

LETTERS TO THE EDITOR

CHRONIC FATIGUE SYNDROME

Sir,

We read with interest the special report by Nijs et al. (1), entitled "Chronic fatigue syndrome: an approach combining self-management with graded exercise to avoid exacerbations". The paper proposes to provide an integrated model for graded exercise therapy (GET) in patients with chronic fatigue syndrome (CFS).

The authors state that current GET programmes for people with CFS exacerbate symptoms. This is a familiar and mistaken criticism of GET, often quoted from the 2001 Action for myalgic encephalomyelitis (ME) (AfME) survey, which reported that 50% of patients with CFS/ME who received graded exercise felt worse (2). A follow-up survey reported that, in many cases, exercise was being undertaken independently, without the supervision of a therapist trained to deliver GET to patients with CFS (3). In other words, it was not GET.

GET programmes have developed considerably in the last few years and recent guidelines that aid therapists in their delivery of GET to patients with CFS have been published by the National Institute of Clinical Excellence (NICE) in the UK (4). These guidelines are based on current practice and the evidence from 5 high-quality randomized controlled trials, which report reduced symptoms and improved physical functioning following GET in patients with CFS, with few adverse events or treatment drop-outs (5).

Current GET programmes are designed so as not to exacerbate symptoms in patients with CFS, and there is no scientific evidence that properly delivered GET causes harm in this group. One of the fundamental components of GET is that it is delivered by an appropriately clinically supervised GET therapist with training and experience in CFS/ME (4). Current levels of activity are determined at the start of treatment and a level of activity that does not exacerbate symptoms is set as a baseline. Exercise and activity are then gradually increased, first in duration and then intensity, designed to meet goals agreed by the patient. The aim of setting a baseline of activity is that it is possible to undertake it even on a "bad" day, to avoid exacerbations in symptoms and the "boom and bust" pattern characteristic of some patients with CFS/ME. It is recommended that duration is increased by less than 20% at any increment up to 30 min per day and then intensity is increased by 10–20% at any increment.

If CFS/ME symptoms are exacerbated, current activity level is reviewed, and no increase is prescribed. If necessary, the baseline is re-established, and if it has had to be reduced, for example, due to an incidental infection, a gradual return to previous exercise and functional routines is encouraged. However, a central concept of GET is that patients maintain their level of exercise as much as possible even after a CFS/ME setback. This is to reduce the many negative consequences of rest and allow the body to habituate to the increase in activity.

GET therapists provide treatment based on the rationale that physical deconditioning, exercise intolerance and avoidance caused by relative inactivity are reversed by gradually and carefully re-introducing regular physical activity, aiming to return a patient to normal health and ability. Physical deconditioning is characterized by both reduced muscle strength and aerobic capacity, which can occur in the most inactive patients. Apart from improvements in CFS and function, a major objective of GET is that patients will eventually be able to undertake the amount of exercise recommended for full health and prevention of disease. The quantity of exercise recommended by the Chief Medical Officer in the UK is 30 min of moderate intensity physical activity at least 5 times a week (6). Regular exercise prevents various diseases, such as cardiovascular disease and type 2 diabetes, reducing premature death by 20–30% and having a positive effect on psychological wellbeing, sleep and the maintenance of a healthy musculoskeletal system.

There is no evidence that GET damages the immune system. Endurance exercise induces a cytokine response in healthy people, but this is at a significantly higher and more prolonged level of exercise than that undertaken by patients with CFS (7, 8). Five studies have examined the effect of acute exercise (not GET) on immune measures in CFS, but these have measured a number of different markers and shown inconsistent findings (9–13). More research is required to investigate the immune response to exercise in CFS patients (and we are currently undertaking such a study), and then to investigate the relationship between the immune markers and GET. It may be that as people become reconditioned their immune system improves, rather than the reverse, as Nijs et al. (1) suggest.

