

ABC of psychological medicine

Fatigue

Michael Sharpe, David Wilks

Fatigue can refer to a subjective symptom of malaise and aversion to activity or to objectively impaired performance. It has both physical and mental aspects. The symptom of fatigue is a poorly defined feeling, and careful inquiry is needed to clarify complaints of "fatigue," "tiredness," or "exhaustion" and to distinguish lack of energy from loss of motivation or sleepiness, which may be pointers to specific diagnoses (see below).

Prevalence—Like blood pressure, subjective fatigue is normally distributed in the population. The prevalence of clinically significant fatigue depends on the threshold chosen for severity (usually defined in terms of associated disability) and persistence. Surveys report that 5-20% of the general population suffer from such persistent and troublesome fatigue. Fatigue is twice as common in women as in men but is not strongly associated with age or occupation. It is one of the commonest presenting symptoms in primary care, being the main complaint of 5-10% of patients and an important subsidiary symptom in a further 5-10%.

Fatigue as a symptom—Patients generally regard fatigue as important (because it is disabling), whereas doctors do not (because it is diagnostically non-specific). This discrepancy is a potent source of potential difficulty in the doctor-patient relationship. Fatigue may present in association with established medical and psychiatric conditions or be idiopathic. Irrespective of cause, it has a major impact on day to day functioning and quality of life. Without treatment, the prognosis of patients with idiopathic fatigue is surprisingly poor; half those seen in general practice with fatigue are still fatigued six months later.

Causes of fatigue

The physiological and psychological mechanisms underlying subjective fatigue are poorly understood. Fatigue may rather be usefully regarded as a final common pathway for a variety of causal factors. These can be split into predisposing, precipitating, and perpetuating factors.

Predisposing factors include being female and a history of either fatigue or depression.

Precipitating factors include acute physical stresses such as infection with Epstein-Barr virus, psychological stresses such as bereavement, and social stresses such as work problems.

Perpetuating factors include physical inactivity, emotional disorders, ongoing psychological or social stresses, and abnormalities of sleep. These factors should be sought as part of the clinical assessment.

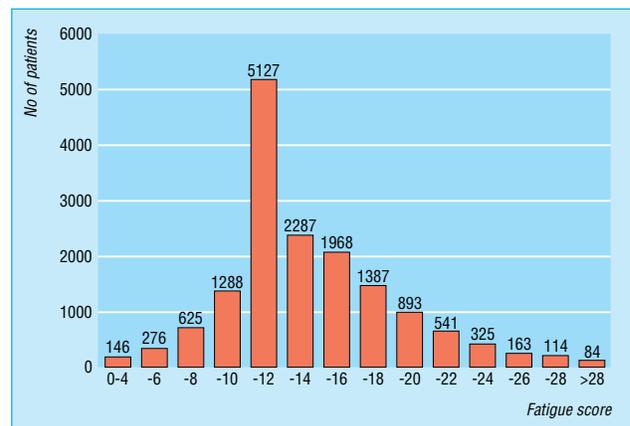
Other physiological factors such as immunological abnormalities and slightly low cortisol concentration are of research interest but not clinical value.

Diagnoses associated with fatigue

Among patients who present with severe chronic fatigue as their main complaint, only a small proportion will be suffering from a recognised medical disease. In no more than 10% of patients presenting with fatigue in primary care is a disease cause found. The rate is even lower in patients seen in secondary care.



Weary 1887 by Edward Radford (1831-1920)



Distribution of the complaint of fatigue in the population

Medical conditions that may present with apparently unexplained fatigue

- **General**—Anaemia, chronic infection, autoimmune disease, cancer
- **Endocrine disease**—Diabetes, hypothyroidism, hypoadrenalism
- **Sleep disorders**—Obstructive sleep apnoea and other sleep disorders
- **Neuromuscular**—Myositis, multiple sclerosis
- **Gastrointestinal**—Liver disease
- **Cardiovascular**—Chronic heart disease
- **Respiratory**—Chronic lung disease

Fatigue is a major symptom of many psychiatric disorders, but for a substantial proportion of patients with fatigue the symptom remains unexplained or idiopathic. In general, the more severe the fatigue and the larger the number of associated somatic (and unexplained) complaints, then the greater the disability and the greater the likelihood of a diagnosis of depression.

Chronic fatigue syndromes

Chronic fatigue syndrome is a useful descriptive term for prominent physical and mental fatigue with muscular pain and other symptoms. It overlaps with another descriptive term, fibromyalgia, that has often been used when muscle pain is predominant but in which fatigue is almost universal. There is also substantial overlap of the diagnoses with other symptom based syndromes, the so called functional somatic syndromes.

