Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

December 2017

Future dates

Open to all members and carers.

For upcoming meeting dates please email: guildfordme@hotmail.co.uk.

Cellular bioenergetics is impaired in ME/CFS:

An open-access peer-reviewed research paper was published on 24th October 2017 that details cellular energy problems in ME/CFS patients

The actual paper can be found here:
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0186802

However, below are two articles that offer an easier to absorb overview. The first article from the New Scientist offers a high level overview, the second article by Cort Johnson offers further depth.

1 New Scientist: blood cells in CFS are drained of energy

Source: http://www.meassociation.org.uk/2017/11/new-scientist-blood-cells-in-chronic-fatigue-syndrome-are-drained-of-energy-04-november-2017/

Thirteen years ago, Cara Tomas was rendered bedbound with chronic fatigue syndrome. It came on suddenly, she says, without warning signs. Even now she has good days and bad days due to the lingering effects of the disease. “A lot of people dismiss it as a psychological disease, which is a big frustration,” she says.

Tomas knows more about CFS than most. A PhD student at Newcastle University in the UK, she has just published a paper demonstrating that white blood cells in people with the disease are as listless as the people themselves often feel.

“Now we’ve shown there’s a physiological difference, it could explain the whole-body fatigue shown by patients,” she says. The finding adds to mounting evidence that the disorder has a biological explanation, and raises the prospects for new treatments and diagnostic tests.

For many years, arguments have raged over whether CFS — also known as myalgic encephalomyelitis, or ME — has a physiological or psychological basis. But the latest research comparing samples of peripheral blood mononuclear cells (PBMCs) from 52 people with the condition and 35 without has reinforced the case for a biological explanation.

Less mighty mitochondria

Across almost all measures of energy capacity, the cells from people with CFS were weaker compared with their healthy counterparts. If other cells are equally compromised, it could explain why people with the condition are often bed- or wheelchair-bound for months, and struggle with even modest physical exertion.

“The CFS cells couldn’t produce as much energy as the control cells,” says Tomas. “At baseline, they didn’t perform as well, but the maximum they could reach under any conditions was so much lower than the controls.”

Tomas and her colleagues measured the efficiency of mitochondria, the energy-generating powerhouses in cells. The mitochondria are the dominant source of energy for all of our cells. The team found that mitochondria in CFS cells can’t produce energy properly. “We’ve shown definitively that it’s a fault in mitochondria,” says Tomas. “It points directly to a physiological, not psychological disorder.”

Tomas measured the oxygen consumption of cells in comfortable and stressed conditions, to see how well they could raise their game with glucose in short supply, a situation forcing the cells to consume more oxygen to compensate. Even at baseline, control cells consumed twice as much oxygen as the CFS cells. The disparity widened dramatically when the cells were stressed.

Metabolically exhausted

In another test that artificially pushed cells to their maximum capacity starting from baseline, CFS cells could only increase their mitochondrial output by 47 per cent, roughly half the 98 per cent increase achieved by control cells.

The implication is that cells from CFS patients can’t raise their output to meet the energy demands of routine physical tasks.

“These exciting results confirm what others have postulated but not been able to prove, namely that cells of patients with CFS are easily metabolically exhausted when put under any form of stress,” says Stephen Holgate of Southampton General Hospital. “In many ways, this is how patients describe their whole-body experience with CFS.”

“This is a major step forwards, supporting previous studies, which demonstrated that mitochondrial function can be impaired in this illness,” says Karl Morten of the University of Oxford. “A major question now is whether the situation in these white blood cells reflects whole-body mitochondrial dysfunction in patients,” he says.

To that end, Tomas is currently taking samples of muscle cells and testing them in the same way as the blood cells. “It would be good if we could get this repeated in muscle cells,” she says. “It’s important the patient population know we are looking into this. Patients sometimes think no one cares, but we do have interest, and want to find out what’s going on.”

2 **Cellular energy production takes a big hit in ME/CFS study**

Source: https://www.healthrising.org/blog/2017/11/11/cellular-energy-hit-chronic-fatigue-study/

The two-day exercise study results suggest that the ability to produce energy after exercise in chronic fatigue syndrome (ME/CFS) is blunted, and the search is on to identify blockages in cellular energy that could explain that. Lead by Cara Tomas, Julia Newton and company have stepped into the fray with the first published "Seahorse" ME/CFS study that I'm aware of.

