

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW? AND WHAT REMAINS UNCERTAIN OR UNKNOWN?



How the history of ME/CFS has defined and complicated research into causation

Long Covid overlaps with ME/CFS

What causes ME/CFS?

Predisposing, precipitating and perpetuating factors

Current and future research



WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?



What causes of 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.

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CONTENTS

- [3](#) **BACKGROUND**
- [4](#) **HOW THE HISTORY OF ME/CFS HAS DEFINED AND COMPLICATED RESEARCH INTO CAUSATION**
- [7](#) **LONG COVID OVERLAPS WITH ME/CFS**
- [8](#) **WHAT CAUSES ME/CFS?**
 - Predisposing factors
 - Precipitating factors
 - Perpetuating factors
- [11](#) **RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM:**
 - Infection and reactivated viral infection
 - Immune-system research
 - Brain and nervous system research
 - Neuroendocrine (brain hormone) research
 - Research into energy production and mitochondrial dysfunction
 - Other possible perpetuating factors
- [18](#) **CONCLUSIONS**
- [18](#) **FUTURE RESEARCH INTO WHAT CAUSES ME/CFS**
- [19](#) **FURTHER INFORMATION**
- [20](#) **THE ME ASSOCIATION**



Use this QR code or the link below to access all the links in this booklet:

<https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

BACKGROUND

Knowing what causes a disease obviously helps to explain what produces the symptoms. It can also lead to the development of diagnostic biomarkers/blood tests and effective forms of treatment that are aimed at the underlying disease process, instead of just managing the symptoms.

Knowing the cause also decides how a disease is classified and which medical speciality should take the lead in patient management.

In the case of ME/CFS, the World Health Organisation (WHO) classifies ME/CFS as a disease of the central nervous system (in section G.93.3 of ICD10) – as does the Department of Health and Social Care. However, ME/CFS is not a disease that most neurologists are happy to deal with. So, at a specialist level, people can be referred to departments dealing with infectious diseases, immunology, rheumatology, virology and sometimes even psychiatry – even though this is not appropriate.

While we have some important clues as to what is causing the debilitating fatigue and the wide range of symptoms that affect different body systems in ME/CFS, we still don't know what is really going wrong.



While we have some important clues as to what is causing the debilitating fatigue, and the wide range of symptoms that affect different body systems in ME/CFS, we still don't know what is really going wrong.

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?



Before summarising what we do and do not know about research into the cause of ME/CFS, it's helpful to understand some of the key events in the history of ME/CFS, why this has led to two different names for this illness, and how this has caused problems for research.

HOW THE HISTORY OF ME/CFS HAS DEFINED AND COMPLICATED RESEARCH INTO CAUSATION

As a result of uncertainty surrounding causation, ME/CFS has, for many years, involved a split of medical opinion between clinicians and researchers who believed that it was a psychological problem that should be treated with cognitive behaviour therapy/CBT (which is designed to change abnormal thoughts and behaviours) and graded exercise therapy/GET (which is based on the belief that problems with mobility are caused by inactivity and deconditioning) and those who believed it was a complex medical disease.

Unfortunately, the psychosocial view of ME/CFS is still held by some members of the healthcare profession. However, there is now a substantial body of evidence supporting the understanding of ME/CFS as a complex, multisystem medical disease – as outlined in this research review. This is not just the position of the ME Association. It is also supported by a wide body of medical opinion, the Medical Research Council, the Department of Health and Social Care and the NICE guideline on ME/CFS.

Before summarising what we do and do not know about research into the cause of ME/CFS, it's helpful to understand some of the key events in the history of ME/CFS, why this has led to two different names for this illness, and how this has caused problems for research.

Following the outbreak of a mysterious infective polio-like illness that affected almost 300 members of staff at the Royal Free Hospital in London in 1955, and closed the hospital for almost three months, the outbreak was written up in *The Lancet* the following year.

The *Lancet* editorial introduced the name ME into medical language and announced that ME was 'a new clinical entity':

Reference 1



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

HOW THE HISTORY OF ME/CFS HAS DEFINED AND COMPLICATED RESEARCH INTO CAUSATION *(continued...)*

Myalgic refers to the muscle pain that often occurs in ME/CFS. Encephalomyelitis refers to the presence of serious and widespread inflammation in the brain (encephalo-) and spinal cord (-myelitis).

