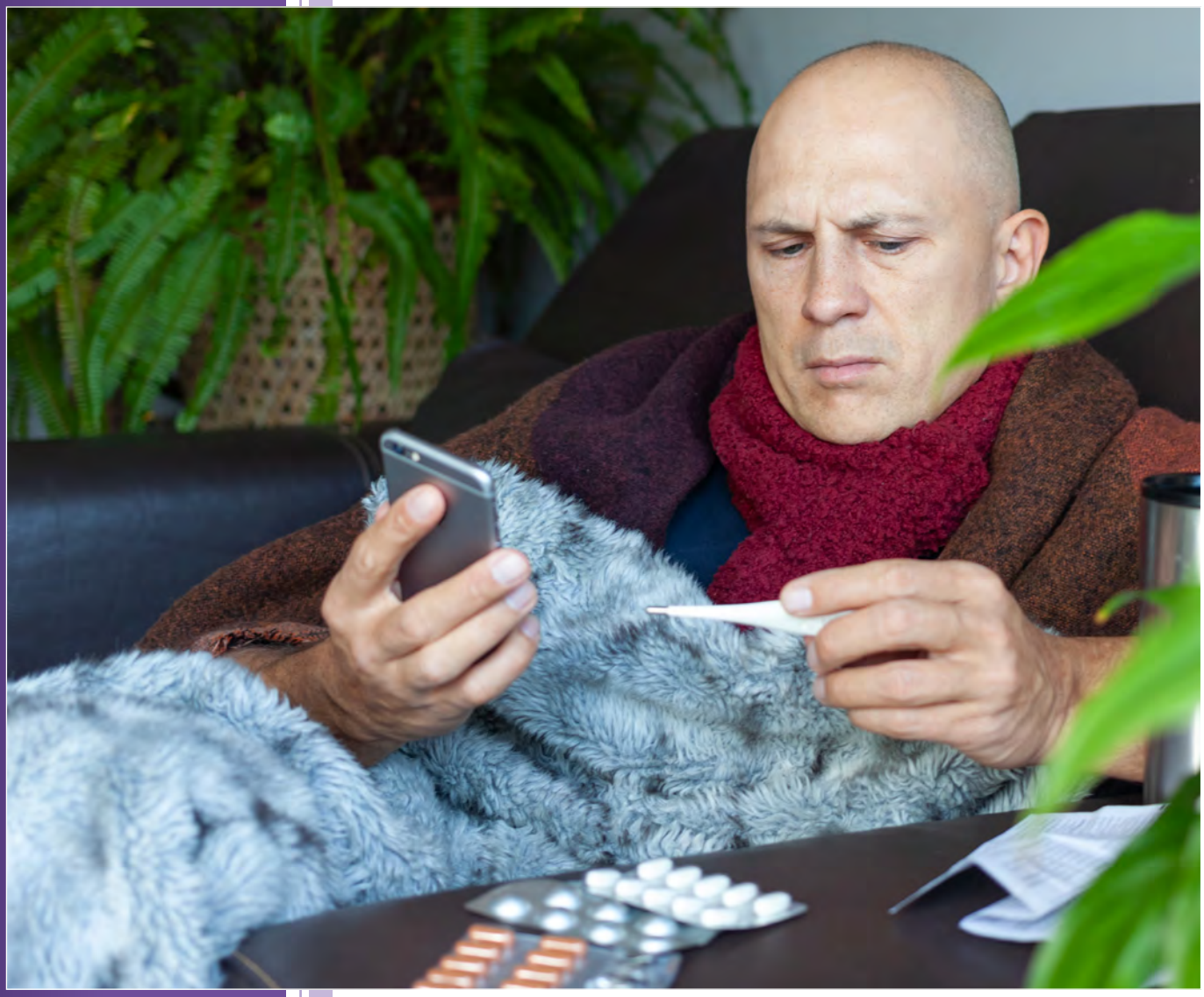
THE ME ASSOCIATION

TREATING ME/CFS

Including research into new and experimental approaches



Including:

How new drugs are assessed and brought into use

Treating ME/CFS

Prescribing new and experimental forms of drug treatment

Looking to the future and the overlaps between ME/CFS and Long Covid

APRIL 2024

Treating ME/CFS was written by **Dr Charles Shepherd, Trustee and Hon. Medical Adviser to The ME Association.**

DISCLAIMER

We recommend that the medical information in this leaflet is discussed with your doctor. It is not intended to be a substitute for personalised medical advice or treatment. You should consult your doctor whenever a new symptom arises, or an existing symptom worsens. It is important to obtain medical advice that considers other causes and possible treatments. Do not assume that new or worsened symptoms are solely because of ME/CFS or Long Covid.

TREATING ME/CFS: Including research into new and experimental approaches

CONTENTS

Significant abnormalities have now been identified involving the role of infection, immune system responses, the nervous system, muscle and mitochondrial function, and hormonal control.

INTRODUCTION

Drugs and other interventions can be used in three different ways when it comes to treating almost any illness.

First is to cure the condition – as when an antibiotic is prescribed to quickly eradicate an acute infection.

