British Journal of Psychiatry (1988), **153**, 287–297

Review Article

Chronic Depression

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Defining chronic depression as persistent symptoms for 2 or more years, a prevalence of chronic depression of 12–15% is found in the literature. A four-part classification of chronic depression is proposed: Chronic Primary Major Depression; Chronic Secondary Major Depression; Characterological or Chronic Minor Depression (Dysthymic Disorder); and 'Double Depression'. The literature indicates several factors predicting chronicity in primary major depression: more at risk are female patients, particularly those with premorbid neurotic personality traits, individuals with unipolar disorders, and those with higher familial loading for such disorders. Other factors are the adequacy and appropriateness of the treatment given, and the length of illness episode prior to treatment being received. Larger studies with well-matched controls are needed.

Kraepelin's (1913) classic work on the functional psychoses emphasised the relatively good prognosis of manic–depressive illness in contrast to schizophrenia. The rather exaggerated interpretation of this thesis has meant that an unremitted depressive illness must be explained away at all costs, the patient usually being relegated to the category of 'treatment-refractory personality disorder'. Chronic depression is a challenge to psychiatry, but we have been slow to study the reasons behind these therapeutic failures and there have been few systematic studies of the aetiology of chronicity.

The aim of this review is threefold: firstly, to establish a definition of chronic depression and to estimate its prevalence; secondly, to look at the classification of chronic depressive illnesses; and thirdly, to review those factors which predict chronicity in primary major depression.

Definition and prevalence of chronicity

Definition

In 1972, Robins & Guze reviewed 20 outcome studies of affective disorders and concluded that a chronic course supervened in 1–28% of cases. This wide variation in the prevalence of chronicity is probably attributable to the different patient populations studied, the non-uniformity of the diagnostic criteria for depression, the assessment methods employed, the differing lengths and intensity of follow-up, and the definition of chronicity used. The last factor is obviously an important one, and has been reviewed well by Bebbington (1982). A depressive illness may be perceived as chronic because of the persistence of affective symptoms (Wertham, 1929; Lundquist, 1945; Bratfos & Haig, 1968; Weissman *et al*, 1976), because of impaired social functioning (Paykel & Weissman, 1973; Bothwell & Weissman, 1977), or, more rarely, because of a change in symptomatology – the illness persisting in a non-affective form (see below).

Social impairment may occur as a consequence of persistent depressive symptoms, even though these may be relatively trivial in themselves (Bebbington, 1982). In 20–26% of patients, it can continue to be a problem after recovery from the illness when the patient is euthymic (Weissman & Paykel, 1974; Carlson *et al*, 1977; Akiskal, 1982). Cassano *et al* (1983) report that social maladjustment may also precede the full manifestation of depressive symptoms. Therefore, although it is an important feature of depression, using this criterion would lead to a higher prevalence of chronicity being reported (Weissman & Paykel, 1974). In addition, there is little agreement on the definition of this term.

Chronicity due to non-affective symptoms has been described by several researchers (Lewis, 1936; Lundquist, 1945; Astrup *et al*, 1959). Astrup and colleagues described three patients with affective illness who developed a defect state despite never previously manifesting any schizophrenic symptoms. Lewis (1936) and Lundquist (1945) described the occasional development of chronic paranoid states. However, it seems inappropriate to use an atypical outcome to define chronicity.

In order to allow comparisons between existing studies, and to be readily applicable to future studies, the definition of chronic depression should be uncontentious and relatively simple to use. The most acceptable available at present defines chronicity simply on the basis of the persistence of affective symptoms for a specified period of time, and was put forward by Cassano *et al* (1983):

TABLE I
Summary of follow-up studies reporting depressed patients with a chronic course

Year	*Study*	*Number of patients*	*Duration of follow-up: years*	*Percentage chronically depressed*
1921	Kraepelin (Germany)	899	10–40	4–5
1945	Lundquist (Sweden)	319	20	9
1948	Huston & Locher (USA)	93	6.5	18
1952	Stendstedt (Sweden)	216	2–20	1–14
1959	Astrup *et al* (Norway)	278	7–19	18
1968	Bratfos & Haig (Norway)	124	>5	23
1973	Morrison *et al* (USA)	202	4.3	20
1974	Taschev (Bulgaria)	614	Lifetime	10.7
1974	Murphy *et al* (USA)	37	2.8–6.5	16

"Chronicity refers to symptomatic non-recovery for a period of 2 or more years and may be a sequel to one or more episodes of depression from which the patient does not recover."

