry, *17:* 103, 1954.

Cohen, R. A. Manic depressive illness. In *Comprehensive Textbook of Psychiatry,* A. M. Freedman, H. I. Kaplan; and B. J. Sadock, editors; ed. 2, p. 1012. Williams & Wilkins, Baltimore, 1975.

* Davis, J. M. Overview: Maintenance therapy in psychiatry. II. Affective disorders. Am. J. Psychiatry, *133:* 1, 1976.

Davis, J. M., Janowsky, D. S., and El-Yousef, M. K. The use of lithium in clinical psychiatry. Psychiatr. Ann., *3:* 78, 1973.

D'Elia, G., and Raotma, H. Is unilateral ECT less effective than bilateral ECT? Br. J. Psychiatry, *126:* 83, 1975.

Engelmann, W. A slowing down of circadian rhythm by lithium ions. Z. Naturforsch., *28:* 733, 1973.

Feinstein, S., and Wolpert, E. A. Juvenile manic-depressive illness: Clinical and therapeutic considerations. J. Am. Acad. Child Psychiatry, *12:* 123, 1973.

Freud, S. Mourning and melancholia (1917a). In *Standard Edition of the Complete Psychological Works of Sigmund Freud,* vol. 4, p. 152. Hogarth Press, London, 1957.

Freud, S. Introductory lectures on psychoanalysis. Part III. General theory of the neuroses. Lecture XXIV (1917b). In *Standard Edition of the Complete Psychological Works of Sigmund Freud,* vol. 16, p. 378. Hogarth Press, London, 1959.

* Gershon, S., and Shopsin, B. *Lithium: Its Role in Psychiatric Research and Treatment.* Plenum Publishing Corp., New York, 1973.

Gibson, R. W., Cohen, M. B., and Cohen, R. A. On the dynamics of the manic depressive personality. Am. J. Psychiatry, *115:* 1101, 1959.

Goodwin, F. K., and Bunney W. E., Jr. A psychobiological approach to affective illness. Psychiatr. Ann., *3:* 19, 1973.

Grinker, R. R., Sr., Miller, J., Sabshin, M., Nunn, R., and Nunnally, J. C. *The Phenomena of Depressions.* Harper & Row, New York, 1961.

Hartman, E. Longitudinal studies of sleep and dream patterns in manic depressive patients. Arch. Gen. Psychiatry, *19:* 312, 1968.

Hoch, P. H., and Zubin, J., editors. *Depression.* Grune & Stratton, New York, 1954.

Jacobson, J. The hypomanic alert: A program designed for greater therapeutic control. Am. J. Psychiatry, *122:* 295, 1965.

Jefferson, J. W., and Greist, J. H. *Primer of Lithium Therapy.* Williams & Wilkins, Baltimore, 1977.

Jovanovic U. Chronobiologic aspects of psychiatry. Waking Sleeping, *1:* 335, 1977.

Klerman, G. L., and Barrett, H. The affective disorders: Clinical and epidemiological aspects. In *Lithium: Its Role in Psychiatric Treatment and Research,* S. Gershon and B. Shopsin, editors, p. 201. Plenum Publishing Corp., New York, 1975.

Kohut, H. *The Analysis of the Self.* International Universities Press, New York, 1971.

* Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* E. and S. Livingstone, Edinburgh, 1921.

Kretchmer, E. *Korperbau und Charakter.* Springer, Berlin, 1921.

Lange, J. Die Endogene und Reaktiven Germutserkrank Heiten und die Manisch-Depressive Konstituten. II. In *Handbuch der Geisteskrank Heiten* (VI spez. teil 2), O. Bumke, editor. Springer, Berlin, 1928.

Leonhard, K. *Aufteilung der Endogenen Psychosen.* Acadamie-Verlag, Berlin, 1957.

Leonhard, K., Korff, I., and Schulz, H. Temperaments in the families of monopolar and bipolar phasic psychoses. Psychiatr. Neurol., *143:* 416, 1962.

Maas, J. W. Biogenic amines and depression: Biochemical and pharmacological separation of two types of depression. Arch. Gen. Psychiatry, *32:* 1357, 1975.

Mendlewicz, J., Fieve, R. R., Rainer, J. D., and Fleiss, J. I. Manic-depressive illness: A comparison study of patients with and without a family history. Br. J. Psychiatry, *120:* 523, 1972.

Ostrow, D., Pandey, G., Davis, J., Hurt, S., and Tosteson, D. A heritable disorder of lithium transport in erythrocytes of a subpopulation of manic-depressive patients. Am. J. Psychiatry, *135:* 1070, 1978.

Pao, P. N. On manic-depressive psychosis: A study of the transition of states. J. Am. Psychoanal. Assoc., *16:* 809, 1968.

Perris, C., editor. A study of bipolar (manic-depressive) and unipolar recurrent depressive psychoses. Acta Psychiatr. Scand., *42:* 1, 1966.

Perris, C. The course of depressive psychoses. Acta Psychiatr. Scand., *44:* 238, 1968.

Post, F. The management and nature of depressive illnesses in late life: A follow through study. Br. J. Psychiatry, *121:* 393, 1972.

Prange, A. J., Jr. The use of drugs in depression: Its theoretical and practical basis. Psychiatr. Ann., *3:* 19, 1973.

Preodor, E., and Wolpert, E. A. Manic-depressive illness in adolescence. Am. J. Youth Adoles., *8:* 111, 1979.

Reich, T., Clayton, R. S., and Winokur, G. Family history studies. V. The genetics of mania. Am. J. Psychiatry, *125:* 64, 1969.

Rennie, T. A. C. Prognosis in manic-depressive psychosis. Am. J. Psychiatry, *98:* 801, 1942.

Schildkraut, J. J. *Neuropsychopharmacology and the Affective Disorders.* Little, Brown, and Co., Boston, 1970.

Schildkraut, J., and Kety, S. Biogenic amines and emotion. Science, *156:* 21, 1967.

Sheldon, W. H., and Stevens, S. S. *The Varieties of Temperament,* Harper & Row, New York, 1942.

Sheldon, W. H., Stevens, S. S. and Tucker, W. B. *The Varieties of Human Physique.* Harper & Row, New York, 1940.

Slater, E. The genetics of manic-depressive insanity: The parents and children of manic-depressives. Z. Gesamte Neurol. Psychiatr., *163:* 1, 1938.

Slater, E., and Cowie, V. *The Genetics of Mental Disorders.* Oxford University Press, New York, 1971.

