

**Dr Sarah Myhill MB BS, Upper Weston, Llangunllo, Knighton, Powys, LD7 1SL**

Tel: 01547550331 Fax: 01547550339 E-mail: [office@doctormyhill.co.uk](mailto:office@doctormyhill.co.uk) Website: [www.doctormyhill.co.uk](http://www.doctormyhill.co.uk)

## **NOTES TO EDITORS**

The scientific paper entitled '*Chronic Fatigue Syndrome and Mitochondrial Dysfunction*' is available here <http://www.ijcem.com/files/IJCEM812001.pdf>, Int J Clin Exp Med (2009) 2, 1-16

**For more information about mitochondria and their clinical reference, see extract from the online book, free for anyone to download, written by Dr Sarah Myhill [www.drmyhill.co.uk](http://www.drmyhill.co.uk)**

**Mitochondria are the engine of the car – they supply energy to every cell in the body. When mitochondria goes slow, everything goes slow!**

Dr Sarah Myhill writes:

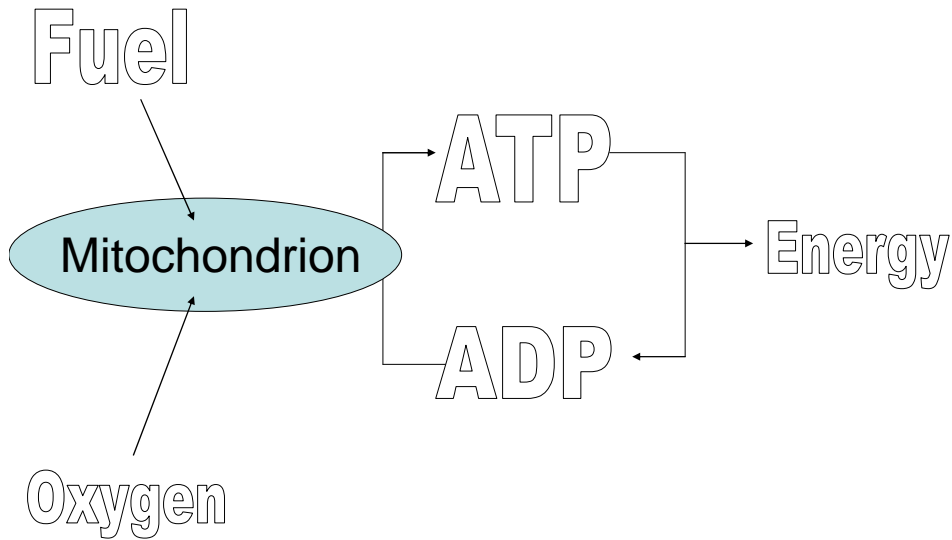
*I think this is one of the most important ideas I have come up with in terms of my understanding of CFS and what to do in order to recover! So please read this very carefully and several times over because for many sufferers it contains the keys to unlock their illness!*

We are made up of lots of different cells – heart, blood, muscle nerve cells etc. All these cells are different because they all have a different job of work to do. To do this job of work requires energy. But the way in which energy is supplied is the same for every cell in the body. Indeed all animals share this same system. The mitochondria in my dog, my cat and my horse are exactly the same as mine. Mitochondria are a common biological unit across the animal kingdom. Energy is supplied to cells by mitochondria which I think of as little engines which power every cell in the body.

Chronic fatigue syndrome is the symptom caused by mitochondrial failure. The job of mitochondria is to supply energy in the form of ATP (adenosine triphosphate). This is the universal currency of energy. It can be used for all sorts of biochemical jobs from muscle contraction to hormone production. When mitochondria fail, this results in poor supply of ATP, so cells go slow because they do not have the energy supply to function at a normal speed. This means that all bodily functions go slow.