Prevalence

If a review of the literature is confined to studies of depression which define chronicity in terms of the persistence of symptoms and follow up the patients for a period of observation of two or more years or until death, it appears that a chronic course evolves in 12–15% of cases (see Table I). The studies quoted span more than 50 years and it is noteworthy that the introduction of a wide variety of new treatments has not significantly altered the prevalence of the disorder. Neither treatment factors nor length of follow-up seem to be as important as the intensity of follow-up: the proportion of chronic cases increases the more intensively the patient population is followed up (Bebbington, 1982). This is an important point: one of the most frequently quoted studies (Winokur & Morrison, 1973) suggested that, if a cohort was followed up for long enough, chronicity was self-limiting. Analysis of their data shows that, at ten-year follow-up, over 83% of their cohort were not traced, which throws this claim into question.

In two recent prospective studies Keller *et al* (1984, 1986*b*) found that approximately 20% of patients with major depressive illnesses had not recovered at two years. The recovery rate slowed with time: 64% of the cohort recovered within six months, 74% within 12 months, but only 79% within two years (Keller *et al*, 1984). Also, for 101 patients who recovered from the index episode of depression, there was a 22% risk of chronicity with the next episode; and the cumulative risk that a member of a cohort of major depressives would eventually fall into an unremitting state of depression was 29% (Keller *et al*, 1986*b*).

Post (1972) and Murphy (1983) have reviewed the prognosis of depression in old age. The former study found a 19% rate for 'chronic psychosis'. In Murphy's study (1983), the follow-up was relatively short. At one year, 48% of elderly depressives had a 'poor outcome', but this group were not further subdivided into those with chronic and those with recurrent illness.

Studies focused on out-patients only have been carried out by Weissman & Klerman (1977) and Rounsaville *et al* (1980). In the former, the prevalence of chronic depression in a cohort of 150 female out-patient depressives was 12%. Rounsaville *et al* (1980) found that over 30% of out-patients presenting with acute major depression also met Research Diagnostic Criteria (RDC) for chronic minor or intermittent depression.

There have been few community surveys of chronicity and most do not refer to major depression. In a study of 511 adults (Weissman & Myers, 1978), the prevalence of chronic intermittent depression was 4.7%. Brown & Harris (1978) found an 8% prevalence of chronicity at two years. Hornstra & Klassen (1977) found 'persistent depression' in 47–105 per 1000 of the population at risk, but it is difficult to know whether they were referring to a clinically defined illness. A more recent survey using DSM-III criteria (Boyd & Weissman, 1981) showed a 4% prevalence of dysthymic disorder, and 75% of those affected had suffered a major depressive episode at some point in life.

Classification of chronic depressions

The term chronic depression has often been used synonymously with 'characterological' depression or 'treatment-resistant' depression. While both

disorders may be included in the category of chronic depressive illness, neither offers an adequate classification in itself. Characterological depression is always chronic, but not all chronic depression is the function of an underlying maladaptive personality (Akiskal, 1983). With regard to depression being treatment-resistant, the definition of the term is problematical as there is little agreement on the standards, range or combination of treatments that should be used before this judgement is made (Ananth & Ruskin, 1974). Also, not all treatment-resistant depressions will become chronic, as the illness may go into spontaneous remission (Robins & Guze, 1972); before the advent of physical treatments for depression, recovery usually occurred within 9–12 months (Kraepelin, 1913).

In most classificatory systems, chronic minor and intermittent depressions (RDC), and chronicity as a function of personality (ICD-9, 'depressive personality') are defined. In 1980, DSM-III (American Psychiatric Association, 1980), replaced the category of neurotic depression with dysthymic disorder. This legitimised the existence of chronic depression but perpetuated the idea that it is a minor illness arising as a consequence of an underlying personality disorder. DSM-III criteria differ from RDC (Spitzer *et al*, 1978) and ICD-9 criteria (World Health Organization, 1978) only in the age of onset of the disorder (RDC and ICD-9 suggesting an onset in early adult life, DSM-III requiring two or more years of minor depression at any age). The emphasis on maladaptive personality has some validity in studies of patients with symptoms of a minor nature (Akiskal *et al*, 1981), but chronic major depression has frequently been reported in patients whose premorbid personality was not overtly abnormal (Wertham, 1929; Nystrom, 1979; Akiskal, 1982; Scott *et al*, 1988). Guensberger & Fleischer (1972) make a plea for a more comprehensive classification of chronic depressions, but as yet no such system of proven validity exists (Keller *et al*, 1986*b*).