In January 1970, two psychiatrists - Colin McEvedy and William Beard - published a highly controversial and influential paper in the British Medical Journal.

Reference 2

They argued that the 1955 Royal Free Hospital outbreak of myalgic encephalomyelitis (ME/CFS) was not a physical illness, but rather an episode of “epidemic hysteria” (mass hysteria). This single paper fundamentally shifted the medical consensus, framing ME/CFS as a psychosomatic or psychiatric condition – an outdated viewpoint that caused widespread medical disbelief and seriously stalled biological research.



In the 1980s, following growing interest in ME among psychiatrists, a large section of the international medical establishment decided to try and rename and redefine ME as chronic fatigue syndrome/CFS – a move that was strongly opposed by the patient community, and many doctors, who felt it was like renaming dementia as a chronic forgetfulness syndrome.

There was also a serious attempt to completely remove ME from medical language because no scientific evidence had emerged since the Royal Free outbreak to show that an encephalomyelitis was present.

This is how a very fractious debate opened up into whether we should call this disease ME, or CFS, or ME/CFS and whether it was medical or psychiatric in regard to both causation and treatment.

Renaming and redefining ME as CFS has led to serious problems when it comes to which definition and inclusion criteria – ME, CFS, ME/CFS – should be used for research purposes. Currently, there is a lack of a universally accepted clinical or research definition for ME/CFS and there are now over 20 definitions.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

HOW THE HISTORY OF ME/CFS HAS DEFINED AND COMPLICATED RESEARCH INTO CAUSATION *(continued...)*

These include the Canadian, Fukuda (historically the most commonly used), International, and Oxford – some of which do not require the presence of post-exertional malaise, a key diagnostic symptom of ME/CFS.

Having broad and varied inclusion criteria skews research findings in relation to both the aetiology and pathophysiology of ME/CFS. So it can be very difficult to draw firm conclusions from different research studies into both causation and treatment when they have been using different research criteria that involve people with different clinical presentations of ME and ME/CFS. The MEA is currently working with Professor Leonard Jason and colleagues on the development of research criteria that would have international agreement.

With no evidence emerging from post-mortem studies to confirm that a widespread inflammatory process is taking place in the brain and spinal cord, some doctors remain sceptical or even hostile to the use of the name ME. So they refuse to use ME in their medical notes and use the name CFS instead. This is why the MEA has proposed changing the E in ME to encephalopathy – which still refers to brain abnormalities but not widespread inflammation – and why we also use the compromise term ME/CFS.



In some people, excessive physical or mental stress at the time of the infection appears to be an important co-factor in increasing the risk of developing ME/CFS.

Fortunately, findings from the growing volume of biomedical research that has examined brain, muscle and immune-system function in ME/CFS, and publication of the 2021 NICE guideline on ME/CFS, which takes a biomedical approach to management, the situation is starting to change. Many clinicians and researchers now follow a medical model of causation and management. However, we still have a long way to go when it comes to discovering safe and effective treatments that are aimed at the underlying disease process.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

LONG COVID OVERLAPS WITH ME/CFS

Following the Covid-19 pandemic, around 10% of those who had been infected with Covid-19, failed to properly recover. A new condition, which covered a wide range of post-Covid symptoms and complications, was named Long Covid (medical name: Post-Acute Sequelae of SARS-CoV-2 infection). A significant proportion of people with Long Covid have symptoms such as debilitating fatigue, post-exertional malaise/PEM and cognitive dysfunction that are diagnostic of ME/CFS. Some research indicates that around 50% of those with Long Covid meet diagnostic criteria for ME/CFS.

Reference 3

Over the past five years, a huge amount of research funding has been allocated into trying to find the cause of Long Covid and effective forms of treatment. Not surprisingly, given these overlaps with ME/CFS, a lot of this research has replicated the muscle/mitochondrial, brain and immunological research that has already been carried out in ME/CFS. Unfortunately, despite all this funding and research effort, no significant breakthroughs have occurred.



