ARE WE AS DEPRESSED AS WE THINK WE ARE?

by

DAVID J. KING, CAROL McMEEKEN and PETER C. ELMES

from

The Department of Therapeutics and Pharmacology,
Queen’s University of Belfast

* (The contents of this paper were first presented at a meeting of The Pharmaceutical Society of Northern Ireland on 23rd February, 1977.)

MEDICAL attitudes to psychotropic drugs in general and antidepressants in particular tend to be casual, and their effects seen as innocuous. Indeed if used as recommended by their manufacturers tricyclic antidepressants are not very effective drugs, although some of their side effects and interactions can be very serious. It has been stated that tricyclics generally have a margin of superiority over placebos of 20-30 per cent, and given an average placebo response of 40 per cent in most psychiatric patients, they thus fail in 30-40 per cent of cases (Lehman, 1966). There are a number of factors contributing to this including a wide individual variation in pharmacokinetics (Alexanderson et al, 1969; Asberg et al, 1971) and poor patient compliance (Willcox et al, 1965), but perhaps the most important, although controversial, is the failure to distinguish depression as an illness from depression as a symptom.

THE ENDOGENOUS-NEUROTIC DISTINCTION

Opposition to an endogenous-neurotic distinction in depressive conditions has come, for different reasons, from two quarters, viz. academic psychiatry and drug companies. The Maudsley group from the time of the late Sir Aubrey Lewis argued that (a) environmental factors could almost invariably be found in every type of depression if one looked hard enough (Lewis, 1934), and (b) statistical analyses of case history material (Kendell, 1968) or of data based on standardised interviews of depressed patients (Kendell and Gourlay, 1970) had failed to show a clustering of two separate syndromes. The drug companies, on the other hand, have opposed the distinction presumably because it would limit the market, particularly if say only 10-20 per cent of depressed patients were deemed to suffer from “endogenous” depression. Consequently their products are often advertised as being effective in both depression (of any type) and anxiety.

Nevertheless many psychiatrists, particularly those working in mental hospitals, daily make a judgment between those depressions which represent an abnormal personality change and are likely to respond to E.C.T. or tricyclic drugs, and those which do not, and will not. This distinction has always been upheld by the Newcastle School who developed a rating scale for doing so (Carney, Roth and Garside, 1965). The North Americans have only recently joined in this argument and it is interesting that a series of papers based on a collaborative study involving nine hospitals, supports the endogenous-neurotic distinction as a predictor of response to antidepressant drugs (Raskin and Crook,
1976). A recent British statistical review of thirty controlled trials of imipramine and placebo in the treatment of depressive illness found that only in those trials where an endogenous-neurotic distinction was made, was imipramine consistently found to be significantly better than placebo (Rogers and Clay, 1975).

A working compromise is frequently adopted whereby every depression is seen as having both constitutional and environmental components which are mutually complementary with regard to aetiological specificity (see Figure 1). This continuum is based on the ideas of Angst (1974). Kendell, who had also adopted a similar continuum, has recently made a very helpful and fair review of the numerous ways of classifying depressions now in use (Kendell, 1976). The degree to which biological factors appear to be present, and thus the extent

![Fig. 1. CONTINUUM OF DEPRESSIONS](image)

of which a favourable response to drugs or E.C.T. can be expected, is judged from the descriptive phenomenology of the presenting symptoms rather than from the recent history. Thus, on the one hand, diurnal variation in mood, early morning wakening, loss of appetite, weight, energy and libido are marked and the environmental factors are seen as non-specific "triggers"; whereas, on the other, the depression is an understandable reaction, given the previous personality and the specific prevailing circumstances, and "biological symptoms" are minimal. In addition to biological symptoms, guilt, remorse, hopelessness, psychomotor retardation and impaired insight are important aspects of the mental state in primary depressive illness. Severity probably varies independently in both types of depression and is not of itself indicative of a good response to drugs, and the terms "deep depression" or "severe depression" are therefore confusing. Confusion can also arise if too much weight is placed on trying to assess the specificity of environmental factors, particularly in older age groups, for such patients are often only too willing to offer "reasons" for feeling miserable. The failure to see agitated elderly patients as "depressed", and miserable
youngsters as primarily “anxious” (or angry), leads to further confusion and confusing support for the drug companies’ claim that antidepressant drugs are equally effective in anxiety and depression.