Squire, L. R. ECT and memory loss. Am. J. Psychiatry, *134:* 9, 1977.

Stenstedt, A. A study in manic-depressive psychoses: Clinical, social and genetic investigations. Acta Psychiatr. Scand., *79* (Suppl.): 197, 1952.

Tsuang, M. T. Schizophrenia and affective disorders: One illness or many. In *Biology of the Major Psychoses,* D. X. Freedman, editor, p. 27. Raven Press, New York, 1975.

Wehr, T. A. Phase and biorhythm studies of affective illness. Ann. Intern. Med., *87:* 321, 1977.

Wertham, F. A group of benign chronic psychoses: Prolonged manic excitements. Am. J. Psychiatry, *86:* 17, 1929.

Winokur, G. Diagnostic and genetic aspects of affective illness. Psychiatr. Ann. *3:* 6, 1973.

Winokur, G., and Clayton, P. Family history studies. II. Two types of affective disorders separated according to genetic and clinical factors. In *Recent Advances in Biological Psychiatry,* J. Wortis, editor, vol. 9, p. 35. Plenum Publishing Corp., New York, 1967.

* Winokur, G., Clayton, P. J., and Reich, T. *Manic-Depressive Illness.* C. V. Mosby, St. Louis, 1969.

Winokur G., and Tanna, V. Possible role of X-linked dominant factor in manic depressive disease. Dis. Nerv. Syst., *30:* 89, 1969.

Wolpert, E. A. Manic depressive illness as an actual neurosis. In *Depression and Human Existence,* E. Anthony and T. Benedek, editors, p. 199. Little, Brown, and Co., Boston, 1975.

* Wolpert, E. A. *Manic-Depressive Illness: History of a Syndrome.* International Universities Press, New York, 1977a.

Wolpert, E. A. Nontoxic hyperlithemia in impending mania. Am. J. Psychiatry, *134:* 580, 1977b.

Wolpert, E. A. Manic-depressive illness: The relations of biology to psychology. In *Developments in Psychiatry.* Vol. II: *Biological Psychiatry Today,* J. Obioles, C. Ballus, E. Gonzalez Monclus, and J. Pujol, editors, part A., p. 530. Elsevier, Amsterdam, 1979.

Wolpert, E. A., Wolpert, G. Y., Holinger, P. G., and Preodor, D. A follow-up study of lithium carbonate treatment of manic-depressive illness. In *Developments in Psychiatry.* Vol. II: *Biological Psychiatry Today,* J. Obioles, C. Ballus, E. Gonzalez Monclus, and J. Pujol, editors, part B., p. 1111. Elsevier, Amsterdam, 1979.

Zung, W. W. K. Evaluating treatment methods for depressive disorders. Am. J. Psychiatry, *124:* 40, 1968.

18.3 Other Specific Affective Disorders

GERALD L. KLERMAN, M.D.

Introduction

Most patients experience affective disorders as episodic; after a time-limited period of symptoms, they return to their normal state. A majority of patients with episodes of affective disorder, whether depression or mania, experience them as brief episodes. Various factors—for example, therapeutic efficacy, inherent constitutional mechanisms, or social supports—may be responsible for the abatement of symptoms. Many patients, however, have recurrences after a symptom-free interval.

In recent years it has become increasingly recognized that a significant proportion of patients suffer from chronic affective disorders, either dysthymic or cyclothymic disorder. Although the two disorders are grouped together in terms of their common clinical course, there is no presumption as to common causes or single treatment. Cyclothymic disorder is probably a mild manifestation of bipolar disorder. Dysthymic disorder probably represents the common clinical outcome of acute depressions of multiple causes, including bipolar major depressive episodes as well as various forms of secondary depressions.

Dysthymic Disorder

Clinical experience and numerous studies have shown that most depressions are episodic. Although a large proportion of adults experience acute depressions—usually without coming to the attention of physicians, let alone psychiatrists—a significant percentage experience their condition as chronic.

For example, Barrett et al. (1978) reporting on a survey of 293 nonpatient air traffic controllers found that a significant percentage, almost 30 per cent, reported some degree of depression during at least 1 month of the year. The vast majority had symptoms that were nonpsychotic and of relatively short duration. Only a small percentage sought medical attention. However, about 9 per cent had been bothered by an enduring depressed mood, with only intermittent periods of normal feeling state during the year of observation. Similarly, Weissman and Klerman (1977a), in a follow-up study of 150 patients treated for acute depression, found that about 12 per cent had a chronic cause that, although distressing, was not sufficiently disabling to require hospitalization.

Most chronic depressions probably represent the inadequately recognized and poorly treated residual of unresolved or partially remitted acute depressions. As the studies summarized in Table I indicate, about 15 to 20 per cent of patients experiencing acute depressions do not make a complete recovery but show some intermittent, fluctuating, and chronic symptoms, often persisting for years.

TABLE I
Studies Reporting Depressed Patients with a Chronic Course†*

Year of Publication	Investigators	Number	Duration of Follow-Up (Years)	Percentage Chronic
1921	Kraepelin	899	10–40	4–5
1945	Lundquist	638	20	9
1948a	Huston, Locher	80	6.8	9
1948b	Huston, Locher	93	6.5	18
1952	Stenstedt	216	2–20	1–14
1956	Watts	387	Up to 8	14
1959	Astrup et al.	278	7–19	8
1968	Bratfos, Haug	207	1–12	28
1973	Morrison et al.	202	4.3	20
1974	Murphy et al.	43	2.8–6.5	16
1974	Paykel et al.	190	0.8	21

* Studies up to 1968 are taken from Robins and Guze (1972). In general, "chronic course" was defined as the patient's having been continuously symptomatic during the observation period or until death. With the exception of the Watts and Paykel et al. studies, which included both inpatients and outpatients, all studies dealt exclusively with inpatients.

† From Weissman, M. M., and Klerman, G. L. The chronic depressive in the community: Unrecognized and poorly treated. Compr. Psychiatry, *18:* 523, 1977a.

DEFINITION

The creation of a separate category in the third edition of the American Psychiatric Association's (1980) *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) for patients with dysthymic disorder (depressive neurosis) represents an important step forward. This advance in diagnosis is particularly important in the era of community psychiatric treatment, inasmuch as most of the patients are not institutionalized and are able to continue in the community. Although they have moderate to severe fluctuating symptom levels, they are able to maintain some degree of occupational, family, and community roles. However, their emotional distress affects their families, co-workers, and friends, since the patients often have serious impairments in social functioning. Many are heavy users of the health care system. A significant proportion complain predominantly of hypochondriacal and bodily ailments and pose major diagnostic and therapeutic problems.

