



The Science and Art of Treating
CFS/ME

**Symptoms, mechanisms and
tools of the trade for recovery**

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CFS, ME and fibromyalgia are not diagnoses

- They are symptoms
- We need to ask the question why?
- What are the mechanisms that are going wrong that result in these awful symptoms?

Fatigue is the symptom we experience when energy demand exceeds energy delivery.

Fatigue is an essential symptom to maintain life!

Without fatigue we would all be dead in 11 days. No-one has survived that long without sleep.

Fatigue is a powerful symptom - it prevents athletes winning gold medals!

Mr. Micawber in Charles Dickens' novel David Copperfield



Mr. Micawber

- "Annual income twenty pounds, annual expenditure nineteen [pounds] nineteen [shillings] and six [pence], result happiness.
- Annual income twenty pounds, annual expenditure twenty pounds ought and six, result misery."

.....and so it is with energy

CFS/ME ...

- ... is the clinical picture that arises when energy demand chronically outstrips energy delivery.
- Diagnosis is all about identifying the reasons for this because that gives clear indications for management.
- Is our energy pot too small?
- Are there wasteful plugholes?

The difference between CFS and ME is..

- All patients with the above symptoms have chronic fatigue syndrome
- In addition, many have a large inflammatory component. Inflammation is common and this punches an immunological hole in the energy bucket. Myalgic encephalomyelitis (ME) is the term used for patients who have both chronic fatigue syndrome and inflammation.
- This distinction is important because this has clear implications for treatment

This gives us the overall strategy

- 1. Look at how energy is being delivered in the body
- 2. Look at how energy is being spent in the body.

Before we look for the biological lesions ...

- Let's look at the clinical picture.
- Poor energy delivery mechanisms, to all tissues of the body, explain the multiplicity of symptoms that we see.
- Every system goes slow!

The cardinal symptoms of CFS

VERY POOR STAMINA

(due to poor recycling of ATP - see later)

DELAYED FATIGUE

(due to loss of ATP via AMP and slow replenishment - see later)

Muscles

No stamina

Muscle weakness

Early switch into anaerobic metabolism with lactic acid production and muscle pain (actually it is not the lactate which is the problem but the acid!)

This is one major cause of the symptoms of fibromyalgia

Brain: cognitive

- Weight for weight the brain needs energy ten times faster than the body – and ATP is not just an energy molecule, it is also a neurotransmitter. Foggy brain is a major symptom. See [http://www.drmyhill.co.uk/wiki/Brain_fog -
_poor memory, difficulty thinking clearly
etc](http://www.drmyhill.co.uk/wiki/Brain_fog_-_poor_memory,_difficulty_thinking_clearly_etc)

Brain - Low mood

- Poor energy delivery to the brain results in low mood and depression.
- This is a mechanism designed to prevent the brain spending energy (we all get depressed in the Winter when we hibernate – it is called Seasonal Affective Disorder)

Brain - stress

- Stress is the symptom we experience when we know we do not have the energy to deal with demands.....
-be they physical, mental, emotional, financial or whatever!

EYE

- Eye – weight for weight the eye needs energy ten times faster than the brain

Inability to read, watch TV

In severe cases photophobia – CFSs have to lie down in a darkened room

Ear

- Noise intolerance
- The business of processing sound is again greatly demanding of energy

Immunity, healing and repair

- The immune system is enormously demanding of energy. We cannot fight infections efficiently, we cannot run a fever without a good energy supply to our standing army – the immune system.
- Joints and connective tissue – the immune system is responsible for healing and repair. This too will go slow when energy delivery is impaired

As we age energy delivery declines, so we do not heal and repair so well and do not run a fever nor fight infections as well as the young.

CFSs are intolerant of heat and cold

- The skin is the largest organ of the body! On a hot day the heart has to increase output by 20% to perfuse the skin. The severe CFSs do not have the energy to do this, making them markedly intolerant of heat.
- If energy delivery is poor then not enough heat is generated to keep warm.

Gut and liver function

Both the gut and liver need a large amount of energy to function

- Liver – at rest the liver consumes 27% of total body energy consumption!!
- Gut – poor energy delivery will result in poor gut function and poor digestion

Clinical pearl: The easiest food to digest is fat! It does not even have to go to the liver first! It requires no processing. It cannot be fermented. Even “normal” people find energy better on the ketogenic diet

Hormone synthesis

- Is likely to be slowed – in CFS there is general suppression of the HPA axis
- Kidneys – many CFSs have low glomerular filtration rates

Cardiac symptoms in CFSs are very common

- Poor energy supply to cardiac muscle means the muscle cannot contract powerfully.
- There is an early switch into anaerobic metabolism producing lactic acid and chest pain. This lactic acid is slow to clear so the pain is much more persistent than typical angina. CFSs are often diagnosed with “atypical chest pain”
- Poor blood supply to pacemaker – cardiac dysrhythmias common
- Poor blood supply to cardiac muscle causes chest pain (angina)
- All these symptoms are worse with exertion

Heart problems compound all the above problems ...

- ... because fuel and oxygen delivery to the mitochondria is further impaired, which means the heart cannot beat powerfully as a pump.
- Indeed patients with severe CFS are effectively in heart failure.
- What are the symptoms of heart failure? The same as CFS! Fatigue, foggy brain, shortness of breath, anxiety

POTs – (postural orthostatic tachycardia syndrome)

ie Low blood pressure and fast pulse resulting in faintness and loss of consciousness on standing

- In severe CFS, energy delivery to the heart is so poor that the sufferer has to lie down (it is much easier pumping blood flat!)
- On standing, cardiac output has to increase. Normally this is achieved by the heart pumping more powerfully. But the CFSs cannot do this! The panic hormone adrenalin is released

POTs - postural orthostatic tachycardia syndrome.

Low blood pressure and fast pulse resulting in faintness and loss of consciousness on standing

- So CFSs can temporarily increase cardiac output through adrenalin making the heart beat faster.
- But this cannot be sustained because there is insufficient energy delivery to do so.
- Blood pressure drops and the CFS passes out (unless she lies down quickly!)

Loss of libido

- This is Nature's way of preventing procreation when there is no energy for such. The business of having babies, as any parent knows, is hugely energy demanding. Much more so for women than the men, hence women suffer this symptom much more than men.

Symptoms of inflammation

- Localised inflammation results in heat, redness, swelling, pain, loss of function
- Generalised inflammation results in flu-like symptoms, fever, sore throat, swollen lymph nodes, rashes, malaise. The immune system is busy – infection, allergy, fermenting gut, auto-immunity

Symptoms of inflammation

- These symptoms plus poor energy delivery symptoms = ME
 - Inflammation + poor energy = ME
 - More detail in my book
- “Sustainable Medicine” – the symptoms, the mechanisms, the tools of the trade and when to use them.

So.....back to mechanisms

- All the above occur when energy demands exceed energy delivery.
- Let's look at energy delivery mechanism first
- THIS IS THE SCIENCE!

A helpful analogy is to think of the body as a car. To get it to go you need:

- Engine.....
- Fuel.....
- Oxygen.....
- Fuel and oxygen delivery
- Accelerator pedal.....
- Gear box.....
- Service and repair
- Tool kit
- Cleaning – oil
- Catalytic converter.....
- A driver.....
- Mitochondria
- Diet and gut function
- Lungs,
- Heart and circulation
- Thyroid
- Adrenal
- Sleep
- Methylation cycle
- Antioxidants
- Detoxification
- The brain in a fit state!

Table 1. Examples of Genetic Deficiencies in Mitochondrial Disease

Category	Other names	Examples of Symptoms	Examples of related diseases	OMIM Records
Complex I Dysfunction	NADH:Q(1) OXIDOREDUCTASE DEFICIENCY	Exercise intolerance, muscle wasting, lactic acidosis, cardiomyopathy, poor growth	Leigh Disease, MELAS, MERRF, Pearson Syndrome,	#252010
Complex II Dysfunction	SUCCINATE CoQ REDUCTASE DEFICIENCY	Short-stature, cardiomyopathy, muscle weakness, loss of motor skills, ataxia,	Kearns-Sayre Syndrome, Leigh Disease	252011
Complex III Dysfunction	UBIQUINOL CYTOCHROME C REDUCTASE	tubulopathy, encephalopathy, liver failure, muscle weakness, myoclonus, ataxia, mental confusion, exercise intolerance, metabolic acidosis	Leigh Disease, Pearson Syndrome	124000
Complex IV Dysfunction	CYTOCHROME c OXIDASE DEFICIENCY	Diminished reflexes, lactic acidosis, proteinuria, glucosuria, and amino aciduria, liver failure,	Leigh Disease, MNGIE syndrome, Pearson Syndrome	220110
Complex V Dysfunction	ATP synthase	lactic acidemia, hypotonia, and neurodegenerative disease, retinitis pigmentosa, ataxia, and mental retardation, cardiomyopathy, lactic acidosis	Leigh Disease, NARP syndrome,	516060

Mitochondria are the engine of our cars

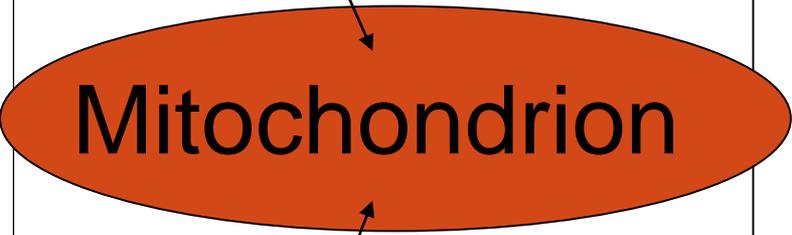
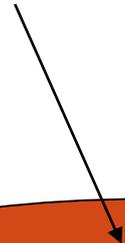
- **They need the correct fuel and oxygen to fuel them. They then convert this fuel to a form of energy that the body can use, namely ATP.**
- **With oxygen we can use fuel via aerobic metabolism. This is highly efficient! The biochemical steps involve glycolysis and oxidative phosphorylation, so that one molecule of glucose makes 36 molecules of ATP in total. (In practice some are wasted as heat, but at least 30 molecules)**
- **By contrast, without oxygen, anaerobic metabolism can only make 2 x ATP from one molecule of glucose.**

- ATP, like money, is the currency of energy. With ATP the cells can do any job of work

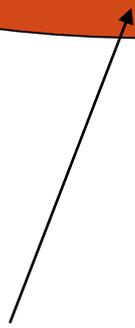
If ATP production is slow, cells go slow because CFS sufferers have slow production and recycling of ATP.

If ATP production is slow, CFSs have poor stamina.

