British Journal of Psychiatry (1989), **154**, 697–704

Point of View

The Damnation of Benzodiazepines

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It is argued that there are two kinds of benzodiazepine dependence: a therapeutic and a morbid kind. The therapeutic dependence is acceptable in that it mitigates the clinical manifestations in patients with long-standing and fluctuating anxious–depressive symptoms. The morbid dependence is an unfortunate complication which can arouse therapeutic concern because it ties patients to an excessive dosage, unless the penalty of a sometimes grim abstinence syndrome is paid on drug reduction. The present, often strident and threatening, damnation of benzodiazepines oversteps the mark and causes avoidable misery to patients whose well-being has become largely and therapeutically dependent on the drug.

In the 1960s, benzodiazepines became available for the treatment of patients with anxiety, sleep disturbance, muscular spasms, and epilepsy. They began to replace barbiturates, which until then had had pride of place in this respect. Benzodiazepines were of equally high therapeutic efficacy, seemed to have few side-effects and, above all, were safe, since overdoses were hardly ever fatal. Oswald (1983), for example, reported that "in the Edinburgh Poisons Unit, having some 2000 admissions per year, the number of unconscious patients admitted had steadily declined year by year since the benzodiazepines came increasingly to be taken, and deaths as a consequence of benzodiazepines are rare".

No wonder that the number of prescriptions for benzodiazepines gradually rose to unexpected heights. Yet this very rise began to undermine their therapeutic popularity. Warning voices started to be heard. The damnation of benzodiazepines was on its way. It was maintained that society was becoming overmedicated; that people, instead of stoutly tackling the vicissitudes of life, recoiled from them with the help of tranquillising drugs; that doctors were too ready to provide a pill for every ill, thus avoiding the more onerous task of helping their patients to come to grips with problems that could be solved or ameliorated.

Psychiatrists were among the first who tried to stem the tide of benzodiazepine prescriptions, warning that benzodiazepines seemed to have become the "opium of the masses" (Lader, 1978). It was generally agreed that doctors should be more careful in prescribing these and other psychotropic drugs, that they should not blindly provide repeat prescriptions for them, but should monitor their patients' medication at relatively short intervals. It also began to be realised that benzodiazepines were often not the best drugs for treating anxious and depressed patients, but that antidepressants (including monoamine oxidase inhibitors) could be superior. Certainly all these considerations had an effect. The number of prescriptions for benzodiazepines began to fall in several countries, including England, in the late 1970s (Marks, 1985*a*). There even emerged voices among the experts which spoke in favour of benzodiazepines. Rickels (1981) remarked:

> "An almost irrational concern with the possible overuse of benzodiazepines can be observed in some who completely disregard the shortcomings of available alternatives – including use of alcohol or marijuana, smoking and overeating – which are certainly much less appealing from the point of view of public health than is the use of benzodiazepines. It should be kept in mind that non-drug psychotherapeutic approaches as alternatives to drugs and support are frequently not available . . . [or] unacceptable alternatives."

Marks (1975*b*) said in a similar vein:

> "There is justification for the argument that the level of use of [benzodiazepines] in women is not too high, but that the level in men is too low. With increased appropriate prescriptions of benzodiazepines, some cases of alcoholism, evolving from self-medication of emotional distress, might be prevented. Also work absenteeism, resulting from significant emotional factors, might be reduced."

Morrison (1974), a Canadian minister of state, when arguing against legally restricting the administration of psychotropic drugs, had this to say:

> "Mental anguish causes at least as much suffering as physical pain and may have somatic consequences. Rational, responsible use of psychotropic drugs to relieve even ill-defined psychological disorder should not be considered as a craven surrender to human weakness. There is nothing really noble about needless suffering."

However, by then the media had joined the chorus of damnation. Their clamour was usually no more than biased and ill-informed sensationalism. Yet the

public was now alerted and alarmed. When Manheimer *et al* (1973) examined, in a nationwide survey, what the attitudes and beliefs of American adults were about such minor tranquillisers as benzodiazepines, they found that 87% agreed with the statement: "it is better to use willpower to solve problems than it is to use tranquilizers"; and 40% agreed that "taking tranquilizers is a sign of weakness". Respondents with the least education were the most likely to agree to those two statements. From the values given by the authors, one can calculate that this trend is highly significant statistically ($\chi^2 = 28.22$ and 51.75, d.f. = 3, $P < 0.0001$).

