

susceptible to toxicity from neuroleptics and/or lithium (Addonizio *et al.*, 1986; West & Meltzer, 1979). Case one was also dehydrated with hypernatraemia – a treatable concomitant. Leukocytosis is a non-specific finding that may reflect recent lithium usage, stress and/or infection. This patient remained afebrile throughout and was appropriately treated with rehydration. In addition, the patient was not reported to have rigidity in the case study, despite indications of rigidity in the discussion. It is often difficult to evaluate whether certain physiological states are secondary to NMS or specific triggering factors.

Case two had confusion with increased levels of creatine phosphokinase. His pulse, blood pressure and temperature were monitored, but no baseline values were given, and no neurological abnormality reported at the time of symptomatic treatment. Case two, the only patient with documented rigidity and fever, was treated with diazepam. This patient was a 61-year-old male who received a total of 15 mg of haloperidol (750 mg of chlorpromazine equivalents). In addition, he had cardiac disease, apparent pre-renal azotemia secondary to dehydration, electrolyte imbalance and was eventually successfully rehydrated. The physiological concomitants of ageing were not kept in mind and one may question the dosage of neuroleptic in this frail individual. We can speculate that his fever was a coincidental occurrence in a dehydrated patient. He simply had extrapyramidal side-effects that were precipitated by neuroleptics.

The main emphasis is that specific criteria and a precise delineation for the diagnosis of NMS remains controversial with some question as to the existence of a specific disorder. It would be unfortunate if pre-occupation with the beguiling designation 'incipient NMS' or even the full blown phenomenon of NMS sidetracks or distorts our perception of what is really going on – that is, in most cases, the concomitants of physical illness and, most importantly neuroleptic-induced rigidity possibly associated with akathisia that is inadequately treated.

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Calcium-channel blockade and depressive illness

SIR: It was with great interest that I read Eccleston & Cole's report of treatment-resistant depression associated with the use of a calcium-channel blocker (*Journal*, June 1990, **156**, 889). The authors suggest that it may be possible to explain this action of dihydropyridines in terms of the monoamine hypothesis on the basis of alterations in intraneuronal concentrations of calcium. This could be mediated by dihydropyridines reducing calcium influx through voltage-sensitive calcium channels, and noradrenaline and 5-hydroxytryptamine (5-HT) altering levels of inositol 1,4,5-triphosphate (IP3) and diacylglycerol, which regulate release of sequestered calcium from intracellular organelles. However, the spatial distribution of calcium in the cell may be more important than the average cell concentration for the control of many cellular functions. For example, it has been demonstrated that transmitter release may require calcium entry through voltage-sensitive calcium channels increasing the levels of calcium just inside the membrane, rather than general cellular increases of calcium mediated by IP3 (O'Sullivan *et al.*, 1989). The fact that dihydropyridines and monoamines can both affect intraneuronal calcium may not alone be explanation enough. Behavioural studies have clearly shown that calcium-channel blockers are able to affect 5-HT_{1A} and 5-HT₂ function in rats, effects which are reported to be independent of whole-brain 5-HT synthesis and potassium-induced release from *in-vitro* brain slices (Green *et al.*, 1990). Where exactly these effects are mediated is open to debate. Since the effects of calcium-channel blockers could not be reversed by using a calcium-channel agonist (Bay K 8644), Green *et al.* suggest that the changes in 5-HT function are not mediated at the calcium-channel level. However, only low doses of Bay K 8644 were used because of its toxicity.

Recent electrophysiological work may be able to shed light on the situation. 5-HT has been shown to be able to directly reduce calcium currents in dorsal raphe cells of rats, an effect that is independent of its previously well characterised inhibition mediated via potassium channels (Penington & Kelly, 1990). The receptor involved appears to be the 5-HT_{1A}.

presynaptic autoreceptor. This is interesting since this receptor has been implicated as a possible locus for the action of antidepressant treatments (Goodwin *et al*, 1985). In addition, electrophysiological evidence suggests that chronic antidepressants lead to a 'down regulation' of 5-HT_{1A}-mediated inhibition (Blier *et al*, 1988). While this has yet to be confirmed for the action of 5-HT on calcium currents, if it is, then clearly antidepressants have an opposing action to calcium-channel blockers by being able to decrease the ability of 5-HT to reduce calcium influx. Therefore the common pathway for the action of dihydropyridines and monoamines in affective disorders could be at the level of the calcium channel itself.

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Investigating psychosurgery

SIR: I was interested to read Al-Sheikhli's letter (*Journal*, June 1990, 156, 903) and, like him, I wondered why psychosurgery had not been considered in Paykel's review of the relevance of research for the treatment of depression. Professor Paykel helpfully replied (*Journal*, June 1990, 156, 904) and pointed out that psychosurgery, while having a place with severe resistant depression, needs more research into efficacy and indications.

However, in this letter my main purpose is to question Professor Paykel's statement that "I understand that the Mental Health Act Commission has comprehensive records ...". The Commission have been involved with a total of about 100 patients and the Act requires only opinions in writing from three

professionals for each patient. By contrast we have now carried out over 1200 operations since the mid-1960s and we have increasingly detailed information on all these patients over this period of time. Our problem is that money for research is not at all easy to obtain but, given better computer facilities, we have the richest possible information available for investigating psychosurgery.

Professor Paykel suggests that the College could take up the fact that more research into the efficacy and indications of psychosurgery is needed. At the foundation of the College a research committee was set up to investigate the value of psychosurgery. One of the main problems was that there seemed to be no treatments that could be used as a control. A protocol was suggested (Research Committee, 1977) but funding proved impossible.

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WHO consensus statement

SIR: We read with interest the WHO consensus statement on prophylactic use of anticholinergics in patients on long-term neuroleptic treatment (*Journal*, March 1990, 156, 412). However, like Barnes (*Journal*, March 1990, 156, 413-414), while we welcomed the statement, we also felt that it was too brief and failed to comment on some benefits of anticholinergic therapy. Such benefits may be of particular relevance in third-world countries where, for example, patients may experience extreme transport difficulties in reaching a hospital should acute neurological side-effects arise. The occurrence of an otherwise preventable acute dystonia may well exacerbate natural fear of 'western' medicine, so adversely affecting future compliance and willingness to return for further psychiatric care. Also, use of those antipsychotics which are less likely to produce side-effects may not be possible in situations where poor availability and relative costs must be taken into account. Other than from Morocco, there were no other African contributions to this WHO statement which may possibly explain why such factors were not considered.