Second is to try and modify what is called the underlying disease process. Good examples here are the use of powerful anti-inflammatory drugs in rheumatoid arthritis, or antidepressants to treat chemical imbalances in depression.

Third is to relieve specific symptoms such as pain or sleep disturbance – something that is normally worth trying in almost any disease, even though the underlying cause of the symptom or disease may not be fully understood.

When it comes to using drugs to treat ME/CFS, there is no curative treatment at present and none on the immediate horizon. The prospect of having a curative treatment will almost certainly have to wait until research provides more substantial information as to what is going wrong in this illness.

However, significant abnormalities have now been identified involving the role of infection, immune-system responses, the nervous system, muscle and mitochondrial function, and hormonal control.

These are the type of abnormalities that can be used as the basis for considering and investigating treatments that are aimed at modifying the underlying disease process. This can involve the development of totally new drugs that are aimed at a specific abnormality (which is extremely expensive to do) or finding new uses for existing drugs - a process known as repurposing. A good example of drug repurposing is the discovery that gabapentin, a drug that is normally used to treat epilepsy, can also be very useful for treating some types of moderate to severe pain.

So until we gain a much clearer picture about the possible role of disease-modifying drugs in ME/CFS, the main use of drug treatments is going to be for the relief of common symptoms such as pain, irritable bowel and gastric symptoms, sleep disturbance and PoTS (postural orthostatic tachycardia syndrome).

Drugs and other approaches that provide symptomatic relief are already covered in separate MEA information leaflets and will not be reviewed in any detail here.

The leaflets can be **downloaded here**.

INTRODUCTION

So what sort of treatments for ME/CFS have already been assessed? How might new drugs be assessed and brought into use? And what sort of completely new treatments might be worth investigating?

HOW NEW DRUGS ARE ASSESSED AND BROUGHT INTO USE

Clinical trials involving drug treatments are normally carried out in what is termed a randomised, double-blind, and placebo-controlled manner.

Before a drug can be licensed for use in a specific condition like ME/CFS, and then recommended for use by NICE, there must be sound and consistent evidence of benefit and safety from a number of 'gold standard' clinical trials.

Clinical trials involving drug treatments are normally carried out in what is termed a randomised, double-blind, and placebo-controlled manner.

In simple terms this means that the participants are divided into two separate groups. Each group is then given either a placebo or the active drug. Neither group knows which drug they are receiving, and nor do the organisers of the trial. The participants are then assessed over a period of time to record side-effects and to what extent those taking the active drug respond in comparison to those taking the placebo.

Drug trials are extremely costly to carry out – so the assessment process often starts with small numbers and pilot studies. If the initial results are encouraging, the process progresses through larger trials into what are called phase-2 and 3- clinical trials – the so-called 'gold standard' of assessment for clinical trials.

If one or more phase-3 clinical trials can demonstrate convincing efficacy and safety, the drug will almost certainly be given what is called a product licence and made available on the NHS. However, as we know from the ME/CFS Rituximab clinical trial in Norway, there were very encouraging signs based on early observations and from small clinical trials. But, when a large phase-3 clinical trial was conducted on Rituximab, the results failed to confirm that it was an effective treatment for ME/CFS.

HOW NEW DRUGS ARE ASSESSED BROUGHT INTO USE

Clinical trials are clearly important but one of the problems is that a lot of clinical and pathological sub-groups come under the current umbrella description of ME/CFS. So a one-size-fits-all approach to treatment is never likely to work.

Consequently, clinical trial analysis must also allow for the fact that there may be just a small sub-group that responds with a particular symptom profile, or an immune system or muscle abnormality - but there is no clinical response from most of the people involved.

Clinical trials are clearly important but one of the problems with ME/CFS is that we have a lot of clinical and pathological sub-groups under the current umbrella.

So a one-size-fits-all approach to treatment is never likely to work.

CAN WE TREAT ME/CFS?

What follows is an A-Z summary of all the treatments that have been assessed, are being assessed or could be assessed to see if they could be safe and effective treatments for ME/CFS. I have included possible drug therapies, supplements, vitamins and non-drug approaches.

Most of the clinical trials that are referred to here are summarised in more detail, along with relevant references, in the Treatment section of the MEA Clinical and Research Guide (the MEA 'Purple Book')

Patient evidence - gained from very detailed surveys of non-drug approaches to management - indicates that pacing is the safest and most effective form of activity management.

Activity and energy management

In our current state of knowledge, activity management remains the most important aspect of managing ME/CFS. This balances physical, mental and emotional activity with rest in a manner that is appropriate and within a person's individual limitations.

Patient evidence – gained from very detailed surveys of non-drug approaches to management - indicates that pacing is the safest and most effective form of activity management.

Unfortunately, we do not have results from any high-quality clinical trials that have assessed the benefits of pacing – although several research studies have advocated its use.

Conversely, we know that graded exercise treatment (GET) has made their condition worse in over 50% of people with ME/CFS who were advised to use GET. And, although the use of GET was supported by some early clinical trials, the large and most influential PACE Trial has been heavily criticised and discredited. The MAGENTA trial, which assessed GET in children, also found no benefit. Consequently, graded exercise treatment (GET) is no longer recommended by NICE and should not be prescribed by health professionals.

