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The Concept of Disease in Psychiatry

SIR: A recent editorial in *Psychological Medicine* on the concept of disease in psychiatry (Häfner, 1987) helped to clarify many problems connected with this issue. I would like to emphasise an approach which might add to our understanding.

For any doctor in therapeutic practice – and to the general public – a disease is what can be treated with a certain success by a physician. This definition is operational in the extreme; nevertheless, it should influence our theoretical thinking.

The estimate of the prevalence of endogenous depression at the beginning of this century was 0.5–1%. At this time patients would be in hospital for months, and all that could be done was custodial care and prevention of suicide. In some institutions opium was administered, with ambiguous results. In the period 1940–1950, the prevalence of endogenous depression was estimated to be 2–3%. Again, the patient had to be admitted to hospital, and could be treated with ECT. The duration of hospital stay would be 4–5 weeks, and the patient would usually be discharged after a satisfactory remission. Nevertheless, understandably, only severe cases were chosen to be treated in this way.

With the introduction of antidepressants, which enabled doctors to treat depressed patients as outpatients, an ever-increasing number of depressive patients has been found in the population, and current estimates of the prevalence reach 10% or more. Again, the influence of the second generation of antidepressants (e.g. mianserin, maprotiline) and of the antidepressive benzodiazepines (e.g. alprazolam, bromazepam) can be observed: their side-effects are fewer and less unpleasant than those of, for example, imipramine and amitriptyline.

It might be speculated that the increasing possibility of drug treatment of distress, considered some 10–20 years ago as a common human condition, has been an important factor contributing to the change in the image of mental illness and to the changes in the diagnostic criteria for depression, as reflected *inter alia* in DSM–III.

For a doctor in routine practice, the differentiation of patients who will respond to neuroleptics from those who will respond to antidepressants is more important than theoretical consideration about the nosological entity of schizoaffective, mixed, or other psychoses. The same is true when deciding whether to begin lithium prophylaxis of a periodic psychosis.

Medicine has been always action-oriented. Physicians have been interested in cases which can be treated, in conditions which can be changed. An ever-increasing interest in genetic and other biological factors in the pathogenesis of mental disorders is due to the perspective of the possibility that errors in the human genome will be accessible to therapeutic intervention. In this light, the changes in opinions about possible biological causes leading to new concepts of nosological classification of alcoholism, panic anxiety, drug dependence, and criminality can be better understood.

The opposite also seems to be true: apart from the ethical and political issues, the failure to treat homosexuality contributed – according to this line of reasoning – to the disappearance of this diagnosis in nosological classification. If – 20–30 years ago – some simple drug treatment had been discovered for homosexuality, this variation of sexual behaviour would have remained in psychiatric nosology – irrespective of the possible theoretical interpretation that this fact alone would mean that homosexuality was an illness.

Therapeutic pragmatism thus may play a decisive role when constructing the concept of disease and when dealing with the problems of nosological classification.

Are mild monosymptomatic headaches, insomnia, tiredness, or feelings of emotional tension illnesses? Patients begin to believe so if they get a pill which helps – and so do doctors. The pharmaceutical industry does not object to such an evolution. This does not decrease the merit of the industry in promoting research in neurophysiology, molecular biology, and other scientific disciplines as long as their progress remains related to the relief of human suffering. A rational concept of disease should serve to further such an aim.

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Combined Minaserin and Tranylcypromine

SIR: The early controversy about the risk of side-effects occurring with combined tricyclic

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antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) is now largely resolved. It seems clear that some combinations are without problems, whereas others, particularly those involving a TCA with prominent 5HT-uptake inhibiting properties, can cause serious symptoms such as disturbed state of consciousness, hyper-irritability of the CNS, and hyperthermia (Graham *et al,* 1982).

The tetracyclic antidepressant mianserin (MIA) does not have 5HT-uptake inhibiting properties, but does have 5HT antagonistic and antihistaminic properties. In animals, agents with 5HT antagonistic properties confer protection against the development of the 'hyperthermic syndrome' caused by some TCA/MAOI combinations. Likewise, antihistamines protect against related syndromes, suggesting that the clinical usage of MIA/MAOI should be without problems. Furthermore, MIA has alpha-2 receptor antagonistic action, and agents with this property when combined with an MAOI such as tranylcypromine (TCP) lead to more rapid beta-receptor sub-sensitivity. This change has been associated with clinical improvement, suggesting that the combination MIA/MAOI could lead to more rapid improvement than if one or other drug is used alone.

The only reported study of combined antidepressants utilising MIA used isocarboxazid as the MAOI, and did show an early response in many cases (Riise & Holm, 1984). This study involved 60 cases, none of whom showed a hyperthermic reaction. Weight gain, however, was a problem. TCP is a MAOI with anorexic and activating properties, whereas MIA frequently has initial sedative and sometimes weight-inducing problems. A combination of MIA/TCP was hypothesised as a way to minimise unwanted effects, yet maintain the rapid onset of antidepressant activity described by Riise & Holm (1984).

At Bentley Clinic, 39 depressed out-patients were commenced on MIA/TCP. They were diagnosed as having DSM–III major depressive disorder with (10) or without (22) melancholia, or dysthymic disorder (7), with 28 subjects completing 4-week trials. Dosage was increased gradually over a few days, usually to 60 mg nocte MIA and 10 mg TCP morning and midday. There were 22 responders; many of them showed marked improvement within the first week, and the majority showed most of their improvement within the first 2 weeks.

