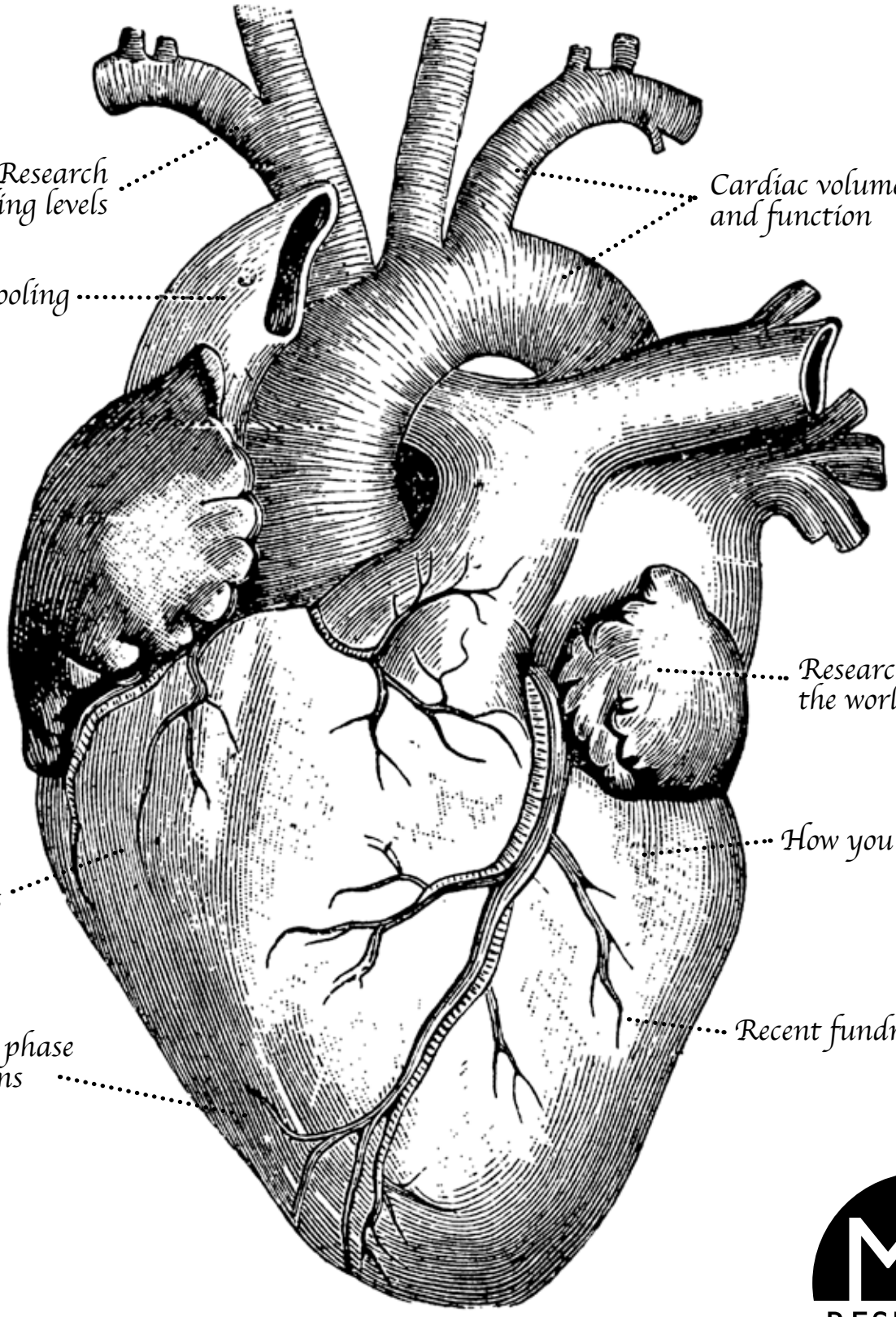
NEWS OF THE ME RESEARCH YOU ARE HELPING TO FUND

breakthrough



ME RESEARCH UK

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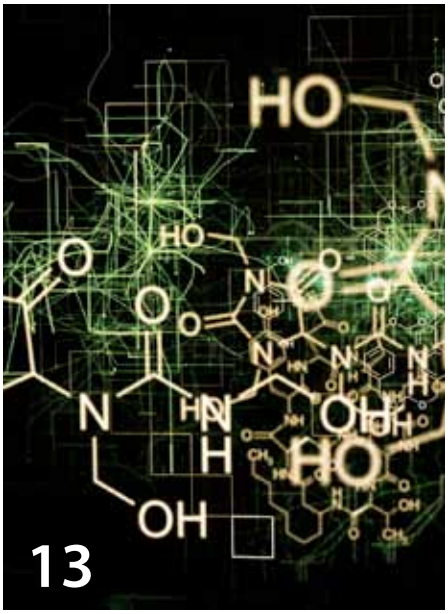

Welcome

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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This issue

In the spotlight

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

The bottom line

Report exposes the low level of funding for ME/CFS

We all know that research funding for ME/CFS is abysmally low, but we can now provide some figures thanks to a report commissioned by the ME/CFS Research Collaborative in the UK. It asked the company ÜberResearch to search its database for relevant information on ME/CFS and comparable diseases.

The report found that ME/CFS received less than 1% of all grants given by UK mainstream funding agencies over the past decade. Also, the nature of the support was low-level and patchy, highlighting the need for increased investment in high-quality studies of biological mechanisms and treatments.

