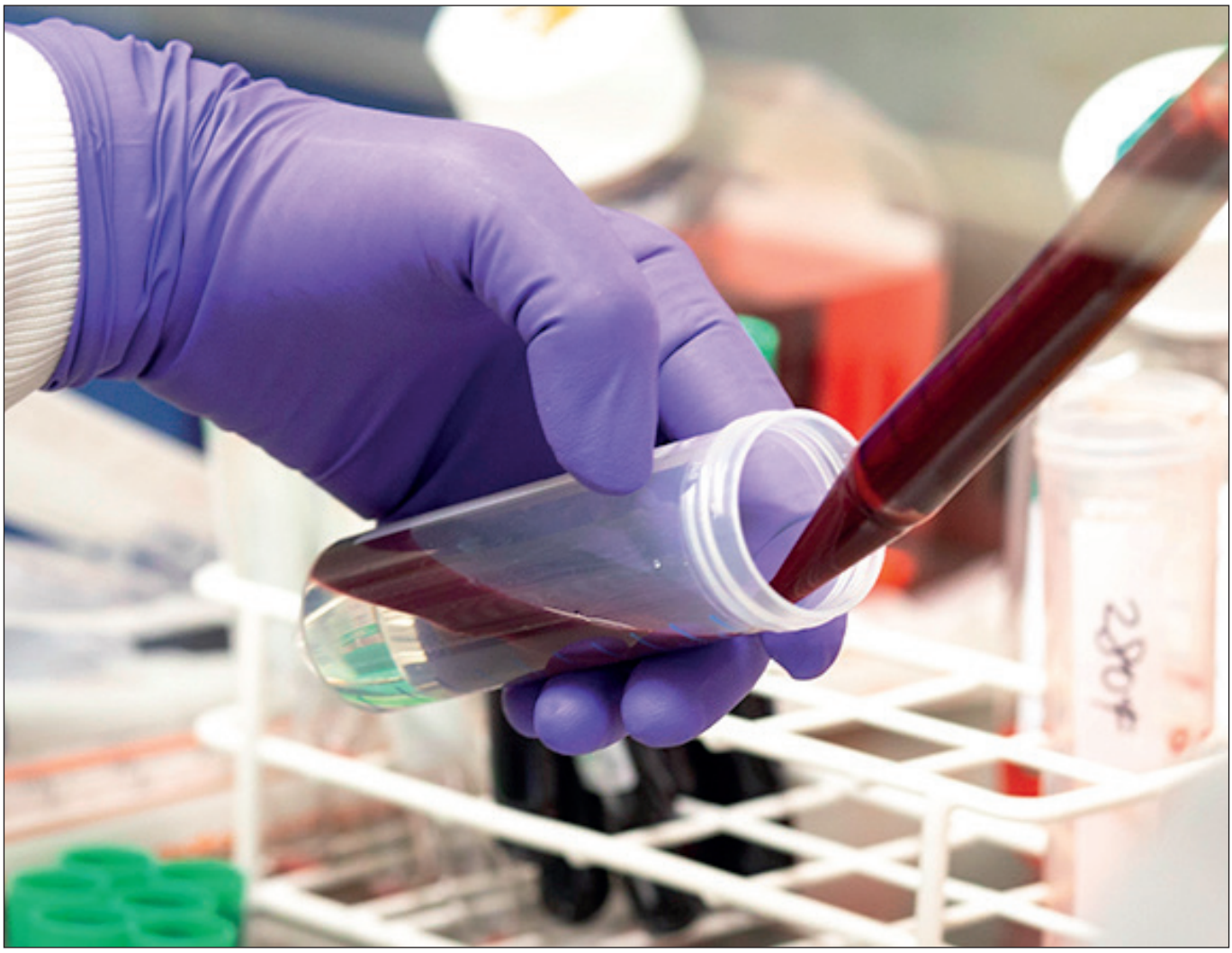
MEE Medical

The magazine for Healthcare Professionals



photograph by Yas Crawford

THE ME ASSOCIATION

This ME Association magazine has been designed solely for doctors and healthcare professionals. It has been estimated that ME/CFS affects around 265,000 adults and children in the UK, so the chances are you will come into contact with someone who has this medical condition.

We hope this quarterly magazine will help to keep you informed of recent developments and contribute to your own understanding. We would like to thank you and your colleagues for the support and help you provide to people with ME/CFS.

If you have any questions then please get in touch: contact@meassociation.org.uk.

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The Countess of Mar
Etain, Lady Hagart-Alexander
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About The ME Association

Biomedical Research

We invest in essential research to discover what causes ME/CFS so that effective treatments can be developed. We are the only charity that funds the vital M.E. Biobank at the LSHTM in London.

Information & Support

We are here to support people with ME/CFS so that everyone gets the help they need. We provide timely and accurate information via an extensive library of leaflets and the telephone helpline. MEA literature can be found online here: **https://meassociation.org.uk/me-association-shop/**

Trustees & Staff

Everyone who works for the charity has experience of ME/CFS, is currently living with the condition, or has a loved one or close friend that has been affected.

ME Connect

The telephone helpline is available 365 days a year to offer support, advice and a listening ear.

The number for ME Connect is **0344 576 5326**. We have a wonderful team of volunteers that are available 10am-12noon; 2pm-4pm; and 7pm-9pm. More information about ME Connect can be found here: **https://meassociation.org.uk/about-the-mea/telephone/**

Membership

We have kept membership subscriptions affordable from just £18 a year, because we know how much of a lifeline ME Essential magazine can be. We put our members' interest at the forefront of all that we do.

Full Membership is available to all adults with ME/CFS, carers and anyone with an interest in the disease. Annual membership costs: £18.00 (UK residents and BFPO); £24.00 (Mainland Europe including Republic of Ireland); £30.00 (Rest of the World)

Join the MEA here: **https://meassociation.org.uk/product-category/mea-membership/**

Collaborations

We collaborate with other charities and belong to Forward-ME and the CFS/ME Research Collaborative (CMRC) because there are times when we need to speak with a single voice and share investment in research.

Fundraising

We are so grateful to every fundraiser – not just for the valuable funds that they raise, but also for the awareness that comes with every single event. ME/CFS still has a long way to go to achieve the kind of medical recognition and social acceptance that other diseases like M.S. have obtained, and any effort on your part can help spread the word and bring us closer to these objectives.

https://meassociation.org.uk/donate/

Welcome to MEE Medical

Introduction by Dr Charles Shepherd, Hon. Medical Adviser to the ME Association

Dear Doctors and Healthcare Professionals

Welcome to the first issue of MEE Medical (ME Essential Medical), the ME Assocation's new quarterly magazine for health professionals. It contains all the medical and research features from the latest issue of ME Essential magazine that we think you will be most interested in reading.

Publication of the important NICE clinical guideline - that had been reviewed over 4 years by a committee of experts, clinicians, and lay members, and was subject to extensive stakeholder consultation - was expected on 18 August, but was withdrawn by NICE at the last minute. The new guideline had been widely welcomed by the patient community, and provided a totally new framework for health professionals on how to diagnose and manage this medical condition. The latest news can be found on the MEA website. We hope to see final publication without too much more delay and we will include a summary of it in the next magazine.

In this issue is a new MEA information leaflet covering the management of hypersensitivities that quite often occur in ME/CFS - including alcohol, light, pain, temperature and touch. We hear from Dr Peter Gladwell at the Bristol ME/CFS service about the use of TENS machines for pain relief, selected Q&As from our regular 'Ask the Doctor' feature covering questions on fluctuating medical conditions, symptoms and triggers.

Meet the Scientist has an interview with Dr Mark Zinn, who discusses Central Autonomic Network Disturbance, and we feature an article from from Phil Prydderch who describes his experience of having severe ME/CFS.

If you have any comments on this publication, or have any questions, please let me know by emailing contact@meassociation.org.uk

Kind regards,
Dr Charles Shepherd
Hon Medical Adviser, MEA

How GPs and other healthcare professionals can help

WHY YOU HAVE RECEIVED THIS PUBLICATION

You have received MEE Medical, our new magazine for health professionals, because a patient has requested it be sent to you. If you would also like to receive the members magazine ME Essential, please join the ME Association as a member: **https://meassociation.org.uk/product-category/mea-membership/**

ME Essential features exclusive articles, medical and scientific developments, Ask the Doctor, stories and opinions from people living with ME/CFS, and keeps members apprised of recent news. Quite simply, it is the best magazine available and the feedback we receive proves it!

ME ASSOCIATION MEMBERSHIP

While our services are primarily aimed at people with ME/CFS, you don't need to have this medical condition to join. Carers, family-members, and healthcare professionals are all represented as members of the charity. The more members we have, the more representative we can be. This is especially useful when we take part in debates, decide to launch a campaign, discuss medical education, or raise awareness in parliament. Membership subscriptions are a vital part of our charity income and together with donations they allow us to help make the UK a better place for people with ME/CFS.

The NICE Guideline on ME/CFS

"It heralded a new beginning and was a guideline we could support, but NICE has paused publication at the last minute" The ME Association

The National Institute for Health and Care Excellence (NICE) has been working on a long-awaited and much-needed new clinical guideline for ME/CFS. The clinical guideline is important as it provides a framework of recommendations to health and social care services in England, Wales, and Northern Ireland – and is recognised in Scotland.

The review began in 2018 after many years of advocacy because the previous guideline was not fit for purpose. The guideline committee – comprising experts, clinicians, and patients – has worked very hard and provided evidence-based recommendations to NICE following an extensive stakeholder consultation period which began last November. NICE then produced a final draft of the guideline which was sent to stakeholders in the first week of August 2021.

The final guideline was expected on 18 August, but at the last minute, and in an unprecedented move, NICE decided to halt the process (https://tinyurl.com/evmzfz45). We don't yet know the full reasons behind this decision, or who in particular might have influenced this move. It would appear that several Royal Colleges have claimed their opinions were not taken into consideration. These views appear to relate to the agreed management recommendations, namely the removal of graded exercise and the recommended energy management.

