The World Psychiatric Association

WPA Educational Programme on Depressive Disorders

Fundamentals

volume

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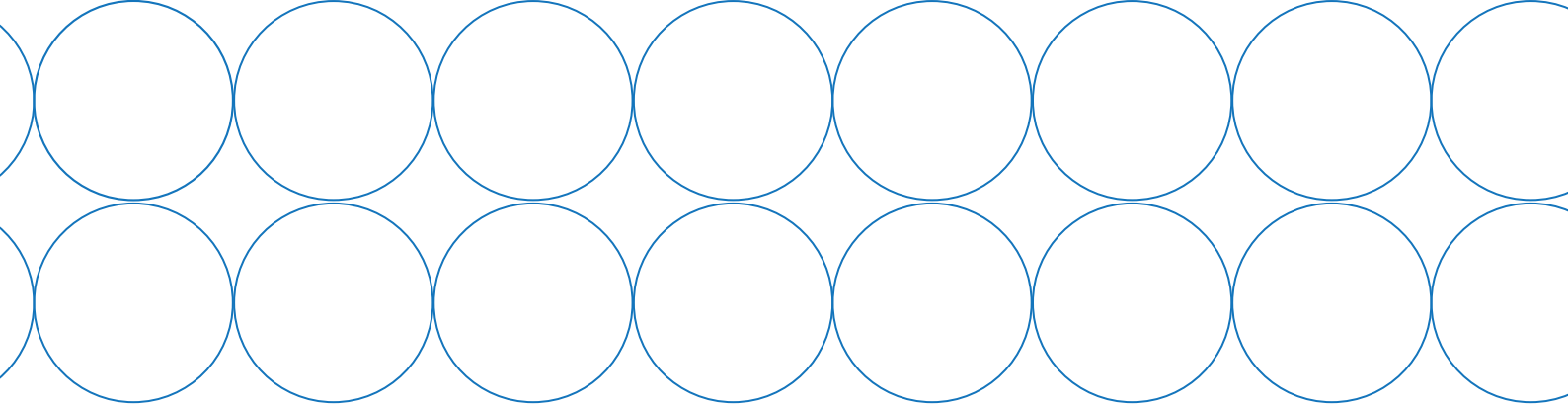

THE WPA EDUCATIONAL SERIES ON DEPRESSIVE DISORDERS

Revision of 2008

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WPA Educational Programme on Depressive Disorders

This programme is designed to be widely used in training psychiatrists as well as health personnel in other branches of medicine in the management of depressive disorders. A previous version of this programme, which was released in 1996, has been translated into a number of languages and used as a basis for the production of local training programmes in several countries.

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VOLUME IV. METHODS OF TRAINING AND EDUCATION ABOUT DEPRESSION

INTRODUCTION

Several important developments made it necessary to update the programme. First, it was necessary to clarify a number of issues concerning the diagnosis and classification of depressive disorders. Recent epidemiological studies, including the World Mental Health Surveys (Kessler et al. 2007), continue to show considerable differences in the prevalence of depressive disorders in different countries. It is likely that most of these differences are due to methodological problems and imperfections in the diagnostic systems (including differences in how the disorders are delineated) currently used in research and practice of psychiatry. On the whole, epidemiological studies indicate that the prevalence of depression is high and increasing. At the same time, there are numerous reports—some produced by groups such as the scientologists and some by other organisations and scientists—stating that the prevalence of depressive disorders is actually stable and that the higher figures are the result of a collusion between the pharmaceutical industry and the medical profession. The need for a clear and authoritative statement about the diagnosis of depressive disorders—for use in practice, teaching, and research—has therefore grown, and this programme needed to be revised to include such a statement.

Another reason for updating this programme was that, in the period between 1996 and 2008, our knowledge of depression has grown and new and important findings needed to be included in the programme. These include findings concerning the comorbidity of depression and physical illness, a new understanding of the ethiopathogenesis of depression, confirmation of the contribution of depression to the global burden of illness, new findings about the high prevalence of depressive disorders in disaster stricken populations, new experiences and evidence about depression in the elderly, and new perspectives concerning pharmacotherapy and psychotherapies.

Depressive disorders in children have also increasingly become a focus of attention among psychiatrists and the general public and the media. The recognition of a risk of suicide at a young age, of the continuity of child and adult depressive disorders, as well as the role of depressive disorders in the causation of physical illness are other reasons for updating this programme.

This new version of the programme consists of four volumes. The Members of the Task Force and the sections of the text for which they had primary responsibility are as follows:

1. Overview and fundamental aspects (O. Gureje, M. Maj)

2. Depressive disorders and physical illness (M. Riba)

3. Depressive disorders in older persons (E. Chiu, H. Chiu)

4. Methods of education about depression (N. Sartorius, D. Goldberg, L. Gask)

5. Depressive disorders in special situations and population groups (O. Gureje, M. Maj, N. Sartorius)

The Task Force who developed the programme included N. Sartorius (Co-chairman), A. Tasman (Co-chairman), M. Benyakar, E. Chiu, H. Chiu, S. Douki, L. Gask, D. Goldberg, O. Gureje, S.V. Ivanov, S. Kanba, M. Kastrup, M. Maj, M. Riba, S. Tyano, and D. Wasserman. Substantial contributions to the text were also received from M. Bradley, S. Chaturvedi, F. Cournos, F. Creed, R. Fahrer, L. Grassi, C. Lyketsos, S. Marcus, K. McKinnon, S.R. Vagnhammar and L. Wulsin. Senior Advisers to the project were: J.J. Lopez-Ibor, F. Lieh Mak, E. Paykel, and C. Stefanis.

REFERENCE

Kessler RC, Angermeyer M, Anthony JC, et al. Lifetime prevalence and age-of-onset distributions of mental disorders in the World Health Organization's World Mental Health Survey Initiative. World Psychiatry 2007;6:168–76.

Note

In the programme, the word "depression" is used to denote the syndrome of depression, as described in the ICD-10 category "Depressive episode" and the DSM-IV category "major depressive episode", unless otherwise specified. All drug dosages mentioned in the text are those recommended by the manufacturers of the relevant drugs.

VOLUME 1

OVERVIEW AND FUNDAMENTAL ASPECTS OF DEPRESSION

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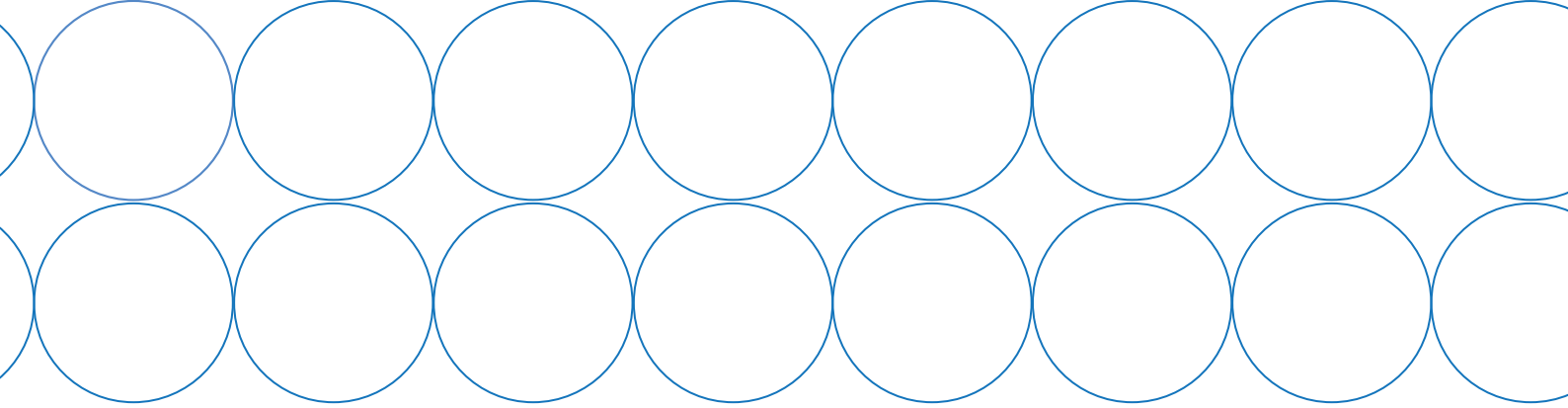

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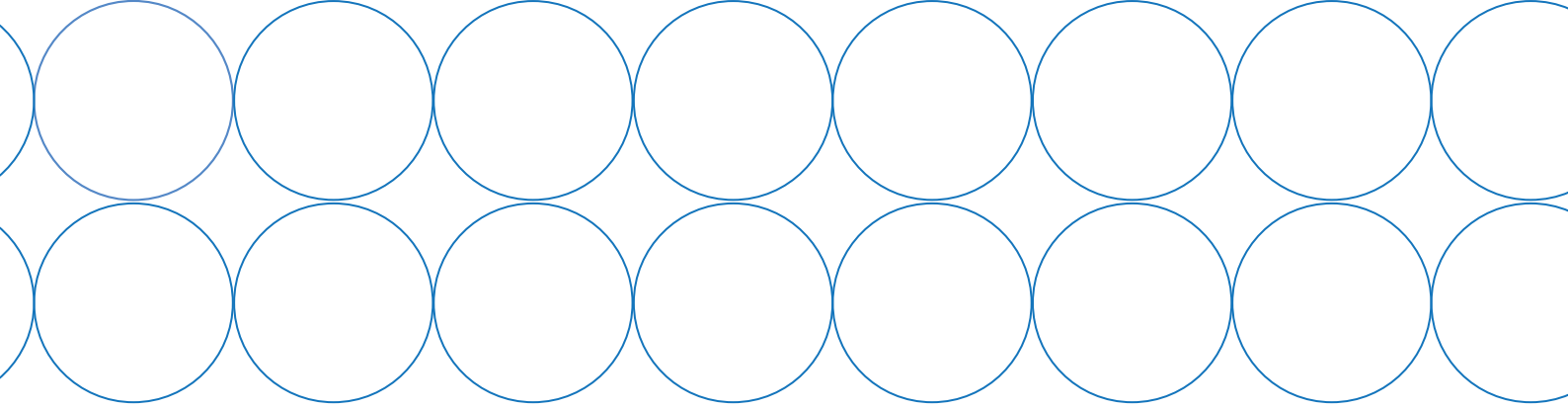

Chapter 1

Concept and Classification of Depressive Disorders

In medicine, the term depression has at least three different meanings: 1) a mood, a feeling, an emotion, an affective state; 2) a symptom of a depressive disorder; and 3) the depressive disorder itself. This text focuses primarily on depressive disorders.

ESSENTIAL FEATURES OF DEPRESSIVE DISORDERS

There are numerous types and variations of depressive disorders, and differentiation is important for effective management. Regardless of the way in which they are grouped, depressive disorders share a number of clinical manifestations:

Mood and affect

Sadness, diminished reactivity to pleasant or unpleasant events, decreased motivation, loss of interest and/or pleasure, lack of feelings, sense of emptiness, apathy, anxiety, tension, irritability, sense of frustration, anger.

Thought-cognition

Diminished concentration, indecisiveness or vacillation, loss of confidence or self-esteem, feelings of worthlessness, unreasonable self-reproach or inappropriate guilt, helplessness, pessimism, hopelessness, death wishes and suicidal ideation.

Psychomotor activity

Retardation: slowing of body movements, stupor, poor facial expression or lack of expression, inhibited interpersonal communication or lack of communication; or

Agitation: restlessness, fidgeting, purposeless and uncontrollable hyperactivity.

Somatic manifestations

Changes in basic functions: insomnia and/or hypersomnia, decreased or increased appetite and body weight, decreased sexual drive.

Changes in vitality: tiredness, fatigability, diminished energy, lack of vigour.

Bodily sensations: pains and aches, feelings of pressure, feeling of coldness, heavy limbs, any other vague and undifferentiated sensations.

Visceral symptoms: gastrointestinal complaints, cardiovascular complaints, other vague complaints about a bodily function.

BIPOLAR DISORDER

Primary care physicians usually see patients who exhibit unipolar depressive disorder, but some patients may have bipolar affective disorder, and physicians should be aware of the differences that exist between the two types of disorder. In bipolar disorder, depressive episodes and manic or hypomanic episodes occur in the same individual.

NORMAL VERSUS ABNORMAL MOOD STATES

Transient feelings of sadness and disappointment are a part of normal life experience. Thus, it is important to clearly differentiate clinical depression from normal adaptive responses to stress, frustration, and loss (e.g., bereavement), manifested as sadness.

CLASSIFICATION OF DEPRESSIVE DISORDERS

Although there are many ways to classify depressive disorders, the ICD-10 (WHO 1992) distinguishes severe, moderate, and mild forms of depressive episodes. Differentiation between these three types of depressive disorder rests upon clinical judgement involving the number, type, and severity of symptoms that are present.

Patients with a severe depressive episode generally are in considerable distress and present with severe symptoms. Marked agitation or retardation may impede their ability to describe symptoms. Personal and vocational functions are severely limited. To meet diagnostic criteria for a severe depressive episode, the patient must meet the general criteria for a depressive episode, have all three typical symptoms, and have at least five additional symptoms (Table 1.1).

TABLE 1.1

Depressive Episode

General Criteria	Typical Symptoms	Additional Symptoms
The depressive episode should last for at least 2 weeks	Depressed mood to a degree that is definitely abnormal for the individual, present for most of the day and almost every day, largely influenced by circumstances, and sustained for at least 2 weeks	Loss of confidence or self-esteem
No hypomanic or manic symptoms sufficient to meet the criteria for hypomanic or manic episode at any time in the individual's life	Loss of interest or pleasure in activities that are normally pleasurable	Unreasonable feelings of self-reproach or excessive and inappropriate guilt
Not attributable to psychoactive substance use or to any organic mental disorder	Decreased energy or increased fatigability	Recurrent thoughts of death or suicide, or any suicidal behaviour
		Complaints or evidence of diminished ability to think or concentrate, such as indecisiveness or vacillation
		Bleak and pessimistic views of the future
		Sleep disturbance of any type
		Change in appetite (decrease or increase) with corresponding weight change

Source: WHO. ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland: World Health Organization; 1992.

Patients with a moderate depressive episode may also have considerable difficulty maintaining personal and vocational role functions, and some symptoms may be quite severe, but on the whole the symptoms are fewer in number and less intense than in severe episodes. The patient with a moderate depressive episode must fulfil the general criteria for a depressive episode, have two of the three typical symptoms, and have four additional symptoms (Table 1.1).

Patients suffering a mild depressive episode, sometimes called minor depression, are generally distressed by the symptoms but continue to maintain personal and vocational role functions, although they often find this difficult. The patient with a mild depressive episode must fulfil the general criteria, have two of the typical symptoms, and have two additional symptoms (Table 1.1).

In the ICD-10 Classification of Mental Disorders for use in primary health care (WHO 1996), the criteria for diagnosis of depressive episodes have been simplified.

DYSTHYMIA

Dysthymia is a disorder characterised by a chronic low-level depressed mood present for 2 or more years, with occasional periods of "wellness" that rarely last more than a few weeks at a time. In addition to the low mood, at least three other symptoms must be present (Table 1.2) (WHO 1996).

OTHER FORMS OF DEPRESSIVE DISORDERS

In addition to the main forms of depressive disorders, certain subforms merit separate descriptions because of their prognostic and therapeutic implications. The descriptions that follow are based on the ICD-10 (WHO 1992).

Psychotic Depression

Psychotic depression is a depressive disorder that presents with psychotic symptoms (e.g. hallucinations and delusions) and significant psychomotor disturbances. In contrast to schizophrenia and schizoaffective disorders, however, these psychotic features are never present without concurrent mood symptoms. Moreover, the content of hallucinations and delusions in psychotic depressive disorder is usually consistent with the predominant mood of sadness (mood-congruent).

Therapeutic implications: Antidepressants combined with either electroconvulsive therapy (ECT) or antipsychotic medication are superior to antidepressants alone.

Melancholia (Somatic Syndrome)

Key features of depressive disorder with somatic symptoms (in ICD-10 nomenclature) are loss of interest or pleasure in activities that are normally enjoyable, lack of emotional reactivity to normally pleasurable surroundings and events, early morning waking, depression worse in the morning, psychomotor retardation or agitation, marked loss of appetite, weight loss, and marked loss of libido. These forms of depressive disorder are more common in older patients.

Therapeutic implications: Patients with severe symptoms of this type are likely to respond to antidepressant drugs in combination with ECT.

Atypical Depression

The atypical subform is usually seen in younger patients and is characterised by numerous reversed vegetative symptoms of increased sleep and appetite, which are quite infrequent in most cases of depressive disorders.

Therapeutic implications: Monoamine oxidase inhibitors are more effective than tricyclic antidepressants (Quitkin et al. 1979).

Seasonal Depressive Disorder

Key features of seasonal depressive disorder are recurrent episodes, a temporal relationship between the onset of the depressive episode and a particular period of the year (e.g., regular onset in fall and offset in spring), seasonal episodes that outnumber nonseasonal episodes, and depressive symptoms disappearing between (seasonal) episodes.

Therapeutic implications: Light therapy seems effective in short-term management.

Rapid-Cycling Bipolar Depression

The rapid-cycling subform of bipolar disorder is associated with frequent occurrences of mood episodes (four or more per year). Mood episodes include depressive episodes, manic or hypomanic episodes, and mixed (manic-depressive) episodes. The mood episodes may follow one another, with or without asymptomatic periods. Rapid cycling may occur spontaneously (usually over the long-term course of bipolar disorder), or it may be speeded by antidepressants. Concurrent thyroid-axis disease may also cause rapid cycling.

Therapeutic implications: Response to lithium is poor in rapid-cycling bipolar disease. Therefore, use of other mood stabilisers, such as anti-epileptics, is a preferred option.

TABLE 1.2

Dysthymia

Criteria	Symptoms
At least 2 years of constant or constantly recurring depressed mood	Reduced energy or activity
Intervening periods of normal mood rarely last for longer than a few weeks; no episodes of hypomania	Insomnia
None, or very few, of the individual episodes of depression within the 2-year period should be sufficiently severe or long-lasting to meet the criteria for recurrent mild depressive disorder	Loss of self-confidence or feelings of inadequacy
During at least some of the periods of depression, at least three of the symptoms listed below should be present	Difficulty in concentrating
	Frequent tearfulness
	Loss of interest in or enjoyment of sex and other pleasurable activities
	Feeling of hopelessness or despair
	A perceived inability to cope with the routine responsibilities of everyday life
	Pessimism about the future or brooding over the past
	Social withdrawal
	Reduced talkativeness

Source: WHO. ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva, Switzerland: World Health Organization; 1992.

Secondary Depressive Disorder

Certain depressive disorders can occur secondary to other mental or physical disorders (e.g., postpsychotic depressive disorder, depression due to carcinoma of the pancreas) or to the use of dependence-producing substances or certain medications (see Volume I, Chapter 3). Although less frequent than primary depression, secondary depression should be considered in the differential diagnosis, particularly when the patient does not respond to treatment as anticipated.

Therapeutic implications: It may be necessary to treat the depressive disorder concomitantly with treatment of the primary condition.

Postpartum Depression

There are three forms of postpartum depression:

1. Postpartum blues is a common phenomenon occurring in one third of mothers in the early postpartum period. It is a transient phenomenon that usually requires no treatment.

2. Mild or moderate postpartum depression occurs in up to 10% of mothers in the year following childbirth. Treatment is the same as for other forms of mild or moderate depression.

3. Postpartum psychosis often presents with a mixed atypical picture. Depression and manic features are common, and there is a high relationship with subsequent bipolar disorder.

Recurrent Brief Depression

The ICD-10 criteria for recurrent brief depression (RBD) are a dysphoric mood or loss of interest for a duration of less than 2 weeks, recurrent presentations, and at least four of the following symptoms: poor appetite, sleep problems, agitation, loss of interest, fatigue, feeling of worthlessness, difficulty in concentrating, and suicidal tendencies.

Mixed Anxiety-Depression Syndrome

Some patients have symptoms of both anxiety and depression, but neither set of symptoms, considered separately, is sufficiently severe to justify a diagnosis. This disorder should be distinguished from depressive disorders with a mixture of anxiety symptoms and anxiety disorders with some depressive symptoms. In mixed anxiety-depression syndrome, some autonomic symptoms (tremor, palpitations, dry mouth, stomach churning) are also present, if only intermittently.

Subthreshold Depression

Recently, particular attention has been paid to depressed patients who do not have the number or severity of symptoms required for a full diagnosis of depressive disease. It has been found that these patients with so-called "subthreshold depression" are at high risk for future depressive episodes, and that they may have substantial limitations in functioning and well-being.

COURSE OF ILLNESS

The outcome of individual episodes of depressive disorders is usually good, and full remission can be achieved in most patients if they are treated appropriately. However, a clinical study involving a 9-year follow-up of patients with major depressive disorder found that patients spent 15% of the time with symptoms at the level of major depression (Judd et al. 1998b). The course and outcome of depressive disorders depend on a variety of factors, ranging from those inherent to the illness and the presence or absence of a personality disorder to the adequacy of support patients receive from family, friends, and others in their social environment.

Follow-up studies of depressed patients show a significant risk for chronicity and relapse (Keller et al. 1986). A review of the literature suggests that approximately 50% of patients with major depression experience only one episode, 20% exhibit a recurrent course of illness, and 30% become chronically depressed (Angst et al. 1990; Merikangas et al. 1994). The majority of recurrent episodes occur within 2 years of

Classification Guidelines
ICD-10, DSM-IV-TR

The 10th version of the International Classification of Diseases (ICD-10) Classification of Mental and Behavioural Disorders is the official classification system used in all 180 member states of the World Health Organization. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), developed and published by the American Psychiatric Association in 1994 (with a text revision published in 2000), was designed to be compatible with the ICD-10. The vast majority of categories exist and are described in the same way in both classifications, so that uniform reporting systems can be used throughout the world. All categories found in DSM-IV are also found in ICD-10, but the latter has some additional categories not present in the former. The ICD-10 classification has several versions, including a user-friendly clinical version (WHO 1992), a research version (WHO 1993), and a version for use in primary health care (WHO 1996).

Historical Note

Depressive disorders have been present and described throughout the ages. For example, depressive disorders were described by Hippocrates (who coined the term melancholia) and Rufus of Ephesus. The term melancholia continued to be used by other medical authors, including Aratalus (AD 120–180), Galen (AD 129–199), and Alexander of Tralles in the sixth century. The first book in Arabic on this topic was written in the 10th century by Ishak Ibn Omran, in Tunis. The 12th-century Jewish physician Maimonides considered melancholia a separate disease entity (Kaplan et al. 1995).

Reactive Versus Endogenous Depression

Depressive disorders were previously distinguished by traditional dichotomies such as neurotic versus psychotic conditions (based on the intensity and quality of symptoms) or reactive versus endogenous depression.

The symptoms considered characteristic for endogenous depression include prominent physiological disturbances (e.g., weight loss, decreased energy, sleep disturbances, and psychomotor retardation or sometimes agitation), absence of environmental precipitants, and lack of reactivity. In contrast, the diagnosis of reactive depression was made in cases that included precipitating events and life stresses and had few significant vegetative disturbances. A fluctuation of symptoms in response to concurrent environmental change and preserved day-to-day functioning were also used for the diagnosis of reactive depression.

The problem with this model is that very few people who are depressed fall neatly into either of these two categories. Most presentations lie somewhere on a continuum between the endogenous and the reactive extremes, without any sharp boundary, and mixed cases are common. In the past, treatment decisions have often been based on this differentiation (e.g., with antidepressants prescribed for endogenous depression and psychotherapy for neurotic depression), but this is no longer considered relevant for treatment choice.

remission. Most studies suggest that the greater the number of past episodes, the higher the risk of recurrence. Residual symptoms, continued sleep disturbance, and the persistence of neuroendocrine abnormalities may also be predictive of a relapsing illness. Compared with patients who are asymptomatic following treatment, those who have residual symptoms are at elevated risk for a more severe course of illness, greater chronicity, and faster relapse or recurrence (Judd et al. 1998a; Judd et al. 2000). Proper monitoring and management of residual symptoms must therefore be part of the maintenance phase of therapy (Karp et al. 2004; Nierenberg et al. 2003). Alcoholism and drug abuse also contribute to increased risk of recurrence.

THE PATIENT PERSPECTIVE

If we are help those suffering from depression, it is essential that we take the patient's perspective fully into account, especially through an examination of personal accounts of mental illness (Gask 1997). This brief review draws particularly on several studies by Karp and a meta-synthesis of studies by Khan and colleagues. In the early 1990s, Karp undertook extensive interviews with people who had been diagnosed and treated for unipolar depression (Karp 1994, 1996) and also performed a case study of a self-help group for affective disorders (Karp 1992). In 2007, Khan and colleagues published a meta-synthesis of qualitative papers that discussed the experience of depression (Khan et al. 2007). For further personal accounts of depression, one should explore those published by Styron (Styron 2001) and the semi-autobiographical review by Andrew Solomon, The Noonday Demon (Solomon 2001). Most of the work cited in this section is based on qualitative research on depression, however, where indicated, the text draws on the results of survey research.

