

Affective (mood) disorders

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Learning Objectives

- Epidemiological factors in mood disorders.
- Aetiological factors in mood disorders, including monoamine hypothesis of depression.
- Clinical features of depressive disorders and mania, and of dysthymia and hypomania.
- Differential diagnosis of depression, including organic (secondary) causes.
- Be able to assess a patient with low mood.
- Be able to talk to a patient about starting an antidepressant or mood stabiliser.
- Be able to talk to a patient about electroconvulsive therapy (ECT) treatment.

Testimony of a bipolar sufferer after a course of ECT treatment for a severe depressive episode

I have been high several times over the years, but low only once.

When I was high, I became very enthusiastic about some project or another and would work on it with determination and success. During such highs I wrote the bulk of two books and stood for parliament as an independent. I went to bed very late, if at all, and woke up very early. I didn't feel tired at all. There were times when I lost touch with reality and got carried away. At such times, I would jump from project to project without completing any, and did many things which I later regretted. Once I thought that I was Jesus and that I had a mission to save the world. It was an extremely alarming thought.

When I was low I was an entirely different person. I felt as though life was pointless and that there was nothing worth living for. Although I would not have tried to end my life, I would not have regretted death. I did not have the wish or the energy to do even the simplest of tasks. Instead I withered away my days sleeping or lying awake in bed, worrying about the financial problems that I had created for myself during my highs. I also had a feeling of unreality, that people were conspiring to make life seem normal when in actual fact it was unreal. Several times I asked the doctor and the nurses to show me their ID because I just couldn't bring myself to believe that they were real.

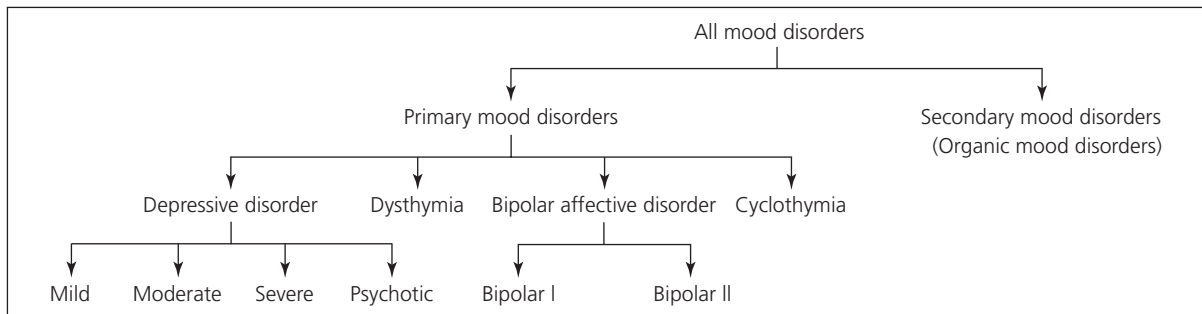


Figure 5.1 Types of mood disorder.

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Classification

Primary versus secondary mood disorder

A **primary mood disorder** is one that does not result from another medical or psychiatric condition. A **secondary mood disorder**, on the other hand, is one that results from another medical or psychiatric condition, e.g. anaemia, hypothyroidism, substance abuse. Once a diagnosis of mood disorder has been made, it is important to consider the possibility of it being a secondary mood disorder, as a secondary mood disorder is often most effectively treated by treating the primary condition, e.g. anaemia, etc.

Unipolar depression versus bipolar affective disorder

Broadly speaking, a primary mood disorder is either unipolar (depressive disorder, dysthymia) or bipolar (bipolar affective disorder, cyclothymia) (Fig. 5.1). To meet the criteria for a bipolar mood disorder, the patient must have had one or more episodes of mania or hypomania. The unipolar–bipolar distinction is an important one to make, as the course and treatment of bipolar affective disorder differ significantly from those of unipolar depression.

Unipolar mood disorders

In ICD-10, depressive disorders are classified according to their severity into **mild**, **moderate**, **severe**, and **psychotic** depressive disorder (Fig. 5.1). If a patient has had more than one episode of depressive disorder, the term **recurrent**

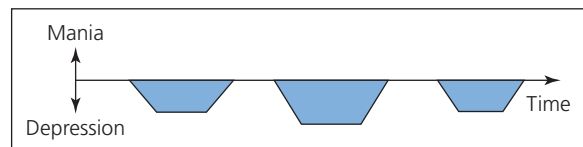


Figure 5.2 Recurrent depressive disorder.

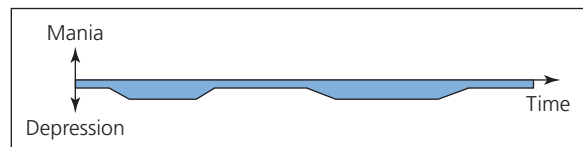


Figure 5.3 Dysthymia.

depressive disorder is used, and the current episode is classified as for a single episode, e.g. ‘recurrent depressive disorder, current episode moderate’ (Fig. 5.2). In DSM-IV the term major depression is used instead of depressive disorder. Major depression is simply subclassified as ‘single episode’ or ‘recurrent’.

Not all people suffering from depressive symptoms have a depressive disorder. **Dysthymia** can be described as a mild chronic depression characterised by depressive symptoms that are not sufficiently severe to meet a diagnosis of depressive disorder (Fig. 5.3).

Bipolar mood disorders

According to ICD-10, bipolar affective disorder consists of repeated (two or more) episodes of depression and mania or hypomania. In the absence of episodes of mania

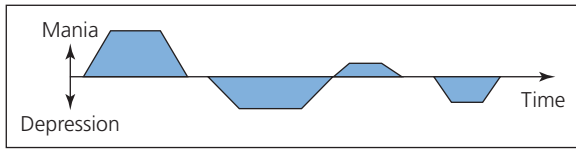


Figure 5.4 Bipolar depression (bipolar I).

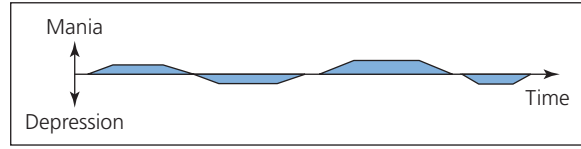


Figure 5.5 Cyclothymia.

or hypomania, the diagnosis is one of recurrent depressive disorder. In the absence of episodes of depression, the diagnosis is either one of bipolar affective disorder or hypomania – i.e. recurrent episodes of mania are diagnosed as bipolar affective disorder. This is not only because sooner or later a depressive episode is almost certain to supervene, but also because recurrent episodes of mania resemble BAD in their course and prognosis.

According to DSM-IV, ‘bipolar disorder’ can be diagnosed after even a single episode of mania, whereas in ICD-10 a single episode of mania is simply diagnosed as a

‘manic episode’. The separation of bipolar disorder into bipolar I and bipolar II in DSM-IV may have implications for treatment response. **Bipolar I** consists of episodes of mania and major depression (Fig. 5.4), **bipolar II** of episodes of hypomania and major depression.

Cyclothymia can be described as mild chronic bipolar affective disorder and is characterised by numerous episodes of mild elation and mild depressive symptoms that are not sufficiently severe or prolonged to meet the criteria for bipolar affective disorder or recurrent depressive disorder (Fig. 5.5).



ICD-10 classification of affective disorders

- F30** Manic episode
 - F30.0 Hypomania
 - F30.1 Mania without psychotic symptoms
 - F30.2 Mania with psychotic symptoms
 - F30.8 Other manic episodes
 - F30.8 Manic episode, unspecified
- F31** Bipolar affective disorder (BAD)
 - F31.0 BAD, current episode hypomanic
 - F31.1 BAD, current episode manic without psychotic symptoms
 - F31.2 BAD, current episode manic with psychotic symptoms
 - F31.3 BAD, current episode mild or moderate depression
 - F31.4 BAD, current episode severe depression without psychotic symptoms
 - F31.5 BAD, current episode severe depression with psychotic symptoms
 - F31.6 BAD, current episode mixed
 - F31.7 BAD, current episode in remission
 - F31.8 Other bipolar affective disorders
 - F31.9 Bipolar affective disorder, unspecified
- F32** Depressive episode
 - F32.0 Mild depressive episode
 - F32.1 Moderate depressive episode
 - F32.2 Severe depressive episode without psychotic symptoms
 - F32.3 Severe depressive episode with psychotic symptoms
 - F32.8 Other depressive episodes
 - F32.9 Depressive episode, unspecified
- F33** Recurrent depressive disorder
 - F33.0 Recurrent depressive disorder, current episode mild
 - F33.1 Recurrent depressive disorder, current episode moderate

- F33.2 Recurrent depressive disorder, current episode severe without psychotic symptoms
- F33.3 Recurrent depressive disorder, current episode severe with psychotic symptoms
- F33.4 Recurrent depressive disorder, currently in remission
- F33.8 Other recurrent depressive disorders
- F33.9 Recurrent depressive disorder, unspecified
- F34** Persistent mood disorders
 - F34.0 Cyclothymia
 - F34.1 Dysthymia
 - F34.8 Other persistent mood disorder
 - F34.9 Persistent mood disorder, unspecified
- F38** Other mood disorders
 - F38.0 Other single mood disorders
 - F38.1 Other recurrent mood disorders
 - F38.8 Other specified mood disorders
- F39** Unspecified mood disorders

DSM-IV classification of affective disorders

- Depressive disorders
 - Major depressive disorder
 - Single episode
 - Recurrent
 - Dysthymic disorder
- Bipolar disorders
 - Bipolar disorder I
 - Bipolar disorder II
 - Cyclothymic disorder
- Mood disorder due to a general medical condition
- Substance-induced mood disorder

Depressive disorders

... I have of late – but
wherefore I know not – lost all my mirth, forgone all
custom of exercises; and indeed it goes so heavily
with my disposition that this goodly frame, the
earth, seems to me a sterile promontory, this most
excellent canopy, the air, look you, this brave
o'erhanging firmament, this majestic roof fretted
with golden fire, why, it appears no other thing to
me than a foul and pestilent congregation of vapours.
What a piece of work is a man! how noble in reason!
how infinite in faculty! in form and moving how
express and admirable! in action how like an angel!
in apprehension how like a god! the beauty of the
world! the paragon of animals! And yet, to me,
what is this quintessence of dust? man delights not
me: no, nor woman neither, though by your smiling
you seem to say so.

