PART I

NOSOLOGY, MEASUREMENT, AND THE EPIDEMIOLOGY OF WOMEN AND DEPRESSION

1

Depression

From Nosology to Global Burden

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Depression is now identified as a major health issue, being a major cause of both psychological and physical morbidity. It is predicted to be second only to ischaemic heart disease in terms of total burden of disease burden to 2020 (Murray & Lopez, 1996). However, the definition of depression has undergone a number of changes over time, reflecting clinical and research fashions, evolving theories concerning psychological and biological causations of disease and the wider social context in which the problem is perceived. The changing fashions have affected how depression is viewed and how the construct is measured. This chapter will explore the evolving concepts involved in the nosology of depression, including a consideration of the implications for both genders.

MELANCHOLIA AND DEPRESSION

Melancholia has had much wider currency than *depression* through most of recorded history (Akiskal, 2000; Rush, 1986). The term referred to the presence of black bile associated with coldness, blackness, and dryness, so that melancholic individuals possessed a temperament that was essentially depressive. In a summary of Greco-Roman concepts, Akiskal (2000) noted the description of Soranus of Ephesus, in the second century BC, who characterised those with melancholia as exhibiting "mental anguish and distress, dejection, silence, animosity towards members of their household, sometimes a desire to live, and at other times a longing for death; suspicion that a plot is being hatched against him, weeping without reason, meaningless muttering, and occasional joviality."

Rush (1986) noted that Burton, in his *Anatomy of Melancholy* (1621), first differentiated grief from melancholy and recognised suicide as

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a manifestation of melancholy. Kraepelin (1921) distinguished manic-depressive insanity from schizophrenia, and then Bleuler (1930) first used the term *affective disorders* to include psychoneurotic depressive reactions and involutional melancholia. Today, the characteristic features of melancholia described many centuries ago are still recognisable in current descriptions of the construct, signifying a severe and disabling form of depression with a high risk of suicide. Much of the nosological discussion of depression in the past has revolved around nonmelancholic forms of depression. Areas of particular interest have included the definition and quantification of the nature of depression in different populations and applications and how the concept differs from normal human experience.

THE CONTEXT FOR CLASSIFYING DEPRESSION

Stress, distress, and disease originally all meant much the same thing (Rees, 1976) and implied a relationship between lack of emotional well-being and external precipitants. Rees (1976) noted that in the fifteenth century, *distress* was first shortened to *stress*, whereas *disease* meant discomfort or lack of well-being. The term *depression* was first used in the 19th century by cardiologists to describe the effects of a state of lowered (cardiac) function. Since then the term depression has been used more widely than melancholia. It covers a broader range of experience than that conveyed by melancholia, but in the process, it has become less meaningful and harder to define.

There are a number of meanings for the word depression, ranging from scientific to economic to psychological (*Oxford English Dictionary*, 1989). Most commonly, in general parlance, depression is used to describe a normal human emotion. It may also be used to convey an affect (the external manifestation of mood), a predicament (a state of being or condition that is unpleasant, trying, or dangerous), a symptom (a complaint reported), a disease (a constellation of symptoms and signs implying an underlying pathological process), or an illness (a manifestation of disease in the social context).

The purpose of classifying depression relates to the context. In a clinical setting, a diagnosis is linked to clinical goals such as making a prognosis about the likely outcome and management planning. The important diagnostic distinctions from depression in this setting are grief (where there can be similar symptoms and signs, but a clear precipitant leading to the grief and no associated loss of self-esteem) and anxiety disorders (which have their own characteristic sets of diagnostic features and often occur prior to or concurrent with depressive episodes).

In a research setting, the concept of *caseness* is used to determine population trends in morbidity, risk factors for epidemiological studies, and health resource planning. The objective is to determine a threshold for inclusion of subjects who are *cases*, irrespective of whether the subject

considers him or herself to be a case, from *noncases*. The definition relates to the severity and subjective impact of the disorder by determining the impact on indicators such as daily psychological and physical functioning and days absent from normal life roles. There are gender implications as women are overrepresented in clinical studies as they engage in more help-seeking than men. This highlights the importance of using data from general population studies to ascertain rates. The reasons for men not seeking help include fears of their own vulnerability and denial concerns about stigma, all related to male sex-role conditioning (Moller-Leimkuhler, 2002). All of these factors can lead to inflation of women's rates relative to men's.

DEBATE ABOUT THE NATURE OF DEPRESSION

Apart from the ongoing debate about what how depression is conceptualised (in terms of reproducible symptom clusters, duration of episodes, and the boundaries with other diagnostic categories), there is a more fundamental question about the nature of diagnostic categories. The question of whether the construct of depression is dimensional or categorical is important in determining how depression is conceptualised (whether on a continuum with normal experience or something that is qualitatively different) and how it is best measured.

