To exercise or not to exercise in chronic fatigue syndrome?
No longer a question

Graded physical exercise is no panacea, but is beneficial

Much remains unknown about the enigmatic clinical disorder chronic fatigue syndrome (CFS). Apart from clear evidence implicating certain infections as a trigger, and reproducible evidence of increased rates of comorbid depression, the aetiology remains obscure.1 Similarly, despite numerous tantalising hypotheses of pathogenesis, including immunological, neuroendocrine and metabolic disturbances, all remain unproven.1 On the positive side, the criteria for diagnosis are well accepted internationally,2 and have been the subject of recent refinements to improve reliability.3 The disorder is well recognised, and about 0.5% of patients attending general practice are identified as having CFS.4 What, then, of treatment for a disorder with so many unknowns?

About 40 controlled trials of treatment interventions for patients with CFS have been published to date.1,5 The most striking features of these studies are, firstly, that no curative treatment has been found, and secondly, there has been a remarkable lack of benefit demonstrated from any of the broad array of antiviral, immunological, hormonal, antidepressant and other treatments evaluated. The sole exception lies in the relief of symptoms and improvement in functional capacity provided by programs incorporating graded physical exercise.

Several studies have incorporated physical exercise as a component of cognitive–behavioural therapy (CBT). The CBT approach in treatment for patients with CFS is based upon the premise that cognitive attributions and behavioural patterns act as perpetuating factors for symptoms. In particular, given that the cardinal phenomenon of fatigue in CFS is characterised by a marked and prolonged exacerbation of symptoms following minor physical activity, patients may reach the conclusion that it is best to avoid exercise. Thus, patients may develop an understandable cognitive attribution that exercise is harmful in the short term (as symptoms worsen) and detrimental in the longer term. This leads to altered behaviour in the form of reduced physical activity with consequent deconditioning. Similarly, as sleep typically takes on a characteristic unrefreshing quality, and fatigue is dominant in the symptom complex, patients may consider that increased sleep holds promise for symptom relief and for rapid recovery. This attribution commonly leads to a behavioural pattern of phase-shifted sleep (late night to late morning) and frequent daytime naps. Accordingly, the CBT approach generally seeks to alter these cognitive attributions and modify the associated behavioural patterns.

Having established CBT as a beneficial treatment approach, subsequent studies have sought to identify the “active” components of the CBT package. In this regard, graded physical exercise therapy has been found in several studies to be significantly better than comparators such as relaxation therapy, notably in reducing symptom severity and gaining improved function.6–8 In particular, Fulcher and...
White\textsuperscript{6} reported that 16 of the 29 patients who completed exercise treatment rated themselves as “much” or “very much” better, compared with eight of the 30 patients in the “flexibility” control group. Similarly, Powell et al\textsuperscript{7} found that 84\% of a selected patient group had significantly improved functional capacity and reduced fatigue 12 months after graded exercise therapy when compared with standard medical care.

The report by Wallman et al (page 444) adds to this evidence with a systematic and well-controlled evaluation of graded exercise versus relaxation over 12 weeks.\textsuperscript{9} Importantly, these authors have incorporated the notion of “pacing” into the exercise program. This concept recognises that individual patients with CFS differ significantly from each other in the amount of physical activity they can achieve before symptoms become exacerbated. In addition, this “threshold” beyond which symptoms worsen may vary over time. Hence, the graded exercise program allowed patients who experienced worsened symptoms to temporarily reduce exercise duration and then to resume once symptoms subsided. Their findings are noteworthy in that multiple parameters of exercise performance, such as resting systolic blood pressure and work capacity, were improved in the active group, indicating that the reconditioning component of the program was indeed effective. In addition, measures of mood and cognitive performance also showed improvement. Interestingly, the proportion of patients who rated themselves as significantly better was not different in the two groups. Unfortunately, no commonly used measure of disability (such as the SF-36)\textsuperscript{10} was included as a primary outcome measure, as would be typical in studies of chronic medical illness. In addition, the durability of the effects was not examined after the completion of the intervention. Finally, although “pacing” was an important component of the exercise intervention, this approach was not formally evaluated against “unpaced” exercise.

Nevertheless, one can safely conclude from these studies that graded physical exercise should become a cornerstone of the management approach for patients with CFS. When applied astutely, including via “pacing”, it may not be realistic to anticipate cure, but it is realistic to expect that patients will feel better and will improve their functional capacity. In combination with appropriate interventions to improve sleep hygiene and to treat any comorbid mood disturbance,\textsuperscript{11} patients with CFS managed in this way often achieve a substantially better quality of life while awaiting recovery.

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\textbf{In diagnosis and prognosis, we should avoid intuitive “guesstimates” and seek a validated numerical aid}

\textbf{One of the axioms} of clinical practice is that, in medicine, there are few, if any, certainties. When assessing the likelihood of a specific disease in a particular patient, or the chance of a future adverse event in a patient with known disease, clinicians are estimating probabilities or risk. These estimates derive from a clinical gestalt — the process of interpreting findings from history, examination and simple investigations (diagnosis), or of disease-specific correlates of complications or death (prognosis).

Clinicians use these estimates of probability or risk to decide whether they should intervene immediately, particularly if effective treatments are available. Alternatively, if the disease likelihood is low, or treatments toxic or only marginally effective, these estimates are used to decide whether to defer treatment and either observe expectantly or conduct more sophisticated tests whose results may substantially alter pre-test likelihood estimates.\textsuperscript{1} If the estimate is too high, patients may incur unnecessary treatments or confirmatory investigations, or, if the estimate is too low, they may suffer the consequences of delayed intervention.

Thus, a fair bit is riding on how accurately we can judge the likelihood of current or future disease. Available research suggests that, for various reasons, we are not that good at it.\textsuperscript{2-4} Common pitfalls include:

- framing a clinical problem in a way that may exaggerate risk;
- overweighting or underweighting certain clinical features;