Shakespeare, *Hamlet*, Act II, scene 2

5

Epidemiology

Figures for the lifetime incidence or lifetime risk of depressive disorders depend on the criteria used to define 'depressive disorders'. Using the criteria for major depressive disorder (DSM-IV), the lifetime risk of depressive disorders is about 15%. The prevalence of depressive disorders at any one time or point prevalence is about 5%. This figure masks an uneven gender distribution, however, as females are more affected than males by a ratio of about 2 : 1. The reasons for this uneven gender distribution are unclear but are thought to be partly biological (genetic predisposition, hormonal influences) and partly sociocultural (social pressures, readiness to admit to depressive symptoms, diagnostic bias in clinicians). Although depressive disorders can occur at any age, their peak prevalence in males is in old age, and in females is in middle age (Fig. 5.6). They are relatively uncommon in children, or present differently (see Chapter 13).

There are important geographical variations in the prevalence rates of depressive disorders, and these can at least in part be accounted for by sociocultural factors. For example, somatic presentations of depression are particularly common in Asian and African cultures and may therefore not so easily be recognised as depression. As a clinician it is important to remember that sociocultural

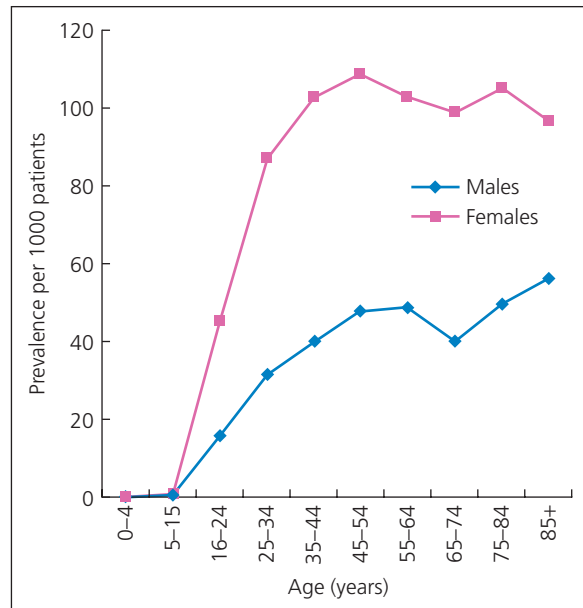


Figure 5.6 Prevalence of 'treated depression' according to age and sex. Note prevalences and peaks. (Adapted from Key Health Statistics from General Practice 1998.)

factors can affect the presentation not only of depression but also of other psychiatric and non-psychiatric conditions (see Table 7.3 on culture-bound syndromes).

Aetiology

Genetics

The prevalence rate for major depression in first-degree relatives is about 15%, compared to about 5% in the general population. Although first-degree relatives are at increased risk of depressive disorders they are *not* at increased risk of bipolar affective disorder or schizoaffective disorder. The concordance rate for major depression in monozygotic twins is 46%, compared to 20% in dizygotic twins. There is thus an important genetic component to the aetiology of depressive disorders. The inheritance pattern is no doubt polygenic, but more research is needed to identify the genes involved.

Neurochemical abnormalities

The monoamine hypothesis of depression suggests that depression results from the depletion of the monoamine

neurotransmitters noradrenaline, serotonin, and dopamine. In its revised version the monoamine hypothesis of depression recognises that depression may not result from an actual depletion of the monoamine neurotransmitters, but from a change in their receptors' function.

Support for the original monoamine hypothesis of depression comes from several findings, notably:

- Antidepressants increase the levels of the monoamine neurotransmitters:
 - Monoamine oxidase inhibitors (MAOIs) inhibit the degradation of monoamines presynaptically.
 - Tricyclic antidepressants (TCAs) inhibit the reuptake of noradrenaline from the synaptic cleft.
 - Selective serotonin reuptake inhibitors (SSRIs) inhibit the reuptake of serotonin from the synaptic cleft.
- Amphetamines and cocaine increase the levels of monoamines in the synaptic cleft and can elevate mood.
- Reserpine decreases the levels of monoamines presynaptically and can depress mood.
- Cerebrospinal fluid levels of 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite, are decreased in depression sufferers.

Other neurological abnormalities

Computed tomographic (CT) and magnetic resonance imaging (MRI) findings in major depression include enlarged lateral ventricles and loss of volume in the frontal and temporal lobes, hippocampus, and basal ganglia; but these findings are inconsistent.

Endocrine abnormalities

The fact that depression occurs in a variety of endocrine disorders (Cushing's syndrome, Addison's disease, hypothyroidism, hyperparathyroidism) suggests that endocrine abnormalities play a role in the aetiology of depressive disorders. **It has been found that plasma cortisol levels are increased in about 50% of depression sufferers and that about 50% of depression sufferers fail to respond to the dexamethasone suppression test.** These endocrine abnormalities may have their origin in disturbances of the hypothalamic–pituitary–adrenal axis.

Immune function

It has been postulated that disturbances in the hypothalamic–pituitary–adrenal axis in depression (see above) may at least in some cases result from changes in immune regulation.

Table 5.1 Organic causes of depression (note that this list is not exhaustive).

Neurological	Stroke, Alzheimer's disease/dementia, Parkinson's disease, Huntington's disease, multiple sclerosis, epilepsy, intracranial tumours
Endocrine	Cushing's syndrome, Addison's disease, hypothyroidism, hyperparathyroidism
Metabolic	Iron deficiency, vitamin B ₁₂ /folate deficiency, hypercalcaemia, hypomagnesaemia
Infective	Influenza, infectious mononucleosis, hepatitis, HIV/AIDS
Neoplastic	Non-metastatic effects of carcinoma
Drugs	L-dopa, steroids, beta blockers, digoxin, cocaine, amphetamines, narcotics, alcohol

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Organic causes

The organic causes of depression are listed in Table 5.1.

Personality traits

Certain personality traits such as neuroticism and obsessiveness and certain personality disorders predispose to depression.

Environmental factors

Early adverse life events such as loss of a parent, neglect, or sexual abuse may predispose to depression in later life, and 'an excess of life events' occurs in the months preceding the onset of a depressive episode. A depressive episode that appeared to result from life events and lacked somatic symptoms used to be called a **reactive depression** and contrasted to an **endogenous** depression, but both epithets and their cognates have been abandoned in favour of the realisation that all depressive episodes ultimately result from a combination of both genetic and environmental factors.

The Brown and Harris study

In 1978, Brown and Harris studied working class women in inner London boroughs and found that certain circumstances acted as so-called '**vulnerability factors**' for depression:

- Loss of mother by death or separation before the age of 11.
- Excess of life events or major difficulties prior to onset of depression.
- Lack of a supportive relationship.
- Three or more children under the age of 14 at home.
- Not working outside the home.

Seasonal affective disorder

Seasonal affective disorder (SAD) is a depressive disorder that recurs every year at the same time of year and may be marked by increased sleep and carbohydrate craving. The condition is thought to result from changes in the seasons, particularly in the length of daylight, and may respond to bright artificial lights (light is given at 2500 lux in the morning and late evening). There is usually complete summer remission and occasionally summer hypomania or mania which, along with Shakespeare, may be at the origin of the expression 'This is very midsummer madness'.

5

'Learned helplessness' and depression

In 1975 Seligman demonstrated that dogs that had learnt that they could not escape from an electric shock did not try to escape from it even once the situation permitted them to do so. In other terms, once the dogs had learnt that they could not exert control over their environment, they permanently gave up the will to do so. Extended to human behaviour, this so-called 'learned helplessness' has provided an influential cognitive-behavioural model of depression.

Man's Search for Meaning

We who lived in concentration camps can remember the men who walked through the huts comforting others, giving away their last piece of bread. They may have been few in number, but they offer sufficient proof that everything can be taken from a man but one thing: the last of human freedoms – to choose one's attitude in any given set of circumstances – to choose one's own way.

Victor Frankl (1905–1997), neurologist, psychiatrist, holocaust survivor, author of *Man's Search for Meaning*, and founder of logotherapy and existential psychotherapy

Frankl observed that those who survived longest in the concentration camps were not those who were physically strong, but those who succeeded in retaining a sense of individual purpose and control over their lives.

Psychological theories

Three of the most influential psychological theories of depression are considered in Tables 5.2 and 5.3.

Table 5.2 Psychological theories of depression.

According to	Depression results from
Attachment theory (Bowlby)	Maternal deprivation
Psychoanalytical theory (Freud)	Loss of the loved object and mixed feelings of love and hatred, so-called ambivalence
Cognitive theory (Beck)	Beck's triad (negative appraisal of the self, of the present, and of the future) and Beck's cognitive distortions (Table 5.3)

Table 5.3 Beck's cognitive distortions in depression.

Cognitive distortion	Explanation
Arbitrary inference	Drawing a conclusion in the absence of evidence, e.g. <i>Everyone on this ward hates me</i>
Overgeneralisation	Drawing a conclusion on the basis of a single incident, e.g. <i>The nurse gave me an evil look – everyone on this ward hates me</i>
Selective abstraction	Focusing on a single event to the detriment of others
Dichotomous thinking	'All-or-nothing' thinking, e.g. <i>If he doesn't come to see me today then he doesn't love me</i>
Magnification/minimisation	Over- or underestimating the importance of an event
Catastrophic thinking	Expecting disaster to strike, e.g. <i>If I take the car out to the shops I'm more than likely to crash it and kill someone</i>
Personalisation	Relating independent external events to oneself, e.g. <i>The nurse left her job because she was fed up with me</i>

Clinical features

The clinical features of depression can be divided into:

- Core features:
 - Depressed mood.
 - Loss of interest and enjoyment.
 - Fatiguability.
- Other common features:
 - Poor concentration.
 - Poor self-esteem and self-confidence.
 - Guilt.
 - Pessimism.
- Somatic features:
 - Sleep disturbance.
 - Early morning waking.
 - Morning depression.
 - Loss of appetite and/or weight loss.
 - Loss of libido.
 - Anhedonia (loss of the capacity to experience pleasure).
 - Agitation and/or retardation.



La Femme qui Pleure by Pablo Picasso, 1937. (© Estate of Pablo Picasso/Artists Rights Society [ARS], © 2004 Tate, London.)
 'Computers are useless. They can only give you answers.'
 Pablo Picasso (1881–1973).

Although the most common symptom of depression is depressed mood, many patients never complain of this and instead present because of other cognitive, behavioural, or somatic symptoms. For example, they may present because they are feeling tired all the time, because they cannot concentrate on their job, or because they can no longer fulfil their marital or social obligations.

Mild depression is the commonest form of depression and tends to present, if at all, to GPs. The patient often complains of feeling depressed and tired all the time, and sometimes also of feeling stressed or anxious ('mixed anxiety-depression'). There are none of the somatic features of depression and, although suicidal thoughts can occur, self-harm is uncommon.

Moderate depression is the classic textbook description of depression that is often treated in primary care but that can be severe enough to be referred to a psychiatrist. Many if not most of the clinical features of depression are present to such an intense degree that the patient finds it difficult to fulfil his or her social obligations. Somatic features are present and anhedonia is characteristic. Suicidal ideation is common and may be acted upon.

