Wetenschap voor Patiënten
(Science to patients)

On Thursday 10 April 2014 dr. Charles Shepherd answered questions in a chatwing-session. These are the Q&A of this session.

Q: Can you tell me exactly what the problems are with the mitochondria?
A: The mitochondria, which are the batteries in cells that help to produce chemical energy in the form known as ATP are not doing so in an efficient manner. It is possible that the initial viral infection, or other immune system stressor, has affected the way they work.

Q: In the overall mitochondria or just those of infected tissue?
A: Mitochondria are present in almost all tissues in the body - they are not just producing energy in muscle cells. Liver has a lot as well - but we have concentrated research efforts in relation to muscle mitochondria.

Q: Are the problems with mitochondria measurable/ provable?
A: Yes, you can look for evidence by taking a sample (biopsy) of muscle and looking for structural changes under the microscope. Professor Mina Behan has done this - including using some of my own muscle!
You can also look at changes in the way chemical reactions are taking place, including the excessive production of lactic acid, using what is called magnetic resonance spectroscopy (MRS). This has also been done on my own muscle - with results published in The Lancet!

Q: Will there be a test available in the near future to show one has problems with the mitochondria?
A: As I said earlier there are tests available - electron microscopy and MRS - that can show abnormalities in the mitochondria, or biochemical changes, that are consistent with mitochondrial dysfunction.

Q: I understand the tests are there for research purposes. But we need them to be on the common laboratory list of our GP's so they can ask for it.
A: I'm afraid these are research based investigations at present. Until the situation becomes more clear, and mitochondrial dysfunction is accepted by the wider medical profession, these tests are not going to form part of routine cynical assessment/diagnosis of ME/CFS.

Q: Is there a linear connection between the severity of the problems with the mitochondria and the severity of the fatigue, pain and other complaints?
A: The research that has been published so far has only involved small numbers of patients, and tended to avoid those with moderate or severe ME/CFS. So we don't have any clear evidence of a link between severity of findings and severity of symptoms.

Q: Is there a link between the increasing of the variable personal boundaries, the fatigue attacks, the muscle fatigue and the shortness of breath, dizziness, headache (orthostatic intolerance)?

A: Yes, all these problems are probably interlinked. I went to a really good physicians workshop on OI (causes, investigation, self-management, drug management) given by Professor Peter Rowe at the IACFS conference in San Francisco. I am currently writing this up for a website report.

Q: How come that the fatigue/exhaustion sometimes takes place a day or 2 days later? (I find this most unfair of ME/CFS, one moment you're busy, and a few hours later or the next day it turns out to have been too much again anyway).
A: The reasons why people have post-exertional malaise and symptom exacerbation are complex and were discussed in some detail in San Francisco. They probably relate to a combination of metabolic/chemical, immune system and possibly blood flow changes to skeletal muscle.

Q: For very severe cases, pacing is nearly impossible because they exceed their limitations by doing almost nothing. I'm almost always in PEM and I get worse and worse. Do you have any suggestions how severe ME-patients can try to stop deterioration? I can understand if you don't have answers.
A: I'm sorry but it's not really possible to go into how pacing should be applied to people with severe ME/CFS in just one line…The bottom line is that any sort of physical and mental activity has to be very low grade (keg passive exercises with a physic) and increased at a very gradual rate.

Q: But why is PEM sometimes 2 houres and sometimes 2 days later?
A: The simple answer is that we just don't know. The research that Professor VanNess et al has been doing (the double dose exercise test measuring Vo2 max) is shedding some light on what may be happening. The MEA is funding Prof Jo Nijs to carry out research into the cause of PEM.

Q: Why do you not mention HPV vaccination as a trigger for ME/CFS while you're mentioning many other vaccinations? Don't you known any cases that HPV is the trigger? Or are there other reasons or don't you acknowledge that HPV vaccination may be a trigger?
A: I have covered HPV in more detail on the YouTube video page for the mitochondria video (n39). I have a number of cases where HPV appears to have triggered ME/CFS but the MHRA here in the UK came to the conclusion that there is no link with this vaccine. I am sceptical about this conclusion.