Lewis (1938) proposed a dimensional or spectrum model, with depression ranging from mild (being normal mood state/adjustment reaction, then anxiety state) to severe (endogenous/melancholic depression and finally psychotic depression). Others, following on from great European clinicians such as Kraepelin and Bleuler, had taken a categorical approach. The models of depression pre–*Diagnostic and Statistical Manual*, third edition (*DSM-III*; American Psychiatric Association, 1980) and in the *Manual of the International Standard Classification of Diseases, Injuries and Causes of Death*, ninth edition (ICD 9; World Health Organisation [WHO], 1977) were predicated on the assumption of two dichotomous groups. One type, variably labelled as *endogenous*, *autonomous*, or *psychotic* depression, was not considered to be the result of a psychosocial precipitant, but to have a biological causation requiring biological treatments. This endogenous form of depression was seen as synonymous with the early accounts of melancholia and viewed as qualitatively different from the other type, variously named *exogenous*, *reactive*, *neurotic*, or *characterological* depression. Kiloh, Andrews, Neilson, and Bianchi (1971) summarised the position, "Psychotic or endogenous depression is a condition . . . with an imputed genetic or biochemical basis, whilst so-called neurotic depression is a diffuse entity encompassing some of the ways in which the patient utilises his defence mechanisms to cope with his own neuroticism and concurrent environmental stress."

One criticism of the binary model was that the endogenous/melancholic type was much more clearly identified as a coherent construct than the neurotic/reactive type. The latter tended to be a default category with features more closely identified with anxiety disorders than depression – the "diffuse entity" that Kiloh et al. (1971) alluded to. Another problem was that the terms *psychotic* and *endogenous* often came to be used interchangeably, with many British writers using the term *psychotic* to denote severity of depression (Carney, Roth, & Garside, 1965) rather than the presence of specific melancholic or psychotic features.

For the endogenous depressions, a further distinction (Leonhard, Korff, & Schulz, 1962) was made between bipolar disorder (subjects having a history of manic and depressive episodes) and monopolar disorder (where there is a history of only manic *or* depressive episodes), based on family history studies. Subsequently, the concept of *monopolar depression* has been retained in the current term *unipolar depression*, whereas purely manic episodes have been subsumed under the category of bipolar disorder (American Psychiatric Association, 1980; Boyd & Weissman, 1981; Spitzer, Endicott, & Robins, 1978; World Health Organisation, 1977). There are some subtle differences in phenomenology between unipolar and bipolar depression (Mitchell, Parker, Gladstone, Wilhelm, & Austin, 2001) but they are not sufficiently characteristic to render this a useful concept.

There are generally smaller gender differences in rates and experience of more biological depressions. There are minimal or absent gender differences in rates of bipolar disorder and melancholic depressions, with differences more in nonmelancholic types of major depression and more minor depressions (Jenkins, 1985), where comorbid anxiety plays a significant role (Breslau, Chilcoat, Peterson, & Schlultz, 2000). Thus, men and women seem to have similar expression of established episodes of major depression (in terms of type of symptoms and severity); the differences are more in comorbidities and coping styles (Nolen-Hoeksema, 1987, 2000; Wilhelm, Roy, Mitchell, Brownhill, & Parker, 2002).

THE CHANGING FORTUNES OF THE CONCEPT OF NEUROTIC DEPRESSION

In the ninth edition of the ICD system, ICD-9 (World Health Organisation, 1977), neurotic depression is defined as a "neurotic disorder characterised by disproportionate depression which has usually recognizably ensued on a distressing experience. . . . there is often preoccupation with the psychic trauma which preceded the illness." A further category, adjustment reaction, covers "mild or transient disorders lasting longer than acute stress reactions . . . often relatively circumscribed or situation-specific, generally reversible"; these may be brief, including grief reactions, or prolonged, lasting up to a few months. The term *adjustment reaction* implies an

understandable reaction to a specific stressor, whereas neurotic depression stipulates a level of depression disproportionate to the presumed stressor. There is also a further category *depressive disorder, not elsewhere classified* for "states of depression, usually of moderate but occasionally of marked intensity, which have no specifically manic-depressive or other psychotic features, and which do not appear to be associated with stressful events or other features specified under neurotic depression."

There were some implicit assumptions in contrasting *neurotic* or *reactive* depressions to *endogenous* or *psychotic* depressions in terms of presumed aetiological factors. The assumption was that neurotic or reactive depressions had an underlying psychological causation (i.e., psychosocial stressors or conflicts), whereas endogenous depression arose more spontaneously and was linked to psychotic depression, two terms that came to be used synonymously (Andreasen, 1982). From the mid-1970s leading up to the publication of the third edition of *DSM* (American Psychiatric Association, 1980), these concepts were rigorously investigated.