The Experience of Depression

Khan and colleagues (Khan et al. 2007), who primarily examined experiences in the United Kingdom across different ethnic groups, noted that depression was most frequently attributed to external sources of stress or conflict, including conflict with work colleagues or family, chronic illness, events in childhood, material disadvantage, and racism (Burr and Chapman 2004; Grime and Pollock 2004; Kadam et al. 2001; Rogers et al. 2001). Rather than emphasising symptoms or feelings of depression, respondents mainly reported an inability to cope and, in particular, disturbances to everyday functioning and social roles (with negative consequences for other family members) (Burr and Chapman 2004; Kadam et al. 2001; Knudsen et al. 2002; Maxwell 2005; Rogers et al. 2001). Metaphors used by respondents to communicate the experience of depression included being "on edge", "churned-up inside", "boxed in", "a volcano bursting", "broken in half", "shut in my own little shell", "a wall of pain", and "prisoner in my own home" (Kadam et al. 2001). Most importantly, patients' assessment of the cause of their problems differed from the psychological model, which underlies cognitive–behavioral therapy and the prescribing of antidepressants.

Karp's collected accounts (Karp 1996) provide a breadth of different experiences and a richness of detail which, as Styron commented in his biographical account, are simply not conveyed by the simplistic listing of nine symptoms in the DSM-IV.

Burr and Chapman challenged traditional psychiatric trans-cultural wisdom about the experience and presentation of somatic symptoms of depression (Burr and Chapman 2004) based on their interviews with South Asian women. Their respondents freely described emotional experiences and their impact on their overall physical well-being. Effects of depression included more traditional emotional symptoms in addition to a range of physical experiences: nausea and vomiting, general aches and pains in the joints, headache, painful menstruation, and asthma attacks.

When asked to describe her experience of depression, a female nurse described her state of mind as follows:

A sense of being trapped, or being caged, sort of like an animal, like a tiger pacing in a cage. That's sort of how I feel. I feel like I'm in a cage and I'm trapped, and I can't get out and it's night-time and the daylight's never going to come (Karp 1996).

Here is a male professor's response to the same question:

When you are really depressed, you know, if you're in your bedroom and someone said there's a million dollars on the other side of the room and all you have to do is swing your feet over the edge of the bed, and walk over and get the million, you couldn't get the million. I mean you literally couldn't (Karp 1996).

Studies of women experiencing post-natal depression in a variety of regions challenge the assumption that socio-cultural contexts associated with childbirth in non-western societies "protect" mothers from depression. In-depth interviews with women in Goa, India revealed that factors unique to the women's cultural background, such as gender preference and the low involvement of husbands in childcare, were perceived as major stressors by the women. Respondents interpreted emotional distress within the context of social adversity, poor marital relationships, and cultural attitudes towards gender rather than as a biomedical psychiatric category (Khan et al. 2007). Some women in Hong Kong with postnatal depression described themselves as being trapped in a situation from which their only means of escape was violent, such as homicide or suicide (Chan et al. 2002). Women attributed their unhappiness to a noncaring husband, and controlling and powerful in-laws.

A Swedish study that examined gender differences in the experience of depression noted that men seemed to talk more easily about physical distress while women talked more readily about emotional distress (Danielsson and Johansson 2005).

Age-related differences in the experience of depression have also been explored. In a focus group in Portland, Oregon, teenagers described an "illness trajectory" similar to that found in adults with depression: a slow growth of distress, a time of "being in a funk", and a period in which they considered whether they were depressed (Wisdom and Green 2004). Elderly patients with depression interviewed in Manchester, England viewed depression as "understandable", a product of social and contextual issues rather than an "illness", a view shared by many of their general practitioners (Burroughs et al. 2006).

Seeking Help

Karp has described the stages through which many of his interviewees passed before coming to terms with depression: 1) having inchoate feelings of distress, 2) coming to feel that something is "really wrong", 3) having a crisis, 4) coming to grips with an "illness identity", and sometimes 5) defining depression as a condition that one can get past (Karp 1994).

Based on their review of studies done in the United Kingdom, Khan et al. (2007) concluded that the experience of depression and failure to cope with everyday life could lead people to seek help from a primary caregiver. Patients who felt overwhelmed by feelings of their inability to cope (Rogers et al. 2001) or whose inaction had led to negative consequences for family members (Maxwell 2005) exhibited a desire to get help. However, engaging with primary care was problematic. Patients used primary care because they saw it as the only place where help was offered, rather than because they believed that primary care services would be effective. Accessing help was viewed as a set of "moral actions" (Maxwell 2005) . The Scottish women in Maxwell's study saw emotions as something that they should be able to control, and they viewed seeking help for non-physical problems as a failure to cope. They sought help only in order to "do right" by their family, for whom they perceived themselves as being unable to care. Some of these feelings were further complicated by a sense of shame and lack of legitimacy, which could lead to the covert presentation of psychological problems (Burr and Chapman 2004; Rogers et al. 2001). Moreover, accessing help could threaten an already weakened sense of self if it led to discussions about treatments that patients found unacceptable (such as medication or referral to specialist mental health services).

In a study of working-age adults with a diagnosis of depression in Manchester, England, some patients unquestioningly accepted a low quality of care (Gask et al. 2003). Patients often felt that they were "wasting their doctor's time" and that doctors were unable to listen to them and understand how they felt. Older patients in the same city had similarly limited expectations of treatment (Burroughs et al. 2006). Older people in London from a range of ethnic backgrounds considered that combating depression was an individual task, with medical support being only a secondary source of aid (Lawrence et al. 2006). They were also acutely aware of their doctors' time.

Stigma Associated with Treatment

The stigma associated with mental health problems has been well documented world-wide (Sartorius and Schulze 2005).

Prior et al. (2006) suggested that stigma is an insufficient explanation for a reluctance to disclose emotional problems to health professionals. However, Khan et al. (2007) found that there was a considerable stigma in seeking treatment for depression, more so among black than white patients according to a study in the United States (Cooper-Patrick et al. 1997).

Taking medication for depression (the commonest treatment that was offered) has been reported to be associated with a potential threat to the sense of self. In contrast, a sense of personal responsibility for coping with depression, the fear of a loss of function in everyday life, and a need to accept help for the sake of others have been reported to play a role in a patient's decision to accept medication (Grime and Pollock 2004; Knudsen et al. 2002; Maxwell 2005). Respondents were wary of telling others that they were taking antidepressants, because of the combined stigma of depression and taking psychiatric medications (Grime and Pollock 2004; Knudsen et al. 2002).

Treatment and Recovery

Karp's interviews with patients in the United States revealed that taking drugs prescribed by doctors involves an exhaustive interpretative process about the meaning of having an "emotional illness", which changes over the course of a "depression career" (Karp 1993). The four stages in the process were identified as resistance, trial commitment, conversion, and, eventually, disenchantment. In Grime and Pollock's study in central England, medication users reported that they perceived themselves as people who needed to take antidepressants in order to get through daily life and were therefore somehow deficient (Grime and Pollock 2004). Respondents spoke of guilt and of letting themselves or others down, and expressed concerns about long-term changes to their personality associated with treatment.

Numerous qualitative studies that have explored nonadherence with antidepressant medications have revealed discomfort with psychiatric diagnoses, denial of the illness, problematic side effects, fears about dependency, and feelings that medication is unhelpful following resolution of the acute phase (Byrne et al. 2006). Bollini et al. (2004) in Switzerland found that denial of the disease and the need to assess its permanence were the main causes of nonadherence rather than side effects. In contrast, Haslam et al.(2004) in England concluded that side effects and fear of dependence were a major problem. An Australian large-scale survey study suggested that those who had sought treatment for depression were less confident about the helpfulness of lifestyle interventions and more positive about the efficacy of antidepressants compared with those without treatment experience. Those with current symptoms were also less likely to rate family and friends as helpful in coping with illness (Jorm et al. 2000).

Surveys of the lay public in Western European countries have revealed that "talking therapies" (i.e., psychotherapy interventions) remain the most popular treatment (Churchill et al. 2000; Riedel-Heller et al. 2005). Respondents expected that discussing their problems would be therapeutic in its own right (Kadam et al. 2001). According to a study performed in the United Kingdom by Glasman and colleagues, patients did not always follow the principles and exercises prescribed by their cognitive-behavioural therapist. They instead reconstructed the principles of cognitive–behavioral therapy in eclectic ways that had meaning and applicability to their attempts to live with psychological problems on an everyday basis. Self-help activity was described as "hard work", and participants reported that there were times when they faced crises or lapses in their ability to use the techniques (Glasman et al. 2004).

Lawrence and colleagues (2006) undertook a study of older people with depression from three ethnic groups in London. They found that, within the black Caribbean group, conversing with God through prayer was seen as an effective means of overcoming depression, while a large proportion of South Asian and white British participants identified families as an important source of help. Emphasis on spirituality as an important means of coping and source of support has also been found in black patients in North America suffering from depression (Cooper-Patrick et al. 1997).

In a study in the United Kingdom by Badger and Nolan (2007), patients reported that they felt that multiple factors contributed to recovery from depression, with two-thirds of the participants indicating that they felt medication had contributed to their recovery. The factors that patients considered important in recovery changed, however, with the passage of time and many perceived personal strengths as important to recovery. Practitioners who acknowledged and encouraged people's roles in recovery and supported multifaceted care were perceived by users as being caring and as offering holistic, individualised care. These investigators concluded that people with depression are eager to regard their recovery as multifactorial and to have their own roles in the recovery process acknowledged. It is also important to note that many patients, even those who would benefit from long-term care, find current conceptions of depression as a "chronic disease" difficult to accept and are more likely to view interventions as "short term and temporary" (Maxwell 2005).

CONCLUSION

There is a limited but important literature that examines depression from the perspective of the patient. In order to more effectively treat patients, professionals should better understand how depression is experienced; why, when, and how help is sought; and attitudes towards treatment and recovery. An important limitation of this literature is the lack of data on depression in low-income individuals and in those in developing countries.

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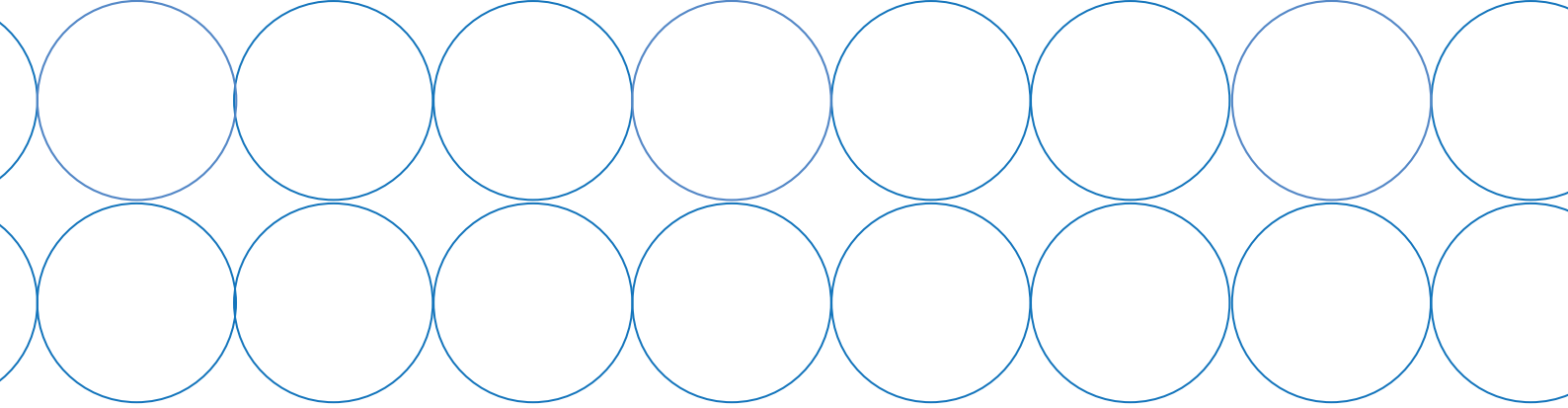

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Chapter 2

Epidemiology And Impact Of Depressive Disorders

EPIDEMIOLOGIC FINDINGS

Several large epidemiological studies of depressive disorders have been conducted in the past few decades. One of the earliest of these, the National Institute of Mental Health (NIMH) Epidemiologic Catchment Area (ECA) study, revealed that 9.5% of the US population over 18 years of age was afflicted by a mood disorder in any 1-year period (Regier et al. 1993). In recent years, other population studies using broadly similar ascertainment tools have been reported. The World Mental Health surveys, conducted in several countries, provide 12-month estimates of the prevalence of major depressive disorder that range from just under 1.0% in Nigeria to over 6% in the United States (Demyttenaere et al. 2004). **Table 2.1** shows 12-month prevalence estimates from studies utilising similar assessment tools. Studies conducted in other regions show comparable rates; for example, the 12-month prevalence of major depression was 6.7% in Australia (Andrews et al. 2001) and 5.7% in Chile (Vicente et al. 2006). Community surveys of children and adolescents as well as those of elderly persons show that depression is also a common disorder in these age groups (See Volume III, Chapters 1 and 3 for reviews of relevant studies concerning depression in the elderly and in children and adolescents).

Depressive disorders are not only frequent in the general population but are among the most prevalent conditions seen in primary care practice. Prevalence studies of depressive disorders conducted in primary care settings report varied figures, all of them relatively high. A major international study conducted at 14 sites in 12 countries found median rates of more than 10% (Ustun and Sartorius 1995).

The prevalence rates of depressive disorders in patients suffering from a physical illness are even higher. For example, studies have reported the occurrence of depressive disorders in 22%–33% of all medical inpatients, in 33%–42% of cancer patients, in 47% of stroke patients during the first 2 weeks after the event, in 45% of patients who

TABLE 2.1

Epidemiological studies: Lifetime and 12-month rates of major depressive disorder

	US (NCS-R)	Europe (ESEMeD)	New Zealand (NZMHS)	Mexico (M-NCS)	Nigeria (NSMHWB)
Lifetime prevalence	16.6	12.8	16.0	7.2	3.3
12-month prevalence	6.2	3.9	5.7	3.7	1.0

NCS-R, National Comorbidity Survey-Replication

ESEMeD, European Study of the Epidemiology of Mental Disorders

NZMHS, New Zealand Mental Health Survey

M-NCS, Mexican National Comorbidity Survey

NSMHWB, Nigerian Survey of Mental Health and Well-Being

Source: Kessler RC and Üstün TB, Eds. (2008). The WHO World Mental Health Surveys: Global Perspectives on the Epidemiology of Mental Disorders. Cambridge University Press, New York, NY.

have had a myocardial infarction (MI) patients during the days immediately following the event, and in 33% of patients 3 to 4 months after an MI (Bukberg et al. 1984; Katon and Sullivan 1990; Robinson et al. 1983; Schleifer et al. 1989) Pain, the most common complaint with which patients present in clinical practice, is particularly likely to be associated with depression. Reports of studies conducted in both community and primary care settings show that depression is highly prevalent among persons with chronic pain around the world (Gureje et al. 1998, 2007). (For a fuller discussion of the epidemiology of depressive disorders in the presence of physical illness, see Volume III on Physical Illness and Depression).

Even though some differences exist, the core symptoms of depressive disorders show many similarities across different countries. Somatic symptoms, psychomotor retardation, and anhedonia are the most commonly encountered symptoms in depressed patients world-wide.

Globally, patients with a depressive illness are more likely to be diagnosed and treated by a primary care physician than by a psychiatrist. In the United States, where the number of psychiatrists is relatively high, 50% of community residents with major depressive illness are seen by primary care practitioners, while only 20% are seen by psychiatrists (Perez-Stable et al. 1990). In the United Kingdom, most patients with depression are treated by general practitioners, and only 10% of these patients are referred to psychiatrists (Goldberg and Huxley 1992). In some other countries, fewer than 5% of all persons with a mental disorder are seen by a psychiatrist (Madianos and Stefanis 1992).

Four decades ago, Watts (1966) coined the term "iceberg phenomenon" to describe the situation in which only a small percentage of patients in a community sought medical help and saw general practitioners, and an even smaller number—the visible part of the iceberg—consulted a specialist. Goldberg and Huxley further developed this concept in their description of the three filters to psychiatric care (Goldberg and Huxley 1980, 1992). Based on their reviews of Western European and North American studies, they found that as few as 10% of the patients in the community are seen by specialists and that this low percentage may related to several factors: the decision to seek care or a display of illness behaviour on the part of the patient (the first filter), the detection skills of primary care clinicians (the second filter); and the willingness of the clinician to refer the cases that are detected to specialists (the third filter).

An important issue in the epidemiology of depressive disorders is the frequent comorbidity with other psychiatric conditions. Up to 30% of people with depressive disorders have been found to have symptoms of anxiety disorder or to suffer from panic attacks (Clayton et al. 1991). In some countries, 10% to 50% of patients with a depressive disorder have been found to have problems with alcohol dependence (Kaplan and Sadock 1991).

Another important finding is the cohort effect in depressive disorders. For example, Klerman *et al.* (1985) reported an apparent increase in risk of lifetime major depression among those born in the United States since World War II, as well as an earlier age of onset for the disorder in recent years. Similar findings have been published in Germany, Canada, and New Zealand (Simon and VonKorff 1992), although such trends have not been consistently observed in other countries (Simon et al. 1995). Whether the observed cohort effect represents a real increase in prevalence and decrease in age of onset or whether it is an artefact is still a matter of debate. There are, however, indications that depressive disorders will become an even greater problem for public health in years to come (Madianos and Stefanis 1992).

IMPACT OF DEPRESSIVE ILLNESS

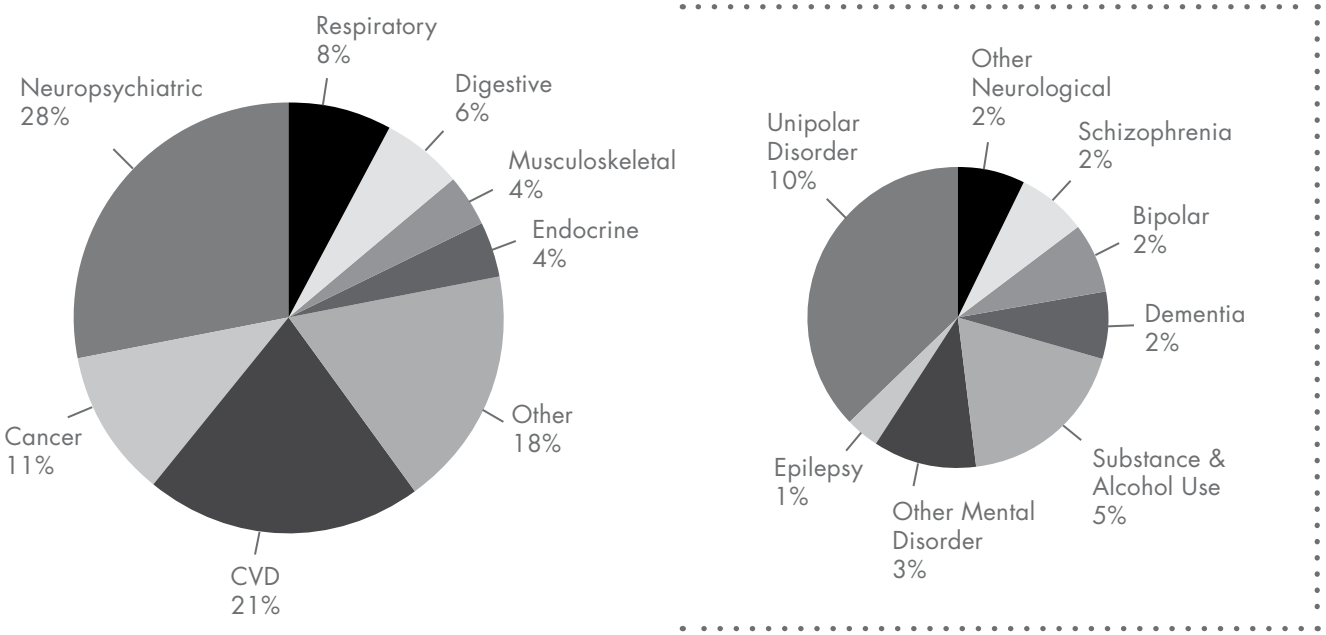
The impact of depression on society has now been well documented (Desjarlais et al. 1995). The Global Burden of Disease study found that depression was the fourth most burdensome of all medical conditions throughout the world in 1990, and predicted that it would become the second most burdensome by 2020 (Murray and Lopez 1996). An important metric that allows comparison of the societal impact of various health conditions was introduced in 1993 by the Harvard School of Public Health in collaboration with the World Bank and the World Health Organization. This metric, disability adjusted life years (DALY), combines information on the impact of premature death and of disability and other non-fatal health outcomes. As described by the World Health Organization (2001), DALY represents the sum of years of life lost due to premature mortality (YLL) in the population and the years lost due to disability for incident cases of the health condition. Using this metric, neuropsychiatric disorders accounted for about 28% of total DALYs lost due to non-communicable diseases in 2005 (**Figure 2.1**). Unipolar depression was the largest contributor to this figure, accounting for 10% of the 28% DALYs lost.

CONSEQUENCES FOR PATIENT AND FAMILY

A large body of evidence suggests that unipolar major depressive disorder is commonly associated with significant psychosocial disability. Even states of sub-threshold depressive symptoms that do not attain diagnostic status have now been found to be associated with considerable levels of disability, and significant increases in disability have been reported with each stepwise increase in depressive symptoms. Patients with depressive disorders report poorer intimate relationships and less satisfying social interactions (Bothwell and Weissman 1977). In addition to potentially reversible limitations in ability to perform activities of daily living at work, home, and school, individuals with depressive disorders commonly experience irreversible consequences of their illness, such as reduced educational attainment and increased likelihood of teenage pregnancy and marital instability (Kessler et al. 1995, 1997, 1998). They may suffer from a variety of different functional limitations, experience significant impairment in their ability to perform everyday activities, and find it difficult to cope with family and job responsibilities (Weissman and Paykel 1974).

FIGURE 2.1

Disability Adjusted Life Years (DALYs) due to non-communicable diseases in 2005: contributions of disease groups and of specific neuropsychiatric disorders



Depressive disorders may also increase the patient's susceptibility to other illnesses. Depression can amplify medical symptoms such as pain and decrease a patient's ability to participate in his or her medical care. Depression has been shown to prolong hospitalisation for other medical illnesses and to worsen their prognosis (Verbosky et al. 1993).

The most tragic consequence of untreated or inadequately treated depression is suicide, and reported suicides probably represent only a fraction of the self-inflicted deaths that occur due to depression (Robins et al. 1959; Roy 1986).

Finally, the stigma associated with the diagnosis and treatment of mental illness compounds the suffering of patients and their families and reduces the probability that those affected will seek medical help.

ECONOMIC CONSEQUENCE OF DEPRESSIVE DISORDERS FOR THE HEALTH CARE SYSTEM AND SOCIETY

The costs associated with untreated or inadequately treated depressive illness are likely to be staggering in all societies. Figures available for highly industrialised countries show that direct costs (i.e. cost of treatments for depression, such as antidepressant medication, psychotherapy, electroconvulsive therapy, psychiatric hospitalisation) are significant; however, the greatest burdens are the indirect costs. These include increased use of the healthcare system for other medical complaints, often somatic symptoms that are masking an underlying depressive illness; prolonged hospitalisations for other medical illnesses; increased absenteeism and decreased productivity at work; and premature death from suicide.

It is estimated that more than 20% of direct health care costs in the European Union result from diseases of the nervous system, most commonly depression. In the United Kingdom, direct costs associated with depression are estimated at £420 million, while indirect costs are estimated at £3 billion (Kind and Sorensen 1993).

As in the United Kingdom, indirect costs in the United States far outstrip direct treatment costs. Greenberg and colleagues (2003) estimated that the economic burden of depression in 2000 in the United States was $83.1 billion. Of this, 31% (or $26.1 billion) represented direct medical costs such as charges for medical and psychiatric care, 7% ($5.4 billion) were related to the costs of suicide mortality, while the largest percentage—62% (or $51.5 billion)—represented indirect workplace-related costs such as absenteeism and reduced productivity, mostly associated with untreated or inadequately treated depressive disorders. The increased risk of physical illness and hospitalisation among those with depressive disorders may also contribute to work absenteeism.

In fact, disability is a significant factor in the costs associated with depressive illness. In a series of population studies conducted in 15 countries across the world, depression was consistently associated with disability than several chronic physical conditions (Ormel et al. 2008). Using the Sheehan Disability Scale (Sheehan et al. 1996), the authors showed that persons with depression had a higher mean disability rating and were more likely to be rated as severely disabled than persons with arthritis, asthma, diabetes and high blood pressure. These results were true for high-income as well as low- and middle-income countries. Paradoxically and compounding the disablement, depressed subjects were less likely to receive treatment even when analysis was focused on participants rated as having severely disabling disorders and this was the case for both affected persons residing in high-income and even more so for those living in low- or middle-income countries.

Another economic consequence of inadequately treated depression is increased use of medical services (Johnson et al. 1992). Depression has been shown to be associated with more visits and calls to the physician, an increase in laboratory tests, and unnecessary prescriptions (Weissman and Klerman 1977). It has been estimated that 66% of undiagnosed depressed patients make more than 6 visits a year to a primary care physician for somatic complaints that actually mask an underlying depression (Katon 1987). The economic

costs associated with depression are partly, but not totally, due to the presence of medical comorbidity. An international study conducted in primary care settings in 6 countries (Spain, United States, Australia, Russia, Israel, and Brazil) found that medical comorbidity was associated with a 17%–46% increase in health care costs in five of the six sites (Chisholm et al. 2003).

A growing body of evidence suggests that the indirect costs of depressive illness can be reduced by effective treatment. Several studies have demonstrated that treatment costs for patients with both medical and psychiatric illness can be reduced by early and appropriate psychiatric intervention for mental illness (Lopez-Ibor 1990; Lyons et al. 1986).

