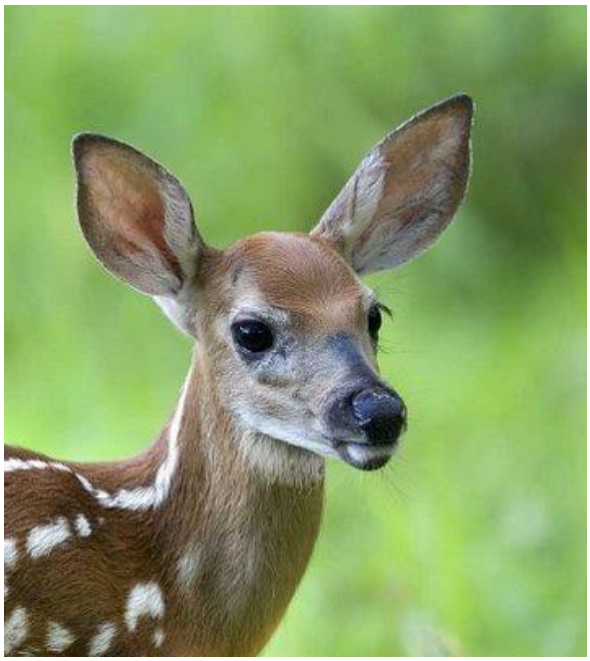


Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

Summer 2012

Future dates

The following ME meetings are open to all members and carers:

19th September (Wednesday) 4pm Home of

Annual General Meeting (AGM)
15th October (Monday) 7.30pm The Seahorse
The Street, Shalford, Guildford, GU4 8BU
Everyone is welcome at the AGM, which includes a review of the group over the last year and a future direction

7th November (Wednesday) 11am The Holiday Inn
Egerton Road, Guildford, GU2 7XZ
(Deadline date for booking for Christmas Dinner, see below)

Booking required !

Christmas Dinner
3rd December (Monday) 7.30pm The Seahorse
The Street, Shalford, Guildford, GU4 8BU
If you would like to come please contact Maggie Lilley on
Tel: before the 7th November
so that we can book seats.

16th January (Wednesday) 11am The Holiday Inn
Egerton Road, Guildford, GU2 7XZ

Booth, Myhill, McLaren-Howard comment on ME/CFS mitochondrial dysfunction paper

By Norman E. Booth, Sarah Myhill, John McLaren-Howard
Source: www.prohealth.com/me-cfs/library/showarticle.cfm?libid=17086
July 4, 2012

Dr. Norman E. Booth, Dr. Sarah Myhill and Dr. John McLaren Howard are pleased to announce the publication of a second paper concerning the link between mitochondrial dysfunction and ME/CFS. ["Mitochondrial Dysfunction and the pathophysiology of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)", published June 30, 2012]

Comment

In 2009 we published our first paper looking at mitochondrial function in ME/CFS patients. What we found is that those patients with the worst mitochondrial function had the worst levels of fatigue and vice versa. There was a very clear relationship between the two. The importance of this paper was that it gave backing to certain treatment interventions and also that it clearly established ME/CFS as a physical condition with physical causes. The mitochondrial function can be used as an objective assessment of fatigue and of course this has obvious practical implications.

Hitherto any assessment of the level of disability had to be subjective and this created great difficulties for patients in cases where their physicians disbelieved the serious nature of their symptoms. For a detailed explanation of the clinical issues please see: www.drmyhill.co.uk/wiki/CFS_-_The_Central_Cause:_Mitochondrial_Failure.

This second paper further explores the above ideas. In this second paper the size of the patient group is much larger with 138 ME/CFS patients involved. Their mitochondrial function tests were compared with 53 normal healthy controls.

The findings of the first paper were repeated and confirmed, but the analysis of this second paper was carried out slightly differently.

It was found on careful inspection of the biochemistry that there were various sub-groups of ME/CFS patients with their own characteristic biochemical pattern. In particular, one of the five parameters measured, namely translocator protein function IN, can be higher as well as lower for patients as compared with controls.

This second paper also attempts to explain what is happening at the biochemical level to result in such an abnormality.

