The authors state that all the patients with the postviral fatigue syndrome had characteristic mitochondrial changes, and some had RNA enteroviral sequences, but as the necessary investigations were not applied to the depressed patients or controls it is not possible to tell whether these findings did in fact distinguish the group with the syndrome.

Another issue that concerns us is that the authors fail to refer to the considerable body of work suggesting that release of prolactin mediated by 5-hydroxytryptamine is suppressed in depressed patients[3,4] and that this response is enhanced by antidepressant treatments, including electroconvulsive therapy.[5] There is a non-significant trend in their study for the depressed patients to have a smaller rise in prolactin secretion than controls, with the patients with the postviral fatigue syndrome having a significantly higher response than that of both the other groups. The finding that the prolactin response seems to be changed in opposite directions in the postviral fatigue syndrome and depression is of particular interest but makes it all the more frustrating that the clinical features of the two groups are not described more fully. Differences in neuroendocrine responses raise the possibility of subdividing poorly defined disease entities in a way that may better reflect underlying neuroendocrine disease, but to capitalise on this we need to know more about the correlations between these responses and individual symptoms.

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1 Bakheit AMO, Behan PO, Dinan TG, Gray CE, O'Keane V. Possible upregulation of hypothalamic 5-hydroxytryptamine receptors in patients with postviral fatigue syndrome. *BMJ* 1992;**304**:1010-2. (18 April.)
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AUTHOR'S REPLY,—In response to Simon Hatcher, all three groups in our study had baseline prolactin concentrations that did not differ significantly from each other. The high mean value in patients with the postviral fatigue syndrome did not represent odd high cases: this is a finding seen in several studies. The reason for suggested high baseline prolactin concentrations is unknown.

As J S Bevan will know, buspirone has more than one action. Some data suggest that it acts as a dopamine antagonist.[1] Clearly, further experiments, which are under way, are necessary for a complete understanding of its mechanisms.

David Curtis and Timothy Bullock raise many issues. We emphasise that 20-30% of our series of patients with the postviral fatigue syndrome have no depression whatsoever and complain predominantly of fatigue and myalgia. When depression occurs it differs clinically from severe endogenous depression in that the patients do not experience guilt or delusions, are well able to enjoy themselves, and have no loss of interest and, usually, normal libido. Though they may have depressed mood, more usually their severe emotional lability is to the fore and is often the conspicuous symptom.

For research purposes we select patients whose illness occurs after a well defined viral illness and in whom the myalgia is so severe that occasionally they have been referred for cardiologists if the pain resembles that of a myocardial infarct. This highlights muscle involvement. We did not carry out muscle biopsies on depressed patients because we believe that this would not be ethical. We are well aware of the decreased release of prolactin mediated by 5-hydroxytryptamine in major depression.[2] The many studies quoted in this paper confirm the decreased response and tend to support our conclusion. Depression and fatigue occur quite commonly in disorders such as idiopathic cyclic oedema, multiple sclerosis, and Parkinson's disease, but these disorders are not primarily depressive illness. The depression in the postviral fatigue syndrome is only one of its symptoms.

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EDITOR,—A M O Bakheit and colleagues recently reported[1] a possible upregulation of hypothalamic 5-hydroxytryptamine receptors in patients with the postviral fatigue syndrome, giving some evidence for hypothalamic functional abnormalities in these patients, which are different from others with depression. There is a growing body of evidence which claims that this clinical condition is organic and cannot be simply perceived as a somatisation disorder in patients with predisposition to psychiatric disease.[2]

We reviewed and quantitatively analysed with Ceretec and single photon emission tomography the brain perfusion of 14 patients fulfilling the Oxford criteria for diagnosis of myalgic encephalomyelitis.[3] They had all had disease for more than six months (more than half the time) manifested with generalised malaise and myalgia, as well as significant physical and intellectual disability. None had any medical condition known to produce fatigue or had recently or in the past had psychiatric disease.

When compared with a group of 24 non-depressed age and sex matched controls (normal volunteers) there was significant reduction of the perfusion to several areas of the brain cortex but particularly the brain stem (table). This original

Brain stem perfusion (mean (SD)) normalised to cerebellum and to visual cortex in 14 patients with myalgic encephalomyelitis and 24 controls

Normalisation area	Patients with myalgic encephalomyelitis	Controls
Cerebellum	0·74 (0·04)*	0·80 (0·04)
Visual cortex	0·75 (0·05)*	0·84 (0·05)

*$p<0·001$, Student's t test for independent samples.

finding confirms that single photon emission tomography with Ceretec is an important tool for investigating patients with myalgic encephalomyelitis, including the chronic fatigue syndrome and the postviral fatigue syndrome. This is the first observation of an organic component of this disease, with significant deficits in brain perfusion, particularly in the hypothalamus and pons.