The term myalgic encephalomyelitis (or encephalopathy) has been used in Britain and elsewhere to describe a poorly understood illness in which a prominent symptom is chronic fatigue exacerbated by activity. This is a controversial diagnosis that some regard as simply another name for chronic fatigue syndrome and that others regard as a distinct condition. This article will focus on chronic fatigue syndrome.

Prevalence and outcome—Chronic fatigue syndrome can be diagnosed in up to 2% of primary care patients. Untreated, the prognosis is poor, with only about 10% of patients recovering in a two to four years. A preoccupation with medical causes seems to be a negative prognostic factor.

Assessment and formulation

History—The nature of the fatigue is an important clue to diagnosis, and it is therefore important to clarify patients' complaints. Fatigue described as loss of interest and enjoyment (anhedonia) points to depression. Prominent sleepiness suggests a sleep disorder. The history should also cover

- Systematic inquiry for diseases often associated with fatigue
- Symptoms of depression anxiety and sleep disorder
- Patients' own understanding of their illness and how they cope with it
- Current social stresses.

Examination—Both a physical and mental state examination must be performed in every case, to seek medical and psychiatric diagnoses associated with fatigue.

Routine investigations—If there are no specific indications for special investigations, a standard set of screening tests is adequate.

Special investigations—Immunological and virological tests are generally unhelpful as routine investigations. Sleep studies can be useful in excluding other diagnoses, especially obstructive sleep apnoea and narcolepsy.

Psychological assessment—It is important to inquire fully about patients' understanding of their illness (questions may include "What do you think is wrong with you?" and "What do you think the cause is?"). Patients may be worried that the fatigue is a symptom of a severe, as yet undiagnosed, disease or that activity will cause a long term worsening of their condition.

Formulation—A formulation that distinguishes predisposing, precipitating, and multiple perpetuating factors is valuable in providing an explanation to patients and for targeting intervention.

General management

Persistent fatigue requires active management, preferably before it has become chronic. When a specific disease cause of fatigue

Psychiatric diagnoses commonly associated with fatigue

- Depression
- Anxiety and panic
- Eating disorders
- Substance misuse disorders
- Somatisation disorder

Diagnostic criteria for chronic fatigue syndrome

Inclusion criteria

- Clinically evaluated, medically unexplained fatigue of at least 6 months' duration that is
 - Of new onset (not life long)
 - Not result of ongoing exertion
 - Not substantially alleviated by rest
 - Associated with a substantial reduction in previous level of activities
- Occurrence of 4 or more of the following symptoms
 - Subjective memory impairment, sore throat, tender lymph nodes, muscle pain, joint pain, headache, unrefreshing sleep, post-exertional malaise lasting more than 24 hours

Exclusion criteria

- Active, unresolved, or suspected medical disease or psychotic, melancholic, or bipolar depression (but not uncomplicated major depression), psychotic disorders, dementia, anorexia or bulimia nervosa, alcohol or other substance misuse, severe obesity

Screening tests for fatigue

- Full blood count
- Erythrocyte sedimentation rate or C reactive protein
- Liver function tests
- Urea and electrolytes
- Thyroid stimulating hormone and thyroid function tests
- Creatine kinase
- Urine and blood tests for glucose
- Urine test for protein

Factors to consider in a formulation of chronic fatigue

	Predisposing cause	Precipitating cause	Perpetuating cause
<i>Biological</i>	Biological vulnerability	Acute disease	Pathophysiology Excessive inactivity Sleep disorder
<i>Psychological</i>	Vulnerable personality	Stress	Depression Unhelpful beliefs about cause Fearful avoidance of activity
<i>Social</i>	Lack of support	Life events Social or work stress	Reinforcement of unhelpful beliefs Social or work stress

can be identified this should be treated. If no disease diagnosis can be made, or if medical treatment of disease fails to relieve the fatigue, a broader biopsychosocial management strategy is required. A discussion with the patient about fatigue and its treatment can be supplemented with written material (see below).

Patients should be told that they are suffering from a common and treatable condition that the doctor takes seriously and for which behavioural treatment can be helpful. While patients may be concerned about possible disease and the need for medical investigation and treatment, it can be explained that no disease has been found, and hence there is no disease based treatment, but that with help there is a great deal that the patients can do themselves.