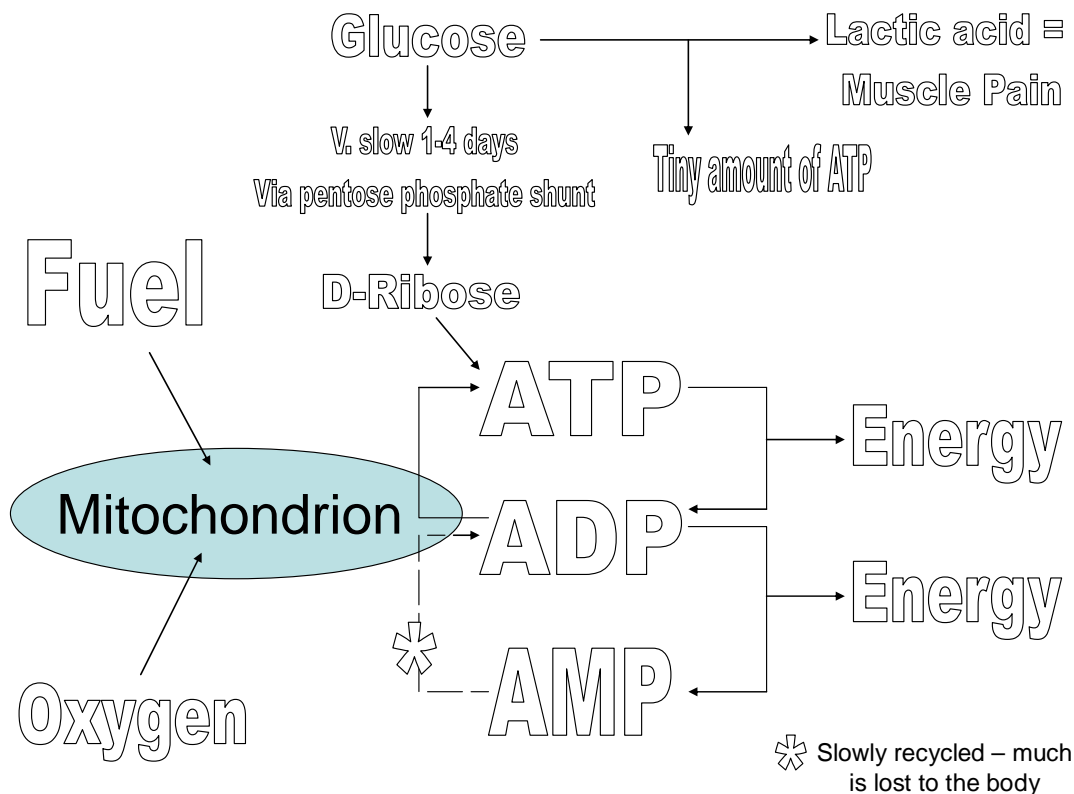
Chronic fatigue syndrome therefore is a symptom of mitochondrial failure and every cell in the body can be affected.

The following cycle illustrates what happens inside every cell:



ATP (3 phosphates) is converted to ADP (2 phosphates) with the release of energy for work. ADP passes into the mitochondria where ATP is remade by oxidative phosphorylation (ie a phosphate group is stuck on). ATP recycles approximately every 10 seconds in a normal person – if this goes slow, then the cell goes slow and so the person goes slow and clinically has poor stamina ie CFS.

Problems arise when the system is stressed. If the CFS sufferer asks for energy faster than he can supply it, (and actually most CFS sufferers are doing this most of the time!) ATP is converted to ADP faster than it can be recycled. This means there is a build up of ADP. Some ADP is inevitably shunted into adenosine monophosphate (AMP -1 phosphate). But this creates a real problem, indeed a metabolic disaster, because AMP, largely speaking, cannot be recycled and is lost in urine.



Indeed this is the biological basis of poor stamina. One can only go at the rate at which mitochondria can produce ATP. If mitochondria go slow, stamina is poor.

If ATP levels drop as a result of leakage of AMP, the body then has to make brand new ATP. ATP can be made very quickly from a sugar D-ribose, but D-ribose is only slowly made from glucose (via the pentose phosphate shunt for those clever biochemists out there!). This takes anything from one to four days. So this is the biological basis for delayed fatigue.

However there is another problem. If the body is very short of ATP, it can make a very small amount of ATP directly from glucose by converting it into lactic acid. This is exactly what many CFS sufferers do and indeed we know that CFS sufferers readily switch into anaerobic metabolism. However this results in two serious problems – lactic acid quickly builds up especially in muscles to cause pain, heaviness, aching and soreness (“lactic acid burn”), secondly no glucose is available in order to make D-ribose! So new ATP cannot be easily made when you are really run down. Recovery takes days!

