Depression

Causes and Treatment

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Chapter 1
The Definition of Depression

Paradoxes of Depression

Depression may someday be understood in terms of its paradoxes. There is, for instance, an astonishing contrast between the depressed person's image of him- or herself and the objective facts. A wealthy woman moans that she doesn't have the financial resources to feed her children. A widely acclaimed movie star begs for plastic surgery in the belief that he is ugly. An eminent physicist berates herself "for being stupid."

Despite the torment experienced as the result of these self-debasing ideas, the patients are not readily swayed by objective evidence or by logical demonstration of the unreasonable nature of these ideas. Moreover, they often perform acts that seem to enhance their suffering. The wealthy man puts on rags and publicly humiliates himself by begging for money to support himself and his family. A clergyman with an unimpeachable reputation tries to hang himself because "I'm the world's worst sinner." A scientist whose work has been confirmed by numerous independent investigators publicly "confesses" that her discoveries were a hoax.

Attitudes and behaviors such as these are particularly puzzling—on the surface, at least—because they seem to contradict some of the most strongly established axioms of human nature. According to the "pleasure principle," patients should be seeking to maximize satisfactions and minimize pain. According to the time-honored concept of the instinct of self-preservation, they should be attempting to prolong life rather than terminate it.

Although depression (or melancholia) has been recognized as a clinical syndrome for over 2,000 years, as yet no completely satisfactory explanation of its puzzling and paradoxical features has been found. There are still major unresolved issues regarding its nature, its classification, and its etiology. Among these are the following:

1. Is depression an exaggeration of a mood experienced by the normal, or is it qualitatively as well as quantitatively different from a normal mood?

2. What are the causes, defining characteristics, outcomes, and effective treatments of depression?
3. Is depression a type of reaction (Meyerian concept), or is it a disease (Kraepelinian concept)?
4. Is depression caused primarily by psychological stress and conflict, or is it related primarily to a biological derangement?

There are no universally accepted answers to these questions. In fact, there is sharp disagreement among clinicians and investigators who have written about depression. There is considerable controversy regarding the classification of depression, and a few writers see no justification for using this nosological category at all. The nature and etiology of depression are subject to even more sharply divided opinion. Some authorities contend that depression is primarily a psychogenic disorder; others maintain just as firmly that it is caused by organic factors. A third group supports the concept of two different types of depression: a psychogenic type and an organic type.

Prevalence of Depression

The importance of depression is recognized by everyone in the field of mental health. According to Kline,[1] more human suffering has resulted from depression than from any other single disease affecting humankind. Depression is second only to schizophrenia in first and second admissions to mental hospitals in the United States, and it has been estimated that the prevalence of depression outside hospitals is five times greater than that of schizophrenia.[2] Worldwide, Murray and Lopez[3] found unipolar major depression to be the leading cause of disability in 1990, measured in years lived with a disability. Unipolar depression accounted for more than one in every ten years of life lived with a disability.

More than 40 years ago, a systematic survey of the prevalence of depression in a sharply defined geographical area indicated that 3.9 percent of the population more than 20 years of age were suffering from depression at a specified time.[4] According to the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*) of the American Psychiatric Association,[5] the probability during one's lifetime of developing a major depressive disorder is 5–12 percent for males and 10–25 percent for females. At any given point in time ("point prevalence"), 2–3 percent of the male and 5–9 percent of the female population suffer from a major depression. Piccinelli[6] reviewed the studies on gender differences in depression and found that the gender differences began at mid-puberty and continued through adult life.

TABLE 1-1. Leading Causes of Disability Worldwide, 1990

	Total years lived with disability (millions)	*Percent of total*
All causes	427.7	
1. Unipolar major depression	50.8	10.7
2. Iron-deficiency anemia	22.0	4.7
3. Falls	22.0	4.6
4. Alcohol use	15.8	3.3
5. Chronic obstructive pulmonary disease	14.7	3.1
6. Bipolar disorder	14.1	3.0
7. Congenital anomalies	13.5	2.9
8. Osteoarthritis	13.3	2.8
9. Schizophrenia	12.1	2.6
10. Obsessive-compulsive disorder	10.2	2.2

Adapted from Lopez and Murray 1998. For up-to-date WHO data, see http://www.who.int/mental_health/management/depression/definition/en/

TABLE 1-2. Prevalence of Major Depressive Disorder by Gender (%)

	Male	*Female*
Lifetime	5–12	10–25
Point prevalence	2–3	5–9

Adapted from *DSM-IV-TR*.