Akiskal *et al* (1981) suggested that individuals whose chronicity of depression dates back to onset in early life (so called 'characterological depressives') should be distinguished from late-onset chronic depressives, whose illness can be viewed as non-recovery from one or more major episodes of depression. In a prospective follow-up of 137 outpatient probands, they put forward a classification of chronic depressions on the basis of 'clinical clustering'. This is a rather simplistic technique, but it offers a starting point for subclassifying these disorders. The authors subdivided chronic depressions into chronic primary, chronic secondary and characterological depressions. A further subtype has been described by Keller & Shapiro (1982), who demonstrated that acute major depressive episodes are often superimposed on a chronic minor depressive subtype (dysthymic disorder). They have coined the term 'double depression' to describe this phenomenon.

Combining and modifying these approaches allows a preliminary classification of chronic depressive illnesses to be put forward.

Proposed classification of chronic depressions

Chronic Primary Major Depression: usually of late onset, an unresolved major depressive episode *without* evidence of a pre-existing chronic minor disorder. The individual may have a unipolar or bipolar disorder.

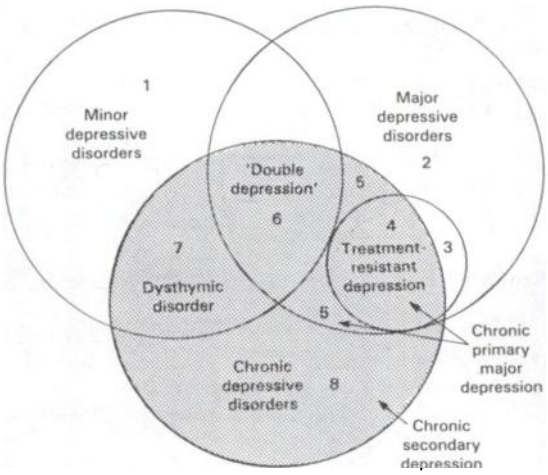
Chronic Secondary Major Depression: an unremitting major depression arising secondary to physical ill-health or non-affective psychiatric disorder.

Characterological or Chronic Minor Depression (Dysthymic Disorder). This covers a heterogeneous group of patients. The disorder has an ill-defined onset in early adulthood and appears to be interwoven with the character style. The symptoms are generally of a minor nature. This group best fits the DSM-III category of dysthymic disorder.

'Double Depression'. In this group, acute major depressive episodes are *superimposed* on an underlying chronic minor disorder. On recovery from the major depressive episode, the individual returns to his or her premorbid dysthymic baseline. The prognosis of the minor depression is poor and recurrence of major depressive episodes is frequent (Keller & Shapiro, 1982).

Relationship between subtypes

According to published research (Akiskal *et al*, 1981; Akiskal, 1982; Cassano *et al*, 1983), chronic primary major depression accounts for approximately 30% of all chronic depressive illnesses. Chronic secondary and characterological disorders have a worse prognosis than chronic primary depressions, but the outcome for all groups is unimpressive. The relationship of chronic minor to chronic major depression is unclear. The minor disorder may be a milder subsyndromal precursor or residuum of the major disorder, differing only in severity (Akiskal *et al*, 1981), or it may reflect a qualitatively different disorder that predisposes to, or arises as a complication of, a chronic major depression. Figure 1 is an



1. *Minor depressive disorder* – a depressive illness that does not meet all the diagnostic criteria, e.g. RDC or DSM-III, for major depression; it persists for more than 2 weeks but less than 2 years; would be equivalent to RDC episodic minor depression
2. *Major depressive disorder* – a primary depressive illness that meets RDC or DSM-III criteria
3. *Treatment-resistant depression (non-chronic)* – a major depressive illness that fails to respond to standard treatments given in adequate dosages for sufficient time, but remits spontaneously
4. *Treatment-resistant depression (chronic)* – as above, but does not remit and persists for more than 2 years
5. *Chronic primary major depression* – that arises as a result of inadequate or inappropriate treatment
6. *'Double depression'* – a major depressive episode superimposed on a chronic minor depressive (i.e. 'dysthymic') disorder
7. *Dysthymic disorder* – a chronic minor depressive illness, also described as 'characterological depression'
8. *Chronic secondary major depression* – major depression of more than 2 years' duration that arises secondary to a physical or a non-affective psychiatric disorder

FIG. 1 Relationship between chronic and non-chronic depressive disorders. ☐ represents all Chronic Depressive Disorders.

attempt to demonstrate the relationship between the subtypes of chronic depression on the basis of our current knowledge.

