

CHAPTER 1

Clinical features of depressive disorders

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Classic phenomenology

Robert Burton published *The Anatomy of Melancholy* in 1621 and it enjoyed great popularity. Samuel Johnson found it to be the only book that ever raised him from his bed 2 hours sooner than he wished to rise. The writings of Milton, Byron and Lamb were all strongly influenced by it. In his account of melancholy, Burton described a state of mind that had been familiar to many before him, and his description must have resonated with the experiences of a large number of his readers. Here was a systematic account of the mental phenomena that had much earlier led the psalmist David to declare:

‘I am a worm, and no man; a reproach of men, and despised of the people.... I am poured out like water, and all my bones are out of joint: my heart is like wax; it is melted in the midst of my bowels. My strength is dried up ... and thou has brought me into the dust of death.’ (Psalm 22: 6–15)

Similarly, Job had described:

‘wearisome nights are appointed to me ... I am full of tossings to and fro unto the dawning of the day.... When I say, My bed shall comfort me, my couch shall ease my complaint; Then thou scarest me with dreams, and terrifiest me through visions ... I have sinned ... I am a burden to myself ... thou shalt seek me in the morning, but I shall not be.’ (Job 7: 3–21)

Melancholy, literally the ‘black humour’, had been one of Hippocrates’ four categories of madness, and it had been established as such throughout medieval teaching. In the 13th century Bartholomeus Angelicus wrote:

‘The patients are faint and fearful in heart without cause, and oft sorry ... feeling like earthen vessels they dread to be touched lest they should break ... they feel they have the world upon their heads and shoulders for it is about to fall.’ (Quoted by Hunter & Macalpine, 1963, p. 2)

For many of Burton’s predecessors, melancholy had been regarded with ambivalence. While few welcomed its ravages, many believed it to be a sign of great sensibility, and some even believed that people with melancholy ‘are accounted as most fit to attempt matters of weightie charge and high attempt’ (Du Laurens, 1599; quoted by Hunter & Macalpine, 1963, p. 52).

In keeping with this, Burton gave to melancholy a bitter-sweet character. In his rhyming prologue, alternate verses had the refrain ‘Naught so sweet as melancholy’, but he left his readers in no doubt as

to the terrifying quality of its most severe forms. He wrote: ‘If there is a hell on earth, it is to be found in a melancholy man’s heart’.

After Burton, 300 years elapsed before there was an account of the phenomenology of melancholy which matched his in both scope and quality. Emil Kraepelin’s *Manic Depressive Insanity and Paranoia*, published in English in 1921, is filled with vivid descriptions which confirm for the reader the appropriateness of Burton’s use of the words ‘hell on earth’. His text is still widely quoted. A decade after Kraepelin, the *Journal of Mental Science* published Aubrey Lewis’s ‘Melancholia: a clinical survey of depressive states’. In about 100 pages, this paper combines meticulous phenomenological analysis with an empirical study of 61 carefully documented patients seen in his practice at the Maudsley Hospital. Taken together, these works of Burton, Kraepelin and Lewis render an account of the clinical features of the depressive disorders that is unlikely ever to be equalled.

Psychiatry in the 19th and early 20th centuries saw a shift in terminology from Burton’s ‘melancholy’ to the current usage of the word ‘depression’. The nature and context of this change have been well described by Berrios (1992). The term ‘depression’ was favoured by physicians who heard in it echoes of a more physiological disorder. Kraepelin legitimised its use by giving it adjectival status in ‘depressive insanity’ and Adolf Meyer was an enthusiast for the more modern usage. The word ‘depression’, however, still has its passionate opponents. In *Darkness Visible*, a personal account of the illness, William Styron wrote:

‘Melancholia would still appear to be a far more apt and evocative word for the blacker forms of the disorder, but it was usurped by a noun with a bland tonality and lacking any magisterial presence, used indifferently to describe an economic decline or a rut in the ground, a true wimp of a word for such a major illness ... for over 75 years the word [depression] has slithered innocuously through the language like a slug, leaving little trace of its intrinsic malevolence and preventing by its very insipidity, a general awareness of the horrible intensity of the disease when out of control.’ (Styron, 1991, p. 37)

Clinical features of depressive disorders

‘The Tower of Babel never yielded such confusion of tongues, as the chaos of melancholy doth variety of symptoms.’ (Burton, 1621, p. 240)

LEE

Many phenomena can be identified as features of depressive disorders. These vary both in the patterns in which they occur and in their intensity. In severe forms symptoms tend to be pervasive and unchanging. In milder forms they may shift constantly, in ways which reflect the dynamic relationships between them.

Some phenomena are exaggerations of normal experience, for example feelings of sadness or guilt. These become significant as symptoms because of their intensity, or their frequency, or their inappropriateness. Other phenomena involve impairments of normal capacities, for example loss of the ability to feel pleasure. A third group emerge as developments from other symptoms, as is seen when marked feelings of guilt evolve into delusions.

There have been many attempts to classify symptoms but none has been widely accepted. This account follows the traditional order of presentation within the mental state, although appearance and behavioural features (including linguistic ones) are considered separately at the end, after an account of histrionic features and depressive stupor. Impaired concentration and memory are discussed alongside other impairments of feeling, energy and thinking; these, together with vegetative (bodily) changes, are often referred to as the 'associated features' of depression.

Painful affects

Depressed mood

'Sorrow sticks by them still continuously gnawing as the vulture did...' (Burton, 1621, p. 236)

Depressed mood is the commonest symptom found in depressive disorders. It has an obvious claim to be the central feature, but it is not essential for diagnosis and it is not easy to delineate. Most definitions refer to sadness, misery or dejection. The mood is painful and oppressive, and frequently without apparent cause. It can be distinguished from normal feelings of sadness or unhappiness which accompany loss or failure by its greater intensity, duration and pervasiveness. A special quality is often described, as if a black cloud were descending. Sufferers feel heavy-hearted and weighed down with their miseries. Tears come unexpectedly and at times for no reason. Those who are severely depressed may be beyond tears, in a state of frozen misery.

This extremely unpleasant state is usually coloured by depressive thinking, and is experienced as gloom, hopelessness, despair, insufficiency, loneliness or unwantedness. One sufferer wrote:

'The gray drizzle of horror induced by depression takes on the quality of physical pain.... I feel the horror like some poisonous fogbank roll in on my mind, forcing me into bed.' (Styron, 1991, pp. 50, 58)

Some patients successfully conceal their mood change and very few offer their mood as a presenting complaint. It is extremely rare for someone depressed for the first time to use the words 'I feel depressed'. Sometimes depressed mood is absent, or it may be masked by irritability, problems with introspection or a cultural tendency to show depression in forms other than mood disturbance.

Anxiety

'A kind of panic and anxiety overtook me ... accompanied by a visceral queasiness.... The flight of birds caused me to stop, riveted with fear ... I have felt the wind of the wing of madness.' (Styron, 1991, pp. 42, 46)

Anxiety is also one of the commonest symptoms in depressive disorders, although sufferers rarely complain of it by name. Often it is experienced as an apprehensive foreboding, as if something terrible is going to happen. Sufferers usually do complain of autonomic accompaniments, which include a dry mouth, palpitations, tremulousness, sweating, blushing, 'butterflies' or a knot in the stomach, choking, difficulty getting breath, dizziness and giddiness. These may be misinterpreted as evidence of a physical illness, which may lead to escalating anxiety. Panic attacks and phobic avoidance may develop. Many sufferers wake early with anxious ruminations and autonomic symptoms, feeling unable to face the day. This is a very useful diagnostic pointer to the presence of a depressive illness.

The feeling of anxiety can be coloured by cognitive features, in particular pessimistic thinking, low self-esteem and a preoccupation with death. Danger is felt to be imminent, as are loss and disgrace. Everyone encountered is a potential thief or is out to pick a quarrel. Friends or relatives will die. The world is upon the sufferer's shoulders and it is about to fall. There is a fear of collapse, of madness, of death or eternal damnation.

Agitation

Agitation is marked anxiety combined with excessive motor activity. Sufferers feel anxious and restless and complain that they cannot keep still. They may continually wring their hands or fidget with a convenient object. They may constantly shift positions. In severe forms they cannot remain seated, and pace up and down, or pick feverishly at their clothes. They often appear scared or startled, with wide eyes and a half open mouth.

Agitation is often accompanied by worrying. The sufferer cannot escape from a round of painful thoughts ridden with anxiety. Agitated patients report feeling frantic, always wanting to be somewhere else but not knowing where to go to. One man described feeling dreadful, badgered and worried. A woman felt she was getting into a terrible state of feverish nervous excitement: 'I know that something has to be done. I don't know what to do.'

Agitation can be distinguished from akathisia (motor restlessness occurring as an extrapyramidal side-effect of neuroleptic medication), from states of gross excitement and from stereotypies. In akathisia, anxiety is usually less prominent than it is in depression and indeed often absent. Gross excitement in depression usually has an aggressive or explosive quality. Motor stereotypies involve the exact repetition of patterns of movement and tend to be comforting, leading to a reduction of anxiety.

Irritability

Alongside sadness and anxiety, those who are depressed may complain of increased irritability, experienced as a

lowered threshold for annoyance and anger in the face of frustration. Sufferers may keep it to themselves, or may exhibit increased argumentativeness, uncharacteristic shouting and quarrelling, outbursts of temper, throwing or breaking things or, in extreme cases, violence to others.

Changes in mood

Fluctuations in mood are common, and may be both abrupt and extreme. About 50% of sufferers show a regular pattern. Most feel worse in the mornings but there can be regular mid-afternoon or evening exacerbation. Diurnal variation, with mood lowest in the morning, is often considered typical of the somatic syndrome of depression (see Box 1.1, below), as is loss of reactivity to the environment.

Reactivity is often harder to assess in hospital, but improvements often follow immediately after admission, with further marked changes following visits from relatives, visits home, changes in other patients and attempts at therapy. Reactivity does not imply a less serious depression, for it is not unknown for patients to be cheerful to the point of misleading those around them as to the need for vigilance, and then unexpectedly to hang themselves.

Impairments of feeling, energy and thinking

Anhedonia: loss of capacity for enjoyment

‘They are utterly unable to rejoice in anything. They cannot apprehend, believe or think of anything that is comfortable to them.’ (Richard Baxter, a 17th-century clergyman, quoted by Hunter & Macalpine, 1963, p. 241)

Anhedonia is the second most common symptom in depressive disorders. Whereas painful sadness is the psychological opposite of pleasure, anhedonia refers to its negation – the absence of pleasure. Anhedonia is part of a wider phenomenon; as Jaspers (1963, p. 111) describes: ‘the feeling of having lost feelings’ is associated with a ‘terrible emptiness – a subjectively felt void’. It is closely linked to feelings of dulled perception and depersonalisation, and also to feelings of insufficiency and lack of vitality.

Those with anhedonia do not experience pleasure even if something good happens. They are not cheered by fine weather, receiving a compliment, winning a game or by a surprise windfall, for example. They cannot enjoy the company of friends and are not happy spending time at their previous hobbies and interests (see also ‘Loss of interest’, below). Kraepelin (1921, pp. 75–76) captures the phenomenon well:

‘[the sufferer is] indifferent to his relatives and to whatever he formerly liked best ... a dull submission ... shuts out every comfort and every gleam of light. ... Everything has become disagreeable to him; everything wearies him, company, music, travel, his professional work. ... Life appears to be aimless ... and meaningless. ... All the joy [of nature] cannot pump a drop of bliss from [his] heart up to [his] brain.’

Lewis (1934) comments on the ‘especial distress’ experienced by his patients from rural districts when they were unable to enjoy the sight of the fields, the sky, the trees and the flowers.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

Anergia: loss of energy

Kraepelin’s description of ‘total lack of energy’ in a depressed man has never been bettered:

‘He drags himself with difficulty from one day to another ... [he] lacks spirit and willpower. ... He cannot rouse himself ... cannot work any longer ... has to force himself to everything. ... The smallest bit of work costs him an unheard-of effort; even the most everyday arrangements, household work, getting up in the morning, dressing, washing, are accomplished with the greatest difficulty and in the end indeed are left undone. Work, visits, important letters, business affairs are like a mountain in front of the patient and are just left, because he does not find the power to overcome the opposing inhibitions. Finally [he] gives up all activities, sits all day with his hands in his lap, brooding to himself in utter dullness. Sometimes a veritable passion for lying in bed is developed.’ (Kraepelin, 1921, pp. 76–78)

Kraepelin did not view loss of energy as tiredness or fatigue but rather as one manifestation of ‘psychic inhibition’, the sufferer being unable to overcome inhibitions to action, which themselves may have resulted from excessive fear and pessimism. The French psychiatrist and philosopher Pierre Janet (quoted by Lewis, 1934, p. 298) held a similar view: ‘The feeling of inadequacy is essentially a fear of action, a flight from action, a checking regulation which stops one action, seeks to replace it with its opposite, and in doing so causes a failure of the action.’

