We conducted a telephone survey of facilities for treatment of patients with comorbidity in such services. Ten residential rehabilitation addiction services were contacted and admission staff questioned on their attitudes to new referrals who were on medication for comorbid psychiatric disorders. The therapeutic orientation ranged from a therapeutic community to a skills-based programme; half were based on the abstinence 12-step approach. Only one of the 10 had psychiatric input and two had general practitioner support. The other seven could call on general practitioner services when necessary. Six would not accept patients on hypnotics, anxiolytics or antidepressants; the other four would work towards the reduction of such medication. Six would accept patients on antipsychotics, four refused. Five would accept patients on mood stabilisation, five refused. All would accept referrals on anti-epileptic medication.

We also asked about attitudes to medication prescribed to help maintain abstinence. Only two of the 10 would accept clients taking acamprosate calcium or naltrexone.

Poor outcome is associated with the failure to identify and address comorbid psychiatric disorders in patients with substance use disorders. Such patients would benefit from long-term residential rehabilitation. However, this is made difficult as many rehabilitation units refuse to take patients on medication. In addition, patients may be denied the benefits of new pharmacological treatments for addiction to reduce cravings, such as acamprosate calcium and naltrexone.

Hall, W. & Farrell, M. (1997) Comorbidity of mental disorders with substance misuse. *British Journal of Psychiatry*, **171**, 4–5.

Regier, D. A., Farmer, M. E. Rae, D. S., *et al* (1990) Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) Study. *Journal of the American Medical Association*, **264**, 2511–2518.

Francis Keaney, Helen Crimlisk, Jenny Bearn
Wickham Park House, Bethlem Royal Hospital, Monks Orchard Road, Beckenham, Kent BR3 3BX

Sir: Hall & Farrell (1997) propose that the SCL-90 questionnaire could be used to detect probable anxiety and depressive disorders among drug-dependent persons. However, we think precaution is necessary.

We assessed the SCL-90 (Derogatis, 1994) in a Dutch population (n=56) of drug-dependent persons who have entered a clinical treatment to screen for psychopathology. The first assessment took place in a pre-detoxification intake, the second assessment took place after detoxification. Results show that all sub-scales of the SCL-90 (with the exception of the hostility scale) decrease substantially (total score diminished 18%), suggesting that high pre-detoxification scores may represent drug-related symptoms, rather than psychiatric disorders. Furthermore, in another study we found that the validity of the SCL-90 to screen for DSM–III anxiety disorders is limited. Typically, satisfactory sensitivity was accompanied by low specificity (Hendriks, 1990).

We agree with the authors that the recognition and treatment of people with comorbid mental and substance use disorders is necessary. Also, staff in addiction services should be trained to identify anxiety and affective disorders in this population. However, before implementing instruments to detect psychopathology in drug-dependent patients, thorough investigation of the psychometric properties is necessary in this specific population, in particular given the potentially drug-induced nature of the reported symptoms.

Derogatis, L. R. (1994) *The Symptom Checklist 90–R: Administration, Scoring, and Procedures Manual* (3rd edn). Minneapolis, MN: National Computer Systems.

Hall, W. & Farrell, M. (1997) Comorbidity of mental disorders with substance misuse. *British Journal of Psychiatry*, **171**, 4–5.

Hendriks, V. M. (1990) *Addiction and Psychopathology: A Multidimensional Approach to Clinical Practice*. Rotterdam: Erasmus University.

I. H. A. Franken, V. M. Hendriks Research Department, Psychiatric Centre Bloemendaal, PO Box 53002, 2505 AA The Hague, The Netherlands

Eosinophilia, agranulocytosis and clozapine

Sir: There has been controversy in the *Journal* recently about the relationship between eosinophilia and clozapine-induced agranulocytosis (Amital *et al*, 1997; Bailey *et al*, 1997). Evidence on the predictive value of eosinophilia for subsequent emergence of neutropenia and/or agranulocytosis in clozapine-treated patients is not robust (Hummer *et al*, 1996; Ames *et al*, 1996). Undue concern about the emergence of agranulocytosis may lead to discontinuation of clozapine which may have significant impact on the future course of the disease.