Factors predicting chronicity in primary major depression

Recent publications (Keller *et al*, 1984; Lancet, 1986; Hirschfeld *et al*, 1986) have emphasised the need to identify predictors of chronicity, but, despite the apparent size of the problem, there have been few convincing or large-scale studies of its aetiology. Some suggest that treatment-resistance underlies the evolution of chronicity (Freyhan, 1978; Perez de Franciso, 1979) and that it is a biological phenomenon, while others have invoked the pathogenic role of premorbid personality (Chodoff, 1972; Akiskal *et al*, 1978). These rather polarised views represent an oversimplification of the situation, but have been seized on readily and incorporated into the published works in this field without sufficient critical evaluation. The rest of this paper reviews the available literature on predictors of chronicity in major depressive episodes in the general adult psychiatric population.

Socio-demographic factors

Older patients are more at risk of developing chronicity than younger patients (e.g. Bratfos & Haig, 1968; Post, 1972; Keller *et al*, 1986*b*), although in the published outcome studies the mean age of onset for chronic depression was the mid-forties to fifties (Akiskal *et al*, 1981; Berti Ceroni & Pezzoli, 1984; Scott *et al*, 1988), i.e. not significantly different from that of affective disorders in general. Most reported that chronicity is more frequent in females (e.g. Kupfer & Spiker, 1981; Berti Ceroni *et al*, 1984; Houillon & Dumont-Girard, 1985). The enhanced female to male ratio is similar to that found in depressive disorders in general, but Winokur & Morrison (1973) showed that after a substantial follow-up period, females were significantly more likely to develop chronicity than males. Berti Ceroni *et al* (1984) suggested that females were at greater risk as they more frequently received inadequate antidepressant treatment. Married patients predominate, but only one study (Keller *et al*, 1984) found chronicity to be significantly associated with being married.

The community studies of Brown & Harris (1978) allude to the importance of social class as a predictor of chronicity (a chronic illness being five times more frequent in working-class than in middle-class females). There has been no confirmation of this finding in in-patient or out-patient studies (Bebbington *et al*, 1981; Akiskal, 1982; Hirschfeld *et al*, 1986; Scott *et al*, 1988). Keller *et al* (1986*a*) found an association between low family income and length of illness; they suggested that this related to the decreased likelihood of these patients actually seeking treatment. Three studies reported a relationship between lower intellectual functioning and chronicity (Kinkelin, 1953; Toone & Ron, 1977; Nystrom, 1979), but the techniques used to estimate this varied considerably. More recent studies have failed to investigate this area.

https://doi.org/10.1192/bjp.153.3.287 Published online by Cambridge University Press

Illness factors

Length of episode

The most important predictor of chronicity is the prior length of illness episode. It has been found in every systematic study of chronicity that the greater the length of the illness episode prior to treatment or prior to entry into the research study, the more likely the illness is to persist. This appears to be the dominant clinical predictor (Keller *et al*, 1986*b*). Toone & Ron (1977) found that incomplete recovery at time of discharge predicted symptomatic chronicity.

Course of illness

Chronicity is more frequent in unipolar as opposed to bipolar disorders (Lundquist, 1945; Morrison *et al*, 1973; Akiskal *et al*, 1981; Scott *et al*, 1988). It has been postulated that depressive episodes in bipolar patients are interrupted by spontaneous shifts into hypomania or euthymia (Akiskal *et al*, 1981).

Symptom profile

Earlier studies, e.g. Kerr *et al* (1970) and Paykel *et al* (1974), suggested that neurotic depressions became chronic more frequently than endogenous depressions. Recent studies have not shown this trend, chronicity being as frequent in endogenous as in neurotic illnesses (Kupfer & Spiker, 1981; Keller *et al*, 1984; Garvey *et al*, 1986; Hirschfeld *et al*, 1986; Scott *et al*, 1988) or more frequent (Lee & Murray, 1988). Schatzberg *et al* (1983) and Akiskal (1983) reported endogenous symptoms in 10–40% of chronic depressives. The situation is probably more complex than this. Prospective follow-up studies have suggested that some endogenous symptoms, e.g. diurnal variation of mood, early morning wakening, etc., 'burn out' as the illness persists (Shaminina *et al*, 1973; Cassano & Maggini, 1985), or become fewer and less intense (Helmchen, 1974; Lehmann, 1974; Akiskal, 1985). 'Cross-sectional' assessment after the onset of the chronic illness may then make it difficult to establish whether the episode initially had an endogenous or neurotic symptom profile.