Severe depression is an exaggerated form of moderate depression. It is characterised by intense negative feelings and psychomotor agitation or retardation. Depressive stupor may supervene upon psychomotor retardation, and urgent ECT treatment may be required (see later). Psychotic symptoms may be present in 10–25% and are usually mood-congruent, e.g. nihilistic delusions, delusions of guilt, delusions of poverty. Suicidal risk is high and, in the retarded patient, may be even more so once treatment is initiated and the mood begins to lift.

Dysthymia

Dysthymia is characterised by mild chronic depressive symptoms that are not sufficiently severe to meet the criteria for mild depressive disorder. Although dysthymia has sometimes been regarded as a 'depressive personality', genetic studies suggest that it is in fact a chronic, mild form of depressive disorder. If it develops into a depressive disorder, it is then referred to as 'double depression' (Fig. 5.7). Its lifetime prevalence is about 3% and, as it is a very chronic condition, its point prevalence is not actually very different. It is more common in females and in the divorced. Dysthymia may respond to drug treatment and to psychological treatments, although to date there is no firm evidence base for the latter.

In depression this faith in deliverance, in ultimate restoration, is absent. The pain is unrelenting, and what makes the condition intolerable is the foreknowledge that no remedy will come – not in a day, an hour, a month, or a minute. If there is mild relief, one knows that it is only temporary; more pain will follow. It is hopelessness even more than pain that crushes the soul. So the decision-making of daily life involves not, as in normal affairs, shifting from one annoying situation to another less annoying – or from discomfort to relative comfort, or from boredom to activity – but moving from pain to pain. One does not abandon, even briefly, one's bed of nails, but is attached to it wherever one goes.

William Styron (born 1925, Virginia), *Darkness Visible: A Memoir of Madness*

5

William Styron is also the author of *Sophie's Choice* and other novels.

When the shadow of the sash appeared on the curtains it was between seven and eight o'clock and then I was in time again, hearing the watch. It was Grandfather's and when Father gave it to me he said I give you the mausoleum of all hope and desire; it's rather excruciatingly apt that you will use it to gain the reducto absurdum of all human experience which can fit your individual needs no better than it fitted his or his father's. I give it to you not that you may remember time, but that you might forget it now and then for a moment and not spend all your breath trying to conquer it. Because no battle is ever won he said. They are not even fought. The field only reveals to man his own folly and despair, and victory is an illusion of philosophers and fools.

William Faulkner (born 1897, Mississippi; died 1962, Mississippi), *The Sound and the Fury* (1929), winner of the Nobel Prize for Literature 1949

Faulkner's depressive disorder may have influenced this celebrated nihilistic passage.

Diagnosis

ICD-10 criteria for depressive episode

In typical depressive episodes of all three varieties described in ICD-10 (mild, moderate, and severe), the individual usually suffers from depressed mood, loss of interest and enjoyment, and reduced energy, leading to increased fatigability and

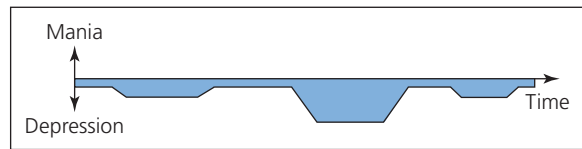


Figure 5.7 Dysthymia and double depression.

diminished activity. Marked tiredness after only slight effort is common. Other common symptoms are:

- (a) *Reduced concentration and attention.*
- (b) *Reduced self-esteem and self-confidence.*
- (c) *Ideas of guilt.*
- (d) *Pessimism.*
- (e) *Ideas of self-harm or suicide.*
- (f) *Disturbed sleep.*
- (g) *Poor appetite.*

Mood varies little from day to day and is often unresponsive to circumstances. In some cases, anxiety, distress, and motor agitation may be more prominent than depressed mood. For depressive episodes of all three grades of severity a duration of at least two weeks is usually required for diagnosis, but shorter periods may be sufficient if symptoms are unusually severe and of rapid onset. The categories of mild, moderate, and severe depressive episodes should only be used for a single (first) depressive episode, and further episodes should be classified under one of the subdivisions of recurrent depressive disorder.

ICD-10 criteria for mild depressive episode

At least two of depressed mood, loss of interest and enjoyment, and increased fatigability should be present, plus at least two of the other symptoms described above, for a minimum period of two weeks. None of the symptoms should be present to an intense degree.

ICD-10 criteria for moderate depressive episode

At least two of the three most typical symptoms noted for a mild depressive episode should be present, plus at least three (and preferably four) of the other symptoms, for a minimum of two weeks. Several symptoms are likely to be present to an intense degree.

An individual with a moderately severe depressive episode will usually have considerable difficulty in continuing with social, work, or domestic activities.

ICD-10 criteria for severe depressive episode

There is considerable distress or agitation, unless retardation is a marked feature. Loss of self-esteem and feelings of uselessness or guilt are likely to be prominent, and suicide is a distinct danger in particularly severe cases. Psychotic symptoms may be present and are usually mood-congruent.

DSM-IV criteria for major depressive episode

- A** Five or more of the following symptoms have been present for the same **two-week** period and represent a change from previous functioning; at least one of the symptoms is either depressed mood, or loss of interest or pleasure:
- A** Depressed mood most of the day, nearly every day.
 - B** Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day.
 - C** Significant weight loss or weight gain or decrease or increase in appetite.
 - D** Insomnia or hypersomnia.
 - E** Psychomotor agitation or retardation.
 - F** Fatigue or loss of energy.
 - G** Feelings of worthlessness or excessive or inappropriate guilt.
 - H** Diminished ability to think or concentrate.
 - I** Recurrent thoughts of death, recurrent suicidal ideation, or suicide attempt.
- B** Symptoms do not meet the criteria for a mixed episode.
- C** Symptoms cause significant distress or impairment to social, occupational, or other important areas of functioning.
- D** The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
- E** The symptoms are not better accounted for by bereavement.

DSM-IV criteria for major depressive disorder, single episode

- A** Presence of a single major depressive episode.
- B** The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorders, delusional disorder, or psychotic disorder not otherwise specified.
- C** There has never been a manic episode, a mixed episode, or a hypomanic episode.

NB: Does not apply if these episodes are substance- or treatment-induced or the direct physiological effects of a general medical condition.

DSM-IV criteria for major depressive disorder, recurrent

- A** Presence of two or more major depressive episodes.
- B** The major depressive episodes are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorders, delusional disorder, or psychotic disorder not otherwise specified.
- C** There has never been a manic episode, a mixed episode, or a hypomanic episode.

NB: Does not apply if these episodes are substance- or treatment-induced or the direct physiological effects of a general medical condition.

! Note that neither ICD-10 nor DSM-IV require the presence of depressed mood for a diagnosis of depressive disorder to be made.

5

Differential diagnosis

- Normal reaction to life event or situation or to fresh insight.

And I gave my heart to know wisdom, and to know madness and folly: I perceived that this also is vexation of spirit.

For in much wisdom is much grief: and he that increaseth knowledge increaseth sorrow.

Ecclesiastes 1:17–18 (KJV)

Psychiatric conditions

- Bereavement.
- Adjustment disorder.
- Seasonal affective disorder (SAD).
- Dysthymia.
- Cyclothymia.
- Bipolar disorder.
- Mixed affective states (during transition from mania to depression and vice versa).
- Schizoaffective disorder.
- Schizophrenia.
- Generalised anxiety disorder.
- Obsessive-compulsive disorder.
- Post-traumatic stress disorder.
- Eating disorder.

Medical or organic conditions

Organic causes of depression are common and often overlooked (see Table 5.1). They are best treated by treating the cause.

Clinical skills: assess a patient with low mood

- Introduce yourself to the patient.
- Explain that you are going to ask him some questions to uncover exactly how he is feeling, and ask for his consent to do so.
- Ensure that he is comfortable.
- First ask open questions about his current mood and feelings, listening attentively and gently encouraging him to open up.
- Ask about the onset of illness, and about its triggers or causes.

Aim to cover:

- The core features of depression:
 - Depressed mood.
 - Loss of interest.
 - Fatiguability.
- The other common features of depression:
 - Poor concentration.
 - Poor self-esteem and self-confidence.
 - Guilt.
 - Pessimism.
- The somatic features of depression:
 - Sleep disturbance.
 - Early morning waking.
 - Morning depression.
 - Loss of appetite and/or weight loss.
 - Loss of libido.
 - Anhedonia.
 - Agitation and/or retardation.
- Ask about anxiety, obsessions, hallucinations, delusions, and mania, to exclude other possible psychiatric diagnoses.
- Take brief past psychiatric, past medical, drug, and family histories.
- Assess the severity of the illness and the effect that it is having on everyday life.
- **Ask about suicidal intent.** If he is suicidal, assess suicidal intent (see Chapter 6).
- Ask him if there is anything he might add that you have forgotten to ask about.
- Thank him and offer him a further course of action.

Adapted from *Clinical Skills for OSCEs* (2003), N. Burton *et al.*

Management

Investigations

Laboratory investigations should be ordered on a case-by-case basis to exclude potential medical or organic causes of depression (see above). Laboratory investigations to consider include full blood count (FBC), urea and electrolytes (U&Es), liver function tests (LFTs), thyroid-stimulating hormone (TSH), erythrocyte sedimentation rate (ESR), vitamin B₁₂ and folate, toxicology screen, antinuclear antibody, HIV test, and dexamethasone suppression test. A CT or MRI scan of the brain might also be considered if clinically indicated.

Treatment

Methods of treatment include:

- Antidepressants:
 - Serotonin-selective reuptake inhibitors (SSRIs).
 - Tricyclic antidepressants (TCAs).
 - Monoamine oxidase inhibitors (MAOIs) and reversible MAOIs.
 - Other antidepressants.
- Other drugs.
- Electroconvulsive therapy.
- Psychological and social treatments.

Antidepressants

History of antidepressants

The first MAOI, iproniazid, was originally developed in the 1950s as a treatment for tuberculosis. Although it revolutionised the treatment of depression, patients had to adhere to a strict diet to avoid its dangerous side-effects (see later).

The first TCA, imipramine, was originally developed in the late 1950s as a treatment for schizophrenia. Although patients no longer had to adhere to a strict diet, they continued to suffer from troublesome and potentially dangerous side-effects.

It took another 30 years for the next class of antidepressants to be developed, and the first SSRI, fluoxetine, only gained regulatory approval in 1987. Since then other classes of dual action and selective antidepressants have been developed, but their exact role in the treatment of depression remains to be established.

! Explanation and reassurance are an important part of treatment in all depressions, and in the acute milder depressions may be the only form of treatment that is needed.

