How is mitochondrial dysfunction linked to chronic disease, and what can we do about it?

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AONM

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Author of award winning books including:
"Chronic Fatigue Syndrome – its mitochondria not hypochondria"
"Ecological Medicine - -the antidote to Big Pharma"
"The Infection Game – Life is an Arms Race"
"The Energy Equation"
"Paleo-Ketogenic – the Why and the How." "Diabetes"
"Green Mother"

There are two major drivers of Western Disease

Energy delivery mechanisms

Inflammation

……and mitochondria are centrally involved in both

This means it is difficult to find a pathology in which mitochondria are not involved!

Central nervous system
Encephalopathy
Stroke-like episodes
Seizures and dementia
Psychosis and depression
Ataxia
Migraine

Cardiac
Hypertrophic cardiomyopathy
Dilated cardiomyopathy
Heart block
Pre-excitation syndrome

Endocrine and diabetes
Diabetes mellitus
Hypoparathyoidism
Hypothyroidism
Gonadal failure

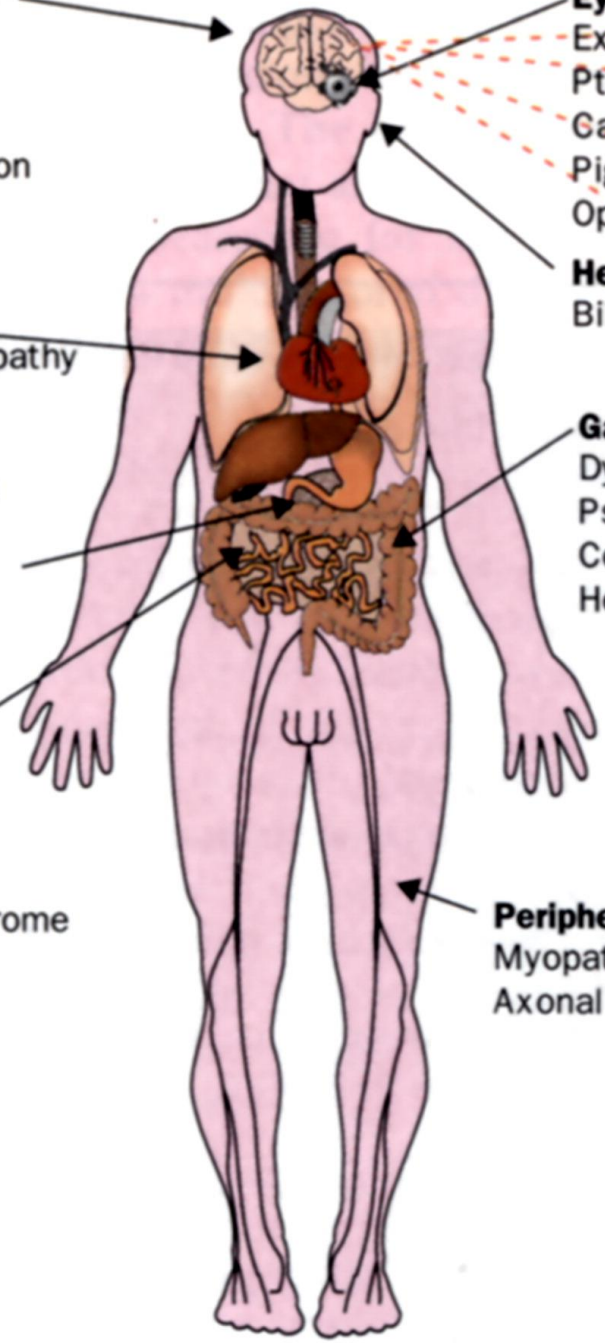
Renal
Renal tubular defects
Toni-Fanconi-Debre syndrome

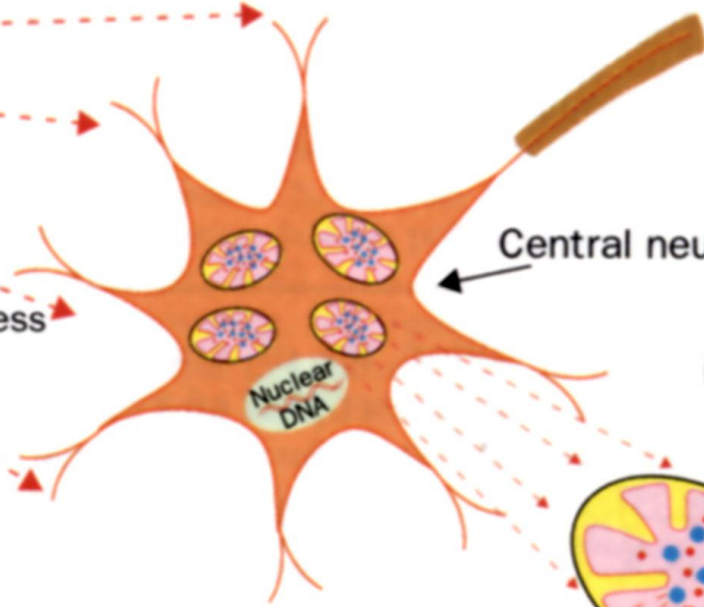
Eye
External ophthalmoplegia
Ptosis
Cataract
Pigmentary retinopathy
Optic atrophy

Hearing
Bilateral sensorineural deafness

Gastrointestinal
Dysphagia
Pseudo-obstruction
Constipation
Hepatic failure

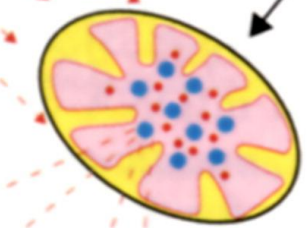
Peripheral nervous system
Myopathy
Axonal sensorimotor neuropathy

