Chronic unexplained fatigue

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"A riddle wrapped in a mystery inside an enigma"

After more than two years' gestation, an independent working group, set up by the previous Chief Medical Officer for England, published its final report on the subject of chronic fatigue syndrome (CFS) in January of this year.¹ This is a topical subject in the English speaking world as two other management reports have been published in the last six months, by the US government and the Australasian Royal College of Physicians.^{2,3} The Canadians are also close to a final draft of their own report. This has occurred at the same time as the release of two independent systematic reviews of management. Remarkably the two teams from Texas (USA) and York (UK) reached such similar conclusions that they combined their findings into the one paper.⁴ The York group has just published their own guidance based on their systematic review.⁵

So, has the mystery of myalgic encephalomyelitis (ME) been resolved? Is everyone agreed on how to manage the enigma of patients presenting with chronic unexplained fatigue? Have we finally solved the riddle of CFS?

On first reading of the management guidelines, the answers seem to be a qualified "yes". All are agreed that CFS and ME are essentially synonymous. All agreed that CFS is a discrete illness, although they further suggested that CFS is either an umbrella term for several different disorders, or that the aetiology is multifactorial. Both the Australasian and English management reports suggested that there are three management options that are worth consideration. These are cognitive behaviour therapy, graded exercise therapy, and "pacing". All agreed that patients have not been well served by the medical profession and that a mutually respectful doctor-patient relationship is essential for optimal care.

So far so good. Closer reading of the reports and awareness of the politics surrounding them qualifies the optimism and spreads some doubt. Five clinicians and two patients resigned just before publication of the English report,⁶ being unable to endorse it. There was a five year delay and much controversy between publication of the Australasian draft report in 1997 and this year's final report.³ There were three main reasons

for the politics and polemic. Firstly, some clinicians were keen on a more biopsychosocial approach to both assessment and treatment, whereas others wanted a more biomedical approach emphasised. Secondly, some clinicians could not agree to recommend "pacing" on the basis of patient group experience alone, without any research evidence of efficacy.⁶ Both systematic reviews concluded that cognitive behaviour therapy and graded exercise therapy were the only two treatments to show promise.^{2,4} Thirdly, some clinicians believed that the reports over-emphasised the severity and chronicity of CFS to the extent of suggesting that recovery was unlikely, when the evidence shows that not to be true.⁷ Other criticisms of the English report include its over-reliance on anecdotal evidence,⁸ and the dangers of both over-medicalisation of chronic fatigue⁹ and the iatrogenic damage consequent upon that.¹⁰

The mystery of CFS deepens if one examines the validity of current definitions of the illness. None of the three current definitions are based on empirical data.¹¹⁻¹³ Fortunately, two large surveys of secondary and tertiary care fatigue clinic patients (one of which was international) seem to delineate two separate syndromes.^{14,15} The first and most common resembles past descriptions of neurasthenia with prominent physical and mental fatigue, exacerbated by minor exertion, and not relieved by rest. Sleep disturbance, muscle aches, and concentration problems are also common. This syndrome is similar to the fatigue syndrome empirically derived from patients recovering from glandular fever.¹⁶ The only substantial difference is the excessive sleep noted after glandular fever, compared to the disturbed sleep noted in those patients with a longer duration of illness. Fatigue syndromes probably vary in both form and aetiology according to duration.¹⁷ The second syndrome, suffered by a quarter of fatigue clinic patients, is similar to a chronic somatisation disorder, with multiple symptoms, greater disability, and more comorbid mood disorders.^{14,15} Unsurprisingly, the latter patients have the worse outcome.¹⁸

What of the riddle of aetiology? Like many disorders in medicine, aetiological factors in CFS are best categorised into

predisposing, precipitating, and perpetuating factors. Predisposing factors are not well established, but being female and relatively young are the most reliable findings.^{1,2,3} Certain infections, such as Epstein-Barr virus, can precipitate CFS,¹⁹ but there is no good evidence of abnormal viral persistence. Perpetuating factors may include excessive inactivity, certain illness beliefs, mood and sleep disorders. Immune and endocrine abnormalities are either inconsistent or of uncertain pathophysiology.^{1,2} Social factors not mentioned in these reports, but found by others, include membership of a self help group and being in receipt of financial benefits.

How can patients with CFS be helped to get better? The systematic reviews are quite clear that the only currently available treatments with good quality evidence of efficacy are cognitive behaviour therapy and graded exercise therapy. In contrast, the committee reports on management were more cautious, highlighting the "potential for harm" of these treatments.¹ The English report's recommendation omitted any suggestion that cognitive behaviour therapy and graded exercise therapy should be more readily available; something that would have been helpful since the unavailability of these treatments is the real issue in this country. The Australasian guidelines were a little less cautious, recommending that "...rehabilitative, behavioural and cognitive approaches should be an integral component of managing people with CFS."

These recommendations were obfuscated by equally promoting "pacing", in spite of the lack of research evidence for its efficacy.⁴ "Pacing" is poorly defined in the literature. In the USA, pacing is based on the "envelope" model of CFS in which energy is perceived as having a fixed level, which should not be exceeded, so patients are discouraged from exceeding their "daily available or perceived energy".²⁰ The English report adapted this model, depending on which "phase" ("acute, stabilisation/transition, and recovery") of the illness a patient is in. According to this report, pacing involves establishing a baseline level of activity, followed by "gradual stepwise increases in activity". This is adapted if "setbacks" occur. The Australian report uses a similar approach but warns that activities must be "...scheduled to stop before they produce a significant exacerbation of symptoms". The one clear difference between pacing and the more active cognitive behaviour therapy and graded exercise therapy is that activity levels are limited by symptoms in pacing, whereas in cognitive behaviour therapy and graded exercise therapy increased symptoms are an expected part of the recovery and regarded as a sign of

active adaptation. The theoretical risk of pacing is that the patient remains trapped by their symptoms in the envelope of ill health. A study that compares these different approaches is overdue.

What can the working clinician conclude from this flurry of reports and guidance of such mixed provenance? CFS probably does exist, but it may be an umbrella term for several disorders. Misdiagnosis is common, with the most likely differential diagnoses being mood and sleep disorders. We do not understand its aetiology, but it is probably multifactorial and both biological and psychosocial factors are likely to be important. Although there is no certain cure for the disorder, active rehabilitation therapies that include a gradual and mutually agreed return to normal activities help the majority of patients. Mood and sleep disorders may also need attention. The role of the doctors in either encouraging or delaying recovery should not be underestimated. Some patients will make a full recovery. Some of those who do not improve may have either a mood disorder or chronic somatisation disorder; the latter being even more of a riddle than CFS itself.

CONFLICT OF INTEREST

Dr White was one of the clinicians who resigned from the English report on CFS/ME.

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