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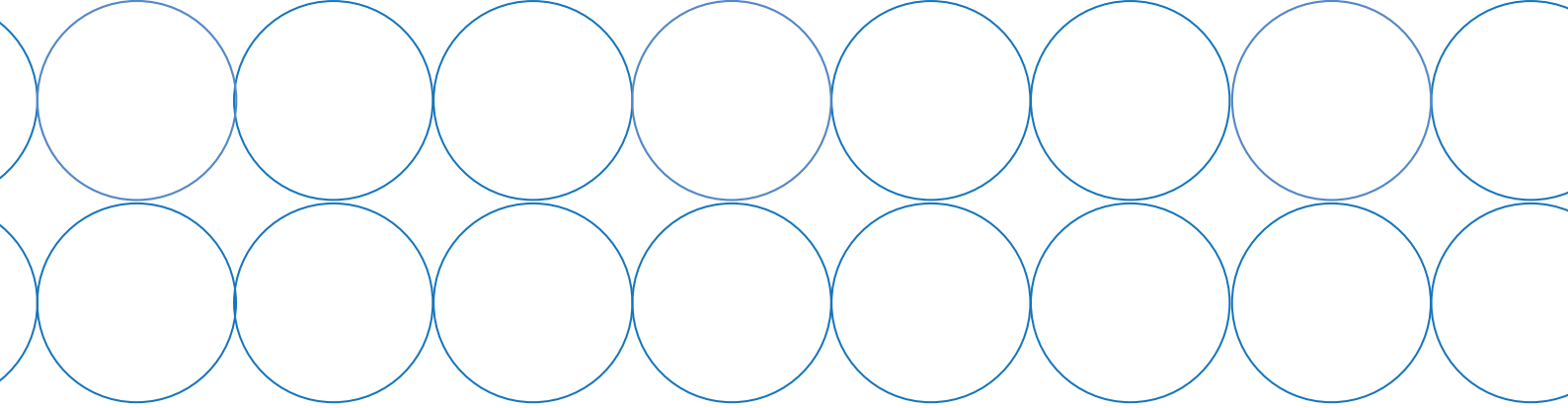

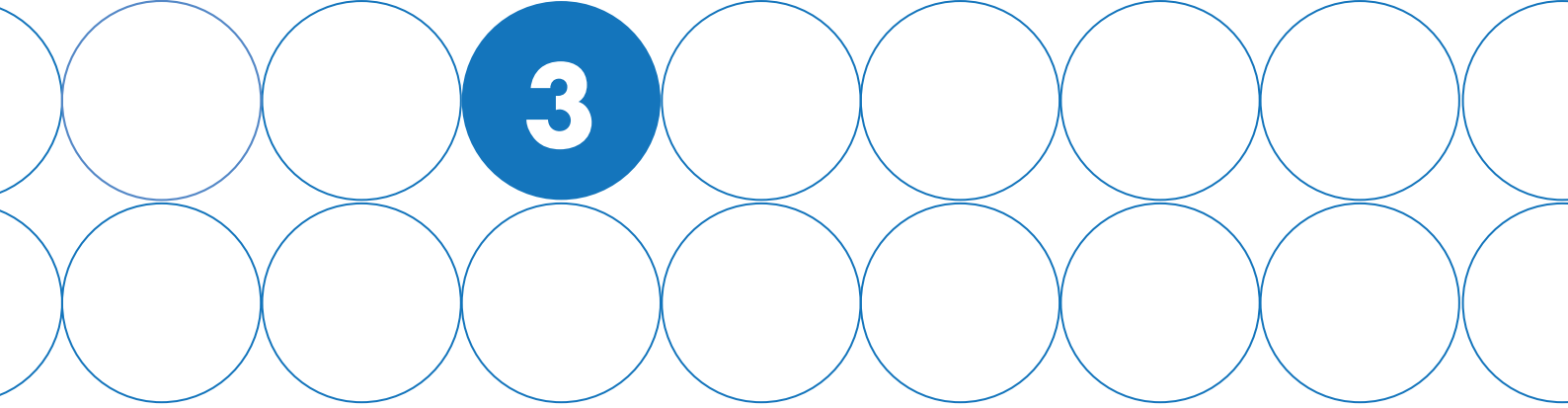

Chapter 3

Recognition, Diagnosis, Differential Diagnosis, and Cultural Aspects of Depressive Disorders

INTRODUCTION

Recent studies demonstrate that many depressive disorders are often not recognised by clinicians. Several studies, for example, reported that more than half of the patients with depressive disorders seen in the primary care setting were not diagnosed as such (Perez-Stable et al. 1990; Üstün and Sartorius 1995; Zung et al. 1993).

This is not surprising, since depressed patients often present with complaints of physical problems. In one study, for example, while depressive disorders were ultimately diagnosed in 20% of patients in primary care settings, only 1.2% cited depressive mood as the reason for their visit (Zung et al. 1993). In addition to the many patient factors that can mask depressive disorders, physicians are often hindered by their own medical training and approach to practice, which lead them to give immediate priority to the treatment of somatic symptoms without much further exploration.

This chapter will briefly review the reasons why depressive disorders are often unrecognised in the general medical sector. We will then describe some screening tools that can facilitate recognition of depressive disorders and provide guidelines that can help clinicians make a differential diagnosis.

OBSTACLES TO RECOGNITION

Stigma

The first obstacle to recognition is that only 1 out of 3 patients with a depressive disorder ever seeks medical help (Regier et al. 1988). The stigma associated with the diagnosis and treatment of mental illness appears to play a role in patients' reluctance to seek, accept, adhere to, and continue treatment. Patients fear, often rightly, that they will subsequently be discriminated against in hiring, promotion, and other occupational opportunities, as well as being socially ostracised. Discrimination against people with mental illness, as opposed to most other medical conditions, is present in some countries' selective third-party reimbursement policies, reporting requirements for driver's licenses, security clearances, and job applications. A survey of physicians disclosed that many cases were not coded for depression in medical records, owing (at least in part) to a desire to protect patients from stigmatisation (Rost et al. 1994).Despite educational efforts, depression is still viewed by many patients and by the lay public as evidence of a temperamental defect, emotional weakness, or lack of willpower. Thus, many people believe that patients with depression could get better if they just worked at it hard enough.

Masked Depression

Recognition of depressive disorders is also hampered by the fact that many depressed patients present to physicians with mainly somatic symptoms. The somatic presentation of depressive disorder, or masked depression, was first described in the 1970s (Lopez-Ibor 1991). In primary care settings, more than half of the patients ultimately found to have a depressive disorder originally presented with somatic complaints (Üstün and Sartorius 1995). This tendency to ignore or deny psychological symptoms and to emphasise the bodily manifestations of psychiatric disorders is seen frequently in the elderly, in patients who lack psychological insight, in the poorly educated, and in those unable to verbally express their feelings (alexithymia). It is also more likely when patients contact physicians who are reluctant to deal with psychological symptoms.

Studies concerning general practitioners show that, while most physicians are aware of the psychological symptoms of depressive disorders, they are less likely to be familiar with the range of physical symptoms produced by such disorders (Ayuso-Gutierrez and Ramos-Brieva 1984). For example, in one study of 100 patients treated for somatic complaints, none was diagnosed with a depressive disorder, even though results of subsequent tests showed that 44% of the patients were mildly to extremely depressed (Munoz et al. 1990). The most commonly encountered somatic symptoms in a depressive disorder are pain (such as headache, backache, or vague, undifferentiated pain), sleep disturbances, gastrointestinal upset, fatigue, and appetite changes (American Psychiatric Association 2000).

Comorbid Medical Illness

Another obstacle to recognition is the confusing picture often presented by patients with a serious comorbid medical illness, such as heart disease, cancer, or stroke. These illnesses can obscure the symptoms of depressive disorder, since symptoms such as fatigue and loss of appetite are common in both. In addition, even if clinicians recognise the depressive symptoms, they may consider them an appropriate response to the patient's serious medical problem (Freeling et al. 1985). However, having a "good reason" for being depressed (such as a serious illness or major life stress) does not exclude the presence, nor diminish the treatability, of comorbid depressive disorder.

Tacit Collusion

Physicians' attitudes can also present obstacles to the recognition of depression. A patient's hesitancy to discuss psychological issues may be reinforced if he or she senses that the physician shares society's prejudices against mental illness or is uncomfortable talking about feelings. Sometimes, what might be called a tacit collusion between physician and patient occurs. Depressive symptoms are not acknowledged because it is easier and more comfortable for both physician and patient to talk about somatic symptoms than about depressive symptoms.

Time Constraints

Sometimes clinicians are concerned that talking about, diagnosing, and treating depressive disorders will be too time-consuming to incorporate into their busy practices. However, the reverse is generally true. Although some extra time is initially required for diagnosis, much time can be saved in the long run by avoiding unnecessary consultations and tests and appropriately treating the depression as early as possible.

Inadequate Medical Education

Many physicians currently in practice receive only limited psychiatric education during medical school or postgraduate training and thus were trained in a narrow biomedical diagnostic framework with minimal exposure to psychiatric problems, particularly milder problems. The World Psychiatric Association has suggested that 20% of medical school curriculum should be devoted to the psychological aspects of medical care, including interviewing techniques and treatment issues.

Several programs have been developed to help primary care practitioners develop skills and confidence in this area, and results are promising. Such programs include Defeat Depression, by the Royal College of Psychiatrists and Royal College of General Practitioners in the United Kingdom (Priest et al. 1995), the Depression, Awareness, Recognition and Treatment Program, organised by the National Institute of Mental Health in the United States (Regier et al. 1988), and Beyondblue, the national depression initiative which was established in Australia in 2000 (Jorm et al. 2006).

DIAGNOSIS OF DEPRESSIVE DISORDERS

A systematic assessment for the presence of a depressive disorder should be included in the normal medical workup. Certain situations and symptoms should increase the clinician's alertness for the presence of a possible depressive disorder. Patients at particularly high risk for a depressive disorder include those who have recently suffered a major adverse life event, such as the death of a spouse, divorce, or loss of a job, and those suffering from a serious medical illness.

Certain patient presentations may also be clues to an underlying depressive disorder. Patients whose somatic complaints are vague and undifferentiated and those who have presented repeatedly for similar complaints may be suffering from a masked depressive disorder. Some patients may present with anxiety symptoms, which are frequently symptoms of an underlying depressive disorder. Older patients may present with cognitive difficulties suggestive of dementia that are really symptoms of depressive illness. These issues will be explored more fully in the next section on differential diagnosis.

Sometimes patients who come to the clinician asking for help for their children are really suffering from a depressive disorder themselves. Their children's problems may in fact be secondary to the effect the parent's depressive disorder is having on the family.

SCREENING AND ASSESSMENT TOOLS

Numerous screening and assessment tools have been developed for use in identifying and diagnosing depressive disorders (see Table 3.1). Screening tools detect the possible presence of psychiatric illness, whereas assessment instruments are mainly used to diagnose a depressive disorder, evaluate its severity, and identify the types of specific symptoms that are present.

DIFFERENTIAL DIAGNOSIS OF DEPRESSIVE DISORDERS

Accurate diagnosis is the key to deciding whether to treat a patient for depression. The time that is spent in making the diagnosis is valuable because, in addition to ensuring its accuracy, the evaluation process helps to establish a doctor/patient relationship, which is essential for effective treatment.

A variety of illnesses and conditions can present in a manner that resembles a depressive disorder; they can-also co-exist with a depressive disorder. Thus, establishing the differential diagnosis is a challenge for the clinician, who must sift through clues from the physical workup, screening procedures, and clinical interview to discover whether the symptoms reflect a depressive disorder or another medical or psychiatric illness.

Particular skill in differential diagnosis is needed in evaluating patients from certain high-risk populations, including those with symptoms of anxiety; with dementia, pseudodementia, or comorbid physical illness; and who have suffered bereavement. Moreover, if the patient has a history of psychiatric disorders (e.g. schizophrenia, obsessive-compulsive disorder, or bulimia), the clinician must determine whether the current presentation is an early sign of a new episode of a pre-existing disorder or an evolving comorbid depressive disorder.

Depressive Disorders Versus Anxiety Disorders

Although depressive disorders and anxiety disorders are distinct clinical syndromes, they often appear together. They also share several symptoms, such as physical restlessness, difficulty concentrating, sleep disturbances, and fatigue.

Anxiety symptoms are often the most prominent, even when due to an underlying depressive disorder, which can further complicate the differential diagnosis. Patients may focus on their anxiety symptoms during the clinical interview because these symptoms appear less stigmatising to patients or cause them more acute distress. The physician understandably wants to provide the patient with relief, and is sometimes tempted to diagnose the anxiety and initiate treatment without further probing. Studies in primary care settings have found that many patients who are ultimately discovered to have depressive disorders were first treated with anxiolytics.

Because symptoms of anxiety are so common in patients with depressive disorders, and because the consequences of not detecting a depressive disorder can be lethal, patients with anxiety symptoms should be screened for the presence of a depressive disorder. If the criteria for a depressive disorder are met, this becomes the patient's primary diagnosis, and the patient should be treated for the depressive disorder—i.e., with antidepressant medication rather than an anxiolytic agent. Effective antidepressant therapy can alleviate all the symptoms of the depressive disorder, including the anxiety symptoms, whereas anxiolytic treatment may have no impact on an underlying depressive disorder. (see Volume I, Chapter 5 for an overview of treatment options for depression).

TABLE 3.1

Screening and Assessment Procedures

Examples of screening tools specifically designed to detect depression:	Zung Scale: a self-report questionnaire completed by patients useful in primary care practice (Zung 1965)	CES-D (Center for Epidemiological Studies-Depression Scale): a self-report depression scale for research in the general population (Radloff 1977).	Beck Depression Inventory (BDI):a screening measure that identifies depressed patients using a structured psychiatric interview (Beck 1961).
Examples of more general brief screening tools used to detect depression as well as other mental disorders:	PRIME-MD (Primary Care Evaluation of Mental Disorders): a patient questionnaire listing 26 symptoms, including symptoms of depression, panic disorder, generalised anxiety disorder, eating disorder, and alcohol abuse (Spitzer et al, 1994).	GHQ (General Health Questionnaire): Goldberg and his group in the UK (1972) used a two-stage procedure for diagnosis. Stage 1 was the GHQ, a 60-item patient self-report questionnaire measuring general well-being and coping. Stage 2 was a clinical interview schedule, which was administered by the physician to arrive at a diagnosis in accordance with ICD guidelines.	SDDS-P C (Symptom Driven Diagnostic System for Primary Care): a screening questionnaire containing 16 symptoms (Weissman et al, 1995).
Examples of assessment instruments that are used to evaluate the severity of depression and record symptoms of depressive disorders:	HAM-D (Hamilton Depression Scale): a rating scale containing symptoms of major depression (Hamilton 1967; Paykel 1990).	GDS (Geriatric Depression Scale): especially helpful for screening older patients (Yesavage and Brink 1983).	SADD (Standardized Assessment of Depressive Disorders): an instrument for recording the results of clinical assessment of patients with depressive disorders (Sartorius and Davidian 1983).
Example of assessment instruments used to evaluate non-depression-specific disorders:	PSE (Present State Examination): a structured interview schedule for conducting the mental status examination and scoring its findings (Wing et al, 1974). It is designed for adult patients and is incorporated in the SCAN system (see Table 3.2).	CIDI (Composite International Diagnostic Interview): a highly structured psychiatric epidemiological interview that is applicable across cultures and provides diagnoses according to both ICD and DSM criteria; designed primarily for administration by laypersons (Robins et al. 1988).	

Depressive Disorders Versus Normal Bereavement

For the clinician, the focus of clinical attention with a bereaved patient is the appropriateness of the patient's grief reaction. As part of their bereavement, some grieving individuals present with symptoms characteristic of a depressive disorder (e.g., feelings of sadness and associated symptoms, such as insomnia, poor appetite, and weight loss). The bereaved individual typically regards the depressed mood as normal", although the person may seek professional help for relief of associated symptoms, such as insomnia or anorexia.

The duration and expression of "normal" bereavement vary considerably among different cultural groups. Table 3.2 presents the DSM-IV-TR guidelines (American Psychiatric Association 2000) for the diagnosis of bereavement. In general, the long-term presence (i.e., more than 6 months) of psychological symptoms, such as incapacitation at work, in school, or in the home, and guilt, low self-esteem, and inability to enjoy previously pleasurable activities, should make the physician suspect a depressive disorder.

Depressive Disorders Versus Physical Illness

As mentioned above, many depressive patients present with masking somatic complaints. In addition, depressive disorders are prevalent in patients with other coexisting physical illnesses, including cancer, heart disease, stroke, and Parkinson's disease (see Volume 2 Physical Illness and Depression). Any chronic disease or prolonged recuperation can precipitate a depressive disorder, as can some treatments.

When a patient with a physical illness presents with depressive symptoms, these are often either attributed to the other physical illness or, when correctly attributed to a depressive disorder, presumed to be a "natural consequence" of the physical illness. This is a faulty assumption because, while most patients with serious illnesses experience sadness and grief, they do not all develop depressive disorders. When a depressive disorder does occur, it warrants recognition as a separate medical illness regardless of precipitating factors. In fact, studies reveal that when a depressive disorder in a patient with a serious comorbid illness is effectively treated, it often improves the prognosis of the other illness as well as the patient's ability to cope and comply with treatment (Evans et al. 2005). Nevertheless, it can be difficult to differentiate symptoms secondary to a comorbid illness, such as fatigue or loss of appetite, from symptoms of a depressive disorder. Physicians are therefore advised to consider all symptoms that might suggest a depressive disorder, even if another possible physical cause is present, and to probe for the presence of psychological symptoms specific to depressive illness, such as loss of interest or pleasure, guilt, and low self-esteem. The presentation can often be confusing, and the physician's clinical judgement will, as always, determine how best to attribute symptoms. A thorough medication history is, of course, essential in this situation. If it is suspected that a medication may be contributing to the depressive symptoms, the clinician will ideally want to substitute a drug less likely to cause depressive symptoms, although unfortunately this is not possible in some cases.

Depressive Disorders Versus Dementia

The high prevalence, comorbidity, and overlapping symptomatology of depression and senile dementia (Alzheimer's disease) among the elderly it especially difficult to differentiate these illnesses (Derouesne and Lacomblez 2004). Moreover, many elderly patients have what has been termed "pseudodementia", a temporary cognitive impairment (such as memory problems, inability to concentrate, and disorientation) due to an underlying depressive disorder or physical illness and its treatment, that may mimic early Alzheimer's disease and further confound the diagnostic process.

Symptoms of early Alzheimer's disease have a gradual onset, while those of pseudodementia due to a depressive disorder tend to progress rapidly. In a depressive disorder, the patient often complains of cognitive defects, while in senile dementia, the patient may attempt to conceal these deficits or be unaware of them. The patient with true dementia may actively try to answer questions during a brief cognitive screen, while the depressed patient will show apathy toward this evaluative process and make little attempt to answer questions.

TABLE 3.2

DSM-IV definition of bereavement

Presenting complaints	Diagnostic features	Differential diagnosis
The patient feels overwhelmed by loss	Normal grief includes preoccupation with the loss of the loved one	If a full picture of depression is still present 2 months after the loss, consider a depressive disorder.
The patient is preoccupied with the lost loved one.	This may be accompanied by symptoms resembling depression such as: • Low or sad mood • Disturbed sleep • Loss of interest • Guilt or self-criticism • Restlessness	Symptoms that are not characteristic of "normal" grief include • Inappropriate feelings of guilt • Thoughts of death other than the survivor feeling that he or she would be better off dead • Preoccupation with worthlessness • Psychomotor slowing • Hallucinatory experiences other than "hearing" the voice of the deceased
The patient may present with somatic symptoms following loss.	The patient may withdraw from usual activities and social contacts	
	The patient may find it difficult to think about the future	

Based on the definition of bereavement in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (American Psychiatric Association, 2000)

Another critical difference between depressive disorders and early Alzheimer's disease is the presence of neurologic symptoms. Patients with early Alzheimer's disease often display progressive dysphagia, apraxia, and agnosia, whereas patients with pseudodementia do not usually have signs of neurologic defects.

A trial of antidepressant medication may be the best tool available to the clinician in making this differential diagnosis, since pseudodementia resolves with antidepressant therapy, while, in true senile dementia, cognition remains poor, although mood may improve.

DIFFERENTIATING BIPOLAR DISORDER FROM UNIPOLAR DEPRESSION

In evaluating depressive symptoms, after excluding medical causes or substance-induced depression, the clinician should systematically consider the possibility of a bipolar disorder. Bipolar disorder, which until recently was often termed "manic-depressive illness" or "manic depression", is defined by the occurrence of one or more major depressive episodes alternating with at least one manic (bipolar I disorder) or hypomanic (bipolar II disorder) episode in the same individual. The DSM-IV-TR also includes cyclothymia and bipolar disorder not otherwise specified within the bipolar disorder category (American Psychiatric Association 2000).

A growing body of evidence suggests that a significant subset of depressed patients suffer from bipolar disorder and that they are more likely than previously thought to present for treatment in primary care settings. Recent studies have shown that 21%–26% of depressed patients in primary care settings were found to have bipolar disorder after careful screening (Hirschfeld et al. 2005; Manning et al. 1997).

The distinction between major depressive disorder (or unipolar depression) and bipolar disorder has extremely important clinical implications for both prognosis and treatment. Whereas antidepressants are the treatment of choice for major depression, current guidelines recommend that mood stabilisers be the first-line treatment for bipolar depression and that, if antidepressants are necessary, they should not be used without concurrent mood stabilisers (Sachs et al. 2000).

Epidemiological Data: Bipolar Disorder As A Major Unrecognised Source of Depression

Bipolar disorders are among the most common mental disorders and their lifetime prevalence is probably higher than was once believed. Recent epidemiological studies suggest that the actual rate of bipolar spectrum disorders in the general population may be as high as 6%. Using a self-report screening tool, the Mood Disorders Questionnaire, Hirshfeld et al. (2003) found a 3.4% lifetime prevalence of bipolar disorders (including bipolar I, bipolar II, cyclothymia, and bipolar disorder not otherwise specified) in a U.S. community sample. In Europe, the Zurich cohort study identified a prevalence of 5.5% for hypomania/mania, as defined by the DSM-IV (Angst 1998).

Unlike unipolar depression, which is more common in women than in men, bipolar disorder appears to have roughly the same distribution across genders, although women appear to have more depressive symptomatology than men (Angst and Sellaro 2000) as well as a higher prevalence of rapid cycling, defined as 4 or more episodes per year (Leibenluft 1996).

Moreover, a high percentage of depressive episodes may occur in the context of bipolar disorder. Some studies have reported that as many as 40% of both inpatients and outpatients diagnosed with depression were subsequently found to have a bipolar disorder (Ghaemi et al. 1999, 2000). In France, Hantouche et al. (1998) found that 28% of a population of depressed patients had bipolar disorders. In northern Italy, Benazzi (1997) found that 49% of the outpatients presenting with depression had a bipolar spectrum disorder.

Bipolar patients are also more likely to suffer from depressive than manic or hypomanic episodes, with the frequency of episodes reported to be twice that in unipolar depression (Goodwin and Jamison 1990). Depression represents about three quarters of the time spent with mood symptoms in bipolar I disorder and over 90% of the time spent with mood symptoms in bipolar II disorder (Judd et al. 2002, 2003).

Bipolar disorders are among the most potentially severe psychiatric disorders. With an early age of onset and high rates of recurrence, bipolar illness often results in chronic morbidity, as well as functional impairment and increased mortality. Patients with bipolar disorder have higher rates of suicide and natural causes of death compared with the general population (Cuijpers and Smit 2002; Goldberg et al. 1995; Harris and Barraclough 1998; Osby et al. 2001). The lifetime risk of suicide attempts among patients with bipolar disorders ranges from 25% to 50% (Jamison 2000), and the risk of completed suicide has been estimated to be 10%–15% (American Psychiatric Association 2000).

Patients with bipolar disorder are also exposed to a substantial degree of psychosocial morbidity: they are 2 to 3 times more likely to be divorced than the general population (Manning et al. 1997), more than twice as likely to have work-related problems, and 5 times more likely to be jailed, arrested, or convicted of a crime than others in a community sample (Calabrese et al. 2003). Calabrese et al. (2003) also found 4 times the incidence of anxiety and panic attacks and twice the incidence of migraine headaches among the population with bipolar spectrum disorders. Comorbid medical illnesses, anxiety and personality disorders, and substance abuse are common among patients with bipolar disorders. Large epidemiological studies have found rates of alcohol and/or drug abuse in more than 40% of patients with bipolar disorder (Regier et al. 1990). Given the serious morbidity associated with bipolar disorders, it is crucial to identify bipolar illness as early as possible in order to help modify its natural course.

The Risks and Consequences of Misdiagnosis

Unfortunately, many patients with bipolar disorders, especially bipolar II disorder, remain unrecognised even in psychiatric settings, often being misdiagnosed with unipolar depression and consequently inappropriately treated. Studies have shown that it can take several years for patients with bipolar disorders to receive a correct diagnosis. In a study based on a questionnaire distributed to patients with bipolar disorder who were members of the Depression and Bipolar Support Alliance (DBSA), Hirschfeld et al. (2003) noted that 69% of respondents reported that they had initially been misdiagnosed. Among the respondents to this survey, 35% reported that they had waited 10 years or longer to receive a correct diagnosis, and many had consulted 5 or more physicians before receiving the correct diagnosis.

