



MANAGEMENT FILE

by DR CHARLES SHEPHERD, our medical adviser

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The nature of fatigue in ME/CFS

FATIGUE AND FATIGUABILITY IN ME/CFS

The key features of ME/CFS fatigue are:

- New and definite onset, often following an acute infection – in other words the fatigue part of ME/CFS has not been a lifelong problem that has progressively become worse over time.
- Affects both physical and mental functioning – ie memory, concentration, information-processing
- Induced and exacerbated by physical activity.
- Often made worse by mental/cognitive activity.
- Results in an on-going inability to sustain physical and mental activities that could previously be achieved without any problem.
- Causes post-exertional malaise and flu-like symptoms after activity has ceased.
- Over-exertion beyond normally tolerated limits has a delayed impact which may be felt later in the day or the following day. This is then followed by a slow recovery period in physical and mental functioning. This may persist for days or weeks.
- Made worse by alcohol, standing, stress and temperature extremes.
- Associated with unrefreshing sleep.
- May come with muscle pain.

WHAT IS FATIGUE?

Everyone gets fatigued or tired at times – it's a perfectly normal part of human life. And people will describe their fatigue in many different ways.

Research into the subject of fatigue indicates that around 10% of the population have some degree of regular fatigue or tiredness. In fact, fatigue is a significant symptom in a quarter of all general practice consultations and it's one of the main problems in about 6% of GP consultations. But there are different types of mental and physical fatigue, and the unique type of fatigue described by people with ME/CFS is a key diagnostic feature of this illness.

So it's important to define what we mean by fatigue and fatiguability in ME/CFS and the way in which it differs from the chronic fatigue that occurs in a wide range of medical and psychiatric illnesses.

- Causes a significant decrease in ability to take part in all aspects – home, social, work, etc – of daily life.
- Often the most disabling symptom of ME/CFS.

ME/CFS is not the same as the 'healthy fatigue' that occurs after exercise and quickly resolves with rest. Neither is it the same as feeling 'tired all the time', or the lack of motivational fatigue that is found in depression and other psychiatric illnesses.

WHAT CAUSES FATIGUE IN ME/CFS?

The simple answer is that we just do not know.

But the effect is that people with ME/CFS have to function with an 'energy battery' that is smaller in size and less efficient than before they were ill. It's rather like putting a defective battery

into a torch – it shines for a while at low intensity and then quickly fades away. After a period of rest and recharge the torch will work again but only in the same inefficient way. Carry on repeating the exercise and the torch eventually fails completely.

From the scientific point of view it seems likely that a number of different explanations may be interacting to cause this fatigue. They predominantly involve what doctors call central and peripheral fatigue.

Central fatigue refers to fatigue that is caused by a problem in the brain or nervous system – which explains why chronic fatigue can be a very significant symptom in neurological illnesses such as multiple sclerosis (MS), Parkinson's disease, post-polio syndrome and following a head injury.

Although not the same as ME/CFS

fatigue, the fatigue experienced by many people with MS does have important similarities to ME/CFS fatigue (eg being made worse by heat). Similar pathological mechanisms may therefore be involved.

Peripheral fatigue is caused by a problem with the muscle itself. And, with exercise bringing on fatigue in ME/CFS, along with weakness and pain in the muscle, this suggests that there is a peripheral component to ME/CFS fatigue as well – at least in some people.

We also know that chronic fatigue can be a significant symptom in infectious and inflammatory conditions such as HIV, hepatitis C infection and rheumatoid arthritis.

To add this complex picture, common ME/CFS symptoms such as unrefreshing sleep, pain, orthostatic intolerance (= problems and symptoms relating to standing) and depression (where it occurs) will also cause significant levels of fatigue.

WHAT DO WE KNOW FROM RESEARCH INTO ME/CFS FATIGUE?

With a strong possibility that central and peripheral components are both involved in ME/CFS fatigue, researchers have tried to find satisfactory explanations that could lead to effective forms of drug treatment. This research has involved brain scans, muscle biopsies and assessing the function of the autonomic nervous system (which controls heart rate and blood pressure responses).

The good news is that some important clues are starting to emerge. The less good news is that none of these findings has so far led to the development of a drug that can reduce chronic fatigue in its broadest sense.

As far as the brain is concerned, changes in the levels of brain chemical transmitters (eg serotonin), decreased blood flow to the brain stem, and autonomic nervous system dysfunction are all possible explanations.

At a more scientific level, one

attractive hypothesis is that a viral infection is followed by damage to a key part of the brain known as the ascending reticular activating system that includes the brain stem, basal ganglia and hypothalamus.

Research into muscle function in people with ME/CFS has found abnormalities in the way in which energy is produced by the mitochondria (the Duracell batteries within muscle cells) from glycogen and the way in which the waste product lactic acid is removed after exercise (which may cause muscle pain). These are abnormalities that cannot simply be explained by inactivity or deconditioning.

Another possibility is that autonomic nervous system dysfunction may be reducing blood supply and oxygenation of skeletal muscle.

Research into the chronic fatigue that occurs in conditions such as arthritis, cancer, and HIV-AIDS suggests that persisting activation of the immune system, with production of immune chemicals called cytokines (which cause fatigue during acute infections), could well be relevant to ME/CFS as well.

CAN ME/CFS FATIGUE BE TREATED WITH DRUGS?

Various drugs have been used to try and reduce the chronic disabling fatigue that is found in various neurological conditions – in particular MS.

