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FEATURES

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Cerebral blood flow and pain

ME/CFS and irritable bowel syndrome

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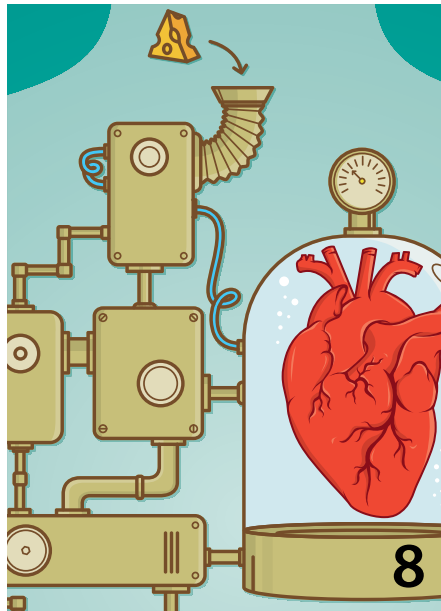
How you can help

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Welcome

Breakthrough magazine is published by ME Research UK, a Scottish Charitable Incorporated Organisation that funds research into Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (also known as ME/CFS). The charity has an international remit, and its principal aim is to commission and fund high-quality scientific (biomedical) investigation into the causes, consequences and treatment of ME/CFS. It also aims to energise ME research by identifying potentially important areas for future biomedical research, producing high quality professional reviews and reports, and presenting research at meetings and conferences. *Breakthrough* is an open access publication and, with the exception of images and illustrations, the content may be reproduced free of charge, subject to the terms and conditions found at:

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In the spotlight

What's happening in the world of ME research and funding



Film maker **Jennifer Brea**
(photo credit Jason Frank Rothenburg)

A year of Unrest

A new documentary is taking the ME world by storm

'Jennifer Brea is about to marry the love of her life when she's struck down by a fever that leaves her bedridden. When doctors tell her "it's all in her head", she turns her camera on herself and her community as she looks for answers and fights for a cure.'

The documentary *Unrest* has become one of the most effective tools in recent years to raise awareness of ME and its effects on people worldwide. Using a combination of professionally shot footage, iPhone videos and Skype interviews, the film explores Jennifer's experiences as her health deteriorates and she struggles to find answers. She also connects with sufferers around the world, and finds a forgotten community of people confined to their homes.

One of the film's great achievements has been its mainstream success, receiving positive reviews from film critics, and prizes at film festivals such as Sundance. There have been screenings of the film throughout the country, and an excerpt was shown at a reception in the Scottish Parliament in January. Closer to home, Dr Vance Spence from ME Research UK attended a screening in Crieff, and answered questions afterwards. He will be attending a further free screening at Perth Theatre on 16th May 2018, to mark ME Awareness Week.

If you have not yet had the chance to watch this 'bracingly inventive and moving' documentary, do seek it out. It is available in the UK on the streaming service Netflix and on DVD.

Regular gifts

The research we report in *Breakthrough* is made possible by donations large and small.

Regular giving allows us to plan for the future because we know, day in and day out, that there is a steady stream of income upon which we can rely.

The easiest way to give regularly is by standing order. It's simple to set up, and your donations are collected automatically from your bank.

Please consider completing the standing order form included with this issue of *Breakthrough* (or via our website) to begin donating quickly, easily and safely.

You can make a difference this month and every month. Your regular gift will allow us to fund more vital research and continue providing information on ME/CFS to patients and professionals in the years to come.



Keeping in touch

We would like to thank everyone who returned the contact form sent out in the last issue of *Breakthrough*. We have updated our contact list and will continue to contact you in the ways you selected.

But it is not too late for supporters who have not yet let us know how they wish to be kept informed of our research news, activities and fundraising opportunities.

A contact form has been printed on the inside back cover of this issue. Just complete it and send it back to us. This will let us know the ways you wish us to communicate with you. If you don't want to hear from us in a particular way then that's your choice and we'll respect it. You can also complete a form on our website: meresearch.org.uk

If we don't hear from you by May 2018, we'll remove your details from our mailing list and we won't contact you again. This means we won't be able to send you further issues of *Breakthrough*.

So, whether you are an individual, group, GP, clinic or MP, please take a few minutes to complete your details and let us keep in touch. Your details will only be used by ME Research UK – we never give your information to other organisations, and you are free to change your mind at any time.



Lightning in a bottle

Controversial therapy is tested in a clinical trial

Can you harness the power of your mind to promote good health? Can you learn to reset your body's systems back to normal? And could this be the answer for people suffering with ME/CFS? These are some of the claims made by advocates of the Lightning Process, a training course designed to give you 'powerful tools to use this brain-body link to influence your health and life'. It is promoted as being effective for a number of conditions, including post-viral fatigue, anxiety, stress, pain, fibromyalgia and ME/CFS.

The process has been endorsed by several TV and sports stars, as well as champions of holistic medicine. And it hit the news again last year following the publication of a randomised controlled

trial looking at its effects in children with ME/CFS.

The Lightning Process involves a period of home study to learn more about the theory behind brain-body interaction. This is followed by a three-day seminar consisting of group sessions in which participants discuss and practise key concepts such as 'mental rehearsal techniques, the use of simple postural exercises, movements and gestures... and self-coaching tools'. The details given are fairly vague, which is not surprising given that the Lightning Process is provided commercially and charges around £620 for the three-day course. However, there have been descriptions published on social media.



Prof. Esther Crawley is a paediatrician at Bristol University who runs a clinic for children with ME/CFS. In an article in the *Guardian* newspaper, she said that more and more of her patients were expressing interest in the process, and asking whether they should try it. This prompted her to set up a randomised trial to look at its effects in 100 children aged between 12 and 18 years.

All participants in the Specialist Medical Intervention and Lightning Evaluation (SMILE) trial were offered medical care aimed at improving sleep and managing activity levels, while cognitive behavioural therapy and graded exercise therapy were also available, if requested or thought necessary. Around half of patients were also randomly selected to undergo the Lightning Process, delivered by a qualified practitioner.

Patients in both treatment groups experienced improvements in their health. However, compared with children who received just specialist medical care, those who also underwent the Lightning Process had better physical function at 6 and 12 months, as measured using the 36-item short form survey. This group also reported less fatigue and depression, better improvement in anxiety, and better school attendance after following the training programme.