The essential feature of dysthymic disorder is a chronic nonpsychotic disturbance involving depressed mood or a loss of interest or pleasure in all or almost all usual activities and pastimes. Usually, associated symptoms are not of sufficient severity to meet the criteria for major depression.

Dysthymic disorder is defined as a long-standing illness of at least 2 years' duration with either sustained or intermittent disturbances in depressed mood and associated symptoms. The disorder may begin in early adult life, often without a clear onset. In the past, patients with this disorder included those with depressive neurosis. Subgroups include patients with masked depression or depressive equivalents.

EPIDEMIOLOGY

Since this is a relatively new diagnostic category, precise data as to incidence and prevalence are lacking. However, a number of studies have indicated that it is a relatively common condition. Hornstra and Klassen (1977) reported a 1-year prevalence of 47 to 105 per 1,000, on the basis of a community survey in Kansas City. Barrett et al. (1978) reported a 1-year prevalence of 60 per 1,000. Weissman and Myers (1978) reported a lifetime prevalence of about 45 per 1,000, using the Research Diagnostic Criteria (Spitzer et al., 1978) for depressive personality, which is similar to the clinical characteristics for dysthymic disorder in DSM-III. It is likely that more

accurate figures will become available as the specific criteria embodied in DSM-III are used in epidemiological studies.

Almost all American studies of depressions report a predominance of women over men in the ratio of two or three to one. That finding is reported also in European studies, including those from England, Bulgaria, and Scandinavia. A detailed discussion of the importance of sex ratio and the predominance of women in all forms of depressive conditions appears in the study by Weissman and Klerman (1977b).

Data on familial patterns are lacking. Insufficient studies using precise diagnostic criteria have been conducted to allow any conclusions. It is likely that family studies will show an excess of first-degree relatives with various forms of affective disorder. Whether they will be specific for unipolar or bipolar forms of affective disorder is not clear. In view of the heterogeneity of onset, homogeneous subgroups will be necessary to establish familial patterns and possible genetic factors (Winokur et al., 1978).

CAUSES

The theories and hypotheses proposed as to causation follow those for affective disorders in general.

Personality characteristics. The large number of patients with depression whose onset is in the late teens and young adulthood suggests psychodynamic features, particularly those related to faulty personality and ego development culminating in difficulty in adaptation to adolescence and young adulthood.

The role of personality in depression has been given considerable attention by the psychiatric community. In a review of psychoanalytic theories of depression and personality, Chodoff (1972) concluded that undue interpersonal dependency and obsessionality often predispose to depression. Several newer approaches from cognitive and behavioral theories have also been applied to depression. Most notable have been the ideas of Beck (1972), Seligman (1974), and Lewinsohn (1974).

In contrast to the theoretical approaches that emphasize predisposition, two alternate formulations about the relationship of personality and depression should be considered: (1) Certain personality features and certain psychiatric disorders—whether genetic, developmental, or familial—may be manifestations of the same underlying process. That is, a personality trait may represent a subclinical expression of a psychiatric disorder, such as bipolar disorder. If that trait has a familial or genetic basis, one expects to find an increased frequency of the trait among relatives, both affected and nonaffected, as well as in patients. (2) Personality qualities may be altered by the experience of the chronic and recurrent affective disorder. Chronic diseases, both medical and psychiatric, often lead to changes in individual personality patterns. The precise extent to which the change may occur in chronic depressions is at present unknown. Kahn (1975) described several pervasive personality traits, especially low self-esteem, that are strongly associated with what he called "the depressive character." Weissman and Paykel (1974) found that personality features such as dependency, guilt, and passivity did not return to normal levels, even though symptom relapse and remission had occurred.

Psychosocial factors. Differences of opinions exist as to the role of psychosocial stressors as precipitants of chronic episodes. One hypothesis (Weissman and Klerman, 1977a) is that the chronic disorder represents the poorly treated or partially resolved residua of prior acute depressions in adult life that likely had psychosocial precipitants. On the other hand, Hornstra and Klassen (1977) in their Kansas City community survey found no relationship between life stress and the depressive symptoms of an enduring nature.

Physiological causes. Many of the chronic conditions may represent the residual effects of secondary depressions due to the chronic use of alcohol, amphetamines, or barbiturates or may be related to long-standing medical illness, such as gastrointestinal, arthritis, thyroid, and other endocrine disorders.

CLINICAL FEATURES

The essential feature of dysthymic disorder is a long-standing nonpsychotic symptom complex of at least 2 years' duration. The major predominant symptom is that of depressed mood. In addition, there is often a loss of interest or pleasure in all or almost all usual activities, pastimes, and sources of pleasure.

The depressed mood may be characterized by the patient's reporting himself as feeling sad, blue, down in the dumps, or low. Life may be described as dark, black, or bleak. The depressed mood and associated features may be either relatively persistent, in which case the disorder is considered chronic, or intermittent, in which case the periods of symptoms are separated by intervals of normal mood, with the capacity to enjoy pleasure and function at some normal level of social activity. The relatively normal periods may last from a few days to a few weeks.

In distinguishing the dysthymic disorder from cyclothymia, one must ascertain whether the return to normal is experienced as a relief from depression or whether there are positive signs of euphoria, increased activity, and poor judgment, in which latter case the patient should be considered cyclothymic.

The patient may have manifestations of the nonpsychotic features of the depressive syndrome, such as impaired self-esteem, slowing of speech and thinking, and loss of appetite. Those features are usually experienced by the patient as discontinuous and ego-alien changes from his usual or former self.

During the depressive periods there are usually the various nonpsychotic and mild features of the depressive disorder. The presence of delusions and hallucinations is by definition inconsistent with the diagnosis of dysthymic disorder. Among the associated symptoms are those commonly associated with depressive episodes, including poor appetite, weight change, sleep difficulty (particularly early morning wakening), loss of energy, fatigability, psychomotor retardation, loss of interest or pleasure in activities, decreased sexual drive, decreased sexual performance, feelings of guilt and self-reproach, complaints of difficulty in thinking, indecisiveness, thoughts of suicide, feelings of helplessness and hopelessness, and pessimism.

