While families would agree that the prime focus of the psychiatric team must be the mental health of the patient, organisations such as ours would argue that a supportive family provides a large contribution to the short- and long-term health of the patient, whether the latter eventually lives in the family home or not.

For the family to be able to support the patient, they must have the understanding and information necessary to provide appropriate care. Ideas on confidentiality need to be re-thought. On admission to hospital, the patient may say 'no' to informing the family, but during their hospital stay and before discharge, they should be asked again. They may well have changed their mind, especially if staff have helped them to understand that sharing their problems with carers makes living with their illness easier (Carstairs *et al*, 1985). When the patient is discharged, staff should be quite sure that the patient is adamant about not informing his/her family. If s/he is adamant but intends to see the family even occasionally, s/he could be told that the family must get some minimum information, essentially phone numbers for emergencies and crises. The release of further information could be negotiated with the patient.

Ways of giving information which do not breach confidentiality (Atkinson & Coia, 1995) include the use of voluntary organisations such as National Schizophrenia Fellowship (Scotland) which can provide support and general information about treatments, the pros and cons of medication and tips on how best to help the user.

Where the family members are going to give support, they need accurate and well-balanced information on both the illness and the individual patient. If they do not get this from the psychiatric team, they may look elsewhere for enlightenment. They may then get suggestions of how to proceed which are neither relevant nor helpful to that particular patient, such as stopping medication and using alternative therapies, going back to work or college or taking up activities which put the person under stress and increase the possibility of relapse.

It is necessary that all psychiatric staff understand that discharging patients without providing information to their family could be detrimental to the patient's welfare. People with severe mental illnesses are looked after in hospital by highly trained professional staff with their own professional support systems. Discharging these patients into the community where families, the unpaid informal carers, are given no support and information, is potentially a recipe for disaster. It simply does not make sense.

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5-HT_2 neurotransmission in major depression

Sir: I read with interest the neuroendocrine challenge study by Sargent *et al* (1998). The conclusion that potentiation in 5-HT_2 neurotransmission is unlikely to be responsible for the antidepressant effect of selective serotonin reuptake inhibitors (SSRIs) is consistent with platelet studies suggesting that up-regulation of 5-HT_{2A} receptors may be a trait phenomenon of major depression (Hrdina *et al*, 1997). However, some additional points should be made to clarify the role of 5-HT_2 neurotransmission in depressive disorder.

First, concurrent use of cyproheptadine, a 5-HT_2 antagonist, to treat sexual dysfunction resulted in a reversal of the antidepressant effect of fluoxetine (Feder, 1991), supporting the role of 5-HT_2 neurotransmission in the antidepressant effect of SSRIs in some depressed patients. Second, short-term lithium treatment appears to reverse the deficit state in an animal model of depression by activating post-synaptic 5-HT_{1C} (current terminology 5-HT_{2C}) receptor sites (Aulakh *et al*, 1994). Further, it seems to enhance cognitive and motivational process by increasing 5-HT_2 neurotransmission (Harrison-Read, 1998). Hence, it is possible that initial increase in 5-HT_2 neurotransmission may account for the improvement in some symptoms of depression and/or for the augmenting effect of lithium carbonate in the treatment of refractory depression. Third, considering the findings that neurotransmission at 5-HT_2 receptors may be a trait marker of major depression (Hrdina *et al*, 1997), the down-regulation of 5-HT_2 receptors with long-term treatment with SSRIs might be responsible for prevention of recurrences of depression (this awaits further investigation). In sum, the participation of 5-HT_2 receptors in major depressive disorder appears to be multifarious and complex.

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Active placebos in antidepressant trials

Sir: Moncrieff *et al* (1998) highlight a methodological flaw in many placebo-controlled studies; anticholinergic side-effects are readily identifiable so it is not possible for these studies to be blinded and they are therefore liable to observer bias. This is the rationale for a meta-analysis of studies that used an active placebo in the form of atropine. Nine studies were identified and a smaller effect size for tricyclic antidepressant (TCA) efficacy was identified, relative to analyses pooling studies that used an inert placebo. They conclude that TCAs may not be as effective as previously assumed and that active placebos are necessary for valid double-blind studies.