Do these results mean ME/CFS patients everywhere should be signing up to the Lightning Process? Well, ME Research UK takes a cautious line. And, despite her findings, Prof. Crawley isn't suggesting people go out and get it either.

First of all, the Lightning Process does not address any of the biological abnormalities that underlie the symptoms of ME/CFS, and which years of biomedical research have helped uncover. Even Phil Parker, who developed the programme, is careful to stress that 'the changed physiology of CFS/ME has to be addressed', 'research is essential' and 'positive thinking or pushing through it will not work'.

Secondly, although apparently well conducted, Prof. Crawley's randomised trial did have its limitations, many of which she herself highlights in the paper, published in the journal *Archives of Disease in Childhood* and freely available on its website.

The trial was conducted in a relatively small number of children, of whom only 81 were included in the analysis. Although this was justified statistically and is perhaps appropriate for an initial exploratory study such as this, therapeutic clinical trials typically recruit several hundred patients in order to provide a more complete picture of the efficacy of a treatment and its potential side effects.

The trial was not blinded; that is, the participants knew whether or not they were receiving the Lightning Process. This was unavoidable given the

nature of the programme, but does raise the possibility that the effects were due to a placebo, clinical trial or other effect. Analysis of the results was performed in a blinded manner, however.

Only subjective, self-reported outcomes were evaluated, with participants reporting their own levels of physical function, fatigue, pain, etc. using various questionnaires. These methods have been validated, are widely used, and definitely have their place in clinical trials. However, there is no denying the value of objective measures that can be applied consistently and are not subject to individual interpretation, and can help clarify the biological changes taking place, if any.

One other limitation acknowledged by the investigators is that they were unable to assess whether the Lightning Process is effective on its own, and the addition of specialist medical care (including cognitive behavioural therapy in some cases) muddies the water somewhat. The process was not tested in children younger than 12 years or in those who are severely affected, and fewer than 30% of eligible children elected to take part in the trial.

According to the ME Association, some ME/CFS patients who have gone through the Lightning Process have experienced initial improvements but have later suffered relapses or a worsening of symptoms. However, the longer term effects of the programme were not reported in the current trial, and perhaps some follow-up investigations are warranted in these children.

The results of this trial were surprising to many of us involved in ME/CFS research, not least the investigators themselves. However, a careful review of the findings makes it clear that they do not yet provide sufficient evidence to recommend the Lightning Process as a viable treatment option for patients with ME/CFS. A conclusion also reached by Prof. Crawley and her team.



A NICE change

NICE to update its ME/CFS guideline after all

In the last issue of *Breakthrough*, we reported on the decision by the National Institute for Health & Care Excellence (NICE) not to update its clinical guideline on the diagnosis and management of CFS/ME. Since its original publication in 2007, ME Research UK (along with other ME/CFS charities and patient support groups) have had real concerns about its usefulness to patients.

As a stakeholder, ME Research UK was given the opportunity to comment on this decision, and we restated our position that the main treatment recommendations of the 2007 guideline are ineffective for most people with ME/CFS or may be causing harm.

And it seems that our comments, and those of the many other stakeholders involved in the consultation process, have been taken seriously. On 20th September 2017, NICE announced that it had decided after all 'to fully update the guideline with a modified scope', citing 'broader issues with the guideline... that

*'an important
step towards
giving patients the
guideline
they deserve'*

called into question the guideline scope and its current relevance' as well as new evidence highlighted during the consultation.

ME Research UK wholeheartedly welcomes this decision. It is what many have been hoping for over the last decade, and an important step towards giving patients the guideline they deserve.

NICE's plan is to replace the guideline by October 2020, and they kicked off the process with a Stakeholder Engagement Workshop in London in January this year. ME Research UK was represented at this workshop by our Vice Chair, Mrs Sue Waddle, who was encouraged by the discussions that took place.

‘Prof. Mark Baker (Director of the Centre for Guideline at NICE) is determined to do the right thing – and he does listen. So, I am hopeful that the outcome will be more favourable in the upcoming guideline than the present version.

‘I also think that I have got through to him... the principle of “first,

do no harm” in regard to graded exercise therapy, and that they may take the unusual step of issuing an Interim Advisory Note before the next version of the guideline is published.’

Following consultation on the scope of the new guideline, its development will begin with the formation of a Guideline Committee consisting

of healthcare professionals providing multidisciplinary contributions, as well as up to four lay members representing patients and carers.

The development process begins in November, and is expected to last around 70 months. According to the timetable, a draft guideline will be available for consultation by April 2020.

