

CORRESPONDENCE

Functional somatic syndromes

Sir—In their review of functional somatic syndromes, Simon Wessely and colleagues (Sept. 11, p 936)¹ include chronic fatigue syndrome (CFS) in a list of overlapping conditions and propose that they be classified together for treatment by a general physician aided by liaison with psychiatrists. They omit to mention that CFS is already itself a term combining the neurological condition formerly known as atypical polio (subsequently named myalgic encephalomyelitis) with other fatigue-inducing conditions.²

This global approach has already led to court cases after unsuitable and damaging treatment was given to children who found themselves in subgroups of CFS² but who were all treated with the same psychiatric approach. I am disappointed that Wessely and colleagues could aggravate a situation that the Chief Medical Officer's working group on CFS and myalgic encephalomyelitis was set up to resolve, before the working group had completed its work.

It is odd that in 1999 CFS should be listed as a functional somatic syndrome at all, since, although its cause may be unclear at present, so many physical abnormalities can be diagnosed by brain imaging and other tests (data available from the Young Action Online website, <http://www.jafc.demon.co.uk/yaonline/does/brain.htm>, accessed Nov 10, 1999). I note that Gulf war syndrome is conspicuous by its absence from this list, whereas in previous years it would not have been.

One of the psychiatrists who labelled the 1955 Royal Free Hospital epidemic of myalgic encephalomyelitis as mass hysteria went on to label an epidemic of winter vomiting disease in another institution as mass hysteria. The cause is now known to be the Norwalk virus which can be seen by electronmicroscopy of patients' discharge-fluid samples, but which cannot yet be grown in culture.

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¹ Wessely S, Nimmuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; 354: 936-39.

² Report from the National Task Force on CFS/PVFS/ME. Bristol: Westcare, September, 1994.

Sir—Are Simon Wessely and colleagues¹ really suggesting that we would be better off classifying chronic fatigue syndrome with tension headaches and premenstrual syndrome, alongside non-cardiac chest pain? Do they honestly believe that the differences between these conditions are of no clinical significance?

Medicine is a science, and science demands precision. Grouping patients because they have much in common or because we do not yet understand the cause of their conditions is not what we expect from well-trained medical specialists.

Wessely and colleagues suggest that acceptance of these disorders as "distinct syndromes" is of limited value, and that keeping them separate adds a "spurious complexity", which undermines understanding and management. If we focus on shared characteristics, they suggest that we can reject the subspecialist with their "idiosyncratic approach" in favour of a broad-based programme.

If we apply Wessely and colleagues' reasoning, we should stop differentiating between breast, pancreatic, liver, prostate, and colon cancer. For instance, they all have at least one thing in common (malignant disease), patients with one form of the disease may develop another, and most patients respond to the same treatments.

And how should we be treating these adult cancer syndromes? Would we prescribe the same regimen for every patient? Of course not. We do not even treat breast cancers in the same way. In fact, we don't gloss over the differences and rely on general physicians. We study any anomalies and value the expertise of the subspecialists. Even if the similarities outnumber the differences, that is no reason to ignore them.

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¹ Wessely S, Nimmuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; 354: 936-39.

Authors' reply

Sir—We have questioned the orthodoxy of considering the large number of medically unexplained or so-called functional syndromes such as CFS and irritable bowel syndrome as separate entities. We have reviewed the evidence suggesting important similarities between these conditions, and we have suggested that, pending more information from research, there is merit in a multidimensional classification based on clinical features and known pathophysiology rather than on presenting symptoms.

Jane Colby takes issue with our thesis, arguing that CFS in general and myalgic encephalitis in particular is not functional and implies that medical rather than psychiatric management is required. Patients with CFS represent only a small number of patients who present with somatic symptoms for which no disease process has been identified and the associated philosophical, moral, and management issues are not unique to this syndrome. Many of these patients have identifiable physiological and psychological disturbances that may underlie their symptoms. Although we welcome research that increases our understanding of these aetiological factors we believe that classification and management should be based on current best evidence rather than on prejudice or belief, especially for vulnerable persons such as children.

Although it is far from their intention, we feel that Ellen Goudsmit and Charles Shepherd actually support our thesis. We agree with them that medical science benefits from appropriate identification of pathologically and clinically valid subgroups of patients. We argue that the classification of functional syndromes is not supported by evidence and therefore stands in the way of the development of a more valid approach. Do they really think that patients with cancer should be studied and managed according to their presentation and type? Do they not agree that there have been advantages in basic research that acknowledges the common biological process underlying all cancers? Do they

not also agree that there have been benefits from the setting up cancer centres for cancers of all types where knowledge and resources can be pooled?

Underlying these criticisms of our thesis is an understandable desire for pathology-based diagnosis and appropriately targeted medical treatment. We have sympathy with this wish. However, we argue that at present both science and patients are best served by an approach based on good evidence rather than merely type of presentation, tradition, or belief; that does not mean that patients should not be subclassified. Indeed we suggest that a more evidence-based classification should be a major goal for research into these important but neglected illnesses.

