WPA Educational Programme on Depressive Disorders

Depression in Population Groups
(children, elderly, women, suicide, transcultural issues)
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# VOLUME 3

DEPRESSION IN POPULATION GROUPS

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PART 1
Depressive Disorders in the Elderly

Professor Helen Fung Kum Chiu, Dr. Cindy Woon-Chi Tam, Professor Edmond Chiu

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Chapter 1
Depression in The Elderly: Clinical Presentation, Detection, and Diagnosis
INTRODUCTION
Depressive disorders in old age are common and disabling. They have a negative impact on the quality of life of both older persons and their caregivers. Moreover, they are associated with increased mortality from natural causes and from suicide. Physicians who are not psychiatrists—internists, general practitioners, and geriatricians—are often among the first to see older persons with depressive disorders and frequently undertake their treatment. Therefore, physicians must have the knowledge and skills to recognise, diagnose, and adequately treat depressive disorders in these patients.

Reluctance to treat the older person with a depressive disorder reflects three misconceptions. The first is that diseases associated with aging are part of the aging process itself—that is, depressive disorders are an inevitable consequence of growing older. The second is that in older persons, adverse events related to the treatment of depressive disorders generally outweigh the disabling aspects of the disorders themselves. The third is that depressive disorders should be treated only by psychiatrists. Such views should be dispelled by the available data presented here.

In this chapter and those that follow, the term “depressive disorders” will be used to denote all clinically significant depressions in older people. A label of “depressive episode” is used when there are sufficient symptoms to fulfill diagnostic criteria for such an episode, such as the ICD-10 criteria for a Depressive Episode (World Health Organization 1993) or the DSM-IV-TR criteria for a Major Depressive Episode (American Psychiatric Association 2000). The ICD 10 criteria for a Depressive Episode are presented in Table 1.1.

There are many types of depressive disorders that can occur in older adults (Table 1.2), and many terms are used to describe these disorders in the literature. Readers are referred to Volume I for a more detailed discussion of the clinical features of depressive disorders in general.

SIGNs AND SYMPTOMs OF DEPRESSive DISORDERS
Are there special symptoms or other features of depressive disorders in later life that distinguish them from depressive disorders at any other age? Consideration should be given to distinctive clinical features, the influence of physical comorbidity, and cultural factors. A transient feeling of sadness can occur at any age as a normal response to loss (for example, in bereavement). It is important to differentiate normal sadness from depressive disorders and to distinguish between the different types of depressive disorders.

Patients with mild depressive illness are troubled by their symptoms but are able to continue personal and vocational functions. Moderate episodes of depressive disorder are intermediate and characterized by major distress; levels of functioning can remain near normal but are maintained only with great effort. Patients with severe depressive disorders are generally in distress and may have marked agitation or retardation. The personal and vocational roles of such patients are severely limited.

SYMPTOMs SPECIFIC TO THE OLDER PATIENT
Two key features distinguish depressive disorders in later life:
• Complaints of sadness are less prominent
• Excessive concerns with physical health are common

Across many cultures, elderly people with depressive disorders complain less of a subjective lowering of mood than do younger patients, even when they appear depressed to the observer (Georgotas 1983). In addition, hypochondriacal preoccupation—an over-concern with and fear of bodily illness—is found consistently more often in older than in younger patients (Gurland 1976). Taken together, these variations predict that older persons with depressive disorders are more likely to consult their physician because of concerns about their general health rather than symptoms specific to a depressive disorder.
TABLE 1.1
Criteria for a depressive episode

At least 2 of the following 3 symptoms:

1. Depressed mood to a degree that is definitely abnormal for the individual, present for most of the day and almost every day, largely uninfluenced by circumstances, and sustained for at least 2 weeks
2. Loss of interest or pleasure in activities that are normally pleasurable
3. Decreased energy or increased fatiguability

An additional symptom or symptoms from the following (at least four):

1. Loss of confidence or self esteem
2. Unreasonable feelings of self-reproach or excessive and inappropriate guilt
3. Recurrent thoughts of death or suicide, or any suicidal behaviour
4. Complaints or evidence of diminished ability to think or concentrate, such as indecisiveness or vacillation
5. Change in psychomotor activity, with agitation or retardation (either subjective or objective)
6. Sleep disturbance of any type
7. Change in appetite (decrease or increase) with corresponding weight change


TABLE 1.2
Types of depressive disorders seen in older people

- Organic mood (affective) disorder
- Bipolar disorder
- Schizoaffective disorders with predominantly depressive symptoms
- Major depressive episode
- Minor depression
- Dysthymia
- Double depression
- Recurrent depressive disorder
- Mixed anxiety/depressive disorder
- Adjustment disorder
- Subsyndromal depressive spectrum
- Dementia with depressive mood
DISTINCTIVE MODES OF PRESENTATION

In addition to the symptoms noted above, certain distinctive modes of clinical presentation are common in older persons with depressive disorders. These include:

- Recent somatic concerns
- Sudden onset of anxiety or obsessional symptoms
- Medically “trivial” deliberate self-harm
- Prominent cognitive dysfunction (“pseudodementia”)
- Recent “out-of-character” behavioural disturbance

Becoming familiar with these modes reduces the chances of overlooking a treatable depressive disorder.

Depressive disorders in later life, as at earlier ages, may present with somatic symptoms, such as pain. If no organic cause is present and the physician is satisfied that the patient is suffering from a depressive disorder, then time must be taken to explain that depressive disorders can produce pain and other physical symptoms; otherwise, such patients repeatedly seek help from a variety of doctors. Often they do not admit to low mood but will acknowledge other symptoms, such as anhedonia, sleep disturbance, and poor appetite.

Onset for the first time in later life of the classic “neurotic” disorders, such as severe anxiety, obsessive-compulsive disorder, and hysteria, is uncommon. Generally, the late first appearance of such symptoms suggests an underlying depressive disorder.

Suicide attempts by older people should be taken seriously. Overdoses are rarely taken simply to attract attention. Any act of possibly deliberate self-harm should lead the physician to explore whether a depressive disorder is present. Even if the act of self-harm is not medically serious (for example, taking four instead of two sleeping pills), it should not be ignored. All older persons who attempt self-harm should be assessed by a qualified person to exclude the presence of a depressive disorder.

“Pseudodementia” is a controversial term. It is often used to describe the condition of older persons with depressive disorders who, on presentation, appear confused or forgetful and show deficiencies in self-care. Characteristically, such patients dismiss queries about memory and orientation by responding, “I don’t know.” In most instances, the onset of confusion is acute and easy to document (Post 1982). The absence of cortical signs such as aphasia or apraxia helps to rule out dementia.

Patients who suddenly present with behavioural disturbances may have a depressive disorder. Common disturbances include aggression, incontinence, and lack of cooperation in situations of enforced dependency, such as a residential or nursing home.

The “vascular depression” hypothesis (Alexopoulos et al. 1997) is the subject of much ongoing research (see Volume III, Part 1, Chapter 3). “Vascular depression” is characterized by psychomotor retardation, limited depressive ideation (such as guilt and poor insight), and pronounced apathy and disability (Alexopoulos et al. 1997; Krishnan et al. 1995). The basis for this condition is thought to be ischemically induced changes in white matter (Baldwin and O’Brien 2002). This subtype is probably less responsive to antidepressant medications (Simpson et al. 1998) but patients may recover with electroconvulsive therapy, although with increased risk of post-treatment delirium.
PHYSICAL COMORBIDITY

Some of the core symptoms of depressive disorders are similar to those of physical ill health. If symptoms such as lack of appetite, fatigue, and altered sleep patterns are attributed to a physical disorder, then a depressive disorder may be inappropriately ruled out. A detailed history can help determine whether a depressive disorder is present. For example, physical pain may cause an individual to sleep poorly; on the other hand, if the patient develops early-morning awakening against the background of an interrupted sleep pattern, the disrupted sleep could be considered symptomatic of a depressive disorder. A comprehensive history can also help the clinician differentiate depressive fatigue from low energy levels caused by physical frailty. Even when there are difficulties regarding symptom attribution, answers to queries about enjoyment of life, feelings of helplessness or hopelessness, and low mood itself may provide evidence of a depressive disorder.

Older patients are at greater risk to be receiving polypharmacy, which can lead to drug interactions resulting in symptoms that mimic depressive disorders or interfere with the metabolism of drugs that are prescribed to treat other physical illnesses (Table 1.3). Based on data from a large Dutch database, Dhondt et al (2002) calculated the population attributable risk percentage (PAR%) for a range of medications. The PAR% is that part of depression in the population that is associated with the use of particular drugs. They found rates of 2.5% for non-selective β-blockers, 5% for calcium antagonists, 15% for benzodiazepines and 3% for systemic corticosteroids. Although it is a mistake to automatically attribute causation to medication, it is likely that drug-induced depression is under-recognised.

When a depressive disorder and a physical disorder coexist, it is not uncommon for the treating physician to ignore the depressive disorder while treating the physical condition; yet treating the depressive disorder can result in great benefit to the patient. Table 1.3 lists medical illnesses that may be associated with depression. A more detailed description of depressive disorders occurring in the context of physical illness is presented in Volume II of this programme “Physical Illness and Depression”.

CULTURAL FACTORS

Cultural factors may influence how people perceive and express symptoms of disease and depressive disorders, as well as their coping strategies and help-seeking behaviour. In addition, older people constitute a special subgroup within a given culture, with their own shared values and beliefs. Physicians should take these factors into consideration when making their assessments.

In India, depression is a common presentation in primary care; however, it is infrequently diagnosed, because it is regarded as a social rather than a health problem (Patel and Prince 2001). In Asia, depressed older people have a high tendency to present with somatic symptoms; they are unwilling to seek help from mental health professionals because they fear that they may be considered insane (Chiu et al. 2003). It is noteworthy that the vocabulary and language used to express emotional symptoms vary across different cultures. For instance, older African-Caribbean individuals in the United Kingdom rarely use terms such as “sad” or “unhappy” to describe emotional distress (Abas 1996; Shah 2007); instead they use terms such as “being low spirited”, “fed up”, and “weighed down”. In addition, beliefs regarding appropriate and acceptable sources of help for people with depression may influence a person’s help-seeking behaviour and pathway to care. Studies have found that older adults from minority ethnic groups in the United Kingdom who suffer from depression have low levels of service use. In a study of multi-cultural focus groups of older adults, conversing with God through prayer was seen as an effective means of overcoming depression within the black Caribbean group, while a large proportion of South Asian and white British participants identified families as an important source of help (Lawrence et al. 2006). There is wide variation in how older persons perceived the role of general practitioners in the management of depression (Lawrence et al. 2006). In some cultures, traditional healers and spiritual leaders may be considered more acceptable sources of help than mental health professionals.
TABLE 1.3
Medical Illnesses and Central-Acting Drugs Associated with Depression.

<table>
<thead>
<tr>
<th>Medical Conditions</th>
<th>Central-Acting Drugs</th>
<th>Substance abuse</th>
<th>Substance withdrawal</th>
<th>Miscellaneous</th>
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<td>Endocrine/metabolic</td>
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<td>Hypo/hyperthyroidism</td>
<td>Antihypertensive drugs</td>
<td>Alcohol</td>
<td>Marijuana</td>
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<td>Cushing’s disease</td>
<td>ACE inhibitors</td>
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<td>Hypercalcemia</td>
<td>Beta-blockers</td>
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<td>Methyldopa</td>
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<td>Pernicious anaemia</td>
<td>Reserpine</td>
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<td>Neurological disorders</td>
<td>Clonidine</td>
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<td>Cerebrovascular disease/stroke</td>
<td>Nifedipine</td>
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<td>CNS tumors</td>
<td>Digoxin</td>
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<tr>
<td>Parkinson’s disease</td>
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<tr>
<td>Alzheimer’s disease</td>
<td>Steroids</td>
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<td>Multiple sclerosis</td>
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<td>Occult carcinoma</td>
<td>Analgesic drugs</td>
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<td>Pancreas</td>
<td>Opioids</td>
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<td>Indomethacin</td>
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<tr>
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<td>AntiParkinsonian drugs</td>
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Case Vignette: Depressive Disorder in Primary Care

A 67-year-old Chinese man with a week-long history of chest discomfort was referred to the general hospital by his family doctor. After assessment and investigations by the cardiologist, he was declared well and discharged. The family doctor re-interviewed him. The patient said that, since his wife had died 8 months previously, he had had difficulty falling asleep and early-morning awakening. His children had noticed that he had lost interest in playing chess with his friends, had become reticent, and preferred to remain at home. He tired easily and had lost his appetite. His son took the patient to see a traditional healer, who prescribed some herbs to enhance his “chi” or energy. For 2 months, the patient continued to be preoccupied with his health and complained to his son about chest discomfort. He saw the family doctor again, who prescribed an antidepressant. Although initially the patient insisted on seeing other specialists, he was persuaded to continue with the antidepressant treatment and, after 7 weeks, he recovered completely.

This case illustrates how concern with physical health is common among older persons of all cultural backgrounds. Unless the diagnosis of underlying depressive disorder is made fairly quickly, much time can be wasted on inappropriate referrals to specialists. Such patients must have their concerns taken seriously, but they need firm persuasion to stay on antidepressants for a sufficient time to allow recovery.

Case Vignette: Psychotic Depression

A 77-year-old man was referred for an urgent psychiatric evaluation following an attack on his wife with a hatchet. Fortunately, no serious harm had been done to her. On questioning, it became apparent that he wanted to kill her as “an act of mercy” to end, as he saw it, their combined troubles. He had intended to kill himself afterward. In retrospect, his wife could see that he had become withdrawn over the past 3 months, had lost weight, and had often appeared preoccupied. This was in contrast to his usual outgoing self. He had suffered a minor stroke 3 months earlier. This event had been his first serious illness but had left little if any physical disablement. She described the stroke as having a “devastating” effect on her husband psychologically, as he had always been so proud of his fitness and masculinity. She had assumed the change in him was due to the stroke, although physically he seemed just the same.

On interview with the patient, it was clear that he had low mood. He blamed himself for what he had done and reported poor appetite, early-morning awakening, and significant weight loss. He also harboured unshakable ideas that he had AIDS because he had a swelling in his groin, which was in fact a hydrocele. He scored 26 on the Mini Mental State Examination, losing some marks because of poor concentration. He responded well to a course of electroconvulsive therapy.

This vignette describes a classic case of psychotic depression occurring in an older person. It illustrates how even the most classic symptoms of mental disorder, such as delusional thinking, can be overlooked in an older patient. It also illustrates hypochondriacal delusions, which occur frequently in depressive psychosis, probably more so than delusions of guilt.
Case Vignette: Pseudodementia

At the request of her family, an 80-year-old woman with confusion presented to her primary care physician. During the interview, she bent forward, avoided eye contact, and was noted to be fiddling with her hands and jewelry. She thought it was Thursday when it was Tuesday, could not give the date, thought that the month was September when it was October, but knew where she lived. Attempts to perform the remainder of the Mini Mental State Examination were unsuccessful, as she became more agitated on questioning, eventually saying: “I don’t know, please just leave me alone; I am sorry, I am not being any help to you, I know I am a nuisance.”

The family reported that 3 months earlier she had lost her cat and quite quickly became distressed, constantly telephoned her daughters without any clear reason, would not eat properly, was tired all the time, and did not sleep well. She appeared quite muddled and was clearly not managing her household. However, when the family came around and coaxed her, she managed for a few days, only to sink back into noncoping, always blaming herself for things not being “right”. She appeared to recognise her family but sometimes mixed up the names of her grandchildren. Before the death of her pet she had seemed quite lucid. The family recalled that she had been seen by another doctor 10 years earlier, following her husband’s death, and had been given tablets for a depressive disorder, which helped her “get over it”.

Since her health was good for her age, the doctor decided to treat her with a sedative tricyclic antidepressant, beginning at a low dose. The family, who had thought that she needed to be placed in a residential facility because of her inability to cope, was told that she might have a depressive disorder rather than dementia, although they feared it was the latter. After 6 weeks, she appeared calm, was no longer confused, and was coping much better.

This vignette illustrates the typical features of a “pseudodementia” caused by a depressive disorder. The confusion was largely restricted to disorientation. Although apparently unable to cope, the patient could do so if coaxed. Thus, she retained skills but had lost motivation. The rapid onset of the symptoms and the patient’s history of a previous depressive disorder were further clues that she had a depressive disorder rather than dementia. Like many older people with depressive disorders, she did not complain of feeling depressed but expressed many depressive ideas. Although she recovered from both her depressive disorder and her confusion, she should be seen regularly over the coming years because she is at risk for developing dementia.
Case Vignette: “Double Depression”

A 72-year-old man presented to his primary care physician with pain from an acute deterioration of his osteoarthritis. The physician was aware that the patient had a long history of depressive disorder and so inquired about his mood. The patient reported that, for the past 6 weeks he had been sleeping poorly, had reduced appetite, had little interest in his main hobby (gardening), and had become very irritable when his grandchildren visited him, eventually asking his family not to visit. He felt hopeless about his future and had an idea that he was a burden, but he was neither delusional nor suicidal. The patient had developed arthritis when he was 54 years old, which had led to his early retirement. At age 57, he developed angina, and a year later, he had one myocardial infarction. His health problems had significantly impaired his physical function. His wife died from cancer when he was 59. Since that time, the patient had felt depressed much of the time, although he had no history of mental illness before then. His symptoms comprised low mood, irritability, being on edge, muscle tension, fatigue, and a feeling of not being able to cope with life. The symptoms waxed and waned, but he would rarely if ever describe his mood as cheerful.

The physician diagnosed a mild depressive disorder and treated the patient with antidepressant medication. His sleep and appetite improved, and he became somewhat brighter and less irritable, but he still had symptoms of low mood and anxiety and found it difficult to motivate himself.

This vignette illustrates a depressive disorder complicating dysthymia. Many sufferers in old age have an onset of dysthymia in midlife. As in this case, antecedent life stressors and poor health are common in this situation. This is in contrast to dysthymia in younger people, which typically begins in adolescence and is associated with a high level of comorbid psychiatric illness, substance misuse, and personality disorder. Dysthymia is a risk factor for depressive disorders and should be treated.
Case Vignette: Recurrent Depression

A 75-year-old woman presented to her primary care physician with typical symptoms of a depressive disorder. She had a first depressive episode at the age of 50, coinciding with the departure of her last child from home and her husband’s onset of Parkinson’s disease. Over the next 10 years, she had two more episodes, each associated with bereavement. Her response to treatment with antidepressants and counselling was good. Between the ages of 60 and 70, she had four more depressive episodes, which again were precipitated by unpleasant life events. Her response to treatment was satisfactory, although she required hospitalization on three of the four occasions. Each episode of illness had lasted longer than the one before.

For the past 5 years, the patient had experienced annual attacks of depressive disorder, some of which were not always clearly associated with a life-event trigger. Her health had shown some deterioration with signs of hip arthritis and mild emphysema, both of which led to a reduction in the patient’s general level of activity. The last depressive episode had occurred 6 months earlier, and the patient had not made a full symptomatic recovery. The local hospital had treated her with lithium over the past 4 years. On this occasion, the primary care physician referred the patient to the hospital immediately. She responded well to treatment but, for the first time, required electroconvulsive therapy. The hospital psychiatrist continued the patient on lithium and changed her antidepressant, with a recommendation that she stay on an antidepressant medication on a long-term basis. The hospital and the primary care team agreed to share the patient’s care, with the former monitoring her lithium and the primary care nurse visiting monthly to offer support.

This vignette illustrates how a depressive disorder can become a recurrent condition. In later life, recurrences may become more frequent, with the disorder assuming a more autonomous course; that is, episodes are not always linked to adverse life events but occur more “out of the blue”. Prompt treatment of each attack lessens the risk of a chronic depressive disorder will develop in which symptoms fail to resolve fully. Prophylactic medication can lead to fairly complex treatment regimens, and care is usually best shared between the primary care and hospital staffs, each of whom should be clear about their role and maintain close communication.
CLINICAL EVALUATION

There is no substitute for obtaining a thorough psychiatric history. It is especially important to assess for a family history of depression, previous episodes of depression, and recent adverse life events, such as bereavement. Information obtained from someone close to the patient can often clarify areas of uncertainty, such as the evolution of symptoms, evidence of change, alterations in behaviour (e.g., social withdrawal), and baseline personality traits. Gaining an understanding of the individual’s baseline personality traits is important in setting realistic treatment goals, because treating a depressive disorder removes symptoms but does not necessarily change lifelong personality traits or habits. Table 1.4 lists key questions clinicians can ask patients and those close to them as part of an assessment for depression. Table 1.5 provides recommendations for interviewing an older patient who is being assessed for depression.

A mental state examination should also be performed. Although neuropsychological tests are not always necessary, it is good practice to include a screening test of cognitive function. The most widely used test is the Mini-Mental State Examination (MMSE), which can be performed in 10–15 minutes (Folstein et al. 1975). Scores on the MMSE may be reduced in individuals with depressive disorders. Cultural factors, literacy, and educational level may also influence MMSE scores.
### TABLE 1.4

**Key questions to ask in assessing for depression in an older patient**

<table>
<thead>
<tr>
<th>Key questions to ask the patient</th>
<th>Key questions to ask someone who knows the patient well</th>
</tr>
</thead>
<tbody>
<tr>
<td>• How is your mood?</td>
<td>• What changes have you noticed in the person?</td>
</tr>
<tr>
<td>• Have you lost interest in anything?</td>
<td>• What is his or her personality normally like?</td>
</tr>
<tr>
<td>• Do you get less pleasure from things you usually enjoy?</td>
<td>• Is there a history of depressive disorder in a blood relative?</td>
</tr>
<tr>
<td>• How long have you had symptoms?</td>
<td></td>
</tr>
<tr>
<td>• Have you been diagnosed before with a depressive disorder?</td>
<td></td>
</tr>
<tr>
<td>• Have there been any important changes in your health within the past year?</td>
<td></td>
</tr>
<tr>
<td>• Have there been any major changes in your life in the preceding 3 months?</td>
<td></td>
</tr>
<tr>
<td>• Have you had any symptoms that might suggest an underlying physical illness (for example, weight loss)?</td>
<td></td>
</tr>
<tr>
<td>• Have you ever thought you would be better off dead?</td>
<td></td>
</tr>
</tbody>
</table>
TABLE 1.5

Interviewing an older patient as part of an assessment for depression

- Introduce yourself. Put the patient at ease. Ask the patient he or she wishes to be addressed. Older people often prefer formality, tend to use formal titles ("nurse" or "doctor"), and may wish to be called by their family name (e.g., "Mr. Smith" or "Mrs. Smith"), regardless of how long you have known them. They may feel patronized when a young health professional uses their first name without asking.

- Be sure the patient can hear you. If there are difficulties, move closer. Do not shout.

- Avoid asking, "What is wrong with you?" Older people, in particular, invest much in their doctor and expect to be told what the matter is. A better opening question is "What brings you here?"

- If the person is physically ill, keep the interview as brief as possible.

- Do not use multiple-choice questions ("Do you feel depressed, sad, happy, or just about right?"). Instead ask, "How is your mood?" Use open-ended questions ("How do you feel?") rather than yes/no questions ("You’re depressed, aren’t you?").

- Because older people understate depressed mood, use alternative wording (e.g., "sad" "low," "miserable"), and ask about anhedonia and depressive thoughts, such as reduced self-esteem, guilt, and worthlessness.

- Inquire about suicidal ideation. Start with a broad question ("Have you felt desperate lately?"). If necessary, move to more specific questions, until you gain an understanding of the person’s state of mind. Asking about suicide does not provoke it.

- Ask about withdrawal, reduced ability to perform and/or interest in performing housework, and lack of interest in family or hobbies.

- Validate the patient’s thoughts ("I understand") and feelings ("I can understand why you feel upset").

- Observe the patient’s demeanour and posture (does the person slump forward with head low and no eye contact?), and look for signs of psychomotor disturbance, such as agitation or retardation.

- The first clinical interview is an opportunity to build a therapeutic partnership with the patient. The interview should include an explanation that a depressive disorder is an illness or a sign of moral weakness or failure; that it is treatable; that it is not an indicator of "senility"; and that antidepressant drugs are not addictive. These are all concerns that arise among older people in many cultures.
SCREENING FOR DEPRESSIVE DISORDERS IN OLDER PATIENTS

Screening questionnaires can be useful in diagnosing depressive disorders in older patients when employed in conjunction with a clinical examination. They can also be useful in situations in which the prevalence of depressive disorders is high (e.g., medical wards, nursing homes), because a high prevalence of depression in the setting increases the positive predictive value of the test. A number of questionnaires can be used to help identify a depressive disorder in older people, including the following:

Geriatric Depression Scale

• Patient Health Questionnaire 9 or 2

• World Health Organization (WHO) Well-Being Index

Geriatric Depression Scale

The most widely accepted screening questionnaire for depressive disorders in older persons is the self-administered Geriatric Depression Scale (GDS) (Yesavage et al. 1982–1983). This 15-item screen takes about 10 minutes to complete. The physician may assist the patient if necessary but should not change the wording, which could compromise the accuracy of the scale.

A cut-off score of 11 or above on the full GDS indicates a probable depressive disorder. The same cut-off has been found to give satisfactory sensitivity and specificity in hospitalized elderly patients with concurrent medical illness (Jackson and Baldwin 1993; Koenig et al. 1988). For the 15-item version, the cut-off in earlier studies was set at greater than 5 for a “case”. If a questionnaire is to be employed in a setting or culture in which it has not previously been used, an adaptation of the questionnaire for that culture is necessary. Many translated versions of the GDS are available and can be found on www.stanford.edu/~yesavage/GDS.html. It has recently been suggested that four questions from the GDS are almost as sensitive as longer versions (Katona and Katona 1997).

Whether the GDS is a useful means of detecting depressive illness in the presence of dementia is less clear. In one study of patients referred to a geriatric medical service, it was not useful for detecting a depressive disorder associated with Alzheimer’s disease (Burke et al. 1989), while it performed reasonably well in another study in patients with mild dementia (O’Riordan et al. 1990).

Patient Health Questionnaire

The Patient Health Questionnaire 9 (PHQ 9) is an instrument for screening for depression in primary care as well as a means of measuring severity of depressive symptoms. This questionnaire contains the 9 items upon which a DSM-IV-TR diagnosis of depressive disorder is based. A shorter version containing only 2 items, the PHQ-2, has been found to be a valid screening instrument for depression in older people (Li et al. 2007), with its brevity an advantage for use in older people. Detailed information on the PHQ and screening for depression in primary care can be found at www.depression-primarycare.org/about/mission.

World Health Organization Well-Being Index

The World Health Organization (WHO) Well-Being Index was developed as a quick depression screen based on an older questionnaire. The 1998 version has been validated in subjects 50 years of age and older (Bonsignore et al. 2001). Items in the WHO Well-Being Index cover areas that include positive mood, vitality, and general interests. Many translated versions are available at www.who-5.org.
STANDARDISED TOOLS FOR ASSESSING MENTAL STATE IN OLDER PATIENTS

A number of standardized tools are available for assessing mental state or severity of depressive symptoms in older persons, including the following:

- Geriatric Mental State Schedule (research)
- Hamilton Depression Rating Scale (severity)
- Montgomery-Asberg Depression Rating Scale (severity)
- Patient Health Questionnaire 9 (severity)

These tools tend to be used primarily in research settings.

The Geriatric Mental State Schedule (Copeland et al. 1976), which is administered on a laptop computer and takes about 30–45 minutes to complete, is widely used. This examination is coupled with a programme that generates a diagnosis.

The Hamilton Depression Rating Scale (Ham-D) (Hamilton 1960) assesses the severity of a diagnosed case of depressive disorder as well as changes over the course of treatment. It can be filled in quickly after a clinical examination of the patient.

Another tool is the 10-item Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979). Both the Ham-D and the MADRS should be used only when a depressive disorder has already been diagnosed.

PHYSICAL AND LABORATORY INVESTIGATIONS

A physical examination and laboratory investigations should be performed whenever the possibility of a depressive disorder is being considered. Of course, resources may limit the extent of investigations that are possible. However, a physical assessment is essential. The physical examination has two goals:

- To establish whether a systemic disorder (e.g., a recent small stroke) might be causing the depressive disorder
- To assess for medical comorbidity (e.g., heart failure) which may worsen the overall disability experienced by the patient and/or influence choice of treatment.

Laboratory investigations are carried out for similar reasons. The following tests are desirable:

- Full blood count (look for anaemia)
- Urea and electrolytes (monitor at baseline because antidepressant may cause hyponatremia)
- Thyroid function and calcium (look for hypothyroidism and elevated calcium level)
- Serum vitamin B12 and folate (look for Vitamin B12 and folate deficiency)
- Fasting glucose and lipid profile (assess for cardiovascular risk factors)

Laboratory investigations should include a full blood count, because anemia may mimic or aggravate a depressive disorder and mean corpuscular volume (MCV) may suggest the presence of underlying alcohol abuse, hypothyroidism, or B₁₂ deficiency. Thyroid function should be tested because of the well-known association between depression and hypothyroidism, and because “apathetic hyperthyroidism” can be mistaken for a depressive
### TABLE 1.6

Estimated impact of different risk factors for depressive disorders in young and elderly adults

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Young: Early-onset depression</th>
<th>Elderly: Early-onset depression</th>
<th>Elderly: Late-onset depression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biological factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic factors</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Structural abnormalities</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Neuroendocrine changes</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Neurotransmitter changes</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>Vascular factors</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Psychological and social factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personality</td>
<td>++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Social support</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Bereavement</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Separation</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Housing problems</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Social/financial problems</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Physical health</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>
disorder. Elevated calcium levels are occasionally associated with depressive disorders, as in primary hyperparathyroidism and metastatic cancer (Petersen 1968). An investigation for $\text{B}_12$, and folate deficiency by direct assay should be done whenever possible, because older patients with a severe depressive disorder can have severe depletions of both. Testing for parasitosis (e.g., intestinal worms, occult bleeding) and syphilis should also be performed when appropriate.

It is important to be aware that elderly people are in a more fragile state of homeostasis because of diminished physiological reserves. A severe depressive disorder in a 75-year-old patient may lead to serious metabolic derangement, which would be unlikely to occur in a healthy 35-year-old patient.

No diagnostic changes specific to depressive disorders are found on the standard 12-lead electroencephalogram (EEG). The main benefit of obtaining an EEG is in helping differentiate a depressive disorder from an organic brain syndrome. A brain scan is carried out in depressed patients only if clinically indicated—for example, the rapid-onset of a depressive disorder with neurological symptoms or signs.

In assessing for depressive disorders in older persons, it is important to keep in mind that the impact of biological and psychosocial risk factors in developing a depressive disorder varies with age. For example, genetic factors are more prominent in early- than in late-onset depression. The estimated influence of various risk factors on the development of a depressive disorder in younger and older people is presented in Table 1.6.

**DIFFERENTIAL DIAGNOSIS**

It is important to remember that depressive symptoms can be produced by a systemic illness (e.g., cancer, early dementia), a subcortical disease (e.g., Parkinson’s disease), the side effects of drugs (e.g., calcium channel blockers), and alcohol or drug abuse.

Mixed anxiety and depressive disorder is frequently seen in older persons. This diagnosis is valid for cases in which both anxiety and depressive symptoms are present but neither group reaches criteria for a clear diagnosis of depressive disorder or anxiety (Akiskal et al. 1997; Judd et al. 1997).

Although bipolar disorder occurs in younger people, patients often live into old age with their disease. Sometimes the pattern of illness can change over time, leading to increased frequency of recurrences. Some episodes may be overlooked, for example, a depressive “swing” presenting with withdrawal or a manic “swing” presenting with irritability.

Minor depression is defined as persistent lowered mood and the presence of 2–4 depressive symptoms (as listed in Table 1.1) that are present continuously for a 2-week period. Minor depression is not insignificant depression.

Dysthymia, a long-lasting depressive disorder, is more common in older people than was previously thought and may predispose to depressive episodes. “Double depression” is a term used to describe a depressive disorder superimposed on dysthymia.

Adjustment disorder describes a condition in which there is a clear onset of disabling depressive symptoms within a month of a stressful life event but the full criteria for a depressive episode are not met.
SUICIDE PREVENTION

In many countries, older people have the highest suicide rates of all age groups, and depressive disorders are the main risk factor for suicide in this group (Lindesay 1991). However, today more suicides (57%) occur in younger people (below 45 years) than in those 45 years of age or older. This is a change from the situation in 1950, when 56% of suicides occurred in the older age group (45 years of age or older) (World Health Organization 1999).

In many developed Western countries, the suicide rates in older people are only slightly increased compared with the rates in younger people. However, in Latin cultures and in some Asian countries like Japan, Korea and China, the suicide rates in older people are very high compared with rates in younger people (Chiu et al. 2001).

Some of the main risk factors for suicide in the elderly are listed in Table 1.7. The single factor that is most predictive of suicide is a previous attempt. Patients at risk for suicide often contact general practitioners, presenting with somatic complaints or fears of being physically ill (Barraclough 1971). It is important that clinicians be aware of this, because the majority of older people who commit suicide have had a consultation with a primary care physician within the 3 months prior to death (Cattell and Jolley 1995), and it is possible that their somatic preoccupations divert attention away from their underlying depressive disorder. The anniversary of bereavement is a time of particular vulnerability and may serve as a trigger for both a depressive disorder and suicide.

Means of suicide in older people vary from culture to culture. Since overdose, especially with benzodiazepines and non-opiate analgesics, is common in Western cultures (Lindesay 1991), physicians should keep this in mind when prescribing medications.

Although the risk factors shown in Table 1.7 are important, it is difficult to predict which patients will actually kill themselves. The primary care team, as well as the family, must be educated to take seriously any statements concerning self-harm, to remove means of committing the act, and to be alert for behaviours such as suddenly altering wills, giving away possessions, or sudden changes in religious interests.

Since pain and disability are associated with suicide, effective management of physical illness and control of pain, including pain associated with terminal disease, can help to reduce the risk of suicide. Appropriate prescription is important, however, since an overdose of prescribed drugs is a common means of suicide in the elderly.

In the United Kingdom, the suicide rate among elderly people fell when the lethal element was removed from domestic coal gas, suggesting that removing a means of suicide may be a viable preventive strategy. In a in Gotland, Sweden, depression-related suicide rates were reduced after the implementation of a depression-training programme for primary care physicians (Rihmer et al. 1995). In Italy, a reduction in the elderly suicide rate was demonstrated after the introduction of a telehelp service (i.e., a programme involving telephone checking and monitoring of clients at risk) (De Leo et al. 1995).
Better organization of services for older people with depressive disorders may also play a role in preventing suicide. An established secondary care team can facilitate communication and instill trust, and perhaps uncover suicidal plans and avert a tragedy. Suicide prevention programmes have been established in a number of developed countries. Because multiple causative factors can lead to suicide, many suicide prevention programmes adopt a broad strategic approach, with detection and treatment of depression always playing an important role. As described above, many older people who commit suicide had a consultation with a primary care physician within 3 months prior to death, so that primary care physicians can act as “gate-keepers” to detect and prevent suicidal behaviour in older persons. An example of an elderly suicide prevention programme is an intervention that was implemented in Hong Kong in 2002 (Chiu et al. 2003). In this programme, five elderly suicide prevention teams, consisting of psychiatrists, nurses, and social workers, work in collaboration with hotline services, nongovernmental organisations, centres for the elderly, and general practitioners to screen for people with depression and those at risk of suicide. Older people identified as being at risk for suicide or with severe depression are seen in fast-track clinics and visited at home by nurses; they also receive telephone monitoring. Another major focus of this programme is provision of training to general practitioners in the detection and management of depression.

The Canadian Coalition for Seniors’ Mental Health (CCSMH) has a useful website that provides guidelines on Assessment and Treatment of Depression, Assessment and Treatment of Mental Health Issues in Long-Term Care Homes (with a focus on mood and behavioural symptoms), and the Assessment of Suicide Risk and Prevention of Suicide (available at www.ccsmh.ca).

**TABLE 1.7**

Risk Factors for Suicide

<table>
<thead>
<tr>
<th>General factors</th>
<th>Psychiatric factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>Past suicide attempt</td>
</tr>
<tr>
<td>Living alone</td>
<td>Agitation</td>
</tr>
<tr>
<td>Inadequate social support</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Significant loss (for example, bereavement)</td>
<td>Guilt</td>
</tr>
<tr>
<td>Chronic medical condition (especially if painful)</td>
<td>Hopelessness</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>Low self-esteem</td>
</tr>
<tr>
<td>Cultural acceptability (in some societies, suicide is more acceptable than in others)</td>
<td>Hypochondriacal preoccupations</td>
</tr>
</tbody>
</table>
REFERENCES


Gurland BJ. The comparative frequency of depression in various adult age groups. J Gerontol 1976;31:283–92.


Katona CI, Katona PM. Geriatric Depression Scale can be used in older people in primary care. BMJ 1997;315:1236. Letter.


PART 1
Depressive Disorders in the Elderly
Chapter 2

Epidemiology and Impact of Depressive Disorders in The Elderly
INTRODUCTION

Many epidemiological studies on depressive disorders in the elderly have been done, with wide variation in prevalence rates reported in different countries. Several problems make it difficult to obtain reliable data in this area. A major problem involves selection of subjects for such studies. For example, some surveys that include only elderly people in institutional homes and hospitals are highly selective and unrepresentative. In addition, older adults may find it difficult to read and respond appropriately to questionnaires in community surveys. Lay interviewers may not be sufficiently trained, which can affect results. The definition of depressive disorders is another problematic issue, because the criteria used for diagnosis will determine the definition of caseness that is used in reporting results. Many older people may have depressive symptoms that do not fulfil the strict criteria for depressive disorders in a given classification system, even though they require treatment. For example, Blazer and Williams (1980) administered detailed standardized questionnaires to 997 elderly subjects in Durham, North Carolina, in the United States and reported that 14.7% of subjects had depressive symptoms but only 3.7% fulfilled criteria for major depression.

PREVALENCE OF DEPRESSIVE DISORDERS IN ELDERLY INDIVIDUALS IN THE COMMUNITY

Table 2.1 shows the variation in prevalence rates of depressive disorders in elderly people (65 years of age and older) reported in community studies. Varying diagnostic criteria for depressive disorders were used in these studies. Very little has been written about the incidence of depressive disorders in the elderly living in the community. Copeland et al. (1987) estimated the annual incidence of depression among elderly people in Liverpool to be at least 2.37%. Rorsman et al. (1990) estimated the incidence of major depression in Lundby County, Sweden, to be 4.3% for men and 7.6% for women of all ages (with very little age variation). Norton et al. (2006) assessed 2,877 elderly (65–100 years of age) residents of Cache County, Utah who did not have dementia. They found that individuals with no history of depression had rates of major depression of 7.88 per 1,000 person-years for men and 8.75 for women; rates of minor depression were 19.23 for men and 24.46 for women. Based on a meta-analysis, the prevalence of clinically significant depression among older people living in the community was reported to be 13.5%, while the prevalence of major depression found to be much lower—around 1.8% (Beekman et al. 1999). Another review found that the prevalence of depressive symptoms ranged from 26% to 40% among older people dwelling in the community in Europe (Copeland et al. 2004). In summary, although rates vary depending on methodology and samples, depressive symptoms are common in older people in the community, but only about 2% suffer from major depression. The prevalence of depressive disorders is also higher among women than men.

DEPRESSIVE DISORDERS AMONG ELDERLY PEOPLE IN LONG-TERM INSTITUTIONAL CARE

Depressive disorders are common among elderly people in nursing homes, and there is concern that such disorders may go undetected or remain untreated even when identified by medical staff. Katz et al. (1989) studied 51 subjects in Philadelphia, Pennsylvania in the United States and found depressive symptoms in 43%. Phillips and Henderson (1991) reviewed 17 surveys of depression in elderly nursing home residents and reported prevalence rates ranging from 5% to 85%. This variation may be due to the use of different diagnostic criteria; however, more recent studies have also demonstrated a higher prevalence of depressive disorders in residential homes than in the community (see Table 2.2).
### TABLE 2.1

Prevalence of depressive disorders in the elderly (people 65 years of age and older) living in the community

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>N</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blazer and Williams 1980</td>
<td>United States</td>
<td>997</td>
<td>3.7</td>
</tr>
<tr>
<td>Ben-Arie et al. 1987</td>
<td>South Africa</td>
<td>139</td>
<td>13</td>
</tr>
<tr>
<td>Copeland et al. 1987</td>
<td>United Kingdom</td>
<td>1070</td>
<td>11.3</td>
</tr>
<tr>
<td>Kua 1990</td>
<td>Singapore</td>
<td>612</td>
<td>4.6</td>
</tr>
<tr>
<td>Livingston et al. 1990</td>
<td>United Kingdom</td>
<td>705</td>
<td>15.9</td>
</tr>
<tr>
<td>Medianos et al. 1992</td>
<td>Greece</td>
<td>251</td>
<td>9.5</td>
</tr>
<tr>
<td>Henderson et al. 1993</td>
<td>Australia</td>
<td>945</td>
<td>1.0</td>
</tr>
<tr>
<td>Komahashi et al. 1994</td>
<td>Japan</td>
<td>1914</td>
<td>0.4</td>
</tr>
<tr>
<td>Beekman et al. 1995</td>
<td>Netherlands</td>
<td>3056</td>
<td>2</td>
</tr>
<tr>
<td>Lobo et al. 1995</td>
<td>Spain</td>
<td>1080</td>
<td>5.5</td>
</tr>
<tr>
<td>Pahkala et al. 1995</td>
<td>Finland</td>
<td>1086</td>
<td>2.2</td>
</tr>
<tr>
<td>Helmchen et al. 1996</td>
<td>Germany</td>
<td>516</td>
<td>17.8</td>
</tr>
<tr>
<td>Liu et al. 1997</td>
<td>Taiwan</td>
<td>1313</td>
<td>6.1</td>
</tr>
<tr>
<td>Steffens et al. 2000</td>
<td>Utah</td>
<td>4559</td>
<td>4.4 (men)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.7 (women)</td>
</tr>
</tbody>
</table>

*Note: In Tables 2.1, 2.2, and 2.3, we refer to the country in which the study took place, although in most cases samples were not representative of the countries’ populations as a whole.*
### TABLE 2.2
Depressive disorders in residential care settings

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann et al. 1984</td>
<td>United States</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>55</td>
</tr>
<tr>
<td>Parmelee et al. 1989</td>
<td>United States</td>
<td>12</td>
</tr>
<tr>
<td>Snowdon 1986</td>
<td>Australia</td>
<td>18</td>
</tr>
<tr>
<td>Ames 1990</td>
<td>United Kingdom</td>
<td>34</td>
</tr>
<tr>
<td>Rovner et al. 1991</td>
<td>United States</td>
<td>13</td>
</tr>
<tr>
<td>Rovner and Katz 1993</td>
<td>United States</td>
<td>15-60</td>
</tr>
<tr>
<td>Alexopoulos et al. 2001</td>
<td>United States</td>
<td>12.30</td>
</tr>
<tr>
<td>Arroll et al. 2002</td>
<td>New Zealand</td>
<td>13.8</td>
</tr>
<tr>
<td>Jongenelis et al. 2004</td>
<td>Netherlands</td>
<td>8.1 (major)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.1 (minor)</td>
</tr>
</tbody>
</table>

### TABLE 2.3
Depressive disorders in residential care settings

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacDonald 1986</td>
<td>United Kingdom</td>
<td>30.6</td>
</tr>
<tr>
<td>Borson et al. 1986</td>
<td>United States</td>
<td>24.4</td>
</tr>
<tr>
<td>Iliffe et al. 1991</td>
<td>United Kingdom</td>
<td>21.2</td>
</tr>
<tr>
<td>Oxam et al. 1990</td>
<td>United States</td>
<td>21</td>
</tr>
<tr>
<td>Evans and Katona 1993</td>
<td>United Kingdom</td>
<td>36</td>
</tr>
<tr>
<td>Alexopoulos 1996</td>
<td>United States</td>
<td>30</td>
</tr>
<tr>
<td>Beratdi et al. 2002</td>
<td>Italy</td>
<td>8.6</td>
</tr>
<tr>
<td>Litcht-Strunk et al. 2005</td>
<td>Netherlands</td>
<td>13.7</td>
</tr>
</tbody>
</table>
DEPRESSIVE DISORDERS IN PRIMARY CARE SETTINGS
Prevalence data from primary care surveys are sparse. General practice surveys usually come from self-selected groups who are likely to have medical comorbidity, and thus represent a skewed sample. Table 2.3 presents data from some of these studies.

DEPRESSIVE DISORDERS IN GENERAL HOSPITALS
Table 2.4 presents data from various studies of the prevalence of depressive disorders in medical inpatients.

IMPACT OF DEPRESSIVE DISORDERS IN OLDER PERSONS
Depressive disorders have an adverse impact on quality of life. In addition, recent evidence from a community sample of older people demonstrated that depressive disorders are associated with significantly increased use of health and social service resources (Livingston et al. 1997)

Recent evidence has suggested that minor and major depression in older people share similar risk factors and carry similar disease burden, including poorer health and social outcomes, functional impairment, and higher health utilisation and treatment costs (Lyness et al. 2004).

The Medical Outcomes Study (Wells et al. 1989) revealed that consequences of depressive disorders, with respect to poor functioning, were comparable to or worse than eight major chronic medical conditions, including coronary artery disease and diabetes. Failure to benefit from rehabilitation and to reach the expected level of functioning following catastrophic illness was strongly associated with persisting depression (Harris et al. 1988).

The report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options (1996), convened under the auspices of the World Health Organization, projected that, by the year 2020, depression will be the leading illness associated with negative impact and disease burden on human well-being, replacing communicable diseases and surpassing other conditions such as ischemic heart disease, neoplastic diseases, and cerebrovascular disease. The latest estimates from the Global Burden of Disease study indicated that unipolar depressive disorders accounted for 4.4% of the global disease burden (65 million disability adjusted life years [DALYs] lost in total), a figure that is in the same range as the total burden attributable to ischemic heart disease, diarrhoeal diseases, or the combined impact of asthma and chronic obstructive pulmonary disease (World Health Organization 2002).
REFERENCES


PART 1
Depressive Disorders in the Elderly
Chapter 3

Aetiology Of Depressive Disorders In The Elderly

As is the case with most chronic illnesses, no single risk factor is responsible for the development of a depressive disorder; rather, it is the accumulation of risks over time that increases the likelihood of a depressive disorder developing. A summary of evidence concerning the impact of various risk factors is given below.
GENETIC INFLUENCES

Generally, the later the onset of a given illness, the less influential genetic factors are in its aetiology. Hopkinson (1964) found that the prevalence of depressive disorders among first-degree relatives of depressed individuals whose illness began after the age of 50 was less than half of that of probands with early-onset depression. As at other times of life, female sex is associated with a greater risk of depression than male sex across the lifespan (Cole and Dendukuri 2003).

IMPACT OF PHYSICAL ILLNESS AND DISABLEMENT

In the elderly individuals with physically illnesses, as in other age groups with physical illnesses, depressive symptoms and disorders are common. The interaction between ill health and depressive disorders is complex and bidirectional; chronic ill health contributes to a poor prognosis for depressive disorders, and the presence of a depressive disorder can also worsen the outcome of a physical illness.

Similarly, psychiatric illness can contribute to the occurrence of somatic disease, and conversely, organic illness facilitates the appearance of psychiatric disturbances (Murphy and Brown 1980). Physical impairment may provoke a depressive disorder, which may in turn increase the degree of disability associated with the original impairment (Prince et al. 1998) and contribute to its chronicity (Murphy and Brown, 1980).

Other factors associated with aging—hearing and visual deficits (Rovner and Shmuely-Dulitzki 1997), declining recognition, and fears of increasing ill health, loss of dignity, and becoming a burden—may also predispose individuals to depressive disorders. Although some of these conditions are intrinsic to the aging process, viewing increasing adversity as an inevitable consequence of aging may lead to a gradual loss of hope.

PERSONALITY FACTORS

Abrams et al. (1987) showed that older patients with a history of major depression have more lifetime personality dysfunction than do the nondepressed elderly. It seems likely that certain personality traits—dependent, avoidant, “anxiety-prone”—may be related to depression in old age (Burvill et al. 1989). However, the relationship between personality traits and late-life depression is difficult to examine because it is often impossible to ascertain previous personality traits in individuals who have developed a depressive illness in old age. Gillis and Zabow (1982) found that elderly subjects in the community who had dysphoria (significant but subsyndromal depressive symptoms) exhibited “lifelong manifestations of undue dependency, poor coping behaviour, and inadequacy in inter-personal relationships”. They concluded that elderly people with dysphoria “become increasingly like themselves” (Gillis and Zabow, 1982). Positive coping styles, self-efficacy and a high level of mastery over the environment can protect against depression (Blazer and Hybels 2005). Depressed patients with avoidant, dependent, or perfectionist traits have been shown to respond more slowly to medication and have greater residual impairment, suggesting a role for early psychological interventions in such cases (Morse and Robins 2005).
SOCIODEMOGRAPHIC FACTORS

Table 3.1 lists some common sources of psychosocial stress for the elderly that may predispose to depressive symptoms. Blazer et al. (1985) found that loss of income, socioeconomic status, or an active role in society may lead to demoralization, lowered self-esteem, and increased risk of depressive disorders. Chronic stress, particularly due to financial problems and chronic physical illness, has been linked to an increased risk of depressive disorders (Turner and Beiser 1990). Poverty, poor social support, living in high crime areas, and social isolation predispose to depression in later life and may lead to a vicious cycle of risk (Arean and Reynolds 2005).

Caregiving is another chronic stressor that places older adults—particularly women—at increased risk for depressive disorders (Livingston et al. 1997; Wijeratne 1997). Ballard et al. (1996) screened over 100 caregivers of individuals with dementia and found that 25% had a depressive disorder. In approximately 30% of cases, the depressive disorder persisted. Factors associated with persistence of depressive disorders in caregivers were the presence of a depressive disorder and problem behaviours in the patient being cared for. A high percentage of caregivers who are not clinically depressed (that is, do not meet the criteria for depressive disorders) have depressive symptoms (Schulz et al. 1990).

An association between education and depressive disorders has been proposed for all age groups, with lower levels of educational attainment usually related to a higher risk of depressive disorders, especially in women (Weissman and Myers 1978). By contrast, some authors have found that being highly educated is also associated with depressive disorders, making the relationship between education and depressive disorders a U-shaped curve (Blazer et al. 1985). However, no studies have prospectively examined the association between education and depressive disorders in elderly patients.