The UK ME/CFS
Biobank

Images by Yas
Crawford:
[https://www.
yascrawford.com](https://www.yascrawford.com)



References: [https://
linktr.ee/causesMECFS](https://linktr.ee/causesMECFS)

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

WHAT CAUSES ME/CFS?

Download this infographic at full size: [Reference 3a](#)



Based on our current level of evidence from people with ME/CFS, their clinicians and research findings, ME/CFS appears to be a three-stage illness involving predisposing, precipitating and perpetuating factors.

Predisposing factors

As with many chronic diseases - arthritis, cancer, heart disease etc - it appears that genetic factors play a role in making some people more likely to develop one of these conditions.

So while ME/CFS is not a genetic disorder in the sense that it can be directly passed from parent to child, there is growing evidence that some people have a genetic make-up that increases the risk of ME/CFS developing when a trigger factor, such as an infection, occurs at a particular time in their life. This genetic predisposition may also help to explain why there are families with more than one member who has ME/CFS.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

PREDISPOSING FACTORS *(continued...)*

New research on brain structure and function suggests that infections, or events prior to the onset of ME/CFS, may help to prime or activate immune-system cells in the brain called microglia.

The DecodeME research study analysed the DNA (genetic material) from nearly 20,000 people with ME/CFS.

Among the key findings are:

- Eight specific regions in the human genome where people with ME/CFS show significant genetic differences compared to the general population.
- Genetic markers that link directly to neurological and immunological functions.
- Genetic markers relating to the body's response to infection and one which has previously been found in people experiencing chronic pain.
- None of the eight genetic signals identified were shared with depression or anxiety.
- Because DNA does not change with the onset of the illness, these genetic variations reflect underlying risk factors and biological causes of ME/CFS.

The DecodeME research study:

Reference 4

New research on brain structure and function suggests that infections, or events prior to the onset of ME/CFS, may help to prime or activate immune-system cells in the brain called microglia. When faced with another infection, this priming of the microglia may then make some people more vulnerable to developing ME/CFS.



Precipitating factors

One area where there is a widespread medical agreement relates to what often triggers, or precipitates ME/CFS.

Reference 5

Most people with ME/CFS, possibly around 75%, pre-date the onset of their symptoms to an infection – normally viral but sometimes bacterial – from which they ‘fail to recover’ and continue to have ‘flu-like symptoms’, along with the very characteristic muscle and brain symptoms that are associated with ME/CFS.

Infections that are known to trigger ME/CFS include Epstein Barr virus (glandular fever), cytomegalovirus, human herpes viruses (HHV6, HHV7 and chickenpox), parvovirus B19, enteroviruses, Chlamydia pneumoniae, Mycoplasma, Borrelia burgdorferi, Brucella melitensis, and Coxiella burnetii (Q fever). Tropical infections, including dengue fever, Ebola virus, zika virus and chikungunya can all cause prolonged fatigue and an ME/CFS-like illness.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

PRECIPITATING FACTORS *(continued...)*

Other types of stressors on the immune system – vaccinations, chemicals such as organophosphate sheep dips, ciguatera fish poisoning, trauma, pregnancy, surgery – can occasionally trigger ME/CFS. So ME/CFS isn't always a post-viral illness and sometimes there isn't any obvious triggering event.

It also appears that stress – physical, mental, emotional, or a combination of all three – around the time of a triggering infection, or during the recovery period, can be an important co-factor in determining how the body responds to an infection and may therefore increase the risk of ME/CFS developing.



ME/CFS isn't always a post-viral illness and sometimes there isn't any obvious triggering event.

Perpetuating factors

What maintains or perpetuates the symptoms remains far more uncertain. One possibility is that, while the triggering infection causes a normal immune system response, this then fails to settle down and return to normal. This on-going immune-system activation then affects some of the normal control mechanisms in key parts of the brain, especially those which regulate the autonomic nervous system, as well energy-producing systems in cellular structures called mitochondria.