Worse than that, lactic acid has to be converted back to pyruvate – but this requires a lot of energy (ATP) to do this. So lactic acid hangs about for a long time causing pain.

The biological basis of treatment is therefore explained:

1. PACE – do not use up energy faster than your mitos can supply it.

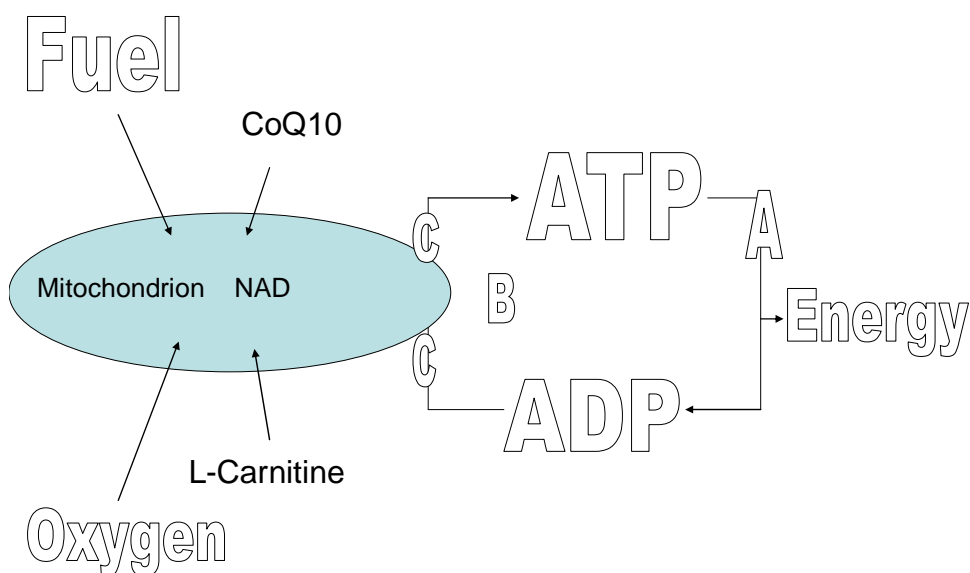
2. FEED THE MITOCHONDRIA - supply the raw material necessary for the mitochondria to heal themselves and work efficiently. This means feeding the mitos correctly so they can heal and repair.
3. Address the underlying causes as to why mitochondria have been damaged. This must also be put in place to prevent ongoing damage to mitos. In order of importance this involves:
  - Pacing activities to avoid undue stress to mitos
  - Getting excellent sleep so mitos can repair
  - Excellent nutrition with respect to:
    - taking a good range of micronutrient supplements
    - stabilising blood sugar levels
    - identifying allergies to foods
  - Detoxifying to unload heavy metals, pesticides, drugs, social poisons (alcohol, tobacco etc) and volatile organic compounds, all of which poison mitos.
  - Optimising gut fermentation – HYPOCHLORHYDRIA and PANCREATIC FUNCTION, GUT DYSBIOSIS
  - Addressing the common problem of hyperventilation
4. Address the secondary damage partly caused by mitochondrial failure such as immune disturbances resulting in allergies and autoimmunity, poor digestive function, hormone gland failure, slow liver detoxification.

**And now for a bit of good news!** You will have read (and will read again) that AMP cannot be recycled. Actually, AMP can be recycled, but it happens very slowly. For practical purposes for patients who are very fatigued, this recycling is so slow that it is clinically insignificant. Interestingly, the enzyme which facilitates this recycling ("cyclic AMP") is activated by caffeine! So the perfect pick-me-up for CFS sufferers could be a real black organic coffee with a teaspoon of D-ribose! Not too much or one can run into calcium problems. See STIFF MUSCLES.

### **The Perfect Test for Chronic Fatigue Syndrome**

The central problem of chronic fatigue syndrome is mitochondrial failure resulting in poor production of ATP. ATP is the currency of energy in the body and if the production of this is impaired then all cellular processes will go slow. It is not good enough to measure absolute levels of ATP in cells since this will simply reflect how well rested the sufferer is. The perfect test is to measure the rate at which ATP is recycled in cells and this test has now been developed by the brilliant medical biochemist Dr John McLaren Howard. He calls it "ATP profiles". It is a test of mitochondrial function.