DANGERS OF ANTIDEPRESSANT DRUGS

The indiscriminant use of tricyclic antidepressant drugs is not only wasteful but dangerous. They are among the most toxic of commonly used psychotropic drugs. In 1973 9 per cent of 2,914 deaths from suicidal, accidental and “undetermined” poisoning, were attributable to tricyclic drugs (Brewer, 1975). Death from tricyclic overdose may vary from 5 to 10 per cent of adult cases to nearly 50 per cent in children (Crane, 1970). A correlation between availability and the frequency of adult self-poisoning has been shown from the poison enquiries recorded at this department (Elmes, 1977). There is also an unnecessary risk of cardiac conduction defects, sudden death, anticholinergic effects, and drug interactions. Jääskeläinen and Viukari (1976) go even further and have argued that since E.C.T. has been giving way to tricyclic antidepressants in the management of depressive illness, there has been an increased length of hospital stay, decreased degree of recovery, more psychomotor impairment and drug toxicity, and a greater number of accidents and suicides.

AVAILABILITY OF ANTIDEPRESSANT DRUGS

In the following calculations all tricyclic, bicyclic and tetracyclic antidepressants and monoamine oxidase inhibitors have been included as “antidepressant drugs”, but not L-tryptophan or lithium. Table 1 shows the increasing number of antidepressant drugs available to general practitioners from 1966-1975. Table 2 shows the increase in the number of drug companies involved. In 1966 7 drug companies were marketing 14 antidepressant preparations containing 7

| Table 1 |
|---------|
|         | 1966 | 1970 | 1975 |
| Number of Antidepressant Drugs | 14   | 18   | 21   |
| Number of Antidepressant Drugs (all strengths) | 21   | 32   | 38   |

| Table 2 |
|---------|
|         | 1966 | 1975 |
| Number of companies producing Antidepressant Drugs | 7    | 11   |
| Number having more than 10% share of market | 4    | 3    |

different drugs; in 1975 this had risen to 11 companies marketing 21 preparations containing 13 drugs. Figure 2 shows the distribution of these drugs expressed as percentages of the total prescribed. In 1966 5 preparations covered three quarters of the market, and 90 per cent of the total market was covered by 4 drug companies; by 1975 10 preparations were competing for the same three

107
quarters of the market, and the top 3 companies shared little more than 50 per cent of the total market between them. Thus an almost 100 per cent increase in the number of antidepressant drugs available in the last 10 years,
from an increasing number of drug companies, means increased competition for smaller percentages of the total market. Not surprisingly the net result would appear to be an expansion in the market. This is illustrated in Figure 3, where it can be seen that there has been a 100 per cent increase in the number of tablets for depression issued per day in the same 1966 - 1975 period. Most of this increase has been due to the introduction of new preparations; the prescribing of preparations available in 1966 being quite similar to their use in 1975.

**PRESCRIBING OF ANTIDEPRESSANT DRUGS IN NORTHERN IRELAND**

Figure 4 shows the steady increase in the prescribing of antidepressants in Northern Ireland between 1966 and 1975, expressed as defined daily doses per 1,000 of population (Elmes, et al, 1976). Amitriptyline is still the single most frequently prescribed antidepressant. These figures take no account of the fact that, apart from their occasional use in enuretic children, the drugs are presumably only prescribed for adults (over 15 years). If the figures are adjusted accordingly it is found that whereas in 1966 4½ adults per thousand were taking a daily dose of an antidepressant drug, this had more than doubled to 9½ adults per thousand in 1975.

No publication has been found in the psychiatric literature which suggests there has been a real increase in primary depressive illness in the past 10 years. Nor can the increase in the use of antidepressants be attributed to increasing secondary depression due to our political troubles, unless the English are more
depressed by them than we are ourselves (see Figure 5). In fact it has been shown that there was a reduction in both types of depression in Belfast in the

Fig. 6. SALES OF ANTIDEPRESSANTS IN NORWAY, SWEDEN AND NORTHERN IRELAND 1971-75

YEAR
12 months following the outbreak of trouble here (Lyons, 1972). The trend of increasing antidepressant prescribing is widespread in the western world and Figure 6 shows that our prescribing of antidepressants is intermediate between that in Norway and Sweden. The problem of increasing use of psychotropic drugs in general seems to be world-wide and is no greater in the West than in the East, nor related to availability of psychotherapy as an alternative (Lall and Parish, 1975).