Whatever sequence of events is involved, there is now a growing body of research evidence to indicate that reactivated viral infections, the central nervous system, neuroendocrine (brain-hormone) system, the immune system, and energy-producing systems are all involved in some interconnected way.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM

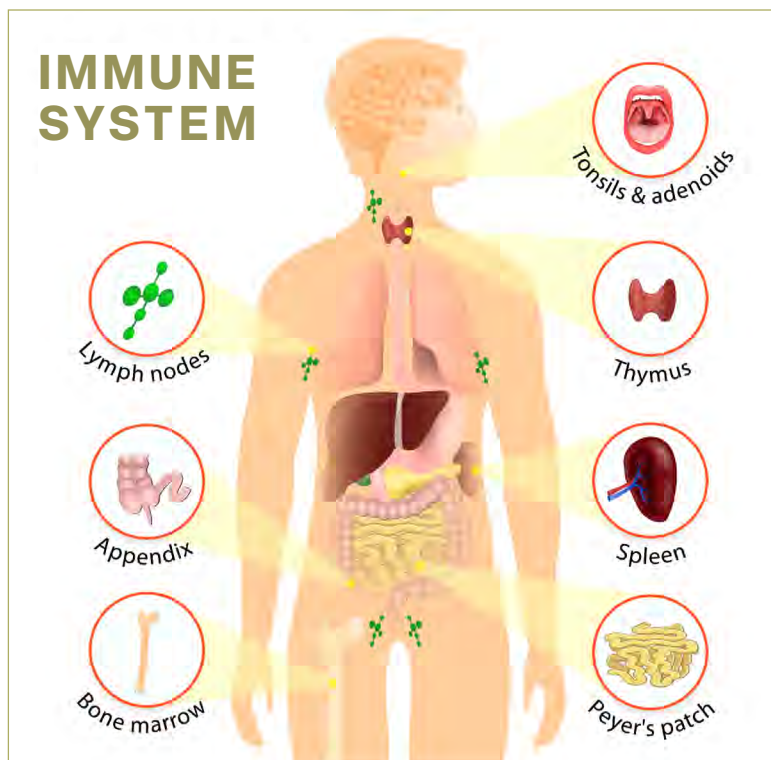
Infection and reactivated viral infection

Although a wide range of infections are known to trigger ME/CFS, most of the research that has investigated infection has not supported a role for persisting viral infection – as happens with hepatitis C, HIV and possibly in some cases of Long Covid.

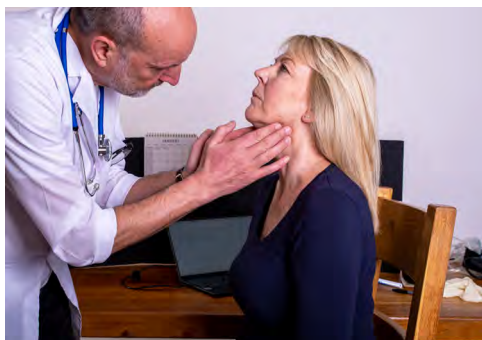
There is, however, some research evidence regarding a role for reactivated viral infection with human herpes virus 6 (HHV-6) and Epstein Barr virus – which causes glandular fever. These are both herpes virus infections that remain dormant in the body after an initial infection and which can be reactivated as a result of an on-going immune system response.

There is also evidence of reactivated viral infection in Long Covid:

Reference 6



A wide range of immunological abnormalities have been reported in ME/CFS. These involve all the different parts of the immune system: natural killer cells, antibodies, auto-antibodies and cytokines.



WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

Immune system research

A wide range of immunological abnormalities have been reported in ME/CFS and they may help to explain some of the flu-like symptoms – sore throats, enlarged glands, feeling feverish – that often occur in ME/CFS.

Research carried at the ME Biobank, which is funded by the ME Association Ramsay Research Fund, has confirmed that an altered immune system state exists in ME/CFS, especially in those with more severe ME/CFS:

Reference 7

These abnormalities involve most of the different components of the immune-system orchestra: natural killer cells, B cells and T cells, antibodies, auto-antibodies and cytokines. However, none of the abnormalities that have been found in research studies are so far consistent or robust enough to regard them as diagnostic, provide a direct link to symptoms, or be useful in relation to management with drugs that can modify the immune-system response.



Of particular interest are abnormalities involving cytokines. These are immune-system chemicals that are produced in response to any type of infection and which result in a range of flu-like symptoms that form part of the body's normal response to an infection. These include loss of appetite, wanting to sleep more than normal, aches and pains in muscles and joints.