Not only does this test measure the rate at which ATP is made, it also looks at where the problem lies. Production of ATP is highly dependent on magnesium status and the first part of the test studies this aspect (A).



The second aspect of the test (B) measures the efficiency with which ATP is made from ADP. If this is abnormal then this could be as a result of magnesium deficiency, of low levels of Co-enzyme Q10, low levels of vitamin B3 (NAD) or of acetyl L-carnitine.

The third possibility (C) is that the protein which transports ATP and ADP across mitochondrial membrane is impaired and this is also measured.

The joy of the ATP profiles test is that we now have an objective test of chronic fatigue syndrome which clearly shows this illness has a physical basis. This test clearly shows that cognitive behaviour therapy, graded exercise and anti-depressants are irrelevant in addressing the root cause of this illness.

To get the full picture I recommend combining this test with measuring levels anti-oxidants such as Co-enzyme Q10, superoxide dismutase (SODase), and glutathione peroxidase together with NAD (an element in the process of energy production). See ANTI-OXIDANTS.

Cell free DNA is very useful because it measures severity of the illness. When cells are damaged and die, they release their contents into the blood stream – cell free DNA measures the extent of this damage. The levels which come back are similar to those from patients recovering from major infections, trauma, surgery or chemotherapy – so this test puts CFS firmly in the realms of major organic pathology. SODase is an important antioxidant which mops up the free radicals produced in all the inefficient chemical reactions in the cells. Dr McLaren Howard also looks at the genes which code for the different types of SODase! It is common to find blockage or polymorphisms typical of toxic stress. See INFLAMMATION.

In fact, all of these blood tests have now been combined as a MITOCHONDRIAL FUNCTION PROFILE (which combines the “ATP profiles” and tests of antioxidant levels) and can be ordered from my practice – see details below.

The two other important co-factors in the production of energy in cells are L-carnitine and D-ribose. The latter is used up so quickly by cells that measuring levels is unhelpful, but low levels of ATP imply low levels of D-ribose. Acetyl L Carnitine is supplemented as routine.

Therefore, the cost of the Mitochondrial Function Profile, which will now include the mitochondrial function studies (ATP profiles), levels of Co-enzyme Q10, glutathione peroxidase, zinc copper SODase, manganese SODase and extracellular SODase together with NAD levels and cell-free DNA is £195, plus £50.00 for the letter of interpretation to the GP.

John McLaren Howard now has specialist equipment to refine these tests further, particularly in respect of oxidative phosphorylation. See PRACTICAL DETAILS should you wish to order this test.

### **Severe CFS is also low cardiac output secondary to mitochondrial malfunction**

Two papers have come to my notice recently, which make great sense of both my clinical observations and also the idea that CFS is a symptom of mitochondrial failure. The two symptoms I am looking for in CFS to make the diagnosis is firstly very poor stamina and secondly delayed fatigue. I think I can now explain these in terms of what is going on inside cells and the effects on major organs of the body. More importantly, there are major implications for a test for CFS and of course management and recovery.

If mitochondria (the little batteries found inside every cell in the body) do not work properly, then the energy supply to every cell in the body will be impaired. This includes the heart. Many of the symptoms of CFS could be explained by low cardiac output because the heart muscle cannot work properly. Cardiologists and other doctors are used to dealing with low cardiac output due to poor blood supply to the heart itself. In CFS the low cardiac output is caused by poor muscle function and therefore strictly speaking is a cardiomyopathy. This means the function of the heart will be very abnormal, but traditional tests of heart failure, such as ECG, ECHOs, angiograms etc, will be normal.

Firstly MicroRespiratory studies which look at oxidative phosphorylation (conversion to ADP to ATP) in more detail. Secondly translocator protein studies which look in more detail at how well ATP and ADP move across mitochondrial membrane. The point is that the blood supply to the heart is fine (fuel and oxygen adequate) but the mitochondria cannot convert this to ATP which is the currency of energy for muscle contraction.

Research by Dr Arnold Peckerman [www.cfids-cab.org/cfs-inform/Coicfs/peckerman.etal.03.pdf](http://www.cfids-cab.org/cfs-inform/Coicfs/peckerman.etal.03.pdf) shows that cardiac output in CFS patients is impaired. Furthermore the level of impairment correlates very closely to the level of disability in patients. Dr Peckerman was asked by the US National Institutes of Health to develop a test for CFS in order to help them to judge the level of disability in patients claiming Social Security benefits. Peckerman is a cardiologist and on the basis that CFS patients suffer low blood pressure, low blood volume and perfusion defects, he surmised CFS patients were in a low cardiac output state. To test this he came up with Q scores.