Walk for ME 2018

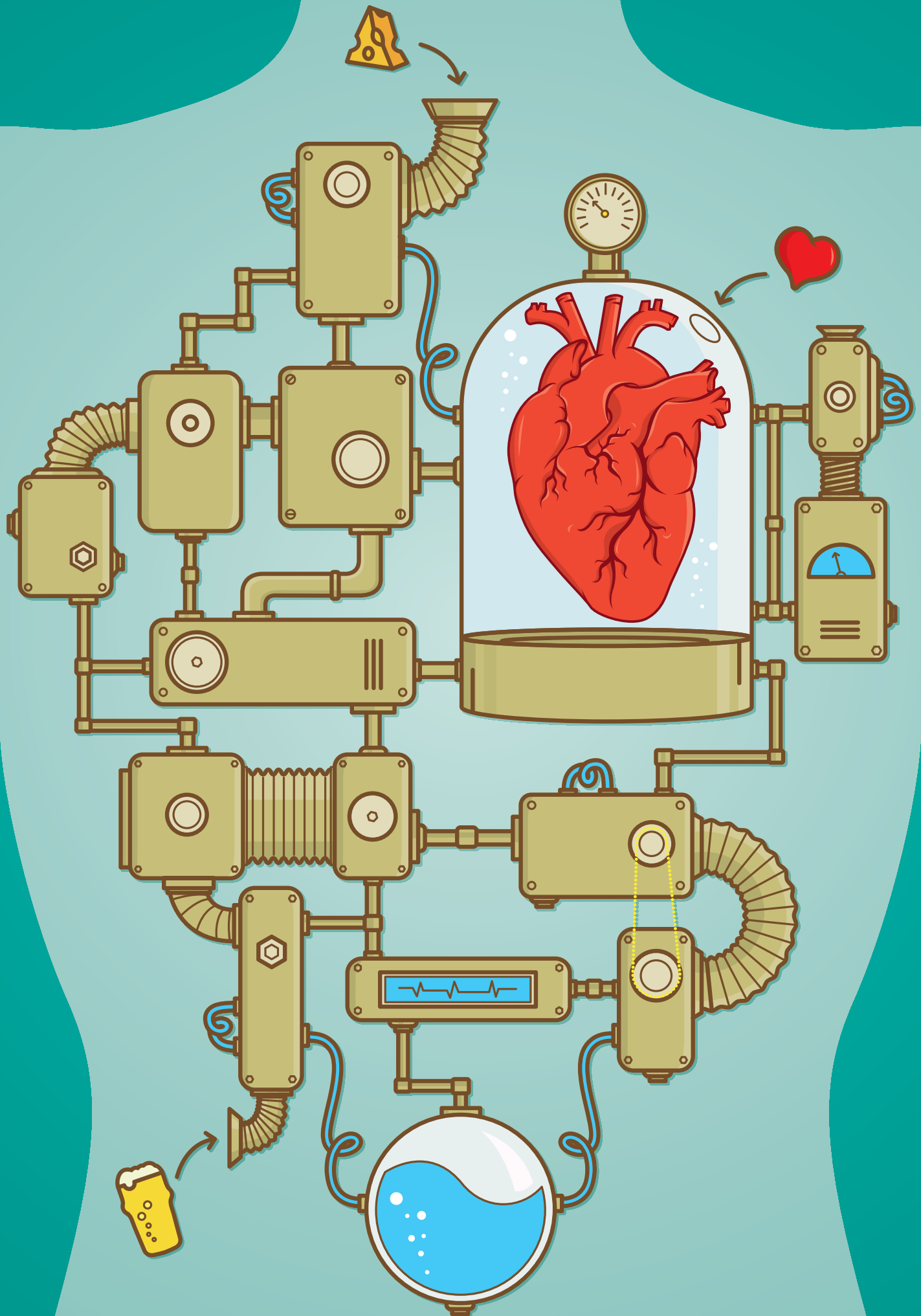
ME Research UK is delighted to be one of Walk for ME’s featured charities for 2018. The original idea behind the event was for family and friends of those affected by ME/CFS to do a sponsored walk on their behalf.

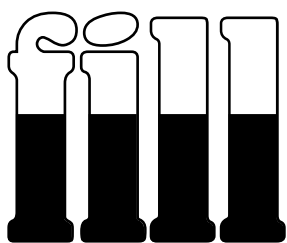
Since then, Walk for ME has had walkers, runners, riders and swimmers across the UK and beyond raising over £100,000 including Gift Aid.

There’s no set date, no required distance and no targets – just the goal of raising funds for research into the illness.

Full details on how to join Walk for ME 2018 can be found on our website: meres.uk/WalkforME.







your heart

New findings from Newcastle show that levels of the cardiac marker **brain natriuretic peptide** are increased in ME/CFS

An increasing amount of research has revealed heart abnormalities in patients with ME/CFS. For example, people with the illness have been found to have a short QT interval and a reduced cardiac output. These changes may occur before any symptoms are apparent.

Much of the recent work on cardiac dysfunction in ME/CFS has been carried out by Prof. Julia Newton and her team at Newcastle University, including studies funded by ME Research UK. In 2012, they used magnetic resonance imaging and cardiac tagging technology to

show that several measures of the heart were lower in ME/CFS patients than in healthy control subjects, including left ventricular mass, stroke volume, cardiac output and end-diastolic volume (see overleaf for a description of these terms).

In further studies, they found a strong association in ME/CFS patients between the total volume of blood and cardiac end-diastolic wall mass.