Prevalence and Severity by Types and Age at Onset

Lifetime prevalence rates for the other mood disorders (see Chapter 4 for distinctions among types) are reported in *DSM-IV*[5] as follows: Dysthymic disorder 6 percent; Bipolar I 0.4–1.6 percent; Bipolar II 0.5 percent; Cyclothymic 0.4–1.0 percent. The National Institute of Mental Health (USA)[7] reports that 18.8 million American adults (9.5 percent of the population age 18 or older) in a given year suffer from some form of depressive disorder. Major depressive disorder is the leading cause of disability in the established market economies around the world.[7]

Twelve-month prevalence and severity rates are provided by Kessler et al.[8] The U.S. National Comorbidity Survey Replication included a nationally representative face-to-face household survey conducted between February 2001 and April 2003. The study employed a structured diagnostic interview, the World Health Organization World Mental Health Survey Initiative version of the Composite International Diagnostic Interview. Participants included 9,282 English-speaking respondents 18 years and older. Twelve-month prevalence and estimates of mood disorders from this study are included in Table 1-3.

TABLE 1-3. Twelve-Month Prevalence and Severity of Mood Disorders (%)

		Severity		
	Total	*Serious*	*Moderate*	*Mild*
Major depressive disorder	6.7	30.4	50.1	19.5
Dysthymia	1.5	49.7	32.1	18.2
Bipolar I–II disorders	2.6	82.9	17.1	0
Any mood disorder	9.5	45.0	40.0	15.0

Adapted from Kessler et al. 2005.

TABLE 1-4. Ages at Selected Percentiles on Standardized Age-of-Onset Distributions of *DSM-IV*/ WMH-CIDI Mood Disorders, with Projected Lifetime Risk at Age 75 Years

	Projected lifetime risk at age 75 (%)	*Age at selected age-of-onset percentiles*							
		5	*10*	*25*	*50*	*75*	*90*	*95*	*99*
Major depressive disorder	23.2	12	14	19	32	44	56	64	73
Dysthymia	3.4	7	11	17	31	43	51	57	73
Bipolar I–II disorders	5.1	11	13	17	25	42	50	57	65
Any mood disorder	28.0	11	13	18	30	43	54	63	73

Adapted from Kessler et al. 2005.

TABLE 1-5. Lifetime Prevalence (%) of Disorders by Age

		Age			
	Total	*18–29*	*30–44*	*45–59*	*>60*
Major depressive disorder	16.6	15.4	19.8	18.8	10.6
Dysthymia	2.5	1.7	2.9	3.7	1.3
Bipolar I–II disorders	3.9	5.9	4.6	3.5	1.0
Any mood disorder	20.8	21.4	24.6	22.9	11.9

Adapted from Kessler et al. 2005.

Age of onset and lifetime prevalence rates (the likelihood of experiencing a mood disorder at some time in one's lifetime) are presented in Tables 1-4 and 1-5.[9]

Descriptive Concepts of Depression

The condition that today we label depression has been described by a number of ancient writers under the classification of "melancholia." The first clinical description of melancholia was made by Hippocrates in the fourth century B.C. He also referred to swings similar to mania and depression.[10]

Aretaeus, a physician living in the second century A.D., described the melancholic patient as "sad, dismayed, sleepless. . . . They become thin by their agitation and loss of refreshing sleep. . . . At a more advanced stage, they complain of a thousand futilities and desire death." It is noteworthy that Aretaeus specifically delineated the manic-depressive cycle. Some authorities believe that he anticipated the Kraepelinian synthesis of manic-depressive psychosis, but Jelliffe discounts this hypothesis.

Plutarch, in the second century A.D., presented a particularly vivid and detailed account of melancholia:

> He looks on himself as a man whom the Gods hate and pursue with their anger. A far worse lot is before him; he dares not employ any means of averting or of remedying the evil, lest he be found fighting against the gods. The physician, the consoling friend, are driven away. 'Leave me,' says the wretched man, 'me, the impious, the accursed, hated of the gods, to suffer my punishment.' He sits out of doors, wrapped in sackcloth or in filthy rags. Ever and anon he rolls himself, naked, in the dirt confessing about this and that sin. He has eaten or drunk something wrong. He has gone some way or other which the Divine Being did not approve of. The festivals in honor of the gods give no pleasure to him but fill him rather with fear or a fright. (quoted in Zilboorg[11])

Pinel at the beginning of the nineteenth century described melancholia as follows:

> The symptoms generally comprehended by the term melancholia are taciturnity, a thoughtful pensive air, gloomy suspicions, and a love of solitude. Those traits, indeed, appear to distinguish the characters of some men otherwise in good health, and frequently in prosperous circumstances. Nothing, however, can be more hideous than the figure of a melancholic brooding over his imaginary misfortunes. If moreover possessed of power, and endowed with a perverse disposition and a sanguinary heart, the image is rendered still more repulsive.

