

LONG COVID AND ME/CFS

ARE THEY THE SAME?

MAY 2022



LONG COVID AND ME/CFS - ARE THEY THE SAME?

This is a review of the important clinical and pathological overlaps that occur between Long Covid and ME/CFS (myalgic encephalomyelitis/chronic fatigue syndrome).

The review also explains how what we have learnt about the management of post-viral fatigue, cognitive dysfunction/'brain fog', orthostatic intolerance, postural orthostatic tachycardia syndrome/POTS, pain management and unrefreshing sleep in ME/CFS can also help people with the same symptoms where they occur in Long Covid.

1. BACKGROUND

It is currently estimated that around 10% of people who catch COVID-19 infection are failing to fully recover and have what has been termed Long Covid or the post-COVID-19 syndrome. This is a diagnosis that is normally being made when a person is still symptomatic three months after the onset of an infection that has probably been due to, or confirmed as being due to COVID-19.

At present, there is no diagnostic blood test for either Long Covid or ME/CFS. The method of diagnosis is very similar for both conditions in relation to a three months or more duration of symptoms along with the exclusion of other possible explanations for the symptoms.

The ME Association (MEA) takes the view that Long Covid and ME/CFS are both examples of a serious and debilitating condition that can follow any type of viral infection. And while a wide range of viral infections can trigger ME/CFS, in previous coronavirus infection outbreaks (e.g., SARS/severe acute respiratory syndrome in 2002-2004 and MERS/Middle East Respiratory Syndrome in 2012) there have been reliable reports in the medical journals of some people going on to develop an ME/CFS-like illness.

While both conditions have some key symptoms in common, and there may be a similar level of fluctuating functional impairment in both, there are also some important differences that distinguish some people with Long Covid from those with ME/CFS.

The picture is further complicated because not everyone with Long Covid is able to confirm a previous infection with COVID-19 and an increasing number of people who had Long Covid, or symptoms suggestive of Long Covid, are now being diagnosed with post-COVID ME/CFS.



Long Covid - Is it the same as ME/CFS? was written by Dr Charles Shepherd (pictured above), Trustee and Hon. Medical Adviser to The ME Association.

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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. If you have been affected by Covid-19 and are unable to recover fully, please consult your doctor. 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 Long Covid or ME/CFS.



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While research is taking place into all aspects of Long Covid, we are only just beginning to understand the complexities of this condition. We clearly need research studies that compare Long Covid and ME/CFS to see whether there are similar disease processes involved in each condition.

And given the many overlaps between both symptoms and causative mechanisms, research into Long Covid could well provide useful information relating to both the cause and treatment of ME/CFS.

■ The NICE rapid guideline – Managing the long-term effects of Covid-19 – outlines the current recommendations for symptom recognition, diagnosis, and management for Long Covid:

<https://tinyurl.com/3fdxxf64>

2. EPIDEMIOLOGY

How many people have Long Covid?

At present, we have no firm indication as to how many people have been diagnosed with Long Covid.

With ME/CFS, research has estimated a prevalence range of between 0.2 – 0.4% of the population - which means that around 250,000 people in the UK could be affected. However, we don't have any really accurate data on the number of people diagnosed with ME/CFS.

This is the most recent data from the Office of National Statistics on Long Covid:

■ An estimated 1.8 million people living in private households in the UK (2.8% of the population) were experiencing self-reported long COVID (symptoms persisting for more than four weeks after the first suspected coronavirus (COVID-19) infection that were not explained by something else) as of 3 April 2022.

■ Of people with self-reported long COVID, 382,000 (21%) first had (or suspected they had) COVID-19 less than 12 weeks previously, 1.3 million people (73%) at least 12 weeks previously, 791,000 (44%) at least one year previously and 235,000 (13%) at least two years previously.

■ Of people with self-reported long COVID, 556,000 (31%) first had (or suspected they had) COVID-19 before Alpha became the main variant; this figure was 249,000 (14%) in the Alpha period, 446,000 (25%) in the Delta period, and 438,000 (24%) in the Omicron period.



There is currently no firm indication as to how many people have been diagnosed with Long Covid

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■ Long COVID symptoms adversely affected the day-to-day activities of 1.2 million people (67% of those with self-reported long COVID), with 346,000 (19%) reporting that their ability to undertake their day-to-day activities had been "limited a lot".

■ Fatigue continued to be the most common symptom reported as part of individuals' experience of long COVID (51% of those with self-reported long COVID), followed by shortness of breath (33%), loss of sense of smell (26%), and difficulty concentrating (23%).

■ As a proportion of the UK population, prevalence of self-reported long COVID was greatest in people aged 35 to 49 years, females, people living in more deprived areas, those working in social care, teaching and education or health care, and those with another activity-limiting health condition or disability.

Source:

<https://tinyurl.com/34vsadre>

While a diagnosis of Long Covid is largely based on a person still having symptoms at 3 months from the onset of the infection, it does not require the presence of the very significant functional impairment that is needed to confirm a diagnosis of ME/CFS.