Today these concepts are often regarded as closer to the phenomenon of obsessional slowness. Loss of energy is now usually framed in terms of unpleasant inappropriate tiredness, listlessness and exhaustion. There may also be an important overlap with hypochondriasis.

Although these observations suggest that anergia is not a unitary phenomenon, the description ‘decreased energy or increased fatigability’ is a central element of the ICD-10 criteria for depression (World Health Organization, 1992). A useful probe is: ‘Have you been getting exhausted or tired-out during the day or evening, even when you have not been working very hard?’. It is important to distinguish the psychological symptom from anergia due to a physical disorder.

Sufferers complain of sluggishness, of feeling sapped and drained, or of lacking strength. Their limbs feel like lead, they have lost their vitality or they feel insufficient in some way. They may describe themselves as worn out, exhausted or even too weak to move. They may feel slowed down almost to the point of paralysis. Styron (1991) wrote that it was as if psychic energy was throttled back to zero. Informants report neglect of children, meals, housework, personal cleanliness and tidiness. Depressed people are often sent home from work because of inefficiency. The combination of exhaustion with inability to sleep may be particularly hard to bear.

Retardation

About half of depressed patients feel that their movements are slowed down. This phenomenon is termed ‘retardation’. Those affected may walk very slowly or may sit perfectly still throughout an interview. Speech may also be slowed, hesitant and laboured, with few

LEE

sentences longer than ten words, and seldom more than one sentence. There may be long pauses before replying ('response latency') and also between each word.

Inefficient thinking and retardation have often been viewed as being unified by the concept of psychic inhibition. Many textbooks follow this line and refer to an observed slowing of thought and action as psychomotor retardation. This practice has been criticised as leading to an overemphasis on objective signs, as against the core phenomenon of the subjective experience of slowness. Lewis (1934) argued that observed slowness in speech and task performance is usually not due to slowness in thought but rather to inattention, preoccupation or difficulty in thinking. None of his patients said that their thoughts were slower or fewer. Many of those whose talk appeared to be slowed described their thoughts as racing. Conversely, many complaints of slowed movement were not borne out by objective testing. These considerations suggest that the term 'retardation' be reserved for a subjective feeling of slowed movement, but nevertheless observable slowness also remains an element of diagnostic criteria.

Inefficient thinking/impaired concentration

'They are inconstant ... persuaded to and fro on every small occasion.... Wavering, irresolute, unable to deliberate through fear.... As a man that's bitten with fleas, their restless minds are tossed and vary.' (Burton, 1621, p. 237)

There are several components to the difficulty in thinking found in depression. These include indecisiveness, a tendency to ruminate and an inability to sustain attention. There is often a difficulty in ordering and calling up thoughts and memories, and occasionally slowness. Most of Lewis's patients described a constant press of thoughts, their thoughts running on, their brain never stopping. Kraepelin similarly described his patients as feeling that too much was in their heads: fresh thoughts were always coming, leading to confusion. As a result their thinking was unclear, muddled and lacking in focus. In many patients apparently laborious and slow thinking is due to disorganisation of thoughts rather than any slowness of the thoughts themselves.

Other patients describe their lack of concentration by saying that their thoughts just drift off. Those who are severely affected cannot read more than a few lines, follow a television programme for more than a few minutes, or follow a conversation. They may feel that they cannot take things in, cannot collect or pull together their thoughts. Their head feels heavy, their mind stupid and confused. They often feel they have no memory and that they have lost their command of previous knowledge. They may have problems remembering where they put things. This difficulty may interact with an increased sensitivity to losses; Styron (1991, p. 57) wrote that 'each momentary displacement filled me with a frenzied dismay'. Indecision may show itself as inconstancy or appear as paralysis, with sufferers considering at length the simplest matters.

Loss of interest

'the enthusiast gradually gives up his hobby, the gardener leaves the weeds alone, the golfer lets his clubs rust.' (Hamilton, 1982)

In both major diagnostic systems – ICD-10 (World Health Organization, 1992) and DSM-IV (American Psychiatric Association, 1994) – this symptom is combined in a single criterion with loss of pleasure. Most definitions also refer to a marked reduction in the range and intensity of interests and hobbies, as well as in work and domestic activities, leisure pursuits, keeping well informed and maintaining an interest in clothes, food and personal appearance.

By these definitions the symptom is a composite phenomenon, related to both feeling and activity. It has three components:

- 1 inability to enjoy interests (anhedonia – see above)
- 2 loss of anticipatory pleasure and concern (apathy)
- 3 reduction of activities.

The distinction between the first two of these, anhedonia and apathy, may reflect disorder of different neurophysiological mechanisms. Apathy also has an element of helpless futility. The third component, reduction of activities, follows from anhedonia and apathy, but also may result from inefficient thinking, inability to sustain concentration, phobic avoidance, fatigue and loss of energy, and motor retardation. Despite the fact that it is not a unitary phenomenon, it is loss of interest as defined by behavioural change that is most easily identified and rated, and therefore this is likely to remain in clinical use.

Bodily symptoms

Disturbances of appetite and weight

As a rule there is little appetite for food or drink, and food lacks any flavour. Occasionally, there may be increased appetite or episodes of ravenous hunger and bingeing. Attitudes to eating and drinking may change quickly, and will usually range from a mild disinclination (due to lack of appetite) to outright refusal. Carers may need to use persuasion and cajolery. Reluctance to eat or drink may result directly from a delusional belief that food is poisoned. Refusal to accept fluids can quickly become life-threatening.

Kraepelin described marked fluctuations in body weight, and these are suggestive of changes in fluid balance. Today the most common clinical picture before treatment is of weight loss due to poor appetite rather than dieting or physical illness. Symptom criteria usually specify losses of more than 5% of body weight in a month, or around 1 kg (2 lb) a month for several months. Typically, a depressed person's weight stabilises after a loss of about 6–7 kg (1 stone), unlike the continuing decline seen in anorexia nervosa and occult malignancy. Sometimes weight is lost without any apparent reduction in food intake. In about 10% of depressive episodes there is a similar degree of weight gain, and this is often associated with hypersomnia.

Constipation is a common complaint, which may be due to reduced intestinal motility, to reduced food intake, or to the side-effects of antidepressant drugs. The complaint may also reflect hypochondriacal cognitive distortions in the mental state.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

Disturbance of sleep

Hippocrates described his melancholic patients as having little or no sleep (he claimed several had not slept for over 2 years). Kraepelin's patients typically lay sleepless for hours in bed, tormented by painful ideas; if they did sleep, they had confused and anxious dreams, then woke dazed, worn out and weary. They would get up late and might lie in bed for days or even weeks.

Three patterns of sleep in depression are traditionally described. Initial insomnia or delayed sleep is present when there is more than a 1 hour delay in sleeping after settling down. A delay of 2 hours or more marks a severe disturbance. Middle insomnia is also common, with either frequent waking or a prolonged period of being unable to return to sleep. People with depression frequently fall asleep shortly before they are due to arise. The third pattern, which is traditionally associated with the somatic syndrome, is early-morning waking. This is defined as waking at least one hour earlier than normal. Waking two or more hours earlier than usual marks a severe disturbance, and this is required to satisfy the 'somatic symptom' criterion in ICD-10. Mood is often lowest after waking early and this is a time when the risk of suicidal behaviour can be high.

Occasionally there is an increased duration of sleep (hypersomnia) or an inverted sleep pattern, with long periods of sleep during the day. There may be discrepancies between observed and reported sleep, which may reflect confusion, histrionic exaggeration, or hypochondriacal and nihilistic features of the mental state. The clinical picture is often distorted by hypnotic medication. A fuller account of the disorders of sleep in depression will be found on page 595.

Loss of libido

This symptom is rarely volunteered but is often present. A tactful approach will help to elicit it, and combining enquiries with routine questions about sleep and appetite is often useful. There is usually a lack of interest in sexual activity compared with normal, and this is often reflected in a diminished frequency of sexual intercourse. Men may suffer from erectile impotence and women may report loss of sexual pleasure. Very occasionally libido is increased.

***Disorders of thought content:
depressive cognition***

Alongside feelings of sadness and anxiety, and together with impaired enjoyment, energy and thinking, and bodily symptoms, there are usually changes in thought content. These include morbid preoccupation and disturbed judgement. In severe depression distorted thinking leads to overvalued ideas and delusions, which may have a melodramatic or even fantastic quality.

Cognitive distortions can relate to the past, present or future, and to the self or to the outside world. Thinking about the past is often dominated by self-reproach and guilt. In the present the self is often viewed as worthless and helpless. Hypochondriacal ideas may be prominent. The outside world is seen as useless, meaningless and, occasionally, persecutory. The future is viewed with apprehension, pessimism, hopelessness

and even nihilism. Thoughts of death are common. Suicidal ideas may follow, particularly in the setting of acute hopelessness and despair, but sometimes they arise independently and unexpectedly.

Thoughts and feelings of guilt

'Their phantasy most erreth in aggravating their sin.... They are continual Self-Accusers ... apprehending themselves forsaken of God.' (Richard Baxter, 1716, quoted by Hunter & Macalpine, 1963, p. 241)

Guilt is one of the most striking features of depressive disorders. Seventy-five per cent of sufferers feel it to some degree. Three phenomena can be distinguished.

- 1 *Pathological guilt.* Those affected blame themselves for some action which others would not take very seriously. They often recognise that this is out of proportion but they cannot help feeling self-blame and dwelling upon it. They may blame themselves for neglecting their children, bills having not been paid, duties having been ignored. Sufferers may feel their friends have been let down; their unwise decisions are regretted intensely. They may feel guilty about having stolen sweets as a child or for having been ungrateful to their parents. Characteristically, sufferers also feel blame for bringing an illness upon themselves. Ideas of worthlessness and self-deprecation are closely associated.
- 2 *Guilty ideas of reference.* Those affected feel that others are blaming them; in more severe forms they feel accused. Insight is preserved and so sufferers recognise the feeling as their own. Intense forms shade into persecutory delusions.
- 3 *Delusions of guilt.* As depressive states deepen, ideas of guilt become less realistic, and insight into their pathological nature is lost. Patients magnify their own role in events and may give an entirely false account of a serious misdemeanour (delusional memory). Delusional guilt sometimes has the quality of glorifying self-aggrandisement. One patient claimed 'I am the chief sinner; there never was anyone in the world as wicked as me.' Patients may believe that they have committed adultery or incest, that they have killed their families, that they have caused a train crash or air disaster, or that they have become possessed by the Devil. Patients may give themselves up repeatedly to the police. Delusional guilt may also involve feelings of responsibility for others. One patient was convinced that she was making other patients ill. Another believed that whenever he ate someone was executed. Great care should be taken to distinguish between delusional memories and accurate recall of painful events for which feelings of guilt are appropriate. Guilt over past incest may be delusional or it may be a highly significant disclosure.

Thoughts of worthlessness and self-deprecation

'But I am a worm, and no man.' (Psalm 22: 6)

In depressive states any premorbid tendency to feelings of inferiority and low self-worth is amplified. Raised standards are applied to the self without a corresponding change with regard to others. Compensatory merits are discounted. People with severe depression often regard

LEE

themselves as worthless and as total failures. There are occasionally delusions of poverty, such as the false belief that one is bankrupt.

Sufferers describe themselves as unwanted, unloved and not worthy of having friends. They feel discontented with themselves. They lack confidence. They have failed at everything, they will lose their jobs, they face ruin. Requests for lists of personal strengths and weaknesses often result in catalogues of faults with no redeeming features. In severe states, feelings border on self-loathing and self-hatred.

It can be hard to distinguish depressive self-deprecation from insight and from long-standing attitudes to the self. For example, there may have been genuine failure at work as a result of impaired concentration, indecisiveness and lack of energy. There may always have been a lack of confidence and low self-esteem. Depression is identified by a fluctuation in self-deprecation with mood, by its intensity and by the fact that it is a change from the normal.

Hypochondriasis

‘Some are afraid that they shall have every fearful disease they see others have, hear of or read.’ (Burton, 1621, p. 235)

People who are depressed have many good reasons to feel that they are physically ill. They may have experienced low mood, loss of appetite and fatigue during a previous physical illness. Depressed mood or muscular tension may be felt as a physical pain in the chest or head. The autonomic symptoms of anxiety all suggest physical disorder.

