Brit. J. Psychiat. (1983), **143**, 308–312

Correspondence

Correspondents should note that space is limited and shorter letters have a greater chance of publication. The Editors reserve the right to cut letters and also to eliminate multitudinous references. Please try to be concise, strictly relevant and interesting to the reader, and check the accuracy of all **references in Journal style.**

CONCOMITANT ADMINISTRATION OF MIANSERIN AND WARFARIN

DEAR SIR,

We wish to report a case in which there was an apparent interaction between the drugs mianserin and warfarin.

A sixty-three-year-old man was admitted to High Royds Hospital suffering from manic-depressive psychosis—depressed type (ICD 9, 296.1). Clinically he was severely depressed and presented a risk of suicide; antidepressant medication was therefore indicated. Two years previously he had suffered a cerebral embolism and consequent left hemiparesis; this was attributed to atrial fibrillation caused by previously undiagnosed thyrotoxicosis. He had made an almost full recovery and had been maintained since that time on anti-coagulant therapy with warfarin. Euthyroid status has been maintained with oral carbimazole.

An ECG was performed prior to antidepressant therapy and ischaemic changes recorded. This finding suggested that mianserin hydrochloride, a tetracyclic antidepressant claimed to possess few cardiotoxic side-effects, would be the most appropriate treatment. We were aware of interactions between some tricyclic drugs and anticoagulants but the hospital pharmacist, British National Formulary and Data Sheet Compendium were consulted and no evidence was found to suggest that warfarin and mianserin might interact in the same way (Committee on Safety of Medicines, 1982).

The prothrombin time had been satisfactory during the six months prior to admission, on a dosage of 8 mg warfarin daily. A prothrombin time estimation was performed prior to the commencement of mianserin; the result was 20 seconds, and British Standard Ratio 1.8. After a week's administration of mianserin 10 mg daily, the prothrombin time was 25 seconds, British Standard Ratio 4.6; that is above the therapeutic range. Mianserin was therefore stopped and at the time of writing the prothrombin time had returned to within the therapeutic range. Thyroid and liver function were both checked prior to administration of mianserin and repeated after the drug was stopped, both were normal and remained unchanged. No other drugs were administered, apart from the daily dose of carbimazole which had been taken for almost two years, and there was no excessive alcohol consumption.

As a result of this experience we conclude that mianserin and warfarin may interact and cause an increase in the prothrombin time, with a risk of pathological bleeding. This may occur because mianserin is plasma protein bound and could therefore displace warfarin from the binding sites on these proteins. The concentration of unbound and therefore biologically active warfarin in the circulation would increase. Both of these drugs are in common use and indications for their concomitant administration cannot be uncommon. The interaction described could have serious and potentially lethal effects. For these reasons we believe that the combination should be avoided and appropriate warnings given to users of the drugs.

H. M. C. WARWICK
R. H. S. MINDHAM

High Royds Hospital,
Menston, Ilkley,
W. Yorks LS29 6AQ

DEPRESSION UNDERTREATED? YES, BUT . . .

DEAR SIR,

I should like to endorse Dr Bridges' opinion in "Points of View" (*Journal*, June 1983, **142**, 621) that 'undertreatment' of depression with antidepressant medication is a serious problem. The problem is perhaps even worse in elderly patients where it is genuinely rare for them to receive adequate doses of tricyclic drugs either from their GP's or from hospital psychiatrists. "A little bit of antidepressant for a little bit of depression" is guaranteed to bring all the problems of unpleasant side effects and no benefits. It is common for a patient to be referred after weeks of Imipramine 10 mg daily or Prothiaden 25 mg twice daily. Doctors are now thoroughly versed in all the unpleasant side effects and risks of using tricyclics in

the elderly and this is presumably the reason for such 'nervous' prescribing, sometimes in marked contrast to the heroic doses of benzodiazepines prescribed to the same patient.