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Managing tuberculosis and HIV infection

EDITOR,—The British Thoracic Society's guidelines on managing tuberculosis and HIV infection are incomplete and contain some points that clinicians who look after people infected with HIV with or without tuberculosis would take issue with.[1] Data that I and a colleague obtained in a retrospective study of nine patients with HIV infection (five English with BCG scars, three Africans and one Indian who had had BCG vaccination but did not have a scar) showed that previous BCG vaccination does not protect people with HIV infection from developing tuberculosis.[2] This should be another strong reason for not vaccinating such people, whatever their immune status. Normal chest radiographs in such people presenting with fever either with or without cough are well reported,[2,3] and induction of sputum with hypertonic saline in patients unable to produce sputum is an important aid to diagnosis apart from invasive procedures such as bronchoscopy with bronchoalveolar lavage and biopsy.

Clinicians should also bear in mind that ethambutol should be included in the initial treatment regimen if central nervous system disease or disseminated disease is present or resistance to isoniazid is suspected.[4] Lifelong chemoprophylaxis with isoniazid after completion of treatment is controversial and, on the basis of current evidence, should be judged on each patient's clinical circumstances. As tuberculosis can be one of the earliest infections to occur in the course of HIV infection,[5] such people should not be universally subjected to chemoprophylaxis with isoniazid throughout the time that they are still immunocompetent. Regular clinical monitoring may be more appropriate until more data are available as the guidelines acknowledge that reactions to antituberculous drugs are commoner in HIV positive people and desensitisation with steroid cover may be considered in difficult cases.[6]

Tuberculosis in people with HIV infection is an important public health issue in the United Kingdom as it is one of the few diseases that can be infectious to both HIV negative and HIV positive contacts and has a good outcome if treated appropriately.

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1 Subcommittee of the Joint Tuberculosis Committee of the British Thoracic Society. Guidelines on the management of tuberculosis and HIV infection in the United Kingdom. *BMJ* 1992;**304**:1231-3. (9 May.)
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EDITOR,—Effective surveillance of tuberculosis is required to monitor the effectiveness of the recent guidelines on the management of tuberculosis and HIV infection[1] and reassure those responsible for controlling infection that in the United Kingdom

the risk of an increase in tuberculosis related to HIV is small.[2]

An audit of cases of tuberculosis (April 1990-March 1991) in Riverside Health Authority showed two problems with the current surveillance of HIV infection and tuberculosis based on notification data. Firstly, tuberculosis in HIV infected people is less likely to be notified than that in other people. In our study only four (40%) of 10 dual infections were notified; in contrast, 50 (74%) of 68 cases of tuberculosis in people not known to be infected with HIV were notified. Furthermore, HIV positive patients given antituberculous treatment without bacteriological evidence being sought were even less likely to be notified (one (18%) of six).

Secondly, a rise in the number of cases of tuberculosis attributable to HIV infection may be masked by the high rates of, and changing trends in, notifications concerning people from the Indian subcontinent (India, Pakistan, Bangladesh)[3,4] owing to the similar age ranges of the two groups of patients (mean ages in our study were 41 and 42 years). Ethnic group and country of origin are not recorded on notifications.

Cooperation between the consultant in communicable disease, microbiologists, and clinicians has corrected the problem of differential reporting from Riverside, and we recommend that other health authorities audit their cases of tuberculosis to ensure that the surveillance data are unbiased. Moreover, to measure the extent of dual infection we have begun locally to record ethnic group and country of origin for all cases of tuberculosis and recommend that other centres with a high prevalence of HIV infection do likewise.

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AUTHOR'S REPLY,—E L C Ong is correct in saying that tuberculosis in people with HIV infection is an important public health issue in the United Kingdom as it is one of the few diseases that can be infectious to both HIV positive and HIV negative contacts and has a good outcome if treated appropriately. This was one of the main reasons for the Joint Tuberculosis Committee formulating the guidelines. The other reason was that the committee was increasingly being asked for advice on aspects of the interaction between tuberculosis and HIV infection. As is discussed in the guidelines, definitive advice on certain points was not available. In those cases the subcommittee, which included physicians regularly treating patients with tuberculosis and HIV infection, had to reach a balanced position on the evidence available when the guidelines were compiled late last year.