The issue of misdiagnosis is particularly serious because antidepressant monotherapy can induce mood destabilisation in patients with bipolar disorder—that is, antidepressants used alone can lead to induction of mania or acceleration of cycling frequency over time, phenomena that have been reported to occur in approximately 25%–40% of patients with bipolar disorder (Goldberg and Truman 2003). Misdiagnosis with a unipolar depressive disorder also prevents patients with bipolar disorder from receiving treatment with mood stabilisers, exposing them to the many serious complications of the natural course of the disease. Delaying appropriate treatment may increase the risk of suicide, impair psychosocial functioning, and contribute to a diminished response to lithium (Franchini et al. 1999; Goldberg and Ernst 2002).

The Challenge of Differentiating Unipolar from Bipolar Depression

Distinguishing between unipolar and bipolar mood disorders is very challenging for two main reasons.

First, the differential diagnosis of unipolar depression and bipolar disorder is based on the presence of at least one episode of mania or hypomania in the patient's history. However, in bipolar disorder, depression is often the first phase of the illness that comes to clinical attention, and patients will frequently experience several episodes of depression before their first manic episode (Lish et al. 1994).

Second, eliciting information about past hypomanic or manic symptoms, even when such a history exists, from a patient who is currently depressed may be extremely difficult. Patients may fail to recall manic or hypomanic symptoms or may have no insight concerning their morbidity. Many patients value their heightened activity and energy during hypomanic states and do not consider them pathologic. Other patients may fear the stigma associated with bipolar disorders (Bowden 2001).

However, several strategies, which are described in the following section, can help clinicians improve their diagnostic accuracy. These diagnostic strategies are not especially time-consuming, and primary care physicians can easily perform such assessments (Kaye 2005).

CLINICAL ASSESSMENT FOR BIPOLAR DISORDER

Screening for Hypomanic and Manic Symptoms

Clinical screening

Diagnostic criteria and guidelines are available in the DSM-IV-TR (American Psychiatric Association 2000) and the ICD-10 (WHO 1992). In practice, the physician should inquire about past periods of mood elation. Manic episodes are generally characterised by symptoms that are the opposite of those seen in depressive episodes: people may become euphoric or irritable, overly active, highly talkative, spend money irresponsibly, and be involved in hazardous adventures. Hypomania involves a lesser degree of mania: a persistent, mild elevation of mood; increased energy, activity, sociability, talkativeness, overfamiliarity, and sexual energy; and marked feelings of well-being and a decreased need of sleep.

Some authors suggest that a two-question screen for mood changes may be sufficient to rule out bipolar disorder. Manning (2003) advises the clinician to ask the following two questions:

> *Have you ever felt that you could get by on much less sleep than you used to?*
>
> *Have you done things that others might think inappropriate, such as spending too much money?*

Benazzi and Akiskal (2005) suggest using the following two questions to screen for bipolar II disorder:

> *Are you a person who frequently experiences ups and downs in mood over life?*
>
> *Do these mood swings occur without cause?*

The authors concluded that the relatively high sensitivity of this measure of risk for bipolar II disorder supports its usefulness as a screening tool.

With both of these screening strategies, a positive response to at least 1 question indicates an increased likelihood of bipolar disorder.

Screening and assessment tools

Two screening tools can help clinicians reduce the risks of a missed diagnosis.

The Mood Disorder Questionnaire (MDQ) (Hirschfeld et al. 2000) is a 1-page self-administered questionnaire with 13 yes/no items and 2 additional questions regarding function and timing of symptoms. In a validation study of the MDQ, a score of 7 or higher yielded a sensitivity of 73% and a specificity of 90%, meaning that the questionnaire can identify 7 of 10 patients with bipolar disorder and eliminate 9 of 10 without it. The MDQ takes about 5 minutes to complete, so that it can be easily integrated into a routine office visit with the patient completing the questionnaire in the office before seeing the physician (Kaye 2005).

Another tool, the Hypomania Check List (HCL) (Angst et al. 2005), was developed specifically to identify bipolar II disorder and has been translated into many languages.

Consultation with family members and others with close ties to the patient may also be extremely useful in identifying previous mood episodes and obtaining a complete family history (Pomerantz 2004).

Features suggestive of bipolar disorders

Until recently, it was believed that there were no differences between unipolar and bipolar depression. Indeed, the description of these types of depression is the same in the current classifications and manuals. Although no single

clinical feature is unique to bipolar or unipolar depression, researchers have identified a number of clinical features that suggest an increased possibility that a patient presenting with depressive symptomatology has a bipolar disorder (Abrams and Taylor 1980; Perlis et al. 2006):

- Patients with bipolar depression have a significantly younger average age of onset compared with those with unipolar depression (21.2 years of age versus 29.7 years of age) (Perlis et al. 2006).
- The risk of recurrence is higher in patients with bipolar disorder: 52.8% experience more than 25 episodes while only 1.1%–3.0% of patients with major depression have that many episodes (Perlis et al. 2006). The duration of depressive episodes is also usually shorter, less than 3 months, in patients with bipolar disorder than in patients with unipolar depression (Ghaemi et al. 2001).
- A family history of bipolar disorder increases the risk of having bipolar disorder (Corwell 1999; Manning et al. 1997).
- Patients with bipolar disorder are more likely than those with unipolar depression to present with the following symptoms:
  - Atypical features, such as feelings of worthlessness, restlessness, hypersomnia, hyperphagia, weight gain, and leaden paralysis (Benazzi 2000; Mitchell et al. 2001)
  - Psychomotor retardation (Benazzi 1999)
  - Psychotic symptoms (Bowden 2001; Goldberg et al. 2001a, 2001b)
- Patients with bipolar disorder report more fears, whereas patients with unipolar depression experience more cognitive, somatic/anxious (muscular, respiratory, genito-urinary), and insomnia complaints (Perlis et al. 2006).
- Another feature that suggests the presence of bipolar illness is a strong association with alcohol and drug abuse and anxiety disorders (Regier et al. 1990).
- A short-term, but not prolonged, response to antidepressants is also suggestive of a bipolar disorder (Kaye 2005). In a study involving 602 patients, almost 20% of patients with unipolar depression who were nonresponsive to treatment with antidepressant medication screened positive for bipolar disorder. This suggests that clinicians should carefully screen for bipolar disorder in patients who have failed to respond to at least one antidepressant. Comorbid anxiety, a feeling that people are unfriendly, a recent diagnosis of depression, a family history of bipolar disorder, and recurrent legal problems may also be useful indicators of bipolar risk among patients who have failed to respond to at least one antidepressant (Calabrese et al. 2006).
- Bipolar depression is also characterised by a more pronounced seasonal pattern than is observed in unipolar depression, with depressive episodes in winter being the most common (Whybrow 1997).
- In women, there is a greater likelihood of mood disturbance during the postpartum period. As many as half of all women with bipolar spectrum disorders experience an episode of depression or mania or a mixed mood state after the birth of a child (Whybrow 1997). In fact, for many women, the first presentation of a bipolar disorder is a postpartum episode (Robling et al. 2000). Thus, any woman without a history of psychiatric problems who develops postpartum depression should be closely monitored, as the risk for developing a bipolar disorder may be especially high (Kaye 2005).

CHALLENGES IN THE TREATMENT OF BIPOLAR DEPRESSION

It is clear from the characteristics described in the previous section that the treatment of patients with bipolar disorder is complicated and challenging and that there are many reasons to consider a psychiatric referral for patients who appear to have bipolar illness.

First, psychopharmacological treatment of bipolar disorders is much more complicated and entails greater risk than that of unipolar depression (Kaye 2005; Potter 1998). Clinicians need to be alert for potential risks in prescribing antidepressant therapy for patients with bipolar depression.

Antidepressant monotherapy is discouraged in current guidelines for the treatment of bipolar disorder (American Psychiatric Association 2002), although the use of antidepressants may be necessary in some patients. Current practice guidelines, for bipolar disorder, including those of the American Psychiatric Association (American Psychiatric Association 2002), recommend that antidepressants be used with caution in bipolar depression, that they be used together with a concomitant mood stabiliser, and that they generally not be continued for long periods of time (Post 2004). Mood stabilisers, which are the standard of care for bipolar disorders, include lithium as well as several anticonvulsant agents, among them divalproex, carbamazepine, and lamotrigine. More recently, the utility of atypical antipsychotic medications (e.g., aripiprazole, olanzapine, risperidone, quetiapine, ziprasidone) has been recognised, increasing the number of treatment options available to clinicians for bipolar disorders. In addition, the high rates of physical and mental comorbidity in patients with bipolar disorder complicate medication algorithms. Polypharmacy tends to be the rule in these patients, with maintenance therapy for the average patient with bipolar disorder involving 3 or 4 active agents to treat mood problems (Post 2004); only 20.6% of patients with bipolar disorders are managed with monotherapy (Kupfer et al. 2002).

Another reason to consider a psychiatric referral for patients with bipolar disorders is the extremely high incidence of comorbid substance abuse, which complicates disease management and increases the risk of nonadherence to treatment and negative outcomes (Kaye 2005).

Finally, a majority of patients with bipolar disorder experience some form of chronic occupational, social, or family difficulty, which may be alleviated to some extent by adjuvant psychosocial interventions (American Psychiatric Association 2002).

In summary, due to the formidable treatment challenges posed by bipolar disorders, it is recommended that any patient suspected of having such a disorder should be referred to a psychiatrist for evaluation and treatment.

CULTURAL ASPECTS OF DEPRESSION

Culture is defined as the learned, shared beliefs, values, attitudes, and behaviours characteristic of a society or population (Bhugra and Mastrogianni 2004). Although many different definitions of culture exist, scientists appear to agree that culture is a dynamic concept. In the age of globalisation, cultures are described as "ever-changing constructs that emerge from interactions between individuals, communities and institutional practices" (Kirmayer 2001). From the standpoint of cultural psychiatry, culture has an impact on the following (Kirmayer 2001):

- Causes, symptoms, and manifestation of mental distress,
- Individual explanatory models, coping mechanisms, and help-seeking behaviour,
- Social response to mental distress and disability.

At the same time, ethnic identity plays an important key role in how people experience their own self-value and affects the social causes and the course of mental disorders. The effects of pluralistic ways of life in multi-cultural societies on people's psyche are relatively unknown (Bibeau 1997). It is assumed that globalisation may amplify the experience of stress in vulnerable individuals and strip cultures of their psychologically protective function, as individual and collective identities are questioned (Kirmayer and Minas 2000).

Acculturation

Hovey (2000) introduced the concept of acculturative stress, which has been shown to be correlated with high levels of depression and suicide ideation, in part probably because of disconnection from protective, culturally mediated social resources (e.g., strong family networks, role models). Hwang and Myers (2007) described a significant correlation between negative life events and the prevalence of depression, which was shown to be higher for more acculturated Chinese Americans.

Haasen et al. (2008) hypothesised that acculturative stress might be comparable to the general experience of stress, the importance of which has been widely described in the aetiology of depression. This is based on the concept that the neuroendocrinological stress response is an adjustment mechanism which ensures survival of the individual when homeostasis is in danger. In the unspecific stress response, the hypothalamo-pituitary-adrenocortical (HPA) axis plays a central role and has been shown to be related to the pathophysiology of depression (Holsboer 2000). Selten and Cantor-Graee (2005) suggested that the chronic experience of social defeat in migrants leads to sensitisation of the mesolimbic dopamine system and puts the individual at increased risk for the development of a disorder of the brain. However, it is challenging to test these hypotheses due to the difficulty of measuring subjective experiences such as acculturative stress or social defeat, which are liable to self-presentation bias.

Diagnostic Considerations

With the increase in global migration and the increasing proportion of migrants presenting for care in mental health care systems, taking into account culture-specific issues in the diagnosis of mental disorders is no longer considered an esoteric practice but rather has widely accepted practice throughout the world (Westermeyer 1985; Minas 2001). Intercultural diagnosis has to grapple with a number of basic considerations, such as the cross-cultural validity of diagnostic categories, the pathoplasticity of mental disorders, the existence of culture-dependent syndromes, cultural variability in symptoms, and theoretical concepts, such as cultural relativism versus cultural universalism.

Classification problems

Historical changes in psychiatric classification systems have had an extremely important and far-reaching impact on the categorisation and differentiation of depressive syndromes (e.g., endogenous vs. reactive depression, psychotic vs. neurotic depression, major depression vs. minor dysthymic disorders). Therefore, it is difficult to compare data, collated at different times and in different cultures, and such comparisons are only possible to a limited extent (Tseng 2003). Furthermore, research on the classification of depression is an extremely controversial issue. Diagnostic terms such as depression, or phobia, have no corresponding terms in many languages outside Europe. In other words, although the experience of a dysphoric mood may be a universal human phenomenon, the concept of a depressive disorder is a long way from being universally accepted. The concept of a depressive disorder was developed in Western culture and focuses on mood swings; in many non-Western cultures, on the other hand, feeling "down" is not necessarily a major symptom of a depressive illness (Bebbington 1993; Patel 2001). Another problem in classifying depression is the clinical validity of differentiating between depression and anxiety. The results of the latest multinational WHO study in general healthcare show that the comorbidity of depression and anxiety is over 50% (Goldberg and Lecrubier 1995). Some researchers have identified local concepts that show a certain similarity to the structure of depression as an alternative to using Western diagnostic terminology (Kleinman and Kleinman 1985; Patel et al. 1995). These methodologically different approaches are reflected in the debate on cultural universalism and cultural relativism (i.e., whether to use etic or emic instruments to identify and assess mental disorders) (Kleinman 1988; Fabrega 1989). Today, an integrative approach is being sought that can combine quantitative and qualitative examination methods (local narrative and explanation models) (Bhui and Bhugra 2001; De Jong and Van Ommeren 2002; Lloyd et al. 1998), and the nature/culture dichotomy has been replaced by an integrative view of culture as a core feature of human biology (Kirmayer 2006).

In addition to differences in classification, other methodological problems can produce for transcultural variations in findings concerning depression. These problems primarily involve differences in study samples, different methods of clinical assessment, and a lack of assessment instruments suitable for the specific culture being studied, or problems connected with the translation and validation of assessment instruments (Ballenger et al. 2001).

Culture-specific aspects of Western classification systems

To date, culture-specific factors have not been included in ICD-10. In English-speaking countries, a manual describing a suggested approach to culture-specific history-taking has been included in the appendix to the DSM-IV and DSM-IV-TR (American Psychiatric Association 1994, 2000; Mezzich 1995). In addition, the inclusion of a discussion of culture-specific aspects in the text sections describing each mental disorder in DSM-IV (American Psychiatric Association 1994) was a huge step towards a more culturally competent and sensitive assessment of mental disorders. The editors of DSM-IV stated that their intention was to improve the intercultural scope of the manual, by "... increasing the awareness of culturally-dependent variations in the expression of mental illnesses and reducing the possible impact of any unintentional interference from the researcher's own cultural background".

A knowledge of an individual's cultural background (e.g., socio-cultural factors, religious beliefs, typical cultural rituals and standards of behaviour, as well as experiences) allow the clinician to more reliably assess signs and symptoms in a migrant who presents for care as representing a normal psychological presentation or being of a psychopathological nature. Reliable and coherent assessment of what is normal or abnormal forms the cornerstone of a diagnosis that takes a universal, cross-cultural approach. Such an approach requires that the clinician clearly distinguish culturally typical standard forms of behaviour from types of behaviour and experiences that are untypical of the patient's original cultural environment but which may play an important role in the illness. Careful biographical history-taking can provide information concerning the patient's ethnic and cultural reference group and identity, the migration process, and the level of acculturation the patient has achieved. The DSM-IV manual for assessing cultural influences is a useful tool that can help clinicians carry out systematic assessment of the patient's cultural background.

Nevertheless, some researchers have criticised the DSM-IV because they believe the diagnostic criteria still represent Western concepts of illness and cannot be unequivocally used in other cultures (Kirmayer 2001). However, given that some form of diagnostic formulation is needed to compare presentations across cultures, it is recommended that concepts of depression be defined in a way that is consistent with both psychiatric models and indigenous convictions, thus fully taking into account patients' sociocultural contexts (Bhui 1999; Bhugra and Mastrogianni 2004).

The diagnostic dimension of migration

Migration is a process that is particularly likely to cause psychosocial stress. In considering the concept of migration, it is important to take into account the individual who has migrated, the motives for and circumstances surrounding the migration, the political and diplomatic relationship between the home and host countries, the relationship between the new and the original culture (e.g., individualistic versus collectivistic outlooks), and the way in which the migrant has been accepted into the host country. All of these factors have a major influence on the opportunities and abilities of a migrant to acculturate. Today, it is safe to assume that migration can be a key trigger in the development of stress-related illnesses, such as depressive or anxiety disorders, addiction, and psychosomatic reactions (Jablensky et al. 1992; Pfeiffer 1994; Tseng 2003).

Depressive syndromes are clearly very common among migrants in the United States and Europe. They are probably the most frequent mental disorders among individuals who migrate to other countries, since they are subjected to significant social and psychological stress that makes them especially vulnerable. Kleinman (2004) estimates that at least 50% of immigrants and members of ethnic minorities in the United States suffer from clinical depression. A study by Oquendo et al. (2004) analysed the frequency of major depression among different ethnic groups in the United States, including Caucasian, African-American and Spanish immigrants to Los Angeles, as well as migrants from Mexico, Cuba, and Puerto Rico. The study found the highest rates of depression

among white and Puerto Rican immigrants; in the case of the Puerto Rican immigrants, this was also associated with an increased prevalence of suicide attempts (with a similar trend also found among Cuban immigrants). A study in Europe (Van der Wurff et al. 2004) on the prevalence and risk factors of depressive illnesses among older Turkish and Moroccan immigrants in the Netherlands found results similar to those in the United States. The incidence of depressive symptoms, identified with the aid of self-assessment instruments, was 33.6% among older immigrants from Morocco and 61.5% among Turkish immigrants; these rates were considerably higher than those found in Dutch nationals (14.5%). Furthermore, the level of education and income of the immigrants was very low and they had a large number of physical handicaps and chronic medical illnesses. Thus, it appears that ethnic origin alone is associated as a strong, independent risk factor for clinically-relevant depressive symptoms.

It is assumed that it is not just the fact of migrating in itself, but also a specific constellation of risk factors (e.g., current living conditions, personal history, physical health) frequently associated with the migration process, that can predispose to the development of a mental illness (Bhugra and Jones 2001; Hovey 2000). Higher rates of mental and/or somatic symptoms may therefore be associated with migrants' stressful living conditions (e.g., low social class, lack of work, inadequate housing conditions, discrimination).

In summary, in evaluating the complex link between migration and psychosocial health, the following factors must be considered:

- Current living conditions (e.g., social and legal status, poverty)
- The heterogeneity of the population of migrants
- The individual's personal history, the premigratory personality, and conditions that led to the migration (e.g. war, torture)
- The concept of migration as a long-term process and the varied family dynamics caused by this process;
- Psychological variables, such as perceived control (internal versus external) over the decision to migrate, the predominant cultural assimilation strategy used to deal with the guest culture, and the subjective experience of migration.

Migration is therefore not a homogeneous event, but can involve a range of processes, factors, and conditions that can be associated with health and illness (Bhugra 2005).

Symptom Manifestation

Several studies have reported on the epidemiology of depression in different cultures. One of the best-known studies was carried out by the World Health Organization (WHO) in five different settings: Basel, Teheran, Tokyo, Nagasaki, and Montreal (Jablensky et al. 1981; Sartorius et al. 1980). The study followed a cohort over a 10-year period and evaluated clinical course, contact with services, and social function (Thornicroft and Sartorius 1993). Using the WHO Standardized Assessment of Depressive Disorders (SADD) (Sartorius and Davidian 1983) as the assessment tool, the study found that the "average" depressive patients seeking care in different cultural settings shared many characteristics despite cultural differences: Extensive similarities across countries were found in symptoms such as lowered mood, sleep problems, lack of energy, and problems concentrating, providing support for the idea that typical depressive symptoms are found in very different cultural settings.

General mood

Cross-culturally, the general mood found to be associated with depression is characterised by a symptom involving intensive "lively melancholy", combined with fear and an inability to experience cheerful emotions. This is also associated with a general lessening of interest in things, including familiar people and surroundings. Loss or gain in body weight may also be seen. Sleep disturbance, which may take the form of sleeplessness or an increased need for sleep, is the most frequently found cross-cultural symptom. Psychomotor activity may be increased (e.g., agitation) or retarded (e.g., apathy). A disturbance in the cognitive capacities may occur, as evidenced

by a reduction in the ability to concentrate and remember. In describing their experience of depression, patients from non-Western countries often tend to employ metaphors based on the state of their inner organs rather than the types of psychological terms that are usual in Western countries (see discussion of somatisation below).

As noted above, cross-cultural variations in the fundamental symptoms of a depressive episode are only slight. However, more marked variations are seen cross-culturally in symptoms such as exhaustion and loss of energy, feelings of inferiority and guilt, ideas concerning death and suicide, and psychotic features. Somatisation, which is listed as a symptom in both the DSM-IV and the ICD-10, appears to be a core symptom of depressive episodes cross-culturally, although up to now it has not been listed as such in the standard diagnostic formulations (Machleidt and Calliess 2007).

Psychotic symptoms

In general, hallucinations and delusions occur less often in depressive episodes in non-Western countries. When they do occur, they may be seen not only in association with psychotic episodes but also with neurotic and psychoreactive disturbances. When visual hallucinations occur in depressive episodes in non-Western settings, they do not suggest, as would be the case in Western societies, the existence of a physical illness as an additional cause. Delusions are especially dependent on cultural influences. When delusional phenomena occur in association with depression in countries other than the United States and Europe, they most often refer to issues such as physical health, religiosity, and persecution, rather than to guilt, inferiority, and poverty, as is often the case in Western countries. Thus, the ideals and anxieties of a culture find special expression in delusions (Pfeiffer 1994).

Feeling of persecution can be an expression of indigenous concepts of illness, in which mental disorders are conceived of as being caused by "aggressive spirits" (e.g., by the neglected spirits of the ancestors) or being produced through witchcraft, curses, the "evil eye" or some other magical influences. For example, among non-Western patients, the strong impression that one is being visited by the dead must be considered as a traditional experience (e.g., many Africans live daily in constant altercation and connection with their deceased ancestors and experience this as being supportive). It would therefore be completely wrong to consider this as a psychotic symptom. The same is true about sensations such as "burning in the head", piercing, or the feeling of being "crawling with worms and ants". Such "creepy-crawly" sensations must be differentiated from true hallucinations or delusions by considering the traditional context in which they occur. Instead, such narratives bear witness to the cultural in which they occur in which there is an everyday struggle against local parasites. On the other hand symptoms must not be ignored simply because they superficially appear to be an expression of the subject's culture.

Worthlessness and feelings of guilt

Although worthlessness and feelings of guilt are among the major symptoms of depression observed in the Euro-American culture, they are not specific to the Judeo-Christian cultural context. Rather, these symptoms are found in many other cultures, although with greatly reduced frequency, particularly when the person is an active member of a religious community. In a WHO study, Sartorius et al. (1983) found that Swiss patients had the highest frequency of feelings of guilt and Iranian patients the lowest. When self-reproach and feelings of guilt occur in subjects outside the Euro-American cultural context, they tend to be directed towards personal relationships in marriage and family and usually include reference to the spirits of the ancestors, friends, and the social position of the subject, and only exceptionally involve metaphysical concerns such as God. A sense of sin is largely absent in East and Southeast Asia (Japan, China, Vietnam) and increases proportionally as Christian influence increases. The more the principle of collective responsibility is replaced by one of personal responsibility and individual accountability as a result of sociocultural changes, the more a sense of individual guilt seems to become relevant in the phenomenology of depression.

Inefficiency

Inefficiency as a symptom of depression is not experienced as a problem in the majority of Southern countries. This contrasts markedly with the Euro-American and East-Asian (e.g., Japan, China) cultural context. This is because, in Southern cultures, the status of a person in family and society is determined by the circumstances of his or her birth, whereas, in industrial countries, efficiency is of major importance in personal assessment. Therefore, in Southern cultures, other, more family-oriented issues, such as physical attractiveness or sexuality and fertility, appear to play a more important role in the manifestation of depression.

Exhaustion and loss of energy

Individuals with depression in East-Asian cultures frequently complain of exhaustion and loss of energy. Weakness is a major symptom in these settings—it is considered to be due to a deficiency in psychic energy, the Qui, and a disturbance in the Yin-Yan-balance with an excess of Yin.

Somatisation

Somatisation, as a depressive syndrome involving a sense of physical discomfort and vegetative symptoms without any evidence of organic cause, is reported in every culture. Thus, the spectrum of depressive presentations ranges from those that focus primarily on psychological symptoms to those that primarily accentuate bodily symptoms. In contrast to the depressive symptoms that appear to be fundamental in Western countries, physical complaints with vegetative syndromes and bodily discomfort are seen as basic symptoms in other parts of the world. The majority of depressive episodes in these settings do not progress beyond this syndrome, although sudden behavioural disturbances (e.g., psychomotor overexcitation, dissociative phenomena) sometimes do occur. Depressive symptoms reported in developing countries include vegetative disturbances (e.g., disturbances in sleep and appetite, generalised weakness, loss of libido, exhaustion) and bodily discomfort (e.g., in the head, heart, abdomen and/or a general discomfort involving sensations such as burning, trembling, or stiffness).