Marital status is a strong predictor of depressive disorders in later life. In general, married adults are at lower risk than their unmarried peers, with the divorced and separated at greatest risk. Interestingly, in the presence of physical disablement, marriage was shown to be a protective factor for men but a risk factor for women (Prince et al. 1998).

TABLE 3.1

Potential sources of chronic stress in the elderly

- Declining health and mobility
- Dependence
- Sensory loss, cognitive decline
- Housing problems
- Major problems affecting a family member
- Marital difficulties
- Socioeconomic decline
- Problems at work, retirement
- Caring for a chronically ill and dependent family member
LIFE EVENTS

Major life events (Murphy 1982; Musetti et al. 1989; Post 1972) seem to increase the probability of developing a depressive disorder in older patients, in whom such events tend to have cumulative effects. Table 3.2 lists a number of life events that may contribute to the development of depressive symptoms in the elderly.

Bereavement, particularly due to the unexpected death of a partner, can have a harsh impact on an older person. Psychiatric symptoms increase substantially in the months immediately following a partner’s death (Clayton 2004). The effect of bereavement on the development of a depressive disorder is more pronounced in men; women may be more successful in using intimacy and a confiding relationship as buffers against their distress (Emmerson et al. 1989).

TABLE 3.2

Life events that may contribute to depression in the elderly

- Bereavement
- Separation
- Acute physical illness
- Medical illness or threat to the life of a beloved person
- Sudden homelessness or loss of residence
- Major financial crisis
- Negative revelation regarding a family member or friend
- Loss of valuable or meaningful object(s)

AGING

Is the aging brain itself particularly vulnerable to depressive disorders? This question has generated considerable interest and debate. Numerous studies suggest that structural, vascular, neuroendocrine, and biochemical changes in the brain (Table 3.3) significantly influence late-life depression.

Structural and Functional Changes

Brain atrophy was the first structural alteration reported in older patients with depressive disorders. Computed tomography (CT) studies in such patients have consistently shown increased cerebral atrophy, as measured by both ventricular brain ratio (VRB) and sulcal widening, compared with younger patients with mood disorders and elderly control subjects. Brain atrophy has also been shown to correlate with certain clinical features of depressive disorders, including melancholic symptoms, psychomotor retardation, cognitive impairment, and increased 2-year mortality (Abas et al. 1990).

Magnetic resonance imaging (MRI) studies have also demonstrated changes that may be linked to late-life depression. Elderly depressed patients show a high prevalence of deep frontal white-matter lesions on T2-weighted images. Subcortical gray-matter disease involving the basal ganglia, caudate, and thalamus has also been reported in as many as 60% of patients with late-life depression. Such lesions, termed leukoariosis or leukoencephalopathy, are suggestive of subclinical cerebral vascular disease (Krishnan et al. 1997). Schweitzer and colleagues (2001) reviewed structural neuroimaging studies in late-life depression published over the past two decades. These studies indicated that there are neuroimaging changes that are commonly observed in patients with late-life depression compared with normal controls. Findings include ventricular enlargement and sulcal widening, and reduction in volume size of frontal lobes, hippocampus and caudate nucleus. White matter lesions are more common in depressed subjects and tend to be more severe.

Functional imaging studies with positron emission tomography (PET) have suggested decreased cerebral blood flow and reduced glucose metabolism throughout the brain, most prominently in the frontal lobes and right hemisphere, both in primary depressive disorder and in depressive disorder secondary to Alzheimer’s disease (Kumar and Miller 1997).
### TABLE 3.3

**Biological factors possibly associated with depressive disorders in the elderly**

<table>
<thead>
<tr>
<th>Biological factor</th>
<th>Description</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in brain structure (structural imaging studies)</td>
<td>CT scans of elderly depressed patients show increased cerebral atrophy (sulcal and ventricular dilation)</td>
<td>Jacoby et al. 1983</td>
</tr>
<tr>
<td></td>
<td>High prevalence of patchy lesions in the frontal deep white matter and basal ganglia on T2-weighted magnetic resonance imaging</td>
<td>Greenwald et al. 1996, Krishnan 1991</td>
</tr>
<tr>
<td></td>
<td>Frontal and temporal lobe atrophy and ventricular enlargement in late-life major depression</td>
<td>Rabins et al. 1991</td>
</tr>
<tr>
<td></td>
<td>Prefrontal lobe atrophy in late-life minor depression</td>
<td>Kumar et al. 1997</td>
</tr>
<tr>
<td></td>
<td>Subcortical hyper-intensities and gray-matter disease involving the basal ganglia, caudate, and thalamus in patients with late-life depression</td>
<td>Coffey et al. 1990, Figgel et al. 1991, Greenwald et al. 1998</td>
</tr>
<tr>
<td></td>
<td>Leukoariosis and the “vascular depression” hypothesis</td>
<td>Krishnan et al. 1997, Lavretsky et al. 1998</td>
</tr>
<tr>
<td></td>
<td>Late-onset depression is associated with white-matter hyper-intensities, a larger ventricular brain ratio, and a history of hypertension</td>
<td>Salloway et al. 2002</td>
</tr>
<tr>
<td></td>
<td>Reduced prefrontal volume and a greater volume of hyper-intensity on magnetic resonance imaging in late life depression</td>
<td>Kumar et al. 2000, Firbank et al. 2004</td>
</tr>
<tr>
<td></td>
<td>Smaller right frontal lobe volume in late onset depression</td>
<td>Almeida et al. 2002</td>
</tr>
<tr>
<td></td>
<td>Local gray matter deficits in the right lateral temporal cortex and parietal cortex in late onset depression</td>
<td>Ballmaier et al. 2004a</td>
</tr>
<tr>
<td></td>
<td>Bilateral gray matter deficits in the anterior cingulate and the gyrus rectus and the orbitofrontal cortex</td>
<td>Ballmaier et al. 2004b</td>
</tr>
<tr>
<td>Metabolic changes in the brain (functional imaging studies)</td>
<td>Decreased frontal lobe and right hemisphere cortical blood flow in patients with depression</td>
<td>Kumar and Miller 1997, Sackeim et al. 1990</td>
</tr>
<tr>
<td></td>
<td>Reduced frontal lobe glucose metabolism correlates with depression in patients with Alzheimer’s disease</td>
<td>Hirono et al. 1998</td>
</tr>
<tr>
<td></td>
<td>Abnormal metabolism of caudate nucleus, basal ganglia and the frontal region during depression</td>
<td>Drevets 2000</td>
</tr>
<tr>
<td></td>
<td>Reduced activation of the dorsal anterior cingulate in patients with severe depression</td>
<td>De Asis et al. 2001</td>
</tr>
</tbody>
</table>

*continued on next page*
<table>
<thead>
<tr>
<th>Biological factor</th>
<th>Description</th>
<th>References</th>
</tr>
</thead>
</table>
| **Neuroendocrine changes** | Dexamethasone nonsuppression is more frequent in geriatric than younger depressed patients | Alexopoulos et al. 1984  
Davis et al. 1984 |
| | Strong correlation between clinical improvement and normalization of the dexamethasone suppression test | Meyers et al. 1993 |
| | High levels of corticotropin-releasing hormone (CRH)-mRNA levels in the paraventricular nucleus of elderly depressed patients | Raadsheer et al. 1995 |
| | Blunted response to thyroid-stimulating hormone (TSH) in geriatric depressed patients | Sunderland et al. 1985 |
| | Variability of response to thyrotropin-releasing hormone (TRH) test in subjects limits its usefulness in the study of late-life depression | Targum et al. 1992 |
| | Association of the inflammatory marker interleukin-6 (an interleukin involved in cortisol production, inflammation, and immune system) with depressive disorder in later life | Penninx et al. 2003 |
| **Neurochemical changes** | Increased turnover of monoamines, norepinephrine (NE), and serotonin (5-HT) in aging brains | Karlsson 1993 |
| | 5-HT1 and 5-HT2 binding sites decrease with age | Sparks 1989 |
| | Age-related reductions in dopaminergic function may predispose individuals to depressive disorders | Wong et al. 1984 |
| | Reduction in homovanillic acid (HVA) levels in cerebrospinal fluid is accompanied by increased monoamine oxidase (MAO)-B activity in brain, plasma, and cerebrospinal fluid | Brown and Gershon 1993 |
Neuroendocrine Dysfunction

Neuroendocrine dysfunction may also influence a person’s vulnerability to depressive disorders. For example, hypothalamic-pituitary-adrenal (HPA) axis/dexamethasone nonsuppression is more frequent in geriatric than in younger depressed patients, and there seems to be an association between response to treatment for depressive disorders and dexamethasone suppression test (DST) normalization in a subgroup of patients. However, attempts to define the DST as a biological marker of late-life depression have failed, because the test is also positive in one third of patients with Alzheimer’s disease and in the presence of leukoariosis (Krishnan 1991), suggesting low specificity for depressive disorders in elderly populations (Alexopoulos et al. 1985).

Hyperactivity of the HPA axis in elderly depressed patients is also supported by studies suggesting increased expression of corticotropin-releasing hormone (CRH) in the paraventricular nucleus of elderly depressed patients, compared with those who are not depressed.

Blunted thyroid-stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) has also been reported in patients with geriatric depression and in one third of Alzheimer’s disease patients. Some decrements may be attributed to the aging process itself and to variability between the sexes (Molchan et al. 1991).

Neurochemical Changes

The concentration, turnover, and availability of the major neurotransmitters serotonin (5-HT), norepinephrine (NE), and dopamine have been shown to be altered in normal aging, dementia, and late-life depression. Specific studies of neurotransmitter abnormalities in late-life depression have yielded inconsistent findings (Schneider 1992).

Although serotonin (5-HT) levels do not seem to change in the normal aging brain, levels of the 5-HT metabolite 5-hydroxyindoleacetic acid (5-HIAA) have consistently been shown to increase with age (Karlsson 1993), again suggesting hyperactivity in serotonergic pathways.

Age-related reductions in function in the dopaminergic system, primarily affecting the caudate nuclei and putamen in people over 70 years of age, have been demonstrated in post-mortem studies and in vivo with PET scans. Increased monoamine oxidase-B (MAO-B) activity in platelet, brain, and cerebrospinal fluid parallel the decrease in dopamine function.

“Vascular Depression” Theory

The importance of chronic ischemic cerebral changes has recently been recognised. A study of depressed patients with and without abnormalities on MRI demonstrated that positive MRI findings correlated with older age at onset of depression, vascular comorbidity, greater psychomotor slowing or Parkinsonism, anhedonia, increased functional impairment, and lower incidence of psychosis (Krishnan et al. 2004).

According to the “vascular depression” theory (Krishnan et al, 1997), vascular damage to striato-pallido-thalamo-cortical pathways leads to depressive disorders by disrupting norepinephrine (NE) and serotonin (5-HT) mood-regulating circuits. Both deep white and gray-matter lesions may be related to cardiovascular pathology, carotid atherosclerosis, and hypertension (D’Mello and Rooker 1997). The presence of subcortical pathology is highly correlated with lack of response to pharmacotherapy and increased risk of developing Alzheimer’s disease (Lavretsky et al. 1998).

Alexopoulos and colleagues at Cornell have further refined the notion of vascular depression by linking it to neuropsychological markers of frontal-executive dysfunction (Alexopoulos et al. 2002). The syndrome of depression with executive dysfunction may be related to cerebrovascular disease or age-related neurodegeneration. Patients present with frontal executive impairment manifested by difficulties with motivation, organisation, planning, sequencing, and abstracting. These patients typically exhibit anhedonia and apathy rather than sadness and have cognitive impairment with psychomotor retardation.
Basal Ganglia Disease And Depression

Basal ganglia diseases share a number of features including prominent subcortical pathology as well as cortical-subcortical pathway dysfunction. The anatomic-physiological correlates of depression in basal ganglia disease involve structures similar to those in major depressive disorder, including the frontal lobes and basal ganglia in stroke studies and hypometabolism of the caudate and inferior and medial frontal lobes in depressed patients with Parkinson’s disease. Additionally, cellular damage to the caudate occurs in patients with Huntington’s disease and Wilson’s disease and may explain the origin of depression in these disorders. The evidence appears to implicate depression as a syndrome with multifactorial causation and dysfunction along separate but functionally linked pathways that involve not only subcortical but also cortical sites, as well as multiple neurotransmitter systems.

In contrast to early-onset depressive disorder, the aging process may play a more important role than genetic factors in the aetiology of late-onset depressive disorder. Nevertheless, early and late-onset depressive disorders can be clinically indistinguishable, and both conditions share a number of underlying risk factors (Alexopoulos et al. 1993; Baldwin 1990; Baldwin and Tomenson 1995; Eagles and Whalley 1985; Musetti et al. 1989). This lends credence to the adage, “Depression is depression at any age” and should be treated whenever it is found (Baldwin 1990).

PROTECTIVE FACTORS

Several biological, psychological, and social factors seem to exert buffering effects (Table 3.4), protecting older adults from developing depressive disorders in response to the precipitating factors discussed in earlier sections of this chapter.

Good physical health is a protective factor against the development of depressive disorders, as are prompt identification and treatment of physical disorders and early correction of sensory losses with devices such as hearing and visual aids.

Having a robust social support system is also protective. This includes the availability of community-based sources of assistance, support of family and friends, and—perhaps most important—the patient’s subjective perception of feeling supported (George 1994). Feeling lonely at the index assessment is significantly associated with the later onset of pervasive depression (Prince et al. 1998).

A capacity for intimacy and involvement in a relationship characterised by mutual trust are considered buffers against emotional distress. Some studies have suggested that, after life events, lack of a close, confiding relationship may be the most important vulnerability factor for the development of depressive disorders. It has also been suggested that men are less likely than women to have such relationships (Murphy 1982).

TABLE 3.4

Protective (buffering) factors

<table>
<thead>
<tr>
<th>Adequate medical support:</th>
<th>Adequate coping behaviour:</th>
<th>Social support:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early detection and treatment</td>
<td>Well-integrated personality</td>
<td>Social network</td>
</tr>
<tr>
<td>Avoidance of polypharmacy</td>
<td>Ability to achieve intimacy</td>
<td>Tangible support</td>
</tr>
<tr>
<td>Nutritional advice</td>
<td>Active efforts for reintegration</td>
<td>Patient’s perceptions of support</td>
</tr>
<tr>
<td>Physiotherapy/fitness programs</td>
<td>Positive coping styles, self-efficacy and a high level of mastery over the environment</td>
<td>Intimacy/confidante relationship</td>
</tr>
<tr>
<td>Early correction of sensory losses, such as hearing aids and cataract treatment</td>
<td></td>
<td>Religious/spiritual beliefs</td>
</tr>
</tbody>
</table>
While no definite aetiology can be established for depressive disorders occurring in later life, it has been established that both biological and social factors have important roles. Advances in neuroimaging techniques have given some support to a possible relationship between neurobiological (especially vascular) events and depressive disorders. Studies of neurochemical and neuroendocrine factors, while not totally consistent or definite, have pointed to a possible disturbance in physiological homeostasis. Personality and social factors may either protect against or increase vulnerability to depressive disorders in later life, suggesting potentially important preventive and treatment strategies. Future research into etiological factors will yield greater understanding of the varying roles of neurobiology, genetics, and psychosocial factors.

**REFERENCES**


PART 1
Depressive Disorders in the Elderly
Chapter 4

Course of Depressive Illness in the Elderly
INTRODUCTION

This chapter covers prognosis and factors relating to morbidity and mortality in depressive disorders in older persons. It is important to recognize that depressive disorders are treatable even in the very old and those with comorbid conditions such as dementia. A majority of older patients recover if given appropriate treatment. A meta-analysis by Cole and Bellavance (1997a) indicated that 60% of patients either remained well or had relapses or recurrences from which they also recovered (Table 4.1).

Although there are fewer data regarding community-dwelling elders, Denihan et al. (2000) studied the 3-year prognosis of depression in a cohort of 127 community-dwelling elderly subjects in Ireland. They found that 34.9% had persistent or relapsed case-level depression and 14% had recovered completely. Beekman et al. (2002) assessed the natural history of late-life depression in the Longitudinal Aging Study in Amsterdam. They found that depressive symptoms were short-lived in only 14% of a cohort of 277 depressed elderly persons in the community, remission occurred in 23%, an unfavourable but fluctuating course was found in 44%, and a severe chronic course occurred in 32% after 6 years. There was a gradient in outcome from baseline sub-threshold depression (best prognosis), to major depression and dysthymia (intermediate prognosis) through to double depression (depression with dysthymia) with poorer prognosis. It is unclear why the outcome in community studies is worse than in hospital studies. Aside from methodological issues, two factors stand out—in the community, detection of depressive disorders was poor, and prescription rates for antidepressants were low. Thus, no treatment or inadequate treatment of depressive disorders could result in poor recovery and chronic depressive illness.

Different types of depressive disorders may lead to different outcomes. Early evidence suggests that depressive disorders in old age, particularly late-onset depression, are associated with brain changes, which may result in lower rates of remission of symptoms in the acute phase of treatment. Psychotic late-life depression is also associated with poor outcome (Murphy 1983).

PROGNOSIS OF DEPRESSIVE DISORDERS IN THE FRAIL AND PHYSICALLY ILL

In their second meta-analysis, Cole and Bellavance (1997b) identified eight inpatient studies involving 265 inpatients with depressive disorders. For the most part, follow-up was short (less than 12 months). Only one in five patients recovered from their depressive disorder. Detection of depressive disorders on medical wards is known to be low (Jackson and Baldwin 1993), with both rates of treatment and adequacy of treatment being suboptimal (Koenig et al. 1997). Evans et al. (1997) studied 42 medical inpatients who had been randomly allocated to either placebo or fluoxetine. Recovery was twice as high in the actively treated group, and superiority of treatment was most marked in those with the most severe medical illness. This suggests that treatment of a depressive disorder should not be postponed because of physical comorbidity, and that both conditions should be treated in parallel.

OUTCOMES OF DEPRESSIVE DISORDERS IN OLDER COMPARED WITH YOUNGER PATIENTS

Contrary to popular belief, depressive disorders in old age are not associated with worse outcomes than at other times in life. Table 4.2 summarizes comparative findings from nine studies. Results from a recent systematic review suggest that response and remission rates to pharmacotherapy and electroconvulsive therapy (ECT) are not significantly different in depression in old age and middle-age, but that relapse rates are higher in late-life depression (Mitchell and Subramaniam 2005).
**TABLE 4.1**

Meta-analysis of studies of prognosis in hospitalised psychiatric patients and outpatients

<table>
<thead>
<tr>
<th>Prognosis Category</th>
<th>Results</th>
<th>Combined results</th>
<th>Results</th>
<th>Combined results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well</td>
<td>25%–68%</td>
<td>43.7%</td>
<td>18%–34%</td>
<td>27.3%</td>
</tr>
<tr>
<td>Relapse with recovery</td>
<td>11%–25%</td>
<td>15.8%</td>
<td>22%–52%</td>
<td>32.5%</td>
</tr>
<tr>
<td>Continuously ill</td>
<td>3%–69%</td>
<td>22.5%</td>
<td>7%–30%</td>
<td>14.2%</td>
</tr>
<tr>
<td>Other (most had died)</td>
<td>8%–40%</td>
<td>22.5%</td>
<td>23%–29%</td>
<td>30.9%</td>
</tr>
</tbody>
</table>

Source of data: Cole and Bellavance 1997a

**MORTALITY RATES**

Having a depressive disorder may shorten life. Table 4.3 shows results from both short-term and long-term studies. A 5% year-on-year mortality would be expected in this older age group, so the results shown in Table 4.3 are well above the expected. It cannot be assumed that those with depressive disorders who died earlier had more severe physical illness. In the study by Murphy et al. 1988, older adults with and without depressive disorders were matched for age, sex, and levels of physical morbidity. Those with depressive disorders nonetheless had statistically higher mortality, chiefly from cardiovascular causes.

Cuijpers and Smit (2002) conducted a meta-analysis of 25 studies involving 106,628 subjects, 6416 of whom were depressed, in order to examine the excess mortality of depression in older people. The overall relative risk (RR) of dying in depressed subjects was 1.81 compared with non-depressed subjects. No major differences were found between men and women, although the RR was somewhat larger in men. The RR in subclinical depression was not smaller than the RR in clinical depression. Vinkers et al. (2004) followed 500 subjects from 85 years of age on for an average of 3 years and found that depression contributed to an increase in both cardiovascular and non-vascular mortality. Interestingly, a recent study found that the association between depression and mortality is gender-dependent and varies according to the severity of symptoms and use of antidepressants (Ryan et al. 2008). In this 4-year follow up study of 7363 community dwelling elderly people, severity of depressive symptoms was assessed with the Centre of Epidemiological studies-Depression Scale (CESD). Depressed men using antidepressants had the highest mortality rate, with increasing severity of depression corresponding to a higher hazard ratio. However, among women, only severe depression in the absence of treatment was significantly associated with mortality.
TABLE 4.2
Comparative Outcome of Depressive Disorder in Older Versus Younger Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Age group (years)</th>
<th>Number of subjects</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meats et al. 1991</td>
<td>≥65 &lt;65</td>
<td>56 24</td>
<td>At 1 year, 68% of older patients and 50% of younger patients well</td>
</tr>
<tr>
<td>Hinrichsen 1992</td>
<td>&gt;60</td>
<td>127</td>
<td>72% recovery at 1 year; not significantly different from National Institute of Mental Health study of mixed-age patients</td>
</tr>
<tr>
<td>Brodaty et al. 1993</td>
<td>18–39 40–59 ≥60</td>
<td>104 77 61</td>
<td>No significant differences between groups at 1 and 4 years</td>
</tr>
<tr>
<td>Hughes et al. 1993</td>
<td>≥60 &lt;65</td>
<td>46 67</td>
<td>Elderly group had greater improvement than younger group on depression score (CES-D)</td>
</tr>
<tr>
<td>Alexopoulos et al. 1996a</td>
<td>Old (mean age 75) Young (mean age 55)</td>
<td>63 55</td>
<td>Time to recovery, using survival analysis: 60% of both groups recovered at 6 months</td>
</tr>
<tr>
<td>Philibert et al 1997</td>
<td>&lt;40 40-59 60-69 ≥70</td>
<td>42 47 53 50</td>
<td>Older age at onset linked with higher rate of mortality; age at onset was not linked with remission of depression</td>
</tr>
<tr>
<td>Tew et al. 1999</td>
<td>&lt;60 60-74 ≥75</td>
<td>133 63 72</td>
<td>Those aged 59 or younger experienced a significantly lower remission rate than those aged 60–74 (54% versus 73%). Those over 75 years of age had a response rate of 67%.</td>
</tr>
<tr>
<td>Tuma 2000</td>
<td>&gt;65 &lt;65</td>
<td>54 56</td>
<td>No significant difference in recovery rate</td>
</tr>
<tr>
<td>Fischer et al. 2003</td>
<td>&lt;35 35-44 45-54 55-64 64-74 ≥75</td>
<td>134 214 264 139 134 138</td>
<td>Older patients were less likely to have remission at the 3-month follow-up</td>
</tr>
</tbody>
</table>
### TABLE 4.3

Studies of Mortality in Depression in Old Age

<table>
<thead>
<tr>
<th>Study</th>
<th>Number</th>
<th>Follow-up (months)</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-term studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murphy 1983</td>
<td>124</td>
<td>12</td>
<td>14%</td>
</tr>
<tr>
<td>Baldwin and Jolley 1986</td>
<td>100</td>
<td>12</td>
<td>8%</td>
</tr>
<tr>
<td>Rabins et al. 1985</td>
<td>62</td>
<td>12</td>
<td>13%</td>
</tr>
<tr>
<td>Hughes et al. 1993</td>
<td>≥60</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;65</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td><strong>Long-term studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murphy et al. 1988</td>
<td>120</td>
<td>48</td>
<td>34%</td>
</tr>
<tr>
<td>Baldwin and Jolley 1986</td>
<td>100</td>
<td>48</td>
<td>26%</td>
</tr>
<tr>
<td>Penninx et al. 1999</td>
<td>61 (major depression)</td>
<td>48</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>392 (minor depression)</td>
<td>48</td>
<td>28%</td>
</tr>
<tr>
<td>Tuma 2000</td>
<td>54</td>
<td>54</td>
<td>33%</td>
</tr>
<tr>
<td>Yaffe et al. 2003</td>
<td>73</td>
<td>120</td>
<td>26%</td>
</tr>
<tr>
<td>Kawamura et al. 2007</td>
<td>158</td>
<td>180</td>
<td>61%</td>
</tr>
</tbody>
</table>
Most deaths occur early in the course of illness (Baldwin and Jolley 1986). O’Brien and Ames (1994) have proposed several possible mechanisms for the increased mortality in depressive disorders, including comorbid physical illness, occult illness (for example, an unsuspected carcinoma), illness effects (for example, pneumonia secondary to inertia caused by psychomotor retardation), treatment effects (for example, some of the older tricyclic antidepressants have been considered to be cardiotoxic), and biological effects (for example, raised cortisol level).

Undertreatment of depressive disorders is another plausible explanation. Cardiovascular mortality is reportedly higher in elderly depressed men whose depressive disorder is inadequately treated (Avery and Winokur 1976) and in elderly depressed women who are not given ECT, compared with those who do receive the treatment (Babigian and Guttmacher 1984). Recent prospective studies have also reported that depressive symptoms are a risk factor for cardiovascular mortality in older European men (Kamphuis et al. 2006) and Japanese women (Kawamura et al. 2007). Similarly, inadequately treated comorbid illness physical may worsen the prognosis for a depressive disorder.

Penninx et al. (1998) found that newly depressed older men, but not women, were approximately twice as likely to have a cardiovascular event as those who were never depressed. In men, recent onset of depressed mood is a better predictor of cardiovascular disease than long-term depressed mood. Anstey and Luszc (2002) also reported that depression was associated with a greater risk of mortality for men than women with incident depression in old age. Chronic depression and remitted depression were also associated with mortality, but this effect was explained by medical conditions.

Although suicide only explains some of the excess mortality among older patients with depressive disorders, it is an important and potentially avoidable form of death (see discussion of suicide in association with depression in the elderly in Volume III, Part 1, Chapter 1).

FACTORS PREDICTING OUTCOME

Table 4.4 summarizes general and clinical factors predictive of poor outcomes in older persons with depressive disorders. Generally, the course of a depressive disorder in older people is less dependent on psychosocial factors than at other times of life; thus, illness factors become increasingly important with age. It is therefore important to treat depressive disorders early to achieve the best long-term results and to offer prophylactic treatment (see below) in situations in which the risk of recurrence is high (e.g., individuals in poor physical health, individuals who have had episodes of a depressive disorder in the previous 2 years). Improving the patient’s social supports and milieu may also improve the outcome.

The presence of cognitive impairment, particularly executive dysfunction, in patients with geriatric depression, leads to worse outcomes as manifested in greater disability (Alexopoulos et al. 1996b), chronicity and slow time to recovery (Alexopoulos et al, 1996a), and higher rates of relapse and recurrence (Alexopoulos et al. 2002). In addition, executive impairment predicts a poor or delayed response to antidepressants in geriatric major depression (Alexopoulos et al. 2000).

DO DEPRESSIVE DISORDERS PREDISPOSE INDIVIDUALS TO LATER DEMENTIA?

This question is often asked by caregivers and patients alike, who may believe that a depressive disorder in later life is the first sign of “senility”. Alexopoulos et al (1993) studied 57 depressed inpatients subdivided by the presence or absence of “reversible dementia”—cognitive impairment that remits after recovery from a depressive disorder. Patients who initially presented initially with a depressive disorder and reversible cognitive impairment had an almost fivefold increased risk of developing dementia, compared with those who had a depressive disorder but intact cognitive function.
In naturalistic studies, such as those summarized in Table 4.1 (Cole and Bellavance 1997a), the risk of dementia was not found to be increased, probably because patients with cognitive impairment are usually excluded from such studies. Cognitive dysfunction may develop during an episode of geriatric depression and then diminish in varying degrees once the depressive symptoms remit. Follow-up data have demonstrated that patients with “pseudodementia” developed dementia at a rate of 9%–25% per year (Alexopoulos and Chester 1992). In an epidemiological community study of dementia, Devanand and colleagues (1996) demonstrated that a depressed mood was common in subjects with cognitive impairment who did not meet the criteria for dementia. The baseline depressed mood in these subjects was associated with a moderately increased risk of incident dementia at follow-up. The evidence suggests that patients who present with cognitive impairment and a depressive disorder are at increased risk of dementia, even though their confusion may lift with treatment of the depressive disorder. For this reason, it is important to conduct a brief cognitive screen at the outset. Patients with reversible cognitive impairment in the context of a depressive disorder need particularly close follow-up.

Findings from epidemiological studies show that depression is a risk factor for cognitive impairment or dementia in later life (Green et al. 2003; Sachs-Ericsson et al. 2005). Possible explanations are that chronic depression may be associated with hippocampal atrophy in older patients (Bell-McGinty et al. 2002) and that depressed patients may adopt unhealthy lifestyles, which can aggravate the risk factors for vascular disease and hence dementia.

### TABLE 4.4

Factors Contributing to Poor Outcomes in Older Persons With Depressive Disorders

**Illness—clinical features:**
- Slower initial recovery
- More severe initial depressive disorder
- Duration of >2 years
- Three or more previous episodes (for recurrence)
- Previous history of dysthymia
- Psychotic symptoms
- Extensive deep white-matter and basal ganglia gray-matter brain disease
- Prior dysthymic disorder

**General factors:**
- Chronic stress associated with crime and poverty
- A new physical illness or chronic physical illness
- Becoming a victim of crime
- Poor perceived (but not necessarily tangible) social support
REFERENCES


Babigian HM, Guttmacher LB. Epidemiologic considerations in electroconvulsive therapy. Arch Gen Psychiatry 1984;41:246–53.


Hughes DC, DeMallie D, Blazer DG. Does age make a difference in the effects of physical health and social support on the outcome of the major depressive episode? Am J Psychiatry 1993;150:728–33.


PART 1
Depressive Disorders in the Elderly
Chapter 5

Management and Prevention of Depression in the Elderly
OVERVIEW

Once the diagnosis of a depressive disorder is clear, comprehensive assessment of the patient’s physical, social, and psychological state (and history) is essential in order to establish an effective management plan. Particularly important factors to be considered include:

• Mobility and activity
• Sensory impairments
• Nutritional state
• Specific physical disorders and their current treatment
• History of depressive or other psychiatric disorders and their treatment
• Family and informal caregiver support network
• Statutory care input
• Unmet needs

Managing depressive disorders in primary care involves a wide range of possible interventions that may be focused on the patient, on his or her living conditions, or on the family or other caregivers. The specific intervention “package” chosen usually involves several elements and is individually tailored to the complexity of the case. The overall objectives are:

• Resolution of depressive symptoms and signs
• Reintegration into the family and social environment, when possible
• Prevention of relapse or recurrence
• Restoration of functioning and social roles

The management of depressive disorders in older persons should always be multimodal and multidisciplinary. The therapeutic objectives may need to be modified to suit individual circumstances, and therapeutic and rehabilitative methods should be adapted flexibly to realistic objectives and available resources. For example, resolution of depressive symptoms may not allow a full return to independence if the symptoms develop in the context of chronic physical illness or disability or in a patient with coexisting dementia. Helping the patient and caregivers to accept some degree of loss and dependency may itself be a management objective. However, an assertive approach to optimizing physical health and social circumstances is central to the management of depressive disorders in old age.

It is also important to keep in mind that considerable societal, physical, and psychological barriers to optimizing the treatment of depressive disorders in older persons may exist. These include the limited education and literacy of many older people, their poverty (and resultant limited access to optimal treatment), and their increased vulnerability to side effects of some treatments. Age-related pharmacokinetic and pharmacodynamic changes resulting in increased risk of drug accumulation (Lotrich and Pollock 2005) must be considered but should not discourage the clinician from attempting treatment. Older people are also particularly vulnerable to side effects of some treatments, such as confusion and memory loss induced by electroconvulsive therapy (ECT) and cardiotoxicity, postural hypotension, and falls related to use of tricyclic antidepressants (Campbell 1991).
Age-related changes in the functions and composition of the human body require adjustments in drug selection and dosage for older individuals. Drug excretion via the kidneys declines with age; elderly individuals are therefore assumed to have mild renal impairment. Metabolic clearance is primarily reduced with drugs that display high hepatic extraction, whereas the metabolism of drugs with low hepatic extraction is usually not diminished. Reduction of metabolic drug elimination is more pronounced in malnourished or frail subjects. In addition, the water content of the aging body decreases while the fat content rises. Therefore, the distribution volume of hydrophilic compounds is reduced in the elderly, while that of lipophilic drugs is increased. Intestinal absorption of most drugs is not altered in the elderly. Aside from these pharmacokinetic changes, one of the characteristics of old age is a progressive decline in counter-regulatory (homeostatic) mechanisms. As a result, the effects of drugs are mitigated less, reactions are usually stronger than in younger subjects, and the rate and intensity of adverse effects are higher. The brain is an especially sensitive drug target in old age. Psychotropic drugs, anticonvulsants and centrally acting antihypertensives may impede intellectual functioning and motor coordination. The antimuscarinic effects of some antidepressants and antipsychotic drugs may produce agitation, confusion, and delirium in the elderly. Hence drugs should be used very cautiously in geriatric patients. If drug therapy is indicated, the dosage should be titrated to a clearly defined clinical or biochemical therapeutic goal starting from a low initial dose.

Older patients may also take longer to recover from depressive episodes, and such delay in response should not be taken as treatment failure. Sackeim et al. (2005) analysed data from two drug trials, one comparing sertraline and fluoxetine and the other sertraline and nortriptyline, in older persons. If there was little or no improvement (30% or less on a recognised mood rating scale) by week 4, then recovery or remission was unlikely, a finding that is no different than is found in younger adults. On the other hand, patients who have started to improve may continue to do so for 8 to 12 weeks. It is useful to consider depression management in units of 4 weeks, with decision points at each of these. Relapse and recurrence commonly occur in older people; these setbacks mandate close follow-up of patients whose symptoms have resolved and energetic attempts at prevention of further relapse or recurrence.

Interventions focused on close family members may play a crucial role in the management of depression in the elderly. Family members may require an explanation that a depressive disorder is not the result of failure of willpower and that appeals to the patient to “pull yourself together” or “make an effort” can increase his or her feelings of helplessness and guilt. The clinician must also encourage family members to come to terms with and express their feelings about the depressed person. These feelings (which may be important contributors to the maintenance of the depression) often include guilt, aggression, and exhaustion.

The following general recommendations may be useful to multidisciplinary care providers for older people with depressive disorders:

- Establish and maintain optimal contact, even in the face of sensory, cognitive, emotional, or behavioural obstacles.
- Avoid assuming that depressive symptoms are an inevitable consequence of aging and/or adverse circumstances.
- Remember that some improvement can almost always be achieved both in patients’ specific symptoms and in their general circumstances.
WHEN TO SEEK SPECIALIST REFERRAL OR HOSPITALIZATION

Table 5.1 summarises situations in which a referral to a psychiatrist may be appropriate. Referral to a specialist should be sought if the diagnosis is in doubt, initial attempts at treatment have failed, the situation is complicated by serious comorbid conditions, insufficient family support is available, or the patient’s safety is at risk because of neglect (poor food and fluid intake, deteriorating self-care) or suicide.

Hospitalization should generally occur only after multidisciplinary discussion and with the agreement of the patient and family. If the patient is at risk and/or has lost insight, appropriate mental health legislation may need to be invoked to allow hospitalization without patient consent. The responsible clinician(s) (usually the general practitioner and specialist together) must assume responsibility for such decisions, after having established the lack of other choices. This information should be imparted to the patient in the presence of the family in order to facilitate acceptance and foster maintenance of a therapeutic relationship.

TREATMENT MODALITIES FOR ELDERLY PATIENTS WITH DEPRESSIVE DISORDERS

A wide range of pharmacological, psychological, and other therapies are effective in treating depressive disorders in older persons (Tables 5.2 and 5.3). These treatment approaches should be thought of as synergistic rather than mutually exclusive and should be integrated wherever possible into an individualized treatment plan.

Pharmacological Treatment

It is perhaps surprising that, despite the clear effectiveness and relative safety of antidepressant drugs in the elderly (discussed below), they are still under-used in older patients. A study in the United Kingdom, for example, revealed that only 10 of 103 elderly patients with a depressive disorder who were identified in a community survey were receiving antidepressants, although one third of them took psychotropic medication, mainly antipsychotics and benzodiazepines (Manela et al, 1996).

Efficacy of antidepressant medications in older patients

In general, antidepressants are as effective in the elderly as in younger patients (Anstey and Brodaty 1995; Gerson et al. 1988; Katona and Judge 1996; Alexopoulos 2005), with clinical trial response rates of 50%–60%. These reviews, as well as a meta-analysis of published studies (Mittmann et al. 1997), also suggest that, in older subjects, there is little difference in efficacy among antidepressant classes (e.g., tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs], reversible monoamine oxidase inhibitors [RIMAs], other atypical antidepressants), although the meta-analysis by Mittmann et al. suggested that the atypical antidepressants mianserin and trazodone may be less effective. A recent systematic review of 26 randomized trials comparing antidepressant classes in patients aged 55 and older found little difference in efficacy between medications (Mottram et al. 2006). However, there was a higher withdrawal rate due to side effects in patients treated with TCAs than SSRIs (Wilson and Mottram 2004). These findings suggest that side-effect profiles should be the major determinant in medication selection.

TABLE 5.1

When to refer to a psychiatrist

- When the diagnosis is in doubt
- When the depressive disorder is severe and is characterized by:
  - Psychotic symptoms (e.g., example, delusions)
  - Severe risk to health because of failure to eat or drink
  - Suicide risk
- When an organic cause is under consideration
- When complex therapy (especially in the case of medical comorbidity) is necessary
- When first-line antidepressant therapy has failed
- When a patient cannot tolerate medication
- When family support is lacking
### TABLE 5.2
Pharmacological treatments for depressive disorders in older patients

<table>
<thead>
<tr>
<th>Medications</th>
<th>Starting dose (mg/day)(^1)</th>
<th>Therapeutic dose range (mg/day)(^1)</th>
<th>Medications</th>
<th>Starting dose (mg/day)(^1)</th>
<th>Therapeutic dose range (mg/day)(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
<td></td>
<td></td>
<td><strong>Selective serotonin reuptake inhibitors (SSRIs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>30–75</td>
<td>25–150</td>
<td>Fluoxetine</td>
<td>20</td>
<td>20–40</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>10</td>
<td>30–75</td>
<td>Fluvoxamine</td>
<td>50–100</td>
<td>50–300</td>
</tr>
<tr>
<td>Dothiepin</td>
<td>50–75</td>
<td>25–150 (75 may be sufficient)</td>
<td>Paroxetine</td>
<td>20</td>
<td>20–40</td>
</tr>
<tr>
<td>Imipramine</td>
<td>10</td>
<td>30–50</td>
<td>Sertraline</td>
<td>50</td>
<td>50–200</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>10–30</td>
<td>30–50</td>
<td>Citalopram</td>
<td>20</td>
<td>20–40</td>
</tr>
<tr>
<td>Lofepramine</td>
<td>140</td>
<td>140–210</td>
<td>Escitalopram</td>
<td>10</td>
<td>10–20</td>
</tr>
<tr>
<td><strong>Serotonin norepinephrine reuptake inhibitors (SNRIs)</strong></td>
<td></td>
<td></td>
<td><strong>Reversible Monoamine Oxidase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 (twice daily)</td>
<td>75–150 (maximum 375)</td>
<td>Inhibitors (RIMAs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Moclobemide</td>
<td>300</td>
<td>150–600</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>20–30</td>
<td>40–60</td>
<td>5-HT2 Receptor Blockers</td>
<td>100</td>
<td>100–300</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trazodone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NASSA</td>
<td>15</td>
<td>15–45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mirtazapine</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mianserin</td>
<td>30</td>
<td>30–90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bupropion XL(^2)</td>
<td>150</td>
<td>150–300</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reboxetine(^3)</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

\(^1\)These are suggested average starting and therapeutic doses for antidepressants in the United Kingdom (British National Formulary, vol 52, September 2006; published by the British Medical Association and the Royal Pharmaceutical Society of Great Britain). Some drugs, notably the tricyclic antidepressants, have a very wide therapeutic range, and higher levels may be used when tolerated. Elderly Asian patients may not be able to tolerate higher doses of tricyclic antidepressants.

\(^2\)The doses are suggested in the manufacturer’s prescribing information.

\(^3\)Katona et al, 1999
Newer antidepressants

Several other newer antidepressants have recently become available. These include venlafaxine (which selectively inhibits reuptake of both serotonin and noradrenaline), reboxetine (a selective inhibitor of noradrenaline reuptake), and mirtazapine (which blocks presynaptic a2 adrenoceptors and facilitates release of both noradrenaline and serotonin).

Venlafaxine and duloxetine are two available serotonin-norepinephrine reuptake inhibitors (SNRIs). These agents may also be useful in patients with comorbid pain. Recent double-blind, placebo-controlled studies of escitalopram and venlafaxine did not show significant difference in efficacy among placebo, fluoxetine, and the two newer antidepressant in 8-week trials (Kasper et al. 2005; Schatzberg and Roose 2006). Duloxetine was found to produce significantly greater improvement compared with placebo in cognition and depression in elderly patients in a recent multi-centre, randomized, double-blind, placebo-controlled study (Wise et al. 2007). Few studies have compared the use of SSRIs and SNRIs in the elderly. Frail nursing home residents showed a poorer tolerance to venlafaxine when compared with sertraline in one study (Osling et al. 2003).

Mirtazapine is another agent with serotonergic and noradrenergic properties. It appears to be useful in elderly patients with insomnia, agitation, or restlessness, and anorexia or weight loss. Bupropion is considered an activating agent, so it may be useful in patients who complain of lethargy, daytime sedation, or fatigue. Very limited evidence from clinical trials is available concerning use of traditional monoamine oxidase inhibitors (MAOIs) in elderly patients (Mittmann et al. 1997).

Placebo-controlled evidence concerning use of antidepressants in the elderly is relatively sparse, particularly in the case of the newer drugs, although some placebo-controlled data are available concerning the SSRIs citalopram (Nyth et al. 1992) and fluoxetine (Tollefson and Holman 1993) and the reversible selective MAO-A inhibitor moclobemide (Amrein et al. 1997). Even though the clinical trial populations in such studies are somewhat unrepresentative—subjects are in relatively good physical health and few “very old” subjects are included—clinical experience suggests that antidepressants do indeed remain effective in older people.

Antidepressant Safety and Tolerability

Considerable age-related changes occur in the absorption, transport, metabolism, distribution, and excretion of antidepressant drugs (Baumann et al. 1998). However, the drug-handling characteristics of those over 65 years of age are far from homogeneous; great variability occurs both within the chronological age bracket of individuals 65 to 100 year of age or older and in the biological age that characterises each individual (Dufour et al. 1994).

On average, a given dose of a TCA will generate higher plasma levels in older patients than younger patients, reflecting reduced creatinin clearance, hepatic blood flow, and plasma protein levels. The elimination half-life of some SSRIs (e.g., citalopram, paroxetine) is significantly increased in older persons, while that of others (e.g., fluvoxamine, fluoxetine) is similar to that in younger patients.

<table>
<thead>
<tr>
<th>Psychological Treatments</th>
<th>Other Treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Supportive</td>
<td>• Electroconvulsive therapy</td>
</tr>
<tr>
<td>• Problem-solving</td>
<td>• Brain stimulation therapies</td>
</tr>
<tr>
<td>• Interpersonal</td>
<td>• Sleep deprivation</td>
</tr>
<tr>
<td>• Family</td>
<td>• Phototherapy</td>
</tr>
<tr>
<td>• Cognitive-behavioural</td>
<td>• Alternative (e.g., herbal)</td>
</tr>
<tr>
<td>• Mindfulness-based</td>
<td></td>
</tr>
<tr>
<td>• Behavioral activation</td>
<td></td>
</tr>
<tr>
<td>• Dynamic</td>
<td></td>
</tr>
<tr>
<td>• Self-help techniques/ exercise</td>
<td></td>
</tr>
</tbody>
</table>

**TABLE 5.3**

Psychological and other treatments for depressive disorders in older patients

**Psychological Treatments**
- Supportive
- Problem-solving
- Interpersonal
- Family
- Cognitive-behavioural
- Mindfulness-based
- Behavioral activation
- Dynamic
- Self-help techniques/exercise

**Other Treatments**
- Electroconvulsive therapy
- Brain stimulation therapies
- Sleep deprivation
- Phototherapy
- Alternative (e.g., herbal)

**Newer antidepressants**

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**Antidepressant Safety and Tolerability**

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Some of the side effects of the TCAs are potentially more hazardous for older patients. These side effects include:

- Anticholinergic-induced aggravation of glaucoma, constipation, urinary retention, and confusion
- Antiadrenergic-induced postural hypotension
- Antihistaminic sedation

Not all TCAs have equal propensity to produce such side effects. In particular, nortriptyline (Miller et al. 1991) and lofepramine (Ghose and Sedman 1987) are relatively well tolerated by older individuals. The most important results of these side effects are probably increases in the risks of accidents and falls (Campbell 1991, Liu et al. 1998), potentially resulting in osteoporosis-related fractures.

Traditional MAOIs have a side-effect profile similar to that of the TCAs in older people, with the additional problem of requiring patients to adhere to a low-tyramine diet. In contrast, the SSRIs are relatively free of the side effects typical of TCAs, although sedation may occur. Their main side effects (nausea, diarrhea, headache, agitation) are less troublesome than those of TCAs in older people. Clinical experience also suggests that the SSRIs are associated with better adherence to treatment in older people. Agitation, inappropriate anti-diuretic hormone (ADH) secretion (Kirby and Ames 2001), and the slight risk of gastro-intestinal bleeding (van Walraven et al. 2001) have been reported to be more common in older patients. Moclobemide has similar kinetics in older and younger depressed patients and is well tolerated by older persons (Amrein et al. 1997).

The dual action antidepressants and SSRIs have resulted in the serotonin syndrome, but more data are needed to identify risk factors in elderly patients. Serotonin syndrome manifests as altered mental status, myoclonous, tremor, hyperreflexia, fever, and autonomic changes.

Practical considerations in prescribing antidepressant medications for older patients

The prescription of an antidepressant is only one of the elements of management and should form part of an integrated approach to the patient. A relationship of trust must be established between the physician and the patient in order to ensure the best possible adherence to treatment. Providing patients and caregivers with appropriate information about the characteristics of antidepressants is likely to increase adherence to the treatment regimen (Table 5.4). A more detailed discussion of educational materials for patients and families is provided in the Appendix to Volume I, Part 1.

The maxim, “Start low, go slow” is particularly useful in treating older patients with antidepressants. Tolerability may be enhanced by starting with divided doses, although for most TCAs (and other antidepressants) it is usually possible to move rapidly to a single daily dose, which promotes adherence. SSRIs can usually be started at a therapeutic dose, but if side effects are troublesome, initial dose reduction and a subsequent slow increase may be helpful.

TABLE 5.4

Information about antidepressants to provide to patients and caregivers

- “Start low, go slow”
- Describe typical side effects
- Inform patients about delay in onset of therapeutic action
- Reassure patients that drugs do not produce dependence
- Stress need for continued treatment following initial response
Patients should be closely followed up during the first few weeks of treatment (ideally, weekly visits) to monitor both side effects and treatment response. Therapeutic response may not emerge until 6 to 12 weeks after antidepressants are started (Lotrich and Pollock 2005; Sackeim et al. 2005).

In 2004, the U.S. Food and Drug Administration added its strongest warning label—the "black box"—on the newer antidepressants. It warns that children and teenagers who take the medications may be at higher risk of suicide. Recent data suggest that there is increased risk of suicidal thoughts and behaviours among children, adolescent, and adults younger than 25 taking newer generation antidepressants. However, for adults between 25 and 64 years of age, the antidepressants appeared to be neutral or possibly protective against these problems, and for individuals aged 65 or older, drugs reduced the risk (Kuehn 2007). One study did suggest an increased rate of suicide in men 66 years of age and older in the first month of treatment with an SSRI, compared to other antidepressant drugs; this effect was not seen during subsequent treatment (Juurlink et al. 2006). Monitoring for suicide risk is recommended in early therapy with an SSRI. Clinical observations suggest that improvement of psychomotor retardation without a concurrent lift in mood symptoms may contribute to this risk.

Adjunctive medication

In general, use of several medications at the same time should be minimised in older subjects to reduce the risk of adverse effects. In some cases, however, adjunctive medications may be helpful. These include the following situations:

- **Delusional depression** is unlikely to respond to antidepressants alone. Although ECT is the treatment of choice, administration of antipsychotic medication in combination with conventional antidepressant treatment may be effective. The risk of extrapyramidal symptoms (particularly, tardive dyskinesia) must be considered and may be reduced by using newer antipsychotic agents, such as amisulpride, aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone.

- **Anxiety symptoms** are often prominent in the context of depressive disorders in old age. They usually resolve along with the depressive symptoms, but symptomatic treatment may be required early in treatment (during the first 2–3 weeks) when the anxiolytic effect of the antidepressant has not yet emerged. Benzodiazepines and low-dose antipsychotics may be effective, but a morning dose, when anxiety is at its peak, is sufficient. It is important to limit the period of administration as much as possible and to reduce the dose progressively once depressive symptoms resolve.

- **Sleep disturbance** may be a prominent and troublesome feature of depressive disorders in old age and may be particularly intolerable for spousal caregivers. Such sleep disturbance may respond to sleep hygiene measures (regular bedtime, a hot sweet beverage). Disrupted sleep may reflect a concomitant physical illness (cardiac insufficiency, pain) that requires treatment in its own right. Like anxiety symptoms, depression-related sleep disturbance usually responds to primary treatment of the depressive disorder. Short-term use of hypnotics (benzodiazepines, zopiclone, zolpidem, chloral hydrate) may be helpful with the same provisos as for anxiolytics. The use of relatively sedating antidepressants (trimipramine, mianserin, mirtazapine) may also be helpful.

- **Appetite and digestion** problems may emerge with or be exacerbated by depressive disorders and their treatment (for example, constipation may be worsened by TCAs). Advice about appropriate diet and/or the use of a mild laxative may be required to alleviate discomfort.