Q: What do you think of oxygen therapy? Can it help with muscle pain or the problems with acid in the muscle?
A: Although there is evidence of hypoperfusion (low blood flow) in certain parts of the brain in ME/CFS I'm not convinced that oxygen therapy is of any value. There can also be dangerus in giving oxygen to people who may not be breathing in a normal manner. Evidence was presented in San Francisco that some people with ME/CFS have very shallow and low oxygen intake breathing because they do so via the abdomen instead of the diaphragm at the base of the chest. You can check your breathing by lying flat on the floor and observing whether it is diaphragmatic or abdominal - shallow or deep. Then try breathing in deeply for three seconds through the nose using the chest and diaphragm - the correct way to do so.

Q: How do you explain that the Japanese all of a sudden find evidence of inflammation, have pet-scans gotten better? And how would for instance scans of peeps with mild flu look like?
A: The Japanese are not the only research group to demonstrate what is called neuroinflammation. My post-mortem group here in the UK have evidence of what is called dorsal root ganglionitis in ME/CFS in tissue from people who have died. This finding has also been published.

The results we have published relate to 4 or 5 cases - would need to check with the paper for precise numbers. I have been discussing this post mortem research and the Japan research research on MEA Facebook if you want to follow it up. An abstract from our paper on DRG is there as well.

Q: Have you heard of stealth viruses?
A: Yes, stealth viruses were implicated in ME/CFS many years ago - but the virologists eventually came to the conclusion that they were not relevant.

Q: Do you think these viruses are relevant?
A: A wide variety of viral infections are capable of triggering ME/CFS and there is some evidence (from Dr Chia in California in particular in relation to enteroviral infection) that there could be persistent viral infection in some cases - as enteroviral infection persists in stomach tissue.
But I'm not convinced there is any link with stealth virus infection...

Q: Is ampligen dangerous?
A: Ampligen has side-effects, some of them can be unpleasant, but I would not say it was a dangerous drug. This is based on my reading. Ampligen is not available/licensed for use in the UK and I do not have any personal experience involving its use.

Q: Are you aware of the study of the University of Nijmegen where they are going to give the immunosupressant Anakinra to ME/cfs patients? What do you think of this?
A: I wasn't aware of the clinical trial you refer to but I do want to see trials involving drugs that can dampen down the immune system - because there is growing evidence of what we call immune system activation, and cytokine production, in ME.
One of the drugs that would fit into this category is Etanercept - which is used to dampen down activity in autoimmune disorders. I will need to translate the drug you refer to - it may be very similar.

Q: But wouldn't it be dangerous if people are not screened for infectious diseases like lyme? I hope they'll have mirtazapine on their hands to treat PML which might occur.
A: Yes, you have to be very careful about the sort of ME/CFS patients you use in clinical trials that involve drugs that can produce serious, or very serious side effects. The same logic applies to Rituximab - which can (rarely) cause a fatal allergic adverse reaction.

Q: Dr Shepherd, I'm deeply concerned about MEcfs discussions in the UK. How can the research collaborative be effective when members hold diametrically opposed views on what makes good science? Eg, PACE.
A: As you know I am a member of the UK ME/CFS Research Collaborative. I take the view that there is a case for having a forum where all sides of the ME/CFS debate can meet and discuss where we agree and disagree. We cannot go on with a situation where everyone sits in their own separate tents.

Q: I found the Stanford & IACFS/ME conferences very inspiring; How long do you think it will be before we see a break-through in #ME/cfs research?
A: Yes, there was a lot of good clinical and research information presented at San Fran - some of which has real practical implications for patient management. I was so inspired that instead of rushing out a report (7,600 words!) I've been spending the last week or so getting it right. I would not want to use the words breakthrough or cure but I think we are heading towards some significant steps in understanding the underlying causes of this illness. The work on neuroinflammation was particularly interesting and I am now discussing how we might try and replicate these PET scans here in the UK - a major hurdle is that these scans

are very costly to do. And if we are dealing with a disease involving low level inflammation then we really need a trial of drugs that can dampen down this over-activity - in the same way that they are used to dampen down disease activity in rheumatoid arthritis etc.

Q: I'd love to read your conference report; I hope it'll be on the MEA website.
A: it is being prepared for the MEA magazine but I hope we will be placing it on the website as well for the benefit of non-members.

Q: Lately a MMA test showed a huge shortage of B12. Is there any link to ME?
A: We discussed B12 in San Francisco. There is no firm evidence of vitamin B12 deficiency in ME/CFS and no firm evidence of benefit from B12 injections. However, there are plenty of anecdotal/patient reports of people gaining benefit and one report demonstrating lowered levels in spinal fluid.