

The debate: myalgic encephalomyelitis and chronic fatigue syndrome

Charles Shepherd

Abstract

Almost every aspect of myalgic encephalomyelitis (or encephalopathy) and chronic fatigue syndrome is the subject of disagreement and uncertainty – something that has undoubtedly hampered recognition, understanding and research. Although the pathogenesis remains the subject of intense medical debate, a number of predisposing, precipitating and perpetuating factors are now starting to emerge. Therapeutic nihilism is no longer appropriate as there is a great deal that can be done to alleviate some of the more distressing symptoms and improve quality of life for these patients.

Key words: Chronic fatigue syndrome ■ Myalgic encephalomyelitis

Mention the terms myalgic encephalomyelitis (ME) (or encephalopathy) or chronic fatigue syndrome (CFS) to a group of health professionals and they will produce a variety of opinions on cause, management, and even their very existence as distinct clinical entities.

Controversy and uncertainty surrounding ME/CFS is nothing new and largely dates back to an editorial in the *Lancet* (1956) that introduced ME into medical language as a severe post-infectious illness involving muscle and brain symptomatology. But medical opinion remained sceptical and it was only during the early 1980s that interest was renewed – one result being the redefinition and renaming of ME as CFS.

In 1998, in an attempt to produce a degree of consensus, particularly in relation to diagnosis and management, the Chief Medical Officer (CMO) appointed a Working Group to produce a report (Hutchinson, 2002). The CMO report concluded that ME/CFS is a genuine and disabling illness that imposes a substantial burden on the health of the UK population, and called for a programme of research, education and the availability of multidisciplinary services.

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Nomenclature: a disease of many names

Myalgic encephalomyelitis/encephalopathy (ME)

As encephalomyelitis describes an unproven pathological process — namely inflammation in the brain and spinal cord — many doctors have become reluctant to use this term. Some, including the author, have suggested that encephalopathy is a more acceptable way of describing the various neurological abnormalities and symptoms.

Chronic fatigue syndrome

CFS is a name that makes no firm assumptions about cause. Two major criticisms of the term CFS are that it fails to reflect the symptomatology and severity of the illness — in the same way that chronic forgetfulness syndrome would be a totally inappropriate description for dementia — and that it has become a convenient label for anyone with unexplained chronic fatigue.

Post-viral fatigue syndrome

PVFS was introduced in the 1980s. While this description is generally acceptable to both doctors and patients, it is obviously not appropriate in the absence of a clear cut viral onset.

Clearly, there needs to be nomenclature upon which both doctors and patients can agree rather than resorting to the ME/CFS compromise – a term that covers a heterogeneous group of patients with differing symptom complexes and responses to treatments.

Symptoms and definitions

ME/CFS is characterized by severe, disabling physical and mental fatigue, both of which are markedly exacerbated by relatively small amounts of exertion. Fatigue is accompanied by post-exertional malaise whereby there is a delayed impact so that symptoms are often worse later in the day, or the next day, following activity. The way in which patients describe their fatigue is very different to normal everyday tiredness.

Other characteristic symptoms, which also often fluctuate in severity, include (Hutchinson, 2002):

- Cognitive impairment, particularly involving short-term memory, concentration, information processing, ability to plan or organize thoughts and a short attention span
- Pain, which is sometimes persistent and may be severe. The pain can be muscular, arthralgic or neuropathic – where it is described as burning or searing in quality; not all patients have pain
- Neurological disturbance presenting as problems with balance, paraesthesiae, increased sensitivity to various

stimuli and autonomic dysfunction presenting as postural hypotension or postural tachycardia

- Headaches, which may be migrainous in character
- Sleep disturbance, which may range from hypersomnia (increased requirements) through to insomnia as the illness becomes chronic
- Sore throats, enlarged glands, on-going flu-like feelings
- Disturbances in temperature control with sensitivity to both heat and cold
- Alcohol intolerance, drug and chemical sensitivities.

