serotonergic neurotransmission, it is likely that lithium acts by a different mechanism.

Secondly, many studies find that lithium can potentiate the antidepressant effect of tricyclics within three or four days (de Montigny *et al*, 1981, 1983; Chiu & Rimon, 1987). Compared with the slow onset of antidepressant action of tricyclics alone, the rapid potentiating action of lithium is not typical of changes in neurotransmission but is more consistent with changes in enzymatic reactions.

It should be emphasised that decreased Na^+/K^+-ATPase activity as a mechanism of therapy-resistant depression is only a tentative hypothesis that remains to be tested. Yet researches along that line are certainly worthwhile, especially if studies on neurotransmission do not yield further breakthroughs

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SIR: There were two purposes to my Annotation (*Journal*, April 1988, **152**, 453–459). The first was to emphasise the need to establish a definition of resistant depression that would be internationally recognised. The second was to speculate on the possible biochemical aetiology of resistant depression, with particular reference to changes in neurotransmitter function. As lithium has been advocated as a combination therapy with tricyclic antidepressants in the treatment of therapy resistance, I commented on the possible causes of such a beneficial interaction. It was not my intention to suggest that only the serotonergic system was involved, or that it was causally related to the condition or to the patients response to treatment. The involvement of serotonin has achieved prominence because its transport, receptor function, etc. can be measured in blood. Despite the assertion of Dr Chiu, there is reason to believe that the synergistic interaction between lithium and tricyclic antidepressants is associated with rapid receptor adaptation, as I indicated in my article. Undoubtedly such changes are associated with, or caused by, other changes in electrolyte flux as well as those in neurotransmitters whose activity in patients still awaits evaluation.

Regarding Dr Worrall's comments, the consensus concerning the efficacy of lithium in the treatment of endogenous depression is that the drug is not as effective as tricyclic antidepressants (e.g. Lader & Herrington, 1981). I agree with Dr Worrall that the reason for the greater efficacy of lithium in treating the depressive component of bipolar rather than unipolar patients is unclear and, in my opinion, will remain so until adequately controlled trials are undertaken in which neurotransmitter function, as well as clinical response, is assessed. Dr Worrall's proposal that there are two distinct groups of depressed patients that differ in the nature of their defect is appealing but, to my knowledge, remains to be proven.

While there may be differences of opinion over emphasis, I'm sure all readers will agree that only more research will provide the answers. If my Annotation has achieved nothing but this then it has achieved its purpose.

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Prescribing for the Long-Term Mentally Ill

SIR: Holloway (*Journal*, April 1988, **152**, 511–514) refers to the paper by Priern *et al* (1978) who point out that, for the purpose of assessing the appropriateness of drug prescribing, cross-sectional data is unsatisfactory and misleading and intimate knowledge of the patients' clinical details and treatment history are essential. Dr Holloway then proceeds to criticise the appropriateness of prescribing on the basis of cross-sectional assessment of mental state supplemented by history of illness and treatment from patients' recollections, with or without case notes. He emphasises that case notes were a "poor