The low level of investment is particularly shocking given the scale and impact of ME/CFS on individuals and society. The illness is at least as disabling as multiple sclerosis and congestive heart failure, and its economic cost is more than £6 billion per year in the UK.

Of course, the report does not include research funding by ME/CFS charities. While this can be considerable in relative terms – ME Research UK has committed £1.4 million for more than 40 studies in the UK and overseas, for instance – what charities can provide is small in real terms compared with the larger sums available to institutional funders such as the MRC and the Wellcome Trust in the UK and the NIH in the USA. It is these institutional funders who need to step up to the plate.

As Prof. Stephen Holgate says in the Foreword, "The report presents hard evidence of the chronic lack of research funding for ME/CFS from major funding agencies. I am delighted that the MRC will now review its highlight notice as a result… and hope that other mainstream funders will reassess their attitudes towards ME/CFS and review their funding policies."

Fundraising by phone

Most people carry a powerful fundraising tool – their mobile phone. We all take text messaging and smart phones for granted, and yet they are an ideal way to donate to charity.

Through JustTextGiving, donations can be sent to ME Research UK at any time. It's simple, quick and easy, and no commission is taken by your provider.

Deducted either from your call credit or added to your phone bill, a single text donation can be £1, £2, £5 or £10. The amount is yours to decide.

To donate, text "MEUK01" and the amount to 70070. For example, to donate £5 the message would read: "MEUK01 £5", and should be sent to 70070. You'll receive a message acknowledging your donation.

Alternatively, to donate £2 now, use the QR code on the back cover of *Breakthrough*. This clever little design does all the work for you, but you'll need a smartphone equipped with a camera and a QR reader app. Just centre the code on your screen and, voilà, as soon as it is done scanning, just follow the instructions. Donation complete.

"CFS should be considered a condition of telomere shortening"

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 at the back 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.

Small caps

New study reports telomere shortening

Telomeres are 'caps' of DNA and protein located at the end of chromosomes to protect them from deteriorating or becoming fused with other chromosomes when cells are dividing. Structurally, they consist of a region of hundreds or even thousands of repetitive sequences of nucleotides, usually repeats of the sequence TTAGGG.

Telomeres become shorter during the ageing process as they shorten every time a cell divides – human blood cells shorten by 30 to 70 base pairs per year on average. This weakens the structural integrity of cells and causes them to age and die faster. It remains unknown whether telomere shortening is simply a sign of cells ageing or whether it contributes to the ageing process more directly.

Prof. Elizabeth Unger's group in Atlanta, Georgia, USA has used real-time polymerase chain reaction (in which multiple copies of a DNA sequence are created) to measure telomere length from DNA isolated from the blood samples of 639 participants in the Georgia CFS Surveillance study. Using a questionnaire, 64 participants were classified as having Fukuda-defined CFS, while 302 fulfilled only fatigue criteria, and 196 were healthy controls.

Overall, their results (presented at an Experimental Biology meeting in 2016) showed that telomere lengths

Spring Prize Draw 2017

Playing our spring 2017 raffle is a fun way to support research into ME/CFS. You could win either the top prize of £500 or one of our other fantastic cash prizes, and you'll also be helping us to continue to invest in the kind of biomedical research highlighted in this magazine.

Enclosed with this issue of *Breakthrough*, you'll find a raffle book of ten £1 tickets, but if you want more books just call us and we'll be happy to send them out.

Selling tickets can help raise awareness of ME/CFS. Completed stubs and cheques (made payable to "ME Research UK") need to be returned to us by 12th July 2017, with the draw taking place two days later on 14th July 2017. More information is on our website and printed on the tickets.

were significantly shorter in CFS patients and fatigue patients than in the healthy people. In fact, the mean telomere length was shorter by 593 and 508 base pairs in the CFS and fatigue groups, respectively. As expected, there was a correlation between telomere length and the age of participants. Given this evidence, the researchers suggest that CFS should be considered a condition of telomere shortening.

As shortened telomeres are also found in a range of other chronic diseases (including cancer, diabetes, Alzheimer's disease and Parkinson's disease), the phenomenon is most likely associated with chronic illness generally rather than with ME/CFS in particular. It is intriguing to note, however, that telomeres are highly susceptible to oxidative stress, which is known to damage DNA; the higher the cellular oxidative stress levels the greater the degree of shortening. Given that ME Research UK-funded work in Dundee has found high levels of oxidative stress and associated arterial stiffness to be a feature in ME/CFS patients, it may be that telomere shortening is intimately linked with ongoing inflammatory processes.

Although the length of telomeres decreases with age, it seems that the process is not inevitable and that they can also increase in length. Furthermore, scientists are currently exploring interventions to lengthen telomeres. Telomerase is the enzyme that repairs shortened or dysfunctional telomeres, and various telomerase-activating drugs are under development, with some success as recent work on blood disorders has shown. Also, statins seem to have a protective role against telomere shortening, although lifestyle factors may have an important role to play. One study has found that lifestyle changes (a plant-based diet, moderate exercise, stress reduction and weekly group support) increased telomere length by about 10% in men with prostate cancer!

Chinese enlightenment

Dramatic rise in acute phase proteins

Most scientific reports confirm something we already know or suspect, but occasionally one arrives that makes us stop and think. Researchers at the Second Military Medical University in Shanghai have been using an animal model to investigate how the body responds to fatigue, and they have discovered raised orosomucoid (ORM) in many tissues, including blood and muscle.