More serious neurological symptoms may occur in a minority of patients, particularly those at the severe end of the spectrum. These include double vision, blackouts, atypical convulsions, and loss of swallowing ability – which may require assisted feeding. As with any chronic disabling illness, some patients go on to develop clinical depression or other disturbances in mood.

A number definitions of CFS have been proposed primarily in an attempt at producing an homogenous group of patients for research purposes. The most recent and widely used (Fukuda et al, 1994), requires the presence of:

Six months or more of persistent or relapsing chronic fatigue resulting in a substantial reduction in previous levels of occupational, educational, social or personal activities, plus the concurrent occurrence of four or more of the following symptoms:

- Cognitive dysfunction
- Sore throat
- Tender cervical or axillary lymph nodes
- Muscle pain
- Headaches of new type, pattern or severity
- Unrefreshing sleep
- Post-exertional malaise lasting more than 24 hours
- Multi-joint pain without swelling or redness.

Research criteria for CFS also require the specific exclusion of a number of medical and psychiatric disorders that may cause chronic fatigue.

The introduction of research definitions has undoubtedly helped to stimulate research but in the absence of subgrouping (e.g. the presence or absence of psychiatric comorbidity) the results often leave many questions unanswered.

A major practical problem is that research definitions have not been designed or modified to cover the routine clinical assessment of patients as well. One group of physicians has recently put forward guidelines, the *Canadian Consensus Document*, that are designed to meet clinical rather than research needs (Carruthers et al, 2003).

Disability assessment and quality of life

Most patients fit into one of four categories of disablement, which are based on an assessment scale devised by Cox and Findley (1998):

- Mild: patients are mobile, can care for themselves, and are usually able to perform light domestic tasks. Some will be working full time or be in education; to work, they often have to stop leisure or social pursuits
- Moderate: there is significantly reduced mobility and restrictions in all aspects of daily living, often associated with peaks and troughs of activity. Some are able to just

about cope with flexible part-time work or education but usually require a prolonged rest period in the afternoon

- Severe: Often require assistance with personal care such as washing and are unable to cope with domestic tasks such as cooking. Mobility is severely affected and they may require wheelchair assistance. Some will be largely housebound
- Very severe: Require help with almost all aspects of daily living. Confined to the house and may be bed-bound.

Studies which have examined functional status and quality of life measures (Komaroff et al, 1996) confirm that the impairment of physical and mental activities can be just as great, or greater, than is found in many other chronic medical conditions.

Epidemiology

Problems with definition, and the lack of any large-scale epidemiological study being carried out here in the UK, mean that estimates of incidence and prevalence have to be viewed with caution. In particular, the use of current case definitions may well be producing an under-estimate of the true prevalence, particularly the numbers with severe ME/CFS.

Overall, the CMO report (Hutchinson, 2002) used current evidence to conclude that:

- The population prevalence is at least 0.2%–0.4%
- The most common age of onset is between early 20s to mid-40s
- In children, the most common age of onset is 13–15, but cases can occur as young as 5
- ME/CFS is about twice as common in women as in men
- It affects all social classes to a similar extent
- It affects all ethnic groups.

Aetiology, pathogenesis and disease associations

Research into the possible aetiology (cause) and pathogenesis (underlying disease process) has largely been carried out on patients who meet one of the international research criteria, normally Fukuda et al (1994) for CFS. Although a number of interesting endocrine, immune, infectious, muscular and neurological abnormalities have been reported, none of them are sufficiently consistent or specific enough to act as a diagnostic test. Neither are they robust enough to fully explain a specific symptom or group of symptoms. A consensus is, however, emerging that ME/CFS may be a three-stage illness involving predisposing, precipitating and perpetuating factors.

Predisposing factors

There is growing evidence, in particular from twin studies being carried out in America (Buchwald et al, 2001), that genetic predisposition plays a role and this may help to explain the slightly higher than expected familial incidence.

