likely to persist despite efforts at treatment."[59] There is no convincing evidence that group treatment or behaviour therapy leads to good results in the majority of cases.[60]

Sadomasochism (F65.5)

The term "sadomasochism" denotes "a preference for sexual activity that involves bondage or the infliction of pain or humiliation ... Sexual sadism is sometimes difficult to distinguish from cruelty in sexual situations or anger unrelated to eroticism. Where violence is necessary for erotic arousal, the diagnosis can be clearly established."[61] There is no reliable information about prognosis and no evidence that any particular form of treatment is effective.

59 M. Gelder, *et al.*, *Oxford Textbook of Psychiatry* (Oxford University Press, 3rd ed., 1996), p.500.

60 *Ibid.*; V. Hartmann, "Notes on group therapy with paedophiles" *Canadian Psychiatric Association Journal* (1965) 10, 283–288; H.R. Beech, *et al.*, "Classical conditioning of a sexual deviation: a preliminary note" *Behaviour Therapy* (1971) 2, 400–402.

61 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.220.

22. Mood disorders

INTRODUCTION

In mood disorders, the fundamental disturbance is a change of mood to depression (with or without associated anxiety) or elation. This mood change is normally accompanied by a change in the overall level of activity and most other symptoms are either secondary to, or easily understood in the context of, such changes. Most of these disorders tend to be recurrent and the onset of individual episodes is often related to stressful events or situations.[1] Mood disorders tend to be cyclic in nature, with stable seasonal fluctuations in the incidence of suicide, and many depressed people experience diurnal variation of mood.

ASSESSMENT, DIAGNOSIS AND CLASSIFICATION

When a patient is examined prior to admission, or immediately following admission, the first task is to assess the kind of disorder (if any) which is troubling him so that, having identified it, conclusions can be reached about its causes, probable course, and treatment. Assessment is the process of collecting information relevant to the diagnosis, management, and treatment of a patient's clinical condition, including therefore this art of distinguishing the presence of a particular disorder, for example mania or depression, from the existence of a characteristic pattern of symptoms or manifestations. A diagnosis is a "short-hand way of describing what is wrong with the patient"[2] and involves assigning the patient's case to a predesignated diagnostic class according to some reliable medical classification of mental disorders.

Classifying mood disorders and using operational criteria

Because some symptoms are commonly features of a number of different conditions — for example, they may occur as symptoms of both schizophrenia and mood disorders — operational definitions specify which combinations of symptoms are adequate to substantiate a diagnosis. They define what a clinician or researcher means when he uses the term "depression" and hence represent a pragmatic approach to the problems of syndromes and an attempt to standardise clinical practice and understanding. Over the past two decades there has been a multiplication of classifications and diagnostic criteria to cope with the different conceptions of mood disorders.[3] Although a core of typical patients meet all of the definitions, there are significant differences in the populations of patients covered by each of them, and each generates

1 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.112.

2 J.M. Pfeffer and G. Waldron, *Psychiatric Differential Diagnoses* (Churchill Livingstone, 1987), p.4.

3 C. Thompson, *The Instruments of Psychiatric Research* (John Wiley & Sons, 1989), p.4.

different values for the incidence of the disorder, its heritability, its responsiveness to therapeutic agents, and its prognosis. The classification of mental disorders in official usage in England and Wales is the International Classification of Diseases, now in its tenth revision (ICD–10), and, more particularly, that part of it dealing with mental and behavioural disorders.

Mood and affect

A distinction is often drawn between an individual's mood and his affect (**1073**). A person's affect is how he appears to be emotionally affected by a particular idea or mental representation; for example, he is happy, sad or indifferent upon being given certain news. Mood is the pervasive and sustained emotion which colours an individual's whole personality and perception of events. Consequently, it is sometimes described as sustained affect and mood disorders are said to involve a morbid change of affect. It should, however, be emphasised that this distinction is not universally made. Some authorities use the words "affect" and "mood" interchangeably, in which case the terms affective disorder and mood disorder are synonymous.

Unipolar and bipolar disorders

Depression and mania may be viewed as lying at two opposite poles and classifications of mental disorder generally distinguish between unipolar and bipolar mood disorders. According to the classical model, the disturbed mood of some people will be confined to either depression or mania — unipolar disorder. The mood of other individuals is more variable, sometimes located at one pole (depression), sometimes at the other (mania). Mood disorders characterised by fluctuations of this kind are referred to as bipolar disorders and the patient's history characteristically includes one or more episodes of both depression and mania. In reality, of course, the mood of most people is rarely either equable — at the equator, to use the same analogy — or polar but located at some point in either hemisphere. When a person first experiences disordered mood, it is impossible to predict with certainty what course the illness will take and whether there will be subsequent episodes. In particular, it is not known whether his mood may later change from depression to mania, or vice-versa, and within what time scale. What is generally known is that a substantial proportion of patients have only one episode of illness and, consequently, single episodes are usually distinguished from bipolar and other multiple episode disorders. A serious initial depressive episode will be classified simply as a "depressive episode." Despite the multiplicity of classifications, a patient with a history of at least three separate episodes of psychotic depression, with complete remission in between and no history of mania, would satisfy the operational criteria for unipolar disorder in most classifications.

COURSE, TREATMENT AND OUTCOME

The risk of suicide is high in both unipolar and bipolar illness. The consensus of several studies suggests that the lifetime risk in manic-depressive illness is at least 15 per cent. and that it is greatest in the early years of illness.[4] Nevertheless, on average, mood disorders carry a considerably better prognosis than schizophrenia. Kendell summarises the position by writing that it "has been shown many times that

[4] S.B. Guze and E. Robins, "Suicide and primary affective disorders" *British Journal of Psychiatry* (1970) 117, 437–438.

patients with affective illness are more likely to make a full recovery from their original illness, spend less time in hospital both in the short and the long run, and experience less social deterioration than those with schizophrenia."[5] While there is some evidence that the interval between episodes gets progressively shorter as time goes on, in both unipolar and bipolar disorders,[6] these averages obscure considerable individual variation in terms of the risk of recurrence and the duration and spacing of successive episodes. Consequently, "the best estimate of the future is provided by [the patient's] own past history."[7] As to the effectiveness of available in-patient treatments, there is "little firm evidence that the long-term outlook of mood disorders has been improved by any of the therapeutic measures at our disposal. Despite the undoubted efficacy of ECT and tricyclic antidepressants in the acute treatment of depression there is little evidence that either treatment has reduced the suicide rate. And despite the proven ability of maintenance treatment with lithium or tricyclic antidepressants to reduce the risk of further episodes no one has yet demonstrated a reduction in the incidence of non-first episodes of either depression or mania in any geographically defined population."[8]

THE ICD–10 CLASSIFICATION OF MOOD DISORDERS

The classification of mental disorders in official usage in England and Wales is the International Classification of Diseases, now in its tenth revision (ICD–10), and, more particularly, that part of it dealing with mental and behavioural disorders. One section or "block" of the classification is concerned with "mood (affective) disorders" (Block F30–F39), within which each type and sub-type of disorder is separately coded. For example, a first manic episode is diagnosed as a "manic episode (code F30)" and a first depressive episode as a "depressive episode (F32)." In many instances, the particular diagnostic category includes different grades of severity, and depressive episodes are distinguished as mild, moderate or severe. These distinctions provide a useful general framework for tribunals because they help to gauge a disorder's severity and have implications for treatment. Inevitably, the ICD–10 classification involves "compromises between scientists with the most influential theories and the practice of senior clinicians at national and international level."[9]

MANIC EPISODES AND BIPOLAR DISORDERS

The ICD–10 classification notes that "bipolar affective disorder" is "characterised by repeated (*i.e.* at least two) episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (mania or hypomania), and on

[5] R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.447.

[6] J. Angst, *et al.*, "The course of monopolar depression and bipolar psychosis" *Psychiatria Neurologia Neurochirurgia* (1973) 76, 489–500.

[7] R.E. Kendell, "Diagnosis and classification," *supra*, p.447.

[8] *Ibid.*, p.448.

[9] J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.17.

others of a lowering of mood and decreased energy and activity (de[illegible]ion)."[10] While this is the characteristic pattern, it has been found that some 80–90 per cent of manic patients will eventually experience a full depressive episode, although the converse is not also true — only 10 per cent of patients suffering from depression will later have a manic episode. It is therefore relatively rare for patients to suffer only from repeated episodes of mania and even these patients resemble those who have at least occasional episodes of depression in terms of their family history, premorbid personality, age of onset, and long-term prognosis. Because this is so, patients who experience a second manic episode are, according to the ICD–10 classification, reclassified as suffering from a "bipolar affective disorder" rather than from recurrent manic episodes, despite the absence of any history of intervening depression.[11]

PERSONALITY DISORDERS AND BORDERLINE STATES

Some people are constitutionally inclined to feeling depressed or "high," seemingly either naturally low-spirited or high-spirited, so that a further problem when attempting to classify mood disorders is the precise relationship between an individual's personality and his mood. Legal and medical classifications of mental disorder generally distinguish between personality disorders and mental illnesses. In the former case, the individual's abnormal mental state is considered to be an expression of his normal — albeit, compared to other people, abnormal — personality, rather than the consequence of a depressive illness overlying and distorting that personality. Some people who are prone to depression may therefore be described as having a depressive personality disorder and treatment with antidepressants may have only a limited beneficial effect in such cases.

Borderline states and persistent mood disorders (F34)

It may nevertheless often be unclear whether a person's depression or unstable mood is a long-standing depressive illness distorting a previously well-adjusted, equable, personality or a manifestation of his ordinary personality. Various terms are used to describe such borderline states, *e.g.* affective personality disorder, cyclothymic personality, depressive neurosis, depressive personality disorder, neurotic depression, persistent anxiety depression. Contemporary descriptions of such states most often reflect the current diagnostic fashion rather than any advance in knowledge or understanding. At present, the idea of neurotic depression is out of vogue. The view enshrined in the latest revision of the International Classification of Mental Disorders (ICD–10) is that persistent mood disorders of this kind are genetically related to commonly accepted forms of mood disorder and sometimes amenable to the same treatments. At present, they are therefore grouped with mood disorders in the same treatments. At present, they are therefore grouped with mood disorders in the classification rather than as forms of personality disorder. For these reasons, persistent and usually fluctuating mood disorders which last for years at a time but in which individual episodes are rarely (if ever) so severe as to warrant being described as mild manic or depressive episodes are now categorised as "persistent mood (affective) disorders." Two kinds of persistent mood disorders are distinguished: cyclothymia and dysthymia.