“Q” stands for cardiac output in litres per minute and this can be measured using a totally non-invasive method called Impedence Cardiography. This allows one to accurately

measure cardiac output by measuring the electrical impedance across the chest wall. The greater the blood flow the less the impedance. This can be adjusted according to chest and body size to produce a reliable measurement (this is done using a standard algorithm). It is important to do this test when supine and again in the upright position. This is because cardiac output in healthy people will vary from 7 litres per min when lying down to 5 litres per min when standing. In healthy people this drop is not enough to affect function. But in CFS sufferers the drop may be from 5 litres lying down to 3.5 litres standing up. At this level the sufferer has a cardiac output which causes borderline organ failure.

This explains why CFS patients feel much better lying down. They have acceptable cardiac output lying down, but standing up they are in borderline heart and organ failure. CFS is therefore the symptom which prevents the patient developing complete heart failure. Actually, everyone feels more rested when they are sitting down with their feet up! The subconscious has worked out that the heart has to work less hard when you are sitting down with your feet up – so we do so because we feel more comfortable!

### **Low cardiac output explains the symptoms of CFS**

The job of the heart is to maintain blood pressure. If the blood pressure falls, organs start to fail. If the heart is working inadequately as a pump then the only way blood pressure can be sustained is by shutting down blood supply to organs. Organs are shut down in terms of priority, i.e. the skin first, then muscles, followed by liver, gut, brain and finally the heart, lung and kidney. As these organ systems shut down, this creates further problems for the body in terms of toxic overload, susceptibility to viruses which damage mitochondria further, thus exacerbating all the problems of the CFS sufferer.

#### **1. Effects on the Skin**

If you shut down the blood supply to the skin, this has two main effects. The first is that the skin is responsible for controlling the temperature of the body. This means that CFS patients become intolerant of heat. If the body gets too hot then it cannot lose heat through the skin (because it has no blood supply) and the core temperature increases. The only way the body can compensate for this is by switching off the thyroid gland (which is responsible for the level of metabolic activity in the body and hence heat generation) and so one could get a compensatory under active thyroid. This alone worsens the problems of fatigue.

The second problem is that if the micro-circulation in the skin is shut down, then the body cannot sweat. This is a major way through which toxins, particularly heavy metals, pesticides and volatile organic compounds are excreted. Therefore the CFS sufferer's body is much better at accumulating toxins, which of course further damage mitochondria.

#### **2. Symptoms in Muscles**

If the blood supply to muscles is impaired, then muscles quickly run out of oxygen when one starts to exercise. With no oxygen in the muscles the cells switch over to anaerobic metabolism, which produces lactic acid and it is this that makes muscles ache and fatigue so much.

As well as the above problem, muscles in the CFS patient have very poor stamina because the mitochondria which supply them with energy are malfunctioning.

When we do translocator protein function tests it is common to find lactic acid stuck onto mitochondrial membranes – this illustrates one of the many vicious cycles in CFS – if TL protein is blocked by lactic acid, mitochondria work less efficiently and therefore one is more likely to switch into anaerobic metabolism and produce more lactic acid!

### **3. Symptoms in the Liver and Gut**

Poor blood supply to the gut results in inefficient digestion, poor production of digestive juices and leaky gut syndrome. Leaky gut syndrome causes many other problems such as hypochlorhydria, allergies, autoimmunity, malabsorption, etc., which further compound the problems of CFS. See MALABSORPTION.

If liver circulation is inadequate, this will result in poor detoxification, not just of heavy metals, pesticides and volatile organic compounds, but also toxins produced as a result of fermentation in the gut again further poisoning the mitochondria. See DETOXIFICATION.