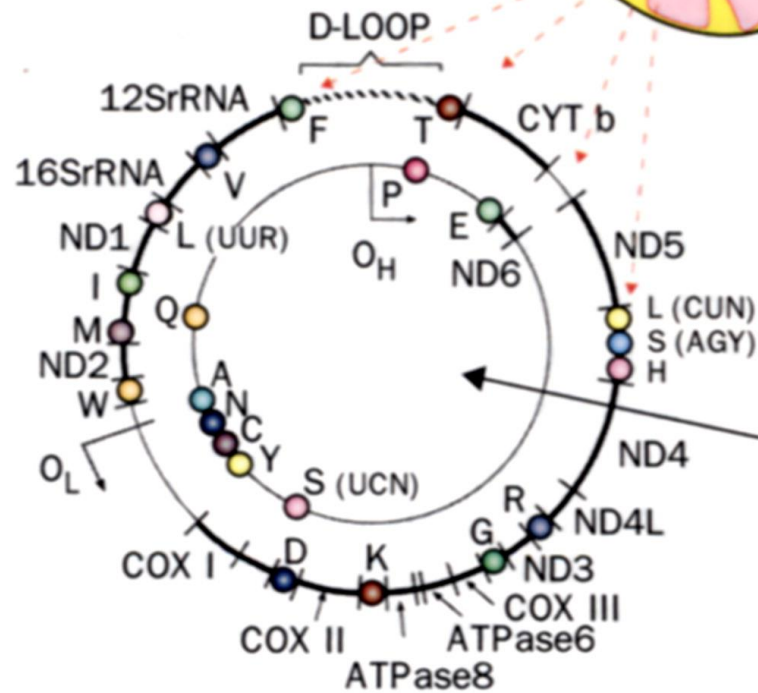




Central neuron

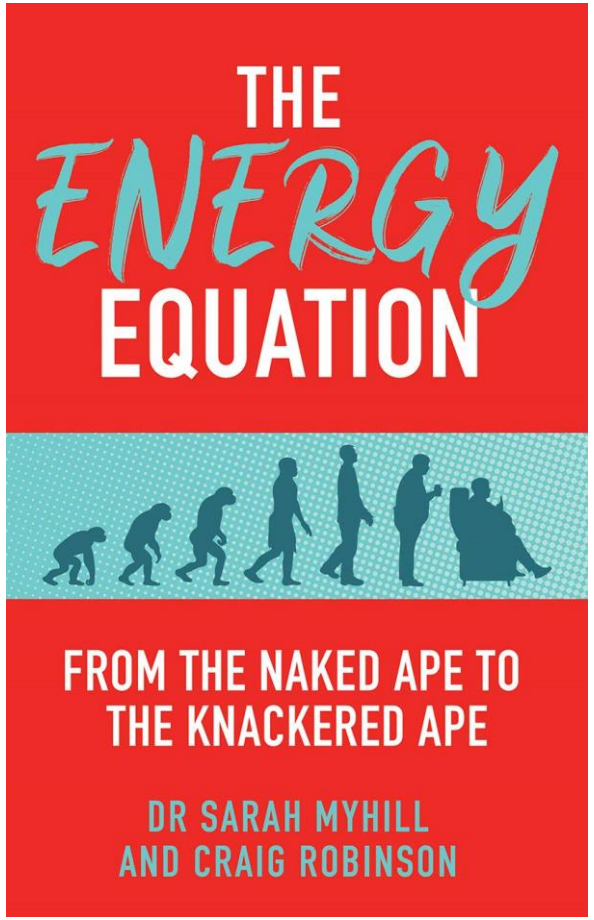
Heteroplasmic mitochondrion





Wild-type (normal) mtDNA molecule

The early stages of mitochondrial failure is often characterised by fatigue



Late stage of mitochondrial failure characterised by

Premature Ageing

Organ failures:

Immune system = cancer

= poor healing and repair so degeneration

Heart = heart failure

Brain = dementia

Liver, kidney, joints, muscles, gut, hormones producing glands……..

How and why do mitochondria go slow?

Wrong fuel in the tank

They are deficient in an essential raw material

They are inhibited by some toxin

The control mechanisms are down (thyroid accelerator pedal and the adrenal gear box)

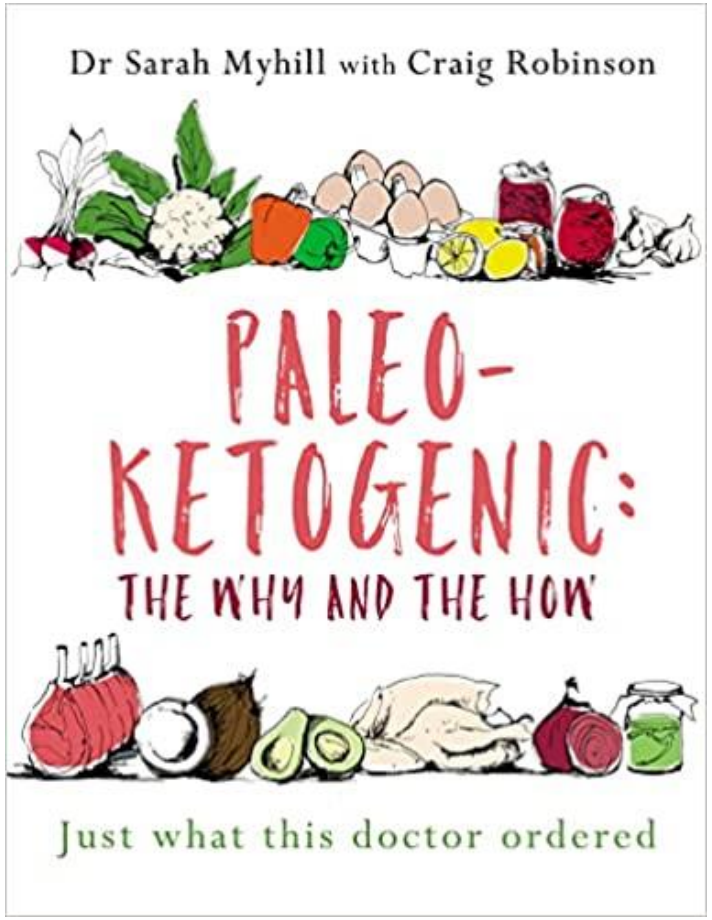
How the body generates energy for life. FIRST the fuel in the tank

Mitochondria work best on ketones – eg work of

Dr Gabriella Segura,

Dr Kiera Clarke.