Anxiety symptoms are said to be significantly more frequent in those who develop chronic depression (Kupfer & Spiker, 1981), but no study has measured anxiety by recognisable criteria. The presence of paranoid delusions (Kay *et al*, 1969; Shobe & Brion, 1971), ideas of reference (Nystrom, 1979) or any single schizophrenic symptom (Astrup *et al*, 1959; Bratfos & Haig, 1968) predict chronicity. While psychotic features could predict a chronic course, the cases described might be classified as schizo-affective using current diagnostic criteria.

Only Keller *et al* (1984) found a link between severity of illness (using admission to hospital as the criterion of severity) and chronicity. Scott *et al* (1988) found that female chronic depressives scored higher than non-chronics on the Beck Depression Inventory (Beck *et al*, 1961), but observer-rated Hamilton scores (Hamilton, 1960) did not confirm this finding.

Past psychiatric history

Age of onset of the first-ever episode of psychiatric illness does not predict chronicity (Hirschfeld *et al*, 1986; Scott *et al*, 1988). Research on number of previous illness episodes is contradictory: Scott *et al* (1988) found that female chronic depressives suffered from significantly more episodes of affective disorder when compared with non-chronic depressives, but this was not supported by others (Akiskal, 1982; Hirschfeld *et al*, 1986; Keller *et al*, 1986*b*). Number of previous admissions but not number of episodes of illness was found to be significantly greater in chronic depressives than in episodic depressives by Toone & Ron (1977). They also reported that patients who had previous admissions for episodes of non-affective illness prior to the presentation of the current depressive episode had a poorer prognosis, a finding supported by Keller *et al* (1984).

Secondary psychiatric complications

Akiskal *et al* (1981) found that rigorously defined secondary psychiatric complications which had not been a feature of previous depressive illness episodes predicted chronicity in some patients. The most frequent problems recorded were drug and/or alcohol abuse, superimposed anxiety states and agorophobia. The only other study to review secondary complications (using recognised criteria) found a similar trend, but it did not reach significance (Scott *et al*, 1988).

Treatment factors

Inadequate treatment

A significant proportion of chronic depressions seem to be due to differing degrees of treatment failure (Quitkin, 1985). Patients referred with chronic depression frequently received substandard treatment or indeed no treatment at all (Kotin *et al*, 1973; Lehmann, 1974; Schatzberg *et al*, 1983). Quitkin (1985) estimated that 30–80% of 'refractory' depressives had received subtherapeutic doses of

tricyclics (TCAs) or monoamine oxidase inhibitors (MAOIs). In Keller *et al*'s (1984) study, 50% of chronic depressives failed to receive active treatment despite the fact that nearly all of them had had a previous depressive episode that responded to antidepressant therapy. Also, symptom profile did not predict treatment; endogenous and neurotic depressives varied only in that the endogenous group received more benzodiazepines. Even severe depressions of greater than six months' duration received no more intensive treatment than those of four weeks' duration (Keller *et al*, 1982), a finding supported by others (Kotin *et al*, 1973; Bridges, 1983; Schatzberg *et al*, 1983). Of the patients in Keller *et al*'s (1982) study who were prescribed drugs, only 34% received TCAs for more than four weeks, and of those only 12% received more than 150 mg/day. There are numerous examples from both the USA and Great Britain of inadequate treatment of chronic depression. Johnston (1974) showed that the longer a depressive illness persisted, the less likely the patient was to receive adequate treatment, while a number of studies (Kiloh *et al*, 1962; Deykin & Dimascio, 1972; Paykel *et al*, 1974) suggested that the longer the episode lasted prior to treatment, the less likely it was to respond to tricyclics. Berti Ceroni *et al* (1984) suggested that inadequate treatment at the onset of the illness predicted chronicity, and that this occurred more frequently in females, even if they had psychotic symptoms. Downing & Rickels (1973) found that placebo response was reduced in depressives whose illness lasted more than six months.

Weissman & Klerman (1977) found that chronicity in 150 female depressives was significantly associated with lack of maintenance treatment, a finding supported by Berti Ceroni *et al* (1984) and Keller *et al* (1986*b*).