Although the clinical presentation with predominant depressive mood, as described above, is most common, it is important to recognize a number of major variants, including the following:

Masked depressions. In patients with masked depressions (Kielholz, 1973; Lesse, 1977), the mood disturbance may not be readily apparent, but the patient may present with chronic pain, insomnia, weight loss, or other bodily complaints. That mode of presentation is most often seen by psychiatrists working in general hospitals and as consultants to medical practitioners.

Hypochondriacal and somatic complaints. A number of studies by psychiatrists working in general hospitals and outpatient medical clinics (Jacobs et al., 1968; Lipsitt, 1970) have documented that a large number of patients with recurrent diagnosed medical complaints, often called hypochondriacs or crocks, are unrecognized intermittent or chronic depressives whose ticket of admission to the health care system is through their bodily complaints. They are usually middle-aged and elderly patients, most often women. They are often referred from one specialty clinic or specialist to another, especially

those related to gynecology, thyroid and other endocrine disorders, gastrointestinal functioning, and arthritis and rheumatic complaints.

Pessimism and hopelessness. Patients with helplessness, pessimism, and discouragement represent another mode of presentation. The difficulties may be directed against the self—as with feelings of self-reproach, low self-esteem, and feelings of failure in life—or inadequate functioning at work or in marriage. Such patients may be labeled as masochistic personalities. On the other hand, their pessimism may be directed outward, with tirades against the world and feelings of having been treated poorly by relatives, children, parents, work, colleagues, or the system. It is important to distinguish those pessimistic depressed patients from paranoid patients, the difference being that the depressives do not have a sense of malicious intent directed at them, as do paranoid persons.

Alcohol abuse. Clinicians must recognize that a high percentage of chronic alcoholics develop secondary depressions. The rates range from 25 to 50 per cent (Pottenger et al., 1978). Whether the depression is psychogenic or pharmacological-toxic in cause is not certain. Guze and other members of the St. Louis group (Guze et al., 1971) believed that the chronic depression of alcoholism, associated with as many as 50 per cent of a large series of alcoholics, was due to a toxic pharmacological effect of alcohol on the central nervous system. The depressive features come after long periods of heavy drinking, often during the rehabilitative phase after acute withdrawal states.

Drug ingestion. Selected drugs—particularly the steroids, amphetamines, barbiturates, and other central nervous system depressants—are known to produce depression after periods of heavy use. A chronic depression secondary to heroin use or long-term methadone use has also been described.

COURSE AND PROGNOSIS

Age of onset. A review of the clinical course reveals important differences related to the age of onset.

Many patients report that their depressive symptoms began in late adolescence or young adulthood and that the symptoms have been of a chronic nature for such long periods as to have become ingrained as part of their characters. A distinction should be drawn between personality features predisposing to depression (Chodoff, 1972) and the clinical personality disorder with guilt, dependency, irritability, and passivity. It is possible for patients to have both conditions—dysthymic disorder and personality constellations predisposing to affective disorders (Chodoff, 1972). In patients with onset early in life, it is important to reconstruct the history carefully, seeking episodes of acute onset, especially in the transition from adolescence to young adulthood. The family history is also valuable to detect a history of affective disorders, since dysthymic patients may have mild forms of major depression whose severity has not been sufficient to reach the criteria for classification as major depression.

The most common period of onset is in maturity and middle age. Such patients give a history of a relatively good social adjustment and normal mood through adolescence and young adulthood, with a gradual or insidious onset of depressive symptoms or poorly remembered episodes of acute depression or residual symptoms after the grief reaction to the death of a parent, sibling, or child. A careful history may reveal that there has, in fact, been an impairment of marital functioning—with disputes, irritability, and poor sexual functioning—impairment of parental functioning—particularly with teenage children (Weissman and Paykel, 1974)—or impairment of occupational functioning.

Onset in old age is often a difficult diagnostic problem because of the need to differentiate depressive pseudodementia from dementia. Many elderly patients present with an impairment of cognitive functions, complaints of decreased memory, inability to concentrate, poor attention, and slowing of functioning. The differential diagnosis of dementia due to central nervous system disorders, such as Huntington's chorea or—more often—senile brain disease, may be difficult. The disorders may coexist, and the issue is not so much dementia versus depression as the coexistence of the two disorders.

Suicide. In all affective disorders, there is an increased risk of suicide. Attention should be given to probing for potential suicide, reconstructing the history of previous suicide attempts, eliciting suicidal ideation, and exploring suicidal fantasies. If they exist, attention should be given to the history of the use of medication, particularly since suicide-prone patients are often heavy users of the health care system. They show a tendency to accumulate partially used bottles of medication. Attention should also be given to accident proneness, particularly in automobile driving.

High risk for medical illnesses. Patients with chronic and intermittent depressions are probably at greater risk for serious medical illnesses than are other persons. Studies indicate a higher than average death rate, often due to cardiovascular disease (Avery and Winokur, 1976). Some suggestions have been made that such patients may be more prone than average to cancer; perhaps there is no true increase in incidence but an increased mortality because depressed persons delay seeking medical attention or are misdiagnosed because of their previous history of chronic complaints.

Hospitalization. Mental hospitalization for dysthymic disorder is currently uncommon, although such hospitalization did occur in the era before the development of modern somatic treatments in the 1940's (electroconvulsive therapy) and the 1950's (psychopharmacology). Before the availability of modern somatic therapies, psychiatric hospitals often had a moderate number of patients with long-standing hospitalizations because of chronic depressive conditions, often with psychiatric features. However, in the current era that situation is rare.

Impairment of social functioning. Currently, the most common impairments lie in the areas of social functioning, manifested by a reduced ability to sustain emotional intimacy, a reduction of sexual interest, lowered sexual performance (often manifested by impotence), and a decreased frequency of intercourse. Moreover, there may be difficulty in maintaining usual levels of social activity, with reduced interest in hobbies and games and less participation in sports or social activities than before the depression developed. There are periods of social withdrawal and lowered initiation of social activities (Paykel and Weissman, 1973). Divorce, unemployment, and business or professional failure may often be the consequence of dysthymic disorder.

Prognosis. The most important determinant of the course and outcome of dysthymic disorder is whether or not the disorder is recognized. If they are left to themselves, patients often have continuing episodes of chronic or intermittent symptoms, with gradual impairment of social functioning. They may have frequent hospitalizations or visits to emergency rooms because of suicide attempts or the aggravation of somatic complaints. When the depression is recognized and treated intensively, the prognosis improves greatly in the majority of cases.

