benefit from clozapine. So what has got into the therapeutic experts of the Committee on Safety of Medicines? Surely the first principle of therapeutics is that those likely to benefit the most should be those who take the largest risk. As things stand now in Britian, clozapine is often reserved for the worst cases of chronic vegetative schizophrenia, with relatively little chance of success. Why should these unfortunate patients, who are less likely to respond, also shoulder the risk of agranulocytosis, while those most likely to respond are denied the drug and left to endure the severe extrapyramidal side effects of the partially effective classic antipsychotic drugs?

Schizophrenia is a devastating and destructive medical condition whose sufferers are third class citizens and third class patients. Clozapine gives them the best chance of recovery to date. The Clozaril monitoring system is working superbly. Clozapine should be available to all patients. We then predict that a cost-benefit analysis would show dramatic improvements.

ROBERT KERWIN

Institute of Psychiatry,
London SE5 8AF

FIONA LOFTS

St George's Hospital,
London SW17

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Clozapine has a unique pharmacological profile

EDITOR,—In their editorial on clozapine Steven R Hirsch and Basant K Puri express the view that the unique and atypical properties of clozapine may be due to the greater antagonism of serotonin S_2 receptors relative to D_2 receptors as well as to a relatively higher affinity for D_1 and D_4 receptors.[1] The standard neuroleptic drugs also have potent antagonist actions on serotonin S_2 receptors in vivo[2] and in vitro.[3,4] Clozapine is unique in that it has antagonist actions on serotonin S_{1C} receptors with a much higher affinity than it does to serotonin S_2 receptors, a property that is not shared by the standard neuroleptic drugs.[3-5] Therefore the unique and atypical properties of clozapine may be due to its antagonistic actions on serotonin S_{1C} receptors as much as to those on serotonin S_2 receptors. Thus neuroleptic drugs may be modelled on another unique pharmacological profile of clozapine: potent central serotonin S_{1C} activity and weaker dopamine D_2 activity.

SERDAR M DURSUN
MICHAEL A REVELEY

Department of Psychiatry,
Faculty of Medicine,
University of Leicester,
Leicester LE2 7LX

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Risperidone is less toxic but equally effective

EDITOR,—Steven R Hirsch and Basant K Puri conclude that clozapine's cost and toxicity are outweighed by its advantages in the treatment of refractory schizophrenia.[1] Whether this is so depends on the availability of alternatives with comparable efficacy and, hopefully, lesser toxicity. The substituted benzamides, such as remoxipride and raclopride, are better tolerated than standard agents but offer no advantage in their therapeutic range. Another newly introduced atypical agent, risperidone, resembles clozapine in its paucity of extrapyramidal reactions, its antidyskinetic activity, and its superior efficacy against negative symptoms and in patients poorly responsive to standard treatment.[2] Risperidone also shares clozapine's liability to cause sedation and hypotension but lacks its haematological, antimuscarinic, and epileptogenic toxicity.

What accounts for the remarkable therapeutic action of clozapine and risperidone? A crucial property of such drugs is not simply a weaker dopamine D_2 antagonism than that of standard agents but rather a relatively stronger antagonist potency at serotonin S_2 compared with D_2 receptors.[3] The strong α_1 adrenolytic activity common to clozapine and risperidone[4] may also be important since noradrenergic input has recently been shown to regulate the reactivity of midbrain dopamine neurones.[5]

Hirsch and Puri point out that the risk of agranulocytosis associated with clozapine and the requirement for regular blood counts contribute substantially to the drug's cost and to noncompliance. Why then do they not mention less toxic atypical antipsychotic drugs with a comparable effect? They suggest that it is too soon to report on the efficacy of such agents. At least with regard to risperidone, this is no longer the case.

DAVID B MENKES

Department of Psychological Medicine,
Medical School,
University of Otago,
Dunedin,
New Zealand

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Compliance no worse than with other neuroleptic drugs

EDITOR,—In their editorial on progress in treating refractory schizophrenia with clozapine Steven R Hirsch and Basant K Puri refer to "considerable lack of compliance."[1] They estimate the noncompliance rate at between 30% and 50% and suggest that this is partly attributable to side effects and the need for regular blood sampling. As the author of a study on non-compliance, I wish to set this in a wider context.

Studies in the United States, Britain, and the former Soviet Union have shown non-compliance rates in schizophrenic patients of up to 32%,[2] and a study in 1967 showed that inpatients who did not comply were mainly those with paranoid delusions.[3] A non-compliance rate of 70% was found in depressed outpatients,[4] and workers in medicine in general have shown high non-compliance rates with aminosalicylic acid in tuberculosis[5] and with drugs for rheumatoid arthritis.

I wonder if this problem is greater with clozapine than with other neuroleptic drugs in those ill enough for long enough to receive it.

J D WILSON

Bracebridge Heath,
Lincoln LN4 2QU

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Home treatment for acute psychiatric disorder

A marvellous advance

EDITOR,—Paul Dedman is lukewarm in his verdict about these new developments in community care, concluding that home based treatment "could be a useful constituent of a comprehensive mental health service" but going no further.[1] Any service for severely mentally ill people that leads consistently to greater satisfaction with psychiatric services, appreciable reduction in use of inpatient beds, and, in some cases, greater improvement in clinical symptoms,[2] is much more than a useful constituent: it is a marvellous advance.

We have made considerable progress since the pioneering work of Stein and Test, and it is probably no longer justified to compare the somewhat unusual community services that offer 24 hour cover and provide total care with standard psychiatric services. Such services are not representative of clinical practice and, as Dedman suggests, may lead to burnout or other problems associated with demotivation of staff. They are also relatively expensive but certainly no more expensive than conventional care.

When the option of home treatment (as opposed to formal domiciliary visits invited by general practitioners) is introduced to ordinary clinical practice[2,3] together with other community focused care through general practice liaison[4] and enhanced day hospital care[5] the benefits are clear and include long term reduction in bed use[6] and, in some cases, reduced cost (unpublished data) as well as the advantages listed above. This community approach involves close working in multidisciplinary teams which are not constrained by the setting in which they first see the patient, and where there is a system for coordinating and reviewing clinical management in community settings. The care offered is similar to that of the care programme approach recently initiated by the Department of Health and, if implemented as planned, could lead to major improvement in our mental health services. The faint applause of Dedman's leader needs some additional decibels of reinforcement.

PETER TYRER
STEPHEN MERSON
NARESH GANDHI

St Mary's Hospital Medical School,
St Charles' Hospital,
London W10 6DZ

BRIAN FERGUSON

East and Carlton Mental Health Team,
Stonebridge Centre,
Nottingham NG3 2FH

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