[10] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.116.

[11] *Ibid.*

CYCLOTHYMIA AND DYSTHYMIA (ICD–10)

Synonyms	*Main features*
	F34.0 Cyclothymia
• affective personality disorder • cyclothymic personality • cycloid personality	A persistent instability of mood, involving numerous periods of mild depression and mild elation, which frequently fails to come to medical attention. The mood swings are usually perceived by the individual as being unrelated to life events. It may persist throughout adult life, cease temporarily or permanently, or develop into more severe mood swings meeting the criteria for bipolar affective disorder or recurrent depressive disorder.
	F34.1 Dysthymia
• depressive neurosis • depressive personality disorder • neurotic depression • persistent anxiety depression	Dysthymia has much in common with the concept of neurotic depression. The essential feature is a very long-standing depression of mood which is never, or only very rarely, severe enough to fulfil the criteria for recurrent depressive disorder of mild or moderate severity, although the criteria for mild depressive episode may have been fulfilled in the past, particularly at the onset of the disorder. Sufferers usually have periods of days or weeks when they describe themselves as well, but most of the time they feel tired and depressed; everything is an effort and nothing is enjoyed. They brood and complain, sleep badly and feel inadequate, but are usually able to cope with the basic demands of everyday life.

THE DIAGNOSTIC CATEGORIES

These observations or assumptions having been made, the classificatory scheme may be summarised as follows—

- Long-standing borderline mood disorders characterised by fluctuations of mood or depression are classified as cyclothymia and dysthymia respectively. However, if a person's mood is sufficiently disordered that he meets the criteria for a depressive or manic episode, this will be the appropriate diagnosis.

- Depressive episodes are distinguished according to their severity as mild, moderate or severe and, in the latter case, psychotic symptoms may or may not be evident. The severity of manic episodes are hypomania or mania and again, in the latter case, psychotic symptoms may or may not be present.

- If a person who has experienced a single depressive episode has a subsequent depressive episode the diagnosis is changed to that of a recurrent depressive disorder. However, if a person who has had a manic episode subsequently experiences either a depressive episode or a further manic episode, the diagnosis is

changed to that of bipolar affective disorder. This diagnosis will also be appropriate in cases where a person who has had a depressive episode subsequently experiences a manic episode.

- Where a patient's mental state during a single episode is highly variable — being characterised by either a mixture or a rapid alternation (usually within a few hours) of hypomanic, manic, and depressive symptoms — this is classified as a mixed affective episode.
- In certain cases, some features of the patient's illness may be characteristic of a mood disorder and other symptoms characteristic of schizophrenia, in which case a diagnosis of schizoaffective disorder (1247) may be made. In yet other cases, the patient's disturbed mood may be attributable to a physical disorder, such as a thyroid disorder, or to substance abuse, so that a different diagnosis is also appropriate.

CLASSIFICATION OF MOOD DISORDERS (ICD–10)

Type and Code	*Brief diagnostic guidelines*	*Sub-types and grades of severity*
• ***Persistent mood (affective) disorders (F34)***	Persistent, usually fluctuating, mood disorders lasting for years at a time, in which individual episodes are rarely (if ever) severe enough to warrant being described as hypomania or mild depressive episodes.	1. Cyclothymia (F34.0) 2. Dysthymia (F34.1)
• ***Depressive episode (F32)***	The category is only used for a single (first) depressive episode. Further depressive episodes are classified as recurrent depressive disorder.	1. Mild (F32.0) 2. Moderate (F32.1) 3. Severe without psychotic symptoms (F32.2) 4. Severe with psychotic symptoms (F32.3) The severity of the current depressive episode is graded using the scale set out in F32, *e.g.* "recurrent depressive disorder, current episode moderate."
• ***Recurrent depressive disorder (F33)***	If a manic episode occurs, the diagnosis is changed to bipolar affective disorder.	
• ***Manic episode (F30)***	The category is only used for a single manic episode.	1. Hypomania (F30.0) 2. Mania without psychotic symptoms (F30.1) 3. Mania with psychotic symptoms (F30.2) The severity of the current episode is graded using the scales set out in F30 and F32, *e.g.* "bipolar affective disorder, current episode hypomanic" or "bipolar affective disorder, current episode moderate depression."
• ***Bipolar affective disorder (F31)***	If there is a history of both manic and depressive episodes, or of more than one manic episode, the diagnosis is revised to bipolar affective disorder.	

DEPRESSION

Major depression is a serious life-threatening illness which is only partially understood. It is often particularly difficult for tribunals to deal with because of the co-existence in some cases of a wish to die together with little medical prospect of any cure. The nature of the illness in its severest form is vividly expressed by an anonymous patient at the Gartnavel Asylum in the 1850s,

> "In the acute form of the disease, the impulse may be as sudden and irresistible as if the victim was blown from a canon's mouth; in the more subdued, but more miserable form, it may be deliberate and slow — no haste, no hurry, but equally certain if left to itself; and no ray of hope pierces that deep sense darkness which weighs upon the soul like lead. Both of these states are the direct offspring of disease, whatever may have been the cause that produced it, and through one or other of these states the suicide must pass."[12]

EPIDEMIOLOGY

Depression affects some 10 per cent. of men and 20 per cent. of women at some stage during their lives and in any one year 2–3 per cent. of men and 5–10 per cent. of women will suffer from it. For about 3 persons in 1000 it is so severe as to result in a hospital admission and of those suffering from a major depressive illness some 15 per cent. will eventually commit suicide. The mean age of onset is 40 with 10 per cent. of new cases occurring in the over–60s and 50 per cent. prior to the age of 40. Depression is approximately twice as common in women as men. It is not clear whether this difference is biologically or socially determined although women in lower socio-economic groups are particularly likely to be affected. Approximately 15–20 per cent. of women suffer depression during the first six weeks after giving birth and between one-fifth and two-fifths of women admitted to a psychiatric unit during the postpartum period have a major depressive disorder. Unemployment is associated with an increased prevalence of depressive symptoms and depression is more common in urban than rural areas. There is no reliable evidence of significant differences in the incidence, prevalence or symptomatology of depression among people of different race or culture. There is, however, some evidence to suggest that the incidence of depression may be increasing rapidly in industrial countries, with a reduction in the age of the first episode.

AETIOLOGY AND PATHOLOGY

No known structural damage to the brain or other clear-cut aetiological factors account for depression and it can be regarded as a final common pathway which may have multiple causes, even in a single case. It should not be expected that so complex a phenomenon would have a single treatment or even that its treatment would be limited to one modality such as drugs.[13] Factors implicated in depression include genetic causes, biochemical imbalance, endocrine abnormalities, upbringing, and life events, such as divorce, separation and desertion.

---

12 Anon., *The Philosophy of Insanity* (1860). The nature of the illness is also captured in Tennyson's poem, "The two voices," in which he described his struggle to resist an inner voice urging him to suicide, and in poems by Hopkins ("O the mind, mind has mountains; cliffs of fall/ Frightful, sheer, no-man-fathomed") and Cowper ("Him the vindictive rod of angry Justice/ Sent quick and howling to the centre headlong;/ I, fed with judgement, in a fleshy tomb, am/ Buried above ground.")

13 E.S. Paykel, *Handbook of affective disorders* (ed. E.S. Paykel, Churchill Livingstone, 1992).

TERMINOLOGY

Depressive states are sometimes categorised as primary or secondary, retarded or agitated, psychotic or neurotic, endogenous or reactive, typical or atypical. Although some of these terms are now falling into disfavour, they will all be encountered in practice and their meaning is therefore considered here.

Primary and secondary depression

It remains common to distinguish between primary and secondary depression. Primary depressive disorders are those which are not the product of any other pre-existing physical or mental disorder. By contrast, the defining feature of secondary depressive disorders is that the individual's depression has developed as a consequence of some other pre-existing disorder. Depressive symptoms may be attributable to drug abuse, prescribed medication (*e.g.* corticosteroids or phenobarbitone) or any one of a vast array of "organic" mental disorders, including hypothyroidism (**1300**), Cushing's syndrome (**1297**), Addison's disease (**1297**), Simmond's disease (**1295**), hypoparathyroidism (**1302**), hypercalcaemia (**1095**), Huntington's chorea (**1286**), cerebral tumours and metabolic disorders such as potassium depletion (**1096**). It is noteworthy that some eight per cent of all patients with depression have a thyroid illness.[14] The importance of the distinction in a tribunal context is that any underlying physical problem may often be easily remedied, leading to a relatively rapid resolution of symptoms.

Retarded and agitated depression

A further distinction sometimes drawn is that between retarded and agitated depression. Motor retardation "implies slowness of the initiation, execution and completion of physical activity."[15] It is frequently associated with retardation of thought, characterised by delayed response to questions, indecision, poor concentration, loss of clarity and poor registration of events. This combined slowing of thought and physical activity is known as "psychomotor retardation." Agitation "implies mental disturbance causing physical restlessness and increased arousal."[16] It occurs with or without retardation in depressive disorders and the two may alternate although retardation is more common. In a tribunal context, the importance of the distinction may be two-fold. Suicidal impulses may be prevented from expression by retardation whereas agitation may render expression more likely. Arising from this, the risk of suicide may increase as the patient's condition begins to respond to treatment and the degree of retardation reduces. However, while severe retardation and stupor may temporarily stifle the expression of suicidal intent, they can lead to a life-threatening deficiency in food and water intake and an inability to voluntarily consent to treatment.

---

14 H.I. Kaplan and B.J. Sadock, *Synopsis of Psychiatry* (Williams & Wilkins, 7th ed., 1994), p.206. Related to this , the Dexamethasone-Suppression Test (DST), which is occasionally used to help confirm a diagnosis of major depression, is associated with a large number of false-positive results. False-positive results are, *inter alia*, associated with phenytoin, barbiturates, carbamazepine, hypertension, dehydration, temporal lobe disease, pregnancy, Cushing's disease, unstable diabetes mellitus, extreme weight loss, acute psychosis, old age. False-negative results are associated with hypopituitarism and Addison's disease.