Fuel

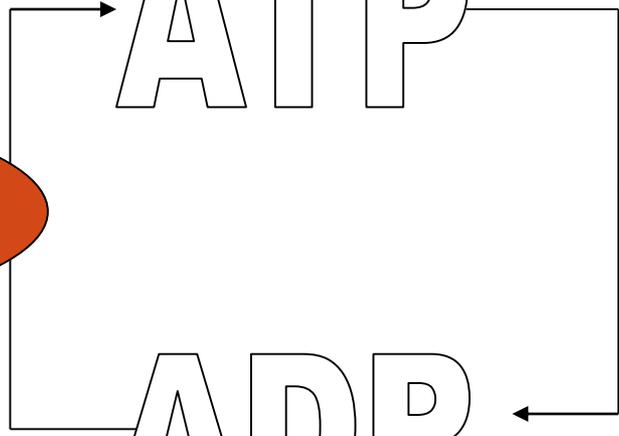


Mitochondrion



Oxygen

ATP



ADP

Energy



What happens when you stress the system?

- By which I mean ask for energy out of mitochondria faster than the mitochondria can supply it.
- ATP (triphosphate) is all converted to ADP (diphosphate), which builds up and gets shunted into AMP (monophosphate).
- AMP cannot be recycled and is lost to the system. Suddenly energy supply dramatically shuts down and the sufferer is pole-axed!
- This creates the first major symptom in CFS, namely very poor stamina.

... and results in delayed fatigue...

- ▶ The body has to make brand new ATP. This it does from a 5-carbon sugar called D-ribose. This is biochemically difficult and takes some days. This results in the symptom of delayed fatigue.
- ▶ In the interim, the body can cheat. It can make tiny amounts of ATP outside mitochondria anaerobically (from glycolysis), but this creates lactic acid which causes pain (note it is the acid that causes pain, not the lactate!).

Glucose

Lactic acid =
Muscle Pain

V. slow: 1 - 4 days
via pentose phosphate shunt

Tiny amount of ATP

Fuel

D-Ribose

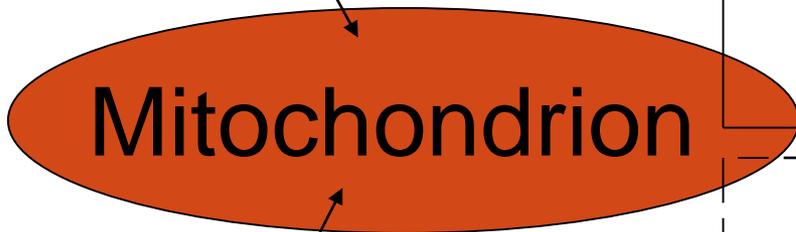
ATP

Energy

ADP

Energy

AMP

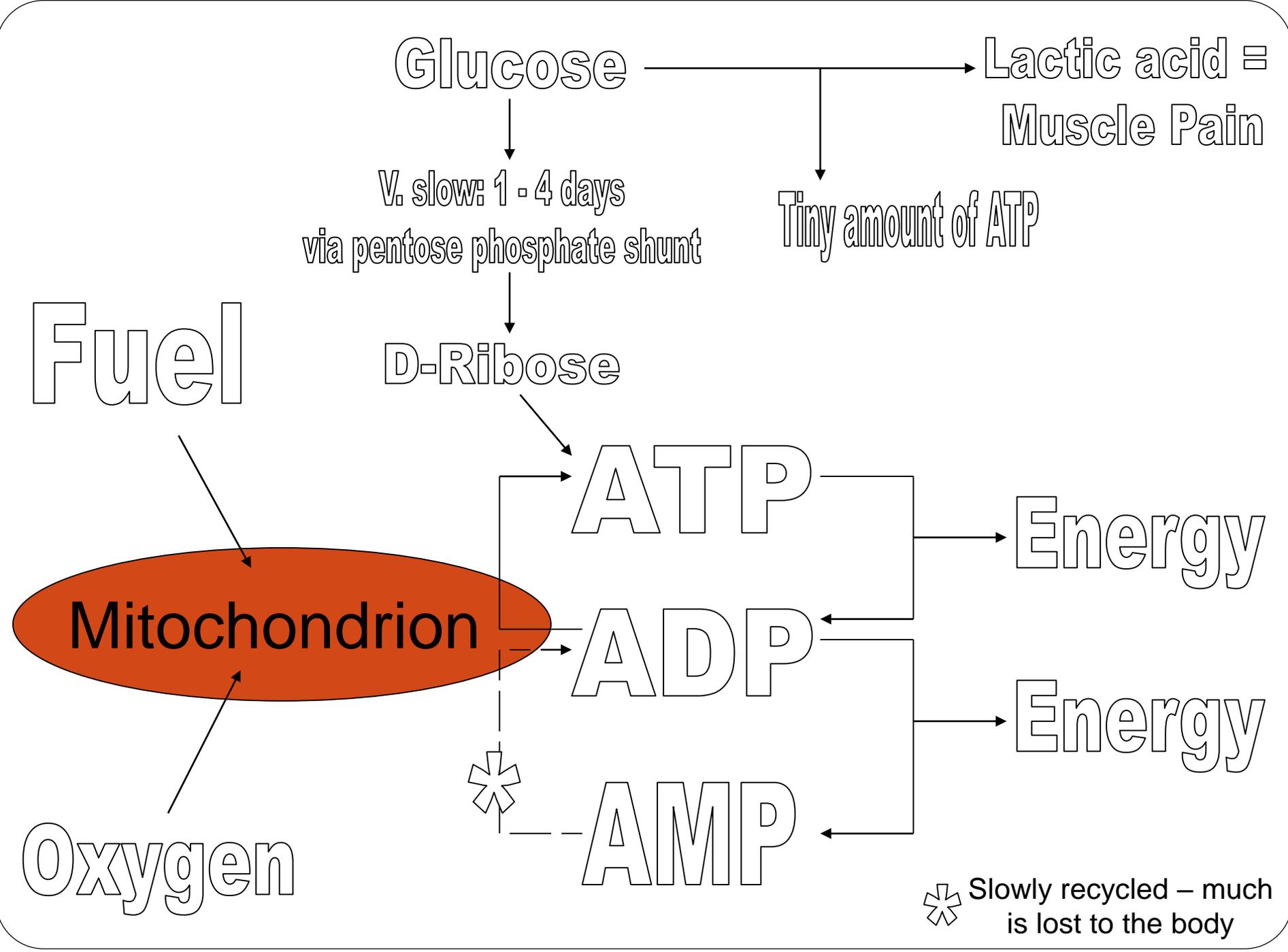


Mitochondrion

Oxygen



* Slowly recycled – much
is lost to the body

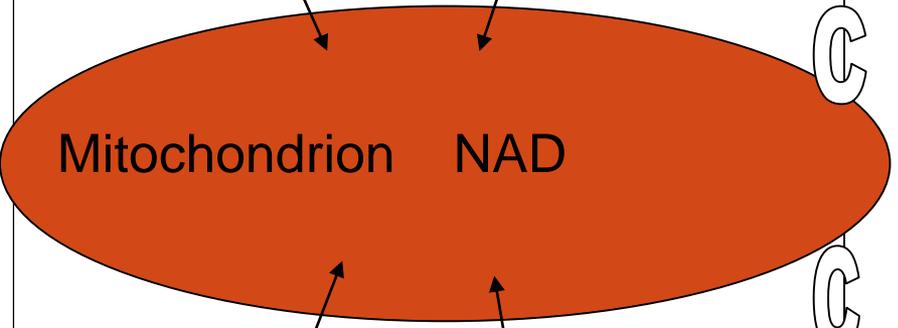


This gives us the basis of a test for mitochondria and therefore CFS

- Thanks to Dr John McLaren Howard we can measure many of these parameters in his mitochondrial function test.
- This has been the most useful biochemical tool clinically!

Fuel

CoQ10



Mitochondrion NAD

L-Carnitine

Oxygen

C

ATP

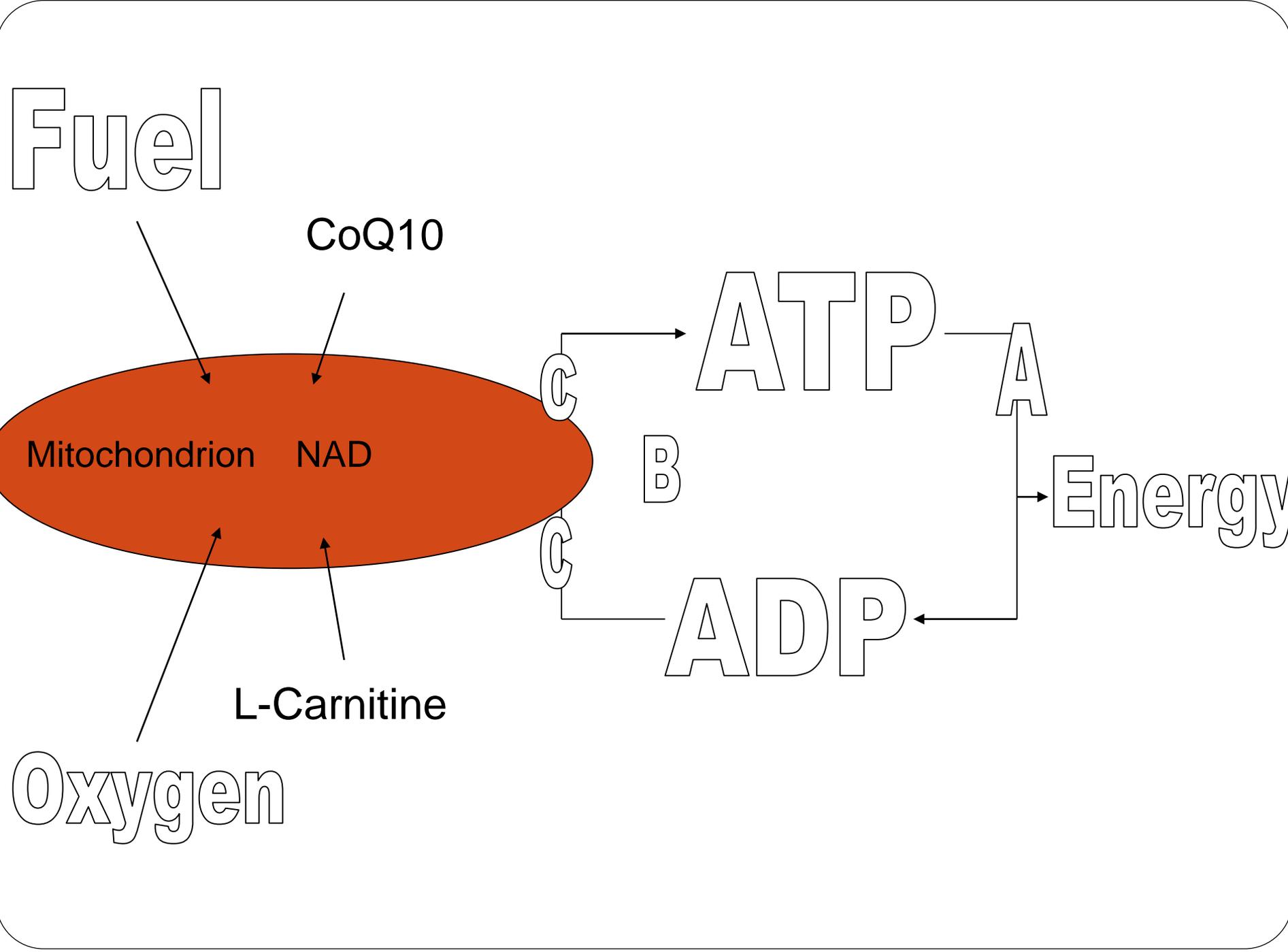
A

B

C

ADP

Energy



The mitochondrial function test looks at...