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Sir—As general practitioners at the sharp end of the patients' presentation of functional somatic symptoms we have tried over the years to make sense of just the dilemma that Simon Wessely and colleagues posed.¹ We agree that the existence of specific somatic syndromes is largely an artifact of medical specialisation. In the UK general practitioners have responsibility for the initial diagnosis and management of undifferentiated presentations, and usually know the patients' situations within the family and community. We do agree with Wessely and colleagues' conclusions, on the basis of working with models drawn from earlier pioneer general practitioners and physicians who looked at the whole person, and saw the individual within the context of their environment and their interaction with it.

This advance from the biomedical system approach towards the biopsychosocial lends itself to a model described by Nixon and King.² Here, a performance-arousal curve is used to suggest that increments in arousal can lead the person to a peak of performance after which he becomes exhausted and develops downslope disorders of function created by impairment of homeostatic control. These disorders include many examples of somatic dysfunction commonly aggravated by chronic hyperventilation. The patient can be taught to recognise his position on the curve and adopt a strategy for restoration. This strategy, known as SABRES, incorporates the need for sleeping adequately, reducing

arousal, overcoming problems of dysfunctional breathing, and re-establishing the balance of rest and effort to obtain optimum performance and restore self-esteem. We have found that these principles can be effectively applied in general practice. This approach is based on the work of Mackenzie³ and Lewis.⁴ It offers triage and a system of restoration of function in patients with impairment of health and performance, but in whom no specific diagnostic category is apparent nor requirement for treatment by a specialist necessary.

We agree with Wessely and colleagues that a new generation of generalists is required, and believe that the general practitioners practising within the UK should be able, with appropriate training, to fulfil that role. Here, assessment, teaching, and rehabilitation return medicine to an enabling process for people who have functional somatic symptoms and for whom specialist investigation is unnecessary, other than to exclude the presence of organic damage due to disease.

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- 1 Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; **354**: 936-39.
- 2 Nixon PGF, King JC. Ischaemic heart disease, homeostasis and the heart. In: Watkins A, ed. *Mind-body medicine*. London: Churchill Livingstone, 1997: 41-73.
- 3 Mair A. Sir James Mackenzie MD. London: Royal College of General Practitioners, 1986.
- 4 Lewis T. *The soldier's heart and the effort syndrome*. London: Shaw, 1918.

Sir—Simon Wessely and colleagues¹ argue that similarities between 12 syndromes justify classifying these syndromes under the larger general category of functional somatic syndromes. Historically, many chronic illnesses have been difficult to define, especially those of unknown aetiology and non-specific and variable signs and symptoms.² However, it is important to remember that multiple sclerosis (MS) is a neurological disease that, like CFS, disproportionately affects women. Earlier medical views of MS parallel current psychogenic assumptions about CFS, since MS was once seen to be caused by stress linked with oedipal fixations.³

Wessely and colleagues assert that core features of the 12 syndromes overlap: this is an overstatement. Fatigue, the central symptom characterising CFS, is included in only six of the 12 case definitions. They also

argue that their hypothesis is supported by their observations that patients with one of these syndromes frequently meet the criteria for another syndrome. In medicine, patients sometimes have more than one illness, yet few would advocate classifying a patient with both cancer and heart disease as having only one syndrome.

The investigators also contend that medical therapies for these syndromes have been ineffective, yet they contradict such generalisations with statements such as "low-dose hydrocortisone therapy is helpful in the management of chronic fatigue syndrome". In addition, their argument that these syndromes cause "unnecessary expenditures of medical resources" can have pernicious public policy implications.

There is a clear need to fund basic science research focusing on issues of variances in criteria; difficulties with current syndromes might be attributable to inadequate formal inclusion and exclusion criteria used to classify patients' data in diagnostic categories. Variance in criteria is likely to occur when explicit criteria do not exist for diagnostic categories.² For example the US case definition of CFS treats two central symptoms, post-exertional malaise and cognitive impairment, as optional rather than required criteria.

Further, Wessely and co-workers mention a strong association between these somatic symptoms and emotional distress. If people with these syndromes present physical complaints to mask psychological problems, then there should be an inverse relation between the number of depression and anxiety symptoms and the number of reported somatic symptoms. This relation has not been shown.⁴ Biases toward psychiatric explanations for these syndromes have been filtered to the media, which has portrayed these syndromes in simplistic and stereotypical ways. Perhaps the dissatisfaction with medical care that the authors cite as common is the stigma they endure due to the trivialisation of their syndromes.

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1 Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; **354**: 936-39.

2 Jason LA, King CP, Richman JA, Taylor RR, Torres SR, Song S. US case definition of chronic fatigue syndrome: diagnostic and theoretical issues. *J Chronic Fat Syndr* 1999; **5**: 3-33.

- 3 Richman JA, Jason LA, Taylor RR, Jahn SC. Feminist perspectives on the social construction of illness states. *Health Care Women Int* (in press).
- 4 Jason LA, Richman JA, Friedberg F, Wagner L, Taylor RR, Jordan KM. Politics, science, and the emergence of a new disease: the case of chronic fatigue syndrome. *Am Psychol* 1997; 52: 973-83.