Precipitating factors

A substantial proportion of people with ME/CFS report that their illness followed an infective episode. A wide variety of viral infections, including glandular fever (White et al,

2004), hepatitis (Berelowitz et al, 1995), meningitis (Hotopf et al, 1996), parvovirus (Kerr et al, 2002) and those caused by enteroviruses (Chia et al, 2005) are known to trigger ME/CFS. Non-viral infections such as *Coxiella burnetii*/Q fever (Ayres et al, 1998) are occasionally implicated as well. Although infections are a common trigger factor, the majority of current evidence suggests that persisting viral infection is not part of the on-going pathology. Immunizations, organophosphate pesticides, toxins and physical trauma are reported as being the principle trigger in a small minority of cases. About a quarter of all patients report a gradual onset to their ME/CFS with no obvious precipitating factor.

Perpetuating factors

There is now a considerable amount of evidence, some of it replicated, to indicate that abnormalities in the central and autonomic nervous systems, possibly linked to a viral trigger and on-going immune system dysregulation, play a

key role in the pathophysiology of ME/CFS. Both ME and CFS are therefore classified as neurological disorders by the World Health Organization in section G93:3 of their 10th International Classification of Diseases (ICD 10).

Key neurological findings include:

- Magnetic resonance imaging (MRI) studies demonstrating punctate areas, i.e. small spot-like lesions of no greater than 5 mm in diameter, of high signal intensity in the cerebral white matter (Buchwald et al, 1992). These appear to be more likely in patients who have no psychiatric comorbidity (Keenan, 1999).
- MRI measurements of brain volume, with two independent groups reporting evidence, suggest that the volume of grey matter is significantly decreased. The study by de Lange et al (2005) reported that the decline in grey matter volume was linked to a reduction in physical activity. Okada et al (2004) reported that the reduction in the right pre-frontal cortex paralleled the severity of fatigue.
- A functional MRI study (de Lange et al, 2004) demonstrating that patients have to exert greater effort to process incoming auditory information and that brain activation, especially in those with no concurrent psychiatric illness, is more diffuse than normal.
- A xenon-computed tomography blood flow study demonstrating a reduction in absolute cortical blood flow (Yoshiuchi et al, 2006) and single photon emission computed tomography (SPECT) hypoperfusion in specific areas of the brain, in particular the brainstem (Costa et al, 1995). The study by Yoshiuchi found that patients devoid of psychopathology were the group most at risk of developing symptoms due to brain dysfunction.
- Brain metabolism studies demonstrating decreased acetylcholine uptake (Kuratsune et al, 2002), increased choline (Puri et al, 2002; Chaudhuri et al, 2003), fluctuations in serotonin status (Badawy et al, 2005) and abnormalities in dopaminergic modulation (Georgiades et al, 2003).
- Cerebrospinal fluid analysis demonstrating higher levels of some cytokines, protein levels and/or white blood cells (Natelson et al, 2005) – an abnormality which suggests that immune dysregulation within the central nervous system may be involved.
- Evidence of autonomic dysfunction (Freeman and Komaroff, 1997; Freeman, 2002) which may help to explain the neurally mediated hypotension (condition in which the body has difficulty regulating the blood pressure, especially when upright) that occurs in some patients, as may disturbances in peripheral cholinergic transmission (Khan et al, 2003).

Additionally, a wide variety of immune system abnormalities have been reported – some of them being consistent with either activation or suppression of various components. However, no consistent pattern of abnormalities has been identified so far (Lyll et al, 2003). One theory is that following a precipitating infection there is an inappropriate and on-going change in immune system function, which may involve cytokine activation – the component that is partly responsible for flu-like symptoms. Immune system dysregulation may also help to explain the increased incidence of allergic illness in some patients.