The PK diet is the single most important intervention and must be done first!



Why we should all be eating a Paleo Ketogenic diet ('PK Diet')

Because this has been established by thousands of years of Evolution

Because this is the starting point to prevent and treat all Western disease

- *"Let Medicine be thy food and food be thy medicine".*
- Hippocrates, c. 460 – c. 370 BC

Humans evolved over two and half million years eating a paleo ketogenic diet. This is the diet which best suits our bowels, body and brains*. If we wish to live to our full potential in terms of quality and quantity of life, this is the diet naturally selected, by survival of the fittest, throughout Evolution.

And take a basic package of supplements

The alarming fact is that foods – fruits, vegetables and grains – now being raised on millions of acres of land that no longer contains enough of certain needed nutrients, are starving us -- no matter how much we eat of them.

U S Senate Document 264

1936

Calories - make sure you are eating sufficient.

An army marches on its stomach

Frederick the Great, Napoleon Bonaparte

Many people chronically undereat in a misguided attempt to keep their weight down. But under-eating puts the body into survival mode – it thinks there is a famine. The body and brain will cut down energy expenditure to deal with this abnormal state of affairs resulting in physical fatigue, foggy brain and depression. You need enough food for energy! See our book “The Energy Equation”.

To calculate your calorie need (also known as basal metabolic rate BMR), use the Mifflin-St Jeor Equation. If you do not fancy the maths, put your vital statistics into - https://www.calculator.net/bmr-calculator.html and that will get your BMR!

Protein – not too little, not too much

Protein Leverage

The body cannot store protein, but daily protein is essential for survival. We have a protein appetite which will make us crave food until that appetite has been satisfied. If you are eating a low protein diet, you will be driven to eat more food. In that process you overeat carbs and fat and so expect to gain weight. Conversely, eat a high protein diet and you tend to undereat and lose weight. Get your protein intake right to help maintain a normal weight. (Note a high protein diet is not desirable as the body then has to deal with the toxic consequences of too much protein! Listen to your body and appetite - it will tell you how much you need!)

Fibre – for the microbiome, fuel and more

Fibre is essential for the healthy gut and body. It is a carbohydrate, but not one that can be digested to sugar. This does lead to confusion with the carbohydrate count of foods because fibre is often included in the analysis. So, for example linseed is 29% carbohydrate of which 27% is fibre. We do not have the gut enzymes to digest fibre, but the lower gut (colon) contains kilograms of friendly bacteria which ferment it. This provides us with a fuel source of short chain fatty acids (yippee! More ketones!) and also essentials such as vitamin K, serotonin, several B vitamins and more are synthesised. The bulking effect of fibre shortens gut transit time to further reduce that toxic load (yes, turds are toxic). The friendly bacteria help to programme the immune system. Fibre protects us from many diseases.

Eat enough fibre until you are crapping like one of Denis Burkitt's Africans. Burkitt, consultant surgeon, observed that indigenous Africans did not suffer Western diseases

Bristol Stool Chart

Seperate hard lumps, like nuts (hard to pass)

Sausage-shaped but lumpy

Like a sausage but with cracks on it's surface

Like a sausage or snake, Smooth and soft

Soft blobs with clear-cut edges (passed easily)

Fluffy pieces with ragged edges, a mushy stool

Watery, no solid pieces. Entirely Liquid

Fats and oils are essential fuels, building materials and hormone precursors.

Fat is the most valuable food known to Man"

ohn Yudkin FRSC (1910 – 1995)

British physiologist and nutritionist, and the founding Professor of the Department of Nutrition at Queen Elizabeth College, London

Forty years of propaganda has given fat a bad name. This is not one jot of evidence for the risible theory that states high fat diet cause high cholesterol and arterial disease. No! No! No! This is a repeat of that said by Mrs Thatcher in response to EU proposals and immortalised by the headline in the Sun newspaper…….. "Up Yours Delors"

"In short, let fat be thy medicine and medicine be thy fat!"

Dr Gabriela Segura, Consultant Cardiologist and Cardiothoracic surgeon

All fats which occur naturally are good fats

Saturated fats

In Nature there is no such thing as a bad fat. All are good. “Bad” fats are Man-made. Man cannot easily destroy saturated fats. These medium chain (8-18 carbon atoms) are tough, straight, stiff molecules in which every carbon atom is “saturated” either with another carbon or a hydrogen atom and are solid at room temperature. Use lard (beef pork or lamb), dripping, goose fat, butter, coconut or palm oil for cooking - when heated (which shakes things up) it retains its normal shape. Cocoa fat is also saturated. Fat is stored in our body as saturated fat and makes a for a perfect pantry – essential fuel for lean times.

Carbohydrates

You may think I am maligning all carbohydrates. No so - they are essential. Five carbon sugars, such as D ribose, are the raw material to make ATP, DNA and RNA – the fundamental molecules of Life! Sugar is used to detoxify nasties in the liver via glucuronidation – 10% of the population have lost this pathway and have a tendency to jaundice because they cannot detoxify bilirubin efficiently. This is called Gilbert's syndrome and sufferers are at greater risk of chronic fatigue syndrome because they are at risk of poisoning. We have even evolved the ability to create sugar in the liver from protein - gluconeogenesis. This reflects not only how essential sugar is, but also its rarity in primitive diets.

PKHW Chapter 4 Get started, get into ketosis and stay on the wagon.

"In order to get from A to B, you first have to leave A".

Purchase a ketone breath meter and learn to use it correctly.