DISCUSSION AND CONCLUSIONS

The figures on antidepressant prescribing reflect a complex situation. There is likely to be an interaction between at least three variables, viz. (a) patients' increasing demands for and expectations from medical remedies, (b) doctors' increasing sophistication and awareness of psychological medicine, and (c) the interest of drug companies in a market of almost unlimited potential. It has been suggested in this paper that this latter factor can by itself change our use of these drugs. This is a particularly great liability in an area where there is so little objectivity in diagnosis or assessment of severity. Clearly the recent increase in antidepressant drug prescribing is not likely to be associated with any increase in depression as an illness, but rather with the use of these drugs for depression as a symptom. It is a modern aspect of an old endeavour, that of trying to treat or ameliorate personal problems with drugs. It is therefore indiscriminate, unnecessary, unlikely to be effective and potentially dangerous. On the other hand more careful attention to the proper clinical diagnosis of depressive illness, adequate dosage and patient compliance is likely to improve the efficacy and predictability of response to antidepressant medications (Knesevich and Biggs, 1976; Asberg, et al, 1971).

SUMMARY

An analysis of the prescribing of antidepressants in Northern Ireland in the last decade shows that there has been a 100 per cent increase in the number of people taking these drugs, to an estimated 9½ adults per thousand each day. This is less likely to be associated with a corresponding increase in either primary or secondary depression, than with an increasing number of drug companies manufacturing a greater number of antidepressant preparations.

REFERENCES

ALEXANDERSON, B., PRICE EVANS, D. A. and SJOQVIST, F. (1969). Steady-state plasma levels of nortriptyline in twins: influence of genetic factors and drug therapy. British Medical Journal, 4, 764.

ANGST, J. (1974). Genetic aspects of depression, in "Factors in Depression", Ed. N. S. KLINE, Raven Press, New York.

ASBERG, M., CRONHOLM, B., SJOQVIST, F. and TUCK, D. (1971). Relationship between plasma level and therapeutic effect of nortriptyline. British Medical Journal, 3, 331.

BREWER, C. (1975). A safer antidepressant? British Medical Journal, iv, 409. (L)
CARNEY, M. W. P., ROTH, M., AND GARSIDE, R. F. (1965). The diagnosis of depressive syndromes and the prediction of E.C.T. response. *British Journal of Psychiatry, 111*, 659.

CRANE, G. E. (1970). Cardiac toxicity and psychotropic drugs. *Diseases of the Nervous System, 31*, 534.

ELMES, P. C. (1977). Annual report of the poisons information service Belfast division 1975. *Ulster Medical Journal, 46*, 46.

ELMES, P. C., HOOD, H. and WADE, O. L. (1976). Prescribing in Northern Ireland: Methods of Analysis. *Ulster Medical Journal, 45*, 56.

JAASKELAINEN, J. AND VIUKARI, N. M. A. (1976). Do tricyclic antidepressants work? *Lancet, i*, 424. (L)

KENDELL, R. E. (1968). “The Classification of Depressive Illness”. Maudsley Monograph No. 18. London: Oxford University Press.

KENDELL, R. E. (1976). The classification of depressions: A review of contemporary confusion. *British Journal of Psychiatry, 129*, 15.

KENDELL, R. E. AND GOURLAY, J. (1970). The clinical distinction between psychotic and neurotic depressions. *British Journal of Psychiatry, 117*, 257.

KNESEVICH, J. W. AND BIGGS, J. T. (1976). Do tricyclic antidepressants work? *Lancet, i*, 802. (L)

LALL, S. AND PARISH, P. A (1975). The price of tranquility. Mind Occasional Paper 4.

LEHMAN, H. E. (1966). Antidepressant drugs of non-MAO inhibitor type. In Workshop Series in Pharmacology Unit, N.I.M.H., N.I.H. No. 1. Eds. D. H. Efron and S. Kety.

LEWIS, A J. (1934). Melancholia: a clinical survey of depressive states. *Journal of Mental Science, 80*, 277.

LYONS, H. A. (1972). Depressive Illness and Aggression in Belfast. *British Medical Journal, 1*, 342.

RASKIN, A. AND CROOK, T. H. (1976). The endogenous-neurotic distinction as a predictor of response to antidepressant drugs. *Psychological Medicine, 6*, 59.

ROGERS, S. C. AND CLAY, P. M. (1975). A statistical review of controlled trials of imipramine and placebo in the treatment of depressive illness. *British Journal of Psychiatry, 127*, 599.

WILLCOX, D. R. C., GILLAN, R. and HARE, E. H. (1965). Do psychiatric out-patients take their drugs? *British Medical Journal, 2*, 790.