The appropriate course of action in a frail elderly person is to start with a very cautious dose and build up slowly over two or three weeks to the full adult dose. Obviously, careful monitoring is the key and an elderly patient should be assessed every few days. I fear it is the commitment to frequent assessment which deters the prescriber from increasing the dose to an effective level.

I would take issue with Dr Bridges on one point, however. He comments that "there is an excessive preoccupation with environmental causes for psychiatric illness" and consequently, he feels, an excessive emphasis on social and psychotherapeutic treatments. I would agree that 'causes' in medicine often have very little to do with 'cures' but would not wish to diminish the status of research into environmental and psychodynamic causes. The fact that depressive illnesses respond rather better to drugs than to psychotherapy does not imply that environmental and psychodynamic 'causes' are unimportant. Take as an example another hazard in old age—the old lady's fractured femur. The fracture is often the end result of osteoporotic bones, loose fitting threadbare carpet, poor lighting and Mogadon, but it is all irrelevant when it comes to putting in the right pin and plate. But what's more important in the long run—developing superior operative hip techniques or tackling the background of poor health and inadequate housing? By all means let us treat depression with adequate doses of efficacious drugs but I hope we won't be seduced by their efficacy into stopping the search for the social and intrapersonal causes.

ELAINE MURPHY

Goodmayes Hospital,
Ilford, Essex

IMIPRAMINE AND AGORAPHOBIA

DEAR SIR,

Richard Stern states that "it might surprise readers in the U.K. to know that Klein advocates very small doses of imipramine, even as low as 10 mgs, to counteract panic attacks (*Journal*, May 1983, **142**, 545–46).

Unfortunately, this is not exact. As we stated clearly in our chapter that appeared in the book on agoraphobia edited by Chambless and Goldstein, we advocate starting with a dose as low as 25 mgs per day, but building up till the spontaneous panics are completely relieved. In our last study, the average dose was over 200 mgs per day, with a substantial number of patients requiring 300 mgs daily.

The reference to low dosage refer exclusively to a small subgroup who respond to imipramine with marked psychomotor stimulation and insomnia. Such patients do respond to apparently homeopathic doses, but this is the exception, not the rule.

The usual flaw in clinical practice is to undertreat with imipramine, and we would not want Stern's comments to support this error.

DONALD F. KLEIN

College of Physicians and Surgeons,
Columbia University,
New York, N.Y. 10032

Reference

CHAMBLESS, D. L. & GOLDSTEIN, A. J. eds. (1982) *Agoraphobia: Multiple Perspectives on Theory and Treatment.* Chichester: John Wiley.

KORO EPIDEMIC IN ASSAM

DEAR SIR,

J. A. Harrington (*Journal* 1982, **141**, 98–99) in his letter described his recent experience on a visit to Thailand where he came across three apparent outbreaks of epidemic psychosis. The report of the first outbreak occurring in North East Thailand, the so called 'Rok Loo' (genital shrinkage disease) is of great interest. Assam, in North Eastern India recently experienced a unique situation in the form of an epidemic of psychological origin. It started in early June, 1982 affecting four western districts of Assam, and lasted until the middle of September. Termed 'Jinjinia Bemar' indicating a disease characterised by tingling sensation of the body, this epidemic started with a rumour that a lethal disease had struck the people bringing instant death or making the person impotent. In the early part of the epidemic, the affected persons did not seek the help of medical men, but tried to combat the epidemic by various preventive measures of indigenous type. These were pouring copious cold water, drinking gallons of lemon water, smearing of chalk paste or lime paste over the ear lobules and also over the private parts, avoiding all outdoor activities. Along with these, religious rites were performed in the different places of religion. People were scared to pursue their outdoor activities. Towards the later part of July people came to consult medical experts and the Department of Psychiatry, Gauhati Medical College surveyed the epidemic in the district of Kamrup where the college is situated.

Both sexes were found to be affected. Often the affected person came for help tying his penis securely with broad ribbons or elastic bands or simply grasping it by hand. The amount of panic generated by the epidemic was stupendous. To start with the diagnosis was a baffling problem for many of our physician