planned reductions of 15 647 beds by 1996. Day hospital places are expected to rise by 6499 over the same period to a total of 34 231. Wide Regional differences in day hospital services are expected to persist: there is a five-fold difference between the 828 places planned by the Northern Region and the 4116 in the North Western Region.

The results of this survey demonstrate a continuation of the long-standing decrease in the number of psychiatric in-patient beds. No acceleration in the rate of discharge of patients in England is expected over the next decade: it will remain about 2300 patients per year. The present total number of both in-patient and day-patient places is 89 126. These results suggest an estimated 78 400 total places after the planned closures: a shortfall of approximately 10 000 places from the current level of service provided by the Regions. The estimated 54 140 in-patient places after closures remains over 6000 places short of the long-standing government target of 47 900 (HMSO, 1984). The Audit Commission (1986) found that Health Authorities have been more successful in planning hospital closures than in implementing successor services. These figures suggest that this will continue to hold throughout the next 5–10 years. Given this, local government authorities may be expected to play an increasingly active role in providing for deinstitutionalised patients (Griffiths, 1988).

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Therapy-Resistant Depression

SIR: We read Professor Leonard's article (*Journal*, April 1988, **152**, 453–459) on the biochemistry of resistant depression with interest. We would like to ask him how his serotonergic hypothesis of resistant depression explains certain experimental findings that are at variance. Most antidepressants enhance electrophysiological responsiveness of cells to iontophoretically applied 5HT (de Montigny & Aghajanian, 1978), yet this is in conflict with receptor binding and behavioural evidence for down-regulation of 5HT function following antidepressant therapy (Peroutka & Snyder, 1980; Goodwin *et al*, 1984). Neither is it explained why ECT would appear to have to have the opposite effect to antidepressants by increasing 5HT mediated behaviour and $5HT_2$ receptor binding (Green *et al*, 1983). It would thus appear that, as yet, no one hypothesis can link together the various mechanisms of actions of the antidepressant therapies on 5HT function.

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SIR: While I agree entirely with the views of Drs O'Shea and Mathews that no one hypothesis can link the various mechanisms of action of antidepressants to changes in 5HT function, I feel that their letter ignores the fact that the healthy, genetically pure laboratory rat differs from a depressed patient. The apparent differences between the biochemical and electrophysiological changes initiated by antidepressants and ECT in rat brain would not appear to apply to the depressed patient. In my annotation, I commented on the similarity of action of antidepressants and ECT on platelet 5HT transport in depressed patients. Thus all antidepressants so far examined normalised the decreased $5HT_2$ receptor function (as shown by reduced platelet aggregation) in those patients responding to treatment; qualitatively similar changes occur in ^{3}H-5HT uptake into platelets from these patients. Such findings suggest that there is a 5HT sub-normality in depression

which is corrected by any effective treatment. Whether this finding in rats has any relevance to the mode of action of antidepressants in man is an open question!

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The Viral Theory of Schizophrenia

SIR: I am grateful to Dr Crow (*Journal*, March 1988, **152,** 431) for updating me on the latest developments in genetic research, and I concede that I will never be in a position to refute his theories on genetic grounds for the reason I have already stated: that the parent science will keep throwing up new discoveries. The problem with the retrovirus theory, as I see it, is more philosophical than genetic.

Dr Crow asserts that there is no compelling evidence for the belief in an environmental contribution and offers in support evidence from population studies. These studies make certain predictions about the distribution of the disease, and Dr Crow infers that his causal theory is likely to be correct because it can be made to fit the predictions. Such an inference is untenable; there is no *a priori* reason to suppose a predictive model causally valid. An analogy can be made to the various theories of astronomy that have had, even at the time of Babylon, sufficient predictive validity to account for the ephemera and yet have been causally incorrect.

He circumvents the problem of monozygotic discordance by enlarging his theory to embrace the development of the central nervous system. The larger theory now consists, in pure terms, of three connected theories: (a) schizophrenia is caused by a genetic disorder, a retrovirus; (b) bilaterality is controlled by a gene; and (c) schizophrenia is a disorder of laterality. This has the appearance of logic, but the logic is unfortunately spurious. This is because all the above theories are of a class known as fictionalist: that is to say, they are not theories about observations but theories about ideas. For example, the first theory, that schizophrenia is caused by a retrovirus, is based on ideas about the hereditary nature of schizophrenia as shown by population studies and the idea that entities such as retroviruses may be important in schizophrenia. There is so far no evidence for schizophrenic retroviruses. Similar caveats operate on statements (b) and (c).

Fictionalist theories are inevitable in conditions when the number of ideas outweigh reliable evidence, such as currently obtain in schizophrenia research. They have a certain validity as conceptual guides to difficult territories, and it is difficult to see how science can proceed without them. They cannot, however, be combined to make larger theories, as Dr Crow does here, any more than works of fiction can be logically combined. Their relationship is entirely arbitrary.

Dr Crow also asserts that the (only) problem with the theory as it now stands is its lack of clarity, which when overcome may enable it to become testable. There are grave doubts about this. The only way that the theories could become clearer is with the emergence of new evidence. But if the criteria for acceptance of a theory are, as for Dr Crow's, logical rather than empirical then new evidence will result in further fictionalist hypotheses by a process of false syllogism whereby two false premises are joined to a true (empirical) conclusion. For example, if empirical research established pathology X as an important covariant of schizophrenia, a new syllogism might arise thus: (a) schizophrenics have retroviruses; (b) retroviruses cause pathology X; thus (c) schizophrenics have pathology X. The conclusion is empirically true, but not the premises. Although the second premise may appear, in this case, more testable, it must be remembered that the number of new syllogisms are limitless in the face of advances in collateral fields. The original theory remains unfalsifiable.

From meiosis onwards, gene and environment are inseparably linked and to tease out one half of the process as if it were acting *in vacuo* is absurd. It is also potentially damaging, as it creates a false determinism, analogous to the 'nurture only' determinism of the 1960s, which may distort the way the patient is perceived and managed. Although I cannot ascribe this to Dr Crow, it is nevertheless likely to be a problem with theories such as these.

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This letter was shown to Dr Crow, who suggested that those interested should refer to the preceding correspondence and the relevant original papers.

SIR: There has been discussion (*Journal*, March 1988, **152,** 429–431) regarding the retrovirus-transposon model for the causation of psychosis. As Dr Crow suggests, one of the good points of the theory is that it is more precise than others, and hence generates testable predictions. Some consequences of the theory are considered here and are drawn from fairly early observations of the mechanisms of viral transformation of normal cells to neoplastic cells.