

Correspondence

EDITED BY LOUISE HOWARD

- Contents** ■ Prescribing of atypical antipsychotics ■ Irish ethnicity and mental health
 ■ Risk of sudden death on high-dose antipsychotic medication: QTc dispersion
 ■ Ethnicity and clozapine metabolism ■ Comprehensiveness of systematic review
 ■ Qualitative research – a rejoinder ■ Active placebos in antidepressant trials

Prescribing of atypical antipsychotics

Sir: Thomas & Lewis (1998) provide a succinct and useful analysis of the issues surrounding atypical antipsychotic drugs. In particular, they rightly emphasise the important role of clozapine for treatment-resistant patients. However, in relation to adverse effects of clozapine, they state that the complications of neutropenia are precluded by blood monitoring. We would question the authors' assertion.

The authors do not state a frequency for blood monitoring, so we presume they are referring to the Clozaril Patient Monitoring Service (CPMS) provided by Sandoz Pharmaceuticals, registration with which is mandatory for patients receiving clozapine in the UK. This level of blood monitoring can certainly reduce the incidence of adverse events, including death, related to neutropenia or agranulocytosis, but we do not believe that such events can be prevented by CPMS monitoring alone. Therefore, we take the view that it would be preferable to state that blood monitoring will reduce the incidence of, rather than preclude, complications associated with neutropenia. There has been at least one death of a patient on clozapine who was monitored precisely in accordance with CPMS procedures and additionally received other white blood cell counts, yet whose agranulocytosis could not be attributed to any other cause and in whom a fatal outcome could not be averted (Mangan & Toal, 1994).

We believe that advice to doctors who might prescribe clozapine should emphasise that clozapine occupies an important place in the treatment of hitherto treatment-resistant schizophrenia, but also that clinical vigilance to signs of infection and possibly additional blood monitoring may be required to minimise the incidence and adverse outcomes of neutropenia and agranulocytosis.

Mangan, B. & Toal, M. J. (1994) Agranulocytosis as a fatal complication of clozapine. *Irish Journal of Psychological Medicine*, 11, 138–139.

Thomas, C. S. & Lewis, S. (1998) Which atypical antipsychotic? *British Journal of Psychiatry*, 172, 106–109.

M. Toal North Cumbria Health Authority, Wavell Drive, Carlisle CA1 2SE

H. Campbell Warneford Hospital, Old Road, Headington, Oxford OX3 7JX

Sir: The recent update on atypical antipsychotics (Thomas & Lewis, 1998) was both interesting and informative. However, the authors seem to endorse the use of divided doses of thioridazine, that is 50 mg t.d.s. (usual dose) and 800 mg (high dose), and trifluoperazine, 10 mg b.d. (usual dose) and 20 mg q.d.s. (high dose). The half-lives of thioridazine and trifluoperazine being 16–30 hours and 13 hours, respectively, there is little justification in using divided doses except in the initial stages when the dose is being titrated. Unnecessary divided dosing can reduce compliance with treatment, impair quality of life, increase side-effects such as drowsiness during working/waking hours, waste nursing time and increase the cost of treatment (Mirza & Michael, 1993; Gelder *et al*, 1996).

Gelder, M., Gath, D., Mayou, R., et al (1996) *Oxford Textbook of Psychiatry* (3rd edn). Oxford: Oxford University Press.

Mirza, K. A. H. & Michael, A. (1993) Cutting costs without cutting corners: a case for sound pharmacotherapy (letter). *Psychiatric Bulletin*, 17, 562–563.

Thomas, C. S. & Lewis, S. (1998) Which atypical antipsychotic? *British Journal of Psychiatry*, 172, 106–109.

R. Appadoo, C. Ashton, T. Carlton Thetford Mental Health Resource Centre, Thetford IP24 2AD

Authors' reply: Toal & Campbell are correct to point out that the blood monitoring performed by CPMS cannot prevent all cases of agranulocytosis. To date, over 15 000 subjects in the UK and Ireland have

been exposed to clozapine and there have been two cases of fatal agranulocytosis (Atkin *et al*, 1996). In the first 14 080 cases, the risk of neutropenia was 2.6% and of agranulocytosis 0.71% (*Clozaril Newsletter*, 1997, issue 18, p. 3). The monitoring service would appear to reduce substantially the risk of developing clozapine-associated fatal agranulocytosis and neutropenia, but cannot completely preclude it. We agree that additional blood monitoring at times of infection would be prudent to ensure that the subject's white blood cell count is sufficient to mount a defence against the infection.

We also agree with Appadoo, Ashton and Carlton's comments. The table at the end of our paper (Thomas & Lewis, 1998, p. 108) was simply designed to compare the costs of the older antipsychotics with some of the newer atypical antipsychotics.

Atkin, K., Kendall, F., Gould, D., et al (1996) Neutropenia and agranulocytosis in patients receiving clozapine in the UK and Ireland. *British Journal of Psychiatry*, 169, 483–488.

Thomas, C. S. & Lewis, S. (1998) Which atypical antipsychotic? *British Journal of Psychiatry*, 172, 106–109.

C. Thomas, S. Lewis University Hospital of South Manchester, Manchester M20 8LR

Irish ethnicity and mental health

Sir: I would like to comment on Bracken *et al's* (1998) article on Irish ethnicity. The authors highlighted the mental health needs of Irish people living in Britain but in considering the Irish dimension in particular and ethnicity in general I would like to draw attention to the gender issues involved. There is a well-established literature on the subjective and objective experiences of Irish women living in British culture and the differences found compared with Irish men (e.g. Hickman, 1995; Gray, 1996). In considering the mental health of this or any ethnic group the contribution of gender to experience of ethnicity should not be ignored. Specific reference to the importance of gender in Irish ethnicity would have added even more weight to Bracken *et al's* arguments.

Bracken, P. J., Greenslade, L., Griffin, B., et al (1998) Mental health and ethnicity: an Irish dimension. *British Journal of Psychiatry*, 172, 103–105.

Gray, B. (1996) Accounts of displacement: Irish migrant women in London. *Youth and Policy: The Journal of Critical Analysis*, 52, 22–29.