DIAGNOSIS

The essential criteria for diagnosis were given in the description of the mood disturbance. The associated symptoms are

those of major depressive episodes except that, by definition, the presence of delusions and hallucinations precludes the diagnosis of dysthymic disorder.

The most difficult differential diagnosis involves the personality disorders, especially histrionic personality disorder, formerly called hysterical personality. Sometimes patients with dysthymic disorder are called borderline, dependent, or narcissistic personalities. The diagnosis of a personality disorder on Axis II is often consistent with the patient's having an acute or intermittent depression. Some evidence indicates that certain types of personality patterns—such as compulsive, dependent, or histrionic personalities—are predisposed to depression with greater frequency than is the general population (Lazare and Klerman, 1968; Chodoff, 1972; Hirschfeld and Klerman, 1979).

The differentiation from histrionic personality has been stressed by a number of observers, including Plutchik and Platman (1977). Patients with somatoform disorders, sometimes called hysteria or conversion disorders, may also have a predisposition to depression, and reports about patients with Briquet's syndrome indicate that about 20 per cent of them experienced depressive episodes in the course of their clinical functioning.

TREATMENT

A number of psychological and somatic therapies have been proposed for treating dysthymic disorder. Among the psychological treatments, the most widely described are those derived from psychoanalytic and psychodynamic theories of personality (Arieti and Bemporad, 1978). Jacobson (1971), Bibring (1953), and other psychoanalysts have written about specific modifications and techniques needed to deal with the long-standing personality difficulties and maladaptations associated with depressive personality features. An analysis of the patient's symptoms must be combined with an analysis of character structure. Psychoanalytic hypotheses relate the development and the maintenance of depressive symptoms and maladaptive personality features to unresolved conflicts from early childhood.

Important modifications of classic psychoanalytic techniques have been described by the interpersonal school, mainly based in the Washington-Baltimore area, and the culturist school, mainly based in the New York area. The interpersonal point of view is derived from the work of Adolf Meyer (Lief, 1948) and Harry Stack Sullivan (1953), who developed general theories of adaptation and interpersonal relations. Specific applications to the long-term psychotherapy of personality features related to affective disorders were described by Mabel Blake Cohen et al. (1954). Partial replication of their hypotheses was developed by R. W. Gibson (1958) on the basis of studies at Chestnut Lodge Hospital in Maryland and at St. Elizabeth's Hospital in Washington, D.C.

The basic thesis is that the adult personality features predisposing to dysthymic disorder develop from a specific familial constellation related to the marginality of the family because of their religious, economic, or cultural membership and associated with excess dependency, sibling rivalry and envy, and high motivation for achievement transmitted to the child destined to become depressive. A number of psychotherapeutic techniques are recommended for dealing with the dependency and manipulation manifested in the therapeutic relationship. Those ideas have been extended by Bonime (1962, 1976), who focused on the long-term maladaptive interpersonal maneuvers used by the chronic depressive to sustain his or her characteristic modes of interpersonal relations. Bonime postulated that those maladaptations serve to manipulate the key figures in the patient's environment, thus protecting the patient from having to undertake any significant changes in life style or relationships. Attempts to get the patient to change are met with increased symptoms and veiled threats of suicide or regression, which serve to perpetuate the pattern of interpersonal relations, often to the frustration of the patient and those in his or her immediate life space.

Intriguing as those formulations are, both as to psychodynamic development or origin and in relation to adult personality functioning and therapeutic techniques, they have unfortunately not been subjected to systematic clinical trials. Although a number of individual case reports exist, there have been no systematic studies with random assignment, systematic follow-up, and quantitative assessments of personality, symptom change, or social adjustment.

Recently, a number of short-term psychotherapies have been developed, and some of them have been subjected to systematic clinical evaluation. They include the cognitive techniques developed by Beck and associates (Beck, 1972; Rush et al., 1977), interpersonal therapy developed by the Boston-New Haven group (Klerman et al., 1974), group therapy developed by the Hopkins group (Covi et al., 1974), and marital therapy as reported by Friedman (1975) in Philadelphia. All those therapies have been shown to produce better results than control conditions.

The efficacy of a number of the techniques has been established for long-term maintenance treatment of chronic patients and those likely to relapse or have recurrences after an acute episode. The Covi et al. (1974) study, the Klerman et al. (1974) study, and the Friedman (1975) report indicate the value of psychotherapy alone in modifying interpersonal relations and personal satisfaction, as well as psychotherapy's enhanced efficacy when combined with tricyclic drug therapy (Lesse, 1977; Klerman, 1978a).

Among the somatic therapies, particular attention should be given to the tricyclic antidepressants. Those drugs remain the main form of pharmacotherapy with demonstrated efficacy for depressions (Klerman and Hirschfeld, 1978). Most patients with chronic depressions report that they have been treated with one or another tricyclic drug. Attention should be given to reconstructing dose levels. A patient should not be considered a failure until the equivalent of 200 mg. to 300 mg. of imipramine has been evaluated for at least 6 weeks. Recently developed methods for assessing blood levels are of great potential value in identifying patients who are not able to absorb or metabolize the compounds.

Monoamine oxidase inhibitors may be of particular value for subgroups of depressed patients who do not show response to tricyclics, especially patients with atypical features marked by anxiety, hysterical, and depersonalization symptoms (Nies et al., 1977).

The value of long-term maintenance therapy for patients with the likelihood of recurrence has been demonstrated in a number of studies (Davis, 1976; Klerman, 1978b). Both lithium and tricyclics have also been proposed for patients with recurrent depressive disorders.

A number of drugs are not of value for long-term treatment. Those drugs include the amphetamines, the barbiturates, and the benzodiazepines. Those drugs are often prescribed for patients with chronic symptoms of insomnia, fatigue, or tension. However, clinical experience and systematic research indicate that they are little better than a placebo and are at times worse. More important, they are apt to be misused and abused by patients, with the possible development of tolerance and dependency.

No discussion of somatic treatment for chronic depression

would be complete without reference to convulsive therapy, especially electroconvulsive therapy (ECT). Although there is controversy about the use of ECT in psychiatry, systematic studies indicate the superiority of ECT over medication, particularly for patients who are suicidal, delusional, or with long-standing complaints (Avery and Winokur, 1976).

A systematic discussion of the selection of medication and ECT for the treatment of affective disorders appears in Shaw's (1977) review, and a clinical description of treatment-resistant depressive disorders appears in Freyhan's (1978) report.