At the ME Association, most of the people with Long Covid that we have been helping over the past eighteen months have been previously fit (some very fit) young adults in their 20s to 50s who were managed at home during their initial COVID-19 infection. Current data suggests that around 90% of people with Long Covid were managed at home and around 40% never had any NHS care.

We are also being contacted about a growing number of children and adolescents with Long Covid.

3. RISK FACTORS FOR LONG COVID AND ME/CFS

In both Long Covid and ME/CFS there is a significant female predominance – possibly relating to the fact that conditions that have an autoimmune component often affect women more than men.

Other risk factors that are emerging for Long Covid include asthma, obesity, living in a deprived area, and poor pre-pandemic health and disability.



We are starting to hear about a growing number of children and adolescents with Long Covid

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It appears that vaccination against COVID-19 is producing a significant decrease in the risk of developing Long Covid if someone does still contract the infection.

4. SYMPTOM SIMILARITIES

4.1 Symptom similarities between Long Covid and ME/CFS

Long Covid has a number of common symptoms that overlap with a post-viral fatigue syndrome (PVFS) or ME/CFS.

So a significant proportion of people with Long Covid have one or more of a cluster of symptoms that are consistent with a diagnosis of PVFS or ME/CFS.

These include:

- debilitating physical and mental fatigue that is activity-induced, is exacerbated by exercise, and is not relieved by rest
- myalgia/muscle pain, arthralgia/joint pain and/or nerve pain/neuropathic pain
- flu-like symptoms and feeling generally unwell
- cognitive dysfunction ('brain fog') – problems with short-term memory, concentration, attention span, information processing and retrieval
- dysautonomia - problems with regulating pulse and blood pressure during changes in posture leading to orthostatic intolerance (difficulty in remaining upright) and postural orthostatic tachycardia syndrome/POTS (a significant rise in pulse rate when moving from lying/sitting to standing resulting in dizziness or feeling faint)
- sleep disturbance which may include both hypersomnia (increased sleep requirements) and insomnia (poor quality sleep) and be described as 'unrefreshing'
- headaches
- poor temperature control
- sensory disturbances – e.g. paraesthesiae ('pins and needles')
- post-exertional malaise/symptom exacerbation

Disabling fatigue is often the main or a very prominent symptom in Long Covid. While it has a lot of similarities to the fatigue that occurs in ME/CFS, damage to the lungs (where there may then be problems with oxygen transfer from the lungs to the blood vessels) and heart may be exacerbating an underlying post-viral fatigue state in people with Long Covid.



A significant proportion of people with Long Covid have one or more of a cluster of symptoms consistent with a diagnosis of PVFS or ME/CFS

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As with ME/CFS, symptoms often fluctuate from day to day and from week to week with some symptoms increasing or decreasing in severity whereas others remain static and new symptoms may appear as time goes on.

4.2 Symptom differences between Long Covid and ME/CFS

A significant proportion of people with Long Covid also have a layer of symptoms that are directly related to involvement of their lungs, heart and blood vessels, liver, kidneys, brain and nervous system, gastrointestinal tract, or skin that occurred at the time of the original infection and which caused damage to or affected the function of these organs.

The more common Covid-specific symptoms include:

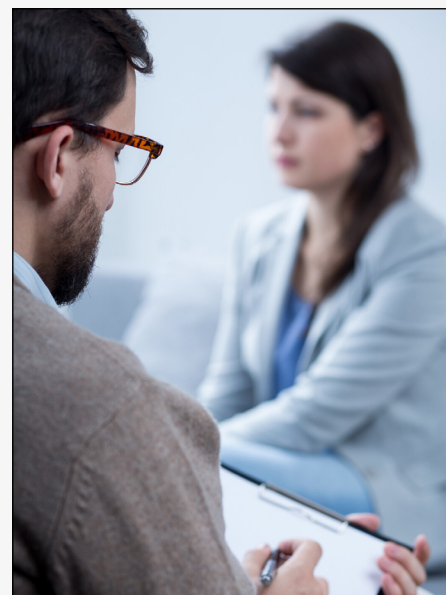
- shortness of breath and/or cough
- chest pains
- heart rhythm disturbances/cardiac arrhythmias
- palpitations on exertion
- periodic fevers
- loss or change of taste (parosmia) and/or smell
- abdominal pain and diarrhoea – which may represent a post Covid irritable bowel syndrome, or an inflammatory bowel syndrome:

<https://tinyurl.com/ye7ruc8t>

- skin rashes - including 'Covid toe'
- hair loss

However, as COVID-19 can affect almost every organ in the body, a much wider range of symptoms has been reported in people with Long Covid. In some cases, these Covid-specific symptoms predominate. In other cases, they are combined with ME/CFS-type symptoms in varying degrees. The mix of symptoms may change over time in relation to both type and severity.

Symptoms involving mental health - anxiety, depression, even post-traumatic stress disorder/PTSD – can also occur, as in ME/CFS. In some cases of Long Covid the mental health symptoms dominate the clinical picture.