You must test because everyone is different - there is no 'one size fits all' guidance here. My joint author Craig can eat 90grams of carbs a day and happily stay in ketosis whereas I have to stick to 30grams of carbs or less a day. Dammit! Men normally move into ketosis more easily because they have a higher metabolic rate, furthermore women have female sex hormones which are conducive to metabolic syndrome.

No ketones on breath testing means we are running purely on sugars. Not desirable in the long term.

Low ketones on breath testing means we are burning some fats. This tells us our glycogen stores are not saturated and blood sugar levels will be completely stable. This is a very desirable state of affairs!

Ketones arise through fat burning and that generates three types of ketone:

Beta hydroxybutyric acid present in and which can be measured in the blood – this is the most accurate measure, but testing strips are expensive. I am mean and a wimp, so I do not use this method.

Acetoacetate is excreted in the urine. Testing is cheap and easy with urine keto-stix but as the body becomes more efficient at matching ketone production to demand, urine tests may show false negatives.

Acetone is exhaled and can be measured with breath testing. This is my preferred method as you can easily test after every meal to ensure you have not overdone the carbs.

“Before you heal someone, ask him if he's willing to give up the things that make him sick.”
Hippocrates

…….THEN you tackle the upper fermenting gut

The Fermenting Upper Gut

The Human gut is almost unique in the mammal world. The upper gut is a sterile carnivorous gut (like a dog's) designed for digesting protein and fat. The lower gut is a fermenting vegetarian gut designed to utilise fibre (like a horse except humans cannot ferment that very tough fibre cellulose). This allows humans to deal with many different foods and part explains our success as a species. This system works perfectly until we overwhelm our ability to deal with sugars and starches. Bacteria and yeast colonise the hitherto sterile upper gut and start fermenting. This creates nasty symptoms and pathology. Why?

1. Foods are fermented to toxins such as ethyl, propyl and butyl alcohols, D lactate, ammonia compounds, hydrogen, hydrogen sulphide and much else. This fermentation is otherwise known as the auto-brewery syndrome. All these nasties have the potential to poison us, and this includes foggy brain. I just need a glass of wine to appreciate that fact!
2. Colonies of microbes, bacteria and fungi build up and are then further colonised by viruses (so called bacteriophages). Fermenting microbes produce bacterial endotoxin, fungal mycotoxins and viral particles.
3. These toxins spill over into the portal vein and so to the liver. The liver uses up much energy and raw materials to deal with these toxins. This is debilitating.
4. The gases generated by upper gut fermentation cause burping and bloating. They may distend the gut, and this is painful.

5. Microbes move into the lining of the gut and this low-grade inflammation results in leaky gut. This means that acid cannot be concentrated in the stomach because it leaks out as fast as it is secreted in. Acid is an essential part of digestion because-

i) it is essential to start the digestion of protein.
ii) it is necessary to absorb minerals.
iii) it sterilises the upper gut and protects us from infections.
iv) it determines gut emptying. A non-acid stomach does not empty correctly and this drive drives reflux, oesophagitis, heartburn and hiatus hernia.

6. Microbes, dead and alive, and undigested foods leak into the blood stream and drive pathology at distal sites. This is a major cause of pathology from inflammatory bowel disease, arthritis , fibromyalgia, connective tissue disease, auto-immunity, interstitial cystitis, urticaria, venous ulcers, intrinsic asthma, kidney disease, possibly psychosis and other brain pathologies such as Parkinson's disease.

7. Chronic inflammation of the lining of the gut results in cancer especially of the stomach and oesophagus. Both are on the increase. Diet is the main reason, followed by acid blocking drugs. These drugs also drive osteoporosis.

8. The inflamed gut results in the inflamed brain

Fermentation of fibre by friendly microbes should take place in the colon, the lower gut. The gasses which result and make you fart are hydrogen and methane. These farts are odourless. Put a match to them and they will explode ……not that I recommend this for diagnostic purposes! If your farts are offensive, then that is because you have overwhelmed your digestion upstream and proteins are fermented in the colon – rotting meat stinks! Short gut transit time will have a similar effect. Professor Gibson, a food microbiologist from the University of Reading, divides people into “inflammables” and “smellies” – the inflammables (hydrogen and methane) have normal gut fermentation and the smellies (hydrogen sulphide) do not! See https://www.reading.ac.uk/food/about/staff/g-r-gibson.aspx for Professor Gibson’s impressive research cv.

To treat the upper fermenting gut there is a three pronged approach

Starve them out with a PK diet.

Normalise digestion (start with mastic gum to encourage chewin)

Kill the little wretches with vitamin C to bowel tolerance (most end up with 6-8 grams daily). Take little and often through the day

Kill the little wretches with Lugol's iodine 15% 3 drops in water at night (appor 50mgs). Take vit C away from iodine

Start with low doses and build up slowly

Now you are in a fit state to tackle the mitochondrial engine

Your engine needs in addition to the correct fuel,

- the raw materials,
- freedom from toxic stress and the
- right control mechanisms (the thyroid accelerator pedal and the adrenal gearbox)
- regular servicing and repair (sleep)

During the 1990s I wondered if part of the pathophysiology of CFS was mitochondrial failure, but we had no test for this. Dr John McLaren Howard of Biolab initially started measuring the activity of respiratory enzymes in mitochondria. However it was clear from initial experiments that there was no correlation between the activity of enzymes and the clinical picture

John went on to develop a new test of mitochondrial function which involved qualitative and quantitative functional testing vis:

How much ATP is present in the cell cytosol and how well it can give up its energy in the cytosol to leave ADP. This is magnesium dependent.

How efficiently mitochondria can recycle ATP from ADP i.e. oxidative phosphorylation – and if going slow whether this is due to micronutrient deficiency or biochemical blocking

How efficiently mitochondria can move ATP out of mitochondria into the cell cytosol and recycle ADP back from the cytosol to the mitochondria again.