Agilent's Seahorse machine is, for the first time, making it easy for researchers to study cellular energetics. During a recent trip to Nancy Klimas's lab at Nova Southeastern (she has one)

Dr. Deth exclaimed at how the Seahorse has greatly expanded researchers' ability to put cells under stress and measure their energy production. With at least five ME/CFS studies using the machine, the Seahorse is a case of technology evolving at just the right time to benefit ME/CFS research.

Because there's no evidence that genetic mutations are affecting mitochondria output in ME/CFS, any mitochondrial problems that are present they are most likely "acquired" during an infection or other event which either damaged them or prevented them from functioning properly.

Since the mitochondria can be inhibited by a number of factors ranging from immune activation to oxidative stress to psychological stress it's probable that a number of different pathways lead to any mitochondrial dysfunction that might be present in ME/CFS.

The metabolomics studies suggest problems with glycolysis are present but studies actually examining mitochondrial functioning in ME/CFS have been pretty rare.

An earlier study using a different means of measuring cellular energy production (ATP Profile test) in neutrophils in whole blood found that "all patients tested have measureable mitochondrial dysfunction which correlates with the severity of the illness." Cell-free DNA measurement showed high levels of damage.

Other studies, however, do not suggest the mitochondrial play an important role in ME/CFS. Mitochondrial content was lower in ME/CFS but ATP production and other measures of mitochondrial health were normal. Likewise, Vermeulen found reduced exercise capacity in ME/CFS but normal ATP production. If an inhibiting factor in the blood plays a role Vermeulen's extraction of PBMC's from whole blood might have played a factor. Vermeulen, however, proposed that reduced oxygen delivery to the issues was the problem.

Most recently, a Stanford study found evidence of greatly increased mitochondrial activity in ME/CFS cells. The Stanford study suggested that left to themselves the mitochondria in ME/CFS might doing just fine and that glycolysis – the anaerobic portion of the energy cycle – might be the issue.

"Our results present an unorthodox view on CFS pathology: the fatigue is not caused by lack of ATP, and instead might be caused by a pathological process linked to non-mitochondrial ATP production such as glycolysis."

That study, which did not use the Seahorse machine, provided yet another twist when the glycolysis results suggested that ME/CFS was a hyper not a hypometabolic conditions. Because the cells were tested outside of the plasma the effect of a possible inhibiting factor in the blood was not taken into account.

Now we have Tomas et. al. using the Seahorse machine to get very accurate direct measurements of cellular energy production in ME/CFS. Like Vermulen, this group used PBMC's isolated from whole blood.

Stuck Cells

The first sign something was wrong came when Tomas assessed the energy production of cells low and high glucose concentrations. (The Seahorse machine allows researchers to add materials to the cells to see the effect they have on energy production.) Tomas expected the addition of glucose would boost up glycolysis – the anaerobic portion of the energy cycle which runs on glucose – and it did – but only in the healthy controls. The inability of the ME/CFS patient's cells to utilize the extra glucose seemed to suggest that something had gone wrong with glycolysis in ME/CFS but a glycolysis stress test indicated that glycolysis was operating normally.

Almost every indicator of energy production was lower in ME/CFS patients' cells whether they were put into low or high glucose levels (basal respiration, ATP production, maximal respiration, reserve capacity, non-mitochondrial respiration, coupling efficiency).

Newton suggested that the ME/CFS cells were kind of stuck in a low energy mode. When given extra glucose they weren't able to use it. When deprived of glucose they weren't able to increase their mitochondrial energy production. A stimulation test in the Seahorse machine didn't stimulate the ME/CFS patient's cells much either. When asked to respond the ME/CFS cells were able to generate about 50% more energy while healthy control cells doubled their energy output. The study was on immune cells not muscle cells but each finding seemed to make sense given ME/CFS patient's inability to mount the energy to engage in exercise.

The healthy controls cells, on the other hand, responded to all three tests – they basically demonstrated the flexibility and capacity that healthy cells need to have to respond adequately to a number of different situations.

Newton's explanation about the healthy control cells being more "adaptable" or responsive to their environment than the ME/CFS patient's cells sounded somewhat like Bob Naviaux's idea of the cells being thrown into a cell danger response and hunkering down and trying to ride out some threat. Unless Naviaux's CDR hypothesis includes cells getting stuck without an outside factor to keep them reined in (which it may), however, it didn't seem to apply: Newton's cells were tested outside of the plasma where the threat is believed present.