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4.3 The overall clinical picture:

A significant proportion of people with Long Covid have symptoms that are directly related to their COVID-19 infection (e.g shortness of breath, chest pains, loss of taste or smell) and some ME/CFS-type symptoms.

Some people with Long Covid have an illness that is dominated by COVID-19 specific symptoms and have no significant component involving ME/CFS-type symptoms.

A further group have an illness that is dominated by ME/CFS-type symptoms and little or no symptoms that are directly related to COVID-19. In this case a diagnosis of post Covid ME/CFS may be more appropriate if they meet with diagnostic criteria for ME/CFS.

The MEA has an information booklet that covers all aspects – clinical history, examination, blood tests - of the diagnosis of ME/CFS:

<https://meassociation.org.uk/mwta>



Some possible overlaps include mitochondrial dysfunction, and the presence of harmful antibodies directed against the body's own tissues

5. THE CAUSE

5.21 What causes Long Covid?

In addition to the overlapping symptoms, there are also some important overlaps as to what may be causing both ME/CFS and Long Covid.

Predisposing factors

In both cases there may be a genetic predisposition. Genome-wide association studies (GWAS) are now being carried out to see if people who develop both Long Covid and ME/CFS have genetic factors that increase susceptibility and response to infections.

Precipitating factors

While Long Covid has, by definition, to date back to a definite COVID-19 infection, the situation with ME/CFS is that it can be triggered by a wide range of viral infections and occasionally non-viral infections. Other types of immune system stressor – such as vaccinations – can also occasionally trigger ME/CFS.

Perpetuating factors

Three separate components appear to be involved in maintaining Long Covid symptoms.



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- First is damage to organs that may have occurred at the time of the infection – the heart and lungs in particular.
- Second are factors that appear to be involved in the causation of other post-viral syndromes such as ME/CFS – in particular immune-system dysfunction involving low level immune system activation and autoantibody production, endothelial dysfunction and mitochondrial dysfunction.
- Third is an area of much uncertainty and the possibility that some other pathology is involved – such as persisting viral infection or the formation of small blood clots/micro-clots.

5.2 Immune system involvement

5.2.1 Cytokines:

One very interesting overlap between Long Covid and ME/CFS is the involvement of immune system chemicals called cytokines – which cause inflammation and many of the flu-like symptoms that are associated with any acute infection.

During the acute stage of COVID-19 there can be what is termed a cytokine storm – with a massive over-production of cytokines causing inflammation in the lungs and serious respiratory complications. There is also research evidence in ME/CFS to indicate that an on-going cytokine response involving what are called pro-inflammatory cytokines fails to 'switch off' after the initial triggering infection.

Cytokines can then pass through what is called the blood-brain barrier and affect an area of the brain called the hypothalamus (which acts as a thermostat for temperature control along with appetite, sleep and hormone regulation), and control centres in the brain for the autonomic nervous system (which controls heart rate and blood pressure during changes in posture and leads to orthostatic intolerance and PoTS).

There is now some research evidence which demonstrates a similar type of cytokine-mediated immune system activation in Long Covid to the one that has already been found in ME/CFS:

<https://tinyurl.com/2p9enxkz>

A combination of infection entering the brain, along with an on-going immune system response, could also lead to activation of structures called microglia in the brain and demyelination (loss of the protective covering) of message-carrying neurons. This has been put forward as one possible explanation for the cognitive dysfunction that occurs in Long Covid – as well as in ME/CFS.



One interesting overlap between Long Covid and ME/CFS is the involvement of immune-system chemicals called cytokines, which cause inflammation and many of the symptoms associated with acute infections

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The Scientist news report:

<https://tinyurl.com/3pnat5rd>

5.2.2 Autoimmunity

There is growing evidence that another component of the immune system response in Long Covid involves the production of autoantibodies – these are potentially harmful antibodies that are directed against the body's own tissues.

Low levels of autoantibodies are also sometimes found in ME/CFS. And while not confirming that ME/CFS (or Long Covid) is what would be termed an autoimmune disease it does suggest that there is an autoimmune component.

5.3 Central nervous system involvement?

Interesting new research from Oxford, which has investigated brain changes in 785 participants from the UK Biobank before and after catching COVID-19, has reported a decrease in grey matter volume and brain damage in areas that are involved with the detection of smell.