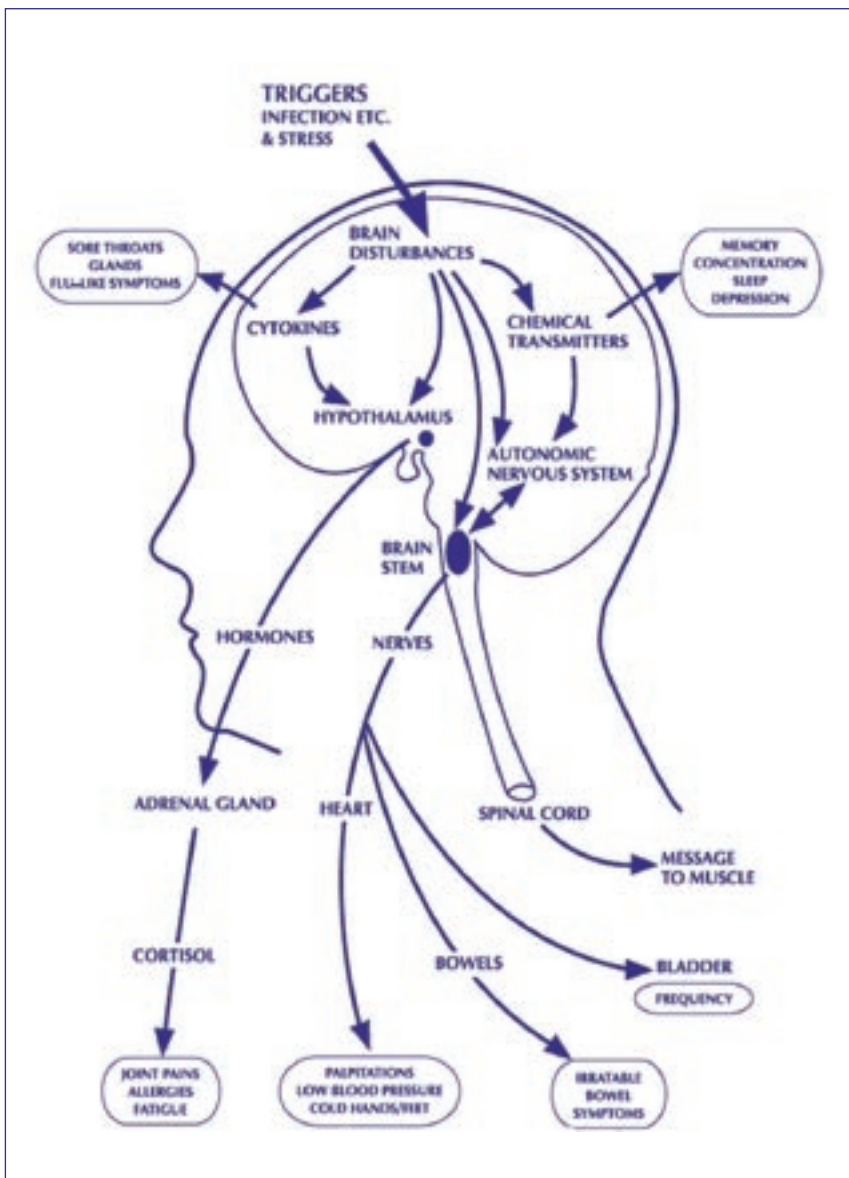


Figure 1: Diagram to illustrate how ME/CFS may involve the central nervous system.

Neuroendocrine hypoactivity of the hypothalamic-pituitary-axis, in particular adrenal activity and reduced output of cortisol, has been consistently reported by several research groups (Papanicolaou et al, 2004) as well as adrenal gland atrophy in one small study (Scott et al, 1999). Disturbances at the level of the hypothalamus may help to explain symptoms such as disturbed thermoregulation.