Psychological Treatments for Depression in Older Patients

Although it is difficult to compare the efficacy of pharmacotherapy and psychotherapy in late-life depression, based on findings from a meta-analysis, Pinquart et al. (2006) reported that outcomes were very similar and that both treatments have reasonable effect sizes, so that patient preference should be a factor in selecting a treatment option.
Supportive psychotherapy

Supportive psychotherapy may be provided within the setting of primary care consultation. The supportive psychological approach combines listening, counselling, and practical support, all within a general framework of “empathy” or solidarity without identification. Listening may involve allowing patients to express their feelings of guilt, incapacity, and helplessness, as well as identifying real or imagined family conflicts and difficulties. Counselling involves mobilising the patient’s existing psychological resources. This approach should be neutral, free of value judgments, and nondirective. It is important to encourage patients to pursue realistic ambitions and to discourage them from making long-term decisions that could be negatively influenced by a distorted perception of reality. For example, patients should be discouraged from moving out of their home when their main motivation for doing so is depression-related dissatisfaction with a current living situation that is, in reality, adequate. Support may also include mobilising help for practical problems, because depressed patients are often unable to take the necessary steps to obtain help or care in the home or to ask for assistance in the management of their own affairs.

Problem-solving therapy

Problem-solving therapy (PST) is a brief structured psychotherapy in which the patient is supported by the therapist in learning about and applying a structured approach to address problems that are causing symptoms. Briefly, PST consists of seven consecutive stages (problem definition, goal definition, generating alternative solutions, decision-making stage, evaluating and choosing solutions, solutions implementation, and evaluating the outcome.), that are applied to at least one problem per treatment session (Haverkamp et al. 2004). PST emphasises the importance of facilitating the patient’s development of a new skill, in which the patient recognises potential solutions to his or her problems rather than solutions being suggested by the therapist. It involves patients developing skills that will empower them to solve any future problems. Alexopoulos et al. compared the efficacy of PST and supportive therapy in a group of depressed elderly subjects with impairment in executive functions. They found that PST was more effective than supportive therapy in leading to remission of depression, and that patients receiving PST had fewer post-treatment depressive symptoms as well as less disability (Alexopoulos et al. 2003). Gellis et al. (2007) found that Brief Problem-Solving Therapy in Home Care was well tolerated and held promise for reducing persistent symptoms in older adults with severe depressive symptoms in an acute home care setting after 6 months.

Interpersonal psychotherapy

Interpersonal psychotherapy (IPT) is a manual-based psychotherapy. Its therapeutic focus is limited to current interpersonal relationships in four broad areas: abnormal grief, role transition, role dispute, and interpersonal deficits. Generally, IPT therapist meets with patients for 12 to 20 weekly 50-minute face to face sessions. IPT seems to be a suitable form of psychotherapy for older primary care patients. Therapists with different therapeutic backgrounds can learn this therapy easily. It was found to be more effective than usual general practitioner’s care for elderly patients with moderate to severe major depressive disorder in real-life general practice (van Schaik et al. 2006).

Family therapy

Family-based approaches may be offered both in primary care settings and following referral to a specialist. The clinician will first try to estimate the level of commitment of those closest to the patient in terms of presence, attitudes toward illness, and implications for their relationships. Some families have a tendency to minimise the depressive disorder, mistakenly considering it to be part of the normal aging process; others will goad the patient into social activities that inspire fear, with the risk of reinforcing feelings of inadequacy. Those closest to the patient could end up exhausted by a situation of long, drawn-out confrontation and may become depressed or aggressive themselves.
Giving support to the patient’s social circle begins by listening attentively in order to foster an atmosphere of confidence. Explaining the nature of the illness and its symptoms, and analysing quirks in the patient’s behaviour are essential. This type of discussion favours the expression of feelings, including anger, aggression, and guilt toward the patient.

During family sessions, the person closest to the patient must be helped to express his or her own feelings of helplessness and frustration; this will help mobilise family solidarity. The family can benefit from simple advice on how to respond to pessimistic or defeatist statements by the patient—by countering the patient’s negativity with the expression of one’s own feelings, such as “I know how you feel.” It is also useful to implement behavioural techniques, such as distancing oneself for progressively longer periods from a patient who abusively demands that he or she be constantly attended to, in order to persuade the patient to take steps to regain his or her autonomy (Blazer 1982).

Cognitive-behavioural therapy

Cognitive psychotherapy has been extensively used and evaluated in the treatment of depressive disorders in older people with depressive disorders. The therapeutic framework emphasises changing dysfunctional thoughts (maladaptive values, attitudes, and thinking patterns) rather than attempting to alter depressed mood directly. The main strategies used in achieving therapeutic change are:

- Identifying negative thoughts
- Evaluating their validity
- Substituting more positive and realistic thoughts
- Modifying dysfunctional attitudes

In practice, cognitive therapy (CT) is often combined with behavioural techniques to form cognitive-behavioural therapy (CBT). The behavioural component aims to break a depressive cycle through graded task assignments that are enjoyable and goal directed, resulting in an increased sense of achievement and self-esteem.

For example, patients who used to enjoy outdoor activity may start a graded program of short walks or gardening. While the acute response to CBT does not seem to have advantages over pharmacology, it may be helpful in the prevention of subsequent episodes of illness.

CT and CBT techniques require specific training but can be administered by clinicians from a variety of professional backgrounds (e.g., psychiatry, primary care physicians, psychology, nursing, social work, occupational therapy). They may be offered in the primary care setting or following referral to a specialist. A course of treatment usually consists of a limited number of sessions (usually about 12 to 16) and may be given on a one-to-one basis or in groups. CBT techniques that have been evaluated for late-life depression include cognitive therapy, social problem solving therapy, problem solving therapy for primary care, and self-management therapy. A review of 18 outcome studies (Koder et al. 1996) confirmed that outcomes in CT or CBT are comparable in older and younger patient groups, with demonstrated superiority to use of no treatment or placebo. CT and CBT seem equally effective if given in individual or group settings. Response to CT or CBT is less likely in patients with co-existing personality disorder, rigid thinking styles, severe depressive disorder, and/or prominent biological symptoms. Response to these techniques is particularly unlikely in patients with depressive delusions or hallucinations.

Short-term treatments, including CBT, IPT, and PST, delivered over a period of 2–4 months, have been shown to be effective in older populations. Research from Project IMPACT demonstrated the feasibility and cost-effectiveness of a primary-care-based treatment program that offered a choice of antidepressant medication and/or a brief, structured form of PST (Unutzer et al. 2002). Psychotherapy and community-based programs for older adults may be particularly helpful for patients with minor depression, for whom pharmacological intervention has not demonstrated consistent effectiveness (Lyness et al. 2006).
**Mindfulness-based cognitive therapy**

Mindfulness-based cognitive therapy (MBCT) is a meditation-based intervention designed to reduce recurrence in people with a history of relapsing major depression. Its aim is to teach participants to disengage from those cognitive processes that may render them vulnerable to future episodes. Early findings suggested that MBCT was promising as a cost-effective addition to clinicians’ repertoire for addressing depression in old age and that it might be a helpful intervention for elderly patients who suffer from recurring depression (Smith et al. 2007).

**Behavioral activation treatment**

Activity scheduling is a behavioural treatment for depression in which patients learn to monitor their mood and daily activities and to increase the number of pleasant activities and positive interactions with their environment. Activity scheduling is an attractive treatment for depression because it is relatively uncomplicated and time-efficient and does not require complex skills from patients or therapists. It had been shown to be effective in a recent meta-analysis (Cuijpers et al. 2007).

**Dynamic psychotherapy**

There has been little formal evaluation of analytic therapies in older people, although psychodynamic group therapy was shown by Steuer et al. (1984) to have efficacy similar to CBT.

**Self-help techniques**

Self-help techniques may be particularly beneficial in milder depressive disorders. These approaches include gentle physical exercise, maintaining a social and activity routine, getting up and going to bed at usual hours, preparing and eating meals as usual, and keeping in touch with friends. Eating regular, well-balanced meals should be encouraged, even if appetite has diminished, in order to keep weight constant and to avoid deterioration in the general state of health.

During periods of insomnia, the patient might be advised to get out of bed, to sit in an armchair, and to try to occupy the mind by watching television, listening to the radio, or reading a magazine. The patient should also be urged to maintain good hygiene and to continue to bathe; men should be encouraged to shave, women to take an interest in their appearance by styling their hair and putting on make-up. These recommendations are accompanied by a recognition of the difficulty, inherent in illness, of accomplishing these tasks. Their role in overcoming feelings of helplessness, hopelessness, and incapacity should be emphasised.

Based on a systematic review of the effects of exercise on depressive symptoms in later life, Sjosten and Kivela (2006) concluded that both aerobic and non-aerobic exercise can be effective in those with depressive disorders or even with sub-syndromal depression. As a sole treatment, the effects may be short-lived but exercise and/or purposeful activity should be considered as part of the management programme for elderly individuals with depression.

**Other Treatments**

**Electroconvulsive Therapy (ECT)**

ECT is an effective treatment for severe depressive disorders in older people, in whom it is also surprisingly safe (Mulsant et al. 1991; Wilkinson 1993). Response rates exceeding 80% can be expected. ECT is the treatment of choice in severe delusional depression in older persons, when retardation, stupor, or suicide is prominent, and particularly when it has been effective during previous episodes.

The rate of ECT-associated mortality is very low, estimated to be about 1 per 10,000 mixed-aged patients treated and comparable to that observed with general anaesthesia in minor surgery. ECT can be safely given to patients with dementia and is effective in these patients, albeit with a high rate of transient delirium (Rao and Lyketsos 2000).

Older patients referred for ECT require a full physical and anaesthetic review. MAOIs and benzodiazepines should be discontinued when possible, Both unilateral and bilateral electrode placement are effective. Unilateral ECT may be associated with diminished neuropsychiatric side effects, particularly if older apparatuses delivering sinusoidal current are used; bilateral ECT, using a brief-pulse technique, more easily avoids subthreshold or ineffective convulsions.
While ECT must be given in a specialist setting, it is important for primary care clinicians to be aware of its availability, effectiveness, and side effects, particularly since widespread lay prejudice exists against its use. The prospect of ECT can cause considerable anxiety, which can effectively be addressed by allowing patients’ misconceptions to be aired (Wilkinson 1993).

It is useful to share the following information about ECT with patients and caregivers:

- Treatment usually consists of 2 sessions a week, with a total of 6 to 12 sessions
- It is not the brief electric shock that is therapeutic but the changes in brain electrical activity that it triggers.
- ECT is carried out after administration of a short-acting general anaesthetic and a muscle relaxant that minimises the bodily convulsion and its associated risks.
- ECT does not damage the brain; however, it may (particularly in older subjects) induce transient (lasting a matter of hours) post-ictal confusion or headache and memory deficits, particularly anterograde amnesia, which resolve over 3 to 6 months.
- ECT rarely causes serious physical or psychiatric complications.

Contraindications to ECT include recent stroke or myocardial infarction, unstable coronary artery disease, and space-occupying brain lesions. The increased risks of ECT in such circumstances must be weighed against the risks of withholding treatment in severe depression, especially if other treatments have failed. Cardiac monitoring by a cardiologist during ECT will reduce the risk.

The main difficulty with ECT is the 50% or so relapse rate after recovery in the ensuing 6-12 months. This warrants the use of medications for prevention, for which the best evidence supports lithium combined with an antidepressant (Sackeim et al. 2001). Maintenance ECT is indicated for those patients who have responded to ECT but who have failed previous trials of medications. In maintenance treatment; ECT is given at a reduced frequency, biweekly to monthly or less often.

Cognitive effects in the elderly are generally minor (Rami et al. 2004). Maintenance phase strategies to prevent depression relapse may include ECT and medication, used either singly or in combination.

**Brain stimulation therapies**

Brain stimulation therapies have been evaluated in the treatment of medication-resistant depression, although there are very limited data concerning these strategies in elderly patients. These therapies include repetitive transcranial magnetic stimulation (rTMS), deep brain stimulation (DBS) used for some patients with Parkinson’s disease, and vagus nerve stimulation (VNS), used in the treatment of epilepsy. The U.S. Food and Drug Administration approved VNS in 2005 for adjunctive use in treatment-resistant depression, defined as patients with chronic depression who have failed at least four adequate antidepressant trials. VNS has not yet been shown to be effective for acute depressive episodes (George et al. 2007). There is now clear evidence for the statistical superiority of left-prefrontal high frequency rTMS compared with sham therapy. However, the clinical benefits are marginal in the majority of reports. There is also still considerable uncertainty concerning optimal stimulation parameters (Mitchell and Loo., 2006). Nonetheless, there is still a dearth of specific evidence concerning the efficacy of DBS, VNS and TMS in the treatment of geriatric depression.

**Alternative Treatments**

**Sleep deprivation** may be dramatically effective in relieving depressive symptoms. The technique usually consists of preventing sleep either for a whole night or for the latter half of the night (after 2 or 3 A.M.), on two or three nights per week (Pitt 1993). However, symptoms usually recur when the usual sleep rhythm is re-established. In responsive cases, maintenance sleep deprivation at home, with spousal co-operation, may be useful. Smith et al. (1999) found that total sleep deprivation might accelerate the clinical response to antidepressant treatment in elderly depressed patients but Reynolds et al. (2005) found the opposite in a recent randomized trial.
Phototherapy has not been evaluated in older persons, but several trials suggest that it is effective in reducing symptoms of seasonal affective disorder (Eastman et al. 1998; Lewy et al. 1998; Terman et al. 1998). Neumeister et al. (1996) suggested that bright light therapy might be efficacious in preventing relapse after partial sleep deprivation.

Herbal remedies are currently being promoted, but evidence of their efficacy has yet to be established through randomized controlled trials. St John’s Wort (SJW) is the popular name for the plant Hypericum perforatum. A number of trials have been published that examined the efficacy of SJW in the treatment of depression. They have been extensively reviewed and most authors conclude that SJW may be effective in the treatment of mild-to-moderate depression (Gaster and Holroyd 2000). However, the active ingredient and mechanism of SJW is still not well understood and the efficacy of SJW in geriatric depression has not yet been established. SJW may be problematic because of its ability to induce CYP3A4, an enzyme involved in the biotransformation of more than 50% of all prescription medications, which can pose a risk for pharmacokinetic herb-drug interactions in the elderly.

REFRACTORY DEPRESSIVE DISORDERS

When patients fail to respond to standard treatments, a full critical review is necessary that should cover the following issues:

• Accuracy of diagnosis or diagnoses
• Adequacy of previous treatment (dose, duration)
• Adherence to with previous treatment
• Maintenance factors (poor social circumstances, occult thyroid disease, chronic pain)

Several regimens have been proposed for the treatment of refractory depression in older individuals in whom no clear reason for prior treatment failure can be identified (Flint 1995). The most important of these are ECT (Benbow 1989) and lithium augmentation (van Marwijk et al. 1990). Lithium can be useful in the long-term treatment of depressive disorders in old age, but its use can be problematic because age-related pharmacodynamic changes can result in both therapeutic and toxic responses at relatively low doses and blood lithium levels. Augmentation with lithium may be effective in about 50% of patients who do not respond to antidepressant monotherapy but toxicity may occur in 11%–23% (Baldwin et al. 2002). In addition, lithium-induced neurotoxicity is common in older subjects, particularly those with Parkinson’s disease and/or cognitive impairment.

In mixed-age patients with more rigorously defined treatment-resistant depression, venlafaxine and ECT have been reported to show rates of recovery of 30% and 50%, respectively (Baldwin et al. 2002). In a study of 53 elderly subjects with prospectively defined treatment-resistant major depressive disorder who had failed to respond to treatment with paroxetine plus IPT, Whyte et al. (2004) observed similar rates and speed of response with an augmentation strategy (using sustained-release bupropion, nortriptyline, or lithium) and a strategy of switching to venlafaxine XR. Venlafaxine XR was generally better tolerated than the augmentation strategies. Dew et al. (2007) examined the likelihood, speed, and predictors of recovery in elderly patients receiving augmentation with bupropion, nortriptyline, or lithium after an inadequate response to standardised treatment with paroxetine plus IPT. Although certainly not uniformly successful, the result was as good as or better than that reported in the comparable STAR*D study in younger adults (Rush et al. 2006). Mazeh et al. (2007) compared the efficacy and tolerability of venlafaxine and paroxetine in elderly patients suffering from treatment-resistant major depression who had not responded to at least two previous adequate trials of antidepressants. Significant improvement in scores on the Hamilton Rating Scale for Depression from baseline to endpoint were observed in both groups of patients. Remission rates were higher for venlafaxine, and tolerability was acceptable with both agents.
More limited, but placebo-controlled, evidence exists concerning the use of phenelzine (Georgotas et al. 1983) and methylphenidate (Wallace et al. 1995). In a 6-week, open, randomized, controlled study with a 2-year follow-up, Kok et al. (2007) studied 29 elderly inpatients with major depressive disorder diagnosed according to DSM-IV criteria who had previously failed to respond to one or more adequate trials of a TCA or venlafaxine. Subjects received either lithium augmentation or the MAOI phenelzine. They found that lithium was more effective than phenelzine in elderly patients with treatment-resistant major depressive disorder; tolerance for both treatments was remarkably good in this group of elderly inpatients with many comorbid medical disorders. These treatment regimens require specialist referral and close monitoring. But primary care clinicians should be aware of the variety of useful treatments available in order to encourage realistic optimism in both patients and caregivers.

**PHASES OF TREATMENT**

The management of depressive disorders in older people (as in earlier phases of life) can be conceptualised as involving interventions in three phases: 1) during the acute phase to achieve resolution of symptoms, 2) during the continuation phase to prevent relapse, and 3) during the maintenance phase to prevent recurrence (Figure 5.1).

The treatment approaches discussed in the preceding sections refer mainly to the acute phase. In view of the high rates of relapse and recurrence of depressive disorders in older persons, the initial management plan formulated for individual patients should include provision for continuation and maintenance treatment. These treatment phases may be influenced by treatment adequacy, aftercare, and prophylaxis, forming a matrix of care.

**FIGURE 5.1**

Response, Remission, Recover, Relapse, and Recurrence
Acute Treatment
Flint and Rifat (1996) evaluated the response of 101 patients with major depression (diagnosed by DSM-III-R criteria) to sequential regimens of antidepressants and ECT. By 28 weeks, 83% of the patients had recovered with one of the regimens.

Continuation Therapy
This refers to the period after remission during which treatment should be continued in order to minimise the risk or relapse. This period is usually specified as 6 months in general adult psychiatry, but the main period of risk in older adults may last as long as 2 years (Flint & Rifat 1997; Old Age Depression Interest Group 1993). Escitalopram has recently been shown to be effective in preventing relapse in major depressive disorder in elderly patients and to be well tolerated as a continuation treatment in 52-week open-label trials (Kasper et al. 2006; Gorwood et al. 2007).

Maintenance Treatment
In the Old Age Depression Interest Group study (1993) of 219 patients with major depression, 69 recovered sufficiently to enter a 2-year double-blind placebo-controlled trial of dothiepin. Survival analysis showed that dothiepin reduced the relative risk of relapse/recurrence by a factor of 2.5 times. There is also evidence for the prophylactic benefit of citalopram (Klysner et al. 2002) and paroxetine (Reynolds et al. 2006). Reynolds et al. (1999) completed a 3-year, randomized, placebo-controlled trial of nortriptyline, IPT, and the combination of the two in the maintenance treatment of patients with major depression who were 60 years of age and older. The study found that the combination had the greatest effect in preventing recurrence, with nortriptyline alone also showing considerable benefit. In contrast, a recent study by the same group (Reynolds et al. 2006) in patients 70 years of age and older who suffered from late-onset depression showed that 2 years of maintenance treatment with paroxetine was effective in preventing recurrence, while maintenance IPT was not found to be useful. The authors suggested that this might be due to differences in the patient groups. They argued that more patients with early cognitive impairment were recruited in the recent study and they might not have been able to fully utilise IPT. Patients with late-onset depression may be a heterogeneous group, some of whom may be in preclinical stages of dementia. Clearly more research is required to examine the role of psychotherapy in maintenance treatment of older adults with depression.

There is an argument for indefinite long-term treatment of any newly presenting episode of major depressive disorder in an older patient. An elderly person in his or her 70s may have an expected life span of 5 years; therefore, the potential to prevent 6 months of morbidity due to a recurrence of depressive illness is an important gain. Thus considerations in this situation differ from those that may apply to a patient in his or her 30s. However, there should not be a general directive to treat indefinitely as it is a matter of weighing up individual risks and benefits, and one should always involve the patient in the decision-making.

Patients with two or more recurrences in the past 2 years, serious ill health, chronic social difficulties, or very severe depression should be offered prophylaxis with either an antidepressant at a dose as close as possible to the treatment dose (Old Age Depression Interest Group 1993) or lithium, which is as effective in older people as it is in younger people (Abou-Saleh and Coppen 1983).

Aftercare
Without planned aftercare, patients can slip through the net and/or their relapses or recurrences can go unnoticed. Given that the highest risk of return of symptoms occurs relatively early, aftercare should be continued for a minimum of 12 months and preferably for 2 years.
PREVENTION OF RECURRENCE

In addition to continuing medication, social and psychological support can prove very beneficial in preventing recurrent episodes of a depressive disorder. Blanchard et al. (1995) have shown the benefits of deploying a psychiatric nurse within the community to manage and follow up patients with depressive disorders. In this study, a multifactorial approach was adopted, using interventions such as social support, counselling, education, and helping the patient attend a day care center. Ong et al. (1987) demonstrated that a support group for discharged elderly patients with depressive disorders, run by a social worker and a community psychiatric nurse, resulted in a significant reduction in relapses and readmissions over a 1-year period. Depression may be prevented by identifying older people with risk factors for depression as well as by directing interventions towards those already identified as being depressed through screening. A recent Dutch study found the latter approach more effective. However, extra resources are needed to ensure that screening tests for depression are used consistently (Schoevers et al. 2006).

Depressive disorders occur frequently in older persons, but they do respond to treatment. General practitioners can successfully treat depressive disorders in older persons, involving the patient’s social support system and make referrals for speciality care when necessary. Many types of treatments are available, but all require respect for the older person, empathy, and continuous updating of the practitioner’s skills and knowledge.

CONCLUSION

There is great potential and opportunity for detecting depression in older people. In addition to relieving great suffering, preliminary evidence suggests that recovery from depression reduces service usage by older people. Models of chronic care that use trained care managers to assist primary care physicians have been found effective in the treatment of late-life depression. As more depressed elderly patients are treated in primary care settings, the implementation of a sustained care management model can have far reaching benefits. Studies suggesting the need for integrated mental health services in primary care settings have spawned a dramatic increase in research on approaches to improving the treatment of geriatric depression in primary care. Three multi-site studies have been carried out, including PROSPECT, IMPACT, and PRISM-E. The PROSPECT study tested the effectiveness of having a non-physician health specialist within the primary care setting, who monitors the patient’s clinical status and supports the implementation of an established treatment protocol consisting of an antidepressant citalopram or IPT (Schulberg et al. 2001). The IMPACT study evaluated the effectiveness of a similar collaborative care model, involving a clinical specialist supporting and monitoring the use of antidepressant medication and PST according to a protocol (Unutzer et al. 2002). The IMPACT study is the largest trial of collaborative care in the elderly that has been undertaken. The results of this trial have already shown improvements in short- and longer-term outcomes of depression; improvements in quality of life; increased satisfaction, and reduction of suicide ideation (Hunkeler et al. 2006; Unutzer et al 2006). Finally, the PRISM-E study compared the outcomes and costs of integrated and speciality referrals models of mental health services for older adults in primary care (Bartels et al. 2004). The results suggest that integrated service arrangements improve access to mental health for older adults who underuse these services.

Collaborative care involves a case manager delivering or facilitating evidence-supported treatments in a primary care setting. The case manager works in collaboration with the primary care physician and mental health specialists. Collaborative care appears to be good value, with healthcare benefits achieved within acceptable cost-effectiveness thresholds.
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APPENDIX
PREPARING EDUCATIONAL MATERIALS FOR PATIENTS AND FAMILIES

- Patient and family educational materials (e.g., booklets, brochures, videos) should be developed for use in a particular country and its cultures. It may be necessary to adapt them for use in various regions within a given country (urban versus rural), so that local values and attitudes are reflected and the language is adjusted to the local dialect.

- Ideally, a booklet or other handouts should be produced in conjunction with a countrywide campaign that raises awareness of depression and explains what it is and how it can be successfully treated.

- Similar materials produced in other parts of the world should be collected to see which parts, if any, can be adapted to a particular country.

- It may be useful to convey the message not only in print but also through visual images. In fact, because of the cognitive impairment often associated with untreated depressive illness, visual images may be more useful than printed text, which requires greater patient effort to understand.

- The text should be concise and simple. Patients who wish to know more about depression should be given a list of books or articles on the topic to read.

- A careful analysis should be made before deciding where and how to distribute materials (e.g., in doctors’ waiting rooms, through health visitors).

- It is recommended that handouts be prepared with the help of the following: psychiatrists, general practitioners, psychiatric nurses, psychologists, social workers, communications specialists, members of facilities for depressed patients, and people who have experienced a depressive disorder.

- Before widespread distribution, handouts should be pilot tested. The simplest way of doing this is for a doctor to present the material to acutely depressed patients, to individuals who suffered from depressive illness in the past, and to relatives of depressed patients. The answers obtained should be carefully noted and discussed with the group producing the materials. The final version should be revised to correct any sections that were not understandable to any of the target groups or did not convey a hopeful message.

- Patient materials should be regularly updated to reflect new developments in the field. Updated versions should be distinguishable from previous versions (e.g., by numbering different versions).

- In countries with a high rate of illiteracy, graphic representations, audiotapes, and videotapes can be very useful.
PART 2
Depressive Disorders in Women

Gender differences in the prevalence of psychiatric disorders have long been recognised. Their importance is illustrated by the significantly different rates of major depressive disorder, which is twice as common in women as in men. Depression has been called the most significant mental health risk for women (Glied and Kofman 1995). Moreover, during their child-bearing and child-rearing years, the risk associated with depression can also to women’s children, who may be adversely affected by maternal depression. In addition to the difference in prevalence, recent studies have found gender-related differences in both clinical presentation and treatment response. Consequently, clinicians must be aware of some special considerations in the diagnosis and treatment of depressive disorders in women in order to improve the recognition, management and outcome of these disorders.


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PART 2
Depressive Disorders in Women
Chapter 1
Epidemiology of Depressive Disorders in Women
PREVALENCE RATES

Higher Prevalence of Depression Among Women

A number of large epidemiological studies from around the world have consistently found that, on average, women experience depression twice as often as men. However, female to male ratios of depression vary among countries, ranging from 1.6:1 in Beirut and Taïwan to 3.5:1 in Munich (Weissman et al., 1996). In the United States, the ECA (Epidemiological Catchment Area), which was the largest survey of psychiatric disorders in North America, reported a female-to-male ratio of depression of 1.96:1, with a lifetime prevalence of 10.2% in women and 5.2% in men (Regier 1988). Similarly, in the NCS (National Comorbidity Survey), a sex ratio of 1.7:1 was found for lifetime prevalence of depression (21.3% in women versus 12.7% in men), as well as for 12-month prevalence rates (Kessler 1993). The same ratio has been reported in ten other countries across the world (Weissman et al. 1996). In the most recent worldwide study, which was carried out by the World Health Organization (WHO) in 14 countries to evaluate gender differences in mental disorders in primary care, the female to male sex ratio for major depressive disorder was 2.1 (Maier 1999).

Gender Differences Vary Across the Lifespan

Gender differences in prevalence vary across the lifespan. Higher rates of depression in women begin at puberty and persist throughout childbearing years, after which they slowly decline (Kessler 1993; Kornstein 2006) (Figure 1.1). Before puberty, girls and boys share similar rates of depression. It’s only after puberty that the gender disparity in depression truly becomes pronounced. One study, which evaluated 10,000 British citizens for risk of developing ICD-10 major depression, found that by age 16, the risk for depression was much higher in women and that this difference continued to increase as a woman entered young adulthood. However, after menopause, women had a lower risk of developing new-onset depression. In late adulthood, the rate of depression in males and females tends to be more alike. (Ustün and Sartorius 1995)

FIGURE 1.1

Depression across the lifespan

Depression Over the Lifespan
Depression Hazard Rates by Age and Sex

<table>
<thead>
<tr>
<th>Hazard Rate</th>
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<tbody>
<tr>
<td>0.0140</td>
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<tr>
<td>0.0120</td>
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<tr>
<td>0.0100</td>
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<tr>
<td>0.0080</td>
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<tr>
<td>0.0060</td>
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<tr>
<td>0.0040</td>
</tr>
<tr>
<td>0.0020</td>
</tr>
<tr>
<td>0.0000</td>
</tr>
</tbody>
</table>

Age Category

0-4 5-9 10-14 15-19 20-24 25-29 30-34 35-39 40-44

Women

Men
IMPACT OF DEPRESSION ON WOMEN AND CHILDREN

According to a WHO Report, depression has been considered “the greatest disease burden for women when compared with other diseases”. Actually, unipolar depression, which is predicted to be the second most disabling illness by 2010 (WHO 2001) already ranks first for women, accounting for 41.9% of the disability from neuropsychiatric disorders among women compared with 29.3% among men (WHO 2000).

Depression is often comorbid with other chronic diseases and can worsen the health outcomes associated with these illnesses, as shown by the WHO World Health Survey (WHS) conducted among 245,404 participants aged 18 years of age and older from 60 countries in all regions of the world (Moussavi et al. 2007). Overall, the 1-year prevalence rate for ICD-10 depressive episodes alone was 3.2%, compared with 4.5% for angina, 4.1% for arthritis, 3.3% for asthma, and 2.0% for diabetes. An average of 3%–23.0% of participants with one or more chronic physical disease had comorbid depression. This result was significantly higher than the likelihood of having depression in the absence of a chronic physical disease (p < 0.0001). Consistently across countries and different demographic characteristics, respondents with depression who had one or more chronic comorbid diseases had the worst health scores of all disease states. The authors concluded that depression produces the greatest decrement in health compared with the chronic diseases angina, arthritis, asthma, and diabetes. Having depression along with a chronic comorbid medical illness incrementally worsens health compared with depression alone, any of the chronic diseases alone, and any combination of chronic diseases without depression. These results indicate the urgency of addressing depression as a public-health priority to reduce disease burden and disability, and to improve the overall health of populations.

Depression is also more common during the period when women become parents, and maternal depression can affect children of all ages, not just very young children during the postpartum period. Maternal depression can and does occur at any time during a child’s life, although it has greatest impact during the child’s early years. Maternal depression can seriously affect interactions between mothers and children, and thus can have an adverse life-long impact on children’s emotional and social development. Maternal depression predicts behaviour problems, developmental delays, and school problems in children, independent of the effects of socio-economic class (Olson and Dietrich 2006). Research in the field has shown that maternal depressive symptoms are linked to a number of different childcare issues. Mothers who are depressed are more concerned with their baby’s health and have more medical visits in the child’s first year of life, including visits to emergency rooms. However, they are less likely to implement recommended preventive safety practices.

Marital conflicts are also increased in the presence of maternal depression (whether preceding or resulting from the depression) and may lead to the development of a negative pattern of parenting. Parents may have a more irritable and hostile style; they may become anxious and overly intrusive in their child’s activities; or they may be withdrawn and nonresponsive. The problem is that parents may exhibit any of these different behaviours and this can vary on day-to-day basis, leaving children unsure of what reaction to expect from their parents. Parents who struggle with depression also have difficulty implementing daily routines of naps, sleep, and mealtimes, and such lack of routine can be a difficult stressors for the child. Over time, the child lacks role models that they can turn to for handling emotional issues appropriately (Olson and Dietrich 2006).
Several studies have suggested that there is an elevated risk for psychopathology among children of depressed mothers. A recent study (Pilowsky et al. 2006) found that about a third (34%) of children of depressed mothers had a current psychiatric disorder, including disruptive behavior (22%), anxiety (16%), and depressive (10%) disorders, while nearly half (45%) had a lifetime psychiatric disorder, including disruptive behavior (29%), anxiety (20%), and depressive (19%) disorders. The same team also demonstrated that helping mothers actually helps the child, whose behavior improves when the mother is treated successfully (Weissman et al. 2006). Figure 1.2 highlights results from this study, the goal of which was to determine whether effective medication treatment for women with major depression is associated with a reduction of symptoms and diagnoses in their children by following the development of their children, who were 7–17 years of age, over 3 months. This study showed that remission of maternal depression has a positive effect on both mothers and their children, whereas mothers who remain depressed may increase the rates of their children’s disorders. As a matter of fact, remission of maternal depression after 3 months of medication treatment was significantly associated with reductions in the children’s diagnoses and symptoms. There was an overall 11% decrease in rates of diagnoses in children of mothers whose depression remitted, compared with an approximate 8% increase in rates of diagnoses in children of mothers whose depression did not. Of the children with a diagnosis at baseline, remission was reported in 33% of those whose mothers’ depression remitted compared with only a 12% remission rate among children of mothers whose depression did not remit. All children of mothers whose depression remitted after treatment and who themselves had no baseline diagnosis for depression remained free of psychiatric diagnoses at 3 months, whereas 17% of the children whose mothers remained depressed acquired a diagnosis. It is interesting to underline that these children weren’t receiving therapy themselves. The improvement resulted only from the mother’s treatment.

**FIGURE 1.2**

Relation between maternal remission status and change in child’s specific diagnoses (Weissman 2006)
Patel and Prince (2006) also showed that depression following childbirth is associated with poor growth in children in developing countries. They described an association between psychological morbidity during pregnancy and low birth weight (<2.5 kg), among a cohort of 270 mothers recruited from a district hospital in Goa, India. As a matter of fact, they found that maternal psychological morbidity was independently associated with low birth weight.

The findings described here support the importance of vigorous treatment for depressed mothers in primary care or psychiatric clinics and suggest the utility of assessing the children, especially children whose mothers continue to be depressed. Healthcare providers are also encouraged to routinely screen adults for depression, especially mothers who ordinarily accompany their children to well-care visits.

RISK FACTORS FOR DEPRESSION IN WOMEN

Many theories have been proposed to explain the higher prevalence of depression in females, as illustrated in Figure 1.3 (Kornstein 1997). Table 1.1 lists a number of commonly reported risk factors for depression in women.

The Artefact Hypothesis

The artefact hypothesis suggests that the greater prevalence of depression in women may not actually be real, but instead may reflect gender differences in symptom reporting and help-seeking behaviour as well as cultural and diagnostic biases. Specifically, this hypothesis posits that, because women are more likely than men to report symptoms of major depression and seek psychiatric care, this could lead to an over reporting of depression in women (Kessler et al. 1993). However, studies that have varied the method of evaluation have found that such factors do not account for the observed gender differences. Besides, the consistency of the female predominance across cultures and in community-based studies as well as clinical studies refutes this theory (Kornstein and Wojcik 2001). The heightened vulnerability of women to depression has been ascribed to a combination of biological factors, gender-related differences in coping styles, and a higher incidence of psychosocial stresses.

## Table 1.1

<table>
<thead>
<tr>
<th>Risk factors for depression in women</th>
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<tbody>
<tr>
<td>- Family history of mood disorders</td>
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<tr>
<td>- Loss of a parent before the age of 10</td>
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<tr>
<td>- Childhood history of physical or sexual abuse</td>
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<tr>
<td>- Use of an oral contraceptive, especially with a high progesterone content</td>
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<tr>
<td>- Use of gonadotropin stimulants as part of an infertility treatment</td>
</tr>
<tr>
<td>- Persistent psychosocial stressors</td>
</tr>
<tr>
<td>- Loss of social support system or the threat of such a loss</td>
</tr>
</tbody>
</table>

Source: Bhatia and Bhatia 1999

## Figure 1.3

Factors that may contribute to gender differences in depression

- **Artifact**
  - Women more likely to report symptoms and seek treatment
  - Possible diagnostic bias

- **Biological**
  - Differences in the brain structure/function
  - Reproductive-related hormonal fluctuations
  - Genetic transmission

- **Psychosocial**
  - Effects of gender-specific socialization
  - Lower social status
  - Abuse
  - Coping Methods
  - Role or life stress

Source: Bhatia and Bhatia 1999
Biological Factors: The Role of Female Hormones

Biological gender differences may explain some of the differences in depressive disorders between men and women. In addition to genetic factors, possible biologic mechanisms may include differences in brain structure and function, and the psychoactive effects of female hormones which have received particular attention. Because the gender gap begins with puberty and disappears after menopause, some researchers believe that hormonal factors play a crucial role in the higher risk for women to develop depression. Estrogen and progesterone have been shown to affect neurotransmitter, neuroendocrine, and circadian systems that have been implicated in mood disorders (Kornstein and Wojcik 2001). Specifically, changes in gonadal hormones, disturbances in the hypothalamic-pituitary-gonadal (HPG) axis and attendant effects on neuromodulators (e.g., serotonin) may all be key mechanisms in the initiation of depression. For example, pregnancy and delivery produce dramatic changes in estrogen and progesterone levels, as well as changes in the HPG axis, that may trigger postpartum depression (Hofecker-Fallahpour and Riecher-Rössler 2005, Riecher-Rössler and Hofecker-Fallahpour 2003).

Psychosocial Factors: Unequal Status and Power

Beyond the biological factors that could explain female-specific depressive disorders, gender differences in depression may also be due in part to psychological and social conditions. Health is also shaped by social gender, as clearly asserted in the WHO’s 1998 World Health Report: “Women’s health is inextricably linked to their status in society. It benefits from equality and suffers from discrimination. Today, the status and well being of countless millions of women world-wide remain tragically low” (WHO 1998).

Many authors (Douki et al. 2007; Kessler et al. 1993; Mirowsky 1996,) support the idea that women’s greater vulnerability to depression is a direct result of their unequal adult status (e.g., having less access to educational or economic resources). Although the same stressors also occur in men, it is usually at a lower rate. Women are more likely than men to shoulder the burden of both work and family responsibilities, for instance. They’re also more likely to have lower incomes, be single parents, and have a history of sexual or physical abuse, all of which can contribute to depression, especially in women who have already experienced depression in the past.

Social conditions

Marital status. Marriage seems to confer a greater protection against depression on men than women. Married women have higher rates of depression than unmarried women, whereas single men are more vulnerable to depression. In unhappy marriages, women are three times as likely as men to be depressed (Wu and DeMaris 1996). In addition, married women who have experienced a larger number of childhood adversities are at significantly increased risk for early-onset depression. Interestingly, married women who are relatively free of childhood adversities are more likely either to report no depressive episodes or to have a later onset of depression (Davies et al. 1997). Single mothers, whether never married, separated, or divorced, are almost three times more likely than married mothers to have experienced a major depressive episode (Davies et al. 1997).

Women also are more sensitive than men to the effects of divorce, especially when it was not their choice. Brown et al. (1995) found that, when marital separation was instigated by the wife, only 10% of these women subsequently developed depression. When the separation was initiated by her partner, approximately half of the women developed depression.
Socioeconomic status (e.g., income and education level) is a risk factor that predicts both lifetime and 12-month prevalence of major depression (Robins et al., 1991; Sartorius et al. 1996). Women are more likely than men to share a number of socioeconomic risk factors for depression, including gender discrimination, lower educational and income levels, segregation into low status and high-stress jobs, or unemployment. Low socio-economic status brings with it many concerns and stressors, including uncertainty about the future and less access to community and health care resources.

Occupational status. Both occupational status and children may influence the risk of depression in women.

Women today have gained the right to work but at what cost? Many women face daily challenges in fulfilling multiple roles and meeting conflicting demands. Firstly, they are mainly represented in sectors of activity that resort traditionally to female manpower, such as education, health, or the textile industry, and generally in subordinate positions. Furthermore, their access to the labour market has resulted in them assuming multiple roles and an overload of responsibilities. Indeed, women today often concurrently hold salaried jobs as well as assuming responsibility for domestic tasks and parenting roles. Thus, in addition to their salaried job, mothers are often far more involved than fathers in meeting household needs and caring for children (and other family members in need). A large community-based survey in Tunisia (Douki et al. 2007) showed that mothers are two to four times more involved in children’s education, schooling, health, and even punishment. It has been demonstrated that the presence of young children at home is also a risk factor for depression in women, especially if a woman works outside the home and had difficulty finding child care. The risk of depressive symptoms is higher among mothers of young children and increases with the number of children in the house (Kornstein 2001, McGrath et al. 1990). Moreover, women’s work exposes them to marital conflicts and to moral and sexual harassment in the workplace. As a result, employment for most women is more a source of exhaustion and stress than of self-development and independence; many develop depressive disorders and finally give up working (Douki et al. 2007).

Immigration and acculturation. A high level of depression is reported in women confronting the impact of immigration and acculturation, especially in minority women who may also face added stress from racial discrimination (National Center for Health Statistics 1994).

Stressful life events

Traumatic events, such as childhood sexual abuse, adult sexual assault, male partner violence, and physical illness can also lead to depression. Research has indicated that women may be more likely than men to experience depression in response to a stressful event. Initial research has also suggested that early trauma has a greater impact on risk for depression than trauma that occurs later in life.

The rate of sexual and physical abuse, during childhood or adulthood, is much higher than previously suspected and is a major factor in women’s depression. A clear relationship between childhood sexual abuse and adult-onset depression has been shown, and this risk factor is considerably more common in women, with the ratio of female-to-male victims estimated to be as high as 12 to 1 (Weiss et al. 1999). Dysregulation of the hypothalamic-pituitary-adrenal axis, resulting in hypersecretion of corticotropin-releasing hormone, is thought to play a major role in linking this trauma with depression. Other types of childhood trauma, such as parental loss, poor parenting, parental drinking, mental illness, and family violence, may also contribute to the development of adult-onset depression. Women who were raped as teenagers or who experience abuse as adults also have a higher incidence of depression. Finally, women are the major victims of violence, particularly domestic violence. In the world, lifetime prevalence rates of wife abuse range from 16% to 50%. Depression is the most common consequence, and domestic abuse is associated a very high risk of severe depression and suicide (WHO 1998).
Gender differences in early developmental socialisation processes lead to different Styles of coping with adverse life events. Parents and teachers tend to have different expectations of girls and boys, which may result in girls becoming more concerned with the evaluation of others and in boys developing a greater sense of mastery and independence. Many girls are trained to be passive and dependent to the point of neglecting their own needs. Such stereotypical gender socialisation is hypothesised to lead to differences in self-concept and vulnerability to depression (Kornstein and Wojcik 2001). Current research has demonstrated that relationships play a more paramount role in women’s self-concept than in that of men and that women are more likely to experience stress in response to adverse events occurring in the lives of others and to place their needs secondary to those of others. These interpersonal orientations illustrate major psychological differences between men and women that may help account for differences in vulnerability to depression.

One cognitive style that is more common in women than men and which increases the risk for depression is ruminative thinking—repetitively and passively focusing on symptoms of distress and their possible causes and consequences. Men, in contrast, tend to respond to negative feelings by using distracting strategies. Nolen-Hoeksama (1995) postulated that this difference in coping styles may contribute to longer and more severe depressive episodes in women.

In conclusion, an integrated, longitudinal model in a population-based sample found recent stressful events to be the single most powerful risk factor for 1-year prevalence of major depression, followed by genetic factors, previous history of major depression, and temperament (Kendler et al. 1993).

ACCESS TO CARE

It is generally thought that women are more prone than men to seek help for health problems and are over-represented in health care settings. However, the number of women coming for care still represents only a portion of those women who are depressed, as demonstrated by community-based prevalence rates, even in developed countries (Alonso et al. 2004; Blazer et al. 1994). When depression is recognised and care is sought, a range of barriers can impede women from receiving needed treatment. These barriers include lack of consumer or provider knowledge about mental health services and treatments, stigma, inability to obtain adequate time off work or other responsibilities to obtain treatment, lack of available transportation, lack of child and elder care (given that women are disproportionately responsible for care of children and elderly family members), and, last but not least, level of insurance copayments, deductibles, and limits. Historically, mental health benefits have been more limited than medical/surgical benefits with higher copayment rates and stricter limits on the number of visits and hospital days. Mental health services also have been a particular target for managed care cost cutting. Concerns have been raised about certain aspects of managed care that make it difficult for depressed women to access appropriate care (Mazure et al. 2002).

In traditional societies, women with mental disorders, especially severe ones, do not benefit from the same protection as men and suffer from worse clinical and social outcomes. Many studies have reported delays in seeking care, poor adherence to treatment, under-representation among psychiatric patients.

In Bangladesh (Ahmed et al. 2000), women suffering from illness report seeking care significantly less often than men. Women represented only 29.5% of the 1,030 patients attending the psychiatric emergency service in Casablanca, Morocco during 10 consecutive months and women represented 38% of the 1,009 patients admitted to a psychiatric hospital in Libya during a calendar year (Avasthi 1991); women were also only 30% of the total inpatient population at the single psychiatric hospital in Tunisia (Douki et al. 2007).
Several explanations for this male predominance in psychiatric care have been proposed:

- The burden of cultural taboos and stigma attached to mental disorders and psychiatric care: women are indeed far more likely than men to be rejected by their family and to be abandoned to institutional care. Likewise, women with mental illness are at greater risk of remaining single or of being divorced by their husbands and separated from their children; they are also at higher risk of sexual or physical abuse, or murder (WHO 2000).

- The important role women play in family functioning: most caregivers are women, who are the first and last resource for taking care of disabled family members, including mentally retarded children, elderly family members with dementia, and adults suffering from major physical or mental illnesses. Women themselves often share the common view that their health is a low priority compared with the role they have in the family.

- Women are physically less aggressive and dangerous than men, a fact that contributes to greater family tolerance towards women for the same acute episode.

- The somatoform expression of depression, which is far more common in women, often leads to the misdiagnosis of a medical condition rather than depression.

Women are therefore more likely than men to receive care for a mental health problem from a general practitioner and, despite improvements in the diagnosis of depression, primary care physicians diagnose depression less often than specialists.
REFERENCES


PART 2
Depressive Disorders in Women
Chapter 2
Depressive Disorders Specific to Women

Women may experience depressive episodes that are specifically related to reproductive events, such as the menstrual cycle, the postpartum period, and the transition to menopause.
**DEPRESSION AND PUBERTY**

Menarche is considered the first time a young woman is at increased risk for depression. Beyond the dramatic hormonal changes that occur at this time, puberty is also often associated with other changes that could play a role in depression, such as emerging sexuality and identity issues, parental conflicts, and evolving social expectations. These psychosocial factors could interact with hormonal changes during puberty and result in an increased risk of depression. When a girl enters puberty and experiences hormonal changes, she may also become more vulnerable to the impact of relationships and stressful life events.

**FIGURE 2.1**

The menstrual cycle and depression  
(Kornstein, 2006)

**THE MENSTRUAL CYCLE AND DEPRESSION**

There are three diagnoses to consider in women presenting with premenstrual depressive symptoms: premenstrual syndrome (PMS), premenstrual dysphoric disorder (PMDD), which is a severe form of PMS, and premenstrual exacerbation of depression, which is a worsening of symptoms of an ongoing mood disorder during the premenstrual period (Figure 2.1).

Premenstrual exacerbation of depression is distinguished from PMS and PMDD in that there is a persistence of symptoms during the follicular phase of the cycle, whereas in PMS and PMDD, the symptoms are only present during the luteal phase. Unfortunately, there is not yet a universally accepted and implemented diagnostic tool that can used to assess for PMS and PMMD. Halbreich and colleagues (Halbreich et al. 2007) recently presented recently the conclusions and recommendations of an international multidisciplinary group of experts who evaluated current definitions, diagnostic criteria, and guidelines for PMS and PMDD, and expressed the hope that the new criteria identified by this group will gain wide acceptance and will eventually be incorporated into the next edition of the *International Classification of Diseases* (ICD-11). These experts concluded that one symptom, whether physical or emotional, is sufficient to make a diagnosis of PMS if the symptom is associated with impairment, occurs for at least 2 days prior to menses, is relieved by the end of the menstrual flow, and abates for a week after the conclusion of menses. These criteria are based upon prospective confirmation.
Premenstrual syndrome (PMS)

Epidemiological surveys have estimated that up to 75% of women of reproductive age experience some physical and emotional symptoms attributed to the premenstrual phase of the menstrual cycle (Johnson et al. 1988). More than 100 psychological and physical symptoms have been reported (Budeiri et al. 1994). This phenomenon is called premenstrual syndrome (PMS) and refers to any combination of symptoms that appear during the last week before menstruation and remit within 1 or 2 days following onset of menses (ICD-10 1992).

PMS is not listed as a mental disorder in the ICD-10, but as a gynaecological problem characterised by the presence of one or more of the following symptoms: mild psychological discomfort, bloating and weight gain, breast tenderness, swelling of hands and feet, aches and pains, poor concentration, sleep disturbance and change in appetite. Usually, most women are able to manage these symptoms through lifestyle changes and conservative therapies. However, some women report premenstrual symptoms that cause severe distress and dysfunction and may seek the help of a health professional. This severe form of PMS has been labelled premenstrual dysphoric disorder (PMDD). Identifying PMDD is important because it is a severely distressing and debilitating condition that requires adequate treatment.

Approximately 50%–80% of menstruating women experience some mild premenstrual symptoms, about 20% report severe PMS symptoms that warrant treatment, and 3%–8% meet strict DSM-IV-TR (American Psychiatric Association 2000) criteria for premenstrual dysphoric disorder.

Premenstrual dysphoric disorder.

PMDD is not included in the ICD-10. However, the DSM-IV-TR classifies PMDD as a category of depression not otherwise specified and includes research criteria for its diagnosis (Table 2.1). PMDD is characterised predominantly by mood symptoms.

Epidemiology

Approximately 3% to 9% of premenopausal women experience PMDD (Ramcharan et al. 1992; Rivera-Tovar and Frank 1990). Onset typically occurs during the teens to late 20s, and symptoms usually peak in women’s 30s and early 40s.

Diagnosis

The diagnosis of PMDD requires the presence of at least 5 of the 11 symptoms, including 1 of the 4 core symptoms confirmed by daily charting for at least two menstrual cycles. The symptoms must have occurred in association with most menstrual cycles during the past year and have interfered with social and occupational roles. Symptoms must occur only during the premenstrual period and remit within a few days after the onset of the follicular phase. To confirm the diagnosis, clinicians should use patients’ self-rated symptoms of PMDD, for two consecutive menstrual cycles. Other components of the evaluation include a physical and gynaecologic examination, a thyroid function test, and measurement of the serum luteal progesterone level or urine luteal hormone surge to document ovulation (Haynes and Parry 1998).