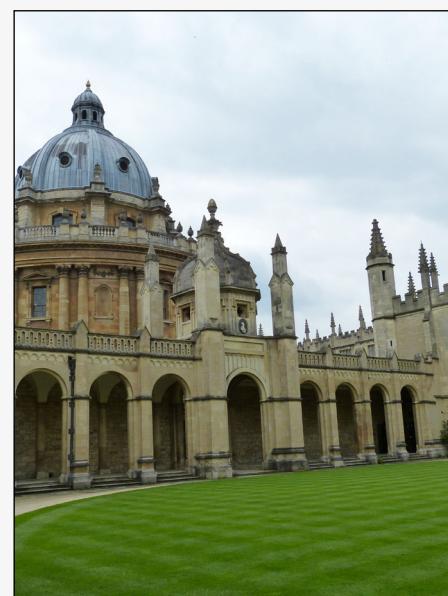
Changes in both grey and white matter volume have also been demonstrated using structural neuroimaging techniques in people with ME/CFS. So this is a finding that could help to explain cognitive dysfunction in both ME/CFS and Long Covid. Link to research paper in Nature:

<https://tinyurl.com/3su4uup4>

5.4 Endothelial damage and blood clots

Damage to the endothelium, the cellular structure that lines the inside of all blood vessels, has been suggested as another possible cause of Long Covid, and this may link in with the persisting formation of small blood clots (micro-clots) in blood vessels. There is now reliable evidence that people with COVID-19, and in some cases of Long Covid, have complications relating to the formation of both large and small blood clots.

While there is research evidence of endothelial dysfunction in ME/CFS, there is no sound evidence of this type of blood clotting problem. Given the lack of clinical evidence for clotting complications occurring in ME/CFS, it therefore seems unlikely that blood clotting abnormalities are involved the pathology of ME/CFS.



Interesting new research from Oxford has investigated brain changes in 785 participants from the UK Biobank before and after catching COVID-19

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5.5 Persisting viral infection?

A reservoir of persisting viral infection in the gastrointestinal tract has been suggested with one research group recently concluding that COVID-19 can infect gastrointestinal tissue and is associated with gastrointestinal symptoms:

<https://tinyurl.com/2p876xwc>

The presence of viral particles in other tissues has also been put forward. This is supported by some preliminary findings from a post-mortem research study from the National Institutes of Health in America. Their report has not yet been peer reviewed:

<https://tinyurl.com/4wdzdae9>

5.6 Mitochondrial defect in energy production

As with ME/CFS, there is evidence of mitochondrial dysfunction in Long Covid – the mitochondria playing a crucial role in the body's energy production – and it is interesting to note that a sustained impairment in cardiopulmonary exercise testing has been found in both ME/CFS and Long Covid:

<https://tinyurl.com/bdznbafe>

5.7 Microfloral dysbiosis

There is also some preliminary evidence of changes to the composition of the natural bacterial and viral population in the intestines – as has been reported in ME/CFS.

5.8 The role of Covid vaccines

One important difference between Long Covid and ME/CFS is the way in which COVID-19 vaccines appear to be producing a significant improvement in symptoms in some people – possibly as a result of 'resetting' the abnormal immune system response. However, in ME/CFS vaccinations are a well-recognised factor in causing an exacerbation of symptoms in some people, and only rarely cause improvement.



One important difference between COVID-19 and ME/CFS is that the COVID-19 vaccines appear to be producing a significant improvement in symptoms in some people

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6. ASSESSING AND DIAGNOSING LONG COVID

Management of Long Covid should consist of carefully assessing people to see if there is any clinical and laboratory evidence of on-going damage (which may be permanent) or dysfunction (which may or may not improve over time) involving the lungs, heart, liver, kidneys, etc. This information can then be used to provide appropriate guidance on the management of individual symptoms relating to this type of organ damage or dysfunction.

What is becoming clear is that basic screening tests such as chest X-rays, standard scans and ECGs are not always the most effective way of picking up the sort of subtle lung and heart damage/dysfunction that can occur in Long Covid, and that sophisticated scanning techniques may provide far more useful information.

A multi-center pilot study being carried out in the UK, which is using Xenon-gas MRI scans to measure oxygen transfer from lungs to blood vessels, has recently reported some significant defects in people with Long Covid that would not be found using more standard tests of lung function.

BBC news report:

<https://tinyurl.com/z3hp9mpk>

As with ME/CFS, it is important to make sure that other possible explanations for Long Covid symptoms are considered. There is a real danger, partly due to problems with accessing face-to-face medical appointments, that any form of continuing ill health following COVID-19 is diagnosed as Long Covid.

Consideration should, for example, be given in women over the age of 40 who may be/are going through the peri-menopause (transitional period before the menopause) or the menopause as to whether some of their symptoms are due to the menopause and falling levels of oestrogen and could be helped by the use of HRT. A similar situation occurs in ME/CFS.

The possibility that COVID-19 has destabilised a pre-existing medical condition, or precipitated symptoms in a condition that has not yet been recognised, must be also considered.

Conditions such as diabetes, inflammatory bowel disease, polymyalgia rheumatica, sleep apnoea and even malignancies can be misdiagnosed as Long Covid when patients are not being properly assessed. This can be reduced by following the same sort of rigorous clinical assessment process, including a range of baseline blood tests, that should occur when ME/CFS



Long Covid clinics are often very good at assessing people for damage to the lungs, heart and other organs that may have been affected by the infection

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is being queried or diagnosed. These tests are described in the MEA publication covering Early and Accurate Diagnosis (see section 4.3).