If it is decided to start an antidepressant, several factors need to be considered in choosing it (Table 5.4). Although it is true that antidepressants are not a solution to life's problems, they do lift the patient's mood and give him a better chance to start addressing them.

The chosen antidepressant should be prescribed at its therapeutic dose and given for an adequate period of time (at least one month). After recovery, the antidepressant should be continued at the same dose for at least six months before being tapered off. Patients should be educated about antidepressants, not least because this significantly improves compliance. They should be told that antidepressants are effective in over 60% of patients but that they can take 10–20 days to start having an effect. Furthermore, it should be explained that although antidepressants are not addictive, they may have trouble-some side-effects that nevertheless tend to resolve in the first month of treatment (see later). If a patient fails to respond to an adequate trial of an antidepressant, check compliance. If the patient has been compliant, the diagnosis is not in doubt, and there are no significant perpetuating factors (e.g. hypothyroidism, alcoholism, social factors), increase the dose to the recommended maximum or tolerated dose. If the patient still fails to respond, try another drug from the same class or another drug from a different class. If the patient continues failing to respond, this is referred to as 'treatment-resistant depression'. A third antidepressant can be tried, although it is important to remember that antidepressants are not the only form of treatment for depression (see later).

Serotonin-selective reuptake inhibitors (SSRIs)

SSRIs such as fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, and escitalopram (the pharmacologically active *S*-enantiomer of citalopram) selectively inhibit the reuptake of serotonin (Fig. 5.8). Generally speaking, they are as effective as TCAs in the treatment of major depression, but may be less effective in the treatment of severe depression in in-patients. They have replaced TCAs as the first line of treatment, notably because of their lesser need for dose titration and their safety in overdose. They are particularly useful in the elderly and the physically ill,

Table 5.4 Factors that may be involved in choosing an antidepressant.

Factor	Explanation or example
Type and severity of symptoms	Prefer an SSRI for anxiety-depression Prefer a sedative antidepressant if there is insomnia
Suicidality	Avoid TCAs and MAOIs as they are more toxic in overdose
Age and physical health	Avoid TCAs in elderly and physically ill patients
Past history of elevated mood	All antidepressants may promote 'rapid cycling'* in bipolar disorder. This is, however, especially true of TCAs
Previous treatment	If a patient has had a previous positive response to an antidepressant, it should not be changed
Patient preference	Patients should be explained the principal side-effects of the main alternatives and given as much choice as possible
Pregnancy	Prefer the SSRI fluoxetine and the TCAs nortriptyline, amitriptyline, and imipramine in pregnancy, and the SSRIs paroxetine or sertraline in breastfeeding

* Rapid cycling refers to four or more episodes of mania, hypomania, and/or depression in a period of one year.
MAOI, monoamine oxidase inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

in mixed anxiety-depression, and in suicidal patients. The response rate to SSRIs is 55–70%, but improvement in mood may be delayed for 10–20 days. Side-effects include dry mouth, nausea, vomiting, diarrhoea, dizziness, sedation, sexual dysfunction, agitation, akathisia, parkinsonism (rare), and convulsions (rare). As fluoxetine, fluvoxamine, and paroxetine are potent inhibitors of the cytochrome P450 isoenzymes, they can also cause important pharmacokinetic drug interactions.

The **SSRI discontinuation syndrome** consists of headache, dizziness, shock-like sensations, paraesthesia, gastrointestinal symptoms, lethargy, insomnia, and change in mood (depression, anxiety/agitation), and occurs most frequently after the abrupt discontinuation of paroxetine. Note that the fact that a discontinuation syndrome has been described does *not* mean that SSRIs are 'addictive'.

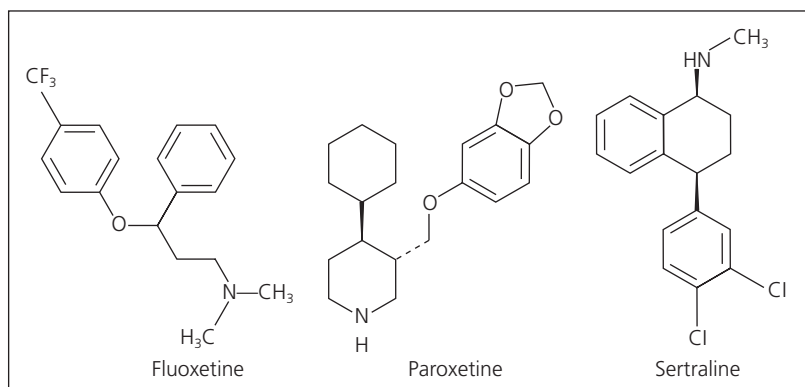


Figure 5.8 Chemical structures of selected SSRIs.

5

! Serotonin syndrome

The **serotonin syndrome** is a rare but potentially fatal acute syndrome resulting from increased serotonin (5-HT) activity. It is most often caused by SSRIs but can be caused by other drugs too, e.g. TCAs or lithium.

Symptoms include:

- Psychological symptoms: agitation, confusion.
- Neurological symptoms: nystagmus, myoclonus, tremor, seizures.
- Other symptoms: hyperpyrexia, autonomic instability.

The principal differential of serotonin syndrome is from neuroleptic malignant syndrome. Management involves the discontinuation of the drug and institution of supportive measures.

Tricyclic antidepressants (TCAs)

TCAs inhibit the reuptake of noradrenaline and serotonin and also have antagonist activities at a variety of neurotransmitter receptors. As their name suggests, they have a three-ringed structure with an attached side chain (Fig. 5.9). Tertiary amines such as amitriptyline, imipramine, and clomipramine are more sedating and cause more anticholinergic side-effects than secondary amines such as nortriptyline, dothiepin, and lofepramine. See Table 5.5 for other common side-effects. Plasma monitoring may be indicated in certain circumstances, e.g. lack of therapeutic response, coexisting medical disorder, or possibility of drug interaction. Although TCAs may be more effective in severe depression in in-patients compared to SSRIs, they must be used cautiously in the elderly and the physically ill, and should be avoided in suicidal patients. Principal contraindications are cardiovascular disease (TCAs delay ventricular conduction time), severe liver disease, glaucoma,

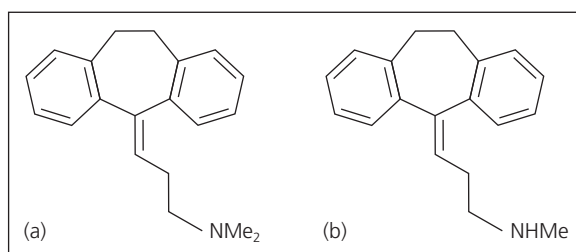


Figure 5.9 Chemical structures of (a) amitriptyline and (b) nortriptyline.

and prostatic hypertrophy. Important drug interactions include dental anaesthetics containing lignocaine (lidocaine) and MAOIs. The response rate to TCAs is 55–70% but improvement in mood may be delayed for 10–20 days. Better sleep is usually the first sign of improvement.

Table 5.5 Principal side-effects of tricyclic antidepressants.

Anticholinergic	Dry mouth, blurred vision, glaucoma, constipation, urinary retention
Antihistaminergic	Sedation, weight gain
α-Noradrenergic blockade	Sedation, postural hypotension
5-HT₂ blockade	Weight gain, sexual dysfunction
Cardiotoxic	Arrhythmias,* myocardial depression
Neurotoxic	Delirium, movement disorders, convulsions

* Electrocardiograph changes indicative of cardiotoxicity include prolonged PR and QT intervals, and ST segment and T-wave changes.

Monoamine oxidase inhibitors (MAOIs)

Patients on irreversible MAOIs (phenelzine, isocarboxylic acid, and tranylcypromine) must adhere to strict dietary and drug restrictions to avoid the so-called tyramine (or 'cheese and chianti') reaction – a hypertensive crisis that can result in subarachnoid haemorrhage. For this reason MAOIs are seldom used, and are generally reserved for the treatment of atypical depression (depression with increased sleep, appetite, and phobic anxiety), resistant depression, and phobic anxiety states.

! The **tyramine reaction** can be caused by:

- Tyramine-containing foods such as cheese (except cottage cheese and ricotta), game, yeast extracts, broad bean pods, pickled herring, beef or chicken liver, and some alcoholic drinks.
- Sympathomimetic drugs, e.g. non-prescription cold remedies.

tyramine. There are two isoforms of monoamine oxidase enzymes, MAO-A and MAO-B. Moclobemide is a reversible MAOI that binds selectively to MAO-A, leaving MAO-B free to metabolise tyramine and eliminating the need for dietary restrictions.

Other side-effects of MAOIs include anticholinergic side-effects, weight gain, insomnia, postural hypotension, tremor, paraesthesia of the limbs, and peripheral oedema.

! A TCA or SSRI should not be started until two weeks after stopping a MAOI (three weeks in the case of clomipramine or imipramine). Conversely, a MAOI should not be started until at least 7–14 days after a TCA or SSRI has been stopped (three weeks in the case of clomipramine or imipramine, five weeks in the case of fluoxetine). Other drugs that interact with MAOIs include pethidine, barbiturates, and insulin.

MAOIs inactivate monoamine oxidase enzymes that oxidise noradrenaline, serotonin (5-HT), dopamine, and

Other antidepressants

Table 5.6 lists some of the other available antidepressants.

Table 5.6 Other antidepressants.

Antidepressant	Class	Notes
Venlafaxine	Serotonin and noradrenaline reuptake inhibitor (SNRI)	Thought to have a more rapid onset of action and greater efficacy than SSRIs, especially in severe depressive disorder Similar side-effect profile to SSRIs; may cause hypertension and heart disease Venlafaxine should not be used in patients with heart disease, uncontrolled hypertension, or electrolyte imbalance Relatively safe in overdose
Reboxetine	Noradrenaline reuptake inhibitor (NARI)	Highly specific noradrenaline reuptake inhibitor Thought to be more effective than SSRIs in severe depression Often used as second line treatment for depression Less likely than SSRIs to trigger mania in bipolar depression or convulsions in epilepsy Commoner side-effects are dry mouth, constipation, and insomnia Safe in overdose
Mirtazapine	Noradrenaline and serotonin-specific antidepressant (NaSSa)	Enhances noradrenergic and serotonergic neurotransmission but no significant effect on reuptake of monoamines Tends to be used as second line treatment for depression Commoner side-effects are weight gain, sedation, and dry mouth. Mirtazapine becomes <i>less</i> sedative as the dose is increased Less sexual side-effects Safe in overdose
Trazodone	Phenylpiperazine	Weak serotonin reuptake inhibitor Mildly sedating, priapism in 0.1% Safe in overdose Commonly used in the elderly

Other drugs

Lithium, tryptophan, triiodothyronine, buspirone (a 5-HT_{1A} partial agonist), or pindolol (a beta blocker and 5-HT_{1A} antagonist) can be used to augment antidepressant treatment.