Beside their unresponsiveness the ME/CFS patient's cells also had lower reserve capacity; i.e. they may have already been operating near their maximum level. The low coupling efficiency suggested that when pushed, they simply didn't have the resources to respond.

All in all it was a remarkable set of findings. At least two thirds of the tests done were abnormally low in whatever situation they were put in.

An earlier model of mitochondrial dysfunction in ME/CFS seems, at least to this laymen's eyes, reflect the situation Newton found. When stressed the cells lacked the capacity to respond. Their reduced mitochondrial capacity had caused the cells to dig into their adenine reserves resulting in long recovery periods after exercise. The model predicted it would take 3-5 times longer for the ATP levels in the muscles of ME/CFS patients to return to normal after exercise than for healthy controls. The model also predicted that short (30 seconds), intense exercise periods would be easier for ME/CFS patients to recover from.

Newton's findings certainly seemed to make sense given the fatigue and energy problems highlighted in ME/CFS but, as she acknowledged, they conflicted with some of the past results.

The combination of the detection of significant differences in OXPHOS alongside the lack of detectable differences in glycolysis has potentially uncovered a previously unknown phenotype of CFS PBMCs Newton et. al.

Newton isolated ME/CFS patients PBMC's from whole blood but still found reduced cellular energy production. The Stanford group did the same thing but found increased energy production with a highlight on increased glycolysis. Newton's finding of reduced energy production in cells found outside the plasma appears to conflicts with the idea that something in the blood is whacking ME/CFS patient's cells ability to produce energy.

Newton's findings of normal glycolysis conflicted with the Stanford group's finding on increased glycolysis and with metabolomic studies pointing to glycolysis issues.

In broad way, though, Newton's findings do fit. Almost all the studies point to problems with cellular energy production that may be manifesting themselves in different ways. A somewhat similar situation may be showing up in exercise studies where different issues (ventilation, VO2 max, anaerobic threshold) are appearing in different patients. Those studies suggest that the exercise incapacity present in ME/CFS is being produced different ways. That may not be surprising given what we know about disease. If the molecular roots of say, lung cancer, differ between patients, it would make sense for a variety of different pathways to cause the energy production problems in ME/CFS.

Conclusion
Newton's rather stunning findings – that the vast majority of tests of cellular energy production were significantly lower in ME/CFS patients' immune cells – made sense. The good news is that most studies are finding evidence of whole body (exercise, metabolomics) or cellular energy production problems. The bad news is that they're coming to different conclusions as to how that's happening.

The cure to the energy production puzzle is, of course, bigger and better studies and they seem to be coming. The Seahorse machine, which looks like it's going to be floating around ME/CFS research circles for a while, will mean more methodological consistency and allow for better comparisons between studies.

Avindra Nath is using one in his NIH intramural study, and Maureen Hanson appears to be using one in two studies, one of which will hopefully be a large, robust study at her NIH funded ME/CFS research centre. Ron Davis has used one, Isabel Barao is using one in her SMCI funded study, and Newton reported she will be seeking larger, longitudinal studies. Anyone, it seems, who wants to know about energy production in ME/CFS is using one.

Avindra Nath's intramural study is small – approximately 40 patients – but with its metabolic chamber, exercise study and other features it's digging into so many different parameters that one wonders if it might be able to uncover different subsets and their pathways all on its own. Brian Vastag reported that the early Seahorse results were so unusual that the researcher involved felt compelled to stop by and chat…

By the time all is said and done the Seahorse will hopefully tell us much about ME/CFS.

Rt Hon Jeremy Corbyn MP pencilled in for Invest in ME conference 2018

The 13th Invest in ME Conference will be held on 1st June 2018. Although speakers are to be determined Jeremy Corbyn has been pencilled in. As speakers are determined they are displayed at the following link:

http://www.investinme.eu/IIMEC13-13-13-Agenda.shtml

Announcing the launch of an innovative patient-centred portal – Natural Health Worldwide

https://naturalhealthworldwide.com

Natural Health Worldwide (NHW) is a new website that launched on 1st June, this year. It is a portal which connects patients from all round the World with NHW health practitioners. These practitioners, also from all round the World, can be Medical Doctors, other qualified Health Professionals or Experienced Patients. Each practitioner has an individual webpage where they can describe their qualifications, their experience and what they specialise in. Patients can search the site by type of practitioner and or illness/problem.