7. TREATMENT

7.1 Treating Long Covid

At present, there is no safe and effective drug treatment for Long Covid. And as with ME/CFS, it's highly unlikely that we are going to find a single successful treatment for every person who has Long Covid. However, a number of drug treatments are now being assessed.

These include:

A clinical trial of an American drug called **AXA1125** in Oxford which aims to improve mitochondrial (muscle energy) function.

MEA website news item on **AXA1125** dated 3 November 2021:

<https://tinyurl.com/mtpdsxbn>

The use of a technique called **apheresis**, which removes disease-causing components from the blood, in Germany. The research into blood clotting forms the basis of the so-called micro-clot model, which proposes that small clots in the blood capillaries that prevent oxygen from reaching the tissues may cause Long Covid symptoms and that this could be treated with anti-clotting drugs.

MEA website news item on **apheresis** dated 26 October 2021:

<https://tinyurl.com/yc8h6wr2>

The MEA has approached clinicians involved in both of these clinical trials to see if it might be appropriate to also include a group of people with ME/CFS.

Another interesting therapeutic development is the finding that some people with Long Covid have symptoms of what is called **mast cell activation syndrome** – where a viral infection destabilises mast cells causing the release of histamine. Where this occurs there are reports that treatment with drugs called histamine H1 and H2 receptor antagonists (e.g. cetirizine and famotidine) and a low-histamine diet can be helpful.

As dysbiosis can affect people with Long Covid (and ME/CFS) researchers in Cambridge have carried out a clinical trial involving a **pre- and probiotic supplement**. They reported benefits in both gastrointestinal and non-gastrointestinal symptoms.

<https://tinyurl.com/m6rx9cs4>



A recent report from the University of Leicester, which looked at people who were treated in hospital, found that most were significantly unwell one year on following the infection

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Other approaches involving drug treatment include the use of colchine to reduce inflammation and a clinical trial involving low dose naltrexone, which is being funded by the Canadian Institute of Health Research:

<https://tinyurl.com/2p83667p>

The MEA has produced a review of treatments that are currently being assessed for Long Covid:

<https://tinyurl.com/2p845tr4>

Politico review of Long Covid treatment trials:

<https://tinyurl.com/2p8f347d>

7.2 Symptom Management

For symptoms that are the same as those found in ME/CFS, the same sort of self-help management strategies and symptomatic relief involving drugs should be discussed with a health professional. The MEA has information leaflets covering all aspects of symptom management that overlap with Long Covid.

Cognitive dysfunction/brain fog:

<https://meassociation.org.uk/d0ad>

Dysautonomia – orthostatic intolerance and PoTS:

<https://meassociation.org.uk/reqf>

<https://meassociation.org.uk/snck>

Pain:

<https://meassociation.org.uk/9eaq>

The MEA also has information leaflets covering the use of specific drugs such as low dose amitriptyline, gabapentin and pregabalin for pain relief in ME/CFS

Sleep and restless legs syndrome:

<https://meassociation.org.uk/wr86>

For Covid specific symptoms there is good support and information available from other medical charities:

Breathing and lung problems – British Lung Foundation:

<https://tinyurl.com/2p8sjxtb>

Loss of taste and/or smell:

<https://tinyurl.com/y44xhvry>

<https://tinyurl.com/2p8nm6vw>



A number of drug treatments are now being assessed, including a clinical trial of an American drug which aims to improve mitochondrial energy production

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7.3 Activity and energy management

Most people with Long Covid have a type of debilitating fatigue and inability to sustain physical and mental activities that is very similar or identical to that which occurs in ME/CFS. In many cases the symptoms will worsen both during and in the days following increased physical activity or exercise. This is referred to as post-exertional malaise or post-exertional symptom exacerbation.

As with ME/CFS it is important to note that physical activity is different to exercise. Physical activity is any muscle movement that requires the production of energy. Exercise is a planned, structured and intentional movement that aims to maintain or to improve strength or cardiovascular fitness. Graded exercise is sometimes recommended following a period of illness that has led to deconditioning or muscle weakness. The aim of graded exercise is to improve muscle strength and fitness.

However, many people with Long Covid appear to have exactly the same sort of complex central (brain) and peripheral (muscular) fatigue that occurs in ME/CFS and which is not caused by deconditioning. So we recommend pacing - the type of activity and exercise management that is used in ME/CFS – and not graded exercise therapy.

Pacing of both physical and mental activity, where the aim is to avoid carrying out or carrying on with any form of physical or mental activity that causes symptom exacerbation, is the most important way of avoiding post exertional malaise. The aim of pacing is to find a stable baseline of activity and avoid 'doing too much' on one day and then feeling unable to do anything the next, due to increased levels of fatigue and other symptoms.

We believe that there is a real risk of harm if inappropriate graded exercise programmes are prescribed to people with Long Covid.