Levels of ATP (A)

Rate of release of energy from ATP (A)

The rate of oxidative phosphorylation, the recycling of

ATP from ADP (B)

Movement of ATP and ADP across mitochondrial membranes (C)

NAD levels (Between Krebs citric acid cycle and oxidative phosphorylation)

Mg levels

Levels of Co-enzyme Q 10

What the mitochondrial function test looks like is on the next slide. There are three sections...

ATP (adenosine triphosphate), studies on neutrophils

ATP is hydrolysed to ADP and phosphate as the major energy source in muscle and other tissues. It is regenerated by oxidative phosphorylation of ADP in the mitochondria. When aerobic metabolism provides insufficient energy, extra ATP is generated during the anaerobic breakdown of glucose to lactic acid. ATP reactions require magnesium. ADP to ATP conversion can be blocked by environmental contaminants as can the translocator [TL] in the mitochondrial membrane. [TL] efficiency is also sensitive to pH and other metabolic-factor changes. [TL] defects may demand excessive ADP to AMP conversion (not re-converted to ADP or through to ATP). Defects in Mg-ATP, ADP – ATP conversion and enzyme or [TL] blocking can all result in **chronic fatigue – a factor in any disease where biochemical energy availability is reduced.**

ATP whole cells:

With excess Mg added (Standard method of measuring ATP)	1.39	nmol/10 ⁶ cells	1.6 – 2.9
Endogenous Mg only (Measured ATP result is lowered during intracellular magnesium deficiency)	0.85	nmol/10 ⁶ cells	0.9 – 2.7
Ratio ATP/ATP ^{Mg}	0.61	> 0.65

ADP to ATP conversion efficiency (whole cells):

ATP ^{Mg} (from above)	1.39	nmol/10 ⁶ cells (1*)	1.6 – 2.9
ATP ^{Mg} (inhibitor present)	0.42	nmol/10 ⁶ cells (2*)	< 0.3
ATP ^{Mg} (inhibitor removed)	0.79	nmol/10 ⁶ cells (3*)	> 1.4
ADP to ATP efficiency [(3* - 2*) / (1* - 2*)] x 100 =	38.1	%	> 60

Blocking of active sites (2*/1*) x 100 = 30.2 % up to 14

ADP-ATP TRANSLOCATOR [TL] (mitochondria, not whole cells):

	<u>ATP</u> (pmol/10 ⁶ cells)	<u>Ref. range</u>	<u>change %</u>	<u>ref. range</u>
Start	270	290 – 700		
[TL] 'out'	342	410 – 950	26.7	over 35% (<i>Increase</i>) (in-vitro test) reflects ATP supply for cytoplasm
[TL] 'in'	194	140 – 330	28.1	55 to 75% (<i>Decrease</i>) (in-vitro test) reflects normal use of ATP on energy demand

Comments

Low ATP.	Poor ATP-related Mg availability.
30% blocking of active sites leading to:	Poor ADP-ATP re-conversion.
Poor provision of mt-ATP and restricted access secondary to 30% block of TLs.	

Interpretation of the mitochondrial function test

- Top third tells us how much ATP is in the cells, and how well it can give up its energy to form ADP. This is magnesium dependent.
- Middle third tells us how efficiently mitochondria can make ATP, i.e. oxidative phosphorylation.
- Bottom third tells us how well mitochondria can move ATP out of mitochondria into the cell and ADP back from the cell to the mitochondria again.

This gives us a mitochondrial function score

- Any one of these processes going slow, or a combination will result in poor energy supply to the cell.
- If these processes are scored and multiplied up, we have a measure of how well those mitochondria can recycle ATP.
- This score accords well with the level of disability in patients who have already sorted out their diet, sleep and pacing.

A study of 71 patients

- All had received the basic workup with respect to diet, supplements, sleep, pacing, thyroid and adrenal function
- The patient and I (Dr Myhill) agreed an ability score between us.
- Bloods were sent to Acumen who undertook the test “blind,” i.e., JMH did not know the ability score
- The ATP profiles were scored by a third party, giving a mitochondrial function score
- The mitochondrial function score was graphed against the ability score (graphed as energy score)
- The study was written up by Dr Norman Booth
- Published in the International Journal of Clinical and Experimental Medicine Jan 2009.

Int J Clin Exp Med (2009) 2, 1-16

www.ijcem.com/IJCEM812001

Original Article

Chronic fatigue syndrome and mitochondrial dysfunction

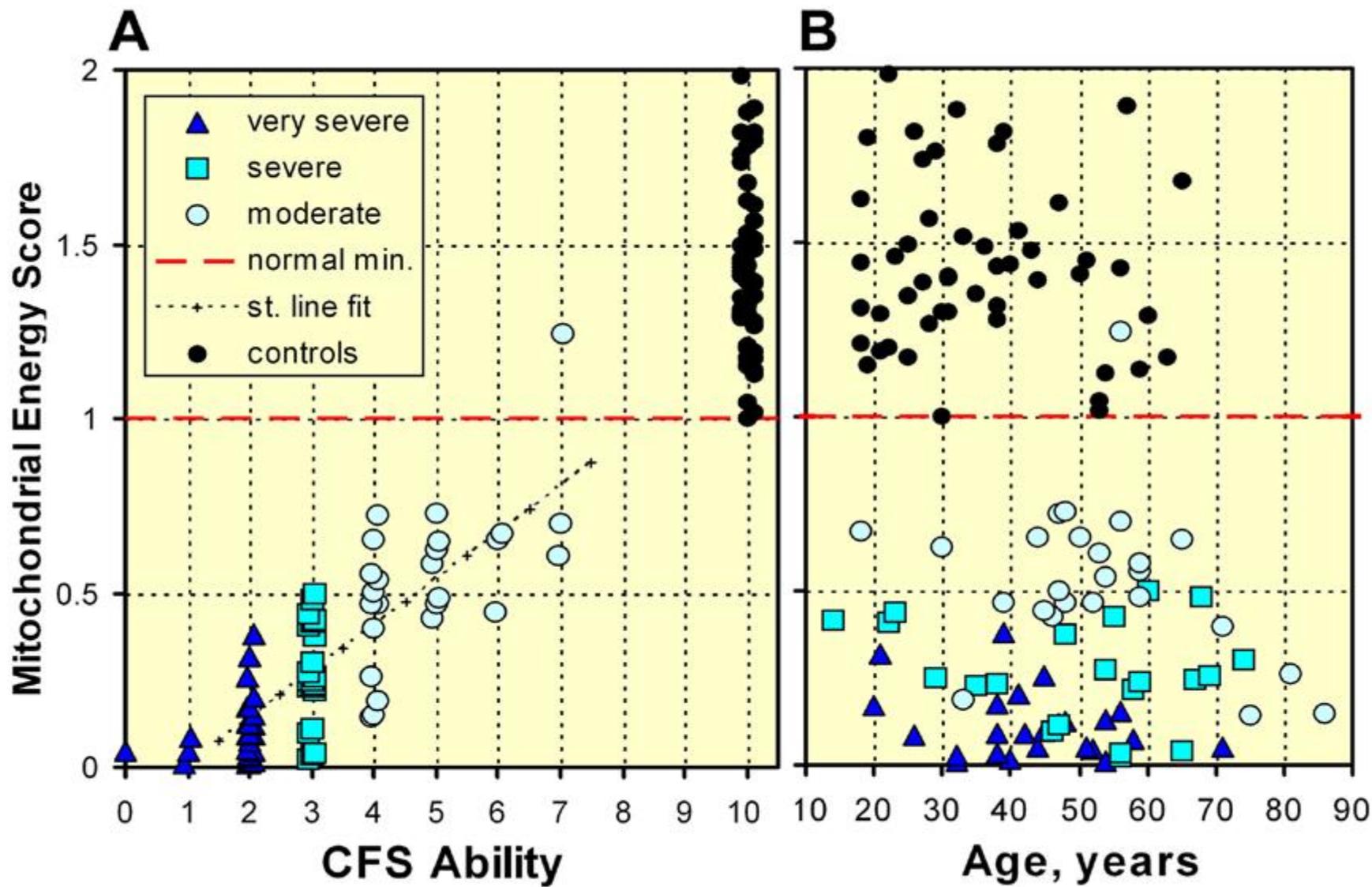
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Abstract: This study aims to improve the health of patients suffering from chronic fatigue syndrome (CFS) by interventions based on the biochemistry of the illness, specifically the function of mitochondria in producing ATP (adenosine triphosphate), the energy currency for all body functions, and recycling ADP (adenosine diphosphate) to replenish the ATP supply as needed. Patients attending a private medical practice specializing in CFS were diagnosed using the Centers for Disease Control criteria. In consultation with each patient, an integer on the Bell Ability Scale was assigned, and a blood sample was taken for the "ATP profile" test, designed for CFS and other fatigue conditions. Each test produced 5 numerical factors which describe the availability of ATP in neutrophils, the fraction complexed with magnesium, the efficiency of oxidative phosphorylation, and the transfer efficiencies of ADP into the mitochondria and ATP into the cytosol where the energy is used. With the consent of each of 71 patients and 53 normal, healthy controls the 5 factors have been collated and compared with the Bell Ability Scale. The individual numerical factors show that patients have different combinations of biochemical lesions. When the factors are combined, a remarkable correlation is observed between the degree of mitochondrial dysfunction and the severity of illness ($P < 0.001$). *Only 1 of the 71 patients overlaps the normal region. The "ATP profile" test is a powerful diagnostic tool and can differentiate patients who have fatigue and other symptoms as a result of energy wastage by stress and psychological factors from those who have insufficient energy due to cellular respiration dysfunction. The individual factors indicate which remedial actions, in the form of dietary supplements, drugs and detoxification, are most likely to be of benefit, and what further tests should be carried out.*

Key Words: Chronic fatigue syndrome; myalgic encephalomyelitis; mitochondria; neutrophils, oxidative phosphorylation.