In the discussion, Moncrieff *et al* acknowledge that the decreased efficacy of TCAs identified in their analysis may arise if atropine had antidepressant properties *per se*. This is dismissed on the evidence that a study by Gillin *et al* (1995) failed to demonstrate antidepressant efficacy of a centrally acting anticholinergic agent relative to a peripherally acting anticholinergic. However, the centrally acting anticholinergic studied was biperidan, a relatively selective M1 antagonist. In contrast, atropine is a competitive antagonist at all

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muscarinic receptors (M1–M5). There is little evidence to suggest that the involvement of central cholinergic pathways in the pathophysiology of depression can be ascribed to the M1 receptor. Thus, the finding by Gillin *et al* is not surprising but does not form a valid basis for dismissing the possibility that atropine may have antidepressant properties.

The question then arises as to the evidence that atropine may indeed have such therapeutic effects. Certainly, there is experimental and clinical evidence to suggest that agents affecting central cholinergic neurotransmission have a profound effect on mood (Janowsky & Overstreet, 1995). Recent work by our group (Cooney *et al*, 1997) using a neuroendocrine strategy supports the hypothesis that overactivity of these neuronal pathways occurs in depressive illness. The area has been advanced further by neuroimaging findings identifying elevation in brain choline (a precursor of acetylcholine) in depressed subjects, which is ameliorated by treatment with nefazodone (Charles *et al*, 1995). Renshaw *et al* (1997) found a relative decrease in choline in the basal ganglia of depressed subjects, highlighting the regional differences in the same neuronal pathways. Of interest, this was most marked in subjects who subsequently responded clinically to fluoxetine. That an abnormality identified in one neuronal system should serve as a marker for response to a drug that acts predominantly through another neurotransmitter system merely emphasises the folly of ascribing behavioural change to discrete neuronal systems, given the complexity of interconnectedness.

Atropine is an agent that has not specifically been subject to clinical evaluation as an antidepressant. It works on a neuronal system that is implicated in depression both directly and indirectly. The point about potential bias made by Moncrieff *et al* is an important one but caution may be needed in accepting their conclusions, as atropine may in fact be more active than placebo.

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One hundred years ago

The out-patient treatment of insanity in general hospitals

By Crochley Clapham, MD, Physician Superintendent, the Grange, Rotherham; Physician to the Royal Hospital, Sheffield

A certain amount of provision for the out-patient treatment of mental disease amongst paupers has been made at our large county asylums, and good work has been done, but there remains a large number of patients of the class slightly above paupers who decline to present themselves for treatment at an asylum and whom it is advisable to provide for elsewhere.

Dr. Henry Rayner (late Superintendent of Hanwell), Lecturer on Mental Diseases at St. Thomas's Hospital, London, has endeavoured to fill this gap by instituting an out-patient department for mental diseases at that hospital, and has advocated the establishment of similar departments at other public hospitals. Dr. Rayner commenced his work at St. Thomas's early in 1893, and I was induced, by his representations and by a paper which he read at the British Medical Association meeting held at Newcastle in that year, to set up a corresponding department at the Royal Hospital, Sheffield, with which I am connected as Honorary Physician.

The weekly Board of the hospital having sanctioned the proceeding, I started in the autumn of 1893 by putting up a notice in the out-patient waiting room to the effect that patients suffering from mental disorder would be seen at 1.30 p.m. every Tuesday, and that it was advisable that patients of this class should be accompanied by a near relation. The response to my notice was immediate and continuous, and for the last four years and a half cases of mental disease have never failed to present themselves on the day set apart by me for their treatment. During this period every form of insanity has passed under my notice at the hospital, and with very gratifying results.

The great object aimed at in the establishment of this department has been to get at the insane of the lower classes in the early stages of their malady, which are so much more amenable to treatment than the more advanced ones. To this end I spoke in my notice of mental disorder and not of insanity, as the latter term is singularly abhorrent to these people.

The first thing to determine, on a case presenting itself, is whether or no it is a suitable one for out-patient treatment, or whether it would be more properly dealt with inside an asylum, thus providing the poor with expert advice gratuitously on a most important point.

Where I have thought it advisable to recommend asylum care, I have always found the relatives ready to fall in with my suggestion, though previously, perhaps, averse to taking action in the matter. However, the great proportion of patients presenting themselves have proved suitable for out-patient treatment and home management.

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