Although current consensus is that the fatigue experienced in ME/CFS is primarily a central problem (i.e. brain), there is some evidence to suggest that in a subgroup of patients there are metabolic (Arnold et al, 1984) and mitochondrial abnormalities (i.e. muscular) (Behan et al, 1991) which cannot simply be explained by deconditioning or a relative lack of activity.

Gene expression research being carried out in both the UK and USA (Whistler et al, 2003) is currently examining how changes in gene expression may contribute to symptomatology and whether these abnormalities could also act as diagnostic biomarkers for ME/CFS.

Maintaining factors linked to the actual illness

To complicate matters further, a number of symptoms and consequences of the illness may also play a role in maintaining or exacerbating ill health and disability. These include the presence of constant pain, and/or any significant sleep or mood disorder such as depression. The role of inactivity and subsequent deconditioning remains controversial with the most recent research examining exercise capacity failing to support any association (Schmaling et al, 2005). Even so, some researchers have put forward a psychosocial model of causation in which the illness is principally maintained by a vicious circle of inactivity, mood disturbance and abnormal illness behaviour and beliefs.

Associated conditions

There are also a number of conditions, including fibromyalgia and irritable bowel syndrome, which appear to be more common in patients with ME/CFS.

Diagnostic assessment

One of the key recommendations in the CMO report was that patients should, wherever possible, receive an early and accurate diagnosis so that a management plan can be put in place as soon as possible. But a recent survey carried out as part of the preparation for an ME/CFS charities report on early and accurate diagnosis (ME Alliance, 2005) found that 53% of adults were still waiting over a year before being diagnosed. The Alliance report recommended a diagnostic timeframe whereby:

- At 4–6 weeks of persisting undue fatigue and other ME/CFS-like symptoms following an acute infection, a diagnosis of a postviral/infectious fatigue syndrome should be considered
- After 3–4 months of persisting symptoms, and where other possible causes of ME/CFS-like symptoms have been excluded through investigation, a provisional diagnosis should be considered
- By 6 months, if symptoms persist, the provisional diagnosis should have been confirmed, provided all other explanations

have been properly excluded, and further advice on management given.

As the symptoms of ME/CFS can sometimes be similar to many other conditions where fatigue is a prominent feature, the diagnostic assessment should always include a detailed clinical history, a full examination, routine investigations and further investigation where appropriate.

Table 1. Differential diagnosis of an ME/CFS-like illness

Endocrine and metabolic
Addison's disease Fluid retention syndrome Haemochromatosis Hypercalcaemia and hypocalcaemia Hypothyroidism Pituitary tumour
Gastrointestinal
Coeliac disease Crohn's disease Irritable bowel syndrome
Infections
Brucellosis Giardia Hepatitis B or C HIV Lyme disease Parvovirus Post-polio syndrome Q fever Toxoplasmosis
Malignancy
Hodgkin's lymphoma
Neuromuscular
Chiari 1 malformation Multiple sclerosis Myasthenia gravis Narcolepsy Rare myopathies
Psychiatric
Depression Hyperventilation Somatisation disorder Stress
Respiratory
Sarcoidosis Sleep apnoea
Rheumatology
Fibromyalgia Sjogren's syndrome Systemic lupus erythematosus

The medical history often provides vital clues, not only about possible causation, but also about what sort of management plan is required. In particular, it should explore other possible explanations where there are less common symptoms or where a symptom such as joint pain is particularly prominent.

Physical signs in ME/CFS are limited and often subtle in nature. One fairly common finding is being unable to perform a standard test of balance (i.e. the Romberg test where a patient is asked to stand up still with their eyes closed). Evidence of vestibular dysfunction — using a Fukuda test — can be demonstrated in a smaller number who complain of dysequilibrium (problems with balance). Those with widespread pain may have tender spots at sites where these are commonly found in fibromyalgia.

The following basic investigations should always be carried out before a diagnosis is confirmed:

- Full blood count and differential
- Erythrocyte sedimentation rate (ESR) or acute phase protein changes
- Blood biochemistry: calcium, sodium, potassium, urea, etc
- Blood glucose
- Creatine kinase (to help exclude muscle disease)
- Thyroid and liver function tests
- Urine tests for renal disease and diabetes.