There were no symptoms to suggest even the beginnings of a 'hyperthermic syndrome'. The most troublesome side-effect was postural hypotension in three underweight cases. Headaches, usually localised in the occiput and described as different to those previously experienced, were complained of in seven cases. Such headaches, in the author's experience, occur not uncommonly with TCP alone. However, with MIA/TCP these headaches impressed as of less severity and frequency. This observation is in keeping with the known prophylactic action of MIA against migraine (Monro *et al,* 1985). Mild sedation occurred in 12 cases, but in most this disappeared after a few days. Later in the study, however, many subjects complained of insomnia, suggesting that the sedative effects of MIA predominated initially, with the activating effects of TCP predominating later. Only one of the 12 dropouts did so because of side-effects, this subject being troubled by nausea and malaise. Anticholinergic effects were minimal in all cases.

A weight increase greater than 3 kg occurred in 3 (14%) and of greater than 2 kg in 6 (27%) subjects. The mean weight, however, showed no change over the 1-month treatment period. Troublesome weight increase greater than when the individual drugs are used alone has frequently been noted in studies of combined TCA/MAOI (Gander, 1967). Thus, even though the weight gain was a problem with some MIA/TCP subjects, it was less than that reported with other combinations.

Combinations of TCA/MAOI have been shown to reduce the chance of hypertensive or 'cheese' reactions to the i.v. administration of tyramine (Pare *et al,* 1982). This protection is thought to be due to the reduced uptake of noradrenaline and tyramine caused by the TCA. MIA, however, does not have this property, so the combination of MIA/TCP would not be expected to provide such protection. Despite careful dietary instructions, one patient ate cheese "to see what would happen" and experienced a transient headache.

Following the completion of the study period, a 65-year-old lady who had continued MIA/TCP because of good response died suddenly. No post-mortem was carried out, but she was known to have a history of hypertension and to have been taking methyldopa concurrently. Caution may thus be necessary with the use of this combination in older subjects and in those with cardiovascular system disorders or those underweight. With these exceptions, MIA/TCP appears to be a safe combination. There is also the suggestion that MIA/TCP has some advantages over the single drugs used alone, so that verification by a controlled study appears worthwhile.

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Psychotropic medication and antisocial behaviour in a mental handicap hospital

SIR: As a contribution to the debate about phasing out mental institutions, I recently reviewed antisocial behaviour and the use of psychotropic medication (as aspects of perceived prospects for discharge) in all 131 patients (average stay 26 years) of a mental handicap hospital.

Thirty patients (23% of the total) were currently taking neuroleptics like chlorpromazine or haloperidol, and had been for years. This is fairly modest compared with the 40–50% found in surveys of the mental handicap literature (Aman & Singh, 1983). However, there was a striking correlation between the use of neuroleptic (and other) psychotropic drugs and difficult or antisocial behaviour as identified by nursing staff in this survey. Fifty-nine patients (45%) were judged to show behaviour of this kind, albeit of varying severity, and nearly two-thirds of these had a history of exposure to long-term neuroleptics; indeed, all but 4 of the 30 patients mentioned above currently taking them showed difficult behaviour. In addition, 34% of those in the 'difficult behaviour' group were or had been on extended courses of benzodiazepines and 22% on antidepressants, increased proportions compared with the rest of the hospital. These associations were even more striking in respect of a core subgroup of 16 patients whose behaviour was judged to be the most intractably difficult in the hospital. Eighty-eight per cent of these had been on long-term neuroleptics, 40% on benzodiazepines, and 31% on antidepressants.

There were few cases of documented psychosis or other specific mental illness (admitting the problems of diagnosing in this field), and it was clear that psychotropic medication had almost always been aimed directly at behaviour. These patients may have been more manageable in hospital as a result, although without obvious improvement in their prospects for a life outside the institution. In almost all cases their behaviour was cited by nursing staff as a major barrier to discharge.

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De Clérambault's Syndrome in Unipolar Depression

SIR: Signer & Swinson (*Journal*, December 1987, **151**, 853–855) described two cases of erotomania in bipolar affective disorder. The delusion appeared during periods of mania, hypomania or euthymia. This association is not uncommon (Guirguis, 1981; Remington & Book, 1984). However, de Clérambault's syndrome is rare in unipolar depression. We have recently seen a patient with this clinical picture.

Case report: Mrs T is a 34-year-old married woman whose mother had bipolar affective disorder; her sister has recurrent depression. Her past medical history was unremarkable. Her first psychiatric illness was at 15, when she had a brief depressive episode. Ten years later she showed clear symptoms of puerperal depression.

At the age of 33, the patient exhibited this affective picture: tearfulness, hopelessness, suicidal ideation, insomnia, loss of energy, poor appetite, loss of interest in hobbies, and slowing of thoughts and movements. There were no obvious precipitant events. A diagnosis of depression was made, and imipramine (150 mg daily) prescribed. She responded well to this treatment. However, the drug was discontinued after three months, and depressive symptoms recurred. At the same time, Mrs T imagined she was the object of affection of her daughter's teacher. He sent a gift to the child, and the patient believed he was really sending a love message to her. Later she claimed he followed her in his red car each day.

When examined, the patient was sad and anxious, with suicidal thoughts, indecisiveness, and feelings of guilt. Imipramine (150 mg daily) normalised the affective state, and delusional erotomania vanished.

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