These experiences may lead a person to suspect a physical illness, but this does not amount to hypochondriasis. When there is also anxious foreboding and a worried, pessimistic mood, hypochondriacal phenomena are likely to emerge. There may be a heightened awareness of bodily sensations, and an abnormally intense and painful preoccupation with the possibility of a fearful disease, or a growing conviction of an unhealthy, rotten or diseased body. In extreme forms there may be beliefs that the sufferer has one or more physical illnesses in the face of evidence to the contrary. Such hypochondriacal delusions can take on a fantastic and even nihilistic quality. The illness may be viewed as a deserved punishment.

Kraepelin described patients who believed that they were incurably ill and expecting a slow and painful death. Some claimed they had lung disease or cancer; others had tapeworms; others could not swallow. Lewis’s patients were particularly concerned with their bowels; one said, for example, ‘they have all gone wrong ... the food just wedges in’. One patient had a sudden blank feeling across his forehead and was sure it was a stroke. More fantastic ideas have involved: organs being withered, burnt or rotten; brains melting, leaving skulls full of filth; and bones out of joint and insects breeding inside the cavity. Patients have reported excruciating pains, disfiguring eruptions on the face, testicles being crushed, food falling down between intestines into the scrotum. Nihilistic hypochondriacal delusions have included beliefs that the body is hollow, that stomach and bowels are no longer there, that no urine is passed, and that genitals have disappeared.

Hopelessness, *tedium vitae* and suicidal thoughts, plans and acts

‘My days are swifter than a weaver’s shuttle, and are spent without hope ... so that my soul chooseth strangling, and death rather than my life.’ (Job 7: 6, 15)

The future may appear bleak and without comfort. Life can seem pointless and not worth living (*tedium vitae*), there being little or no hope of recovery, so that more pain and anguish will follow. Fleeting thoughts of suicide are common and often plans are made. When hope is lost, suicide may begin to appear as a logical solution, as a relief from intolerable pain or even as an atonement for real or delusional guilt. Thoughts of joining loved ones who have already died are particularly ominous, as is the writing of a suicide note, settling one’s affairs and taking precautions against being found. Threats to take the lives of children or a partner to save them from the effects of the suicide should also be taken very seriously. While suicidal acts usually arise out of a sense of extreme despair, they may emerge suddenly and without warning in states of milder depression, often in association with impaired impulse control, and with the sufferer unable to account for the motives.

Many risk factors for suicide have been identified, but these can be difficult to apply in practice. Three useful clinical predictors are hopelessness, suicidal plans and previous attempts. Kraepelin regarded psychic inhibition (see ‘Anergia’, above) as protective against suicide, and warned against the increasing risk when retarded patients recovered their volition while remaining hopeless. Many clinicians have encountered the unexpected suicide of a patient who appeared to be recovering. The decision to take one’s life is often accompanied by a sense of calmness, and suicidal plans may be concealed behind apparently cheerful behaviour. A detailed account of suicide is given in Chapter 7.

Suicidal thoughts and acts are not the only results of depressive thinking about the future. If recovery is felt to be unlikely, or impossible, then concordance with treatment may be poor. Pessimism can interact with perceptions of the world as cruel and desolate, and with an extremely apprehensive mood. The resulting thought content can range from regret that society’s values are decaying to a conviction of imminent global catastrophe.

The self may be perceived as potentially dangerous. One patient reported by Du Laurens (1597, quoted by Hunter & Macalpine, 1963), believed that if he were to pass water then his whole town would be drowned by the volume of his urine. He was reportedly treated by his attendants convincing him that the town was engulfed in a raging fire which needed his intervention. Today patients are more likely to be convinced of impending nuclear holocaust or financial ruin, and it may be that altruism can no longer be relied upon for a cure. Delusions of catastrophe have a nihilistic quality: everything will be destroyed, nothing can be done. In extreme forms, as Jaspers (1963) describes, the future vanishes.

Delusions

As already indicated, these will sometimes occur as an end-point of severe cognitive distortion. Five main types can be identified:

- 1 delusions of guilt
- 2 delusions of poverty
- 3 hypochondriacal delusions
- 4 delusions of catastrophe
- 5 nihilistic delusions.

All of these are regarded as mood congruent. Persecutory delusions, delusional jealousy and delusions of bodily change are also sometimes found in depressive illnesses. Examples of delusions of guilt, poverty, hypochondriasis and catastrophe have already been given.

Cotard (1882) described a syndrome of nihilistic delusions often associated with hypochondriasis. The central feature is the delusion of negation: for example, a patient goes beyond the belief that his bowels are not working to the point where his bowels cease to exist. Such nihilistic delusions can refer to parts of the body, the self, the world or even the future.

Persecutory delusions commonly take the form of beliefs that the patient is under surveillance, that there is a plot, an organisation such as the CIA is pursuing the patient, other patients are detectives or secret agents, food is poisoned, and so on. The persecution is usually felt to be justified, as a development from guilty ideas of reference, but some patients show resentment at its unjust nature and may even loudly proclaim their innocence.

Disorders of experience

Depersonalisation

Depersonalisation is not a common symptom of depression, but when present it is striking. Sufferers feel unreal, as if they were acting a part, or as if they were a robot. Insight into the abnormality of this phenomenon is retained. The feeling is highly unpleasant but difficult to describe, and hence metaphor is often used. One patient said, 'I've got this dreadful feeling as if I'm unreal, a sort of dead feeling, wooden inside. I've changed; I do things mechanically.' Jaspers analysed depersonalisation as resulting from a loss of sense of awareness: of the self as an active agent; of temporal continuity of the self; and of the distinction between the self and the outside world. Depersonalisation is also closely linked to the phenomenon of anhedonia. It should be distinguished from:

- 1 a perception of parts of the body as unfamiliar
- 2 dysmorphophobia (the perception of one's appearance as changed)
- 3 delusions of bodily change
- 4 nihilistic delusions of non-existence.

Exploring the reasons behind a person's feelings of depersonalisation sometimes uncovers hidden delusions.

Only about a half of those presenting with depersonalisation are depressed and so it is not a diagnostic sign. It sometimes occurs in healthy persons under stress, in association with intense anxiety, or following sensory deprivation. It may occur in many other psychiatric conditions, including organic disorders (especially temporal lobe seizures), schizophrenia, generalised and phobic anxiety disorders, post-traumatic stress disorder and after the use of hallucinogens. Very

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

occasionally it occurs as a primary phenomena alongside derealisation (see below). It is categorised as such in ICD-10 as depersonalisation disorder, a sub-class of the dissociative disorders.

Theories of the mechanisms underlying depersonalisation have been reviewed by Sierra & Berrios (1998). Functional imaging studies have identified reduced neural responses in emotion-sensitive areas of the brain, accompanied by increased responses in regions associated with emotional regulation. Depersonalisation may have a protective effect in acute anxiety but in depressive disorders it is often associated with a chronic course and it can be difficult to treat. Glutamate hyperactivity has been postulated, but early results from a small randomised controlled trial of lamotrigine, which inhibits glutamate release, were disappointing.

Derealisation

Derealisation is another uncommon but often striking feature of depression. In mild forms, the person's surroundings lack colour and life, and other people may seem to be making a pretence of their emotions. In more severe forms everything seems artificial or unreal, like a stage set populated with actors. One patient described it as follows: 'People seem changed, like machines; things look mysterious. It's as if I were in a dream, watching a film.' Lewis analysed the phenomenon as a combination of various changes, including:

- 1 altered perceptions of the environment, for example appearances of unreality, mystery, acting and soullessness
- 2 changes in consciousness, for example bewilderment, muddle, impressions of mystery and confusion
- 3 loss of the ability to recall images with vividness
- 4 changes in the experience of time.

Derealisation should be distinguished from nihilistic delusion. Derealisation is an experience, not a belief, and insight into its abnormal nature is retained.

Obsessive-compulsive phenomena

Obsessive-compulsive symptoms occur in 20–35% of depressive episodes, often as an exaggeration of pre-morbid traits. The core phenomenon is the experience of intrusive thoughts or impulses which are recognised as one's own and which are entertained or carried out against conscious resistance. The sufferer recognises them as senseless and tries to stop but cannot. In time the experience of conscious resistance may fade.

Obsessional thoughts in depressive disorders usually have aggressive or obscene themes. For example, knives may be avoided for fear of harming the self or others, or there may be a strong impulse to shout obscenities while in a church service. There may be recurrent and apparently senseless thoughts of killing one's family. The obsessional nature of such thoughts is usually protective against harmful actions, but any switch from an obsessional to a delusional quality in thoughts with suicidal or homicidal themes is extremely ominous.

Repeated checking is a frequent problem. For instance many people with depression cannot remember whether they have locked doors and may return to check. This

LEE

is not a true obsessional symptom unless they can remember locking the door but still need to check again to satisfy an inner compulsion.

A few of those who gain obsessional symptoms during a depressive episode fail to lose them on recovery. One interesting hypothesis is that such symptoms may have a dual role in depression, acting both as markers of a propensity for psychosis and also as defences against disintegration of the psyche (Stengel, 1945).

A full account of obsessive-compulsive phenomena is given in Chapter 15.

Hallucinations

In states of normal grief, seeing and hearing the deceased is not uncommon, but in depressive illnesses hallucinations are rare. When they occur they are usually auditory, in the second person and consistent with depressive themes of guilt, death, personal inadequacy, disease, nihilism or deserved punishment. They are often isolated phenomena and are seldom in the foreground of the clinical picture. Often there is little more than an indistinct muttering. Kraepelin reported his patients as hallucinating the crackling of hell or the hammering of a gallows being erected. When a voice is recognised it is often that of a relative or partner. Typically only a few words are distinct. A parent may be heard to say in a condemnatory tone: 'You have let everybody down' or 'You deserve to die'. On closer examination, many of these phenomena are not true hallucinations but rather illusions, auditory misinterpretations, or pseudo-hallucinations (i.e. they are heard within the mind and not located in physical space by the patient). Kraepelin describes vividly how the vascular murmur of the ear becomes a reproach: 'Whore, whore, whore...', which is then attributed to the Devil. When true hallucinations do occur they are often more frequent at night and are often described as emanating from the sufferer's body, for example as a voice speaking from inside the stomach.

Command hallucinations also occur, most often instructing the patient to harm him- or herself, or others. These should be examined carefully for evidence of passivity phenomena, in which the patient feels impelled to act under the controlling influence of an outside force. The association of command hallucinations with passivity phenomena is an extremely dangerous development.

Visual distortions are sometimes seen. Faces can take on an ominous or spectral quality. A shadow may be seen at the window. Worms may swarm in the patient's food. True visual hallucinations are rare, but they can appear as an invitation or enticement to suicide. One patient saw a clear vision of a noose and believed this was a signal that she should hang herself.

Hallucinations in other modalities are even rarer, but can include the perception of a strong smell of putrefaction emanating from a house or from the person's own body. Very occasionally hallucinations occur simultaneously in more than one sensory modality.

Schizophrenia-like and mood-incongruent psychotic features

There are patients whose illnesses appear to be typically depressive but who experience somatic hallucinations,

or passivity phenomena, or describe thought insertion, or express bizarre nonsensical or absurd delusions, or delusions of external influence, or persecutory delusions unrelated to deserved punishment. Both Kraepelin and Lewis reported such features in their classic descriptions of melancholy, and they were especially prominent in Kraepelin's categories of 'paranoid' and 'fantastic' melancholy. Many of these phenomena constitute first-rank symptoms of schizophrenia, and if they are prominent they point to an ICD-10 diagnosis of schizoaffective disorder (see Chapter 9).

Delusions or second-person hallucinations that are affectively neutral or not in keeping with a depressed mood occur in up to a third of all patients with psychotic depression and do not in themselves point to schizoaffective disorder. These can be specified in ICD-10 as mood-incongruent psychotic features, although there is little agreement about the value of making such a distinction.

Histrionic features

Kraepelin wrote that hysterical disorders were observed 'extraordinarily often' in melancholia. Aubrey Lewis devoted many paragraphs to 'neurotic features', which comprised a mixture of psychosomatic and conversion symptoms and histrionic behaviours. Although such features are familiar to most clinicians, they now receive scant recognition in many textbooks.

Kraepelin's account included noises in the ears, shivering in the back and special sensitivity to the influence of the weather. He also described fainting fits, giddiness, hysterical convulsions, choreiform clonic convulsions and psychogenic tremor. Lewis portrayed many conversion-type symptoms, such as vomiting or headaches under stress or in unwelcome situations. His account of histrionic behaviour included exaggerated and melodramatic talk, attitudes of extreme dependence, threatening a hunger strike, clutching arms with a very appealing manner, seeking endless sympathy and pedantic formality. He described over-intimacy, letters like novelettes and strong affective relationships which quickly changed from strong attachment to active dislike. Some of his patients were 'always seeking attention, calling out, asking for interviews, self-pitying, and copying symptoms from others'. Others were 'laughing and crying alternately with neither giving the impression of much depth'. One patient was always stealing another patient's pillows; another's eyes kept revolving. Many were worried about their eyes or ears, and multiple pains, which resolved quickly.