NHW has a philosophy of providing healthcare that is as 'natural' as possible, with many of the practitioners using diet, supplementation and other non-prescription drug approaches. However, this does not exclude the use of prescription drugs, where appropriate. Initially the focus of the site is on conditions such as ME/CFS, Adrenal and Thyroid problems, Lyme Disease etc, However, NHW expects to widen its coverage as the site grows.

Dr Sarah Myhill is the website founder and has funded its development – this website is her gift to patients. Dr Myhill stands to gain nothing from NHW, having divested herself of all financial interests.

The motivation for this project can be seen from two perspectives. First, over the years, Dr Myhill has had to turn away thousands of patients and wanted to develop a portal that would provide an excellent and accessible service for these often neglected and ignored patients. NHW does just that, bringing practitioners to those patients in an easy one-stop shop.

Secondly, NHW is part of a wider agenda, which has the aim of empowering patients to take control of their own health-care. So much of modern medicine can be driven by vested financial interests and in the process, the patient is almost completely forgotten. Dr Myhill had the vision of swinging the pendulum back in favour of the patient and away from those vested interests.

To achieve this empowerment, three key areas were identified:

1. The knowledge to work out why you have symptoms and disease - Dr Myhill has undertaken an extensive book-writing exercise, with 3 books published already and 2 more on the way this year*
2. Direct access to relevant medical tests – this is achieved via the NHW website
3. Direct access to knowledgeable Health Practitioners who can further advise and guide patients, together with access to safe and effective remedies – this is achieved via the NHW website

Appointments are booked through the website and can be conducted by Skype, Facetime, 'phone or email. This makes the process very convenient and also caters to a forgotten patient population – the housebound and bedridden. After each appointment, patients rate their practitioners on 'Knowledge', 'Value for Money' and 'Approachability', as well as having the opportunity to leave more discursive comments. The rating system means that practitioners build reputations and this will help inform subsequent patients as to who may be the best practitioner for them.

Patients can also access lab tests via the site and there is also an extensive phlebotomists' listing in the UK, again making the process quick, easy and accessible to all.

The hope is that NHW will contribute to the future of healthcare being more patient-centred, with access to health practitioners, lab tests, and the necessary knowledge, all putting patients back in control and giving them the choices that they both need and deserve.

Interested patients – please register here - https://naturalhealthworldwide.com/patient_sign_up.php All patients who register in June or July will be entered into a free mystery prize draw.

Interested practitioners – please register here - https://naturalhealthworldwide.com/practitioner_sign_up.php

Other media and general enquiries – please email office@naturalhealthworldwide.com

Craig Robinson

*Dr Myhill has published:

- "Diagnosis and Treatment of CFS and ME – it's mitochondria not hypochondria" - http://drmyhill.co.uk/wiki/CFS/ME_-_my_book_Diagnosis_and_Treatment_of_Chronic_Fatigue_Syndrome_and_Myalgic_Encephalitis
- "Sustainable Medicine – whistle blowing on 21st century medical practice" - http://drmyhill.co.uk/wiki/My_book_"Sustainable_Medicine_-_Whistle-blowing_on_21st_century_medical_practice"
- "Prevent and Cure Diabetes – delicious diets not dangerous drugs" – [co-authored with Craig Robinson] http://drmyhill.co.uk/wiki/My_book_"_Prevent_and_Cure_Diabetes_-_delicious_diets_not_dangerous_drugs"

Due out this year are

- "The Paleo Ketogenic Diet – getting the best of both worlds" - [co-authored with Craig Robinson]
- "Life is an Arms Race – fighting infections" - [co-authored with Craig Robinson]

Negative phase III clinical trial result from Norway for Rituximab in ME/CFS

Source: http://www.meassociation.org.uk/2017/11/me-association-statement-negative-phase-iii-clinical-trial-result-from-norway-for-rituximab-in-mecfs-27-november-2017/

By Dr Charles Shepherd, Hon. Medical Adviser, ME Association.

