Letters to the Editor

Immune responsiveness in chronic fatigue syndrome

Sir,

The paper by Milton and colleagues¹ challenges the hypothesis that patients with postviral fatigue syndrome (myalgic encephalomyelitis) have a persisting viral infection along with consequent immune dysregulation. The protocol employed in the study suggests that their conclusions may not be valid.

Firstly, the 31 patients were selected from a group attending a 'muscle clinic' who complained of 'unexplained chronic fatigue'. Of these only 15 had a clear history of a precipitating viral illness – a key diagnostic feature of postviral fatigue syndrome. Secondly, although other research groups have also demonstrated that raised levels of Coxsackie B virus IgG and IgM antibodies are not diagnostic of the syndrome,² these findings cannot be used to exclude the possibility of persisting viral infection within either muscle or the central nervous system.

As far as muscle is concerned, Gow and colleagues³ have recently detected enteroviral RNA sequences in muscle biopsies of 53% of patients with a well-defined postviral fatigue syndrome compared to 15% in a control group, and Archard *et al.*⁴ have shown that this persisting enterovirus is poorly replicating.

Demonstrating the presence of persisting virus within the central nervous system is obviously far more difficult without autopsy material. However, Daugherty *et al.*⁵ in America have published the results of MRI scans and cognitive function tests on 20 patients (with age and sex matched healthy controls) showing abnormalities consistent with an organic brain syndrome similar to that seen in patients who are positive for human immunodeficiency virus.

Thirdly, a large number of papers have been published in the UK, America and Australia documenting laboratory evidence of various changes in immune regulation. The differences in results may well be related to variable factors such as duration and severity of the illness as well as age of the patients. If there is any consensus it appears to be in the area of abnormalities within natural killer lymphocyte subsets where researchers on both sides of the Atlantic have come to similar conclusions.⁶

I would accept that chronic fatigue syndrome is a perfectly acceptable umbrella term to cover a wide heterogeneous group of patients suffering from persisting fatigue – an extremely common symptom in primary care. However, if conclusions are to be drawn about the virology, immunology and neuromuscular pathology of a particular subgroup, that is, those with postviral fatigue or myalgic encephalomyelitis, then researchers must adhere to the guidelines laid down at Oxford⁷ which the authors refer to but have not followed. These state very clearly that post-infectious patients do form a distinct subgroup, and that to fulfil research criteria there must be 'definite evidence of infection at onset or presentation'.

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We have shown this letter to Drs Milton, Edwards and Clements, who reply as follows:

Thank you for giving us an opportunity to comment on the points raised in Dr Shepherd's letter.

First, we have investigated patients in the broad category of chronic fatigue syndrome, not those classified under the sub-heading postviral fatigue syndrome.¹ We think this is reasonable since there is no obvious clinical difference between those patients with and without evidence of an episode of viral infection as an initiating feature of their chronic fatigue. Of course those patients with such a viral onset should also be investigated as a separate group, but with patients of long duration of fatigue it is often difficult to ascertain accurately whether there was any preceding viral infection.

Second, the evidence provided by the finding of enteroviral RNA in the muscle of more patients than controls is indeed suggestive of a persistent viral infection, but as it is not known whether the presence of viral RNA in the cells alters their metabolism,² the significance of this finding is as yet unknown. Our point in this regard is that we find no altered cellular immune responsiveness to enteroviruses in our patients. We do make the point in discussion that the small number of patients who had increased circulating immune complexes came mostly from those patients who had an indication of a viral origin of their fatigue.

Third, regarding immune regulation, of which there are various contradictory reports, the possible involvement of natural killer cells awaits an elucidation of the function, if any, of the various sub-sets thereof in viral containment.³

In summary, we would restate that we find no indication, in the limited number of parameters we have investigated, of persistent viral infection or altered immune regulation in patients with chronic fatigue syndrome, though we provide no hard evidence against it.

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Myotonia dystrophica – first presentation as severe left ventricular failure complicating dilated cardiomyopathy

Sir,

Myotonia dystrophica is an autosomal dominant multi-system disorder which in adults affects the specialized cardiac conduction tissue frequently, but the myocardium itself only rarely clinically,¹ although electron microscopic studies show early myocardial involvement.² Cardiomyopathy has been described,^{3,4} but we are unaware of reports of first presentation of myotonic dystrophy with dilated cardiomyopathy and left ventricular failure.

A previously well, 30 year old infertile man presented with breathlessness at rest and paroxysmal nocturnal dyspnoea. There was no significant family or drug history. He was orthopnoeic and hypotensive (blood pressure 90/70 mmHg) with a raised jugular venous pressure. His pulse was 112/min and regular. There was a prominent left ventricular third heart sound, accentuated pulmonary second sound and a soft systolic murmur in the mitral area. He was also noted to have frontal baldness, drooping eyelids, wasting of the masseters, myotonia, small firm testes, and lenticular opacities on slit lamp examination. There was no significant muscle weakness.

Electrocardiography showed a sinus tachycardia, complete left bundle branch block and left anterior hemiblock. Chest X-ray confirmed left ventricular failure. Echocardiography revealed a moderately dilated left ventricle, hypokinesia of the interventricular septum and left ventricular posterior wall, E point septal separation of 25 mm and a reduced aortic valve opening of 1.2 cm. These parameters were suggestive of moderate to severe left ventricular dysfunction complicating dilated cardiomyopathy.

Dilated cardiomyopathy is rare in adults with myotonia dystrophica. Why this should be so is unknown, as cardiac conduction tissue, which is commonly involved, both sub-clinically and clinically, has a close embryologic

link with cardiac muscle. Perhaps the susceptibility of the myocardium to the biochemical defect affecting conduction tissue is determined by hitherto unknown genetic or environmental risk factors. It is also uncommon for patients with myotonic dystrophy to present with severe left ventricular failure as our patient did. Cardiac muscle involvement is commonly occult throughout life and there is no consistent correlation with skeletal muscle involvement.¹ Electrocardiological and electrophysiological studies show abnormal sinus node function in about 20% and His-Purkinje disease in 80% of patients.¹ Isolated left bundle branch block and left anterior hemiblock may occur in 13–24% of patients.⁵ But it is rare for a combination of left anterior hemiblock and complete left bundle branch block to occur in the same patient. This may have been a marker of severe cardiac muscle involvement.

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Intussusception in ileostomy in a pregnant woman

Sir,

Intussusception in stomata is rare^{1–3} and only two cases have been reported previously in the literature reviewed since 1950.^{4,5} A case of intussusception of ileostomy in a woman pregnant with twins is presented and its mechanism described.

A 31 year old woman with ileostomy presented with 'prolapse' of her stoma, associated with colicky abdominal pain. She was 21 weeks pregnant with twins. Abdominal examination showed a uterus compatible with her date of pregnancy, multiple scars, no area of tenderness and normal bowel sounds. Her haematological investigations were within normal limits.