The course of PMDD parallels that of a recurrent major mood disorder, in that it becomes more severe, extends in duration, and becomes more refractory to treatment over time (Haynes and Parry 1998).
A. In most menstrual cycles during the past year, five (or more) of the following symptoms were present for most of the time during the last week of the luteal phase, began to remit within a few days after the onset of the follicular phase, and were absent in the week postmenses, with at least one of the symptoms being either (1), (2), (3), or (4):

1. markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts
2. marked anxiety, tension, feelings of being “keyed up,” or “on edge”
3. marked affective lability (e.g., feeling suddenly sad or tearful or increased sensitivity to rejection)
4. persistent and marked anger or irritability or increased interpersonal conflicts
5. decreased interest in usual activities (e.g., work, school, friends, hobbies)
6. subjective sense of difficulty in concentrating
7. lethargy, easy fatigability, or marked lack of energy
8. marked change in appetite, overeating, or specific food cravings
9. hypersonia or insomnia
10. a subjective sense of being overwhelmed or out of control
11. other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of “bloating,” weight gain

Note: In menstruating females, the luteal phase corresponds to the period between ovulation and the onset of menses, and the follicular phase begins with menses. In nonmenstruating females (e.g., those who have had a hysterectomy), the timing of luteal and follicular phases may require measurement of circulating reproductive hormones.

B. The disturbance markedly interferes with work or school or with usual social activities and relationships with others (e.g., avoidance of social activities, decreased productivity and efficiency at work or school).

C. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as Major Depressive Disorder, Panic Disorder, Dysthymic Disorder, or a Personality Disorder (although it may be superimposed on any of these disorders).

D. Criteria A, B, and C must be confirmed by prospective daily ratings during at least two consecutive symptomatic cycles. (The diagnosis may be made provisionally prior to this confirmation.)

To meet criteria for PMDD, women should have no other concurrent psychiatric disorder or unstable medical condition but may have a history of a past psychiatric disorder. Indeed, women with a history of postpartum depression and mood changes induced by oral contraceptives may be at increased risk for PMDD. A history of non reproductive-related clinical depression also appears to be a risk factor, as does a history of PMDD. Conversely, longitudinal studies (Pearlstein et al. 1990; Rubinow 1992) indicate that women who experience PMDD are at greater risk for future depression during pregnancy, the postpartum period, and the perimenopausal period, thereby suggesting a biochemical relationship between depression and the disorder. There is a lack of consensus in the literature regarding the pathophysiology of PMDD. Although no single cause has been established, current research implicates mechanisms related to the serotonin system as being relevant to its aetiology and treatment.

Management

Without treatment, PMDD may become a chronically recurring illness, with a course similar to that of major depressive disorder. Both nonpharmacological and pharmacological measures have been employed in the treatment of PMDD. Treatment includes conservative interventions (such as lifestyle and stress management), cognitive-behaviour therapy, suppression of ovulation (oral contraceptives may help, although they may exacerbate symptoms in some patients), and antidepressants, which have been demonstrated to improve symptoms and quality of life in women with PMDD. (Freeman 2005).

Patients with mild to moderate symptoms of premenstrual disorder may benefit from nonpharmacologic interventions such as education about the disorder, lifestyle changes (e.g., physical exercise), and nutritional adjustments (caffeine restriction, complex carbohydrate consumption, and moderation of alcohol intake) [Pearlstein 1996]. The use of calcium supplementation to reduce symptoms has recently attracted interest.

Patients who fail to respond to conservative measures may also require pharmacological management, typically beginning with a selective serotonin reuptake inhibitor (SSRI). Serotonergic antidepressants such as fluoxetine, citalopram, sertraline, and clomipramine are effective when used intermittently during the luteal phase of the menstrual cycle. Patients who do not respond to a serotonergic antidepressant may be treated with another SSRI. Low-dose alprazolam, administered intermittently during the luteal phase, is considered as a second-line treatment. A therapeutic trial of a gonadotropin-releasing hormone (GnRH) agonist such as leuprolide may be considered when other treatments are ineffective. However, the risk of serious side effects and the cost of these medications limit their use to short periods (Bhatia and Bhatia 2002). In at least one study, ovulation suppressors produced a more salutary response on physical symptoms of PMDD, but were less effective in treatment of severe premenstrual depression. (Freeman et al. 1997). In contrast the SSRIs improve affective symptoms but have a more variable effect on the somatic symptoms of the disorder (Halbreich et al. 2002). A recent, large epidemiological study found that, among women with PMDD, some women experienced positive mood changes and other women negative changes following institution of oral contraceptives. The authors concluded that oral contraceptives do not influence premenstrual mood in most women, and that premenstrual mood is most likely to deteriorate in women with a history of depression and to improve in women with early-onset premenstrual mood disturbance or dysmenorrhea (Joffe et al. 2003).
DEPRESSION DURING PREGNANCY

Contrary to what was previously thought, pregnancy does not provide protection against mental disorders. However, it is also not a risk factor for depression. The prevalence rates of depression are now known to be similar in pregnant and nonpregnant women. During pregnancy, up to 70% of women experience depressive symptoms and 10%–16% fulfil the DSM-IV diagnostic criteria for major depressive disorder (Klein and Essex 1995). Up to 18% of women suffer from subsyndromal depressive symptoms (Marcus et al. 2003). Sleep and appetite dysregulation are viewed as part of the normative experience of pregnancy, and the vast majority of women with depressive symptoms as well as major depressive disorder during pregnancy are undertreated (Marcus et al. 2005). Untreated depression is an important risk factor for unfavourable pregnancy outcomes, including poor weight gain, difficulty obtaining prenatal care, and increased alcohol and drug use (Ryan et al. 2005). Human studies demonstrate that perceived life-event stress, as well as depression and anxiety in pregnancy, predicted lower infant birth weight, decreased Apgar scores, prematurity, and smaller head circumference (Rahman et al. 2007).

Table 2.2 lists some common risk factors for developing depressive disorders during pregnancy. The strongest predictor of depression during pregnancy is a previous history of major depressive disorder. Other risk factors include young age, poor social support, living alone, marital conflict, and unwanted pregnancy (Altshuler et al. 1998; Poffenbarger 1982). Various medical disorders, such as anaemia, gestational diabetes, and thyroid dysfunction, may also contribute to depressive symptoms in pregnancy (Llewellyn et al. 1997).

The same diagnostic criteria for depressive disorders apply to pregnant women; however, one can’t use the same diagnostic instruments to assess for depression during pregnancy, because many somatic symptoms occur as normal consequences of pregnancy and should not be counted as evidence for a diagnosis of depression. One therefore has to use specific instruments that do not include symptoms such as sleeping difficulties or changes in appetite in making the diagnosis of depression. The Edinburgh Postnatal Scale (Cox et al. 1987) is therefore often used to assess for pregnancy both during pregnancy and postnatally.

Pregnancy raises crucial management issues. Treatment options are basically the same as for nonpregnant women and include nonpharmacological interventions and/or antidepressant medications. Treatment should be tailored to the severity of the depressive disorder, risk of recurrence, and the wishes of the woman and her family. Research investigating both interpersonal therapy (IPT) and cognitive-behavioural therapy (CBT) in the treatment of depression during the puerperium suggest positive outcomes when these therapies are delivered by appropriately trained treatment providers (Cooper et al 2003; O’Hara et al. 2000). For those

### TABLE 2.2

Risk factors for depressive disorders in pregnancy

- Young age and poor social support (Altshuler et al. 1998; Poffenbarger 1982)
- Unwanted pregnancy (Poffenbarger 1982, Altshuler et al. 1998)
- Higher number of prior pregnancies (O’Hara 1986)
- Previous depressive disorders (Marcus et al. 2003)
- Single marital status, marital conflict (Marcus et al. 2003)
- Alcohol use during pregnancy (Marcus et al. 2003)
- Bereavement in the second or third trimester (Kumar and Robson 1984)
- Anemia, gestational diabetes, thyroid dysfunction (Llewellyn et al. 1997)
women who are reluctant to begin or continue pharmacotherapy, these treatments may be useful alternatives. Likewise, for women who choose to use pharmacotherapy but have significant psychosocial stressors, these treatments may be essential augmentation strategies.

When managing depression during pregnancy, it is important to weigh the risks of treatment against the risks of untreated mental illness to both the mother and foetus. Both acute and prophylactic treatment of severe depressive disorders during pregnancy requires an individual risk/benefit analysis. The goal in treating depression during pregnancy is to try to minimise foetal exposure to both medication and to the illness itself. Depression during pregnancy may harm women, because of the increased risk of suicide and because they may not provide themselves with adequate self-care, diet and sleep and may consume alcohol and drugs—depression has been shown to reduce women’s motivation to seek and adhere to prenatal care (Stewart et al. 2006). Depression is also associated with poor obstetrical outcomes, including an increased risk of preterm delivery and low birth-weight infants, which may be related to poor prenatal care. Untreated depression may also affect mother-child bonding and may be a cause of chronic depression and treatment resistance (Stewart 2005).

The Potential Risks of Antidepressants

Teratogenicity

Antidepressant medications, which all cross the placenta, are associated with potential reproductive risks of intrauterine foetal death, morphologic teratogenicity (major birth defects or major and minor physical malformations), growth impairment, and neonatal toxicity (Cohen and Rosenbaum 1998; Wisner et al. 1999). Moreover, the risk of an impact on behavioural development (e.g., abnormal emotional behaviours in the offspring) cannot be excluded. Recent animal studies have reported that serotonin and SSRI treatment have an impact on behavioural phenotypes, which led to the hypothesis that serotonin may have a critical role in the maturation of brain systems that modulate emotional function (Ansorge et al. 2004). Limited safety data are available concerning exposure to antidepressants during pregnancy and most involve single case reports, case series, and epidemiological studies.

No antidepressants have been approved by the U.S. Food and Drug Administration for use during pregnancy and there is still a scientific debate about the teratogenicity of these drugs. A great many early studies involving both the SSRIs and tricyclic antidepressants (TCAs) suggested that neither class was likely to contribute to major congenital anomalies above the 1%—3% baseline risk seen in the general population of pregnant women (Chambers et al. 1996; Cohen and Rosenbaum 1998; Kulin et al. 1998; Koren et al. 1998; McElhatton et al. 1996; Nulman et al. 1997). Moreover, in a meta-analysis of 414 cases of first trimester exposure to TCAs, no significant association between exposure to these antidepressants and congenital malformations was found (Altshuler et al. 1996). However, more recent studies do suggest that first trimester exposure to SSRIs may contribute to preterm delivery and minor malformations.

Paroxetine was recently reclassified as a category D agent during pregnancy. This was in part due to a GlaxoSmithKline report (2005) suggesting that infants exposed to paroxetine during the first trimester had an increased risk of congenital malformations (4% versus 2% in the general population), particularly cardiovascular anomalies (3% vs. 1% in the general population). A recent meta-analysis (Bar-Oz et al. 2007) confirms the concerns regarding increased cardiovascular risk, but also notes that a detection bias might contribute to these findings because of a 30% increased rate of ultrasound during pregnancy, and 2-fold increased rate of echocardiograms in the neonates. Finally, Chambers, et al. (2006) suggested that persistent pulmonary hypertension of the newborn may be associated with late trimester use of SSRIs.
However, a very recent meta-analysis reported that the use of newer antidepressants, such as SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs), noradrenaline reuptake inhibitors (NARIs), noradrenergic and specific serotonine inhibitors (NaSSAs), and dopamine norepinephrine reuptake inhibitors (DNRIs), is not associated with an increased risk of major malformations above the baseline of 1%–3% in the general population (Einaron and Einaron 2005). Finally, a survey of aggregate data now available—positive, negative, and equivocal—makes it clear that neither the SSRIs as a group nor individual SSRIs are major teratogens on the order of thalidomide or isotretinoin (Alwan et al. 2007; Louik et al. 2007; Greene 2007). In particular, this study reported an incidence of all congenital heart malformations of approximately 7 per 1000. Even among infants exposed to paroxetine in utero, the absolute incidence of right ventricular outflow tract lesions is unlikely to exceed 1%, and the incidence of all congenital heart defects is unlikely to exceed 2%. The authors conclude that “the available information, do suggest that any increased risks of these malformations in association with the use of SSRIs are likely to be small in terms of absolute risks”.

Neonatal complications

Based on a review of the literature, Wisner et al. (1999) reported that the development of children whose mothers took tricyclic antidepressants or fluoxetine during gestation did not differ from that of controls. However, one study did report decreased birth weights in infants exposed to fluoxetine in the third trimester (Chambers et al. 1996). Monitoring and interventions for patients with identified risk factors (e.g., poor weight gain) are therefore recommended. In addition, direct drug effects and withdrawal syndromes may occur in some neonates whose mothers are treated with antidepressants near term. Recent research also suggests that, like the older TCAs, the SSRIs may be associated with difficulties in neonatal adaptation including irritability, hypertonicity, and feeding and sleep difficulties.

Neonatal side effects occur in about 30% of infants exposed to antidepressants (Levinson-Castiel et al. 2006). Such side effects can occur with any antidepressant but paroxetine may pose a greater risk (Sanz et al. 2005). They begin within minutes to hours after birth and usually last 1–2 days (Oberlander et al., 2004). Neonatal side effects may include withdrawal hepatic immaturity, but also mild respiratory distress, tremor, jitteriness, increased REM sleep, decreased muscular tone, low blood sugar, and rarely, seizures or heart rhythm abnormalities (Källén 2004; Oberlander et al. 2004; Zeskind and Stephens 2004).

Finally, another consideration with the use of antidepressants during pregnancy is their potential for adverse effects. For example, TCAs can cause adverse effects such as constipation, urinary retention, and additional weight gain, which could cause great discomfort in a pregnant woman.

The Potential Risks of Mood Stabilisers

Lithium has been linked to teratogenicity, especially cardiac malformations, although some evidence suggests that this danger may have been overestimated (Jacobson et al. 1992). Lithium also has been linked to fetal renal and thyroid dysfunction (See Volume II, Chapter 4). Likewise other mood stabilisers have been implicated in a substantial risk for anomalies. Valproate increases the risk of major malformations and other serious pregnancy complications approximately fivefold if it is used during the first trimester (Cohen 2007; Ernst and Goldberg 2002; Viguera et al. 2007; Worley 2007; Wyszynski et al. 2005). The overall incidence of major malformations is 11% (Kaneko et al. 1999). Thus, if a mood stabiliser has to be given during pregnancy, lithium is currently considered the one with the lowest risk of teratogenicity.
Treatment Strategies

In selecting a treatment strategy for use during pregnancy, the benefits and risks of antidepressant pharmacotherapy have to be evaluated and compared with other nonpharmacologic treatment alternatives, including electroconvulsive therapy (ECT), cognitive-behavioural therapy (CBT), and interpersonal therapy (IPT) (Spinelli 1997; Stuart et al. 1997) as well as sleep deprivation (Parry et al. 2000), and bright light therapy (Oren et al. 2002). CBT and IPT should be the first choice for patients with mild-to-moderate past episodes of depression. Mild depressive symptoms during pregnancy may improve with psychosocial therapy, and these techniques can be helpful in resolving interpersonal and psychosocial conflicts, resulting in a positive outcome without exposing the mother or foetus to drugs. ECT is probably the best option for severe and refractory depression. It is a relatively safe and effective treatment for major depression in pregnant women, particularly in high-risk situations, such as depression with suicidal ideation or psychosis (Cohen and Rosenbaum 1998; Miller 1994). Pregnant women with moderate-to-severe or recurrent major depression are also candidates for pharmacological interventions.

Guidelines for Antidepressant Choice During Pregnancy

The choice of an antidepressant medication during pregnancy should include consideration of any history of the patient having a positive response to a medication in the past as well as available data regarding a drug’s safety in pregnancy and lactation, its dosing flexibility, and safety in overdose (Llewellyn et al. 1997). When available, it is best to use the patient’s psychiatric history to guide treatment decisions. For example, if the woman has had previous depressive episodes, it is probably safer to maintain her on medication throughout the pregnancy, rather than to expose her to a risk of recurrence. Indeed, discontinuation of antidepressant therapy in patients with medication-responsive illness is associated with an increased risk of relapse (Kupfer et al. 1992). If pharmacotherapy is indicated, it is preferable to use just one medication if possible, in order to avoid exposure to multiple drugs (Nonacs and Cohen 2003).

Because fewer data and studies exist concerning the newer antidepressants, it is recommended not to use compounds for which information on teratogenic risks associated with exposure to them is incomplete or absent as first-line agents in the pharmacological treatment of depression during pregnancy and breast-feeding. Many authors consider the SSRIs as first-line therapy for depression severe enough to justify the use of medication, given findings concerning their reproductive safety and their favourable side effect profile (Bhathia and Bhathia 2002).

The American Psychiatric Association’s Practice Guideline for Major Depressive Disorder in Adults (American Psychiatric Association 2003) suggests that clinicians consider use of better studied agents, the SSRIs fluoxetine (if the woman does not plan to breast-feed) or sertraline if she plans to breast-feed. A TCA and or an SNRI may be introduced if SSRIs are ineffective. It is important to avoid use of bupropion or maprotiline if pre-eclampsia is present.

Among the TCAs, desipramine and nortriptyline are preferred during pregnancy because of their long history of use, lower relative anticholinergic potency compared with other TCAs, lower risk of orthostatic hypotension, and the established relationship between their plasma concentration and therapeutic effect (Cohen and Rosenbaum 1998, Wisner et al. 1999). However, if a woman has responded to another TCA, preferential consideration should be given to its use during pregnancy.

Adjustment of antidepressant dosages may be needed, because antidepressant levels have been reported to decrease during pregnancy, possibly as a result of pregnancy-associated altered volume of distribution. Dosage requirements of nortriptyline, clomipramine, and imipramine in pregnant women have been reported to be 1.6 times (range 1.3–2.0) higher than those needed in nonpregnant women (Wisner et al. 1993). The physician should consider a partial dose taper during the last month of pregnancy to minimise neonatal side effects.
Recurrence rates for patients with major depression during pregnancy are estimated to be as high as 50% within 6 months following discontinuation of antidepressant treatment (Altshuler et al. 1998). Therefore, antidepressant prophylaxis in these patients should be considered. Similarly, patients with a history of severe major depression may benefit from prophylactic reintroduction of antidepressants either during the latter portion of the third trimester or immediately after delivery.

In summary, clinicians should keep the following key principles in mind in selecting treatment options for depression in pregnant women:

• Seek to minimise foetal exposure to both medication and illness
• History should guide therapy
• If medications are indicated, monotherapy is preferable.

**POSTPARTUM DEPRESSION**

During the postpartum period, women may suffer from three types of mood changes: postpartum blues, postpartum depression, and postpartum psychosis (Figure 2.2).

**Epidemiology of Postpartum Mood Changes**

About 25%–40% of mothers suffer from mood lability and mild depression during the first week after parturition, which is referred to as postpartum blues or postpartum dysphoria; about 10%–15% of mothers suffer from a depressive disorder; and 1 or 2 of every 1,000 women present with psychosis during the infant’s first year (Riecher-Rössler & Rhode 2005). These disorders have traditionally been called “postpartum disorders” (Table 2.3).

**Postpartum depression** (PPD) is one of the most common mental disorder following childbearing and has potentially serious long-term adverse consequences for the mother, her family, and the developing child. Yet up to 50% of cases of postpartum depressive disorders are not detected (Briscoe 1986). As noted above, postpartum depressive disorders affect 10%–15% of childbearing women (O’Hara et al. 1990, 1991a; O’Hara and Swain 1996; Cox et al. 1987). There has been some controversy as to whether the risk for depression is increased in postpartum women compared to women of comparable age groups who have not delivered a baby. According to a case-control study (Cox et al. 1993), there is a threefold risk of a depressive disorder in the month following childbirth, compared with monthly incidence rates in nonchildbearing women. Most methodologically sound studies, however, find prevalence rates comparable to those of the normal population (O’Hara et al. 1990). Thus, as concluded by Riecher-Rössler and Hofecker-Fallahpour (2003), there might be an enhanced prevalence of mild subthreshold depression and possibly also a slightly enhanced incidence of major depression in the first postpartum weeks, but, thereafter, the risk seems to be similar to that of other women of the same age group who have quite a high risk for depression anyway. The 1-year-prevalence rate of depression reaching the diagnostic threshold for major depression does not seem to be enhanced.

The rarest and most severe postpartum mood disorder is postpartum psychosis (PPP), with a prevalence rate of approximately 0.1%–0.2% after childbirth (O’Hara et al. 1991a). It starts typically in the 2 to 6 weeks after delivery, but the onset may occur as early as the first 48 to 72 hours postpartum. PPP evolves rapidly and is characterised by depressed or elevated mood, disorganised behaviour, mood lability, delusions, and hallucinations. It is considered a psychiatric emergency, given the risks of suicide and infanticide and requires inpatient treatment.

On the contrary, postpartum blues is very common and generally transient, and although, in 20% of patients, it may herald the development of a major depression in the first postpartum year (O’Hara et al. 1991b). About half of new mothers find themselves sad, angry, irritable, anxious, and prone to tears soon after giving birth. These symptoms (also called “baby blues”) typically peak on the fourth or fifth day after delivery and remit by the tenth postpartum day. Patient education and reassurance are generally adequate treatment measures (Nonacs and Cohen 1998). However, if symptoms and depressed mood persist for 2 weeks, patients should be evaluated for postpartum major depression, particularly if they have a history of depression (O’Hara et al. 1990, 1991a). As a matter of fact, Vigueria et al. (Vigueria et al. 2000) found that the rate of recurrence of bipolar illness in pregnant women was 52% during the 40 weeks following delivery when lithium was discontinued.
**FIGURE 2.2**

Spectrum of postpartum mood changes (Kornstein, 2006)

Spectrum of Postpartum Mood Changes

Transit, Nonpathological  | Serious, Disabling  | Psychiatric Emergency

Postpartum Blues  | ↑risk for MDD

Postpartum Depression

Postpartum Psychosis

**TABLE 2.3**

Mental disorders in the postpartum period

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum blues</td>
<td>Mild depression with mood lability and tearfulness during the first postpartum week, self-limiting</td>
</tr>
<tr>
<td>Postpartum depression</td>
<td>All types of depressive disorders, during the first postpartum months/year</td>
</tr>
<tr>
<td>Postpartum psychosis</td>
<td>Depressive, manic, schizo-affective, schizophrenic, or atypical symptoms during the first postpartum months</td>
</tr>
</tbody>
</table>

Source: Riecher-Rössler & Rhode 2005
Risk Factors for Postpartum Depression

As at other phases of life, the risk of depression during the postpartum period is influenced by genetic vulnerability. The main risk factor that has been identified is an individual predisposition to affective disorders. About one-third of all women with postpartum depression have already suffered from similar previous episodes. There is also often a family history. Apart from individual, partly genetic predisposition, the only additional predictors that have consistently been identified are anxiety and depression already present during pregnancy, baby blues, stress related to child care or general stress, little social support, and marital problems. However, it is not clear to what extent these predictors are of pathogenetic relevance and to what extent they are early consequences of the depression that is beginning (Riecher-Rössler and Hofecker-Fallahpour 2003). A history of major depression (puerperal or not) and an absence of social support can double the risk of developing PPD (Cooper et al. 1996). Factors including negative life events during pregnancy, marital conflict, single marital status, poor health functioning, alcohol use during pregnancy and lower socio-economic status have been identified as risk factors for PPD (Cooper et al. 1996) (Table 2.4).

Evidence to support a biologic basis for PPD is lacking. Changes in the reproductive hormonal milieu associated with pregnancy, particularly the postpartum decrease in oestrogen concentration, may contribute to the onset of depressive symptoms. Studies of the potential role of other biologic factors, including prolactin, oxytocin, cortisol, and β-endorphins, have failed to identify a single specific etiology. Therefore, the combination of a rapidly changing hormonal environment, biologic vulnerability, and psychosocial factors may contribute to the development of this affective illness (Altshuler et al. 1998). Giving birth to a child with all its consequences seems to act as a major stressor—not only in the sense of a psychosocially stressful life event, but also in the sense of a biological stressor.

The sudden drop in oestrogen levels might contribute particularly to the mood lability of the blues and to the outbreak of psychosis (Mahé and Dumaine 2001), which has a 20-fold increased incidence in the first postpartum month, but it might also be relevant in postpartum depression, especially if oestrogen deficiency is sustained. Thus, Bloch et al. (2000) recently found that artificially inducing a drop in oestrogen levels provoked depression in 63% of women with a history of postpartum depression, but not in women without such a history.

On the other hand, there is hardly any life event that is more emotionally stirring than giving birth to a child. In the time period thereafter, the mother has to cope with massive psychosocial changes in almost all areas of her life, with multiple burdens, role changes, -conflicts, losses, and feelings of ambivalence. Thus, new motherhood can also be a severe psychosocial stressor, a fact that is well known from life-event research.

Diagnosis of Postpartum Depression

DSM-IV-TR (American Psychiatric Association 2000) defines postpartum depression (PPD) as a major depressive episode that has its onset within 4 weeks of delivery. The same DSM-IV criteria for a major depressive disorder apply to the diagnosis of PPD. However, the similarities between symptoms of a major depressive episode, PPD, and the normal sequelae of childbirth (such as sleep and

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**TABLE 2.4**

Risk factors for postnatal depressive disorders

- Family or personal history of depressive disorders
- History of previous postnatal depressive disorders
- Ambivalence about pregnancy
- Recent life events (for example, bereavement)
- Marital problems
- Lack of social support
appetite disturbances, weight loss, lack of energy, diminished concentration, and indecisiveness) often complicate the diagnosis of PPD (Llewellyn et al. 1997). The Edinburgh Postnatal Depressive Scale (EPDS), a simple, brief, 10-item self-rating inventory, has been shown to be an effective tool in diagnosing PPD (Cooper et al. 1996). In a large community study, the EPDS had a specificity of 92.5% and a sensitivity of 88%, indicating its validity as a screening tool for PPD (Murray and Carothers 1990).

Management of Postpartum Depression

According to Riecher-Rössler and Hofecker-Fallahpour (2003), “therapy—although in principle the same as that of other depressive disorders—has to put a special emphasis on the needs of the postpartum period. Education about the fact that this is a disease and not due to failure as a mother is of utmost importance to relieve the patients from feelings of guilt. Counselling and practical advice for the mother and her family is often needed as well as the help of a midwife, a family nurse, a social worker and/or other health-care professionals. A good mother–infant bonding should be a main concern from the start. This means that the mother should not be separated from her infant for longer periods of time. However, she needs a great deal of help in order to allow for relaxed contacts with the infant. Baby massage and mother–infant play therapy can be helpful, especially if there are bonding problems”. The same authors noted, “If hospitalisation is needed, mothers are often very reluctant to comply, as they cannot bear the separation from their child, and develop even more feelings of guilt. Also mother–child bonding is severely hampered by the separation. Mother–baby units have therefore been implemented, which allow the admission of mothers together with their infants. Fathers should be involved as much as possible, as father–infant bonding seems just as important, especially when the mother suffers from recurrent illness.” Finally, these authors advised “If medication is needed, some experts advise mothers to stop breastfeeding, as all antidepressants are secreted into breast milk”.

In summary, in selecting treatments for PPD, the key point to keep in mind is that:

- Nonpuerperal depression and puerperal depression are treated similarly unless the mother is breast-feeding.

As during pregnancy, the transition to motherhood may provide challenges for many women. Both IPT and CBT are treatments which have demonstrated efficacy during the postpartum period (O’Hara et al. 2000). For women who have unique needs related to inadequate housing, finances, or their support system, the help of a care manager, who may provide connection to community services or entitlements may prove helpful. The role of family or other support systems to help women with the infant’s overnight feedings cannot be overemphasised. One of the best pieces of advice for depressed women in the postpartum period is to get adequate sleep at night in order to re-establish proper circadian rhythm. Often this requires the help of a significant other. Resumption of physical activity as postpartum healing permits, and maintaining adequate nutrition also facilitates recovery from depression.

Treatment of breastfeeding mothers requires a careful risk/benefit assessment; as during pregnancy, the clinician must weigh risk of treatment against risk of untreated illness to mother and infant, knowing that all antidepressants are excreted in human milk and that maternal depression has adverse effects on infants. Although pharmacotherapies carry some risks, untreated depression may lead to significant problems. If depression is not treated, poor self-care, poor nutrition, and newborn neglect may have an adversely effect on infant development and maternal-child bonding. Recent research suggests that virtually all medications taken by women are secreted into the breast milk. Concentrations vary enormously and are dependent upon medication dosing relative to milk production, and whether the foremilk or the hindmilk is sampled (Stowe et al. 2000). Some additional factors to consider are the severity of illness, the patient’s psychiatric history, her previous history of medication response, and available safety data concerning use of the medication in lactation.
Breast-feeding during maternal pharmacotherapy is acceptable if the risk-benefit analysis is carefully considered and the mother and infant are closely monitored. Current data on the use of antidepressants during lactation do not warrant any absolute recommendations (Epperson 1999). Therefore, the final decision should be based on multiple considerations by women, their families, and their physicians. The decision to treat a breast-feeding woman with antidepressants must involve a case-specific risk-benefit assessment, pending the accumulation of more clinical experience and data.

Data regarding the effects of antidepressants on breast-fed infants are limited. SSRIs are commonly used by lactating women. Drug exposure to the infant can also be minimised if the mother takes the medication just after completion of breast-feeding.

Use of mood stabilisers during lactation are somewhat more problematic, and lactating women general avoid lithium during lactation due to the remote chance of dehydration and lithium toxicity developing within the infant. The American Academy of Pediatrics (1994) considers the use of valproic acid “compatible” with nursing, however rare adverse effects have been observed in nursing infants.

An overall increase in depressive symptoms in thyroid antibody–positive women followed for up to 8 months postpartum reinforces an association between thyroid disturbance and early-onset postpartum depressive disorders and the need to check thyroid function in postpartum women complaining of mood disturbance. (Harris et al. 1992).

Although oestrogen is superior to placebo in treating postnatal depressive disorders (Gregoire et al. 1996), there is no evidence that women suffering from such disorders have progesterone or oestrogen insufficiency. Preliminary research indicates that transdermal oestrogen can also be effective in the treatment of severe cases of depression (Gregoire et al. 1996). However, the relatively hypercoagulable state of women during postpartum places them at risk for thromboembolism when oestrogen is used as a treatment agent during this time.

The effectiveness of oestrogen (sublingually) was also reported by Ahokas et al. (1998, 2001 in studies in which they titrated the oestrogen levels to physiological levels in order to avoid the risk of thromboembolism. However, no double blind, placebo-controlled studies of this treatment have yet been done.

Psychotherapy, including IPT, CBT and counselling, is an appropriate option for women who have mild-to-moderate symptoms and has been used successfully in PPD. In particular, specific psychotherapies for mothers of younger children have been developed by many authors (Stuart and O’Hara 1995; Meagher and Milgrom 1996; Clark et al. 1991; Hofecker et al. 2005).

Women who are severely depressed and at risk of harming their baby or themselves will need extra support from family and health services, and may require admission to hospital. Protective services may also additionally be needed for women whose capacities are so limited that they are unable to care for their children. Support services (family and community) and respite care may be provided by protective services in such cases.

ECT may be of value in patients who have severe depression with psychosis and an increased risk of suicide.

In conclusion, most postpartum depressive disorders should be treated. Longitudinal studies show that about one quarter of affected mothers are still depressed at the child’s first birthday (Kumar and Robson 1984).
Postpartum Affective Psychosis

Postpartum psychosis has an incidence of 1:500 to 1:1000 live births across cultures—a rate that has remained broadly the same for 150 years (Kumar 1994). Women with a history of bipolar disorder or puerperal psychosis are at particularly high risk, between 1:3 (Kendell et al., 1989) and 1:2 (Marks et al. 1992). Biological factors are more important than psychosocial or obstetric factors in the etiology of postpartum psychosis. A family history of affective psychosis increases the risk, suggesting a genetic role (Brockington et al. 1982). Sudden fluctuations in hormone levels following labour may precipitate psychosis in genetically vulnerable women, possibly by leading to changes in neurotransmitter activity. Most patients present within 2 weeks of delivery as severe cases of psychosis, often accompanied by perplexity or confusion (Kendell et al. 1989). Suicidal and infanticidal ideation may occur.

Some women can be managed at home, but most require hospital admission (Oates and Gath 1989). When mother and baby are admitted together, all contact between the two should be supervised by staff to ensure the safety of the baby. Antidepressants, atypical antipsychotics, mood stabilisers, and ECT are used when appropriate, as for postnatal depressive disorders. While there is emerging research regarding the use of antipsychotics during lactation, the available evidence is insufficiently powered to draw any firm conclusions about the use of these agents in breast-fed infants.

Prognosis for postpartum psychosis is good; with high response rates to adequate treatment trials. However, relapse can occur, so women should be closely monitored after returning to their homes. Women of childbearing age with histories of bipolar disorder should be advised of the risk of postpartum psychosis and monitored very closely postpartum. Recent data suggests that continuation of lithium during pregnancy may significantly decrease rates of postpartum relapse of bipolar illness (Blehar et al. 1998; Viguera et al. 2000).

DEPRESSION AND MENOPAUSE

Definitions

It is important to distinguish the three phases related to menopause that succeed one another during this stage of life, which actually lasts many years (Table 2.5). Menopause which usually occurs in women around the age of 50 is the point at which a woman has permanently ceased menstruating. Perimenopause, which typically starts 5–7 years before menopause, is the interval between regular ovulatory menstrual cycles and complete cessation of ovarian function. Postmenopause is defined formally as the time after which a woman has experienced 12 consecutive months of amenorrhea without a period.

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<th>TABLE 2.5</th>
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<td><strong>Definitions</strong></td>
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<td><strong>Menopause</strong></td>
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<td><strong>Perimenopause</strong></td>
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<td><strong>Postmenopause</strong></td>
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DePressIon anD menoP aUse

Definitions

It is important to distinguish the three phases related to menopause that succeed one another during this stage of life, which actually lasts many years (Table 2.5). Menopause which usually occurs in women around the age of 50 is the point at which a woman has permanently ceased menstruating. Perimenopause, which typically starts 5–7 years before menopause, is the interval between regular ovulatory menstrual cycles and complete cessation of ovarian function. Postmenopause is defined formally as the time after which a woman has experienced 12 consecutive months of amenorrhea without a period.
Epidemiology

The prevalence of depressive disorders does not seem to increase during menopause (Hunter 1996), and is no more likely to occur during menopause than at any other time in a woman’s life (Nolen-Hoeksema 1995). On the contrary, epidemiological studies suggest that the risk of depression decreases in women after age 50. A large 5-year longitudinal prospective study of women between the ages of 45 and 55 years examined the effect of menopause on depression (Avis et al. 1994). The study, which controlled for prior depression, menopausal symptoms, and concurrent hormonal treatment, showed that the onset of natural menopause was not associated with an increased risk of depression.

However, the risk of depression may be heightened during perimenopause, when hormone levels fluctuate erratically. Several studies and community surveys have found a peak in the prevalence of major depression during the menopausal transition. For example, Ballinger et al. (1990) reported a significant increase in psychiatric morbidity among perimenopausal women ages 45 to 49 years.

More recent studies suggest that some women are particularly vulnerable to development of depression when entering the perimenopause. In a large, methodologically very thorough study, Freeman et al. (2006) have recently shown that new onset of depressive disorder was 2½ times more likely to occur during the menopausal transition as compared with premenopausal women. The Harvard Study of Mood and Cycles (Cohen et al.) showed similar results. Recurrence of depression may also occur more often in association with the menopausal period of life. There are some studies suggesting that women with a history of mood symptoms accompanying alterations in reproductive hormones, such as mood symptoms occurring during the postpartum and premenstrual phases, may be at particular risk for experiencing major depression during menopause (Hay et al. 1994). With regard to an increase of depressive disorders in the postmenopausal period, studies are even more contradictory, with more recent studies tending to be negative.

Risk Factors

The gonadal source of oestrogen production is lost at the menopause. As oestrogens have important neuro- and psychoprotective activities, this loss may trigger or aggravate mental disorders in vulnerable women. Oestrogens, 17-b-estradiol in particular, exert multiple positive functions in the brain, as they seem to improve both cerebral blood flow and glucose metabolism, promote neuronal sprouting and myelinisation, enhance synaptic density and plasticity, facilitate neuronal connectivity, act as antioxidants, and inhibit neuronal cell death. As long ago as the early eighties the identification of oestrogen receptors in the limbic system led to the assumption that oestrogens not only play a role in the modulation of endocrine functions but must also have a “neuro-modulating function”. It was observed in laboratory animals that the effect of oestrogens is in some respects similar to that of antipsychotics. Oestrogens modulate cerebral neurotransmission in many ways and influence both mood and cognition. They appear to have significant effects on the dopaminergic, serotonergic, noradrenergic, glutamergic, and cholinergic systems. Concurrently, ample evidence has been collected to show that oestrogens exert several positive effects on mental state. They may improve affective symptoms, reduce aggressivity, and influence suicidal behaviour. They may also act as stress protectors and effectively improve cognitive function. Oestrogens have therefore even been called “nature’s psychoprotectants”.

In addition to the obvious physical ageing occurring in association with menopause, this phase of life is often associated with emotional stressors such as children leaving home, frequent sexual and relational problems, worries about the health of partner, parents, or self, stressful confrontation with the process of biological ageing itself, and the need to re-evaluate life expectations.
Environmental events and developmental life stressors, such as changes in family structure, caring for an elderly parent, having children leave or return home, involvement in outside work in addition to running a household, and reappraisal of one’s future role, have also been shown to affect mental health during this life stage. These psychosocial factors may contribute more to common menopausal symptoms such as fatigue, anxiety, and sadness than to physiologic changes associated with menopause (Desai and Jann 2000). Life changes particularly losses, and other interpersonal role transitions have been associated with onset and maintenance of depression in women (Weissman et al, 2000).

The risk of depression seems to be greater in women who have severe vasomotor symptoms, such as hot flashes and night sweats. Affective changes at the time of menopause may be secondary to the occurrence of vasomotor or other physical symptoms, rather than menopausal status itself (Avis et al. 1994). However, most women who experience uncomfortable menopausal symptoms don’t develop depression and sometimes depression may be the first symptom to appear, even before the vasomotor symptoms. Other physiological changes, including insomnia, which may accompany the decline in oestrogen during the menopause transition, may predispose some women to changes in mood (Eichling and Sahni 2005). Women with a previous history of PPD, premenstrual syndrome, or depressive episodes are at increased risk for developing a depressive illness at menopause (Stewart et al. 1993). In the longitudinal study by Avis et al. (1994), prior depression was the variable that was most predictive of subsequent depression in postmenopausal women. Hysterectomy with removal of the ovaries can lead to an abrupt onset of menopause with more severe symptoms, including mood changes and sometimes depression.

**FIGURE 2.3**

**Depression and menopause**

1Soares CN, Cohen LS. CNS Spectrums. 2001;6:167-174

Management

Very few studies of antidepressants have controlled for menopausal status, but some data suggest that there may be differences in treatment response between premenopausal and postmenopausal women. As a whole, available data suggest that women tend to respond less well than men to tricyclic antidepressants, while they tend to respond better to SSRIs and monoamine oxidase inhibitors ((MAOIs). These differences appear to be particularly true in premenopausal women, whereas postmenopausal women tend to respond somewhat more like men.

Data on the role of hormone replacement therapy (HRT) in managing mood disorders in the peri- and postmenopause is confusing and most studies to date have yielded inconsistent findings. Although there is evidence of improved well-being in healthy women taking HRT (Pearce et al, 1995), there is little evidence to suggest that HRT improves depressive disorders in menopausal women (Morrison et al. 2004). Thus, women who have depressive symptoms during menopause should be treated with conventional treatments, such as antidepressant drugs and psychotherapy. In contrast, HRT may reduce the likelihood of depressive disorders in women who have undergone a surgical menopause (Sherwin and Gelfand 1985).

Several studies have shown that oestrogen alone may be effective for perimenopausal depression. A 12-week, double-blind, placebo-controlled study (Weissman and Olfson 1995) evaluated subjects with major depressive disorder (MDD), dysthymia, or minor depression who were treated with either an HRT patch or placebo. There was significant improvement in depressive symptoms in women taking HRT. The remission rates for those on HRT were significantly higher than remission rates of those on placebo, suggesting that modulating oestrogen during perimenopause may be helpful in reducing risk of depression during this period.

Most researchers in this area have reported that oestrogen replacement alone can provide relief of vasomotor symptoms, and minor cognitive and mood symptoms. This therapy is also useful in preventing osteoporosis.

Studies have also reported positive therapeutic effects of oestrogens on depression. In women suffering from hot flushes, mild depressive symptoms may also be present and can be treated effectively with oestrogens without referral to a psychiatrist. Zweifel and O’Brien (1997) have conducted a meta-analysis on 26 studies of mild depression. They concluded that oestrogen treatment has the potential to reduce mild depressive symptoms in women with a natural menopause. The therapeutic effect was most pronounced in perimenopausal women, as opposed to postmenopausal or mixed study groups. The same therapeutic effect has also been demonstrated in severe major depression (Schmidt et al. 2000; Soares et al. 2001, Rasgon et al. 2001, Cohen et al. 2003; a review see Riecher-Rössler and de Geyter 2007).

For women who have prominent complaints of insomnia, estradiol may play a role in stabilising sleep. Behavioural management and sleep hygiene as well as novel new agents such as zolpidem may also provide short term relief from insomnia and prevent further deterioration in mood symptoms (Soares and Murray 2006). Some studies also suggest that HRT may enhance antidepressant response in postmenopausal women taking SSRIs.

Menopause is certainly a physiological event, but it is accompanied by hormonal and other biological alterations as well as manifold psychosocial changes. All these changes can trigger or aggravate mental disorders in some women, probably on a basis of genetic susceptibility. Oestrogen replacement may in these cases be an effective therapeutic measure. Nevertheless, antidepressants remain the treatment of choice if the patient has major depression, especially given the recent concerns about hormonal therapies.
DEPRESSION AND USE OF ORAL CONTRACEPTIVES

Twin studies suggest that there may be a familial risk of developing depressive disorders during oral contraceptive use (Kendler et al., 1988). Some early studies showed an association between depressive disorders and the use of oral contraceptives with high-dose progestins (Grant and Pryse-Davies, 1968); others studies found that oral contraceptive users may develop a pyridoxine deficiency (Rose et al., 1972) and that depressive symptoms in this situation may benefit from pyridoxine supplementation (Adams et al., 1973). There does seem to be some evidence that oral contraceptives have a positive effect on mood among women of all ages whose hormones are in a state of flux. In adolescent girls a recent placebo controlled study using oral contraceptives showed improvement in CES-D scores in girls treated with both placebo and oral contraceptives (O’Connell et al., 2007). Some studies have explored use of oral contraceptive use by women in the postpartum period and have found a significant improvement in mood when estradiol was used for women with postpartum depression (Gregoire et al., 1996). In another randomised controlled trial, estradiol was found to enhance mood in perimenopausal women (Soares et al., 2001). Estradiol did not significantly improve mood in post-menopausal women with depression, however (Morrison et al., 2004). A recent assessment of women with major depressive disorder who were under 40 years of age and were participating in the STAR*D trial suggested that women on progestin-only agents had more comorbid general medical conditions, hypersomnia, weight gain, and gastrointestinal symptoms than women on combined agents, or those using no oral contraceptives. Those on combined hormone contraception demonstrated fewer depressed symptoms on the 16-item Quick Inventory of Depressive Symptomatology (Young et al., 2007). There is some suggestion that long-acting depot progestins (Norplant, Depo-Provera), may be more problematic for mood, particularly in women who are predisposed to depression and have elevated mood scores when they initiate these medication (Westhoff et al., 1998a and b). The recent introduction of lower dose oral contraceptives may have led to a decrease in associated depressive symptoms.

STERILITY

Other issues surrounding reproductive life can lead to depression, particularly infertility. In societies where a woman’s value is equated her capacity to procreate, preferably, sons, sterility is a definite risk factor for depression. Kamel reported depression rates of 32.5%, and anxiety rates of 55% in a Bahraini sample of 70 infertile women; likewise, Nasr et al. found 46.6% of depression and 42.9% of anxiety in a Tunisian sample of 105 infertile women (Douki et al., 2007).
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PART 2
Depressive Disorders in Women
Chapter 3
Non-Specific Depressive Disorders in Women
MAJOR DEPRESSIVE DISORDERS

Although the same diagnostic criteria are used for both genders, the presentation and course of depression are sometimes different in women (Table 3.1).

Gender Differences in Presentation

Several differences between genders in symptomatology, comorbid conditions, and coping styles have been described.

Symptoms

Compared with men, women are more likely to present two subtypes of major depressive disorder: major depressive episodes with atypical features and major depressive episodes with seasonal pattern.

Major depressive episode with atypical features or atypical depression (AD) (Angst and Gamma 2003; Kornstein 1997; Kornstein et al. 1996; Young et al. 1990). The DSM-IV-TR (American Psychiatric Association 2000) defines depression with atypical features as a subtype of depression characterized by mood reactivity, which means being able to experience improved mood in response to positive events. In contrast, sufferers from melancholic depression generally cannot experience positive moods, even when good things happen. Additionally, atypical depression is characterised by reversed vegetative symptoms, namely substantial gain in appetite or weight and oversleeping (sleeping at nighttime, as well as sometimes daytime napping, that lasts at least 10 hours total or 2 hours more than is normal for the person). Diagnostic criteria for atypical depression are shown in Table 3.2. Atypical features occur two to three times more often in women than in men. They are also associated with depression beginning at an earlier age (e.g., in the teens) and possibly with more chronic depressive episodes. Personality and anxiety disorders may also be more common.

Major depressive disorder with seasonal pattern (Seasonal affective disorder) (Liebenluft, 1995, Burt and Hendrick 2001). Women are six times as likely as men to have seasonal affective disorder (SAD), a condition in which depressive episodes recur in a seasonal pattern. In winter-SAD, which is more common in the northern hemisphere, symptoms of depression are limited to the fall and winter months, whereas in summer-SAD, which is observed more often in the southern hemisphere, depression occurs in the spring and summer. The changes in mood and behaviour that characterise SAD (especially the winter type) run in families and appear to be largely due to a biological predisposition. Possible aetiologies implicated in SAD are changes in circadian rhythm, altered melatonin secretion, or serotonin dysfunction. This type of depression is characterised by atypical or reverse vegetative symptoms, including subjective dysphoria, hypersomnia, severe fatigue with a heavy feeling in the arms and legs, increased appetite and carbohydrate craving, and weight gain. Treatment of SAD is based on the use of artificial light therapy (2500 lux of light for 1–2 hours or 10000 lux of light for 30 minutes generally administered in the morning). In some cases, adjunctive pharmacotherapy (especially SSRIs) is helpful in maintaining remission from symptomatic season to season.

Other differences in symptomatology (Kendler et al. 1993; Young et al. 1990). The symptoms of depression in men and women tend to be fairly similar overall, except that women tend to report a greater number of depressive symptoms than men. Major depressive episodes that meet full DSM-IV-TR criteria are more prevalent in female than male depressed patients (Angst et al. 2002). In the large European DEPRES I and II study, women were significantly more likely to meet five or more criteria for depression than men (female/male ratio 1.96). However, women also appear to be more likely to present with more anxiety and somatic symptoms (e.g., headaches, stomach upset) than men, whereas some features of depression appear more prevalent in men (e.g., a tendency to overreact, anger attacks) (Winkler et al. 2005).

Comorbidity

The presence of comorbid conditions is generally associated with a more serious course of depressive illness. Moreover, the presence of comorbid conditions can complicate the evaluation and treatment of both the depression and the other conditions that are present. Data from both the Epidemiologic Catchment Area study (Regier et al. 1990) and the National Comorbidity Survey (Kessler et al. 1994) show that depressed
TABLE 3.1

Gender differences in presentation of depression

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Women versus men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime prevalence</td>
<td>20% versus 10%</td>
</tr>
<tr>
<td>Age of onset</td>
<td>May be earlier</td>
</tr>
<tr>
<td>Duration of episodes</td>
<td>May be longer</td>
</tr>
<tr>
<td>Course of illness</td>
<td>May more often be recurrent or chronic</td>
</tr>
<tr>
<td>Seasonality</td>
<td>More frequent</td>
</tr>
<tr>
<td>Association with interpersonal stressful life events</td>
<td>More frequent</td>
</tr>
<tr>
<td>Association with work stressors</td>
<td>Less frequent</td>
</tr>
<tr>
<td>Atypical symptoms, reverse vegetative symptoms</td>
<td>More frequent</td>
</tr>
<tr>
<td>Suicidal behaviour</td>
<td>Suicide attempts versus completed suicide</td>
</tr>
<tr>
<td>Comorbid anxiety disorders</td>
<td>Greater</td>
</tr>
<tr>
<td>Comorbid eating disorders</td>
<td>Greater</td>
</tr>
<tr>
<td>Comorbid alcohol or substance use disorder</td>
<td>Less frequent</td>
</tr>
<tr>
<td>Comorbid hypothyroidism</td>
<td>Greater</td>
</tr>
<tr>
<td>Comorbid migraine headaches</td>
<td>Greater</td>
</tr>
<tr>
<td>Comorbid antisocial, narcissistic or obsessive-compulsive disorder</td>
<td>Less frequent</td>
</tr>
<tr>
<td>Effect of exogenous and endogenous gonadal steroids on mood</td>
<td>Greater</td>
</tr>
</tbody>
</table>

Sources: Bhatia and Bhatia 1999; Kessler et al. 1999; Kornstein et al. 2002
women have higher rates of comorbidity than depressed men, especially with regard to anxiety disorders, somatisation, and eating disorders. In contrast, depressed men are more likely to have a comorbid substance use disorder. Depressed women also had a higher prevalence than men of both lifetime and 12-month comorbidity of three or more disorders. In the Epidemiologic Catchment Area study, 51% of respondents with major depression had a comorbid anxiety disorder, with a female-to-male ratio of 3 to 1. Phobia and panic disorder were the most prevalent comorbid anxiety disorders in depressed women. Comorbid generalised anxiety disorder is also frequently in association with major depression. Data from the NIMH showed no gender difference in overall prevalence rates of comorbid personality disorders; however, obsessive-compulsive, passive-aggressive, antisocial, and narcissistic personality disorders were diagnosed significantly more often in men than women (Kornstein et al. 1996).

Women also appear to be particularly vulnerable to medical conditions such as thyroid disorders, rheumatological conditions, and migraine disorders, all of which can make depression more difficult to treat successfully (Pajer 1995; Kornstein 1997). Thyroid screening is recommended for depressed women who are 45 year of age or older, or for women with a personal or family history of thyroid disease. Migraine headaches in women are often influenced by reproductive hormonal changes associated with menarche, the menstrual cycle, pregnancy, and oral contraceptive use. Other comorbid general medical disorders common in depressed women include chronic fatigue, fibromyalgia, chronic pelvic pain, and irritable bowel syndrome. Clinicians should also keep in mind the increased risk of myocardial infarction among those with a history of depression in treating depressed women patients.