However, patients on benzodiazepines found themselves at least partially exonerated when it was convincingly shown that, for some of them, willpower was of no avail. Even when they were on a therapeutic dosage, they could no longer free themselves from their medication because, when trying to do so, they were overwhelmed by distressing and even unbearable symptoms. They had become drug dependent in an unpleasant way.

The term drug 'dependence' was introduced by the World Health Organization in 1964 to replace the term 'addiction', which had given rise to confusion because it had been differently understood by physicians, lawyers, and sociologists. It was defined (World Health Organization, 1974) as:

> "a state, psychic and sometimes also physical, resulting from the interaction between a living organism and a drug, characterized by behavioural and other responses that always include compulsion to take the drug on a continuous or a periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence."

The 'compulsion' mentioned in this definition is certainly too strong a word, when the dependence is merely a need to "avoid the discomfort of [a drug's] absence".

The definition of dependence usually incorporates some deficit, but it is an ethical and not a medical deficit because the patients have been enslaved and robbed of their freedom of choice. It has nothing to do with the occurrence of side-effects, which are present with almost all medications. For instance, the insulin-dependent diabetic has side-effects which are clinically more conspicuous and troublesome than those with patients on benzodiazepines, where the detection of side-effects often needs a laboratory toothcomb.

The term 'drug dependence' may conjure up the image of dishevelled, pleasure-craving, doped individuals, leading disreputable lives on the outskirts of society. Yet patients on benzodiazepine medication are quite obviously not of this egregious kind. They lead fairly normal lives, even when they are plagued by anxious-depressive symptoms that are not fully controlled by the drug. They do not frantically search for a drug supply, and hardly any of them develop the sort of drug tolerance that would force them to increase their dosage to an excessive level. Benzodiazepine dependence is thus of a special kind.

To analyse this dependence adequately, it will be helpful to have a suitable conceptual framework. I propose to use the framework I set out in my book *The Concepts of Illness, Disease and Morbus* (Taylor, 1979). It bases itself on logistic theories about sets and classes.

We might start with the statement that any particular class of patients is characterised by a particular kind of morbidity – or, briefly, by a particular 'morbus'. Unfortunately, this is a purely theoretical statement which does not lead us very far. In practice, we deal only with diagnosed patients and diagnosed morbi.

How then do we diagnose morbi? There are several possible and involved answers to this question (e.g. Scadding, 1967; Kendell, 1975). I prefer to be guided by actual usage. In everyday life, a morbus is diagnosed when symptoms are observed in persons that are in some ways abnormal and that call out for some form of treatment. We shall say that such symptoms cause 'therapeutic concern', allowing this term to do duty also for concerns that are diagnostic or prophylactic. These concerns can be aroused in the patients themselves and/or their lay or medical environment. Therapeutic concerns are thus subjective experiences, influenced by individual inclinations as well as cultural trends and fashions. There is nothing definitive and absolute about them. That is why the diagnosis of morbi has undergone so many changes in medical history. There was, for instance, a time – and it lasted two centuries (Hare, 1962; Engelhardt, 1974) – when masturbation was denounced as an evil morbus in need of punitive forms of prevention and treatment. The same could once be said of homosexuality, but today it is a 'psychosexual disorder' only for those "homosexuals for whom changing sexual orientation is a persistent concern" (DSM-III; American Psychiatric Association, 1980), i.e. only when therapeutic concern is aroused in the persons concerned.

Therapeutic concerns evoked in doctors do not, and should not, immediately give rise to therapeutic procedures, unless these are urgently and quickly needed. Before treatment comes the task of establishing what kind of morbus we are dealing with – the task of diagnosis. This is based on the observations made by clinicians, the medical theories

they entertain, and the information they can gather from the patient and his environment. In modern times, medical theories have been fashioned by ideas that were originally propounded by Virchow (1858). According to him, the most significant component of a morbus is its cellular pathology and the somatic consequences deriving from it. He attached the name 'disease' firmly to these pathological changes in cells and soma. It became the task of doctors to infer such Virchowian diseases from their clinical observations. Developing Virchow's ideas, Feinstein (1967) has recently suggested that a morbus can be divided into three components.

The first component he called, in agreement with Virchow, a *disease*. But diseases are nowadays no longer exclusively based on a cellular and somatic pathology. Today we also have to take into account molecular pathologies. Indeed, it appears that, for the most part, functional anomalies, including psychological ones, are mediated by abnormal molecular events. When such events are in the foreground, the term 'disorder' is often used instead of 'disease'; and the otherwise outmoded term '(molecular) mechanism' still has its adherents, for example, among psychopharmacologists.