Such features can be regarded as pathoplastic effects of a histrionic premorbid personality, or as a re-emergence of childhood and infantile behavioural patterns, with acute fears of abandonment, fierce attachments and possessiveness. One should be cautious about assuming the former, for it is striking how apparently histrionic 'personality' features often disappear completely when a patient recovers fully from a depressive illness.

Depressive stupor

Kraepelin described stupor as a syndrome rather than a symptom. His patients usually lay mute and motionless

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

in bed, at most withdrawing timidly from approaches, sometimes demonstrating catalepsy, sometimes merely aimless resistance. They sat helpless before food but often allowed themselves to be spoon-fed. They held fast what was pressed into their hand, turning it slowly about, without knowing how to get rid of it. Unable to care for their bodily needs they frequently became dirty. Now and then periods of excitement were interpolated. Kraepelin described how, after the return of consciousness, memory was 'very much clouded and often quite extinguished'.

Depressive stupor is usually conceptualised either as an end-point of severe retardation or as an extreme form of psychic inhibition. Severe forms, with a complete failure to respond to the surroundings, are now rarely seen. More commonly patients present in a pre-stuporous phase, having stopped eating and drinking, still speaking a few words, but spending most of their time staring into space. When patients recover they usually give a clear account of their experiences, describing the state as an extremely painful one. The fact that Kraepelin's stuporous patients had only patchy recall on recovery has led to suggestions that some were showing clouding of consciousness, perhaps due to dehydration or nutritional factors. Stupor is included in ICD-10 alongside hallucinations and delusions as a psychotic feature of severe depression. Stupor is also discussed in Chapter 20 (see page 490).

Appearance, behaviour and talk

The appearance of depression is usually easier to recognise than it is to describe. It is often identified directly rather than inferred from any combination of elements. The following features are common, but few may be present, and there may even be smiles and apparent jocularity.

Most sufferers appear sad, dejected, downcast, miserable or guilty, much of the time. They may look stony faced, frightened or apprehensive. Worry may be evidenced by a furrowed brow, and the corners of the mouth may be turned down. Posture is often stooped or drooping and sufferers may sit head in hands, looking at the floor. Tears may be close, or there may be actual crying, weeping or sobbing. Their general manner may signal an attitude of dependency, hostility or even indifference.

Evidence of self-neglect is common. Those affected may be untidy and unkempt, dirty and smelling, with unwashed hair. Clothes may be unusually drab, or dirty and stained. Night-clothes may be worn in the middle of the day. There may be signs of weight loss or dehydration, or evidence of self-harm (e.g. scars or bruises). Agitation or retardation may be apparent, as described above. There may be a poverty of movement, gesture and speech. Talk is likely to be soft or monotonous, and may die away, often with sentences left incomplete. There may be hesitancy, monosyllabic replies or even muteness.

Changes in social behaviour

Depressive illnesses can provoke many changes in social behaviour and these are often the most prominent features of the clinical presentation.

Inefficiency at work may lead to threats of redundancy or to unemployment. Unpaid bills and failure in budgeting may cause financial crises. Irritability, loss of feeling and social withdrawal can lead to a breakdown of relationships with friends or family. Marital discord is a common presenting problem. It may be hard to distinguish between cause and effect in a person with chronic depression who complains of an unhappy marriage.

Alcohol and other drugs are often used to provide relief from depressive symptoms, especially low mood, anxiety and insomnia. A presentation with alcohol or drug misuse may mask an underlying depressive illness. Equally, a hidden alcohol problem commonly underlies treatment-resistant depression. Antisocial behaviours are sometimes released by depressive illnesses. Shoplifting, promiscuity, sexual aberrations, violence and physical and sexual abuse are all ways in which a depressive illness can present itself.

Hypochondriacal features may lead to repeated medical consultations, especially when somatic symptoms closely mimic a physical illness. This is a fairly common mode of presentation of depressive disorders, particularly in those who have difficulty in describing their feelings.

Most importantly of all, depressive illnesses can result in increased risk-taking, self-harm, suicide and even homicide. An episode of deliberate self-harm is one of the commonest ways in which a depressive illness is revealed.

Of course, phenomena such as unemployment, marital discord, antisocial behaviour and deliberate self-harm can have many other causes. They are sometimes associated with depressive illnesses, and when they occur one possibility among many is that the individual is suffering from a primary depressive illness.

Diagnostic criteria and classification

No clinical feature described here is either necessary or sufficient for the diagnosis of a depressive episode. For each, there are episodes where the phenomenon is absent and yet the diagnosis remains one of depression. Conversely, each can occur as a symptom of another disorder. Depressive disorders therefore show a pattern of family resemblance, and diagnoses are best made using polythetic criteria, with multiple elements. Both ICD-10 (World Health Organization, 1992) and DSM-IV (American Psychiatric Association, 1994) employ this approach.

Core features

There have been many attempts to isolate core features. The most obvious candidate is depressed mood, which appears in most accounts, ranging from *The Anatomy of Melancholy* to current textbooks. Burton, however, was very aware that depressed mood was not essential. He wrote: 'Some indeed are sad and not fearful, some fearful and not sad; some neither fearful nor sad' (Burton, 1621, p. 234). Kraepelin did not even view depressed mood as a central feature. He believed the underlying

LEE

process to be a depression of function: 'simple psychic inhibition'. Bleuler and Janet held similar views, Janet stressing the importance of a feeling of inadequacy (see Lewis, 1934, p. 301). Jaspers (1963) argued for two independent central features: 'an unmotivated profound sadness' and 'a retardation of psychic events'.

Two other features, low self-esteem and anhedonia, have found support as candidates for core features of the disorder. ICD-10 and DSM-IV criteria include both depressed mood and anhedonia as core features. DSM-IV requires that at least one of these must be present for a diagnosis of a depressive syndrome. ICD-10 is closer to the Jaspersian tradition, in that it includes increased fatigability as a third core feature and requires two out of three features for the diagnosis of depression to be made. Thus in both current systems there can be patients diagnosed as depressed who are 'neither fearful nor sad'. Robert Burton would have approved.

Classification

The bewildering range of depressive disorders has led to a search for organising principles. Variation can be accounted for by differences in severity and by the shaping ('pathoplastic') effects of personality and circumstances. However, many psychiatrists believe that there must also be a heterogeneous group of disorders behind the variability, and there have been many attempts to find a useful and valid division into subtypes. Few areas in psychiatry have generated more heated debate and yet remained for so long in a state of confusion. There have been two main themes running through the literature: an endogenous/somatic distinction of subtypes, and a unipolar/bipolar distinction.

From endogenous depression to the somatic syndrome and beyond

First, can depressive illnesses be divided into two main types on the basis of aetiology, clinical features and response to treatment? Timothy Bright (1586, quoted by Hunter & Macalpine, 1963, p. 37) noted 'how diverslie the word melancholy is taken'. He identified cases where melancholy was 'not moved by any adversity present or imminent', in which 'the melancholy humour ... abuseth the mind' and for which physical treatment was needed. He described a second type of melancholy where 'the perill is not of body' but 'proceedeth from the mind's apprehension'; this required 'cure of the minde', that is, psychotherapy. For the four centuries and more since, Bright's distinction between endogenous and exogenous forms has reappeared in various guises, in particular as the division between endogenous and reactive depressions, and that between psychotic and neurotic depression, which had been embodied in the *International Classification of Diseases* until ICD-10, which introduced the somatic syndrome (see below).

With hindsight we can see how this simple and apparently sensible distinction led to confusion. Three main elements characterise Bright's 'melancholy humour' or what we would now term the endogenous category:

- 1 the absence of an external cause
- 2 a biological clinical picture
- 3 response to physical treatment.

Problems arise whenever cases meet one of these criteria but not the others. For example, Paykel *et al* (1984) have shown that the clinical picture of depressive illnesses is mostly independent of the presence or absence of an external cause. It follows that the aetiological division between endogenous and reactive depression may bear little relation to the biological clinical picture or to response to particular forms of treatment.

Further problems have arisen from the use of the terms 'psychotic' and 'neurotic' to attempt to identify the distinction that Bright made. Kendell (1968) has discussed how the patients encountered in asylum practice by Kraepelin, and identified as suffering from manic-depressive psychosis, differed from those seen in the consulting rooms of early psychoanalysts, who described their patients as suffering from depressive neuroses. This selective experience by different groups of clinicians with very different aetiological models may have led to an artificial polarisation between two forms of what may nevertheless have been the same illness.

In addition, both 'psychotic' and 'neurotic' have had several meanings. A diagnosis of 'manic-depressive psychosis' or 'psychotic depression' according to Kraepelin and the tradition of the *International Classification of Diseases* (again, before ICD-10) did not require the presence of hallucinations or delusions. For most psychiatrists now the word 'psychotic' is used to convey precisely the fact that hallucinations or delusions are present. The term 'neurotic' has been used to refer to milder depressive episodes, to episodes showing 'neurotic' clinical features, to 'reactive' episodes, to chronic fluctuating depressive disorders, to depressive disorders that respond to psychotherapeutic interventions or to depressive episodes arising on the background of a neurotic personality. It has been no surprise to find that the diagnosis of 'neurotic' depression lacks both reliability and validity.

One escape route from this confusion would be to adopt the position argued by Lewis (1938), namely that all the variability in depressive illness is due to the effects of severity and pathoplastic factors, together with a variation between episodic and chronic forms. This unitarian approach has been central to the development of DSM criteria and also underpinned the tenth revision of ICD, in which the neurotic-psychotic distinction was finally abandoned.

It was the advent of the Research Diagnostic Criteria (RDC) in the United States that marked the first step in this direction (Spitzer *et al*, 1978). Neurotic depression was rejected on the grounds that it was an amorphous category, and depressions were divided into major and minor on the basis of severity. 'Psychotic' major depression was restricted to cases showing delusions or hallucinations. Subtypes were proposed, including endogenous depression (RDC) or melancholia (in the subsequent DSM criteria), and operational criteria for these included pervasive anhedonia, loss of reactivity, early-morning waking and weight loss. DSM-III-R (American Psychiatric Association, 1987) further introduced a classification of depressions into three levels

Box 1.1 ICD-10 criteria for the somatic syndrome

At least four of the following:

- marked loss of interest or pleasure
- loss of emotional reactions
- waking in the morning 2 hours or more before usual time
- depression worse in the morning
- objective evidence of marked psychomotor retardation or agitation
- marked loss of appetite
- weight loss (5% or more of body weight in the past month)
- loss of libido

of severity – mild, moderate and severe – and this has remained in DSM-IV.

A similar approach was taken in ICD-10, with four main levels of severity (see Box 1.2, below), with ‘psychotic’ being restricted to hallucinations, delusions or depressive stupor. ‘Melancholic’ features were designated as ‘somatic’ (an optional ‘syndrome’). ‘Biological features’ had been considered as an alternative term to ‘somatic symptoms’ and this would reflect the usage of many psychiatrists, but ‘somatic symptoms’ remained in the final version.

It is the somatic syndrome (ICD-10) (see Box 1.1) or melancholic subtype (DSM-IV) that has the strongest echoes of Bright’s endogenous form of depression. The clinical features identifying this symptom cluster have emerged consistently from discriminant function and factor analytic studies, and have been repeatedly shown to predict both response to physical treatments (including electroconvulsive therapy and antidepressants) and an increased risk of recurrence. Most proponents claim that pervasive anhedonia and loss of reactivity are central defining characteristics and that these probably reflect a distinct pathophysiology. Others have suggested that retardation is the central phenomenon.

Critics of the approach taken by ICD-10 and DSM-IV continue to argue against the relegation of what they feel to be a crucial diagnostic distinction to merely an optional subtyping into melancholic or somatic features, while perhaps less meaningful distinctions based on severity are promoted. It is probably true that most psychiatrists can cite criteria to separate major and minor depression, whereas only a minority will reliably identify the somatic syndrome. Contrary to the hopes expressed in ICD-10 and DSM-IV, most depressive episodes previously described as ‘neurotic’ or ‘reactive’ cannot be classified as minor depressions or dysthymia (see below), but fall squarely into the major depressive category, so that samples of patients with major depression ascertained for research purposes may be unduly heterogeneous.