Precipitating factors

Gender differences also exist in factors that can precipitate depressive episodes. Women have been shown to be more sensitive than men to becoming depressed following a stressful life event (Bebbington et al. 1988). A study by Kendler et al. (2001) examined the role of stressful life events and found that women were 3 times more likely than men to develop depression after experiencing

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**TABLE 3.2**

Criteria for atypical features specifier for a major depressive episode

| A. Mood reactivity (i.e., mood brightens in response to actual or potential positive events) |
| B. At least two of the following: |
| 1. Significant weight gain or increase in appetite |
| 2. Hypersomnia (sleeping too much, as opposed to the insomnia present in melancholic depression) |
| 3. Leaden paralysis (i.e., heavy, leaden feelings in arms or legs) |
| 4. Long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment |
| C. Criteria are not met for melancholic depression or catatonic depression during the same episode. |

a traumatic event. The stressors determined to be significant included the death of a relative, illness, or change in residence. One stressor that was found to be significant in men, but not in women, was financial stressors. Indeed, many studies confirmed that the type of stressor may be of significance, with women being more sensitive to family events and men to financial difficulties (Kessler and McLeod 1984). As already mentioned, seasonal changes are also more likely to trigger depressive episodes in women than in men. Of those suffering from SAD, nearly 80% are women (Leibenluft et al. 1995). In addition, many women experience depressive symptoms in relation to events in the reproductive cycle (e.g., premenstrually, during the postpartum period, and during the menopause). Hormonal therapies, including hormonal contraceptives, hormone replacement therapy, and infertility medications may also be associated with depressive symptoms (Kornstein 1997).

Gender Differences in Course

Some studies have noted an earlier age at onset of major depression in women (Kessler et al. 1993; Kornstein et al. 1996; Fava et al. 1996). In the National Comorbidity Survey, this difference was most pronounced in early adolescence, with age at onset of the first major depressive episode in females reported to be as early as age 10 (Kessler et al. 1993). Whereas men more commonly become symptomatic in their twenties, women often become symptomatic in mid-adolescence (Ernst and Angst 1992). Evidence from several longitudinal studies suggests that women have longer episodes of depression and are more likely than men to develop a chronic or recurrent course (Bhatia and Bhatia 1999). The results of the STAR-D study (Marcus et al. 2005) also showed a significantly earlier onset of the first major depressive episode in women, as well as longer current major episodes in women than men.

Gender Differences Across the Lifespan

Interestingly, gender differences in symptomatology are already apparent in adolescent depression. In a study of 383 depressed adolescents with a mean age of 15.8 years, Bennett et al. (2005) found that depressed girls were more likely to exhibit guilt, body image dissatisfaction, self-blame, self-disappointment, feelings of failure, concentration problems, difficulty working, sadness/depressed mood problems, fatigue, and health worries than their male counterparts. In contrast, depressed boys had higher clinician ratings for anhedonia, depressed morning mood, and morning fatigue.

In contrast, gender differences in the presentation of depressive symptoms in elderly individuals have not been formally studied, and it is not known whether there are gender-related differences in depressive symptoms in elderly individuals. One common presentation in elderly patients has been described as “masked depression”, because the depressed mood may be absent or hidden by somatic complaints—which may even be the presenting symptoms (Casper et al. 1985). Depressed women may not recognise the feeling of depression, but may complain more of anxiety and “nerves” (Blazer 1989). Chronic abdominal distress, nonlocalised pain, and other unresponsive pain syndromes, may all suggest the presence of depression.

In depressions with psychotic features, it seems that delusions of poverty (delusions regarding the lack of money or clothes despite proof of the contrary) are more common in women, whereas delusions regarding somatic concerns and cancer are more common in men; (Holroyd, 2001).

Gender Differences in Clinical Management

The standard assessment of women with major depression should include a careful evaluation of symptoms at presentation, including their number, type (e.g., typical versus atypical), and severity (e.g., presence of suicidal ideation or psychosis). The assessment should also explore comorbidity, triggers for episodes (e.g., such as stressful life events, seasonal pattern, or reproductive events), possible premenstrual exacerbation of illness, current or recent pregnancy, and whether the woman is breast-feeding. The evaluation should also assess the course of the depressive episode, the patient’s personality (strengths, coping skills), and psychosocial factors (e.g., victimisation, role stress, social support from family members) (Desai and Jann 2000; Kornstein, 1997; Pajer 1995). Treatment interventions in the clinical management of major depression include education, psychosocial therapy, pharmacotherapy with antidepressant agents, and ECT. The American Psychiatric Association
has provided clinical practice guidelines for the treatment of major depression in adults, which are the same in women and men (1993). Special gender-related treatment issues are also discussed in Volume II, Chapter 4 and Volume III, Part 2, Chapters 2 and 6.

BIPOLAR DISORDER

Although bipolar disorder occurs equally in both genders, there are significant differences in its clinical features, course, and treatment.

Gender Differences in Clinical Presentation

Women have higher prevalence rates of mood episodes than men, especially depressive episodes (Kessler et al. 1994). Bipolar II disorder, characterised by episodes of hypomania and depression, occurs more frequently in women than in men (Dunner 1998). Women with bipolar disorder are approximately two times as likely as men with the disorder to experience rapid cycling, defined as four or more affective episodes per year, with the percentage of rapid cycling patients who are female ranging from 58% to 92% (mean of approximately 71%) (Leibenfult 1997). Why rapid-cycling bipolar disorder should occur more often in women is unclear; it may result from women’s greater likelihood of being treated with antidepressants, which may precipitate rapid cycling. Hypothyroidism has been implicated in rapid cycling, with 30%–90% of patients with rapid cycling bipolar disorder reported to have hypothyroidism; and thyroid dysfunction is more common in women (Freeman et al. 2001).

Finally, women appear to experience a seasonal pattern of mood disturbances more often than men, with women’s depressive episodes more commonly occurring in the fall and winter than in the spring and summer (Faedda et al. 1993).

Women with bipolar disorder may experience a premenstrual relapse or exacerbation of symptoms. Daily charting of moods will allow the clinician and patient to better assess the relationship between phases of the woman’s menstrual cycle and mood changes. For women whose mood consistently deteriorates during the premenstrual phase, it is helpful to obtain blood levels of medication both premenstrually and in the week postmenses, as serum levels of mood stabilisers may fluctuate across the menstrual cycle.

Gender Differences in Clinical Management

Special considerations in treating women with bipolar disorder are summarised in Table 3.3. Because women taking lithium are at significant risk of developing lithium-induced hypothyroidism, especially when they are over 40 years of age, thyroid function should be monitored at least every 6 months. Because it can induce hormone clearance and metabolism, carbamazepine may reduce the efficacy of oral contraceptives; women with bipolar disorder who are taking carbamazepine and oral contraceptives should therefore be advised to use a different or additional form of contraceptive. Similarly, postmenopausal women taking carbamazepine may need higher doses of hormone replacement therapy to reduce vasomotor symptoms associated with hypo-oestrogenemia (e.g., flashes, night sweats).

TABLE 3.3

Special considerations in the treatment of women with bipolar disorder

- Symptoms may recur or worsen premenstrually
- Medication levels may fluctuate across the menstrual cycle
- Carbamazepine may render oral contraceptives ineffective through its induction of liver enzymes
- Psychotropic agents may produce disturbances in the menstrual cycle
- Mood stabilisers, especially valproic acid and carbamazepine, are associated with relatively high rates of foetal anomalies when used during the first trimester of pregnancy
- Women with bipolar disorder are at high risk for postpartum depression
- Thyroid function should be monitored at least every 6 months in women taking lithium, given the significant risk of developing lithium-induced hypothyroidism

Source: Freeman et al. 2001
REFERENCES


PART 2
Depressive Disorders in Women
Chapter 4

Depression and Suicide in Women
Depression is a significant risk factor for suicidal behaviour in both sexes. Women, especially those younger than 30 years of age, more often attempt suicide, but the rate of completed suicide is higher in men (Hirschfeld and Russell, 1997). The male-to-female ratio for completed suicide is greater than 4:1 (Moscicki 1994). This difference is probably related to the tendency of men to use more lethal and immediate methods (such as fire arms and hanging), whereas women more often take overdoses of medication. Self poisoning is the most common method of suicide for females (39.1%) (CDC, 2005). Men are also less likely to seek psychiatric help that may prevent suicide. Significant risk factors for suicide by women are listed in Table 4.1 (Bhatia et al. 2000). Some researchers believe that suicide rates are vastly underestimated because many suicides are recorded as accidental deaths. Similarly, self-inflicted injury may also be concealed or may not come to medical attention (Stewart et al. 2006).

Among women, some populations seem to be at particular risk. For example, the U.S. National Center for Health Statistics (1994) indicated that Asian American women over the age of 65 have the highest female suicide rate among all ethnic and racial groups. In addition, Asian American adolescent girls have the highest rates of depressive symptoms of all racial groups and have the highest suicide rate among all women between 15 and 24 years of age (National Center for Health Statistics 1994). Likewise, the 2001 British Confidential Enquiry into Maternal Deaths described suicide as the leading cause of maternal death within the year following childbirth. This finding was made possible only by data linkage and the examination of indirect causes of maternal death, which illustrates the silent nature of mental illness as a cause of mortality and morbidity. Stewart recommend that indicators beyond the usual obstetrical factors must be included and that the period being monitored be lengthened beyond the current 42 days to improve maternal mortality rates in developed countries (Stewart et al. 2006).

During the initial visit, every patient with depression should be screened for suicidal thoughts, intent, and plan, as well as the availability and lethality of a method for committing suicide. This screening may provide an opportunity for life-saving intervention (Hirschfeld and Russell 1997). Outpatient management is appropriate for patients with less severe depression who have infrequent suicidal thoughts, who are willing to contract for safety and let go of their instrument of suicide, who have good social support, and who are willing to return for regular follow-up (Bhatia et al. 2000; Bhatia and Bhatia 1999; Mosciki 1994).

Psychotherapy may be used alone in women with mild to moderate depression, or it may be used adjunctively with antidepressant drug therapy. Because women are more prone to self-poisoning than men, it is recommended that clinicians prescribe only one week of an antidepressant at the initial visit with a depressed female patient (especially if prescribing an agent that is potentially lethal in overdose, such as a tricyclic antidepressant). It is also important to enlist the aid of at least one of the patient’s family members or friends to monitor intake of the prescribed antidepressant so that the patient does not hoard the medication for use in a suicide attempt.

Hospitalisation is necessary for patients with severe depression, psychosis, substance abuse, severe hopelessness, or limited social support. Patients should also be hospitalised if they display a strong urge to act on suicidal thoughts or if they have a specific suicide plan that is likely to be successful. Women who have severe depression accompanied by active suicidal thoughts or plans should usually be managed in conjunction with a psychiatrist. (Bhatia and Bhatia 1999)
TABLE 4.1

High-Risk Factors for Suicidal Behaviour in Women

<table>
<thead>
<tr>
<th>Risk for suicide attempts</th>
<th>Risk for completed suicide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threatened loss of intimate relationship</td>
<td>Severe clinical depression, especially with psychosis</td>
</tr>
<tr>
<td>Living alone</td>
<td>Substance abuse</td>
</tr>
<tr>
<td>Current psychosocial stressors</td>
<td>History of suicide attempts</td>
</tr>
<tr>
<td>(e.g., recent loss of job)</td>
<td>Current active suicidal ideation or plan</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>Divorced or widowed</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>One or more active or chronic medical illnesses</td>
</tr>
<tr>
<td>(e.g., borderline personality disorder)</td>
<td>Feelings of hopelessness</td>
</tr>
<tr>
<td>Clinical depression</td>
<td></td>
</tr>
</tbody>
</table>

REFERENCES


PART 2
Depressive Disorders in Women
Chapter 5
Cultural Issues Related to Depression in Women

The findings covered in the first 4 Chapters of this Volume have focused largely on depression in women in Western cultural settings. Gender differences in depression are well documented in westernised, developed societies, but there has been little quantitative cross-cultural research on this topic.
GENDER DIFFERENCES IN PREVALENCE

Cultures around the world do not appear to display a similar difference in rates of depression as reported in Western societies. Some studies suggest that gender differences in depression may be related to whether or not the society or group under study is “traditional” (Loewenthal et al. 1995). The first community-based epidemiological survey in Tunisia (Sraïri 1995) which involved 5000 adults, found a very slight gender difference of 1.2, with a lifetime prevalence of 9% in women versus 7.4% in men. Carta et al. (1991) found no gender differences in depression in a Sardinian community study. Likewise, Loewenthal et al. (1995) found a similar prevalence of case depression among men as among women in a sample of 339 Jewish individuals (157 men and 182 women) affiliated with orthodox synagogues. A previous study carried out by the same team (Loewenthal and Goldblatt 1993) found men more depressed than women, with husbands more depressed than their wives. In a recent study (Hopcroft and Bradley 2004), the authors examined gender differences in depression across 26 westernized and non-westernized countries using data from the U.S. General Social Survey and the World Values Survey. They reported that young women across all types of countries are more likely to report depressive symptoms than young men, but the gender difference in depression among those over 50 is only found in westernized, developed countries.

GENDER DIFFERENCES IN RISK FACTORS

Cultural phenomena can give rise to particular risk factors of developing depressive disorders. As a matter of fact, cultural attitudes toward menstruation seem to increase a woman’s vulnerability to premenstrual depression (Bancroft 1993). Similarly, negative beliefs about menopause (Avis et al. 1994) are associated with an increased risk of depressive disorders, while, in cultures with positive attitudes toward menopause, women tend to report few symptoms (Flint 1975). In some traditional societies, menopause constitutes a high-risk phase of life. For example, menopause, which put an end to any hope of procreation, is named in Arabic “age of despair”. A recent study carried out in Tunisia among a thousand women between 45 and 64 years of age found a 34% prevalence rate of depressive disorders (Ayari 2005). Likewise, it has been shown that postpartum depression occurs as frequently in developing countries as in developed countries, but that there were cultural differences in risk factors. In India, a study found that low income, birth of a daughter when a son was desired, relationship difficulties with mother-in-law and parents, adverse life events during pregnancy, and lack of physical help were risk factors for the onset of postpartum depression (Chandran et al. 2002). Lee et al. (2004) showed that conflict with a mother-in-law was also an important source of household distress in many Asian societies. The cultural practice of peiyue—Chinese custom of mandated postpartum family support—was associated with better social support and a slightly lower risk of postnatal depression.

GENDER DIFFERENCES IN CLINICAL PRESENTATION

Gender-related differences in risk factors for depression may be explained by gender differences in clinical presentation across various cultures. It is well recognized that culture can influence the experience and communication of symptoms of depression. For example, in non-Western cultures, depression may be expressed largely through somatic complaints, (e.g., bodily aches and pains) rather than sadness or guilt. Gender differences in clinical presentation have not been thoroughly studied across ethnicities. Nevertheless, some studies have reported some findings in this area. Contrary to what has been reported in western countries, women in developing countries are less likely than men to meet the current diagnostic criteria for a major depressive episode, which may in part explain the underdetection of depression in women in these settings using current screening instruments.
In a study comparing depressive symptomatology in France and in Maghreb (Darcourt et al. 2003) using the Hamilton Depression Rating Scale, more gender-related clinical differences were found in the Maghrebian population than in the French sample. Maghrebian women had lower scores for retardation and higher scores for anxious and somatic symptoms than men. In contrast, in France, only one item differed between genders, with muscle tension more elevated in women than men (1.93 versus 1.03). In two studies in Tunisia (Bouattour 2001; Douki et al. 1991), the first of which included 1100 subjects of both genders and the second of which included 250 depressed women, the female subjects appeared to display a different pattern of symptoms than men. Two subtypes of depression were more prevalent in females:

**Hostile depression**

The occurrence of anger, irritability, and hostility in depression has been recognised for many years. More recently, anger attacks have been proposed as a specific form of depression (Painuly et al. 2004). These attacks are characterised by a tendency to overreact, a rapid onset of intense anger, and a crescendo of autonomic arousal occurring in response to trivial provocations or stress. Children are often the main victims of these episodes of “acting out”, which are then followed by deep feelings of guilt and sadness. Patients with this clinical profile also complain about chronic headaches, insomnia, lack of concentration, and difficulty maintaining relationships. Conjugal conflicts are often associated with this type of depression.

**Masked depression**

Depression may be disguised as somatic complaints such as headache, joint or muscle pain, back pain, tiredness, fatigue, weakness, and constipation and other gastrointestinal problems. This type of patient often first presents to the general practitioner and costly laboratory tests may be undertaken in an attempt to identify an organic source for the symptoms.

Kleinman (2004) has described somatic symptoms as an alternative “idiom of distress” that is prevalent in cultures where psychiatric disorders carry great stigma. He explained that Chinese immigrants to the United States may display boredom, pain, fatigue, or dizziness rather than sadness as the symptom of their depression, since the more “normal” display of depressive symptoms is culturally, morally, and experientially unacceptable to large numbers of Chinese.

The expression of depression is also very dependent on educational background. Somatisation and anger are correlated with a low level of education and verbalisation, which are more common in women. This cultural pattern is changing over time, as progress is made in education, urbanisation, and individualisation, evolving towards a western-type clinical depression.

Depression in women frequently has a chronic course. In Bouattour’s study (2001), females represented 73% of the 1100 subjects on sick-leave for more than 1 year. Women are often misdiagnosed and do not receive appropriate treatment. Instead, they are frequently told that they are tense, nervous, and/or run down and they may be prescribed vitamins or anxiolytics. They may also be advised to lose weight, learn to relax, get a change of scenery, or get more exercise. The root of their symptoms is not explored and these women continue to complain of being tired and empty.

**GENDER DIFFERENCES IN COPING STYLES**

Gender differences in depression may be explained in part by differences in ways of handling stress and psychological suffering. Thus, Loewenthal et al. 1996 found similar rates of depression in women and men in their sample of Jewish individuals. These findings suggest that specific cultural-religious values may have an important effect on the prevalence of depressive disorders in both genders. These values include the esteem attached to women’s central role in family management, and low use of alcohol and suicide as escape routes from depression by women in this cultural
group (Loewenthal et al. 1995). Srâiri (1995) also suggested that depression in men is probably overestimated in Islamic cultures because it is not masked by comorbid alcohol abuse. It is also important to consider cultural forms of resilience, as suggested by Kleinman (2004) and Loewenthal et al. (1995). In traditional societies and minority groups, people under stress may benefit from the support of strong extended-family ties. As for women, another work on Jewish communities (Loewenthal and Goldblatt 1993) suggested that the high esteem attached to their role in family management could protect them from developing depressive disorders.

**CONCLUSION**

Gender differences in depression vary with culture. A comparison of cultures may help to ascertain the extent to which cultural and social construction has created this clear difference in rates and clinical presentation of depression. Just as there are probably more types of depression than are currently defined, there may be an intrinsic difference in what constitutes depression in women and men.

**GENDER DIFFERENCES IN SEEKING HELP**

Culture confounds diagnosis and management of depression by influencing not only the experience of depression, but also by affecting help-seeking behaviour and the pathways to care that individuals use. In some cultures, traditional healers and spiritual leaders may be considered more acceptable sources of help than mental health professionals, especially for women, given the fact that they are generally less educated and more exposed to stigmatisation. Women are more likely than men to share common cultural beliefs such as beliefs in “evil spirits” or “evil eyes”. They may often interpret psychological problems as punishment for some wrongdoing that has been committed by them or by their family members or ancestors. Conversing with God through prayer may be seen as an effective means of overcoming depression. Family is also identified as a major source of help (Lawrence et al. 2006). In addition, women are often less willing than men to seek help from mental health professionals because they fear that they may be considered insane and that this will compromise their chances of marriage.
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PART 2
Depressive Disorders in Women
Chapter 6
Treatment Considerations
GENERAL PRINCIPLES

When a woman presents with depression, it is important for the clinician to assess for any relationship between the depression and menstruation, pregnancy, postpartum status, or menopause, all of which involve special considerations in management. Particularly in women with histories of depression, longitudinal monitoring for recurrence of depression at vulnerable points in the female cycle may allow for the rapid implementation of treatment and the prevention of relapse.

Clinicians must also be alert for the possible relationship between depression and medications, such as birth control pills or hormone replacement therapy (Pajer 1995). If there is a link with any treatable cause of depression, it should be addressed first. If the patient’s depression does not respond to this intervention, further treatment is required.

In providing pharmacological treatment to women of reproductive age, it is important to keep in mind the possibility of pregnancy and the potential effects of antidepressants on a foetus or neonate. Therefore, sexually active women should be advised to use an effective method of contraception. For women who are planning to conceive and who may require continued use of medication during pregnancy, choosing an antidepressant that appears safe during pregnancy may avoid the need to switch medications following conception.

Some women who suffer from depression experience premenstrual exacerbation of their symptoms despite successful treatment of depression at other times of the month. In such cases, it may be useful to chart the timing of the symptoms; an increase in antidepressant dose 7—10 days before onset of menses may help maintain euthymia throughout the cycle.

Women are at increased risk for depression during the first 4—8 weeks following delivery, and this is particularly true for women with a history of depression. For many of these women, prophylaxis with an antidepressant or a mood stabiliser may be essential in preventing a recurrent episode.

SPECIAL CONSIDERATIONS IN PHARMACOTHERAPY

Gender differences in pharmacokinetics and in responses to pharmacological treatment have been noted. Such differences should be considered in choosing a treatment strategy for depressed women.

Gender Differences in Pharmacokinetics

A growing body of data has demonstrated that sex-specific differences in physiology can affect drug pharmacokinetics and pharmacodynamics (Kashuba et al. 1998). Currently, little is known about these pharmacokinetic differences because many more men than women have participated in investigational drug studies. Nonetheless, certain gender-related differences merit consideration (Yonkers et al. 1992). Gender differences involve drug absorption and bioavailability, drug distribution, and drug metabolism and elimination. For example, women have, on average, a lower body weight, a slower gastric emptying time (especially during high progesterone phases of the reproductive cycle), lower gastric acid secretion, a higher percentage of body fat (which increases the volume of distribution for many drugs), decreased hepatic metabolism (possibly because of oestrogen’s inhibitory effect on some microsomal enzymes), and lower renal clearance compared to men. Oestrogen and progesterone, both highly protein-bound, may compete with psychotropic medications for protein binding sites. Medication levels may thus vary as a result of hormonal changes associated with the menstrual cycle, pregnancy or menopause, as well as due to the use of exogenous hormones such as oral contraceptives or hormone replacement therapy. Such differences may lead to higher plasma levels and longer half-lives of drugs, as well as a greater sensitivity to side effects in women. Thus, female patients with depression may require lower dosages of antidepressants than their male patients.

Other factors that may require adjustments in antidepressant dosage in women include age, pregnancy, and concurrent oral contraceptive use. Some studies have reported that the use of long-term, low-dose oral contraceptives may decrease
the hepatic metabolism of imipramine in women (Frakiewitz 2000). This finding suggests that plasma concentrations of other antidepressants that are significantly metabolized by the CYP3A4 iso-enzyme in the liver would also be affected by concurrent oral contraceptive use.

Gender Differences in Treatment Response
Gender differences in treatment response to antidepressant medications have been described. According to several studies, women appear to respond less well than men to tricyclic antidepressants (TCAs), while they appear to respond more favourably to selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase inhibitors (MAOIs). A meta-analysis by Hamilton et al. (1996) of 35 studies that reported imipramine response rates separately by gender showed significantly higher response rates in men.

The largest study that has compared antidepressant response rates by gender is a study by Kornstein et al. (2000) that examined response rates to sertraline and imipramine in the treatment of chronic major depressive disorder and double depression. The results showed a significant gender x treatment interaction, with women responding more favourably to sertraline and men to imipramine. Differences in tolerability were also noted, with the women who were receiving imipramine discontinuing their participation in the study more frequently than those receiving sertraline. In addition, an interaction between treatment response and menopausal status was found: perimenopausal women responded significantly better to sertraline than to imipramine, whereas there was no difference in response rates to the two drugs among postmenopausal women. This positive response to SSRIs in chronically depressed women was also observed in patients with dysthymia. However, many authors suggest that the well-known better adherence to treatment in women may explain these differences;

The Potential Role of Oestrogen
In addition to looking at the effect of age and menopausal status on antidepressant response rates, some recent research has focused on whether hormone therapy may enhance response rates. With regard to depression, oestrogen is obviously particularly helpful during the perimenopausal period. In these cases, a therapeutic trial seems justified, especially in mild depression or if there is an additional indication for oestrogen replacement such as hot flushes. As an alternative to treatment with oestrogen, an SSRl can also be used. If oestrogen alone is not sufficient, or in more severe depression, antidepressants must be added. In these cases oestrogen may enhance endogenous serotonergic activity and thus induce a better response to an SSRI. To achieve optimum outcome, pharmacotherapy may need to be combined with psychotherapy; social support is also often needed.

More research is needed concerning the use of hormone therapy during the postmenopausal period.

Riecher-Rössler and de Geyter (2007) recently discussed the crucial issue of potential negative effects of oestrogen, such as thromboembolism or risk of endometrial cancer. To reduce the risk of such negative effects, the authors suggest administering oestrogen in combination with progestin in women with an intact uterus. However, even in such women, the Women’s Health Initiative (WHI) study (Rossouw et al. 2002) has demonstrated that the risks of stroke, coronary heart disease, pulmonary embolism, and breast cancer are still significantly increased in women receiving combined oestrogen plus progestin. The WHI study has been criticised by many experts and by the International Menopause Society, however, mainly because the study population was much older than that around the natural menopause (mean of 63 years of age at inclusion).
Many of the complications noted in the WHI study such as stroke, pulmonary embolism, and myocardial infarction are caused by the vascular effects of oestrogens in the presence of manifest arteriosclerosis. The biased conclusions due to the recruitment of many older patients have now been partially counteracted by reanalysis, in which at least the cardiovascular complications can be reduced by an early introduction of hormone replacement therapy. This has opened a window of opportunity in which at least a cardiovascular benefit can be obtained in healthy menopausal women when replacement therapy is started soon after menopause. In addition, combined treatment with both oestrogens and progestin is needed to prevent endometrial hyperplasia and endometrial cancer in women with an intact uterus. This combined treatment has been shown to carry a small incremental risk of breast cancer during long-term use. If oestrogen can be used as monotherapy, particularly in women after hysterectomy, the risk of developing breast cancer appears to be smaller (although the difference was not statistically significant).

Augmentation

Several augmentation strategies to enhance antidepressant response have shown possible advantages in women (Kornstein and Wojcik 2001); for example, augmentation with triiodothyronine may be more beneficial in women than in men. The notion that oestrogen may enhance response to SSRIs in postmenopausal women has been suggested by two studies that analysed response rates to fluoxetine and sertraline with and without concomitant oestrogen replacement therapy (ERT) (Schneider et al. 1997, 2001). These researchers found that there were significantly more responders to sertraline among those taking ERT than in the women not receiving ERT (79% versus 58%). In addition, there was a trend for greater remission rates among the women taking ERT. Thus, there is some preliminary evidence suggesting that oestrogen may improve response and remission rates with SSRIs in postmenopausal women, although clearly more research is needed, particularly studies that are better designed to address this issue.

Oestrogen has also been used effectively as a treatment in some women with refractory depression, PPD, and perimenopausal mood disturbance. Oestrogen has also been shown to be effective in some women in the treatment of acute depression, augmentation of partial antidepressant response, and prophylaxis against recurrence (Joffe and Cohen 1998). Oestrogen appears to have multiple neuromodulating effects, including those mediated by its effects on the serotonergic system. These effects may lead to an antidepressant benefit in certain groups of women. However, in women with heightened sensitivity to normal hormonal changes, oestrogen’s central nervous system effects may confer added risk for mood disorders (Joffe and Cohen 1998). These are also some suggestions that lithium and stimulants may be more effective as augmentation agents in women.

**PSYCHOTHERAPY**

Few studies have examined gender differences in response to psychotherapy for depression. Sex was not a predictor of response to cognitive-behavioural therapy (CBT) or interpersonal therapy (IPT) in the NIMH Collaborative Research Program (Kornstein and Wojcik 2001). CBT in severe depression was found to be as effective in women as in men in a study by Thase et al. (1994). However, according to McGrath (1993), CBT groups were especially effective in women.

Problem-solving types of individual therapy, such as CBT, and group therapy, such as IPT, have been shown to be effective treatments for major depression. McGrath et al. (1990) suggested that psychosocial therapies may be more helpful for women than for men with major depression; however, but other studies have reported no gender differences in treatment outcome after psychotherapy. It appears that both genders may benefit from treatments that enhance the use of psychosocial resources, especially peer support.
Psychosocial therapies for women with depression should address issues that particularly affect women, such as competing roles and conflicts. Commonly used treatments include psychotherapy to correct interpersonal conflicts and to help women develop interpersonal skills, CBT to correct negative thinking and associated behaviour, and couples therapy to reduce marital conflicts. In patients with mild to moderate depression, psychosocial therapies may be used alone for a limited period, or they may be used in conjunction with antidepressant medication.

CONCLUSION

With the exception of hypertension, major depression is more commonly encountered than any other condition in the primary care setting (Sartorius et al. 1996). It has been established that women have a greater risk of depression than men, particularly during the childbearing years. Depression in women not only harms the patient but can also have an adverse effect on the family, particularly the children. Depression among mothers is common, yet it is not necessarily recognized by healthcare professionals, and sometimes not by the women themselves. Gender differences in clinical presentation, comorbidity, and course can make diagnosis challenging. In addition, events related to women’s reproductive life—menstrual cycle, pregnancy, lactation, menopause—may trigger depressive episodes and/or complicate their management. Clinicians should consider gender differences both in assessing and treating depression in order to achieve the optimal response. Table 6.1 summarises some common treatment-related differences between women and men. When recognised, major depression can usually be successfully treated, resulting in significant improvements in the productivity and the quality of life of women and their families. Targeted prevention treatment is also recommended, focusing on times of heightened risk for depression and using longitudinal monitoring for recurrence of depression at vulnerable points in the female cycle. Finally, the bio-psychosocial origins of depression in women may require a multidimensional approach to treatment, including campaigns to unveil this “silent cause of mortality and morbidity” (Stewart, 2006).
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Women versus men</th>
</tr>
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<tbody>
<tr>
<td>Frequency of seeking help</td>
<td>May be greater</td>
</tr>
<tr>
<td>Absorption of antidepressants</td>
<td>Greater</td>
</tr>
<tr>
<td>Ratio of body fat to muscle</td>
<td>Greater</td>
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<tr>
<td>Volume of drug distribution</td>
<td>Larger</td>
</tr>
<tr>
<td>Plasma concentration of antidepressant</td>
<td>May be higher</td>
</tr>
<tr>
<td>Antidepressant dosage</td>
<td>May need to be lower</td>
</tr>
<tr>
<td>Side effects of antidepressants</td>
<td>More frequent</td>
</tr>
<tr>
<td>Effect of progesterone</td>
<td>Increased microsomal and monoamine oxidase enzyme activity with decreased monoamine neurotransmitters</td>
</tr>
<tr>
<td>Effect of oestrogen</td>
<td>Decreased microsomal and monoamine oxidase enzyme activity with increased monoamine neurotransmitters</td>
</tr>
<tr>
<td>Duration of therapy</td>
<td>May need to be longer</td>
</tr>
<tr>
<td>Efficacy of CBT and IPT</td>
<td>Similar</td>
</tr>
<tr>
<td>Efficacy of combined medication and psychotherapy</td>
<td>Similar or may be greater</td>
</tr>
<tr>
<td>Need for treatment of comorbid anxiety, panic, phobic and eating disorders</td>
<td>Greater</td>
</tr>
<tr>
<td>Need for thyroid screening</td>
<td>Greater</td>
</tr>
<tr>
<td>Comorbid antisocial, narcissistic or obsessive-compulsive disorder</td>
<td>Less frequent</td>
</tr>
<tr>
<td>Effect of exogenous and endogenous gonadal steroids on mood</td>
<td>Greater</td>
</tr>
</tbody>
</table>

Source: Bhatia and Bathia 1999
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PART 3
Depressive Disorders in Children and Adolescents

Depression is one of the most ancient disorders to be documented and studied over the history of psychiatry. It was once thought that only adults suffer from depression. However, child and adolescent psychiatrists have been studying the normal development of minors over the last 30 years, and this work has led to the suggestion that any deviance from this normal development be considered abnormal. As part of this work, each age group with its unique features has been studied and described.

With the development of valid and reliable measurement scales, we have discovered that the basic clinical manifestations of depression are similar from childhood into adulthood. At the same as we have identified a number of features unique to childhood and adolescent depression, including some age-specific risk factors, different reactions to treatment, and particular patterns of comorbid condition. One of the difficulties researchers have faced in this area was the need to develop ways to ask children and adolescents and their caregivers the right questions and to better understand their body language with its diverse manifestations.
Another element that has contributed significantly to our understanding of the complex developmental pathways of depression has been cumulative data coming from longitudinal studies. This information has helped us to understand, first, the influence of psychosocial factors (e.g., life events such as loss, abuse, neglect and chronic illness; relationships with parents, peers, and teachers), and, second, the gene–environment interaction involved. Longitudinal studies have also showed us that one clinical presentation can turn into another disorder over time. For example, conduct disorder in girls during childhood, may change into depression in adolescence.

This growing body of information led us to conclude that it was essential to add a module on early depression, its clinical manifestations, and age-specific therapeutic procedures to this programme on depression. By broadening the scope of coverage in this programme, we hope to help paediatricians, family practitioners, and all mental health service providers better detect early signs of depression, starting in infancy, and thereby promote early intervention and improved quality of life for all children, adolescents, and adults.


Professor Sam Tyano
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Chapter 1
Overview of Depression in Children and Adolescents
CONTINUUM OF DEPRESSIVE DISORDER

Depressive disorders exist on a continuum and are classified on the basis of age, severity, pervasiveness, and presence or absence of mania. At the mildest end of the spectrum is adjustment disorder with depressed mood occurring in response to a clear stressor. Dysthymic disorder is further along the spectrum; it refers to a chronic condition with fewer symptoms than major depression but with a course that lasts at least 1 year. Major depression is the most severe depressive disorders, characterised by either sad or irritable mood and at least five other symptoms, such as social withdrawal, worthlessness, guilt, suicidal thoughts, sleep disturbances, decreased concentration and motivation, and appetite disorders. This chapter does not include the bipolar end of the spectrum (i.e., disorders that include mania or hypomania). Readers are referred to Volume I of this programme for a discussion of bipolar disorders in general and to Parts 1 and 2 of Volume III for discussions of how bipolar disorders may present in elderly patients and women. Volume III, Chapter 5 also includes a discussion of suicide in minors.

There are a number of key questions concerning paediatric depression:

- Is paediatric depression similar to adult depression?
- Is depression with onset during the pre-school years or childhood the same as depression with adolescent onset, or do these presentations represent separate disorders that differ in their manifestations as well as etiology?

THE HISTORY OF THE CONCEPT OF PAEDIATRIC DEPRESSION

In countries where there has been considerable resistance to the application of psychiatric diagnoses, especially depression, to young children, the history of paediatric depression dates back only a couple of decades. The societal expectation that childhood should be carefree and happy has led to reluctance to consider the possibility of early onset mood disorders. There was also an inclination to avoid pathologising normal and transient phenomena in children’s behaviour (Meade and Luby 2006). It is still a common belief that the behavioural and emotional disturbances that appear early in life are transient, and it is not uncommon to hear statements such as “he or she will grow out of it…”.

Gaining acceptance for the notion of depression in infancy was even harder. Early reports by Spitz (1946) on depressive clinical symptoms in infants and toddlers suggested that early and severe psychosocial deprivation had impinged on the emotional development of infants. He was the first psychiatrist to point out that infants and toddlers could experience psychic pain that can ultimately lead to an infant’s death, independently of the availability of food and shelter. He named the syndrome anaclitic depression. Unfortunately, the understanding Spitz gained were ignored by clinicians for over 50 years, possibly because they were based on children who were separated from their mothers in extreme war related circumstances and had lived in orphanages (Keren and Tyano 2006).

The existence of childhood depression was questioned during the 1960s, as it was believed that children’s immature superego (the intrapsychic structure traditionally linked to depression) would not permit the development of depression. In the 1960s and 1970s, depression in school-age children was considered to be impossible because of their assumed underdeveloped sense of self and limited emotional development and cognitive skills.

The situation has been similar with regard to adolescents. In 1971, Cytryn and Meknew were among the first to report depressive symptoms (e.g., sadness, withdrawal, impaired functioning, social isolation, helplessness, and hopelessness) in young adolescents with chronic medical illness.
This clinical presentation was first understood as mimicry of adult depression or masked depression, when depression was present but masked by other behaviours included somatic complaints, school problems, and conduct difficulties. Only later was it viewed as an entity in itself with distinct features, course, and response to medications.

EPIDEMIOLOGY

The rates of depression rise with age, so that depression is much more common in adolescents than among children (Agnold et al. 2002). Epidemiological data about depression in infancy are still not precise, but 3 studies conducted in different countries have found that the prevalence of infant depression ranges from 0.5% to 3% (Keren and Tyano 2006).

The prevalence of depressive disorders in prepubertal children is 1%–2%. Among children 8–13 years of age, it was found that the risk of recurrence was 40% within 2 years, and 72% within 5 years (Kovacs et al. 1984).

Prevalence rates of depression rise among adolescents and range from 3% to 8%, with a lifetime prevalence of approximately 20% by the end of adolescence (Lewinsohn et al. 1998; Reinerz et al. 1993). The duration of depressive episodes ranges between 3 and 6 months in community samples, and between 5 and 8 months in samples referred for care (Birmaher et al. 2002; Kovacs 1996). In community and clinical samples, approximately 20% of adolescents have a persistent depression that lasts 2 or more years (Birmaher et al. 2000; Lewinsohn et al. 1998). To compare, the prevalence of depressive disorders in adults has been reported to be 10.4% (World Health Organization 2001). Adolescent-onset depression is associated with a strong risk for recurrence in adulthood. Longitudinal studies have shown that the risk of recurrent depression ranges between 40% to 70% within 1–2 years of follow-up (Fergusson and Woodwards 2002; Lewinsohn et al. 2000; Pine et al. 1999).

GENDER DIFFERENCES

Adult depression is characterised by a strong gender imbalance in prevalence rates. The gender ratio of 3:1 (female: male) in the prevalence rates of mood disorders first emerges in adolescence. Until puberty, girls are not more prone to depression than boys. Increases in depressive symptomatology in girls begin to be detected at age 12 and are observable at the diagnostic level by the age of 13 and older (Angold et al. 2006; Reinerz et al. 1993). Once depression is established, there are no gender-related differences in its duration, severity, relapse, and recovery rates (Kessler 2000).

It is not yet clear why the prevalence rates of depression increase during adolescence, particularly in girls, although variables such as biological, psychosocial, and cognitive factors have been studied (Orvaschel et al. 1997). Girls enter puberty earlier than boys, with the psychosocial and biological consequences that accompany this change. It has been hypothesised that girls may have more risk factors for depression than boys, including the role of hormones during puberty, negative experiences of physical changes, and intensification of stereotypical gender roles (Petersen et al. 1991; Pine et al. 1999). During adolescence girls tend to be more occupied with their body image, are more likely to be exposed to sexual abuse, and may experience more pressure to conform to restrictive societal roles than boys (Nolen-Hoeksema and Girgus 1994). Moreover, from a young age, girls are culturally socialised to be more dependent than boys. Girls focus more on or are more preoccupied by their internal feelings, in contrast to boys who are often encouraged to translate their feelings into actions; thus depression in boys is more likely to manifest as external behavioural disturbances and acting out. All of the psychosocial influences described above may cause adolescent girls to be acutely more self-conscious about themselves and their performance, and to experience more pain if they experience negative judgement and rejection by peers.
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PART 3
Depressive Disorders in Children and Adolescents
Chapter 2
Developmental Aspects of Depression: Follow-up Studies
A transactional model regarding normal and abnormal development was proposed by Sameroff (1987, 2003). This model suggested that what is constant in children's development is not a set of "traits", but the processes by which these traits are maintained. The development of the child is seen as a product of ongoing dynamic interactions between children and the experiences provided by their families as well as the wider social context. Multiple factors, consisting of genetics, biology, culture, life events, and psychology, influence the child's development. Instead of thinking in terms of syndromes, pathways of development are considered. Multiple pathways can lead to the same outcomes, and the same initial pathway can also lead to multiple outcomes (Cicchetti and Cohen 1995). Change is possible at many turning points in children's developmental pathways and early caregiving facilitates change; however, change becomes more difficult the longer a pathway is pursued.

To our knowledge, only a few studies have examined the course of depression from infancy or pre-school onset to later years of childhood or adolescence. However, some studies, such as McFarlane's (1954) research on normal children from 21 months to 14 years of age, looked at various experiences such as "somberness" and found a few peaks around the ages of 5–7 years and 9–13 years that supported the existence and impact of developmental changes. Given the biological changes in the brain that have been associated with affective symptoms in high-risk infants and pre-schoolers, the identification of depressive symptoms during infancy and pre-school years seems to be critical. The body of research on depression among pre-schoolers has demonstrated that some pre-school behaviours are stable and predictive of later functioning (Campbell 1995; Campbell and Gilliom 2000) and that intervention during these years is effective and results in observable treatment gains well after the completion of therapy (Hood and Eyberg 2003; Webster-Stratton and Hammond 1997). In a 4-year study, in which they have monitored the permanence of pre-school onset psychopathology, Lavigne and colleagues (1998) reported considerable stability in mood diagnoses. Among 2- and 3-year-old children who met diagnostic criteria for an emotional disorder, 40% continued to have an emotional disorder up to 4 years later, while 60% had met diagnostic criteria for either a mood disorder or a disruptive behaviour disorder as defined by the DSM-IV (American Psychiatric Association 1994).

Behaviourally inhibited children were found to be more vulnerable to developing depression in later years. While this association was found to occur only in males in one study (Hofstra et al. 2002), other researchers (Caspi et al. 1996; Roza et al. 2003) did not find gender differences. Roza and colleagues (2003) concluded that the lack of gender differences in their study indicated that the reported higher frequencies of mood disorders among females were not caused by problem behaviour in childhood, but were due to factors such as environmental influences during adolescence or genes that came into expression later in life. Furthermore, longitudinal epidemiological and family studies, as discussed by Thapar and Rice (2006), have shown that childhood anxiety often preceded later depression, especially in families suffering from depression. This link appeared to be indirectly mediated through an increased vulnerability to life events.

Harrington et al. (1996) found that childhood depression was associated with psychosocial adversity and was not a precursor of adult depression. In contrast, adolescent onset depression was more often seen as early onset of adult depression and perhaps had a genetic base. Similarly, it was found that adverse environmental factors (e.g., early abuse, early adverse life events and lack of maternal support) accounted for most of the variance in childhood depression. Among adolescents, genetic factors such as maternal depression were more significant, especially for girls (Scourfield et al. 2003). Findings from twin studies have been consistent in showing similar age-related effects. A number of other studies
have also reported that environmental factors had a significant influence only on younger children (Rice et al. 2002; Thapar and McGuiffin 1994). In 2004, Gutman and Sameroff published their study “Continuities in depression from adolescence to young adulthood: Contrasting ecological influences”. In this study, they examined multiple social setting variables that influence depression in males and females from adolescence to young adulthood, using longitudinal data from 372 families living in a large eastern urban area. They found that variables related to depression differed for males and females depending on the developmental period being examined. Overall, family and peer variables in adolescence had a more significant impact on change in depression for males, whereas contemporary variables in young adulthood had a more significant impact on change in depression for females.

In summary, we cannot yet fully answer the question of whether depression in infancy, childhood, and adolescence is the same disorder with the same etiology and course as in adulthood, since more longitudinal studies of infant depression are needed. Nevertheless, all of the currently available data indicate that childhood depression may indeed be a different disorder (which appears to have a stronger reactive nature) than depression in adolescence and adulthood (which appears to have a more genetic basis).
REFERENCES


PART 3
Depressive Disorders in Children and Adolescents
Chapter 3
Aetiology of Depression in Children and Adolescents

Paediatric depression is a complex mental health problem that has multifactorial etiology, involving genetics, neurobiology, and environmental factors. Biochemical changes have been found in the brain of depressed children. These changes can result from genetics, but psychological and environmental factors can also cause depression. Among infants, a major question is whether depression can be endogenous, as in older children and adolescents, or whether it is always reactive to environmental adverse factors. It is also important to compare the course and prognosis of infant depression with the reactive type of depression (Keren and Tyano 2006).
GENETIC FACTORS

Family, adoption and twin studies have shown evidence for familial aggregation of major depressive disorder (MDD) in family members. Family studies found a higher risk of psychopathology in offspring of depressed patients (Nomura et al., 2002; Orvaschel et al. 1988). The rate of major depression in children was inversely associated with the age of onset in parents. The children of parents who had an onset of MDD before the age of 20 had the highest risk of MDD (Weissman et al. 1988). Parental depression was associated with an earlier onset of depression in the children, more severe symptoms, increased impairment, and higher recurrence rates (Leib et al. 2002).

Adoption studies have shown less conclusive results. Wender and colleagues (1986) have found evidence supporting a genetic effect on the transmission of MDD. Cadoret et al. (1985) found a similar trend towards such an effect, although it did not reach the level of significance. Twin studies have demonstrated that a greater concordance of depressive symptoms among monozygotic (identical) than zygotic twins (McGuffin et al. 1991). Family studies have shown a two- to four-fold increased risk of depression in first-degree relatives (Kovacs and Devlin 1998; Weissman et al. 2005). Other studies have also suggested a greater genetic component in adolescent versus childhood onset depression, supporting the view that depression with onset in early childhood may be a response to environmental risk factors (Glowinski et al. 2003; O’Connor et al. 1998; Rice et al., 2004; Scourfield et al. 2003; Thapar and McGuffin 1994; Thapar and Rice, 2006; Todd et al. 1993).

As mentioned above, the fundamental question of whether the etiology of depression in infancy and childhood is endogenous versus reactive is still not answered. In an extensive study of preschool depression, Luby et al. (2004) concluded that infant depression, similar to melancholic depression in adults, could be seen in children between the ages of 3.5–6 years. However, it could be argued that these children had experienced a familial transmission of depression in their early years through parenting behaviours, not necessarily due to genetic or biologic factors (Keren and Tyano 2006).

ENVIRONMENTAL FACTORS

Table 3.1 outlines some of the major environmental risk factors, including life events, psychosocial factors, and parent child relationships, which have been found to be associated with childhood depression.

Table 3.1

<table>
<thead>
<tr>
<th>Environmental Risk Factors for Childhood Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Exposure to traumatic circumstances, such as war, car accident, or natural disaster</td>
</tr>
<tr>
<td>• Death of a close person</td>
</tr>
<tr>
<td>• Relocation of family</td>
</tr>
<tr>
<td>• Divorce of parents</td>
</tr>
<tr>
<td>• Living in an abusive family where children regularly witness, or are victims of parental aggression, rejection, or scapegoating</td>
</tr>
<tr>
<td>• Strict and punitive treatment of children</td>
</tr>
<tr>
<td>• Severe parental psychopathology</td>
</tr>
<tr>
<td>• Chronic or life threatening illness</td>
</tr>
</tbody>
</table>
GENE-ENVIRONMENT INTERACTION

Gene-environment interaction is defined as the influence different environments may have on different genotypes in shaping the development of the phenotype. Most human illnesses, particularly psychiatric ones, have complex aetiologies and result from various interactions between genetic vulnerabilities and environmental factors, such as infectious, chemical, physical, nutritional, and behavioural factors.

Interaction between environmental factors and genes can occur through several mechanisms. Adversity may “turn off” genes in an enduring fashion through methylation of vulnerable sites in the promoter region, environmental factors may “turn on” pathogenic genes, or genes may favour behavioural traits that may cause a subject to “choose” a specific malicious environment.

A functional polymorphism in the promoter region of the 5-HT transporter (5-HTTLPR) moderates the influence of stressful life events on depression. Subjects with one or two copies of the short (s) allele of the 5-HTTLPR polymorphism have been found to exhibit more depressive symptoms and suicidality in relation to stressful life events than individuals who are homozygous for the long allele (Caspi et al. 2003). Lower expressing alleles, LG, S, of the 5-HTTLPR predicted greater severity of depression and greater severity of major depression in association with moderate to severe life events compared with the higher expressing LA allele (Zalsman et al. 2006a). Children with the s/s genotype of the 5-HTTLPR and no positive supports had the highest depression ratings. The presence of social support has been reported to reduce the risk associated with the s/s genotype. Thus, variations in the 5-HTTLPR has been shown to moderate the development of depression after stress, and social support has been shown to have the capacity to further moderate the risk for depression (Kaufman et al. 2004). In adolescents, a significant interaction between genotype and environment risk factors for the 5-HTTLPR has been found only in female subjects (Eley et al. 2004; Zalsman et al., 2006b).

NEUROBIOLOGICAL FACTORS

The aetiology of depression in children and adolescents can not always be deduced from adults; some neurobiological systems develop during childhood and adolescence and continue to change with time. Maturation of the serotonergic system reaches adult levels in childhood, while maturation of the noradrenergic system continues through puberty, and the dopaminergic system matures as late as early adulthood. Neurobiological factors unique to children and adolescents suffering from depression are outlined in Table 3.2.

The Serotonergic System

Abundant data reinforce the role of serotonin in depression and in aggression in adults as well as in children and adolescents. Whole-blood serotonin was found to be lower in children and adolescents with mood disorders compared with in controls and children with conduct disorder (Hughes et al. 1996) and children with schizophrenia and schizoaffective disorders (Rogeness et al. 1985). When serotonin levels have been measured in adolescents who were admitted to the emergency room, they were found to be significantly lower in violent compared with non-violent youth (Tyano et al. 2006). Results with phosphoinosifide hydrolysis mediated by the 5HT2 receptor have indicated blunted signal transduction in high lethality suicide attempters (Mann et al. 1992a and b). There are now an impressive number of studies linking low cerebrospinal fluid 5-hydroxyindolacetic acid (CSF 5-HIAA) and/or blunted prolactin response to fenfluramine challenge with suicidal behavior, especially lethal suicide attempts, regardless of psychiatric diagnosis (Mann et al., 1992b; Malone et al. 1996).