This model of illness, in which an infection triggers an inappropriate or protracted immune-system response, is one that the MEA has proposed for many years. Further support for this theory comes from an interesting research observation that people who are given interferon alpha (a type of cytokine) as a treatment for hepatitis C can develop an ME/CFS-like illness as a side-effect:

Reference 8

And while some research has identified low levels of autoantibodies – these are antibodies that attack the body's own tissues – these findings are again not consistent and do not provide the necessary evidence to say that ME/CFS is an autoimmune disease:

Reference 9



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

Brain and nervous system research

Using a variety of ways of investigating brain structure/anatomy and function in ME/CFS, there is now evidence of abnormalities involving the brain and central nervous system. However, as with immune system dysfunction, these findings are not always consistent and often lack replication by other research groups.

One abnormality that does appear to be linked to symptoms involves what is called the autonomic nervous system (ANS). This is a part of the brain and nervous system that is not under conscious control and which sends 'speeding up' or 'calming down' messages to vital organs such as the heart, bowel and bladder.

This finding is of practical importance because dysautonomia (the medical term for ANS dysfunction) probably helps to explain symptoms such as orthostatic hypotension, where blood pressure falls on standing and may cause fainting, and postural orthostatic tachycardia syndrome (POTS) – where the pulse rate rises on standing.

Reference 10



Brain scans have demonstrated a range of abnormalities including changes in blood flow to key parts of the brain, which could help to explain the cognitive dysfunction such as problems with short-term memory, concentration, etc.

The autonomic nervous system also controls the size of tiny blood vessels supplying the skin, which may help to explain why some people with ME/CFS have cold hands and feet. ANS dysfunction may further explain why irritable bowel and bladder-type symptoms are very common in ME/CFS.

Brain scans have demonstrated a range of abnormalities including changes in blood flow to key parts of the brain, which could help to explain the cognitive dysfunction (= problems with short-term memory, concentration, etc), as well as other brain-related symptoms such as poor temperature control and pain.

One neuroimaging study of particular interest, was carried out by Dr Durval Costa at the Middlesex Hospital in London:

Reference 11



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

This research compared blood flow to an important part of the brain called the brain stem in people with ME/CFS, healthy controls and depression. The ME/CFS patients had a marked decrease in blood flow (hypoperfusion) and as the brain stem helps to regulate a wide range of body functions – heart rate and blood pressure, sleep patterns, balance, etc – this could be another important clue in symptom explanation. Changes in cerebral blood flow have also been reported in Long Covid and linked to fatigue:

Reference 12

An interesting study using functional magnetic neuroimaging (fMRI) has reported that symptoms of fatigue in ME/CFS were associated with reduced responsivity of the basal ganglia, possibly involving the disruption of projections from the globus pallidus to thalamic and cortical networks.

Reference 13

Involvement of the basal ganglia has also been suggested as the cause of fatigue in other neurological conditions such as Parkinson's disease and those involving immune-system activation.

Neuroimaging research from Japan has demonstrated abnormalities that are consistent with low-level inflammation in the brain (neuroinflammation), possibly caused by immune-system activation.

Reference 14



Research relating to brain neurochemical imbalance has reported on higher levels of glutamate and N-acetyl-aspartate:

Reference 15

- and also the possibility of decreased dopamine production in Long Covid:

Reference 16

Analysis of cerebrospinal fluid has shown abnormalities in cell numbers and proteins. Reduced levels of GM-CSF with increases in cytokines IL-8 in some patients and in IL-10 in others supports a hypothesis that some of the symptoms of ME/CFS may be due to immune dysfunction within the central nervous system:

Reference 17



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

Post-mortem research carried out here in the UK, and funded by the MEA Ramsay Research Fund, has found an abnormality called dorsal root ganglia (= inflammation of the dorsal root ganglia) in a small number of cases. The dorsal root ganglion are part of the peripheral nervous system that lies just outside the spinal cord and help to relay messages about sensation and pain back to the brain. The MEA is now working with the Manchester Brain Bank on post-mortem research into ME/CFS:

Reference 18

Dr Abhijit Chaudhuri, a consultant neurologist who advises the MEA on neurological research, has written a review of fatigue in neurological disorders, including ME/CFS:

Reference 19

Neuroendocrine (brain hormone) research

Research into the way in which control centres in the brain regulate the output of various body hormones in ME/CFS indicates that there may be a down-regulation of what is called the hypothalamic-pituitary-adrenal (HPA) axis.