Second line tests, which may be appropriate in certain circumstances, include:

- Antibody screening tests for specific infections, e.g. hepatitis B/C; Lyme disease; parvovirus
- Screening for coeliac disease if there are irritable bowel-type symptoms or unexplained anaemia (Skowera et al, 2001)
- Autoimmune and rheumatology screen if joint pains are prominent
- MRI scan if another neurological illness seems possible on the basis of symptoms and signs
- Pituitary and endocrine function tests if there are symptoms and signs suggestive of an endocrine disorder.

There is insufficient evidence to justify testing for antiviral activity, the RNaseL test (Gow, et al 2001) or urinary markers (Chalmers, et al 2006).

Children and adolescents

ME/CFS also occurs in children and adolescents and is one of the most common causes of long-term absence from school (Dowsett and Colby, 1997). Although the main symptoms are very similar to those seen in adults, children may have additional symptoms such as abdominal pain, nausea and sinus congestion. Liaison with the school in relation to home tuition and part-time schooling, where appropriate, forms a key part of any management programme. The Royal College of Paediatrics and Child Health has produced a guideline (2004) on issues relating to diagnosis and management, and there are separate support charities dealing with this area of ME/CFS.

Management

General principles

Having established a diagnosis, or provisional diagnosis, patients with ME/CFS require a flexible management plan

that is based on both the stage and severity of their illness, as well as the type of symptom complex that is present. In most cases the best person to coordinate such a plan is their GP. Management should be multidisciplinary and may involve dietitians, nurses, occupational therapists, physiotherapists and psychologists.

Important issues such as benefit entitlement, along with negotiations with employers and educational authorities, often form an additional component of any management plan. The Department of Work and Pensions have made it clear that, where appropriate, people with ME/CFS are entitled to the full range of sickness and disability benefits. In relation to employment and services, ME/CFS is an illness that is recognized under the Disability Discrimination Act.

Patients should have access to a local hospital service where further advice can be given on diagnosis and/or management, and where referral to other specialist services is available.

The Department of Health has recently allocated £8.5 million of ring-fenced money to support the establishment of 36 local multidisciplinary teams, 11 specialist teams for children and adolescents, and 13 clinical network coordinating centres throughout England. Some of these new services are able to arrange domiciliary visits for more severely affected patients. Unfortunately, no such initiative has yet taken place in Scotland, Wales or Northern Ireland. The ME Association is collecting feedback on the new services and has a list of their locations and referral requirements.

The management of ME/CFS is currently the subject of a new guideline being prepared by the National Institute for Health and Clinical Excellence. This guideline is due for publication in 2007.

Pharmacological treatments

A wide variety of drug treatments have been advocated for ME/CFS but no single approach has been shown to significantly affect the underlying disease process. The following interventions have all been assessed, or are being assessed, to some extent in clinical trials:

- Amantadine: a drug for which there is some evidence that it can reduce central fatigue in neurological conditions, such as multiple sclerosis
- Ampligen: an antiviral and immunomodulatory drug currently being tested in America, where a Phase 2 clinical trial has recently been completed
- Central nervous system stimulants, e.g. modafinil (Randall et al, 2005; Turkington et al, 2004) and methylphenidate (Blockmans et al, 2006)
- Eicosapentaenoic acid (EPA): an omega-3 fatty acid supplement (Puri, 2004)
- Hydrocortisone to correct any hypocortisolaemia (McKenzie et al, 1998; Cleare et al, 1999)
- Isoprinosine: partly in relation to the immune dysfunction involving natural killer cell activity (Diaz-Mitoma et al, 2003)
- Midrodine: for neurally mediated hypotension (Naschitz et al, 2004)