This qualitative testing allowed us to calculate a mitochondrial function score because…..

…….any one of these processes going slow, or a combination will result in poor energy delivery from mitochondria to the cell cytosol.

- If these processes are scored and multiplied, we have an objective measure of how well mitochondria can produce and recycle ATP.
- Initial experience suggested that the mitochondrial energy score accorded well with the level of disability in patients who had already sorted out other aspects of energy delivery such as diet, thyroid function, adrenal function and of course sleep.
- So we went on to test this in 71 patients

A study of 71 patients (2005-2008)

- All had received the basic work up with respect to diet, supplements, sleep, pacing, thyroid and adrenal function
- The patient and I (Dr Myhill) agreed a clinical ability score (Bell scale) between us.
- Bloods were sent to Acumen who undertook the test “blind” ie Dr John McLaren Howard did not know the ability score
- The ATP profiles were scored 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 Professor Norman Booth, Mansfield College Oxford University
- 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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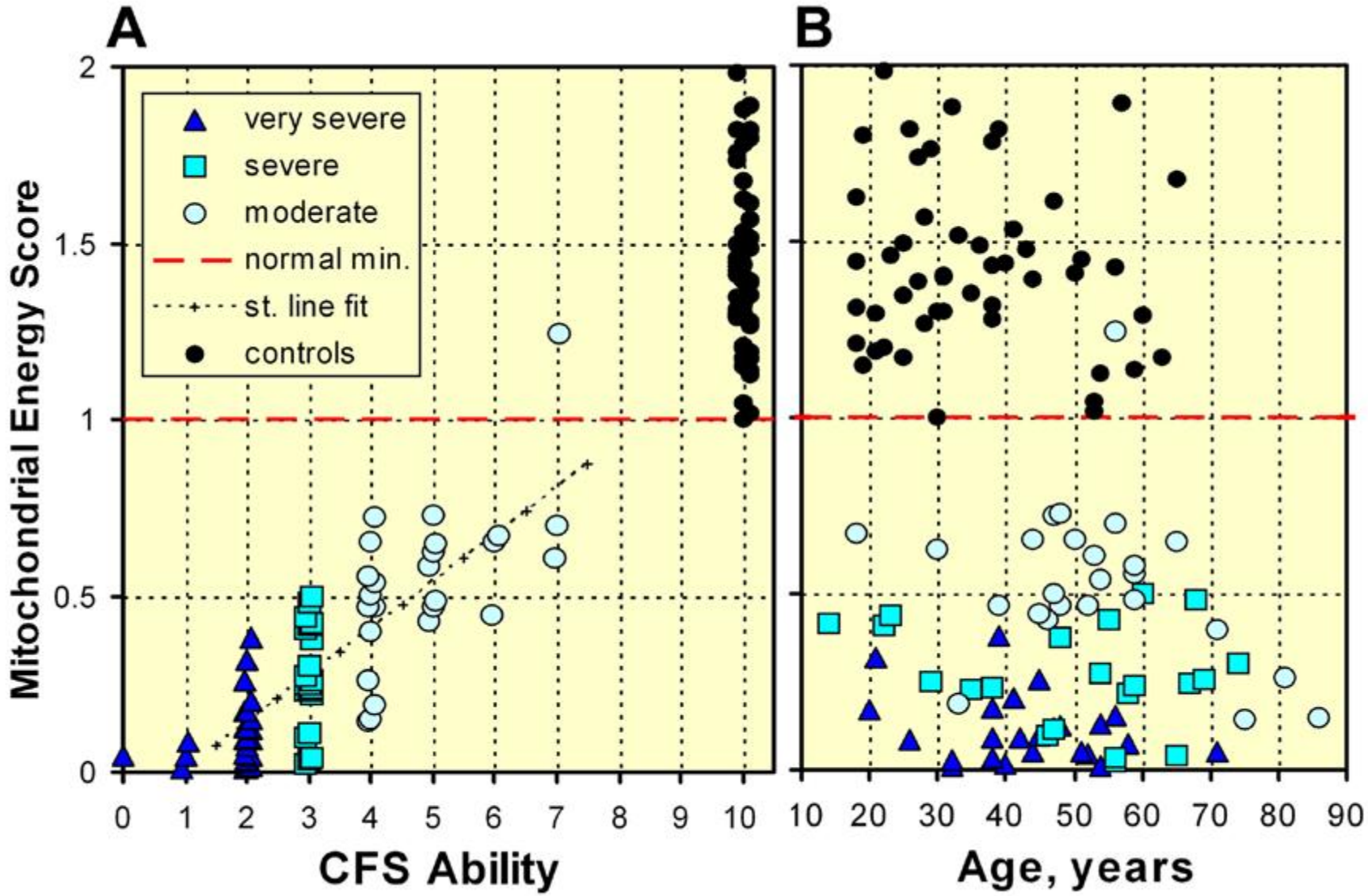
Abstract: This study aims to improve the health of patients suffering from chronic fatigue syndrome (CFS) by interventions based on the biochemistry of the illness, specifically the function of mitochondria in producing ATP (adenosine triphosphate), the energy currency for all body functions, and recycling 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.


A
B
very severe
severe
moderate
normal min.
st. line fit
controls
Mitochondrial Energy Score
0
0.5
1
1.5
2
0 1 2 3 4 5 6 7 8 9 10
CFS Ability
10 20 30 40 50 60 70 80 90
Age, years

We continued to collect data and were soon able to look at patients who requested follow up repeat testing. This became the subject of a third paper to address the question as to whether the prescribed regimes were clinically effective.