So we do now require good-quality research studies to investigate the role of activity and energy management in ME/CFS in a way that takes account of stage, severity and fluctuation of symptoms. As with any clinical trial, this also needs to include objective outcome measures - including the use of Actometers to measure energy expenditure, walking distance and also information regarding benefit and employment status.

Health professionals would then be in a better position to provide sound guidance on activity management.

CAN WE TREAT ME/CFS?

■ The MEA has a new information booklet covering all aspects of activity and energy management and Pacing:

Pacing: Activity and Energy Management

Antidepressants

Low doses of antidepressants – in particular sedating tricyclic drugs such as amitriptyline – can sometimes be very useful in relieving pain, improving disrupted sleep patterns, and helping with sensory symptoms.

Low doses of antidepressants – in particular sedating tricyclic drugs such as amitriptyline – can sometimes be very useful in relieving pain, improving disrupted sleep patterns, and helping with sensory symptoms. Higher doses over a prolonged period may be necessary when someone with ME/CFS also develops true clinical depression.

However, there is no evidence from clinical trials to indicate that any of the antidepressant drugs that are currently in use are an effective form of treatment for ME/CFS. In other words, they have no effect on the underlying disease process and do not restore health and function.

One possible exception may be the use of antidepressant drugs known as SSRIs (selective serotonin reuptake inhibitors) which increase the level of serotonin in the brain. This is because there is some research evidence to indicate that a disturbance involving a brain chemical transmitter called serotonin is involved in causing central (brain) fatigue.

A large clinical trial of fluoxetine (Prozac) has failed to demonstrate any benefit in ME/CFS. However, there is some anecdotal evidence to indicate that some people with ME/CFS appear to gain benefit from an SSRI called sertraline (Lustral). This came from a small, uncontrolled trial carried out in Glasgow by Professor Peter Behan. But we also know that a significant proportion of people with ME/CFS are very sensitive to SSRI medication and feel worse as a result.

In other words, a sub-group of people with ME/CFS may have low levels of serotonin and could therefore benefit from an SSRI whereas others have normal, or elevated levels of serotonin, and are therefore very sensitive to this type of medication. So the use of any SSRI drug, even at a very low dose, has to be done very cautiously.

■ The MEA has a leaflet covering all aspects of depression and the use of antidepressant drugs in ME/CFS:

CAN WE TREAT ME/CFS?

Depression – Antidepressants & Other Treatment Options

Antiviral drugs

Viral (and sometimes bacterial) infections are very common trigger factors in the development of ME/CFS. A debate continues as to whether some of these triggering infections (enteroviral infections, in particular) may then persist at a cellular level – as happens in the case of HIV, hepatitis C infection and possibly Long Covid – and play a role in causing ME/CFS symptoms. However, almost all the current evidence indicates that persisting viral infection is not involved in the underlying disease process.

Two antiviral drugs have been assessed so far in clinical trials in people with ME/CFS.

There is however limited evidence to indicate that some types of dormant viral infection – herpes viruses such as Epstein Barr Virus (EBV) and Human Herpes Virus (HHV-6) in particular – become reactivated in ME/CFS, as they can in Long Covid.

Two antiviral drugs have been assessed so far in clinical trials in people with ME/CFS.

One small clinical trial found no benefit from using **acyclovir** – a drug that is very effective at treating herpes virus infections. A small trial in America carried out by Professor Jose Montoya's group at Stanford, who used **valganciclovir** (trade name: **Valcyte**), indicates that this antiviral drug could be of value in carefully selected patients with clinical and laboratory evidence of reactivation of HHV-6 and EBV infection.

The ME Association followed the Montoya research up and met with representatives of Roche Pharmaceuticals (who manufacture Valcyte) to discuss the possibility of a UK trial. Unfortunately, the pharmaceutical company decided not to pursue this line of research.

In the case of Long Covid, where there is some evidence of persisting viral infection, clinical trials are being carried out to assess the use of an antiviral drug called **Paxlovid**.

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Vagal nerve stimulation is a treatment that is being used in a number of conditions, including epilepsy. Several clinical trials have been conducted into its use in both ME/CFS and Long Covid.

Image: Mikedanroz (Wikimedia Commons)

Autonomic nervous system dysfunction (dysautonomia) and cardiac function

The autonomic nervous system consists of two groups of nerves – the parasympathetic and sympathetic – that play a key role in regulating heart rate and blood pressure. There is evidence of significant autonomic nervous system dysfunction in both ME/CFS and Long Covid, including orthostatic intolerance (an inability or difficulty to remain in an upright position) and a condition called PoTS (postural orthostatic tachycardia syndrome) where there is a significant increase in heart rate when moving from lying to standing.

Autonomic nervous system dysfunction helps to explain why a significant proportion of people with ME/CFS have abnormal blood pressure and pulse-rate responses when they stand up and consequently feel faint. These findings have resulted in the assessment of drugs such as **beta blockers**, **fludrocortisone**, **ivabradine**, **Midodrine** and **pyridostigmine** that can help to modify the effects of autonomic dysfunction on cardiovascular responses to changes in posture.