The MEA has an information leaflet providing detailed guidance on energy management and pacing:

<https://meassociation.org.uk/h8qj>

The section of activity and energy management on pages 28-32 in the new NICE guideline on ME/CFS is also very helpful here:

<https://tinyurl.com/4y7datwr>



Most people with Long Covid have a debilitating type of fatigue that is very similar or identical to that which occurs in ME/CFS

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7.4 Education and employment

Not surprisingly, there are especially high rates of Long Covid in people who are/were employed in the health service, social care, the teaching professions, hospitality, retail and transport. So they require information and guidance on the sort of modifications to hours, duties, travel etc that will need to be made if/when someone has reached the point where a phased or modified return to education or employment is possible.

Unfortunately, it is becoming clear that many people with Long Covid are experiencing the same sort of practical problems that occur in ME/CFS in relation to obtaining reasonable adjustments and modifications if they are still able to participate in some form of employment or education.

And while Long Covid has not been classified as a named disability within the 2010 Equality Act, the fact that some people with Long Covid clearly have an illness that is causing a significant and long-term (ie likely to remain for a year or more) reduction in their ability to carry out normal daily activities means that on an individual basis these people should be classified as being disabled in relation to modifications and reasonable adjustments to normal routines at work, school and college.

7.5 Long Covid Clinics

There is now a network of around 90 hospital-based Long Covid clinics where adults can be referred by their GP. There are also 14 clinics for children and adolescents. As with referral services for ME/CFS, these NHS clinics are mainly in England with only a small number of Long Covid services in Northern Ireland and Scotland. There are no Long Covid clinics in Wales at present.

Data on demographics indicates that referrals are heavily weighted towards white females between the age of 35 and 64 and that many people from deprived communities are not being referred.

Feedback to the MEA indicates that these clinics are often very good at assessing people for damage to the lungs, heart and other organs that may have been affected by the initial infection, but not so good at having the necessary time to spend on personalised management. Many of these services also lack the necessary expertise to deal with ME/CFS-type symptoms.



There are especially high rates of Long Covid in people who are/were employed in the health service, social care, the teaching professions, hospitality, retail and transport who require information and guidance regarding work modifications

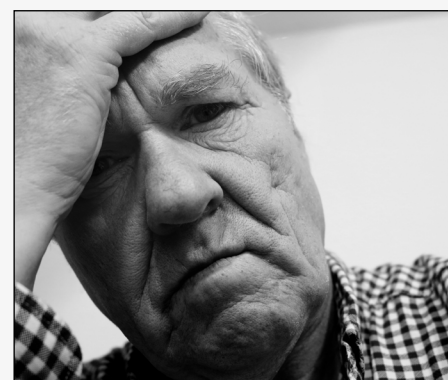
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Some people with Long Covid are clearly being helped by a package of pulmonary (lung) rehabilitation, appropriate activity and energy management programmes and (if required) the psychological support that many of the Long Covid clinics provide.

However, some of these Long Covid referral services are not being open-minded about all the different and possible causes of Long Covid (especially the fact that a significant proportion of people with Long Covid have post-exertional malaise and meet with other diagnostic criteria for ME/CFS) and seem unwilling to accept that activity and energy management involving convalescence and pacing is going to be far more helpful than a 'one size fits all' approach that is based on graded exercise.

So we continue to be surprised and disappointed that the Long Covid medical community is still not making use of the lessons that we have learnt on how to manage key symptoms - especially debilitating fatigue, cognitive dysfunction, dysautonomia and sleep disturbance - that are common to almost any serious post-viral disease state.

There have been proposals to establish joint Long Covid and ME/CFS clinics in some parts of the UK. The MEA position is that they should normally be kept separate at present - due to the need to have specialist input for the heart and lung problems in Long Covid - but to establish links to ME/CFS clinics so patients can be referred for help with management of ME/CFS-type symptoms.



The overall outlook in Long Covid appears to be very uncertain - as with ME/CFS

8. PROGNOSIS

What happens to people with Long Covid?

The overall outlook in Long Covid appears to be very uncertain - as with ME/CFS. Many people are finding that their condition fluctuates in severity – often more dramatically than occurs in ME/CFS. Some people stabilise and improve whereas others deteriorate and now have a severe form of Long Covid. While some are clearly improving, those who achieve a full, sustained recovery from Long Covid appear to be in a minority.

Research studies are now starting to report on prognosis in Long Covid and the recent report from the University of Leicester PHOSP COVID study, which is looking at people who were treated in hospital, found that most were still significantly unwell one year on following the infection.



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Reference:

<https://tinyurl.com/2p8hszu4>

A study from France on 968 people with Long Covid who had mainly been managed at home reported that 85% were still symptomatic one year after the onset of symptoms.

Reference:

<https://tinyurl.com/yhtufz9a>

9. HOW CAN THE ME/CFS MEDICAL AND PATIENT COMMUNITY HELP THOSE WITH LONG COVID?

The MEA is trying to build bridges with the Long Covid patient and medical communities by providing information and guidance on the management of symptoms that overlap with ME/CFS.

This includes using ME Connect and our social media platforms to provide information and support to people with Long Covid with increasing numbers of people with Long Covid joining in discussions on MEA Facebook – where they are very welcome.