Neuroendocrine Studies

Some of the core symptoms of depression, such as changes in appetite and sleep patterns, are related to the functioning of the hypothalamus. Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been a focus of adult depression studies.
## TABLE 3.2

Neurobiological factors in children and adolescents suffering from depression

<table>
<thead>
<tr>
<th></th>
<th>Childhood</th>
<th>Adolescence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serotonergic System</strong></td>
<td>Whole-blood serotonin was lower</td>
<td>Whole-blood serotonin was lower Low CSF 5-HIAA and/or blunted prolactin response to fenfluramine challenge in suicidal youth</td>
</tr>
<tr>
<td><strong>Neuroendocrine Studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cortisol and dehydroepiandrosterone</strong></td>
<td></td>
<td>High evening cortisol levels and low levels of morning DHEA</td>
</tr>
<tr>
<td><strong>Dexamethasone suppression test</strong></td>
<td></td>
<td>Higher rates of dexamethasone non-suppression</td>
</tr>
<tr>
<td><strong>Corticotropin releasing hormone</strong></td>
<td>No significant difference</td>
<td>Lower ACTH secretion after CRH infusion</td>
</tr>
<tr>
<td><strong>Growth hormone</strong></td>
<td>Secreted lower levels of growth hormone after insulin-induced hypoglycemia, clonidine, L-dopa, desmethylimipramine, and growth hormone-releasing hormone</td>
<td>Mostly, no difference in lower GH secretion in response to clonidine, L-dopa, dextroamphetamine</td>
</tr>
<tr>
<td><strong>Thyroid hormone</strong></td>
<td>Inconclusive findings</td>
<td>Inconclusive findings</td>
</tr>
<tr>
<td><strong>Sex hormones</strong></td>
<td></td>
<td>Weak association</td>
</tr>
<tr>
<td><strong>Sleep Studies</strong></td>
<td>Shorter REM latency, increased sleep latency, and an increased REM time (one study)</td>
<td>Shorter REM latency, REM density differences, and less sleep efficacy</td>
</tr>
<tr>
<td><strong>Neuroimaging Studies</strong></td>
<td>No findings available</td>
<td>Smaller left subgenual PFC and larger third and fourth ventricles</td>
</tr>
</tbody>
</table>
Cortisol and Dehydroepiandrosterone
High baseline levels of plasma cortisol over 24 hours and lower concentrations of dehydroepiandrosterone (DHEA) in saliva have been reported in depressed adults compared with controls. Most studies did not find a difference between baseline cortisol secretion in depressed children and adolescents and controls. Dahl et al. (1991) found that cortisol secretory patterns were very similar between depressed adolescents with MDD and normal controls, except that the depressed adolescents showed significantly elevated cortisol levels around sleep onset and that these elevated levels were related to severity of illness. High evening cortisol levels and low levels of morning DHEA were found to be correlated with major depression in patients who were 8 to 16 years of age (Goodyer et al. 1996).

Dexamethasone Suppression Test
Administration of dexamethasone has been shown to suppress the release of cortisol in healthy subjects. In adults, HPA hyperactivity has been shown to be correlated with non-suppression in depressed patients. The dexamethasone suppression test (DST) has also been reported to normalise after recovery from a depressive episode. Reviews of DST in children and adolescents have found rates of non-suppression which were about twice as high in inpatients as in outpatients. As in adults, higher rates of dexamethasone non-suppression were related to the severity of illness; it was more frequent in inpatients than in outpatients, more frequent in psychotic and recurrent depression, and was a predictor of suicide (Casat et al. 1989; Dahl et al. 1992; Kaufman et al. 2001; Zalsman et al. 2006b).

Corticotropin Releasing Hormone
Studies of depressed adults have found blunted adrenocorticotropic hormone (ACTH) secretion after an infusion of corticotropin releasing hormone (CRH), and higher concentrations of CRH in cerebrospinal fluid (CSF) compared with normal subjects. No significant differences were found in levels of either cortisol or ACTH in depressed prepubertal children compared with normal subjects at baseline or after CRH stimulation (Zalsman et al. 2006b). However, in a study of adolescents, depressed inpatients and subgroups with melancholia had significantly lower ACTH secretion after CRH infusion (Birmaher et al. 1996a).

Growth Hormone
Higher daytime growth hormone (GH) secretion, lower GH secretion during the first hours of sleep, and blunted response to clonidine have been reported in depressed adults compared with controls. Depressed children have been found to secrete lower levels of GH than controls in response to insulin-induced hypoglycemia, clonidine, L-dopa, desmethylinamipramine, and growth hormone-releasing hormone (Dahl et al., 2000; Jensen and Garfinkel 1990; Puig-Antich et al. 1984; Ryan et al. 1994). Furthermore, blunted GH response to insulin-induced hypoglycemia has been reported to persist even when the MDD remits. Children and adolescents with heavy family loading for depression have been found to secrete lower levels of GH compared with controls; however, no difference was found in pre-GH releasing hormone and nocturnal GH secretion levels (Birmaher et al. 1996b; Birmaher et al. 2000; Zalsman et al. 2006b). Studies in adolescents have found a different pattern than in children and adults, with no difference in GH secretion in response to clonidine, L-dopa, and dextroamphetamine in depressed adolescents compared with controls (Kaufman et al. 2001).
**Thyroid Hormone**

Lower levels of transthyrotopin in the CSF, lower levels of thyroid stimulating hormone (TSH) in response to thyrotopin releasing hormone (TRH) stimulation, and lower nocturnal TSH and serum T3 levels have been found in depressed adults compared with controls. However, studies of T3 levels, free thyrotoxin index, and free T4 in depressed children and adolescents have been inconclusive (Zalsman et al. 2006b).

**Sex Hormones**

No gender differences have been found in the prevalence of depression in prepubertal children. After 13 years of age, however, there is an increase in the prevalence of depression in girls which is maintained until menopause. However, studies of the link between gonadotropins, gonadal steroids, and adrenal androgens have not found strong associations with depression (Angold and Costello 2006). To date, however, none of these markers are sufficiently specific to contribute to the diagnosis of major depression.

**Sleep Studies**

Sleep disturbances are considered a hallmark of depression. Sleep studies in depressed adults have found prolonged sleep latencies, disturbances in sleep continuity, shorter rapid eye movement (REM) latencies, increased REM densities, and decreased delta (stage 3 and stage 4) sleep. Findings in sleep studies of depressed children and adolescents have not been as compelling as in depressed adults, and findings in these studies could be attributed to differences in severity of illness and age. Studies in depressed adolescents have found shorter REM latency, REM density differences and less sleep efficacy. Greater rates of sleep changes were found in inpatient than outpatient adolescents and in association with psychosis and suicidality. Of the few studies that have been conducted in children, one study has found a shorter REM latency, an increased sleep latency, and an increased REM time in an inpatient sample of depressed children (Birmaher et al. 1996b; Kaufman et al. 2001; Zalsman et al. 2006b).

**Neuroimaging Studies**

Imaging studies of depression in adults have used brain magnetic resonance imaging (MRI) and computed tomography (CT) scans to assess structural and functional abnormalities. Findings from these studies have shown smaller prefrontal cortex (PFC) and basal ganglia; decreased blood flow (BF) and metabolism in the dorsolateral and the dorsomedial PFC, and anterior cingulate gyrus ventral to the genu of the corpus callosum; increased BF and metabolism in the ventrolateral and orbital portions of the PFC, the amygdala, and the medial thalamus in depressive subjects compared with controls. Some abnormalities have been found to be reversible with effective antidepressant therapy. MRI morphometric measures have demonstrated smaller left subgenual PFC and amygdala. Structural studies of depressed young adults and adolescents have found smaller left subgenual PFC. Smaller PFC and larger third and fourth ventricles have been found in depressed adolescents. Larger pituitary and amygdala/hippocampal ratios have been correlated to the severity of anxiety symptoms. Patients suffering from depressive disorders have been found to have a higher lateral ventricular volume/total cerebral volume ratio when compared with hospitalised psychiatric controls (Drevets 1998, Zalsman et al. 2006b).
REFERENCES


PART 3
Depressive Disorders in Children and Adolescents
Chapter 4
Clinical Manifestations of Depression in Children and Adolescents
Presenting Symptoms

Childhood is a period of dramatic developmental changes, and children sometimes feel sad or needy. Typically, young children as well as adolescents may demonstrate transient and normative behavioural and emotional difficulties as well as mood fluctuations. However, depressed youngsters experience disturbing symptoms that are well beyond the range of normal sadness. It can sometimes be complicated to distinguish between normal and clinically relevant behaviour for several reasons. Symptoms are expressed in various ways depending on the child’s developmental stage. For example, children and adolescents with depression may have difficulty identifying and accurately describing their internal emotional or mood states; instead of communicating their negative feelings, they may act out and be irritable toward others, which, in turn, may be interpreted and treated as misbehaviour.

Depression is an illness that damages affect, thinking, and behavioural functioning. The affect is sad; there is a decline in enjoyment, and increased irritability and sensitivity to rejection and failure. Thinking patterns of depressed children are negative and pessimistic, and these children tend to judge themselves harshly, to diminish the value of personal achievements, and to perceive the future as gloomy and hopeless. These thinking patterns, in turn, further reinforce feelings of depression. Various behavioural difficulties may also be present, including school avoidance, complaints about physical pains, and sleeping and eating problems. When a child does not seem capable of handling the feelings on her or his own and seems overwhelmed, and if the symptoms persist, particularly if they are dangerous or seriously interfere with the child’s daily functioning, it is time to seek help from a child and adolescent mental health specialist.

Some of the typical presenting problems parents report when they seek help for their children are listed in Table 4.1.

### Table 4.1

Presenting Symptoms

- Frequent sadness, recurrent crying
- Hopelessness and helplessness
- Decreased interest in activities or a decline in enjoyment from activities the child previously enjoyed
- Occupation with death themes
- Constant boredom
- Social isolation and relationship difficulties
- School absences or poor school performance
- Destructive behavior
- Low self esteem and feelings of guilt
- Extreme sensitivity to rejection and failure
- Increased sensitivity to rejection and failure
- Complaints about physical pains such as stomach pains or headaches
- Concentration Difficulties
- Major changes in sleep and eating patterns

Not all the symptoms must be present simultaneously. However, two or three behavioral signs from this list do indicate that the child might be depressed and require professional help.
SIGNS AND SYMPTOMS AMONG PRESCHOOL CHILDREN

Luby and colleagues (2003b) demonstrated that the DSM-IV diagnostic criteria for depression (American Psychiatric Association 1994) captured the most severely affected preschoolers but missed a substantial number of children between 3.5 and 6 years of age who were suffering from less severe symptoms. These children, however, were identified using modified DSM criteria developed for use with infants and preschool aged children. The goal of these preliminary modifications was to create a developmentally sensitive diagnostic system, with items adapted to correspond to preschoolers’ developmental abilities. The strict 2 weeks duration criteria was put aside, because it was found that only the most severely affected preschoolers met it, while preschoolers with less severe but still clinically meaningful depressive syndrome did not meet the duration criterion. Items related to schoolwork were adapted to assess “activities and play”, the term “sad or depressed” was changed to “sad or unhappy” to match the way young children are viewed by their parents, and preoccupation with death and suicide was adapted to include persistent themes of death and suicide in play.

Luby and colleagues (2003a) have found evidence to support a specific symptom constellation in preschool depression; these symptoms include sad/grouchy mood, anhedonia, appetite and weight problems, sleep problems, lower activity and energy levels, low self-esteem, trouble thinking and concentrating, death or suicide themes in play/talk, and whining/crying. High internal consistency of these symptoms has been demonstrated, indicating that these symptoms cluster together as is expected in valid clinical syndromes. Anhedonia emerged as the most specific symptom in the depressed group of subjects—that is, children who have not been able to enjoy activities as they previously did are most likely to meet the modified diagnostic criteria for preschool depression. The most sensitive symptom has been the experience of irritability/sadness, which was evident in 98% of depressed preschoolers.

In the past, clinicians often believed that children demonstrated “masked” symptoms such as somatisation and regression instead of presenting with depressive symptoms (Cytryn and Meknew 1972). Luby et al. (2003a) found that, although symptoms of somatisation were evident, typical symptoms of depression occurred at higher rates.

In summary, in young children, as in adults, typical symptoms of depression provide the best clinical diagnostic markers and anhedonia is specifically correlated with depression severity scores (Luby et al. 2004).

SIGNS AND SYMPTOMS AMONG CHILDREN

Sadness is not obvious among young children, and the typical presenting symptoms of depression often include boredom, loss of interest or pleasure in most activities, complaints about being tired most of the time or lack of energy to engage in normal activities, irritability and mood swings ranging from deep sadness to sudden angry outbursts, dissatisfaction, school absences, avoidance of social activities, and physical complaints without medical explanations. When asked directly, these children can sometimes say they are unhappy or sad. Depression among children is often detected in its late stages because most of the symptoms are internal and more difficult to detect, unlike anxiety, attention difficulties, or behavioural problems.

The experience of restlessness, agitation, and decreased concentration may confuse parents or teachers and lead them to think that the child has attention deficit disorder, when in fact the child is depressed. It is not uncommon for children who are being evaluated for one condition to be diagnosed with the other, since the two different disorders often coexist (American Academy of Child and Adolescence Psychiatry 1998).
Case Vignette: - Infancy

A 2.5 year-old boy was referred to a community infant mental health unit because of his severe delay in language development, hyperactivity, and general lack of interest. He would run away from his parents when returning home from the kindergarten. He was an only child and did not eat or did he sleep well and rarely laughed. He was diagnosed with pervasive developmental disorder and attention deficit disorder by a child neurologist. The parents asked for a second opinion. They perceived the child as “dumb”, were resentful and disappointed with him, and did not believe he would ever talk. On examination, he looked sad and poorly groomed and did not approach his parents, but he did explore the room and toys. The child hardly spoke but did say the words “my” and “I”. When faced with a difficulty, he did not ask his parents for help but turned to the therapist. Over the next four sessions, a full and gloomy picture of the context into which this boy was born has emerged. The mother has been suffering from a severe obsessive compulsive disorder since her teenage years and was never treated. Her family history was loaded with psychopathology. After the birth of her son, she became overwhelmed with compulsive cleaning and became increasingly angry with her baby, whose care interfered with her compulsions. She therefore kept him in his crib to prevent him from touching things and messing them up. The baby became irritable, but the parents had attributed this to his bad temperament. The mother washed the child endlessly, because she feared his stools, and he has had severe temper tantrums at bathing and diaper changing times. The child was put at a daycare centre at the age of 8 months, where he has shown partial improvement, but there has been no improvement at home. The child was diagnosed with depression reactive to the maternal obsessive-compulsive disorder on the first DC:0-3 axis, and mother-child relationship disorder was diagnosed on the second axis. The child did not meet any diagnostic criteria for pervasive developmental disorder. After 1.5 years of triadic psychotherapy, the child had improved in all domains, was communicative, and had a good relationship with his father, but he was still tense with his mother and had difficulties with peers.
Case Vignette: - Childhood
A 6-year-old girl was referred to a private mental health unit by her parents for treatment of various problems such as sadness, excessive crying, decrease in verbal communication, and eating problems. The girl’s parents reported that she preferred to stay at home and did not meet with friends for social activities in the afternoons. Instead, she remained in her room, watching TV and playing there. The parents thought that the girl’s behavior was caused by her disappointment after a recent sudden decision to keep her in kindergarten for another year. Because of this decision, she had to separate from her friends who would be starting first grade. The child was the second daughter in a family of three children. The family lived in a communal environment (“a kibbutz”), and both her parents were “newcomers” to that kibbutz. The parents themselves had very different backgrounds. The patient’s father and older sister have been diagnosed with dyslexia. The patient was a well developed, happy, and social baby. Language difficulties were detected when she was 3 years old, and she attended speech therapy for 3 years. She also attended occupational therapy for a short period of time, to enhance her graphic-motor abilities. She has had two short episodes of elective mutism in the past, which ended after psychological guidance was given to the parents and kindergarten teachers. On examination, the patient was a beautiful slender girl, who sat with her head turned downwards, spoke softly and very little, and maintained only minimal eye contact with the therapist. She did not let her parents leave the room and sat very close to them during the whole interview time. She smiled while interacting with her parents but was emotionally inhibited in her interactions with the therapist. The patient was willing to draw, but did not play. At the end of the evaluation process, the clinician was concluded that the patient had difficulties in her interpersonal relationships, felt insecure, and had low self-esteem. She was introverted and passive, as was reflected in her withdrawn behavior and silence. She was diagnosed as suffering from depression and was treated individually for 2.5 years. Her parents also met with the therapist on a monthly basis. Following this intervention, the patient showed improvement in all domains, but she still remained inhibited and socially withdrawn.
Case Vignette: Adolescence

The patient’s depression started 2 months before his examination at my clinic. The depression had gradually worsened and was accompanied by suicidal thoughts, reaching the intensity of a psychotic depression. The patient was later admitted to a day-care psychiatric department and treated pharmacologically with a combination of antidepressant and antipsychotic medications. The patient described his experience as follows.

“The depression started 2 months ago. I was active in the Hanoar Ha’oved V’halomed [The Association of Working and Learning Youth] and had started a training programme to become a group leader. My friends have slowly left the programme and I was affected by their leaving and felt alone. During the summer camp, I functioned great but I started to feel a lack of meaning inside me. Initially I felt dejected; I cried a lot, which was not typical of me in the past. After a week or so, the tears dried up, but inside of me I have felt extremely sad. I had difficulties falling asleep— I used to do sport, went for runs to exhaust myself, so I could fall asleep. I felt insecure in social situations. I had a friend who bullied me. I preferred not to talk with friends so I would not get hurt. I have, therefore, avoided going to school. School depressed my soul. I am envious of my twin brother whose social life is great.

I feel that the society is fake, pathetic, and dramatic and I do not belong to it. I feel that I constantly examine our society’s ailments through a pair of dark glasses. I get my mind off the depressive thoughts a little bit by watching TV. I really want to read books about Buddhism but find it hard to concentrate. I manage to do some sport, it’s relaxing, then I think less and feel less vulnerable, my mood improves, and I feel more whole. But when I do nothing, I am more vulnerable. I feel distant from my father who puts sunglasses on things he does not want to see and has a good time with his girlfriend. I feel that my mother understands me better, but I could not express my feelings to her [the parents divorced and all 4 grownup male children live with the father]. Even you cannot understand what I am going through, in terms of intensities.

I have thoughts about the meaningless and senseless of my existence and I sometimes consider jumping out of the window in my room (on the 4th floor). But I know that there is hope and I want help. After the talk with Vered, the therapist, I feel better, it goes up from minus 20 to minus 10, but it is temporary and goes away after half a day, when I start to think about the things that depress me. I feel divided. When I feel bad, it is like a stone sinks to the bottom. In this state, I feel that there is no point in making an effort because in 2 months time I would not be alive anyway. I frequently think about God and tell myself that God does not care. My deterioration is like a book I have started reading and then could not stop”.

During a later meeting, the patient said: “…I feel like flesh that goes on living, nothing is real except the pain. Contact with people even with my parents seems to me unreal. I stood this week in front of the window, thought of jumping. At this stage I have decided to survive and live. But it is not something I can commit to in the future”. At this stage he was admitted to the day-care psychiatric ward.
**SINGNS AND SYMPTOMS AMONG ADOLESCENTS**

Young people often experience mood swings during adolescence, but some adolescents are especially prone to distressing periods of depression. Depression interferes with adolescents’ ability to form and maintain close relationships with family members, friends, and early romantic partners, and it also hinders school performance. Teenagers may be suffering from a depressive disorder if their mood is consistently sad or if they perceive their life and future as grim and bleak. Depressed teenagers may be withdrawn and uncharacteristically lack energy and initiative. They may neglect their appearance and appear looking dirty, with mismatched clothes and dishevelled hair. Their movements may be slowed down and voice quality may be monotonous. Depressed adolescents may also show heightened sensitivity to rejection and signs of low self-esteem. For example, a depressed teenager may say things such as “I’m stupid…no one loves me…I’m bad”.

Often, there is a negative affect on social and academic functioning; the teenager’s concentration may be poor, school grades may deteriorate, and there may be decreased interest in extracurricular activities. While teenagers are naturally more likely to sleep late in the morning whenever possible, a depressed teen will nap excessively throughout the day or go to bed early in the evening. Complaints about headaches or stomach-aches are often reported by depressed teenagers. Dangerous and self-injurious behavior may also occur. Depressed adolescents may use drugs or alcohol, in some cases as self-medication to try to relieve their depression. During adolescence, teens with severe depression may also present with other emotional problems, including delinquent behavior, school attendance problems, anxiety disorders, substance abuse, and eating disorders (American Academy of Child and Adolescence Psychiatry 1999). For a discussion of suicidal risk and behaviors in adolescents, readers are also referred to Volume III, Part 5.

**DIAGNOSTIC AND CLASSIFICATION MANUALS**

**DC 0-3 R**

The DC 0-3 R diagnostic classification for infants and toddlers younger than 3 years of age reflects a developmentally sensitive modification of DSM-IV criteria. Empirical testing of these operational criteria is still needed (Zero to Three, National Center for Clinical Infant Programs 2005).

**Type I. Major depression** is defined as follows: Five of the following symptoms must be present most of the day, more days than not, for at least 2 weeks and must include one of the first two symptoms:

A. Depressed mood as indicated by either the child’s direct expression (such as “I am sad”) or observation by others (such as “the child appears sad or tearful”).

B. Markedly diminished interest in all, or almost all, activities.

C. Significant weight loss or gain (a change of more than 5% of body weight in a month, significant decrease or increase in appetite, or failure to make expected weight gains).

D. Insomnia or hypersomnia.

E. Psychomotor agitation or retardation.

F. Fatigue or loss of energy.

G. Evidence of feeling of worthlessness or inappropriate guilt in play (such as self-punitive actions and play) or in the child’s direct expression.

H. Diminished ability to think or concentrate or difficulty in solving problems, responding to caregivers, or sustained attention.

I. Recurrent references to or themes of death or suicide or self harm attempts. The child may demonstrate these symptoms through thoughts, activities, play, or potentially harmful behavior.
### TABLE 4.2

Comparison of diagnostic criteria for depression in children from three classification systems

<table>
<thead>
<tr>
<th></th>
<th>DSM-IV-TR</th>
<th>ICD</th>
<th>DC 0-3 R</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>All the rest</td>
<td>Modified - infants and preschoolers</td>
<td>Younger than 3</td>
</tr>
<tr>
<td><strong>Name</strong></td>
<td>Major depressive episode</td>
<td>Depressive episode</td>
<td>Type I. Major depression</td>
</tr>
<tr>
<td><strong>Minimal duration</strong></td>
<td>2 weeks</td>
<td>Not necessarily persistently 2 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td><strong>Symptoms required</strong></td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>Key symptoms</strong></td>
<td>1. Depressed or irritable mood 2. Diminished interest</td>
<td>1. Depressed mood 2. Diminished interest 3. Reduced energy</td>
<td>1. Depressed mood 2. Diminished interest</td>
</tr>
<tr>
<td><strong>Specifiers</strong></td>
<td>Mild = 2 of 3 key symptoms Severe = 3 of 3 key symptoms</td>
<td></td>
<td>Type II: 3–4 symptoms, at least 1 of which is one of the key symptoms</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Causes distress and impaired functioning</td>
<td>Observable themes in play</td>
<td>Play themes</td>
</tr>
<tr>
<td><strong>Exclusion criteria</strong></td>
<td>Not a mixed episode, not due to medical causes, bereavement and without mood incongruent psychotic symptoms</td>
<td>History of manic/hypomanic episode, psychotic symptoms, depressed stupor, psychoactive substance abuse</td>
<td></td>
</tr>
</tbody>
</table>
**Type II: Depressive disorder** not otherwise specified requires the presence of three or four of the nine symptoms described for Type I, with at least one of them being one of the first two symptoms for at least 2 weeks.

**DSM-IV and ICD-10 Criteria**

The diagnostic classification systems, DSM-IV-TR of the American Psychiatric Association (APA 2000), and the ICD-10, of the World Health Organization (WHO), differ in some ways in their classifications of mood disorders. However, both systems use the adult criteria to diagnose depressive disorders in minor. The ICD includes one additional diagnostic category called Childhood Behavioural and Emotional Disorders (F92). This disorder includes the criteria for Conduct Disorder (F91) in comorbidity with Depression (F30-39). Symptoms of this disorder include feelings of despair, anhedonia, guilt, and sometimes sleep and eating disorders. In the DSM-IV-TR system, features such as irritable mood are considered an alternative to depressed mood when practitioners are assessing children. It is important to keep in mind research findings such as those collected by Sorensen et al. (2005) in Denmark. They studied 199 child psychiatry patients and found that more children met the DSM-IV-TR criteria for major depressive disorder/depressive episode than the ICD-10 diagnostic criteria for the equivalent emotional disorders. Differences in the diagnostic criteria of the various diagnostic systems and specific features important in the process of diagnosing depression in children are outlined in Table 4.2.

**DSM-IV Criteria for Major Depressive Episode**

A. Five (or more) of the following symptoms have been present—**but not necessarily persistently**—during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

**Note:** Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

1. **Depressed mood** most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.

2. **Markedly diminished interest or pleasure** in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).

3. **Significant weight loss** when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.

4. **Insomnia** or hypersomnia nearly every day.

5. **Psychomotor agitation** or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

6. **Fatigue** or loss of energy nearly every day.

7. **Feelings of worthlessness** or excessive or inappropriate guilt (which may be delusional) — **that may be evident in play themes**—nearly every day (not merely self-reproach or guilt about being sick).

8. **Diminished ability to think or concentrate,** or indecisiveness, nearly every day (either by subjective account or as observed by others).

9. **Recurrent thoughts of death** (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. **Suicidal or self-destructive themes are persistently evident in play only.**

B. The symptoms do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

*Modified DSM criteria for use with infants and preschool aged children from Luby JL et al. 2003a are shown in bold.

ICD-10 criteria for Depressive Episode

**Depressive episode –(general criteria)**

G1. The depressive episode should last for at least 2 weeks.

G2. There have been no hypomanic or manic symptoms sufficient to meet the criteria for hypomanic or manic episode at any time in the individual’s life.

G3. **Most commonly used exclusion clause.** The episode is not attributed to psychoactive substance use or to any organic mental disorder.

ICD-10 criteria for Mild Depressive Episode

A. The general criteria for depressive episode must be met.

B. At least two of the following three symptoms must be present:

1. Depressed mood to a degree that is definitely abnormal for the individual, present for most of the day and almost every day, largely uninfluenced by circumstances, and sustained for at least 2 weeks.

2. Loss of interest or pleasure in activities that are normally pleasurable.

3. Decreased energy or increased fatigability.

C. An additional symptom or symptoms from the following list should be present, to give a total of at least four:

1. Loss of confidence or self-esteem.

2. Unfavorable feelings of self-reproach or excessive and inappropriate guilt.

3. Recurrent thoughts of death or suicide or any suicidal behavior.

4. Complaints or evidence or diminished ability to think or concentrate, such as indecisiveness or vacillation.

5. Change in psychomotor activity, with agitation or retardation (subjective or objective).

6. Sleep disturbance of any type.

7. Change in appetite (decrease or increase) with corresponding weight change.

ICD-10 Criteria for Severe Depressive Episode Without Psychotic Symptoms

Note: if important symptoms such as agitation or retardation are marked, the patient may be unwilling or unable to describe many symptoms in detail. An overall grading of severe episode may still be justified in such a case.

A. The general criteria for depressive episode must be met.

B. All three of the symptoms in criterion B, depressive episode, must be present.

C. Additional symptoms from depressive episode, criterion C, must be present, to give a total of at least eight.

D. There must be no hallucinations, delusions, or depressive stupor.
REFERENCES


PART 3
Depressive Disorders in Children and Adolescents
Chapter 5
Comorbid Conditions in Depressed Children and Adolescents
PHYSICAL ILLNESS

While the great philosophical distinction between mind and body in western thought can be traced to the Greeks, it is to the influential work of René Descartes (1596–1650), French mathematician, philosopher, and physiologist, that we owe the first systematic account of mind-body dualism. The study of the relationship between mind and matter is still deeply rooted in the clinical approach of both primary care physicians and specialists today. Many studies have found evidence of “organic” alterations in neurotransmitters, brain anatomy and function, neuroendocrine and immunological pathways in depression, a so called “functional” disorder. Current opinions about the interrelation of mind and body suggest that mental processes emerge from brain functioning, and that subjective mental experience affects our brains and bodies (Kendler 2005). The association of physical illness and depression has been demonstrated in many studies in adults. Psychiatric disorders have been found to be prevalent among individuals with physical illness, with depression accounting for 50% of these disorders. Yet many depressed patients report only somatic symptoms as the reason for their visit. Depression can be a presenting symptom of several diseases, such as hyperthyroidism, hypothyroidism, cancer, lupus erythematosus, acquired immune deficiency syndrome, anaemia, diabetes, and epilepsy. On the other hand, depressed patients are more susceptible to diseases, especially heart disease but also diabetes and cancer. Depression has been found to affect quality of life, daily functioning, and symptom burden (Steptoe et al. 2007).

A few studies have examined physical and psychiatric comorbidity in children, with less conclusive results. In a study of 700 children who were 1–10 years of age, poor physical health predicted an increased risk of future depression, and a diagnosis of major depression predicted an increased risk of future poor physical health (Cohen et al. 1998). A study of 1,410 older adolescents found similar results (Lewinsohn et al. 1996). Interview-based studies have shown increased rates of depression in children with a chronic illness while studies using rating scales, especially self-report scales, have been inconclusive (Bennett 1994; Burke and Elliot 1999; Cohen et al. 1998; Spady et al. 2005). Studies that specifically examined the self-reports of children with cancer found no difference in depressive symptoms from a children in a healthy control group and sometimes even found significantly lower rates of depression. These low rates of reported depressive problems could have been explained by the children’s denial and repressive coping style (Phipps et al. 1995). Interview-based studies have suggested that 5%–23% of ill children and adolescents meet criteria for major depression (Burke and Elliot 1999).

Children suffering from conditions that directly involve the central nervous system have shown higher rates of psychiatric disorders (Meltzer et al. 2000). A few studies have investigated depressive comorbidity with specific illnesses. One review found that children with severe asthma, inflammatory bowel disease, and diabetes had higher rates of depression (Burke and Elliot 1999). A previous review has found that children with sickle cell disease or asthma were at a higher risk of depression than children with cancer, cystic fibrosis, or diabetes (Bennet 1994).

Depression has been found to change the course of physical illnesses. Psychiatric disorders have been linked to increased risk of ketoacidosis, and depression was specifically linked to high levels of HbA1c and increased risk of retinopathy, in juvenile diabetes (Kovacs et al. 1995; Lernmark et al. 1999; Rewers et al. 2002). Depression has been also linked to increased mortality in children with asthma (Miller and Strunk 1989; Strunk 1987).

Several studies of children who are ill have shown similar trends with regard to the influences of age and gender on depression as have been found in physically healthy youth. For instance, adolescents are at greater risk for depression than pre-adolescents, and female adolescents are at a greater risk for depression than male adolescents. Most studies have also found a family history of depression to be a risk factor for the development of depression. Several studies have found that the length of time since the initial diagnosis was not related to depressive symptoms, while a 10-year prospective longitudinal study of juvenile diabetes found that most depressive symptoms developed within the first year of the onset of the illness (Kovacs et al. 1997).
Case-Vignette

A 3-year-old girl was referred to a paediatric hospital day unit, because of loss of appetite and interest in her surroundings. The paediatrician asked at once for a psychiatric consultation, with a strong suspicion of depression. The physical examination did not reveal any abnormality. The child looked very sad, had absolutely no interest in toys, and looked at the consultant with a despairing look; she also whined and clung to her parents. The girl’s developmental, emotional, and social history had been completely normal before this. Her parents explained the relatively abrupt change in the child’s behavior as a reaction to their move to a new home some 4 months earlier. No other stressors could be identified. The observed parent-child interaction was adequate and no relational disturbance could be diagnosed. The absence of past developmental and emotional difficulties, the absence of significant parental psychopathology, the normal family functioning, and the low stressogenic impact of the factor reported by the parents (i.e., moving into a new home) made the child psychiatrist sceptical about the diagnosis of major depression. She sent the child back to the paediatrician, with a request for a further medical work-up. An abdominal computed tomography (CT) scan revealed a malignant tumour. Obviously, this child (as well as her parents) did not know at the time she first presented for evaluation that she had a life-threatening illness; therefore, her depressive-like symptoms could not be understood as a reaction to being ill.

This short vignette exemplifies the need to distinguish between depression as a psychological reaction to the child’s knowledge that she or he has a bad illness, and depression as an intrinsic, biologic component of a severe physical illness, such as a carcinoma. In adults, carcinoma of the pancreas is a well-known cause of depression. The depression appears before the characteristic physical symptoms appear. The case presented here shows that the same phenomenon may occur in children as young as 3 years of age.

This clinical observation leads to two conclusions. First, it is recommended that all clinicians—paediatricians as well as child psychiatrists—keep in mind that major depression in young as well as in older children and adolescents is usually associated with risk factors within the child and his or her environment (as noted above). Second, it would be interesting to undertake research concerning the specific physical illnesses that have an intrinsic component of depression. (For a detailed discussion of depression in relation to HIV/AIDS, see Volume II, Chapter 8.)
The severity of the medical condition has not been consistently related to the development of depressive symptoms. One study found that depressive symptoms were related to the perceived severity of the illness and disability rather than its objective severity (Burke & Elliot 1999; Ondersma et al. 1997; Spady et al. 2005).

The high incidence of depression in chronic illnesses and symptoms that may be associated with both the medical illness and depression, such as disturbed sleep, appetite, and energy, can make differential diagnosis difficult; yet it is extremely important if identify depression if it is present. Feelings of guilt, worthlessness, and suicidal ideation indicate a high probability of major depressive disorder (American Academy of Child and Adolescent Psychiatry1998).

**ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER**

It has been assumed that comorbidity between depression and attention-deficit/hyperactivity disorder (ADHD) is an artefact of their overlapping symptoms, since the diagnostic criteria for both disorders include psychomotor disturbance and impaired ability to concentrate. However, studies that have removed overlapping symptoms have found that both diagnoses can be present without one being a diagnostic artefact of the other (Biederman et al. 1996; Milberger et al. 1995). Only a few studies have examined the occurrence of ADHD among depressed children, and the rates of comorbidity that have been reported differ. Masi et al. (1998) reported high rates of ADHD comorbidity among depressed children (30%) and adolescents (15%). Based on a review of several studies, Angold and Costello (1993) found that between 0% and 57.1% of those suffering from depression also met criteria for ADHD, and that between 0% and 45.5% of those with ADHD also met criteria for depression. ADHD in combination with high levels of depression is associated with an increased risk of the other. Given their dissimilarities, this association was unexpected. It is very difficult to compare prevalence rates across studies, because of the many differences in diagnostic precision, methodology, assessment techniques, and sample characteristics across studies. However, based on a large meta-analysis of child and adolescent community samples, Angold and Costello (1993) found that 22.7%–83.3% of the sample with depression also met criteria for oppositional defiant disorder (ODD) or CD, whereas 8.5%–45.4% of those with ODD or CD also met criteria for depression. In a longitudinal study of school-age children suffering from affective disorders, Kovacs et al. (1988) also found comorbid CD among 16% of the children during the index depressive episode, and among 23% of the children during the full study observation. The risk that the depressed children would develop CD by the age of 19 was 36%. Furthermore, in most of these cases, CD persisted after the depression had remitted.

Longitudinally, youth who suffer from both conduct problems and depression are at higher risk for long-term problems in functioning compared with youth who suffered from depression without conduct problems (Harrington et al. 1991; Kovacs et al. 1988). Children and adolescents who have been diagnosed with major depression and have also shown disruptive behaviours compared with those diagnosed with “pure” major depression were significantly more likely to receive treatment, had poorer global functioning, and had more academic problems (Lewinson et al. 1995), as well as lower levels of social competence (Renouf et al. 1997).

In summary, children in whom depression and disruptive behaviour disorders co-occurred had accentuated emotional symptoms and functional impairment.

**OBSESSIVE-COMPULSIVE DISORDER**

To our knowledge, no large-scale study has examined the incidence of comorbid obsessive-compulsive disorder (OCD) in depressed children and adolescents. In a study by Goodyer and colleagues (2001), of 68 children with a first episode of major depressive disorder 24% had comorbid OCD at presentation. Moreover, having comorbid of OCD at presentation was a risk factor for persistent depression at 72 week follow-up (Goodyer et al. 2001).
REFERENCES


PART 3
Depressive Disorders in Children and Adolescents
Chapter 6
Diagnostic Assessment of Depression in Children and Adolescents
ASSESSING PEDIATRIC DEPRESSION

One of the difficulties in assessing and identifying pediatric depression is the covert nature of many of its symptoms. A diagnosis of depression requires an evaluation of internal states that are more difficult to assess accurately, especially among young children. In the past, it was thought that young children could not be asked directly as they were not accurate reporters of information; therefore, parents were considered the better source of information. Today, although children are also evaluated directly, it is still common to use parents’ reports. When using parents’ reports, one should remember that it is only another source of information, the parents’ subjective opinion of their child’s internal state. Furthermore, many parents who have been depressed may have trouble accurately describing their child’s symptoms (Stark et al. 2000). Parents who are themselves depressed may either view everything in negative terms and therefore exaggerate their child’s problems, or they may be so preoccupied with their own depressive symptoms that they fail to see their child accurately. In such situations, parents are often unaware of their child’s sadness, suicidal thoughts, or sleep disturbances.

Since depression is a covertly experienced disorder and given the limited cognitive and language abilities of young children, it is important to evaluate depression among children by observing their play, either with their parents or individually. Various studies have found that, during a structured parent-child-dyadic task, depressed preschoolers displayed less enthusiasm and had less positive experiences with their caregivers. In addition, depressed children showed significantly less symbolic play and greater engagement in non-play behavior than healthy, nondepressed children (Statlets and Luby 2006).

PSYCHIATRIC INTERVIEW

Evaluation frequently requires conducting separate or conjoint initial interviews with the child and the parents or caregivers. Several interviews are also usually required to gather collateral information from teachers, primary care physicians, and social services professionals. The assessment interviews should include an evaluation of global functioning, comorbid psychiatric diagnoses, psychosocial and academic performance, negative life events, psychiatric family history, social support, medical and medication history, and substance use. A physical examination and laboratory tests, as indicated, are also important components of the evaluation. During the assessment, it is vital for the clinician to be alert for ethical and cultural factors that may influence the presentation, description, or interpretation of symptoms as well as attitudes towards treatment.

ASSESSMENT TOOLS

Assessment tools such as parent report measures such as the Child Behavior Checklist (Achenbach 1991), self-report questionnaires such as the Children’s Depression Inventory (Kovacs 1981), and interviews such as the Schedule for Affective Disorders and Schizophrenia for School-Age Children K-SADS (Chambers et al. 1985), can be used to assess the presence and severity of depressive symptoms.

Child Behavior Checklist (CBCL)

Competence Scale

The CBCL (Achenbach 1991) questionnaire is not a specific measure for depression. Rather, it evaluates the amount and quality of the child’s activities and measures behaviour problems (total, externalizing, and internalising). It was designed to record the competence and well-being of children aged 4-18 years. The scale has 20 items which are filled out by parents or other caregivers for the younger age group or by the patient on the teenagers’ form. The information that is gathered is divided into three subscales: activities (sports, solitary activities, chores); social
(participation in organised activities, number of friends and frequency of contact with them, behaviour with others, and ability to work and play independently); and school (performance in academic subjects, special class placement, school problems). It is a useful tool for assessing children’s social adjustment.

Sample Item:
Please list the sports your child most likes to take part in.

For each sport listed, the respondent is asked the following:

• Compared to others of the same age, about how much time does he/she spend in each? (Less than average, average, more than average, or don’t know).

• Compared to others of the same age, how well does he/she do in each one? (Below average, average, above average, or don’t know).

Children’s Depression Inventory (CDI)
The CDI (Kovacs 1981) is a self-report measure of depression symptoms designed for use with children and adolescents 7–17 years of age. The CDI assesses a range of depressive symptoms, including disturbed mood, impaired hedonic capacity, vegetative functions, self-evaluation, and interpersonal behaviours. The full scale has 27 items, and the child rates her or his own behavior or feelings by selecting one of three statements that best describes his or her behavior within the previous 2 weeks. A short form of the CDI is available, which includes 10 of the CDI items; this short version was developed to provide a quick measure of the extent to which the child exhibits depressive symptoms. The CDI was designed to be used as a screening instrument or as a measure of symptom severity, and structured age and gender norms are available for the scale. Responses to the CDI should be integrated with other sources of information (e.g., other self-rating scales for children), since the CDI has yielded high levels of false-negative diagnoses.

Sample Items:

Negative mood subscale:
• I am sad once in a while (0)
• I am sad many times (1)
• I am sad all the time (2)

Anhedonia subscale:
• I have fun in many things (0)
• I have fun in some things (1)
• Nothing is fun at all (2)

Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS)
The K-SADS (Chambers et al. 1985) was originally developed in 1977 based on the Schedule for Affective Disorders and Schizophrenia (SADS) for adults. It is a semi-structured interview for school age children (i.e., children between 6 and 18 years of age) that covers the major psychological disorders of childhood, including depression. Both the child and the caregiver are interviewed separately. The K-SADS has been used for many years and has been revised and updated. Several versions are available, but clinicians and researchers usually prefer the K-SADS-PL, which is a present and life-time version (Kaufman et al. 1997). The K-SADS may be especially good at detecting children who meet diagnostic criteria for major depressive disorder. It has a high degree of precision in assessing depressive symptoms, their onset, severity, duration, and associated impairment. The use of the instrument requires clinical experience and specific supervised training. Kaufman and colleagues have suggested that the interview be used as part of a comprehensive battery that includes information gathered from a variety of sources.
PSYCHOLOGICAL TESTING

Intelligence Tests

Intelligence tests are frequently administered as part of the assessment procedure. They are often used to measure whether or not a child is functioning at his or her chronological age and could be expected to meet teaching demands at school for average children of the same chronological age. It is important to keep in mind that intelligence is not some kind of disembodied skill that exists apart from the rest of the child’s personality. IQ scores are themselves related to many aspects of children’s lives, such as their performance at school and their peer relationships. In addition, the test provides data concerning general areas of strengths and weaknesses, coping techniques, motivation, characteristics of thinking that may be related to personality variables, the presence of distorted thinking, and capacity for concentration. One of the most widely used intelligent tests is the Wechsler Intelligence Scale. Three versions of this test are available:

1. The Wechsler Preschool and Primary Scale of Intelligence (WPPSI) is for preschool and young children, between 2.5 and 7 years of age.

2. The Wechsler Intelligence Scale for Children (WISC) is for children between 6 and 16 years of age.

3. The Wechsler Adult Intelligence Scale (WAIS) is for use in individuals who are 16 years of age and older.

PROJECTIVE TECHNIQUES

Projective techniques involve using ambiguous or unstructured material to assess an individual’s particular personality, inner emotions, and conflicts. The examiner either presents amorphous stimuli, such as a serious of inkblots, or else presents stimuli that have a number of different meanings, such as a set of pictures that is used as a basis for stories told by the person.

The Rorschach test is a psychological evaluation method, in which the examiner is trying to assess personality characteristics and emotional functioning. It uses a series of 10 inkblots, which the child views one at a time after being instructed to tell the examiner everything the blots look like. The child’s scores are interpreted in terms of a number of personality variables.

The Thematic Apperception Test (TAT) was designed to draw on a subject’s unconscious to reveal repressed aspects of personality, motives, and needs for achievement, power and intimacy, and problem-solving abilities. The TAT consists of thirty ambiguous pictures, but only 10 pictures are used in an average administration. The evaluator instructs the person to tell a story identifying the people in the picture, explaining their thoughts and feelings, and describing their past, present, and future. The heroes in the stories are thought to represent various aspects of the individual’s self concept. The Children’s Apperception Test (CAT) was designed based on the concept that children will more readily identify with and therefore tell more meaningful stories about animals than about human figures. Unlike for the Rorschach test, there is no standard scoring procedure for the TAT and CAT.
REFERENCES


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Depressive Disorders in Children and Adolescents
Chapter 7
Treatment modalities
There are different therapeutic modalities for depression. The preferred treatment is a combination of pharmacotherapy and psychotherapy. Still, among preschoolers and young children antidepressant drugs are less common, and psychotherapy is mostly recommended.

**PHARMACOTHERAPY**

Treatment for depression in children is a recent development, data is still scarce, studies present methodological problems such as insufficient sample size, difference in primary endpoint, high dropout rate, short duration of treatment, low final doses, and few studies research different age groups.

To date the use of antidepressants in children and adolescents is still controversial. The efficacy in treating depression in adults made treating children and adolescent seem like a reasonable option. In 1998 the American Academy of Child and Adolescent Psychiatry (AACAP, 1998) issued the practice guidelines recommending Selective serotonin reuptake inhibitors (SSRIs) as initial therapy in MDD in children and adolescent after the first randomized, controlled double-blind trial (RC-DB) showed superior results over placebo (Emslie et al, 1997). This recommendation was followed by a significant increase in prescribing SSRIs for youths. With the accumulation of data showing negative results and reports of an increase risk of suicidal ideation and behavior with SSRIs treatment the Food and Drug Administration (US FDA, 2005), the European Medicines Agency (EMA, 2004), and the British Medicines and Healthcare products Regulatory Agency (MHRA, 2004) issued advisories concerning the risk of suicide and self-harm associated with the use of antidepressant medication in children and adolescents. Other issues concerning treatment with antidepressants in children such as an increased risk of manic conversion or the long-term effects of these drugs on the developing CNS have not been studied enough (Moreno et al, 2007; Leckman & King, 2007; Moreno et al, 2006; Kratochvil et al, 2006).

**TABLE 7.1**

**When to refer a child to a mental health professional**

- Collect parental report of symptoms and behavioral changes, as well as duration of symptoms and any possible precipitating event
- Guide parents and professional (pediatrician, family doctor, school teacher or school counselor) to talk to the child and show interest and the desire to help and understand the child’s feelings.
- Try to determine whether the child seems capable of handling the feelings, or whether the child is overwhelmed by the feelings, and his daily functioning is impaired.
- Rule out underlying physical illness that could also produce depressive symptoms.
- If symptoms persist, particularly if they are dangerous or seriously interfere with the child’s life, child’s physician should make a referral to a child and adolescent psychiatrist or other mental health professional experienced in working with children.
Placebo response
The placebo effect varies greatly among studies but still is one of the most reproducible finding in clinical trials. In adult studies the placebo effect average is about 30%, in trials of SSRI treatment in children and adolescents it is as high as 50%. Several explanations for these findings were suggested such as less severe illness and the dependant and suggestible nature of this population. Since the etiology of depression in children is considered to be more psychosocial then genetic compared to adolescents and adults, the attention, empathy and therapeutic alliance may play a greater role in response to treatment. Participants in clinical trials show better outcomes than non-participants, and establishing a therapeutic alliance, providing patients with empathy, attention, and intense clinical care seem to be an essential part of the treatment in children and adolescents (Moreno et al, 2007).

Tricyclic antidepressants
Studies of tricyclic antidepressant (TCA) treatment in children were conducted since the 1980’s. In most of these studies TCA were not significantly more effective the placebo (Kramer & Feiguine, 1981; Petti & Law, 1982; Kashani et al, 1984; Preskorn et al, 1987; Puig-Antich et al, 1987; Birmaher et al, 1998; Geller et al, 1990; Kutcher et al, 1994; Kye et al, 1996; Klein et al, 1998; Sallee et al, 1998). Two Meta-analysis of TCA studies found a small effect size for these drugs. The later also found a better response among depressed adolescents compares to children (Maneeton & Srisurapanont, 2000; Hazell et al, 2004). Several explanations for these findings were suggested, different levels of maturation of the noradrenergic system, lower noradrenergic receptor sensitivity, and methodological problems. With no prove of significant efficacy, potential lethal side effects and the risk of over dose, TCA are not standard treatment for depression in children and are reserved for more severe chronic cases (Moreno, 2007).

The AACAP recommends a full physical examination before starting treatment with TCA. Electrocardiogram, liver function test, blood pressure (sitting and standing), pulse, and weight should be tested at baseline and monitored regularly. Starting dose should be increased gradually and not exceed 1-3 mg/kg per day (AACAP, 1998).

Selective serotonin reuptake inhibitors
In adults there is no significant difference in the efficacy of different members of the SSRI group, data gathered so far from clinical trials in children and adolescents does not show such uniformity. These results may be attributed to specific characteristics of different drugs having a more pronounced effect in children, different effect in different age groups, or to the scarcity of data rather then an actual effect. The first trial testing fluoxetine in adolescents found no difference between drug and placebo groups (Simeon et al, 1990). The second, a single-site, RC-DB trial found fluoxetine to be superior to placebo in the primary endpoint (Emslie et al, 1997). A larger, multi-site RC-DB trial failed to show difference between fluoxetine and placebo in the primary endpoint, however three of seven secondary endpoints were positive (Emslie et al, 2002). The Treatment for Adolescent Depression Study (TADS), a multi-site randomized controlled trial, compared fluoxetine, cognitive behavioral therapy (CBT), a combination of both treatment, and placebo (March et al, 2003). Fluoxetine was superior to placebo in one of the two endpoints (Kratochvil et al, 2006).

A Meta-analysis weighing the risks and benefits of SSRI treatment in both published and unpublished data found a favorable risk-benefit profile for fluoxetine. Published and unpublished data found little evidence for efficacy of paroxetine treatment; moreover, patients in the treatment group had an increased risk for serious adverse events. Two published RC-DB trials of sertraline treatment found a slight improvement in response rates with an increased risk of serious adverse events (Wagner et al, 2003). Unpublished data showed no benefit in remission rates. One RC-DB tail
found a reduction in depressive symptoms and no serious adverse events with citalopram treatment (Wagner et al, 2004), while two unpublished trials showed no significant reduction in depressive symptoms but showed an increased risk for suicide attempts (Whittington et al, 2004; Moreno et al, 2006; Moreno et al, 2007). A recent Meta-analysis of antidepressants treatment for MDD, OCD and non-OCD anxiety disorders in children and adolescents found an overall increased risk of suicidal ideation/suicide attempt associated with treatment. For MDD, only a moderate pooled risk difference was found with SSRI treatment and no benefit over placebo was found in children under 12 years except for fluoxetine (Bridge et al, 2007).