Antipsychotics can be used in addition to antidepressants if there are psychotic symptoms.

Electroconvulsive therapy (ECT)

History of ECT

In pre-modern times it was observed that convulsions induced by camphor could improve schizophrenia and depression. In 1933, the German psychiatrist Sakel began the practice of using insulin injections to induce convulsions, but a period of panic and impending doom prior to convulsing made the treatment very difficult to tolerate. The Hungarian psychiatrist Meduna replaced insulin by metrazol, but similar problems remained. Then in 1938 the Italian neuropsychiatrist Cerletti began the practice of using electric shocks. Cerletti's method, first tested on a vagrant that he found at the train station in Rome, soon superseded Sakel's insulin injections and Meduna's metrazol injections as the most popular (or least unpopular) method of inducing convulsions. The advent of suitable short-acting anaesthetics and muscle relaxants in the 1950s made the electric shocks much safer by reducing complications such as muscle pains and bone fractures. Since then many drugs have been invented, but ECT is still occasionally used as an alternative form of treatment. Its mechanism of action is unclear, although it is known to decrease 5-HT₁ and increase 5-HT₂ receptors in the brain.

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Indications

Table 5.7 lists the main indications for the use of ECT.

Contraindications

! As it is a potentially life-saving treatment, there are no absolute contraindications to ECT.

Relative contraindications include:

- Raised intracranial pressure.
- Cardiovascular disease.
- Dementing illnesses.

Table 5.7 Indications for ECT.

Indication	Notes
Depression	By far the most common indication for ECT. Especially indicated in the presence of psychotic features, pronounced psychomotor retardation, or high suicidal risk. Efficacy is <i>at least equal</i> to that of antidepressants and speed of action is faster
Mania	Use restricted to acute mania that is refractory to drug treatment or if drug treatment is contraindicated
Schizophrenia	Use is uncommon and restricted to acute episodes of schizophrenia in the presence of catatonia or affective symptoms

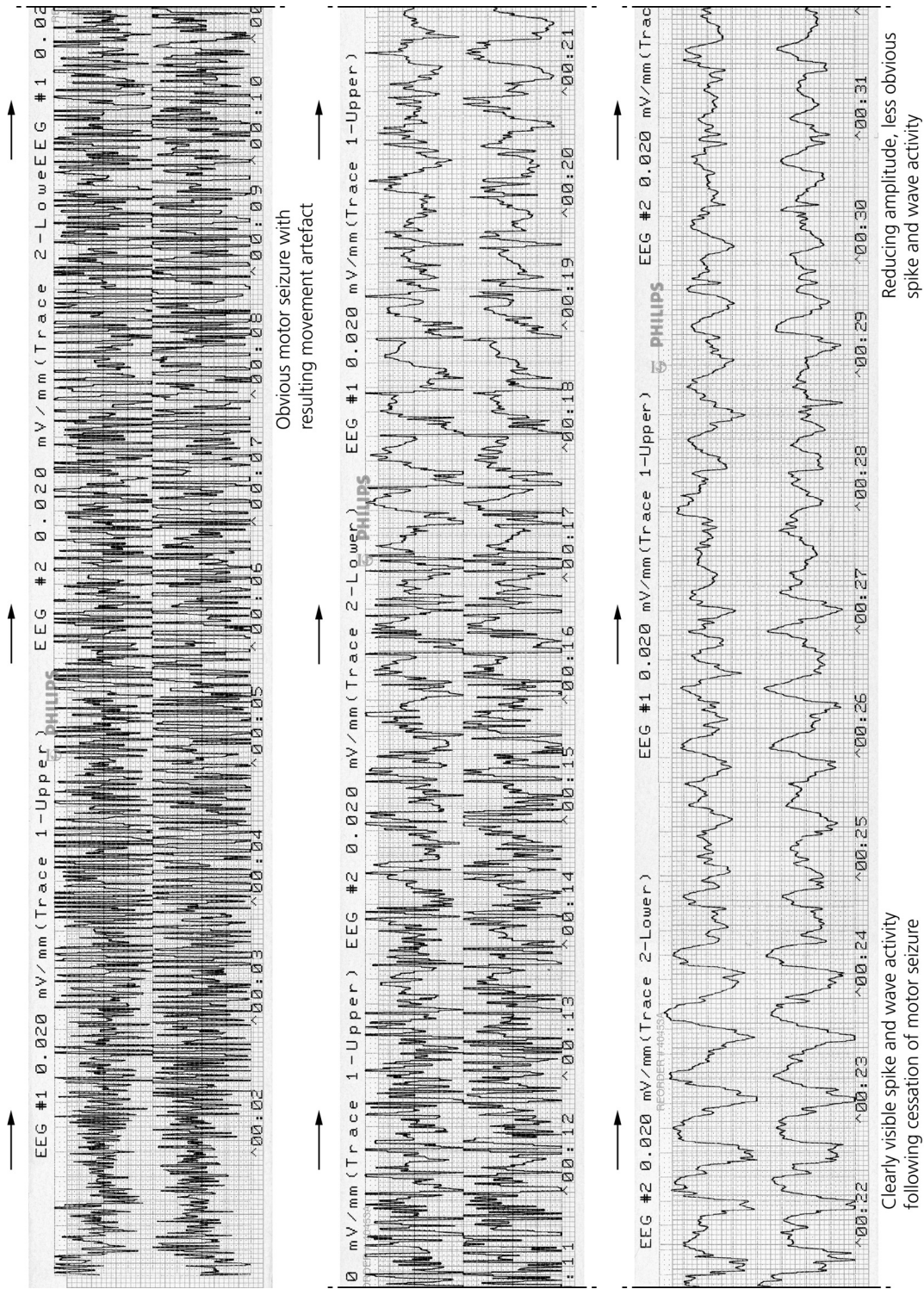
- Epilepsy and other neurological disorders.
 - Cervical spine disease.
- Pregnancy and old age are *not* contraindications to ECT.

Method

The patient has a standard anaesthetic such as propofol and a muscle relaxant such as suxamethonium, and the seizure duration is monitored using an electroencephalograph (EEG) recording (Fig. 5.10). The modern approach is to deliver constant current, brief-pulse ECT at a voltage that is above the patient's seizure threshold. The choice of bilateral or unilateral (usually right-sided) ECT should be made on a case-by-case basis as, although bilateral ECT is more effective than unilateral ECT, unilateral ECT has less cognitive side-effects. Most patients respond to a course of 4–8 ECT treatments, usually delivered over the course of 2–4 weeks. Prior to starting a course of ECT treatments, a patient should have a physical examination, an electrocardiograph (ECG), and blood tests including FBC and U&Es – and should be 'nil by mouth' from the previous midnight. Informed consent is needed except if being treated under the provision of the Mental Health Act (see Chapter 3).

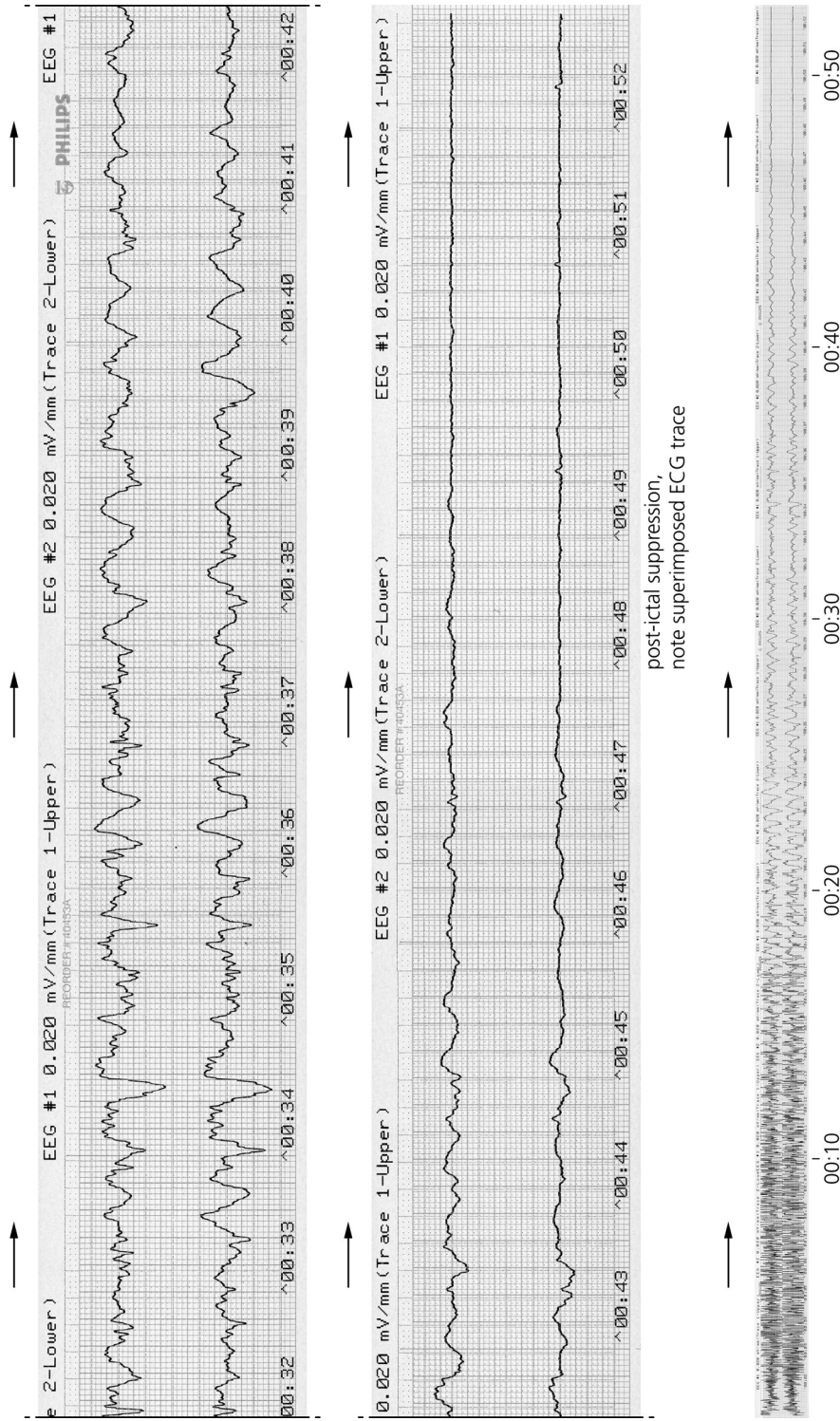
Common side-effects

- Side-effects of anaesthesia.
- Headache.
- Muscle aches.
- Nausea.
- Confusion.
- Temporary anterograde memory impairment.