15 A. Sims, *Symptoms in the Mind* (Baillière Tindall, 1988), p.272.

16 *Ibid.*

Psychotic and neurotic depression

It was until recently commonplace to distinguish between psychotic and neurotic depression. Most often, the distinction being drawn was between psychotic patients, with florid symptoms such as nihilistic delusions, and "neurotic people" who retained a normal level of insight into their condition and whose perception of reality was not significantly impaired. However, both terms eventually acquired multiple meanings and the distinction became increasingly blurred. For example, the label neurotic depression might, depending on the author, mean that the condition was non-incapacitating, non-psychotic, non-remitting, non-situational, that the patient had a depressive personality, or any combination of these and similar features. Consequently, the use of the term "neurotic", and the traditional division between the neuroses and psychoses was abandoned in the tenth revision of the International Classification of Diseases. The term "psychotic" is nevertheless retained as a convenient descriptive term "to indicate the presence of hallucinations, delusions, or a limited number of several abnormalities of behaviour, such as gross excitement and overactivity (or) marked psychomotor retardation."[17]

Endogenous and reactive (exogenous) depression

The term "endogenous" literally means originating or growing from within and it was invented by Moebius in 1895 to describe a condition which was associated with heredity and had a strong genetic component. For many years, it was customary to distinguish between endogenous and reactive, or exogenous, depression and the distinction is still sometimes made. Endogenous depression, having a strong genetic component, often occurred without any obvious external cause or trigger while, in contrast, reactive depressive disorders appeared to be a response to an obviously stressful situation, such as a bereavement, separation or redundancy. Again, the term "endogenous" acquired a range of other meanings over the years as claims were made that this form of depression was associated with characteristic symptom patterns. The word was, for example, used as a short-hand term for a constellation of vegetative signs such as weight loss, early morning waking and fatigability; to describe persistent depressed mood qualitatively different from the normal depressions of every-day life and associated with unremitting hopelessness; and as a synonym for "psychotic depression," indicating the presence of stupor, hallucinations or delusions (the endogenous–reactive, psychotic–neurotic divide). The resulting ambiguity eventually led to the term being dropped from the third revision of the main American classification (DSM–III) and also from the ICD–10 classification, being replaced by the concepts of melancholic and somatic depression respectively — or, more specifically, "major depression with melancholia" and "depressive episode with somatic symptoms."

Atypical depression

Inevitably, tribunals periodically deal with cases involving patients diagnosed as suffering from "atypical depression." Recent research suggests that this may be a distinct type of depressive disorder associated with weight gain and increased appetite, oversleeping and hypersomnia, chronic fatigue and significant elements of anxiety intermixed with the depression, sometimes expressed in the form of

[17] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.3–4. The meaning of these terms is also considered on page 1036.

agoraphobia or panic attacks.[18] ording to the ICD classification, atypical presentations are particularly common in adolescence. In some cases, anxiety, distress, and motor agitation may be more prominent at times than the depression, and the mood change may also be masked by added features such as irritability, excessive consumption of alcohol, histrionic behaviour, hypochondriacal preoccupations and exacerbation of pre-existing phobic or obsessional symptoms.[19]

SOMATIC SYMPTOMS

According to the ICD–10 classification, these symptoms have special clinical significance. In particular, this somatic syndrome will almost always be present in a severe depressive episode. The most typical somatic symptoms are specified in the classification and given in the table below. It should be noted that the classification states that the somatic syndrome is not usually regarded as present unless "about four of these symptoms are definitely present."[20] There is a caveat to this. If two or three are present but they are unusually severe, a diagnosis of a mild depressive disorder with somatic symptoms may be justified.[21]

TYPICAL SOMATIC SYMPTOMS

- loss of interest or pleasure in activities that are normally enjoyable
- lack of emotional reactivity to normally pleasurable surroundings and events
- waking in the morning 2 hours or more before the usual time
- depression worse in the morning
- objective evidence of definite psychomotor retardation or agitation (remarked on or reported by other people)
- marked loss of appetite
- weight loss (often defined as 5 per cent. or more of body weight in the past month)
- marked loss of libido

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.120.

DEPRESSIVE EPISODES (F32)

The description of a typical depressive episode given in the ICD–10 classification is based upon three "typical" symptoms and a number of "other common symptoms." These are set out in the table below and some of them may be sufficiently marked that a syndrome of somatic symptoms is apparent (see above).

[18] F.M. Quitkin, *et al.*, "Phenelzine and imipramine in mood reactive depressives" (1989) *Archives of General Psychiatry* 46, 787–793.

[19] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.120.

[20] *Ibid.*

[21] *Ibid.*, p.122.

TYPICAL DEPRESSIVE EPISODE

THE TYPICAL SYMPTOMS	OTHER COMMON SYMPTOMS
A. depressed mood	A. reduced concentration and attention
B. loss of interest and enjoyment	B. reduced self-esteem and self-confidence
C. reduced energy leading to increased fatigability and diminished activity	C. ideas of guilt and unworthiness (even in a mild type of episode)
Typically, the lowered mood varies little from day to day, and is often unresponsive to circumstances, yet may show a characteristic diurnal variation as the day goes on. Marked tiredness after only slight effort is common.	D. bleak and pessimistic views of the future
	E. ideas or acts of self-harm or suicide
	F. disturbed sleep
	G. diminished appetite

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.119.

The number of symptoms and their duration

As to the number of symptoms which must be present and for how long before a depressive episode is diagnosed, the general position may be summarised as follows—

- A definite diagnosis of a mild depressive disorder "usually" requires that at least two of the three typical symptoms, plus at least two of the other common symptoms listed above, are present for at least a fortnight, although none should be of an intense degree.[22]
- A diagnosis of a moderate depressive disorder requires that at least two of the three typical symptoms, plus at least three (and preferably four) of the other common symptoms, are present for at least a fortnight. Several symptoms are likely to be present to a marked degree but this is not essential if a particularly wide variety of symptoms is present overall.[23]
- A diagnosis of a severe depressive episode usually requires that all three of the typical symptoms and at least four of the other common symptoms are present for at least a fortnight, some of which should be of severe intensity, although the diagnosis may be reasonable and justified if the symptoms are unusually severe and of rapid onset.[24]

22 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.121.
23 *Ibid.*, p.122.
24 *Ibid.*, pp.120 and 123.

The severity of depressive episo

The classification of depressive episodes specifies three levels of severity — mild (F32.0), moderate (F32.1), and severe (F32.2). Severe depressive episodes are of two kinds — severe depressive episode without psychotic symptoms (F32.2) and severe depressive episode with psychotic symptoms (F32.3). For each grade of depression, the classification describes the usual consequences for the individual in terms of how disabling the illness is and the likely care setting.

THE SEVERITY OF A DEPRESSIVE EPISODE

Severity	*For a definite diagnosis*	*Interference*	*Care setting*
• **Mild**	At least <u>two</u> typical symptoms are present plus at least <u>two</u> of the other common symptoms for a minimum duration of about 2 weeks, but none to an intense degree.	• The individual is usually distressed by the symptoms and has some difficulty in continuing with ordinary work and social activities, but will probably not cease to function completely.	Individuals with mild depressive episodes are common in primary care and general medical settings
• **Moderate**	At least <u>two</u> typical symptoms are present plus at least <u>three</u> of the of the other common symptoms for a minimum duration of about 2 weeks. Several symptoms are likely to be marked but this is not essential if a particularly wide variety of symptoms is present overall.	• The individual will usually have considerable difficulty in continuing with social, work or domestic activities.	Variable. May be able to continue to work.
• **Severe without psychotic symptoms**	<u>All three</u> of the typical symptoms are present plus at least <u>four</u> of the other common symptoms, some of which should be of severe intensity. Although the depressive episode should usually last at least 2 weeks, the diagnosis may be justified after less than 2 weeks if the symptoms are particularly severe and of very rapid onset. Loss of self-esteem or feelings of uselessness or guilt are likely to be prominent.	• It is very unlikely that the sufferer will be able to continue with social, work, or domestic activities, except to a very limited extent. He usually shows considerable distress or agitation, unless retardation is a marked feature. Suicide is a distinct danger in particularly severe cases.	Psychiatric in-patient units deal largely with patients suffering from the more severe grades.
• **Severe with psychotic symptoms**	A severe depressive episode meeting the criteria given in which delusions, hallucinations, or depressive stupor are also present. The delusions usually involve ideas of sin, poverty, or imminent disasters, responsibility for which may be assumed by the patient. Auditory or olfactory hallucinations are usually of defamatory or accusatory voices or of rotting filth or decomposing flesh. Severe psychomotor retardation may progress to stupor.		

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.119–124.

Using psychiatric rating scales to assess severity

The severity of a depressive episode may be measured using psychiatric rating scales. Where a depression measure yields a global score, it is important to realise that the same numerical score may have very different clinical meanings. Thompson has summarised the main rating scales used in cases of depression in a tabular form, from which it can be seen that the scales differently weight the different features of depression.

DEPRESSION RATING SCALES

	HDRS	Bech	MADRS	BDI	Zung	Wake	Carroll
Mood	8	18	30	9.5	15	25	8
Vegetative	28	18	30	29	35	33	35
Motor	12	18	0	0	5	8	15
Social	8	9	0	5	0	8	0
Cognitive	28	27	30	52	35	0	27
Anxiety	16	9	10	0	5	17	15
Irritability	0	0	0	5	5	8	0

- *Mood* includes sadness, loss of enjoyment, distinct quality to mood, weeping and diurnal variation.
- *Vegetative* includes sleep disturbance, appetite change, weight change, loss of libido, constipation and fatigue.
- *Motor* includes retardation, agitation and restlessness.
- *Social* includes withdrawal, isolation and inability to function at work or other tasks.
- *Cognitive* includes thoughts of hopelessness and helplessness, suicide, illness and guilt, as well as loss of insight and indecision.
- *Anxiety* includes psychic and somatic and phobic anxiety.
- *Irritability* includes both inwardly and outwardly directed hostility.

Abbreviations: HDRS = Hamilton Rating Scale; Bech = Bech-Rafaelson Melancholia Rating Scale; MADRS = Montgomery Asberg Depression Rating Scale; BDI = Beck Depression Inventory; Zung = ; Wake = Wakefield Depression Inventory.

Source: Professor C. Thompson, The Instruments of Psychiatric Research (John Wiley & Sons, 1989), p.5.