Sir—Simon Wessely and colleagues¹ cite rather conservative figures for the frequency of patients with functional somatic syndromes in primary care populations of around 20%. Other research suggests an even higher prevalence of patients with medically unexplained syndromes.² Their thesis centres around the proposition that the many different functional somatic syndromes, which continue to be named and studied separately by respective subspecialties, may be more fruitfully studied through what they describe as "dimensional classification". Their work parallels Hyams³ recent efforts, although his similar conclusions are more limited.

Wessely et al suggest both a common clustering of symptoms and an underlying common pathway, which others have described as an illness superhighway. Two tentative but empirically tested models might help us to understand first the nature of the bidirectional brain-body autonomic and messenger-molecule communication pathways that constitute this superhighway, and second the supra-hypothalamic variables that lead to potential dysregulation of these mechanisms and the production of functional symptoms. Chrousos and Gold^{4,5} describe the structure and bimodal function of the stress response mechanisms and present them as the fulcrum of the brain-body connection. They focus on the hypothalamus and explain the action of these mechanisms in the body.^{4,5} Their analysis of the bimodal functioning of the stress response mechanisms is supported by a large array of specific studies.

Wickramasekera² proposes three key clusterings of variables that predispose individuals to the development of functional medical symptoms. Further variables are proposed to account for the specific events that precipitate the patient's experience of symptoms, and the factors that perpetuate or modulate the time course and intensity of the reported symptoms. The core predispositional risk factors include repressive coping style, negative affectivity, and hypnotic vulnerability. His innovative use of electrophysiological monitoring technology is an important potential clinical advance in meeting the challenge to elucidate

the key predispositional and often similar perpetuating variables in these patients.

To Wickramasekera's list of variables I would add various forms of trauma, whether experienced during childhood or adulthood. Finally, the emerging school of Darwinian medicine and evolutionary psychiatry invites us to be open to the possibility that the many functional medical symptoms, with which these patients present, may be having powerful behaviour modifying and even possible social roles that without this perspective are difficult to detect and appreciate.

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- 1 Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999; 354: 936-39.
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Sublingual cobalamin for pernicious anaemia

Sir—Georges Delpre and colleagues (Aug 28, p 740)¹ advocate sublingual therapy for cobalamin deficiency as an alternative to oral and parenteral cobalamin supplementation in patients with pernicious anaemia, food-cobalamin malabsorption in the elderly, vegetarianism, and in other deficiency states. Certainly most patients would prefer sublingual or oral vitamin B₁₂ if given the choice.

There are at least four forms of cobalamin—cyanocobalamin, hydroxocobalamin, and two coenzyme forms, which are biochemically active (methylcobalamin and adenosylcobalamin).² Hydroxocobalamin can only be given parenterally because oral preparations are not commercially produced.

Hydroxocobalamin is a potent cyanide antagonist, whereas cyanocobalamin is not. Since our original study³ I have focused on the neuro-ophthalmological manifestations of deficiency diseases and degenerative neuropathies. The precise role of

chronic cyanide intoxication in the pathogenesis of such disorders has merited particular attention.⁴

Oral or intramuscular cyanocobalamin is ineffective in the treatment of tobacco amblyopia and in patients with pernicious anaemia who smoke. Patients with tobacco amblyopia who have normal serum vitamin B₁₂ concentrations need not continue therapy with intramuscular hydroxocobalamin once their visual acuity and visual field have returned to normal, as long as they stop smoking.

Patients with Addison's pernicious anaemia who smoke require permanent therapy with parenteral hydroxocobalamin, as do smokers with low serum vitamin B₁₂ concentrations from other disorders.

Irrespective of whether patients with tropical (nutritional) amblyopia have normal or low serum vitamin B₁₂ concentrations, they also require treatment with parenteral hydroxocobalamin, and not with oral or parenteral cyanocobalamin in view of the fact that cyanocobalamin is not a cyanide antagonist.

Because confusion persists among doctors over the various forms of vitamin B₁₂ available for therapeutic use and about their possible adverse effects in neuro-ophthalmological disease, I strongly urge manufacturers to withdraw parenteral cyanocobalamin in favour of hydroxocobalamin for therapeutic use.⁵ I know of no disorder in which cyanocobalamin is preferable to hydroxocobalamin. I am particularly concerned that patients with tobacco/alcohol amblyopia have been given parenteral cyanocobalamin instead of hydroxocobalamin. The diagnosis may then be questioned, treatment stopped, and the patient condemned to a life of poor sight.

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- 1 Delpre G, Stark P, Niv Y. Sublingual therapy for cobalamin deficiency as an alternative to oral and parenteral cobalamin supplementation. *Lancet* 1999; 354: 740-41.
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- 5 Freeman AG. Cyanocobalamin—a case for withdrawal: discussion paper. *J R Soc Med* 1992; 85: 686-71.