(a) **Figure 5.10** EEG activity following the delivery of bilateral constant current, brief-pulse ECT at a voltage above the patients' seizure threshold. *Continued on next page.*

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(b) Figure 5.10 Continued.

Note that mortality is similar to that of general anaesthesia in minor surgical procedures and mostly results from cardiovascular complications such as arrhythmias. Although memory impairment is a recognised side-effect, most patients receiving ECT treatment actually feel their memory improving as their depression lifts. Interestingly, emerging evidence suggests that the use of repetitive transcranial magnetic stimulation (rTMS) may in some cases provide a safer alternative to ECT in depression and other psychiatric disorders.

Psychological and social treatments

Explanation and reassurance are an important part of treatment in all depressions, and in the acute milder depressions may be the only form of treatment that is appropriate. It should be stressed that depression is common and treatable and, especially, that it is not a sign of personal or moral failure. Although drug treatments are the most readily available treatment option, psychological and social treatments can in some cases be more effective. They are often preferred by patients because they are (correctly) seen to address underlying problems rather than simply treating symptoms. Types of psychological treatments that are most appropriate for depression are listed in Table 5.8. The type of psychological treatment that is chosen depends both on the patient

and on the resources available. Although there is no substantial evidence for a marked benefit from combining psychological treatment and drug treatment, this should be considered in treatment-resistant cases.

Course and prognosis

The average length of a depressive episode is about six months, but about 25% of patients have episodes of more than one year. After a first depressive episode, about 80% of patients have further depressive episodes. These episodes tend to become progressively longer and the interepisode intervals progressively shorter. About 10% of patients develop a chronic unremitting disorder, and about 10% of patients eventually have a manic episode and convert to bipolar affective disorder.

5

! The overall lifetime suicide rate for major depression is about 7% in males and 1% in females, but the figures for severe depression requiring in-patient treatment are significantly higher.

Pyotr Il'yich Tchaikovsky (1840–1893)

Born in 1840, the composer Tchaikovsky suffered from depression throughout most of his short life. He began suffering from depression after his mother died in 1854 and never completely recovered. During his depressive episodes, he experienced not only a pervasive melancholy, but also insomnia, lack of appetite, and other classic symptoms of depression. Although he suffered greatly from these symptoms, there is no doubt that he found in them a source of inspiration.

Tchaikovsky died only nine days after the première of his sixth symphony, the *Symphonie Pathétique*, a piece of inconsolable anguish and grief. Some say that he died from cholera and others, by suicide.

Table 5.8 Psychological treatments used in depression.

Psychological treatment	Involves
Counselling	Identification and resolution of current life difficulties Explanation, reassurance, and support
Cognitive-behavioural therapy	Identification of cognitive distortions and associated behaviours; cognitive restructuring
Interpersonal psychotherapy	A systematic and standardised treatment approach to personal relationships and life problems
Individual dynamic psychotherapy	Effecting change through a higher level of self-understanding
Family therapy	Effecting change by addressing the dysfunctional aspects of family relationships that precipitated the depressive episode

Puerperal disorders

The puerperium is characterised by unique hormonal and psychological stresses that lead to a number of clinically distinct psychiatric disorders.

Maternity blues

Maternity blues (also called 'baby blues') is a minor mood disturbance occurring in about 50% of mothers on the third or fourth day postpartum. The condition is more

common in primiparous mothers and is thought to result from a precipitous decline in sex steroids and the psychological stresses of childbirth and mothering. It consists of tearfulness, irritability, and – characteristically – lability of affect. No specific treatment other than explanation and reassurance is required, and the condition usually resolves spontaneously in a matter of days.

Postnatal depression

Postnatal depression occurs in about 10–15% of mothers in the first month postpartum. The condition is thought to result from the stresses of mothering, and from feelings of anxiety and guilt about caring for the baby. It is more common if the mother has a past psychiatric history or lacks social support. Tiredness, irritability, and anxiety are often more prominent than depressed mood, and the baby may be at short-term risk of neglect and harm. Treatment involves explanation and reassurance and, in some cases, antidepressants or psychological treatments. If hospital admission is required, it should be to a mother-and-baby unit so that the mother–baby relationship is maintained and bonding is not compromised.

Puerperal psychosis

Puerperal psychosis occurs in about 0.2% of mothers, and is more common if the mother is primiparous or has a psychiatric history or family history of psychiatric illness. Onset is about 7–14 days' postpartum. Puerperal psychosis can present in one of three clinical pictures: delirious, affective (bipolar disorder and schizoaffective disorder), and schizophreniform. The delirious picture results from puerperal sepsis and is in effect an organic psychosis. It has thus become relatively rare since the advent of antibiotics. Puerperal psychosis puts the baby at high risk of neglect and harm. The mother may be deluded about the baby and may, for example, believe that it is abnormal or evil. Hospital admission is often required

Table 5.9 Puerperal disorders compared in terms of incidence and time of onset post-partum

Puerperal disorder	Incidence (%)	Time of onset post-partum
Maternity blues	50	3–4 days
Postnatal depression	10–15	<1 month
Puerperal psychosis	0.2	7–14 days

and treatment involves antidepressants and antipsychotics. ECT often leads to a dramatic recovery and may, depending on clinical features and severity, be the treatment of choice. Although most cases recover, the relapse rate for puerperal affective disorders is 25%.

Mania and bipolar affective disorder

Nessun maggior dolore
 Che ricordarsi del tempo felice
 Nella miseria.
*[There is no greater pain
 Than to recall happy times
 In times of misery.]*

Dante, *Inferno*, V

! Reminder

According to ICD-10, bipolar affective disorder consists of repeated (two or more) episodes of depression and mania or hypomania. In the absence of episodes of mania or hypomania, the diagnosis is one of recurrent depressive disorder. In the absence of episodes of depression, the diagnosis is either one of bipolar affective disorder or hypomania – i.e. **recurrent episodes of mania are diagnosed as bipolar affective disorder**. In DSM-IV a single episode of mania is sufficient to meet the criteria for bipolar disorder.

Epidemiology

The lifetime risk for bipolar disorder ranges from 0.3% to 1.5% and because bipolar disorder is a chronic disorder, the prevalence rate is fairly similar. All races and both sexes are equally affected. The mean age of onset is 21 years and, although the age of onset is variable, a first episode of mania after the age of 50 should lead to an investigation for a primary cause such as organic brain disease or endocrine and metabolic disorders. Interestingly, the prevalence rate is higher in higher socioeconomic groups and, it is thought, in creative artists. In *Touched by Fire: Manic Depressive Illness and the Artistic Temperament*, Kay Redfield Jamison estimates the prevalence of bipolar affective disorder to be 10–40 times higher amongst artists than amongst the general public.

I am come of a race noted for vigor of fancy and ardour of passion. Men have called me mad; but the question is not yet settled, whether madness is or is not the loftiest intelligence – whether much that is glorious – whether all that is profound – does not spring from disease of thought – from moods of mind exalted at the expense of the general intellect. They who dream by day are cognizant of many things which escape those who dream only by night. In their grey visions they obtain glimpses of eternity . . . They penetrate, however ruderless or compassless, into the vast ocean of the 'light ineffable'.

Edgar Allan Poe, quoted in Kay Redfield Jamison,
*Touched by Fire: Manic Depressive Illness and
the Artistic Temperament*

Aetiology

Genetics

First-degree relatives of a bipolar patient have an approximate 10% lifetime risk of bipolar affective disorder, and also have increased risks of unipolar depression and schizoaffective disorder. The concordance rate for bipolar affective disorder in monozygotic twins is 79% (higher than in either depressive disorders or schizophrenia), as compared to only 19% in dizygotic twins. Furthermore, children of bipolar patients remain at increased risk of affective disorders even after adoption by unaffected foster parents. There is thus a strong genetic component to the aetiology of bipolar affective disorder (stronger than in any other psychiatric disorder). The inheritance pattern is most likely to be polygenic, but more research is needed to identify the genes involved.

Neurochemical abnormalities

The monoamine hypothesis of depression suggests that mania results from increased levels of noradrenaline, serotonin, and dopamine, and it has been observed that drugs such as cocaine and amphetamines can exacerbate mania. Unfortunately, neurochemical abnormalities in mania have not been as extensively studied as in depression.

Other neurological abnormalities

Findings of neuroimaging studies suggest ventricular enlargement and structural abnormalities in the pre-

frontal cortex, striatum, and amygdala, but these findings are inconsistent.

Life events/environmental factors

Life events, severe stresses, and disruptions in the circadian rhythm may provoke the onset of a first manic or hypomanic episode, and it has been established that there is an increased risk of manic episodes in the early postpartum period. There is also an excess of manic episodes in late spring and summer.

Clinical features of mania or manic episode

As previously noted, bipolar affective disorder consists of repeated (two or more) episodes of depression and mania or hypomania. Manic episodes usually begin abruptly and last for a median duration of about four months. Depressive episodes last for a median duration of about six months and rarely last for more than a year, except in the elderly. The frequency and severity of episodes is very variable, as is the proportion of manic to depressive episodes. **Rapid cycling** is more common in females and refers to four or more episodes of mania, hypomania, and/or depression in a period of one year (DSM-IV only).

5

Clinical skills: mental state examination in mania

Appearance	<i>Colourful clothing, unusual combinations of clothing, too much make-up</i>
Behaviour	<i>Hyperactive, entertaining, flirtatious, hypervigilant, assertive, aggressive</i>
Speech	<i>Pressured speech, neologisms, clang associations</i>
Mood/affect	<i>Euphoric, irritable, labile</i>
Thought	<i>Optimistic, self-confident, grandiose, pressure of thought, flight of ideas, loosening of associations, circumstantiality, tangentiality, mood-congruent delusions or less commonly mood-incongruent delusions</i>
Perception	<i>Hallucinations</i>
Cognition	<i>Poor concentration but intact memory and abstract thinking</i>
Insight	<i>Very poor insight</i>

Pressure of thought

I roll on like a ball, with this exception, that contrary to the usual laws of motion I have no friction to contend with in my mind, and of course have some difficulty in stopping myself when there is nothing else to stop me . . . I am almost sick and giddy with the quantity of things in my head – trains of thought beginning and branching to infinity, crossing each other, and all tempting and wanting to be worked out.

John Ruskin, quoted in Kay Redfield Jamison, *Touched by Fire: Manic Depressive Illness and the Artistic Temperament*

Flight of ideas

They thought I was in the pantry at home . . . Peekaboo . . . there's a magic box. Poor darling Catherine, you know, Catherine the Great, the fire grate, I'm always up the chimney. I want to scream with joy . . . Hallelujah!