Reference 20



References: <https://linktr.ee/causesMECFS>

The hypothalamus acts as the body's thermostat in relation to appetite, sleep and temperature control – all of which can be affected in ME/CFS.



Dr Abhijit Chaudhuri, Professor Peter Behan and some Australian researchers have postulated that the fluctuating nature of ME/CFS symptoms could be caused by ion channel dysfunction and whether ME/CFS is an ion channelopathy

Reference 20a

The hypothalamus and pituitary are tiny glands inside the brain that play a key role in the control and production of hormones elsewhere in the body. In the case of ME/CFS, some studies have reported a minor defect in the output of the hormone cortisol from the adrenal glands, which sit above the kidneys. This lowered level of cortisol (= hypocortisolaemia) could be related to symptoms such as fatigue and low blood pressure.

The hypothalamus also acts as the body's thermostat in relation to appetite, sleep and temperature control – all of which can be affected in ME/CFS.

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

The MEA Ramsay Research Fund has funded several research studies into mitochondrial function in ME/CFS at the Universities of Liverpool, Newcastle and Oxford.



**The MEA Ramsay
Research Fund**

Leading the way in ME/CFS research

[https://meassociation.org.uk/
ramsay-research](https://meassociation.org.uk/ramsay-research)

Research into energy production and mitochondrial dysfunction

An abnormality involving skeletal muscle biochemistry in ME/CFS, where there is an abnormally prolonged and excessive production of lactic acid following exercise, was first described back in 1984 in *The Lancet*. This research, in which I was involved and used my own leg muscle, was carried out in Oxford by Professor George Radda and colleagues. It examined what happened at a biochemical level during exercise using magnetic resonance spectroscopy (MRS).

Reference 21

Since then, structural and functional abnormalities involving the mitochondria – a key part of the cell where nutrients are converted into an energy-carrying molecule called adenosine triphosphate (ATP) – have been reported in a number of research studies.

Reference 22

More recently, abnormalities in cellular energy production and mitochondrial function have also been reported in Long Covid.

Reference 23

The MEA Ramsay Research Fund has funded several research studies into mitochondrial function in ME/CFS at the Universities of Liverpool, Newcastle and Oxford.



References: [https://
linktr.ee/causesMECFS](https://linktr.ee/causesMECFS)

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

RESEARCH INTO THE ROLE OF THE IMMUNE SYSTEM *(continued...)*

Other possible perpetuating factors

More recent research into the possible cause of both ME/CFS and Long Covid has identified other pathways that may be involved in causation. These include:

The microbiome - a collection of bacteria and other organisms that normally inhabit the gastrointestinal tract - and the gut-brain axis, which describes how the microbiome and the immune system it supports can influence what happens in the brain and central nervous system.

Reference 24

Endothelial dysfunction – the endothelium being the lining of blood vessels which can be affected by an inflammatory event such as a viral infection.

Reference 24a



Symptoms such as pain and sleep disturbance could also help to maintain the underlying disease process through their action on brain chemical transmitter systems and immune-system function.



Researchers are also making use of new techniques such as metabolomics - the study of substances called metabolites in cells and tissues. Metabolites are small molecules that are made when the body breaks down food, drugs, chemicals, or its own tissue. Metabolites can be measured in blood, urine, and other body fluids. Metabolomics may help us to find important clues about disease pathways which in turn lead to diagnostic tests and treatments.

Reference 25

Symptoms such as pain and sleep disturbance could also help to maintain the underlying disease process through their action on brain-chemical transmitter systems and immune-system function – as can problems with mental or emotional health which can occur in any long-term health condition.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?



FUTURE RESEARCH INTO WHAT CAUSES ME/CFS

Historically there has been a serious disparity between government research funding for ME/CFS and most other long-term health conditions. There has also been an unacceptable bias towards funding ME/CFS research that is based on a flawed psychosocial model of cause and management - especially the PACE trial.