The vagus nerve is a very important part of the autonomic nervous system and sends regulatory messages to the heart, lungs and gut. Vagal nerve stimulation is a treatment that is being used in a number of conditions, including epilepsy. Several clinical trials have been conducted into its use in both ME/CFS and Long Covid. 'Physios for ME' will shortly be conducting a UK trial into the use of transcutaneous* vagal nerve stimulation.

* This is a non invasive method of stimulating the vagus nerve via electrodes which are attached to the ear.

Reference: Physios for ME

Other research into cardiac (heart) function in ME/CFS has produced findings that may relate to both symptoms and treatment. Of particular interest here is low blood volume and the possibility that intravenous (by drip) saline therapy could be of benefit to some people with ME/CFS.

Anecdotal reports from America – where saline therapy is sometimes prescribed – indicate that it can be helpful. However, inappropriate fluid expansion can also be dangerous. So this type of fluid replacement must be regarded as experimental at present and should only be considered where an experienced doctor is involved. It cannot be recommended more widely until clinical trials have confirmed both efficacy and safety.

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■ The ME Association has information leaflets covering the diagnosis and management of Orthostatic Intolerance and PoTS. This includes information on the various drug treatments that are sometimes prescribed for people with PoTS:

Orthostatic Intolerance

Postural Orthostatic Tachycardia Syndrome (PoTS)

Cognitive behaviour therapy (CBT)

In the 2021 Nice Guideline on ME/CFS, CBT is a form of management that is recommended as an option that can be considered. But this is controversial because CBT may still be recommended on the basis that it can treat ME/CFS through altering what are called abnormal illness beliefs and behaviours. This is not the type of CBT that is recommended by NICE.

A more practical form of CBT may help people cope with the consequences of having a long-term physical illness – as can be the case in a number of other conditions.

CBT may still be recommended on the basis that it can treat ME/CFS through altering what are called abnormal illness beliefs and behaviours. This is not the type of CBT that is recommended by NICE.

Patient surveys carried out by the ME Association indicate that the vast majority of people do not find that CBT is an effective form of treatment for their ME/CFS but it may help some people to cope with emotional and psychological effects of having a long-term condition.

■ The ME Association has an information leaflet covering the use of CBT in ME/CFS:

Cognitive Behavioural Therapy (CBT)

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At present, there is no sound evidence of thyroid gland dysfunction (i.e. hypothyroidism) in ME/CFS, although one research study has reported on an unusual aspect of thyroid dysfunction where ME/CFS patients had relatively higher levels of another thyroid hormone called reverse T3 or rT3.

Hormones

Although research has revealed that a number of hormonal abnormalities occur in ME/CFS, evidence from clinical trials means that the use of hormonal replacement remains very speculative and, in some cases, potentially dangerous.

One hormonal abnormality that has attracted considerable attention in both ME/CFS and Long Covid is hypocortisolaemia. This refers to a slightly lowered level of cortisol in the blood. Cortisol is a vital hormone that is produced by the adrenal glands but whose output is under the control of the hypothalamus and pituitary glands in the brain.

The explanation for this abnormality remains uncertain and any form of cortisone supplementation therefore has to be managed with great caution. This is because steroids, including cortisone, are drugs that can cause unpleasant side-effects. And, once started, they may then be difficult to discontinue due to suppression of the natural output of the hormone from the adrenal glands. Two clinical trials have assessed the value of using very low doses of **hydrocortisone**. The results were not sufficiently conclusive to recommend supplementation.

A report in The Lancet indicated that the use of an **oestradiol patch and cyclical progestagen** may be of value in women who have a premenstrual exacerbation of symptoms along with low levels of plasma oestradiol (a naturally-occurring oestrogen).

At present, there is no sound evidence of thyroid gland dysfunction (i.e. hypothyroidism) in ME/CFS, although one research study has reported on an unusual aspect of thyroid dysfunction where ME/CFS patients had relatively higher levels of another thyroid hormone called reverse T3 or rT3. This appeared to be due to a shift in hormone production, where the body preferred to convert T4 to rT3 instead of producing T3. The low T3 levels found in ME/CFS patients coupled with this switchover to rT3 could mean that T3 levels are reduced in body tissues.

Some doctors are willing to prescribe **thyroid supplements** to people with ME/CFS. However, the use of thyroid supplements in people with normal thyroid function tests has serious dangers and cannot be recommended in our current state of knowledge, especially in people who may also have a degree of hypocortisolaemia.

Melatonin is a naturally occurring hormone that is produced by the pineal gland in the brain. It helps to keep the 'body clock' functioning normally, especially in relation to the induction of sleep at night. We

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know from patient surveys that a significant number of people with ME/CFS successfully use melatonin to help sleep disturbances, especially when this is more severe. The NICE guideline on ME/CFS makes no recommendation for using melatonin in ME/CFS. Consequently, most people find that doctors are unwilling to prescribe melatonin on the NHS and have to purchase it via the internet – which is not a safe and reliable source for this type of treatment unless done through an internet pharmacy.