However, there are a great many improvements to the new guideline that have been overlooked by these Colleges and in the many reports from the news-media. We have been waiting 14 years for a clinical guideline that provides safe and practical recommendations and gives due consideration to the most vulnerable in the patient community.

This further delay, after 4 years of evidence-based review is of real concern and as we have no idea when the guideline might finally emerge – or what it will look like – it could have a detrimental effect on people who are waiting for a diagnosis and for those with a diagnosis who need practical help from health and social care services.

The final draft of the new guideline that we saw on 04 August was good and much improved. It promised real and much-needed support. NHS primary and secondary care would have continued to play key roles in making an accurate diagnosis, providing ongoing accessible care, and helping people manage ME/CFS safely and effectively.

The ME Association is a steering group member at Forward-ME and we helped to produce a press release and statement that endorsed the new guideline. We then had to issue a rapid response when it was announced that the process had been suspended hours before publication.

NICE has announced that a roundtable meeting will be held in September (it will probably have happened by the time you read this article) and it is our hope it will enable stakeholders including the Royal Colleges to reach agreement and for the guideline to be published quickly.

Without the support of these representative bodies, we could have a guideline that is not implemented effectively – and nobody would want to see that. Forward-ME will attend the meeting and listen to the Colleges and to what NICE has to say. We want the guideline to be published without further amendment but we won't know more until this meeting has occurred.

NICE TIMELINE

- Mid-September 2021: Roundtable Discussion – date to be announced.
- 18 August 2021: Intended publication date.
- 17 August 2021: NICE announce delay in publication process.
- 04 – 11 August 2021: Final draft guideline stakeholder consultation.
- March 2021: NICE extend publication date to 18 August 2021.
- November – December 2020: Draft guideline stakeholder consultation.
- December 2019: NICE extend publication date to December 2020.
- January 2018: NICE agree to review and update clinical guideline.

More information

To read all about the story so far, the statements from the MEA and Forward-ME, and for all the news-media articles, visit the website:

https://tinyurl.com/8jkdh72h

DR SHEPHERD'S INITIAL REACTION TO THE NICE DELAY

"We should have been welcoming the arrival of a completely new NICE guideline on ME/CFS today. A guideline that acknowledged ME/CFS as a serious and complex medical condition.

"It was a guideline that contained sensible advice on activity, energy, and symptom management – along with a revised timeline and advice for early and accurate diagnosis, and it placed special emphasis on the care and management of children and young people and those who have severe or very severe ME/CFS.

"Instead, we are discussing the huge disappointment felt by

the patient community to yesterday's announcement from NICE to cancel publication today and to pause proceedings while discussions take place around objections to the new recommendations regarding CBT and GET – objections that were discussed and resolved as part of the long review process."

"On a personal basis, having spent a considerable amount of my time over the last four years working with colleagues on the preparation of this new guideline, I feel frustrated and angry. The action of a small number of people who have persuaded the leadership at the Royal College of Physicians, the Royal College of Paediatrics and Child Health, and possibly other Royal Colleges, to put pressure on NICE to reconsider what had already been agreed by the guideline committee, is reprehensible…"

■ To read more of Dr Shepherd's initial reaction to the news, visit the website:

https://tinyurl.com/9azvjsva

British Medical Journal:

Working together to find the cause and effective treatments for ME/CFS, by Dr Charles Shepherd, Hon. Medical Adviser, ME Association

As a charity that funds biomedical research into myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), we are not aware of any researchers who hold negative views about the patient community (BMJ: Newman M. Chronic fatigue syndrome and long covid: moving beyond the controversy).

Patients, researchers and charities, are all working together on research initiatives such as Decode ME (www.decodeme.org.uk), the ME Biobank (https://cureme.lshtm.ac.uk/the-uk-mecfs-biobank), and cardiorespiratory exercise testing.

People with ME/CFS feel let down by the medical establishment because, until recently, almost all biomedical research has been funded by the charity sector. Almost all government funding has gone into research based on a flawed psychosocial model of causation involving abnormal beliefs and behaviours and deconditioning. This research resulted in the current NICE guideline recommendations, published in 2007, for cognitive behavioural therapy (CBT) and graded exercise therapy (GET).

Having reviewed clinical trial and patient evidence for these interventions. NICE now states in the introduction to the draft of its updated guideline on ME/CFS that: **"…because of the harms reported by people with ME/CFS, as well as the committee's own experience of the effects when people exceed their energy limits, the draft guideline says that any programme based on fixed incremental increases in physical activity or exercise, for example graded exercise therapy (GET), should not be offered for the treatment of ME/CFS."** - *The draft NICE guideline ME/CFS (2020)*

It also emphasises that CBT is not a treatment or cure for ME/CFS.

People with ME/CFS who have not been listened to by health professionals and told that their symptoms are "all in the mind" deserve an apology. This attitude has meant that biomedical research into the underlying cause of ME/CFS has not taken place at the speed it should.

NICE has warned that current recommendations regarding GET for ME/CFS are not appropriate for people with Long Covid. This new cohort of patients with post-viral illness should not have to suffer the same mistakes that have been inflicted on people with ME/CFS. ■

Announcing the Launch of Doctors with M.E.

To improve patient outcomes worldwide by empowering medics, scientists and policymakers with up-to-date practices and scientific rigour, fostering collaboration between professionals, the industries they serve, patients and the public.

To build a future where every surgery, hospital, agency, insurance provider and employer is enabled with accurate information that supports their patients, clients, shareholders and wider stakeholders.

Visit the Doctors with M.E. website for more information: **https://doctorswith.me**

ABOUT DWME

Doctors with M.E. empowers medics, scientists, industry and policymakers with evidence-based practices and scientific rigour, distributing regionally produced content to a global audience, as the international umbrella body representing our professions.

Statement from the Countess of Mar (Extract):

"I am truly heartened by the formation of Doctors with ME. Their appearance has been like a dream come true for me. They have the understanding and drive to take ME into the world of real medicine based on the foundation of their personal experiences, knowledge, and ability to communicate. Thanks to them, I am sure that very soon people with ME will feel as positive as I do about their own future."

Statement: Countess of Mar on Doctors with M.E: **https://tinyurl.com/857kaa87**

Statement from DwME on the Draft NICE Guideline for ME/CFS (Extract):

"Doctors with M.E. (DwME) welcomes and supports this change in treatment recommendations, and we await publication of the final guideline in August 2021. NICE undertook an extensive evidence review and consultation process that involved a wide range of stakeholders, including many clinical experts and patient groups. DwME fully supports NICE's decision to no longer recommend GET as treatment for ME/CFS..."

Statement from DwME on the draft NICE Guideline for ME/CFS: **https://tinyurl.com/3daunhyp** ■

The Howes-Goudsmit Prize for Severe ME Research

Nigel Speight and Willie Weir

The ME Association is pleased to announce the establishment of the Howes-Goudsmit Prize for Severe ME research. This award has been created because of a very generous donation from Dr Ellen Goudsmit, a disabled scientist who helped to create awareness of ME in both the UK and the Netherlands and who has studied ME for over 40 years.

The prize, which will amount to £5,000 per year for the next ten years, has been named The Howes-Goudsmit Prize after Mrs Sandra Howes and the late Mrs Felicie Goudsmit. Mrs Howes had Severe ME, was a board member of the ME Association, and spent years writing about the disease. Mrs Goudsmit was a carer and, as such, became very familiar with the many challenges of dealing with severe disability.

The 2021 Howes-Goudsmit Prize has been awarded – by unanimous decision – to Helen Baxter, Dr Nigel Speight, and Dr William Weir. They co-authored an important item of research into the recognition and management of life-threatening malnutrition in Severe ME.

2021 PRIZEWINNERS

Helen Baxter, Dr Nigel Speight, and Dr William Weir

The research paper, which includes five case reports, was published in the medical journal Healthcare back in April. The recipients issued the following statement:

"We are delighted to receive this award in recognition of our paper.

"We would like to thank both the ME Association for choosing our paper and Dr Ellen Goudsmit for establishing this award to recognise research in the field of severe ME.

"We would also like to take this opportunity to thank the patients with very severe ME and their families who participated in the research and allowed their stories to be told.

"We hope the paper will continue to raise awareness of nutritional difficulties in severe ME."

The Research:

Life-Threatening Malnutrition in Very Severe ME/CFS: **https://tinyurl.com/amnbz94d**

ABSTRACT

Very severe Myalgic Encephalomyelitis (ME), (also known as Chronic Fatigue Syndrome) can lead to problems with nutrition and hydration.

The reasons can be an inability to swallow, severe gastrointestinal problems tolerating food or the patient being too debilitated to eat and drink. Some patients with very severe ME will require tube feeding, either enterally or parenterally. There can often be a significant delay in implementing this, due to professional opinion, allowing the patient to become severely malnourished.

Healthcare professionals may fail to recognise that the problems are a direct consequence of very severe ME, preferring to postulate psychological theories rather than addressing the primary clinical need. We present five case reports in which delay in instigating tube feeding led to severe malnutrition of a life-threatening degree. This case study aims to alert healthcare professionals to these realities.

THE HOWES-GOUDSMIT RESEARCH PRIZE

The prize will be given to an individual or an organisation who has made a significant contribution to research into severe ME – this being defined as causing significant impairment, usually leaving the individual house or bed-bound and/or unable to eat a diet that can sustain him/her.

The research must involve the care or management of people with severe ME and/or raising awareness of severe ME. It should relate to the situation in the United Kingdom but will not be restricted to people or organisations who are based there.

If there are no suitable candidates in any one year the prize will not be awarded and will instead be rolled over to the following year(s).

The decision on who to award the prize will be made by ME Association Trustees who will consult with a person or persons who suffer from severe ME before making their decision.