Identifying unhelpful beliefs—Potentially unhelpful beliefs should be discussed. If a patient has a simple aetiological model (such as “It is all due to a virus”) an alternative approach based on a biopsychosocial formulation can be outlined. This has the advantage of highlighting potential perpetuating factors, as these may be regarded as obstacles to recovery. Doctor and patient can then work together to overcome these. It is rarely productive to argue over the best name for the illness; instead, the emphasis should be on agreeing a positive and open minded approach to rehabilitation.

Managing activity and avoidance—Gradual increases in activity can be advised unless there is a clear contraindication. It is critical, however, to distinguish between carefully graded increases carried out in collaboration with patients and “forced” exercise. It is also important to explain that erratic variation between overactivity on “good” days and subsequent collapse does not help long term recovery and that “stabilising” activity is a prerequisite to graded increases.

Depression and anxiety—If there is evidence of depression a trial of an antidepressant drug is worth while. Patients with fatigue are often sensitive to the side effects of antidepressants. However, if they are given adequate information about what to expect when treatment begins, with small doses, most patients can tolerate them. Randomised trials have shown psychological therapies such as cognitive behaviour therapy to be equally effective for mild to moderate depression.

Managing occupational and social stresses—Patients who remain in work may be overstressed by it. Those who have left work may be inactive and demoralised and may not wish to return to the same job. These situations require a problem solving approach to consider how to manage work demands, achieve a return to work, or to plan an alternative career.

Referral for specialist management

Most patients with fatigue are managed in primary care, but certain groups may require referral to specialist care:

- Children with chronic fatigue
- Patients in whom the general practitioner suspects occult disease
- Patients with severe psychiatric illness
- Patients requiring specialist management of sleep disorders
- Patients unresponsive to management in primary care.

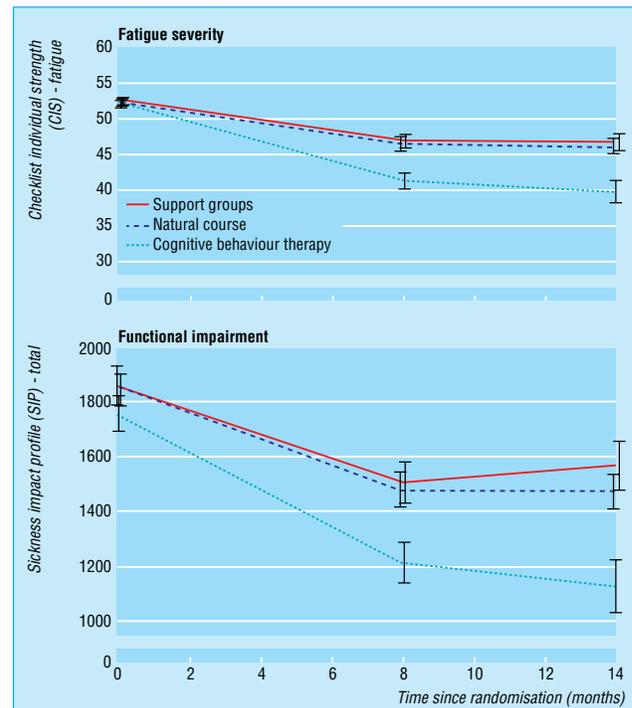
Referral may be to a physician or psychiatrist as is deemed most appropriate. Psychologists may be able to offer cognitive behaviour therapy. Where available, joint medical and psychiatric clinics are ideally suited to the assessment of chronic fatigue and related problems. It is essential there is close liaison between primary and specialist care to ensure a clear, consistent, and encouraging approach by all concerned.

Management of chronic fatigue

- 1 Assessment
 - Empathise
 - History
 - Examination
 - Limited investigation
 - Biopsychosocial formulations
- 2 Treat treatable medical and psychiatric conditions
- 3 Help patient to overcome perpetuating factors
 - Educate
 - Reduce distress
 - Gradual increase in activity
 - Solve social and occupational problems
- 4 Follow up



Patients should be encouraged to gradually increase their activity. (“Mrs Bradbury’s establishment for the recovery of ladies nervously affected,” from *On insanity* by William B Neville London 1836)



Efficacy of cognitive behaviour therapy for treating chronic fatigue syndrome

What is cognitive behaviour therapy?

- Brief pragmatic psychological therapy
- Targets beliefs and behaviours that might perpetuate symptoms
- An established treatment for depression and anxiety
- Has been adapted for somatic complaints of pain and fatigue
- Requires a skilled therapist

Rehabilitation

Rehabilitation based on behavioural principles is currently the most effective specialist treatment approach.

Cognitive behaviour therapy is a collaborative psychological rehabilitation that incorporates graded increases in activity but also pays greater attention to patients' beliefs and concerns.

Graded exercise therapy is a structured progressive exercise programme administered and carefully monitored by a therapist.