These include:

- **amantadine** - an antiviral drug that also affects the level of the brain chemical transmitters, acetylcholine and dopamine. Amantadine has been shown in some trials to be effective in reducing central fatigue in MS
- **methylphenidate** – an amphetamine-like brain stimulant
- **modafinil** – another central stimulant drug that is an effective form of treatment for narcolepsy, the daytime sleeping disorder
- **injections of vitamin B12** – which most doctors are reluctant to use unless there is sound evidence of vitamin B12 deficiency

These drugs have also been assessed in small clinical trials in ME/CFS but with conflicting or uncertain results. Consequently, they are not normally prescribed for people with ME/CFS.

Where fatigue is caused by a muscle problem, the list of possible drug interventions is much smaller or non-existent – especially when it comes to established muscle diseases such as muscular dystrophy. Despite all the claims for muscle energy supplements, there is no sound evidence that supplements such as carnitine, creatine, co-enzyme Q10, or magnesium are of any real benefit in reducing fatigue in ME/CFS.

Other drugs that have been tried or suggested for ME/CFS fatigue include low doses of hydrocortisone (to correct the lowered level of cortisol that may be present in ME/CFS), thyroxine (which should not be given to people with normal thyroid function tests) and drugs known as cytokine modulators that inhibit cytokine activity.

Antidepressants, while sometimes improving fatigue levels in people with depression, have not been shown to be an effective form of treatment for ME/CFS.

It should also be noted that a number of common drugs – prescription and over-the-counter – can cause fatigue as a side-effect. These include antidepressants, antihistamines (for allergies), beta-blockers (for heart disease), and diuretics (water-losing tablets). So these sort of drugs have to be used with much more care than usual in people with ME/CFS.

SELF-HELP MANAGEMENT

With no effective drug treatment for what is normally the most debilitating symptom in ME/CFS, simple self-help measures remain the most effective forms of management:

Pacing

This refers to balancing rest and activity – both physical and mental – in order to cope with a very significant reduction in both size and efficiency of the human energy battery.

For most people, this means a radical change to the way in which they use up their available physical, mental and emotional energy during the day – especially avoiding any form of over-activity that is going to have to be paid for later.

The bottom line to successful energy management in ME/CFS is establishing a baseline of physical and mental activity which you feel comfortable with on a day-to-day basis. People also need to accept that progress is probably going to be gradual and erratic. To achieve this, it helps to split up the day into small and easily manageable chunks of physical or mental activity which are interspaced with periods of rest and relaxation.

Avoid fatigue-inducers

Try to avoid anything that is going to cause or increase your fatigue levels.

Obvious ones include:

- Alcohol
- Dehydration
- Hot weather
- Heavy or irregular meals
- Stress

So this means:

- Making sure you drink plenty of non-caffeinated fluids, especially during hot weather, is important – especially if you have any orthostatic symptoms. Hot weather often produces a major increase in fatigue levels in ME/CFS – so keep cool with measures such as a fan and light cotton clothing.
- Avoiding heavy meals because they divert blood to the intestines and produce fatigue in healthy people. Stick to small regular meals that contain complex carbohydrates. This should help to maintain a steady level of blood sugar throughout the day.
- Learning how to relax through tapes, relaxation classes or even something like gentle yoga classes – if stress is a factor.

Sort out pain, sleep and orthostatic intolerance

Any kind of sleep disturbance – unrefreshing sleep, erratic sleep – or pain is going to exacerbate fatigue levels. Unfortunately, sleep problems and pain are two very common symptoms of ME/CFS. So it's important to do all you can, with the help of your doctor, to reduce pain levels and get a decent night's sleep. Equally, new research indicates that orthostatic intolerance, and the problems it causes, is strongly linked to the level of fatigue. This is an aspect of ME/CFS that also needs to be addressed.

Help in the home

Work, social and family life require a great deal of physical, mental and emotional energy. While someone who normally spends their day at work should be able to go on sick leave, the same situation cannot always apply to those who are looking after a home and children on a full time basis.

This may mean that people with ME/CFS are left with still trying to cope with domestic tasks while their partners are out at work. So it's important to look at all the practical and financial help that might be available from family, friends, social services (home helps, meals on wheels) and state benefits (eg DLA).

For people who are more severely affected there various disability aids and adaptations that may be appropriate.

Keeping a diary

Keeping a simple daily diary may help you to identify things which either exacerbate or reduce fatigue levels.

CBT and GET

According to the NICE guideline on ME/

CFS, these are the most effective forms of treatment currently available.

Consequently, they are often recommended in the NHS clinics to people with mild to moderate ME/CFS. CBT and GET are also often claimed to be helpful in reducing fatigue levels.

The ME Association feels that the benefits of both CBT (cognitive behaviour therapy) and GET (graded exercise therapy) are being exaggerated and are not supported by evidence collected from patients. The patient evidence collected by the MEA, and contained in our 2010 Management Report, indicates that CBT is ineffective in many instances and GET can make people worse if it is used inappropriately.

FURTHER INFORMATION FROM THE MEA

- ◆ The *MEA Management File on Muscle Energy Supplements* contains detailed information on carnitine, creatine, co-enzyme Q10, etc
- ◆ Section 7:3 of *ME/CFS/PVFS: An Exploration of the Key Clinical Issues* summarises the results of clinical trials into the use of amantadine, hydrocortisone, methylphenidate and modafinil in ME/CFS. It also summarises research findings into various supplements.
- ◆ The practical approach to balancing activity with rest is described in the two MEA information leaflets covering *Energy Management* and *Pacing*.
- ◆ The management of orthostatic intolerance, pain, sleep disturbance and stress are covered in four separate MEA Management Files.

Medical information contained in this leaflet is not intended to be used as a substitute for medical advice or treatment from your own doctor.

The ME Association recommends that you always consult your own doctor or healthcare professional about any specific problem.

We also recommend that any of the medical information provided by The MEA in this leaflet is, where appropriate, shown to and discussed with your doctor.