To this end, Dr. Booth provides an alternative method of assessing mitochondrial function. He noticed that the percentage inhibition of ATP closely correlates with TL-in factor – this is probably because the biochemistry of these two measured quantities is so closely associated.

So instead of using TL-in to calculate the mitochondrial energy score, he used percentage ATP inhibited – this provided a solution to the problem of translocator protein IN being higher in some patients than in controls, a factor which in itself is abnormal.

Dr. Booth then went on to plot the relationship between mitochondrial energy score and the number of factors within the normal region to achieve an extremely close correlation.

Importantly this test identifies a clean separation between the ME/CFS cases and the healthy controls.

So this first part of the paper very much confirms the work of the first paper published in 2009 which is that those patients with the worst ME/CFS had the worst mitochondrial function and vice versa.

It must be remembered that patients attending a clinic for ME/CFS are usually the most severely fatigued – no mildly ill patients were tested. Within these limitations the ATP profile is an exclusive and sensitive test for ME/CFS. However, we cannot claim that it is specific to ME/CFS because there are many other neurological illnesses and metabolic syndrome also associated with mitochondrial dysfunction.

Dr. Booth went on to analyze sub-groups within the main group.

When mitochondria are stressed, i.e., energy demand exceeds energy delivery, in the short term they can switch into an alternative means of making ATP, of which there are 2 possibilities identified. Dr. Booth called these patients cohort 1 and cohort 2.

In cohort 1, the mitochondria switch into anaerobic metabolism with increased glycolosis in order to produce ATP.

In cohort 2, there was an alternative process to supply additional ATP. This alternative process involves the adenylate kinase reaction in which two molecules of ADP combine to make one of ATP and one of AMP. The problem with this reaction is that for every molecule of ATP generated, so is one of AMP. This is not recycled, but mainly lost in the urine. So there may be short term metabolic benefits here, but in the longer term metabolic disaster ensues as the energy molecules literally leak away. It takes time to replace these leaked molecules of ADP (leaked in the form of a 'lost' AMP molecule) and so this may explain one of the clinical features of ME/CFS, namely delayed fatigue.

A vital feature of ATP studies is that they identify the mechanisms by which mitochondria 'go slow'. Essentially they can 'go slow' for one of three common reasons:

1) Either there is substrate deficiency, i.e. lack of essential co-factors for mitochondria to work such as Co-enzyme Q10, magnesium, vitamin B3, or acetyl-L-carnitine,

2) Or secondly, because mitochondria are blocked by toxins. Typically the blockage can be of oxidative phosphorylation and/or translocator protein function. Dr. John McLaren Howard has developed several further tests to look at the nature of these blockages. These tests include microrespirometry studies, translocator protein function studies, intracellular calcium studies and so on.

3) The third possible mechanism for mitochondria malfunctioning has to do with membrane function. The membranes of mitochondria need to be of just the right consistency in order to hold the bundle of enzymes in the correct 3D configuration to allow efficient movement of substrate from one enzyme complex to another. To this end, again Dr. John McLaren Howard has developed cardiolipin studies which look in more detail at mitochondrial membrane structure and function.

Many of the above tests have been available in research laboratories, some John has developed through his own brilliance and initiative. What is so wonderful is how he has given these cutting edge research tests a clinical application.

This is extremely helpful for patients and clinicians because we can see exactly why mitochondria are 'going slow' and thereby correct deficiencies using both nutritional supplements, correct gut function, as well as being able to tailor detoxification regimes to individual patients.

This second paper also goes on to look at cell free DNA in ME/CFS patients.

Cell free DNA is a measure of DNA in the bloodstream that is not bound up within cell membranes. It can only, therefore, come from damaged cells and therefore is a measure of cell damage within the body.

What we found is a strong negative correlation with mitochondrial energy scores, ATP levels and the rate of oxidative phosphorylation. What this means is that those patients with mitochondria that perform extremely poorly have the highest level of cell damage and vice versa. This makes perfect biochemical sense – if mitochondria 'go slow' one can expect there to be the production of free radicals which have the potential to damage tissues.

Therefore addressing these issues of poor antioxidant status is an essential part of the package of treatment for ME/CFS patients.