This was published in January 2013. *Int J Clin Exp Med 2013;6(1):1-15 www.ijcem.com /ISSN:1940-5901/IJCEM1207003 Original Article:*
Targeting mitochondrial dysfunction in the treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) – a clinical audit
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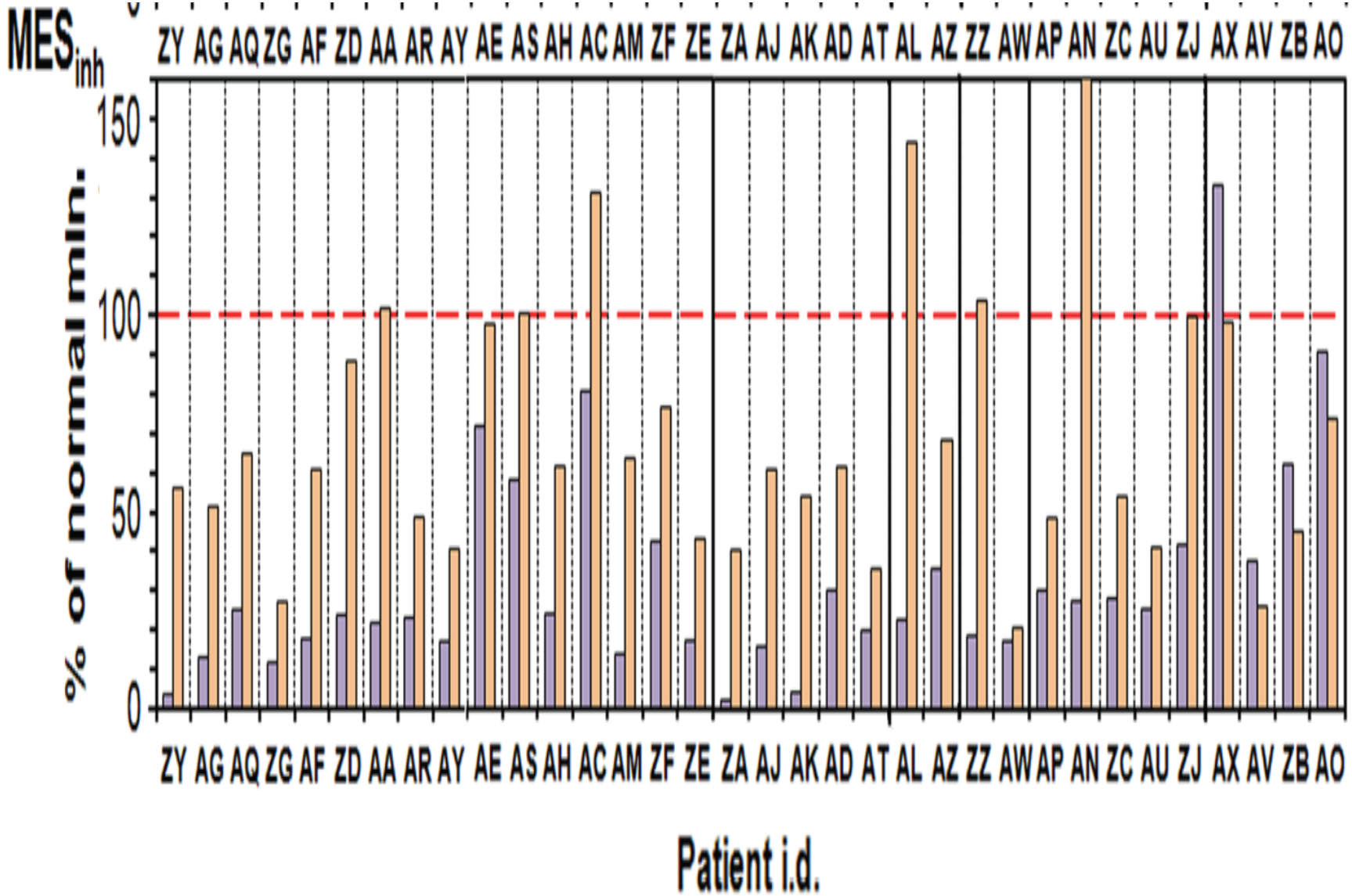
Abstract: We report on an audit of 34 ME/CFS patients who attended a private practice and took the ATP Profile biomedical test. The results revealed that all of these patients had measurable mitochondrial dysfunction. A basic treatment regime, based on

1) eating the evolutionary correct stone-age diet [*Now PK diet*] ,
2) ensuring optimum hours of good quality sleep,
3) taking a standard package of nutritional supplements, and
4) getting the right balance between work and rest, was recommended for all patients.

Additions to the basic regime were tailored for each patient according to the results of the ATP Profile and additional nutritional tests and clues from the clinical history.
Mitochondrial function is typically impaired in two ways:
substrate or co-factor deficiency, and
inhibition by chemicals, exogenous or endogenous.
For the former, additional nutrients are recommended where there is a deficiency, and for the latter, improvement of anti-oxidant status and selective chelation therapy or far-infrared saunas are appropriate.
We show case histories of nine patients who have taken the ATP Profile on three or four occasions, and a before-and-after treatment summary of the 34 patients who have had at least two ATP Profile tests separated by some months. Finally, we summarize the results for the 30 patients who followed all aspects of the treatment regime and compare them with the 4 patients who were lax on two or more aspects of the treatment regime.
All patients who followed the treatment regime improved in mitochondrial function by on average a factor of 4.


MES$_{inh}$
ZY AG AQ ZG AF ZD AA AR AY AE AS AH AC AM ZF ZE ZA AJ AK AD AT AL AZ ZZ AW AP AN ZC AU ZJ AX AV ZB AO
150
100
50
0
% of normal mln.
ZY AG AQ ZG AF ZD AA AR AY AE AS AH AC AM ZF ZE ZA AJ AK AD AT AL AZ ZZ AW AP AN ZC AU ZJ AX AV ZB AO
Patient i.d.

Acumen tests are no longer available, but Professor Koenig in Germany is now offering similar tests via AONM. We have the clinical experience to know what works from the above papers further borne out by the clinical experience of 1,036 patients who have undergone mitochondrial testing.