No detailed epidemiological study has reported whether BCG vaccination before HIV infection reduces the incidence of tuberculosis. Small studies of nine patients, such as that mentioned by Ong,[1] clearly do not have the power to answer this question. The recommendations for the treatment of tuberculosis in HIV infection follow the treatment guidelines issued previously by the Joint Tuberculosis Committee, which allow the addition of ethambutol if the clinician believes that there is a risk of resistance to isoniazid.[2] The earlier guidelines emphasised that the advice to continue prophylaxis with isoniazid indefinitely after the completion of standard treatment was based on current available evidence.[3] It was also pointed out that studies to determine what chemoprophylaxis should be given, for how long, and under what circumstances are being undertaken by the World Health Organisation.[4]

It is inevitable that some aspects of the guidelines can be criticised as a position had to be taken on certain points to which the answer is not yet known. The subcommittee considered that it was better to make recommendations based on the current evidence available than to avoid such points, which would have led to vague and weak guidelines. When the answers to those points are available revised updated guidelines can then be produced.

Matthew Hickman and colleagues are correct to emphasise the need to notify all cases of tuberculosis in patients with HIV infection. Notification of 74% cases in people suspected to be negative for HIV and of 40% of cases in HIV positive people clearly shows undernotification of tuberculosis generally and dual infection in particular. The Joint Tuberculosis Committee's guidelines clearly state that all cases of tuberculosis should be notified, and each district will have to ensure, as Riverside Health Authority has now done, that this is carried out so that contacts can be traced. Only by scrupulously notifying all cases of tuberculosis in HIV positive people can the impact of the interaction between tuberculosis and HIV infection in the United Kingdom be monitored.

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Ernest Saunders: diagnostic dilemma

EDITOR,—Three expert medical witnesses, called by the counsel to Ernest Saunders during the hearing of his appeal against conviction in April 1991, testified that he was suffering from Alzheimer's disease. From a review of newspaper reports of evidence heard on 24 April 1991 by the Appeal Court, the diagnosis of Alzheimer's disease was based on a degree of frontal atrophy on computed tomography, Mr Saunders's inability to repeat more than three numbers backwards, his mistaken identification of Gerald Ford rather than George Bush as the American president, and an occasion when he had wandered off in the wrong direction after leaving Dr Patrick Gallwey's consulting room.[1-4]

Dr George Perkin, a consultant neurologist called by the crown, told the court that there was no definite correlation between an abnormal brain scan and dementia and that he did not agree that Alzheimer's disease could be diagnosed in Mr Saunders's case without the results of further psychometric tests and longer assessment. Dr Perkin considered depression, rather than dementia, to be responsible for Mr Saunders's symptoms. The diagnosis of Alzheimer's disease was accepted by the Appeal Court judges and Mr Saunders's sentence reduced.

It now seems that the diagnosis of Alzheimer's disease was certainly incorrect. Dr Gallwey had treated Mr Saunders for depression between February and November 1988, and the observed cognitive deficits were probably related to a depression as Dr Perkin suggested at the appeal. Atrophy on computed tomography may be seen in depression in late and middle life[5] and is in no way diagnostic of Alzheimer's disease.

We are concerned that what may have been recently portrayed in the press as an unprecedented spontaneous recovery from Alzheimer's disease may damage the credibility of members of our profession who give evidence in cases in which those involved have genuine Alzheimer's disease or other dementias. This case and its aftermath draw attention to the difficulties of making a clinical diagnosis of Alzheimer's disease. These are now well recognised, in that research on patients with the disease necessitates the use of internationally agreed diagnostic criteria.[6] Though use of such criteria may not always be appropriate in routine or, indeed, forensic clinical assessment, we believe that, when a clinical diagnosis of Alzheimer's disease needs to be made with authority, it should surely be supported by recognised neuropsychological tests.

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Time to abolish "gold standard"

EDITOR,—A few years ago at a clinical discussion on the usefulness or otherwise of the newly described fructosamine assay in the regular management of diabetic patients[1] someone stated that "the gold standard in detecting early complications in diabetics was the measurement of cell membrane thickness in a muscle biopsy sample by electron microscopy." I was taken aback—not by the impracticability of the proposed test but by the phrase "gold standard."

As a practising biochemist for nearly 40 years I had never heard these words used to describe any biological test. Because the subject is in a state of perpetual evolution gold standards are, by definition almost, never reached. Instead, as progress is made conclusions may be drawn with an increasing degree of confidence. Even Jeffreys *et al* in their milestone paper on how the uniqueness of our genetic fingerprint may be shown (odds of up to 10^{19} against duplication) never used the term.[2] How, therefore, can its application to often quite complex clinical procedures be justified? In these matters complexity is the antithesis of certainty.

From the initial incident described above I became alerted to this presumptuous appellation, and in my general reading of the medical literature I have noted a steady increase in its use. This subjective impression has been confirmed by a