Inappropriate treatment

The use of inappropriate treatments has been noted by several authors (Lehman, 1974; Weissman & Klerman, 1977; Akiskal, 1982). Keller *et al* (1982) found that 19% of major depressives received only anti-anxiety drugs and that benzodiazepines were used more frequently in the elderly. Akiskal (1982, 1986) reported the significantly greater use of 'depressant' drugs in chronic depressives, 21% of chronic depressives being treated with catecholamine-depleting anti-hypertensive drugs, compared with 3% of episodic depressive controls.

Family and personal history

Family history

Six studies have reviewed the family history of affective illness in the first-degree relatives of chronic depressives. Four reported a significantly greater familial loading in the chronic as compared with the non-chronic depressives (Kinkelin, 1953; Nuller *et al*, 1972; Akiskal *et al*, 1981; Scott *et al*, 1988), although only the latter two used recognised criteria for identifying affective disorders in first-degree relatives (Andreasen *et al*, 1977). The studies of Toone & Ron (1977) and Garvey *et al* (1986) did not support these findings, but the former sample comprised both primary and secondary depressives and the latter study failed to use recognised criteria for establishing such a history. A family history of unipolar illness was identified in 40–50% of chronic patients by Akiskal *et al* (1981) and Scott *et al* (1988). The latter study found that this increased familial loading was only significant in female patients; other studies did not distinguish between the sexes in their data analysis. The family history was often multiple, with several first-degree relatives affected by severe illnesses. There was no evidence of increased loading for bipolar disorder. No study has commented on any family history of chronic depression.

Personal history

Developmental object loss has not been found to be associated with chronicity in major depression (Weissman & Klerman, 1977; Akiskal *et al*, 1981; Hirschfeld *et al*, 1986; Scott *et al*, 1988). Scott *et al*'s (1988) study is the only one to look at Brown & Harris's (1978) predisposing factor of 3 or more children under 14 years. This was not significantly more frequent in chronic than in non-chronic depressives.

Personality

Kay *et al* (1969) suggested that premorbid personality predicted outcome in depressive disorders. Kerr *et al* (1972) found that neurotic and hysterical traits were significantly correlated with poor prognosis. Lee & Murray's (1988) follow-up of 'Maudsley depressives' confirmed the findings on neuroticism. Weissman & Klerman (1977) and Hirschfeld *et al* (1986) found that female chronic depressives had significantly higher scores on the Neuroticism scale of the Eysenck Personality Inventory (Eysenck & Eysenck, 1974) than episodic depressives, although the personality assessments were made after the onset of the illness. To try to overcome the possible 'colouring' of the personality assessment because the individual is depressed, Scott *et al* (1988) asked the patients to rate their personality "as they would have done prior to

the onset of the illness''. They found the same trend of higher Neuroticism in female chronic depressives, but it just failed to reach statistical significance. This technique has been used by other researchers (e.g. Kendall & DiScipio, 1968), who felt that the responses obtained were both valid and different from those achieved without such a directive, but it is not clear if this technique can be applied reliably to chronic depressives.

Akiskal *et al* (1981), using Schneider's depressive typology (1958), found that 44% of chronic depressives as opposed to 28% of non-chronic depressives fulfilled the criteria for depressive personality. Nystrom (1979) suggested that depressives with hysteroid, aesthenic, syntonic or sensitive personality traits (as measured on Sjobring's (1973) personality classification) had a poor outcome. Hirschfeld *et al* (1986) found that chronic depressives showed more emotional instability, less objectivity and a greater tendency to 'break under stress'. They suggested that this meant that chronic patients were more 'thin-skinned', but the assessments were again completed after the onset of the illness episode. In a single case study, Rowe (1971) showed a potential role for repertory grids in the assessment and prediction of chronicity. She predicted non-response to treatment on the basis of the patient's personal constructs, which classified 'good' people as ill and 'bad' people as well. So far, no large-scale studies have assessed the value of this approach.

