Correspondence

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Contents ■ Haematological monitoring with clozapine therapy in India ■ Chromosome 22q11 deletions and aggressive behaviour ■ Well-being in the families of people with schizophrenia ■ 5-HT_2 neurotransmission in major depression ■ Active placebos in antidepressant trials

Haematological monitoring with clozapine therapy in India

Sir: Clozapine was introduced in India in 1995 and some brands of the drug are now available for the equivalent of around £0.25 for 300 mg clozapine. Unfortunately, affordability is still a problem for many people with schizophrenia, as added to drug costs are the costs of weekly haematological monitoring (£0.25–0.75) and travel. The frequency and duration of haematological monitoring are factors that influence the cost and acceptability of therapy.

Studies from the USA (Alvir *et al*, 1993) and the UK (Atkin *et al*, 1996) reported a drastic fall in the incidence of agranulocytosis or neutropenia after the first 12 months of clozapine treatment. Long-term haematological data from India are lacking, but surveillance over four years in the UK (Atkin *et al*, 1996) did not find Asians from the Indian subcontinent to be at increased haematological risk. The UK study also found the risk of agranulocytosis in the second year of clozapine (0.07%) to be similar to that reported with phenothiazine treatment (0.08%), where counts are checked only on clinical indication.

Recommendations on long-term monitoring vary widely, from weekly monitoring in the USA (American Psychiatric Association, 1997), to fortnightly or monthly monitoring in Europe (Alvir *et al*, 1993). In India many centres monitor counts weekly for the first 18 weeks of clozapine therapy. Thereafter, counts are checked monthly for the duration of therapy, though some centres check counts fortnightly between 18 and 24 weeks. Early detection and management of neutropenia and agranulocytosis before sepsis supervenes is crucial in preventing mortality (Krup & Barnes, 1989). While weekly haematological monitoring for the duration of clozapine therapy would aid early detection of low counts, it is questionable whether monthly monitoring would achieve this.

With the available data, indefinite routine monitoring does not appear to be justified. I therefore invite comment from your readers on the proposition that routine haematological monitoring be discontinued after 16–18 months of clozapine therapy, except in those at higher risk such as the elderly.

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Chromosome 22q11 deletions and aggressive behaviour

Sir: We read with great interest the work by Murphy *et al* (1998) on the prevalence of velo-cardio-facial syndrome (VCFS) in a population of subjects with idiopathic learning disability. In both case reports of patients with 22q11 microdeletions described by Murphy *et al*, aggressive behaviour was a significant feature of the clinical presentation. Patients with deletional forms of VCFS are hemizygous for the gene encoding catechol-O-methyltransferase (COMT). A codon 158 polymorphism encodes common high and low COMT enzyme activity variants found in humans (Lachman *et al*, 1996*a*). Hemizygosity for the low-activity allele is associated with ultra-rapid cycling bipolar disorder that occurs in a subset of VCFS patients (Lachman *et al*, 1996*b*). Most of these rapidly cycling patients are difficult to manage because of increased aggressiveness.

Strous *et al* (1997) recently showed that the low-activity COMT allele is associated with increased violent behaviour in people with chronic schizophrenia. This finding is consistent with previous studies showing that dopaminergic and noradrenergic stimulation increase aggressive behaviour in animals (reviewed by Volavka, 1995). These observations suggest that the low-activity COMT allele could be the common denominator that leads to increased aggression in VCFS and other psychiatric conditions.

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Well-being in the families of people with schizophrenia

Sir: In this wide-ranging discussion it was encouraging that Szmukler & Bloch (1997) considered the importance of the well-being of the family, not just the risk of violence on the part of the person with psychosis. When the psychosis first manifests itself, family members suffer. Their hurt and bewilderment lowers their self-confidence, which may be further undermined by psychiatric staff not listening to them nor trying to answer their questions. Their own health may deteriorate to the point where they may abandon their relative or become incapable of supporting her/him.

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