1993). The putative aetiopathological association of psychosis and multiple sclerosis (MS) is, however, difficult to discern from the multiple confounding factors: the variability of neurological presentation, the frequent existence of substantial cognitive impairment even at the early stages of MS, the use of steroids in treatment, and the marked psychological distress and psychosocial dysfunction which accompany MS.

We have studied the relationship of bipolar affective disorder to MS, and have described seven patients in whom mania appeared as the initial presentation of demyelination (Hutchinson *et al*, 1993). The mean age at onset of psychosis was 29.8 years (range 21–52), which is earlier than that of the patients described by Dr Feinstein *et al*. Affective symptoms antedated the emergence of neurological findings by just under two years in two patients and five years or more in the remaining patients. Subsequent psychotic episodes were unrelated temporally to neurological exacerbations or steroid treatment. A family history of affective illness was noted in only one patient. In contrast to the findings of Feinstein *et al*, we were unable to discern any distinct pattern of white matter lesions evident on magnetic resonance imaging (MRI). We agree with the assertion of Dr Feinstein *et al*, supported by earlier clinical and epidemiological research (Minden & Schiffer, 1990), that an aetiological association exists between the pathological process of MS and psychosis. Some recent findings may suggest a genetic basis to this association (Schiffer *et al*, 1988). The nature of relationship between psychosis and MS merits closer scrutiny both from a nosological perspective and with regard to the effective management of MS patients who exhibit psychotic symptoms.

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Adaptive behaviour scale in Down's syndrome

SIR: We are interested in two particular points in Collacott's article (*Journal*, November 1992, **161**, 675–679): the significant decline in Adaptive Behaviour Scale scores with advancing age in Down's syndrome, and the increased variance of the scores in the older age group.

We have been looking for some time at a possible association between raised mean cell volume (MCV) and cognitive decline in Down's syndrome, previously noted by Hewitt *et al* (1985), and have conducted a small local study to examine this idea further. Sixty-three Down's syndrome subjects from three hospitals were selected from an original group of 113, by excluding patients with known possible causes of macrocytosis (hypothyroidism, anaemia, B12/folate deficiency, and treatment with anticonvulsants). By means of a carer interview all patients were rated on a simple scale (available from the authors) designed to measure functional disability: ability to wash, dress, feed and toilet themselves, etc. The average disability score was then compared between those with normal MCV (less than 96 fl), and those with high MCV (greater than 97 fl). Within the two groups, scores were further divided into those less than 50 years, and those older.

Although the results did not reach significance, there was a trend towards higher MCV subjects being more disabled, this being most pronounced in the older group. The variance of disability scores was also greater for the older group, in keeping with Collacott's findings, and at least partially accounted for by the high/low MCV split. We have speculated in an article soon to be published in the *Journal* that the raised MCV found in Down's syndrome, and the premature appearance of dementia, may follow free radical stress, a process which is probably accelerated in Down's syndrome and which may also be relevant to ageing. It seems possible that from an early age some of these individuals are less able to handle the additional oxidative stress, and it is this group that show earliest intellectual deterioration. The extent of macrocytosis may help to identify these subjects before any measurable cognitive decline has occurred.

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Fluoxetine and suicidal behaviour

SIR: Power & Cowen (*Journal*, December 1992, **161,** 735–741) have performed a comprehensive overview of available data. However, it is of concern that they believe many clinicians are still disquietened despite the balance of evidence suggesting there is no association between fluoxetine and suicidal behaviour. The quote from an American psychiatrist merely highlights the media involvement and the fact that medical care in the USA may be compromised by threats of litigation.

Both the Committee on Safety of Medicines (CSM) and the Food and Drug Administration (FDA) have issued statements on fluoxetine. In September 1991 the FDA reviewed all the data and concluded that there was "no credible evidence" to link fluoxetine to suicidal or aggressive behaviour. A recent CSM Current Problems (1992) and a Manufacturing Chemists Association (MCA)/CSM paper (Price *et al*, 1992) also lend extra weight to this, stating "there is little to support the suggestion that fluoxetine induces suicidal or aggressive behaviour".

Drs Power and Cowen rightly concentrate on the scientific aspects of the controversy. They remark on the fact that development of suicidal ideation in patients taking antidepressants is not new. In the Damluji and Ferguson (1988) case studies two of four patients on desipramine who were subsequently switched to fluoxetine made a complete recovery with no recurrence of suicidal ideation.

The hypothesis of a rare idiosyncratic reaction, perhaps in the context of induced akathisia, is proposed. The data available to support this hypothesis are far from established. A recent paper by Baldessarini *et al* (1992) failed to show a dopamine-inhibiting effect of fluoxetine either with acute or repeated doses. The suggestion is also made that, of the selective serotonin (5-hydroxytryptamine, 5-HT) reuptake inhibitors (SSRIs), fluoxetine is most activating. Although data varies (and most work has been done at 40 mg) it is, in fact, not the case. Kerr & Hindmarch (1991), in their review of the cognitive and behavioural effects of the 5-HT reuptake inhibitors, conclude that these drugs are essentially neutral.

We will continue to be vigilant in our collection of safety data for fluoxetine. As the SSRIs in general become more commonly used, it may be that specific effects become more clearly delineated and clinicians will learn to manage these as they have those of the older tricyclic antidepressants which are arguably more toxic to patients.

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Periodic psychosis associated with the menstrual cycle and childbirth

SIR: I agree with Crammer (*Journal*, December 1992, **161,** 859) that the relationship between mental states and monthly cycles is complex, and add that a better understanding of this relationship may help untangle the biological basis of certain mental disorders. However, I am sorry that the relationship between the mental state and the menstrual cycle was not more convincing in my case report (*Journal*, September 1992, **161,** 402–404). The graph presents an accurate record of the timing of the patient's mental state and menses, as far as it is possible to demonstrate such things pictorially. As stated in the text, three of six psychotic episodes began in the week prior to menses, and two in the fortnight before.

Sometime after writing the report, my patient moved and was unfortunately lost to follow-up. It later transpired that she did not take any medication after losing contact. During this period she had a stable relationship and became pregnant, sustaining the longest period of good health that she had enjoyed for a number of years. Both she and her relatives were so struck by the disappearance of her regular relapses that they believed she was now free from her illness. After a full-term and uncomplicated delivery she returned home. However, three days later she disclosed to a midwife ideas about killing the baby. On the fourth post-partum day she was admitted to a local psychiatric unit, perplexed, anxious, and experiencing accusatory auditory