These abnormal results clearly show that the effect on mitochondria is a systemic effect, not just confined to the neutrophils that are being tested. Very often we see levels of cell free DNA of a similar magnitude to those in patients who are experiencing a serious illness such as cancer, stroke, autoimmunity, or severe viral infection. Again this underpins the fact that ME/CFS is a physical condition with clear indications of marked cell damage.

This puts ME/CFS firmly in the realm of major organic pathology.

Implications for the treatment of ME/CFS

These bio-medical tests have been extremely helpful in the diagnosis and management of ME/CFS patients. This is because they clearly identify the biochemical lesions that underpin the cause of this illness. Furthermore, identification of these lesions has clear implications for management using the standard methods of nutritional and environmental medicine.

We are currently preparing a third paper which looks at the efficacy of these interventions in patients by measuring mitochondrial function tests before and after such interventions and correlating these with the clinical picture.

For further information as to what these interventions are please see www.drmyhill.co.uk/wiki/CFS_-_CFS_Book_published_by_Dr_Sarah_Myhill, which is available on line without charge.

It bears repeating that this paper would not have been remotely possible without the brilliance of Dr. John McLaren Howard at Acumen Laboratory, who has developed these wonderful tests for looking at mitochondrial function, together with the analytical mind of Dr. Norman Booth, who has analyzed the data in detail to identify the biochemical metabolic pathways involved.

A layperson's notes on the ME/CFS mitochondrial dysfunction paper (the one discussed in the article above)

Source: www.prohealth.com/library/showarticle.cfm?libid=17134

Our ME/CFS group often sources research articles from a website called 'Prohealth'. One of Prohealth's readers made notes about the mitochondria dysfunction paper that was discussed on pages 2 to 4 earlier. These notes may help some to better understand the paper.

I am a physicist, not a medical researcher. I had to teach myself the basics of biochemistry to treat my ME/CFS since the doctors were clueless. I read the full paper trying to glean the essential things, and here is what I came up with, in English we can understand.

The fuel for our cells is ATP, or adenosine TRI-phosphate. The ATP is made of ADP, which is DI-phosphate. The mitochondria take ADP and make ATP for our cells to use. The mechanism that does this is the Krebs Cycle, which starts with pyruvic acid.

About 70%-90% of the ME/CFS group were very low in ATP before the study.

Intracellar Magnesium is also low in 90% of the ME/CFS patients. Magnesium is one of the natural resources needed for the Krebs Cycle.

Blood samples from the patients were taken for this study. The samples were checked for mitochondrial function. Then the samples were mixed with a substance (azide) that blocks ATP production by the mitochondria. Then the azide was washed off, and the cells were allowed to recover. The recovery time was recorded and compared to the severity of ME/CFS symptoms.

They found that ME/CFS blood does not recover as well as the normal blood. But, the ME/CFS blood is not as affected by the blocking of ATP as the normal blood. The conclusion is that ME/CFS patients already are using an alternative ATP cycle to compensate for the dysfunctional Krebs Cycle in their bodies, so they don't make enough ATP overall.

The alternative ATP cycles are much less efficient than the primary one, and they create more waste products that make their bodies more acidic and create more damage in their tissues. So, we get tired because we don't make enough ATP and we make too many waste products. And the negative effects can be delayed, so that we feel worse the next day.

Waste products include lactate (lactic acid), which is transported to the liver to be recycled into glucose. But, if the liver isn't functioning properly (such as the mitochondria in the liver are dysfunctional), then the lactate isn't processed fast enough, and it accumulates.

Two ways that ATP is blocked are: (a) the sites on the mitochondria are blocked by something so the ADP can't get in, and (b) there aren't enough natural resources for the Krebs Cycle.

The study found that ME/CFS patients also have a problem with a Krebs Cycle key player called translocator protein TL, which has not been studied before but is important for getting the ADP in and ATP out of the mitochondria.

Natural resources that are needed for the full ATP cycle: pyruvic acid, ADP, CoQ10, reduced niacinamide (NADH), Magnesium (Mg), inorganic phosphate.