Neurotic or reactive depression was characterised partly by the lack of features characterising endogenous depression and was associated with reactivity of mood to environmental stimuli, initial insomnia, self-pity, or doubt rather than guilt and anxiety symptoms (World Health Organisation, 1977). It was defined more by what supposedly caused it rather than by a standard set of symptoms and signs. The concept of neurosis (embedded in that of neurotic depression) implied anxiety driven by conflict of motivations and had origins in psychoanalytic thought.

Neurotic conditions were reflected in diagnostic classifications until the mid-1970s, when Akiskal, Bitarm, Puzantian, Rosenthal, and Walker (1978) criticised the concept of neurosis as covering a multiplicity of conditions, including nonpsychotic depression, mild depression, coexisting neurotic symptoms, reactive/psychogenic depression, and characterological depression. Akiskal's views were important in the construction of new constructs for the third edition of the *Diagnostic and Statistical Manual* (American Psychiatric Association, 1980). These were termed major depression, adjustment disorder, and dysthymia.

The endogenous type of depression has to a large extent been replaced by the construct of major depression. The category of major depression has a set of features that are intended to increase interrater reliability (Kendell & Jablensky, 2003). These developments have been thought to have changed the focus "from a clinically-based biopsychosocial model to a research-based medical model" (Wilson, 1993). The *DSM-III* categories were intended to be descriptive rather than presuming any specific aetiology and have continued into *DSM-IV* with only minor modifications (American Psychiatric Association, 1994a). The 10th edition of the ICD (World Health Organisation, 1992) has now derived similar constructs based on similar premises. This classification system used *depressive episode*

(DE) for a syndrome very similar to major depression and notes that it includes the diagnoses of depressive reaction, psychogenic depression, and reactive depression. The ICD-10 system grades severity on number of symptoms, so that the category of mild DE involves a lower threshold for symptoms to the DE category, with moderate DE having more, while severe DE has superimposed extra symptoms, with or without psychotic symptoms. The concept of neurosis is still present in the category of neurotic, stress-related and somatoform disorders rather than for depression.

The increased interest and confidence in description of symptoms and signs without placing them in a context suggesting aetiology has come at a price. It represents a "significant narrowing of psychiatry's clinical gaze" (Wilson, 1993) at the expense of description of the psychological inner life of depressed people and (arguably) ongoing critical evaluation of the concepts.

Some Americans, notably Winokur (1985) and Wolpe (1986), have argued that the concept of neurotic depression is useful, albeit flawed, and have recommended revisiting the concept – in the light of current thinking. Winokur (1997) conceptualised the depressions as endogenous/psychotic and "those that occur in the context of marked emotional instability," a looser category (p. 105). Wolpe (1986) saw neurotic depressions in terms of their presumed relationship to anxiety states. He proposed a number of purer subtypes, in which depression was hypothesised to be a consequence of various types of anxiety states. These included severe conditioned anxiety (based on erroneous cognitions), anxiety-based interpersonal inadequacy, and an overreaction to bereavement. Wakefield (1998) criticised the drive for a set of atheoretical *DSM* categories as a failure to differentiate between the actual disorder the disorder and its symptoms. He noted that the importance of the role that anxiety plays in the onset of neurotic disorders and the impossibility of doing this without making references of the causation of under lying psychic conflicts.

There are gender implications in that women tend to rate higher on scales reflecting neuroticism and anxiety and have higher rates of anxiety disorders (Breslau et al., 2000). The greatest gender differences in rates of depression are within the potential childbearing age bands (Kessler, McGonagle, & Swartz, 1993; Wilhelm, Mitchell, Slade, Brownhill, & Andrews, 2003), when women also have higher rates of anxiety disorders that have been thought to be contributory (Breslau et al., 2000). This effect could be mediated as an effect of gonadal hormones on limbic system hyperactivity and may carry a biological advantage at times when women needed to be alert (Parker & Brotchie, 2004).

METHODS OF RATING DEPRESSION

The method of measuring depression will also reflect whether it is seen as dimensional (in which caseness is determined by a minimum score on a

dimensional scale) or categorical (i.e., certain characteristics are necessary for inclusion in the category).

