1% (Ungerstedt, 1971). Many researchers counter this argument by pointing out that these systems are highly arborized and have a wide sphere of influence. That these neurones arborize widely is true, but their influence is probably no more widespread than that of cholinergic or other putative neurotransmitter systems (Aston-Jones *et al,* 1983).

Is it not reasonable to suggest that disorders of higher cognitive functioning such as schizophrenia, must primarily involve neurones at the highest cortical level? Yet at present we concentrate our energies on monoamine neurones in the medulla, pons and mesencephalon. Whatever the sphere of influence of these neurones there can be little doubt that they are relatively small in number and anatomically vary little from the rat to man.

Surely the time has come to look at these systems realistically and focus our attention on neurones at a higher level. In this regard psychiatrists are obviously dependent on advances in neurophysiology and neurochemistry. Whilst waiting for such advances, let us not delude ourselves into believing, we have found the root of madness.

TIMOTHY G. DINAN

Wellcome Research Fellow,
St. George's Hospital Medical School,
London SW17

References

ASTON-JONES, G., SHAVER, R. & DINAN, T. (1983) The physiology of cortically projecting neurons in rat basal forebrain. *Society for Neuroscience.* Abstr. 106, **15,** 355.

UNGERSTEDT U. (1971) Stereotaxic mapping of the monoamine pathways in the rat brain. *Acta Physilogica Scandinavica Suppl,* **367,** 1–48.

BRIEF PSYCHOTHERAPY IN FAMILY PRACTICE

DEAR SIR,

In response to Dr Williams' letter (*Journal,* January 1984, **143,** 101–2), the points made had indeed been covered in the original article (*Journal* 1983, **143,** 11–19), and we acknowledged the high probability of a type two error. The figures provided by Dr Williams are quite correct, but one would expect there to be a differential effect between treatment groups for a larger number of subjects to demonstrate an effect. In fact, a reverse trend was found in that the control group improved more than either of the treatment groups.

Secondly the problems of finding patients suitable for controlled therapeutic trials of psychotherapy were discussed, and Dr Williams has merely emphasised those issues. He goes on to point out that "The results of such a study are applicable to only seven per cent of those patients with significant psychiatric morbidity who present to general practitioners, and thus of limited relevance to the practical management of psychiatric disorder in general practice". What he appears to have failed to appreciate is that it is in fact only these patients with persistent psychiatric morbidity in whom we were interested. The vast majority of psychiatric disorders presented by patients in general practice remit (Johnstone & Goldberg, 1976). There were 128 patients who were persistently symptomatic for at least six months of whom 27 were allocated to the control group. Of the remaining 101 persistently psychologically symptomatic patients, 35 refused interview, 25 declined treatment and 12 dropped out of therapy leaving 36 patients who completed psychotherapy. A more realistic appraisal then is that 36 out of 101 patients with the type of disorder specified, persistent psychological morbidity for at least six months, might be suitable for dynamic psychotherapy.

We look forward with interest to the results of the studies by workers at the General Practice Research Unit with regards to social casework in the primary care setting as until now only anecdotal evidence of its efficacy exists.

HENRY BRODATY
GAVIN ANDREWS

The Prince Henry Hospital,
P.O. Box 233,
Matraville, N.S.W. 2036,
Australia

Reference

JOHNSTONE, A. & GOLDBERG, D. P. (1976) Psychiatric screening in general practice: A controlled trial. *The Lancet, i,* 605–8.

MIANSERIN AND WARFARIN

DEAR SIR,

I refer to the letters of Warwick and Mindham (*Journal,* September, 1983, **143,** 308) and Ancill and Pinkerton (*Journal,* February, 1984, **144,** 213–4) concerning a case of concomitant administration of warfarin and mianserin which resulted in an abnormally high prothrombin time. I would like to report a case where such an interaction did not occur.

An otherwise healthy 53 year old female developed cardiac arrhythmias and pulmonary oedema while on tricyclic antidepressant therapy for a severe depressive phase of a manic-depressive psychosis (ICD 9, 296.1). On recovery she was stabilised on digoxin and anticoagulant therapy with warfarin 8 mgs. daily, a dose she has remained on since. A month after commencing warfarin she was prescribed mianserin on the grounds that it is non-cardiotoxic. She responded to a dose of mianserin built up to 120 mgs./day, but

unfortunately she became hypomanic, at which point it was discontinued. After a further five week period she was again depressed, and was recommenced on mianserin.

