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-cardiototoxic 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