In making their decision ME Association Trustees will not award the prize to any person or organisation which has previously expressed sexist or racist comments, holds views that are inconsistent with respect for an individual or group, or has carried out threatening behaviour towards a patient or researcher.

The recipient, or recipients, of the prizes will be asked to take part in the consultation process during the following year.

Where possible, the prize shall be awarded during ME Awareness Week which takes place around 12th May each year. ■

The Shame

An ME Association member and blogger shares their experience of what it's like to have ME

I'm ashamed to say I have M.E.

I've collapsed in the street and when I've managed to explain that I don't need an ambulance, it's just M.E, I see the compassion disappear. As if I've said, don't worry, I just want the attention.

My M.E. isn't that bad anymore. I'm not always bedbound. It's been 27 years so I don't really know what being normal is supposed to feel like. But now I can disguise how I am feeling.

On good days I can walk around a shop and buy food as long as I don't carry a heavy shopping basket or stand in a queue. I can walk slightly further to the non-disabled parking bay because if I use my blue badge to park in the disabled space I'll worry that someone will see me walking and judge me harshly.

I drive home and then sit in the car pretending to be busy so I don't have to talk to my neighbour because talking and standing will wipe out the next two days. They'll also wonder why I've gone from seemingly normal to holding onto the fence and walking like a spaceman.

If I'm on a bus and a person with a pram is getting off at the same time, I wait until the next stop, or hide behind other passengers, so I don't have to look like a selfish person for not helping. I never sit in the priority seats in case I'm asked to move for a person who's visibly in need. Mostly I avoid buses.

I'm entitled to having a Disabled parking bay outside my home, but my neighbours would know I was ill and question why I seemed perfectly fine walking the dogs the other day.

I suspect one of my neighbours knows because she no longer asks, "How are you today?" she asks, "How's your health doing?" I don't even like sympathetic people because it puts me on the spot and there's never an easy explanation.

I was taken to hospital with a suspected heart attack once because of bad chest pains. Then my legs collapsed. I told the doctor's I felt it was probably M.E. and they said, "No, M.E doesn't do that."

When eventually I was told that I was fine and all tests were normal, they no longer cared that my legs still weren't working because they knew I had M.E and M.E. symptoms don't count.

I started having different symptoms. Numbness, brain zaps, collapsing without warning. I was checked out for Multiple Sclerosis. I was disappointed not to have it. I desperately wanted to have something people recognised as life-altering and didn't need to be explained.

I was using my wheelchair that week, the doctor looked concerned and tried all the tests. When it turned out I didn't have MS, his attitude changed towards me. He looked at me like I was a con artist.

I never blame M.E. for making me feel ill, I always blame myself. I blame myself for putting away the washing, for texting too much, for standing in the shower, for taking jeans out of the wardrobe, for lifting a heavy shoe, for reading, for writing this…

Ironically, I have had some good things happen to me because of my 27 years with M.E. Looking back:

I wouldn't have met my husband if I didn't have a relapse, which prompted me to leave my boyfriend because he couldn't cope with looking after me again.

I wouldn't have got my beautiful dogs if I'd been able to work full-time.

I wouldn't look young for my age if I'd been able to have a social life.

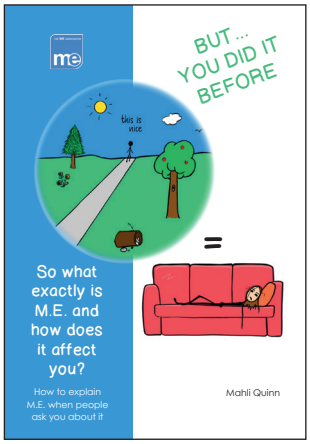
I wouldn't have found out who my real friends were if I hadn't been ghosted by the ones who couldn't handle the tedium of illness.

I wouldn't have experienced the joy of symptom-free days.

I can't yearn for what might have been if I hadn't had M.E. It's too late for that. Doctors have been my prison guards. I am ashamed to say I have M.E. but the real shame lies with the medical profession.

If their attitude had been at least as good as it is for others with a chronic illness, if they chose to believe me and treat me with fairness then perhaps I wouldn't carry my shame and the stigma associated with this medical condition would have been extinguished decades ago. ■

Photograph courtesy of an MEA member for The ME Association's Real ME Campaign



The ME Association recently published a wonderfully illustrated comic from digital artist Mahli Quinn that helps to explain M.E. to others: **https://tinyurl.com/uvhv2af3**

Dr Charles Shepherd, Hon. Medical Adviser for the ME Association, discusses:

Sensitivities, intolerances and hypersensitivities in ME/CFS

INTRODUCTION

This article provides information and practical self-help management tips on how to cope with most of the common sensitivities, intolerances, and hypersensitivities that can affect people with ME/CFS.

Most people with ME/CFS will develop a sensitivity, an intolerance, or a hypersensitivity to one or more things that we all come into contact with and are often part of normal everyday life. The terms sensitivity and intolerance are to some extent overlapping whereas hypersensitivity implies a far more severe problem.

Common sensitivities experienced by people with ME/CFS – particularly when they are severely or very severely affected – might involve alcohol, chemicals and smells, drugs, food, light, noise, pain, temperature, and touch.

Although the cause remains uncertain, and probably differs between sensitivities, one possible explanation in the case of ME/CFS is that a viral infection, or whatever immune-system stressor triggered ME/CFS in the first place, resets control centres and chemical transmitter systems in the brain that are responsible for how we recognise and then react to things like alcohol and chemicals.

With some sensitivities the problem may lie in what is called the peripheral nervous system – part of the nervous system that lies outside the brain and spinal cord and which transmits information about pain, touch, etc., from the body and skin back to the brain.

And while there is patient and some research evidence to indicate that various types of allergic disease are more common in people with ME/CFS, possibly as a result of the immune-system dysfunction that is present, the sensitivity problems covered here are not being caused by immune mediated allergic reactions. One allergic condition where we receive fairly regular reports is hay fever – where there is hypersensitivity to plant pollen. This was covered in some detail in a Question and Answer in the Autumn/Winter 2020 (156) edition of ME Essential. We are planning to cover allergies and ME/CFS in a separate information leaflet in due course.

Allergy research reference:

Straus SE et al. Allergy and the chronic fatigue syndrome. The Journal of Allergy and Clinical Immunology. 1998, 81 (5 Pt 1): 791–795:

https://tinyurl.com/45t8vxkd

Unfortunately, apart from avoiding any known trigger factors where possible, there is no simple solution to any of these problems. And drug treatments are not usually the answer.

ALCOHOL

Alcohol intolerance is a characteristic diagnostic symptom of ME/CFS with many people reporting that it occurred right at the very start of their illness. As a result, even small amounts of alcohol can produce a hangover-type effect. So most people decide to avoid alcohol completely.

We don't know why this happens. ME/CFS does not affect liver function, where alcohol is metabolised/broken down - so it's unlikely that the problem lies there. A more plausible explanation, which links in with increased sensitivity to drugs that act on the central nervous system, is that there is a similar sensitivity that involves changes to chemical transmitter systems in the brain that are influenced by alcohol.

The only published research is a small study that looked at the incidence of alcohol intolerance in ME/CFS (Woolley et al). Two-thirds of those interviewed reported decreased use of alcohol - the most common reasons being increased tiredness, hangover feelings, nausea and an exacerbation of sleep disturbance.

We also don't know whether drinking alcohol again after a period of abstention is going to cause any harm, or delay to any natural recovery process. Based on patient evidence it seems that this is a safe thing to do so if

this is one of your pleasures in life - providing intake is not in excess, is limited to times when your illness is stable or improving, and that you are not experiencing any adverse effects after drinking alcohol.

Research reference:

Woolley J et al. Alcohol use in chronic fatigue syndrome. Journal of Psychosomatic Research. 2004, 56, 203 – 206:

https://tinyurl.com/5yym3c3w

Chemicals, smells and multiple chemical sensitivity (MCS)

A wide range of everyday products can cause problems for people who have chemical sensitivities. They can do so via contact on the skin, or through ingestion or smell. Common triggers include:

- pesticides and insecticides
- agricultural chemicals
- moulds and mycotoxins (toxic chemicals produced by moulds/fungi)
- synthetic fragrances – including perfume, fragrances and deodorants
- laundry detergents and fabric softeners
- cigarette smoke and wood-fire smoke
- petrochemical solvents and plastics
- building materials
- preservatives, food colourings, artificial sweeteners, and additives such as tartrazine
- air pollution
- some types of essential oils

Where people have multiple sensitivities a diagnosis of multiple chemical sensitivity (MCS) may be appropriate. MCS on its own can cause a wide range of symptoms – common ones being:

- headaches,
- fatigue,
- confusion and memory problems,
- depression,
- shortness of breath,
- joint and muscle pains,
- skin rashes,
- dizziness and gastrointestinal problems.

As many of these MCS symptoms overlap with ME/CFS, having MCS is very likely to exacerbate some aspects of ME/CFS.

Unfortunately, NHS services for people with MCS can be poor or even non-existent. And although some private doctors and alternative practitioners claim to specialise in MCS, this may involve expensive investigations and treatments – many of which are unproven and need to be viewed with a considerable degree of caution.

Practical tips that may help:

- Air purifiers
- Avoiding scented cleaning products and toiletries

DRUGS

People with ME/CFS are often more sensitive to the side-effects of drugs. This can involve both prescribed and over-the-counter medications, especially those that affect chemical transmitter systems in the brain such as antidepressants and anaesthetics and some types of pain-relieving drugs.

Consequently, it is often advisable to start with a low dose of this type of drug, especially antidepressants, and proceed cautiously with gradual increases in dose over a period of weeks. The use of liquid preparations can be useful if a very low dose is required, or swallowing tablets causes difficulties.