Over a 22 week period the daily dose of mianserin, varying between 0 and 120 mg, was not related to the degree of anticoagulation achieved (prothrombin ratio) with a constant dose of warfarin. This fails to confirm the finding of Warwick and Mindham of a risk of pathological bleeding. Mianserin, because it is non-cardiotoxic and has a unique mode of action, will not infrequently be indicated in depressed patients with pre-existing cardiovascular disease and who may therefore also require anticoagulation with warfarin. This report suggests mianserin can be prescribed in such cases, but it is also clear that prothrombin time needs to be closely monitored, particularly when the drug is commenced or discontinued.

R. K. SHELLEY

Trinity College Dublin,
St. James Hospital,
Dublin 8.

NEUROLEPTIC MALIGNANT SYNDROME

DEAR SIR,

In 1968 Delay and Deniker described signs and symptoms of a drug fever resulting in hyperpyrexia associated with neurologic and autonomic abnormalities, in relation to treatment with phenothiazines, which they called 'neuroleptic malignant syndrome'. The hallmarks of NMS are hyperpyrexia, altered consciousness, muscular rigidity and autonomic dysfunction. The drugs implicated include major tranquillisers — phenothiazines, butyrophenones and thiothixenes. Therapeutic doses rather than toxic doses of these drugs may be involved, and there is no relationship to the duration of therapy. The mechanism of action seem to be strongly related to the disturbance of dopaminergic systems within the hypothalamus and basal ganglia (Smego & Durrack, 1982).

Since Delay and Deniker's coinage of the term many cases have been reported in the American and continental literature, but only two such cases have been published in the United Kingdom (Allen & White 1972; Cope & Gregg 1983).

We (Singh & Sabir) have encountered a further case which presented with all the hallmarks of neuroleptic malignant syndrome as described above. The patient was a 22 year old mentally handicapped girl in an acute schizophrenic state for the treatment of which she had to be admitted to hospital. The mild degree of mental handicap was not due to brain damage, but social and environmental causes. The causal relationships with the drugs for the triggering of neuroleptic malignant syndrome could be traced not to an individual drug, but to various drugs, which were used for the treatment of acute schizophrenia during the first weeks in hospital. She was treated with all the known drugs implicated in precipitation of this syndrome — that is a thiothixene, a butyrophenone and a phenothiazine, with the addition of a barbiturate (amylobarbitone sodium) used initially for the first few nights for insomnia. The schizophrenic illness relapsed in an acute state in spite of a maintenance dose of a long acting intramuscular thiothixene, flupenthixol, which had had to be discontinued soon after admission. Initially a butyrophenone (Dropindol up to 10 mgs BD) was used, with amylobarbitone sodium 200 mgs at night, and after a test dose fluphenazine decanoate (10 mg) was gradually introduced and increased to 50 mgs fortnightly, in four weeks time. However, 5 days after the first 50 mg dose of fluphenazine decanoate the patient collapsed in the hospital grounds, and developed all the classical signs and symptoms of the neuroleptic malignant syndrome: hyperpyrexia of 41°C, muscular rigidity, loss of consciousness, and absence of sweating. All the drugs were immediately discontinued, and she responded to supportive treatment initially and later at an Intensive Care Unit, recovering completely by the third day. Her schizophrenic illness responded satisfactorily to a small dose of pimozide and she was eventually discharged home.

One interesting feature of our case was the unusually hot weather on the day when the patient developed the signs and symptoms of the disorder. The lack of sweating in spite of hot weather was noticed by the nursing staff and could have given warning of the impending catastrophe. It is also interesting to review the literature to see if sunlight has any role in the triggering mechanisms as well, particularly in view of more frequent reports of this syndrome from hot countries.

T. HARI SINGH

Hensol Hospital,
Pontyclun, Mid-Glamorgan

References

ALLEN, R. C. & WHITE, H. D. (1972) Side effect of long acting phenothiazines. *British Medical Journal,* **2,** 221,

COPE, R. V. & GREGG, E. M. (1983) Neuroleptic malignant syndrome. *British Medical Journal,* **286,** 1938.

DELAY, J. & DENIKER, P. (1968) Drug induced extra pyramidal-syndromes. In *Handbook of Clinical Neurology: Diseases of the Basal Ganglia.* By P. J. Vinken & G. W. Bruyn. New York: Elsevier North Holland.

SMEGO, R. A., JR. & DURRACK, D. T. (1982) The neuroleptic malignant syndrome. *Archives of Internal Medicine.* **142,** 1183-4.