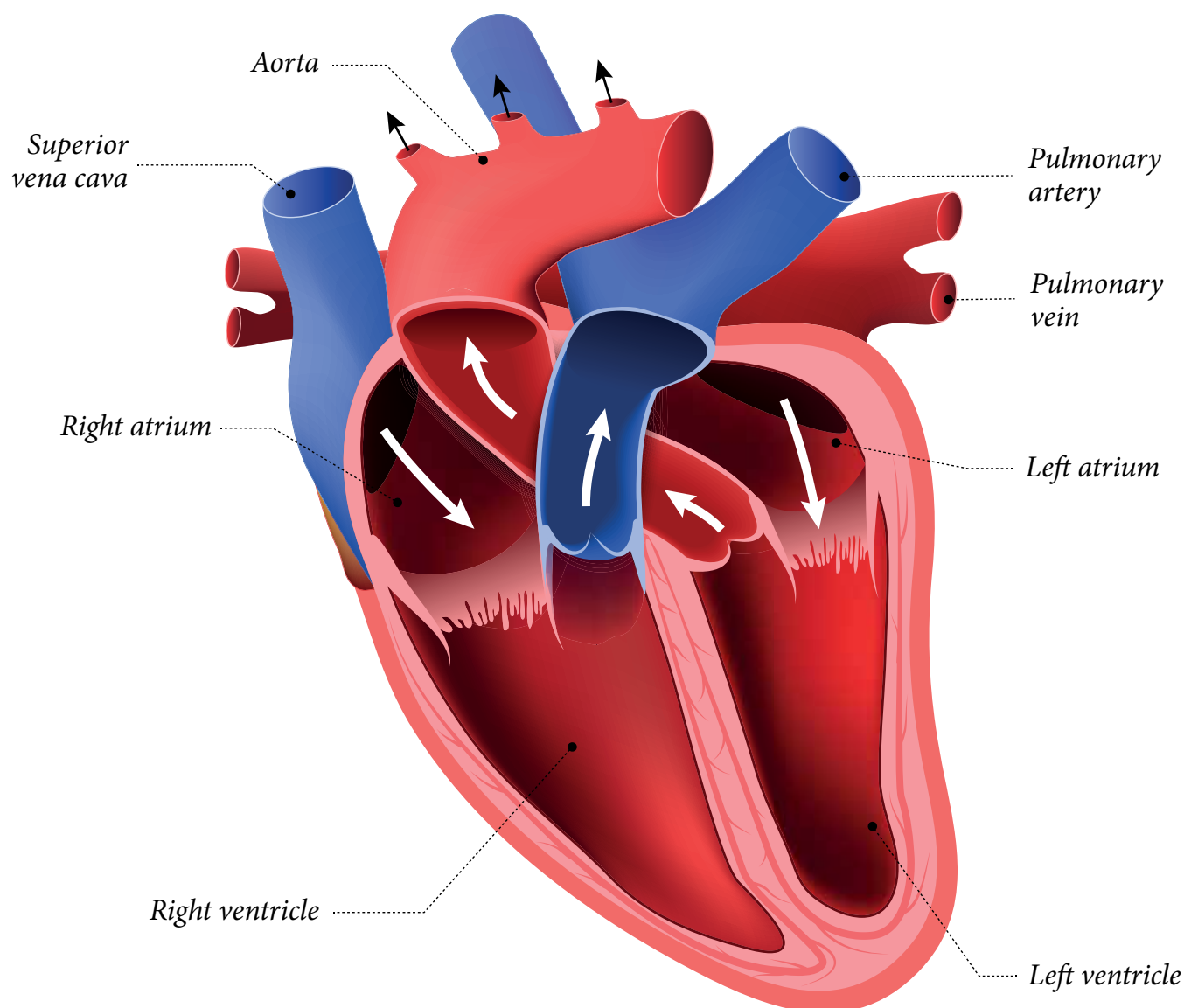
Brain natriuretic peptide

Continuing their work in this area, the team has recently published a paper in the journal *Open Heart* looking at levels of brain natriuretic peptide (BNP) in ME/CFS, and correlating these with

measures of cardiac dysfunction. Despite its name, BNP is a hormone that is actually secreted by the muscle cells of the heart, and is produced when the ventricles are overstretched to accommodate an increase in blood volume.

Circulating BNP causes a decrease in blood pressure and in cardiac output, and has found use clinically as a diagnostic and prognostic marker of heart failure.

In their current study, the investigators recruited 42 patients with ME/CFS and no other illness, as well as 10 sedentary control subjects matched for age and sex. The participants' hearts were examined using magnetic reso-



‘BNP may be a convenient way to identify patients who would benefit from cardiac treatment’

nance techniques to provide a number of measures of cardiac function, including cardiac volumes at the end of systole and at the end of diastole. In addition, blood samples were taken, and plasma BNP levels were measured using an enzyme immunoassay.

Increased BNP levels

The first important finding was that BNP levels were significantly higher in ME/CFS patients than in sedentary control subjects, with mean levels of approximately 500 versus 300 pg/mL, respectively. Furthermore, both end-systolic and end-diastolic cardiac volumes were significantly lower among patients

with high BNP levels (defined as being greater than 400 pg/mL) than in those with low BNP levels.

BNP tends to be a sign of cardiac volume overload, so this association is not what one would normally expect to see. One explanation suggested by the researchers is that the high level of BNP is causing an excessive production of urine, which reduces the total volume of circulating blood (as seen in their earlier study), leading to a smaller cardiac volume.

It is important to note that none of these measures was related to the duration of illness, indicating that the results are unlikely to be due to decon-

ditioning (i.e. they were not the result of the heart adapting to less physical activity).

What might these results mean to patients? One possibility put forward by the investigators is that measurement of BNP levels may be a convenient way by which to identify those ME/CFS patients with cardiac abnormalities who would benefit from specific treatments, although additional studies would be needed to confirm this.

This approach may also be valuable in identifying a specific cardiac subgroup of ME/CFS patients, and better understand the diverse nature of this illness. ●

A guide to some of the terms used

Cardiac output – Amount of blood pumped by the heart per minute

Diastole – Period of the heartbeat during which the chambers of the heart relax and refill with blood

End-diastolic cardiac volume – Volume of blood in each ventricle after they have refilled

End-systolic cardiac volume – Volume of blood left in each ventricle after they have contracted

Left ventricular mass – Thickness of the wall of the left ventricle

QT interval – Measure of the electrical activity of the heart

Stroke volume – Amount of blood pumped by the left ventricle in one contraction

Systole – Period during which the ventricles contract and pump blood out into the arteries

Rituximab biomarker study update Negative trial results stall the search for an immunosignature

In the last issue of *Breakthrough*, we reported on a newly funded study aimed at developing a biomarker to help predict patients who will respond to treatment with rituximab. Unfortunately, this study will not now be going ahead.

Rituximab is an antibody that attacks B cells and has been used to treat some cancers and autoimmune disorders. Following promising results in patients with ME/CFS, a randomised, placebo-controlled trial of rituximab was started in 2014 at five centres in Norway.

As the drug appeared to be effective in only some individuals, Prof. David Patrick at the University of British Columbia planned to use blood samples from the Norwegian patients to develop an immunosignature to help distinguish those likely to respond to the treatment.

ME Research UK awarded Prof. Patrick a grant to carry out this work, but unfortunately in November there was a major setback when one of the Norwegian investigators, Dr Olav Mella, announced preliminary negative results of the rituximab randomized trial.

Although we are still waiting for publication of the full trial results, it is likely they will not show any benefit of rituximab in ME/CFS patients. With this in mind, Prof. Patrick and ME Research UK jointly made the decision not to proceed with the immunosignature study since, in these trial patients at least, there would be nothing to show.

This is disappointing news as rituximab has been one of the greatest hopes in recent years for an effective treat-

ment for ME/CFS. It is still to be seen whether this is the end of the road for rituximab as far as ME/CFS is concerned. There are signs that researchers are still interested in exploring its potential further, however, and it may yet prove to be beneficial for a subgroup of patients.



Prof. David Patrick from the University of British Columbia



the BIG hurt

Do **cerebral blood flow and heart rate variability** contribute to the pain that ME/CFS patients experience following exercise

Chronic widespread pain is a fact of life for many people with ME/CFS, and around a third of patients report that pain limits their everyday activities and can be more disabling than fatigue. But we are only just beginning to understand what the causes might be.

