



If one falls to the right side, the fire burns low because we do not have the raw materials to feed it so energy levels are low. One would see this in starvation, or chronic poor oxygen supply from lung disease or anaemia.

If one falls to the left side, there is too much free radical production, which overwhelms the antioxidant mopping up system. The free radicals then inhibit mitochondrial function directly and the fire burns low and again we see low levels of energy.

There is a further complication. Mitochondria have to adjust the level of their fire from second to second so that energy supply is coupled to energy demands. Mitochondria need to supply energy at a millisecond's notice! In the micro-respirometry studies that John McLaren-Howard does, we often see uncoupling of oxidative phosphorylation so this link is lost and energy is wasted.

#### Why is this important?

Using his methods of assessing heart function (also a measure of mitochondrial function), Dr Cheney has shown that CFS sufferers respond to oxygen very differently from healthy controls. People with normal energy levels who function in the middle of this redox state perform better with additional oxygen. Their fire glows brighter! In contrast, CFS sufferers get worse. Cheney postulates that this is because they are sitting to the left side – with low levels of energy and poor anti-oxidant status. They cannot cope with free radicals which are already making their mitochondria go slow. Give them oxygen and this creates further pro-oxidant stress which worsens the situation by pushing them further to the left. Indeed, this is how he distinguishes experimentally between people with CFS and normals.

#### Why is this relevant to viral infection?

A paper published in 1991 by Fauci looked at the ability of viruses to replicate according to redox status of the host. What was so fascinating about this paper is that in those individuals with normal redox status viruses were unable to replicate and so their hosts were markedly resistant to viral infection. This explains why when we see an epidemic of infectious disease such as influenza, not all people are equally affected. Some have no symptoms, whereas others are completely flattened. In those people with poor redox state, the virus was able to replicate easily and it is high numbers of viruses in a human host which dictate the severity of the illness. Furthermore, if the immune system moves into “overdrive”, one can get a “cytokine storm” resulting in massive tissue damage and possible death. Indeed, this is what kills people in flu epidemics.

So, if one gets an acute viral infection, and one cannot drag oneself back from the left pro-oxidation side into a normal redox state, one will be stuck with low levels of energy because the mitochondria cannot work. A recent article in the New Scientist (29.8.09) shows that some viruses generate oxygen. If this were the case, it could partly explain how viruses keep one in this pro-oxidant state. The virus has manipulated the host's biochemistry to suit itself and allow it to multiply!

#### So how does one get rid of a chronic infection?

The majority of people I see improve without resorting to anti-microbials by putting in place all the interventions to restore mitochondrial function and good anti-oxidant status. These include:

STONEAGE DIET

NUTRITIONAL SUPPLEMENTS

SLEEP

PACING

Correcting MITOCHONDRIAL FUNCTION

Correcting ANTI-OXIDANT status

DETOX regimes

Etc

However, Cheney has seen good results by treating CFS sufferers using artesunate. This is derived from the Chinese herb artemesia. It is of proven benefit in treating malaria. But, interestingly, it is active against a wide range of other infections including schistosomiasis, cytomegalovirus, hepatitis B, Human Herpes Virus simplex type 1, Human Herpes Virus type 6, hepatitis C, Epstein Barr virus, bovine viral diarrhoea virus and probably others. Artemesins have also been shown to be effective against bacterial infections, yeast infections and also they have powerful anti-cancer activity. What is most remarkable is that side-effects are minimal and rare.

This begs the question as to how one drug can have such a broad spectrum of activity against so many different pathogens? The answer is that it has an effect on the redox state of the host – it pushes it back to the right. It creates a terrain in which bugs cannot replicate! In a normal redox state mitochondria can work normally, energy levels are restored, the body warms up (many pathogens are markedly heat sensitive- that is why we run a fever to get rid of bugs) and the immune system has the energy to kill infection. **BUT THIS WILL ONLY WORK IF ALL OTHER INTERVENTIONS ARE IN PLACE. Without normal mitochondrial function, normal antioxidant status, etc. artemesins cannot work!**

#### Using Artesunate

The dose is 2-4mgs per kg body weight daily given by mouth in two doses. I would suggest 100-200mgs twice daily for one week, then go to a maintenance dose of 100-200mgs alternate days, gradually tailing off until there is clinical improvement and stability.

Side effects are remarkably few – see below:

Possible side effects: Artemether has been remarkably well-tolerated, and appears less toxic than quinine or chloroquine; adverse effects include bradycardia, electrocardiogram abnormalities, gastrointestinal disturbances (nausea, abdominal pain, diarrhoea - oral therapy only), dizziness, injection site pain, skin reactions, and fever. Transient decreases in neutrophils and reticulocytes have been reported in some patients treated with artemether.

Drug induced fever has been observed with artemether. Mild reactions were seen in patients to whom artemether had been administered intramuscularly. These included nausea, hypotension, dizziness and tinnitus. These side effects were also reported: dark urine, sweating, somnolence, and jaundice. There were no deaths or any other side effects. No irreversible side effects were seen.

Slight rise of SGOT and SGPT may occur in individual cases. Neurological side effects have not yet been observed in clinical use but clinical trials suggest that coma may be prolonged in patients treated with artemether and there was an increased incidence of convulsions in one trial in cerebral malaria. Transient first degree heart block has been documented in three patients receiving artemether.

Neurotoxicity has been observed in animal studies but not in humans.

Cardiotoxicity has been observed following administration of high doses of Artemether.

Using artesunate in CFS is still experimental although Cheney has reported some good results. I cannot emphasise enough how important it is to put in place all the other interventions – artesunate is the icing on the cake! No cake and the icing does not work!