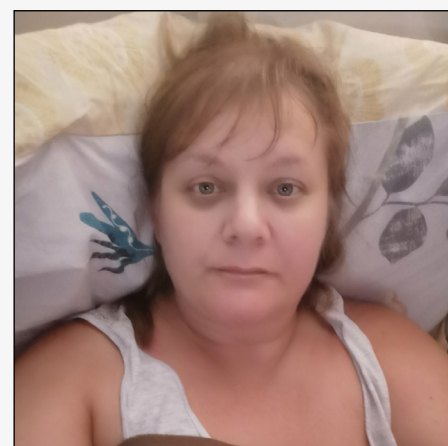
This collaboration has not been helped by some members of the Long Covid patient community assuming that ME/CFS is a psychological illness and not therefore wanting to acknowledge any possible connection or collaboration.

Many health professionals and researchers also have very limited or inaccurate knowledge about ME/CFS and are not aware of research findings in ME/CFS that may well be relevant to Long Covid.

10. HOW CAN RESEARCH INTO LONG COVID HELP PEOPLE WITH ME/CFS?

This interaction with the Long Covid patient and medical communities should be a two-way process given all the funding and interest into the cause and treatment of Long Covid that is occurring. The MEA is therefore trying to encourage research that also includes people with ME/CFS in studies that are looking at both causation and treatment of Long Covid.

In particular, we are very keen for this research to start making use of blood samples from people with ME/CFS, multiple sclerosis and healthy controls that are available for research purposes at the ME Biobank. The MEA Ramsay Research Fund would be happy to consider research funding proposals here.



The MEA is trying to build bridges with the Long Covid patient and medical communities by providing information and guidance on the management of symptoms that overlap with ME/CFS



LONG COVID AND ME/CFS

What do Long Covid & ME/CFS have in common?

SIMILARITIES

Post-viral fatigue syndromes (PVFS): Neurological

Both Long Covid and ME/CFS are caused by an apparent failure to recover from a viral infection.

Fluctuating illness: Unpredictable

Both conditions cause symptoms that fluctuate in intensity and severity

Treatment: Management

There are no effective drug treatments for either condition

Risk factors: Gender

It has been estimated women are up to 4 times more likely to have ME/CFS than men and a similar ratio is emerging for Long Covid

KEY SYMPTOMS IN COMMON

Post-Exertional Malaise (PEM)

A worsening of symptoms following even minor physical or mental exertion

Fatigue

A profound exhaustion that is debilitating in nature and worsened by activity

Muscular aches and pains

Similar to the myalgia experienced with infections like the Flu

Sleep

Sleep quality is often poor and unrefreshing, meaning people wake feeling as bad or worse than before

Cognitive dysfunction

'Brain fog', can include short-term memory lapses, difficulty in concentrating...

Dizziness and nausea

Often caused by problems regulating pulse and blood pressure

Bowel and bladder

Many people report irritable-bowel-type symptoms such as a change in bowel habits

LONG COVID & ME/CFS

The ME Association believes that Long Covid (Post-acute Covid-19) and ME/CFS (Myalgic Encephalopathy/Encephalomyelitis) can generally be viewed as examples of post-viral syndromes or post-infectious fatigue syndromes..

But while they share symptoms in common and can cause similar functional impairment, some people with Long Covid are experiencing symptoms that are caused by organ damage and will require additional support from medical specialists.



WHAT DO LONG COVID & ME/CFS HAVE IN COMMON?

■ Post-viral fatigue syndromes (PVFS): Neurological:

PVFS is recognised as a neurological disease by the World Health Organisation, NHS, and UK Government. ME/CFS is included in this definition. Both Long Covid and ME/CFS are caused by an apparent failure to recover from a viral infection. Long Covid is triggered by Covid-19 and its variants and c.80% of ME/CFS cases are triggered by viral infections such as Glandular Fever (Epstein-Barr virus).

■ Fluctuating illness:

Unpredictable: Both conditions cause symptoms that fluctuate in intensity and severity, and an illness that can follow a pattern of relative remission and relapse. For some the illness can get progressively worse until a period of relative stability is obtained. Both can cause significant functional impairment affecting cognition, mobility, and a person's ability to perform everyday tasks. Employment and education are likely to be affected.

■ Treatment:

Management: There are no effective treatments for either condition. Both have NICE clinical guidelines, but the Long Covid guideline is not as detailed or helpful in terms of ongoing management advice and support. NHS England has been commissioned to provide secondary care specialist services (clinics) for Long Covid and for ME/CFS. They are tasked with diagnosis, triage, and delivering personalised management advice that should be based around a technique known as 'pacing'. Provision of services in Wales, Northern Ireland, and Scotland is virtually non-existent with patients having to negotiate ongoing care and support with primary care (GPs).

■ Risk factors:

Gender: It has been estimated women are up to four times more likely to have ME/CFS than men and a similar ratio is emerging for Long Covid. Such gender imbalances also occur in autoimmune conditions. The explanation is uncertain but may be due to genetic abnormalities, the way that a woman's immune

system responds to viral infections and/or hormones. Medical attitudes towards illnesses that are seen as being 'women's diseases' can be dismissive and cause a delay in diagnosis or misdiagnosis – it can also make it harder for men to receive appropriate care and support.