In rare instances, patients should be considered for psychosurgical procedures. Recently developed methods, particularly those evaluated in Britain, indicate the possible value of psychosurgery for some selected groups of patients (Price, 1978). The National Commission for the Protection of Human Subjects, the Ryan Commission, reviewed some 600 patients who received psychosurgical procedures and reported evidence of improvement, particularly in patients with chronic symptoms marked by pessimism and obsessive-compulsive manifestations.

Detailed descriptions of the psychotherapeutic approaches appear in Arieti and Bemporad's (1978) book, the use of psychotherapy in combination with antidepressant drugs was described by Klerman (1978a), and the use of psychopharmacology and ECT was described by Shaw (1977).

Cyclothymic Disorder

DEFINITION AND HISTORY

The term "cyclothymia" was first coined by Kahlbaum in the mid-19th century for what was then called circular insanity. The following quote from Kraepelin (1921) summarizes the late 19th-century clinical wisdom concerning cyclothymia:

> There are certain temperaments which may be regarded as rudiments of manic-depressive insanity. They may throughout the whole of life exist as peculiar forms of psychic personality without further development; but they may also become the point of departure for a morbid process which develops under peculiar conditions and runs its course in isolated attacks.

Following Kraepelin, the common usage is to regard cyclothymia as a personality condition manifested by a chronic nonpsychotic disturbance involving numerous periods in which there are symptoms characteristic of either the manic or the depressive syndrome or both. Usually, those periods are not of sufficient intensity to meet the full criteria for bipolar disorder. Furthermore, the patient usually experiences them as ego-syntonic and usually does not present himself for psychiatric treatment. However, members of his family, relatives, and co-workers may be disturbed by the patient's mood swings and behavior fluctuations and recommend treatment.

With the recent success of lithium in the treatment of full-blown manic episodes and in the prevention of recurrence in patients with bipolar disorder, increasing numbers of patients with cyclothymic disorder are coming to the attention of psychiatrists, and there is a new focus on patients with the disorder (Akiskal et al., 1977; Tellenbach, 1977). However, there are only a few systematic studies, the most important being by Akiskal et al. (1977). Until further quantitative research is done, the conclusions described below must be regarded as tentative.

EPIDEMIOLOGY

The only epidemiological study is the one reported by Weissman and Myers (1978) from the New Haven Community Study. The authors reported a lifetime prevalence of cyclothymia of less than 1 per cent, using the criteria from the Research Diagnostic Criteria. That figure is likely a major underestimate because of the variability of the diagnostic criteria and the reluctance of persons with cyclothymic disorder to identify themselves as patients.

Indirect estimates of the frequency of cyclothymic disorder may be found in clinical studies, particularly those by Akiskal et al. (1977), which identified 46 patients from a pool of 500 outpatients, about 10 per cent of the patients in a clinic population. Similarly, Winokur and Reich (1970) reported on a family study of personality attributes among first-degree relatives of probands with manic-depressive disorder and found a higher than expected frequency of those personality traits among the relatives. However, that was a study of personality attributes and cannot by itself be regarded as indicative of the frequency of cyclothymic disorder. The distinction is made difficult by a lack of adequate psychometric studies as to the boundary between traits and disorder.

CAUSES

There is a general consensus, following Kraepelin, that cyclothymia is a mild or attenuated form of bipolar disorder. That consensus is based on a number of sources of evidence, including: (1) the symptomatic and phenomenological similarity between symptoms and the behavior of persons with cyclothymic disorder and the full-blown bipolar disorder, (2) the distribution of affectively disordered biological relatives among family members (Akiskal et al., 1977), (3) observations based on follow-ups that a significant proportion evolve into the clinical picture of bipolar disorder, showing pharmacological similarities in response to treatment, including the tendency for hypomanic response to tricyclic therapy and favorable response to lithium. Gershon (1978) and associates did some of the important genetic studies and demonstrated an increased frequency of cyclothymic personality disorders in the biological relatives of probands with bipolar disorders. Similar findings were also reported by Akiskal et al. (1977).

Although the genetic hypothesis as to cause is the most favored, there are important psychodynamic and cultural hypotheses. These hypotheses derive in large part from the observation of patients in long-term psychotherapy, particularly by Jacobson (1971) and by Mabel Blake Cohen et al. (1954). In the psychodynamic theories, emphasis is placed on early childhood experience, often with the postulation of trauma and fixation during the early oral stages of infant development. Attempts are made to describe a specific family constellation, but the differentiation of cyclothymic disorder from other forms of bipolar disorder is not clear.

CLINICAL FEATURES

The essential features of cyclothymic disorder are chronic disturbances involving frequent periods during which there are nonpsychotic symptoms characteristic of both depressive and manic syndromes. However, the symptoms are usually not of sufficient severity or duration to meet the criteria for a full-

blown manic episode or depressive episode. Usually, the manifestations of the mood cycles alternate biphasically, or they may be intermixed. In other cases there may be periods as long as several months of relatively normal mood. During the periods of affective change, the symptoms related to either depression or mania are present in a mild form. During the elated phase, the patient may have an elevated, expansive, or irritable mood. There may also be decreased sleep need, increased productivity, unusual self-imposed working habits, a sense of increased capacity for attention and concentration, and sharpened or unusual creative thinking. Characteristic of the hypomanic or elated phase are episodes of buying sprees, with financial extravagance, gifts, and excessive indulgence. The sprees may be so severe as to produce business failure and bankruptcy. There may be frequent job changes, periods of sexual promiscuity, or religious or political changes.

COURSE AND PROGNOSIS

The typical manifestations of the personality changes begin to appear in mid to late adolescence. During that developmental phase, the patient is often described as moody, with periods of being high and low. The moods may be experienced as aggravations or accentuations of normal adolescent development. There is a variability in the intensity of either the elated phase or the depressive phase and in the duration and the degree of periodicity.

During adulthood these patients may be very adaptive, particularly during the hypomanic or elated phase, when their optimism, social gregariousness, good humor, high drive, and ambition may make them successful in business, professional life, public service, or academic pursuits. However, there may be excessive periods of maladaptive features. During the depressed phase the patient may be underactive, have difficulty in concentrating, be underresponsive, and perform at lower levels than normal. Conversely, during the periods of elation or hypomania, the patient may behave inappropriately socially, with excessive sexual behavior, poor management of funds, and poor judgment in family, business, and social activities. As the patient proceeds through adulthood, the periods of depressive or hypomanic mood swings may become so intense or so long as to make the clinical diagnosis possible.