ATP is also essential as a neurotransmitter for our brains and neurons, which might explain why we have such terrible brain fog. We don't make enough for all the requirements.

Possible solutions:

Supplement with Magnesium in a bioavailable form, such as Magnesium Citrate or Magnesium Threonate.

Supplement with CoQ10, niacinamide (Vit B3), pyruvate

Do not supplement with inorganic phosphate, since high levels are shown to cause serious health problems

Treatment of ME/CFS and Fibromyalgia with D-Ribose: An open-label, multicenter study

By Jacob Teitelbaum, Janelle Jandrain, Ryan McGrew
Source: http://www.prohealth.com/me-cfs/library/showarticle.cfm?libid=17081
July 4, 2012

Note this study did not involve 'blinding' and was not placebo controlled - patients all were supplemented with D-ribose. At least one blinded, controlled trial is in the works, led by Leslie J Crofford, MD, at the University of Kentucky.

Objectives
Chronic Fatigue Syndrome and Fibromyalgia (CFS/FMS) are debilitating syndromes affecting about 2%-4% of the population.

Although they are heterogeneous conditions associated with many triggers, they appear to have the common pathology of being associated with impaired energy metabolism.

As D-ribose has been shown to increase cellular energy synthesis, and was shown to significantly improve clinical outcomes in CFS/FMS in an earlier study, we hypothesized that giving D-ribose would improve function in CFS/FMS patients.

Design, Location, and Subjects
An open-label, unblinded study in which 53 US clinics enrolled 257 patients who had been given a diagnosis of CFS/FMS by a health practitioner.

Interventions
All subjects were given D-ribose (Corvalen™), a naturally occurring pentose carbohydrate, 5-g twice a day for 3 weeks.

Outcome measures
All patients were assessed at baseline (1 week before treatment), and after 1,2, & 3 weeks using a Visual Analog Scale (1-7 points) rating energy, sleep, cognitive function, pain and overall well being.

Results
203 patients completed the 3 week treatment trial. D-ribose treatment led to both statistically ($p<.0001$) and clinically highly important average improvements in all categories:

61.3% increase in energy

37% increase in overall well being

29.3% improvement in sleep

30% improvement in mental clarity

15.6% decrease in pain.

Improvement began in the first week of treatment, and continued to increase at the end of the 3 weeks of treatment. The D-ribose was well tolerated.

Conclusions
In this multi-centre study, D-ribose resulted in markedly improved energy levels, sleep, mental clarity, pain relief, and well-being in patients suffering from fibromyalgia and chronic fatigue syndrome.

Dr Myhill on D-ribose

Source: http://drmyhill.co.uk/wiki/D-ribose

The pathological defect in patients with chronic fatigue syndrome is slow recycling of ATP. Normally there is enough ATP in a heart cell to last about ten beats - this means that roughly speaking ATP needs to be re-cycled every ten seconds. Top athletes like Steve Redgrave probably recycle ATP every five seconds, but patients with fatigues may only be able to recycle ATP every minute. Therefore I can do in ten seconds what Steve Redgrave can do in five seconds, but it might take one of my fatigue syndrome patients a minute to achieve the same!

ATP in releasing energy is converted to ADP (2-phosphates) which is recycled back through mitochondria to ATP (3-phosphates). However, if the system is really pushed then the body can extract energy from ADP by converting it into AMP (1-phosphate). The problem is that AMP is very slowly recycled, if at all, and most is lost from the cell. This means that the body has to make brand new ATP. This it does from D-Ribose and this it can do very quickly. The trouble is the body making D-Ribose. Normally this is made from glucose. However if the cell is lacking in energy then any glucose lying around can be converted to lactic acid to generate energy. The problem here is twofold - first of all the lactic acid causes pain. Secondly any glucose that is swilling around is not available to make D-ribose.

Even when glucose supply is plentiful, production of D-ribose in the cell by the glucose pentose shunt is very slow.