This is not surprising in itself as ORM is one of the major 'acute-phase proteins' which increase or decrease in blood plasma when inflammation is present. ORM is produced by many tissues – although mainly the liver – and its manufacture is influenced by factors such as tissue injury, infection, tobacco smoke, or the presence of other proteins produced by cells. Oddly enough, its precise biological function remains poorly understood, but we know that it is involved in immunity and in the metabolism of various drugs.

The clear relationship between ORM and fatigue in their experimental model led the researchers to wonder whether the protein might, in fact, be increased in people with ME/CFS. And their results proved very surprising. ORM levels were dramatically elevated in the blood of ME/CFS patients compared with healthy people (average levels of 2.78 versus 0.44 mg/mL, respectively). In fact, ORM levels were less than 1 mg/mL in all the healthy controls, but greater than 1 mg/mL in all except one of the ME/CFS patients. ORM expression was not related to serum cortisol level, as might have been expected.

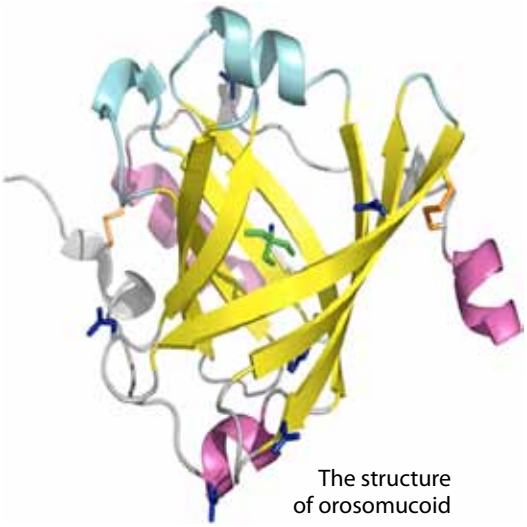
There is no other evidence of an association between raised ORM and ME/CFS, apart from the presence of ORM2 (one of the two isoforms of ORM) in the cerebrospinal fluid of ME/CFS patients, reported in a study in 2005. We already know that levels of ORM (and other acute phase proteins) are raised by infection and inflammation, and that concentrations of ORM in the blood are increased in smokers compared with past

or never smokers, although not to the extent seen in the ME/CFS patients in this study.

Also, raised levels of ORM, in combination with other markers, are linked with mortality in elderly people, as well as in some pathological conditions. Interestingly, another member of the acute phase protein family, C-reactive protein, is also greatly increased in ME/CFS patients, as ME Research UK-funded work has shown, with potential consequences for cardiovascular health. The publication of these result in *CNS Neuroscience & Therapeutics* in 2016 will hopefully bring this unusual finding to a wider audience.

Of course, whether ORM will become a valid biomarker for a diagnosis of ME/CFS is still anyone's guess. The next step is for the group in Shanghai to confirm and extend its findings (hopefully with funding from the National Natural Science Foundation of China which kindly funded their previous investigations), and for researchers elsewhere to test for ORM and related acute phase proteins in the blood of their ME/CFS patients. We'll watch this space with interest.

"Whether ORM will become a valid biomarker for diagnosis is still anyone's guess"



The structure of orosomucoid

Focus on funding

Leaving a legacy

Why is it important?

Each year, ordinary supporters make an extraordinary difference to their favourite causes by leaving a gift in their Will. These gifts, known as legacies, are an increasingly vital source of funds for charities such as ME Research UK.

A legacy does not have to be an enormous sum. Any gift left in a Will, no matter how large or how small, is important to the charities you support. Through a legacy you can make a direct and lasting contribution to ME Research UK.

Making your Will

Including ME Research UK in your Will is straightforward. You can include the charity when your Will is first drawn up, or you can add us to an existing Will by asking your solicitor to attach a written instruction, called a codicil. This ought to be done by your solicitor, so please don't make changes yourself. The codicil will need the signature of a witness.

Your legacy can be in the form of a set sum of money, financial assets such as shares, or in property and valuables. Currently all gifts to a charity such as ME Research UK are free from Inheritance and Capital Gains Taxes, so the full value of your gift will go to help the work of ME Research UK.

Types of legacy

- A Pecuniary Legacy allows you to give a specific sum of money.
- A Residuary Legacy involves leaving all or part of the residue of your estate after pecuniary legacies and other liabilities have been met.

We hope you will consider leaving a legacy to ME Research UK. If you do, please contact us, or complete the Legacy Pledge Form (available on our website), which is not legally binding, and send it to us for our records.

No matter how big or how small your gift, by donating you help ME Research UK to fund the biomedical research we all want to see.

trials of the heart

A new study from Newcastle looking at measures of **cardiac volume and function** in patients with ME/CFS

Over the years, a few scientific reports have pointed to the presence of abnormalities of heart (cardiac) function in ME/CFS. These abnormalities include relatively short QT intervals and a reduction in cardiac output or function.

ME Research UK-funded investigations by Prof. Julia Newton and colleagues at Newcastle University have also thrown up some intriguing findings. When the research group looked at the function of the heart using cardiac tagging, they found a dramatic increase in residual torsion in ME/CFS patients compared with control subjects. Patients had twice as much residual torsion as healthy people, indicating that their heart muscle was taking longer to relax.

