Drug Treatment of Disease

SEDATIVES AND TRANQUILLIZERS: PART II*

BY

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Tranquillizers

In recent years over twenty so-called tranquillizers have been marketed by drug manufacturers to replace or to reinforce the older types of sedatives already discussed. Unfortunately some of these drugs have been offered to general practitioners long before they have been properly tested in Great Britain, and false claims and even some disasters have occurred. We have seen, for instance, the spate of suicides by depressive patients following the unwise advocacy of reserpine as a tranquillizer for general use and in the treatment of hypertension before this fatal complication of treatment had been fully realized. Many cases of jaundice likewise followed the enthusiastic claims made for chlorpromazine long before most British psychiatrists had had any real opportunity to test it out and to find its potential advantages and dangers. Again, it is now known that chlorpromazine can greatly increase depression in an already depressed person (though perhaps not to the same extent as reserpine), with the consequent risk of suicide. It is thus inadvisable to try out new tranquillizers in general practice until they have been thoroughly tested in Great Britain, and tested in circumstances which will prevent the disasters that have happened in recent years.

The writer has, so far, been able to try out only some of these new tranquillizers in a way which justifies their detailed discussion in an article of this nature. Others may be useful, but some have proved of little use at all, and should never have been put on the market or advertised for general use.

Chlorpromazine

This drug unfortunately produces jaundice in some patients, but the benefit it gives often makes this a worthwhile risk if the patients are properly selected for it. It is of far greater value in the sedative treatment of the psychotic patient in hospital than the neurotic patient outside. But there is now some evidence that chlorpromazine, if given in sufficiently large doses (200–400 mg. a day), may abort the development of acute schizophrenic illnesses in some of those persons predisposed to them. General practitioners may find it advisable to give this drug immediately to patients in the very earliest phases of the illness and while awaiting, for instance, the taking of further expert advice on future treatment. Since its introduction in psychiatry, this drug has also enabled many schizophrenic patients to be treated much more speedily than previously, and some can now stay on as out-patients instead of having to go into hospital for insulin-coma and other treatments. Even when other treatments, such as full or modified insulin, E.C.T., and leucotomy also have to be used, chlorpromazine seems to be a drug of considerable value as a maintenance treatment, tending to prevent relapses. However, quite large doses are generally necessary, doses which can, in fact, markedly aggravate other neurotic and psychotic conditions. Indeed, schizophrenics may need to be given initially up to 1,000 mg. a day, and maintenance doses of 150–400 mg. a day may also be necessary later on. At present we do not yet know

how long these large doses have to be kept up; but relapses often occur within a month of the patient being taken off the drug even after prolonged use.

There are also many elderly senile patients, suffering particularly from agitation, in whom ordinary sedatives produce confusion and increasing upset of memory. Such patients are often greatly helped by the use of chlorpromazine in lower doses—say, 100–200 mg. a day. By damping down their agitation it may enable them to be nursed at home rather than in hospital. In ordinary neuroses chlorpromazine should be given much more hesitantly. Doses in the region of 100 mg. a day can help some patients with anxiety and depression, but the administering of this drug alone in cases of depression can increase the symptoms, sometimes to the point of suicide, and general practitioners must always be on their guard against this. Anxiety states, anxiety hysteria, and obsessional states are really little helped by this drug, and the barbiturates will be found much cheaper and much more effective. Chlorpromazine, however, may be used to reinforce small doses of barbiturates, and to prevent larger doses producing undesirable states of barbiturate addiction.

Several substitutes and equivalents have been produced for chlorpromazine, some of them claiming that jaundice is avoided as a complication of their use. These may be tried where jaundice has occurred, but whether they are as effective as chlorpromazine is as yet far from certain.

Reserpine

This drug has also had a recent vogue in the sedative treatment of anxiety states and in schizophrenia. Some excellent results have been reported in schizophrenic illnesses when the dose is pushed to as high as 8–10 mg. a day, and a maintenance dose of around 3–6 mg. a day is used later. But there are many undesirable features attaching to the use of this drug. Suicidal depressions are very common, and it is doubtful whether much better results are obtained with reserpine than with the skilled use of chlorpromazine in a proper high dosage. Smaller doses of reserpine (1–2 mg. a day) can, however, be given to supplement larger doses of chlorpromazine.

Some tension states are also undoubtedly helped by much smaller doses of reserpine—about 0.25 mg. three times a day. But it is difficult to delimit these, and one should try to use every other drug first, because of the drug's liability to produce such severe depressive reactions. The physician should be especially careful in treating anyone who has a prior history of a neurotic or psychotic attack of depression.

Meprobamate

This expensive sedative has had a great vogue in the U.S.A. But testing in Great Britain indicates that it has only limited uses as compared to, say, the much cheaper barbiturates. It is helpful in treating withdrawal states in the alcoholic. It relaxes muscle tension, and some patients with reactive tension depressions do seem to be helped by it; these patients may put on weight while on this drug.