In a world-wide study, Simon et al. (1999) found that approximately half of depressed patients across cultures reported somatic symptoms and that the number of unexplained somatic symptoms was on average three to four times higher among depressed patients than in individuals without a major-depression. This marked relationship between major depression and somatic was consistently found across all investigation centres and the finding was independent of the type of centre, the culture, and the socio-economic status of the patient. However, the quality of the doctor-patient relationship was found to play an important role in the symptom presentation. The more trustworthy the doctor-patient-relationship was, the lower the rate of presentation of physical symptoms. The tendency of patients with major depression to present with somatic symptoms can therefore be interpreted as follows: The presentation of somatic symptoms does not imply that a patient is incompetent or unwilling to report psychological symptoms; rather, it appears that, when patients visit a general health care centre, they believe it is more appropriate to present with somatic symptoms. This kind of "facultative somatisation" can be considered an "admission ticket" and an "opening move" in the doctor-patient-relationship in a general healthcare centre that is seen across different cultural and socio-economic settings. The more confidence the patient has in the doctor-patient-relationship and the more the patient feels that he or she is taken seriously, the greater the probability that this "admission ticket" will be dispensed with.

Somatisation (i.e., a presentation involving multiple somatic symptoms) can be considered a universal basic syndrome that is characteristic of depression in the same way that the pure psychological symptoms specified in classification manuals are considered a basic feature of depression. However, when depressed patients present primarily with somatic symptoms, general practitioners may miss the presence of the depression. When the doctor allows, or encourages, a more psychological expression of suffering, somatic complaints often decrease significantly. Thus, while somatic presentations of depression are common in every culture, there is evidence that the type of interaction that occurs between patient and doctor greatly influences the likelihood that the patient will express distress somatically (Gureje 2004; Simon et al. 1999).

Suicidal ideas and attempts

Suicide attempts exhibit various characteristics depending on the motivation involved. For example, a suicide attempt by means of a threat or a demonstration of a suicidal act can be an appeal to the community for sympathy. In highly traditional and patriarchal cultures, in which the head of the house is considered responsible for the fate of those entrusted to him, this may serve as a means of exerting pressure. Suicide attempts may not involve any intention of causing death, but rather have the characteristics of a conventional gesture. Such attempts may represent the person's effort to surmount otherwise insoluble conflicts and redefine the situation, as might occur with an indebted Chinese merchant or a student who fails exams. Suicidal impulses can also be expressed by alien types of behaviour or risky ventures. On the other hand, less dangerous modes of action can act as an equivalent to suicide, such as taking part in trance rituals or running away blindly into the jungle. Another form of suicidal action is self mutilation (e.g., cutting off the penis, which is considered the seat of life; cutting off a finger, as is done sometimes in New Guinea as an expression of grief at the death of a relative).

Thus, it appears that the suicidal tradition in different cultures still exists under the surface today. However, no where today is suicide considered a culturally obligatory duty, and ritual suicide only occurs in individual cases. However, even today, suicide in difficult life situations is still considered an alternative by some Indians and Japanese. A focus on national traditions can also lead to a revival of such customs (Calliess et al. 2007).

Psychopathological symptoms and patterns across cultures

Based on data gathered in the cross-cultural WHO Collaborative Study of Psychological Problems in General Health Care (Üstün and Sartorius 1995), Krueger et al. (2003) detected patterns of association among psychopathological syndromes across cultures. They identified a structure of comorbidity among 7 psychopathological syndromes: depression, somatisation, hypochondriasis, neurasthenia, anxious worry, anxious arousal, and hazardous use of alcohol. The best fitting model was a two-factor model that differentiated between so-called internalising syndromes (depression, somatisation, hypochondriasis, neurasthenia, anxious worry, anxious arousal) and an externalising syndrome (hazardous use of alcohol) across 14 countries (Brazil, Chile, China, France, Germany, Greece, India, Italy, Japan, The Netherlands, Nigeria, Turkey, United Kingdom, United States). Thus the results indicated a very close relationship between the 6 internalising syndromes independent of culture. Average levels of each psychopathological syndrome varied substantially from country to country.

In conclusion, the data reviewed here suggest that the diversity of depressive symptomatology found in many individuals in many different cultures can be captured by a dimensional model. Thus, the relationship among psychopathological syndromes are similar throughout the world. It should be noted that, based on the analysis by Krueger et al., somatisation, as well as anxiety and depression, were placed within the internalising dimension. This finding appears to be related to the fact that ethnic minorities living in Western countries tend to express or experience emotional distress in somatic terms more than members of Western cultures.

Explicit differences in observed patterns of average symptoms were also seen across cultures. Primary care patients in Asian countries (China, Japan, India) reported fewer, whereas patients in Latin American countries (Chile, Brazil) reported more symptoms of common forms of psychopathology than their counterparts in Western countries (Europe, United States). Thus culture has an important influence on levels of symptomatology.

These findings suggest the hypothesis that culture affects mental distress by modulating levels of psychopathology within specific countries within the framework of cultural similarities in the latent structure of psychopathology, as indicated by the internalising dimension. This theoretical formulation is close to the structuralist theory, which suggests that "universal structural features may be present against the background of cultural heterogeneity in manifestations of these features (de Saussure 1915/1966; Levi-Strauss 1955/1967)" (Krueger et al. 2003). "Emotion" as a basic psychological construct may be one of those latent culturally universal and culturally specific features.

Depression and pain

An association between depression and pain has repeatedly been noted in the literature. Using data from the large epidemiological sample evaluated in the U.S. National Comorbidity Survey (NCS) (Kessler et al. 1997), Hernandez and Sachs-Ericsson (2006) examined ethnic differences in reports of pain among Hispanics and Caucasians who had a current health problem and the role of depression. Hispanics with a current health problem reported higher levels of pain. When the interrelation of ethnicity, pain, and depression was analysed, these researchers found that depression was positively associated with reports of pain in both groups. The reports of pain were greater among depressed Hispanics than depressed Caucasians. Thus, depression was identified as a moderator of the relationship between ethnicity and pain reports, with ethnic differences in pain reports even greater among those who were depressed. The temporal relationship between pain and depression may be bi-directional, so that pain may precede the onset of depression or vice versa. Being Hispanic in the United States may be associated with a burden of stressful life experiences that may in turn influence bio-psychological mechanisms that affect sensitivity to pain and vulnerability to depression.

Depression and heart disease

An association between depression and heart disease has been reported across Western countries. Ormel et al. (2007) evaluated the association between depression and heart disease and between anxiety disorders and heart disease in 17 countries in Europe, the Americas, the Middle East, Africa, Asia, and the South Pacific using data from a World Mental Health survey. The evaluation involved a cross-cultural assessment of the total population and of 50 years of age and older. The results of this analysis indicated that the well-known association between heart disease and depression (major depressive disorder and dysthymia), which was replicated in this study, was not stronger than the association between anxiety disorders and heart disease. A consistent association was also found between depressive and anxiety disorders. Even though the countries included in this study differed markedly in culture, level of socio-economical development, and many other variables the outcomes showed strong cross-cultural consistency. This suggests "that efforts to understand causal relationships between heart disease and psychological illness should consider culture-independent mechanisms that hold true for mood and anxiety disorders." The depression-anxiety-heart disease link should also be analysed in the contexts of chronic somatic disease and psychiatric disturbances to detect the general background dynamics.

Depression and diabetes

Recent studies have found that the risk of depression may be doubled in those with diabetes compared with the general population. Other psychological disturbances, such as symptoms of anxiety, may also be more prevalent in patients with diabetes. Psychological morbidity has also been shown to be associated with the development of diabetes complications, poor diabetes self-care, and worsening glycaemic control. For example, in a primary care sample of Hispanic patients with diabetes in the United States, an association was found between increasing depression and poor glycaemic control (Gross et al. 2005).

A cross-cultural comparison of anxiety and depression in adults with type 1 diabetes in the United Kingdom and the United States found a number of cultural differences and similarities (Lloyd et al. 2003). In both samples, there was a high correlation between depressive and anxiety symptoms; however, the subjects in the United Kingdom were more likely to report higher levels of anxiety, while levels of depression did not differ between the two samples. Symptoms of anxiety in the subjects in the United Kingdom were associated with depression, less physical activity, and greater frequency of blood glucose monitoring, whereas in the U.S. subjects, depression was correlated with anxiety and smoking. The country of origin was an independent explanatory variable for these outcomes. It is not yet clear, however, whether these findings are a consistent pattern cross-culturally.

An increased risk of comorbid depression, diabetes, and high Body Mass Index has been reported in adults 65 years of age and older, especially in African Americans who are known to have a higher risk for diabetes. Associations were also found with functional and cognitive impairment. Of African American women with type-2-diabetes, one third had high levels of depression. Two depressive symptoms, anhedonia and lowered frustration, were found to be directly associated with an increased risk of cardiovascular disease (Collins-McNeil et al. 2007). A strong association with depressive symptoms was found in about 30% of individuals who had been newly diagnosed subjects with diabetes in a rural community in Bangladesh; while depressive symptoms are common in this culture, they are particularly prevalent in those with diabetes (Asghar et al. 2007).

Depression and posttraumatic stress disorder

In a highly traumatised refugee population, persons who exhibit symptoms of posttraumatic stress disorder (PTSD) after trauma often also have depressive symptoms. At follow-up, such individuals may develop major depression or other symptoms or become asymptomatic (Mollica et al. 2004). Evidence is emerging that individuals who suffer from comorbid PTSD and depression (e.g., Bosnian refugees, combatants) display substantial levels of psychosocial impairment and three- to five-fold more severe symptoms compared with those with PTSD alone. In diverse populations who have been affected by trauma, the prevalence of comorbid PTSD and depression ranges from 20% to more than 40%, with PTSD appearing to be the primary disorder in most cases, while comorbid depression develops as a secondary condition. Some evidence suggests that exposure to physical abuse and threat to life is more likely to lead to PTSD, whereas loss of close attachments increases vulnerability to depression (Momartin et al. 2004). In their study of Bosnian refugees who were resettled in Australia 5 years after the trauma, (Momartin et al. (2004) found that threat to life emerged as the only predictor of pure PTSD, whereas threat to life and traumatic loss were both strong predictors in the group with comorbid PTSD and depression. Individuals with comorbid depression and PTSD showed higher rates of severe or extreme PTSD and high levels of global functional impairment, distress, and social and occupational impairment, whereas those with pure PTSD were close to subjects with no psychiatric diagnoses on these parameters. It is evident that different events lead to depression and PTSD, suggesting that the pathways leading to these disorders may be somewhat distinct. There is a high degree of consistency in these findings across cultures.

Therapeutic issues

In treating members of ethnic minorities, a basic tool for clinicians is to continuously on their own cultural attitudes and values in order to facilitate a dialogue on cultural concepts of mental illness, treatment strategies, and roles of patient and therapist (Fox 2005). When different personal elements, both biological and cultural, are taken into account, minority patients can be treated with available interventions as successfully as Caucasian patients (Schraufnagel et al. 2006). Treatment will hardly be effective, however, without a shared concept of a patient's illness and its aetiology. In a study of illness representations in South Asian immigrants and European Americans (Karasz 2005), the results showed that the former identified the depressive symptoms described in a vignette in largely social and moral terms, while the European Americans focused on biological explanations as well as situational stress or life events. It can be hypothesised that illness representations mirror central cultural values. Immigrants of Hispanic origin, for instance, were found to equate "depression" with "problems at home", referring to the disintegration of the family as an emotional and instrumental supportive system (Cabassa et al. 2007).

Diagnostic assessment models, such as the cultural formulation presented in the DSM-IV-TR (American Psychiatric Association 2000; Lewis-Fernandez and Diaz 2002), provide clinicians with a window into their patients' worlds by helping them to inquire about patients' cultural background and identity, explanatory models of illness, and how their psychosocial environment influences their illness and functioning. The cultural formulation in the DSM-IV was developed by a multidisciplinary group of experts with the goal being to make the diagnostic manual more culturally sensitive by including

cultural perspectives and research findings in the psychiatric diagnostic system (Borra 2008). The cultural formulation may be seen as an ideographic statement that puts an emphasis on the patient's personal experiences in the light of his or her culture and the cultural reference groups (Borra 2008).

The interview described in the cultural formulation focuses on five aspects:

1. The cultural identity of the patient and his or her relation to the culture of the country of origin and host country. In order to elicit information on this, questions may focus on issues such as the patient's cultural reference group; language preference and abilities; degree of involvement with country of origin and level of engagement in the host country.

2. Cultural explanations of the person's illness, including issues such as the meaning and perceived severity of the patient's symptoms in relation to the norms of the cultural reference group; predominant idioms of distress; local illness categories used by the patient and his or her family; explanatory models the patient and reference group prefer; and help-seeking behaviour

3. Cultural factors related to the psychosocial environment and levels of functioning, including culturally relevant interpretations of social stressors and available social support; level of functioning and disability; and role of religion and kin networks in providing support.

4. Cultural elements of the relationship between the patient and the clinician, including individual cultural and social differences between patient and clinician and problems caused by such differences in the diagnostic and therapeutic process.

5. Overall cultural assessment for diagnosis and care, which focuses on cultural considerations that specifically influence comprehensive diagnosis and care (Lewis-Fernandez and Diaz 2002; Borra 2008).

Thus, an open intercultural dialogue concerning the patient's understanding of his or her problems conveys respect for the patient's attitudes and traditions and can be the first step in establishing a sustainable therapeutic alliance. However, under certain conditions, using a psychoeducative approach that teaches the patient about Western biopsychosocial models for the aetiology of depression and how to differentiate depression from normal feelings of grief or sadness may have an exculpatory effect (Lawrence et al. 2006). In addition, by reflecting on different interpretations of social situations and expectations in the therapeutic context, the clinician can gain a deeper understanding of problems associated with acculturation in the patient's everyday life.

In the psychiatric or psychotherapeutic treatment of immigrants, it very helpful to involve interpreters if the therapist does not speak the patient's mother tongue. Even if the patient can manage the host country's language in everyday situations, there may be limits on the patient's ability to describe emotional experiences in the language of the host country. Unconsciously memorised contents are activated in the mother tongue and emotions are experienced more immediately. The phenomenon of language independence (Marcos and Alpert 1976) can lead to a separation of affect and content when a person uses a second language, because emotions, memories, and associations that have been experienced in one's mother tongue may not be accessible in the cognitively learned second language. Moreover, language is an important factor in a person's identity and cultural expression (Grinberg and Grinberg 1990).

The impact of cultural factors on depression and its treatment should generally be considered within the patient's specific cultural context. Cultural concepts of illness and attitudes towards treatment will differ substantially if measured in native populations in different countries in contrast to findings from ethnic minority groups in Western societies. Hence, strategies for treating depression treatment need to be tailored for the patient's specific condition and situation. For instance, Western-socialised therapists tend to focus on individualisation and insight. However, in certain situations (e.g., in a community with a similar

cultural background), an orientation towards social values and role expectations may be more adaptive and helpful for the individual. In contrast, in areas that require self-actualisation (e.g., in the workplace), an adherence to traditional values aiming at inter-individual goals may help to resolve intrapsychic or interpersonal conflicts. Therefore, it is important for to define therapeutic goals in accordance with the patient's cultural background (e.g., self-organisation based on interindividual relatedness) (Sato 2001). Psychiatrists from individualistic cultures sometimes assume that cohesive family structures impede personal growth and do not allow individualisation. However, such cohesive social and family patterns can provide the basis for the development of a self-contained identity that is suited to one's position in a hierarchical structure (Fisek 2001). This implies that psychiatrists should not only refrain from automatically setting Western-oriented therapeutic goals (e.g., not focusing too much on autonomy), but should systematically access specific cultural resources. For example, a family characterised by traditional roles can provide patients with support and orientation. Given that, in many traditional cultures, the family is the entity that forms attitudes and makes decisions, it is generally helpful to involve important relatives in the therapeutic process. In addition, decision-making concerning treatment is a family matter in many areas of the world (Kastrup 2008). If a depressed patient makes a decision that is not in line with the family's decision, the patient may end up taking the entire responsibility for his or her health situation and may lose any family support (Okasha 2000). Especially when family problems are among the factors that are contributing to the illness, involving the family may prevent unsolvable conflicts between family and therapist.

Cultural factors also need to be differentiated from those related to migration, even though these dimensions are frequently confounded in both research and practice. For patients who have migrated because of (institutionalised) repression in their home country, any contact with state authorities can trigger traumatic experiences, and they may also distrust health professionals. Especially after forced migration, an internal feeling of relatedness to the home country and plans for returning home can interfere with necessary steps that the person needs to take concerning work and housing in the host country. Hence, the psychiatric interview should not only focus on cultural factors but also consider such factors related to the migration. Asking a patient about his migration biography can provide crucial insights into the conditions that brought him or her to the new country and shed light on possible factors that may be contributing to the illness. Clinicians need to keep in mind that the experience of migration and its consequences can have a long-term impact on psychological functioning.

Culture-Related Issues in Treatment

Patients' attitudes toward treatment vary greatly from culture to culture as well as from one social group to another. In some societies, antidepressant medication may "legitimise" the illness, whereas in others, it further stigmatises the disorder. Expectations of medication are also affected by culture. Many individuals expect a powerful, immediate response, and most will discontinue medication as soon as they feel better.

Pharmacokinetic variations in the metabolism of medications also exist among ethnic groups. However, it is not yet possible to say whether these differences have any impact on the dosage variations observed in several countries, which seem to depend much more on physicians' attitudes and training than on any ethnic differences.

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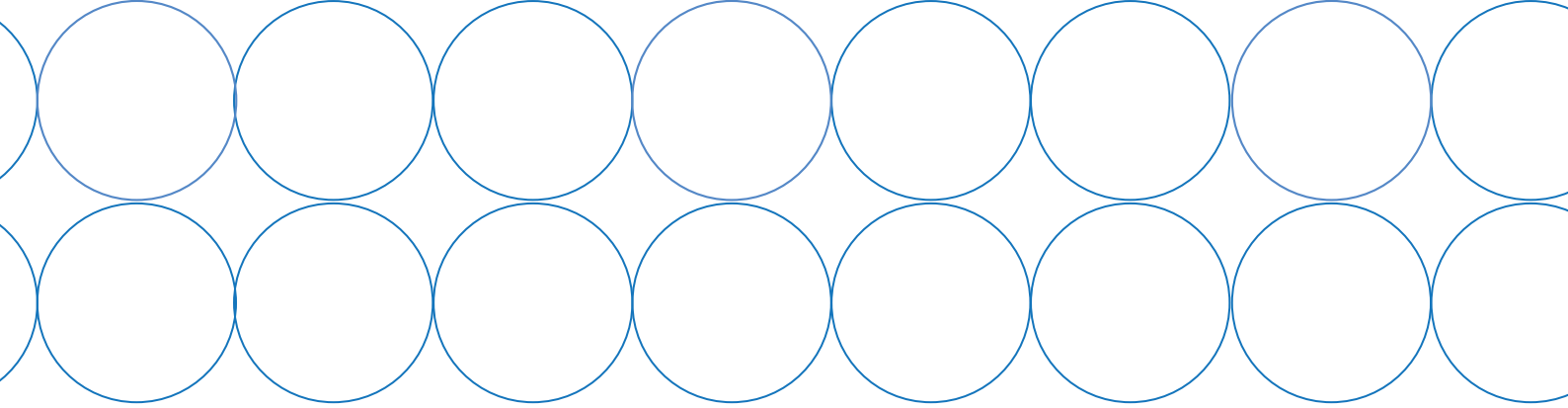

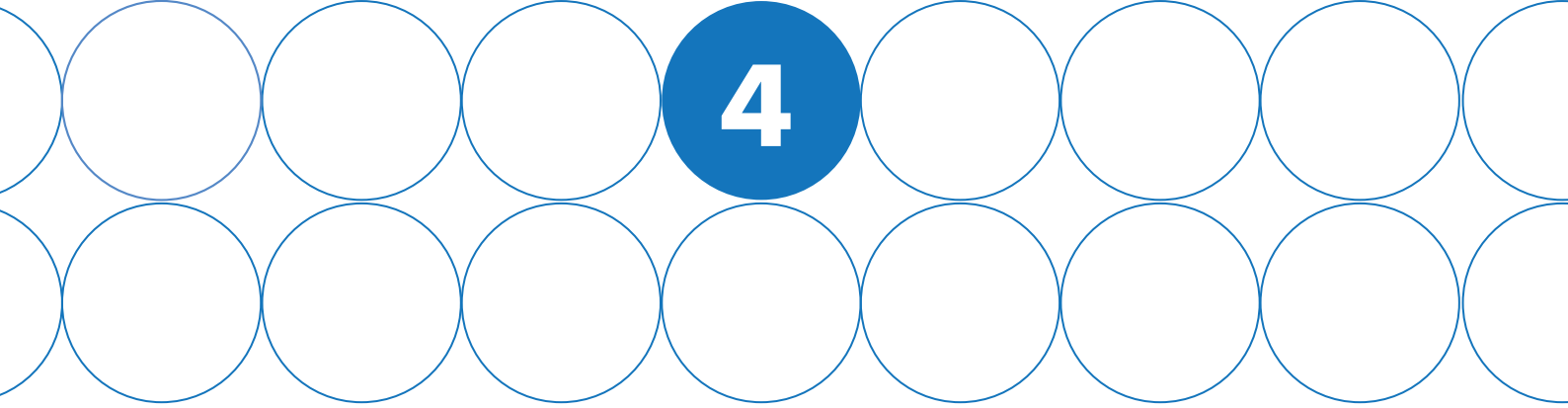

Chapter 4

Etiology and Pathogenesis of Depressive Disorders

Depression is a heterogeneous disorder related to multiple complex factors ranging from genes to environment. Many hypotheses have been advanced about the etiology and pathogenesis of depressive disorders. The overview that follows summarizes findings about the role of genetic and neurochemical factors in depression and reviews the results of brain imaging studies. It also discusses the role of physical illnesses, psychosocial factors, and premorbid personality characteristics in the occurrence and course of depressive disorders.

NEUROBIOLOGICAL FACTORS

Genetics of Depression

Family, twin, and adoption studies provide ample evidence of the importance of genetic and familial factors in the development of mood disorders. Family studies consistently show aggregation of illness in relatives of persons with mood disorders. In a large study, 25% of relatives of bipolar probands had bipolar or unipolar illness themselves, compared with 20% of relatives of unipolar probands and 7% of relatives of controls (Gershon et al, 1982).

The relative contributions of genetic and environmental factors to a particular disorder are determined by measuring the degree of similarity between a set of identical (monozygotic [MZ]) twins, and comparing this with similar data for a set of non-identical (dizygotic [DZ]) twins. The analysis proceeds by assuming that the genes are indeed identical in the MZ twins, who will therefore have perfect correlation for variance due to genetics, while the variance for DZ twins is assumed to be 0.5 since they only share half their genes. Variance due to common, family environment is also assumed to be perfect for both MZ and DZ twins, and anything left over is attributed to a residual term covering unique (or non-shared) environment. The similarity between the MZ twins is now considered to be due to the sum of the effects of genetic factors and shared environment, while the similarity between the DZ twins is due to half the genetic factor, plus the shared environment. Comparisons of the within-pair correlations for the two sets of twins will thus result in rough estimates of the variance due to genes, shared environment, and unique environment (Kendler et al. 1987; Kendler and Prescott 1999; Thapar and McGuffin 1998). These studies all showed the same thing: shared family environment had no contribution whatever, genetic factors accounted for around 40% of the variance, and environment unique to the individual accounted for a large part of the rest. It should be noted that the genes that control depression are almost the same as those that control anxiety (Kendler et al 1987), and about half of the genetic variance that was identified is associated with "neuroticism" measured in adult life (Kendler et al, 1993).

However, the assumption that the environment is the same for each MZ twin is not correct. Each of us has a "unique environment", and this will cause each one of us to experience life differently. It is therefore never correct to assume that a "shared family environment" is truly shared—even a pair of MZ twins may try to ensure that they have different clothes and are perceived as separate individuals, and will in turn perceive their parents in somewhat different ways. Such different experiences may cause different genes to become active, and it is therefore not justifiable to attribute all of the differences between identical and fraternal twins to genetic causes.

Linkage studies have sought to identify candidate genes for depression. These studies have looked at genes such as serotonin and dopamine receptors, G protein, and cAMP response element-binding protein (CREB) genes (Taylor and Fink 2006), but the results are not yet conclusive (Levinson 2006). More recent studies on candidate genes have focused on the genes involved in neurotrophic and neurotoxic processes, inflammation, the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, and sleep and circadian rhythms.

Gene–Environment Interactions

One of the genes responsible for the transport of serotonin (a neurotransmitter implicated in depressive phenomena) is the 5HT transporter gene on chromosome 17 (17q11.2). People can have with two copies of the long allele, two copies of the short allele, or a heterozygous condition with one short and one long copy. This gene appears to moderate the serotonergic response to stressful events. In a cohort study of children born in Dunedin, New Zealand, Caspi et al. (2003) found that those with the homozygous long version (31% of this population) are relatively resilient in that they tend not to develop depression even when they have experienced several stressful events. Heterozygous subjects (51% of this population) are more likely to become depressed if they experience stressful events. Finally, those who are homozygous short (17%) show a very strong relationship between stressful events and developing depression. Without stress, the gene does not manifest itself, but in the presence of stress one's genetic make-up will

determine how likely you are to become depressed. These observations fit with the finding that most of the discordance between the results found for MZ and DZ twins is due to discordance for health while only a small part is discordance for illness. Thus, genetic factors may largely be controlling resilience to adult stressors, rather than entirely controlling factors related to depression.