KEY SYMPTOMS IN COMMON

■ Post-Exertional Malaise (PEM):

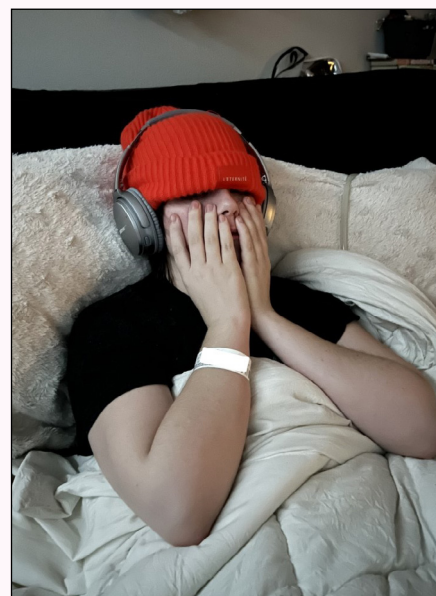
A worsening of symptoms following even minor physical or mental exertion. There is often a delay in symptom exacerbation of 12 to 48 hours. This exacerbation can last for days or weeks and lead to relapse.

■ Fatigue:

A profound exhaustion that is debilitating in nature and worsened by activity. It is not relieved by rest and is a constant symptom for most people that prevents them from initiating or completing daily tasks. It can impact mobility and exacerbate other symptoms like sleep quality and cognitive dysfunction.

■ Muscular aches and pains:

Similar to the myalgia experienced with infections like the Flu, it is often constant and ►





intrusive. It can cause disruption to sleep and periods of rest. It is a symptom that can be exacerbated by activity and exercise.

■ Sleep:

People will experience periods when they need to sleep more than is normal often when their illness is in an acute phase or during periods of relapse when other symptoms are at their worst. But sleep quality is often poor and unrefreshing, meaning people wake feeling as bad or worse than before. Sleep can also be interrupted by an inability to enter deep sleep, or by night sweats, insomnia, and bad dreams (night terrors) that lead to poorer quality sleep that is of shorter duration.

■ Cognitive dysfunction:

'Brain fog'. Symptoms can include short-term memory lapses, difficulty in concentrating or sustaining attention, difficulty with processing incoming information (reading, listening) and retrieving stored information, trouble finding the right word, remembering, mixing up commonly used words, problems with carrying out everyday tasks that involve any form of sustained mental activity.

■ Dizziness and nausea:

Often caused by problems regulating pulse and blood pressure. The body is unable to supply sufficient blood quickly enough to the brain, which can cause dizziness and nausea. It can be diagnosed as orthostatic intolerance or Postural Orthostatic Tachycardia Syndrome (PoTS). People will find these symptoms occur when trying to stand from a prone position. They will often be unable to remain standing and it can lead to fainting. It is important to get these symptoms checked and properly diagnosed as there are treatments available.

■ Bowel and bladder:

Many people report irritable-bowel-type symptoms such as a change in bowel habits – diarrhoea and/or constipation – an increased or urgent need to go to the toilet, abdominal pain, bloating, a feeling of incomplete bowel evacuation; and non-bowel symptoms that might include backache, gynaecological problems, and an increased need to pass urine including when asleep.

■ 'Flu-like':

Many people describe the symptoms they experience with ME/CFS and Long Covid as being 'flu-like' in nature. These include recurrent sore throats, headaches, and the muscular aches and pains, fatigue, sleep problems, nausea, and cognitive dysfunction described above. Some people with Long Covid are reporting significant and periodic spikes in body temperature. This is not something that occurs in ME/CFS and if it does it should be properly investigated to exclude another infective illness. ■

11. FURTHER INFORMATION

We have produced another MEA information booklet that covers all the overlaps between Long Covid and ME/CFS along with the diagnosis and management of Long/Post-Covid fatigue and Long/Post-Covid ME/CFS in more detail than here. This booklet covers the management of all the common ME/CFS-like symptoms that overlap with Long Covid in some detail. This is a free download from the Covid-19 literature section in the MEA website shop:

<https://meassociation.org.uk/rcti>

MEA position statement on the overlaps between Long Covid and ME/CFS:

<https://meassociation.org.uk/lbrb>

Article for the BMA/BMJ publications with contributions from Drs Nina Muirhead, David Strain, Amy Small and myself. It also covers the ME/CFS and Long Covid overlap:

<https://tinyurl.com/mryz98ne>

'Nature' review of Long Covid and the overlaps with other post infection syndromes, including ME/CFS:

<https://tinyurl.com/2p844mzy>

Wong TL and Weitzer D. Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) - A Systemic Review and Comparison of Clinical Presentation and Symptomatology. *Medicina* 2021 May; 57(5): 418.

<https://tinyurl.com/4wz95ra8>

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