These accounts bear a striking similarity to modern textbook descriptions of depression; they are also similar to contemporary autobiographical accounts such as that by Clifford W. Beers.[12] The cardinal signs and symptoms used today in diagnosing depression are found in the ancient descriptions: disturbed mood (sad, dismayed, futile); self-castigations ("the accursed, hatred of the gods"); self-debasing behavior ("wrapped in sackcloth or dirty rags . . . he rolls himself, naked, in the dirt"); wish to die; physical and vegetative symptoms (agitation, loss of appetite and weight, sleeplessness); and delusions of having committed unpardonable sins.

The foregoing descriptions of depression include the typical characteristics of this condition. There are few psychiatric syndromes whose clinical descriptions are so constant through successive eras of history (For descriptions of depression through the ages, see Burton.[13]) It is noteworthy that the historical descriptions of depression indicate that its manifestations are observable in all

aspects of behavior, including the traditional psychological divisions of affection, cognition, and conation.

Because the disturbed feelings are generally a striking feature of depression, it has become customary to regard this condition as a "primary mood disorder" or as an "affective disorder." The central importance ascribed to the feeling component of depression is exemplified by the practice of utilizing affective adjective checklists to define and measure depression. The representation of depression as an affective disorder is as misleading as it would be to designate scarlet fever as a "disorder of the skin" or as a "primary febrile disorder." There are many components of depression other than mood deviation. In a significant proportion of the cases, no mood abnormality at all is elicited from the patient. In our present state of knowledge, we do not know which component of the clinical picture of depression is primary, or whether they are all simply external manifestations of some unknown pathological process.

Depression may now be defined in terms of the following attributes:

1. A specific alteration in mood: sadness, loneliness, apathy.
2. A negative self-concept associated with self-reproaches and self-blame.
3. Regressive and self-punitive wishes: desires to escape, hide, or die.
4. Vegetative changes: anorexia, insomnia, loss of libido.
5. Change in activity level: retardation or agitation.

Semantics of Depression

One of the difficulties in conceptualizing depression is essentially semantic, namely, that the term has been variously applied to designate a particular type of feeling or symptom; a symptom-complex (or syndrome); and a well-defined disease entity.

Not infrequently, normal people say they are depressed when they observe any lowering of their mood below their baseline level. A person experiencing a transient sadness or loneliness may state that he or she is depressed. Whether this *normal* mood is synonymous with, or even related to, the feeling experienced in the abnormal condition of depression is open to question. In any event, when a person complains of feeling inordinately dejected, hopeless, or unhappy, the term *depressed* is often used to label this subjective state.

The term depression is often used to designate a complex pattern of deviations in feelings, cognition, and behavior (described in the previous section) that is not represented as a discrete psychiatric disorder. In such instances it is regarded as a syndrome, or symptom-complex. The cluster of signs and symptoms is sometimes conceptualized as a psychopathological dimension ranging in intensity (or in degree of abnormality) from mild to severe. The syndrome of depression may at times appear as a concomitant of a definite

psychiatric disorder such as schizophrenic reaction; in such a case, the diagnosis would be "schizophrenic reaction with depression." At times, the syndrome may be secondary to, or a manifestation of, organic disease of the brain such as general paresis or cerebral artereosclerosis.

Finally, the term depression has been used to designate a discrete nosological entity. The term has generally been qualified by some adjective to indicate a particular type or form, as for example: reactive depression, agitated depression, or psychotic-depressive reaction. When conceptualized as a specific clinical entity, depression is assumed to have certain consistent attributes in addition to the characteristic signs and symptoms; these attributes include a specifiable type of onset, course, duration, and outcome.

One such classification system, the diagnostic manual of the American Psychiatric Association (APA),[5] illustrates some of these aspects. The APA categorizes the mood disorders into (1) depressive disorders (unipolar depression) and (2) bipolar disorders. In the former, there is no history of a manic or hypomanic episode, and in the latter there is such a history.

The depressive disorders include major depressive disorder and dysthymic disorder. Major depressive disorder is defined by one or more major depressive episodes. Such episodes include 2 weeks of depressed mood or loss of interest, along with a minimum of four additional depression symptoms. Dysthymic disorder is defined in part by at least 2 years of low-level depressed mood, where the person is depressed for more days than not. The bipolar disorders are usually accompanied by major depressive episodes, and are divided into two types, Bipolar I and Bipolar II disorder.[5] The classification of the mood disorders will be considered in more detail in Chapter 4.