FOODS

The situation regarding causation may be more uncertain as some reactions to foods have a clear allergic basis (e.g. peanut allergy) whereas other people are intolerant or sensitive to one or more foods.

Food intolerance and sensitivity can play a role in both irritable bowel syndrome and migraine-type headaches – both of which are more common in people with ME/CFS.

Wheat/gluten sensitivity can cause coeliac disease – a condition that is sometimes misdiagnosed as ME/CFS because it causes fatigue and irritable bowel-type symptoms (IBS). Screening for coeliac disease with an antibody blood test should always be arranged before a diagnosis of ME/CFS is confirmed, especially in people who have IBS-type symptoms.

With lactose intolerance, people become intolerant to milk and dairy products because they lack an enzyme called lactase. This is a chemical that breaks down lactose in dairy products. Symptoms, some of which are very similar to irritable bowel syndrome, include bloating, diarrhoea, and stomach pains/cramps.

The best way to identify foods that may be causing a problem is normally through the use of what is called an elimination diet where specific foods, or food groups, are excluded from the diet for a period of time to see if this is linked to any improvement. Undertaking this type of assessment really requires help from a dietitian – preferably one who understands ME/CFS.

There are also a wide range of food allergy tests available both privately and on the NHS. However, some of those offered by commercial companies and alternative practitioners are of very questionable value. So do check with your GP before relying on a commercial food allergy test or purchasing expensive allergy treatments.

More information:

We have a range of leaflets available to download from the MEA website shop all about diet and nutrition in ME/CFS including a review of dietary trends, malnutrition, the FODMAP diet and irritable bowel type symptoms. We also have a leaflet covering irritable bowel-type symptoms and ME/CFS:

https://tinyurl.com/4urthurk

LIGHT

Sensitivity to light, especially bright light from fluorescent or incandescent light bulbs or strong sunlight, is known as photophobia. This can produce uncomfortable or painful feelings in the eye as well as excessive blinking or squinting, watering, and eye strain, and lead to people either avoiding bright light or taking measures to restrict exposure.

Photophobia tends to be more common and pronounced in

SENSITIVITIES, INTOLERANCES AND HYPERSENSITIVITIES IN ME/CFS

people with severe and very severe ME/CFS. However, it's important to note that photophobia can also be a sign of an underlying eye condition such as:

- dry eyes
- blepharospasm - where the eyelids close uncontrollably
- uveitis - inflammation inside the eye
- keratitis - inflammation of the cornea, the clear layer in front of the eye
- cataracts
- retinal damage

So it's important to have your eyes checked by either your GP or an optician before concluding that photophobia is just another symptom of ME/CFS.

Wearing sunglasses with polarising lenses will help to eliminate glare, especially when out of doors. Blackout curtains can also help to restrict light coming into a room. However, it's important to note that constant use of light-limiting measures indoors can make photophobia worse by artificially adapting the eyes to conditions that are too dark.

Opticians are a good source of information and guidance on how to manage photophobia. They can help with:

- Reaction lenses in glasses that will adapt to changing light,
- An anti-reflective coating to glasses that will help if you have to cope with high-intensity indoor lighting in a shop or office,
- Tinted glasses,
- Yellow tinted glasses – which turn dazzling headlights yellow and may help with night driving.

Bright light is also a common trigger factor for migraine-type headaches – which appear to be more common in people with ME/CFS and are often accompanied with an increased sensitivity to smell and noise.

Practical tips and commercial products that may help:

- Blackout blinds or curtains,
- Blackout eye masks,
- Reducing the brightness on a computer screen or loading a programme to recue brightness,
- Theraspecs are therapeutic glasses that are designed to filter out harmful blue light which might trigger migraines etc.

NOISE

Increased sensitivity to what most people would regard as everyday sounds, and not necessarily loud noise, is called hyperacusis. Sound not only becomes unpleasant – it can also cause pain. People with hyperacusis are also more likely to hear ringing, buzzing or other strange noises in their ears – which is called tinnitus.

There is no effective drug treatment for hyperacusis. Management is therefore limited to self-help measures such as sound therapy, which can involve wearing an ear piece that makes white noise.

Wearing noise reduction headphones or ear plugs may be helpful but they should only be used when really necessary, e.g., when trying to sleep, as permanent use can make you prone to noise sensitivities at an even lower frequency. One way around this might be to have 'white noise' in the background e.g., a fan, when sleeping.

More information:

The British Tinnitus Association has useful information and guidance on both hyperacusis and tinnitus.

Practical tips and commercial products that may help:

- Flare audio ear plugs. or mouldable ear plugs from a pharmacy,
- Noise cancelling headphones,
- Ear defenders – e.g., Peltor
- SensGard hearing protection products,
- white noise machines/ sounds.

PAIN

Hypersensitivity to pain, where the body over-reacts to any form of painful event – such as even a minor injury, is called hyperalgesia. It also occurs in fibromyalgia, shingles, HIV infection and diabetic neuropathy. It can also be caused by longer-term use of opiate pain-killing drugs.

If the problem is more severe it may be worth asking for a GP referral to a hospital-based pain management service.

The MEA has an information leaflet covering the general management of pain in ME/CFS and leaflets covering the use of all the main drugs that might be prescribed to help reduce pain in ME/CFS (eg Amitriptyline, Gabapentin, Pregabalin)

Research reference:

- MEA information about the NICE Guideline on Chronic Pain & ME/CFS:

https://tinyurl.com/4tt2dpbp

- Meeus M, et al. Evidence for generalized hyperalgesia in chronic fatigue syndrome: a case control study. Clinical Rheumatology. 2010, 29 (4): 393–398:

https://tinyurl.com/4pt4s3xv

Temperature regulation – and coping in hot weather

People with ME/CFS almost always have problems with temperature control. This is

probably related to a problem with a tiny 'thermostat' gland in the brain called the hypothalamus - which plays a key role in temperature regulation and control.

In addition, the autonomic nervous system, that controls the size of tiny blood vessels, becomes more sensitive to changes in temperature.

Having ME/CFS therefore makes people more sensitive to changes in external temperature, humidity, and to things like hot baths/showers. Most will be more sensitive to hot or cold weather. Conversely, others may find that ME/CFS symptoms are more manageable in the warmer summer or cooler winter months.

Practical tips that may help:

To keep you cool when experiencing hot temperatures:

- Wear lightweight and loose-fitting cotton clothes and pyjamas and a wide-brimmed hat if you have to go outside in the heat
- Drink plenty of fluids to stay hydrated – but avoid too many caffeine-containing drinks
- Eat small regular meals and switch from hot meals to salads
- Reduce activity levels in hot temperatures and stay indoors between 10am and 6pm – unless you really need to go out
- Be aware of warning signs of heat-related illness/heat stroke – nausea, headache, confusion, muscle cramps, feeling faint
- Close the curtains and windows during the day in any room you want to stay cool, especially those that face the sun. Once the heat starts to cool down windows can be opened again in the evening and at night
- Buy an electric fan for when if it's really hot
- Take a cold 'hot water bottle' to bed at night and keep a cold-water spray handy during the day
- Have a bowl of cold water and a flannel by the bedside at night to cool down
- Run cold water over wrists and submerge feet in cold water – if you can manage it, then a cool shower before sleep can also help
- Be aware that some drugs (e.g., antidepressants, antihistamines) can also affect temperature-control mechanisms
- Switch to low-energy light bulbs – as conventional incandescent light bulbs emit more heat – and avoid charging electric equipment in the bedroom overnight
- Strange as it might seem but a cup of hot tea can actually help to lower body temperature. It does so by stimulating sensory nerves in the mouth which then trigger an increase in sweating. This works best in hot dry weather and if you are wearing lose clothing that allows the skin to breathe.

There are also various types of commercial cooling towels and other cooling products available that you might find helpful.

More information:

We have an MEA information leaflet that discusses the management of temperature dysregulation and cold hands and feet in more detail: **https://tinyurl.com/r383ywzk**

TOUCH

Sensitivity to what can be just light touch on the skin from another person, bedding, clothes, and furniture is known as cutaneous or tactile hyperaesthesia. It tends to occur in people with more severe ME/CFS.

Interestingly, this sort of tactile sensitivity can occur in people who have nerve pain/damage in conditions like diabetes as well as in the autistic spectrum disorder – where it may have a developmental origin as touch is one of the first senses to develop after birth. It has also been described in people with COVID-19 infection.

You can read the article here: **https://tinyurl.com/nsmfbepd**

In some cases, sensitivity to touch creates an unpleasant sensation in the skin but it can also cause pain. ■


July 2021

SENSITIVITIES, INTOLERANCES AND HYPERSENSITIVITIES IN ME/CFS

ME CONNECT HELPLINE: 0344 576 5326

by Dr Charles Shepherd
Non-Medical Adviser to the MEA

INTRODUCTION

This leaflet provides information and practical self-help management tips on how to cope with most of the common sensitivities, intolerances, and hypersensitivities that can affect people with ME/CFS.

Most people with ME/CFS will develop a sensitivity, an intolerance, or a hypersensitivity to one or more things that we all come into contact with and are often part of normal everyday life. The terms sensitivity and intolerance are to some extent overlapping whereas hypersensitivity implies a far more severe problem.

Common sensitivities experienced by people with ME/CFS – particularly when they are severely or very severely affected – might involve alcohol, chemicals and smells, drugs, food, light, medicines, pain, temperature, and touch. Although the cause remains uncertain, and probably differs between sensitivities, one possible explanation in the case of ME/CFS is that a viral infection, or whatever immune system stressor triggered ME/CFS in the first place, resets control centres and chemical transmitter systems in the brain that are responsible for how we recognise and then react to things like alcohol and chemicals.

With some sensitivities the problem may lie in what is called the peripheral nervous system – part of the nervous system that lies outside the brain and spinal cord and which transmits information about pain, touch, etc., from the body and skin back to the brain.