Hamilton Rating Scale (HRS)

The Hamilton Rating Scale (HRS) is the most widely user observer scale for rating depressed patients and it is a measure of severity and not a diagnostic instrument. Over 20 items (*e.g.*, mood, guilt, suicidal tendencies, diurnal variation) are rated on a 0–2 or a 0–4 scale. The scale is generally considered to have high reliability,

validity and international accep e but has been criticised for failing to differentiate adequately between moderate and severe depression.

Beck Depression Inventory

There are two forms of the Beck Depression Inventory. The short form is for use by general practitioners in screening patient for depression. The long form is designed to provide a quantitative assessment of the severity of depression. It is not designed for diagnostic purposes, that is as a way of determining whether a person is or is not clinically depressed. As with the Hamilton Rating Scale, the inventory has generally been found to be reliable but has been criticised for failing to differentiate adequately between moderate and severe depression, and for being open to observer bias when the interviewer rates the patient.

Zung Self-Rating Depression Scale (SDS)

The scale has been criticised for insensitivity to clinical differences at the lower end of the severity range and awkward wording of items. Severity is measured almost exclusively by reference to the frequency of a symptom rather than its tolerability.

RECURRENT DEPRESSIVE DISORDER (F33)

Recurrent depressive disorders are characterised by repeated episodes of mild, moderate or severe depressive episodes without any history of independent episodes of mood elevation and overactivity fulfilling the criteria of mania. The diagnosis requires at least two depressive episodes each lasting for a minimum of two weeks and separated by several months without significant mood disturbance. According to the ICD classification, individual episodes generally last between three and twelve months, with a median duration of about six months, and they are often precipitated by stressful life events. Recovery is usually complete between episodes. In cases of recurrent depressive episode, the severity of the present episode may be graded in the same way as a single episode.

MANAGEMENT AND TREATMENT OF DEPRESSION

The management of severe depressive episodes may necessitate hospital admission and, if there is a significant risk of suicide, continuous observation. In-patient treatment almost invariably includes medication (**1208**) or ECT (**1132**). Cognitive therapy (**1154**) or some other kind of psychological treatment may be indicated. Several trials suggest that the relapse rate following cognitive therapy is lower than after drug treatment alone. In rare, intractable cases psychosurgery is occasionally offered (**1130**). The outcome for mood disorders is generally more favourable than for schizophrenia. However, cases requiring in-patient treatment tend to be severe, chronic, recurrent, or accompanied by a high risk of suicide. As to these patients, there is "little firm evidence that the long-term outlook of mood disorders has been improved by any of the therapeutic measures" available.[25] In particular, there is "little evidence" that ECT and tricyclic antidepressants have reduced the suicide rate

[25] R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.447.

or that maintenance treatment with tricyclic antidepressants reduces risk of further episodes, and no one has demonstrated a reduction in the incidence of non-first episodes of either depression or mania in any geographically defined population.[26] After an interval of eighteen years, Lee and Murray reinterviewed 94 per cent. of 89 individuals who had originally received in-patient treatment for depression in 1965–66. Although 61 per cent. had been first admissions the overall outcome was poor despite the frequent use of tricyclic antidepressants and lithium throughout the follow-up period. Only 11 of 89 patients had a good outcome (*i.e.* no further admissions, no suicide attempts and good social functioning at follow-up) and 25 had a very poor outcome (suicide or other unnatural death, repeated episodes of illness and poor social functioning at follow-up). There was a striking relationship between the symptomatology of the index illness and outcome, those with the most psychotic or endogenous symptoms having the worst outcome.[27] Alcohol abuse is a high-risk factor in most suicide indicators and a disproportionate percentage of depressed persons drink excessively. Where the alcoholism is primary and the depressive disorder consequent upon it, medication and treatment is of little benefit without abstinence. In Desmond Kelly's famous phrase, it is like painting over rust.

THE NEED FOR HOSPITAL ADMISSION

According to Kendell, "the decision whether or not to admit the patient to hospital, or to try to persuade them to come into hospital, is largely governed by three considerations — the risk of suicide, the need for ECT, and whether or not the patient is still at work. The most important of these is the risk of suicide, and the patient should always be questioned about this. Merely having had thoughts about suicide, or having wished not to have to wake up in the morning, are not necessarily cause for alarm, for they are almost invariable in severe depressions. But if the patient is preoccupied with thoughts of suicide, planning how he might kill himself, or frightened that he might do so, he probably needs to be under observation in hospital. So too does anyone who is seriously depressed and living alone. Age, sex, previous suicidal attempts and alcohol intake are other important determinants of risk. Whether the patient is still at work is important partly as an indication of the severity of the illness and partly because anyone who is already unable to work has much less to lose by coming into hospital. And in the writer's view anyone who is ill enough to need ECT needs to be either an in-patient or a day patient."[28]

ANTIDEPRESSANT MEDICATION

Anti-depressants may be divided into four broad categories: (1) tricyclic and related antidepressants; (2) MAOIs; (3) SSRIs and related antidepressants; and (4) other medication with antidepressant properties, such as flupenthixol and tryptophan. The choice of anti-depressant is governed by various considerations including their effectiveness, safety and comparative cost; the tolerance of side-effects; the age of

26 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.447.

27 *Ibid.*; A.S. Lee and R.M. Murray "The long-term outcome of Maudsley depressives" *British Journal of Psychiatry* (1988) 153, 741–751. A 15 year follow-up of 145 Australian patients ... produced rather similar findings. Although "the overall prognosis was rather less gloomy, only 20 per cent. had no further episodes of depression and 9 per cent. committed suicide. See L.G. Kiloh, *et al.*, The long-term outcome of depressive illness *British Journal of Psychiatry* (1988) 153, 752–757.

28 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies, supra*, p.451.

patient; the existence of a concurrent illness or the administration of concurrent drug therapy; the psychiatrist's familiarity with the available drugs; and the type of depression from which the patient suffers. An extensive review of the literature by Appleton showed that some 70 per cent. of patients responded to tricyclics compared to 40 per cent. for placebos and, in general terms, it appears that approximately 20–30 per cent. of additional recoveries occur with the assistance of medication when compared with no treatment or treatment with placebo.[29] Medication also has a short-term prophylactic role in terms of reducing the risk of relapse. While the results of research studies vary, the risk of relapse is approximately halved if tricyclics are continued for a period of six to eight months following remission whereas cessation within two months of remission leads to a relapse rate variously described as between 20 and 50 per cent. Assuming that medication is effective, and some 30 per cent. of patients fail to respond to tricyclic medication, Appleton's view is that tricyclic medicines should be continued for between three and twelve months at a dosage of 100–150mg of imipramine or equivalent.[30] There is some evidence that a "maintenance dose" of 75–100 mg per day is less effective[31] although higher doses may encourage non-compliance because of their side-effects.

TRICYCLIC AND RELATED ANTIDEPRESSANTS

These antidepressants, which inhibit the re-uptake of the monoamines serotonin and noradrenaline, are called tricyclics because of their three-ringed chemical structure. The first of them, imipramine, was introduced in 1959. Some of the newer related drugs have four rings and may be referred to as tetracyclics.

Efficacy

In 62 of the 93 trials reviewed by Morris, patients receiving tricyclic antidepressants showed greater improvement than those receiving a placebo.[32] The actual response relative to placebo may be greater than this because the initial dosage advice is now generally considered to have been too low.[33]

The choice of tricyclic

There is little evidence that tricyclics differ from one another in clinical efficacy but they do differ in their side-effects. The pronounced sedative action of amitriptyline may be useful if there is some immediate gain through a reduction of anxiety and tension. However, some patients complain of over-sedation in which case a less sedative preparation such as imipramine may be preferred. Clomipramine may be effective when a depressive illness has obsessive-compulsive features and imipramine where there is retardation. Safer drugs like mianserin are valuable for patients who are likely to attempt to kill themselves or who develop intolerable anticholinergic side-effects on amitriptyline or imipramine.

29 W. Appleton, *Practical Clinical Psychopharmacology* (Williams & Wilkins, 3rd ed., 1988).

30 *Ibid.* Prien and Kupfer found that treatment needed to be continued for four months after full recovery but no longer. R.F. Prien and D.J. Kupfer "Continuation drug therapy for major depressive episodes: how long should it be maintained?" *American Journal of Psychiatry* (1986) 143, 18–23.

31 E. Frank, *et al.*, "Three year outcomes of maintenance therapies in recurrent depression" *Archives of General Psychiatry* (1990) 47, 1093–1099.

32 J.B. Morris and A.T. Beck, "The efficacy of antidepressant drugs, A review of research (1958–1972)" *Archives of General Psychiatry* (1974) 30, 667–674.

33 W. Appleton, *Practical Clinical Psychopharmacology* (Williams & Wilkins, 3rd ed., 1988).

TRICYCLIC AND RELATED ANTIDEPRESSANTS (B.N.F. 4.3.1)