An objective measure of fatigue

- The mitochondrial function test therefore gives us an objective measure of how fatigued the patient is (all other factors being equal).
- This is very useful for assessing the degree of disability and monitoring recovery.

The test also tells us what and where the biochemical lesion is...

- Magnesium deficiency
- ATP deficiency (correct with D-ribose)
- NAD (niacinamide deficiency)
- CoQ10 deficiency
- Need for acetyl L carnitine
- Need for B12

....and if there is evidence of blocking.

- Of oxidative phosphorylation
- Of translocator proteins (necessary to transport ATP out of mitochondria and recycle ADP back into mitochondria)

If there is blockage this can be investigated further by....

- **Micro-respirometry studies (to look at ADP to ATP conversion i.e. oxidative phosphorylation)**
- **Translocator protein studies (to see how well ATP and ADP move across mitochondrial membranes)**
- **Cardiolipin studies (look at how the mitochondrial membrane is made up)**
- **DNA adducts and fat biopsies**

If the body is a car, then to get it to go you would need:

- ▶ Engine.....
- ▶ Fuel.....
- ▶ Oxygen.....
- ▶ Accelerator pedal.....
- ▶ Gear box.....
- ▶ Service and repair
- ▶ Tool kit
- ▶ Cleaning – oil
- ▶ Catalytic converter.....
- ▶ A driver.....
- ▶ Mitochondria
- ▶ Diet and gut function
- ▶ Lungs, heart, circulation
- ▶ Thyroid
- ▶ Adrenal
- ▶ Sleep
- ▶ Methylation cycle
- ▶ Antioxidants
- ▶ Detoxification
- ▶ The brain in a fit state!

Let's move to the practical reality

● How to get well

- In this section, for reasons of pragmatism and brevity, I am going to roll together the mechanisms with the tools of the trade. Medicine is not a science, it is an art!

The overall strategy

- Improve energy delivery mechanisms
- Reduce energy expenditure

Energy expenditure

- Housekeeping duties (basal metabolic rate) takes up 66% of all energy expenditure. We can't change that much!
- Physical energy – PACING physically
- Mental energy – PACING mentally

Holes in the energy bucket

- Emotional
- Immunological – inflammation

Allergy,

Fermenting gut,

Infection

Healing and repair

Autoimmunity

There are not enough therapists for patients

- My job is to give you the Rules of the Game and the Tools of the trade.
- Only one person can get you well, and that is you.
- As I older, (and perhaps wiser), I find that the very basic things – done very well – get you a long way!

The first appointment

- This is so standard that now you do not need an appointment to see anyone!
- You can do it all yourself and the tools of the trade are freely available.
- However you do need the knowledge, discipline and some physical, mental and emotional energy to put it all in place!

Sustainable Medicine

- ▶ The treatment of ALL disease, from optimising athletic performance and extending life to treating heart disease, cancer and dementia starts with a Basic Package of Treatment
- ▶ This is detailed in my book Sustainable Medicine
- ▶ What follows is what we should all be putting in place, regardless of our current state of health, all the time!
- ▶ The most important aspects of these for all CFSs are highlighted

- Sustainable Medicine section 4 - the tools of the trade to correct and treat mechanisms of disease.
-
- *"Give us the tools, and we will finish the job"*
- *Sir Winston Churchill 1874-1965*
-
- The tools of the trade divide quite neatly into two sections: first, those we should all be doing all the time to reduce the possibility of ill health arising in the first place, and then secondly the "bolt-on" extras that should be employed where a specific condition has been identified.

- 2. The Basic Package – what we should all be doing all the time:

-
- I – Stone-age diet
- II-- Multivitamins, minerals, essential fatty acids
- III--Sleep
- IV– Pacing activity – (exercise or not)
- V-- Sunshine and light
- VI--Reduce the chemical burden
- VII--Sufficient physical and mental security to satisfy our universal need to love and care, and be loved and cared for
- VIII -Avoid infections and treat aggressively

- 2 - The Basic Package – what we should all be doing all the time:



- 1 -- Stone Age Diet



- *“The Cure is in the Kitchen” Dr Sherry Rogers, environmental physician*



- I spend more time talking about diet than all other subjects put together. Changing one’s diet is the most difficult but perhaps the most important thing one needs to do for good health. Anyone eating a modern western diet high in sugar and refined carbohydrates can expect to become fat, feel fatigued and/or die prematurely from heart disease, cancer and/or dementia.

- Sugar, for some, may be essential in the blood stream but it is not essential as a food. For millions of years Man evolved with very low carbohydrate diets. He was fuelled by fat, protein and vegetable fibre. Indeed Dr Heinz Reinwald recognises three ages of nutrition:
 -
 - The Stone Age, of over 2.5 million years ago to about 10,000 years ago, when the diet was ultra-low carbohydrate and largely ketogenic.
 - The glucogenic from 10,000 BC to about 1850 - when increasingly humans were fuelled by starches from the agrarian revolution
 - The glucotoxic from 1850 to date, when the Industrial Revolution allowed wholesale access to cheap additive sugars and refined carbohydrates.

- ▶ CFSs are evolutionarily carnivorous relics!

The majority of CFSs have to return to the most primitive diet, i.e., a ketogenic diet, to fully recover. I suspect this for 3 reasons:

1. Allergy to modern foods - grains, dairy yeast
2. Because their body's preferred fuel is ketones (fat and fibre, not sugar and starches)
3. Because fermenting gut is extremely common if not universal in CFS.

- The ketogenic diet is of proven benefit in the prevention and treatment of cancer, heart disease and dementia.
- Fuel the body with fat and fibre, not sugar and starch.
(This is not a high-protein diet)
- Starve out infection and microbes in the fermenting gut
- Stephen Phinney and Jeff Volek "The Art and Science of Low Carbohydrate Performance"

- **II -- Micronutrients: Multivitamins, minerals, essential fatty acids**

- Westerners all need to take micronutrients for life for the reasons given previously. My standard package is:
- Multivitamins - containing at least 25mgs of B1, B2, B3, B5, B6 vitamins, 1mg of folic acid, 1mg of B12, vitamin A 2,000iu, vitamin E 50mgs and vitamin K 0.2mgs .
-
- Multi-minerals - the following doses of elemental weight are per 2 stone of body weight (12.5Kgs) – Calcium 60 mgs, magnesium 70 mgs, potassium 40 mgs, zinc 6 mgs, iron 3 mgs, boron 2 mgs, iodine 0.3 mg, copper 0.2 mg, manganese 0.2 mgs, molybdenum 40 mcg, selenium 40 mcg, chromium 40mcg. These doses should be taken up to a maximum dose for a 10 stone (62.5kg) person, ie up to five times the amounts listed above. Use one gram of mix per litre of water – this can also be used to make hot drinks. I do not include sodium chloride (salt) because this is contained in so many foods. If absent then sea salt should be used, approx one gram per 2 stone of body weight per day.
-
- Vitamin D – at least 2,000iu daily but up to 10,000iu daily
-
- Hemp oil – one dessertspoonful, together with 2 capsules of fish oil.
-
- Vitamin C at least 2 grams, possibly up to 10 grams at night.
-
- These doses assume that nothing comes from the diet; as the stone-age diet is adopted and sun bathing becomes possible, these doses can be reduced.

▶ III -- Sleep



▶ One cannot create energy and function without doing some damage. All living creatures, right down to bacteria, require rest when systems are shut down to allow healing and repair. We call this sleep. Without a good night's sleep on a regular basis, all other interventions are to no avail!

▶ Regular hours of quality sleep

▶ Use a sleep dream

▶ Perhaps use hypnotics (start with melatonin 3-9mgs, Nytol 1-2 at night) together with a sleep dream to establish a Pavlovian conditioned response.



▶ d--Circadian rhythms – timing is vital

- ▶
- ▶ *“The early bird gets the worm, but the second mouse gets the cheese.”*
- ▶ *Willie Nelson 1933 -*
- ▶



- ▶ **Re-establishing the circadian rhythm** – Modern Western lifestyles destroy our natural circadian rhythm because of light (inhibiting melatonin production at night), noise (disturbing sleep), diet (hypoglycaemia and adrenalin disturbing sleep), drugs of addiction (withdrawal symptoms), caffeine and other such. Interventions that help include:
 - ▶
 - ▶ Bright light, ideally sunshine, by day
 - ▶ Complete darkness at night
 - ▶ Peace and quiet at night
 - ▶ High-fat breakfast for energy delivery - diet should be Stoneage!
 - ▶ Physical and mental exercise during the day
 - ▶ Bed by 9pm, asleep by 9.30pm – the best quality sleep occurs before midnight
 - ▶ Melatonin 1-9mgs at night, perhaps other medications – see sleep section in this book
 - ▶ Take thyroid hormones in the morning on waking ideally with food (T3 sooner) – levels of TSH peak at midnight, T4 peaks at 4am and T3 at 5am.
 - ▶ Take cortisol and DHEA on waking
 - ▶ Perhaps use caffeine in day to fire up – none after 2pm
 - ▶ Perhaps B12 injections in morning to fire up
 - ▶ Other things as I [and the patient!] learn more!