- Ondansetron: a 5-HT₃ receptor antagonist which may also have an effect on central fatigue in ME/CFS (Spath et al, 2000) and chronic liver disease (Jones, 1999).
- Oestradiol patches and cyclical progestagens: in those where an oestrogen deficiency state appears to be present (Studd and Panay, 1996)

Although some of these drugs, such as hydrocortisone, have demonstrated some degree of benefit, their use at present remains highly speculative. EPA supplements are available over the counter and are being quite widely used by ME/CFS patients at present. Thyroid supplementation has also been advocated, even in the presence of normal thyroid function tests, but most doctors believe this is unwise and potentially harmful (Shepherd, 1997).

Patients with ME/CFS are often sensitive to the side-effects of drugs, particularly those which act on chemical transmitters systems in the brain and nervous system. Therefore, it is usually advisable to 'start low and go slow', depending on the response.

Symptomatic relief

With no effective drug treatment currently available, the role of medication is largely confined to symptomatic relief, an approach that should be combined with appropriate self-help strategies and, where safe and appropriate, the use of complementary therapies.

Pain

Over-the-counter analgesics are seldom adequate where pain is a significant feature of the illness. In this case drugs, such as a low dose of amitriptyline (e.g. 10 mg at night) or gabapentin (again starting with a low dose of 100 mg) may be helpful, especially where the pain has neuropathic features. Other pain relief options that could be considered include the use of acupuncture, a TENS machine, or referral to a hospital pain clinic. The cautious use of antispasmodics, such as baclofen, may be helpful where painful muscle spasms occur.

Irritable bowel syndrome

Where this co-exists, and conditions such as coeliac disease have been excluded, this should be managed with relief of specific symptoms along with the possibility of trying an exclusion diet to see if there is intolerance to any specific food groups.

Sleep disturbance

Self-help strategies, such as trying to regulate times of going to bed and getting up, relaxing rather than sleeping during the day, and controlling noise, light and temperature in the bedroom, should be discussed. A low dose of amitriptyline may again be helpful, and where someone has difficulty in initiating sleep a course of a short-acting hypnotic may be worth trying (Moldofsky, 2002). Some people with ME/CFS, who have more severe sleep disturbances, claim that melatonin has been helpful, although there is only limited evidence to support this (Van Heukelom et al, 2006).

Depression

Clinical depression, where it occurs, must be taken seriously. For those with mild to moderate depression the options

include cognitive therapy, antidepressant medication or St John's Wort. The choice of antidepressant medication will need to take account of the type of depression, the presence of symptoms such as pain or sleep disturbance, and any drug side-effects which may exacerbate existing ME/CFS symptoms. Suicidal intentions, especially where these co-exist with social isolation, poor symptom control, financial or relationship difficulties, probably indicate the need for specialist referral.

Non-pharmacological management

Energy management: pacing and graded exercise therapy

The most important aspect of management is achieving the right balance between activity and rest, in relation to both physical and mental activities. Finding the right balance will depend on the stage and severity of the illness as well as the degree of variability of symptoms.

Feedback from patients to the CMO report indicated that over 90% found an approach known as pacing, to be the most helpful. In practice, this means finding a level of activity at which patients feel comfortable. Physical and mental activity can then be gradually increased and interspaced with periods of rest and relaxation, but always keeping within individual limitations.

Graded exercise therapy, which has demonstrated some benefits in some mobile patients in clinical trials (Fulcher and White, 1997; Wearden, et al 1998), was reported as only being helpful by 35% in patient feedback with 50% saying that it had made them worse.

Any form of activity programme must therefore be planned with care and the informed consent of the patient (Shepherd, 2001). And from the medico-legal point of view, health professionals who prescribe exercise programmes must do so with just as much caution as would be taken with medication.

There is some limited evidence to suggest that supplements such as carnitine (Vermeulen et al, 2004) and nicotinamide adenine dinucleotide (Forsyth et al, 1999) may be of value in reducing physical fatigue.