One idea that might help to explain the mechanisms underlying the pain in ME/CFS is that of central sensitisation. Briefly, central sensitisation is an increased sensitivity of cells in the spinal cord and brain to stimuli such as pres-

sure, heat, cold or chemicals. The concept is believed to underlie many chronic pain conditions, and has been extensively explored in fibromyalgia research.

Evidence for central sensitisation

A few years ago, Prof. Jo Nijs and colleagues at Vrije Universiteit Brussel in Belgium reviewed the scientific evidence for central sensitisation in ME/CFS, and concluded that its presence is consistent with many of the symptoms of the illness.

Since then, the team has continued work in this area and has recently completed two studies looking at different aspects of central sensitisation in

ME/CFS. The results of one strand of this work were published this year in the journal *Pain Physician*.

In healthy, pain-free individuals, a painful stimulus has been shown to result in a decrease in cerebral blood flow (supplying the brain), leading to symptoms such as fatigue, dizziness, memory loss and headaches. These symptoms are also characteristic of ME/CFS and can be induced by physical exercise, suggesting that cerebral blood flow might play a significant role in the illness.

The researchers' hypothesis was that ME/CFS patients may have an inadequate cerebral blood flow response



to exercise, so altering pain sensitivity in these individuals. To test this, they asked 20 women with ME/CFS and 20 healthy, pain-free sedentary women to undergo a number of measurements while performing a 12-minute cycling test.

Cerebral blood flow

Throughout the experiments, cerebral blood flow was monitored using an ultrasound technique, while heart rate variability was measured using finger plethysmography. Heart rate variability is the natural variation in the intervals between consecutive heartbeats, and is another indication of cardiovascular health which has been shown to be abnormal in chronic pain. To control for the effects of emotional stress, the measurements were repeated while participants underwent an emotional stress test.

In addition, before and after each cycling or emotional stress test, the investigators measured the temporal summation of pressure pain. This is essentially a measure of the accumulation in pain

experienced following repeated pressure stimuli, and is a useful way of evaluating the excitability of sensory nerves.

As expected, pain scores during the temporal summation test reduced following exercise in the healthy control group, indicating active modulation of

‘cerebral blood flow does not play a role in the pain experienced following exercise’

the painful stimuli. However, there was no change after exercise in the ME/CFS group, suggesting that pain modulation is dysfunctional in these patients.

Cerebral blood flow increased during physical exercise, while heart rate variability decreased, but these changes were what one would normally expect,

and there were no differences between the ME/CFS patients and healthy controls. Furthermore, there were no significant associations between any of the parameters assessed.

So these results seem to contradict the original hypothesis of the study, and indicate that cerebral blood flow and heart rate variability changes after exercise are not altered in ME/CFS, and are unlikely to be the cause of the abnormal pain response in these individuals.

The researchers point out that this was a relatively small number of participants, and the exercise was fairly mild, although the changes seen were substantial, and normal pain modulation was seen in the healthy controls.

In conclusion, cerebral blood flow and heart rate variability do not appear to play a role in the increase in pain experienced following exercise in ME/CFS patients. It is disappointing when a promising idea has negative results, but there are still plenty of other threads to pursue in future research. ●

inside out

A new study looking at the link between irritable bowel syndrome and ME/CFS

Irritable bowel syndrome (IBS) is a relatively common condition characterised by a number of symptoms affecting the digestive system, including stomach cramps, bloating, diarrhoea and constipation. The symptoms can be different between individuals, and are often triggered by stress or particular foods.

Interestingly, the prevalence of ME/CFS is estimated to be 35 times higher among people with IBS than in the rest of the population. And, conversely, there is also a high prevalence of IBS among people with ME/CFS.

But that's not the only link between the two conditions. Both ME/CFS and IBS are often reported to occur after an infection, and are also both associated with abnormal activation of the immune system, as indicated by raised levels of various cytokines and immune cells.

There is also evidence of changes to the gut microbiome in both ME/CFS and IBS. The microbiome generally refers to the collection of around 100 trillion microorganisms, including bacteria, that live on or inside the human body. Many of these bacteria are beneficial to us and essential to our survival. In the gut, they live on the membranous lining, or mucosa, and break down our food and help protect us against infection. This whole area has become a hot topic of research in many diseases.



The similarities between ME/CFS and IBS suggest that the two conditions may be part of a spectrum of illness, with shared pathophysiological changes in response to infection. This is the fascinating idea that Prof. Yan Yiannakou and his team in Newcastle are planning to investigate in a new project recently awarded funding by ME Research UK.

Prof. Yiannakou suggests that if the two conditions are linked in this way, then 'patients with ME/CFS alone would have mucosal immune and microbiome changes that are similar to, though less pronounced than, patients with both ME/CFS and IBS'.

To explore this, the team will recruit four groups of individuals: 25 patients with ME/CFS alone, 25 with IBS alone, 25 with both ME/CFS and IBS, and 25 healthy control subjects. Follow-