Andrew Sims, *Symptoms in the Mind: An Introduction to Descriptive Psychopathology* (1988)

Case study

Ten months ago Mrs S, a community psychiatric nurse, started feeling brighter and more energetic. At work she took on many extra hours and extra rôles, but to her surprise one of her colleagues reported her as unsafe. She promptly resigned, claiming that she needed more time to devote to her many plans and projects. By then she couldn't stop her thoughts from racing and was sleeping only three or four hours a night. She rented a launderette and set out to transform it into a multipurpose centre. Then she bought three houses to rent out to the poor. She became very outgoing and acted completely out of character, dressing garishly, smoking marijuana, and getting herself arrested for being 'drunk and disorderly'. Four months ago her mood began dropping and she felt dreadful and ashamed. Today she is feeling better but has had to sell her house to pay off her debts. Her psychiatrist suggested that she start on a mood stabiliser, but she is understandably reluctant to take his advice.

Hypomania

Hypomania is a lesser degree of mania and as such its clinical features are very similar to those of mania. **The mood is elevated, expansive, or irritable but, in contrast to mania, there are no psychotic features and no**

marked impairment of social functioning. The differential diagnosis of hypomania includes mania, cyclothymia, hyperthyroidism, anorexia, and agitated depression. Hypomania may herald mania, and in such cases the diagnosis should be one of just mania.

Cyclothymia

Cyclothymia can be described as mild chronic bipolar affective disorder and is characterised by numerous episodes of mild elation and mild depressive symptoms that are not sufficiently severe or prolonged to meet the criteria for bipolar depression or recurrent depressive disorder. Cyclothymia usually develops in early adult life and is more common in the relatives of bipolar disorder patients. Unless it progresses to bipolar affective disorder (15–50% of cases), it rarely comes to medical attention.

Diagnosis

ICD-10 criteria for manic episode

ICD-10 specifies three degrees of severity for manic episode: **hypomania, mania without psychotic symptoms, and mania with psychotic symptoms.**

ICD-10 criteria for hypomania

A lesser degree of mania in which abnormalities of mood and behaviour are too persistent and marked to be included under cyclothymia but are not accompanied by hallucinations or delusions. There is a persistent mild elevation of mood (for at least several days on end), increased energy and activity, and usually marked feelings of well-being and both physical and mental efficiency. Increased sociability, talkativeness, overfamiliarity, increased sexual energy, and a decreased need for sleep are often present but not to the extent that they lead to severe disruption of work or result in social rejection. Irritability, conceit, and boorish behaviour may take the place of the more usual euphoric sociability.

ICD-10 criteria for mania without psychotic symptoms

Mood is elevated out of keeping with the individual's circumstances and may vary from carefree joviality to almost uncontrollable excitement. Elation is accompanied by increased energy, resulting in overactivity, pressure of speech, and a decreased need for sleep. Normal social inhibitions are lost,

attention cannot be sustained, and there is often marked distractability. Self-esteem is inflated, and grandiose or over-optimistic ideas are freely expressed.

Perceptual disorders may occur, such as the appreciation of colours as especially vivid (and unusually beautiful), a preoccupation with fine details of surfaces or textures, and subjective hyperacusis. The individual may embark on extravagant and impractical schemes, spend money recklessly, or become aggressive, amorous, or facetious in inappropriate circumstances. In some manic episodes the mood is irritable and suspicious rather than elated.

The episode should last for at least one week and should be severe enough to disrupt ordinary work and social activities more or less completely.

DSM-IV criteria for manic episode

- A A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting as least one week (or any duration if hospitalisation is necessary).
- B During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
 - 1 Inflated self-esteem or grandiosity.
 - 2 Decreased need for sleep.
 - 3 More talkative than usual or pressure to keep talking.
 - 4 Flight of ideas or subjective experience that thoughts are racing.
 - 5 Distractability.
 - 6 Increase in goal-directed activity or psychomotor agitation.
 - 7 Involvement in pleasurable activities that can have painful consequences.
- C The symptoms do not meet criteria for a mixed episode.
- D The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to require hospitalisation to prevent harm to self or others, or there are psychotic features.
- E The symptoms are not due to a substance or a general medical condition.

DSM-IV criteria for hypomanic episode

- A A distinct period of persistently elevated, expansive, or irritable mood, lasting throughout at least four days, that is clearly different from the usual non-depressed mood.

- B During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
 - 1 Inflated self-esteem or grandiosity.
 - 2 Decreased need for sleep.
 - 3 More talkative than usual or pressure to keep talking.
 - 4 Flight of ideas or subjective experience that thoughts are racing.
 - 5 Distractability.
 - 6 Increase in goal-directed activity or psychomotor agitation.
 - 7 Involvement in pleasurable activities that can have painful consequences.

NB: These symptoms are exactly the same as those listed under manic episode.

- C The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.
- D The disturbance in mood and the change in function are observable by others.
- E The episode is not severe enough to cause marked impairment in social or occupational functioning, or to require hospitalisation, and there are no psychotic features.
- F The symptoms are not due to a substance or general medical condition.

DSM-IV criteria for mixed episode

- A The criteria are met both for a manic episode and for a major depressive episode (except for duration) nearly every day during at least a one-week period.
- B The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to require hospitalisation to prevent harm to self or others, or there are psychotic features.
- C The symptoms are not due to a substance or a general medical condition.

Differential diagnosis

Psychiatric disorders

- Mixed affective states (simultaneous manic and depressive symptoms).
- Schizoaffective disorder.
- Schizophrenia.
- Cyclothymic disorder.

- Attention-deficit hyperactivity disorder.
- Drugs such as alcohol, amphetamines, cocaine, hallucinogens, antidepressants, L-dopa, steroids.

Medical/neurological disorders

- Organic brain disease of the frontal lobes such as cerebrovascular accident, multiple sclerosis, intracranial tumours, epilepsy, AIDS, neurosyphilis.
- Endocrine disorders, e.g. hyperthyroidism, Cushing's syndrome.
- Systemic lupus erythematosus.
- Sleep deprivation.

Management

5

Investigations

Laboratory investigations should include a serum and/or urine drug screen, liver, renal, and thyroid function tests, FBC, ESR, and a urine test (including pregnancy test). The aim of these investigations is to rule out drug abuse, establish baselines for the administration of mood-stabilising medication, and uncover possible medical causes for the patient's symptoms. Other, more specific, investigations such as antinuclear antibody and urine copper level should be considered on a case-by-case basis. A pretreatment ECG is important prior to starting lithium and some other drugs. If the patient is already on lithium, a lithium level should be taken.

Treatment

Methods of treatment:

- Mood-stabilising and other drugs.
- Electroconvulsive therapy.
- Psychosocial treatments.

Mood-stabilising and other drugs

Choice of medication in bipolar affective disorder is to a large extent determined by the patient's current symptoms.

- **Acute manic episode:** antipsychotics, benzodiazepines, and mood stabilisers such as lithium, valproate, carbamazepine.
- **Acute depressive episode:** antidepressants and mood stabilisers. Note that antidepressants alone may over-treat the patient into mania.

- **Maintenance treatment to prevent relapses:** mood stabilisers.

The Australian John Cade described the antimanic properties of lithium in 1949, but the drug took another 20 years to enter mainstream practice. Today it is commonly used for the prophylaxis of classic bipolar disorder and recurrent depressive disorder, and in the treatment of acute manic/hypomanic episodes. It is also the only mood stabiliser that has been demonstrated to have a specific antisuicide effect. Despite its popularity and number of side-effects, its mode of action is unclear. It is understood to have a range of effects in the central nervous system, including effects on cation transport, intracellular second messenger systems, and certain neurotransmitters and neurotransmitter receptors.

Lithium should only be started if there is a clear intention to continue it for at least three years, as poor compliance and intermittent treatment may precipitate rebound mania. The starting dose of lithium should be cautious and depends on several factors, including the preparation used (lithium carbonate or lithium citrate). Lithium is eliminated unchanged by the kidney and its half-life is related to renal function. It is therefore important to check renal function before starting the drug. The therapeutic range is **0.5–1.0 mmol/L** (0.8–1.0 mmol/L for the acute treatment of mania), although this can vary slightly from hospital to hospital.

! Toxic effects of lithium are usually experienced beyond 1.5 mmol/L and include gastrointestinal disturbances such as anorexia, nausea, vomiting, diarrhoea; nystagmus, coarse tremor, dysarthria, ataxia; and, in severe cases, loss of consciousness, seizures, and death.

Serum levels should be taken at 12 hours' postdose (usually in the morning) and monitored at 5–7-day intervals until the patient is stabilised, and at 3–4-monthly intervals thereafter. Renal and thyroid function should also be monitored.

Once started on lithium some patients stop taking it because of its side-effects (Table 5.9).

In addition to the side-effects listed in Table 5.9, lithium is teratogenic, and the risk of cardiovascular malformations in the foetus is 0.5/1000 to 1/1000 births. The most common cardiovascular malformation is Epstein's anomaly (downward displacement of the tricuspid valve into the right ventricle). As lithium is excreted into breast milk, breastfeeding is not advised.

Table 5.9 Side-effects of lithium.

Short-term effects	Long-term effects
Fine tremor	Weight gain
Gastrointestinal disturbances	Oedema
Muscle weakness	Goitre and hypothyroidism – check thyroid function tests before starting therapy and monitor every six months
Polyuria	Hyperparathyroidism
Polydipsia	Cardiotoxicity (T-wave flattening on ECG) – record baseline ECG before starting therapy
Stuffy nose, metallic taste in the mouth	Nephrogenic diabetes insipidus
	Irreversible renal damage – check U&Es before starting therapy and monitor every six months
	Exacerbation of acne and psoriasis
	Raised leucocyte and platelet count

Lithium has a response rate of 75% in the treatment of acute manic episodes, but takes several days to produce an effect. If tolerated and effective, it should be continued long term. If not, it can be stopped abruptly but, because of the risk of rebound mania, should only be stopped gradually over the course of 2–3 months after successful long-term treatment. Patients on lithium should be advised to drink plenty of fluids and to avoid reducing their salt intake, as dehydration and sodium depletion can precipitate lithium toxicity.

The use of anticonvulsants including valproate, carbamazepine, and lamotrigine in the prophylaxis of bipolar affective disorder is increasing. Anticonvulsants enhance the action of the inhibitory neurotransmitter gamma aminobutyric acid (GABA), but their precise mode of

Table 5.10 Some lithium–drug interactions.