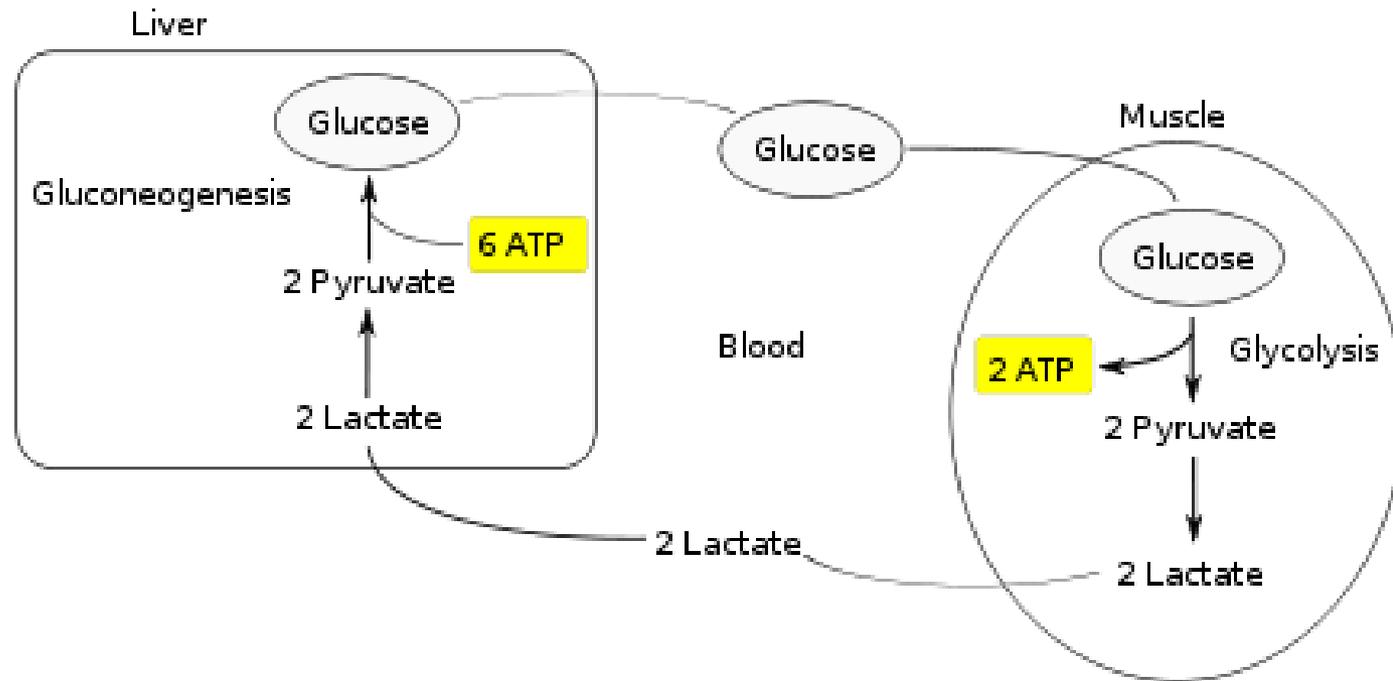
- *IV: Exercise – this must be the right sort to give benefit*
- In CFS we call this pacing! This is desperately boring but essential
- **WHY?**
- If energy demands exceed delivery then we move into anaerobic metabolism. This is extremely inefficient. One molecule of glucose burnt aerobically produces up to 36 molecules of ATP.
- One molecule of glucose burnt anaerobically produces 2 molecules of ATP.

But worse than that.....

-we produce lactic acid. The acid causes all sorts of other symptoms – it inhibits mitochondria directly and causes pain.
- So we must get the lactic acid back to pyruvate (another fuel for mitochondria)
- To do this we use the Cori cycle in the liver.

The Cori cycle

Look at how much ATP is needed to recycle lactate! Three times as much!



The Cori cycle

- Anaerobic metabolism generates 2 molecules of ATP per molecule of glucose
- To convert lactic acid back to glucose needs 6 molecules of ATP.
- Athletes can do this in a few minutes
- CFSs take many minutes, possibly hours, some days! This is because their mitochondria cannot make ATP fast enough!
- CFSs experience angina because of lactic acid burn of the heart – but this is called “atypical” because it does not settle quickly with rest. Angiograms are normal because the blood supply to the heart is fine.

So failure to PACE.....

- ▶puts huge energetic demands on the body and makes things MUCH WORSE!
- ▶ This is why advice to exercise is so very damaging in CFS. My personal view is that to advise such amounts to medical negligence.

(Would one advise a patient in heart failure to exercise? I don't think so!)

▶ **V -- Sunshine and light**

▶ *"Good day sunshine" The Beatles [dates – various]*

▶ Sunshine on the skin is highly desirable for at least three reasons:

▶ **To make vitamin D from UV light** - Western cultures have become almost phobic about any exposure of unprotected skin to sunshine. Indeed the US Environmental Protection Agency advised that ultraviolet light, and therefore sunlight, is so dangerous that we should "protect ourselves against ultraviolet light whenever we can see our shadow". That advice is just nuts! The deaf blind author Helen Keller (1880 – 1968) agrees:

▶ *"Keep your face to the sun and you will never see the shadows."*

▶ The best source of vitamin D is sunshine – not so much that the skin burns, but enough to tan. One hour of whole body exposure to Mediterranean sunshine can produce 10,000 to 20,000 iu of vitamin D. We need at least 2,000iu daily and probably more for optimal health. No studies have shown any toxicity in doses up to 10,000iu daily. Further excellent information at <http://www.vitamincouncil.org/>

▶ I use high dose vitamin D routinely in the treatment of multiple sclerosis, any condition associated with inflammation (allergy, infection, autoimmunity), osteoporosis and arthritis. My ME/CFS patients are nearly always deficient. Note that the normal blood levels for NHS labs are set very low at 30-60ng/ml. I like to see levels at 75-200ng/ml.

▶ Whilst sunshine exposure is a risk for basal and squamous cell cancer, these are relatively benign, easily treated and rarely kill. At the first sign of sun damage to skin I recommend Curaderm, extract of eggplant. It is highly effective in treating solar keratosis, early basal cell carcinoma (rodent ulcers) and early squamous cell carcinomas. If there is no sign of remission after 8 weeks of use, then consultant opinion is necessary. There is increasing evidence that sunshine is not a risk factor for the aggressive melanoma. If it were then this tumour would have the same distribution as other skin tumours. It does not.

▶ Do not use sun tan lotions. There is evidence to suggest that they increase cancer risk directly or, because they give a false sense of security, then they increase cancer risk indirectly through complacency. Once there is a risk of burning, head for the shade or cover up.

- **To make us happy** – absence of full spectrum light results in SAD (Seasonal Affective Disorder). This is no fun but evolutionarily desirable – it helps us conserve energy through long cold winters because we do not want to do things – boring, but with survival advantage. Sunshine is addictive – indeed one measure of addiction is how much money we are prepared to spend on such. Holidays in hot climates are expensive but still highly desirable!
-
- **To receive heat in the form of far infra red** - such free heat means we do not have to generate so much heat from our own mitochondria. This too has survival benefits as an energy conservation method. Indeed the mitochondria of native Africans run slower than Caucasians and much slower than Inuit Indian Eskimos. The latter have a high metabolic rate and are excellent at fat burning, which is essential to deal with the cold. They need abundant food to fuel this demand. By contrast native Africans run their mitochondria slow, and this makes them much more susceptible to metabolic syndrome and all its complications. They are metabolically highly efficient.
-
- We use this form of heat in FIR saunas to detoxify chemicals. However I suspect this is just one of many possible benefits of FIR about which we have much more to learn. The heat from muscular activity radiates as infrared. This warming reduces friction in connective tissue to reduce stiffness.

- **VI -- Reduce the chemical burden**

- We live in an increasingly polluted world containing an increasing number of toxic chemicals which are toxic to our genes, to our brains, to our internal metabolism and to our immune system. These “nasty” toxic chemicals contribute to our ever increasing incidence of cancer and birth defects, our declining fertility due to life time exposure and also make us more susceptible to chronic fatigue syndrome.
- It is impossible to completely avoid every “nasty” chemical. I have yet to do a fat biopsy or measure toxic metals in urine following a DMSA challenge and find a normal result. We live in equilibrium with our environment and the best we can do is keep the total toxic load as low as reasonably possible, Anything that can be done to reduce the toxic chemical load will be helpful in allowing our bodies to recover.
- Dr Paula Baillie Hamilton in her book "The Detox Diet" explains how chemicals in foods and the air interfere with internal metabolism to make us fat and lethargic - indeed she points out that farm animals are deliberately fed hormones, antibiotics and pesticides to make them fat and lethargic, and therefore they do not have to eat so much in order to put on weight (cheap meat!). Effectively we are treating our farm animals to produce a metabolic syndrome. Many chemicals are persistent and concentrate up through the food chain - it is very likely that if Westernised humans were a farm animal, they would be declared too toxic to eat.

- **Reduce your chemical exposure:**

- **Foods**

- **Water**

- **Air**

- **Cosmetics**

- **Garden and agricultural chemicals**

- **Social and prescription drugs**

- **Outdoor air pollution**

- I believe the late Dr Dick van Steenis did more for the Health of the Nation than any other doctor through his campaigning work against polluting industry.

- **Good nutrition**

- This is highly protective against toxic stress - this is further reason to take nutritional supplements. One example of this came out of the research into thalidomide. This drug prescribed to women in pregnancy as a "pregnancy safe hypnotic" caused serious birth defects if the women took it during early pregnancy. But not all babies were affected. This drug was tested in rats - no offspring were abnormal. This was a mystery to researchers, until someone had the bright idea of putting the rats onto nutritionally depleted diets. Then the baby rats developed the foetal abnormality of phocomelia ("flipper limbs"). It was a combination of toxic stress (the drug) and nutritional deficiency that caused the problem to become apparent.

- **VII -- Sufficient physical, mental and financial security which satisfies our universal need to love and care, and be loved and cared for.**
- It is beyond the scope of this book to discuss the psychological and spiritual imperatives that we must fulfill for optimal physical and psychological health and I am no expert. I am deeply grateful for a loving carefree childhood with a Mum who was a brilliant cook. This love flowed further to my two gorgeous daughters Ruth and Claire, but as they became more independent my affections embraced my pets – horses and more recently my lovely puppy Nancy. Pets are far more emotionally intelligent and sensitive than humans! I think it is essential for anyone living alone, or in an emotionally lacking relationship, to have a loving pet.
- My horizons are constantly changing. When my girls were little, my hobby was watching them have fun. Most recently I want my house, which is too big for one, to become the Marigold hotel for horse and dog lovers! Humans evolved to live in tribes, certainly not to live alone and probably not just within a single family. A complex social life is vital to good mental health.
- Simply identifying the above needs is often helpful to patients. Knowing what they need, they then come up with innovative solutions.

▶ **VIII -- Avoid infections**

- ▶ Acute infections clearly cause short term misery, but I am more concerned by their potential to switch on ME/CFS, allergies, auto-immunity and cancer. Even arterial disease may have an infectious component – it is clearly driven by inflammation. Many cancers we know are infection driven such as cervical cancer (Human Papilloma Virus, HPV), stomach cancer (Helicobacter pylori), Kaposi's sarcoma (HIV infection), Burkitt's lymphoma (Epstein Barr Virus), hepatoma (hepatitis B), lung cancer (tuberculosis), and so on. We also know that many cases of autoimmunity are infection driven. I suspect that the upper fermenting gut will eventually prove to be the major risk factor for oesophageal, stomach and colon cancer.
- ▶ Avoiding infection is an important part of long-term good health.