The use of **dehydroepiandrosterone (DHEA) supplements** is unwise. This is because there is no sound evidence of DHEA deficiency in ME/CFS and this hormone has been linked to cancer.

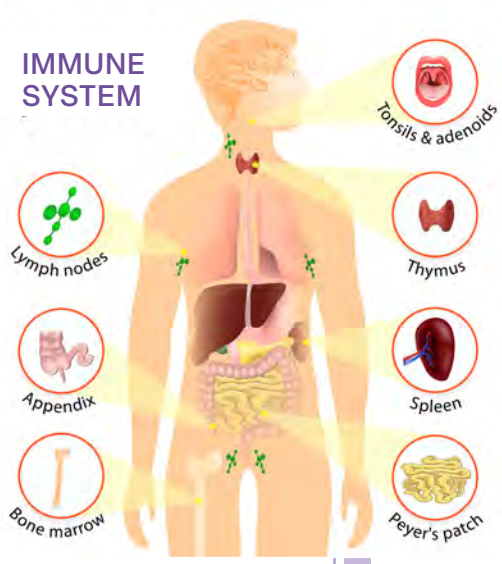
■ The MEA has information leaflets covering the Management of the Menopause and research into female hormone status in ME/CFS, Thyroid Function and Thyroid Function Tests, and Sleep – the latter includes information on Circadin (prescription-only melatonin):

Menopause – Female Hormones & HRT

Thyroid Disease and ME/CFS

Sleep Management

Various markers of immune system dysfunction can be found in people with both ME/CFS and Long Covid.



Drugs that can modify the immune system response

Various markers of immune-system dysfunction can be found in people with both ME/CFS and Long Covid. These include raised levels of immune-system chemicals called cytokines, abnormalities in natural killer (NK) cell function, B- and T-cell function, and the production of autoantibodies – potentially harmful antibodies that are directed against the body's own tissues, rather than infections and allergens.

A plausible hypothesis for this type of immune-system dysfunction involves a triggering infection that results in an on-going immune system activation and over-production of cytokines – chemicals that cause people to feel unwell when they have any type of infective illness.

A considerable number of immunological treatments have therefore been assessed as possible forms of treatment for ME/CFS. The list includes Ampligen, immunoglobulin (IgG) injections, alpha interferon, inosine pranobex (trade name: Imunovir), rituximab, staphylococcus toxoid vaccine and tumour necrosis factor inhibitors.

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Ampligen is a very expensive American drug that is claimed to have both antiviral and immunomodulatory properties. Ampligen has not been approved for use in ME/CFS by the Food and Drug Administration – the US drug regulator – and is unlikely to be made available in the UK until this approval has been given.

There have been several small trials assessing the value of **immunoglobulin injections** in ME/CFS with conflicting results. A clinical trial involving Long Covid is currently taking place.

Inosine pranobex/Imunovir is an immunomodulatory drug that has a potential to enhance natural killer cell activity. Anecdotal reports indicate that some people find this drug to be helpful and some specialists are willing to prescribe it. Most doctors are generally unwilling to do so because the NICE guideline does not recommend the use of any immunomodulatory drugs in ME/CFS.

There have been several small trials assessing the value of immunoglobulin injections in ME/CFS with conflicting results. A clinical trial involving Long Covid is currently taking place.

Rituximab (a monoclonal anti-CD20 antibody) is an anti-cancer drug that causes depletion of B lymphoctye cells in the body. It was reported to be beneficial in a preliminary trial carried out in Norway but a further large phase-3 trial failed to confirm these findings.

Tumour necrosis factor/cytokine inhibitors are widely used in more severe rheumatoid arthritis to dampen down inflammation in the joints. Preliminary results from a pilot study involving six ME/CFS patients indicated that one drug in this group (**etanercept**) could be of benefit but needs to be tested in larger clinical trials. Another drug in this group called **anakinra** has also been assessed in a clinical trial in The Netherlands but there were no significant benefits.

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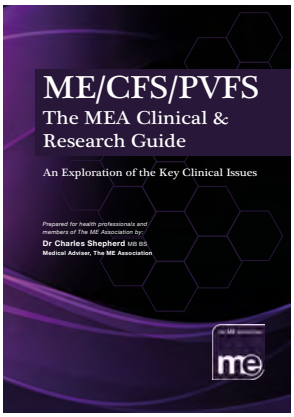

ME Association ME/CFS/PVFS Clinical & Research Guide

The most comprehensive, evidence-based summary of ME/CFS/PVFS currently available. It contains everything that health professionals, patients, and the people who care for them need to know about this devastating neurological disease.

Purchase The 2022 Clinical & Research Guide here

Muscle energy supplements

Activity-induced muscle fatigue is the key clinical feature of ME/CFS and there is now sound research evidence in both ME/CFS and Long Covid of biochemical abnormalities in the way that the mitochondria – a core 'battery like' component of muscle cells – produce energy in response to physical exertion. These mitochondrial abnormalities cannot be explained by simple deconditioning or inactivity.

Not surprisingly, this finding has led to the production of various muscle energy supplements, many of which are promoted by commercial supplement manufacturers, as possible forms of treatment.