Neurochemical Studies

Psychoactive drugs have provided researchers with powerful tools for studying the biochemical basis of behaviour. One hypothesis based primarily on pharmacological data is that a disturbance in biogenic amine metabolism is the predisposing factor in mood disorders. In its simplest form, "the monoamine hypothesis" postulates that depressive disorders are associated with a relative deficit of one or more of the biogenic amines, while mania is linked to a relative excess. Schildkraut (1965) proposed that noradrenalin (NA) was an important neurotransmitter involved in depression, while Coppen (1967) postulated that serotonin (5-HT) played a more important role than NA in depression. However, these monoamine hypotheses do not address the fact that the onset of a therapeutic effect normally requires 2–4 weeks. The time lag in the onset of the effect of antidepressants is believed to be due to the desensitisation of the alpha-adrenergic receptor or 5-HT1A auto receptors, which occurs over a few weeks. However some of the newly developed antidepressants do not alter the density of these receptors. A number of dopaminergic drugs have also been shown to successfully treat depression. As a result, it is currently believed that a diversity of pathophysiological mechanisms may underlie depressive disorders, suggesting that there may not be a single shared mechanism of action for antidepressants. While it is recognized that these proposed explanations for mood disorders are oversimplifications, they nevertheless serve as an important stimulus for further research into the biology of mood disorders.

A more consistent finding in depression is the hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, which is revealed by the dexamethasone suppression test (DST) (Carroll et al. 1982). A major drawback of the DST that has been reported is its modest sensitivity to depression. A more accurate test was subsequently introduced in which the DST was combined with a corticotropin-releasing factor (CRF) challenge (Holsboer et al. 1987). Patients who were depressed displayed higher adrenocorticotropic hormone (ACTH) and cortisol responses to CRF when pre-treated with dexamethasone.

Although data are inconclusive, gamma aminobutyric acid (GABA) and some neuropeptides (particularly vasopressin and endogenous opioids) have also been implicated in the pathophysiology of mood disorders.

The exciting finding that the new neurons are produced (neurogenesis) in the hippocampus throughout the lifespan (Eriksson et al. 1998) has changed the way we think about the pathogenesis of psychiatric disorders. Many studies have indicated that antidepressants and electroconvulsive therapy (ECT) increase neurogenesis (Malberg 2004). While acute and chronic stressors produce a down-regulation of neurogenesis, antidepressants can reverse the stress-induced down-regulation of neurogenesis. One way in which antidepressants may produce neurogenic effects is by increasing neurotrophic factors such as brain-derived neurotrophic factor (BDNF). Almost every antidepressant activates CREB, which is a downstream component in the cAMP cascade system; in its phosphorylated form, pCREB induces BDNF expression (Nibuya et al. 1996), which in turn leads to neurogenesis. Coinciding with studies of these basic mechanisms of antidepressants, imaging studies performed in chronically depressed patients have found a reduction in the hippocampal volume and the cortex (Botteron et al. 2002; Sheline et al. 1996), suggesting that these changes in the hippocampal volume and/or the cortex may be caused by depression. Furthermore, it has been reported that antidepressant treatment can reverse depression-induced decreases in hippocampal volume (Vermetten et al. 2003). However, it is still not clear whether such changes appeared before the onset of the disease or whether they were a direct cause of the disease.

A number of alterations of the somatic immune system have been observed in major depression; particularly increased levels of pro-inflammatory cytokines (Maes et al. 1997) and reduced receptor sensitivity (Kanba et al. 1998). Central cytokines may also possibly be involved in the pathogenesis of depression. Stress increases intekeukin-1 in the rat brain (Shintani et al. 1995). Chronic treatment with different classes of antidepressants has been reported to significantly increase the production of IL-1 receptor antagonist (IL-1ra) mRNA in specific regions of the rat brain (Suzuki et al. 1996).

Although the data are still inconclusive, other substances that would be expected to have antidepressant action are non-peptide antagonists for the substance P preferring neurokinin-1 (NK1) receptor, drugs that down regulate N-methyl-D-aspartic acid (NMDA) receptor function. A body of evidence also exists suggesting that some transmitters could be involved in the pathophysiology of depression including GABA, neuroactive steroids, opioids, and cholecystokinin (Slattery et al. 2004)

Brain Imaging of Depression

Well replicated findings from structural neuroimaging studies in depression include an increased rate of deep white matter hyperintensities and a smaller frontal lobe, hippocampus, cerebellum, caudate, and putamen (Steffens and Krishnan 1998). Bipolar disorder has been reported to be associated with a larger third ventricle, in addition to a larger basal ganglia and amygdala. Functional imaging studies have indicated both the metabolism and the blood flow in the dorsolateral prefrontal cortex, left hippocampus are decreased in depressed patients, while the metabolism and blood flow in the amygdala and the ventrolateral and posterior orbital cortex are increased (Taylor and Fink 2006). In addition, a reduction in the volume and metabolism of the subgenual prefrontal cortex (SGPFC) has also been reported (Drevet et al. 1997).

Depression and Physical Illness

Depressive disorders are linked with various physical illnesses, such as endocrinopathies (e.g., hypothyroidism, Cushing's syndrome, Addison's disease), carcinoma, neurological disorders, infectious disease, and collagen diseases (e.g., systemic lupus erythematosus, rheumatoid arthritis). Chronic diseases that cause pain and limit social interaction are frequently accompanied by demoralization and depressive disorders (Table 4.1).

Cerebrovascular diseases that are visualized with MRI in the deep white matter and the basal ganglia are associated with late-onset depression. The concept of vascular depression (previously called arteriosclerotic depression) (Krishnan et al. 1995) has been discussed (Krishnan et al. 1997; Alexopoulos et al, 1997). However, the etiological link between depression and vascular disease needs further exploration.

Finally, a host of drugs used in clinical practice have been reported to sometimes precipitate depressive disorders. For example, interferon therapy is strongly related to the occurrence of depression, which sometimes results in an interruption of the interferon therapy itself (Dieperink et al. 2000). High rates of depression have also been reported in individuals with drug dependence (Kokkevi and Stefanis 1995; Stefanis and Hippius 1994).

TABLE 4.1

Medical Conditions Associated With Depressive Disorders

Metabolic and Endocrine Disorders	Infectious Diseases	Degenerative Disorders	Other Somatic Disorders
Addison's disease	Encephalitis	Alzheimer's disease	Carcinoma
Anemia	Endocarditis	Huntington's disease	Chronic pyelonephritis
Cushing's syndrome	Hepatitis	Multiple sclerosis	Lupus erythematosus
Diabetes	Mononucleosis	Parkinson's disease	Ménière's syndrome
Hyperparathyroidism	Syphilis		Pancreatitis
Hyperthyroidism	Tuberculosis		Postconcussional syndrome
Hypocalcemia			
Hyponatremia			
Hypothyroidism			
Korsakoff's syndrome			
Liver dysfunctions			
Porphyria			
Uremia			
Wilson's disease			

ENVIRONMENTAL FACTORS

The Importance of Secure Attachment

Secure attachment to the caregiver (usually the mother) in the first few months is of critical importance in modifying the excitability of the HPA axis and thus the vulnerability to stress in later life. Attachment theory proposes that infants develop 'internal working models' of relationships that serve as a psychological blueprint for interpersonal functions with others in childhood and later life. Insecure attachment produces a baby with poor social development and more anti-social behaviour, which in the presence of negative experiences leads to anxious traits. Thus, maternal attachment is the first life experience that can modify—in either direction—the excitability of the HPA axis. Maternal separation increases HPA sensitivity, as does maternal depression. Severe chronic privations, such as being brought up in an orphanage since birth, are also associated changes in the sensitivity of the HPA axis—with cortisol hypersecretion frequently reported. In children, early parental loss by death or separation engenders an increased risk for developing future psychiatric illnesses, such as major depression and anxiety (Mireault and Bond 1992).

Recent work with both rats and monkeys has greatly advanced our knowledge of the effects of early maternal deprivation. Rat mothers can be bred who display much maternal licking, grooming, and nursing behaviour ("high LGN mothers"), while others can be bred who only rarely display such behaviours. The high LGN mothers produce offspring that have dampened HPA axes in adult life, and will show dampened responses to stress. The low LGN offspring show the opposite—hyperreactivity and increased stress responses in adult life. Yet if neonates of high LGN mothers are given to low LGN mothers, and the latter's offspring are given to high LGN mothers, the phenomenon is just as strong—it is the environment, not the genes, that produces the anxious adult rat. Even more impressive—when females born to low LGN mothers but who have experienced high LGN mothering have their own litters, they continue to manifest high LGN behaviours. Good mothering is being transmitted without the presence of altered genes, but which alter subsequent gene expression. The offspring of these rats will have increased hippocampal glucocorticoid receptor mRNA expression, higher central benzodiazepine receptor levels in the amgydala, and lower corticotrophin releasing factor mRNA in the paraventricular nucleus of the hypothalamus (Francis et al. 1999). High LGN behaviour in the rat mother produces differences in HPA responsiveness in the offspring during their adult life, which is in turn associated with differences in DNA methylation, and changes in transcription factor (NGFI-A) binding to glucocorticoid receptors (Weaver et al. 2004).

In monkeys, those experiencing maternal separation at 1 week of age show fewer social behaviours and an increase in self-comforting behaviours (for example, thumb sucking) over the course of their development; in contrast, monkeys experiencing maternal separation at 1 month of age show increased seeking of social comfort later in life. Sabatini and colleagues (2007) examined changes in mRNA content in amygdala tissue collected from infants at 3 months of age. Samples were taken from three groups:1) infants separated from their mothers at 1 week; 2) infants separated from their mothers at 1 month; and 3) infants who were maternally reared. The neural systems involved may be related to one gene, guanylate cyclase 1 3 (GUCY1A3), which showed differential expression between the group separated after 1 week and the maternally reared group, and between the groups separated at 1 week versus 1 month. The expression of this gene was positively correlated with acute social-comforting behaviour and longer-term close social behaviour. This gene is expressed at adult levels by 1 week of age and its expression was found to be greater in the amygdala than in all of the other brain areas examined.

Events in Childhood

Maltreatment of children (physical and sexual abuse) has significant biological consequences for neural systems and chemical codes for behaviour. Child maltreatment has been found to be associated with cortisol hypersecretion in some studies but with cortisol hyposecretion in others. Children subjected to physical or sexual abuse display a wide range of common mental disorders in adolescence—not only much higher rates of depression, but self-harm behaviours and eating disorders, as well as problems obtaining satisfactory sexual relationships. Girls are at greater risk than boys for sexual abuse.

The effects of poor parenting practices are less dramatic than those associated with poor infant attachment. Poor parenting—whether overinvolved or depriving—is associated with an increased risk of depression and/or anxiety in the children later in life. Marital discord—often associated with separations and violence—exerts an effect on children independent of the effects of parenting. Children who have experienced parental divorce and parental death also have higher rates of depression and anxiety in adult life. Concepts of self-worth, peer popularity, and social competence develop during childhood and problems in the development of these concepts can have important consequences for the later development of common mental disorders. The development of friends is the most important non-family activity that occurs in childhood, and those who do not develop friendships may have difficulties handling negative life events in later life.

During middle childhood children begin to adjust their self-perceptions as a result of failure at key tasks. It is usually at this stage of life that feelings of shame, helplessness, and hopelessness first emerge, and the germs of later depressive illness may become manifest, as early cognitive changes occur, especially in those who have a tendency to persistently ruminate and perseverate about real or supposed shortcomings.

Hammen and colleagues (2000) reported that young women who had experienced one or more significant childhood adversities (e.g., family violence, parent psychopathology, alcoholism) had a lower threshold for developing a depressive reaction to stressors compared with women who had not experienced such adversities.

Life Events and Social Conditions

Life events refer to discrete changes in a person's environment that may cause some form of threat or stress to the individual. Research on life events prior to the onset of depressive disorders shows a five-fold higher prevalence of undesirable events, which may occur throughout at least the 6-month period preceding the onset of illness. *Loss events* such as bereavement, divorce, severe illness in a close relative, or job loss have been shown to be particularly important. There is a substantial genetic component in individuals' experience of stressful life events, but this is entirely mediated by personality variables, notably neuroticism (harm avoidance) and a personality dimension called "openness to experience". About half the variation in normal personality is genetically determined.

Several investigators have confirmed the finding by Brown and Harris (1978) that events involving loss are more likely to occur before episodes with predominant depression, while threat and danger are more likely to occur before episodes of predominant anxiety. Not only is depression more prevalent among those who are poor, unemployed, or experiencing adverse living conditions, but it is also associated with lack of an intimate relationship, humiliating life situations, or entrapment in a life situation that cannot readily be modified (Brown et al. 1995).

Premorbid Personality

Individuals with certain personality types are at greater risk for depressive disorders. An example is the hypothesized association between unipolar depressive disorder and a trait pattern described as the melancholic type (Tellenbach 1961) or Shimoda's Shuuchaku Kishitu (Shimoda 1941). This pattern includes features such as orderliness, conscientiousness, rigidity, obsessiveness, meticulousness, placing a high value on achievement, and dependency on close personal relationships. In recovered patients, passivity, interpersonal dependence, and low scores on emotional stability increase the risk of relapse (Hirschfeld et al. 1983). A longitudinal study performed in Zurich identified neuroticism as the most prominent premorbid personality trait for unipolar disorder (Clayton et al. 1994). Presumably, these features are important because they influence the way people respond to stressful life events.

PSYCHODYNAMIC PERSPECTIVES OF DEPRESSION

In the early 1900s, Sigmund Freud published a landmark paper, "Mourning and Melancholia". Freud was interested in what differentiated normal grief from depression (melancholia). In this work, Freud suggested that the origin of depression involved a psychological process which he characterized as "aggression turned inward". In his formulation, this problem can arise when a close relationship ends either through death, illness, conscious decision, or accident.

The psychological work of grief, to Freud, involved withdrawing the emotional attachment felt toward the person who is no longer present. In certain circumstances, especially when the relationship is an ambivalent one, loving feelings may be mixed with hateful or angry feelings toward the other person. Due to a variety of possible causes, a specific individual may be unable to resolve the aggressive feelings toward the lost person.

Freud hypothesized that, since a psychological resolution is necessary, certain individuals may resolve their aggression toward the lost person by using a defence mechanism he called introjection, resulting in turning the aggression toward the self. The clinical evidence for this occurrence would be seen in the shift from the normal sadness and associated feelings and experience of loss in grief toward the guilt, self-criticism, and suicidal ideas characteristic of melancholia (depression). Because of the way defence mechanisms operate (i.e., outside conscious awareness), the individual cannot explain what has happened.

The treatment approach in Freud's formulation involves, as a first step, helping the patient to become consciously aware of the aggressive feelings toward the lost individual. This is followed by working to resolve the aggressive feelings, now that the patient is aware of them. This formulation of the aetiology of depression, and recommended treatment, has been followed with much benefit by many patients throughout the last century.

Clinically driven advances in theory and treatment techniques in psychoanalysis led to the introduction of another important approach in recent decades. In the 1970s and 80s, the American psychoanalyst Heinz Kohut developed a psychoanalytic body of thought which has come to be known as self psychology. Kohut believed the maintenance of psychological equilibrium relies on a combination of regulatory capacities both within the individual and resulting from important relationships. He believed that normal development involves an ongoing need for external psychological support that begins at birth but is continually transformed throughout life. Kohut used the term cohesive self to describe the state in which adequate self-awareness, self-esteem, and self-regulation (including regulation of interpersonal relationships) exist to allow the individual to function in a reasonably adaptive way.

In Kohut's view, the loss of a relationship with someone who has been a source of significant external psychological support can produce a state of self-fragmentation, due to the affected individual's inadequate capacity to maintain self-cohesion. A variety of clinical manifestations of this self dysregulation can occur, including depression. Treatment in this situation aims to re-establish external support, leading to a return to self-cohesion and internal regulation.

This theoretical view also accounts for another source of stress to self-cohesion which may result in depression. As noted above, the ability to maintain a cohesive sense of self relies on the capacity to maintain internal self regulation. Stress may come from loss of an external support, as discussed above. However, stress may also from internal loss of self regulation due to what is known as a narcissistic injury. A narcissistic injury is one in which there is an injury to the self, resulting from loss of one or more components of an individual's identity, a blow to self esteem, or trauma. The resulting self fragmentation may produce a state of depression. In this case, reestablishment of external supports is not the goal of treatment; rather, the external support is seen as providing a bridge while internal self cohesion is re-established either via a return to previous self cohesion or the development of a new and modified self. Many transitions in life roles (e.g., loss of a job or relationship) involve a loss of previous roles. While not as dramatic as the death of a loved one, such losses can still produce a state of injury to the self and resulting depression.

Neither cognitive behavioural therapy (CBT) nor interpersonal therapy (IPT) use a psychological formulation based on the theoretical perspectives discussed above. It can been seen, however that the identification of "automatic thoughts" and "schemas" in CBT, or the provision of external psychological support in IPT can be seen as dealing with the types of psychological processes described above.

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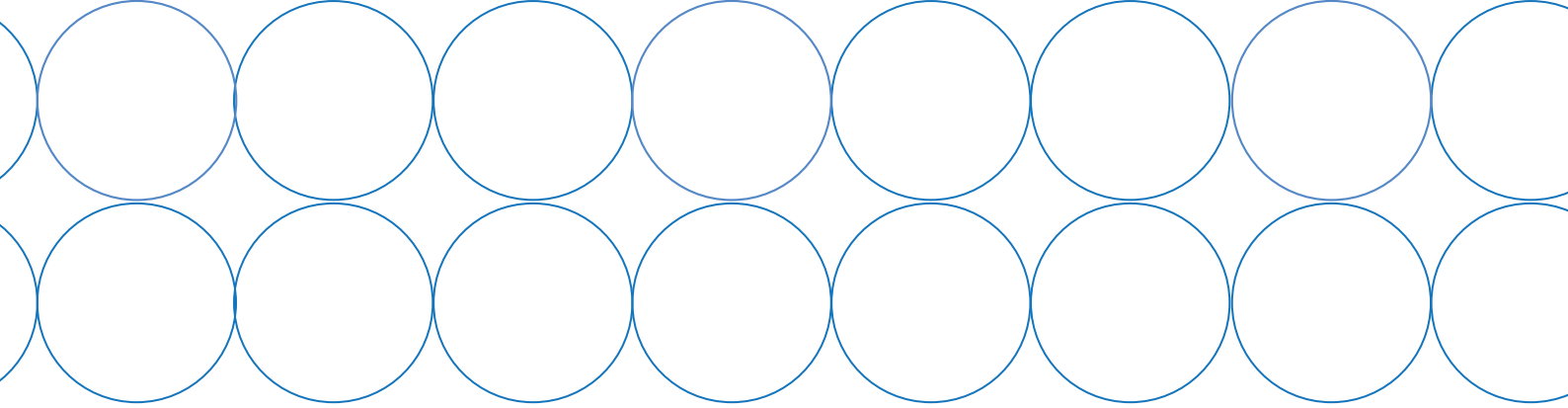
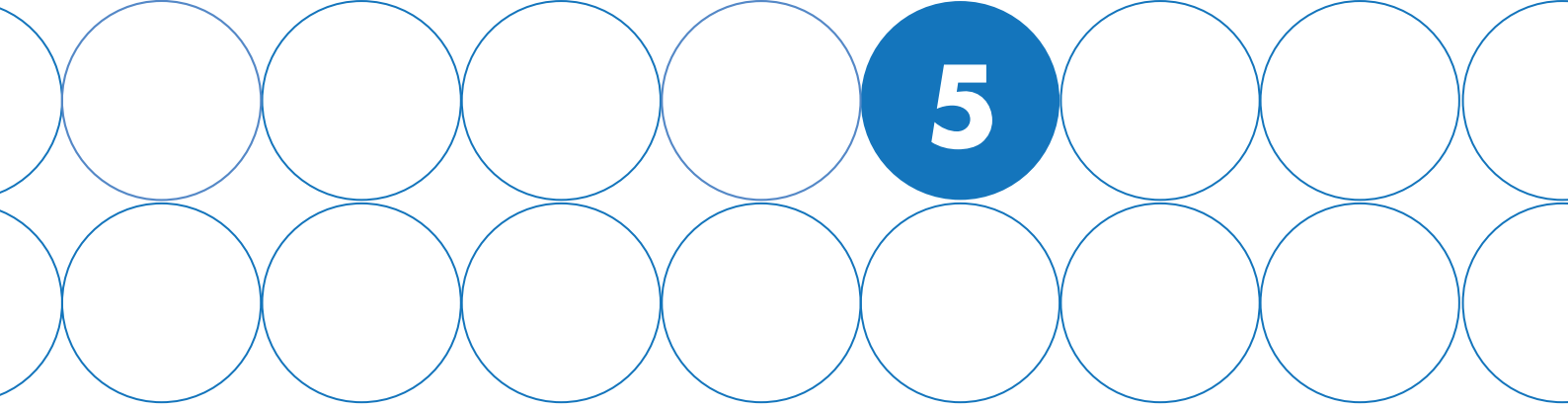




Chapter 5

Management of Depressive Disorders

INTRODUCTION

Management of depressive disorders can be one of the most rewarding aspects of primary care practice. Studies consistently show that most patients with a depressive episode can be effectively treated. Treatment generally returns patients to their premorbid level of functioning, usually within 1 to 2 months. Recent studies have also shown that recurrence can be prevented in most cases.

Management of depressive disorders can usually be accomplished within the framework of the primary care physician's practice. Very mild forms of depressive disorders often subside without treatment, and it is therefore important that the physician understand the point at which to initiate treatment. Only selected patients will require consultation with or referral to a specialist. The extra time the primary care physician spends in diagnosis and patient/family education during the early phase will save time in the long run, because subsequent visits are likely to be shortened and the patient will be less likely to contact the physician frequently for vague somatic complaints.

This chapter describes the different modalities available for the treatment of depressive illness: various classes of antidepressant medication, different forms of formal psychotherapy, and electroconvulsive therapy (ECT). It then discusses the indications for these modalities during the acute, continuation, and maintenance phases of treatment for depressive illness. Finally, this chapter discusses issues related to clinical management, including the importance of the therapeutic alliance between patient and physician, working with the family to help them become as an ally in treatment, patient/family education, and follow-up and assessment of the patient who is in treatment. The primary care physician, particularly one who knows the patient and family, is in an excellent position to form a therapeutic alliance with the depressed patient and help him or her overcome the serious obstacles to treatment adherence—pessimism, poor motivation, low energy, social isolation, and guilt— that are inherent in this illness.

AIMS OF TREATMENT

Once a depressive disorder is diagnosed, the primary aim of treatment is to decrease symptoms and suffering earlier than would occur in the natural course of the illness. Treatments and interventions with the highest probability of success and lowest risk of troublesome adverse events should be tried first whenever possible. Thus, the initial objectives of treatment, in order of priority, are:

- To reduce and ultimately remove all signs and symptoms of the depressive disorder
- To restore psychosocial and vocational functioning to the premorbid state
- To minimise the likelihood of relapse and recurrence

OVERVIEW OF TREATMENT MODALITIES

Today clinicians around the world have three major modalities (or a combination of these three) available for the treatment of depression: pharmacotherapy, formal psychotherapy, and ECT. Each treatment modality has potential value in selected patients, and the advantages and disadvantages of each are discussed in the sections that follow.

Pharmacotherapy

Numerous randomised, controlled clinical trials have demonstrated the effectiveness of antidepressant medications in the treatment of all forms of depressive episodes, dysthymic disorder, and the depressive phase of bipolar disorder. For patients with a moderate or severe depressive episode, and even for patients with episodes somewhat below this level of severity, antidepressants have been shown to be more effective than placebo and superior to psychotherapy (Elkin et al. 1989; Paykel et al. 1988; Wells et al. 1989). Efficacy of pharmacotherapy has not been demonstrated, however, in clinical trials for patients with depressive symptoms at the very mild end of the clinical range.

Therapy with antidepressant medications is effective even in the presence of significant life stress, such as a serious medical illness (e.g., cancer, heart disease) or job loss; it should not be withheld in a persistent depression solely because the condition is understandable and stress is contributing to it. Barring contraindications, antidepressant medication is the first line of treatment for moderate and severe depressive and dysthymic disorders.

Meta-analysis of studies on treatment with antidepressant medication for patients with depressive episodes indicate that, in general, most antidepressants have comparable efficacy and that drug-placebo comparisons are similar across medications. Furthermore, the efficacy of medications studied to date in depressed but otherwise medically fit geriatric patients is similar to that found in younger adults.

In contrast to antidepressants, antianxiety agents (with the possible exception of alprazolam) have not been demonstrated to be effective in the management of depressive illness. Anxiolytics may act on the anxiety symptoms that are often present in depressive disorders, thus diminishing the overall severity of the condition; however, because they are not treating the underlying depressive disorder, the risk of suicide and depressive symptoms persists.

Benefits of Treatment

The overall benefits of successful treatment include symptomatic remission; improved interpersonal, marital, and occupational functioning (DiMascio et al. 1979); and reduced potential for suicide, as well as the prevention of possible future episodes. In addition, early detection and treatment of depressive disorders can reduce health care overutilisation and long-term treatment costs. It is also reasonable to expect that successful treatment of a patient's depressive disorder will facilitate treatment of concomitant general medical conditions and may improve the individual's long-term prognosis.

Each treatment approach has its own advantages and disadvantages. Antidepressant medications 1) are easy to administer; 2) are effective in mild, moderate, and severe forms of depressive episodes; and 3) require little patient time. The advantage of structured, targeted psychotherapy for depression is that it has no physical side effects, such as those encountered with medications or ECT. Roughly, it can be said that medications and ECT work better in resolving symptoms, while psychotherapy works better in resolving problems. A combination of pharmacotherapy and psychotherapy has the advantages of both modalities.