DIAGNOSIS

The diagnosis is usually readily obtained by getting a history from the patient or his relatives and friends as to the degree of mood swing. However, there may be important differential diagnostic features, particularly from histrionic, antisocial, and sociopathic personalities (Plutchik and Platman, 1977). Akiskal et al. (1977) described those patients as being pseudocyclothymic. The histrionic features may be particularly difficult to differentiate from cyclothymic disorder because of elements of increased sexuality, changes in mood, and sociability in each condition. The family history may be helpful in the differential diagnosis, as may be the patient's response to treatment, especially lithium.

Important differential diagnostic considerations apply to mood swings associated with the ingestion of drugs, particularly steroids, amphetamines, and drugs of the hallucinogenic type. Mood swings have also been described as part of the secondary affective disorder related to chronic alcoholism.

In patients over the age of 40 showing the onset of mood swings, attention should be given to searching for organic features. Krauthammer and Klerman (1978) described the concept of secondary mania and collected reports of a number of medical conditions that may manifest themselves in elated episodes. Although there have been no careful descriptions of secondary cyclothymia, it is likely that such cases do exist but are insufficiently recognized.

TREATMENT

There are reports of occasional attempts at psychotherapy, particularly long-term psychotherapy, with cyclothymic disorder, but no systematic studies are available. The most significant treatment advance has been the advent of lithium. Several investigations report positive results after its use in cyclothymic disorders (Gershon and Shopsin, 1973).

Suggested Cross References

An overview of affective disorders is presented in Section 18.1, and the major affective disorders are discussed in Section 18.2. The personality disorders are discussed in Chapter 22, and the somatoform disorders are discussed in Section 21.2. Affective disorders in children are discussed in Section 43.15. Community psychiatry is discussed in Chapter 45. The theories of Adolf Meyer are discussed in Section 10.2 and the theories of Harry Stack Sullivan in Section 9.3. Psychotherapies are discussed in Chapter 30 and organic therapies in Chapter 31.

REFERENCES

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders,* ed. 3. American Psychiatric Association, Washington, D.C., 1980.

* Akiskal, H. S., Djenderedjian, A. H., Rosenthal, R. H., and Khani, M. K. Cyclothymic disorder: Validating criteria for inclusion in the bipolar affective group. Am. J. Psychiatry, *134:* 1227, 1977.

* Arieti, S., and Bemporad, J. *Severe and Mild Depression: The Psychotherapeutic Approach.* Basic Books, New York, 1978.

Astrup, C., Fossum, A., and Holmboe, R. A follow-up study of 270 patients with acute affective psychoses. Acta Psychiatr. Neurol. Scand., *34* (Suppl.): 1, 1959.

Avery, D., and Winokur, G. Mortality in depressed patients treated with electroconvulsive therapy and antidepressants. Arch. Gen. Psychiatry, *33:* 1029, 1976.

Barrett, J., Hurst, M. W., DiSalla, C., and Rose, R. M. Prevalence of depression over a 12-month period in a nonpatient population. Arch. Gen. Psychiatry, *35:* 741, 1978.

Beck, A. T. *Depression: Causes and Treatment.* University of Pennsylvania Press, Philadelphia, 1972.

Bibring, E. Mechanism of depression. In *Affective Disorders,* P. Greenacre, editor, p. 13. International Universities Press, New York, 1953.

Bonime, W. Dynamics and psychotherapy of depression. In *Current Psychiatric Therapies,* J. Masserman, editor, p. 137. Grune & Stratton, New York, 1962.

Bonime, W. The psychodynamics of neurotic depression. J. Am. Acad. Psychoanal., *4:* 301, 1976.

Bratfos, O., and Haug, J. O. The course of manic-depressive psychosis: A follow-up investigation of 215 patients. Acta Psychiatr. Scand., *44:* 89, 1968.

* Chodoff, P. The depressive personality. Arch Gen. Psychiatry, *27:* 666, 1972.

Cohen, M. B., Baker, G., Cohen, R. A., Fromm-Reichmann, F., and Weigert, E. V. An intensive study of twelve cases of manic-depressive psychosis. Psychiatry, *17:* 103, 1954.

Covi, L., Lipman, R. S., Derogatis, L. R., Smith, J., and Pattison, J. Drugs and group psychotherapy in neurotic depression. Am. J. Psychiatry, *131:* 191, 1974.

Davis, J. M. Overview: Maintenance therapy in psychiatry. II. Affective disorders. Am. J. Psychiatry, *133:* 1, 1976.

Freyhan, F. A. Treatment-resistant or untreatable? Compr. Psychiatry, *19:* 97, 1978.

Friedman, A. S. Interaction of drug therapy with marital therapy in depressed patients. Arch. Gen. Psychiatry, *32:* 619, 1975.

Gershon, E. S. The search for genetic markers in affective disorders. In *Psychopharmacology: A Generation of Progress,* M. A. Lipton, A. DiMascio, and K. F. Killam, editors, p. 1197, Raven Press, New York, 1978.

Gershon, S., and Shopsin, B. *Lithium: Its Role in Psychiatric Research and Treatment.* Plenum Publishing Corp., New York, 1973.

Gibson, R. W. The family background and early life experience of the manic-depressive patient: A comparison with the schizophrenic patient. Psychiatry, *21:* 71, 1958.