"I was disappointed to learn – while at the Royal Society screening of the documentary, Unrest, in London last Thursday – of the preliminary (but unpublished) results from the phase III clinical trial of Rituximab, that has been carried out in Norway.

"This large, multicentre, 'gold standard' clinical trial, involved 152 people with ME/CFS receiving either Rituximab or a placebo, with initial treatment followed by maintenance treatments at 3, 6, 9 and 12 months, and a two year follow up.

"The ME Association has consistently taken the position that Rituximab could be one of the most promising developments in the search for a safe and effective drug treatment that is targeted at the underlying disease process in ME/CFS.

"We also know that the physicians involved in this research – Drs Oystein Fluge and Olav Mella from the Haukeland University Hospital in Norway – have taken great care in the way that they have devised the protocols for the clinical trials that have been carried out and reported.

“Despite the headline negative finding, we believe that this trial will still provide useful insights and contribute to a better understanding of M.E., and we also have the results from the Cyclophosphamide clinical trial to look forward to. We are very pleased that this knowledgeable, and valued, research team will continue with their work, trying to find answers to the M.E. puzzle.

“The ME Association Ramsay Research Fund had set aside around £60,000 to help support this research, or to help fund a clinical trial of Rituximab here in the UK, if such funding was required, and applied for by a reputable research or clinical trials group. No research grant applications have been received.

“It is difficult to comment further on these very basic preliminary results, and my understanding is that no further comment will be made by those involved until the study is published early next year. However, we do believe that it is correct and helpful for the patient community to be notified about the disappointing key conclusions prior to publication.

“Any decision – including if it is going to be sensible for the charity sector to be raising or spending further large sums of money on research involving the theoretical basis to this treatment (i.e. immune system dysfunction, involving the B-cell component of the body’s immune system), or further clinical trials to assess the safety and efficacy of Rituximab – will have to wait until more detailed information becomes available about the outcome of this phase III clinical trial, and the scientists involved have expressed their opinion as to whether further such research is justified.

“Based on the results from the clinical trials that have been published so far – along with the rather mixed evidence from people with M.E. who have been prescribed Rituximab outside formal clinical trials – it does appear that this type of immunotherapy could still be relevant to at least a sub-group.

“If it is agreed by experts in this area of immunotherapeutics (and we will be seeking expert advice), that we should continue to explore the role of Rituximab as a possible treatment for ME/CFS – and try to find immune system biomarkers that could help to identify the sub-group of people with M.E. who are most likely to respond to such treatment – the ME Association will continue to invite applications for research grants to the Ramsay Research Fund.

“Medical journals are less enthusiastic about publishing negative research findings or negative results from clinical trials. However, given the enormous amount of interest in Rituximab, from both people with M.E. and the medical community, I am confident that these results from Norway will be accepted for publication in due course.

“The ME Association is currently considering a number of other research applications – some of them quite large – and trustees will discuss the latest news about the Rituximab clinical trial at their Board meeting in December. A decision will then be made as to whether the £60,000 currently set aside, should remain as a ring-fenced sum for funding Rituximab research, or used for other biomedical research applications.”

Dr Charles Shepherd,
Hon Medical Adviser, ME Association.

Norwegian Cyclophosphamide trials

Is Cyclophosphamide the new Rituximab? Although the previous newsletter article shows Rituximab to be a disappointment, trials in Norway are investigating an alternative chemotherapy drug called cyclophosphamide. Results are yet to be published.

Refer to the following link for further information
https://helse-bergen.no/en/avdelinger/kreftbehandling-og-medisinsk-fysikk/research-and-development/mecfs-research

Unrest - impact so far

Source: https://www.healthrising.org/blog/2017/12/16/unrest-flies-high-dr-oz-talks-mecfs-ms-magazine-delivers/

Page 9 of our September 2017 newsletter detailed 'Unrest' the film by Jen Brea. The following is an excerpt of an article about its impact

From the beginning Jen Brea's vision has been a very large one of which Unrest was just a part. Unrest has always been more than about making a film; it's a strategic attempt to produce a worldwide shift in how people view ME/CFS. ME Action – which Jen co-founded – was simply another part of the strategy. It's served as a platform for ME Action and for Unrest. Jen's fantastically successful Ted talk – seen by over 400,000 people – was another part of a well thought out and brilliantly executed strategy to educate people and incite action, both within and outside the ME/CFS community.