- ▶ How to avoid infection:
- ▶ **Keep warm** – cold kills. When the Mistral wind blows in France, death rates increase.
- ▶ **Drink clean water and eat clean food**
- ▶ **Care with sexual partners.** Passionate love is a form of insanity that makes us do insane things and take insane risks!
- ▶ **Avoid insect bites** with the potential for blood-to-blood transmission of pathogens. We are seeing epidemics of Lyme disease from biting insects.
- ▶ **Treat breaches of the skin thoroughly** - keep clean and wrap up. All animal bites get infected! I have seen infections of heart valves and inter-vertebral discs arising from such.
- ▶ **Eat a low-carb diet** and especially avoid sugar and fruit sugar – these are the substrates that microbes love to ferment. New cases of diabetes may be picked up because of recurrent thrush, fungal toenails or staphylococcal skin infections.
- ▶ **Dental hygiene** - the commonest chronic infection is streptococcus mutans, which causes dental decay with gum disease resulting downstream. Dental decay is a marker symptom of many other diseases, including the clinical picture of metabolic syndrome and of course upper fermenting gut! Avoid sugar, brush teeth regularly and perhaps use herbal antiseptic mouthwashes such as neem.
- ▶ **Identify and treat hypochlorhydria** – An acid stomach is a major line of defence against infection. Inhaled microbes stick to the mucous lining the airways and are coughed up and swallowed – so most end up in the stomach. This should be an acid bath to sterilise the upper gut. This is particularly important where there is hypochlorhydria. Hypochlorhydric are at greater risk of food poisoning and recurrent infections.
- ▶ **Do not graze** – this never allows the stomach time to become fully acidic between meals.
- ▶ **Take probiotics** regularly – these are of proven benefit in, for example, avoiding traveller's diarrhoea.
- ▶ **Take micronutrients** as per Basic Package – these are essential for normal immune function
- ▶ **Vitamin C** – this is toxic to bacteria, viruses and fungi (and, incidentally, cancer cells). It is harmless to normal cells. It is a fabulous defence against infection. Taken by mouth it is poorly absorbed, but that helps protect against infection via the gut.

- ▶ **Do not be obsessed with hygiene and chemical disinfectants** – these may be counter-productive. You can never sterilise a surface – microbes will always be present. The immune system needs normal exposure to everyday microbes for correct programming. Mothers are usually fastidious with first born babies, less so with the rest – first born children are more likely to suffer from allergy.
- ▶ *“A child who is protected from all controversial ideas is as vulnerable as a child who is protected from every germ. The infection, when it comes- and it will come- may overwhelm the system, be it the immune system or the belief system.” Jane Smiley 1949 –*
- ▶ **Symptoms of acute infection should not be suppressed with drugs.** Symptoms arise to make us do the things we need to reduce numbers of microbes (cough, wheeze, sneeze etc), or rest to conserve energy and resources for fighting infection efficiently. Only too often my ME/CFS patients tell me they had an infection and continued to work by dint of taking paracetamol, caffeine, antihistamine and pseudoephedrine, then turn to addictions to cope with the stress, so allowing their virus to get topside. This is short-term gain, long-term pain.

▶ **I -- Tools to treat acute infection**

▶ **All of the above!**

- ▶ **Feed a cold, starve a fever.** The gut and liver are greatly demanding of energy – empty the gut by fasting and energy is freed up for the immune system to burn hot and run a fever.
- ▶ **Hydrate with water, salt and minerals.** Where there is fluid loss through sweating, diarrhoea and/or vomiting, rehydrate. My recipe is one litre of water with 2 grams of salt (a teaspoon is 5 grams, so a mean half) and one gram of multi-mineral mix (as in the basic package micronutrients) drunk ad lib.
- ▶ **Rest** – again this allows the immune system the essential energies to deal with infection. Do not exercise! Some athletes claim they can run off an acute infection – this may be because that generates heat which kills microbes, but it is a high risk policy.
- ▶ **Encourage a fever** – keep warm.
- ▶ **Do not use symptom-suppressing medication for all the reasons given in part 3!**
- ▶ **Vitamin C taken in sub-diarrhoeal doses** at the first sign of a cough or cold will often prevent the illness from progressing. High dose vitamin C should be used in any acute infection. Many doctors use high dose intravenous vitamin C in the treatment of infection and cancer with good results reported. Up to 50 grams (50,000mgs) daily are used iv – this demonstrates how safe this vitamin is.
- ▶ **High-dose probiotics** - I suggest kefir 1-3 cupfuls daily
- ▶ **Use antiviral herbal preparations** such as colloidal silver 20ppm one dessertspoonful rinsed round mouth, gargle and swallow 3-4 times daily, Echinacea 25 drops held in mouth and swallowed 3-4 times daily and/or propolis 600mgs three times daily help many. It is really a case of trying as many things as you can until you find a combination that suits you.
- ▶ **Zinc drops or lozenges** - 10mgs four times daily into the mouth kills microbes. Zinc is the commonest mineral deficiency that results in poor immunity. It is directly toxic to microbes. I use an infection spray which contains vitamin C, zinc and colloidal silver in DMSO for topical use on skin and mucous membranes.

- **IMMUNOLOGY**

- *From transient infection*

- *to chronic disease*

- Can some infections “scar” the immune system?

- Carl Nathan

- ▶ Da Fonseca *et al.* propose that a long-gone infection may set the stage for chronic disease by impairing the immune system's checks and balances. They base this proposal on the observation that most of the mice that had cleared a gastrointestinal tract infection by *Yersinia pseudotuberculosis* within 3 weeks had persistently leaky lymphatic vessels draining the intestine and persistently enlarged, inflamed lymph glands in the mesentery (a broad membrane in the abdomen). These changes lasted up to 42 weeks (the last period examined), which is roughly equivalent to 28 years of a human life span.

Second appointment

The bolt-on Extras – the therapeutic tools of the trade

- We do not have all the tools to treat all the problems, but the body is fabulous at healing itself. We only have to get the package 51% right and the body will do the rest. Only 49% right and one is on the slippery downhill slope. Many tools multitask. For example, ATP is the energy molecule but also a neurotransmitter. Also, high-dose vitamin B12 may be used to improve mitochondrial function, for detoxing via the methylation cycle, as an anti-oxidant, and for its anti-inflammatory properties by damping down the pro-inflammatory fire of the NO/ON/OO cycle.

▶ **II -- Tools to treat poor energy delivery**

▶ a--Poor mitochondrial function:

▶ Broadly speaking, mitochondria go slow either because they lack substrate to work efficiently, or because they are blocked by toxic stress (there are other reasons!). Dr Stephen Sinatra's excellent book "The Sinatra Solution" identifies the common biochemical bottlenecks that result in poor function – his ideas find good biochemical support in the tests of mitochondrial function that I do with my ME/CFS patients. The ageing process is determined by mitochondria, so as we age perhaps we should all be taking additional supplements to support our mitochondria. Dr John McLaren Howard, Dr Norman Booth and I published a third paper in January 2013 which showed that those CFS patients taking the package of supplements to support mitochondrial function and remove sources of toxic stress (chemicals from the outside world or products of the upper fermenting gut) improve biochemically, and that improvement is paralleled by clinical improvement. This paper can be seen at <http://www.ijcem.com/files/IJCEM1207003.pdf>

▶ The package that I use is as follows:

▶ Co-enzyme Q 10 200-500mgs daily (the oil of the engine). It is virtually impossible to overdose with co-Q 10.

▶ Acetyl L carnitine 1-2 grams daily (the fuel pipe that delivers the acetate fuel into mitochondria)

▶ Vitamin B3 slow-release niacinamide 1500mgs (essential step between Krebs Citric Acid cycle and oxidative phosphorylation)

▶ Magnesium 400mgs orally, perhaps injections – I think of Mg as the spark plug of the engine

▶ D-ribose 5-15 grams – the raw material to make new ATP, the energy molecule.

▶ Vitamin B12 1-2mgs daily, ideally by injection.

▶ **Blocking of mitochondria** – this may result from exogenous toxins (see detox regimes), endogenous toxins (see fermenting gut) or because of poor membrane quality (consume high-dose hemp oil with quality fish or shell fish oils).

- ▶ B - Thyroid function – the accelerator pedal of our car
- ▶ UK citizens are not subject to Best Practice with respect to prescribing thyroid hormones. All relate to the prescribing of thyroid hormone for underactive thyroid glands (hypothyroidism).
- ▶ **The threshold for thyroid stimulating hormone (TSH) is set too high**
- ▶ **Population reference range versus individual normal range – they are not the same:**
- ▶ **Poor conversion of inactive T4 to active T3**
- ▶ **Thyroid hormone receptor resistance:**

▶ c--Adrenal function – the gear box

- ▶ Where there is complete failure of the adrenal gland, most commonly due to autoimmunity, treatment is life saving and must be overseen by a consultant endocrinologist. However in clinical practice this is rare. What I most often see is adrenal fatigue or partial adrenal failure. This can be diagnosed with an adrenal stress test. This is done on 4 saliva samples taken through the day. Arguably saliva tests are better than blood tests because the latter can be coloured by protein binding. Saliva tests are a measure of the free available hormone.
- ▶ **Interpretation of the Adrenal Stress Test for DHEA and cortisol**
- ▶ Levels of DHEA and cortisol vary according to the level of stress and for how long that stress has been applied. Increasing cortisol production is the normal response to short-term stress and is highly desirable, so long as the stress is removed and the adrenal glands can recover. On-going, unremitting stress means the adrenal gland and the whole body is in a constant state of alert, does not get time to recover and eventually packs up. So, there are several stages of adrenal function gradually leading to failure:
 - ▶ Normal levels of cortisol and DHEA, normal circadian rhythm
 - ▶ Raised cortisol, normal DHEA –
 - ▶ Raised cortisol and raised DHEA -
 - ▶ High levels of cortisol, low levels of DHEA
 - ▶ Cortisol levels low, DHEA levels low
- ▶ In addition to absolute levels, this test may indicate poor diurnal rhythm of hormones. If levels of DHEA are low in the morning this may indicate low melatonin at night. In this event I prescribe 3-9mgs of melatonin nocte, especially if sleep is disturbed.
- ▶ Pregnenolone 50mgs sublingually is a good all-rounder – it is upstream of DHEA and cortisol. Levels decline with age. We increase our need for this with stress.