The benefits of treatment for depression usually far outweigh the risks.

Disadvantages of Different Treatment Modalities

Antidepressant Medications

The disadvantages of antidepressant medication include 1) the need for repeated medical visits to allow the clinician to monitoring the effects of the medication and titrate the dose as needed; 2) unwanted side effects; 3) more severe medical reactions, including allergic reactions; 4) potential use of medications in suicide attempts; 5) failure of many patients (estimates range between 10% and 40%) to complete treatment; 6) need for adherence to the medication regiment. Clinicians and patients must weigh the risks of side effects against the potential benefits of treatment. Side effects from antidepressants range from relatively minor but annoying problems (e.g., dry mouth, constipation), to moderately severe effects (e.g., orthostatic hypotension) to substantial adverse effects (e.g., conduction abnormalities in cardiovascular disorders).

Psychotherapy

Although structured, targeted psychotherapy of depression (e.g., cognitive, behavioural, interpersonal psychotherapy of depression) does not have the physiological side effects associated with medications; other disadvantages may emerge when it is chosen as sole therapy. The quality of the therapy affects the outcome, suggesting that the availability of trained and competent therapists is pivotal. Disadvantages include the following: 1) formal psychotherapy of depression has rarely been tested in patients with moderate, severe, or psychotic depression; 2) many patients (10%–40%) fail to follow through with the full course of treatment; 3) the most common forms of psychotherapy (e.g., long-term dynamic psychotherapy) have not been tested for efficacy in randomised, controlled trials; 4) psychotherapy is not effective for all patients with depressive disorders; 5) some therapies may differ from others in overall efficacy or in specific effects (e.g., marital therapy may be more effective than other less specific therapies in improving marital relationships); 6) while theory suggests that formal psychotherapy reduces the likelihood of recurrence, available data for already established recurrent depressive disorders do not support this claim (Shea et al, 1992); 7) therapy sessions are time consuming and may be inconvenient; 8) some patients and therapists are reluctant to consider somatic treatment alternatives (medication, ECT) when psychotherapy proves ineffective after a reasonable trial; and 9) formal psychotherapy of depression may be expensive.

Combination Treatment

The disadvantages of combined treatment (e.g., medication plus some type of formal psychotherapy) include the separate disadvantages discussed above for each modality. Patients with milder, transient depressive disorders may not require, respond to, or tolerate medication; those attaining remission with medication alone may have spent unnecessary time and money on formal psychotherapy. If the depressive disorder recurs, both treatments will again be required, because it will be impossible to determine whether one alone would have been sufficient. There is no evidence, however, that the combination has a worse outcome than either treatment alone, and formal psychotherapy may work in areas not affected by medication.

Electroconvulsive Therapy

ECT provides rapid symptom relief, which is especially useful in severely ill suicidal patients; it may work in patients who are refractory to other treatments, and it may be used when a patient's medical condition makes drug therapy risky.

ECT also has a number of disadvantages: 1) it has not been rigorously tested in milder forms of depressive illness; 2) it can be costly, since it may entail hospitalisation; 3) it is associated with specific and significant side effects (e.g., retrograde and anterograde amnesia); 4) use of ECT involves the additional risks of general anaesthesia; 5) it is often associated with a significant social stigma; 6) it is relatively or completely contraindicated when certain medical conditions are present; and 7) prophylaxis with antidepressant medication may be required, even when a good response to ECT is attained.

OVERVIEW OF PHARMACOLOGIC TREATMENTS FOR DEPRESSION

Antidepressant medications can be classified on the basis of their predominant mode of action on monoamine transmission (Table 5.1) (Ban TA 2001). The material in the following sections is based on the packaging labels.

Tricyclic Antidepressants

Tricyclic antidepressants (TCAs) have been in use for approximately 45 years, and, thus, extensive data about their efficacy and tolerability are available. This class includes compounds with predominant serotonergic (S-TCA), noradrenergic (N-TCA), or mixed serotonergic/noradrenergic (S/N-TCA) activity.

Anticholinergic and anti-histaminergic side effects of the TCAs have a substantial effect on their tolerability and thus on treatment adherence. Sedating properties may help in the treatment of depression-related sleep disturbance, but daytime drowsiness and sedation often lead to discontinuation of treatment. Over the long term, increased appetite may result in weight gain and the development of metabolic syndrome.

TABLE 5.1

Antidepressant medications

	Starting dose (mg/day)*	Dose range (mg/day)*
Mixed serotonergic/noradrenergic tricyclic antidepressants		
Amitryptiline	25–75	150–300
Amitriptylinoxide	30-60	180-300
Dibenzepine	120-180	240-720
Dosulepine/ Dothiepin	75	75-150
Doxepin	25-75	150-300
Imipramine	25-75	150-300
Melitracen	20	20-30
Protriptyline	10	20-60
Predominant serotonergic tricyclic antidepressants		
Clomipramine	25–50	100–250
Monoamine oxidase inhibitors		
Phenelzine	15	30–40
Isocarboxacid	20	20–60
Tranylcypromine	10	20–40
Moclobemide[1]	150–300	300–600
Selective serotonin and noradrenaline reuptake inhibitors		
Venlafaxine	75	75–375
Duloxetine	40/60[2]	60–120
Milnacipram	50	100–200
Selective noradrenaline reuptake inhibitors		
Reboxetine	4	8–12
Serotonin modulating antidepressants		
Trazodone	50–100	200–600
Nefazodone3	100	300–600
Dopamine and noradrenaline reuptake inhibitors		
Bupropion	100	200–300
Noradrenergic and specific serotonergic antidepressants		
Mianserin	30	60–120
Mirtazapine	15	30–45
Melatonergic antidepressants		
Agomelatine	25	25–50

*Dosages recommended by the producer

1Reversible monoamine oxidase-A inhibitor

2Recommended starting dose is 40 mg in the United States and 60 mg in Europe

3Nefazone has been withdrawn from the market in some countries

Postural hypotension, urinary retention, and the potential for cardiac arrhythmias may cause serious problems, particularly in older patients, patients with heart disease, and men with prostatic hypertrophy. These side effects often lead to inadequate treatment, due to patients' nonadherence to treatment or physicians' tendency to prescribe these drugs in lower than effective doses. Moreover, the TCAs have greater cardiotoxicity in case of overdose than the newer more selective antidepressants.

Although the TCAs are generally very inexpensive and are cheaper than any other antidepressants, the potential for nonadherence and inadequate treatment complicates an assessment of relative costs.

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors (MAOIs) have a long record of efficacy, particularly for depressive episodes with atypical features.

Interactions between irreversible MAOIs and sympathomimetic medications (including common drugs such as decongestants) or tyramine-containing food (e.g., cheese, red wine, smoked or pickled meats) can precipitate potentially life-threatening hyperthermia and hypertensive crises and increase the risk for myocardial infarction and stroke. The risk of developing a serotonin syndrome due to the concomitant use or accidental combination of other serotonin-enhancing antidepressants must also be taken into account. Depending on the half-life of the substances used, a drug-free interval of at least 2 weeks before or after the use of an irreversible MAOI is necessary to minimise the risk of severe adverse events. When an MAOI is prescribed following fluoxetine, the drug-free interval must be increased to 5 weeks because of the long-half life of fluoxetine.

A reversible MAOI, moclobemide, which does not seem to affect dietary tyramine, is available in some countries. This drug preferentially inhibits MAO-A. Several multicentre clinical trials have found moclobemide to be more effective than placebo in the treatment of depressed patients. Its most frequently observed side effects are dry mouth, somnolence, headache, dizziness, and psychomotor agitation.

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are the most prescribed medications for the first-line treatment of depression in many countries, since they have been shown to be as efficacious as the TCAs, but with a more tolerable side-effect profile because of their receptor selectivity. There is some evidence that the SSRIs may not be as efficacious as the TCAs in the subgroup of inpatients.

The safety and tolerability profile of the SSRIs compares very favourably with the TCAs. Specifically, anticholinergic side effects are less common during SSRI therapy, which results in a lower discontinuation rate. SSRIs have also proven safer than TCAs in cases of overdose.

Nevertheless, clinicians need to be aware of the side-effect profile of SSRIs. The most frequent side effects following short-term treatment are gastrointestinal disturbances such as nausea, diarrhoea and emesis. Also common are restlessness and agitation, sleep disturbances, dizziness, and headache. During long-term SSRI treatment, sexual dysfunction, including loss of libido, anorgasmia, and disturbances of erectile or ejaculatory function in men, may occur. Rare side effects are weight gain, anticholinergic effects and extrapyramidal motor side effects.

The SSRIs are generally not associated with sedation, although this varies somewhat among agents. Interestingly, recent clinical trials have shown the nonsedating SSRIs relieve the symptoms of anxiety associated with depression as quickly and effectively as amitriptyline, a sedating TCA. Finally, the SSRIs (and the TCA clomipramine) may be an especially good choice in patients with comorbid obsessive-compulsive disorder (OCD).

Selective Serotonin and Noradrenaline Reuptake Inhibitors

Selective serotonin and noradrenaline reuptake inhibitors (SNRIs) represent a group of newer antidepressants that act on both serotonin and norepinephrine reuptake. Today, three SNRIs are currently available: venlafaxine, milnacipran, and duloxetine. Compared with venlafaxine, duloxetine more potently blocks serotonin and noradrenaline transporters in vitro and in vivo.

It has been suggested that the three SNRIs have similar efficacy. Several meta-analyses have also suggested that venlafaxine has superior efficacy compared with the SSRIs, with a stronger finding of superior efficacy when both treatment response and remission are used as criteria to evaluate efficacy.

SNRIs have a favourable tolerability profile compared with the TCAs. Most of the adverse events associated with the SNRIs resemble those of the SSRIs, but they tend to decrease or disappear with continued treatment. Hypertension may occur more frequently with high doses of venlafaxine than with low doses. The fatal toxicity index for venlafaxine in cases of overdose seems to be between that of the SSRIs and the TCAs.

Selective Noradrenaline Reuptake Inhibitors

The only available selective noradrenaline reuptake inhibitor (NARI) is reboxetine. Reboxetine was found to be similar to fluoxetine in efficacy for depressive disorders, and more effective in a subgroup of severely depressed patients.

Reboxetine is safer and better tolerated than the TCAs: its use is not associated with increased risk of seizures, orthostatic hypotension, or cardiovascular side effects. Reboxetine has a different side-effect profile than the SSRIs, with advantages in terms of agitation, nervousness, anxiety, sexual dysfunction, and gastrointestinal events. Increased heart rate and blood pressure may be observed.

Noradrenergic and Specific Serotonergic Antidepressants

The structurally similar tetracyclic antidepressants mianserin and mirtazapine represent the group of α2 adrenergic and 5HT2 receptor blocking antidepressants (noradrenergic and specific serotonergic antidepressants, NaSSAs).

Both mianserin and mirtazapine are described as being as effective as TCAs. In addition to its antidepressant effects, mirtazapine significantly improves sleep parameters associated with insomnia. NaSSAs have a substantially better side-effect profile than the TCAs. The safety profile of the NaSSAs is similar to that of the SSRIs, but typical serotonergic side effects, such as sexual dysfunction and gastrointestinal complaints, are less frequent in patients treated with mirtazapine.

The most frequently reported adverse events during mirtazapine therapy are antihistaminergic effects, such as initial somnolence and dizziness, together with increased appetite and cumulative weight gain over the long term. Weight gain often reduces patients' adherence to treatment and may sometimes facilitate development of a metabolic syndrome.

Serotonin Modulating Antidepressants

Nefazodone and its structural analogue trazodone block 5-HT2 receptors but only weakly inhibit the reuptake of serotonin and noradrenaline; these agents are referred to as serotonin modulating antidepressants (SMAs). These drugs are reported to work as well as the TCA imipramine and other older antidepressants. The sedating properties of nefazodone and trazodone make them particularly suitable for agitated patients and those suffering from insomnia.

The SMAs have a more favourable tolerability profile than the TCAs, with lower anticholinergic and antihistaminic activity. The most commonly reported side effects are sedation, dry mouth, nausea, somnolence, and dizziness. Trazodone may increase the risk of priapism. Patients treated with SMAs report fewer complaints of nervousness, insomnia, and sexual dysfunction than those receiving SSRIs. Nevertheless, several case reports concerning the potential of nefazodone to cause severe hepatotoxicity and even fulminant hepatic failure make reliable clinical monitoring crucial. The original manufacturer has withdrawn nefazodone from the market, but in some countries, including the United States, generic versions of the drug are available.

Dopamine and Noradrenaline Reuptake Inhibitors

Bupropion has been reported to have antidepressant efficacy that is at least equal to that of the SSRIs. Despite some contradictory results, its good efficacy combined with a lower rate of mood switches than seen with the SNRIs suggests that bupropion may be recommended especially for the treatment of bipolar depression.

Compared with SSRIs, bupropion shows a lower rate of serotonergic side effects, such as sexual dysfunction, gastrointestinal complaints, insomnia, and agitation. Although generalised seizures are considered a rare consequence of bupropion treatment, the risk of seizures must be taken into account in treatment planning. Generalised seizures seem to be a relatively frequent complication in cases of accidental or intentional overdose.

New Developments

Investigators have recently been studying agomelatine, an agent with a mechanism of action involving agonism at melatonergic MT1 and MT2 receptors and selective antagonism at serotonergic 5-HT2c receptors. This potential antidepressant is currently under review by authorities in Europe.

Summary

Despite the development of a variety of new antidepressants with different pharmacodynamic profiles, the hope of finding agents with better efficacy and clinical effectiveness than the older antidepressants has not yet been fulfilled. The main advantages of the newer antidepressants are overall better tolerability and safety compared with the older agents. Although the newer antidepressants are better tolerated and cause fewer and less serious side effects, their specific side-effect profiles must still be taken into account during treatment. The latency of several weeks until onset of sufficient therapeutic effects also remains a serious and clinically relevant problem with all currently available antidepressants.

A further general problem in the pharmacotherapy of depression is possible non-response to initial antidepressant treatment. About 50% of depressed patients do not respond adequately to an adequate first course of antidepressant treatment (treatment of sufficient duration at an adequate dose) (about 30% do not show satisfactory improvement and about 20% drop out) (Davis et al. 1993). Half of these patients fail to respond to a second antidepressant treatment trial. If several antidepressant treatment trials have not been efficacious, the range of appropriate pharmacological treatment strategies includes dosage adjustment, switching to an antidepressant from a different another class, switching to an antidepressant from the same class, combination therapies involving more than one antidepressant, and pharmacological and non-pharmacological augmentation strategies.

SELECTING AN ANTIDEPRESSANT

As discussed above, all currently available antidepressants demonstrate comparable efficacy in general population samples. Although an individual patient may respond better to one drug than another, this response cannot be reliably predicted before initiation of therapy. Therefore, antidepressant selection depends largely on factors that affect adherence such as side-effect profile and dosing regimen.

Adherence is an especially important issue because:

- Disease characteristics, such as lack of motivation and hopelessness, make the patient with a depressive disorder especially prone to nonadherence.
- The prolonged period between initiation of therapy and full therapeutic effect can be very discouraging for the patient.
- The long-term therapy currently recommended for many patients prone to recurrence further increases the risk of nonadherence; patients are more likely to miss doses when they are asymptomatic and undergoing long-term treatment.
- The stigma associated with mental illness in many societies may make patients reluctant to take medication (particularly in situations in which others are present).

In view of similar efficacy among agents and the importance of therapeutic adherence, factors that should be considered in the selection of an antidepressant medication include:

- Short- and long-term side effects
- Other factors that influence adherence compliance, such as dosing regimen (preferably once a day), impact of drug characteristics on the patient's lifestyle (e.g., sedation, dietary restrictions), and cost of medication
- Concurrent nonpsychiatric medical illnesses (e.g., heart disease) that may increase the risk of certain medications
- Previous positive or negative response to antidepressant medication
- History of a first-degree relative's response to a medication
- Patient age
- Physician's experience with the different agents
- Patient preference

FORMAL PSYCHOTHERAPEUTIC TECHNIQUES

Psychotherapy, a generic term, refers to a variety of verbal and nonverbal techniques and procedures that differ in their immediate, intermediate, and long-term objectives. Here we use the term formal psychotherapy in recognition of the fact that there is a strong, although unspecific, psychotherapeutic element in everyday clinical practice, which can be differentiated from formal psychotherapeutic approaches that use specific techniques.

Evidence for the efficacy of formal psychotherapy used alone in the management of depressive disorders is largely limited to a number of randomised, controlled trials of short-term, structured forms of psychotherapy, including cognitive-behavioural therapy (CBT) (Churchill et al. 2000), interpersonal psychotherapy (IPT) (de Mello et al. 2005), behaviour therapy (BT), marital therapy (MT), family therapy, and brief dynamic psychotherapy (BDP) (Table 5.2). These trials have generally enrolled patients with less severe forms of depressive disorders than those participating in medication trials. Results indicate that the formal, time-limited therapies are more effective than wait-list comparisons. In trials comparing formal psychotherapy to use of standard antidepressant medications, psychotherapy and medication have often been equally effective. The evidence is best for CBT and IPT. However, unlike antidepressant medication trials, only one large formal psychotherapy trial has included a placebo contrast cell. In that study, CBT and IPT (the two techniques tested) were less effective than drug treatment for patients with moderate to severe depression (Elkin et al. 1989). For patients with milder illness, psychotherapy and medication showed comparable efficacy, but response was more rapid with medication. There is also now good evidence that CBT reduces relapse rates when used alone or in combination with antidepressants (Paykel 2007).

Clinical experience shows that patients with psychotic features or severe vegetative symptoms are less able to engage in the activities essential to the therapeutic process and therefore should not be treated with psychotherapy alone. The presence of personality disorders may also reduce or slow the response to cognitive, interpersonal, and other time-limited, symptom-focused psychotherapies alone, as well as to medication. Marital dissatisfaction may also predict higher rates of relapse and recurrence after maintenance IPT.

Consequently, the use of psychotherapy alone to reduce the symptoms of depressive disorders, whether they are dysthymic or depressive episodes, may be considered a first- line treatment only if the depression is relatively mild, and psychotic or melancholic features are absent. There is a good evidence base for these recommendations only for two forms of time-limited, formal psychotherapy: CBT and IPT. If formal psychotherapy is ineffective, or if it fails to achieve a full symptomatic remission within 12 weeks, medication should be seriously considered, since there is strong evidence for its specific efficacy. CBT has its effects primarily on depressive symptoms rather than psychosocial problems.

FORMAL PSYCHOTHERAPY USED IN COMBINATION WITH ANTIDEPRESSANTS

In randomised, controlled trials of combinations of medication and formal psychotherapy, some studies have found only a modest advantage for combination therapy compared with medication or psychotherapy alone, while others have found no advantage, particularly with regard to symptom reduction. On the other hand, some evidence indicates that combined treatment may have a broader effect than medication alone (Thase et al. 2007; Weissman 1979;). In particular, psychotherapies have been found to improve interpersonal relationships and social adjustment (Thase et al. 2007). Cognitive therapy combined with antidepressants has also been found to reduce relapse rates (Paykel 2007).

Combination treatment may be useful if:

1. Either treatment alone is only partially effective.

2. The clinical circumstances suggest two different and discrete targets of therapy (e.g., symptom reduction to be addressed with medication and psychological/social/occupational problems to be addressed with formal psychotherapy).

3. The previous course of illness has been chronic—either episodic with poor interepisode recovery or of prolonged duration (e.g., lasting more than 2 years).

It may also be helpful to add CBT to medication when the patient is vulnerable to relapse as indicated by features such as residual symptoms that have not responded to antidepressant medication, a history of previous relapses or recurrences, or return of depressive symptoms as the dose of medication is reduced.

ELECTROCONVULSIVE THERAPY

ECT is associated with numerous myths and misconceptions, at least partly fuelled by widespread misinformation and by inflammatory articles in the lay press. This is unfortunate, since ECT can be a very effective and safe treatment for a selected group of seriously ill patients, including:

- Patients with severe or psychotic depressive disorders who are acutely suicidal or dangerously delusional and either have not responded to adequate medication trials or have an underlying medical condition that makes the use of antidepressant or antipsychotic medication risky.

- Severely depressed patients with significant neurovegetative symptoms, psychomotor disturbances (e.g., retardation), or a decline in their ability to function who do not respond to more than one trial of antidepressant medication or cannot tolerate medication.

- Patients in life-threatening situations that require a rapid response, such as a high risk of suicide or refusal to eat or drink.

The presence of somatic or psychotic symptoms and previous good response to ECT appear to predict positive response to ECT (Lykouras et al. 1993).

The Procedure

In ECT, a generalised seizure is provoked by application of an electric stimulus to the patient's head. Today it is recommended that ECT be done with anaesthesia, which reduces the risk of side effects (such as fractures) and increases the acceptability of the procedure. Patients are anaesthetised before the procedure with a short-acting hypnotic compound and a muscle-depolarising agent. Treatments are generally administered three times a week, on an in- or outpatient basis, for a total of 6–12 treatments.

Pre-treatment Clearances

Before initiation of treatment, the clinician must address psychological and medical issues. The mere mention of ECT often evokes high levels of anxiety among both patients and families. Thus, patients and families need to be educated regarding the benefits and adverse effects of both ECT and other treatment alternatives and the risks of not adequately treating a severe depressive episode. When the clinician feels the patient and family adequately understand the procedure, a consent form should be signed by the patient and the family and/or guardian.

Pre-treatment evaluation must include a complete medical and anaesthetic history, a physical examination and electrocardiogram, and laboratory studies where appropriate, to rule out electrolyte imbalances and cardiopulmonary or neurologic risk factors.

Adverse Effects

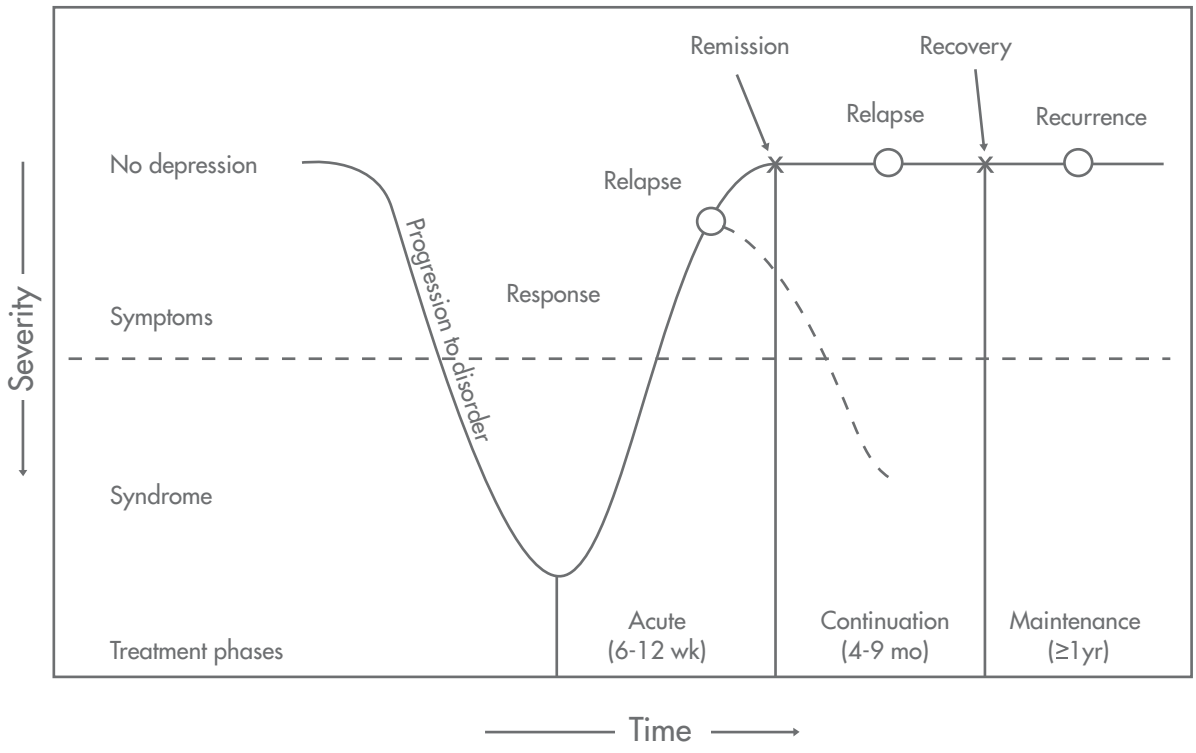
Common adverse effects associated with ECT are transient post-treatment confusion and memory loss. Although memory impairment during a course of treatment is almost always the rule, follow-up data indicate that almost all patients return to cognitive baseline by 6 months post-treatment. Some patients do complain of persistent memory difficulties, however. Unilateral application of the electric stimulus to the nondominant hemisphere and use of equipment that produces square-wave instead of sinusoidal currents reduce the risk and severity of memory impairment.

THE THREE PHASES OF TREATMENT FOR DEPRESSION

As discussed in Chapter 1 of this Volume, recent reviews of the literature have revealed that depressive disorders are often recurrent. Therefore, the treatment of these disorders is generally viewed in three phases—acute, continuation, and maintenance (or prophylaxis) phases— with demarcations between the different phases often somewhat blurred (Figure 5.1).

FIGURE 5.1

Phases of Treatment



The Acute Treatment Phase

The acute treatment phase begins with the initiation of treatment and continues until complete or nearly complete remission of symptoms. Generally, if a particular antidepressant is going to work for an individual patient, some modest signs of symptom resolution may begin to appear after 1 or 2 weeks of full-dose therapy. A partial response (40% to 50% symptom reduction) should occur by weeks 4 to 6, and full therapeutic response to the medication, as evidenced by complete or nearly complete symptom resolution (recovery or remission), usually takes between 10 and 12 weeks.