According to the AACAP SSRI’s produce less serious side effects and require simpler monitoring. Liver function tests, weight, height should be tested at baseline and monitored regularly (AACAP, 1998).

**TABLE 7.2**

**Fluoxetine**

- To date, Fluoxetine is the only antidepressants with proven favorable risk/benefit profile for the treatment of depression in children and adolescents. The risk/benefit profile is unfavorable for paroxetine, venlafaxine, sertraline, citalopram, escitalopram and mirtazapine.

- The reported increased suicidal risk with antidepressants warrants a close monitoring of treated children and adolescents for symptoms such as irritability, hostility, self-harm and self-destructive actions, particularly at the beginning of treatment.

- Adolescents more then children seem to benefit with antidepressants treatment.

- Drug Metabolism is age dependant thus doses and frequency of administration needs to be adjusted when prescribed in children and adolescents.

**Other antidepressants**

Two multi-sited and one one-site RC-DB trials found no efficacy with vanlafaxine treatment (Emslie et al, 2004a; Mandoki et al, 1997).

Two RC trials with nefazodone found no difference between treatment and placebo in primary endpoint, one of these trials showed a difference in some of the secondary endpoints (Emslie et al, 2002).

Two RC-DB trials of mirtazapine failed to show efficacy (Moreno et al, 2006)

**Continuation and maintenance treatment**

The mean duration of a depressive episode is 7 to 9 months, about 90% remit within 1 to 2 years. Relapse rate in children and adolescents range between 34% and 50% with greater rates during the 6 to 12 months. Recurrence rate between 54% and 72% was found in children and adolescents followed for 3 to 8 years. However, few studies of long-term follow up were conducted. In a one year naturalistic study subject were randomized for 8 weeks of treatment with fluoxetine or placebo. 39% of recovered subjects had a recurrence of depression within one year. The risk for recurrence was 2.3 times greater for patients who discontinued fluoxetine, however, recurrence occurred even in patients still treated with fluoxetine (Emslie et al, 1998). In an ad-on study children and adolescents who responded to fluoxetine were re-randomized to continue medication or switch to placebo for 36 weeks. Fewer patients treated with fluoxetine then placebo met criteria for relapse and time to relapse longer with fluoxetine treatment (Emslie et al, 2004b).

The AACAP recommendations include continuing therapy for at least 6 months. Children and adolescents with two or three episodes of a MDD should receive maintenance treatment for at least 1 to 3 years. Patients with a second episode accompanied by psychosis, severe impairment, severe suicidality, and treatment-resistance, and patients with more than 3 episodes, should be considered for longer treatment (AACAP, 1998).
ELECTROCONVULSIVE THERAPY

Electroconvulsive therapy (ECT) is an effective treatment for depression in adults with minimal effects events and few contraindications. Despite these facts, ECT remains a controversial treatment especially for special populations such as adolescents. ECT is rarely used in adolescents, when used is usually a treatment of last resort. A recent review of the literature found 200 relevant articles, most of them case reports, few are open studies, and no randomized control trials were found. Only one study compared adolescents with bipolar disorder patients who received ECT with a group of adolescents with bipolar disorder patients who refused treatment. Only two studies compared adults and adolescents who received ECT (Stein et al, 2006).

Efficacy

In reviews about the efficacy of treatment in children and adolescents (Bertagnoli et al, 1990; Rey & Walter, 1997; Ghaziuddin et al, 1999; Stein et al, 2004), most studies presented methodological problems such as heterogeneous diagnoses, small sample size, and retrospective study design. With the exception of a single report (Guttmacher & Cretella, 1988) that showed lack of efficacy, all published reports found ECT effective. Efficacy in one review ranged between 60% and 100% in children and adolescents with depression, another review found ECT effective in 80% to 100%, and an improvement of 90% in adolescents with treatment resistant depression (Stein et al, 2006).

Adverse effects

Three reviews reported mild adverse effects such as headache, confusion, nausea or vomiting, muscle aches, and transient, mild memory disturbances. More serious adverse effects include prolonged seizures, and risks associated with general anesthesia. When compared with matching controls, standardized neuropsychological batteries did not show significant differences in long-term memory, attention, new learning and objective memory scores (Cohen et al, 2000) and no difference in school achievement 2.5 years after treatment (Taieb et al, 2002). In a review of 60 published reports no fatalities were reported (Rey & Walter, 1997; Stein et al, 2006).

PSYCHOTHERAPY

Psychotherapy is a complex and rich process that can reduce symptoms, provide insight, and improve a child or adolescent’s functioning and quality of life. There are different kinds of psychotherapy:

- Infant-parent psychotherapy - apply to infants
- Play therapy - apply to children
- Individual Psychodynamic psychotherapy – apply to adolescents
- Parental guidance - apply to parents of children and adolescents
- Cognitive behavioral therapy (CBT) – apply to adolescents
- Interpersonal therapy (IPT) – apply to adolescents

Infant-parent psychotherapy

Infant-parent psychotherapy is a multifaceted method of intervention that uses joint work with parents and infants under 3 years old, with the ultimate goal of improving parent-infant relationships and the child’s socioemotional functioning. It utilize a combination of intervention modalities that include insight oriented psychotherapy, unstructured developmental guidance and emotional support. Processes created in the therapeutic relationship can lead to enduring changes in the parent’s and infant’s experience of each other, the quality of their relationship, and their sense of themselves. Intervention in infancy should apply parent-infant psychotherapy, setting out a support system, therapy and medications for ill parents, and placement outside the home, according to the specific characteristics of the environmental trigger factors (Lieberman et al, 2000).
Play therapy

Play therapy involves the use of toys, blocks, dolls, puppets, drawings and games to help the child recognize, identify, and verbalize feelings. The psychotherapist observes how the child uses play materials and identifies themes or patterns to understand the child's problems. Through a combination of talk and play the child has an opportunity to better understand and manage their conflicts, feelings, and behavior.

Individual psychodynamic psychotherapy

Psychodynamic psychotherapies are based on the assumption that a child’s behavior and feelings will improve once the inner struggles are brought to light. It can help adolescents to understand themselves, identify feelings, improve self-esteem, change maladaptive patterns of behavior, interact more effectively with others, and cope with ongoing and past conflicts. Therapy offers support and empathy while encouraging exploration of the depressed feelings and symptoms. It helps the adolescent to deal with feelings rather than act them out. Therapy emphasizes understanding the issues that motivate and influence a child’s behavior, thoughts, and feelings, and help identify a child’s typical behavior patterns, defenses, and responses to inner conflicts and struggles.

Because of their developmental struggle with autonomy from authority figures, adolescents pose a particular challenge to clinicians. The establishment of good rapport is essential for building trust. The issue of confidentiality is key and, from the outset, the clinician should explain the ground rules governing when a parent or other third party will be informed of what is discussed with the patient.

Parental guidance

A critical component of early treatment of depression is education of the child and the family about the disorder and its treatment to help them become informed partners in the treatment team. Education on depression allows proceeding with less parental self blame, and blame of the child (she’s manipulative, or lazy). Education should be offered to all family members because the symptoms of depression usually affect all of them. With the help of education, the depressed child and family members can develop a concept of depression as an illness, identify affect, address psychosocial deficits, learn the importance of complains with treatment, and reduce feelings of stigmatization. It may include the signs and symptoms of depression, the role of psychiatric medication, common misconceptions about depression and medication, relapse and recurrence, impact on school performance and academic functioning, and the impact of peer and family relationships (AACAP, 1999).

Cognitive behavioral therapy (CBT)

CBT was initially developed as adult treatment. The technique does not developmentally fit children, and it is common in use among adolescents.

Cognitive Behavioral Therapy (CBT) is the most studied nonpharmacologic intervention for the treatment of depression in youth (Weisz et al, 2006). At it’s core, the intervention is based on cognitive vulnerability model, as it was put forth by Beck (1979), although current CBT treatment programs do not ignore the biological behavioral and environmental bases of depression. From cognitive perspective, depressive disorders are characterized by disturbance in cognition that is activated by specific vulnerabilities to stressful events. Once activated the disturbance in cognition produces a negative distortion in perception about the self, the world, and the future. Beck (1979) hypothesized that depressive schemes are formed through early learning experiences, especially those within the family, and the most central
scheme is the self-scheme. The self-scheme of depressed individuals is unrealistically negative and characterized by a sense of loss or feeling of not being loved, and may account for selective attention to, and personalization of, salient events. This would lead to imbalance in information processing, in which fewer instances of positive self-relevant information are processed and internalized into the overall sense of self. Lack of positive self-scheme, or existence of pervasive negative self-scheme, is hypothesized to lead to a negative bias in information processing that serves to confirm the depressed individual’s negative sense of self and the world (Stark et al, 2000).

CBT approach embodies behavioral theories of depression as well as cognitive models. Social learning theory is the most prominent of the behavioral models, and it suggests that depression is caused and maintained by the disruption in adaptive behavior, like using pleasant activities to elevate mood, caused by stressful life events (Weersing & Brent, 2006).

CBT techniques for youth depression target these hypothesized cognitive distortions and behavioral deficits to improve current mood and prevent further episodes of depression. Overall, CBT programs aims are to teach depressed youth specific CBT mood regulation skills through encouraging the practice of skills in and between sessions. CBT manuals differ substantially in the extent to which they emphasize the primacy of cognitive or behavioral strategies, the overall number of sessions, group versus individual setting, and general level of structure (Clarke et al, 1990).

Weersing & Brent (2006) described common CBT techniques and general sequence of treatment across youth depression protocols:

- Psychoeducation and mood monitoring – providing parents and youths information about the course and characteristics of depression and of the CBT model of treatment. Teaching youths to monitor their moods, thoughts, and behaviors.

- Pleasant activity scheduling and behavioral activation- promoting engagement in activities that provide opportunity for mastery or pleasure, and to promote a long term focus on creating a rewarding, non stressful and mood elevating environment.

- Cognitive restructuring- Helping youths to explore their automatic thoughts and core schemes and assess the accuracy and consequences of their views. Teaching youths to engage in “rational” thinking about themselves, the world, and the future.

- Additional CBT skill building techniques used in many programs- Relaxation; Social skills and conflict management; Problem solving skills.

It is difficult to draw strong conclusions from the current CBT literature on the treatment of depression in youth. Reviewing the all published CBT depression trials for children and adolescents that have appeared in peer reviewed, English language journals, Weersing & Brent (2006) concluded that although the protocols share some common elements, they do differ in major terms that might influence conflicting results. In different studies factors like sample, treatment manuals (dose of treatment, emphasis on cognitive versus behavioral techniques and group versus individual setting) and design (selection of control or comparison conditions) influenced the results. However there are some evidence to indicate that CBT is more appropriate for adolescents with mild to moderate depression, and may not be helpful for: adolescents with severe depression and functional impairment, families with maternal depression, and in cases with externalized comorbidity.
Interpersonal therapy (IPT)

Interpersonal therapy (ITP) for adolescents (ITP-A) is the most recently developed psychotherapeutic intervention and has been noted to be efficacious in the treatment of depressive symptoms in adolescents (Brunstein et al, 2006). It was initially developed as a time limited, focused treatment for depressed adult outpatients. Mufson and colleagues were the first to adapt ITP to treat depressed, nonbipolar, nonpsychotic adolescents (ITP-A). It is implemented for the purpose of reducing depressive symptoms and enhancing interpersonal functioning, through examination of the depressive symptoms as a result of grief reaction, life transitions, family conflicts between parents and child, conflict with peers, or social withdrawal and social deficits. ITP-A is a manualized treatment, limited in time- 12 weekly sessions. Depressed adolescents are educated about how their depression and quality of interpersonal relationships affect one another. It focuses largely on current interpersonal issues that are areas of great concern and importance for adolescents (Mufson et al, 2004).

ITP-A focuses on four identifies problem areas (Brunstein et al, 2006):

- **Grief** caused by death- adolescents that lost someone close and the onset of depression is associated to the loss. Grief is considered abnormal when it is prolonged, distorted, delayed or chronic. Treatment goals are to facilitate appropriate mourning process, establish a more realistic view of the deceased and the relationship, and re-establish relationship that can substitute for what was lost.

- **Interpersonal dispute-** when a patient and at least one significant other person have different expectations about their relationship that leads to frequent conflict. During adolescence disputes frequently involve parents. Treatment goals are to identify the dispute, and modify the communication or expectations so some resolution of the dispute can be established.

- **Interpersonal role transition-** can occur because of developmental changes or other life changes. Difficulties take place when a patient is having a difficult time adjusting to the change that requires a new social role. Treatment goals are to mourn and accept the loss of the old role, foster more positive view on the new role, and help the adolescent to achieve a sense of competence and mastery in the new role.

- **Interpersonal deficits-** lack of social and communication skills to establish and maintain appropriate relationships within and outside the family. Treatment goals are to reduce social isolation and encourage formation of new relationships.

**Combined treatment**

Meta-analysis through the late 1990s indicated that effect sizes for CBT on measures of depression were among the highest in youth psychotherapy literature (Lewinsohn & Clarke, 1999). Within the last 2 years a series of new findings has complicated the definite picture of CBT effects. The most well-known is the Treatment for Adolescents with Depression Study (TADS). Funded by the National Institute of Mental Health, the Treatment for Adolescents with Depression Study (TADS) is intended to evaluate the short-term (12 weeks) and longer term (39 weeks) effectiveness of four treatments for adolescents with DSM IV moderate to severe MDD. TADS patients exhibit the full spectrum of clinically ill depressed teens seen in clinical practice. The four treatment modalities are clinical management with fluoxetine (FLX), cognitive-behavioral psychotherapy (CBT), their combination (fluoxetine plus CBT), and clinical management with a sugar pill (placebo). The outcome of the study is unambiguous and the clinical implications are straightforward.
Thus, the results for the 12 weeks period are unambiguous. They demonstrate that the combined treatment accelerated recovery relative to the CBT, and for some outcomes to the FLX alone, while minimizing the risk of suicidality relative to FLX alone. Taking risk and benefits into account, it was concluded by March and colleagues (2006) that the combination of FLX and CBT appears superior to either monotherapy as a treatment for moderate to severe major depression disorder in adolescents. The rates of response defined as much or very much improved were: 71.0% for the combination of FLX and CBT, 60.6% for FLX alone, 43.2% for CBT alone, and 34.8% for placebo. Thus, the combination of FLX and CBT appears to produce the greatest improvement in symptoms of major depression. FLX alone is effective, but not as effective as the combination of FLX and CBT. CBT alone is less effective than FLX and not significantly more effective than placebo.

Almost 30% of TADS participants had suicidal ideation at the start of the study; 2% had intense suicidal ideation. Suicidality decreases substantially over 12 weeks of treatment. Improvement in suicidal ideation is greatest for the combination of FLX and CBT and least for FLX alone. CBT psychotherapy may protect against harm-related behavioral events in patients taking FLX.

In spite of the persuasive results, as Brent (2006) commented, even under the best circumstances with combination treatment, only 37% of the TADS subjects have remitted by 12 weeks. It may be that we need additional time or treatment to bring depressed patients to full remittance, or that we are getting to the adolescents too late and that more effort should be put into early detection.

TABLE 7.3

Key components of IPT-A

- Explanation of the medical model of depression—depression is a medical illness, and normal performance and activities are being affected.
- Psychoeducation—nature of depression disorder, treatment options, improvement and recovery.
- Interpersonal inventory—detailed review of significant relationships.
- Modify communication patterns
- Interpersonal problem solving
- Active parental involvement

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SUGGESTED READING


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PART 4
Cultural Aspects of Depression

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BACKGROUND

Due to the process of globalisation, professionals in the mental healthcare system are more and more often confronted with the necessity of assessing depressive disorders in patients from ethnic backgrounds different from their own. Low mood, lack of energy, sleep problems, and loss of interest in social environment are all symptoms that may be found in most cultural settings, and there is evidence that racial and ethnic background does not significantly influence the prevalence of depressive traits. We know that depression is influenced by an interaction between genetic, biological, and psychological vulnerability and social adversities. A key question, however, is whether differences in symptomatology can be explained by differences in social or biological conditions rather than differences in cultural conditions.

In many cultures, depressive traits are often seen as a natural reaction following losses or severe life events; similarly, depressive traits in old age may be interpreted as a condition that does not require intervention. However, in some cultures, severe pathological grief reactions are viewed as a sign of genuine grief more than as a pathological phenomenon, which may lead to severely depressed individuals not receiving adequate treatment. Even in depressive episodes with a marked biological component, culture may have a pathoplastic effect by modifying depressive manifestations. Thus, it is important to recognise the interaction between culture and depression whenever interviewing a patient who is suspected of having a depressive episode.

This chapter provides an overview of cultural aspects of depression, including issues related to epidemiology, diagnostics, symptomatology, provoking factors, comorbidity, therapeutics, prognostic factors, and training for health professionals.

The Influence of Culture on Mental Disorders

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).

EPIDEMIOLOGY

Depression constitutes an important global public health problem of increasing importance. This is due both to its high lifetime prevalence and to the significant disability it causes. Enormous body of research deals with rates of major depression or dysthymia in particular ethnic minority groups in certain countries and communities (e.g., Gonzales et al. 2001; Jang et al. 2005; Leavey et al. 2007; Lerner et al. 2005; Miller et al. 2004; van der Wurff et al. 2004). Given that the majority of the studies refer to a specific group (e.g., with regard to ethnic and cultural background, age, and gender) in a specific context, it is difficult to extract a generalisable pattern from the results that explain differences among groups (Lincoln et al. 2007).
According to the World Health Report (2001), globally, approximately 360 million persons suffer from mood disorders. Depressive disorders are the fourth most important contributor to the global burden of disease, while in adults 15–44 years of age, they are the leading cause of DALYs (disability-adjusted life years) lost world-wide. In 2002, depression accounted for 4.5% of the worldwide total burden of disease (in terms of DALYs). The lifetime risk for major depression has been reported to be 12%–16%, compared with a lifetime risk of 1%–5% for bipolar disorder. The World Health Organization (WHO) has predicted that, by 2020, depression will be the second most important cause of disability. Although measures of disability may differ, they have consistently demonstrated that persons with depressive disorders show clearly impaired physical functioning, impaired role functioning, increased work impairment, and high utilisation of health services (Lecrubier 2001). In addition, the high rates of comorbid physical and mental disorders in individuals with depressive disorders add still further to the burden and disability associated with the illness.

Depression is very prevalent, and depression is ranked number 5 in women and number 7 in men on a global level as a cause of morbidity (World Bank 1993). However, the burden does depend on the region, with the burden estimated to be 8.9% in high-income countries compared with 1.2% in Africa. Nevertheless, depression is also associated with a heavy disease burden in developing countries and is predicted to become a leading cause of disease burden in these regions as well (Murray and Lopez 1997).

It is estimated that 5%–10% of the population at any given time is suffering from identifiable depression requiring psychiatric or psychosocial intervention. Individuals under 45 years of age are much more likely to suffer from depression than those who are 45 years of age or older. This means that, in all cultural settings, depressive illness is more likely to affect people during their most productive years of life.

The rate of occurrence of depression does not vary significantly by race or ethnicity. Socio-economic and educational differences may contribute to some of the differences observed between ethnic groups, but when these factors are statistically corrected for, no variation in risk by ethnic groups is found (WHO 2006).

In the Cross National Collaborative Group study (Weissman et al. 1996), which included comprised 10 countries, the lifetime prevalence of depressive disorder was found to vary greatly, ranging from 19% in Beirut to 1.5% in Taiwan.

There are clear gender differences in the risk of having a depression. On a global level, women have a risk that is 1.5–2 times higher of developing depression compared with men. In all countries of the Cross National Collaborative Group, there was a higher prevalence of depression among women, ranging from a female: male ratio of 3.1 in West Germany to 1.6 in Beirut and Lebanon (Weissman et al. 1996). It is believed that certain factors, such as the need to maintain multiple roles as homemakers, professionals, wives, and mothers, may explain the higher frequency of depression in women.

How Common Is Depression in the Community?

Until the middle of the twentieth century, it was commonly-believed that mental disorders regularly occurred less frequently in developing countries than in industrialised nations. Today we know that stress factors can occur regardless of the level of industrial development in all cultures, and that mental disorders are found all over the world (Sartorius 2000). Investigations carried out by the World Health Organization (WHO)—the international pilot study on schizophrenia (WHO 1973), the study on the determinants of serious mental disorders (Jablensky et al. 1992), and studies on depressive disorders in different countries (Sartorius et al. 1983)—appear to indicate that the incidences of mental disorders, in particular their serious forms, do not differ significantly from one another globally. However, socio-cultural factors do have a significant impact on the incidence of minor mental disorders and culture-specific disorders (Jilek and Jilek-Aall 2000).
As a result, until the end of the 1950s it was assumed that depression in developing countries, in particular in Africa and Asia, was an uncommon illness compared with the Western hemisphere. In particular, it was thought that suicides due to depressive illnesses were exceptions. This viewpoint was very much rooted in the tradition of the founder of comparative psychiatry, Emil Kraepelin. During his studies on Java in 1904 he noticed that "...there was hardly any occurrence of more serious forms of depression". Self-reproach, or a tendency to suicide in depressed people, was hardly observed (Bendick 1989). Multi-centre studies that investigated the prevalence of depressive disorders in different countries and continents during the second half of the twentieth century—particularly during the 1970s and 1980s—showed this hypothesis to be false. They proved that depressive disorders occur at different levels of frequency in all known cultures (Jablensky et al. 1992).

Given the availability of well-defined diagnostic categories and reliable operational criteria, the frequency of depression in the community can be measured. In the WHO study on mental illness in general health care which covered 14 countries world-wide, the prevalence of current depression as diagnosed according to ICD-10 criteria in general health care centres varied from 2.6% in Nagasaki and 4.0% in Shanghai to 16.9% in Manchester and 29.5% in Santiago (Goldberg and Lecrubier 1995). The wide differences were attributed to four possible causes: true differences in depression rates, differences in concepts of disease, differences in help-seeking tendencies, or differences in demographic characteristics of the help-seeking population (Goldberg and Lecrubier 1995).

Depressive disorders are frequently identified in primary care. In the WHO collaborative study concerning psychological problems in primary health care (Wittchen et al 1999.), data were collected from primary care centres in 15 countries. A main finding from the study across countries was that 11.7% of patients coming to services had a disorder fulfilling ICD-10 criteria for depression. However, the primary reason patients contacting healthcare services was rarely a psychological problem. Rather, patients tended to present with multiple disorders, including depression, with the result that the depression often remained undiagnosed, and even when the depression was diagnosed, treatment usually focused on the other chronic diseases.

**NEUROBIOLOGICAL ASPECTS**

There are no data on neurobiological aspects in the pathogenesis of depression specifically referring to migrants. Furthermore, studies on acculturation and depression show inconsistent results concerning the actual impact of acculturation on the development of a depressive disorder (See Volume I, Chapter 3 for more discussion of acculturation and depression).

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 has become a 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) (Fabrega 1989; Kleinman 1988). 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 the International Classification of Diseases, 10th Edition (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”.

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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 atypical 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).

Diagnosing Mental Illnesses in Migrants
In diagnosing mental disorders in migrants, clinicians need to be particularly alert for three types of issues, which are both theoretically and practically important: language, culture-specific issues, and migration-specific issues. It is assumed that issues related to the last two areas play a significant role in the problems of migrants who are undergoing acute psychological crises: however, migration- and culture-specific factors can each have a different impact on the intrapsychological conflict that may arise involving the person’s feelings towards the both the home and host country, which is part of the migration process. How these specific factors are dealt with in individual cases will depend mainly on protective and pathogenic factors that are not specific to migration, but rather are related to the current psychological developmental challenges the person is facing (Calliess et al 2007a).

The literature on migration often makes no clear differentiation between the terms culture-specific and migration-specific. For research purposes, however, it is vital though to differentiate these areas and the different types of influence they may have on, for example, the frequency of disorders and problems that may arise in treatment. Results of studies on increased psychological morbidity in migrants (Cantor-Graae & Selten 2005) do not indicate whether increased vulnerability is associated with a migration background, or with acculturation problems in the host country due to cultural differences, or a combination of both factors (Berry 1997, Bhugra 2005).

In diagnosing mental disorders in patients who are migrants, clinicians should consider culture and migration-specific factors as well as the person’s level of integration into the host country, since these three dimensions determine the conflicting influences in which the diagnosis of acute psychological crises in migrants takes place.

The greater the proportion of biological factors involved in the onset of a mental illness, the less impact cultural factors are likely to have on the aetiology of the illness. Conversely, the lower the pathogenetic component in the aetiology of the disorder, the more a pathoreactive effect will make itself felt (Tseng 2001). Despite the worldwide incidence of serious mental disorders, these factors can lead to a vastly different picture of the epidemiology, symptomatology, and courses of illnesses in different cultural settings (Pfeiffer 1994; Sartorius et al. 1977, 1978). Therefore, diagnosticians from other cultures can encounter substantial difficulties in differential diagnoses, due to the great variation in symptoms that may present depending on the patient’s culture of origin.
Thus, culture can play a key role in the expression and type of illness. This is seen in the culturally relevant question that arise, for example, about the view of suicide in certain countries (i.e., whether suicide is today ever considered a suitable strategy for resolving conflicts in a seemingly hopeless situation in certain cultures). Likewise, migrants in a mental crisis may tend to describe somatic symptoms first and foremost, because the dichotomy between body and soul, which is so typical of Western cultures, may be not be part of their original culture.

At the same time, migration and the culture shock associated with it, involving a change from a traditional society with a collectivistic approach to a modern, individualistic society, can lead directly to problems in migrants that range from decompensation of mental coping mechanisms to actual mental illness. Thus, migration can be a trigger for mental disorders, because the protective function of the original culture is missing (Cantor-Graae & Selten 2005). In this situation, a variety of differential diagnostic problems can arise, especially if clinicians do not take into account problems with acculturation arising as part of the migration process and manifestations of serious mental disorders that are the result of a change of culture or due to trauma.

**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.

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, nowhere 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. 2007b).

PRECEPTING FACTORS

Given the lack of clearly defined, empirically validated risk factors for depression that have consistently been identified across ethnic groups, it is reasonable to consider the emergence of depressive disorders as the result of an interaction of various factors, some, but not all of which, are related to cultural or ethnic issues. Factors that influence the aetiology of depressive disorders in ethnic minority groups (i.e., specific determinants besides the factors that are valid for any individual such as biopsychological vulnerability, physical health, or critical life events) can be related to the individual or may occur on a microsocial or macrosocial level (Marsella 2003). Variables to be taken into account include the following:

- Concept of personhood or selfhood held by a particular cultural tradition (e.g., idiocentrism vs. allocentrism) (Triandis et al. 1985)
- A person’s ethnicity and degree of identification with his or her cultural heritage;
- Personality factors (e.g., locus of control);
- Degree and mode of acculturation (e.g., role confusion and conflict versus bicultural identity);
- Characteristics of the society or community (e.g., individualistic versus collectivistic; traditional versus modern) (Hofstede 1980)
- Factors related to the individual’s status as a member of an ethnic minority group (e.g., racism, social drift, marginalisation)
- Factors related to migration (e.g., uprooting due to war or natural disasters, distance from important persons or family members, alienation, legal status).

The following sections discuss each of these factors in relation to depression.

Cultural Personal Characteristics

It has been hypothesised that personal cultural characteristics such as concepts of the self (e.g., idiocentrism versus allocentrism) may influence the risk for depression moderated by coping mechanisms. Idiocentrism and allocentrism represent individualism and collectivism at the level of the individual (Triandis et al. 1985). Idiocentric persons view the individual as the basic unit of social perception, with the self defined as an autonomous identity and personal goals having primacy over in-group goals. In contrast, allocentric persons define the self in terms of in-group relationships; in these persons, in-group goals have primacy over personal goals and cognitions are context-dependent (Bhugra 2005). In a study with American and Chinese college students, idiocentrism was correlated with high self-esteem, high depression, high suicide ideation, and low social support, while allocentrism was related to lower levels of suicide ideation in both cultures, with the relation being stronger for women (Zhang et al. 2007). Since the self-rating of idiocentrism/allocentrism of American and Chinese students seemed to depend rather on cultural-specific response styles than objective differences, the authors suggested that the evaluation of social connectedness versus idiocentrism in comparison to one’s personal reference group is crucial in the relationship with depressive symptoms and suicide ideation.

Ethnic Identity

Ethnic identity can have either a beneficial or detrimental effect with regard to depression. The concept of ethnic identity refers to a sense of commonality transmitted over generations by the family and reinforced by the surrounding community. Ethnic identity develops as the product of ethnic socialisation of children as they acquire the values, attitudes, behaviours, and perceptions of the ethnic group to which they belong and come to perceive themselves as members of this group. Bhugra (2005) proposed a model that focuses on cultural identity and cultural congruency to explain mental disorders in immigrants. He pointed out that the deleterious effects contextual dissonance
has on self-esteem may be mediated by dissonant communications and cultural environments in comparison with reference groups. Kennedy et al. (2005) found that there was an association between a close identification with their cultural heritage and suicidal ideation in immigrant undergraduates, no data were offered to explain this finding. A Canadian study provided more insight about the context-specific effects of ethnic identity on depressive mood (Beiser and Hou 2006). That study found that the impact ethnic identity had on depression was dependent on the particular challenges the person had to handle: When Southeast Asian refugees encountered racial discrimination or unemployment, attachment to their ethnic identity amplified the risk of developing a depressive mood. By contrast, a strongly held ethnic identity provided psychological advantage for individuals experiencing difficulties with the dominant language.

**Personality Factors**

Internal locus of control, as a personality trait, has been established as a variable that enhances the probability for positive outcomes in depression when faced with physical or psychological problems, especially in Western societies (Lerner et al. 2005; Steptoe et al. 2007). An external locus of control (i.e., events being attributed to fortune, the stars, chance), which takes responsibility away from the individual, may provide a more adaptive way for some individuals to cope with stressors associated with migration and acculturation, because this view is linked with less threatening cognitions (Bhugra 2004). The lower rates of common mental disorders in Asian groups in the United Kingdom may reflect acceptance of an external locus of control in these individuals. Culture-related personality factors are thus an example of the interplay between migration- and culture-related aspects in the aetiology of depression in ethnic minority groups.

**Acculturation**

Studies on the impact of acculturation on depression have found different results, in part due to differences in the concept and measurement of acculturation that was used. Acculturation may also have influenced response characteristics.

Acculturation has been described as a long-term, multi-dimensional and mutual process that varies both intra-culturally and within families (Berry 1990,1997,2002). Depending on individual characteristics, such as gender, age, education, motivation, and expectations associated with migration, as well as situational variables including the predominant attitude towards immigration in the host society, persons and groups develop long-term strategies for adaptation and dealing with the challenges of acculturation. According to Berry, acculturation strategies involve two dimensions:

- Interest in maintaining a relationship with one’s cultural heritage and an appreciation of one’s cultural identity
- Interest in contact and interaction with members of the host society and appreciation of positive relationships with other cultures.

Depending on whether the general attitude towards these issues is positive or negative, four types of acculturation have been defined:

- **Integration**: individual wants both to maintain original culture and have daily interactions with other groups;
- **Assimilation**: individual does not wish to maintain cultural identity and seeks daily interactions with other cultural groups;
- **Segregation**: individual places value on retaining original culture and wishes to avoid interacting with individuals from different cultural groups;
- **Marginalisation**: individuals has little interest in or possibility of maintaining his or her cultural identity and little interest in having relationships with other groups.
Although marginalisation can be a strategy that people choose as a way of dealing with their acculturative situation, it can also result from failed attempts at assimilation (involving cultural loss) combined with failed attempts at participating in the larger society. Such cases may be due in part to discriminatory attitudes and practices of the dominant group.

When greater levels of conflict are experienced and the experiences are judged to be problematic but controllable and surmountable, the process should be conceptualised in terms of acculturative stress. Only under certain conditions, when acculturation experiences overwhelm the individual, is a psychopathology paradigm appropriate for the understanding of acculturation.

The integration strategy, which optimally leads to the development of a bicultural identity, can generally be assumed to be the most adaptive and healthy way of acculturation. It is associated with involvement in two cultural communities (i.e., having two social support systems) and having a flexible personality. In sharp contrast, marginalisation involves rejection by the dominant society, combined with loss of one’s own culture, resulting in hostility and greatly reduced levels of social support. Marginalisation is the type of acculturation that has been found to be most often correlated with psychosocial problems and psychiatric disorders (Berry 1990; Schmitz 1994).

A bicultural identity is not simply a midpoint between having an ethnic and, for example, an American identity; rather, it is the result of identification with two cultures. The gratifications and stressors inherent in having a bicultural identity compared with a strong ethnic identity or a predominant identification with the host country have been shown to vary as a function of generational status, experience of discrimination, and developmental stage (Phinney 2002).

It is important to note that the outcome of any acculturative strategy by an individual or group strongly depends on the conditions prevailing in the larger society with respect to immigration and multiculturalism. Integration can only be freely chosen and successfully pursued by nondominant groups when the dominant society has an open and inclusive orientation toward cultural diversity. Policy strategies (e.g., regarding host country citizenship and permission to work) have an impact on public perceptions of migrants and psychological reactions to them, which will have a strong influence on acculturative stress. Acculturation is necessarily a mutual process (Berry 2002). The acculturation strategies described above are affected by the dominant culture and society (institutions, policy, healthcare system). Hence, characteristics of the larger society play a significant role for individuals facing the task of immigration and acculturation and may enhance the risk for depressive decompensation under certain conditions.

Given the complexity, duration, and multidimensionality of acculturation, it is not surprising that studies concerning acculturation and depression have shown inconsistent results. One the one hand, there is evidence indicating that mental health problems seem to increase as immigrants acculturate (Escobar 1998; Hwang et al. 2005; Nazroo 1997). If acculturation is based on length of residence, it may be confounded with the experience of migrating as a child and the resulting existential destabilisation. On the other hand, some studies have found that increasing levels of acculturation were associated with reduced risk of depression. For example, in a study of older Mexican Americans, less-acculturated individuals were at a significantly higher risk for depression than highly acculturated participants after adjusting for education, income, psychosocial, behavioural, and health problems (Gonzalez et al. 2001).
Thus, it seems useful to conceptualise level of acculturation as a proxy that may identify at-risk-groups but tells little about actual mechanisms leading to a depressive episode. The concept of acculturation comprises associated stressors as well as the results of a successful acculturation process. The widely accepted approach developed by Berry (1990, 1997, 2002) suggests that research on outcomes and consequences of acculturation, such as implications for mental health, may be insufficient when based on the idea of acculturation as a unidimensional and unidirectional process measured in terms of “level” or “degree”.

Acculturative stress (which is probably an unavoidable consequence of acculturation during at least some portion of the process) has been shown to correlate with high levels of depression and suicide ideation (Hovey 2000). Acculturation is probably associated with a disconnection from protective culturally mediated social resources (e.g., strong family networks, role models). The deleterious effect of negative life events on the prevalence of depression was found to be higher among more acculturated Chinese Americans (Hwang and Myers 2007). Acculturation implies that one has to learn to conform, adapt, meet the demands of, and negotiate two different environments. For Chinese Americans, this process may involve becoming more individualistic and less collectivistic and may lead to changes in ethnic identity, social attitudes, expectations, and coping styles. This may lead to a movement away from traditional networks, thus reducing levels of social support. Increased acculturation may also increase exposure to culturally incongruent stressors (e.g., intergenerational conflict, culture clash, discrimination, shifts in family dynamics). Hence, the impact of acculturation on depression will differ different depending on the specific cultural characteristics of individual involved and the host culture.

Characteristics of the Society
Distinctive characteristics of the society from which a person comes, such as basic value systems, are assumed to have a multi-dimensional impact on the development of mental disorders such as depression (Bhugra 2005; Bhugra and Mastrogianni 2004). A study that examined levels of psychiatric morbidity in relation to cultural values from 11 nations found that values representative of traditional societies (conservatism, hierarchy, and self-mastery) were negatively correlated with psychiatric diagnoses and symptoms (e.g., depression), whereas values typical of modern/post-modern societies (autonomy and egalitarian commitment) were positively correlated with psychiatric diagnoses and symptoms (Maercker 2001).

In a cross-cultural study on the impact of modernisation on depression, which included participants from rural Yorubaland in Nigeria, Yorubas living in urban Nigeria, and residents from rural Canada and urban United States, the prevalence of depression was lowest in rural Nigeria and highest in the urban United States (Colla et al. 2006). The results suggest that a traditional way of life seems to serve as a protective factor for some of the stressors associated with modernisation.

People exposed to the rapid changes associated with globalisation have to cope with insecurity and unpredictability. Some of the consequences are negative, in particular, when these changes are imposed on people who have no power to influence how the change will affect them (Brundtland 2001).

Social upheaval and adversities such as war, poverty, violence, and natural disasters, may disrupt communities and be a risk for the development of depressive episodes. In addition, a huge number of migrant workers lack social support and upheaval in their family structures may be a key stress factor (Patel 2006) and risk factor for depression. However, it is not only the migrant labourers who are at risk—the women
who are left behind, alone and dependent on the migrant workers’ remittances, also face an increased risk of depression (Patel 2006). Governments and health policies should take into account the impact of such social upheavals and take steps to reduce their negative effects and thereby reduce the risk of depressive episodes.

**Status as a Member of an Ethnic Minority Group**

Factors related to the person’s status as a member of an ethnic minority group and their impact on the risk for developing a depressive disorder vary depending on age, gender, and social status (Clarke et al. 2008). For instance, it has been suggested that social stressors associated with minority race-ethnicity vary across the life span. Minority children may be sheltered from the negative impact that discrimination in the labour market and other areas of adult life has on adult mental health (Gore and Aseltine 2003). Social stressors also seem to be most severe for middle class minorities who have the highest expectations but face the greatest competition in labour markets (Jackson and Stewart 2003).

**Factors Related to Migration**

Transitions associated with migration, independent of the individual’s specific cultural background, can place ethnic minority members at a high risk for depression (see discussion of “The Diagnostic Dimension of Migration” earlier in this chapter). In a study of pregnant immigrant women, Zelkowtiz et al. (2004) found that stressful life events, lack of social support, and unsatisfactory marital relations were significantly related to depressive symptoms in this group. Interestingly, women who reported more depressive symptoms described networks that included fewer women, fewer relatives, and fewer members of their own ethnic group. They did not have the possibility of relying on the social support systems that were available in their countries of origin, especially during pregnancy. Also, stress associated with migration, such as problems with housing, discrimination, and prejudice, were more common among women who reported depressive symptoms. Furthermore, stressors requiring active, action-oriented coping strategies (e.g., learning the language of the host country, dealing with an aversive work situation), should be differentiated from burdens demanding psychological coping mechanisms. According to one of the few long-term studies on migration (Mirdal 2006), the former play a greater role at the beginning of the migration process, while the latter become increasingly salient after a long period of residency in the host country, when individuals may be more likely to critically consider the consequences of their migration and their possibly unrealistic hopes and expectations.

Even though it can be helpful for clinicians to have an understanding of culture-specific factors in the aetiology of depression, clinicians treat an individual within a larger socio-economic context that is not limited to the person’s ethnic background (Bhugra and Mastrogianni 2004). The decontextualisation of depression involves the danger that one may assign one’s own ethnocentric meanings and interpretations to the problems, independent of the context in which they emerged and are sustained (Marsella 2003). It is also helpful to consider the presence of cultural resources and protective factors, such as mourning or religious rituals, nutritional patterns, family strengths, and coping or support systems, that the person may be able to access despite social disadvantages (Bhugra 2004, Breslau et al. 2006). The divergent results of the studies in this area show that many culture-related factors can function as protective as well as risk factors and that these factors should be considered from both points of view in the treatment of ethnic minority patients affected by depression.
COMORBIDITY

Comorbidity refers to the tendency for individuals to meet criteria for multiple disorders. Concurrent comorbidity refers to the situation when two disorders overlap in time, while successive comorbidity describes a situation in which two disorders do not overlap in time.

Correlates and Risks

Comorbidity is an important factor in major depression that affects both its course and outcome. A study of major depression and its correlates in primary care settings in six countries (Australia, Brazil, Israel, Spain, Russia, United States) found that those patients with medical conditions (angina, arthritis, asthma/chronic bronchitis, cancer, chronically inflamed bowel, heart attack and failure, hypertension, diabetes, kidney disease, major paralyses, and ulcer), dysthymia, and anxiety disorders had a poorer outcome after 9 months of treatment than those without such comorbidity (De Almeida Fleck et al. 2005; Herman et al. 2002). No difference was found for alcohol risk.

In a population of socio-economically disadvantaged African American young adults aged 19–22 years of age living in a large metropolitan area, major depressive disorder and comorbidity were significant mental health problems (Ialongo et al. 2004). About two thirds of the participants diagnosed with an episode of lifetime MDD also met the criteria for at least one other disorder, including generalised anxiety disorder, antisocial personality/conduct disorder, attention-disorder/hyperactivity disorder, and alcohol/substance dependence/abuse. Participants with MDD were 13 times more likely to have generalised anxiety, 4 times more likely to have an episode of alcohol dependence, 3.7 times more likely to have at least one other disorder (see above), and almost three times as likely to have two, three, or more other disorders than participants without MDD. The risks were generally comparable across genders. Thus, a lifetime episode of MDD appeared to be associated with increased psychopathology and substance dependence in young African Americans.

In a study of correlates of depression in older Chinese adults in Hong Kong (Chi et al. 2005), the following health-related factors were found to be associated with a high probability of being depressed: poor self-rated physical health status, long-term pain, vision problems, higher level of impairment in activities of daily living (ADL) besides financial problems, poor social support, and having lived in Hong Kong for fewer than 20 years. These findings are consistent with those in other countries, including Western countries.

Some evidence of patterns of comorbid physical and mental illness has emerged in research concerning Latinos in the United States that has looked at specific ethnic subgroups, including Mexicans, Cubans, Puerto Ricans, and others (Ortega et al. 2006). Lifetime anxiety was associated with diabetes and cardiovascular disease, while depression was only associated with asthma in the Latino group as a whole. When results were stratified by subgroups, anxiety was associated with asthma among Puerto Ricans, with diabetes in Cubans, and with diabetes and cardiovascular disease in Mexicans, whereas depression was associated only with asthma in Puerto Ricans and Mexicans. Comorbid anxiety and depressive disorders were associated with asthma in the entire group and in the Mexican subgroup. These findings replicate the link that has been established between anxiety and cardiovascular disease among Latinos but not the link between depression and cardiovascular disease and diabetes that has been reported. This may be due to cultural protective factors. In addition, no link between mental illness and acculturation has been found in many migrant populations cross-culturally. Thus these findings demonstrate that Latinos may show a different pattern of psychiatric and medical comorbidity than the general population and a unique pattern in their ethnic subgroups.
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 biopsychological 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-economic 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. 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-
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 psychoeducational 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.

Psychopharmacology

Ethnic variations in response to psychotropic medication as a result of both pharmacokinetic and pharmacodynamic differences are known to exist (Bhugra 2004). Genes that encode enzymes responsible for the metabolism of drugs, as well as genes controlling the function and response of targets, may be involved in ethnic differences. Lin (2001) reported ethnic differences in the activity of the cytochrome P450 enzymes CYP2D6, CYP2C19 and CYP3A4, which are the most commonly involved in psychotropic drug metabolism. A recent large study of black and Hispanic outpatients (Lesser et al. 2007) showed that patients from ethnic minority backgrounds, particularly blacks, had a less robust response to antidepressant treatment (citalopram). Once socio-economic and demographic differences and clinical comorbidities were taken into account, however, these differences were less pronounced. Thus, future investigations need to clarify the impact of severe psychosocial stressors (e.g., crime, racial discrimination, family disruptions, poor housing) on the relation between race/ethnicity and symptom remission, since these factors may be associated with increased chronicity. Socioculturally tailored treatment and prevention interventions may be more efficacious than standard treatment programmes for patients in ethnic minority groups (Van Voorhees et al. 2007).

Recent evidence on ethnicity and preferences for depression treatment, based on an investigation involving 78,753 individuals with significant depressive symptoms including African Americans, Asian/Pacific Islanders, Hispanics, and white Americans, implies that patients from racial and ethnic minority groups prefer counselling for depression treatment over medication more than do white patients (Givens et al. 2007). Beliefs about the effects of antidepressants, prayer, counselling, and alternative treatments (Machleidt 2007) partially mediate preferences for depression treatment.
Treatment Gap and Access to Care

Antidepressant medications and brief, structured forms of psychotherapy are effective for 60%–80% of those affected by depression and can be delivered in primary care settings. However, looking at depression from a global perspective, fewer than 25% of those affected by depression (in some countries fewer than 10%) receive adequate care, and this treatment gap is highly dependent on the cultural setting (WHO 2008a). Barriers to effective care include lack of resources, lack of trained providers, and social stigma associated with mental disorders including depression.

According to Kohn et al. (2004) the median treatment gap for depression—measured as the percentage of individuals needing care minus the percentage that actually receives adequate care—is 56.3%. However, there are large regional differences, with the European region having an average gap of 45.4% but a gap of up to 70.2% found in the Eastern Mediterranean region and 67% in Africa. Not only do we see differences between countries, but also within countries, since cultural differences seem to matter when it comes to access to care. Thus, a study of different ethnic groups in the United States found large differences and showed that the burden of depression seemed higher among black than white in the United States (Williams et al. 2007).

Up to 20% of those attending primary health care in developing countries suffer from depressive and /or anxiety disorders. In many centres, these patients are not recognised and therefore not treated. Individuals in economically disadvantaged regions of the world have the least access to care (WHO 2008a)

Governments should recognise the treatment gap and develop strategies to overcome such inequities in access to health care. In developing countries, where a majority of the population is based in rural areas, primary health care facilities are the main source of medical care, and it is of paramount importance that primary care providers in these settings receive training in the identification and treatment of depression.

PROGNOSTIC FACTORS
AND OUTCOME

A comprehensive approach to the aetiology, outcome, and prognosis of depressive episodes should include cultural factors. However, such factors are frequently underestimated because the focus tends to be on biological and psychological factors (Marsella 2003). Two key types of factors linked to the socio-cultural context can influence the emergence and prognosis of depressive episodes:

- Societal stress factors (e.g., poverty, violence, war)
- Psychosocial factors (e.g., family conflicts, unemployment, migration)

Physical health symptoms also seem to play an important role in the prognosis of depression and have been found to be associated with depression. For example, an association between physical health problems and depression has been found in elderly South Asians who adhered to traditional values (Lai & Surood 2007).

A relationship between ethnic background and outcomes of depression has also been found, showing that blacks had a poorer response to antidepressant treatment and that the poorer outcome could not be explained by differences in socio-demographic background (Lesser et al. 2007). Others have shown that cultural differences in expectations and beliefs may lead to differences in treatment adherence (Bhugra and Mastrogianni 2004). However, these researchers also emphasised the need to look for genuine differences without being biased by ethnic stereotypes.

Suicide is the most negative outcome of depression and it is estimated that 15% of those suffering from depression commit suicide (WHO 2008a). Suicide is the 13th leading cause of death globally (WHO 2005) and is on the increase globally. Among young and middle-aged, especially male, individuals, suicide is the leading cause of death in the European region (WHO 2005). Groups who are marginalised, for example, due to migration or being imprisoned, are at particularly high risk of suicide.
Suicide prevention among depressed individuals constitutes a major public health problem worldwide. First, a large proportion of depressed individuals are not recognised or referred for adequate treatment. Steps should thus be taken to train health professionals to better recognise depressive episodes and, when identified, to refer depressed patients for proper treatment. However, it is also necessary to increase the awareness of personnel in other settings (e.g., correctional institutions, specialised psychiatric treatment facilities) in which individuals may be at increased risk for suicide.

The role of the family is crucial when caring for and providing support to a depressed individual (see also Volume I, Chapter 5 for further discussion of interventions with families). In many cultural settings around the world, little help may be available from mental healthcare services; in such situations, the role of the family becomes decisive. Families can play an important role in the management of depression in a number of ways:

- By helping the patient to start and continue with treatment
- By providing supervision and support to minimise the risk of suicide
- By providing emotional support to the patient and showing affection and patience
- By helping the patients to resume his or her activities and role in life and letting the patient gradually take over more of his or her own responsibilities (WHO 2006).

From a cultural perspective, it may be an advantage to live in an extended family, because this reduces the risk of any family member having to assume responsibility as the only caregiver, and it also increases the chances that the patient will have the help of supportive relatives. However, severe depressive disorders may consume family resources; in such cases, consumer organisations and/or self-help groups may be useful sources of support and assistance. With respect to depression in women, it is important to keep in mind that autonomy to exercise some control in response to severe events is protective, but that women may find it difficult to achieve such autonomy in some cultures.

TRAINING

Given the complex treatment needs of depressed patients from different ethnic backgrounds, staff working in mental health care settings needs to possess adequate competencies to deal with this diversity (Kastrup 2008). Training on both pre- and post-graduate levels should provide systematic training to provide a better understanding of cultural perspectives and diversity (Fox 2005). Curricula for medical students and residents should include training concerning differences among cultures and their impact on the presentation and treatment of illnesses (e.g., how cultural factors can affect the manifestation and treatment of depression) (Fox 2005).

Cultural Competence

Acquiring cultural competence on a post-graduate level is a dynamic process. As part of the process of providing psychiatric training, it is important to increase clinicians’ awareness of their own cultural identity and prejudices and help them learn to question their own stereotypes and show empathy across cultures (Kastrup 2008). In “Clinicians Guide to Cultural Psychiatry” Tseng (2003) outlined a number of important ingredients of cultural competence:

- Need for increased cultural sensitivity and awareness of the existence of different lifestyles and attitudes and ability to accept these differences without prejudice,
- Acquisition of cultural knowledge and respect (e.g., an increased understanding of differences in illness-behaviour that will allow the clinician to provide culturally relevant assessment and care),
- Focus on cultural empathy and understanding patients’ own perspective,
- Recognition of culturally relevant relations and interactions, and the impact of the person’s cultural background on his or her help-seeking behaviour,
- Ability to provide cultural guidance, and an understanding that particular forms of treatment may be suited for particular ethnic groups and that we should always consider culture-related factors in addressing patients’ problems.
Training
Given the pluralism of modern day societies, medical doctors should receive formal training in cross-cultural studies. Although this has been recognised by a number of agencies, such as the European Board of Medical Specialists, few medical schools currently provide such training (Qureshi et al. 2008). Physicians should be trained in interviewing techniques that elicit information concerning the patient’s cultural background, cultural identity, culture-related stressors, cultural explanatory models, and cultural factors related to his or her psychosocial environment and functioning; physicians should also receive training concerning cultural elements that can play a role in the relationship between patient and clinician (Marsella 2003). Training in cultural competence involves gaining an awareness of the ways in which culture, migratory status, and race can affect psychopathology, psychosocial development, and therapeutic transactions (Qureshi et al. 2008).