Examples include **carnitine**, **co-enzyme Q10**, **creatine**, **magnesium**, **NADH (nicotinamide adenine dinucleotide)** and **D-ribose**. Some of these supplements have been assessed in small clinical trials but the results are not impressive.

Based on this very weak research evidence, the only supplement that may be worth trying is carnitine. These clinical trials are summarised in more detail, and referenced, in the MEA's **The 2022 Clinical & Research Guide** (The 'Purple Book').

AXA1125 is an experimental drug containing various amino acids that has been developed by an American company. It may improve mitochondrial function and energy production and has been used to treat non-alcoholic fatty liver disease. AXA1125 is now being assessed in clinical trials by researchers in Oxford as a possible form of treatment for Long Covid.

A number of commercial supplements, often containing multiple ingredients, have been promoted to people with ME/CFS on the basis that they can improve mitochondrial function and/or energy production. There is no evidence from clinical trials that these products are effective. The ME Association does not therefore endorse their use.

■ The MEA has an information leaflet covering the four most common muscle energy supplements:

Muscle Energy Supplements

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Nervous system stimulation

A case report and a small trial have assessed the use of **modafinil** (brand name: **Provigil**). Modafinil is a drug that stimulates the central nervous system and so helps to reduce daytime sleepiness and improve mental alertness in narcolepsy and sleep apnoea. One case report described how modafinil was of considerable benefit in one person with severe ME/CFS. However, a more recent placebo-controlled trial involving 14 patients queried its value.

Methylphenidate, another type of nervous system stimulant, has also been assessed in a clinical trial but cannot be recommended for individual use. The 'drugs bible' for doctors – the British National Formulary – does not recommend the use of central nervous system stimulants for patients with fatigue.

Vitamin supplements are probably unnecessary – unless there are significant dietary restrictions.

Vitamins, minerals, probiotics and supplements

There is no sound evidence of any significant deficiency of any of the main common vitamins, including vitamin B12, in ME/CFS.

Uncertainties and controversy surround the use of **vitamin B12** in ME/CFS. The NICE guideline does not recommend the use of any vitamin treatments but some doctors are willing to try vitamin B12. This is not on the basis that people with ME/CFS are deficient in vitamin B12, or any sound research evidence. It is based on the theory that vitamin B12 supplementation could help to improve nervous system repair. Before considering this form of treatment, it is important to make sure there is no evidence of pernicious anaemia being present. The ME Association has been looking at the possibility of funding a clinical trial to assess the use of vitamin B12 injections.

This lack of evidence means that vitamin supplements are probably unnecessary – unless there are significant dietary restrictions. Taking large doses of over-the-counter single **vitamin supplements** can also cause serious side-effects and is not recommended.

One important exception is that some people with ME/CFS are at risk of developing Vitamin D deficiency – especially those who are housebound and/or on restrictive diets. So **vitamin D supplementation** should be discussed with a doctor if you are at increased risk of vitamin D deficiency due to a lack of sunlight on the skin (the main way in which

CAN WE TREAT ME/CFS?

Eicosapentaenoic Acid (EPA) appears to be a safe supplement to use and it may just be worth a try for a month or two – if you can afford the cost.

vitamin D is produced). People with moderate or severe ME/CFS, and who are mainly or totally housebound, are at particular risk and should probably take a supplement. Vitamin D level can be checked with a simple blood test.

There are theoretical reasons why treatment with **essential fatty acids (such as Efamol Marine) and Eicosapentaenoic Acid (EPA)** could be of benefit in ME/CFS. The results from clinical trials are conflicting in the case of Evening Primrose Oil (EPO). For EPA a small clinical trial described some benefit, especially for improving cognitive function. EPA appears to be a safe supplement to use and it may just be worth a try for a month or two – if you can afford the cost.

Folic acid deficiency in ME/CFS has been reported – so folic acid supplementation should always be discussed with a doctor, especially by anyone who is intending to get pregnant, or is pregnant.

Probiotics can be helpful in some cases of irritable bowel syndrome where this co-exists with ME/CFS and there is some preliminary evidence from clinical trials in Long Covid that pre- and probiotics could be of benefit. If research into the possible role of the microbiome (the viruses and bacteria that inhabit the gut) identifies clear abnormalities in Long Covid or ME/CFS, the use of specific probiotics could become more widespread.

■ The MEA has information leaflets on EPO and EPA, Vitamin supplements, Vitamin B12 and Vitamin D. The information leaflet on Irritable Bowel Syndrome symptoms covers the use of probiotics and dietary modification:

Vitamins and Supplements

Stomach & Irritable Bowel Symptoms

CAN WE TREAT ME/CFS?

We received reports that a small number of people with ME/CFS in the UK and overseas are apparently being prescribed or are obtaining an antipsychotic drug called Aripiprazole (trade name = Abilify) and using it as a treatment for ME/CFS.

The ME Association does not recommend that anyone with ME/CFS attempts to obtain or to take this drug, even in small doses, until such time as more appropriate research – double-blind placebo controlled clinical trials – can better determine safety and efficacy.