Drug	*Proprietary*	*Indications*	*BNF guideline doses*	*Notes*
Amitriptyline Hydrochloride	▪ Amitriptyline (tablets) ▪ Lentizol (capsules) ▪ Tryptizol (tablets, mixture, injection)	*Depressive illness, particularly where sedation is required*	*By mouth* initially 75mg daily, increasing to maximum 150mg daily. Usual maintenance dose 50–100mg daily. *IM or IV injection* 10–20mg q.d.s.	More sedative than imipramine and has more pronounced anticholinergic effects. Often used where anxiety or agitation are apparent. Some 70 per cent. of depressed in-patients respond.
Amoxapine	▪ Asendis (tablets)	*Depressive illness*	Initially 100–150mg daily. Maximum dose 300mg daily. Usual maintenance dose of 150–250mg daily.	Chemically related to the antipsychotic loxapine. Tardive dyskinesia reported and endocrine disorders in women.
Clomipramine Hydrochloride	▪ Clomipramine (capsules) ▪ Anafranil (capsules, syrup, injection, tablets)	*Depressive illness, phobic and obsessional states*	*By mouth* initially 10mg daily, maximum 250mg daily, usual maintenance 30–50mg daily. *IM injection* initially 25–50mg daily, maximum 100–150mg daily. *IV infusion* initially 25–50mg increasing to usual dose of 100mg daily for 7–10 days.	Strongly sedative.
Desipramine Hydrochloride	▪ Pertofran (tablets)	*Depressive illness*	75mg daily initially, usual maximum dose of 200mg daily (in resistant depression max. 300mg daily with plasma concentration monitoring). Usual maintenance 75–100mg daily.	Slight stimulant effect. *Discontinued in 1997.*
Dothiepin Hydrochloride	▪ Dothiepin (tablets, capsules) ▪ Prothiaden (tablets, capsules)	*As for amitriptyline*	Initially 75mg daily, increasing as necessary to 150mg daily or in some circumstances (*e.g.*, hospital use) 225mg.	Similar to amitriptyline.
Doxepin	▪ Sinequan (capsules)	*As for amitriptyline*	Initially 75mg daily, increased as necessary to 300mg daily. Range 30–300mg daily.	May have fewer unwanted effects than amitriptyline.
Imipramine Hydrochloride	▪ Imipramine (tablets) ▪ Tofranil (tablets, syrup)	*Depressive illness*	Initially up to 75mg daily, increased gradually to 150–200mg (up to 300mg in hospital patients). Usual maintenance 50–100mg daily.	Less sedating than Amitriptyline.
Lofepramine	▪ Lofepramine (tablets, syrup) ▪ Gamanil (tablets)	*Depressive illness*	Range 140–210mg daily.	Less sedating than Amitriptyline. Safe in overdose. May cause agitation in the elderly. Hepatic disorders reported.
Nortriptyline	▪ Allegron (tablets)	*Depressive illness*	Low dose initially increased as necessary to 75–100mg daily. Maximum 150mg. daily in hospital patients (plasma concentration monitoring above 100mg).	Less sedating than Amitriptyline.
Protriptyline Hydrochloride	▪ Concordin (tablets)	*Depressive illness, particularly with apathy and withdrawal*	Initially 10mg 3–4 times daily. Usual range 15–60mg daily.	Strongly stimulant. Anxiety, agitation, restlessness more common.
Trimipramine	▪ Surmontil (tablets, capsules)	*As for amitriptyline*	50–75mg daily, increased as necessary to maximum 300mg daily for 4–6 weeks, then reduced to usual maintenance dose 75–150mg daily.	Sometimes advocated for MAOI combination therapy. Strongly sedative.
		Related antidepressants		
Maprotiline Hydrochloride	▪ Ludiomil (tablets)	*As for amitriptyline*	Initially 25–75mg, maximum 150mg daily.	Antimuscarinic effects may be less frequent than with Amitriptyline but rashes common. Increased risk of convulsions at higher doses.
Mianserin Hydrochloride	▪ Mianserin (tablets)	*As for amitriptyline*	Initially 30–40mg daily, increased gradually as necessary. Usual dose range 30–90mg.	Tetracyclic. Safe in overdose. Leukopenia, agranulocytosis, jaundice reported.
Trazodone Hydrochloride	▪ Molipaxin (tablet, capsules, liquid)	*As for amitriptyline*	Initially 150mg daily, maximum 300 mg daily or (in hospital patients) 600mg daily.	Chemically unrelated to other anti-depressants. Mechanism of action unclear. Fewer antimuscarinic and cardiovascular effects compared to Amitriptyline.
Viloxazine Hydrochloride	▪ Vivalan	*Depressive illness*	300 mg daily, maximum 400mg daily.	Less sedating than Amitriptyline. Fewer and milder antimuscarinic and cardiovascular effects.

Dosage and response

The normal adult dose of most tricyclic antidepressants is 150mg per day. The elderly will usually only be able to tolerate half this amount. According to Kendell, and the guidelines in the British National Formulary, it is important to start with a maximum dose of 75mg per day in everyone so as to minimise the impact of sedative and anticholinergic side-effects.[34] Initial response to tricyclic medication generally takes ten to fourteen days and six weeks may be required for maximum therapeutic effect; improvement in somatic symptoms is often the first feature to be noted.[35] This means that little or no improvement in a section 2 patient's condition may be apparent by the time his case is heard but, providing the dose is adequate, maximum response should have been achieved by the date of any section 3 hearing. After a year, the therapeutic effect of tricyclics wanes and after two years of continuous treatment they are probably of little or no benefit.[36] Because of their delayed action "no patient under the age of 60 years should be deemed to have failed to respond to a tricyclic drug until they have taken 150mg/day for at least three weeks. If there is no improvement within this time it is usually better to increase the dose still further (*i.e.* to 200 or 250mg/day of amitriptyline) than to change to a different drug, unless side-effects have prevented an adequate dose being taken or poor compliance is suspected. This probably applies to the newer tetracyclic drugs as well, though at present there is little evidence either way."[37]

Predicting who will respond

Some 30 per cent. of depressed patients fail to respond to tricyclics. The general reasons for treatment failure have already been summarised (**1150**). In relation to depressive disorders, there is some evidence that "endogenous depression" tends to respond better than do "neurotic" depressive disorders,[38] and unipolar psychotic episodes respond fairly poorly, ECT being likely to achieve a better response.[39] Symptoms commonly found to be susceptible to improvement are depressed mood (sadness), guilt and worthlessness, and decreased involvement in work and interests (lassitude).[40] According to Kendell, the "most appropriate treatment for patients with severe depressions which have failed to respond both to a tricyclic drug in full dosage and to ECT is very uncertain. Possible strategies include an MAOI in high dosage, combining a tricyclic and an MAOI in moderate doses, combining lithium with a tricyclic or an MAOI, prescribing an MAOI and tryptophan. For non-responders whose illnesses are "reactive" or "neurotic" in character the best alternative treatment is usually either an MAOI or cognitive therapy.[41]

34 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.449.

35 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.141.

36 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies*, *supra*, p.449.

37 *Ibid.*

38 E.C. Johnstone, *et al.*, "Neurotic illness and its response to anxiolytic and antidepressant treatment" *Psychological Medicine* (1980) 10, 321–328.

39 W. Appleton, *Practical Clinical Psychopharmacology* (Williams & Wilkins, 3rd ed., 1988).

40 See J.C. Nelson, *et al.*, "Drug-responsive symptoms in melancholia" (1984) *Archives of General Psychiatry* 41, 663–668; S.A. Montgomery & M. Asberg, "A new depression scale designed to be sensitive to change" (1979) *British Journal of Psychiatry* 134, 382–389; P. Bech, *et al.*, "The Hamilton Rating Scale: Evaluation of objectivity using logistic models" (1981) *Acta Psychiatrica Scandinavica* 63, 290–299; M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.141.

41 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies*, *supra*, p.451.

Adverse effects

Approximately 400 deaths due to tricyclic overdoses are reported annually and they are considerably more dangerous than phenothiazines in overdose. Even a week's supply of an antidepressant at full dosage can be lethal and a dose of imipramine or amitriptyline above 600mg is likely to produce serious effects. Symptoms usually appear within four hours.[42]

Prescribed medication

The side-effects of medication taken according to prescription include drowsiness, torpor, a feeling of detachment, tremor and confusional reactions in the elderly, postural hypotension, constipation, urinary retention, delayed ejaculation, weight gain, headache and nausea.

SELECTIVE SEROTONIN RE-UPTAKE INHIBITORS (SSRIs)

Serotonin is stored in synaptic vesicles and, following its release into the synaptic cleft, the main method of inactivation is via re-uptake by presynaptic neurones (**1270**).[43] The SSRIs are a structurally diverse group but they all selectively inhibit this re-uptake, having no significant effect on noradrenaline or dopamine reuptake.

Efficacy

The evidence suggests that the drugs are as effective as amitriptyline, have fewer side-effects and comparatively safe in overdose. The latter is necessarily an important consideration if there is a significant risk of suicide. Opinion varies as to whether SSRIs or tricyclics should be used as the initial treatment in cases of major depression because it is not yet firmly established that they are as effective in treating severely depressed patients.[44] They may, however, be particularly effective where a depressive disorder is associated with obsessional or phobic thoughts.

Adverse effects

SSRIs are less cardiotoxic than tricyclic antidepressants, much safer in overdose, non-sedating and lack antimuscarinic (anticholinergic) effects. They are also not associated with weight gain. The fact that SSRIs have fewer debilitating adverse effects may mean that patient compliance with prescriptions is higher than when a tricyclic antidepressant is prescribed.[45] The most common adverse effects include nausea, loss of appetite, dry mouth, diarrhoea, constipation, insomnia, headache, dizziness, tremor, sweating, and sexual problems such as retarded ejaculation. Gastro-intestinal side-effects (diarrhoea, nausea and vomiting) are dose-related.[46] Akathisia and extrapyramidal effects have been reported with fluoxetine.[47] It is hazardous to combine an SSRI with an MAOI or to prescribe the latter drug within several weeks of stopping the former.

42 M. Lader and R. Herrington, *Biological treatments in psychiatry* (*supra*), p.151.

43 B.K. Puri and P.J. Tyrer, *Sciences Basic to Psychiatry* (Churchill Livingstone, 1992), p.103.

44 M.V. Rudorfer and W.Z. Potter, "Antidepressants: a comparative view of the clinical pharmacology and therapeutic use of the 'newer' versus the older drugs" (1989) *Drugs* 37, 713–738.

45 F. Song, *et al.*, "Selective serotonin reuptake inhibitors: a meta-analysis of efficacy and acceptability" (1993) *British Medical Journal* 306, 683–687.

46 *British National Formulary* (March 1996) 31, 176.

47 J.F. Lipinski, *et al.*, "Fluoxetine-induced akathisia: clinical and theoretical implications" (1989) *Journal of Clinical Psychiatry* 50, 339.

SSRIs AND RELATED ANTIDEPRESSANTS (B.N.F. 4.3.3)

Drug	*Proprietary*	*Guideline doses*
Fluoxetine	Prozac (capsules, liquid)	*Depressive illness* 20mg daily. *Bulimia nervosa* 60mg daily. *Obsessive-compulsive disorder* initially 20mg, maximum 60mg daily (if no response after several weeks).
Citalopram	▪ Cipramil	20 mg daily increased to maximum 60mg daily.
Fluvoxamine Maleate	▪ Faverin (tablets)	100mg daily, maximum 300mg daily.
Paroxetine	▪ Seroxat (tablets, liquid)	Usually 20mg mane, maximum 50mg daily
Sertraline	▪ Lustral (tablets)	Initially 50mg daily, maximum 200mg daily, usual maintenance dose of 50mg daily. Doses of 150mg or greater should not be used for more than 8 weeks.
	Related antidepressants	
Nefazone Hydrochloride	▪ Dutonin (tablets)	Initially 100mg twice daily, increased after 5–7 days to 200mg twice daily. May be gradually increased to maximum 300mg twice daily.
Venlafaxine	▪ Efexor (tablets)	Initially 75mg daily increased if necessary after several weeks to 150mg. *Severely depressed or hospitalised patients* — Initially 150mg daily, increasing in steps every 2/3 days to maximum 375mg daily then gradually reduced.

