We believe that the use of a single red alert coupled with careful consideration of its significance by CPMS, together with the facility for independent expert haematology review, is the optimal management system for preventing potentially fatal agranulocytosis, and is the only way in which people with severe schizophrenia can obtain the benefits of clozapine with minimal risk.

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Obsessive–compulsive symptoms and clozapine

SIR: Eales & Layeni (*BJP*, May 1994, **164**, 687–688) report exacerbation of obsessive–compulsive (OC) symptoms with clozapine therapy within the context of pre-existing OC symptoms. These symptoms may also arise *de novo* – often shortly after beginning clozapine treatment (Baker *et al*, 1992; Buckley & Meltzer, 1994). Such OC phenomena are surprisingly recalcitrant to standard pharmacotherapy (Buckley & Meltzer, 1994). The obsessions are readily distinguishable from partial delusions and are not merely the misrepresentation of a change in either the intensity or quality of delusions consequent upon clozapine therapy. OC symptoms in schizophrenic patients in general (Rosen, 1957) and now within the context of clozapine therapy offers a glimpse of the putative neurobiological heterogeneity as it may pertain to phenomenology and treatment response. Such observations lend support to the heuristic validity of using treatment response (to typical *and* atypical antipsychotic drugs) to define subgroups of schizophrenic patients (Schulz *et al*, 1989).

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Strength of the genetic effect in schizophrenia

SIR: McGuffin *et al*'s proposition (*BJP*, May 1994, **164**, 593–599) that schizophrenia may be a purely genetic illness is not convincing.

McGuffin *et al* realise that the major obstacle to their contention is discordance between monozygotic twins. Accordingly, McGuffin *et al* describe genetic processes – mutation, unstable DNA sequences, imprinting, and inactivation – that are not hereditary in any easily identifiable pattern. Similar mechanisms, they posit, may be at work in schizophrenia.

Yet in the various disease entities they cite, nothing near the phenomenon of 50% discordance obtaining for schizophrenia in monozygotic twins is to be found. In Huntington's disease, where an expanded tandem repeat sequence accounts for the pathology, penetrance is 88% (Gusella *et al*, 1993). In fragile-X mental retardation, penetrance for the sons of the daughters of normal transmitting males is 80% (Warren & Nelson, 1994). Penetrance for heterozygote carriers of the gene for retinoblastoma is 85–95% (Naumova & Sapienza, 1994). The random X inactivation of Duchenne's muscular dystrophy, an X-linked illness, also does not seem readily applicable to schizophrenia.

On the other hand, the hypothesis that environmental stress imposed upon a genetic diathesis may cause schizophrenia is not merely "orthodoxy". While McGuffin *et al* discuss physical stressors, psychosocial factors should not be too easily dismissed. Tienari *et al* (1994) have shown that adopted-away children of schizophrenic mothers are far more likely to develop schizophrenia if their adoptive family is characterised by emotional disturbances. Moreover, contrary to accepted wisdom, life events may often precede the onset of schizophrenia (Van Praag, 1993). These are findings impossible to explain if we limit ourselves to a purely genetic aetiology.

The genetic mechanisms referred to by McGuffin *et al* may certainly explain a small percentage of cases of schizophrenia, but considerable room remains for positing an environmental influence in the aetiology of schizophrenia.

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SIR: Although many hypotheses are put forward by McGuffin *et al* to account for the 'non-genetic' causes of schizophrenia, they have possibly overlooked one significant cause of the new appearance of schizophrenia in a patient with no family history: ambiguous paternity.

Estimates of the incidence of non-paternity vary from 2.8% to 30%. Rates of non-paternity depend on the population being investigated. For instance, Macintyre & Sooman (1991) report that one study of the correlation between antibody formation in artificial insemination and blood group had to stop because it had revealed that in the population being surveyed, 30% of the children could not have been sired by their mothers' husbands.

Published data have revealed non-paternity rates of 5% on the basis of ABO and rhesus markers (Johnstone, 1957), and Bellis & Baker (1990) predict a non-paternity rate of 6.9–13.8%. Via DNA fingerprinting, Le Roux *et al* (1992) estimated that, in a population with genetic disease, the rate of children not sired by the declared father was 2.8%.

There is no reason not to expect a similar phenomenon in a psychiatric subpopulation, where the relationships may be even more unstable. However, neither standard textbooks nor a literature search revealed any reference to non-paternity when discussing the heredity of psychiatric illness. Although this phenomenon may not account for all, it can explain part of the discrepancy between the observed and expected heredity. Non-paternity warrants further investigation when studying family histories.

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Lithium prophylaxis in recurrent affective illness

SIR: Guscot & Taylor (*BJP*, May 1994, **164**, 741–746) draw attention to some of the reasons for non-compliance with lithium. I profoundly disagree with the concept of separate specialised clinics which the authors propose would lessen the gap between efficacy and efficiency. This philosophy reflects a general trend in the National Health Service away from the 'generalist' towards fragmentation of services and the deskilling of staff, leading to resentment and demoralisation.

Specialist clinics with research-orientated staff on short-term contracts may not serve the patients' need for personal doctoring: long-term relationships, based on trust and mutual respect, characterised by consultations with staff who have taken the patients through relapses, and have knowledge of the family and social network. There is a need for some specialist services, but surely affective illnesses are the bread and butter of general psychiatrists.

This leads to the conundrum of training psychiatrists. How can programmes that rotate every six months possibly serve patients with long-term illnesses? The problems lie at the root of medical education, which lays emphasis on the seductive rewards of treating acute illness using an authoritarian medical model. I propose that this is an important source of non-compliance which specialist clinics cannot even provide sticking plaster for.

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Dyskinesia and withdrawal from alcohol

SIR: Duke *et al* (*BJP*, May 1994, **164**, 630–636) found that tardive dyskinesia (TD) in schizophrenic