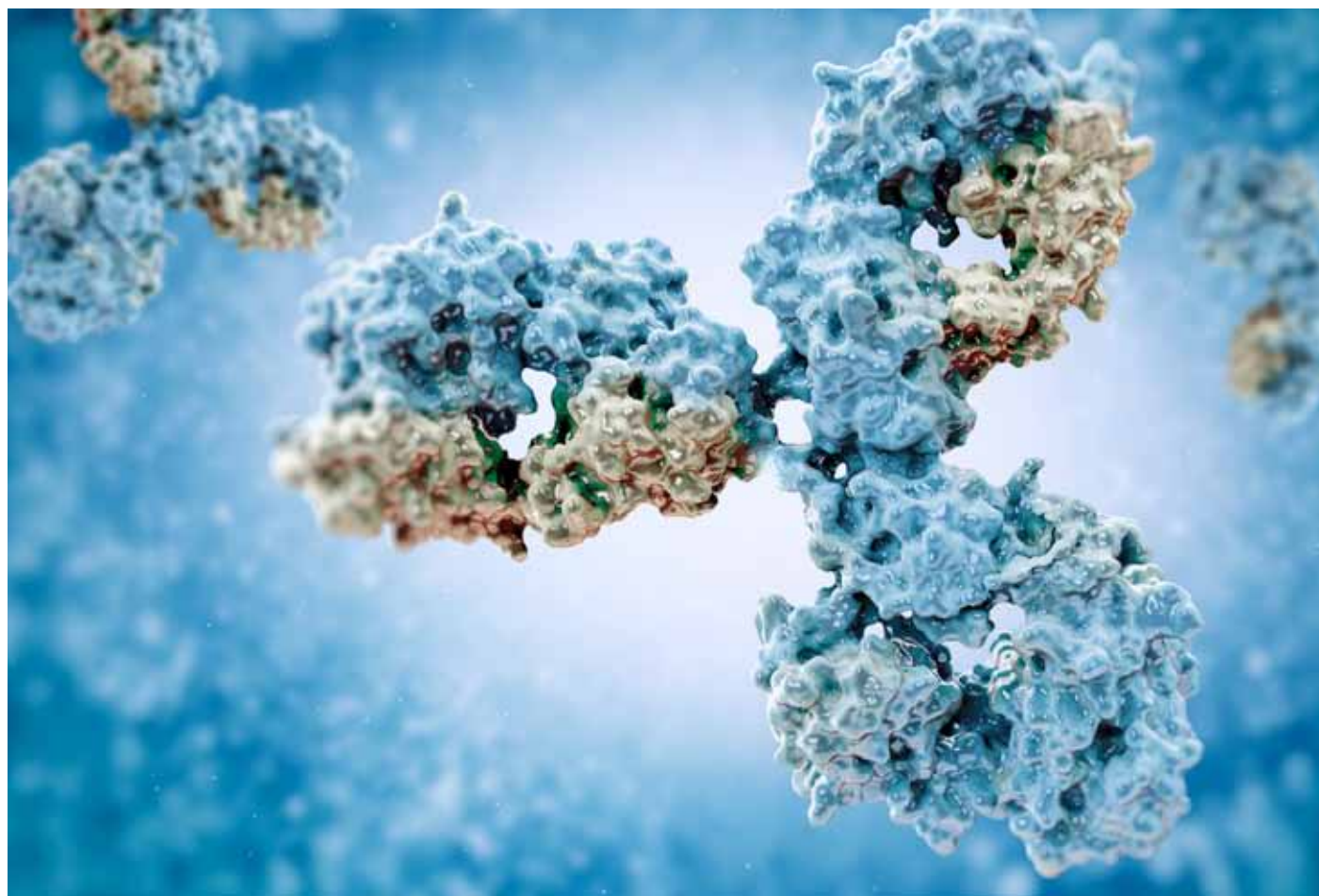
ing clinical assessment, blood samples will be collected to analyse a variety of markers of immune activation, while stool samples will be taken from which to measure changes in the faecal microbiome using DNA analysis.

In addition, in five individuals from each group, biopsies of the colon will be taken in order to analyse the mucosal immunology and microbiome more directly. This whole process is particularly challenging and involves invasive tests, so its feasibility and acceptability to patients need to be explored.

These are relatively small groups of patients, but Prof. Yiannakou hopes to assess the feasibility of the techniques, and provide pilot data on which to base larger studies examining the links between the gut microbiome and immune system in ME/CFS and IBS. ●

Research bites

Our round-up of recent research from around the world



Antibody removal

Scheibenbogen et al., PLOS One, 2018

A lot of recent research evidence suggests that ME/CFS is an autoimmune disease; that is, the immune system is attacking the body's own healthy cells. In the last issue of *Breakthrough*, we wrote about a German study we are funding to look at the function of $\beta 2$ adrenergic receptor autoantibodies in the illness. The same team has also recently published work exploring a method of removing these antibodies using a technique called immunoadsorption. This involves passing the blood through a special machine to filter out the offending autoantibodies, and the technique has been used to purify blood in the treatment of other autoimmune diseases, and for kidney transplantation. It also has the advantage of being relatively free from adverse effects.

In this study, ten patients with ME/CFS and elevated $\beta 2$ autoantibodies were treated for five days, following which autoantibody levels were measured and the participants' symptom severity was assessed using a questionnaire. After treatment, $\beta 2$ autoantibody levels had fallen in nine out of ten patients, and levels were still decreased 6 months later. Seven patients also experienced an improvement in symptoms, and in some cases this lasted for several months. Although this was only a relatively small number of patients, the results demonstrate the potential of immunoadsorption as a treatment for ME/CFS. We are keenly awaiting the results of the study we are funding, as well as further research that may spring from this pilot work.



Comparison with MS

Kingdon et al., Pharmacoeconomics Open, 2018

We regularly make comparisons between patients with ME/CFS and those with multiple sclerosis (MS), perhaps partly because neither illness has a clear cause or definitive treatment. In their recent study using data from the UK ME/CFS Biobank, researchers from the London School of Hygiene and Tropical Medicine looked at the impact of each disease on measures of disability, employment and income. ME/CFS patients were more physically disabled than those with MS, spent less time at work, and had a lower income. While the recognition and awareness of MS is certainly greater, these results indicate that ME/CFS may actually have a greater impact on individuals' day-to-day life, and consequently on society.



Can probiotics help?

Corbitt et al., Probiotics and Antimicrobial Proteins, 2018

As we discuss elsewhere in this issue, there is a high prevalence of irritable bowel syndrome (IBS) among ME/CFS patients, and *vice versa*, and we have recently funded a pilot study to explore this link further. Probiotics are used to restore the natural balance of bacteria in the gut, and there is some evidence they can help relieve the symptoms of IBS, although questions remain about their effectiveness. This review looked at 25 studies investigating probiotic supplementation in these two conditions. While there was substantial data supporting their use in IBS, the evidence was poor and limited for any benefits of probiotics in ME/CFS patients, indicating that more research into this issue is needed.



Ventricular lactate

Natelson et al., Fatigue, 2017

A few years ago, we reported on a study using magnetic resonance spectroscopy to measure levels of a metabolite called lactate in the cerebrospinal fluid of ME/CFS patients. Lactate levels were higher in patients than in healthy controls, and the same team has now followed up this work by comparing lactate between individuals with ME/CFS and those with fibromyalgia. The hypothesis was that this metabolite might be able to distinguish between the two conditions, which share many of the same symptoms. However, there was no difference in lactate levels between patients with ME/CFS, those with fibromyalgia, and those with both conditions. We may have to search elsewhere for that elusive biomarker.