MONOAMINE OXIDASE INHIBITORS (MAOIs)

The enzyme monoamine oxidase is responsible for the metabolic degradation of the neurotransmitters noradrenaline, serotonin and dopamine. MAOIs inhibit the enzyme, thereby causing an accumulation of amine neurotransmitters (**1270**) and this has an antidepressant effect. Unfortunately, the enzyme is also responsible for inactivating other amines such as tyramine which is present in food, drink and drugs. When monoamine oxidase is inhibited, tyramine is not broken down and this results in dangerously elevated blood pressure. Such a hypertensive crisis may occasionally be fatal. Consequently, patients taking MAOIs must avoid tyramine-rich foods, such as cheese (which is responsible for 80 per cent. of all reported fatalities) and yeast products, alcohol and certain drugs.

Efficacy

Early studies showed that MAOIs had only a very limited effect over and above placebo but it is now clear that the initial dosage guidelines were only half the therapeutic level.[48] As with tricyclics, the drugs must be given for several weeks and in adequate dosage and "in the case of phenelzine this usually means 60–90 mg/day,

[48] W. Appleton, *Practical Clinical Psychopharmacology* (Williams & Wilkins, 3rd ed., 1988).

or whatever dose is needed to provide 80–90 per cent. inhibition of platelet MAO activity if the assay is available. There is a long tradition that MAOIs are particularly effective forms of treatment for patients with atypical or "neurotic" depression characterised by anxiety, panic attacks, hypochondria, hysterical features or agoraphobia. Five recent studies have confirmed this by demonstrating a vastly superior patient response to MAOIs compared with imipramine in persons suffering from atypical depression.[50] Because of the dietary restrictions, MAOIs tend to be reserved as a second-line treatment for major depressive disorders, being used only for conditions which are refractory to treatment. Nevertheless, recent studies indicate that MAOIs are generally equivalent to tricyclic antidepressants in their efficacy, including as a treatment for "endogenous depression."[51]

MONOAMINE-OXIDASE INHIBITORS (B.N.F. 4.3.2)

Drug	*Proprietary*	*BNF guideline doses*
Phenelzine	▪ Nardil (tablets)	Initially 15mg t.d.s., increased if necessary after 2 weeks to 15mg q.d.s. (hospital patients maximum 30mg t.d.s.). Then reduced to lowest possible maintenance dose – 15mg on alternate days may be adequate.
Isocarboxazid	▪ Isocarboxazid (tablets)	Initially up to 30mg daily, increased after 4 weeks if necessary to max. 60mg daily for up to 6 weeks under close supervision only; then reduced to usual maintenance dose 10–20mg daily (but up to 40mg daily may be required).
Tranylcypromine	▪ Parnate (tablets)	Initially 10mg b.d. Doses above 30mg daily under close supervision only.
	Reversible MAOIs	
Moclobemide	▪ Manerix (tablets)	Initially 300mg daily, adjusted according to response. Usual range 150–600mg daily.

Adverse effects

Because the effects of non-compliance with dietary restrictions are severe, prescriptions are restricted to patients who can be relied upon to adhere to the necessary regime. However, selectively prescribed, there is no evidence that MAOIs are less safe than tricyclic anti-depressants and, indeed, the number of recorded deaths per million MAOI prescriptions is generally considerably less. There is no proven advantage in prescribing tricyclic anti-depressants and MAOIs together and it may be hazardous to do so.

[49] R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.450.

[50] F.M. Quitkin, *et al.*, "Phenelzine and imipramine in mood reactive depressives" (1989) *Archives of General Psychiatry* 46, 787–793.

[51] E.S. Paykel, "Monoamine oxidase inhibitors: when should they be used" in *Dilemmas and difficulties in the management of psychiatric patients* (ed. K. Hawton & P.J. Cowen, Oxford University Press, 1990), pp.17–30; P.J. Cowen, "Depression resistant to tricyclic antidepressants" (1988) *British Medical Journal* 297, 435–436.

Reversible MAOIs (Moclobemide)

Many of the dangerous interactions associated with MAOIs do not apply to the newer drug moclobemide, which is known as a reversible MAOI. However, there is little evidence that it is as effective as the older MAOIs as a treatment for atypical depression.

MANIC EPISODES AND BIPOLAR DISORDERS

In the ICD–10 classification, the terms mania and severe depression are used to denote the opposite ends of the spectrum of mood disorders.[52] Three degrees of severity of manic episode are specified in the ICD classification, all of which share the common underlying characteristics of elevated mood and an increase in the quantity and speed of physical and mental activity: hypomania; mania without psychotic symptoms; and mania with psychotic symptoms. If a patient who has had a manic episode (F30) has a subsequent manic episode, the diagnosis is revised to bipolar affective disorder (F31). This reflects the fact that the vast majority of such patients will eventually experience an episode of depression. The frequency of episodes and the pattern of remissions and relapses are very variable.

AETIOLOGY, PATHOLOGY AND EPIDEMIOLOGY

While many hypotheses have been advanced, the underlying aetiology and pathology are not known. Most studies have found a raised incidence of life events preceding the onset of manic illnesses. Bipolar disorder is less common than unipolar disorder. The first episode may occur at any age from childhood to old age but the mean age of onset of bipolar illness is 21 years. The initial episode occurs before the age of 30 in over 60 per cent of cases and before the age of 50 in almost 90 per cent. of cases.[53] The lifetime risk of bipolar disorder is about 1 per cent. While the risk is the same for men and women it may be somewhat greater for people in higher socio-economic classes.

MANIC EPISODES (F30)

Manic episodes are characterised by elevated mood and an increase in the quantity and speed of physical and mental activity. They usually begin abruptly and last for between two weeks and four of five months, with a median duration about four months.[54] The length of subsequent episodes appears to be similar[55] although the interval between episodes decreases as their number increases.[56]

---

52 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.112.

53 J Angst, *et al.*, "The course of monopolar depression and bipolar psychosis" (1973) *Psychiatrica, Neurologica, Neurochirurgia* 76, 486–500.

54 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.116.

55 J Angst, *et al.*, "The course of monopolar depression and bipolar psychosis," *supra.*

56 P. Roy-Byrne, *et al.*, "The longitudinal course of recurrent affective illness: life chart data from research patients at the NIMH" *Acta Psychiatrica Scandinavica* 71, 1–34.

Differential diagnosis

Mania with psychotic symptoms may sometimes be difficult to distinguish from schizophrenia in cases where the psychotic state obscures the basic mood disorder. The manifestations of some other medical conditions may also include symptoms most commonly seen in manic episodes, including thyrotoxicosis and hypoparathyroidism. The possibility that the condition has been induced by prescribed or non-prescribed drugs must always be borne in mind. Drugs associated with manic symptoms include amphetamines, cocaine, corticosteroids, MAOIs and anticholinergics (procyclidine and benzhexol).

The severity of manic episodes

Three degrees of severity of manic episode are specified in the ICD classification, namely hypomania (F30.0); mania without psychotic symptoms (F30.1); and mania with psychotic symptoms (F30.2).

HYPOMANIA (F30.0)

Hypomania is a lesser degree of mania, an intermediate state without delusions, hallucinations, or complete disruption of normal activities, which is often but not exclusively seen as patients develop or recover from mania.[57] Thus, it covers the range of mood disorders and activity levels which lie between cyclothymia **(1197)** and mania; the abnormalities of mood are too persistent and marked to be included under cyclothymia but are not accompanied by hallucinations or delusions.[58]

SYMPTOMS OF HYPOMANIA

- Persistent mild elevation of mood for at least several days on end.
- Increased energy and activity.
- Usually marked feelings of well-being and both mental and physical efficiency.
- Increased sociability, talkativeness, overfamiliarity and 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.
- Concentration and attention may be impaired, thus diminishing the ability to settle down to work, but this may not prevent the appearance of interests in quite new ventures and activities, or mild over-spending.

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.113.

---

57 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.113.

58 *Ibid.*, p.112.

Diagnostic guidelines

The diagnostic guidelines provide that several of the features listed in the above table, consistent with elevated or changed mood and increased activity, should have been present for at least several days on end, to a degree and with a persistence greater than that described for cyclothymia (**1197**). Hallucinations and delusions should be absent. While "considerable" interference with work or social activity is consistent with a diagnosis of hypomania, if disruption of these is "severe or complete" then mania should be diagnosed.[59]

MANIA WITHOUT PSYCHOTIC SYMPTOMS (F30.1)

The diagnostic guidelines for mania state that the episode should last for at least one week and be severe enough to disrupt ordinary work and social activities more or less completely. The mood change should be accompanied by increased energy and several of the symptoms referred to in the table below. Pressure of speech (**1078**), decreased need for sleep, grandiosity, and excessive optimism, should be evident.

SYMPTOMS OF MANIA WITHOUT PSYCHOTIC SYMPTOMS

- The individual's mood is elevated out of keeping with his 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. However, in some manic episodes the mood is irritable and suspicious rather than elated.
- Normal social inhibitions are lost, attention cannot be sustained, and there is often marked distractibility.
- 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 beautiful and subjective hyperacusis.
- The individual may embark on extravagant and impractical schemes, spend money recklessly, or become aggressive, amorous, or facetious in inappropriate circumstances.

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.114.

[59] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.113. Similarly, the American DSM–IV classification states that by definition the disturbance in hypomania is not severe enough to cause marked impairment in social or occupational functioning or to require hospitalisation, which is required for the diagnosis of a manic episode.

MANIA WITH PSYCHOTIC MPTOMS (F30.2)

The term "psychotic" is used in the ICD–10 classification as a convenient descriptive term to indicate the presence of hallucinations, delusions, or a limited number of several abnormalities of behaviour, such as *gross* excitement and overactivity. The clinical picture is that of a more severe form of mania than mania without psychotic symptoms (F30.1).[60] While the diagnostic guidelines for mania set out in the table above should be satisfied, psychotic symptoms of the kind described below should also be evident.