For the second component, Feinstein used the expression *host*. It is meant to refer to the non-diseased part of a patient's body, as well as to his personality and social situation (age, sex, occupation, social status, cultural background and family influences).

The third component is the clinical *illness*, i.e. the symptoms of which the patient and his social environment become aware, as well as the signs which can be elicited clinically and in the laboratory.

We are now in a position to return to our consideration of drug dependence in general, and benzodiazepine dependenc in particular. When a drug dependence arouses therapeutic concern, it is counted as a morbus. We are then dealing with a *morbid drug dependence*. This has two varieties. The first is a morbid psychological dependence. It occurs with such drugs as amphetamines, cannabis, and cocaine. It is characterised by a compulsive craving for the pleasurable experiences the drug arouses. The second variety adds to this psychological dependence a morbid physical dependence. Among the drugs responsible for it are heroin (and other opiates), alcohol, barbiturates, nicotine, and occasionally caffeine. Benzodiazepine dependence belongs to this variety.

A morbid physical drug dependence makes its appearance when a drug has produced a special kind of pathological change in the brain and the periphery, consisting of molecular transformations (mechanisms) which become so closely intertwined with the normal run of psychophysiological functions as to become indispensable. Unfortunately the molecular transformations are unstable, and have to be maintained by a regular supply of the responsible drug. Reducing the drug supply too abruptly plays havoc with the normal psychophysiological functions, and this leads to an avalanche of distressing and sometimes almost unbearable clinical symptoms. These are usually denoted by such terms as 'abstinence syndrome', 'withdrawal symptoms', or just 'withdrawal' (naming the cause but meaning the effect). Eventually, as we shall see, 'withdrawal symptoms' and 'withdrawal' are given a narrower designation to distinguish them, at least terminologically, from cognate symptoms occurring at the same time.

Let us consider heroin dependence as an illustration of a morbid physical drug dependence. An occasional heroin injection gives rise to transient molecular transformations in the brain. These do not constitute a disease because their clinical manifestations, consisting largely of a temporary analgesia and euphoria, do not arouse therapeutic concern. Indeed, they are therapeutically useful in alleviating intolerable pain. It is only when heroin injections are regularly repeated that the molecular transformations incorporate themselves as indispensable elements in normal physiological functioning. The transformations, or mechanisms, then constitute a disease, or disorder, namely a morbid physical drug dependence, which threatens the appearance of the clinical illness known as an abstinence syndrome.

Little or no attention is usually paid to the fact that physical drug dependence is not invariably of a morbid kind. There is also a therapeutic *physical drug dependence*. It receives little or no attention because it is not a morbus, nor a socio-medical nuisance. The patients concerned have no frantic compulsion to secure their therapeutic drug; they have, at most, an anxious need to "avoid the discomfort of [the drug's] absence" (World Health Organization, 1974) and to assure themselves that the drug is available to them.

Therapeutic physical drug dependence occurs when a drug is successful in the treatment of a chronic or intermittent morbus, with molecular anomalies causing functional clinical disturbances. This is best illustrated by a morbus which has been expressly called 'drug-dependent', namely the metabolic morbus of 'insulin-dependent diabetes'. The diabetic patients involved are obliged for therapeutic reasons to accept their dependence on regular insulin injections. It is through these injections that their diabetes becomes more or less

clinically 'silent', or 'covert', or 'subclinical'. Stopping the insulin injections abruptly would not cause an abstinence syndrome. There would merely be a gradual return of the clinical manifestations of diabetes in their usual intensity and without any admixture of distressing new symptoms.

There are, of course, other functional disturbances which bring about a therapeutic drug dependence. Of particular interest in the present context is the morbus of epilepsy. Among the antiepileptic drugs which can keep this morbus in check is the benzodiazepine clorazepam. It is noteworthy that there has never been an outcry against the use of this benzodiazepine by epileptic patients who are therapeutically dependent on it. Epilepsy, after all, arouses a very much stronger therapeutic concern than drug dependence, even in the most determined abolitionists of drug enslavement.

Examples of other drugs giving rise to a therapeutic dependence in chronic or intermittent morbi are: vitamin B_{12} in pernicious anaemia, factor VIII in haemophilia, glyceryl trinitrate in angina pectoris, antacids in oesophageal reflux, β-adrenoceptor agonists in bronchial asthma, neuroleptic drugs in schizophrenia, and antidepressants and lithium in manic–depression.