Guze, S. B., Woodruff, R. A., and Clayton, P. J. Secondary affective disorder: A

study of 95 cases. Psychol. Med., *1:* 426, 1971.
Hirschfeld, R. M. A., and Klerman, G. L. Personality attributes and affective disorders. Am. J. Psychiatry, *136:* 67, 1979.
Hornstra, R. K., and Klassen, D. The course of depression. Compr. Psychiatry, *18:* 119, 1977.
Huston, P. E., and Locher, L. M. Involutional psychosis: Course when untreated and when treated with electric shock. Arch. Neurol. Psychiatry, *59:* 385, 1948a.
Huston, P. E., and Locher, L. M. Manic-depressive psychosis: Course when treated and untreated with electric shock. Arch. Neurol. Psychiatry, *60:* 37, 1948b.
Jacobs, T. J., Gogelson, S., and Charles, E. Depression ratings in hypochondria. N. Y. State J. Med., *68:* 3119, 1968.
Jacobson, E. *Depression.* International Universities Press, New York, 1971.
Kahn, E. The depressive character. Folia Psychiatr. Neurol. Jap., *29:* 292, 1975.
Kielholz, P. *Masked Depression.* Hans Huber, Bern, 1973.
Klerman, G. L. Combining drugs and psychotherapy in the treatment of depression. In *Depression: Biology, Psychodynamics, and Treatment,* J. O. Cole, A. F. Schatzberg, and S. H. Frazier, editors, p. 213. Plenum Publishing Corp., New York, 1978a.
Klerman, G. L. Long-term treatment of affective disorders. In *Psychopharmacology: A Generation of Progress,* M. A. Lipton, A. DiMascio, and K. F. Killam, editors, p. 1303. Raven Press, New York, 1978b.
Klerman, G. L., DiMascio, A., Weissman, M. M., Prusoff, B., and Paykel, E. S. Treatment of depression by drugs and psychotherapy. Am. J. Psychiatry, *131:* 186, 1974.
Klerman, G. L., and Hirschfeld, R. M. A. The use of antidepressants in clinical practice. J. A. M. A., *240:* 1403, 1978.
Kraepelin, E. *Manic-Depressive Insanity and Paranoia.* E. and S. Livingstone, Edinburgh, 1921.
Krauthammer, C., and Klerman, G. L. Secondary mania: Manic syndromes associated with antecedent physical illness or drugs. Arch. Gen. Psychiatry, *35:* 1333, 1978.
Lazare, A., and Klerman, G. L. Hysteria and depression: The frequency and significance of hysterical personality features in hospitalized depressed women. Am. J. Psychiatry, *124:* 48, 1968.
Lesse, S. Psychotherapy in combination with antidepressant drugs in patients with severe masked depressions. Am. J. Psychiatry, *31:* 185, 1977.
Lewinsohn, P. A behavioral approach to depression. In *The Psychology of Depression: Contemporary Theory and Research.* R. Friedman and M. Katz. editors, John Wiley & Sons, New York, 1974.
Lief, A., editor. *The Commonsense Psychiatry of Adolf Meyer.* McGraw-Hill, New York, 1948.
Lipsitt, D. R. Medical and psychological characteristics of "crocks." Psychiatr. Med., *1:* 15, 1970.
Lundquist, G. Prognosis and course in manic-depressive psychoses: A follow-up study of 319 first admissions. Acta Psychiatr. Neurol., *35* (Suppl.): 1, 1945.
Morrison, J., Winokur, G., and Crowe, R. The Iowa 500: The first follow-up. Arch. Gen. Psychiatry, *29:* 678, 1973.
Murphy, G. E., Woodruff, R. A., Jr., Herjanic, M., and Super, G. Variability of the clinical course of primary affective disorder. Arch. Gen. Psychiatry, *30:* 757, 1974.
Nies, A., Robinson, D. S., Bartlett, D., and Lamborn, K. R. MAO inhibitors in clinical practice: Principles based on recent research. Psychopharmacol. Bull., *13:* 54, 1977.
Paykel, E. S., Klerman, G. L., and Prusoff, B. A. Prognosis of depression and the endogenous-neurotic distinction. Psychol. Med., *4:* 57, 1974.
Paykel, E. S., and Weissman, M. M. Social adjustment and depression: A longitudinal study. Arch. Gen. Psychiatry, *28:* 650, 1973.
Plutchik, R., and Platman, S. R. Personality connotations of psychiatric diagnoses. J. Nerv. Ment. Dis., *165:* 418, 1977.
Pottenger, M., McKernon, J., Patrie, L. E., Weissman, M. M., Ruben, H. L., and Newberry, P. The frequency and persistence of depressive symptoms in the alcohol abuser. J. Nerv. Ment. Dis., *166:* 562, 1978.
Price, J. S. Chronic depressive illness. Br. Med. J., 1200, May 6, 1978.
Robins, E., and Guze, S. Classification of affective disorders: The primary-secondary, the endogenous, and the neurotic-psychotic concepts. In *Recent Advances in the Psychobiology of the Depressive Illness,* T. A. Williams, M. M. Katz, and J. A. Shield, Jr., editors, p. 283. Department of Health, Education, and Welfare, Washington, D. C., 1972.
Rush, A. J., Beck, A. T., Kovacs, M., and Hollon, S. Comparative efficacy of cognitive therapy and pharmacotherapy in the treatment of depressed outpatients. Cog. Ther. Res., *1:* 17, 1977.
Seligman, M. Depression and learned helplessness. In *The Psychology of Depression: Contemporary Theory and Research,* R. Friedman and M. Katz, editors. John Wiley & Sons, New York, 1974.
* Shaw, D. M. The practical management of affective disorders. Br. J. Psychiatry, *130:* 432, 1977.
Spitzer, R. L., Endicott, J. E., and Robins, E. *Research Diagnostic Criteria for a Selected Group of Functional Disorders,* ed. 3. New York State Psychiatric Institute, New York, 1978.
Stenstedt, A. A study in manic-depressive psychosis: Clinical, social, and genetic investigations. Acta Psychiatr. Neurol. Scand., *79* (Suppl.): 1, 1952.
Sullivan, H. S. *The Interpersonal Theory of Psychiatry.* W. W. Norton, New York, 1953.
Tellenbach, H. Psychopathologie der cyclothymie. Nervenarzt, *48:* 335, 1977.
Watts, C. A. H. The incidence and prognosis of endogenous depression. Br. Med. J., *1:* 1392, 1956.
* Weissman, M. M., and Klerman, G. L. The chronic depressive in the community: Unrecognized and poorly treated. Compr. Psychiatry, *18:* 523, 1977a.
Weissman, M. M., and Klerman, G. L. Sex differences and the epidemiology of depression. Arch Gen. Psychiatry, *34:* 98, 1977b.
Weissman, M. M., and Myers, J. K. Affective disorders in a U. S. urban community: The use of research diagnostic criteria in an epidemiological survey. Arch. Gen. Psychiatry, *35:* 1304, 1978.
* Weissman, M. M., and Paykel, E. S. *The Depressed Women: A Study of Social Relationships.* University of Chicago Press, Chicago, 1974.
Winokur, G., Behar, D., Vanvalkenburg, C., and Lowry, M. Is a familial definition of depression both feasible and valid? J. Nerv. Ment. Dis., *166:* 764, 1978.
Winokur, G., and Reich, T. Two genetic factors in manic-depressive disease. Compr. Psychiatry, *11:* 93, 1970.