Cardiac MRI

The Newcastle researchers have been continuing their investigations, and their most recent report was published in the journal *Open Heart*. In these experiments, cardiac magnetic resonance imaging (MRI) of the heart was performed in 47 patients with ME/CFS (excluding those with depression) who had been ill for 14 years on average, and in 47 matched control subjects. The results were fascinating.

Stroke volume was 23% lower in ME/CFS patients than in healthy controls, while volumes at the end of diastole were 25% lower, volumes at the end of systole were 29% lower, and heart wall masses at the end of diastole were 26% lower. In essence, these findings confirm, in a larger and different group of patients, the reductions in cardiac volume observed previously in pilot studies in Newcastle.

The patients' length of illness was not related to any cardiac MRI or volume measurements, suggesting that deconditioning (which would be greater the longer a person was ill) was unlikely to be the cause of these abnormalities.

Prof. Julia Newton leads the research group at Newcastle University

"These findings confirm the presence of cardiac abnormalities in people with ME/CFS"

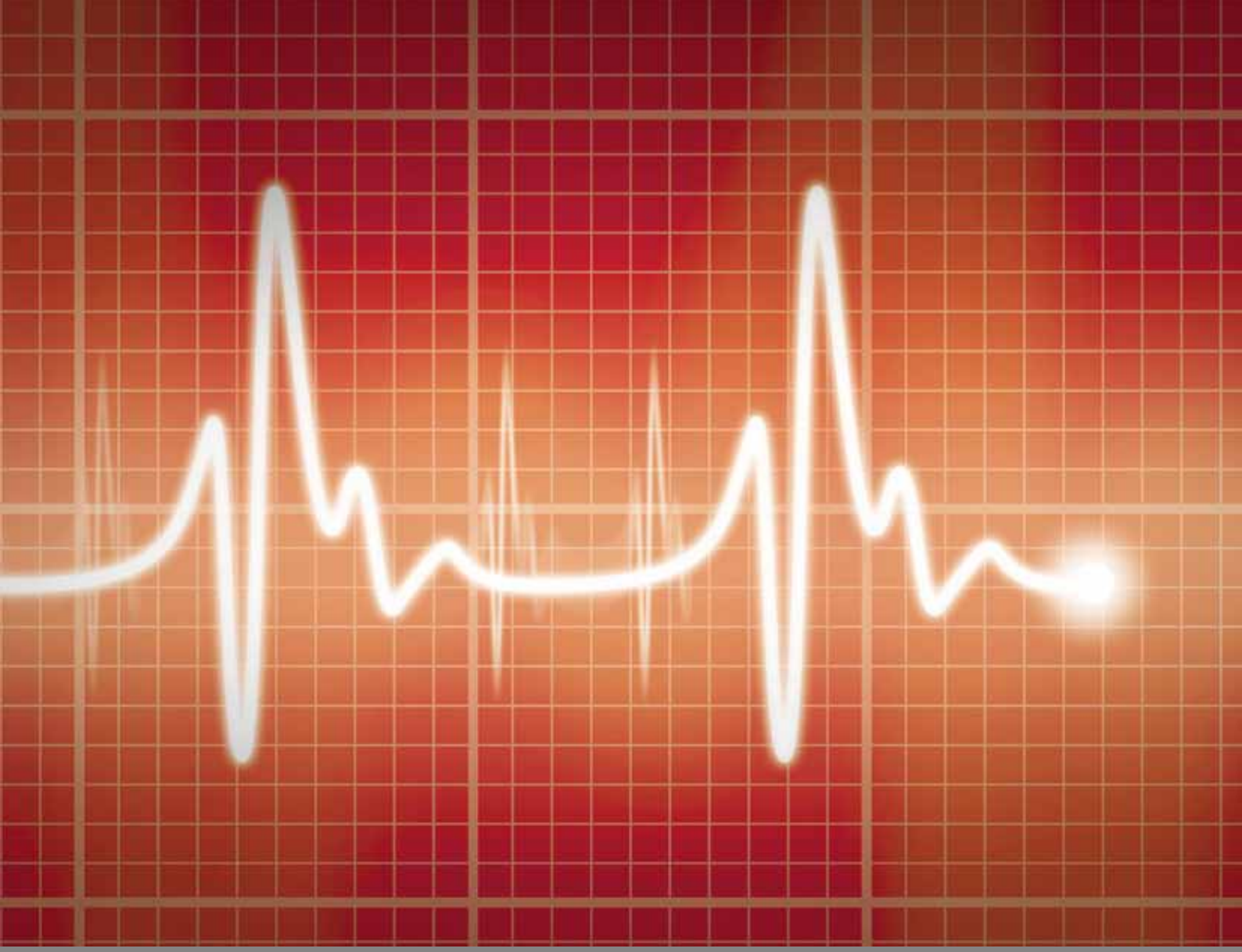
Also, the total volume of blood (including both plasma and red cells) was 4% lower in the ME/CFS group than in the healthy controls, though this difference was not statistically significant. In 63% of patients, however, the volume of red blood cells was below 95% of the expected levels for healthy people, and there were strong positive correlations between blood volume measurements and the mass of the heart wall at the end of diastole.

Red blood cell volume

The finding that the red blood cell volume was low is intriguing, and it may be that blood volume plays at least a part in the symptoms experienced by ME/CFS patients. One possibility is that low blood volume may be due to problems with the venous circulation, as nearly two-thirds of the blood in the circulation is stored in the venous system, which is controlled by the autonomic nervous system, also affected in ME/CFS.