The clinical condition for which benzodiazepines are most commonly prescribed consists of a mixture of anxiety symptoms, depressive worries, and sleep disturbances – a mixture that we shall term 'anxiety illness'. This illness does unfortunately not command much respect and therapeutic concern. It is, as we have seen, often viewed with disdain and disparagement as a mere weakness of character. The clinical manifestations of an anxiety illness betoken the existence of a disease in the form of pathological molecular changes in the brain. These may be no more than transient responses to disturbing experiences, in which case, psychological and perhaps also social help is indicated, but drug therapy may not be required. Indeed, if benzodiazepines or some other psychotropic drugs are prescribed, most patients do not persevere with them (e.g. Williams *et al*, 1982; Catalan *et al*, 1984; Williams, 1987).

Yet the pathological cerebromolecular transformations of an anxiety illness may establish themselves and acquire some autonomy, although still remaining, of course, under the influence of emotional experiences. When such pathological transformations persist and give rise to the constant or intermittent clinical symptoms of an anxiety illness, benzodiazepines may be administered successfully for a long period, leading to a therapeutic drug dependence.

Benzodiazepines can, however, also cause a morbid drug dependence, so that stopping their administration abruptly is followed by temporary and often very unpleasant abstinence symptoms. This was demonstrated by the application of large doses to animals. Such toxic amounts obviously caused pathological cerebromolecular changes which, like those after heroin injections, incorporated themselves as indispensable elements of normal brain functions. The pathological changes therefore had to be maintained at the risk of grave perturbations of cerebral activities. It then turned out that the non-toxic therapeutic doses of benzodiazepines which are given to human patients could have the same result. Patients with an anxiety illness would then have two kinds of pathological molecular changes in their brains: the original disorder responsible for the anxiety illness, and now a new disorder responsible for the morbid benzodiazepine dependence. The two disorders could then be expected to produce different clinical manifestations; one, the original anxiety illness, and the other, the new abstinence syndrome. The latter would run a time-limited course lasting, at most, until the drug and its metabolites had left the body and the drug-induced pathological changes had come to an end. This phase would then be followed by the return of the initial anxiety in its unmitigated form, as it was no longer muffled by benzodiazepines. It happens at times that an abstinence syndrome is not followed by anxious–depressive symptoms, perhaps because the initial diagnosis had been wrong or because the original molecular disorder had disappeared or become subclinical. In that case, the patients had, at least for some time, swallowed pills they did not, or did no longer, need, and had been unnecessarily subjected to an unpleasant abstinence syndrome.

The presence of two pathological mechanisms in the brains of patients with a morbid benzodiazepine dependence has usually been assumed in the literature (e.g. Owen & Tyrer, 1983; Rickels *et al*, 1983; Petursson & Lader, 1984). Yet there are difficulties with this assumption. In the first place, it predicts a difference between the clinical manifestations of an anxiety illness and those of an abstinence syndrome. Strenuous efforts have been made to establish this difference, but they have not been strikingly successful. Some apparently specific abstinence features have been pointed out as possibly distinctive, but it turned out that they did at times occur in healthy subjects, especially on stressful occasions, such as before an examination (Merz & Ballmer, 1983; Rodrigo & Williams, 1986).

Moreover, the clinical picture of the abstinence syndrome is also subject to psychological and social

influences. There have, for instance, been 'pseudo-withdrawal' symptoms in patients who expected possible withdrawal symptoms and produced them, when this was not justified objectively (Winokur & Rickels, 1981; Tyrer *et al*, 1983). Moreover, a doctor's personal expectations can unwittingly have a suggestive effect on patients. This can happen to a keen crusader against the careless use of benzodiazepines. It may have happened to Ashton (1984), who found that the abstinence syndrome in her patients had unusually distressing components and could last "a year or more".

It is understandable that patients who still suffer from an anxiety illness after they had endured an unpleasant withdrawal procedure may look favourably on the assertion that their continuing symptoms had been drug-induced. This frees them from the stigma of having weak characters and being neurotic freaks. It allows them to feel that the blame does not lie with them, but with their doctors or the pharmaceutical industry who had failed to warn them of the vexatious morbid addiction which benzodiazepines may produce. Patients are now encouraged to take legal steps to obtain redress. One may therefore expect that compensation neurotic elements will further affect the clinical picture and muddy the waters. A sober assessment of patients who had been fully weaned from benzodiazepines has revealed that, one to five years later, 60% of them still had their anxiety illness and that about 50% had resumed some psychotropic medication (Golombok *et al*, 1987).