Accelerated ageing

Rajeevan et al., Journal of Translational Medicine, 2018

The central idea behind this new study is that ME/CFS shares many of the characteristics of accelerated ageing, a condition which has been implicated in several other diseases such as rheumatoid arthritis and multiple sclerosis. Accelerated ageing generally refers to a premature decline in the immune system, and one way to assess it is by measuring the length of telomeres, the caps which protect the end of our chromosomes from damage. In a group of 64 patients meeting the criteria for CFS, the relative telomere length was significantly shorter than in non-fatigued individuals, and the researchers concluded that ME/CFS could therefore be included among those conditions associated with accelerated ageing.



European biomarker hunt

Scheibenbogen et al., Journal of Translational Medicine, 2017

EUROMEME is a network of scientists and doctors from across Europe who have joined forces to collaborate on ME/CFS research, and one of their objectives is to identify biomarkers that can help in the diagnosis and management of the disease. To that end, they have established a database of 39 relevant biomarker studies from the last few years, looking at a range of immunological, infection-related, metabolic and neurological parameters.

The investigators looked at the quality of the studies conducted, as well as the consistency of their results. The conclusion of their analysis is that there is not yet any single biomarker available for the diagnosis of ME/CFS, possibly due to there being few studies, with low patient numbers and a lack of control subjects.

Importantly, the paper then goes on to outline strategies to improve this situation, including standardization of sample collection, using a uniform clinical case definition, and defining patient subgroups based on symptoms and severity. They also highlight the importance of reproducing results in individuals from different countries, performing multicentre studies and, crucially, increasing funding for ME/CFS research. Let's hope that EUROMEME can help achieve these worthwhile goals.



Spatial vision

Ahmed et al., Vision, 2018

Dr Hutchinson and her team at the University of Leicester have been leading the way in investigating the many visual problems experienced by people with ME/CFS (and some of her studies have been supported by ME Research UK). These problems include difficulties focusing, reduced eye movements and pattern-related visual stress. In this recent work, the researchers have been looking at spatial vision, which is the ability to discriminate between distinct features. Simply put, this was tested by asking participants to distinguish narrowly spaced gratings of vertical or horizontal lines, and ME/CFS patients were less able to make out the closer spaced lines, something that may explain the difficulties people with ME/CFS have with reading.

Dr J Gordon Parish

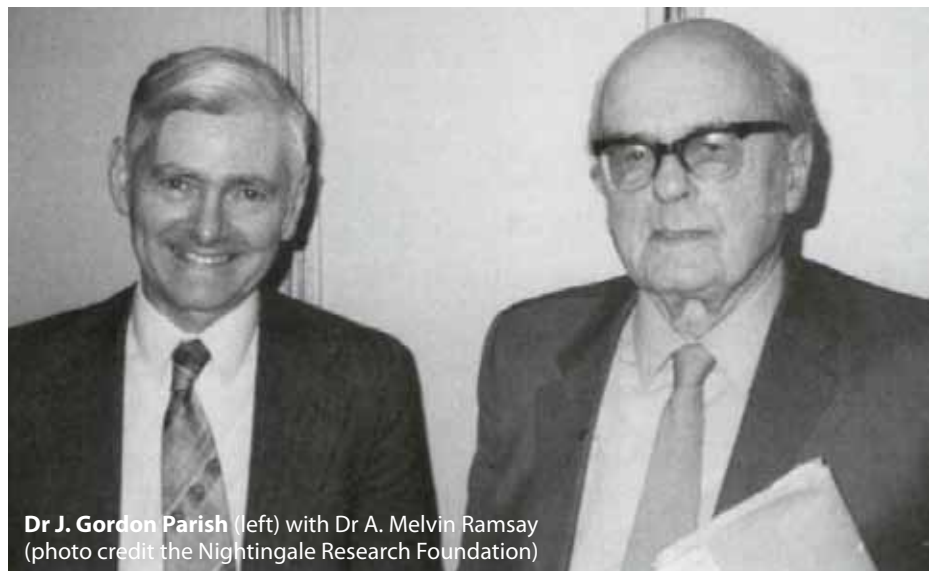
An appreciation of his life and work,
by Dr Neil Abbot

It was with great sadness that we learned of the death of Dr J. Gordon Parish, aged 92, on September 13th at his home in the village of Stanley in Perthshire. Dr Parish was one of the group of trustees who founded ME Research UK (originally called MERGE) in 2000, becoming a valued patron thereafter.

Without his intellectual and financial support, particularly in the very early days, the charity would not have survived and prospered. He was a great advocate of the need to recognise ME as a distinct clinical entity, and through the years he kept a close interest in the scientific projects funded by ME Research UK, particularly those on muscle and brain which he saw as key to understanding the biology of the disease. He also wrote the occasional article for *Breakthrough* magazine, including 'Myalgic encephalomyelitis – a muscle/brain disorder'.

After his war-time medical training, Dr Parish took up posts in the north of England, and it was while working in Durham in the mid 1950s that he contracted ME, recovering thereafter but suffering recurrences of the original illness at various times over the next 60 years. Afterwards, the family moved to Canada but returned to England where Dr Parish ended his working life as a Consultant in Rehabilitation Medicine at Mary's Hospital in Colchester.

It was there that he saw many patients with an ME-like illness simi-



lar to his own, and Dr Parish became dedicated to their care and convinced of the need for scientific investigation of the disease. It was his firm belief that ME had an infectious cause, probably viral, and he devoted much of his spare time to writing scientific letters and articles, and to identifying outbreaks of the illness as they appeared in the scientific literature.

By the end of the 1970s, he had identified 47 possible epidemics of ME across the world, from Los Angeles (1934) to Southampton, England (1979). Over time, he not only tabulated these epidemics (the results of which are available on our website) but brought together an extensive archive of the literature on each, which he made available to researchers. A summary of the information he collected appears as Chapters 1 and 16 of *The Clinical and Scientific Basis*

of ME/CFS, published by the Nightingale Research Foundation in 1992.