The DSM-IV cultural formulation discussed in the section on “Diagnostic Formulations” earlier in this chapter may be a source of guidance for such training (American Psychiatric Association 1994). Clinicians should also keep in mind the importance of involving family members and perhaps even cultural mediators in order to develop a culturally acceptable treatment strategy. It is also important to be aware of cultural non-equivalence in language and concepts in order to minimise cultural barriers to successful treatment (Marsella 2003). The greatest challenge in training clinicians to assess and treat patients from culturally backgrounds different from their own involves developing attitudinal competence, because this requires the clinician to question his or her own cultural and racial preconceptions (Qureshi et al. 2008). Agencies and organisations who provide mental health services should be aware of both organisational and clinical barriers to obtaining cultural competence and seek ways to overcome them.

Communication
Individuals suffering from depression may have difficulty expressing their need for care, and the extent to which this occurs may vary depending on the patient’s cultural background. To successfully treat patients from different cultural backgrounds, health professionals must acquire certain competencies. First, they should be able to identify depressive disorders in persons from a different cultural background who present with different illness behaviour and different manifestations of depression. Second, the relationship between patient and health professional in more traditional societies may be hierarchical, so that the patient will be less likely to express frustration with the therapist or disclose intimate problems. The authoritarian communication style seen in many non-Western cultures may be particularly relevant to the care of female patients. Thus, women may hesitate to talk about their depressive symptoms and, even if they overcome this reluctance, the doctors who are treating them may exhibit a gender bias that could lead them to over- or under-treat these women (WHO 2008b). Medical doctors need to be aware of this problem, because it can often result in women failing to receive adequate treatment for their depressive disorders. When communicating with patients, physicians should also be aware that traditional beliefs (e.g., that supernatural causes may be involved) can influence attitudes towards depressive illness and result in negative responses to and stigmatisation of depressed persons. Health professionals can play an important role in educating the patient and family in this area.

In summary, an important focus for future medical training is to increase professionals’ knowledge of cultural diversity and their experience in communicating across cultural boundaries. Mental health professionals also need to become more sensitive to the importance of learning about each patient’s background and incorporating relevant cultural and historical factors into the information that guides the clinical consultation.
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PART 5
Prevention of Suicide: Issues for General Practitioners

Dr. Danuta Wasserman, Dr. Susanne Ringskog Vagnhammar
DEFINITIONS AND RISKS

Definitions of Suicide

• Suicide is a deliberate, wilful, self-inflicted, and life-threatening act resulting in death.

• Suicide attempt, or parasuicide, is an act with non-fatal outcome, in which an individual deliberately initiated a non-habitual behaviour that without intervention from others will cause self-harm or deliberately ingests a substance in excess of the prescribed generally recognised therapeutic dosage, and which is aimed at realising changes which the subject desired via the actual or expected physical consequences (Schmidtke et al 1997).

Both of these definitions refer to the result of the act and to the intention underlying it. Often it is difficult to understand an individual’s real intention behind a self-destructive act. The suicidal process, leading to the suicide attempt or the suicide, can continue over a long period, during which time the suicidal decision can silently grow stronger and stronger if it is not recognised and halted by the people surrounding the individual. General practitioners should pay attention to information provided by these other people (e.g., close friends, relatives, and neighbours), because they may notice changes in the person’s behaviour that the person will not report.

It is important to keep in mind the strong relationship between a suicide attempt and completed suicide: having made a suicide attempt greatly increases the risk of dying from suicide at a later time, especially in males (Hawton et al. 2003) and elderly people (Wasserman 2001).

Classification of Suicidal Behaviours: Steps in the Suicidal Process

Plutchik and van Praag (1989) pointed out that a suicidal continuum exists, ranging from suicidal ideas, to gestures, to tendencies, to mild suicide attempts, to serious suicide attempts, and finally to completed suicide. Certain characteristics may help general practitioners and other clinicians identify a patient who is in a suicidal process and at risk for suicide with suicidal intention. People at risk of suicide often have feelings of depression, anxiety, dysphoria, anger, helplessness, impaired social adjustment, aggression dysregulation, a history of suicidal behaviour, delinquent behaviour in adolescence, a history of violent behaviour, truancy from school or no attendance, and/or problems with the law. The most crucial risk factors are feelings of hopelessness and weariness of life. Actually, it has been proved that hopelessness is the link between depression and suicide (Botsis et al. submitted). Besides feelings of hopelessness and helplessness, a specific cognitive state is very often experienced by suicidal subjects. This cognitive state consists of ambivalence, constriction of thinking, and what is often referred to as “perturbation”. The individual in suicidal crisis, thinks in an “all or nothing” way. He is not able to think about or find alternative solutions to his or her problems. This sort of cognitive disturbance is also known as dichotomous, narrowed, or “tunnel vision” thinking. All of these factors may lead to death wishes and suicidal thoughts, which can naturally range from unclear, diffuse, vague thoughts, to clear and intentional thoughts and then to actions directed towards self-harm or suicide. A reliable and valid measurement of hopelessness, based on Beck’s Hopelessness Scale, is the simple question ‘The future looks dark to me’ (Aish and Wasserman 2001).
Suicide World-Wide

Most countries in the world record mortality rates, including suicide, using the WHO International Classification of Diseases (ICD). The latest version, ICD-10, was updated in 1997. However, several uncertainties surround these figures. Using ICD-10, suicide is registered as either “certain” or “uncertain”. In the uncertain cases, it is not always clear whether the victim caused the injury that led to death on purpose or if some other cause was responsible for the death. Suicides presented in the national statistics can contain a combination of both certain (approximately 75%–80%) and uncertain (approximately 20%–25%) cases. The uncertain deaths in the American literature are called “equivocal suicides”. Some records may include only those victims who are older than 15 years of age at the time of death.

In addition, it is very difficult to obtain accurate information about the number of attempted suicides. The only figures recorded are those that involve cases in which hospital treatment was administered, which excludes many other attempts, in which medical care was not needed or was not sought. Changes in treatment methods and, as a result, fewer registrations of attempted suicide, make it difficult to compare the occurrences of suicide attempts over time nationally and internationally.

Globally, in the year 2000, 1 million people committed suicide. The number of suicide attempts is considered to be ten to twenty times higher and varies across different age groups (Bertolote 2001). In 1998, suicide world-wide was estimated to represent 1.8% of the total global burden of disease (WHO 2007).

It is estimated that 1.53 million people will die from suicide in the year 2020 (Wasserman 2001). Consequently, suicide, as a consequence of mental illness such as depression, is a major public health problem. Action is called for at all levels—from local to international—and among different sectors of society including those providing health and social services. There is also a great need to improve quality of and access to health services and education.

Increase in Suicides World-Wide: A Comparison

To be able to reduce suicide rates, it is important continuously monitor suicide rates in individual countries and in different geographical regions. This is usually carried out for the whole population, but it is also important to monitor the rates with respect to different variables within the population, such as sex, age, and marital and socio-economic status. Since the 1950s, WHO has monitored suicide rates and disseminated the results. However, it should be noted that the monitoring and comparisons are based on information given by the countries themselves. Therefore, the reliability and validity of the data collection vary and should be improved. In addition, only 130 of the 194 countries in the world report information about suicide to WHO. In addition, there may also be deaths due to suicide that are not reported as suicide, which would lead to an underestimation of the actual number of suicides, pointing to the fact that the problem of suicide is greater than it appears to be (Wasserman 2001).

In the last 45 years, suicide rates have increased by 60% world-wide. Suicide is now among the three leading causes of death among individuals of both sexes who are 15–44 years of age; these figures do not include suicide attempts, which can be up to 10–20 times more frequent than completed suicide. Although suicide rates have traditionally been highest among elderly males, rates among young people have been increasing to such an extent that they are now the group at highest risk in a third of both developed and developing countries (Wasserman et al. 2005).

As more countries are collecting data on suicide, particularly Eastern European countries that were formerly part of the Soviet Union, European and world-wide averages and projections are shifting. Eastern European countries that were formerly part of the Soviet Union report high suicide rates, while the lowest rates of suicide are seen in Eastern Mediterranean countries and in countries in which the predominant religions are Islamic or Jewish. In most Latin American countries, suicide rates are even lower than in Israel. Comparing data between countries and continents continues to be a difficult and often impossible task. However, as more countries collate information on suicide rates and methods, this provides a growing opportunity to compare their progress with policies and strategies for suicide prevention.
Suicide and Gender

With some exceptions, more men than women commit suicide world-wide. At the same time, it is a well-known paradox that depression, which is one of the most common mental health disorders associated with suicide, is only half as common in men as in women—yet still more than twice as many men as women commit suicide. One explanation for this gender paradox is the hypothesis that depression in men may escape diagnosis and treatment, because some men may have atypical symptoms of depression (irritability, aggression, acting-out, substance abuse, and antisocial behaviour (van Praag 1996), or they may possibly have a lower tolerance for stress due to genetic factors (Wasserman 2006). In addition, men often have difficulties communicating and may not turn to medical care for help (Murphy 1998). Moreover, since prehistoric times, men and women have shown different reactions to stress, with “fight-and-flight” behaviour more characteristic of men and “tend-and-befriend” behaviour more characteristic of women (Taylor et al. 2000).

Another fact that could, in part, explain the male predominance in suicides is that, when trying to commit suicide, men generally use more violent methods than women, and these more violent methods have the greatest risk of a fatal outcome. It should be noted that, in a few countries (e.g., China), more women than men commit suicide. Differences in cultural values might in part explain this situation. Recent findings have also shown that some individuals may be genetically predisposed to react with suicidal behaviours under low stress due to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis (Wasserman et al. 2007).

The Stress-Vulnerability Model:

Development of the Suicidal Process from Ideation to Suicide

The stress-vulnerability model (Figure 5.1), which was outlined by Wasserman (2001), is an extension of Mann’s (1998) neuro-biological stress-diathesis model. It is crucial to study the suicidal process not only at the individual level but also at the interpersonal (communicative) level, in relation to other external factors at the community level (for example the social integration of the individual), and in relation to the cultural and physical environment. The model describes the suicidal process from the stage of ideation to a suicide attempt. It usually starts with a non-verbal or non-observable suicidal propensity, which later on could be verbalised or identifiable to others. Suicidal behaviours are not looked upon as an illness, but as a process that is influenced by many different risk factors, including problems with relationships; exposure to violence, stress, poverty, and/or unemployment; psychiatric or somatic diseases; and/or alcohol and drug abuse.

Risk Factors

It is important for clinicians, including general practitioners, to recognise factors that elevate the risk for suicide. The main risk factors are mental disorders, especially depression. However, acute triggers—called precipitating factors—for suicidal behaviour should also be considered. Suicidal individuals have often experienced many losses. Severe stressful life events during the year before the suicidal occurrence are also very common. Suicidal triggers can include separations or conflicts in relationships of any kind, economic problems, unemployment, loss of integrity, negative or traumatic life events, a relapse or exacerbation of illness, and chronic states of pain. The more risk factors an individual has at any given time, the greater the risk that he or she may act in a suicidal way. Key risk factors include genetic influence, environmental influence (in its widest sense), violence, mental trauma (bullying, neglect), and losses of all kinds. Migration is in itself a stress factor: for example, immigrants commit 15% of all suicides in Sweden. Violation, mental illness, alcohol and/or drug abuse, and, most of all, loss of hope all correlate highly with suicide.
FIGURE 5.1
The Stress Vulnerability Model

Risk Factors
- Social stress, poverty
- Unemployment
- Separation, losses, conflicts in relations
- Different negative and traumatic life events
- Narcissistic injury
- Relapse or exacerbation of illness
- Economic problems, bullying, harassment

Acute Triggers for Suicidal Behavior
- Violence and psychic trauma
- Relationship problems
- Stress

Observable behavior
- Suicide attempt
- Suicidal communication
- Death wishes
- Suicidal ideation

Non-observable behavior
- Cognitive style and personality
  - A great sense of personal value
  - Confidence in oneself and one’s own situation and achievements
  - Seeking help when difficulties arise
  - Seeking help when important choices must be made
  - Openness to other people’s experiences and solutions
  - Openness to new knowledge
  - Ability to communicate
- Family patterns
  - Good relationships with family members
  - Support from family
  - Devoted and consistent parenting
- Cultural and social factors
  - Adoption of specific cultural values and traditions
  - Good relationships with friends, workmates, neighbors
  - Support from relevant people
  - Non-drug using friends
  - Social integration, e.g., through work, participation in sport, different associations, church activities, etc.
  - A sense of purpose with one’s life
- Environmental factors
  - Good diet
  - Good sleep
  - Light
  - Physical exercise
  - Non-drug, non-smoking environment

Protective Factors
- Suicidal resilience, inherited and/or acquired during antental life, upbringing and adult life

Many suicidal processes fade away due to individual coping or treatment.
It is well-documented that early social environment (family) of suicidal individuals is often markedly disorganised. Dysfunctional family cohesion and adaptability, rigid and hostile family systems, rejection by one or both parents, lack of affectionate relationships, exposure to family violence, physical and/or sexual abuse, usually by an alcoholic father, are severe traumatic events for the child and adolescent that are highly associated with suicide attempts and suicide in adulthood (Botsis 1997). In addition, psychological risk factors such as low self-esteem, low ego strength, disturbed reality testing, and problems with body image among adolescents are also important risk factors associated with suicidal behaviour (Plutchik et al. 1995). Moreover, a suicidal role model in the family or in the close surroundings or loss of either parent before a child was 12 years of age creates an elevated risk of suicide (Wasserman and Culberg 1989; Wasserman 2001). Finally, an earlier suicide attempt increases the risk of suicide by 30%.

Protective Factors

Factors protecting against suicide include:

1. Cognitive style and personality: feelings of personal value, confidence, a readiness to seek help, and openness to others; experiences that promote clear thinking, and emotional, intellectual and aesthetic enrichment.

2. Family patterns: good relationships with and support from family members, experience of good and caring parents, all of which promote a sense of belonging and of emotional security.

3. Cultural and social factors: adoption of cultural values/traditions; good relationships with friends and colleagues; good social integration with others.

4. Environmental factors: good diet, adequate sleep and physical exercise; adequate amount of light; healthy social networks.

These protective factors naturally belong to a safe and caring environment when the individual was growing up. However, effective, co-ordinated psychiatric and social care can also promote the development of protective factors in vulnerable people later in life.

When investigating a possible suicidal process in a patient, the general practitioner or other clinician should map risk factors, protective factors, and current stressors in the patient. This information will help the clinician find ways to enhance the patient’s protective factors and initiate a personalised suicide-protective treatment. However, general practitioners and other clinicians should be aware that protective factors can also mask the development of a suicidal process.

The availability of suitable treatment is, of course, the crucial protective factor in response to manifest suicidal behaviour. Contact between the general practitioner, the psychiatric clinic, and its inpatient service needs to be established and maintained in an ongoing way. Legal means may need to be used to protect the suicidal person from putting himself or herself into danger. Regular contact between the general practitioner and the patient’s family and/or close friends provides ongoing valuable information about the patient’s mental status, and the doctor can also encourage the family and friends to provide the patient with a first line of support. Contact with societal facilities, church/other religious institutions, retired people’s organisations and other networks surrounding the patient can create extra supportive or protective environments.

**STRATEGIES IN SUICIDE PREVENTION**

In order to prevent suicide and suicide attempts, action is needed at many levels, from the local to the national, and by many different actors. Strategies in suicide prevention can be grouped according to two perspectives: health care and public health (Wasserman 2001) (Figure 5.2).

The health care strategy aims to increase and improve access and quality of health care. Early identification and diagnosis and adequate treatment are needed in order to prevent suicide in patients with disorders such as depression and bipolar disorder. Therefore, psychiatric staff and general practitioners needs to receive continuous training regarding prevention, treatment, and rehabilitation of suicidal patients. General practitioners need to learn how to identify patients at risk, give them satisfying and successful treatment, and provide them with high-quality rehabilitation (Wasserman 2001).
The public health strategy targets population groups such as employers, teachers, parents, and students. The public health perspective focuses on influencing the attitudes of those in work places, organisations, and schools to increase their awareness of suicide in certain targeted populations, with the goal being to increase identification of and support for vulnerable individuals. The public health strategy also involves interactions with mass media, in particular, promoting ethical reporting of information and publication of accurate articles regarding suicide and suicide attempts. Another key component of public health suicide prevention strategies involves restricting means to commit suicide (e.g., controlling availability of drugs and poisons; public safety measures limiting licenses for weapon use). Many factors increase the suicide risk in regard to a population, such as unemployment, drug and/or alcohol abuse, unsecured traffic environments (e.g., unprotected underground rails or bridges in the vicinity of psychiatric hospitals), and lack of national or local suicide prevention programmes. Measures to reduce these risks should be promoted.

A study by Luoma et al. (2002) examined rates of contact with primary care and mental health services by individuals who committed suicide based on data from 40 studies. Three of four suicide victims had contact with primary care providers within the year before the suicide, while approximately one-third of the suicide victims had contact with mental health services during that year. Nineteen percent of suicide victims had contact with mental health care services within a month before their suicide, and 32% received mental health care during the year before the suicide. On average, 45% of suicide victims had contact with primary care providers within 1 month of suicide, with older adults having higher rates of contact with primary care providers within 1 month of suicide than younger adults. Most people who commit suicide are well known to psychiatric care, where they may have experienced a number of treatment failures.
Women have more contact with psychiatric care services, while men more often consult a general practitioner, but often without mentioning psychiatric symptoms or suicidal thoughts. This provides a challenge for the general practitioner—who is “listening with the third ear” as Theodor Reik put it (Reik 1948), discerning possible mental health problems and suicidal ideation behind somatic complaints. The general practitioner has a unique opportunity to prevent suicide attempts and suicide. The important factors are to be open to a discussion of suicidal thoughts and plans and to have the opportunity to refer patients for psychiatric evaluation and treatment.

EDUCATIONAL PROGRAMMES

Examples of educational programmes which incorporate different aspects of the public health and health care perspectives have been shown successes when addressing public and targeted risk groups’ perceptions of mental ill-health (particularly depression) and suicide.

The Depression/Awareness, Recognition and Treatment (D/ART) multi-phased health information and education programme in the USA, which is a state funded programme, incorporates both professionals and the public (Reiger et al 1988). A positive evaluation after 6 months of this programme showed that there were significant increases in knowledge about depression (O’Hara 1996).

The Defeat Depression Campaign, which was run in the United Kingdom from 1992-1996 by the Royal College of Psychiatrists, also included a programme of support for General practitioners and a broad media campaign providing education to the general public. Positive recorded effects include an increased awareness of depressive disorders (Paykel et al 1997) and a reduction in suicide rates (Paykel 2001). However, no sustained improvement was seen in the delivery of care to patients (Rix et al 1999).

An Australian programme ‘Beyond Blue’ has shown similar positive results with regard to increases of knowledge of depression in the general public (Hickie 2004, Jorm et al 2005, Beyond Blue 2008).

A Scottish suicide prevention programme “Choose life” showed a reduction in male suicide and undetermined deaths in the duration of the programme, from 34.1 / 100,000 in 2002 to 29.1 / 100,000 in 2003 (Platt et al 2006, Mackenzie et al 2007).

Similar successes can be seen with the United States Air Force Suicide Prevention Programme (AFSPP) who implemented 11 initiatives including leadership involvement, education in basic training, guidelines for commanders and community support and education. A significant reduction in suicides was noted from the start of the programme in 1995 (15.8 /100,000) until 1999 (5.6 /100,000) (Knox et al 2003).

An educational suicide prevention programme was implemented in 2001 and 2002 in Nuremberg, Germany (population. 500,000), with control region Würzburg (population. 270,000) by the Nuremberg Alliance Against Depression. During the two intervention years, the number of suicidal acts (suicide and attempted suicide) decreased by 24% in the intervention region with rates remained stable in the control region and a 47% reduction in the 5 high risk suicide methods: Jumping from a height, Hanging, Firearms, Drowning, Pedestrian accidents with vehicles (Hegerl et al 2006, Althaus et al 2007).

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The European Alliance Against Depression (EAAD) was formed in 2004 and is based on Nuremberg intervention to this educational method across Europe (Hegerl et al 2004). Evaluation of the work is underway.
DIAGNOSTICS

Psychiatric Diagnoses and Suicide

The majority of people who died from suicide in Europe and North America had a pre-existing mental disorder. Multiple diagnoses in one and the same patient were often seen. Of these, 45% or more were diagnosed with depression. Comorbidity of mood disorders with substance-related disorders (e.g., depression and alcoholism) was the type of comorbidity most frequently found in general population studies of suicide. Other diagnoses included schizophrenia, personality disorders, anxiety disorders, and adjustment disorders (Bertolote et al. 2003).

Depression

The lifetime prevalence of depression is between 22%–24% in women and 15%–16% in men. Since depression is such a common illness, it is of vital importance that general practitioners have knowledge of the disorder—how to diagnose it as well as how to start treatment for it, and, most important, to take it seriously. It is well known that most people who commit suicide turn to their general practitioner or other provider of somatic medical care some time before their fatal step. The risk of suicide is high in patients with untreated depression, especially if comorbid conditions and negative life events are present. Lifetime suicide mortality from major depressive disorder is approximately 10%–15%.

Suicidal thoughts are very common among children and adolescents who are depressed. Suicide attempts are less common, but in a survey of school pupils in Sweden who were 16–17 years of age, 2%–4% of the boys and 6%–9% of the girls reported that they had made suicide attempts (Olson and von Knorring 1999).

In some men, depression is expressed as aggression, a tendency to abuse alcohol and/or drugs, and acting-out behaviour. Men generally appear to be less likely to seek medical care when suffering from psychiatric complaints and they may inadvertently reject caregivers, leading to more men than women committing suicide. Therefore, it is important not to overlook these atypical symptoms of male depression, but instead to address them with suicide-preventive antidepressant treatment. It is vital for the general practitioner to listen to the patient’s family and to ask a number of key questions: Has the patient changed his attitude or behaviour lately? Has something upsetting happened in his life? Could there be a depression explaining the change? Could alcohol misuse or other risk-taking behaviour be masking depression? Had their depression been recognised and treated, it is very possible that many men could have been saved from suicide.

Completed suicide most often occurs in those who are middle-aged and older, while most suicide attempts are committed by people between 15 and 30 years of age. When old people say they have plans to commit suicide, the median time before they have actually committed suicide has been found to be just 1 month (Waern 2000). However, depression in elderly patients is sometimes difficult to recognise, since it may express itself through atypical symptoms, such as a) restlessness, psychomotor agitation, nervousness, clinginess, paranoid tendencies and/or b) somatic complaints such as tiredness, headache, palpitations, pain, dizziness, stomach complaints, back problems, shortness of breath, and the complaint of “never getting well”.

General practitioners are often in the unique position of having a long-standing relationship and knowledge of the elderly person and thus can discern depressive tendencies, distinguishing them from somatic problems associated with illness that was previously present. Elderly patients also tend to have confidence in their general practitioners. Thus they may more readily accept it when their general practitioner points out the presence of depressive symptoms and acknowledge the need to treat their depressive as well as their somatic symptoms.

The lifetime suicide risk in bipolar disorder is high—around 20% (Möller 2001).
Anxiety disorders

Fawcett (2001) reported that panic disorder has been associated with increased rates of suicide and attempted suicide. The degree of increased suicide risk is related to the severity of the anxiety symptoms, which are not always recognised by general practitioners when patients present with major affective disorders. Suicide risk is highest in those with both anxiety and affective disorders (Fawcett 2001).

Alcohol and drug abuse

The mortality of individuals with alcohol dependence is four times that of the normal population, with half the increased mortality due to violence and half due to suicide. Longitudinal follow-up studies show that approximately 7% of individuals with alcohol-dependence die because of suicide; retrospective studies indicate that as many as 15%–20% of people who with alcohol dependence or abuse take their own lives (Wasserman 2001). In Finland, 34% of the total number of suicides over 12 months were associated with alcohol dependence, while another 9% were associated with alcohol abuse (Lönnqvist 2001).

Alcohol dependence usually subsides with advancing years; however, a study of suicides that took place over the course of a year in people who were 65 years old suggested that as many as one third of these individuals had alcohol dependence, which had not been treated (Waern 2000). Alcohol dependence is the “invisible elephant in the room” of medicine and accounts for many somatic symptoms. General practitioners have the opportunity for early detection of individuals with alcohol dependence, who may be at risk for suicide. Treating the alcohol dependence is also a suicide prevention strategy. Drug abuse is often associated with aggression, violence, and criminality and is also associated with an increased risk of suicide attempts (Carlsten 2000, Johansson 2002). Approximately 7% of drug addicts die because of suicide (Wasserman 2001).

Psychotic diseases

Psychotic illnesses, such as schizophrenia, schizoaffective disorder, affective psychosis (mania or depression) (Hawton et al. 2005), drug-elicited psychosis, and organic psychosis, are all associated with an increased risk of suicide. Ten percent of individuals with schizophrenia die as a result, most often during the first years of the illness (Hawton et al. 2005).

Suicide and comorbidity

Comorbid depression and alcohol/drug abuse are associated with the highest suicide rates. Alcohol abuse is much more common and has many more psychiatric side effects than is usually realised. The general practitioner is in a key position to detect these problems and provide treatment (or refer for treatment) for the depression and the alcohol abuse or dependence (Värnik et al. 2007). Elevated levels of alcohol consumption lead to mortality rates that are four times higher than in the general population; approximately half of these deaths—due to suicide—have violent causes (Wasserman 2001). As noted above, approximately 7% of patients suffering from alcohol dependence die from suicide (Wasserman 2001). Of people who commit suicide, 15%–50% have alcohol abuse or dependence (Värnik et al. 2007). Most people with alcohol dependence who commit suicide are young people or middle-aged men. However, the association between alcoholism and suicide in women and the elderly may be under reported. A third of elderly people who died from suicide had problems with alcohol which had not been treated (Waern 2000). It should also be noted that high levels of alcohol consumption often lead to generally risky behaviour, with the individual being more impulsive and having more uncontrolled and confused thoughts.
Somatic Diseases and Suicide

Some somatic disorders are linked to an elevated risk of suicide. This may be the case when the disorder is chronic, causes limitations in daily functioning, has a negative prognosis, or is associated with complicated or continuous pain. Patients such as this are often referred back from specialised medical and psychiatric clinics for follow-up by general practitioners, and it is important that the general practitioner keep this elevated suicide risk in mind.

However, somatic illness, in itself, is not enough to elicit suicidal behaviour. Individuals with somatic illness who become suicidal usually also experience feelings of loneliness and being abandoned; they may also have feelings of hopelessness.

The following somatic diagnoses, in particular, can be associated with an increased risk of suicidality:

- Cancer, especially in the period before the diagnosis is made and communicated to the patient and in the period shortly afterwards (Lönnqvist 2001)
- Neurological disorders, such as multiple sclerosis (MS), Huntington’s chorea, spinal chord injuries, epilepsy, migraine, traumatic brain injury, stroke, and also mental retardation.
- Conditions involving difficult and chronic pain
- Tinnitus in elderly men who are socially isolated and have psychological complaints
- Crohn’s disease and ulcerous colitis.

Since the 1980s, available treatment options for human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) have increased considerably. Therefore, the once very high suicide incidence seen with these conditions has decreased and is now comparable to that seen with other somatic diseases.

Special Groups

Child and adolescent suicide

Children do not acquire an adequate concept of death until they are approximately 10 to 12 years of age. Therefore, suicides in people younger than 10 years old are seldom classified as suicides. Children who express suicidal thoughts, or make suicide attempts, often live under difficult circumstances and experience severe family problems, which they can neither solve nor talk to outsiders about (Orbach 1988; Pfeffer et al. 1988).

The risk for suicidality in children may be related to risk factors in the parents. Such psychosocial risk factors include mental problems in the parents, as well as young parental age, low socioeconomic status, dependence on social welfare services because of sickness, unemployment or criminal behaviour, the parent being a single parent, and family conflicts (Mittendorfer-Rutz et al. 2004 and 2008).

Youth suicides and risk factors

In adolescents between 15 and 19 years of age, suicide ranks as the third highest cause of death. A rising trend of suicides among young men has been observed, which may be due to the increasing prevalence of depression and substance abuse in this population. Men seem to be more vulnerable to social stressors, in part because they show less help-seeking behaviour but also due to genetic factors (Wasserman 2006). According to a longitudinal Swedish study that followed child psychiatry patients for 10 to 40 years, the risk group for adolescent suicide seemed to mainly consist of socially underprivileged children cared for by the social welfare system. Some of these children, especially boys, also consistently put themselves into dangerous situations (Engqvist and Rydelius 2006).
Suicides in the elderly

Generally speaking, the risk of dying from suicide increases with advancing age (Wasserman 2006). A number of factors are associated with suicidal behaviour in old age, including being a widower, social isolation, impaired physical health, high suicidal intent, and mental illness. Relationship problems have also shown to be a prominent factor (DeLeo, 2003). Apart from these problems in old age, having moved to a home for older people may also pose difficulties and lead to feelings of loneliness and loss of context. General practitioners most often see older people when they present with concerns about their somatic health. However, it is important not to forget about the mental health of these patients, because existential issues may become more prominent and thoughts of suicide may appear as individuals age and experience a variety of different kinds of loss.

Rates of suicide may be higher among older people living in residential or care homes for the elderly than among those who have stayed in their original residences. For example, Suominen et al. (2003) found that 0.9% percent of all suicides in Finland over a 1-year period (12/1,397) took place in old age homes. In 75% of these case, a depressive syndrome was identified after death based on psychological autopsy data, but only one third of these individuals were identified as having depressive symptoms before their deaths. Predictors of mortality were older age, male gender, lower level of functioning, and presence of passive self-harm behaviours such as refusing to take medication or to eat or drink.

Studies in France have also reported higher rates of suicide among individuals living in retirement homes compared with those who remained in their own homes, with women 64 to 75 years of age having the highest suicide rates (Casadebaig et al. 2003).

Suicide in prisons

The suicide rate in prisons is higher than in the male population in general. The WHO Department of Mental Health has produced a special document, “Preventing Suicide: A Resource for Prison Officers” (WHO 2000b) with information about prison suicides and how to prevent them. This document and other resources are available from at http://www.who.int/mental_health/resources/suicide.

ASSESSMENT

Suicide Risk Analysis

General practitioners are referred to a special document developed by the WHO Department of Mental Health “Preventing suicide. A resource for general practitioners” (WHO 2000a), also available at http://www.who.int/mental_health/resources/suicide.

Factors that can increase the risk of completed suicide are summarised in the checklist in Table 5.1. In interviewing an individual who has made a suicide attempt, it is important to take the individual’s whole situation into account. What finally triggered his attempt? How serious and how stable is still his suicidal intention? Is the risk unchanged?

There is a risk of suicide if:

• an individual has a psychiatric condition, especially depression;
• he or she has already exhibited suicidal behaviour;
• there is a history of suicide in the family or among his acquaintances.

Has the person communicated his suicidal intention? Communication means there is a part of him open to persuasion to hang on to life. Elderly people are often very serious when they communicate their suicidal intention, but communication from anyone at any age regarding suicidal ideation should be taken seriously. Waern (2000) has shown that, in elderly people, the median time between the suicidal message and completed suicide is just 1 month.

A previous suicide attempt should be regarded as a significant risk factor. In addition, if there has been completed suicide or suicide attempts in the family, this increases the risk for future suicidal behaviour (Hawton et al. 2003; Hultén 2000).
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<tr>
<td><strong>TABLE 5.1</strong></td>
<td>Checklist of risk factors for suicidality</td>
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<td>1. Psychiatric symptoms</td>
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<td>Depression___</td>
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<td>Strong anxiety___</td>
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<td>Psychotic ideation___</td>
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<td>Violent tendencies___</td>
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<td>Alcohol or other substance abuse___</td>
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<td>2. Suicidal model (in the family or close environment)</td>
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<td>3. Previous suicide attempt (when, method)</td>
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<td>4. Severe somatic illness</td>
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<td>5. Social network (failing or missing)</td>
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<td>6. Suicidal intention</td>
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<td>Hopelessness___</td>
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<td>Thoughts about death___</td>
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<td>Suicide wishes/impulses___</td>
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<td>Suicide note___</td>
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<td>Suicide plan/method___</td>
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<td>7. Acute problem</td>
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<td>8. Suicidal communication</td>
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Suicidal Communication

When an individual is contemplating suicide, he often gives a message communicating this intention. General practitioners should be extra sensitive to detect this important message. As noted above, many individuals see their general practitioner some time before committing suicide; however, in this meeting, they often do not disclose their suicidal thoughts. As many as 41% of individuals who commit suicide have visited medical facilities during the 4 weeks before the suicide (Isometsä et al. 1995). Among elderly patients, 80% consult a doctor before their suicide, complaining of a poor somatic condition (DeLeo 2003).

There are four types of suicidal communication (Wasserman 2001):

1. Direct verbal communication, in which people explicitly express thoughts or plans about suicidal behaviour.
2. Indirect verbal communication, in which people express less explicit thoughts, such as “I can’t go on like this”.
3. Direct non-verbal communication, for example, purchase of guns, bullets or drugs
4. Indirect non-verbal communication, for example, suddenly, and without rational reason, taking actions such as writing a will or arranging for insurance policies.

The suicidal communication, therefore, may be direct or indirect, verbal or non-verbal. If it is direct, it is not difficult to identify. General practitioners must take such statements words seriously. They need to sit down with the person and spend time talking the situation through and should also invite close relatives and friends to participate.

If the message is indirect, the general practitioner must pay special attention to reports from others in the person’s environment. For example, has there been a change in the individual’s behaviour or habits lately? Has he put his papers and financial affairs into order and, at the same time, hinted at death as a possible solution to his problems? Only those close to the individual can give information on these topics, especially concerning non-verbal communication. When a person seeks medical help for somatic complaints, this can also sometimes reflect indirect communication of suicidal thoughts.

Suicidal individuals often tend to regress into a psychologically vulnerable state, in which they are oversensitive to rejection and to the ambivalence of significant others. Therefore, it is important that these significant others pay attention to the suicidal communication and take it seriously. If suicidal behaviour persists over time, the general practitioner needs to inform people around the patient and provide education to them concerning how to respond to the individual and how to calm the situation down rather than escalate it.

The responses of significant others and healthcare personnel in response to a suicidal communication may be coloured by so-called counter-transference reactions (e.g., these individuals may show disproportionate feelings of irritability, impatience, lack of interest, or ambivalence towards the suicidal person). This holds true especially if the person is repetitively suicidal. If the suicidal patient does not “get better”, he or she can elicit feelings of guilt, incompetence, anxiety, fear, or anger in the person providing treatment. This, in turn, may lead to underestimation of the depth and seriousness of the patient’s problems (Wolk-Wasserman 1987). General practitioners needs training to help them recognise their own feelings and reactions to these difficult patients in order to be able to make an adequate judgement of the patient’s suicide risk.

Relationship between Attempted Suicide and Suicide

If an individual has made a suicide attempt once or several times, this heightens the risk of completed suicide. Hawton et al. (2003) did a follow-up of 11,583 patients 15 years after an act of deliberate self-harm and found that 300 of the individuals had died from suicide; thus, the suicide risk in this sample was 66 times greater than in the general population. Therefore, it is important to always ask a suicidal patient if he has ever made a suicide attempt in the past, because this considerably heightens the risk of completed suicide.
Predictors of Completed Suicide

Although the risk factors for suicide are well known, it is nevertheless difficult to predict a suicide. The following characteristics do indicate a higher risk of suicide:

• Male sex
• Over 45 years of age
• Separated, divorced, or widowed
• Unemployed or retired
• Chronic somatic illness
• Major psychiatric disorder, especially depression
• Addiction to alcohol or other substances
• Use of violent methods for suicide attempt
• Having left a suicide note

Suicide Rating Scales

Rating scales can be useful tools in the diagnosis of depression and suicidal ideation. Such scales include Beck’s Depression Inventory (BDI) (Beck et al. 1961) and the Montgomery Åsberg Depression Rating Scale (MADRS) ((Montgomery and Åsberg 1979; Svanborg and Åsberg 1994). The MADRS has two advantages. First, it can be self-administered and, second, the two last items, which ask about self-image and suicidal ideation, are good starting points for discussing these difficult and intimate matters with patients.

Beck’s Hopelessness Scale (Beck et al. 1974) is used to predict suicidal behaviour. The individual’s perception of his future, whether ‘dark’ or ‘bright’, has proven to have strong predictive value. Aish and Wasserman (2001) showed that this 20-item scale might even be replaced with just one item, “My future seems dark to me, and I am detecting suicidal tendencies”.

More important than rating scales, however, is the personal interview conducted by the general practitioner. He or she should not be afraid to ask the patient about possible suicide thoughts or plans, and should also ask if the patient has ever made a suicide attempt before and if there is any history of suicide in the family or close environment. These factors, if present, are known to considerably increase the risk of suicide.

Around the world, self-poisoning is the main method used in attempting suicide. Therefore, all physicians, both somatic and psychiatric and including general practitioners, must be cautious when prescribing large quantities of medicines and consider the risk associated with possible suicidal ideation and plans (Fleischman et al. 2005). Hawton et al. (2004) showed that prescribing smaller quantities of medication can help reduce the number of suicide attempts. General practitioners should also ask about guns and medicines at home which could be used in suicide attempts, and relatives should be informed about the potential risks of these items.

Assessment of Suicide Risk

When assessing the suicide risk of a patient, the checklist shown in Table 5.1 below may be helpful in remembering important items.

TREATMENT

Pharmacological Treatment of Individuals Who Are Suicidal

Of individuals who die due to suicide, 80%–90% had a psychiatric diagnosis. This means that treating the underlying psychiatric condition has a suicide preventive effect.

Antidepressant drugs are used to treat for both severe and moderate depression. Mild to moderate depression can also be efficiently treated using different forms of psychotherapy or supportive therapy (Wasserman 2006).
Lithium is used for to treat bipolar disorder (manic-depressive states). Lithium treatment should be monitored by psychiatric specialists.

Antipsychotics are used to treat schizophrenia and other psychotic states as well as bipolar disorder, especially mania. Low doses of antipsychotics may also be helpful in stabilising negative emotions in individuals with personality disorders, especially those with emotionally unstable personality disorder. Antipsychotic drug treatment should be monitored by psychiatric specialists.

Antidepressant therapy should always be combined with supportive therapy, which could be provided by a psychologist, nurse, or other staff member with psychotherapist training in the general practitioner’s office. When suicidal patients were asked what was lacking in the psychotherapeutic treatment they received, most said they felt it was the opportunity to discuss existential matters (Wasserman 2001, 2006).

In choosing an antidepressant medication for a suicidal patient, one wants to have a sedative effect. This can either be inherent in the drug itself or a sedating medication can be added to the antidepressant for a short period. SSRIs are considered a first choice, and can be combined with a short duration of benzodiazepine treatment, since SSRIs may augment initially anxiety. In children younger than 12 years of age, only fluoxetine showed an antidepressant effect, according to a recent meta-analysis by Bridge et al. (2007).

Antidepressants prescribed to suicidal patients should also be relatively safe in overdose (e.g., an SSRI, mianserin, or mirtazapine) (see Wasserman 2006 for further information). However, it is important to remember that no drug is entirely safe. If you consume too many, the SSRIs can be lethal. Therefore, the smallest possible amount should be prescribed, or else arrangements should be made for a family member or outpatient nurse to take responsibility for the medication during this critical period. It is especially vital for general practitioners to keep the risk of intentional overdose in mind, since such practitioners may routinely prescribe large quantities of medications for somatic illnesses.

To the depressed patient, every day is a day of suffering. Therefore, it is wise to start treatment as soon as possible.

Both adherence to and effectiveness of pharmacological treatment depend at least partly on the relationship between the patient and the general practitioner. If the patient trusts his general practitioner, he will take the medicine and follow the doctor’s advice. If he does not trust the general practitioner, the opposite is the case.

By calling the patient on the phone a couple of days after he or she started the medication and seeing the patient at closely spaced intervals during the first phase of treatment, the general practitioner can make sure that the patient is taking his medicine and reacting well to it. In this way, the general practitioner establishes a trusting relationship, which is a key requisite for ameliorating the patient’s condition: the physician is sending the important message that he or she cares.

Suicide and Antidepressant Use

Of people who die due to suicide, approximately 60% or even more according to some studies, suffer from depression—but only 15% received prescriptions for antidepressants. Studies have also shown that only 3%-6% of individuals who died from suicide had received adequate doses of antidepressants (Isacsson et al. 1994).

There are several explanations for this undertreatment of depression:

• First, not all individuals respond to antidepressant medication (only approximately 70%).
• Second, the patient’s adherence to treatment depends, for the most part, on the doctor/patient relationship, as discussed above.
• Third, many patients distrust medication and do not even want to try it.
• Fourth, many patients suffer numerous medication side effects will stop taking pharmacological treatment shortly after it is initiated, if the general practitioner does not provide follow-up and explanations.


The general practitioner should stay in close contact to monitor the patient’s reaction to the medication. Many SSRIs initially augment anxiety and may make the patient feel worse at the beginning of treatment, and the patient needs to be informed about this. Some antidepressant medication has even been reported to produce suicide ideation in some patients. Therefore, the patient should be seen again soon after the medication is been started to assess his or her psychological status and suicide risk.

The increase in anxiety due to antidepressants mentioned above may occur within days of starting the drug, whereas an antidepressant effect does not generally appear until after approximately 10–14 days. Therefore, it is important to contact the patient 2 or 3 days after the medication has been started (e.g., by telephone or contact with the nurse)—such personal contact can play an essential role in successful treatment. It is then imperative that the patient be seen in person within 2–3 weeks, and that regular contact continue to be maintained with the patient and family after that visit. This ensures that the patient and his or her family know that there is someone they can call, if they need to. These contacts are as important as the medication itself. In fact, such contacts play a major role in ensuring that the patient continues to take the medicine.

Lack of optimal response can be the result of poor adherence, but it can also result from the fact that some individuals may have a faster metabolism and need higher doses of medicine to achieve therapeutic drug levels. Therefore, if the patient does not respond to pharmacological treatment at usual therapeutic doses, the serum concentration of the drug should be tested. This can be done when the medication is at steady state, which occurs after approximately ten times the half life (T\(1/2\)) of the drug. The blood sample should be taken in the morning before the morning dose of medication in order to obtain the lowest concentration of the medicine during the day.

Psychological Treatment of Suicidal People

Psychotherapy is a form of counselling that can help patients develop problem-solving strategies. One crucial requirement for successful psychotherapy is a good and trusting relationship between therapist and patient. A number of different kinds of evidence-based therapy are available:

- **Cognitive-behavioural therapy (CBT)** focuses on changing the way one views oneself and others and changing negative attitudes to more positive ones. CBT can be carried out both on a short and long-term basis.

- **Dialectical behaviour therapy (DBT)** focuses on patients with personality disorders and has proven successful with patients who make repeated suicide attempts. DBT is an individually based therapy but also contains exercises that are done in a group setting to give the patient the chance to apply new approaches to the handling of difficult situations.

Both CBT and DBT view suicidal behaviour as a learned coping response and problem-solving strategy that originates under conditions of extreme emotional pain or anxiety. As a group, suicidal patients have a low tolerance for enduring emotional pain and anxiety. Suicidal behaviour, therefore, can be considered an extreme form of emotional avoidance (see the Clinical Manual for Assessment and Treatment of Suicidal Patients by Chiles et al. 2005), to which the individual turns when all other problem-solving strategies he or she can think of have been exhausted. It can also be viewed as an effort by the individual to gain control over unwanted feelings, thoughts, memories or physical sensations and the anxiety that goes with these states. The goal of CBT and DBT in this situation is to help suicidal individuals find alternative ways of solving their emotional problems. One aspect of these therapies is teaching patients to accept opposites and to see a phenomenon from different angles at the same time; rather than viewing things as either black or white (i.e., encouraging the patient to see that two extremes can exist together with a zone of grey in
It is also important to identify triggering situations that make the patient feel hopeless and suicidal. These situations can be broken down into smaller pieces, each of which can be tackled in alternative, constructive ways, rather than allowing the patient to generalise in a negative way (e.g., thinking “Here I go again, abandoned once more, no one ever wants me”).

The “Reasons for Living Inventory” (Strohsal et al. 1992) is a list of items that can be a helpful tool in working with a suicidal patient. The patient may have suicidal thoughts, but the fact that he or she is willing to discuss this with the general practitioner means the patient is open for new perspectives. Just sitting down with the patient, taking him or her seriously, and discussing these matters conveys to the patient a sense that he or she is being treated with a respect that may feel missing in his or her usual surroundings.

Finally, it is important to discuss suicidality openly. If the patient feels that this is a forbidden topic, his suicidal thoughts may go on living their own life, without being questioned or contradicted. Instead, the clinician should use the fact that the patient is alive as a starting point to reinforce his or her will to live.

Another type of psychotherapy that may be useful with suicidal patients is transference focused therapy (TFP). TFP focuses on the patient’s past and current life, in order to help the patient formulate and understand his or her destructive lifestyles and behaviours.

Reducing Repetition of Deliberate Self-harm

The following strategies can help reduce repeated suicidal behaviours:

1. Protect the patient against repeated suicide attempts and against suicide. Suicide attempts greatly increase the risk of completed suicide and of irreversible self-inflicted harm.

2. Reduce feelings of hopelessness. Aaron Beck (1974) showed that hopelessness correlates with completed suicide more strongly even than depression. The general practitioner has often known the person for a long time and is thus in a good position to remind the suicidal and hopeless person of his competencies, experiences of success, and past happiness to show him that this moment of darkness will also pass. This art of offering vicarious hope is vital in providing care to the suicidal person.

3. Treat the patient with pharmacological (antidepressants) and psychological methods or refer for specialist treatment.

4. Improve the person’s subjective quality of life by encouraging him or her to network with significant others, healthcare personnel, and societal resources and facilities.

5. Societal resources that can help with housing and employment can be important elements in ameliorating the life situation of a suicidal individual, and the general practitioner can play a key role in promoting these connections.

Importance of Combining Pharmacological and Psychological Treatments for Suicidal Individuals

Most patients suffering from depression become free of symptoms when they receive a combination of both pharmacotherapy and psychotherapy treatment. However, patients suffering from a very deep depression, such as a major depressive disorder or even a psychotic depression, may first need to be treated with biological agents (e.g., antidepressant medication) so that they can improve enough to be able to engage productively in psychotherapy. In this situation, contact with the psychiatrist during the early phase of treatment should be frequent and supportive (Wasserman 2006).

Training for General Practitioners and their Staff

It is not always possible for a general practitioner refer a depressed patient for psychotherapy or specialist services. It is therefore good to know that the supportive contact the general practitioner provides to the patient during medication treatment is also of great value. Research has shown that it is the quality of the relationship between therapist and patient that is a decisive determinant of what the patient will gain from medication treatment. Such treatment must sometimes be continued on a long-term basis or may need to be restarted if the patient experiences a relapse in depression and suicidal thoughts.
Supporting Healthcare Staff

Patients often see other personnel and healthcare staff in the office more often than they actually see their general practitioner, so that it is important for these personnel to learn about and practice suicide prevention strategies. Personnel should be encouraged and praised in these efforts and should also be offered the opportunity for clinical supervision and continuing education. Working with depressed and suicidal patients can often be very demanding. Moreover, studies have shown that mental healthcare professionals are often extra-sensitive people, and have more suicidal thoughts and behaviour than is found in the population in general. General practitioner have to take responsibility for their patients and, to a great extent, also for their staff—no chain is stronger than its weakest link.

Training General Practitioners in the Treatment of Depression and Suicide Prevention Strategies

Studies have shown that suicide rates in patients decrease when general practitioners are provided with training in the treatment of depression and in suicide prevention strategies. On the island of Gotland, Sweden, Rutz et al. (1989) educated general practitioners about how to diagnose and treat depression and how to identify patients at risk for suicide and refer them for further treatment. This intervention resulted in a 60% decrease in suicides among women. However, it was found that the education project had to be repeated after some years.

Hegerl et al. (2006) implemented a program to improve the care of patients with depression that involved the following four levels of intervention:

- Level one: training of family doctors and support staff
- Level two: public relations campaign providing information about depression
- Level three: co-operation with community facilitators (e.g., teachers, priests, local media)
- Level four: support for self-help and high-risk groups.

The project took place in Nuremberg (480,000 inhabitants) and lasted for 2 years. Compared with results in a control region, the investigators observed a 19.4% reduction in the number of suicidal acts during the first year of the intervention. During the second year of the intervention, the rate of reduction increased to 24%. There was also an 18.3% decrease in suicide attempts. The reduction that was observed was most noticeable for high-risk suicide methods.

Szanto et al. (2007) investigated the effectiveness of a similar intervention, a depression-management educational programme for general practitioners, in a region of Hungary with a very high suicide rate. In this study, 28 general practitioners and their nurses, who were serving 73,000 inhabitants, participated in a 5-year educational program. During the same period, a depression treatment clinic and a psychiatrist telephone consultation service were also established in the intervention region. The annual suicide rate decreased from the pre-intervention average of 59.7 per 100,000 inhabitants to 49.9 per 100,000, a 16% decrease. In rural areas of the intervention region, the female suicide rate decreased by 34%.

A study by Oyama et al. (2006) in rural Japan evaluated a long-term (10 year) community-based suicide prevention programme focused on reducing suicide among the elderly. This programme incorporated both screening for depression in elderly patients and subsequent health education provided via primary and public health nursing services. Results indicated a reduction in the suicide risk in older people in the intervention area, with a significant effect among older women but not men in the same areas.
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Casadebaig F, Ruffin D, Philippe A. Suicide in the elderly at home and in retirement homes on France. Rev Epidemiol Sante Publique 2003;51:55–64.


Murphy GE. Why women are less likely than men to commit suicide. *Compr Psychiatry* 1998;39:165–75.


USEFUL LINKS TO PROGRAMMES

Defeat Depression Campaign
http://www.rcpsych.ac.uk/campaigns/previouscampaigns/defeatdepression.aspx

Beyond Blue

United States Air Force Suicide Prevention Programme (AFSPP)
http://www.nrepp.samhsa.gov/programfulldetails.asp?PROGRAM_ID=68

Choose life
http://www.choselife.net/home/Home.asp

European Alliance Against Depression
http://www.eaad.net/enu/documents-2.php