- Provide mitochondria with the correct fuel in the tank
- Provide mitochondria with the raw materials to work
- Reduce the toxic stress that is inhibiting ADP to ATP synthesis and translocator protein function
- Sort the control mechanisms – both thyroid and adrenal hormones and
- You need to put these interventions in place in the correct order

What are these raw materials that mitochondria need daily for the enzyme systems to work…….

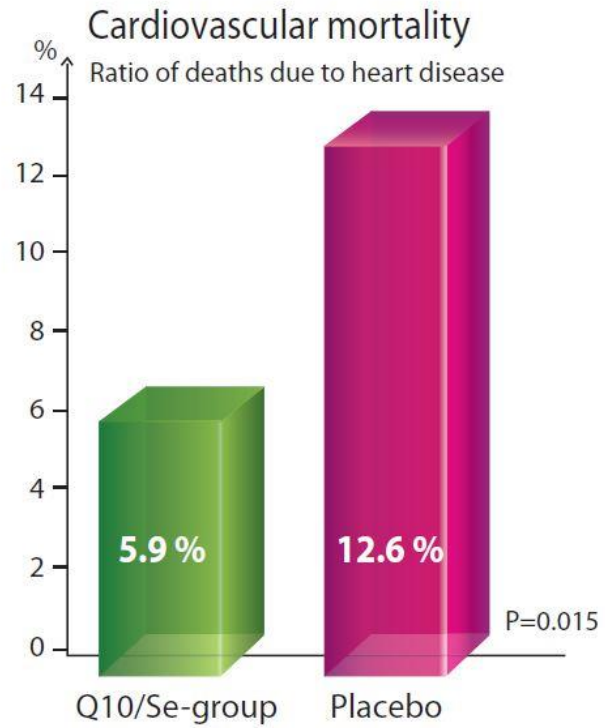
We do not need to test, experience shows that the below are the common essentials

- Co Q 10 100-300mgs as ubiquinol
- Magnesium 300mgs (absorption greatly enhance by vit D 10,000iu daily). Possibly Mg injections
- Niacinamide 1500mgs daily
- Acetyl L carnitine 500-2,000mgs
- Vit B12 1-5mgs daily (possibly injections)
- D ribose 5-15grams daily – but has to be part of the PK diet carb count. I suggest using this as a rescue remedy to shorten recovery time if the patient has over-done their activity.

These tests of toxicity and nutrition can be accessed at other labs for example:
Biolab for co Q 10, NAD activation for niacinamide, red cell magnesium

Genova, Great Plains

Kisel-10 study A total of 443 male and female volunteers aged 70-88 years took part in the five-year study, which was carried out by researchers from Linköping University and Karolinska University Hospital. The trial was headed by Associated Professor Urban Alehagen, a cardiologist from the Heart Center of Linköping University, in collaboration with, among others Professor Ulf Dahlström



A significant reduction of cardiovascular mortality in the Q10/Se-group (5.9% vs. 12.6%; P=0.015).

Problem	Remedy
Lactic acid	Must pace activity more carefully
Products of the fermenting gut	PK diet, vitamin C to bowel tolerance, iodine mastic gum
Diamino compounds eg dyes from hair, foods, drugs	Avoid
Parabens (widely used disinfectant eg in toothpaste) Polybrominated biphenyls - fire retardants in soft furnishings Pesticides Nickel (jewellery) mercy (dental amalgam) and other toxic metals	Avoid Get rid with heating regimes (eg sauna, hot bath, sunbathing followed by washing off in shower) Detoxify with multi-minerals and glutathione 250mgs daily May need chelation therapy – I use oral DMSA(captomer) 15mg/kg weekly dose
Malondialdehdye – a result of poor anti-oxidant status	Improve anti-oxidant status especially with vitamin B12 injections and vitamin C to bowel tolerance
Mycotoxins, viral proteins, immunogloblins	Look for an infectious cause. See “The Infection Game”

Broadly speaking there are four groups of toxin that demand different methods of diagnosis and treatment:
First avoid……..then get rid

- Products of the upper fermenting gut
- Pesticides and volatile organic compounds (measure with urine test and detox with heating regimes).
- Toxic metals (measure with urine test with DMSA and detox with several nutritional interventions. Toxic metals are not excreted with heating regimes)

- Bacterial endotoxin and fungal mycotoxins, immune mediators (cytokines, immunoglobulins etc) – for diagnosis and treatment see “The Infection Game”

I have now collected data from over 30 patients who have undergone tests of toxicity both before and after these heating regimes. The tests have been chosen for particular situations but include fat biopsies, translocator protein studies and DNA adducts. The tests prove to my satisfaction that heating regimes are effective. These heating regimes include sauna: traditional and far infrared (FIR); and Epsom Salt hot baths. I would expect sun-bathing and exercise to be just as effective. Indeed, similar research was conducted by Dr William Rea in America and he used similar regimes of massage, gentle exercise, saunaing and showering to achieve very similar biochemical results.
Journal of Nutritional & Environmental Medicine (1996) 6, 141-148

My experience, roughly speaking, is that 50 episodes will halve the body load. One would expect chemicals to come out exponentially - so one never gets to zero, but one ends up in some sort of equilibrium with the environment which is a low as reasonably possible. Indeed, because we live in such a toxic world, I think we should all be doing some sort of heating regime at least once a week - -I am lucky enough to be able to exercise – I deliberately overdress to make sure I get hot and sweaty then shower off subsequently – what a treat that is!