- **V -- Tools to detoxify:**
- a-- General approach
- **Remove the polluting source** - there is no point doing detox regimes without also addressing the issue of where the toxins are coming from. The upper fermenting gut is a major source of toxic stress. I would not advocate chelation therapy for toxic metals such as mercury until the source of the toxin, such as dental amalgam, has been removed.
- **Ensure good energy delivery** - the business of detoxing is greedy for energy and resources. Most occurs in the liver, which at rest consumes 27% of total body energy production! This is more than the brain and heart combined!
- **Ensure good micronutrient status** - most toxins are rendered water soluble first by oxidation by cytochrome P450 enzymes and then tacking on a group such as glucuronide, glutathione, sulphate, amino acid or other such. So for example if I measure levels of glutathione in the body in someone who is not taking supplements, almost invariably there is a deficiency. Glutathione is in great demand for detoxing and also for glutathione peroxidase – a vital antioxidant.

- b--Correct the methylation cycle -
- Simply taking the basic package of nutritional supplements of vitamins and minerals will go a long way towards correcting poor methylation. But there is a particular vicious cycle here – vitamins B12 and folic acid, essential parts of the methylation cycle, need to be methylated before they can be of use! Sometimes they must be given in the methylated form to be effective. The following regime helps:
 - Methylcobalamin 1 mg sublingually (ideally by injection) daily
 - Methyltetrahydrofolate 800mcg (ActiFolate) daily
 - Pyridoxal-5-phosphate 50mgs twice daily
 - Glutathione 250mgs daily
 - Phosphatidyl serine 100mgs twice daily

Getting rid of toxic metals

- Use trace minerals
- Use glutathione 250-500mgs and/or methionine 250-500mgs
- Vitamin C 4 grams daily
- High-dose iodine 12.5mg once daily ,e.g ., Iodoral
- DMSA strips out many toxic metals remarkably well
- Clays such as kaolin and bentonite, zeolite
- Mobilising toxic metals can make the patient worse
- Whatever regime is used, retest toxic metals in urine

Getting rid of pesticides and volatile organic compounds through heating regimes:

- ▶ The source of heat does not matter too much – exercise, hot baths, sauna and sunshine should all be effective. However many patients, especially my severe ME/CFS patients, are intolerant of heat.
- ▶ The idea behind FIR saunaing is that toxic chemicals that have been dumped by the body in fat, including subcutaneous fat, are shaken up and boiled off through the skin where they dissolve on the lipid layer on the skin surface. Showering these chemical off is as important as saunaing – otherwise they are simply reabsorbed. It is not necessary to sweat for FIR sauna to be effective.
- ▶ Roughly speaking fifty FIR saunas will halve the load – chemicals come out exponentially so a further fifty saunas will reduce the total load to 25% of total and so on. One can never get rid of every last molecule! One ends up in a state of equilibrium with the environment – and of course all environments are polluted.
- ▶ I have done fat biopsies and/or DNA adducts and/or gene studies on 27 patients before and after FIR saunas. Levels of pesticides and VOCs come down reliably well. It may be there are other techniques that work just as well such as exercise (not for my ME/CFS patients), traditional saunas (again not tolerated by ME/CFS patients) and hot Epsom Salt baths (500grams of Epsom salts in 15 gallons of water – soak for 30 mins – indeed Epsom salt baths may be additionally effective because as the chemicals come out magnesium and sulphate are absorbed so providing valuable detox raw materials). These techniques all should, in theory, work just as well. However I do not yet have data to support such.
- ▶ Some people are made ill even by FIR sauna – I suspect this partly results from chemicals being mobilised into the blood stream where they cause an acute poisoning.
- ▶ FIR saunaing does not get rid of toxic metals.

IX -- Doctors – they are potentially dangerous people using potentially dangerous tools! Prescription drugs, vaccinations, medical investigations.

- *'Physician, heal thyself' [and leave the rest of us alone!]*
- *Luke 4.23, The Bible, King James' Version [adapted!]*
- After cancer and heart disease, the most common cause of death in modern western society is the medical profession – drug side effects, medical investigations, doctors' mistakes (including sloppy hand writing) abound. Indeed when doctors go on strike (Israel, New York, Columbia, Los Angeles and others), the death rate falls by up to 50%. Hospitals are dangerous places with the potential to pick up infections (MRSA, clostridium difficile). Malnutrition, dehydration and insomnia erode resistance to disease and ability to heal.
- After 20 years of NHS practice I left partly because I felt I did not have the clinical freedoms I required to practise to the standards I wanted within the constraints of the NHS. Indeed at one stage I was reprimanded because my prescribing costs were too low and therefore I was considered to be a bad doctor!!

3. The Bolt on Extras – the therapeutic tools of the trade

- We do not have all the tools to treat all the problems, but the body is fabulous at healing itself. We only have to get the package 51% right and the body will do the rest. Only 49% right and one is on the slippery downhill slope. Many tools multitask. For example, ATP is the energy molecule and a neurotransmitter. Also, high dose vitamin B12 may be used to improve mitochondrial function, for detoxing via the methylation cycle, as an anti-oxidant and for its anti-inflammatory properties by damping down the pro-inflammatory fire of the NO/ON/OO cycle.

How did the illness begin?

- Sudden post viral?
- Gradual onset?

http://www.drmyhill.co.uk/wiki/Valacyclovir_in_the_treatment_of_post_viral_fatigue_syndrome

- **Purpose:** Beginning in 1993 at a single chronic fatigue syndrome (CFS) treatment center, we began studies that demonstrated Epstein–Barr virus (EBV) nonpermissive replication. In the most recent study performed, EBV nonpermissive replication is the cause of 28.3% of 106 consecutive CFS cases, and is etiologic with human cytomegalovirus (HCMV) and/or human herpes virus 6 (HHV-6) as a coinfection in an additional 52.8% of CFS cases. Therefore, EBV is causally involved in 81% of cases of CFS. Further, EBV CFS is effectively treated with long-term valacyclovir. Coinfection HCMV and HHV-6 CFS requires valganciclovir with valacyclovir."

Patients and results:

- The validated Energy Index Point Score[®] (EIPS[®]) (Please see here '[EIPS](#)' and below) monitors severity of CFS illness and its recovery. A specific CFS diagnostic panel identifies EBV CFS subsets. Four separate EBV CFS therapeutic studies of several hundred CFS patients describe valacyclovir administration and long-term patient recovery. With valacyclovir, serum EBV titers (EBV, early antigen (diffuse); EBV, viral capsid antigen, immunoglobulin M), 24-hour electrocardiography Holter monitors; and cardiac dynamic studies improve.
- **Conclusion:** Nonpermissive EBV infection is causal in a significant proportion of CFS cases. EBV CFS is safely and effectively treated with long-term valacyclovir.

Treatment regimes

- Valacyclovir was prescribed at a dose rate of 1 gram every six hours (i.e. 4 grams per day). For overweight patients the dose was 1.5 grams every six hours, and for small patients correspondingly less. A “Herxheimer” response with worsening of symptoms and a worsening score continuing for two to six weeks after treatment began was a good prognostic omen. Increasing energy score and decreasing symptoms were apparent in the fifth to sixth month of continuing Valacyclovir. As the drug was continued, EIPS values of 7 and above were achieved and activities of normal living restored.
- The above clinical improvements were accompanied by improvement in ECG monitoring.

Cost

- These regimes work well. Valacyclovir long term used to be an expensive therapy. Lerner's costing for valacyclovir tablets for 1 gram every six hours was of the order 25-30 thousand dollars per year. The cost has recently come down a lot as the patent has run out. I can now obtain Valciclovir 500mg x 42 for £19.49, so around £107.18 for a month's course. There is no doubt that Valacyclovir is a very useful treatment for patients, and my recommendation at present is to reserve this for those who do not respond to the standard nutritional work ups.
- Also monitor creatinine at one month, 3 months, 6 months and one year (if all well).

Lyme disease

[http://www.drmyhill.co.uk/wiki/Lyme Disease and other Co-infections](http://www.drmyhill.co.uk/wiki/Lyme_Disease_and_other_Co-infections)

- Enzyme-linked Immunosorbent Spot Assay (Elispot - LTT). This is a promising test that has been tested clinically, demonstrating a specificity of 96.7%. Most importantly, after these Lyme patients had been treated, 90.7% showed negative or greatly reduced lymphocyte reactivity and, more significantly, this negative or reduced reactivity correlated well with clinical improvement. It looks like this will be the most helpful test for diagnosing Lyme and monitoring response to treatment. Indeed this test, called Elispot-LTT has received FDA and CDC approval. Further information about the technique used in this test can be found at [Elispot](#)

The Elispot is available from **ArminLabs**
to diagnose and monitor the following infections:

- Borrelia Burgdorferi
- Chlamydia pneumoniae
- Chlamydia trachomatis
- Ehrlichia/Anaplasma
- Yersinia species
- Epstein Barr Virus (EBV)
- Cytomegalo Virus (CMV)
- Herpes Simplex Virus 1 / 2

Gradual onset of fatigue

- Metabolic syndrome
- With lots of other symptoms – allergy or fermenting gut
- Hypothyroidism
- Poor mitochondrial function
- Poor adrenal function

Gut problems

- These are extremely common if not universal in CFS.
- Almost all gut symptoms are due to either allergy or fermenting gut
- Bloating, burping, reflux, foggy brain typical of fermenting gut
- Pain, constipation/diarrhoea more typical of allergy
- BUT OVERLAP!

Fermenting gut causes problems for many reasons

- Foods feed microbes instead of you
- Microbes ferment foods to toxic substances such as alcohol, D lactate, hydrogen sulphide and many others
- The liver uses a large amount of raw materials and energy to cope with this toxic load

Fermenting gut causes problems for many reasons - Hypochlorrhydria

- Malabsorption of minerals
- Protein cannot be digested
- Upper gut cannot be sterilised so
 - i) increase susceptibility to infections
 - li) overgrowth of microbe - bacterial yeast and parasites. These spill over into the blood stream (bacterial translocation)

Fermenting gut causes problems for many reasons: bacterial translocation

- Bacteria in the brain could explain mental disease (see Nishihara's work)
- Any part of the body can sensitise to bacteria, resulting in arthritis, interstitial cystitis, muscle pain, skin rashes, asthma, arteritis, polymyalgia rheumatica, etc., etc.