In medicine, a clinical entity or disease is assumed to be responsive to specific forms of treatment (not necessarily discovered as yet) and to have a specific etiology. There is a considerable body of evidence indicating that the clinical entity depression responds to certain drugs and/or electroconvulsive therapy (ECT), but there is no consensus as yet regarding its etiology. This issue will be further considered in Part II, "Experimental Aspects of Depression."

Depression and Normal Moods

There is little agreement among authorities regarding the relationship of depression to the changes in mood experienced by normal individuals. The term *mood* is generally applied to a spectrum of feelings extending from elation and happiness at one extreme, to sadness and unhappiness at the other. The particular feelings encompassed by this term, consequently, are directly related to either happiness or sadness. Subjective states, such as anxiety or anger, that do not fit into the happiness-sadness categories are not generally included. Some authors[14] believe that all individuals have mood swings and that normal individuals may have "blue" hours or "blue" days. This belief

has been supported by systematic studies of oscillations in mood in normal subjects.[15]

The episodes of low mood or of feeling blue experienced by normal individuals are similar in a number of ways to the clinical states of depression. First, there is a similarity between the descriptions of the subjective experience of normal low mood and of depression. The words used to describe normal low mood tend to be the same used by depressives to describe their feelings—blue, sad, unhappy, empty, low, lonely. It is possible, however, that this resemblance may be due to depressed patients' drawing on familiar vocabulary to describe a pathological state for which they have no available words. Some patients, in fact, state that their feelings during their depressions are quite distinct from any feelings they have ever experienced when not in a clinical depression.

Second, the behavior of the depressed patient resembles that of a person who is sad or unhappy, particularly in the mournful facial expression and the lowered voice. Third, some of the vegetative and physical manifestations characteristic of depression are occasionally seen in individuals who are feeling sad but who would not be considered clinically depressed. A person who has failed an examination, lost a job, or been jilted may not only feel discouraged and forlorn, but also experience anorexia, insomnia, and fatigability. Finally, many individuals experience blue states that seem to oscillate in a consistent or rhythmic fashion, independently of external stimuli, suggestive of the rhythmic variations in the intensity of depression.[15]

The resemblance between depression and the low mood of normals has led to the concept that the pathological is simply an exaggeration of the normal. On the surface, this view seems plausible. As will be discussed in Chapter 2, each symptom of depression may be graded in intensity along a dimension, and the more mild intensities are certainly similar to the phenomena observed in normal individuals who are feeling blue.

In support of the continuity perspective, Hankin et al.[16] used Meehl's[17] taxometric procedures to examine the structure of depression in a sample of children and adolescents. Taking into account the skewness of depressive symptoms, the authors reported youth depression to be a dimensional, not categorical, construct. In discussing the implications of their findings, Hankin et al.[16] point out that by using continuously distributed scores, the statistical power of the research is enhanced, thus aiding the ability of researchers to ascertain correctly the true causes and consequences of depression.

Similar to the findings of Hankin et al.,[17] Haslam and Beck[18] used taxometric procedures to test for discreteness (discontinuity) of 5 hypothesized subtypes of major depression, including endogenous, sociotropic, autonomous, self-critical, and hopelessness forms. The study used self-reported symptom and personality profiles of 531 consecutively admitted outpatients diagnosed

with major depression. The features of the respective subtypes were not found to covary as predicted, except for the endogenous subtype.[18]

It could be contended that many pathological states that seem to be on a continuum with the normal state are different in their essential character from the normal state. To illustrate this, an analogy may be made between the deviations of mood and deviations of internal body temperature. While pronounced changes in body temperature are on the same continuum as are normal temperatures, the underlying factors producing the large deviations are not an extension of the normal state of health: A person may have a disease, for example, typhoid fever, that is manifested by a serial progression in temperature and yet is categorically different from the normal state. Similarly, the deviation in mood found in depression may be the manifestation of a disease process that is distinct from the normal state.

There is no general consensus among the authorities regarding the relation of depression to normal mood swings. Some writers, notably Kraepelin and his followers, have considered depression a well-defined disease, quite distinct from normal mood. They have postulated the presence of a profound biological derangement as the key factor in depression. This concept of a dichotomy between health and disease has generally been shared by the *somatogenic school*. The *environmentalists* seem to favor the continuity hypothesis. In their view, there is a continuous series of mood reactions ranging from a normal reaction to an extreme reaction in a particularly susceptible person. The psychobiological school founded by Adolph Meyer tends to favor this view.

The ultimate answer to the question whether there is a dichotomy or continuity between normal mood and depression will have to wait until the question of the etiology of depression is fully resolved.