While the unitarian approach has found support from the longitudinal studies of Angst and colleagues, who present evidence for a spectrum of depressive disorders (Angst & Merikangas, 1997), others still remain strongly wedded to the notion of two distinct illnesses, and have accused DSM and ICD-10 of leading depression research into a blind alley. To be fair, the authors of ICD-10 have acknowledged that while the

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

status and future of the biomedical pole of Timothy Bright’s distinction is still uncertain, there remains widespread clinical and research interest in its survival.

Unipolar and bipolar disorders

The second major theme running through the history of the classification of the affective disorders involves the relationship between mania and depression. Kraepelin believed that mania and depression were definitely ‘manifestations of a single morbid process’ and he argued strongly for their unification in a single disorder, manic-depressive insanity. This term was to be used even where no manic attacks ever occurred. Many believe that this synthesis was as significant as his separation of manic-depressive insanity from dementia praecox, but it has always had its critics. Diagnoses in ICD-9 (World Health Organization, 1978) followed Kraepelin, so that a single episode of severe depression was described as ‘manic-depressive psychosis: depressed type’. This often misled the lay public, who wrongly interpreted the diagnosis as implying that manic attacks were to be expected.

Leonhard (published in English in 1979) has been credited with rediscovering the distinction between unipolar and bipolar affective disorders. Two further independent empirical studies embodying this distinction appeared almost simultaneously (Angst, 1966; Perris, 1966) (see also Chapter 3, page 51) and their remarkably consistent findings have had a major effect on the subsequent psychiatric literature, which has emphasised the differences between those patients who show unipolar depressive histories and those who show bipolar histories (i.e. of both depression and mania).

Despite these findings, as yet there has been no clear difference shown in clinical features or pathophysiology between unipolar and bipolar depressive episodes. Most of the evidence remains consistent with the hypothesis that bipolar illness represents no more than an increased genetic loading for a unitary affective disorder. There is also increasing support for the concept of a bipolar spectrum (Akiskal *et al.*, 2000). Kraepelin may yet be proved to have had an equally penetrating insight, but the unipolar/bipolar distinction is now widely regarded as the most robust sub-classification of the affective disorders. It was no surprise to find that ICD-10 followed the DSM approach in distinguishing between unipolar and bipolar disorders.

The two main classificatory systems

ICD-10

As indicated above, the ICD-10 classification is a radical departure from its predecessors in finally abandoning the distinction between manic-depressive psychosis and depressive neurosis. An operational definition is given for a depressive episode (outlined in Box 1.2), which is based on a 2-week duration of symptoms. Four levels of severity are defined, mainly on the basis of symptom numbers, but also taking into account functional impairments.

A useful distinction can be made between symptoms, syndromes, episodes and disorders. Symptoms comprise the clinical features described earlier in this chapter,

LEE

Box 1.2 An outline of ICD–10 criteria for a depressive episode

A

- Depressed mood most of the day, nearly every day
- Loss of interest or pleasure
- Decreased energy or increased fatiguability

B

- Loss of confidence or self-esteem
- Unreasonable self-reproach or guilt
- Recurrent thoughts of death, or suicide, or any suicidal behaviour
- Impairments of thinking (subjective or objective)
- Agitation or retardation (subjective or objective)
- Sleep disturbance of any type
- Decreased or increased appetite with corresponding weight change

The symptoms should not be attributable to psychoactive substance use or to any organic disorder.

For a mild episode: At least four symptoms are present during the same 2-week period. At least two of these should be from group A. The patient is usually distressed by the symptoms but will probably be able to continue with most activities.

For a moderate episode: At least six symptoms are present during the same 2-week period. At least two of these will be from group A. The patient is likely to have great difficulty in continuing with ordinary activities.

For a severe episode: At least eight symptoms are present during the same 2-week period, including all three from group A. Suicidal thoughts and acts are common.

For a severe episode with psychotic symptoms: As for a severe episode, but with the additional presence of either hallucinations or delusions or stupor so severe that social activities are impossible. There may be danger to life from suicide, dehydration or starvation.

Adapted with permission from ICD–10.

differing from the normal by virtue of their intensity, pervasiveness and inappropriateness. These can be combined, as in ICD–10, as elements of operational criteria to define mood syndromes. Mood syndromes can occur as part of any disorder, but when they occur on the basis of a mood disorder the result is a mood episode. Episodes occurring singly or in combination define a mood disorder.

In ICD–10, the move from depressive episodes to bipolar and unipolar disorders appears complicated but follows simple rules. If a manic or hypomanic episode has already occurred, then the present episode is classified as ‘bipolar disorder, current episode mild/moderate/severe/severe with psychotic symptoms’, as defined in Box 1.2. If only episodes of depression have occurred previously, then the present episode

is classified as ‘recurrent depressive disorder, current episode mild/moderate/severe/severe with psychotic symptoms’, defined similarly. If no previous affective episode has occurred, then a current episode of depression remains classified at the episode level, again with definitions as in Box 1.2. ICD–10 also allows for the specification of the presence within mild and moderate episodes of the somatic syndrome (Box 1.1), but assumes that in severe episodes this syndrome will almost invariably be present. Severe episodes with psychotic symptoms can be further divided on the basis of mood congruence. ICD–10 also provides provisional criteria for seasonal pattern (see Box 1.3, below).

DSM–IV

The DSM–IV classification of the affective disorders is similar to that in ICD–10. This reflects both a conscious effort by the authors of each to bring the two systems together, and also the fact that the two approaches share a common ancestry in DSM–III–R. In general, the DSM–IV system is simpler and avoids making a distinction between single and recurrent episodes. It also includes a wider range of useful specifiers, including seasonal pattern, atypical features, catatonic features, rapid cycling and postpartum onset (within 4 weeks of childbirth). Longitudinal characteristics can also be identified, including the degree of any remission and chronicity.

DSM–IV criteria for a mild depressive episode are more stringent than those in ICD–10, in that they require five symptoms rather than four. In DSM–IV diagnosis requires one out of two essential features (sadness, anhedonia) compared with two out of three (sadness, anhedonia, anergia) in ICD–10. There is an additional requirement of clinically significant distress or impairment of functioning. Depressive episodes induced by a drug of misuse or medication, or by an organic factor or as part of normal bereavement are excluded. The somatic syndrome is called melancholia, and the criteria for this differ from those in ICD–10. Psychotic features do not include stupor but are restricted to delusions and hallucinations.

Seasonality: seasonal affective disorder

For over 2000 years there has been speculation about seasonal influences on the incidence of mania and melancholia, and in particular about the possible connection between the winter months and depression. Most clinicians can identify patients with bipolar illnesses or recurrent depressive illnesses that show a remarkably consistent seasonal pattern, and it is possible that these constitute a significant subtype of the mood disorders. During the decade 1980–90 this idea received a major impetus from the finding that winter depression may respond to a specific treatment, phototherapy (see below). As a result, criteria for seasonal pattern were incorporated into DSM–III–R and these have been modified in DSM–IV and ICD–10 (Box 1.3). Community and clinic surveys show that about 10% of all patients with major mood disorders meet these criteria.

Summer and winter depressions have been recognised, but it is winter depression that has been most studied; it has been popularised as ‘seasonal affective disorder’ (SAD) (Wehr & Rosenthal, 1989). Patients with

Box 1.3 An outline of the ICD-10 criteria for seasonal affective disorder

- Three or more episodes of mood disorder must occur with onset within the same 90-day period of the year for 3 or more consecutive years.
- Remissions also occur within a particular 90-day period of the year.
- Seasonal episodes substantially outnumber any non-seasonal episodes that may occur.

SAD typically describe lowered levels of energy and activity, anxiety, dysphoria and irritability, impaired concentration, social withdrawal and decreased libido. Most also report a distinctive constellation of symptoms, which include hypersomnia, increased appetite and overeating and carbohydrate craving. Most are mild to moderate in severity but a significant number (11% in one series) require in-patient treatment. In Washington, DC, at latitude 38.9, the illness has been reported as beginning in November, when the hours of daylight fall below 10. Patients in the United States typically report their worst months as January and February, compared with November and December for those in Europe. Untreated episodes usually resolve by springtime and some sufferers report mild euphoria and increased levels of energy, activity and libido, with decreased need to sleep, in the summer months. Most meet the criteria only for unipolar disorders, although some meet bipolar II criteria and very occasionally bipolar I disorders are found (see Chapter 2 on bipolar I and II disorders). Familial risks of affective disorders in SAD are similar to those found in non-seasonal depressive illnesses. It is not clear whether SAD is inherited as a distinct entity or whether seasonality and depression are separate heritable traits that happen to coincide in certain individuals.

The underlying pathophysiology of SAD remains a fascinating intellectual and scientific puzzle. Early hopes that the seasonal pattern and response to phototherapy could be explained in terms of changes in melatonin secretion have not been fulfilled. These have been replaced by theories of disordered brain serotonin regulation, or phase-advanced circadian rhythms. There is likely to be biological and genetic heterogeneity. One intriguing hypothesis is that patients with SAD generate a biological signal of change of season that is absent in healthy volunteers but is similar to that which mammals use to regulate seasonal changes in their behaviour.

Prevalence estimates for SAD vary between 0% and 10%. Studies within the United States have shown consistently higher rates at northern latitudes, but wider comparisons suggest that the influence of latitude on prevalence is relatively small, with other factors such as climate, genetic vulnerability and sociocultural context playing a more important role. Estimates within Europe cluster around a mean of about 3%. Follow-up studies show diagnostic instability, with only about a third of cases remaining seasonal after 5–8 years. In Switzerland two-thirds of those where the picture had changed reported improvement, which suggests that SAD is not necessarily the prodrome of a more serious disorder.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

Phototherapy

About a half of patients studied have shown a clinically significant response to a week of treatment with bright light. Early studies found response to be dependent on both the intensity of light and its duration. While 2500 lux for 2 hours daily was initially recommended, 10000 lux for 30 minutes has proved a more practical and equally effective option. There may be a differential response, with the typical depressive symptoms in SAD responding to bright light whereas the atypical symptoms respond to light treatment at all intensities. Exposure of the eye to the light is important; skin absorption does not modify circadian rhythms and is ineffective in SAD. Early-morning treatment is superior but leads to an increase in reported side-effects, including jumpiness, headaches and nausea, which occur in up to 15% of those treated. Dawn simulators (which produce a gradually increasing signal over 1.5 hours, peaking at 250 lux) may be an effective alternative approach.

Patients who respond to light treatment are usually advised to continue this until springtime and prophylactic treatment beginning in the autumn has been advocated.

Conventional antidepressant treatments have also been reported to be effective in SAD.

Recurrent brief depressive disorder

Not all episodes of depression last for 2 weeks or more, and some remit after just a few days. Thus, while some brief episodes can meet criteria for mild, moderate or even severe depressive syndromes, they may fail to be classified as depressive episodes because of their short duration. When such brief depressions recur frequently, the cumulative morbidity can be very significant.

Criteria for recurrent brief depressive disorder are included in ICD-10: brief depressive episodes must have occurred at least once a month over the previous year, and not solely in relation to the menstrual cycle. A prevalence rate of 10% has been estimated, with only half of those affected seeking treatment.

In contrast to dysthymia (see below), patients with recurrent brief depressive disorder are not depressed most of the time. The occurrence of this disorder in those who also have histories of more prolonged depressive episodes has been shown to carry a particularly high risk of suicidal behaviour.

Although recurrent brief depressive disorder may yet prove to be an important clinical diagnosis, it has not been widely used and its significance has perhaps been overshadowed by the development of the depressive spectrum concept and a focus on the importance of all forms of sub-threshold depressive syndromes.

Persistent disorders: dysthymia/cyclothymia

In Chapter 7 of his *Manic Depressive Insanity*, Kraepelin (1921) identified four fundamental states which he viewed as ‘permanently slighter’ forms of the disorder. These were described as depressive, manic, irritable and cyclothymic ‘temperaments’. He maintained that these occurred in about one-third of his manic-depressive patients, and that they provided evidence of the illness even during the ‘free’ intervals between attacks. He also believed that such states occur in others who have never experienced an episode of illness.

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Box 1.4 An outline of the ICD–10 criteria for dysthymia

A period of at least 2 years with constant or constantly recurring depressed mood. Intervening periods of normal mood rarely lasting longer than a few weeks. No episodes of hypomania.

Very few of the individual episodes of depression within the 2-year period are sufficiently severe or long lasting to meet the criteria for recurrent mild depressive disorder.

During at least some of the periods of depression at least three of the following are present:

- reduced energy or activity
- insomnia
- loss of self-confidence or feelings of inadequacy
- difficulty concentrating
- frequent tearfulness
- loss of interest in enjoyment of sex and other pleasurable activities
- feelings of hopelessness
- perceived inability to cope with routine responsibilities
- pessimism about the future or brooding over the past
- social withdrawal
- reduced talkativeness.

Early onset: late teens or 20s.
Late onset: 30–50 years of age, often after an affective episode.