A 22-year-old White male with a two-year history of paranoid schizophrenia with recurrent suicidal ideas was started on clozapine after he failed successive trials with thiothixene, haloperidol, and risperidone. The clozapine dose was gradually increased to 400 mg/day by day 18. Prior to clozapine treatment, he had a white blood cell (WBC) count of 9300 cells/mm^3, with 4.0% eosinophils (absolute count 400 cells/mm^3) and 56% neutrophils (absolute count 51 000 cells/mm^3). On day 22, the WBC count was 10 000 cells/mm^3 with 15.7% eosinophils (1600 cells/mm^3) and 59.7% neutrophils (5600 cells/mm^3). On day 27, the WBC count was 9100 cells/mm^3 with eosinophils increasing to 22.8% (2100 cells/mm^3) and neutrophils decreasing to 46.3% (4100 cells/mm^3). Clozapine was discontinued after consultation with a haematologist and the Department of Veterans Affairs National Clozapine Coordinating Center. Two weeks after the discontinuation of clozapine, the patient had a WBC count of 7300 cells/mm^3 with 18% eosinophils (1300 cells/mm^3) and 36% neutrophils (2900 cells/mm^3). All the blood cell counts returned to normal by eight weeks. Six months later he died from a self-inflicted gun shot wound to the brain while on a combination treatment with loxapine and risperidone.

Eosinophilia may occur in up to 40–60% of patients on clozapine and is usually considered transient and asymptomatic (Gerlach *et al*, 1989, Banov *et al*, 1993, Bailey, 1997). Cases of symptomatic eosinophilia associated with a decreasing neutrophil count have been reported (Galletley *et al*, 1996). Sometimes, it acts as a precursor of neutropenia; genetic differences are postulated to explain this variability (Hummer *et al*, 1996). Current guidelines from the manufacturer recommend discontinuation of clozapine if the eosinophil count goes above 4000 cells/mm^3. Galletley *et al* (1996) suggest developing guidelines for discontinuation of clozapine in patients with eosinophilia and or decreased neutrophil counts. We believe that eosinophilia is of virtually no clinical utility in predicting clozapine-induced agranulocytosis (Ames *et al*, 1996; Bailey 1997). Premature discontinuation of

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clozapine in such patients may be unjustified as the patients may be denied proper treatment.

Ames, D., Wirshing, W. C., Baker, R. W., et al (1996) Predictive value of eosinophilia for neutropenia during clozapine treatment. *Journal of Clinical Psychiatry*, **57**, 579–581.

Amital, D. Gross, R., Amital, H., et al (1997) Coexistence of eosinophilia and agranulocytosis in a clozapine-treated patient (letter). *British Journal of Psychiatry*, **170**, 194.

Bailey, P. (1997) Clozapine treatment, eosinophilia and agranulocytosis (letter). *British Journal of Psychiatry*, **171**, 90.

Banov, M., Tohen, M. L. Friedberg, J. (1993) High risk of eosinophilia in women treated with clozapine. *Journal of Clinical Psychiatry*, **54**, 466–469.

Galletley, C., Wilson, D. & McEwen, S. (1996) Eosinophilia associated with decreasing neutrophil count in a clozapine-treated patient (letter). *Journal of Clinical Psychiatry*, **57**, 40–41.

Gerlach, J., Jorgensen, E. O. & Peacock, L. (1989) Long term experience with clozapine in Denmark: research and clinical practice. *Psychopharmacology*, **99**, S92–S93.

Hummer, M., Sperneruntenweger, B., Kemmler, G., et al (1996) Does eosinophilia predict clozapine-induced neutropenia? *Psychopharmacology*, **124**, 201–204.

M. D. Adityanjee, V. Chowdary Jampala Psychiatry Service, Veterans Affairs Medical Center, 4100W. Third Street, Dayton, OH 45434, USA

Madan S. Mohan Department of Psychiatry, Wright State University School of Medicine

Establishing cost-effectiveness of antipsychotic drugs

Sir: In commenting on the work of Aitchison & Kerwin (1997), Robert & Kennedy (1997) make a plea for more long-term, large-sample, randomised, controlled trials evaluating the health–economics of antipsychotic prescribing. While I agree that such studies would indeed be useful, I feel that open, mirror-image studies like that of Aitchison & Kerwin have greater practical value. As a manager of a trust drugs budget, I need to know the cost-effectiveness of drugs used under normal clinical circumstances in an environment similar to, or the same as, my trust. Indeed, purchasers of health care often demand parochial health-economic trials before they will consider funding, showing only a passing interest in large-scale multi-centre, randomised controlled trials, despite their scientific rigour. This is because, with all their inclusions, exclusions and intensive observations, these studies only indirectly reflect clinical practice.

