*Brit. J. Psychiat.* (1971), **118**, 375–80

# Correspondence

## TREATMENT OF PHOBIAS

DEAR SIR,

The article by D. Kelly *et al.* (*Journal*, April 1970 pp. 387–98, has evoked critical comment concerning the absence of a control group and lack of double blind techniques (A. B. Mawson, July 1970), and there have been rejoinders by the authors defending the value of more 'open' studies as preliminary to more definitive evaluations. A subsequent letter by Hugh Freeman in the September number of the *Journal* confuses the issue of 'neglect of practical and humane considerations which are unfortunate by-products of the development of academic psychiatry' and the 'pursuit of methodological purity.' We believe there is a great danger of increased human suffering from prescribing treatment for which there is no proven efficacy. Should we now prescribe megavitamins for all schizophrenics because some preliminary reports suggest it is useful? The history of medicine is replete with examples of treatment which have been discarded when subsequent controlled studies have shown them to be useless. The false hopes engendered by such meaningless treatment is responsible for much human suffering. There is no substitute for properly controlled studies in establishing the efficacy of any treatment.

The second area we should like to comment on concerns one of the stated functions of the paper. The authors declared that they will 'report the results of treatment with these drugs (MAOI) and compare them with the results of other kinds of treatment.' They include a discussion of studies concerning the utility of psychotherapy, behaviour therapy, chlordiazepoxide, antidepressants combined with ECT and modified leucotomy in the treatment of various phobic states. They state that in their work, when patients complained of disturbed sleep, in addition to MAOI they were given amitriptyline or trimipramine. However, they fail to mention the work done with imipramine in the phobic anxious state.

As early as 1962, in a pilot study, Klein and Fink reported that they treated 14 patients who had 'noted the onset of inexplicable "panic" attacks accompanied by rapid breathing and palpitation. Their activities became progressively constricted until they were no longer able to travel alone.' They reported that with imipramine the panic attacks ceased and 79% were rated improved and 21% much improved.

In a subsequent double-blind study Klein (1967) reported on 21 phobic anxious patients randomly assigned to treatment with placebo, imipramine or chlorpromazine. Patients treated with chlorpromazine had an increase in their symptoms. The patients treated with imipramine were significantly better than those treated with placebo at the 0.001 level (Mann-Whitney U Test, one-tailed), as measured by global improvement. Actually, 100% of the imipramine-treated patients showed marked improvements as compared to 33% of the placebo-treated patients.

Kelly *et al.* report that 42% of their patients had lost their panic attacks by the end of one month. We have only anecdotal information about the specific efficacy of imipramine for panic attacks in phobic anxious patients. In at least 40 patients personally observed by our colleagues and us, approximately 95% were without panic attacks at the end of a month's treatment with imipramine.

Imipramine has also been shown to be useful in the treatment of school phobia associated with panic attacks. In a pilot study reported by Rabiner and Klein (1969) 24 of 28 (85%) children with this disorder returned to school in 6 weeks after being started on imipramine. In a controlled double-blind study, accepted for publication in the *Archives of General Psychiatry*, Gittelman-Klein confirmed the pilot work, demonstrating the utility of imipramine in 85% of school phobias associated with panic attacks. Interestingly, 50% of the placebo group were able to return to school

Kelly *et al.* report that up to half of their patients treated with MAOI also received tricyclic antidepressants. If this group were analysed separately a rough assessment of the role of the latter medication might have been obtained. However, without random assignment this is a dubious conclusion.

We would suggest that in the light of the pilot and double-blind studies done with imipramine, its greater safety than the MAOI, and the not very marked difference between the MAOI improvement rate and the placebo rates reported above, imipramine should be the first drug treatment tried with these patients. Comparative double-blind, random assignment, studies would be of great interest.

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[As indicated in the January issue, this correspondence is now closed. The above letter was, however, received before this could be made known.—Eds.]

## DANGERS OF FLUPHENAZINE

Dear Sir,

Although more informed comment will doubtless follow, we feel that Dr. West's letter (December 1970 p. 718) requires reply.

Firstly, it is probably scarcely necessary to point out that fluphenazine in oral form is by no means 'a new drug'—our own practical recollection takes us back to the early 1960s. The innovation is its availability as a sustained release phenothiazine. If, therefore, there is any doubt, it must be concerning the agents in which the injection is made available, the uncertainty of chemical interaction or the possibly altered form in which the compound becomes systemically available. As we understand it, this latter is likely to be a serum protein bound form rather than injection site release, but admittedly the situation is by no means certain.

Beyond this, however, over two years practical experience, and more recently an intensive period of in-patient study (which we hope, subsequently, to report in greater detail), have already confirmed for us the efficacy of such a slow release preparation where patient rejection is a cause for concern and when used in suitably selected cases. Our own impression confirms the occurrence of side-effects reported by Dr. West's references (with the possible exception of depression), but we feel this simply shows that we have been provided with a much more sophisticated tool than the manufacturers originally led us to believe, and that the problems of stabilization and maintenance call for considerable skill in establishing an effective yet trouble-free regime. Already, in a number of clinical cases which previously had developed clear patterns of hospital recidivism, the taking of such care has proved eminently worthwhile.

Being well aware of some cautionary reports, we would be the first to deprecate the use of long-term maintenance phenothiazines where this is avoidable and to stress the need for keeping such cases under continuous review. We feel, however, that one should also take cognisance of the small but increasing number of cases who, because of the advent of injectable phenothiazine, are remaining in the community as otherwise they would not have been able to do.

Of course, this comes back to Dr. West's original point, that relatively speaking the body of evidence is still small; but surely, beyond the utmost rigours of laboratory assessment and local trial, every drug ultimately has to stand the test of extended usage. Here particularly we are discussing a compound which has already brought much purposeful life to those who previously were denied it.

Like your correspondent, we await accumulating information, but on the facts already available we deplore the use of such an emotive phrase as 'thalidomide of the 70s' which seems to carry undertones of a regressive doctrine.

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Dear Sir,

At the present time there are two long-acting injectable phenothiazines (L.A.P.) available in the United Kingdom, Moditen enanthate (fluphenazine enanthate) and Modecate (fluphenazine decanoate). Both these preparations are metabolized in the body to free fluphenazine or fluphenazine hydrochloride. The pharmacological action is, therefore, identical to oral fluphenazine, a drug which has been in use for some years. It is essential to appreciate that there is no evidence that the specific action of fluphenazine differs from that of phenothiazines. The potential benefits of long-acting phenothiazines come from their duration of action, the mode of administration, and the associated administrative regime of management.

The side-effects of fluphenazine are shared by all other phenothiazines, although the sedative effects may vary. It is true that once injected the drug remains active for several weeks, but this need not increase the risks to the patient provided that care has been taken to stabilize the patient on oral medication *before* transfer to the long-acting injectable form. All the side-effects listed in Dr. West's letter are known to occur with oral phenothiazines. It is well recognized that only fifty per cent of out-patients take their medication regularly, and it is