D-ribose as a nutritional supplement is therefore useful because it is immediately available for the generation of new ATP

Because D-ribose is a simple sugar, it is extremely well absorbed. The clinical experience of cardiologists using D-ribose to treat heart failure due to mitochondrial failure is that it is very effective and free from side effects. The dose depends on the severity of the illness, but the clinical experience is that sufferers should be started on high doses and then it can be adjusted to a maintenance dose. Therefore I recommend that my CFS patients use 5 grams (1 scoop) three times a day. Effects should be seen within a few days. Whilst levels of energy improve and continue to improve then I recommend staying on 15 grams daily. At the point at which it levels off, experiment with lower maintenance doses. However, should the sufferer overdo things on a particular day then it is as well to take extra D-ribose in order to rescue the situation.
Two problems I sometimes see:

1. The fermenting gut. If there are bacteria or yeast in the upper gut then D-ribose may be fermented to produce alcohol and gas. In this event I suggest reducing the daily dose to 5 grams, holding it in the mouth as long as possible - some will be absorbed here. Space doses throughout the day.
2. Corn sensitivity. D-ribose is derived from corn and some CFSs who are corn sensitive will react allergically to it. I do not know of a corn free preparation of D-ribose.

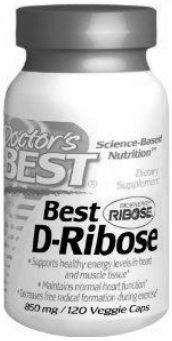
D-ribose is going to work best when the other aspects of mitochondrial metabolism are addressed, namely Co-enzyme Q10, L-carnitine, magnesium, niacinamide, detoxificiation and antioxidant regimes where appropriate.

Anything which can be done to prevent damage to mitochondria will also be extremely helpful. There are many ways in which mitochondria can be damaged such as viral infection, pesticides, heavy metals, hormone imbalances, allergies, low blood sugar or high blood sugar, micronutrient deficiencies, lack of sleep, etc. D-ribose is, therefore, an adjunct to my standard work up for treating chronic fatigue syndrome. Clinically I expect D-ribose to improve the symptom of delayed fatigue in sufferers as well as improve stamina.

D-Ribose examples

Having used D-ribose myself I would recommend that it is always taken with food. I've spoken to a few ME people who have used D-ribose who have, like me, experienced a sugar low experience sometime after taking D-ribose on it's own without food. By a sugar low experience I mean having spontaneous craving for food and being shaky and weak. Diabetics or those with blood sugar issues should avoid D-ribose. By Neil Perrett, Newsletter Editor.

Below are some buying examples of D-ribose.



Doctor's Best Best D-ribose Featuring Bioenergy Ribose (850mg), Vegetable Capsule, 120-Count

Amazon uk £19.76

Precision Engineered - D-Ribose (850mg) 120-Count

Holland and barrett £19.99

President Obama asks NIH & DHHS to elevate the priority of CFS

Source: www.prohealth.com/library/showarticle.cfm?libid=17163

In an unprecedented step, President Obama has asked the National Institutes of Health and the Department of Health and Human Services to elevate Chronic Fatigue Syndrome in priority, assigning his Deputy Chief of Staff to follow their efforts.

When President Obama promised Courtney Miller to "see if they could do more" for CFS research at a Reno Town Hall meeting last year, he was the first U.S. President to say the words Chronic Fatigue Syndrome. Now he has lived up to his promise, becoming the first President ever to ask the nation's health agencies to elevate the priority of CFS!

Thank you, President Obama!

In a July 25, 2012 letter addressed to Mrs. Miller, President Obama describes a report given him by Dr. Francis Collins, Director of the National Institutes of Health. The important part of the letter is the last paragraph which speaks to the future:

He has asked his Deputy Chief of Staff for Policy, Nancy-Ann DeParle, to "stay in touch with Dr. Collins at NIH and Dr. Koh at HHS about my interest in their efforts on CFS."

Mrs. Miller's communications with the White House confirm that the President's wish to have CFS elevated in priority in the Department of Health and NIH has been conveyed at the highest level.

"President Obama kept his promise in the most important way he can for CFS/ME patients," said Courtney Miller, "by leading a stronger federal commitment to CFS/ME research and a better quality of life for patients. CFS is a health crisis for more than 1 million Americans, and President Obama has thrown in on our side!"

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.