SYMPTOMS OF MANIA WITH PSYCHOTIC SYMPTOMS

- Inflated self-esteem and grandiose ideas may develop into delusions, and irritability and suspiciousness into delusions of persecution. In severe cases, grandiose or religious delusions of identity or role may be prominent, and flight of ideas and pressure of speech may result in the individual becoming incomprehensible.
- Severe and sustained physical activity and excitement may result in aggression or violence, and neglect of eating, drinking, and personal hygiene may result in dangerous states of dehydration and self-neglect.
- If required, delusions or hallucinations can be specified as congruent or incongruent with the mood. "Incongruent" should be taken as including affectively neutral delusions and hallucinations; for example, delusions of reference with no guilty or accusatory content, or voices speaking to the individual about events that have no special emotional significance.

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, p.115.

BIPOLAR AFFECTIVE DISORDERS (F31)

It has been noted that the diagnosis of a manic episode (F30) is only used for a first manic episode and also that a significant proportion of manic patients subsequently experience further periods of mania or depression. Bipolar affective disorder is characterised by two or more episodes in which the patient's mood and activity levels are significantly disturbed, this disturbance consisting on some occasions of an elevation of mood and increased energy and activity (mania or hypomania), and on others of a lowering of mood and decreased energy and activity (depression).[61] However, as patients who suffer only from repeated episodes of mania are comparatively rare, and resemble those who also have at least occasional episodes of depression in terms of their family history, premorbid personality, age of onset, and long-term prognosis, patients who experience a second manic episode are reclassified as having a bipolar affective disorder even if there is no history of depression.

[60] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.115.

[61] *Ibid.*, p.116.

Sub-types and diagnostic guidelines

The main sub-types of bipolar affective disorder are listed below, from which it can be seen that the sub-types are distinguished according to the type of disordered mood which defines the current episode. The diagnostic guidelines are two-fold—

- The first is that the current episode meets the usual criteria for the particular kind of mood disorder. So, for example, a definite diagnosis of "bipolar disorder, current episode hypomania" requires that the patient's present condition meets the diagnostic guidelines for hypomania already given.
- The second diagnostic guideline relates to the nature of the previous episode, or episodes, and rests on the distinction to which reference has been made. Namely, that while a person who experiences a second manic episode is reclassified as having a bipolar disorder, a person who has an episode of depression is only reclassified as having a bipolar disorder if and when he subsequently has a manic episode.
- Accordingly, if the present illness meets the criteria for a manic episode the second diagnostic guideline is simply that there has been at least one previous episode of any type of mood disorder.[62] However, if the current episode is depressive, a diagnosis of a bipolar affective disorder requires that there has been a manic episode or a mixed affective episode (alternating mania and depression) at some time in the past.

SUB-TYPES OF BIPOLAR AFFECTIVE DISORDER (F31)

Patient's current condition fulfils the criteria for a manic episode

- Bipolar disorder, current episode hypomanic (F31.0)
- Bipolar affective disorder, current episode manic without psychotic symptoms (F31.1)
- Bipolar affective disorder, current episode manic with psychotic symptoms (F31.2)

Patient's current condition fulfils the criteria for a depressive episode

- Bipolar affective disorder, current episode mild or moderate depression (F31.3)
- Bipolar affective disorder, current episode severe depression without psychotic symptoms (F31.4)
- Bipolar affective disorder, current episode severe depression with psychotic symptoms (F31.5)
- Bipolar affective disorder, current episode mixed (F31.6)
- Bipolar affective disorder, currently in remission (F31.7)

Source: ICD–10 Classification of Mental and Behavioural Disorders: Clinical descriptions and diagnostic guidelines. WHO, Geneva. 1992, pp.116–119.

62 Excluding, of course, cyclothymia and dysthymia.

COURSE AND PROGNOSIS

Prior to the introduction of modern drug therapies the mortality rate of in-patients with mania was approximately 20 per cent., with two-fifths of the deceased dying from exhaustion.[63] Manic episodes usually begin abruptly and last for between two weeks and four to five months with a median duration of about four months.[64] The "risk of recurrence is high, particularly if the first episode occurs before the age of 30 years ... once someone has had a manic illness in adolescence or early adult life they are almost certain to have further illnesses, and in the long run some of these further illnesses are almost certain to be depressions."[65] Indeed, the manic episodes tend to become less frequent and the depressive episodes more frequent with the passage of time. Characteristically, recovery is usually complete between episodes.

MANAGEMENT

The treatment of manic episodes may require hospitalisation. According to Kendell, it is usually advisable to admit the patient to hospital, "for the risks of attempting to treat even hypomania on an out-patient basis are considerable. Because he feels fine, and cannot be convinced that he is ill, the patient rarely takes medication regularly. He may also squander money he can ill afford, get himself into all manner of embarrassing situations which may jeopardise his job or his position in the community, and endanger himself and other people by reckless behaviour.[66] Considerable nursing skill is required. The "patient's boisterous overactivity, sudden whims and capacity for causing mayhem have to be restrained. An experienced nurse can often do this by distracting his energies into other and less dangerous channels, or by winning his co-operation by entering his mood of playful good humour. A less skilful nurse tries to forbid or physically restrain, which annoys the patient and easily provokes him to violence."[67] As mood returns to normal, observation is important because of the considerable risks of relapse or a sudden swing into depression.

ANTIPSYCHOTIC DRUGS USED TO CONTROL MANIA

Following admission, the initial treatment normally includes the use of an antipsychotic (**1141**). Haloperidol and droperidol are widely believed to control motor overactivity more effectively than chlorpromazine but they can also cause severe extrapyramidal side-effects. In severe illnesses, chlorpromazine in doses of up to 1000mg daily or haloperidol in doses of up to 40mg per day are used because of their more immediate effect on over-activity. The sedative effects of antipsychotics are immediate and this may partly explain why manic symptoms generally begin to respond after a few days. Sedation can be hastened by intravenous administration. In one large-scale trial, chlorpromazine was found to control disturbed behaviour in highly active patients within a few days while the effects of lithium were delayed until the tenth day. However, the two were equally effective for mildly ill patients and lithium produced fewer side effects, leaving the patient feeling less sluggish and fatigued.

63 I.M. Derby, "Manic-depressive exhaustion deaths" (1933) *Psychiatric Quarterly* 7, 435–439.

64 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.116.

65 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.446. However, the proportion of patients having a single manic episode has been variously estimated at between one and 50 per cent.

66 *Ibid.*

67 *Ibid.*, p.448.

ANTIPSYCHOTIC DRUGS USED TO CONTROL MANIA (NOT DEPOTS)

Introductory note: Many of the drugs are not recommended for children, and reduced doses are recommended for children or the "elderly."

Drug	*Proprietary*	*Indications*	*BNF guideline doses*
Chlorpromazine Hydrochloride (CPZ)	▪ Chlorpromazine (tablets, elixir, injection, suppositories) ▪ Largactil (tablets, syrup, suspension, injection)	*Mania, short-term adjunctive management of severe anxiety, psychomotor agitation, excitement, and violent or dangerous impulsive behaviour.*	*Mania — by mouth* initially 75mg daily, usual maintenance dose of 75–300mg daily but up to 1g daily may be required in psychoses. *By deep IM injection* for relief of acute symptoms, 25–50mg every 6–8 hours.
Droperidol	▪ Droleptan (tablets, oral liquid, injection)	*Tranquillisation and emergency control in mania*	*Tranquillisation and emergency control in mania — by mouth* 5–20mg repeated every 4–8 hours if necessary. *By IM injection*, up to 10mg repeated every 4–6 hours if necessary. *By IV injection*, 5–15mg repeated every 4–6 hours if necessary.
Fluphenazine Hydrochloride	▪ Moditen (tablets, depot injection see **1263**)	*As for Chlorpromazine*	*Mania — by mouth* initially 2.5–10mg daily, adjusted according to response to 20mg daily. Daily doses above 20mg "only with special caution."
Haloperidol	▪ Haloperidol (tablets) ▪ Dozic (oral liquid) ▪ Haldol (tablets, oral liquid, injection, depot injection) ▪ Serenace (tablets, capsules, oral liquid, injection)	*As for Chlorpromazine*	*Mania — by mouth* initially 1.5–3mg twice or thrice daily; 3–5mg twice or thrice daily in severely affected or resistant patients. *By IM injection*, 2–10mg with subsequent doses every 4–8 hours according to response (up to hourly if necessary) — severely disturbed patients may require initial dose of up to 30mg.
Oxypertine	▪ Oxypertine (tablets, capsules)	*As for Chlorpromazine*	*Mania* — Initially 80–120mg daily, adjusted according to response. Maximum 300 mg daily.

Drug	*Proprietary*	*Indications*	*BNF guideline doses*
Perphenazine	▪ Fentazin (tablets)	*As for Chlorpromazine*	*Mania* — Initially 4mg t.d.s., thereafter adjusted according to response. Maximum dose 24 mg. daily.
Pimozide	▪ Orap (tablets)	*Mania, hypomania, short-term adjunctive treatment of excitement and psychomotor agitation.*	*Mania, hypomania* — Initially 10mg daily in acute conditions, thereafter adjusted according to response to maximum of 20mg daily.
Prochlorperazine	▪ Prochlorperazine (tablets) ▪ Stemetil (tablets, syrups, sachets, injection, suppositories)	*Mania*	*By mouth*, 12.5mg b.d. for 7 days, thereafter adjusted according to response to usual daily dose of 75–100mg. *By deep IM injection*, 12.5–25mg twice or thrice daily.
Thioridazine	▪ Thioridazine (tablets, oral solution) ▪ Melleril (tablets, suspension, syrup)	*As for Chlorpromazine*	*Mania* — 150–600mg daily; maximum 800 mg. daily for up to 4 weeks (hospital patients only).
Trifluoperazine	▪ Trifluoperazine (tablets, oral solution) ▪ Stelazine (tablets, spansules, syrup)	*As for Chlorpromazine*	*Mania — by mouth*, initially 10mg daily, increased by 5mg after 1 week, then at intervals of 3 days according to response. *By deep IM injection*, 1–3mg daily to maximum of 6mg daily.
Zuclopenthixol Acetate	▪ Clopixol Acuphase (injection, oily)	*Mania*	*By deep IM injection into the gluteal muscle or lateral thigh*, 50–150 mg, if necessary repeated after 2–3 days (1 additional dose may be needed 1–2 days after the first injection). Treatment should not exceed 2 weeks — maximum of 4 injections and maximum cumulative dose of 400mg per course.