Several authors (Weygandt, 1908; Kraepelin, 1913; Kraines, 1957; Weitbrecht, 1969) have suggested that any character abnormalities found in chronic depressives represent a deterioration in the personality as a secondary consequence of a prolonged illness. Kraepelin (1913) described such cases, and Kraines (1957) reported that the exaggeration of premorbid neurotic traits was a common feature of chronic depression. Akiskal *et al* (1981) noted that the illness was often classified as characterological by those who had not seen the patient during the acute phase. Scott *et al* (1988) suggested that while many chronic depressives were categorised as having 'personality disorder' during the course of the chronic illness, this diagnosis was rarely recorded in their case-notes during previous illness episodes. Weissman & Akiskal (1984) suggested that hostility and dependence might be state rather than trait phenomena, but did not offer research data to support this idea. The European literature has suggested that changes in personality resulting from the morbid process may lead to the development of a 'depressive defect state' (Regis, 1923; Digo, 1955; Weiser, 1969; Helmchen, 1974).

Life events

There is evidence to support the view that independent, undesirable life events occur significantly more frequently before and after the onset of the illness episode in chronic depressives than in non-chronic depressives (Murphy *et al*, 1974; Akiskal, 1982, 1986; Scott *et al*, 1988). In the latter two studies, 40–60% of chronic depressives suffered loss events both before and after the onset of the illness. These events were often multiple and were thought to act as maintaining factors for the illness episode. Studies which included only events occurring in the six months prior to the onset of the illness do not show significant differences between chronic and non-chronic depressives (Weissman & Klerman, 1977; Hirschfeld *et al*, 1986).

The most frequently reported events in females were loss of 'significant others' or serious illness in an immediate family member. These events seemed to be particularly important as they robbed the patient of an important source of support at a critical moment (Cassano *et al*, 1983; Weissman & Akiskal, 1984), or left her with the burden of caring for a physically or functionally impaired relative (Scott *et al*, 1988). Akiskal *et al* (1981) reported that 21% of chronic depressives were living with a disabled spouse, compared with only 3% of non-chronic depressives; they demonstrated similar figures for multiple deaths within the family. Scott *et al*, (1988) noted that the most frequent independent life event in male chronics was redundancy (not due to illness). Berti Ceroni & Pezzoli (1984) suggested that lack of job, dependency on family and lack of intimacy were important, but no details of how these factors were analysed was available.

Klein (1974) and Oules (1974) both pointed out that chronic depressive state may arise as a result of realistic but unresolvable life situations, and Niederlander (1968) reported the development of a 'survivors' syndrome' in those faced with overwhelming life stresses. It is unclear how these syndromes relate to chronic major depression.

Although there is a lack of accurate assessment in the literature, it is obvious clinically that dependent life events also maintain the illness. It is rare for the spouse of a chronically depressed patient to remain neutral (Fennell & Teasdale, 1983); marital and family conflict are common (Nystrom, 1979; Paykel & Hale, 1985) and may influence the course of the illness.

Biological factors

The evidence for biological factors predictive of chronicity is weak and there have been no major

studies looking specifically at this issue. Coppen (1974) pointed out that chronic patients are often excluded from studies as researchers tend to focus on acute depressives, who are more representative of the general clinical population. Three studies of patients with chronic major depression (mean length four years) showed that they have reductions in REM latencies on their sleep EEGs similar to those of primary depressive controls (Hauri *et al*, 1974; Kupfer, 1976; Akiskal, 1982). The latter two studies also found similar DST non-suppression rates in chronic and non-chronic depressives; they suggested that these findings support the view that chronicity has an affective rather than a characterological basis.

Coppen (1974) stated that the few chronic depressives he investigated were indistinguishable from non-chronic depressives on measures of lumbar 5HIAA concentration or plasma free tryptophan concentration. Marshall *et al* (1985) found that chronic depressives showed a significant reduction in whole blood 5HT and an increase in platelet tryptophan when compared with normals. This reduction in 5HT was akin to that found in acute major depressive disorders, but the levels were lower in those with chronic illnesses. The small sample size in this study suggests that replication will be needed before much weight can be given to the results. In contrast, Le-Quan Bui *et al* (1984) found that whole blood 5HT was not significantly less in patients with dysthymic disorder than in normals.

Akiskal (1986) suggested that a blunted TRH test response predicts chronicity in primary major depressives, but this assertion is not strongly supported in the available literature. Scott *et al* (1988) found that female chronic depressives had a significantly greater prevalence of thyroid dysfunction than episodic depressives (independent of previous drug treatment). The significance of this is uncertain, but is of interest when compared with Johnstone *et al*'s (1986) recent CAT scan findings of enlarged ventricles in manic–depressives with hypothyroidism.