Dr Parish was the last survivor of a handful of British medical doctors who diagnosed and treated people with ME, and who became leading advocates of the need to recognise, diagnose, investigate and treat the disease (notable others include Dr A. Melvin Ramsay, Dr John Richardson and Dr Betty Dowsett). Through their valiant efforts, extending from the 1950s to the present day, the existence of ME and its effects on the lives of patients and their families was not lost to history.

As Dr Vance Spence, Chairman of ME Research UK, says, 'The ME world owes an enormous debt to their quiet persistence, their professional approach and their dedication to keeping the flame alive.' ●



Friends united

Some of the many activities undertaken by our supporters to raise funds for ME research.

Top of the world

Well, almost! Now safely back home, intrepid supporters Alex Blackall, Josh Blackall and Mike Cleveland journeyed to Everest base camp for ME Research UK. They climbed a total of 4,785 m and covered 203 km over 10 days, with no guides or porters to carry anything. Many, many thanks to all three of them.

Royal route

Sy Cane chose what must be one of the UK's most picturesque and historic

routes, when he ran this year's Hampton Court Half Marathon in support of ME Research UK. The route looped around Thames Ditton, the historic Royal Borough of Kingston upon Thames Marketplace, and the iconic three mile stretch of the Barge Walk beside the Thames, with full views of Hampton Court Palace. Congratulations and thanks to Sy who completed the race in an impressive 2 hours 5 minutes. Apparently, even King Henry VIII was there to cheer the competitors on!

Golden years

Lilian and Ricky Kujawa recently celebrated their golden wedding with family and friends. After a church renewal of vows, the couple enjoyed afternoon tea with their guests. They adopted a no gifts policy, but left out an ME donation box and raised a magnificent total. Lilian has suffered with ME for 40 years, and appreciates the need for funds for research and a diagnostic test. The family now exchange charity donations at Christmas instead of gifts, helping



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01 Gail Sumner is over the moon with her triathlon performance

02 Celebrating at Everest base camp are **Alex, Josh and Mike.**

03 Sy Cane is ready for his half marathon beside the Thames

04 Lilian and Ricky Kujawa celebrate 50 years of marriage

to fund further research into ME. The family appreciate the efforts of all of those involved in Perth and elsewhere. And we'd like to thank Lilian, Ricky and all their guests for their support.

Over the moon

Gail Sumner sent us this report from the South Manchester Sprint Triathlon, which she completed in September last year. "The weather was kind to everyone and I was over the moon to finish 6th in my age group out of 41 competitors. Having been unable to work or exercise for the last few years, building myself up to this has been a major focus of my

life. I cannot believe what I have been able to do! As a physiotherapist, I have worked with people with ME and see the devastation it causes every day. What a fantastic achievement, and we are very grateful for Gail's support. She says her next goal is to do an olympic triathlon.

Swinging into action

Last September, Abbie and Debbie Grant organised an evening of swing dance in Fareham to raise awareness of ME and funds for research. Swing with ME was a huge success and lots of dancers came out to support the event, raising a fantastic total for ME Research UK.

Abbie and Debbie presented the funds to our vice chair Sue Waddle who said, 'It is thanks to supporters such as Abbie and Debbie that ME Research UK can continue to fund biomedical research into ME/CFS. Research that is vital to understanding and, one day, curing an illness which affects over 200,000 people in the UK alone. We are so grateful for all they have done in raising awareness of the illness and for helping support research, not only in the UK, but worldwide.' Thank you to Abbie and Debbie for all your hard work, and to Hampshire CC Pal Heyre for showing such an interest in ME/CFS and in our charity.



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Right on target

Congratulations to supporter Jason Croxall who completed the Ikano Bank Robin Hood half marathon in September. Jason says, 'I crossed the finish line with a time of 2:30:45. It was an absolute bulls-eye for my target and I'm over the moon! I'm honoured to have run for the cause, and my brother Jack was even there to see me off and congratulate me at the finish line. Brother Jack is acclaimed author Jack Croxall who's published the well-received *Tethers Trilogy*, and a short story about his experience with ME/CFS.'



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05 Jason Croxall shows brother Jack his finishing medal

06 Just about to donate her hair for charity is **Aine McAnulla** and son Mark (reproduced by kind permission of the *Ulster Herald* and photographer Michael Cullen)

07 Angus Hunter finishes his half marathon in spectacular surroundings

08 Abbie and Debbie Grant (front left and right) present a cheque to Sue Waddle



08

Getting the chop

Many thanks to Aine McAnulla who raised awareness of ME/CFS and funds for research by having her hair chopped, with the lost trusses being donated to the Little Princess Trust. Aine's son Mark is affected by ME/CFS. Speaking to the *Ulster Herald* and *Tyrone Herald*, she explained that, 'Mark continues to push on and fight every day to maintain a normal functioning life. He deals with the bad days when he cannot get out of bed, but makes the most of every other day he can.'

Temple run

Angus Hunter competed in last December's Angkor Wat half marathon in support of ME Research UK. Despite a last minute change to the route due to an urgent convocation of 10,000 monks, Angus posted a personal best time. 'My suffering is momentary compared to those with ME, and has motivated me to achieve more than I otherwise might, and in so doing also hopefully raised more funds and greater awareness of the condition.' It certainly has – thank you, Angus!

We want to keep in touch

We want to be sure you're happy with the way we contact you. So, from 1st May 2018, we will only keep sending you *Breakthrough* magazine and other information if we know you are OK with this.

If you DO want to keep hearing from us, please complete this simple form letting us know how you wish to be contacted, and return it to us at the address below.

If you DO NOT want to keep hearing from us, you don't need to do anything. Your details will be removed from our records on 1st May 2018, after which we will not contact you again.

It's quick and easy to change your mind at any time, just let us know. We take the security of your personal information very seriously and we will never sell your data to anyone else.

1. How would you like to be contacted? You can choose all options, or just one or two.

- ☐ **Post** – You'll receive our free *Breakthrough* magazine and news on ways to support us
- ☐ **Phone**
- ☐ **Email** – Keep up to date with research and find out how to support us

2. Complete your details.

Name

Address

Telephone no.

Email address

*3. Return this form to: ME Research UK, The Gateway,
North Methven Street, Perth, PH1 5PP.*