Another difficulty with the assumption that a morbid benzodiazepine dependence is based on the presence of two different pathological mechanisms in the brain results from this conjecture being too closely fashioned on the model of heroin dependence. When heroin dependence occurs in patients suffering from a painful disease, the drug does not directly affect the disease. It merely masks some of its clinical manifestations. It is possible to be otherwise with benzodiazepines. They may affect the anxiety-causing molecular disease directly, controlling it is a way that silences, or at least muffles, its clinical expressions. When this control is abruptly lifted, a molecular upheaval can then sometimes occur that manifests itself clinically in what has been called a 'rebound phenomenon'. It consists in a transient intensification of the anxiety illness. This rebound phenomenon was first described by Kales *et al* (1978), when benzodiazepine medication had been suddenly discontinued in patients treated for insomnia. It was soon noticed that patients with anxiety illnesses responded similarly (Kales *et al*, 1983; Fontaine *et al*, 1984; Lader & Lawson, 1987).

Rebound phenomena are not only observed with benzodiazepines. They have also been reported with tricyclic antidepressants (Kramer *et al*, 1961; Mirim *et al*, 1981; Charney *et al*, 1982); with lithium (Klein *et al*, 1981); with β-adrenoceptor blockers (Garbus *et al*, 1979; Rangno & Langlois, 1982); with antipsychotic drugs (Gardos *et al*, 1978); with L-dopa, corticosteroids, oral coagulants, and other drugs. All these medications are thus capable of producing a morbid dependence. Yet they have not been denounced on account of that, probably because they had never been overprescribed, perhaps because their rebound responses are not common and not usually severe, and perhaps because the medicinal need for them is widely appreciated, since they control illnesses which rouse much therapeutic concern.

Theoretically, there should be some difference between rebound phenomena and withdrawal symptoms. Rebound phenomena should consist of the intensified symptoms of the decontrolled disorder, whereas withdrawal symptoms should feature the opposite of the drug effects, including actual or possible side-effects. In the case of morbid benzodiazepine dependence, withdrawal symptoms (in a narrow sense) greatly resemble rebound phenomena, but also contain the additional feature of a perceptual hypersensitivity to light, sound, and touch, which is not a common ingredient of anxiety illnesses.

The great resemblance between rebound and withdrawal symptoms seems to speak in favour of the assumption that a morbid benzodiazepine dependence is due to just one kind of cerebromolecular disorder. Lader & File (1987) have advanced such a hypothesis. They state:

> "[We] argue that the two phenomena [of rebound and withdrawal] cannot be distinguished and therefore that each reflects the same common mechanism of dependence".

They mention that we already have a glimpse of some part of this mechanism as it contains a molecular formation that has been experimentally identified. It consists in:

> "high affinity, stereo-specific binding sites for the benzodiazepines. These sites are found on a supramolecular complex with γ-aminobutyric acid (GABA) receptors and with a chloride ionophore (channel across the cell membrane) which also has binding sites for drugs such as the barbiturates (Olsen, 1982)."

Lader and File go on to consider further particulars about the cerebromolecular pathology of the abstinence syndrome.

> "One possibility is that withdrawal [i.e. the cerebromolecular disease] is due to a change in endogenous ligands that act at the benzodiazepine receptor. The benzodiazepine receptor is unusual in that as well as the benzodiazepines that act there to lower anxiety levels and seizure thresholds, it can also mediate the action of the so-called 'inverse agonists' which have behavioural effects in the opposite direction, i.e. they increase anxiety and promote seizures. While no endogenous ligand has yet been identified with certainty, there is evidence that both a benzodiazepine-like and an inverse agonist-like ligand might exist." (See also File, 1988)

This account seems to provide an inkling of the cerebromolecular pathology that is involved in the pathogenesis of an anxiety-causing disease, in its control by benzodiazepines, and in its decontrol that issues in abstinence phenomena.

Not all patients who abruptly stop their benzodiazepine medication develop an abstinence syndrome – only some do. Research has shown that the incidence of abstinence syndromes, and therefore of morbid drug dependence, increases with the length of more or less continuous benzodiazepine medication. The actual figures published are unreliable, as they have been derived from variously biased, and often very small, samples of patients. According to Marks (1985*b*):

> "below 4 months [of regular benzodiazepine medication] the incidence of [morbid] dependence is virtually nil, unless alcohol, other sedatives, or narcotics are also being taken. Up to about one year's continuous use, the incidence of significant withdrawal phenomena is estimated to be less than 5%. Over one year of continuous use, the incidence appears to rise steeply."