Other case reports exist showing chronic depression in patients with copper and zinc deficiency (Hansen *et al*, 1983), temporal lobe dysrhythmias (Matarazzo, 1976), latent herpes simplex virus (Carranzo-Acevedo, 1974), and undiagnosed carcinoma of the pancreas (Fras *et al*, 1967; Pomara & Gershon, 1984) or abdominal lymphoma (Fras *et al*, 1967). Occult neoplasia is often cited as a possible cause of chronic depression, but Akiskal (1986) reported that it accounted for only 2.6% of cases.

Akiskal (1982, 1986) reported chronicity in primary depression with superimposed medical illnesses occurring months to years after the onset of the affective episode. Rheumatological diseases were especially common in the chronic depressives, occurring in 47% of his sample. Cassano *et al* (1983) suggested that the pain and disability impeded the individual's social and work roles, thus maintaining the depression.

Conclusion

Using the definition of chronic depression as persistent symptoms for two or more years, it is suggested that the prevalence of chronicity is 12–15%. The cumulative risk that an individual from a cohort of patients with major depression will eventually develop a chronic illness is about 30% (Keller *et al*, 1986*b*). It is estimated that chronic depressives comprise 5–15% of the 'new long stay' population (Mann & Cree, 1976; McCreadie *et al*, 1983).

Hirschfeld *et al* (1986) pointed out that there are at least two pathways to chronicity: non-recovery from a major depressive episode, or the insidious development of a minor illness over many years, usually referred to as characterological depression. The introduction of 'dysthymic disorder' into DSM–III is an acknowledgement of the existence of chronic depression. Its focus on the less severely depressed and on the aetiological role of personality has offered recognition of the latter pathway, but has tended to deflect attention away from chronicity in major depression. In order to overcome this difficulty it would be advantageous to follow the proposal of Akiskal (1983) and limit the operational territory of the term dysthymia to the characterological depressions only. The classification proposed in this paper, incorporating the current views on the subtypes of chronic depression (Akiskal, 1983; Keller, 1985), will hopefully be of use in furthering our understanding in this area.

This review has focused mainly on chronicity in primary major depression. It was hoped that by selecting a relatively homogeneous group it might be possible to establish some of the factors predictive of chronicity. The clearest feature to emerge is that chronicity in major depression is multifactorial, but the number and quality of the studies available is insufficient to allow any dogmatic conclusions to be drawn. Female patients, particularly those with neurotic premorbid personality traits, suffer from chronic depression more frequently, especially if they fail to receive maintenance treatment. Individuals with unipolar disorders are more at risk, and those with a higher familial loading for such disorders are more vulnerable. Whether this represents a genetic predisposition is not clear; as yet, no specific biological markers have been identified. Evidence for a non-specific increase in the prevalence of thyroid

dysfunction in females is of interest, but requires further verification.

Other factors that predict chronicity are the adequacy and appropriateness of the treatment given, and the length of the illness episode prior to treatment being received. This review highlights the iatrogenic aetiology of chronicity in a significant number of patients. It is hoped that this problem will be resolved in the future by the early introduction of adequate and appropriate antidepressant treatment. Length of illness episode is the most powerful predictor of chronicity, but whether it represents a dependent or an independent variable is uncertain. Multiple loss events or debilitating physical illness may maintain the illness episode.

In recent years, studies of chronic depression have employed more sophisticated methodologies than previously, but many of these studies involved small patient samples. It is recommended that larger studies with well matched 'controls' should be undertaken to replicate the reported findings. Prospective work would help to delineate the role of personality more clearly, and to distinguish secondary complications from predisposing or precipitating factors. The paucity of biological research in this area is disappointing, and expansion is needed. The exclusion of chronic depressives from previous studies seemed to be a function of the atypical nature of the illness, and because of the belief that personality disorder rather than affective illness predominated. The few biological studies available on chronic major depression tend to contradict the latter view. Future enquiries should also involve attempts to define the relationship between chronic minor and chronic major depression. This will have implications for the classification of affective disorders and for our understanding of the functional illnesses in general. With increased knowledge about the evolution of chronic depressive illnesses, it is hoped that we can develop more systematic approaches to primary and secondary prevention for those at risk. The morbidity and mortality associated with chronicity in major depression are such that more intensive study of this disorder is already long overdue.

Acknowledgements

I would like to particularly thank Professor Donald Eccleston and Dr Alan Kerr for their advice and help in the preparation of this paper; also Drs Dunleavy, Ferrier and McKeith for constructive comments on earlier drafts, and Andrea Fairbairn for help with translations.

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