And while there is patient and some research evidence to indicate that various types of allergic disease are more common in people with ME/CFS, possibly due to a type of immune system dysfunction that is present, the sensitivity problems covered here are not being caused by immune mediated allergic reactions.

One allergic condition where we receive fairly regular reports about is hay fever – where there is hypersensitivity to plant pollen. This was covered in some detail in a Question and Answer in the Autumn/Winter 2020 (134) edition of ME Essential. We are planning to cover allergies and ME/CFS in a separate information leaflet in due course.

Allergy research reference:

Straus SE et al. Allergy and the chronic fatigue syndrome The Journal of Allergy and Clinical Immunology. 1998, 81 (5 Pt 1): 791–795.

https://tinyurl.com/4898vskd

Unfortunately, apart from avoiding any known trigger factors where possible, there is no simple solution to any of these problems. And drug treatments are not usually the answer.

ALCOHOL

Alcohol intolerance is a characteristic diagnostic symptom of ME/CFS with many people reporting that if occurred right at the very start of their illness. Even very small amounts of alcohol can produce a hangover-type effect. So most people decide to avoid alcohol completely.

We don't know why this happens. ME/CFS does not affect liver

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Sensitivities, Intolerances, and Hypersensitivities in ME/CFS was written by Dr Charles Shepherd (pictured above), Trustee and Non Medical Adviser To The ME Association.

Sensitivities, intolerances, and hypersensitivities in ME/CFS is available as a leaflet from the ME Association's website shop. If you feel your patient would benefit from reading it, please offer them this link: **https://meassociation.org.uk/me-association-shop/**

From the MEA website

ME/CFS Research Published

All research relating to ME/CFS can be located in the ME Association: Index of ME/CFS Published Research. It is a FREE resource, available to anyone, and updated at the beginning of each month: **https://tinyurl.com/b4ufz48f**

Disputed therapies for myalgic encephalomyelitis abandoned – Times Article

The Times has an article covering the new NICE guidelines on ME/CFS and states that GET and CBT will no longer be recommended as a treatment to Doctors. The article covers NICE's view that the research used to promote these treatments were flawed: **https://tinyurl.com/3xcatvd5**

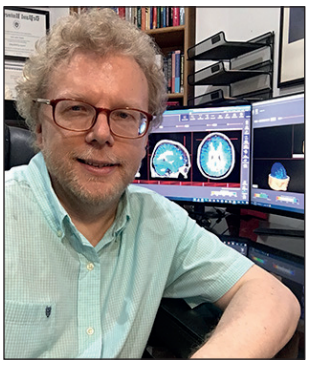
Meet the Scientists: Leonard Jason & Madeline Johnson: risk factors for suicide in people with ME/CFS

Leonard Jason is a professor of psychology and Director of the Centre for Community Research at DePaul University in America. He has a long history of research in the field of ME/CFS.

Madeline Johnson is co-author of several research studies into ME/CFS and is a research assistant to Leonard Jason. Later this year she will be starting her PhD studies in chronic illness amongst paediatric populations.

Guest Blog by Dylan Murphy: **https://tinyurl.com/jsmd8nda**

Mark Zinn is the co-founder of the Neuro Cognitive Research Institute. He has expertise in quantitative and tomographic methods of EEG analysis to test theoretical premises in research involving neuro cognitive disorders.



Meet the Scientist: Central Autonomic Network Disturbance in people with ME/CFS

A conversation with Dr. Mark Zinn, by Dylan Murphy

Mark Zinn is the co-founder of the Neuro Cognitive Research Institute along with his late wife Marcie. He has expertise in quantitative and tomographic methods of EEG analysis to test theoretical premises in research involving neuro cognitive disorders. He has also served as a research consultant 2011-2014 at the Stanford School of Medicine to study cognitive impairment in infection-associated chronic diseases such as ME.

In 2015 he and his wife went to work with Professor Leonard Jason at DePaul University to study neuronal dysregulation within specific brain regions and brain systems contributing to the disrupting of brain network efficiency in patients with ME. Dr. Zinn's ongoing research into the brain regions involved in the autonomic nervous system is an attempt to understand how brain dysregulation helps bring about symptoms in people with neurocognitive diseases. He is the author of numerous research papers in the field of neurocognitive research. His latest research paper* that he co-wrote with his late wife Marcie and Leonard Jason is the subject of the conversation below.

How did you get involved in the field of ME research?

I got involved in the research about 11 years ago, soon after my wife Marcie was diagnosed with herpes encephalitis. Fortunately, she came into contact with Dr. Jose Montoya at Stanford Medical Center and he diagnosed her with ME. He invited Marcie to be on the team for the newly formed Stanford ME/CFS initiative to conduct a major research project involving quantitative EEG**.

I became involved in the project to help with analyzing the data using eLORETA*** (3-dimensional analysis of EEG signals). The results were very promising and our presentation was well received at the 2014 Stanford ME/CFS Symposium as well as the IACFS/ME Conference in San Francisco where we first met Dr. Leonard Jason. Having finished our project at Stanford, Marcie and I decided to move to Chicago in 2015 to continue our work with Dr. Jason at DePaul University. I went on to get my PhD. in psychology with Dr. Jason as my mentor.

ME is a disease of the central nervous system associated with neuro inflammation and dysfunction of the autonomic nervous system. As your recent study has observed current research has demonstrated a need for understanding the effects of physical activity on neurological processes in ME, specifically the central autonomic network (CAN).

Your latest research examines the autonomic nervous network and its relationship to post-exertional malaise (PEM) in people with ME. Can you briefly explain what the autonomic nervous network is?

The central autonomic network is a set of brain regions that work in together in a tightly coordinated fashion for regulating our internal "steady state". It is involved everything you do throughout the day and night, controlling your body states by making adjustments like a thermostat. Depending on momentary demands, it optimizes your blood circulation, heart-rate, blood pressure, body temperature, digestion, sleep/wake cycle, cognition, and many other functions. Signs and symptoms of autonomic dysregulation include difficulty standing upright (orthostatic intolerance), debilitating fatigue, lightheadedness / dizziness, nausea and GI symptoms, brain fog, irregular heartbeat, and shortness of breath.

In your research paper you note that brain regions that are associated with central fatigue are also involved in central autonomic processing, thus implicating the central autonomic network as a prime target for further investigation.

How does this relate to the main objective of your study?

From the Stanford eLORETA study, we learned that certain brain regions with abnormal function were closely tied to autonomic function. The objective of the pilot study was to measure effects of physical exertion in the brain but just targeting key regions known to be involved in maintaining and regulating the autonomic nervous system.

How did you seek to measure post-exertional malaise in the participants of your pilot study?

To study post-exertional malaise, we decided to

record the participants' EEG before and after performing moderately strenuous exercise involving a basic handgrip challenge. A defining aspect of PEM is that it often lasts 24 hours or more. So we had everyone come back the next day and measured their EEG again to assess for changes that might occur after a 24-hour period.

Your study aimed to quantify the effects of physical exertion on central autonomic function in people with ME. What statistically significant findings did your study observe?

In the patient group, we observed a significant reduction in brain activity immediately following the exercise and the reduction worsened after 24 hours. But in control group, we observed a significant increase immediately after exercise, and further increased after 24 hours. With the EEG, we were also able to look at brain rhythms and we found that certain frequencies predicted this change more than other frequencies. So, for example, frequencies involved in driving sensorimotor signaling during task performance predicted greater likelihood for autonomic dysregulation following exercise. Similarly, frequencies having to do with cognitive inhibition and attention also predicted greater likelihood for more autonomic dysregulation following exercise.

If the findings of your study are confirmed by further research how might this be of use to the diagnosis, treatment and understanding of ME?

Overall reduced activation within the central autonomic network may serve as a neurobiological indicator for PEM, which is the most debilitating feature of this illness. Our research protocol could be used in the clinic for measuring subtle changes in brain function triggered by moderate exercise in order to capture features of PEM. In the ME research field, there has been a lot of mixed and contradictory findings, but there may be more agreement within the context of the central autonomic network. In addition, patients with severe ME may have a difficult time with performing maximal cardiopulmonary exercise tests, and this is a practical method that could be done on most patients, even at the bedside. Quantitative EEG adds sensitivity for confirming neurological aspects of PEM and monitoring treatment effectiveness over time. More research is needed to sort all the diagnostic and treatment implications, but these results are promising.

What further actions are needed by public health authorities to help improve the life outcomes for people with ME?

The healthcare system and general public need to be made aware of reasons for the wide-ranging autonomic symptoms reported by patients with ME. When there are no major indications on routine tests, patients are typically told there is nothing wrong, but there may be follow-up tests for autonomic dysfunction from post-viral/immune responses in the brain, resulting in extreme fatigue. People with ME may look fine on the outside while their body is failing to maintain steady-state on the inside. Objective findings of PEM validate the illness while demonstrating that worsening symptoms are due to an underlying neurological condition that needs to be taken seriously. There needs to be funding set aside for the intensive study of the central autonomic network in relation to nearly all aspects of this debilitating disease.

Do you have plans for any future ME research that would follow up your Central Autonomic Network (CAN) study?

I plan to make the CAN the main focus of my research, adding heart-rate variability as a peripheral autonomic measure to study mind-heart interactions. Our NIH grant application for conducting a much larger study on CAN functioning in ME was dismissed by the ME/CFS special interest panel, sadly. Getting funding has been difficult and this pilot study was done without any funding whatsoever. We've submitted another grant application to NIA to study neurological factors in neuro-covid symptoms in older and younger people as well as adolescents. This will involve collaborations with researchers at Northwestern University and Lurie Children's Hospital in Chicago.

* Mark Zinn, Marcie L. Zinn, Leonard A. Jason DePaul University, Central Autonomic Network Disturbance in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Pilot Study, 2021-06-30, Neuro Regulation 8(2) 73-86, DOI: https://doi.org/10.15540/nr.8.2.73

Marcie Zinn who was a distinguished researcher and ME advocate died on 28th December 2019 after the above manuscript was completed.