LITHIUM

The mainstay of treatment is Lithium although several anticonvulsants and calcium channel blockers may serve as alternatives. Lithium is a natural substance which occurs in food and water and small amounts can therefore be found in the body. It acts in a quite different way from neuroleptics. Its side-effects are much less unpleasant and, if it works, it controls all the symptoms of the illness, including the racing thoughts, instead of simply sedating the patient and slowing him down. However, it takes several days to act, which is a serious disadvantage if the patient is aggressive and disruptive so that immediate control of disturbed behaviour is necessary.[68]

Indications

Lithium helps to control acute episodes of mania and reduces the risk of relapse. Its primary use is in the prophylaxis of bipolar affective disorder. It has the advantage of minimising the risk of a swing into depression.

Contra-indications

Lithium is excreted mainly by the kidneys. Any impairment of renal function virtually excludes treatment and it is usually necessary to determine renal function before deciding on the treatment. However, according to Kendell, if lithium is to be used to treat an acute manic episode in a young adult with no history of renal disease it is not necessary to wait for the results of detailed tests of renal function. Indeed, those which involve collecting an accurate 12 or 24 hour urine sample are usually impracticable until the patient has become more co-operative.[69] Cardiac and thyroid function must also be normal before starting lithium. Lithium impairs the uptake of iodine by the thyroid gland and can induce hypothyroidism.

Efficacy

The precise mechanism of action is unknown but lithium has been shown to be effective in preventing attacks of recurrent depression and mania and, to a lesser extent, in treating them. Inevitably, some people taking lithium do not respond to the treatment or respond only partially. More specifically, lithium treatment of manic patients is unsuccessful in about a quarter of cases, and between a third and one half of patients maintained on lithium relapse in a two year period.[70] In terms of predicting who will respond, Lader and Herrington have summarised the relevant research findings:[71] the more typical the patient the more likely he is to respond; a family history of manic-depressive illness predicts a good response[72]; pyknic body build is twice as common among responders as non-responders; response is associated with cyclothymic traits and non-response with withdrawn, anxious and obsessive personalities; a history of schizophrenia, schizo-affective disorder, or of four or more affective episodes per annum during the two to three year period preceding treatment, is associated with a poor prognosis.

68 See R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993).

69 *Ibid.*, p.448.

70 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.206.

71 *Ibid.*, p.210. A pyknic build is characterised by a short, stocky, well-rounded body.

72 J. Ananth and J.C. Pecknold, "Prediction of lithium response in affective disorders" *Journal of Clinical Psychiatry* (1978) 39, 95–100.

Dose and plasma concentratio.

Lithium has a low therapeutic index — toxic concentrations are not much greater than therapeutic concentrations — and it is therefore necessary to keep a regular check on serum lithium levels. Serum levels are estimated between eight and 12 hours after the last dose and guideline lithium levels are given in the table below. Lower levels apply to older patients. Serum estimations are initially frequent, up to twice weekly, but may be reduced to every three months once the treatment has been established. When lithium is used as a treatment for mania, rather than prophylactically, higher serum levels may be necessary. The serum level usually needs to be at least 1.0 mmol Li^+/l to control manic behaviour[73] but should not exceed 1.5 mmol Li^+/litre.[74] Toxicity generally occurs at levels over 2.0 mmol Li^+/l.[75] The dose needed to sustain a level of 1.0 mmol Li^+/l "may produce some toxic effects but there is little risk involved when the patient is under constant observation and the serum level can be checked at any time."[76] Lithium estimations should complement clinical observation and not form a "blind substitute"; some patients are helped despite lithium concentrations below 0.5 mmol and others show signs of incipient toxicity with concentrations hardly exceeding 1.0 mmol.[77]

LITHIUM (B.N.F. 4.2.3)

Drug	*Proprietary*	*BNF guideline doses*	*BNF plasma concentrations*
Lithium Carbonate	▪ Camcolit (tablets)	*Treatment* initially 1.5–2g. daily. *Prophylaxis* initially 0.5–1.2g. daily.	"Doses are adjusted to achieve a plasma concentration of 0.4–1.0 mmol Li^+/litre (lower end of the range for maintenance therapy and elderly patients) on samples taken 12 hours after the preceding dose. It is important to determine the optimum range for each individual patient." (B.N.F., 34, p.172).
	▪ Liskonum (tablets)	*Treatment* initially 450–675mg. twice daily. *Prophylaxis* initially 450mg twice daily.	
	▪ Priadel (tablets, liquid)	*Treatment and prophylaxis* initially 0.4–1.2g. daily.	
Lithium Citrate	▪ Li-Liquid (oral solution)	*Treatment and prophylaxis* initially 1018–3054mg daily.	
	▪ Litarex (tablets)	*Treatment and prophylaxis* initially 564mg twice daily.	
	▪ Priadel (tablets, liquid)	*Treatment and prophylaxis* initially 1.04–3.12g. daily.	

Adverse effects

Side-effects early on during treatment include dry mouth, increased thirst, nausea, mild stomach cramps, tremulousness, and decreased libido. Certain side-effects sometimes persist after the body has adjusted to lithium, including excessive weight gain, skin rash and thyroid changes. Hypothyroidism and kidney damage may

73 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.448.

74 *Drugs in psychiatric practice* (ed. P.J. Tyrer, Butterworths, 1982).

75 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.200.

76 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies, supra*, p.448.

77 M. Lader and R. Herrington, *Biological treatments in psychiatry, supra*, p.201.

occasionally be long-term effects. Toxic interactions have been repo between lithium and antipsychotic drugs such as haloperidol and thioridazine. Lithium toxicity is characterised by diarrhoea, vomiting, increased tremor, dysarthria (**1078**), drowsiness, and ataxia (**1063**) and in the most severe cases by restlessness, confusion, nystagmus, fits, delirium and eventually death.[78]

Combining lithium with other drugs

Haloperidol is commonly combined with lithium, the former providing immediate control of symptoms while the effects of lithium build up to the point where the antipsychotic medication can be withdrawn.[79] However, according to Kendell, there is no evidence that lithium and haloperidol are more effective in the control of severe mania than haloperidol alone. Furthermore, "there are reports of patients developing an acute brain syndrome, followed in some cases by lasting extrapyramidal and cognitive deficits, on large doses of the two drugs together."[80]

CARBAMAZEPINE

In cases of resistant mania or bipolar affective disorder, carbamazepine (CBZ) is sometimes used instead of, or in conjunction with, lithium. It may also be used as a prophylactic although one study showed that while lithium doubled the mean time in remission, carbamazepine only increased it by 50 per cent.[81] Because it may depress the white cell count, regular checks on this are necessary, particularly early on during treatment. The drug is available as Carbamazepine (tablets), Tegretol (tablets, liquid, suppositories), and Tegretol Retard (tablets). The BNF guideline dose is 400mg initially, increased until the symptoms are controlled, with a usual range of 400–600mg daily and a maximum of 1600mg. Common adverse effects include mild leukopenia, nausea and vomiting. Carbamazepine decreases blood levels of haloperidol and tricyclic antidepressants and suppresses circulating levels of T_3 and T_4 (**1298**).

CALCIUM CHANNEL BLOCKERS

Calcium channel blockers such as verapamil and nifedipine, which are usually prescribed for heart conditions such as angina, have also been used to treat mania and they may act by blocking serotonin receptors.

ELECTROCONVULSIVE THERAPY (ECT)

ECT has a role for patients with severe manic illnesses which do not respond to medication (**1132**). One recent trial demonstrated that bilateral ECT given three times a week was more effective than lithium.[82]

---

78 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.208.

79 J. Biederman, *et al.*, "Combination of lithium carbonate and haloperidol in schizo-affective disorder" *Archives of General Psychiatry* (1979) 36, 327–333; M. Lader and R. Herrington, *Biological treatments in psychiatry, supra*, p.203.

80 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), pp.448–449.

81 S.E. Watkins, *et al.*, "The effect of carbamazepine and lithium on remission from affective illness" *British Journal of Psychiatry* (1987) 150, 180–182; M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.210.

82 J.G. Small, *et al.*," Electroconvulsive treatment compared with lithium in the management of manic states" *Archives of General Psychiatry* (1988) 45, 727–732.

23. Schizophrenia and related psychoses

INTRODUCTION

The majority of people detained under the Mental Health Act 1983 are diagnosed as suffering from a form of mental illness known as schizophrenia. Schizophrenia is commonly thought of as a psychiatric term for a range of experiences which the majority of the population describe as "madness." For this reason, to be diagnosed as having schizophrenia carries a stigma which other diagnoses do not. Beyond the public perception, what schizophrenia is is difficult to define. Innumerable definitions and models have been suggested but it is impossible to point to any single defining pathology, symptom or cluster of symptoms, common to all people so diagnosed. It is therefore important to realise at the outset that schizophrenia is a model, an organisational concept the purpose of which is to make it easier to comprehend the variegated phenomena of illness than it would otherwise be.[1] Whether the various presentations collectively classified as forms of schizophrenia do indeed share a particular unifying pathology, and are homogenous at some fundamental level, or instead represent several different kinds of illness or disease process, has still to be established. For the moment, the description of schizophrenia given in the International Classification of Diseases gives an idea of the broad range of experiences associated with the diagnosis[2] —

> "The schizophrenic disorders are characterised in general by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect ... The most intimate thoughts, feelings, and acts are often felt to be known to or shared by others, and explanatory delusions may develop, to the effect that natural or supernatural forces are at work to influence the afflicted individual's thoughts and actions in ways that are often bizarre. The individual may see himself or herself as the pivot of all that happens. Hallucinations, especially auditory, are common and may comment on the individual's behaviour or thoughts ... Perplexity is also common early on and frequently leads to a belief that everyday situations possess a special, usually sinister, meaning intended uniquely for the individual. In the characteristic schizophrenic disturbance of thinking ... thinking becomes vague, elliptical, and obscure, and its expression in speech sometimes incomprehensible. Breaks and interpolations in the train of thought are frequent, and thoughts may seem to be withdrawn by some outside agency. Mood is characteristically shallow, capricious, or incongruous. Ambivalence and disturbance of volition may appear as inertia, negativism, or stupor. Catatonia may be present."

---

1 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.278. Janzarik once described the history of schizophrenia as a history not of medical discoveries but of intellectual models on which the orientation of psychiatry is based.

2 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.86–87.