Acute Treatment Goals

The primary goal during the acute treatment phase is reduction and ultimately complete alleviation of depressive symptoms and return of the patient to his pr her premorbid level of functioning. Setting the stage for longer-term treatment is also an important consideration during the acute phase, since patients at high risk for recurrence are often treated for long periods of time, sometimes indefinitely. If clinicians are attuned to the possibility of long-term therapy, they will usually try to select an antidepressant with a favourable long-term side-effect profile and convenient dosing regimen.

Treatment Selection

To reduce the risk of mortality and morbidity and to minimise any long-term effects that an untreated depression may have on the patient's life (e.g., disruption of family relationships and career), it is important to obtain symptomatic relief as quickly as possible. In addition, there is now evidence suggesting an association between a longer period of untreated depression and a poorer long-term prognosis (NIMH/NIH Consensus Development Conference Statement 1985).

Consequently, physicians are advised to select treatments with demonstrated efficacy and to monitor patients closely and frequently to assess treatment response, so that changes can be made promptly when treatment is ineffective. As discussed earlier in this chapter, antidepressant medication is the best way to meet these goals for most patients with a moderate to severe depressive episode (Elkin et al. 1989), provided the patient is not opposed to taking medication and does not have a medical illness that makes pharmacotherapy risky. For patients with mild depression, either antidepressant medication or formal psychotherapy would be a viable alternative.

If a patient or first-degree relative has previously responded well to a particular antidepressant, it would be advisable to initiate treatment with that medication. When that is not the case, treatment should be initiated with an agent likely to foster both short- and long-term adherence.

Medication Management

Appropriate clinical management during the acute phase is essential in promoting adherence to treatment and ultimately in achieving a favourable treatment outcome. During the acute phase of treatment, the clinician must begin to develop a trusting therapeutic relationship with the patient and family, provide good patient/family education, and negotiate a treatment plan that is acceptable to patient and family. All of these important aspects of clinical management are discussed later in this chapter. This section focuses on specific principles for initiating and monitoring antidepressant medication, which is the preferred treatment for most patients with moderate to severe illness.

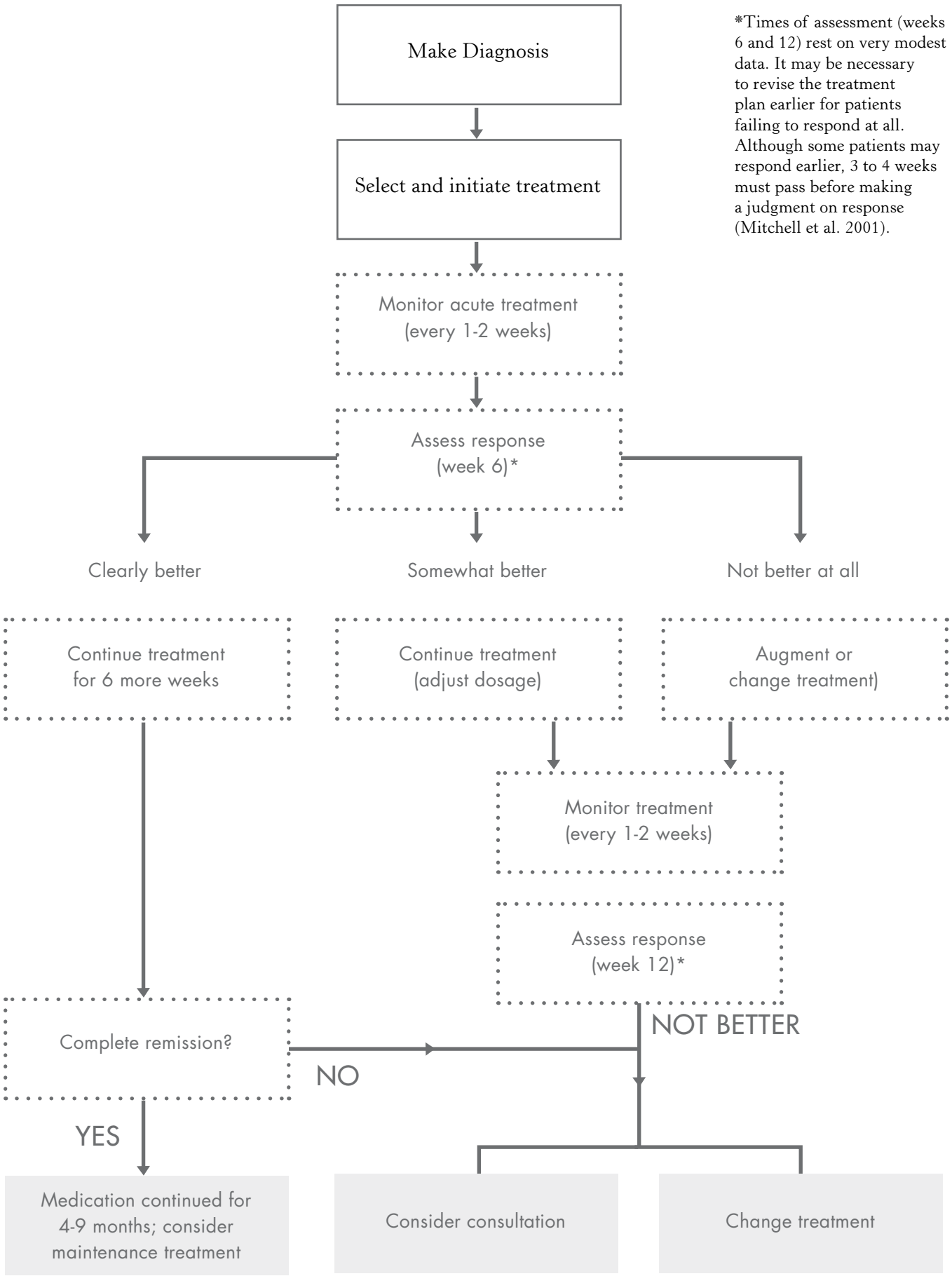
The flowchart in Figure 5.2 provides guidelines for the management of antidepressant medication during the acute phase of treatment. Once treatment is initiated, the patient should be monitored every 1 to 2 weeks, or more often in the case of very severe depression or if the patient requires titration of a TCA.

Assessment at 4 to 6 weeks: Although some patients may respond earlier, 3 to 4 weeks must pass before making a judgement on response (Mitchell et al. 2001).

- If a convincing effect is not apparent within 4 weeks, the first question to ask is whether the patient has taken the medication as prescribed. Nonadherence is a major cause of nonresponse. The major cause of nonadherence is that the treatment that has been prescribed is not consistent with the patient's illness concept. If this is the case, treatment must begin again (see the section on "Clinical Management" later in this chapter).

FIGURE 5.2

Overview of Treatment for Depression



*Times of assessment (weeks 6 and 12) rest on very modest data. It may be necessary to revise the treatment plan earlier for patients failing to respond at all. Although some patients may respond earlier, 3 to 4 weeks must pass before making a judgment on response (Mitchell et al. 2001).

- If the patient has taken the medication as prescribed, the next question is whether the dosage was high enough. Doses for some patients need to be titrated to the top of the recommended range.
- If the patient does not respond to a full therapeutic dose, comorbidity or an alternate diagnosis should be considered. Substance abuse or an underlying medical condition should also be considered as possible causes for the depression.
- If the diagnosis, adherence to treatment, and adequacy of dosage are confirmed, the physician should consider switching to another medication or using augmentation therapy (Figure 5.2).

When there is partial or no response at 6 weeks, the primary care clinician may wish to consult a specialist regarding medication change or augmentation. Since patients respond differently to different medications, the clinician may switch to an antidepressant within the same class (if the drug is well tolerated) but with a different biochemical profile, or to an agent in a different class. Alternatively, clinicians can consider trying to potentiate the effect of the current antidepressant by the addition of lithium carbonate. Several controlled clinical trials have demonstrated that 50%–60% of patients experience rapid clinical improvement when lithium carbonate is added to their antidepressant (Kaplan et al. 1995). When the persisting symptoms are largely cognitive rather than vegetative, the clinician may want to continue the treatment for another 6 weeks and then consider adding formal psychotherapy. For patients with psychotic depression, initial therapy may need to combine an antipsychotic with an antidepressant, or ECT may be advisable.

Formal Psychotherapy

If formal psychotherapy alone is the initial acute treatment and there is no response by 6 weeks, or only a partial response by 12 weeks, clinical experience and the strong evidence for the efficacy of pharmacotherapy suggest the initiation of antidepressant medication.

Continuation/Maintenance Treatment Phases

The continuation phase of treatment begins at the time of complete or nearly complete symptom remission and generally continues for approximately 4 to 9 months. The rationale for treatment during this period is the belief that drugs suppress depressive symptoms without immediately correcting the pathophysiological abnormality that is causing them. Thus, the goal of continuation treatment is to prevent relapse—that is, a re-emergence of symptoms within an episode of depression.

Maintenance treatment, on the other hand, is believed to prevent recurrence—that is, the emergence of new episodes of depression. The maintenance treatment phase begins after continuation therapy (at approximately 4 to 9 months) and can be continued for varying lengths of time depending on the estimated risk of recurrence and the severity of illness. Maintenance treatment is discussed in more detail later in this chapter.

Indications for Continuation Treatment

Sufficient evidence supports the importance and efficacy of continuation treatment, indicating that all patients, regardless of whether they have residual psychosocial problems, should continue to receive the same dose of the same medication for 4–9 months after remission. Continuation antidepressant treatment may also be used after an acute response to ECT.

Cognitive therapy may be useful as an adjunct to medication in lessening the risk of relapse and recurrence in circumstances which indicate vulnerability, such as residual symptoms that have not responded to antidepressant medication, a history of previous relapses or recurrences, or a return of symptoms as the medication dose is reduced. Only limited evidence supports the usefulness of continuing other forms of psychotherapy alone after an acute treatment response to psychotherapy. Logic suggests, however, that psychotherapy to improve psychosocial functioning may be beneficial for selected patients who have responded to and are continuing to receive medication.

Indications for Maintenance Treatment

Depressive disorders are recurrent disorders in many patients. Because of the risk of significant morbidity and potential mortality associated with every new episode of depression, the current trend is to provide long-term maintenance treatment (prophylactic treatment) for patients who are considered at high risk for recurrence. Long-term maintenance treatment generally refers to a period of 5 years or more; in many patients indefinite, perhaps lifetime, treatment is indicated.

The indications for maintenance therapy are outlined in Table 5.3. Maintenance treatment is strongly recommended for patients with bipolar disorder. A patient who has had three or more episodes of major depressive disorder runs a 90% risk of a new episode, and long-term prophylaxis is also strongly recommended in this situation.

Other clinical issues that affect the decision of whether to institute maintenance medication include time between previous episodes, severity of episodes, risk of suicide during previous episodes, degree of disability associated with episodes, acuteness of episode onset, family history of depressive illness, and patient preference. If a patient feels that long-term medication is a sign of persistent illness and fears becoming dependent on permanent medication, the clinician should try to educate the patient regarding the likelihood of recurrence based on that patient's particular course of illness. Prophylactic treatment may be postponed if the patient refuses to accept it, but practitioners must also consider their own position when they agree to care for patients with recurrent depressive disorders without maintenance medication.

TABLE 5.3

Indications for maintenance medication

Very strongly recommended	Strongly recommended
Three or more episodes of major depressive disorder	Two episodes of major depressive disorder and 1. Family history of bipolar disorder 2. History of recurrence within 1 year after previously effective medication was discontinued 3. Family history of recurrent major depression* 4. Early onset (before age 20) of the first episode 5. Both episodes were severe, sudden, or life threatening in the past 3 years.

Source: NIMH/NIH Consensus Development Conference Statement, Am J Psychiatry 1985

*A family history is a positive, clear-cut history in one or more first-degree relatives.

Maintenance Antidepressant Selection and Dosing

Factors that play an important role in promoting short-term adherence have an equal if not greater impact on long-term adherence. Ideally, the clinician will have considered these factors (including tolerable side effects and ease of use) at the time acute treatment decisions were made, so that the patient can be maintained on the same medication that has successfully treated the acute depressive episode. Side effects that may be particularly troubling on a long-term basis are weight gain and sedation. Since asymptomatic patients on long-term therapy are likely to miss doses occasionally, an agent with an extended half-life may have the advantage of preventing breakthrough symptoms if two or three doses are missed (e.g., during a weekend trip).

In 1992, Kupfer and colleagues demonstrated the efficacy of long-term maintenance treatment in preventing recurrent depressive episodes (Kupfer et al. 1992). One of the unique features of the Kupfer study was that patients received full-dose imipramine; this was in contrast to earlier studies in which patients received reduced maintenance doses of medication and no efficacy was demonstrated.

Maintenance Psychotherapy

Patients who continue to exhibit psychosocial problems (e.g., marital, occupational, educational, or interpersonal) after good symptomatic response to medication may benefit from psychotherapy that focuses on these residual psychosocial difficulties. Maintenance psychotherapy alone—defined as at least one session a month—does not appear to be effective in preventing a recurrence, although it may delay the onset of the next episode (Frank et al. 1990).

Symptom Breakthrough

Approximately 10%–20% of patients report some depressive symptoms during continuation/maintenance treatment. The presence of residual symptoms without full remission indicates a strong tendency for relapse, and medication should be continued (Paykel al. 1995). In most cases, the symptom breakthrough is brief, mild, and self-limited, requiring only support and follow-up. If the breakthrough is severe or prolonged, however, the antidepressant regimen should be re-evaluated.

Blood levels should be checked if the patient is receiving an agent whose therapeutic effect correlates with blood levels and that has a narrow therapeutic window. In this situation, symptoms may be the result of toxicity rather than lack of efficacy, and blood levels, where appropriate, will help to make this determination. If toxicity is not the problem and the patient is not receiving the maximum therapeutic dose, the clinician may choose to titrate the dose upward. If this higher dose is effective, it should be maintained until treatment discontinuation. If the patient does not respond to the increased dosage, or if the patient is already receiving the maximum dose, the clinician may consider augmentation with another agent or switching to a different antidepressant medication. At this point, the clinician may want to consult a specialist.

Discontinuing Medication

Based on the criteria outlined above, the clinician may choose to recommend discontinuing medication after 6 to 9 months of sustained treatment (for patients who have had a single, non-life-threatening episode), or much later in the case of recurrent or life-threatening illness. The patient must obviously concur in this decision. If the patient is reluctant to discontinue medication, it may be continued for an additional 3 to 6 months, but the clinician and patient should also discuss the patient's concerns about medication discontinuation.

In discontinuing an antidepressant, the dose should be tapered off over 8–12 weeks if the patient has been receiving a therapeutic dose for 3 months or longer. Abrupt discontinuation of TCAs may cause insomnia, aches, pains, nausea, or a recurrence of the depressive episode.

If the depressive symptoms recur during tapering or shortly after discontinuation, it generally means that the depressive episode has not run its course, and the full therapeutic dose should be reinstated. However, it is important to distinguish between a re-emergence of depressive symptoms and the patient's temporary worry or anxiety about treatment discontinuation. A review of the clinician's records or use of self-assessment severity measurements by the patient may help clarify this issue.

After the medication is discontinued, the patient should be encouraged to report any recurrence of symptoms to the physician. If a new episode occurs, it will usually do so no earlier than 16 to 20 weeks after medication discontinuation (Prien and Kupfer 1986). Prompt treatment of a new episode with the same medication that successfully treated the previous episode is recommended. Patient education regarding recurrence and physician follow-up are discussed more fully in the next section.

CLINICAL MANAGEMENT

Clinical management is the cornerstone of treatment for patients with depressive disorders. In spite of their proven efficacy, the treatments discussed in this chapter will not be successful if the patient is not able to willing to adhere to therapy and if the physician is not consistently assessing the patient's response to treatment and altering the treatment plan as necessary.

Barriers to Successful Treatment

Numerous barriers to successful treatment exist that appropriate clinical management can help overcome. Depending on the individual patient, obstacles may include:

- Patient (and sometimes family) resistance to the diagnosis because of societal stigma or misconceptions, such as viewing depressive illness as a weakness of character or as punishment from God, or as a sign of permanently losing one's mind.
- Symptoms of the depressive disorder (e.g., hopelessness, lethargy, lack of motivation, withdrawal) that may make adherence to a treatment regimen difficult.
- The delayed onset of therapeutic benefit from medication and psychotherapy.
- Misconceptions about the actions of antidepressant medications (e.g., believing that these drugs are addicting or mind altering).

All of these potential barriers to a successful treatment outcome are really barriers to adherence. Stigma, resistance to the diagnosis, misunderstanding of the illness and its treatment, and depressive symptoms such as hopelessness and difficulty concentrating all threaten the patient's willingness and ability to adhere to treatment. Medication side effects and cumbersome dosing regimens are also major impediments to adherence. Numerous studies have documented significant nonadherence to treatment in patients in general. For patients with mood disorders, rates of nonadherence of 4%–90% have been reported, with this very wide range reflecting the variety of assessment methods that were used. In a study of primary care patients being treated for depressive illness, 20%–30% did not adhere to treatment (Kupfer et al. 1992).

In addition to interventions targeting the factors described above, patient education, discussed in more detail later in this section, can also improve adherence. Such education should include providing the patient with explicit instructions and an opportunity to ask questions, discussing difficulties frequently encountered in complying with the proposed treatment, and encouraging the patient to report problems. It may be helpful to schedule a separate appointment dedicated to the provision of information and education and, with the patient's permission, to enlist the support of a family member or significant other.

Elements of Clinical Management

Treatment plans for all patients should incorporate the following clinical management issues:

- Development of a trusting therapeutic alliance (see below) between a knowledgeable, confident, non-judgemental physician and patient (possibly with the family as well),
- Information/education regarding the illness, treatment options, and prognosis, provided in terms understandable to the patient and family and in a setting in which they feel comfortable asking questions,
- Involvement of the patient in treatment decisions, since collaborative decisions increase adherence and thereby treatment effectiveness,
- Initiation of a treatment plan using methods with solidly established efficacy,
- Frequent monitoring and follow-up to assess patient adherence, side effects, and response to treatment and to address any concerns; subsequent adjustment of treatment when necessary to ensure optimal outcome,
- Long-term follow-up and patient/family education to ensure prompt recognition of relapse or recurrence.

The Therapeutic Alliance

Clinical management begins with the development of a trusting relationship between the patient and physician, a therapeutic alliance that may also extend to family members or close friends. The physician must be able to listen to the patient and address his or her concerns. The following guidelines are useful for physicians in this respect:

- The physician should be self-assured regarding his or her own competence and be able to convey this to the patient and family in order to calm any anxieties they may have about the illness. If the physician is insecure, this will likely be transmitted to the patient and family and increase their anxiety. This means that the physician must have adequate knowledge and experience.
- Information about the depressive disorder should be presented clearly and accurately by the physician, who should take care not to deny or minimise the seriousness of the disorder but also not to magnify the consequences by calling it incurable or overemphasising the risk of suicide. The physician's presentation should be void of any moral judgement and signify to the patient, both in attitude and statement, that this is a medical illness like any other; the patient is no more at fault when depressed than he or she would be if stricken with heart disease or diabetes.
- Education and treatment should be individualised to meet the needs of the patient.
- The physician should seek to provide the patient with the best treatment available in the community, focusing on therapies with scientifically proven efficacy and making sure to use those therapies appropriately (e.g., adequate dosages of medication).
- When the physician does not seem to be achieving an optimal outcome or when the patient seems to be at high risk for suicide, the physician should be willing to consult a psychiatrist. It should be noted that such consultation does not remove the primary care physician from daily management.

Patient/Family Education

The co-operation of a knowledgeable patient is crucial to the success of the treatment plan. Guidelines for patient education from the primary health care version of ICD-10 (WHO 1996) are provided in Table 5.4. It is important to understand the patient's personality and his or her preconceived view of depressive illness, so that information can be provided in the most helpful context. The physician must recognise that he or she cannot expeditiously change the patient's view of the world, so health education must be provided in a way that fits with that view. For example, patients who believe that their well-being is dependent on their own behaviour may feel responsible for the depressive illness and want to fight it on their own. For these patients, it may be helpful for the physician to attempt to describe medication as a "tool" in the patient's hands, reinforcing the view that responsibility for optimal treatment lies within the patient's domain.

TABLE 5.4

Health education for patients and relatives (ICD-10 Primary Health Care Version)

Health Education	Counselling of Patient and Family
1. Depression is common, and effective treatments are available. 2. Depression is not weakness or laziness; patients are trying hard to cope.	1. Ask about risk of suicide. Has the patient often thought of death or dying? Does the patient have a specific suicide plan? Has he/she made serious suicide attempts in the past? Can the patient be sure he or she will not act on suicidal ideas? Close supervision by family or friends, or hospitalization, may be needed. Ask about risk of harm to others. 2. Plan short-term activities which give the patient enjoyment or build confidence. 3. Encourage the patient to resist pessimism and self-criticism, not to act on pessimistic ideas (e.g., ending marriage, leaving job), and not to concentrate on negative or guilty thoughts. 4. Identify current life problems or social stresses. Focus on small, specific steps patients can take to reduce or better manage these problems. Avoid major decisions or life changes. 5. If physical symptoms are present, discuss the link between physical symptoms and mood. 6. After improvement, make a plan with patient concerning action to be taken if signs of relapse occur.

Source: ICD-10 Primary Health Care Version (WHO 1996)

Similarly, the patient with a psychosocial orientation may see the depressive disorder in strictly psychological terms and request psychotherapy, even when medication is advisable, while the patient with a biological orientation may request medication when it is not indicated.

Before any meaningful education, the clinician must also understand the patient's current view of the illness, a view that has been formed from sources such as past experience, newspapers and other media, and information provided by friends and relatives. Each patient may have specific concerns that need to be addressed, such as a belief that only crazy people go to a psychotherapist or that people taking antidepressants become drug addicts.

It is helpful to assess the views and availability of immediate family members or significant others and to involve them in the educational process, if possible. A knowledgeable, supportive relative can reinforce adherence and provide encouragement to the patient. In some cultures, the support of a spouse, particularly the husband, is crucial in achieving acceptance of the illness and adherence to treatment. Treatment decisions are left exclusively to family members in some cultures.

Providing patients with educational materials (e.g., booklets, videos) to reinforce their discussions with physicians can be especially helpful. Patients usually forget much of what they are told, because of anxiety or because of cognitive disturbances associated with depression, so such printed materials play a useful role. These materials should be written in the patient's native language and appropriate to his or her level of understanding.

SPECIAL CIRCUMSTANCES

The Suicidal Patient

As previously discussed, the most tragic outcome of a depressive illness is suicide. It is estimated that 10%–15% of patients with affective disorders commit suicide (Guze and Robins 1970). The patient who is acutely suicidal may require involuntary hospitalisation or consultation with a psychiatrist. It is the clinician's responsibility to attempt to assess suicidal risk during the patient interview. The physician should provide a non-judgemental atmosphere and progress from general questions about thoughts of death to specific questions about thoughts of suicide, and ultimately find out if the patient has formulated a specific suicide plan.

If the patient is resistant to this line of questioning, the physician should leave it for a while and return to it later until he or she is satisfied that a full response has been elicited. Some useful questions include:

1. Do you think about death?
2. Do you ever feel life is not worth living?
3. Do you wish you were dead?
4. Do you think about harming yourself?
5. Do you have a plan?
6. What has helped you not to do it?

If patients say that they do think about harming themselves, the physician should ask for specific details. Studies show that patients with a specific plan for harming themselves are at greater risk for suicide than those with only general thoughts. Patients are also at a high risk for suicide if they cannot answer the question "What kept you from committing suicide?" Additional risk factors include physical illness, history of previous suicide attempts, alcoholism, social isolation, and male gender (suicide risk is higher in males). Table 5.5 summarises considerations about when to refer a patient to a psychiatrist or hospitalise a patient.

The Patient Who Refuses Treatment

If the physician does not perceive the patient who is refusing treatment as being at great risk, then it is advisable to continue to meet with the patient a few times, providing education and support. Since the patient's co-operation in treatment is so crucial to a successful outcome, it is preferable to delay treatment for a time in order to establish the patient's confidence in the clinician rather than trying to force treatment on a patient who may not be ready for it. Some studies have found that providing reading materials can be more helpful in reducing symptoms than no treatment at all.

TABLE 5.5

When to refer to a Psychiatrist/When to hospitalise

Treatment in Primary Care Practice	Refer to a Psychiatrist	Hospitalisation
Clear-cut, precise diagnosis of a Depressive disorder	Complicated clinical picture with symptoms of several psychiatric disorders	Suicide attempts or suicide risk*
First episode, with mild or moderate symptoms	First episode of depressive disorder of severe degree, with suicidal thoughts	Deep stupor, food or dehydration problems
History of similar episodes, remitted without psychiatric intervention	History of previous severe episodes that required psychiatric intervention	Agitated delusional state
Patient wishes to be treated by his/her own physician	Patient wishes to be treated by a specialist	Need to avoid negative secondary consequences of the depressive disorder (e.g., misunderstandings or overstressed relations between spouses)
	Concomitant illnesses or treatments that may be contraindications to treatment with antidepressants	

*If there is acute danger of suicide, patients should be hospitalized even against their will, in these cases, patients should be carefully informed about what is being planned for them, and local legal regulations should be followed.

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