Overall, these findings using state-of-the art imaging techniques confirm the presence of cardiac abnormalities in people with ME/CFS. It remains to be seen, however, whether these are caused by the disease and its consequences, or whether (for instance) a pre-existing reduced cardiac volume may make people more vulnerable to the development of illness.

As regards low blood volume, there is anecdotal evidence that the symptoms of ME/CFS improve in some patients after treatment with intravenous fluid (although the procedure is not without drawbacks and risks). The team in Newcastle therefore intends to explore interventions to restore fluid volume in ME/CFS patients in further studies. ●



A guide to some of the terms used

Cardiac output
The volume of blood pumped by the heart per minute, typically 4 to 8 litres per minute in a healthy adult. A lower than normal cardiac output can be a sign of heart failure.

Diastole
That phase of the heartbeat when the heart muscle is relaxing in between contractions, allowing its chambers to refill.

Left ventricle
The largest chamber of the heart, from where blood is pumped into the main arteries and around the body. (The right ventricle pumps blood to the lungs to take on oxygen.)

Magnetic resonance imaging (MRI)
A technique to visualise the internal organs by applying a very strong magnetic field to the body. Pulses of radio waves then knock the protons of the water molecules out of alignment, and when they realign they send out radio signals that distinguish the different types of tissues.

QT interval
This refers to the electrical activity of the heart (as represented in the ECG trace above). The QT interval is the length of time it takes for an electrical impulse to spread throughout the heart, causing it to contract. A shorter than normal QT interval can lead to an abnormal heart rhythm.

Residual torsion
A measure of how completely the heart muscle relaxes in between contractions. A higher residual torsion indicates that the heart is taking longer to relax.

Stroke volume
The amount of blood pumped by the left ventricle of the heart in one contraction. This is typically 60 to 100 millilitres in a healthy adult.

Systole
That phase of the heartbeat when the heart contracts, pumping blood out of its chambers, into the arteries.

diving in

An Australian team is planning to **pool DNA samples** in a search for new biomarkers that may also help identify disease mechanisms

Thanks to recent technological advances, the genome of any individual (a complete set of their DNA) can be surveyed rapidly from a single sample of tissue using machine automation. This technology has allowed genome-wide studies to be undertaken in a range of many different diseases.

Human genomes vary greatly, however, so hundreds or thousands of patients with a particular disease (as well as healthy control subjects) need to be recruited to ensure valid results, and sequencing studies can therefore be very expensive indeed. This is a particular problem in illnesses such as ME/CFS where funding is scarce and where it can be hard to access large numbers of well-defined and clinically assessed patients.

DNA pooling

One way to avoid recruiting thousands of research participants, thereby reducing costs and time, is DNA pooling. The basic idea is that DNA from many different patients is pooled together into a single DNA mixture, which is then sequenced, considerably reducing the library set-up costs involved in preparing samples individually.

Prof. Brett Lidbury and colleagues at the Australian National University in Canberra are conducting an ongoing programme which aims to find biomarkers for ME/CFS using a range of sources: bioinformatics, genetics and pathological testing. Prof. Lidbury has a background in virus–host interactions, particularly the Ross River virus which is endigenous to Australia and can cause long term post-viral syndromes (and has been suspected to have a role in ME/CFS). Today, much of his work is on ME/CFS, and his team benefits from access to a large well-defined group of patients recruited by the CFS Discovery Clinic in Victoria. Full

The team at the Australian National University: (L to R) Dr Alice Richardson, Dr Claudio Mastronardi, Dr Guifang Shang, Prof Patricio Arcos-Burgos, Prof Brett Lidbury and Ben Signor

"We're looking for patterns which can help with biomarker detection and provide clues to disease mechanisms"

clinical histories, as well as pathological and physiological data are available for these individuals.

ME Research UK has provided funding to the group to acquire additional genetic data using DNA pooling. They will apply two-dimensional DNA sequencing to attempt to identify ME/CFS-associated genetic changes across the entire genome in a clinically well-defined group of 100 patients and up to 40 control subjects. Two DNA pooling techniques will be used: a pooling/bootstrap genome-wide method which has been developed and used for the detection of genetic markers of Alzheimer's disease by Prof. Lidbury's collaborators on this project; and a 2D DNA pooling method for rare variant detection.

The team recently completed a pilot study in which they successfully applied machine learning methods to pathological and clinical data alone, which revealed patterns associated with both the presence and the severity of ME/CFS. So when the genetic data is ultimately available from the DNA pooling studies, it will be possible to apply similar machine learning techniques and statistical analyses to an integrated data set combining genetic, clinical and pathological information.

Biomarker pattern detection

Prof Lidbury explains that "We're looking for patterns in the data which can help with biomarker pattern detection and provide clues to disease mechanisms. With complex diseases like this, we need to look at many factors simultaneously, and cross-disciplinary studies are necessary to integrate the findings from different avenues of research investigation.

"I've been very fortunate to have spent a large proportion of my career involved in curiosity-driven fundamental research. My plan now is to work on tangible solutions that translate to patient benefit. For the moment this is focused on biomarker discovery, which may (hopefully) also lead to ideas for therapeutic interventions." ●

Meeting of minds

Annual conference of the CMRC

The third UK CFS/ME Research Collaborative Annual Science Conference was in Newcastle in 2016. There was a range of presentations and a patient–researcher workshop, and some of the researchers we have supported were in attendance, as the photo above shows.