Marks (1985*a*) says: "Even after many years of daily use a majority of patients experience either no problems or minimal problems". Trewin *et al* (1986), for instance, abruptly withdrew benzodiazepines "without any obvious clinical embarrassment" in 127 geriatric patients who had taken these drugs for years. According to Petursson & Lader (1984), the incidence of abstinence symptoms can be 25–45% after two years of regular benzodiazepine consumption, and 75% after six to eight years.

In general, it can be said that the likelihood of a therapeutic benzodiazepine dependence turning morbid increases with age, the severity of the anxiety-causing cerebromolecular disease, the number of social problems afflicting a patient, and the shorter the half-life of the benzodiazepine used. Other significant factors seem to be the length and regularity with which alcohol and psychotropic drugs, including benzodiazepines, had been used in the past. Rickels *et al* (1983) noticed that:

> "withdrawal incidence was considerably affected by the length of prior sedative-benzodiazepine therapy, ranging from 5% in patients with no prior drug therapy to 43% in patients with eight months or more of prior drug therapy."

Smith (1983) reported that 90% of patients with withdrawal symptoms had a past history of alcoholism, even when they were not currently drinking. It thus seems that prolonged use of psychotropic substances can affect the cerebromolecular system involved in the pathology of anxiety-causing diseases in such a way that some kind of precarious balance is established, which collapses with a flood of rebound symptoms when the psychotropic substance is suddenly and inconsiderately withdrawn. For this reason, it is a sound injunction to monitor psychotropic medication at regular intervals in order to keep the dosage and length of therapy as low and short as possible.

Early in the history of the present crusade against excessive benzodiazepine prescriptions, doctors were advised that withdrawal symptoms had nothing to do with a return of the, now uncontrolled, anxiety illness. (Rebound phenomena were still unknown then.) Therefore the patients should not be given further doses of benzodiazepines. They were therefore sternly left to suffer the misery of their abstinence syndrome, and doctors had an opportunity to study that syndrome closely. The result was an outpouring of papers describing morbid benzodiazepine dependence in detail. The medical world was impressed. Officialdom and the media took notice. The damnation of benzodiazepines was on its way.

Today it is recognised that abrupt drug withdrawal should be avoided, as far as possible. When abstinence symptoms occur, patients should be put back on benzodiazepines or some other suitable drug, preferably of a long-acting kind. Such medication should then be gradually and slowly tapered off in a samaritan rather than puritanical spirit. Whether this will be completely successful in the end depends on the chronicity of the anxiety illness involved. There is certainly a group of patients who need prolonged, and perhaps continuous, benzodiazepine medication, so that they can live a tolerable life and take fairly full advantage of their abilities. No dire harm is likely to befall such patients. As Tyrer & Murphy (1987) put it:

> "From present evidence, there is no unequivocal permanent handicap caused by benzodiazepines in short- or long-term dosage. . . . At the present state of knowledge it is too punitive to withdraw benzodiazepines from long-term users who do not want to stop treatment."

Unfortunately, the increasingly strident and threatening clamour against the therapeutic use of benzodiazepines compels doctors today to be unusually circumspect, and to temper their medicinal advice with a (recorded) caution of the side-effects patients might experience in the first few days (e.g. somnolence, clumsiness, perhaps an aggressive outburst), and of the possibility of a traumatic morbid dependence on prolonged medication. One cannot expect the general public to have much respect and therapeutic concern for patients with an anxiety illness. Yet they are in special need of our sympathy and understanding for the stigma they endure and the wretchedness they suffer, which can drive some of these unfortunates to seek a despairing exit through suicide.

Addendum

There is a belief abroad that benzodiazepines usually lose their therapeutic power during prolonged administration. There is no convincing evidence for this belief. Indeed, the evidence to the contrary is stronger. Whenever rebound phenomena occur, they prove that benzodiazepines had been active in suppressing the clinical expression of a cerebromolecular pathology. Moreover, when patients have been fairly well adjusted on benzodiazepines for a long time but succumb, after a successful withdrawal procedure, almost immediately to a modified recurrence of their anxiety illness, the proof that there had been a continuing therapeutic activity of benzodiazepines could hardly be stronger. Of course, it then also follows that the patients are in need of further medication and perhaps even of further prescriptions for benzodiazepines. This would help the patients, even though it is anathema to a narrow-minded damnation chorus.

Acknowledgement

My thanks are due to Miss Susan Friedland for her bibliographic help.

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