Drug	Explanation
Carbamazepine	Can result in neurotoxicity; prefer valproate
Diuretics, especially thiazides	Sodium depletion increases lithium levels, resulting in lithium toxicity
NSAIDs	NSAIDs can increase lithium levels, resulting in lithium toxicity
ACE inhibitors	As above

ACE, acetylcholinesterase inhibitor; NSAIDs, non-steroidal anti-inflammatory drugs.

action in the prophylaxis of bipolar affective disorder is as yet unclear.

Valproate in the form of semisodium valproate (Depakote) is used alone or as an adjunct to lithium or other drugs in the treatment and prophylaxis of bipolar affective disorder, and in the USA has become the most frequently prescribed mood stabiliser. It produces a quicker onset of action than either lithium or carbamazepine, and is of particular benefit in rapid cycling bipolar affective disorder. Side-effects include nausea, tremor, sedation, weight gain, alopecia, blood dyscrasias, hepatotoxicity, and pancreatitis. Valproate can cause neural tube defects and other foetal malformations if used in pregnancy. The therapeutic range is 50–125 mg/L.

Carbamazepine is used in the treatment and prophylaxis of bipolar affective disorder, and is thought to be of particular value in treatment-resistant cases and in rapid cycling. Although in the UK it is sometimes regarded as a safer alternative to lithium, it can have potentially serious side-effects. These include nausea, headache, dizziness, sedation, diplopia, ataxia, skin rashes, rare but potentially fatal blood dyscrasias, and hepatotoxicity. Bloods should be monitored for leukopenia, hyponatraemia, and raised LFTs. Carbamazepine can cause spina bifida if used in pregnancy, but it is not excreted in breast milk and so can be used in breast-feeding mothers. As it is a strong inducer of hepatic microsomal enzymes, it increases the metabolism of many other drugs. The therapeutic range is 4–12 mg/L.

Atypical antipsychotics may also be used in the acute treatment of mania and in the prophylaxis of bipolar affective disorder, although specific licensing agreements for their use are evolving at the current time. Antidepressants can be used to treat depression but the risk of overtreatment to a hypomanic or manic episode is significant (this is the so-called ‘manic switch’).

! All the commonly used mood stabilisers (lithium, valproate, and carbamazepine) are teratogenic and should ideally be avoided in the first trimester of pregnancy.

Electroconvulsive therapy (ECT)

See earlier (p. 74).

Psychosocial treatments

Education about the symptoms, course, and treatment of the disorder, education about the importance of drug

compliance, advice about lifestyle (e.g. avoidance of triggers for relapse such as sleep deprivation and substance misuse), and identification of early signs of relapse are an important aspect of the patient's management.

Hospitalisation

Most cases of bipolar affective disorder can be managed on an out-patient basis. Hospitalisation is required in severe cases if the patient can no longer function in the community or if he is a danger to himself and/or to others.

Course and prognosis

The average length of a manic episode is about four months. After a first manic episode, about 90% of patients experience further manic and depressive episodes, and the interepisode interval tends to become progressively shorter. The prognosis is therefore quite poor, but is more so in rapid cycling, and less so in bipolar II. About 10% eventually commit suicide, but the rate of attempted suicide is significantly higher.

5

Virginia Woolf (1882–1941)

I married, and then my brains went up like a shower of fireworks. As an experience, madness is terrific I can assure you, and not to be sniffed at; and in its lava I still find most of the things I write about. It shoots out of one everything shaped, final, not in mere driblets as sanity does. And the six months . . . that I lay in bed taught me a good deal about what is called oneself.

Quoted from a letter from Virginia Woolf to her dear friend Ethel Smyth

She felt very young; at the same time unspeakably aged. She sliced like a knife through everything; at the same time was outside, looking on . . . far out to sea and alone; she always had the feeling that it was very, very dangerous to live even one day.

Virginia Woolf, *Mrs Dalloway*

Virginia Woolf, the novelist and member of the Bloomsbury Group, suffered from bipolar affective disorder from the age of 13. She committed suicide at the age of 59 by walking into the River Ouse with a large rock in her pocket (artistically portrayed

in *The Hours*, a film loosely based on the novel *Mrs Dalloway* and starring Nicole Kidman as Virginia Woolf). This is her suicide note to her husband and carer:

Dearest, I feel certain I am going mad again. I feel we can't go through another of those terrible times. And I shan't recover this time. I begin to hear voices, and I can't concentrate. So I am doing what seems the best thing to do. You have given me the greatest possible happiness. You have been in every way all that anyone could be. I don't think two people could have been happier till this terrible disease came. I can't fight any longer. I know that I am spoiling your life, that without me you could work. And you will I know. You see I can't even write this properly. I can't read. What I want to say is I owe all the happiness of my life to you. You have been entirely patient with me and incredibly good. I want to say that – everybody knows it. If anybody could have saved me it would have been you. Everything has gone from me but the certainty of your goodness. I can't go on spoiling your life any longer. I don't think two people could have been happier than we have been.
V.

Summary

Depressive disorders

Classification

- In ICD-10 depressive disorders are classified according to their severity into mild, moderate, severe, and psychotic depressive disorder.
- In DSM-IV the term 'major depression' is used instead of depressive disorder. Major depression is simply subclassified as single episode or recurrent.

Epidemiology

- The lifetime risk of depressive disorders is about 15%. The point prevalence is about 5%.
- Females are more affected than males by a ratio of about 2 : 1. Peak prevalence in males is in old age, but in females is in middle age.

Aetiology

- Genetic factors and environmental factors are both involved in the aetiology of depressive disorders.

- The monoamine hypothesis of depression suggests that depression results from underactivity of monoamine projections.
- Organic causes of depression include neurological conditions, endocrine conditions, metabolic abnormalities, infections, and drugs.

Clinical features

- The clinical features of depression can be divided into core features, other common features, and somatic features.
- Dysthymia is characterised by mild chronic depressive symptoms that are not sufficiently severe to meet the criteria for mild depressive disorder.

Differential diagnosis

- The differential diagnosis of depression is from other psychiatric disorders and from secondary depression (depression due to medical or organic causes).

Management

- Methods of treatment include antidepressants, other drugs, electroconvulsive therapy, and psychological and social treatments.
- Psychological and social treatments are often preferred by patients because they are seen to address underlying problems rather than simply treating symptoms.

Prognosis

- The average length of a depressive episode is about six months. After a first depressive episode, about 80% of patients have further depressive episodes.

Disorders of the puerperium

- Maternity blues occurs in about 50% of mothers on the third or fourth day postpartum.
- Postnatal depression occurs in about 10–15% of mothers in the first month postpartum.
- Puerperal psychosis occurs in about 0.2% of mothers at about 7–14 days postpartum.

Mania and bipolar affective disorder

Classification

- In DSM-IV a single episode of mania is sufficient to meet the criteria for bipolar disorder.
- Bipolar I consists of episodes of mania and major depression, bipolar II of episodes of hypomania and major depression.

Epidemiology

- The lifetime risk for bipolar disorder ranges from 0.3% to 1.5%. The mean age of onset is 21 years. All races and both sexes are equally affected.

Aetiology

- Although genetic factors and environmental factors are both involved in the aetiology of bipolar affective disorder, genetic factors play an especially important rôle.
- The monoamine hypothesis of depression suggests that mania results from overactivity of monoamine projections.

Clinical features

- The frequency and severity of episodes is very variable, as is the proportion of manic to depressive episodes.
- In hypomania the mood is elevated, expansive, or irritable but in contrast to mania, there are no psychotic features and no *marked* impairment of social functioning.
- Cyclothymia is characterised by numerous episodes of mild elation and mild depressive symptoms that do not meet the criteria for bipolar depression or recurrent depressive disorder.

Differential diagnosis

- The differential diagnosis of mania and bipolar affective disorder is from other psychiatric disorders, drugs, and medical and neurological conditions.

Management

- The choice of medication in bipolar affective disorder is to a large extent determined by the patient's current symptoms:
 - Antipsychotics, benzodiazepines, and/or 'mood stabilisers' for an acute manic episode.
 - Antidepressants and mood stabilisers for an acute depressive episode.
 - Mood stabilisers to prevent relapses.
- Psychological treatments include education about the symptoms, course, and treatment of the disorder, education about the importance of drug compliance, advice about lifestyle, and identification of early signs of relapse.

Prognosis

- After a first manic episode, about 90% of patients experience further manic and depressive episodes, and the inter-episode interval tends to become progressively shorter.

Recommended reading

- Darkness Visible: A Memoir of Madness* (2001) William Styron. Vintage.
- The Noonday Demon* (2002) Andrew Solomon. Vintage.
- Depressive Illness: The Curse of the Strong* (2003) Tim Cantopher. Sheldon Press.
- Churchill's Black Dog and other Phenomena of the Human Mind* (1997) Anthony Storr. HarperCollins.
- An Unquiet Mind* (1997) Kay Redfield Jamison. Picador.
- Touched with Fire: Manic Depressive Illness and the Artistic Temperament* (1996) Kay Redfield Jamison. Simon & Schuster.

Self-assessment

5

Simply answer with true or false. Answers on p. 172.

- 1 Poor self-esteem is a core feature of depression.
- 2 The peak prevalence of depressive disorders in females is in middle age.
- 3 Somatic presentations of depression are particularly common in Asian cultures.
- 4 Monoamine neurotransmitters include noradrenaline, serotonin, and GABA.
- 5 One of the vulnerability factors for depression is loss of a parent by death or separation before the age of 11.
- 6 According to attachment theory, depression results from loss of the loved object and mixed feelings of love and hatred (ambivalence).
- 7 Alcohol is a common cause of depressive symptoms.
- 8 The SSRI discontinuation syndrome occurs most frequently upon discontinuing imipramine.
- 9 The tyramine reaction is a hypertensive crisis that can result in subarachnoid haemorrhage.
- 10 Trazodone is a mildly sedating antidepressant that is commonly used in the elderly.
- 11 Pregnancy is a contraindication to ECT.
- 12 Interpersonal psychotherapy involves effecting change through a higher level of self-understanding.
- 13 In the DSM-IV classification, bipolar II consists of episodes of mania and major depression.
- 14 If a patient has only recurrent episodes of mania, a diagnosis of bipolar affective disorder can be made.
- 15 The concordance rate for bipolar disorder in monozygotic twins is higher than in either depressive disorders or schizophrenia.
- 16 The average length of a manic episode is six months.
- 17 Rapid cycling refers to four or more episodes of mania in a period of one year.
- 18 Serum levels of valproate should be taken at 12 hours' postdose and monitored at 5–7-day intervals until the patient is stabilised, and at 3–4-monthly intervals thereafter. Renal and thyroid function should also be monitored.
- 19 Toxic effects of lithium are usually experienced beyond 1.5 mmol/L.
- 20 Side-effects of carbamazepine include nausea, headache, dizziness, sedation, diplopia, ataxia, skin rashes, blood dyscrasias, and hepatotoxicity.