Below is a link to a short video that the three of them put out to explain their research into neurocognitive impairment in pwME:

https://www.youtube.com/watch?v=aN0Fh0kiUiI

** An electroencephalogram (EEG) is a recording of brain activity.

*** "state-of-the-art electrical neuroimaging techniques such as swLORETA (standardized weighted low-resolution electromagnetic tomography) allow for accurate mapping of neuronal activities of the brain in three dimensions. Electrical neuroimaging operates at the millisecond timescale which allows for a reliable linkage of brain states and brain regions linked to a patient's symptoms. Furthermore, it is far more practical in terms of cost and portability. These advantages allow researchers and clinicians to objectively measure brain function happening in real time and analyze waveform patterns for assessing the effects of disease on cognitive and behavioral functions."

Definition taken from the Neuro Cognitive Research Institute website. ■

Ask the Doctor

These questions were submitted to **Dr Charles Shepherd** by ME Association members and feature within the 'Ask the Doctor' section of our Autumn 2021 members' magazine, ME Essential.

WHAT TRIGGERS ME?

Most people I know with ME say their illness started with or followed an infection - from which they never recovered. But there are a few who don't recall a clear and sudden onset to their deterioration in health. So are we really sure that infections are always the cause of ME?

DR SHEPHERD RESPONDS...

Patient and research evidence indicates that most people with ME/CFS, possibly around 75%, predate the onset of their illness to a very specific acute viral infection.

A wide range of viruses are known to trigger ME/CFS. This includes common viral infections like chickenpox through to more unusual tropical viral infections such as Ebola virus (in Africa) and Zicca virus (in South America). Glandular fever (Epstein-Barr virus) is a well-recognised trigger factor for post-viral fatigue syndromes and ME/CFS in children and adolescents - where it is estimated to cause a prolonged post-viral illness or ME/CFS in around 10% of cases.

Although far less common, non-viral infections can also trigger ME/CFS. Examples include giardia (which causes a nasty gastrointestinal illness) and Q fever (an illness caught from contact with sheep).

In a minority of cases, some other form of immune-system stressor - such as a vaccination, pregnancy, trauma or a surgical operation - appears to be the main triggering event. In the remainder there is no clear triggering event with symptoms appearing more gradually.

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 of ME/CFS.

In summary, it's a complicated picture overall. In our current state of knowledge, my conclusion is that some form of significant stress on the immune system, often in the form of a viral infection, is the main factor in the development of ME/CFS in the majority of cases. In addition, as with conditions like heart disease and arthritis, some people have a genetic predisposition to developing ME/CFS when the right trigger factor comes along.

THE MEA CLINICAL AND RESEARCH GUIDE

Research into the role of infections, and all the other possible trigger factors for developing ME/CFS, is summarised and referenced in the Research section of the MEA purple book:

tinyurl.com/4f55bhmc

This is free for doctors and health professionals by calling 01280 818963 or emailing admin@meassociation.org.uk

NEW SYMPTOMS – WHEN SHOULD I SEE THE DOCTOR?

I know that in addition to all the well-known symptoms associated with ME there are a considerable number of other symptoms that can sometimes occur. But when should I go and see my doctor if I develop a new symptom? Or when an existing symptom isn't quite the same as it used to be?

In my case I've always had a problem with balance and I know you have described this as 'walking on rubber' - which is exactly how it feels at times! However, I'm now having what are best described as occasional dizzy spells where I feel very "off balance". I also suspect that my hearing isn't quite as sharp as it used to be.

I've mentioned this problem to my new GP, who checked my blood pressure, looked inside my ears and said it was probably caused by ME - but come back if things don't improve! I don't want to be seen as a hypochondriac, turning up at the doctors every time I don't feel well. But at the same time, I don't want to find that something important, or treatable, is being missed.

DR SHEPHERD RESPONDS...

It is always a good idea to speak to your GP if/when a new symptom - affecting either physical health or mental health - develops during the course of ME/CFS, even if the symptom is one that is often reported in ME/CFS.

This is because it's quite possible that a new symptom is being caused by a completely different condition, possibly one that has symptoms that are also present in ME/CFS. For example, an overactive thyroid gland (thyrotoxicosis) can cause sweating, palpitations and anxiety. An underactive thyroid gland (hypothyroidism) can cause gastric problems, increased sensitivity to the cold and cognitive dysfunction. All of which are symptoms that can appear in the course of ME/CFS.

In the case of balance problems, which are very common in ME/CFS, a change in nature to having actual dizzy spells, or spinning round sensations (vertigo), is something that you must see your doctor about. This is a problem that could be caused by a fall in blood pressure when you move from

lying to standing - known as orthostatic hypotension. The loss of blood supply to the brain can then cause dizziness, nausea, sweating and feeling faint, or even fainting. But it could also be caused by a problem involving the way in which the ears, eyes and brain co-ordinate messages about body position and which is not related to your ME.

So it is important to go back to your doctor if these new symptoms continue, or get worse, because you may need to have some further investigations carried out, or be referred to the ENT department at the hospital, to find out why these episodes are happening. I would also advise that you have a proper hearing test done - if this has not been checked already.

BLOOD-BORNE TRANSMISSION OF FIBROMYALGIA - COULD THIS NEW RESEARCH FINDING ALSO APPLY TO ME/CFS?

There was an interesting report in The Guardian newspaper about some new research into fibromyalgia. This suggests that there is an immunological abnormality involving antibody production and that removing these harmful antibodies could be an effective form of treatment. This is a brief summary of what they found:

The researchers in London took blood from 44 people with fibromyalgia and injected purified antibodies from each of them into different mice. The mice rapidly became more sensitive to pressure and cold, and displayed reduced grip strength in their paws. Animals injected with antibodies from healthy people were unaffected.

Prof Camilla Svensson from the Karolinska Institute in Sweden, who was also involved in the study, said: “Antibodies from people with fibromyalgia living in two different countries, the UK and Sweden, gave similar results, which adds enormous strength to our findings.”

The mice recovered once the antibodies had been cleared from their systems, which took a few weeks. This suggests that therapies such as plasma-exchange, which are designed to reduce antibody levels and are available for other autoimmune disorders, such as myasthenia gravis, may be effective in fibromyalgia patients.

Given the important overlaps between ME and fibromyalgia, do you think this research is worth repeating in ME?

DR SHEPHERD RESPONDS...

The results from this small research study suggest some form of immunological involvement, possibly autoimmune, in fibromyalgia.

We already know that people with ME/CFS have evidence of abnormalities in various parts of the immune-system response, including in some cases the production of autoantibodies. These are antibodies that, instead of being protective, are capable of attacking the body’s own tissues and organs.

However, the occasional presence of low levels of autoantibodies in people with ME/CFS is best described as being suggestive of an autoimmune component to ME/CFS - we cannot conclude that ME/CFS is an autoimmune disease on this basis.

It would clearly be interesting to repeat this research in people with ME/CFS and I will be discussing this with my colleagues at the ME Biobank - where we have blood samples and anonymised clinical data on people with ME/CFS - in due course.

If it turns out that removing these antibodies in people with fibromyalgia using plasma exchange leads to symptom improvement this could also be relevant to ME/CFS. However, having been involved with a small trial that was carried out by Professor Peter Behan in Glasgow many years ago, that involved plasma exchange, there was no evidence of benefit.

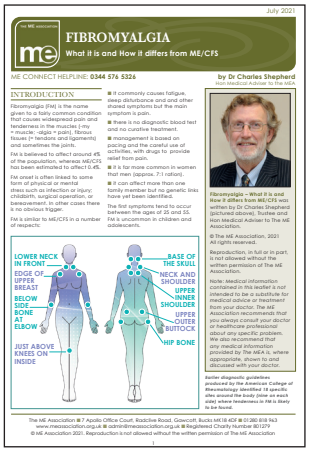
One very important note of caution here is that if this research was to be repeated in ME/CFS this would involve the use of animals - something that the MEA has always been very reluctant to do.

- This research was covered in more detail in an MEA website research review:

tinyurl.com/3wfvnyc9

- The MEA has a recently updated information leaflet covering all aspects of fibromyalgia and the overlaps with ME/CFS:

tinyurl.com/38ydk4hw


July 2021

FIBROMYALGIA

What it is and How it differs from ME/CFS

ME CONNECT HELPLINE: 0344 576 5326

by Dr Charles Shepherd
Joint Medical Adviser to the MEA

INTRODUCTION

Fibromyalgia (FM) is the name given to a fairly common condition that causes widespread pain and tenderness in the muscles (-my = muscle; -algia = pain), fibrous tissues (= tendons and ligaments) and sometimes the joints.

FM is believed to affect around 4% of the population, whereas ME/CFS has been estimated to affect 0.4%.

FM onset is often linked to some form of physical or mental stress such as infection or injury; childbirth, surgical operation, or bereavement. In other cases there is no obvious trigger.

FM is similar to ME/CFS in a number of respects:

- it commonly causes fatigue, sleep disturbance and other related symptoms but the main symptom is pain.
- there is no diagnostic blood test and no curative treatment.
- management is based on pacing and the careful use of activities, with drugs to provide relief from pain.
- it is far more common in women than men (approx. 7:1 ration).
- it can affect more than one family member but no genetic links have yet been identified.

The first symptoms tend to occur between the ages of 25 and 55.

FM is uncommon in children and adolescents.

Fibromyalgia - What it is and how it differs from ME/CFS was written by Dr Charles Shepherd (now retired), Trustee and Joint Medical Adviser to the ME Association.

Note: Medical information contained in this leaflet is not intended to be a substitute for medical advice or treatment from your doctor. The ME Association recommends that you always consult your doctor or healthcare professional about any specific problem. We do not endorse any medical information provided by The MEA is, where appropriate, shown to and discussed with your doctor.