Two of Kraepelin’s fundamental states can be found in modern classifications: ‘depressive temperament’ emerges as ‘dysthymia’ and ‘cyclothymic temperament’ as ‘cyclothymia’. The ICD–10 criteria are summarised in Boxes 1.4 and 1.5. There is no consensus on how these disorders should be regarded; they probably include a mixture of subclinical mood disorders, chronic reactions to adverse circumstances, partial remissions of mood episodes and disorders of personality structure (Akiskal, 1983). The term ‘double depression’ has been coined to describe a depressive episode occurring against the background of dysthymia (Keller & Shapiro, 1983). Follow-up studies (Angst & Merikangas, 1997) suggest that there is little diagnostic stability over the long term for many subtypes of depression, including dysthymia and brief recurrent depressive disorder. There is increasing support for the concept of a spectrum of manifestations within depressive disorders. In this way an individual might experience a depressive episode as either an antecedent to or as a sequel to sub-threshold disorders, such as dysthymia.

Dysthymia has a 1-year prevalence of 1–3% in general population surveys, and is more common in women, the unmarried and those with low income. Comorbid psychiatric disorder is found in over two-thirds of those affected and there is familial aggregation with other depressive disorders. Early-onset cases begin typically in adolescence or early adult life; it has been hypothesised that these are the consequence of either traumatic developments in childhood or an inherited

Box 1.5 An outline of the ICD–10 criteria for cyclothymia

A period of at least 2 years of instability of mood involving several periods of both depression and hypomania.

None of these periods meets the criteria for a manic episode, or moderate or severe depressive episodes, although such episodes may precede or follow the period of mood instability

During at least some of the periods of depression at least three of the following have been present:

- reduced energy or activity
- insomnia
- loss of self-confidence or feelings of inadequacy
- difficulty in concentrating
- social withdrawal
- loss of interest in or enjoyment of sex and other pleasurable activities
- reduced talkativeness
- pessimism about the future or brooding over the past

During at least some of the periods of mood elevation at least three of the following have been present:

- increased energy or activity
- decreased need for sleep
- inflated self-esteem
- sharpened or unusually creative thinking
- increased gregariousness
- increased talkativeness or wittiness
- increased interest and involvement in sexual and other pleasurable activities
- over-optimism or exaggeration of past achievements

Early onset: late teens or 20s.
Late onset: 30–50 years of age, often after an affective episode.

liability to mood disorder. Cases of later onset often arise following an episode of major depression or are associated with enduring health problems and chronic life difficulties. Both forms can give rise to considerable subjective distress and disability, and cumulative levels of morbidity have been estimated as equivalent to those resulting from major depressive disorders.

There is an increasing consensus that treatment of dysthymia is warranted. All classes of antidepressants have been found to achieve symptom response rates of the order of 65%, with residual impairments of social adjustment improving further with cognitive, group and interpersonal psychotherapies. Particular claims have been made for low doses of sulpiride and amisulpride; indeed, in Italy the first marketing authorisation for amisulpride was with the sole indication of dysthymia. There is emerging evidence supporting the use of other atypical antipsychotics, such as olanzapine and risperidone.

Cyclothymia typically begins early and shows a chronic course. Its lifetime prevalence has been estimated at 0.4–3.5%, with men and women equally affected. Cyclothymia may be over-represented in psychiatric

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

out-patient clinics. There is a familial aggregation with both unipolar and bipolar disorders, and some of those with cyclothymia go on to develop frank bipolar illnesses. Mood swings are typically unrelated to life events and cyclothymia may be difficult to diagnose without prolonged assessment or an exceptionally good account of previous behaviour. Misuse of psychoactive substances is a frequent concomitant. Low doses of mood stabilisers have been suggested as a rational treatment for cyclothymia but evidence for their efficacy is limited.

It has long been recognised that cyclothymia is likely to be a heterogeneous condition, with at least some cases being a mild or subclinical form of bipolar disorder. Akiskal and Angst, among others, have advanced the concept of the bipolar spectrum (see, e.g., Akiskal *et al*, 2000). About half the spectrum is occupied by bipolar illness or closely related disorders, while the remainder (including most of those diagnosed with cyclothymia) fall into the 'soft' bipolar spectrum, intermediate between bipolarity and normality. The combination of cyclothymia with a depressive disorder, characterised by increased risk taking and irritability, has been identified as a likely bipolar subtype that can be easily mistaken for an emotionally unstable personality disorder.

Classification on the basis of family history

The best way to resolve the problem of classifying depressive disorders would be to demonstrate genetic heterogeneity. There have been tantalising glimpses of this possibility. Winokur *et al* (1971) distinguished two groups on the basis of age at onset. The group with age at onset before 40 years was predominantly female. This group showed a higher incidence of alcoholism and sociopathy in male relatives, and a high incidence of depression in female relatives. The other group showed a predominance of males with a family history of depressive disorders alone. On this basis, the authors proposed a division into those with a family history of depression alone (pure depressive disease), those with a history of alcoholism or sociopathy in first-degree relatives (depressive spectrum disease) and 'non-genetic' cases (sporadic depressive disease). This classification has received some support from clinicians. Neuro-endocrine treatment and outcome correlates have been found, but attempts to replicate these validating studies have been inconsistent. Research with twins shows that the familial patterns observed are mainly due to environmental rather than genetic factors, which undermines the 'genetic' basis of the hypothesis. Recent developments in molecular genetics have opened up promising horizons for new hypotheses along similar lines to Winokur's proposal, but no practical classification has yet emerged.

Other classifications

'Agitated' and 'retarded' depressions have often been identified but criteria to separate these show little validity and they have been dropped from classificatory systems. The adjectives 'agitated' and 'retarded' are still used as clinical descriptors and both phenomena may

occur at the same time. 'Involuntary melancholia' was a term used by Kraepelin to describe depression occurring in late middle age with agitated and hypochondriacal features, often on the background of an obsessional personality. This diagnosis has been shown repeatedly not to meet validating criteria and is now obsolete. Researchers in the United States favoured a distinction between 'primary' depression (occurring *de novo*) and 'secondary' depression (following on from other disorders). While this approach enabled the definition of more homogeneous groups of depressive disorders for research purposes, it was received with little enthusiasm in the UK. The distinction is difficult to apply rigorously in clinical practice, and the validating evidence to support it is weak.

Measurement

The severity of a depressive syndrome depends on the number of symptoms, their intensity, their frequency, their duration and their pervasiveness. Subjective distress and impairments in functioning are also relevant. Not all of these factors covary and some may be negatively correlated. Despite this, experienced clinicians and their patients are able to make global assessments of severity which correlate surprisingly well. An example of guidelines for global assessment is given in the ICD-10 criteria for distinguishing mild, moderate and severe depressive episodes (see Box 1.2).

Most scientific approaches to the measurement of depression involve rating instruments. These are of two types. Observer ratings involve an examination of the subject, and ratings are completed by the interviewer. Self-ratings are made directly by the subject. While self-rating scales are more economical and are therefore useful for large-scale surveys, they have disadvantages. Those with milder depression tend to overrate their symptoms, while those with psychotic depression underrate them.

Good scales show test-retest and inter-rater reliability and have face validity, predictive validity and internal consistency (see Chapter 27, page 698). Data should be available for normative populations and to enable comparison with other instruments. Effective scales are short, clear and easy to administer, but if they are too short then reliability is sacrificed. A few of the better scales are discussed below.

Hamilton Rating Scale for Depression

After over 40 years of use, the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) remains the most popular observer rating scale for measuring the severity of depression. It meets most of the above criteria, although it has been criticised for being too long. Seventeen items are rated on scales of either 0-4 or 0-2, using a clinical interview and all available information. The assessment refers to the previous 1-2 weeks, and this limits its usefulness as a repeated measure of progress. Some argue that it is biased towards biological features of depression: over half the 17 items relate to anxiety, somatic features or insomnia. Nevertheless, it remains for many the instrument of choice for rating severity in those diagnosed as suffering

LEE

from a depressive episode. The accuracy of other scales is often tested by the strength of their correlation with the HRSD. Concerns have been raised that the scale is not always used according to its instructions, and that it is often used inappropriately as a diagnostic tool to screen for the presence of a depressive episode.

Montgomery–Asberg Depression Rating Scale

The Montgomery–Asberg Depression Rating Scale (MADRS; Montgomery & Asberg, 1979) is a shorter observer rating scale than the HRSD. It was derived from the Scandinavian Comprehensive Psychiatric Rating Scale. Ten items were selected as the most sensitive to response to treatment. It satisfies most of the above criteria and although it also requires a clinical interview, it is in theory easier to administer than the HRSD, and can be completed in under 20 minutes. It is widely used to measure change in depressed patients.

Beck Depression Inventory

The Beck Depression Inventory (BDI; Beck *et al.*, 1961) is probably the best-known self-rating scale for depression, and it too has retained its popularity for over 40 years. It was designed to be read to the subject, who chose from set responses. In this way it overcame the main objection to self-rating scales, namely the uncertainty that the subject is following the instructions correctly. Now it is usually given in a self-report form. It satisfies most criteria mentioned above, but lacks discriminatory power among those with very severe depression. In contrast to the HRSD, all but 6 of the 21 items relate to psychological phenomena. It can be repeated after short intervals and can be seen as complementary to the HRSD and the MADRS.

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) is a brief self-assessment scale that was designed to detect states of depression and anxiety in hospital medical out-patient clinics. Questions are carefully worded to avoid response bias, and refer to the previous week. Five of the seven items in the depression sub-scale relate to loss of the pleasure response, in order to avoid confounding with symptoms of physical illness, and on the basis that anhedonia may be the central feature of a biogenic depressive illness. The scale is easy to administer and it can be used both as a screening instrument and as a measure of severity.

Visual Analogue Scale

The Visual Analogue Scale (Zealley & Aitken, 1969) is one of the easiest ways of estimating global severity or the severity of individual symptoms. The rating can be made by either a clinician or the subject. A line 10 cm long is drawn and the end-points are identified as the extremes of the phenomenon to be measured. When rating sadness the end-points might be 'Not sad at all'

and 'As sad as I can imagine'. The rater makes a mark at the point on the line that best represents the present state. Despite its simplicity, this technique can produce useful information that correlates well with results from more sophisticated instruments. It is very useful for making repeated measures of a rapidly changing phenomenon such as diurnal variation in mood. One drawback is that ratings suffer from contrast effects, rapid changes being rated higher than slower ones.

Course and outcome

In *The Anatomy of Melancholy*, Burton devoted most of his chapter on 'prognostics' to suicide. Suicide does remain 'the greatest, most grievous calamity', which is 'a frequent thing and familiar' among depressed people, and is 'the doom of all physicians' (Burton, 1621, p. 260). It is considered in Chapter 7 in the present book.

Regarding the course and outcome of depression, Burton (p. 260) quoted Montanus:

'This malady doth commonly accompany them to the grave: Physicians may ease it, and it may lay hid for a while, but they cannot quite cure it, but it will return again more violent and sharp than at first.'

Three hundred years later, a more optimistic perspective was provided by Kraepelin, who separated manic-depressive insanity from dementia praecox on the grounds that it was a 'remitting' disorder.

Throughout most of the 20th century an optimistic view held sway, despite follow-up studies in the first three decades which catalogued an impressive array of long-term morbidity and mortality (e.g. Poort, 1945). The advent of modern 'effective' treatments and the promising results of short-term therapeutic trials reinforced that optimism and it was widely assumed that the prognosis of depressive illnesses had improved. However, few of the therapeutic trials lasted longer than 2 years, so that if later recurrence and long-term chronicity were a feature of the natural history of depressive disorders, they would rarely have been recorded. More recent long-term follow-up studies of depressed in-patients from Sydney (Kiloh *et al.*, 1988) and London (Lee & Murray, 1988) revealed a picture similar to that found in the earlier era (before the advent of pharmacotherapy). These studies, taken together with prospective studies from the US National Institute of Mental Health (NIMH) that showed cumulatively high rates of relapse and failure to recover (Keller *et al.*, 1986) led to a less sanguine but perhaps more realistic appraisal of the serious long-term import of a severe depressive illness. This has been followed by a reframing of severe depressive illnesses as lifelong disorders more akin to hypertension or diabetes.