In screening populations, an instrument is applied to a wide range of patients to detect those who may benefit from closer assessment, including identifying whether individuals are likely to be cases. Screening tools may include self-report measures, such as the Center for Epidemiological Studies-Depression Scale (CES-D) (Radloff, 1977), the K-10 (Kessler et al., 2002), and the Beck Depression Inventory (BDI) (Beck et al., 1961); clinician-rated tools, such as the PRIME-MD (Spitzer et al., 1994); or case finding instruments (used by clinicians or lay interviewers, of which the most widely used is the Composite International Diagnostic Interview (CIDI) (World Health Organisation, 1996). Upon identification of subjects at increased risk, assessment tools are used to assist in making a diagnosis. These may be clinician rated, such as the CORE (Parker et al., 1994) for melancholic depression, or self-report instruments, such as the BDI (Beck et al., 1961). Finally, outcome measures are used to quantify the effect of interventions and progress of patients. Self-report measures such as the BDI, and clinician-rated instruments such as the Hamilton Depression Rating Scale (HDRS) (Hamilton, 1960) and the Montgomery–Asberg Rating Scale (Montgomery & Asberg, 1979) are commonly used.

In general, women tend to score slightly higher on these types of self-report measures. This seems to reflect differences in perception of distress as well as their tendency to report a wider emotional range in both directions (Wilhelm, Parker, & Dewhurst, 1998). Only more recently has there been much emphasis on positive affect and on whether positive affective states, such as happiness and contentment, are the polar opposites of negative affective states. This approach is reflected in measures of positive and negative emotion (e.g., the Positive and Negative Affect Schedule [PANAS; Watson, Clark, & Tellegen, 1988]) and positive and negative attitudes to life (e.g., the Life Orientation Test [LOT; Scheier & Carver, 1985]).

DEPRESSION CATEGORIES IN CURRENT DIAGNOSTIC SYSTEMS

The current diagnostic systems in clinical and research use are the International Classification of Diseases (ICD), originating in Europe under the auspices of the WHO, and the *Diagnostic and Statistical Manual*, currently in its fourth edition, originating in the United States. The prevailing definition of a depressive episode equates with the construct of major depression based on operational criteria (symptoms and signs), with cut-offs for inclusion in a diagnostic category and minimal reference to presumed aetiology. The DSM system relies on a multiaxial classification to provide other important contextual information, with the diagnosis of psychiatric disorder (i.e., symptom diagnosis) located on the first axis, with four further axes describing personality, any concurrent medical conditions, predisposing life events, and level of functioning in the preceding year.

DIAGNOSTIC SYSTEMS USING OPERATIONAL CRITERIA

The development of the Present State Examination (PSE; Wing, Cooper, & Sartorius, 1974) in England included an index of definition for subthreshold, threshold, and definite cases, which fitted with the then-current *International Classification of Disease* (World Health Organisation, 1977) categories. The Research Diagnostic Criteria (RDC; Spitzer, Endicott, & Robins, 1978), which were developed from an earlier diagnostic system (Feichner, Robins, & Guze, 1972), similarly relied on strict operationalised criteria intended to increase interrater and test-retest reliability of diagnosis for research purposes. In the RDC, primary depression was divided into major (unipolar) depression and bipolar depression (subjects who had also experienced manic episodes). Two new categories, minor depression and intermittent depressive disorder, were also included. These categories were intended to afford a broad coverage of depressive experience and to encompass the endogenous and neurotic depression categories that had been discarded.

As the RDC system was intended for use in both clinical and nonclinical situations, allocation to RDC categories also requires the imposition of functional impairment criteria (i.e., seeking professional help, taking medication for the episode, or a subjective judgement of a significant impact on life of the episode) studies The *DSM-III* criteria were intended for clinical use rather than primarily for research, with the term *disorder* intended to imply that the episode is clinically significant. The reader is referred to a paper comparing *DSM-III* and RDC criteria if more specific information is required (Williams & Spitzer, 1982).

In the 1950s, the advent of antidepressant medications brought a new focus to the discussion of depression types. The biogenic amine dysfunction theory of depression (Akiskal & McKinney, 1973) was advanced in response to the greater appreciation of the potential role for neurotransmitters, stating that depression was maintained by dysfunction of the noradrenergic transmitter system in the central nervous system. Not long after, Beck published the first book on his cognitive treatment of depression (Beck, Rush, Shaw & Emery, 1979), which was part of the vanguard for a plethora of structured psychological approaches for depression. Although it was cognitive therapy, the theory stated that depression was precipitated and maintained by negative thinking patterns, there was a presumption of a final common pathway at a cellular level, such as that suggested by Akiskal.

With the advent of the structured definitions in the later DSM and ICD systems, *clinical depression* has become synonymous with *major depression*, a depressive episode with functional impairment warranting treatment. Akiskal et al. (1978) had argued against the inclusion of the subjective experience of conflict and other personal experiences that were difficult to