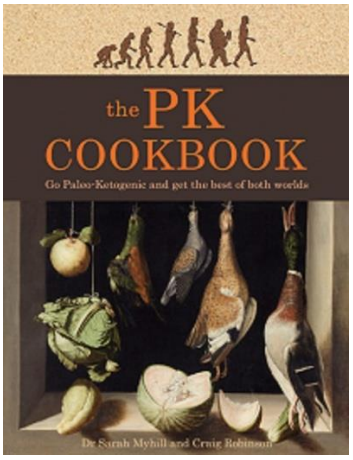
Through this expanded sense of community and connection, and by coming together to take action around the campaign, we are doing so much more than raising awareness, we are organizing – building the capacity, networks, and human infrastructure required to achieve massive, long-term change..Unrest

The strategy is working well. As of last week, Unrest had received 521 screenings in 22 countries!. The film and Jen Brea have been reviewed or interviewed 229 times!. The film's screening in the very heart of the push for CBT/GET – the British Parliament – and the advocacy campaign associated with it, undoubtedly opened eyes and sparked some re-thinking. The film prompted the CDC – the conservative CDC – to do its first ever continuing medical education event (CME) in a theatre. That event drew over 100 CDC health professionals. The fact that doctors could get continuing medical education credits by watching the film and participating in the educational event was in itself an extraordinary validation of the film.

Unrest's biggest coup, however, may be in making the latest cut for Oscar consideration. With 180 entries, the competition was undoubtedly fierce, but little Unrest, just a dream in the eye of a very sick, ex-Harvard graduate with no film experience five years ago, is now vying with 15 other documentaries for the biggest stage of all (33 million viewers). That's a pinch yourself accomplishment. Unrest now has about a thirty-three percent chance of being one of the five films considered for an Oscar. It's going against documentaries produced by the New York Times and Netflix, but its compelling story with its oh so compelling star, and its focus on gender bias in the medical field, might just give it the edge it needs.

Dr Myhil's - the PK cookbook

Source: http://drmyhill.co.uk/wiki/My_book_The_PK_Cookbook_-_Go_Paleo-ketogenic_and_get_the_best_of_both_worlds



Dr Sarah Myhill has been helping sufferers recover from debilitating chronic conditions for over 30 years with an approach that combines all the benefits of current scientific knowledge and medical testing and treatments with an expanding appreciation of the importance of nutrition and lifestyle. Her book with Craig Robinson, "Prevent and Cure Diabetes", saw her arrive at the conclusion that the diet we should all be eating is one that combines Paleo principles (eating pre-agricultural, seasonal foods) with ketogenic ones (fuel the body with fats and fibre, not with carbs or protein). That book tells us WHY; now, in this down-to-earth, highly practical cookbook, Sarah and Craig tell us HOW.

£14.99 from Amazon UK or direct from Dr Myhill's online shop: https://www.salesatdrmyhill.co.uk/book---the-pk-cookbook---one-copy---to-uk---419-p.asp

HEALTHCARE RE-INVENTED

NHW
NATURAL HEALTH WORLDWIDE

Natural Health Worldwide is a new portal offering patients an easy way to make appointments to discuss their medical situations and get opinions from a range of medical doctors, natural health professionals and experienced patients from all across the world.

EMPOWERING PATIENTS

1. Click to connect with specialist Practitioners from all around the world
2. Arrange appointments from the convenience of your own home
3. Choose Skype, Email, FaceTime or Phone

PUTTING PRACTITIONERS AND PATIENTS DIRECTLY IN TOUCH

NATURAL HEALTH WORLDWIDE.COM

4. Rate your Practitioner using NHW's unique star rating system
5. Select the best NHW star-rated Practitioner to suit your needs
6. Book medical tests via NHW's recommended labs - often a Practitioner referral is not needed.
   Phlebotomist details available

WE ARE ACCEPTING PATIENTS NOW!

"Empowering Patients"

Putting patients directly in touch with Practitioners oriented towards a natural approach via skype, phone and email. We strive to remove barriers and empower patients to make their own choices giving them quick access to opinions and tests, all at the click of a button.

- Dr Sarah Myhill, site founder

NHW
NATURAL HEALTH WORLDWIDE

The Guildford & West Surrey ME/CFS Group newsletters aim to inform members of relevant news and treatment options. Use of the treatments is done at your own risk.