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RESPONSE TO LETTER TO THE EDITOR BY LUCY V. CLARK AND PETER D. WHITE

Prevention of symptom exacerbations in chronic fatigue syndrome

We would like to thank Dr Clark and Professor White for their special interest in our integrated model for rehabilitation of those with chronic fatigue syndrome (CFS), as recently presented in this journal (1). We are pleased with their comments and with the opportunity provided by the journal to respond to their Letter to the Editor.

Clark & White challenge that exercise therapy can worsen the health status of patients with CFS and, on the other hand, explain in detail how their approach to graded exercise therapy for CFS prevents worsening of symptoms. They state that “a level of activity that does not exacerbate symptoms is set as a baseline” and “a baseline is set to avoid exacerbations in symptoms and the ‘boom and bust’ pattern characteristic of some patients with CFS”. They even explain what to do “if CFS symptoms are exacerbated”. By doing so, they acknowledge the possibility that exercise therapy can very easily worsen the health status of patients with CFS. From the way they explain their current approach of graded exercise therapy (GET) in CFS, it appears that they are making great efforts to avoid exacerbations in their patients. Avoiding exacerbations in response to exercise therapy was the main message of our special report, as evidenced by the title. England is fortunate to have specialized centres for the treatment of CFS; however, this is not the case worldwide. Many clinicians are treating patients with CFS as part of a mixed caseload of patients. These clinicians often struggle with their early attempts to apply exercise programmes to people with CFS, and our integrated approach combining self-management with graded exercise was intended to provide such clinicians with both a theoretical and practical framework to overcome this issue.

As explained in our special report, it is clear that there is no evidence that GET programmes, on average, cause harm

to CFS patients (2). However, it would not be fair to neglect the possibility that during the course of a GET programme, CFS patients are likely to experience an acute symptom exacerbation. To quote our own paper: “initial success of exercise therapy in CFS is most likely due to the realization by sufferers that exercise can be undertaken safely without the consequence of relapse” (1). Hence the importance of self-management (pacing) prior to, and incorporated in, exercise interventions for CFS (3).

For these reasons we feel that the views of Clark & White expressed in their letter and the content of our manuscript are generally in agreement. We concur with their notion that exercise therapies for CFS have developed considerably in the last few years, and they are now much more in line with both the biological and psychological impairments seen in those with CFS.

Clark & White challenge our view that too vigorous exercise has detrimental effects on the immune system. They state that the studies examining the interactions between the immune system and exercise have yielded inconsistent findings. Is this true, or could it be that the various studies have each focused on different immune markers? No 2 studies in CFS have examined similar immune markers and their response to exercise, implicating that it is not possible to generate *inconsistent* findings. Clark & White further indicate that 5 studies have examined the effect of acute exercise on immune measures in CFS, but overlooked at least 2 studies (4, 5). One of these showed that increased oxidative stress in response to exercise is related to an increase in pain post-exercise (4). However, it should be noted that none of these studies have examined the effects of GET on the immune system in CFS, and that further controlled studies examining the acute effects of exercise on immune measures are required.

The immune system is an extremely sophisticated and complex grouping of cellular and humoral mechanisms, each of which can be assessed by a large number of markers. It seems plausible that too-vigorous exercise affects a number of these mechanisms, at the same time leaving many others unaffected. We support the notion of Clark & White that appropriately paced exercise in CFS might benefit certain aspects of the immune system, and applaud their ongoing research efforts to examine this further. One aspect of resting cellular immune function (i.e. the dysfunctioning of the 2.5A synthetase RNase L pathway) has repeatedly been shown to predict exercise (in)capacity in CFS patients (6, 7). These studies were conducted independently of each other and in different continents (American and European CFS patients). We are currently examining whether exercise influences intracellular immunity in CFS, and whether acute symptom changes following exercise are related to intracellular immune dysfunctions.

We feel that the debate addressing rehabilitation of patients with CFS progresses towards an international consensus, and that efforts have been made to tailor conservative interventions to address the biological and psychological impairments seen in this underestimated illness.

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