(L to R) Prof. Julia Newton (Newcastle University), Dr Vance Spence (ME Research UK), Dr Sarah Knight (Murdoch Childrens Research Institute, Australia), Victoria Strassheim (Newcastle University), Dr Clive Carter (Leicester NHS Trust) & Prof. David Patrick (University of British Columbia, Canada).

Research bites

Our round-up of recent research from around the world

Inflammation of the nose and throat

Hotta et al., Immunological Research, 2016

In some people, ME/CFS starts after a vaccination or immunisation. One Belgian study of over 1,500 patients found a small cluster of cases (around 5%) where hepatitis B vaccination could have been involved, but flu vaccines and human papillomavirus (HPV) vaccines have also been suggested as triggers. It's interesting, then, that Japanese researchers have found a possible association between HPV vaccination, ME/CFS symptoms and nose and throat inflammation (chronic epipharyngitis, which may impact on autoimmunity generally).

They examined the epipharynx in 41 teenage girls who had developed symptoms after HPV vaccination. Most (83%) were unable to attend school, and their symptoms included general fatigue (in 95.1%), sleep disturbance (87.8%), muscle weakness (75.6%) and cognitive problems (68.3%). On examination, severe inflammation was found in all 41 patients. Sixteen girls were willing to come into hospital for treatment of the inflammation, and 13 reported a marked reduction in the symptoms of ME/CFS after treatment, with four eventually achieving a 'cure'.

Chronic epipharyngitis is poorly recognised; in fact, the term is rarely used in the modern medical literature, particularly outside of Japan. Still, it is surely worth other researchers around the world testing for and treating nose and throat inflammation in their own ME/CFS patients, particularly as 'sore throat' was a prominent symptom in older epidemics of myalgic encephalitis and is part of some definitions used today.

Gut bacteria

Giloteaux et al., Microbiome, 2016

When researchers from Cornell University sequenced regions of microbial DNA from stool samples of ME/CFS patients and healthy control subjects, they found that patients had fewer bacterial species known to be anti-inflammatory, something that is also seen in ulcerative colitis and Crohn's disease. There were also fewer different kinds of bacteria in the patients, and specific markers of inflammation were found in the blood, possibly caused by bacteria entering the bloodstream from a leaky gut. Overall, they found that a combination of gut bacteria and blood microbial markers could correctly classify 83% of patients as having ME/CFS, a finding which brings us closer towards an objective yet non-invasive diagnostic test for the disease.

Genome-wide associations

Schlauch et al., Translational Psychiatry, 2016

The gene sequences that differ between human beings are largely made up of single nucleotide polymorphisms (SNPs). Most are 'silent' but others have important consequences, and many scientists are using genome-wide technologies to identify SNPs linked to various diseases. The most comprehensive genome-wide study in ME/CFS was published recently by a consortium of researchers from the USA, Hungary and Russia. From 42 ME/CFS patients, 659,094 SNPs passed quality control, and 23 were found to have a strong association with the illness. These tended to be linked to T-cell receptors (critical for immunity), neurotransmission, and the fight against infection, and these SNPs can now be targeted by research groups around the world.

Gender differences in ME/CFS

Faro et al., Reumatologia Clinica, 2015

Four times more women than men get a diagnosis of ME/CFS, but is the illness the same in women and men? Spanish researchers examining 1309 patients (91% women and 9% men) found that twice as many men as women reported an infectious illness onset, and that men were younger when they were diagnosed. More of the men were skilled workers and were unmarried. Importantly, women were more likely to have other conditions alongside ME/CFS (thyroid disorders, fibromyalgia, etc.). Immune and muscular symptoms were less frequent in men, and women had worse scores for overall physical health. As neuro-immunity differs between the sexes, these findings may well reflect real differences in the disease and how it develops.

Getting professionals to care

Bayliss et al., BMC Family Practice, 2016

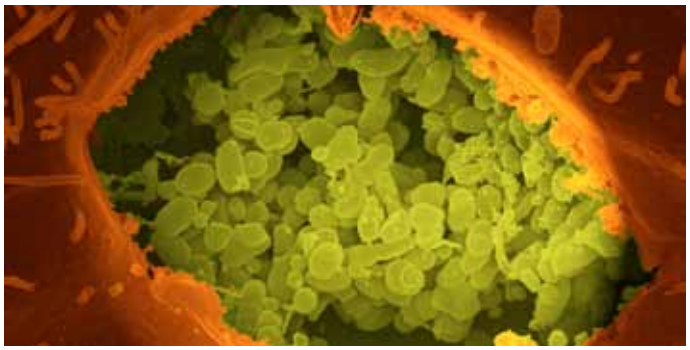
How can the diagnosis and management of ME/CFS patients be improved? The METRIC study in Manchester developed resources to help, including online training for GPs in 21 sample practices. Each GP who completed the training received £50. The team experienced difficulty recruiting GP practices, partly due to scepticism about the illness. Over time, only 10 of the 21 practices completed the training, due to time pressures and the low priority placed on hard-to-manage conditions; as one said, "It's not top of anyone's agenda." GPs tended to think that diagnosis and management of ME/CFS should take place in a specialist care setting – another argument, surely, for dedicated Centres of Excellence across the country.

Are you intolerant to milk?

