it only appears to do so in older patients, who have high cholesterol levels and low-normal thyroid activity.

Lithium is now known to prevent recurrent affective disorders, particularly manic depression. Serum lithium levels must be kept within a safe but effective range; 60 per cent or more of manic depressive patients can now be stabilised with this drug.

DISCUSSION

Dr P. J. Dally

The general action of an antidepressant drug is to lift the mood of pessimism, restore energy and drive, reduce the anxiety that so often goes with depression and also to reduce autonomic over-activity.

It is very important to give antidepressant drugs for a reason. One should use them to treat manic-depressive illness (the only specific, clearly defined, depressive illness). They are useful in treating depressive reactions to stress, in a predisposed individual's life, and which are frequently masked. In addition one often needs to give antidepressant drugs to patients who are dying, and who are unable to tolerate it. They may also be used prophylactically, immediately after childbirth and to treat a patient who is highly predisposed to breakdown, as after bereavement.

So, general practitioners knowing their patients, knowing whether they are predisposed to depression, are in the best position to use these drugs prophylactically for a few weeks or a few months to prevent the onset of a depressive episode.

The newer ones such as doxepin, although they have fewer side-effects, are undoubtedly less effective as antidepressants but they are useful tranquillisers. With tricyclic drugs there is always a therapeutic delay, while the side-effects on the other hand occur immediately. This is sometimes difficult to deal with and involves very much your patient's trust in you. He has to accept your warnings that these side-effects are only temporary.

The length of treatment is important since most depressions will resolve spontaneously. But in some cases, particularly where there has been a great deal of stress in the background which cannot be put right, the patient may have to continue indefinitely on an antidepressant drug. If you try to substitute a placebo, he will relapse. We have patients who have been on amitriptyline or imipramine for ten years or more. They are leading a perfectly ' normal ' life and working regularly and yet before treatment they had broken down continuously and were unable to work.

The antidepressant drug, in these cases, is acting as a prop and one has to recognise it. In addition the doctor also acts as a prop, but doctor plus a placebo is not as effective as doctor plus the antidepressant.

Mr B. Inglis

Are you sure that ' doctor plus placebo ' is not as good as ' doctor plus antidepressant '?

Dr P. J. Dally

Yes.

Mr B. Inglis

Why, in that case, has it not been possible to do adequate clinical trials to demonstrate this?

Dr P. J. Dally

There is no reason why it should not be done. I would be only too happy to do it if the Department would provide us with the money and extra personnel.

Professor A. L. Cochrane

I find it depressing to have been listening to lectures consisting entirely of statements of opinions. Consider another field I know well, the treatment of tuberculosis. Since about 1950 the chest physicians have taken the trouble to do randomised controlled trials on every single drug that came out.

The same thing could be done in psychiatry but I think that the fault lies with the psychiatrists. I have sat on at least two Medical Research Council committees where we have pleaded with psychiatrists to do randomised controlled trials. Money, statisticians, and social workers would all have been made available. Of course there are particular difficulties in doing randomised controlled trials in psychiatry because it is very easy for a psychiatrist to spot the drug in question by its side-effects. There are rather complex ways of getting around this, but I do feel that the psychiatrists have missed the boat very badly. I think it is up to them to do the trials.

Dr P. J. Dally

I do not think you can compare psychiatric illness with pulmonary tuberculosis which is quite straight forward chronologically and bacteriologically.

Professor A. L. Cochrane

But they were the first people to do randomised controlled trials, and they worked out the techniques. We should now take over from them and make use of their techniques.

Dr P. J. Dally

If depression was as straight forward as tuberculosis, I agree entirely—we would be absolutely disgraced if we had not organised proper controlled trials.

Professor A. L. Cochrane

Some of the antidepressant trials were very badly organised, and produced distorted results, but I am sure that if there are real differences, then it is only by going on doing them that the problem is going to be solved.

Dr P. J. Dally

You must have some classification of what you are trying to treat.

Mr G. Teeling-Smith

In severe depression there is no question of matching the effects of drugs against placebos. Nevertheless we should try to use as scientific a basis as possible in the assessment of psychotropic drugs—as we do with other drugs.

Dr R. Steel

What about the new ones coming out? Would there not be a case for testing these against proven drugs without the ethical difficulty?

Dr P. J. Dally

This would be extremely time consuming and it seems quite unnecessary to introduce all these new drugs. They do not appear nearly as effective as the antidepressants already in use.

Dr P. A. Parish

Although it seems quite unnecessary, psychiatrists prescribe them!

Dr P. J. Dally

I agree. I think they are seduced by the advertisers.

Dr P. A. Parish

What worries me is that psychiatrists tend to think that using a new drug implies some knowledge greater than that of their contemporaries in general practice, which just is not true.

Dr J. B. Harman

I think really that there is a difference between the drugs available for depression and the sort of drugs available to treat tuberculosis, which has been quoted as an example. The antidepressant drug groups contain a large number of minor variations and therefore a new drug is different in this sense, but not very different. This is not the case with drugs that are effective against T.B. They are usually quite different and therefore worth testing.

If a new class of antidepressant came out which might work, then it would be useful to have some controlled trials. However, when one knows to begin with that there is not going to be very much difference, then one will not get any reliable results. no matter how much money is spent.

Dr M. Marinker

We are going round in circles. We cannot do trials on these drugs until we prove their value, and we cannot prove their value until we do trials. We have no evidence except the clinical impressions of enthusiasts.

Professor W. Linford-Rees

The National Institute of Mental Health about two years ago carried out a survey of all trials carried out on antidepressant drugs. Although the improvement rate for the uncontrolled trials was higher than for the controlled trials, the evidence from the controlled trials did provide strong statistical evidence that the antidepressant drugs were more effective than placebos. These trials were carried out when these drugs were first introduced; nowadays, it is probably not ethical to compare new drugs with placebos but you can compare them with a well established drug like amitriptyline. If they are superior, then this is in favour of the drug, if they are equally efficacious but with fewer side-effects then this is still in favour of the new drug.

I would not like the conference to go away with the impression that no fully controlled double blind trials have been held throughout the world, as they number many hundreds.

THE USE OF MAJOR TRANQUILLISERS

PROFESSOR W. LINFORD-REES

Chlorpromazine and reserpine were the first major tranquillisers to be introduced. They differed from previous drugs in their efficacy in controlling abnormal behaviour and relieving emotional distress without significantly interfering with clarity of consciousness.

Major tranquillisers and neuroleptics act predominantly on subcortical structures, including the hypothalamus, the limbic system, and the reticular activating system.