Let us conduct more long-term, controlled studies, but let us also note carefully the results of open, uncontrolled trials which better reflect the real world.

Aitchison, K. J. & Kerwin R. W. (1997) Cost-effectiveness of clozapine: a UK clinic-based study. *British Journal of Psychiatry*, **171**, 125–130.

Robert, G. & Kennedy, P. (1997) Establishing cost-effectiveness of atypical neuroleptics. *British Journal of Psychiatry*, **171**, 103–104.

David M. Taylor Bethlem and Maudsley NHS Trust, Maudsley Hospital, Denmark Hill, London SE5 8AZ

Sir: In their excellent article, Robert & Kennedy (1997) reference two reviews in the Cochrane Library (*http://archie.cochrane.co.uk,info/*) (Adams & Soares, 1997). These are now completed. One, on clozapine, has been available for some time and has been updated every three months since publication (Wahlbeck *et al*, 1997). This will soon contain what data are available from recent trials that have, at last, looked at economic outcomes. The review on risperidone is also complete (Kennedy *et al*, 1997) and the next version of the Cochrane Library will contain this as well. What few data there are on cost-effectiveness will be presented. A similar review on olanzapine is starting. Every attempt is made to keep the systematically conducted reviews on the Cochrane Library up-to-date. Abstracts of completed reviews and titles of those underway are readily available (*http://archie.cochrane.co.uk/info/abstracts/abidx.htm#G06@*).

Adams, C. E., Soares, K. (1997) The Cochrane Collaboration and the process of systematic reviewing. *Advances in Psychiatric Treatment*, **3**, 240–246.

Kennedy, E., Song, F., Hunter, R., et al (1997) Risperidone for schizophrenia. The Cochrane Library (CD-ROM). The Cochrane Collaboration; Issue 3. Oxford: Update Software.

Robert, G. & Kennedy, P. (1997) Establishing cost-effectiveness of atypical neuroleptics. *British Journal of Psychiatry*, **171**, 103–104.

Wahlbeck, K., Cheine, M., Essali, M. A., et al (1997) Clozapine vs 'typical' neuroleptic medication for schizophrenia. The Cochrane Library (CD-ROM). The Cochrane Collaboration; Issue 3. Oxford: Update Software.

Clive E. Adams Summertown Pavilion, Middle Way, Oxford OX2 7LG

Disorders of the mother–infant relationship

Sir: Professor Kumar's (1997) questionnaire study of 44 women with disorders of maternal 'bonding' has confirmed the duration of the disorder and the importance of parturition stress. I am surprised that he failed to find a link with unwanted pregnancy and disorders of prepartum affiliation because these are supported by other studies (Arbeit, 1975). He seems not to have considered the child's contribution to this relationship.

My most serious concern, however, is his remark about treatment. There is no discussion of treatment in the text, but the table of "clinical implications" states that "there are as yet no specific therapies". The word 'specific' presumably means therapies tailor-made to address this particular problem, not any other. The principles of treatment were set out in my earlier account (Brockington, 1996, pp. 347–360): they include specific elements directed at mother–infant interaction. Professor Kumar's negative remark about therapy may give a misleading impression to sufferers and their therapists. These are severe disorders, they are common and neglected, but, provided the disordered mother–infant relationship is identified, and not subsumed under a label such as 'postnatal depression', the treatment response is excellent.

Arbeit, S. A. (1975) *A Study of Women During their First Pregnancy*. PhD Thesis, Yale University.

Brockington, I. F. (1996) *Motherhood and Mental Health*. Oxford: Oxford University Press.

Kumar, R. C. (1997) "Anybody's child": severe disorders of mother-to-infant bonding. *British Journal of Psychiatry*, **171**, 175–181.

I. F. Brockington Department of Psychiatry, The University of Birmingham, Queen Elizabeth Psychiatric Hospital, Mindelsohn Way, Birmingham B15 2QZ

Neuropsychological and imaging differences in dementia with Lewy bodies and Alzheimer's disease

Sir: We agree with the recent editorial by Miller (1997) that recognition of the characteristic features of the different dementias has become increasingly important, especially in view of new treatment possibilities. We are surprised, however,

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