Rowe et al., Acta Pediatrica, 2016

Food intolerances have a significant role in ME/CFS. Gluten is a good example; many patients have tried a gluten-free diet and some say it helps reduce gut discomfort and general symptoms like brain fog and muscle pain. Now, a report from Johns Hopkins University suggests that milk protein may also be contributing to symptoms. The researchers examined quality of life before and after a six-month period of 'dietary milk-protein restriction' in 17 young ME/CFS patients (31% of those tested) who were found, unexpectedly, to be milk-protein intolerant.

At the start of the study, health-related quality of life was significantly worse in the patients who were milk-protein intolerant than in 38 patients who were not. However, six months after the milk-free diet, quality of life had improved to a greater extent in those with milk-protein intolerance, and there was no longer a difference in quality of life between the two groups. Also, patients on the milk-free diet had improvements in upper gastrointestinal and general symptoms within two weeks of starting the diet. While stopping or reducing milk consumption is not the answer to ME/CFS, it's worth being aware that the symptoms of ME/CFS may be made worse in some people by a common foodstuff like milk. The authors point out that people with ME/CFS can clarify their own situation by a two-week trial of a milk-free diet.



Q-fever at post-mortem

Sukocheva et al., BMC Infectious Diseases, 2016

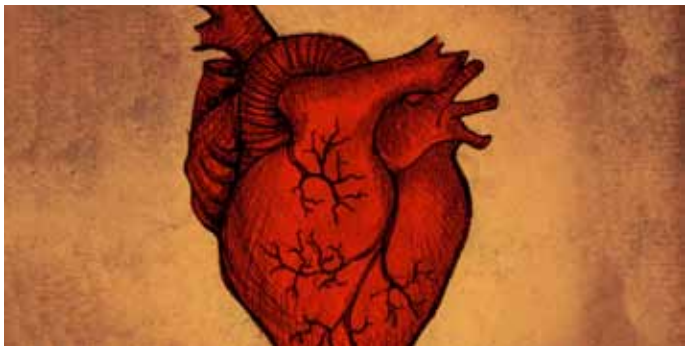
Misdiagnosis is common in ME/CFS. A 19-year-old woman was ill for 10 years after an acute encephalitis-like illness. No cause for her illness was found, and she was given various diagnoses including 'post viral syndrome'. After her death, researchers studying Q-fever (*Coxiella burnetii* infection) tested her post-mortem specimens, finding distinct evidence of persistent infection with the bacterium. Coxiella antigens were found in many organs, such as the spleen, liver and heart, and Coxiella DNA was found in the heart, lung, spleen and liver but not brain or bone marrow. The authors say, "The most compelling and coherent explanation… is one of a severe attack of primary Q-fever and a subsequent multisystem organ dysfunction."

Downgrade for psychosocial therapies

Agency for Healthcare Research and Quality report, 2016

In 2014, an evidence review by the US Agency for Healthcare Research and Quality (AHRQ) found that exercise and behavioural therapies can improve the lives of ME/CFS patients. Since then, a report from the National Institutes of Health has suggested that the very broad 'Oxford definition' should be retired from use, so the AHRQ reanalysed its data after excluding studies using the Oxford definition. The new analysis found "insufficient evidence of the effectiveness" of graded exercise on any outcome, or of cognitive behavioural therapy on function, employment and global improvement. This is an important development, which NICE should take into account when it updates its clinical guidance on ME/CFS in future.

"Stopping milk consumption is not the answer… but the symptoms of ME/CFS may be made worse in some people by milk"



Heart abnormalities

Olimulder et al., Netherlands Heart Journal, 2016

Some investigations, including those we have funded at Newcastle University, have found heart (cardiac) abnormalities in ME/CFS patients, notably an increase in 'residual torsion', meaning that the heart muscle takes longer than normal to relax. A Dutch research group has continued the work, using cardiac magnetic resonance imaging to measure the dimensions of the heart and its function in women (12 with ME/CFS and 36 healthy). They found that the size, mass and functioning of the left ventricle was lower in the patients, though still within the normal range. In seven patients, they found particular abnormalities. As the researchers say, cardiac imaging could usefully be part of the clinical investigation of patients.

Mortality in ME/CFS

Roberts et al., The Lancet, 2016

Do people with ME/CFS die earlier, for whatever reason, than people in the general population? Researchers at King's College London examined the medical records of 2,147 people referred by their GPs to the CFS service in London. Over a seven-year period (2007 to 2013), only 17 of the patients had died: 8 from cancer, 5 from suicide and 4 from other causes. When these mortality rates were compared with matched population data from the Office of National Statistics, the overall rate of deaths from all causes was no higher in ME/CFS patients than in the general population. These headline findings will come as a relief to many patients and their families in the UK worried about the effects of illness in the long-term.

Rex Alexander & the Caravelles playing at the 60s dance organised by **June Warne**

Friends united

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

Back to the sixties

Laura Gilbert's mum, June Warne, worked hard to organise a sixties dance in Melbourne, East Yorkshire. The aim was to have fun, but also to raise much needed funds for ME research. The band playing that night was Rex Alexander & the Caravelles, who specialise in music from the fifties and sixties. And they helped create a night full of memories, including songs such as *Stray Cat Strut*, *Sweet Caroline*, *I Hear You Knocking* and *Oh, Pretty Woman*.

Halcyon days

Two years ago, Hal Bransby raised money for us by cycling from sunrise to sunset on the longest day of the year, covering 211 miles. This time, Hal took part in the cycle festival Eroica Britannia Bakewell, based on the original L'Eroica cycle ride held every year in Tuscany. It's a celebration of good old-fashioned cycling before carbon fibre, power meters and energy gels, and the 100-km ride has to be made on a pre-1987 bike. Hal's steed was a 1974 Viscount with a steel frame, down-tube shifters and toe clips, and he was wearing a very itchy period jersey too!