Both may be used in conjunction with antidepressant drugs. Both have been found to be effective in randomised trials of hospital referred cases of chronic fatigue syndrome. Some general practitioners are able to provide graded exercise or cognitive behaviour therapy in their practice or clinic. Others may wish to refer to a trained therapist.

Conclusion

Fatigue is a ubiquitous symptom that is important to patients and has a major impact on their quality of life. It remains poorly understood and has hitherto probably been not been given adequate attention by doctors. Early and active management of fatigue in primary care may prevent progression to chronicity. Patients who have developed a chronic fatigue syndrome can benefit from specific treatments. Paying more attention to the symptom of fatigue may help to avoid the distress and poor outcome that is associated with patients feeling that their problems are neither accepted nor understood. It may also reduce the numbers who turn to a variety of unproved, and even harmful, alternative approaches.

Michael Sharpe is reader in psychological medicine, University of Edinburgh. David Wilks is consultant in infectious diseases, Western General Hospital, Edinburgh.

The ABC of psychological medicine is edited by Richard Mayou, professor of psychiatry, University of Oxford; Michael Sharpe; and Alan Carson, consultant neuropsychiatrist, NHS Lothian, and honorary senior lecturer, University of Edinburgh. The series will be published as a book in winter 2002.

BMJ 2002;325:480-3

What is graded exercise therapy?

- Explanation of fatigue as a physiological consequence of inactivity, poor sleep, and disturbed circadian rhythms
- Discussion, agreement, and implementation of graded exercise plans
- Monitoring of progress and setting of appropriate new targets

Evidence based summary

- Chronic fatigue syndrome is a descriptive term for a disabling syndrome that probably has multiple causes (physical and psychological)
- Graded exercise and cognitive behaviour therapies are effective in treating chronic fatigue syndrome

Wessely S. Chronic fatigue: symptom and syndrome. *Ann Intern Med* 2001;134:838-43

Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD, Ramirez G. Interventions for the treatment and management of chronic fatigue syndrome: a systematic review. *JAMA* 2001;286:1360-8

Further reading

- Wessely S, Hotopf M, Sharpe M. *Chronic fatigue and its syndromes*. Oxford: Oxford University Press, 1998
- Campling F, Sharpe M. *Chronic fatigue syndrome: the facts*. Oxford: Oxford University Press, 2000
- Reid S, Chalder T, Cleare A, Hotopf M, Wessely S. Chronic fatigue syndrome. *Clinical Evidence* 2001 (Nov)

The painting *Weary* is held at Russell-Cotes Art Gallery and Museum, Bournemouth, and is reproduced with permission of Bridgeman Art Library. The graph of distribution of fatigue in the population is adapted from Pawlikowska T, et al *BMJ* 1994;308:763-6. The box of diagnostic criteria for chronic fatigue syndrome is adapted from Fukuda K, et al *Ann Intern Med* 1994;121:953-9. The print of "Mrs Bradbury's establishment for the recovery of ladies nervously affected" is reproduced with permission of Wellcome Library. The graph showing efficacy of cognitive behaviour therapy is adapted from Prins JB, et al *Lancet* 2001;357:841-7.

My first patient

Friday had been a busy day. I saw my name on the list of candidates who had satisfied the examiners in the final examinations. I shook hands with the dean, swore the Hippocratic oath, signed up with the Medical Defence Union, and went to a party.

The next day I was driving in my old Austin 10 to see my parents when I noticed a man walking on the opposite side of the road suddenly fall to his knees and collapse face down on the ground. I stopped the car and got out. At the same time another car drew up, and a large man alighted. He looked at me and then said, rather imperiously I thought, "Leave this to me, I am a doctor."

Conscious of my newly acquired status, I looked at him and, rather less confidently, said, "Well, as a matter of fact, I am a doctor."

We stood there for a moment, almost frozen in time, like two gladiators each waiting for the next move.

I then noticed that we had been joined by a third man. He looked us up and down and then, casting his eye on the motionless figure lying on the pavement, said in his rich local accent, "Why now, don't you be bothering yourselves with that silly old bugger. He does this every Saturday after he's drunk the

pub dry, so as someone will pick him up and give him a free ride home."

At that the "patient" rose to his feet, dusted himself down, and walked away. My colleague and I looked at each other and then dissolved into helpless laughter.

I returned to my car and drove off. Shortly, I passed the "patient," who was striding along quite briskly, if a little unsteadily. I did not offer him a lift.

K D Stephenson *retired general practitioner, Darlington*

We welcome articles of up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake*, or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.