Clinical prognosis studies

Knowledge of the course and outcome of psychiatric disorders is gained by combining clinical experience with the findings of clinical prognosis studies. Ideally, the follow-up of a typical cohort of sufferers will allow useful estimation of the rates at which patients recover, of the likelihood of recurrence, of the chances of chronicity and other complications, and of the risks of increased mortality from suicide and other causes.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

While shorter-term follow-up studies (1–5 years) give a fairly accurate picture of recovery and early relapse, they underestimate recovery among those with apparently chronic illnesses. More importantly, they also underplay the long-term risks of recurrence. Longer follow-up studies give a clearer picture of the lifetime impact of a disorder, by showing the risks of poor outcome due to repeated recurrences, cumulative chronicity, accumulating secondary handicaps and the evolution of secondary disorders. While longer-term studies will almost always be naturalistic, with no attempt to control for treatments, this has the advantage of giving a clearer picture of the likely ranges of outcomes under normal clinical conditions.

A well-designed follow-up study will identify prospectively a representative cohort, will make diagnoses according to well-established criteria, and will follow this series closely and comprehensively. Outcomes will be established according to clearly defined criteria, and analyses will use actuarial techniques in order to allow for deaths and patients lost to follow-up. There should be sufficient numbers to allow for generalisable findings, but not so many that intensive follow-up becomes impossible. Where predictors of outcome are sought, then the follow-up examinations should be conducted blind to initial assessments.

Since the NIMH, London and Sydney studies were published in the 1980s, several other long-term outcome studies of depression have met most of these criteria. There has been a growing understanding of the importance of comprehensive follow-up, as investigators have found up to half of severely ill survivors had lost contact with mental health services and so were difficult to trace. Studies using comparable methods have enabled us to explore whether there were improvements in outcome between 1960 and 2000. There is surprisingly little evidence that modern treatment approaches and prophylactic strategies are affecting either recovery or recurrence rates, although there are some grounds for hoping that they may be modifying episodes and ameliorating some of their more disabling and enduring consequences.

Recovery

Kraepelin (1921) described depressive episodes which ranged in length from days to more than a decade. Durations of several years were commonplace. Since 1945 the median length of depressive episodes has fallen to 6 months. Recovery rates are often thought to depend on severity of illness but there has been no convincing demonstration that out-patients or even those seen in primary care recover at different rates to in-patients.

In the early months of episodes of depression the cumulative likelihood of recovery rises quickly, so that by 6 months about half will have remitted. By 2 years about three-quarters will have remitted, and the remainder are defined as chronic. Chronic depressive episodes continue to remit slowly, so that by 5 years a further 15% of the initial cohort will have recovered, making 90% in all. The remaining 10% of episodes may be very prolonged, but the chances of eventual remission never disappear entirely.

Recovery has been shown to be faster for bipolar patients and from episodes with somatic features.

Secondary depressive episodes are slow to remit, although successful treatment of underlying disorders or substance misuse can lead to rapid recovery. The presence of hallucinations or delusions predicts a slower recovery, as do neurotic personality traits. Mood-incongruent and hypochondriacal features have also been shown to predict longer episodes. While the pattern of previous episodes is a useful guide to future course, this can be misleading, as a recurrent disorder with short episodes can unexpectedly become chronic.

The bodily symptoms of depression often remit more rapidly than cognitive features such as pessimism and low self-esteem. Cognitive distortion can be persistent and troublesome, as may continuing phobic avoidance, obsessional features and impairments of concentration. Symptoms often remit in a gradual and fluctuating way, which can be disheartening. Social impairments can also persist, with loss of confidence, social withdrawal, and difficulties both at work and in personal relationships. These social changes are sometimes found even where there is complete symptomatic remission. About a quarter of all those who have apparently recovered from depressive episodes show significant and enduring residual problems of one kind or another.

Relapse and recurrence

Many of those who recover from a depressive episode experience a return of symptoms, and the risks of this occurring are best described using survival analysis, a technique borrowed from the life-table approach used by insurance companies. There are two phases to the cumulative risk of symptom return. The first phase, within a few months, can be seen as signifying a re-emergence of the original episode. It has been proposed that the term 'relapse' be kept for this pattern, while 'recurrence' be used for those cases where a new episode of illness occurs after a longer period of full remission.

As many as one-third of depressive episodes may show the phenomenon of relapse. Predictors of relapse differ from those of recurrence and include severity, chronicity and premorbid personality difficulties, together with older age, poor social support, continuing adversity and further life events.

Estimates of recurrence rates vary with the samples studied and the length of follow-up. Most community studies show lifetime risks of around 50%. Angst (1988) argued that if followed long enough and closely enough virtually all moderate and severe depressive episodes would lead to recurrence. Recent studies suggest that, provided only genuinely first-episode cases are followed, as many as 50% of patients will suffer only a single episode, even in hospital series. This is an important message for clinicians and patients alike.

Two powerful predictors of recurrence emerge consistently from follow-up research. The first is the presence of residual symptoms after apparent recovery, which increases the recurrence risk threefold to about 75% in 2 years. The second factor is previous episodes of depression. This doubles the recurrence risk, with each new episode increasing the risk again by a further 16%. Other factors identified as likely to increase recurrence risks include the presence of somatic or psychotic features, an early age of onset, occurrence as part of a bipolar disorder and having a

LEE

first-degree relative admitted with depression. Many of these factors have been shown to have independent effects. In both the London and Sydney series discussed above, in-patients with somatic features and previous admissions had a 50% risk of being readmitted again within 2 years. Findings such as these suggest that for some depressed people little may have changed since Burton's quotation from Montanus.

Very poor global outcome

One of the most alarming findings from recent follow-up research is the extent of the cumulative risk of poor long-term outcome. It appears that each new episode of depression brings with it a renewed and considerable risk of chronicity. The cumulative risk of experiencing an episode lasting over 2 years may be as high as one in three. Factors predicting chronicity (i.e. slow recovery) are outlined above under 'Recovery'. A positive family history, previous episodes and thyroid disorder in women have also been implicated.

Very poor long-term outcome can result from failure to recover or from an interaction between residual symptoms and secondary handicaps such as unemployment, divorce and social isolation. Alcoholism may be a complicating factor. A very small number of sufferers also develop chronic schizophrenic illnesses, or chronic paranoid states, and very occasionally a chronic defect state occurs without other schizophrenic symptoms. In the London series up to a quarter of the survivors showed one or other of these various forms of very poor outcome after 18 years. Those with very poor outcome fell into two groups: the divorced and single, who had multiple hospital admissions; and those with very unhappy marriages, few admissions and a relative isolation from mental health services.

Mortality

The mortality risk for depressed in-patients is doubled (Tsuang & Woolson, 1977), through both suicide and an increased risk of physical disorders, especially arteriosclerotic and other vascular disorders (Angst, 1988). It was long held that 15% of in-patients with depression eventually ended their lives by suicide, but this figure was probably inflated as a result of bias from recurrent cases admitted to specialist centres. The estimated lifetime risk has been lowered to 6% (Inskip *et al.*, 1998) and this may still be an overestimate when considering all cases in secondary care. Most suicides occur outside hospital. The risk for in-patients is at its highest in the 2 years following discharge.

Switches from unipolar to bipolar disorder

One in ten of those who begin with a depressive episode go on to develop an episode of mania. The likelihood of such a switch drops markedly after the third episode of depression, by which time more than two-thirds of those who will show a bipolar disorder have already done so. The two main predictors of a switch are an early age at onset and a family history of bipolar disorder. Other predictive factors include retardation, hypersomnia,

hypomania precipitated by antidepressants, melancholia, delusions and hallucinations, and occurrence in the year after childbirth.

Differences in course and outcome between unipolar and bipolar disorders

There are surprisingly few differences, but those that exist are clear cut. Bipolar disorders tend to begin at an earlier age and have shorter episodes (with a median duration of 4 months) but more frequent recurrences. There appear to be no differences in rates of recovery, chronicity, suicide or overall mortality. After onset, the average proportion of lifetime spent ill has been estimated as 20% for both bipolar and unipolar patients (Angst, 1988). Outcomes among bipolar patients tend to be either very good or very poor. Mixed episodes and rapid-cycling disorders (four or more episodes in a year) are more likely to have very poor outcomes, but otherwise there are no reliable predictors among bipolar patients.

Prognosis for the individual patient

The best predictions of future course are often based on knowledge of a person's previous history, together with baseline risks for the disorder. Clinicians will also weigh the predictive factors outlined above, and consider personal strengths and vulnerability alongside the continuing supports and stresses in the environment. Maintaining factors and further life events will contribute to delays in recovery. Vulnerability factors such as unemployment and a lack of a confiding relationship will increase the risk of recurrence. Therapeutic factors are also important. Delay in adequate treatment is strongly associated with a chronic course. Outcome will very much depend on concordance with treatment and on whether adequate biomedical and psychosocial measures are available, both for immediate treatment and for prophylaxis in recurrent disorders. The task of translating therapeutic approaches with demonstrated efficacy into effective treatment programmes in clinical settings remains a major public health challenge.

Bereavement

'The chambers of the mansion of my heart, in every one whereof thine image dwells, are black with grief eternal for thy sake.' (James Thomson, 1932)

Human grief is universal and many of the experiences of bereaved people overlap with clinical features of depression. In 'Mourning and melancholia' Freud (1917) based an aetiological theory of depression on these similarities. This was the first of many models of the process of mourning, which have drawn on diverse perspectives, including psychoanalysis, behaviourism, ethology, social anthropology and developmental psychology. Of these, attachment theory (Bowlby, 1982) has been particularly influential in shaping understanding of the painful process of adjusting to the death of a loved person.

A helpful distinction can be made between the *situation* of bereavement, the *process* of mourning and

the *experiences* of grief. Thus, bereavement describes the situation of having lost someone significant through his or her death. Mourning is the process of adjusting to bereavement. Grief refers to the personal experience of mourning. Among the bereaved there are very wide cultural variations in the practices and rituals of mourning. These are both derived from and serve to reinforce existing religious and social conventions. By contrast, many of the phenomena of grief are ubiquitous; for example, weeping and feelings of painful sadness occur throughout the world.

Uncomplicated mourning

Many authors have attempted to describe stages in the mourning process. In a very influential account, Lindemann (1944) studied the phenomenology of normal grief in 101 bereaved subjects. Robertson & Bowlby (1952) observed 2–3-year-old children temporarily separated from their mothers and identified a progression from preoccupation and protest, through despair, towards detachment, and this has proved to be a valuable analogy. One of the best syntheses of different models has been that of Brown & Stoudemire (1983), who combined the work of Lindemann and Bowlby, as well as others. They distinguished three phases:

- 1 shock
- 2 preoccupation with the deceased
- 3 resolution.

In the first phase, shock, intense mental and somatic distress is defended against by mechanisms of numbing, denial and disbelief, with associated feelings of depersonalisation and derealisation. Bereaved people at this time may appear dazed or immobile. They will often describe intermittent feelings of intensely distressing mental pain, tension and anxiety, which may be experienced as tightness in the throat, choking with shortness of breath, a need for sighing, empty feelings in the abdomen or a lack of muscular power.

Usually within about 2 weeks the first phase evolves into a second, of intense preoccupation with the deceased. More structured phenomena of separation occur, such as pining and yearning, searching behaviours in the hope of reunion, and anger directed at third parties, the self and the deceased. The bereaved person will spend long periods thinking about the deceased and will dream frequently of that person. One in ten will report brief hallucinatory experiences. Past conflicts will be reviewed and intense guilt will be experienced by at least one person in three. Mechanisms of identification may be evidenced by the appearance of traits and activities of the deceased. This second phase is also characterised by social withdrawal and a range of fluctuating depressive symptoms, including sadness, anhedonia, fatigue, insomnia and anorexia. The tasks of this second phase of the mourning process have been described as reliving memories, working through feelings, reparation and gradually restructuring the representation of the lost person from one of reality to one of memory. This process of internalisation involves a freeing of the self from the bondage of the deceased, and the formation of a new adjustment to the environment.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

Over a period of months to years, this process gradually merges into a third and final phase, characterised by a subjective feeling of acceptance, the capacity to remember the deceased without excessive pain, and a reorganisation of life towards the possibility of new attachment. Phenomena from the second phase may sometimes re-emerge, and these are often more sharply focused at times of significant anniversaries.

Relationship with depressive disorders

Although clinical depression and mourning share many phenomena, and the boundary between them is not always clear, this does not imply that they are the same syndrome. Clayton & Darvish (1979) found that 42% of bereaved spouses examined at 1 month showed sufficient depressive symptoms to meet criteria for a depressive episode. By 1 year this figure had fallen to 15%. When depressive episodes do occur after bereavement, they have been shown to be no different in form from those precipitated by other major life events, but there is still controversy as to whether they warrant a different treatment approach using models of the mourning process. Parkes (1985) and others have described features that may distinguish normal mourning from depressive disorders: pangs of grief, angry pining, anxiety when confronted by reminders of loss, brief hallucinations, somatic symptoms and identification-related behaviours all point to normal mourning; the presence of retardation, generalised guilt and suicidal thoughts after the first month all suggest the development of a depressive episode.