TrekFest: the peaks

Danni Pudney trekked 25 km for ME Research UK recently, as part of Trek-Fest which includes two of the UK's most breath-taking national parks – the Brecon Beacons and the Peak District. Danni says, "My mum is a wonderful, brave, caring and independent woman. She inspires me everyday, and has recently been diagnosed with SEID

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01 Richard Davies considers the gruelling cycle ahead of him

02 Once more skydiving for ME Research UK is **Amber Blackmore**

03 Stacey Permaul and Michael McNicol on their happy day

04 Danni Pudney conquers the peaks on TrekFest

[the suggested new name for ME]."
The whole family has had to learn a lot about ME since then, and they explain that they've met some amazing people with the illness along the way.

Wedding bells

Stacey Permaul and Michael McNicol celebrated their wedding last summer at Oxenfoord Castle outside Edinburgh, and asked their guests to give us donations in lieu of presents. Michael's brother, Andrew, has had ME for quite a few years, and as Stacey explained to the guests, "Mike and I are incredibly lucky to be sharing our wonderful day with you all. We know Andrew would love to have been here too, so we are asking you to help his chosen charity instead of giving lovely plates and towels… Forget the toaster, we'd love a donation!"

Skydive 2016

For the last two years, Amber Blackmore has taken on the huge challenge of skydiving from 15,000 feet, and in 2016 she did it once again. The venue was Dunkeswell Airfield in Devon, and the dive was part of the official world record skydive attempt for the most people to skydive in daylight over a period of 24 hours. Though the world record attempt had to be cancelled, Amber was unfazed and jumped another day for us. Go, Amber!

Celtic Wiseman Perpetual

Martin Wiseman has been bedbound with ME/CFS since August 2008, so his old school friend, Richard Davies, completed the inaugural Celtic Wiseman Perpetual, a gruelling 75 mile cycle ride around Devon and Cornwall to raise awareness of the illness. Richard smashed his fundraising target in the process, and he placed details of his looping route online so other cyclists could follow and donate to ME Research UK.

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05 Jenny Holmes glows with pride after completing her Blacklight Run

06 Fundraising teamwork with **Jamie** and **Georgie** as they plan ther first skydive

07 Sean Wilson is one of our many supporters who took part in the Walk for ME 2016

08 Friends **Helen Millard** (right) and Josie prepare to lose their hair

Jenny's blacklight run

Supporter Jenny Holmes completed the 5 km Blacklight Run, a unique night-time run focussed less on speed and more on UV neon glowing fun. Its rules are simple: wear a white shirt and finish the run covered in UV neon glow powder. There's an after-run party too, so by the end everyone looked like the cast of Ghostbusters.

Georgie and Jamie's skydive

Georgie and Jamie have come together to throw themselves out of an aeroplane to raise funds! Georgie was a competitive swimmer and rower before developing ME, and Jamie's mum was diagnosed with ME many years ago. Their first event is a 15,000 feet jump, and their aim is that "other people don't have to suffer from this debilitating illness in the future".

Walk for ME 2016

We'd like to thank everyone who took part in Walk for ME 2016, particularly-those who chose to support us – walkers like Louise Kay, Heather Bennett, Angela Dyson, Helen Oliver, Shauni Hyslop, Sean Wilson, the Chamberlain family, Rebecca Thomas, Suzy Elsor, Louise Kay and Claire Browne. Thanks also to the originators of this event – you've really made a difference!

Beyond the call

Helen Millard has shaved off all her hair! Her friend Josie had just begun chemotherapy for lymphoma, and Helen offered to match her lost hair for ME Research UK. Helen's support for a dear friend is fitting since Josie was "always thinking of others, not herself".

Standing Order Form

To allow us to press ahead with our mission to Energise ME Research globally, please consider setting up a Standing Order by completing this form and sending it to: **ME Research UK, The Gateway, North Methven Street, Perth PH1 5PP**.

Name of account holder(s)

Address

Postcode

Telephone number

Name of Bank or Building Society

Branch address

Branch postcode

Instruction to your Bank or Building Society

To the Manager, Please arrange to debit my/our account with the amount detailed below, once every month until further notice.

Account number

Branch sort code

Debit amount (£)

Payment date each month

Date of first payment

Pay to: Clydesdale Bank, 158/162 High Street, Perth PH1 5PQ, UK, Account: ME Research UK, Account no: 50419466, Branch code: 82-67-09

☐ ***Tick*** *if you would like us to treat this, any future donations to ME Research UK (SC036942), and all payments in the previous 4 years, as Gift Aid donations, meaning your donation can increase in value by a quarter at no extra cost to you. You confirm that you are a UK taxpayer and understand that if you pay less Income Tax and/or Capital Gains Tax than the amount of Gift Aid claimed on all your donations in that tax year it is your responsibility to pay any difference. Please notify us if you wish to cancel this declaration, change your name or home address, or no longer pay sufficient tax on your income and/or capital gains. If you pay Income Tax at the higher or additional rate and want to receive the additional tax relief due to you, you must include all your Gift Aid donations on your Self-Assessment tax return or ask HM Revenue and Customs to adjust your tax code.*

Signature

Date

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