IV -- Tools to improve gut function:

- **Reduce bacteria and yeast in the mouth**
- **Low/zero carb ketogenic diet**
- **Improve digestion: acid supplements with food**
- **90 mins later alkalise with magnesium carbonate, possibly take digestive enzymes and bile salts.**
- **Probiotics**
- **Transdermal supplements**
- **Vitamin C to bowel tolerance at night**
- **Antimicrobials – prescription or herbal**
- **Anti-fungals – prescription or herbal**
- **Worms**
- **Faecal bacteriotherapy**
- **Bacteriophages**

III --Tools to treat inflammatory conditions:

- ▶ **Allergen avoidance: foods, food additives, biological inhalants, chemicals and microbes**
- ▶ Just as with infection, it is a number's game. Allergy is all about total load and if this can be reduced below a critical threshold then tolerance develops.
- ▶ **Foods** – the stoneage diet is an excellent start and may be all that is necessary to reduce the total load. Where there are obvious and known reactions to foods, avoid them. If this becomes impossible then rotation diets are helpful – the idea here is to eat a food once every four days so one allergic insult does not come on top of another. Quick and efficient digestion of foods means large antigenically interesting molecules are rapidly broken down to minimise the potential for sensitisation so improving gut function is important. Apply the tools to treat the upper fermenting gut.
- ▶ **Biological inhalants** – largely speaking these are large, water soluble molecules. Simple masks filter out much of the allergens – if I am grooming my horse or moving hay I just tie a tea towel over my nose and mouth, otherwise I risk a session of sneezing and wheezing. In the event of any reaction, a shower and change of clothing is very helpful. House dust mites thrive in soft furnishing and soft toys.
- ▶ **Chemical sensitivity** – many sufferers are exquisitely sensitive – I know those who react to wash powders on neighbours' clothes on the washing line, perfume on passers-by and discharges from polluting industry. Sometimes avoidance is impossible. Air filters are helpful. Sufferers may be reacting to POPs contained within their own fat so reducing the endogenous load of POPs using tools for detoxification is helpful.
- ▶ **Microbes** – the main source is microbes from the upper fermenting gut so use the tools to treat such.

Tools to help to damp down the pro-inflammatory biochemical fire of the NO/ON/OO cycle

- ▶ **Correct poor anti-oxidant status** - simply taking the basic package of nutritional supplements of vitamins and minerals will go a long way towards correcting poor antioxidant status. However I routinely measure levels of antioxidants and deficiencies are common. I would use in response to the following deficiencies:
- ▶ Superoxide dismutase – copper 1mgs at breakfast, manganese 3mgs midday, zinc 30mgs at night - these timings reflect the time of day these nutrients are best absorbed.
- ▶ Glutathione peroxidase – glutathione 250-500mgs, selenium 200-500mcgms at night
- ▶ Co-enzyme Q 10 – co Q 10 250-500mgs daily
- ▶ Other important antioxidants such as vitamins A, C, D, E are part of the Basic Package. There are many natural anti-oxidants within our diet which are additionally helpful. These are found in vegetables, nuts, seeds and berries.
- ▶ **Vitamin D** – vitamin D evolved in response to sunshine on the skin as an anti-inflammatory to protect the skin from pro-oxidant stress from ultraviolet light. It then diffuses through the body where it has generalised anti-inflammatory actions. It is protective against infection and improves muscular strength. It protects against allergy, auto-immunity, metabolic syndrome, osteoporosis and cancer. The incidences of all these conditions increase the further away from the Equator you live. It is important to measure blood levels in anyone with any of these conditions since absorption can be variable. I like to see levels between 75 and 200nmol/l. To achieve this requires up to 10,000iu daily.
- ▶ **Vitamin B12 by mouth and by injection** – this provides instant anti-oxidant cover and protection whilst the other antioxidants are being corrected by supplements. See above for details and dose.
- ▶ **Alkalinisation** – the use of bicarbonates and carbonates has been long recognised as a way to switch off allergy reactions, especially to foods. I suggest magnesium carbonate 500mg-2,000mgs last thing at night, or at least away from mealtimes. We need a window of time, at least 90mins after food, to achieve an acid stomach to allow normal gut function. Magnesium carbonate may be additionally useful if acid supplements are being used to treat hypochlorhydria.
- ▶ **Low dose naltrexone (LDN)** – naltrexone is an opiate blocker used in high doses, such as 50mg, to block the effect of opiates. LDN is used in tiny doses such as 1-4mgs at night. The idea is to slightly block the action of the body's own endogenous opiates (endorphins) which results in an increase in endogenous production. Endorphines are natural anti-inflammatories. This property gives LDN wide clinical application from the treatment of cancer, auto-immunity and neurodegenerative disorders. See <http://www.lowdosenaltrexone.org/> for detailed information.
- ▶ **Exercise, music, singing, love and laughter** – all are addictive because they increase endorphins with anti-inflammatory actions arising downstream. Some addictions are useful!

- ▶ **Desensitising techniques to turn off allergies – enzyme potentiated desensitisation (EPD) and neutralisation** - the mainstay of treating allergy is avoidance. Problems arise when allergens are multiple or unavoidable. The technique I use is EPD but comparative studies of EPD and neutralisation give similar long term outcomes. Both treatments are fabulously safe because the concentrations of antigens in the mixes are extremely low. Both have been proven in placebo controlled double blind trials. Both techniques can be used to desensitise to foods, biological antigens (pollen, dusts, animal dander etc), microbes and chemicals.
- ▶ EPD seems to work by reprogramming the immune system to respond appropriately. The idea here is that the bone marrow constantly sends out new white cells which mature and are programmed by the status quo. EPD reprograms these naive cells to respond appropriately to the antigens present in the injection. It may take several injections before sufficient cells are correctly programmed and allergy is switched off.
- ▶ Food Drops – see http://www.drmyhill.co.uk/wiki/Oral_immunotherapy:_switching_off_food_allergies_using_food
- ▶ Probiotics - lactobacillus rhamnosus was successful in switching off peanut anaphylaxis when given with tiny doses of peanut. It can be easily grown at home.
- ▶ **Homeopathy** – I am no expert, but I have seen many patients who are greatly helped by homeopathy. I suspect one possible mechanism of action is it reprogrammes the immune system to respond appropriately. Homeopathic doctors tell me that their remedies work much better when the Basic Package is also applied!

In conclusion

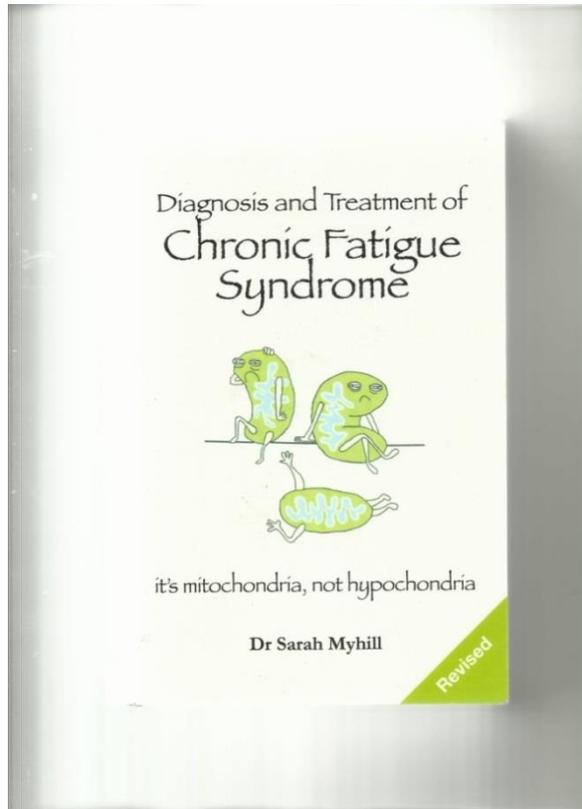
- ▶ Always ask the question why – look for causes
- ▶ Put in place the Basic Package of treatment -see “Sustainable Medicine” and “Chronic Fatigue Syndrome: it’s mitochondria not hypochondria”
- ▶ Use test for the Bolt-on Extras - many can be done at home on DIY blood samples, stool samples, saliva samples – will be available through my website on a “standard interpretation” basis

To recover you need.....

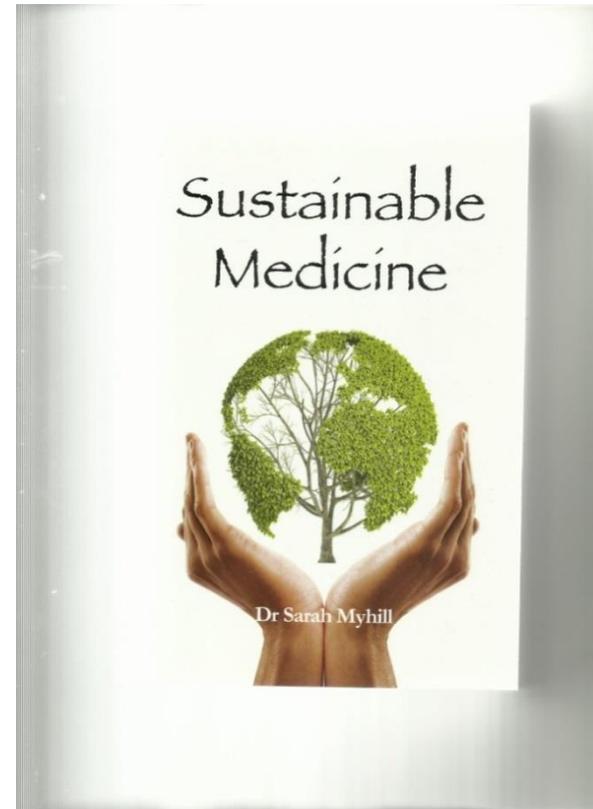
- The knowledge - get the books “CFS –it’s mitochondria not hypochondria” and “Sustainable Medicine”. For up-to-date stuff see http://www.drmyhill.co.uk/wiki/Main_Page
- The tests to diagnose – which I shall be making available on a “no-interpretation” basis (standard interpretations on my website)
- The tools of the trade – largely diets and supplements
- Additional expert guidance.....

The Knowledge is within.....

Chronic fatigue syndrome



Sustainable Medicine



Tests to diagnose and the tools of the trade

<http://www.drmyhill.co.uk/wiki/Category:Tests>

Mitochondrial function tests we must ration simply because the laboratory is overwhelmed.

We are currently looking for other laboratories to do mitochondrial function tests

Expert help from: The Natural Health Service thenaturalhealthservice.org

- Any doctor, therapist or expert patient can make their opinion available online by phone, email, Skype or face-to-face with no admin staff required
- Opinions can be costed at nothing initially until a “reputation” has been established from feedback from customers
- All participants, therapists and customers agree to a “no fault” service – no sueing!