Complicated mourning

The development of a depressive episode is only one of the ways in which mourning can be complicated. Compared with normal cultural patterns, mourning can be absent, delayed or abnormally prolonged; there may also be unusual behaviours, such as extreme preoccupation with the deceased. There may be excessive identification with, or idealisation of the lost person. Patterns of extreme denial, avoidance and compulsive self-reliance can emerge. Health-related behaviours such as smoking and drinking alcohol may increase to pathological levels. Mourning may be further complicated by secondary physical and other psychological disorders, which in turn may modify and colour the experience of grief. Several studies have shown widowers to have increased risks of death, particularly from cardiovascular disorders, in the year following bereavement.

Criteria that describe complicated mourning, or traumatic grief, have been proposed, and two factors have been identified: 'separation distress', which features searching, yearning and loneliness; and 'traumatic distress', which includes numbness, distrust, anger and a sense of futility about the future. These two factors can be separated from the depressive syndrome and are independently associated with enduring functional impairments. It has been proposed that the presence of complicated mourning at 6 months or longer after bereavement suggests a need for professional intervention.

LEE

In non-clinical samples about 10% of bereaved people show complicated mourning, usually in the form of chronic grief. Delayed or absent mourning is relatively rare. In a large survey of consecutive referrals to a general psychiatric clinic, about one-third of all patients met criteria for either moderate or severe traumatic grief, with an average duration of almost 10 years. Conversely, in one traumatic grief clinic, 52% of attendees met criteria for major affective disorders and 30% met criteria for post-traumatic stress disorder.

Risk factors for complicated mourning

Freud (1917) predicted that mourning would be complicated by depression in those whose relationships were marked by intense ambivalence, but Bowlby (1982) observed that the loss of ambivalently loved persons was often consistent with healthy mourning. He stressed the role of anxious attachments to parents as precursors of insecure adult relationships and subsequent difficulties in negotiating mourning. In this way overdependence might lead to chronic grief, while patterns of compulsive self-reliance would result in the denial of loss and the delayed onset of grief. Indeed, empirical research has shown that, contrary to Freud's hypothesis, high levels of ambivalence are associated with lower intensities of grief, whereas the predictions of Bowlby appear to be confirmed.

Parkes (1985) identified clinging behaviours and inordinate pining as early signs of prolonged grief. Other factors that have been suggested as increasing the risks of complicated grief include a sudden, unexpected or unlikely bereavement, potentially stigmatised losses such as abortions, suicides and deaths from AIDS, and deaths where the bereaved may be held to be to blame. Violent or severely traumatic deaths may induce symptoms in the bereaved that resemble those of post-traumatic stress disorder. Multiple losses and deaths resulting from negligence appear to be very hard to cope with. Mourning may also be complicated if previous losses remain unresolved, and in the presence of pre-existing physical and mental health problems, including substance misuse. Low socio-economic status, perceived lack of social support, poor coping skills, absence of contact with organised religion and the need to care for dependent children are also risk factors.

The loss of a child has been shown to result in more intense grief, greater somatisation and an increased risk of secondary depressive disorders. Feelings of guilt and powerlessness are common. The outcome may be increasing marital stresses, overprotection of other children, idealisation of the lost child or unreal expectations of a 'replacement' child.

The loss of a spouse may bring with it many practical problems. These include increased responsibilities for dependent children, financial hardship and social isolation. Persisting sexual feelings can cause frustration, conflict and guilt. Elderly people who lose their partners may be particularly vulnerable to social isolation and the loss of support and care. Those bereaved after a lifetime together commonly experience extremely prolonged feelings of grief.

The death of an elderly parent seems to be the least likely form of bereavement to result in complicated mourning. Painful but healthy grief is often followed by a period of increased creativity and fruitful reparation.

Appendix. A practical scheme for diagnosing and describing depression

- Do the clinical phenomena amount to depressive symptoms?
- If they do, then are they sufficient to constitute a depressive syndrome?
- Can one then exclude other disorders and bereavement, so that one can say that a depressive episode is present?
- Is the episode mild, moderate or severe?
- Are there psychotic features?
- If so, are they mood congruent or mood incongruent?
- Does the episode show the somatic syndrome?
- Are there any other very prominent features (agitation, retardation, panic attacks, obsessional or histrionic features)?
- Does the episode show chronicity, having lasted for more than 2 years?
- Is this the only episode, or is the episode part of a recurrent depressive disorder or a bipolar disorder?
- Is there evidence of a seasonal pattern, rapid cycling or a post-partum onset?
- If the depressive symptoms do not amount to a depressive syndrome or episode, is the patient suffering from dysthymia or cyclothymia, or recurrent brief depressive disorder? Or is this a depressive episode in partial remission?

References

- Akiskal, H.S. (1983) Dysthymic disorder: psychopathology of proposed chronic depressive subtypes. *American Journal of Psychiatry*, **140**, 11–20.
- Akiskal, H. S., Bourgeois, M. L., Angst, J., *et al* (2000) Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *Journal of Affective Disorders*, **59**, suppl. 1, S5–S30.
- American Psychiatric Association (1987) *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn, revised) (DSM–III–R). Washington, DC: APA.
- American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders* (4th edn) (DSM–IV). Washington, DC: APA.
- Angst, J. (1966) *Zur Ätiologie und Nosologie Endogener Depressiver Psychosen. Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie*. Berlin: Springer.
- Angst, J. (1988) Clinical course of affective disorders. In *Depressive Illness: Prediction of Course and Outcome* (eds T. Hegalson & R. J. Daly). Berlin: Springer-Verlag.
- Angst, J. & Merikangas (1997) The depressive spectrum: diagnostic classification and course. *Journal of Affective Disorders*, **45** (1–2), 31–40.
- Beck, A. T., Ward, C. H., Mendelson, M., *et al* (1961) An inventory for measuring depression. *Archives of General Psychiatry*, **4**, 561–571.
- Berrios, G. E. (1992) History of the affective disorders. In *Handbook of Affective Disorders* (2nd edn) (ed. E. S. Paykel). Edinburgh: Churchill Livingstone.
- Bowlby, J. (1982) Attachment and loss: retrospect and prospect. *American Journal of Orthopsychiatry*, **52**, 664–678.

CLINICAL FEATURES OF DEPRESSIVE DISORDERS

- Bright, T. (1586) *A Treatise of Melancholie*. London: Vautrollier.
- Brown, J. T. & Stoudemire, G. A. (1983) Normal and pathological grief. *Journal of the American Medical Association*, **250**, 378–382.
- Burton, R. (1621) *The Anatomy of Melancholy*. Oxford: Cripps. (Page numbers quoted in the text are from the fifth edition published in Philadelphia by J. W. Moore in 1853.)
- Clayton, P. J. & Darvish, H. S. (1979) Course of depressive symptoms following the stress of bereavement. In *Stress and Mental Disorder* (eds J. Barret, R. M. Rose & G. L. Klerman). New York: Raven Press.
- Cotard, M. (1882) Du delire de negations. *Archives de Neurologie, Paris*, **4**, 152–170. Translated into English by M. Rohde in *Themes and Variations in European Psychiatry* (eds S. R. Hirsch & M. Shepherd), pp. 353–373. Bristol: Wright.
- Freud, S. (1917) Mourning and melancholia. *The Standard Edition of the Complete Psychological Works*, Vol. XIV, pp. 243–258. London: Hogarth Press.
- Hamilton, M. (1960) A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry*, **23**, 56–62.
- Hamilton, M. (1982) Symptoms and assessment of depression. In *Handbook of Affective Disorders* (1st edn) (ed. E. S. Paykel). Edinburgh: Churchill Livingstone.
- Holy Bible. Authorised King James Version (1967). London: Oxford University Press.
- Hunter, R. & Macalpine, I. (1963) *Three Hundred Years of Psychiatry (1535–1860)*. London: Oxford University Press.
- Inskip, H. M., Harris, E. C. & Barraclough, B. (1998) Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. *British Journal of Psychiatry*, **172**, 35–37.
- Jaspers, K. (1963) *General Psychopathology*. Translated into English by J. Hoenig & M. W. Hamilton from *Allgemeine Psychopathology* (7th edn). Manchester: Manchester University Press. (Page numbers quoted in the text are from the edition published by Johns Hopkins University Press in 1997.)
- Keller, M. B. & Shapiro, R. W. (1983) Double depression: superimposition of acute depressive episodes on chronic depressive disorders. *American Journal of Psychiatry*, **139**, 438–442.
- Keller, M. B., Lavorie, W., Rice, J., et al (1986) The persistent risk of chronicity in recurrent episodes of nonbipolar major depressive disorder: a prospective follow-up. *American Journal of Psychiatry*, **143**, 24–28.
- Kendell, R. E. (1968) *The Classification of Depressive Illnesses*. Maudsley Monograph, No. 18. London: Oxford University Press.
- Kiloh, L. G., Andrews, G. & Neilson, M. (1988) The long-term outcome of depressive illness. *British Journal of Psychiatry*, **153**, 752–757.
- Kraepelin, E. (1921) *Manic Depressive Insanity and Paranoia*. Translated into English by R. M. Barclay from the 8th edn of *Lehrbuch der Psychiatrie*, Vols III and IV. Edinburgh: E. & S. Livingstone. (Page numbers quoted in the text are from the Classics in Psychiatry edition published by Ayer Company Publishers.)
- Lee, A. S. & Murray, R. M. (1988) The long-term outcome of Maudsley depressives. *British Journal of Psychiatry*, **153**, 741–751.
- Leonhard, K. (1979) *The Classification of Endogenous Psychoses*. Translated into English by R. Berman from the 8th edn of *Aufteilung der Endogenen Psychosen*. New York: Irvington.
- Lewis, A. J. (1934) Melancholia: a clinical survey of depressive states. *Journal of Mental Science*, **80**, 277–378.
- Lewis, A. J. (1938) States of depression: their clinical and aetiological differentiation. *BMJ*, **ii**, 875–878.
- Lindemann, E. (1944) Symptomatology and management of acute grief. *American Journal of Psychiatry*, **101**, 141–148.
- Montgomery, S. A. & Asberg, M. (1979) A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*, **134**, 382–389.
- Parkes, C. M. (1985) Bereavement. *British Journal of Psychiatry*, **146**, 11–17.
- Paykel, E. S., Rao, B. M. & Taylor, C. N. (1984) Life stress and symptom pattern in out-patient depression. *Psychological Medicine*, **14**, 559–568.
- Perris, C. (1966) A study of bipolar (manic depressive) and unipolar recurrent depressive psychoses. *Acta Psychiatrica Scandinavica*, **42**, suppl. 194.
- Poort, R. (1945) Catamnestic investigations on manic-depressive psychoses with special reference to the prognosis. *Acta Psychiatrica et Neurologica*, **20**, 59–74.
- Robertson, J. & Bowlby, J. (1952) Responses of young children to separation from their mothers. *Courrier de la Centre Internationale de l'Enfance*, **2**, 131–142.
- Sierra, M. & Berrios, G. E. (1998) Depersonalisation: neuro-biological perspectives. *Biological Psychiatry*, **44**, 898–908.
- Spitzer, R. L., Endicott, J. & Robins, E. (1978) Research Diagnostic Criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 773–782.
- Stengel, E. (1945) A study of some clinical aspects of the relationship between obsessional neurosis and psychotic reaction types. *Journal of Mental Science*, **91**, 166–187.
- Styron, W. (1991) *Darkness Visible*. London: Jonathan Cape.
- Thomson, J. (1932) *The City of the Dreadful Night*. London: Methuen.
- Tsuang, M. T. & Woolson, R. F. (1977) Mortality in patients with schizophrenia, mania, depression and surgical conditions: a comparison with general population mortality. *British Journal of Psychiatry*, **130**, 162–166.
- Wehr, T. A. & Rosenthal, N. E. (1989) Seasonality and affective illness. *American Journal of Psychiatry*, **146**, 829–839.
- Winokur, G., Cardoret, R., Dorzab, J., et al (1971) Depressive disease: a genetic study. *Archives of General Psychiatry*, **24**, 135–144.
- World Health Organization (1978) *Mental Disorders: Glossary and Guide to Their Classification in Accordance with the Ninth Revision of the International Classification of Diseases (ICD-9)*. Geneva: WHO.
- World Health Organization (1992) *International Classification of Diseases and Related Health Problems (10th revision) (ICD-10)*. Geneva: WHO.
- Zealley, A. K. & Aitken, R. C. P. (1969) Measurement of mood. *Proceedings of the Royal Society of Medicine*, **62**, 993–996.
- Zigmond, A. S. & Snaith, R. P. (1983) The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, **67**, 361–370.