### **4. Effects on the Brain**

Last October I attended a conference sponsored by the late Dr John Richardson. A Canadian physician Dr Byron Hyde showed us some functional scans of the brains of CFS patients. If I had not known the diagnosis, I would have diagnosed strokes. This is because the blood supply to some area of the brain was so impaired. The default is temporary and with rest, blood supply recovers. However, this explains the multiplicity of brain symptoms suffered from, such as poor short term memory, difficulty multi-tasking, slow mental processing and so on. Furthermore brain cells are not particularly well stocked with mitochondria and therefore they run out of energy very quickly. Brain mitochondria are particularly dependent on blood sugar levels. Many brain symptoms are caused by HYPOGLYCAEMIA.

### **5. Effects on the Heart**

There are two effects on the heart. The first effect of poor micro-circulation to the heart is disturbance of the electrical conductivity which causes dysrhythmias. Many patients with chronic fatigue syndrome complain of palpitations, missed heart beats or whatever. This is particularly the case in patients with poisoning by chemicals since the chemicals are also directly toxic to nerve cells.

The second obvious result is poor exercise tolerance. Heart muscle fatigues in just the same way that other muscles fatigue. Symptomatically this causes chest pain and fatigue. In the longer term it can cause heart valve defects because the muscles which normally hold the mitral valve open also fatigue.

THIS APPROACH TO TREATING HEART DISEASE IS EXACTLY THE SAME REGARDLESS OF THE CONVENTIONAL DIAGNOSIS. So patients with angina, high blood pressure, heart failure, cardiomyopathy, some valve defects as well as patients with cardiac dysrhythmias often also have mitochondrial problems and will respond in the same way to nutritional therapies and detox therapies.

### **6. Effects on Lung and Kidney**

The lung and kidney are relatively protected against poor micro-circulation because they have the largest rennin-angiotensin system, which keeps the blood pressure up in these vital

organs. Therefore clinically one does not see CFS patients with kidney failure or pulmonary hypoperfusion.

### **Explanation of the Fatigue Problems in CFS Patients.**

Energy to the body is supplied by mitochondria, which firstly produce NAD (nicotinamide adenosine diphosphate) from Krebs's citric acid cycle and this is used to power oxidative phosphorylation which generates ATP (adenosine triphosphate). These molecules are the "currency" of energy in the body. Almost all energy requiring processes in the body have to be "paid for" with NAD and ATP, but largely ATP. The reserves of ATP in cells are very small. At any one moment in heart muscle cells there is only enough ATP to last about ten contractions. Thus the mitochondria have to be extremely good at re-cycling ATP to keep the cell constantly supplied with energy.

If the cell is not very efficient at re-cycling ATP, then the cell runs out of energy very quickly and this causes the symptoms of weakness and poor stamina. The cell literally has to "hibernate" and wait until more ATP has been manufactured.

In producing energy, ATP (three phosphates) is converted into ADP (two phosphates) and ADP is re-cycled back through mitochondria to produce ATP. However, if the cell is pushed (ie stressed) when there is no ATP about, then it will start to use ADP instead. The body can create energy from ADP to AMP (one phosphate), but the trouble is that AMP cannot be re-cycled. The only way that ADP can be regenerated is by making from fresh ingredients, but this takes days to do. This explains the delayed fatigue seen in chronic fatigue syndrome.

*So to summarise, the basic pathology in CFS is slow re-cycling of ATP to ADP and back to ATP again. If patients push themselves and make more energy demands, then ADP is converted to AMP which cannot be recycled and it is this which is responsible for the delayed fatigue. This is because it takes the body several days to make fresh ATP from new ingredients. When patients overdo things and "hit a brick wall" this is because they have no ATP or ADP to function at all.*

### **Implications for Treatment**

Many patients I see get well with my standard work up with respect to vitamins and minerals, diet, pacing and sleep. All these things must be put in place to repair and prevent ongoing damage to mitochondria so allowing them to recover. For mitochondria to recover they need all the essential vitamins, minerals, essential fatty acids and amino acids to manufacture the cellular machinery to restore normal function. The mitochondrial function tests then allow us to identify lesions which can be corrected by attention to nutritional supplements, improving antioxidant status, detoxing, hyperventilation or whatever. CFS sufferers have limited reserves of physical, mental and emotional energy and this test allows us to direct those energies into the most fruitful line of approach.

### **Examples of some test results:**

ATP profiles – this patient has low levels of ATP, low magnesium, poor conversion of ADP to ATP with blockage of the active sites together with poor translocator protein function – no wonder there is severe fatigue!