Both patients developed complete dysphagia and reduced gag reflexes prior to the administration of medication for NMS, followed by the development of right lower zone pneumonia, probably due to aspiration. Dantrolene and lorazepam have muscle relaxing properties, and bromocriptine has been associated with reflux oesophagitis (Katzung, 1989). They could have slowed the recovery of the swallowing reflex and worsened aspiration. The first patient received cisapride, a pro-kinetic agent (Walker, 1994), which seemed to be associated with the return of bowel sounds although no improvement in swallowing occurred. Patients who develop NMS should have their gag reflex assessed early and if reduced or absent a nasogastric tube would be recommended to reduce the risk of aspiration.

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Clozapine-induced neutropenia – or not

SIR: We wish to bring attention to a point of concern between clinicians and the Clozapine Patient Monitoring Service (CPMS), which may increasingly become an issue as more patients receive clozapine.

Because of the danger of neutropenia (3%; Veys, 1993) and its potentially fatal sequelae, it is absolutely right that regular blood counts be taken.

However, we have had experience of two patients whose survival prospects (through lower suicide risk) and quality of life were radically improved by clozapine. Despite suffering from severe schizophrenic illness unresponsive to conventional neuroleptics, they were able to be discharged from hospital. Both, unfortunately, then had one abnormal 'red alert' result. Because of the inevitable delay between blood sampling and the results, both patients had continued to take clozapine until the request for the emergency sample was made. In both cases these repeat samples taken 24 h after the 'red alert' sample showed a near doubling of the neutrophil count, with values well into the normal range.

It is known that neutrophil counts vary according to such factors as time of day, physical activity and presence of viral illness (Lewis, 1974). We understand the caution of the pharmaceutical company and the conditions of its licensing agreement, but is it not possible that one isolated result may be due to factors other than clozapine?

We do not question that patients who have had a true clozapine-induced neutropenia should not be rechallenged with the drug (Safferman *et al*, 1992), but we have seen the tragic consequences of stopping clozapine. Is it not over-reacting to stop clozapine on the basis of one blood result, considering the impact on the lives of patients denied its benefits?

As clinicians, in consultation with the patient, relatives and multi-professional team, we would be prepared to take the risk of continuing clozapine in these cases, but we are not permitted to do so. Would it not be possible to amend the regulations so that there must be two consecutive 'red alert' results in 24 h before clozapine is stopped?

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Administrative problems limiting electroconvulsive therapy

SIR: In the case report of NMS with prolonged hospitalisation, tracheostomy, intubation, and artificial ventilation (*BJP*, January 1994, **164**, 120–122), Cape notes that the patient "also had one

ECT in hospital with a degree of improvement but administrative problems precluded further treatments." This experience was early in the course of treatment; the patient went on to lengthy hospitalisation and eventual resolution. It is difficult to envisage what administrative problems could have been so compelling as to preclude the further administration of a treatment which seemed useful. ECT is an effective treatment for NMS (Davis *et al*, 1991); is safely administered under the most complex conditions of systemic disease (Abrams, 1992); and is reported as life-saving in similar cases of NMS or malignant catatonia (Mann *et al*, 1990; Rummans & Bassingthwaighte, 1991).

Could the administrative problems that precluded the continued administration of such a life-saving treatment as ECT reflect a prejudice against the use of ECT or a lack of training and experience?

The authors also make much of the surprising outcome – the patient's state changed for the better after prolonged hypoxia, artificial intubation, and ventilation. Such 'surprising' changes in behaviour were commonplace when both insulin coma and leucotomy were accepted medical psychiatric treatments. The frequent appearance of behavioural improvement after prolonged insulin coma or induced severe seizure states after leucotomy led many to suggest that the beneficial effects of these treatments on behaviour was the consequence of prolonged organic mental syndromes. Such observations became the basis for hypotheses of the mode of action of these somatic treatments (APA, 1978). While the present experience does not justify a recall of these therapies, the common thread makes the change in this patient's behaviour more understandable.

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B37 repeats are normal in most schizophrenic patients

SIR: Two groups recently reported abnormal expansions of the CAG repeats in the brain transcript B37, in patients with dentatorubral-pallidoluysian atrophy (DRPLA). Normal chromosomes had 7–34 repeats while DRPLA was associated with 49–75 repeats (Koide *et al*, 1994; Nagafuchi *et al*, 1994). Both groups stressed the clinical heterogeneity of this condition and Koide *et al* (1994) reported two patients who had been diagnosed by psychiatrists as schizophrenics, who also had expansions of the B37 CAG repeats. These patients had 57 repeats, at the lower end of the abnormal range.

Schizophrenia is a disease in which genetic factors play a significant role. However, no linkage studies have been successfully replicated (Kendler & Diehl, 1993). The inheritance patterns of this disease show features compatible with variable penetrance and anticipation (reviewed by Ross *et al*, 1993). These features and the finding of B37 expansions in 'schizophrenic' individuals implicated B37 as a possible candidate gene for schizophrenia. We examined 55 unrelated schizophrenic patients from the USA, UK and Italy for abnormal expansions at this locus (Fig. 1). Unrelated families in which there were at least two siblings with schizophrenia were identified from three main sources: a USA national registry of families identified from treatment centres within a NY county catchment area (Suffolk county) and throughout the USA (40 families); a cohort of cases receiving clinical care at a district hospital in northwest London and its surrounding regions and other cases associated with the National Schizophrenia Fellowship (12 families); families recruited in a similar manner by

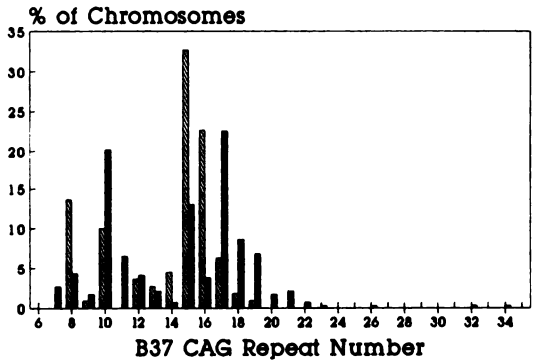

Fig. 1 B37 CAG repeat numbers in schizophrenic patients (hatched bars) (this study) and normal Japanese (solid bars) (data from Koide *et al*, 1994).

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