Read the
MEA WARNING

Other drugs

Other speculative forms of drug treatment that are being assessed include aripiprazole, cyclophosphamide, drugs that slow down memory loss in dementia/Alzheimer's disease, low-dose naltrexone (an opiate/morphine antagonist) and Nimodipine (a drug that may help to increase blood supply to the brain).

Aripiprazole (brand name Abilify): This is a powerful antipsychotic drug that is being assessed in America on the basis that it could have immunomodulatory and anti-inflammatory properties. No proper clinical trials have been carried out and the MEA has issued a warning that this is not a treatment that should be used until we have robust information on both efficacy and safety.

MEA WARNING

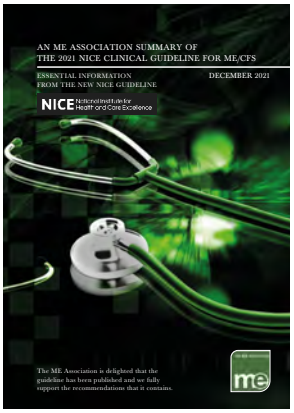
Cyclophosphamide: Researchers in Norway, who carried out the Rituximab trial, have also been carrying out a trial involving the use of cyclophosphamide. This is a drug with powerful anti-inflammatory effects and is used in conditions like rheumatoid arthritis when other drugs fail to work. But it can also cause serious side-effects.

Dementia drugs: Results from a clinical trial published in 2004 found no benefit from the use of **galantamine hydrobromide** – a selective acetyl cholinesterase inhibitor that has been used to treat cognitive decline in people with dementia. A clinical trial involving the use of **donepezil** (brand name: **Aricept**), which is another drug that is normally used to reduce memory decline in dementia, failed to produce any significant improvement in cognitive dysfunction in people with Long Covid.

Low dose naltrexone: One small clinical trial has indicated that **low-dose naltrexone (LDN)** could be of benefit in fibromyalgia – a condition involving widespread pain that can co-exist with ME/CFS. This is on the basis that a low-dose of naltrexone may have immunomodulatory and anti-inflammatory effects. There are now several clinical trials taking place into the use of LDN for Long Covid and ME/CFS.

Nimodipine: This is a calcium channel-blocking drug that dilates blood vessels and and increases blood flow, possibly to the brain. There are anecdotal reports of benefit but no results from clinical trials to assess efficacy and safety.

This booklet is recommended reading. It lets you know what to expect from the NHS and social care services with regard to symptom recognition, diagnosis, management, referral, and ongoing care and support.



NICE Guideline on ME/CFS: An ME Association Summary

PRESCRIBING NEW AND EXPERIMENTAL FROMS OF DRUG TREATMENT

All the supplements referred to in this publication can be obtained from pharmacies, health food stores and internet suppliers.

The drug treatments can only be obtained on prescription. However, most doctors are going to be reluctant or unwilling to prescribe drugs they are unfamiliar with and that have not been licensed or approved or recommended for use in a specific illness.

This is mainly because if anything goes wrong as a result of side-effects, a doctor could then be sued by a patient if he/she has been using an unfamiliar drug that has not yet been licensed for the treatment of ME/CFS – even where a patient initially stated that they would take responsibility for any adverse effects.

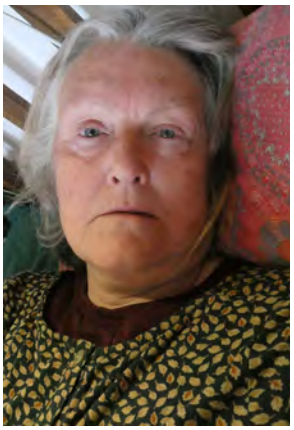
An additional obstacle to using speculative forms of treatment is the fact that the new NICE guideline does not recommend any specific or speculative drug treatments for ME/CFS.

LOOKING TO THE FUTURE AND THE OVERLAPS BETWEEN ME/CFS AND LONG COVID

The huge amount of funding and research interest into the cause and treatment of Long Covid means that in addition to learning more about the cause of post viral disease there is an urgent search for effective forms of treatment for a condition that has many symptoms that overlap with ME/CFS. In fact, around 50% of people with Long Covid meet diagnostic criteria for ME/CFS.

Among the treatments that are now being assessed in clinical trials for Long Covid, and which are also relevant to ME/CFS are antiviral drugs, AXA1125, low dose naltrexone, pre- and probiotics. One very controversial area of treatment involves the theory that small blood clots (microclots) may be present in Long Covid and that treatments such as apheresis (where clots are removed from the blood) or anticoagulant drugs could be an effective form of treatment.

And as we learn more about the underlying disease processes in both Long Covid and ME/CFS, it's possible that we will also be assessing other 'cutting edge' treatments and preventative measures.



The huge amount of funding and research interest into the cause and treatment of Long Covid means that, in addition to learning more about the cause of post viral disease, there is an urgent search for effective forms of treatment for a condition that has many symptoms that overlap with ME/CFS.

LOOKING TO THE FUTURE AND THE OVERLAPS BETWEEN ME/CFS AND LONG COVID

Examples might include:

- Stem cell therapy – which is now being assessed as a way of repairing damaged neurons in conditions like multiple sclerosis and Parkinson's disease.