Nutrition, vitamins, minerals and supplements

A large amount of sometimes confusing and conflicting information about the value of changes in diet and the use of various supplements is widely available in self-help books and on the internet. However, there is very little evidence to support most of these claims and adding further lifestyle restrictions may cause more harm than good.

Eating a healthy balanced diet, identifying any food intolerance through reputable methods, and maintaining a good fluid intake (especially if postural hypotension is present) are all common sense advice. There is no need to recommend expensive vitamin or mineral supplements and the use of megadose products should be avoided.

Psychological therapies

Cognitive behaviour therapy (CBT) is sometimes advocated as a treatment for ME/CFS but as with graded exercise the feedback from patients to the CMO report did not

match the results obtained in clinical trials (Deale, et al 2001; Prins, et al 2001). There is a wide variety of CBT on offer with some therapists basing their programmes on the theory that ME/CFS is perpetuated by abnormal illness beliefs and behaviour whereas for others it is principally about practical ways of coping with key aspects of the illness such as activity, pain and sleep disturbance. CBT may be helpful for people who are having difficulty with developing appropriate self-help strategies or where there are co-existent psychiatric problems or psychosocial distress. As with activity management, any programme must be properly discussed with the patient and based on informed consent.

Alternative and complementary therapies

Although patients often report that alternative and complementary therapies have been helpful, others are persuaded to spend large sums of money on products and services which are dubious at best and fraudulent at worst (Campbell, 1997). Very few of the popular approaches have been subjected to properly controlled clinical trials in ME/CFS, homeopathy being an exception (Weatherley-Jones, et al 2004), but they may be worth a try, especially where someone has faith in what they are doing and they are using a reputable practitioner. Acupuncture, for example may be of help in relieving pain and headaches. There is no evidence to indicate that treatments involving anti-candida programmes are of any value.

Prognosis

As with the epidemiology, sound knowledge about prognosis is limited by the use of different definitions and by a shortage of good quality studies.

Research findings, as reviewed in the CMO report, indicate that:

- Prognosis is extremely variable
- Most patients will improve to some degree, often over quite a long period of time, but only a small minority fully recover and return to previous levels of health and functioning
- Many patients follow a fluctuating course with relapses and periods of relative remission. Overall, they tend to stabilize at a much lower level of functioning compared to when they were well.
- A significant minority become severely and permanently disabled
- Progressive deterioration is unusual and calls for a full clinical review in case another condition has not been recognized
- Children and adolescents have a much better prognosis than adults.

The length of time that people have ME/CFS differs greatly. In some, the illness may resolve within a period of two to three years whereas others remain ill for decades. And where the illness has lasted for more than 5 years, full recovery is unusual.

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Further information and advice

The ME Association is a registered charity that provides information and support to people with ME/CFS as well as funding research. ME Connect is a telephone helpline service manned by trained volunteers. Contact the MEA at:

The ME Association
 4 Top Angel,
 Buckingham
 MK18 1TH
 Telephone helpline numbers: 0870 444 1835 (members); 0870 444 1836 (non-members).
 Website: www.meassociation.org.uk

'Living with ME' (Vermilion, 1999) is a self-help paperback guide written by Dr Charles Shepherd.

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KEY POINTS

- ME/CFS is recognized by the Department of Health as a genuine and disabling illness.
- ME, CFS and PVFS are classified by the World Health Organization as neurological disorders.
- Up to 250 000 people in the UK have ME/CFS – including some children and adolescents.
- Under the umbrella of ME/CFS are patients with a variety of clinical presentations and responses to treatment.
- Abnormalities in endocrine and immune system function, gene expression and neurological function have been identified.
- Management should be multidisciplinary and may involve a combination of drug treatments, self-help strategies and complementary approaches.
- Prognosis is variable and although many patients improve over a period of time, very few return to normal levels of health and functioning.