As a result, most of the biomedical research into the cause and treatment of ME/CFS has been funded by the ME/CFS charity sector, including the MEA Ramsay Research Fund.

Again, there are now signs of a very significant shift at an international level towards funding research that is firmly based on the biomedical model of cause and treatment.

Here in the UK, the DecodeME genetic research is being taken forward with government and charity funding in SequenceME. This will enable the whole human genome to be mapped out in both ME/CFS and Long Covid.

Reference 26

The Rosetta Stone study at Imperial College, funded by the MEA Ramsay Research Fund, is a world-leading study that is examining the overlaps between Long Covid and ME/CFS

Reference 27

The ME Biobank is supplying anonymised clinical data and blood samples to a growing number of researchers all over the world

Reference 28

CONCLUSIONS

Linking all the different symptoms of ME/CFS and the research findings together helps to explain why ME/CFS is often described as a complex multisystem disease. However, whilst it is possible to link these findings together and produce a disease model that is being proposed here, the only way that firm conclusions about causation are going to be reached is through large and well-designed research studies using carefully selected patients.

Until we have a better understanding of the underlying disease pathways in ME/CFS, and the various clinical and pathological sub-groups, progress in developing both diagnostic biomarkers and effective forms of drug treatment is likely to be slow.

However, important clues are steadily emerging and drug treatments are being assessed on the basis of these abnormalities.



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

FURTHER INFORMATION

■ MEA information booklet: What you need to know about ME/CFS?



This booklet provides a summary of what you need to know about ME/CFS and is based on the evidence-based NICE Guideline, expert medical opinion, and

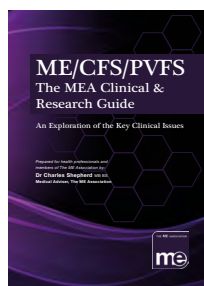
the result of medical research.

It considers key symptoms, diagnosis, multidisciplinary care, and what might cause the disease.

Reference 29

■ The Research chapter in the MEA purple book (ME/CFS/PVFS – Clinical and Research Guide) provides a much more detailed review of key research findings along with references to all the relevant research papers.

Reference 30



The MEA Ramsay Research Fund provides funding for biomedical research into the cause and treatment of ME/CFS. It also funds all the basic running costs of the ME Biobank and collaborates with the Manchester Brain Bank on post-mortem research into ME/CFS.

Reference 31

Use the QR code to link to the MEA's Clinical and Research Guide, **ME/CFS/PVFS: An Exploration of the Key Clinical Issues (The Purple Book)**.

UK DELIVERY ONLY for hard copies. Please allow up to 14 days for delivery.

KINDLE VERSION: If you prefer an electronic copy or you are overseas you can purchase the Kindle version separately on Amazon:

<https://meassociation.org.uk/4nop>



References: <https://linktr.ee/causesMECFS>

WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

THE ME ASSOCIATION

Changing attitudes and improving lives...



“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 effectively and fund 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. All our staff and volunteers have knowledge and understanding of these medical conditions. We provide a personalised service and we're here when you need us most. You can contact us via our telephone support line (this is a FREEPHONE number) or by email. Please see back page for more details. You can also join ME Connected (Discord online community). To view the ME Connect telephone support line 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 £2m in medical research in the last 10 years.

■ **MEDICAL EDUCATION:** We arrange training for healthcare professionals, offer a medical magazine called 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.

References: <https://linktr.ee/causesMECFS>



WHAT CAUSES ME/CFS?

WHAT DO WE KNOW?

THE ME ASSOCIATION

Changing attitudes and improving lives...



“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.”

The ME Association
7 Apollo Office Court
Radcliffe Road,
Gawcott
Buckinghamshire
MK18 4DF

Tel: 01280 818963

Email: admin@meassociation.org.uk

Registered Charity
Number 801279

■ **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: <https://meassociation.org.uk/medm>



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](#).



References: <https://linktr.ee/causesMECFS>





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/mec

Contact ME Connect
HOW TO GET IN TOUCH:
by phone or email



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

For all information relating to ME Connect visit: <https://meassociation.org.uk/mec>

meassociation.org.uk