- Faecal microbiome transplants (FMT) – if research involving the microbiome indicates that there are significant changes in gut microbiology in ME/CFS. A clinical trial of faecal microbiota transplantation has been taking place in Norway and another one is planned to take place at the Quadram Institute in Norwich.

- Vaccination against specific infections, such as Epstein Barr virus/ glandular fever, that are common trigger factors for ME/CFS.

FURTHER INFORMATION

- If you or your doctor require further information, or references to the use of any of these treatments in ME/CFS, these can be found in the treatment and reference sections of the 2022 edition of our clinical and research guide:

ME/CFS/PVFS: An Exploration of the Key Clinical Issues

- Please let us know if you are using any of these experimental and speculative forms of treatment and what effect they are having.

HOW WE CAN HELP

"Thank you for producing such a helpful magazine. The standard is consistently high and each edition is interesting and varied. I need all the help I can get and this magazine is consistently encouraging, realistic, and helpful."

■ **COMMUNITY:** We provide a safe and welcoming community for people affected by ME/CFS and Long Covid who come together and benefit from sharing their experiences. We provide membership, an essential support service, excellent website resources and we host engaging discussions on the most popular social media channels. Knowing that you are not alone can be a great comfort and we are happy to answer your questions and share helpful tips.

■ **MEMBERSHIP:** We put the interests of members at the heart of everything we do. Your subscription means that we can support more people, campaign more effectively and fund more medical research. Members receive the exclusive ME Essential magazine which carries the latest news, medical information, personal stories, and feature articles. **Join us today**.

■ **SUPPORT:** ME Connect is the charity's support and information service. We listen and we understand. We provide a personalised service and we're here when you need us most. We have knowledge and understanding of these medical conditions. To view the ME Connect telephone helpline opening hours please visit: **https://www.meassociation.org.uk/me-connect**

■ **INFORMATION:** We produce reliable and timely information written by topic experts and have the **largest range of free literature covering all aspects of life with ME/CFS and Long Covid**. We can show you how to recognise and manage symptoms, get an accurate diagnosis, a referral to specialists, and to obtain the healthcare that you deserve. We also provide an **e-newsletter** and free access on the website to **Medical Matters** and other relevant information.

■ **RESEARCH:** We fund medical research via the **Ramsay Research Fund** and are especially interested in research that can find diagnostic markers, causes, and treatments. We support the UK ME/CFS Biobank and the Manchester Brain Bank, and have invested over £1m in medical research in the last 10 years.

■ **MEDICAL EDUCATION:** We arrange training for healthcare professionals, offer a medical magazine, ME Medical, and are working with the Government, NHS, Royal Colleges of Medicine, and Local Authorities to implement the recommendations of the 2021 NICE Clinical Guideline on ME/CFS – the successful result of 14 years lobbying and hard work.

"The MEA is doing exactly what it said it would by providing support, actively lobbying for recognition, improvements to health and social care, and funding biomedical research."

HOW WE CAN HELP

■ **LOBBYING:** We campaign to raise awareness and bring about positive change. We believe in collaboration and work with the NHS and social care services, the Department of Health and Social Care, the British Association of Clinicians in ME/CFS (BACME), Forward-ME, the ME Research Collaborative (MERC), DecodeME, the All-Party Parliamentary Group (APPG) on ME, Physios4ME, the Chronic Illness Inclusion project (CII), Hidden Disabilities Sunflower, and Long Covid initiatives.

■ **HEALTH & SOCIAL CARE:** The charity works with healthcare providers to successfully implement the NICE Guideline recommendations on ME/CFS and Long Covid to ensure that everyone receives the very best healthcare, wherever they live in the UK. We want well-trained healthcare professionals providing excellent services because timely intervention can lead to better health outcomes and improved quality of life.

■ **DONATIONS:** In order to help more people and invest in medical research we depend on your generosity. If you feel able to make a donation or want to raise funds in other ways, please get in touch with the fundraising team: fundraising@meassociation.org.uk or you can **make a direct donation via the website.**

WHAT ARE ME/CFS AND LONG COVID?

We answer key questions about these medical conditions and compare similarities and differences. You'll also find the NICE Guideline reproduced in full in an easy-to-use **database**.

MEDICAL MATTERS

Medical Matters is an easy to use online supplement to the more detailed literature. The same topic experts provide answers to commonly asked questions.

NHS REFERRAL SERVICES

If you need to locate an ME/CFS specialist service or Long Covid Clinic then we can help. We have listed all secondary care referral services in an easy-to-use **database**.

THE ME ASSOCIATION

me

ME CONNECT

The Support and Information Service for people affected by ME/CFS/PVFS and Long Covid

Freephone 0808 801 0484

For opening hours visit:
meassociation.org.uk/me-connect

Contact ME Connect
3 WAYS TO GET IN TOUCH:
by phone, email or social media private message

HERE TO LISTEN

We are here to listen, validate and empathise with any issues you might be facing.

VITAL SUPPORT

We are here to help you reach an informed decision.

SAFE ENVIRONMENT

We provide a safe, confidential and understanding environment where you can be heard and understood.

We're here for you!

meconnect@meassociation.org.uk

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