Another group of patients which meprobamate helps are those who show mixed hysterical and obsessive phobic symptoms. These patients, when taking short-acting barbiturates, become easily addicted to them; they may also become addicted to meprobamate, and withdrawal symptoms have been reported; but so far this has not yet proved too serious a complication. Meprobamate does not help patients

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with pure obsessional states or deep endogenous depressions. Only 1-2 400-mg. tablets three times a day, and not more, should be prescribed where indicated.

Conclusions

Clearly sedation should not be given to patients without attempts also being made to deal with environmental and other stresses that may be a cause of the anxiety and tension. But it is a commonplace in general practice that the giving of judicious rest to the nervous system by sedation can often make problems which had temporarily seemed insuperable to a patient become quite easy to handle again. It is worth bearing in mind that the normal brain generally

adjusts to its environment, and, as was very obvious during the last war, the normal brain can tolerate very bad environments indeed for very long periods of time. Likewise the last war also showed in a most convincing manner what is just as true in peacetime—namely, that once breakdown happens it is comparatively easy to abort acute neurotic reactions if only proper sedative treatment is given in time. But neurotic reactions are much less easy to treat when new abnormal patterns of behaviour and thought have been allowed to become thoroughly ingrained in brain function through the lack of adequate sedation early on in the illness. It may truly be said that a grain of sedative in time saves nine.

THE PHARMACEUTICAL HOUSE AND THE DOCTOR

BY

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Recent correspondence in this and other journals has included statements that doctors are inundated by literature from pharmaceutical houses and that visits from representatives of these firms are not only unnecessary and time-consuming but contribute to the cost of drugs and the expense of the National Health Service.

The Survey

It was decided to ascertain the opinion of doctors themselves on this matter, knowing that only the few who feel strongly on the subject tend to write to the press; it was realized, however, that it would be difficult to obtain a true picture. Surveys are notoriously liable to error, whether in design, method of procedure, or interpretation, but a survey seemed to be the only practicable means.

It was considered that the effectiveness of the survey would depend on two factors: (1) the form of the questions, and (2) the way in which they were presented to the doctor.

The Questions.—(1) These must take only a very short time to answer. (2) They must be such that the answer would be unequivocal.

The Presentation.—(1) The doctor must be assured of his anonymity. (2) He must be asked but not pressed to answer.

Bearing these points in mind, a punch-card was designed with all the questions on one side, so arranged that only a tick or cross was needed in the appropriate spaces.

Knowing the almost universal distaste for questionnaires arriving by post, we gave supplies of blank cards to our representatives and instructed them as follows: "Carry out

Please indicate your choice in the appropriate square				
1. Do you see medical representatives?	ALMOST ALWAYS ☐	OFTEN ☐	SELDOM ☐	HARDLY EVER ☐
2. How many times per annum would you prefer them to call on you?	THREE TIMES ☐	TWICE ☐	ONCE ☐	NEVER ☐
3. Do you read advertisements for pharmaceutical preparations? ..	ALMOST ALWAYS ☐	OFTEN ☐	SELDOM ☐	HARDLY EVER ☐
4. Which journal?	B.M.J. ☐	LANCET ☐	OTHER ☐	
5. Do you prefer information on preparations?	AS ADVTs. IN JOURNALS ☐	DISCUSSED WITH REPS. ☐	SENT IN THE POST ☐	
6. Would you be willing to co-operate in any future survey of this kind?	YES ☐	BY INTERVIEW BY POST ☐	NO ☐	

Front of card.

This is an attempt to find out the views of doctors on methods used by pharmaceutical firms.

All replies are anonymous but an analysis of the results obtained will be sent on request.

For office use only	
General practice	
Consulting physician	
Consulting surgeon	
Hospital staff	
Area	

Back of card.

an interview in the usual way, and, when you are about to leave, ask a doctor politely for his co-operation in filling in the answers to some questions which are of interest to us,—pointing out that this will take only about a minute. If any doctor prefers not to do so, do not press him, but record the number of such refusals each day." The representatives were further instructed to complete the back of the card themselves but not to enter the doctor's name anywhere.

All doctors visited were to be presented with cards, and all completed cards were to be returned to us each day.

Classification of Responses.—Cards were appropriately punched on receipt and were filed until enough had been received. The number used in the survey represents 10% of the total number in the National Health Service.

Results

The results are shown in the Table, from which the following observations can be made:

1. Less than 3.5% of the doctors interviewed failed to reply. This figure may be misleading because it takes no count of doctors with whom the representative failed to obtain an interview; but of those who replied, more than 80% said that they almost always see medical representatives.

2. Percentage variations in the replies to certain questions were so slight even in widely separated areas that a strong presumption seems justified that the answers are a true representation of medical opinion and not due to the influence