Earlier diagnostic guidelines produced by the American College of Rheumatology identified 18 specific tender points on the body (as illustrated) where tenderness in FM is likely to be found.

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Ask the Expert

There is evidence to suggest that appropriate management on ME/CFS at a very early stage (i.e. addressing key symptoms and advising on a period of convalescence followed by gradual and flexible increases to physical and mental activities) may minimise long-term morbidity and severity.

Where symptoms persist beyond three months and the person concerned has been unable to resume a normal way of life, serious consideration should then be given towards making a provisional diagnosis of ME/CFS.

The timescale should be shorter in children and adolescents, and, where a child or adolescent has missed around four weeks of school, action must be taken to speed up the diagnostic process.

As a GP, you are likely to be the first port of call for patients presenting with ME/CFS symptoms, yet these patients can remain undiagnosed for many months and, often, years.

Please watch the short diagnosis video on our website here: **https://tinyurl.com/cnu96mj9**

If you have further questions, Dr Shepherd would be glad to discuss these with you. Please email contact@meassociation.org.uk

Research Roundup

Katrina Pears, Research Correspondent for the ME Association, reports on the most recent research relating to ME/CFS.

s fibromyalgia a condition of the immune system? - Passive transfer of fibromyalgia symptoms from patients to mice

Goebel A, Krock E, Gentry C, Israel MR et al.

What was investigated in this paper?

The aim of this research was to determine whether administrating immunoglobulin G (IgG) (a type of antibody) from Fibromyalgia (FM) patients to mice transferred characteristic FM symptoms. The authors hypothesised that fibromyalgia (FM) may have an autoimmune basis due to previously reported altered levels of cytokines suggesting immune processes are dysregulated in FM. As well as this FM is higher among those with autoimmune rheumatological conditions caused by autoantibodies.

What are the key findings?

The key finding of this paper found that the transfer of IgG from FM patients to mice resulted in mice displaying several key FM symptoms. The mice displayed increased sensitivity to noxious mechanical and cold stimulation, lower pain threshold in pressure and reduced paw grip strength.

Importantly, when IgG was transferred from healthy controls to mice, there was no effect. Similarly, IgG depleted serum from FM patients had no effect. This shows that the findings were due to the IgG being injected and that FM is an antibody-dependent illness.

All effects on the mice were reversible and FM symptoms reversed after 2-3 weeks of IgG from FM patients stopping being administered. The effects were also shown to be dose-dependent.

What are the implications from this research?

"Our results suggest that therapies which reduce the total IgG titer, such as plasmapheresis or immunoadsorption (e.g., with protein A columns), or which specifically reduce autoreactive IgG (using antigen-specific adsorption) may be effective for FMS. Alternatively, symptomatic therapies that interfere with the binding of autoreactive antibodies or prevent their functional consequences may also provide effective treatment approaches."

The research methods used in this paper highlights possible future research for autoreactive IgG in the pathophysiology of ME/CFS and long-COVID. It has already been established that sera from COVID-19 patients contain a wide range of functional autoantibodies, which has been proposed to influence the symptoms of patients.

Are patients with ME/CFS at a higher risk of developing COVID-19? - The SARS-CoV-2 receptor angiotensin-converting enzyme 2 (ACE2) in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: analysis of high-throughput epigenetic and gene expression studies

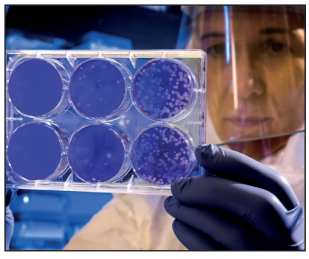
Malato J, Sotzny F, Bauer S, Frietag H et al.

What is the background behind this study?

Typically, genes encode proteins and, when we talk about gene expression, it means the amount of transcription of a gene that can be found in a biological sample at the time of sample collection. Gene expression is affected by both genetic variation and epigenetic modifications. Genetic variation relates to changes in the nucleotide sequence of the gene, whilst epigenetic modifications refer to all the additional changes that occurs from the translation of the encoding nucleotide sequence into the respective encoded protein.

DNA methylation is an epigenetic modification in which a chemical called methyl is added to pairs of cytosine/guanine nucleotides present along the human genome. In particular, the methylation of these pairs in the adjacent nucleotide sequence of a gene makes the opening of the respective chromosomes more difficult for the respective gene translation. Hence, low methylation levels (hypomethylation) of these pairs typically indicate an easiness to express a gene by a given cell, whilst high methylation levels (hypermethylation) pairs indicate the opposite.

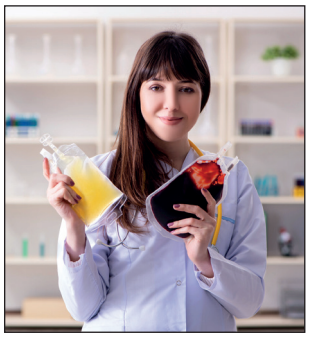
Previous studies investigated the expression and DNA methylation of all the genes present in the human genome in patients with ME/CFS and healthy controls. Finding that when compared to healthy controls, patients have altered expression of different genes and methylation levels of these cytosine/guanine pairs located in specific positions of the genome.



However, it was not known whether these alterations could include the ACE2 enzyme, which is the receptor used by SARS-CoV2 to enter the human cells. In particular, low levels of ACE2 in patients could imply a higher risk of developing severe symptoms of COVID-19.

What are the implications of this research?

If patients with ME/CFS have a decreased expression of ACE2, then they could be at a higher risk of developing severe symptoms of COVID-19. As a possible implication, patients with ME/CFS alongside patients of other diseases but with comorbidities affecting ACE2 levels could be considered a priority group for vaccination. However, it should also be noted that vaccination could aggravate ME/CFS symptoms.



Are we closer to finding a biomarker to ME/CFS? - Altered Endothelial Function in ME/CFS Blood Plasma

Blauensteiner J, Bertinat R, León LE, Riederer M et al.

What was the background to this study?

This study examined molecules which help make proteins (mircroRNAs) in the layer of cells lining blood vessels (endothelium).

Previous studies have placed endothelial dysfunction as another piece in the complex ME/CFS jigsaw. However, no studies have investigated the cellular mechanisms that modulate endothelial function, particularly the production of nitric oxide (NO), and if they are altered in ME/CFS.

NO is a gas released by the endothelium, a layer of cells lining blood vessels, responsible for modulating the blood flowing throughout the body. Endothelial cells actively regulate the immune system, and NO helps to regulate blood and oxygen supply throughout the body.

Endothelial dysfunction is linked to inflammation and oxidative stress which can be caused by inadequate NO production. It is thought that vascular abnormalities such as these could play a part in the complex pathophysiological nature of ME/CFS.

Samples used in this study were provided by the UK ME/CFS Biobank (UKMEB).

What are the main findings to this study?

The study reports that a set of well-described circulating markers used to modulate the production of NO is altered in plasma from ME/CFS patients.

The levels of five microRNAs (miRs) were altered in ME/CFS patients compared to healthy controls. miRs have been found to be altered in many diseases (such as cardiovascular disease) and have been proposed as biomarkers allowing the ability to predict, diagnose and monitor disease.

These findings reinforce clinical evidence reporting decreased NO production in a subset of people with ME/CFS measured by flow-mediated dilatation (FMD) and/or peripheral arterial tonometry.

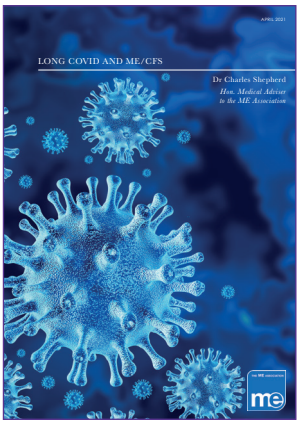
What are the implications and value of this research?

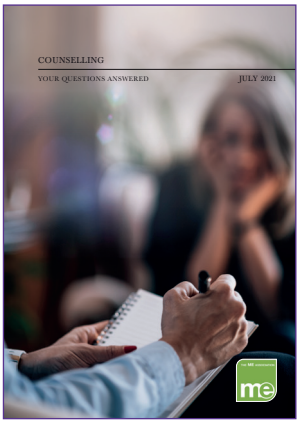
The authors propose that combining this set of circulating markers along with clinical evaluation might allow a more sensitive characterisation of endothelial function in people with ME/CFS.

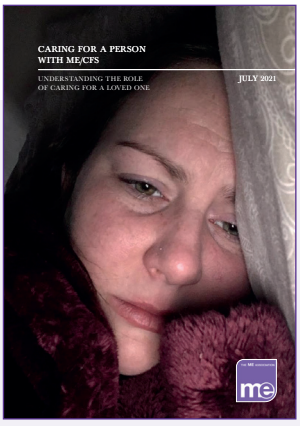
The results are significant as they demonstrate that endothelial dysfunction (ED)-related miRs are observed in up to 60% of the ME/CFS population. This is in line with clinical evidence reporting that ED might be a trait observed in a subset (up to 40-50%) of the ME/CFS population.

The authors propose that a combination of clinical evaluation of endothelial function using assessment methods of FMD and/or EndoPAT, along with the detection of a set of circulating miRs, might allow a more sensitive characterization of ED in a subset of ME/CFS patients, which could help to provide an objective diagnostic test for the disease. ■

ME/CFS Literature







The ME Association has the largest selection of information about ME/CFS anywhere in the UK. All leaflets can be downloaded from the shop and, while we do make a small charge to cover costs, we also ensure a good number of leaflets are free.

Many of our leaflets and booklets have been recently updated and we are constantly updating to keep information as current as possible.

Categories include:

Benefits and Insurance ■ Carers and Social Care ■ Covid-19, Long Covid & ME/CFS ■ Education and Employment ■ Medical & Management

Visit the website shop at:
https://meassociation.org.uk/me-association-shop

TENS for pain relief

People living with long-term pain may be offered a trial of a TENS machine to help ease their symptoms. Might it help people living with ME, and what could it bring to your pain management toolkit? **Physiotherapist Dr Pete Gladwell** draws on patient experience and research to explain the effects and potential benefits of TENS.

TENS (Transcutaneous Electrical Nerve Stimulation) devices were developed in the 1960s and can help in pain management by delivering low-power electrical impulses across the skin. TENS machines are usually small battery-powered devices with wires leading to self-adhesive pads, although wireless devices are also now available. Traditionally, the pads were placed on either side of, on top of or close to the painful area, so it was always thought of as a treatment for localised pain. It has therefore been overlooked as a potential treatment for widespread pain such as that experienced by people living with Fibromyalgia Syndrome (FMS) and ME. However, some recent research has shown that it can help with pain at rest, and pain on movement, for people with FMS.

TENS works through different mechanisms. Research shows that TENS stimulation operates through the "pain gate", a natural system that helps to block the messages going up through the spinal cord. The brain would otherwise respond to these signals by generating the lived experience of pain. The up-to-date term for the pain gate is "segmental inhibition". Other evidence suggests that the TENS machine also stimulates some of the opioid systems, or natural pain-killing systems, within the body. A third mechanism relates to other chemicals (neurotransmitters such as GABA) which are released when people use TENS. A fourth mechanism is the distraction mechanism; the tingling sensation can simply take your mind off the pain.

TENS is likely to help some people and not others

When TENS is switched on you get a tingling sensation under the pads. The usual advice is to aim for a strong, but comfortable sensation. The right sensation for you can be found by exploring the controls on the TENS machine. For some people, using a TENS machine leads to pain relief. For others, the sensation just takes their mind off the pain for a while. Unfortunately, for some people it is not helpful, or they find the sensation unpleasant. In our pain clinics we encourage people to change the sensation to suit them, but it still may not work as people's experience of pain is diverse.

People should NOT use TENS if they have epilepsy, a heart-rhythm disorder, a pacemaker fitted or if they are pregnant (except for pain relief during labour). Pads should only be placed on healthy, intact skin. If you are unsure, speak to your healthcare professional.

As far as we can tell, the TENS machine can be tried for all pain conditions, providing there is no health reason preventing its use. People with widespread pain may feel that it is difficult to choose a specific area to treat, but recent research shows that it is possible to select treatment areas such as the back of the neck and the lower back, to see if the TENS machine can offer an overall, systemic benefit. The Randomized Controlled Trials exploring exactly this approach for people with FMS showed that using TENS in this way can relieve pain at rest, pain experienced during movement, and it also reduced fatigue levels. It should be noted that TENS has not been evaluated for people with M.E., but the FMS research indicates that it is a reasonable option to consider trying.

Different Strategies

We asked people who had experience of using TENS about the ways that they used their TENS machine, the benefits they got and how they overcame their problems. From this research, there seemed to be five main strategies that people had worked out to gain the most from their TENS machine:

- Use the TENS machine only on a bad day or during a flare-up to help cope and get through the worst of the pain
- Use TENS during a rest break, perhaps in combination with relaxation techniques. This could also be done before bed, or in the night if awake with pain.
- Use TENS for activities (such as walking, or sitting) which would otherwise have been made more difficult because of pain

- Use TENS on and off all day to help with most daily activities
- Use TENS in the morning, to help with the extra pain and stiffness that some people experience first thing.

These different methods show how a range of people can find using a TENS machine beneficial by using different strategies.

Others found that TENS use could help them to fall asleep more easily. These aspects are currently the focus of research on the benefits of TENS machines.

It is down to each individual to try out different approaches to see what may help them, and it helps to build up confidence in using TENS and trying out different ways of using it.

Hints and Tips

- The preferred type of sensation is personal. There are some people who feel that

the stronger the sensation, the more effective the TENS machine will be. The settings on most machines can be adjusted to suit individual preferences and can be tweaked during a treatment session.

- Despite being hypoallergenic, the pads can aggravate the skin. The older style rubber pads with gel are an alternative that can be less of an irritant. However, some people do continue to react to the pads. In this case it is important to limit use to short periods where pain relief is crucial and to change the position of the pads regularly to avoid the problem.
- Be persistent! Sometimes patients need to practice with TENS for a few weeks before they feel sure that they are getting the benefits. Changing the settings and changing strategies can help you work out whether TENS can work for you.

For more information

- An information video and written sheet together with a personal TENS diary can be found on the North Bristol NHS Trust Pain Clinic website at **https://tinyurl.com/3amdhftf**

Dr Pete Gladwell is Clinical Specialist Physiotherapist in the Pain Management Service and the ME/CFS Service at North Bristol NHS Trust.

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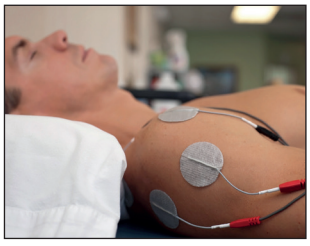


Severe ME Week took place in August and was a time to remember those ME/CFS patients who suffer with Severe and Very Severe ME on a daily basis. This is Phil Prydderch's story.

Severe ME

My name is Phil, and I'm 42. Four years ago, I would have described myself as quite an active person who was rarely ill. I liked the outdoors, camping and hiking – my wife and I would regularly walk 8-9-mile walks over the moors and mountains in North East Wales, from my parents' village near Wrexham, to Llangollen. I also frequently ran 10km, taking part in organised events across Sussex, Surrey and Kent, near where I live. I had a job that took me out in the field every week, and two energetic young sons to keep up with.

But in 2018 everything changed. I caught a flu virus. Although I didn't go to hospital, I was bed-ridden for 12 days and it was the worst I've ever felt. This happened shortly after moving home, with all the stress involved with that, at a time when my career had taken off and I was in a very demanding, public-facing role at work. Although I seemed to recover from the flu and returned to work, my mental and physical health began to unravel. By mid-2019 I was signed off work for five months.

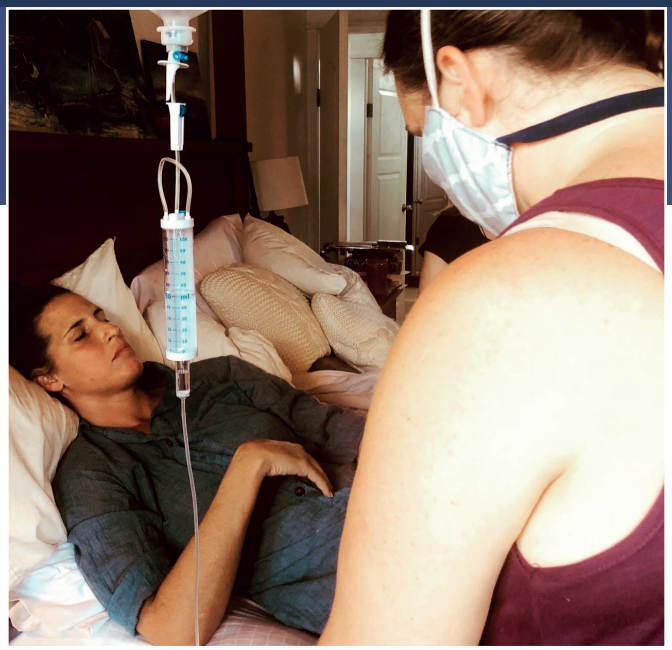
I was formally diagnosed with ME/CFS in May 2021, on top of a Fibromyalgia diagnosis in November 2019. For the past two years, my incredibly supportive employer has given me the space to try and phase back to work. But the reality is that I struggle to do more than two days a week, leaving me with little energy or ability to do anything else, and so Ill Health Retirement now looks likely.

This illness has changed my life. From being an active, fit and healthy person, I now rarely manage to leave my home. I'm very often stuck in bed. On better days, I might manage to help a little around the house and very occasionally maybe even walk a gentle mile with the dog. Life is so different.

ME/CFS is a devastating and debilitating illness. It has robbed me of life as it once was and severely affects the lives of my family too, as my wife often now has to look after me, alongside a demanding job and two growing boys.

But I won't give up. This isn't the life I planned for. I'll build a different life. One that is still meaningful and fulfilling, but in different ways. ■

Learn more about ME/CFS with the Online CPD Training Course!



Myalgic Encephalomyelitis Chronic Fatigue Syndrome

The CMRC [1] Medical Education Group is led by Dr Nina Muirhead [2] (an NHS surgeon with ME/CFS, pictured left), who has launched in partnership with Study PRN an accredited training module for health professionals about ME/CFS.

■ The course was produced by medical experts in ME/CFS.

Why take this course and who is it for?

■ The course has been designed for HCPs and anyone with a professional interest in the condition.

■ It will help you identify symptoms, determine a diagnosis and consider effective treatments using case study examples.

What might the benefits ot taking the course be?

■ The module works with you to determine correct answers and your knowledge about ME/CFS will be improved as a result.

■ We hope HCPs will learn more about ME/CFS from this module, and that this knowledge will lead to better healthcare outcomes and improved relationships with patients.

StudyPRN

TAKE THE COURSE

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"Great to have a well designed, succinct but very informative and up to date course on ME/CFS. I will be forwarding the link and urging other professionals to follow this short, but excellent course."

[1] The CFS/ME Research Collaborative chaired by Professors Stephen Holgate and Chris Ponting.

For more information visit:
www.meassociation.org.uk/research/cfsme-research-collaborative/

[2] Dr Nina Muirhead (BA (Oxon) BMBCh (Oxon) MRCS DOHNS MEd PGDipDerm). Dr Muirhead is also associated with or alumni of: Oxford University, Open University, Cardiff University, Buckinghamshire Healthcare NHS Trust, the Royal College of Surgeons, and the Royal College of Physicians.

The ME Association