Epsom salt baths are ideal as one detoxs through the skin an dabsorbs magnesium and sulphate – which further help. You can order from https://epsomsalts.co.uk/ in kilogram amounts. 500grams per bath – if you do not have a bath use a portable bathtub in your shower

Zinc, selenium and magnesium	Displace toxic metals from binding sites in the body…….	Zinc 50mgs, selenium 500mcgms Magnesium 300mgs - no oral max dose but diarrhoea if too much
Glutathione	……..so the toxic metals can be picked up by glutathione and excreted	No max dose but 250-500mgs is usual
Vitamin C to bowel tolerance	Vital anti-oxidant – the final repository of free radicals	The dose is key and everyone is different
	Binds to toxic metals so they can be excreted in urine	Vitamin C also pulls out friendly minerals so it is vital to take sunshine salt to replace the ‘lost’ ‘good’ minerals
Iodine	Binds to toxic metals so they can be excreted in urine	Lugol’s iodine 15% 3 drops at nigh t (approx. 50mgs)
High fat diet. Several dessertspoons of organic hemp oil	“Washes out” the polluted fats in the body and replaces with clean. Phospholipids can be given intravenously to good effect	Oral fats and oils probably work as well as IV but it takes much longer
Vitamin B12 and correcting homocysteine	Improves the methylation cycle - sticking a methyl group onto toxins renders them water soluble so they are peed out	B12 extremely safe. Take at least 5mgs sublingually daily. Consider B12 injections.
	If homocysteine low then correct with	Methyl B12 as above, methyl B6 (pyridoxal 5 phosphate) 50mgs and methyltetrahydrofolate 800mcgms daily
Adsorbant clays	Mop up toxins in the gut	3 grams at night

Now the mitochondria are sorted, THEN we tackle the control mechanisms – the thyroid accelerator pedal and the adrenal gearbox

Both thyroid hormones and adrenal hormones impact on energy delivery mechanisms through their effects on mitochondria.

Thyroid hormones “base load” metabolic rates, They do this is two ways – firstly they speed up the rate at which mitochondria run AND they determine the numbers of mitochondria (a faster engine and a bigger engine)

Adrenal hormones adjust for second to second, minute to minute, hour to hour fine tuning

This is why it is so important to do things in the correct order – without mitochondria in a fit state to respond, you are “flogging a dead horse”
https://quadrant.org.au/opinion/zegs-take/2012/10/flogging-her-dead-horse/

Energy delivery mechanisms - thyroid and adrenal function

- The thyroid and adrenal glands that allow us to closely match energy delivery to energy demands. To do otherwise is disaster:

- If you cannot immediately gear up energy production to deal with, for example, a predator then the prey is caught and dies

- If you spend energy wastefully then one my not survive winter or a famine

Symptoms of an underactive thyroid are all those of poor energy delivery mechanisms – but there are also thyroid specific symptoms

Mechanism	Symptom	Notes
Fluid retention and oedema	Puffy face	Compare current looks with old photographs
	Large tongue	You may see indentations from where teeth lie against the tongue
	Obstructive sleep apnoea perhaps with snoring	Because the tissues of the throat are swollen, and this constricts the airways
	Voice changes	The vocal cords are puffy
	Swollen, puffy legs, most obvious in the ankles at the end of the day	A cause of non-pitting oedema
	Nerves get squashed E.g., carpal tunnel syndrome Sciatica	
Poor fat burning	Ketogenic hypoglycaemia (on a PK diet you need thyroid hormones to fat burn – if low, then fat burning is done with adrenalin, and this gives all the symptoms of low blood sugar) Inability to lose wt even when keto-adapted	The symptoms of low blood sugar are not due to low blood sugar but the adrenalin (and other hormonal) responses to low blood sugar.

SLEEP DISTURBANCE	POOR QUALITY UNREFRESHING SLEEP	THIS IS WELL RECOGNISED IN HYPOTHYROIDISM BUT THE MECHANISM UNCERTAIN. IT MAY BE IN PART SLEEP DISTURBANCE BY KETOGENIC HYPOGLYCAEMIA
	Being an owl (drop off to sleep late, wake late) and so feeling “jet-lagged”	There are at least three groups of hormones for quality sleep and correct diurnal rhythm. Light inhibits melatonin production, dark stimulates such. Melatonin stimulates the pituitary and so TSH spikes at midnight. Then T4 spikes at 4am, T3 at 5am and this stimulates the production of adrenal hormones which wake you up.
Proximal myopathy i.e., as symmetrical weakness of proximal upper and/or lower limbs	May present with difficulty climbing hills or stairs, trouble getting out of or bath or off the floor or even up from a chair. Or getting on to a horse! Press-ups become impossible!	Often misdiagnosed as lack of fitness
Constipation	I am not sure of the mechanism of this – probably a combination of poor energy delivery, being cold together with oedema of the gut	Constipation is often an early symptom to improve once the underactive thyroid has been corrected
Headaches	Again, I am not sure of the mechanism of this	But clinically, headaches often settle

Signs of energy delivery mechanisms

Symptom	Mechanism	Notes
Low core temperature E.g., below 36.6 degrees centigrade	Poor energy delivery	Monitoring core temperature is helpful to get the dose of thyroid and adrenal supplements right – see chapter 4
Low blood pressure E.g., below 110/70	Poor energy delivery to the heart and so it cannot beat powerfully	This may well be masked by the adrenalin of metabolic syndrome (a pre-diabetic condition) or ketogenic hypoglycaemia
Slow pulse, i.e., less that 70bpm in a non-athlete	The thyroid is largely responsible for the resting pulse rate	A normal person, not in athletic training should have a resting pulse of 70-75 beats per minute Again, this may be masked by adrenalin as above

Which tests to ask for to start to assess the thyroid:

- The bare minimum of testing that is required is the measure levels of:
- TSH
- free T4
- free T3

(if there are abnormalities then check for thyroid antibodies to look for autoimmune damage. Why? With one autoimmune disease there is increased risk of others. AND to prevent such we need to address the risk factors namely vit D deficiency, metabolic syndrome and vaccination)

A trial of thyroxine, NDT, or glandulars such as Metavive)

Start low dose and increase in small increments every 2 weeks

Monitor pulse and blood pressure and core temps – pulse should be less than 85bpm, BP 120/80 or less, core temp 37degrees C or less AND the symptoms

NDT start with ¼ grain – build up in ¼ grain weekly increments and monitor response as above.

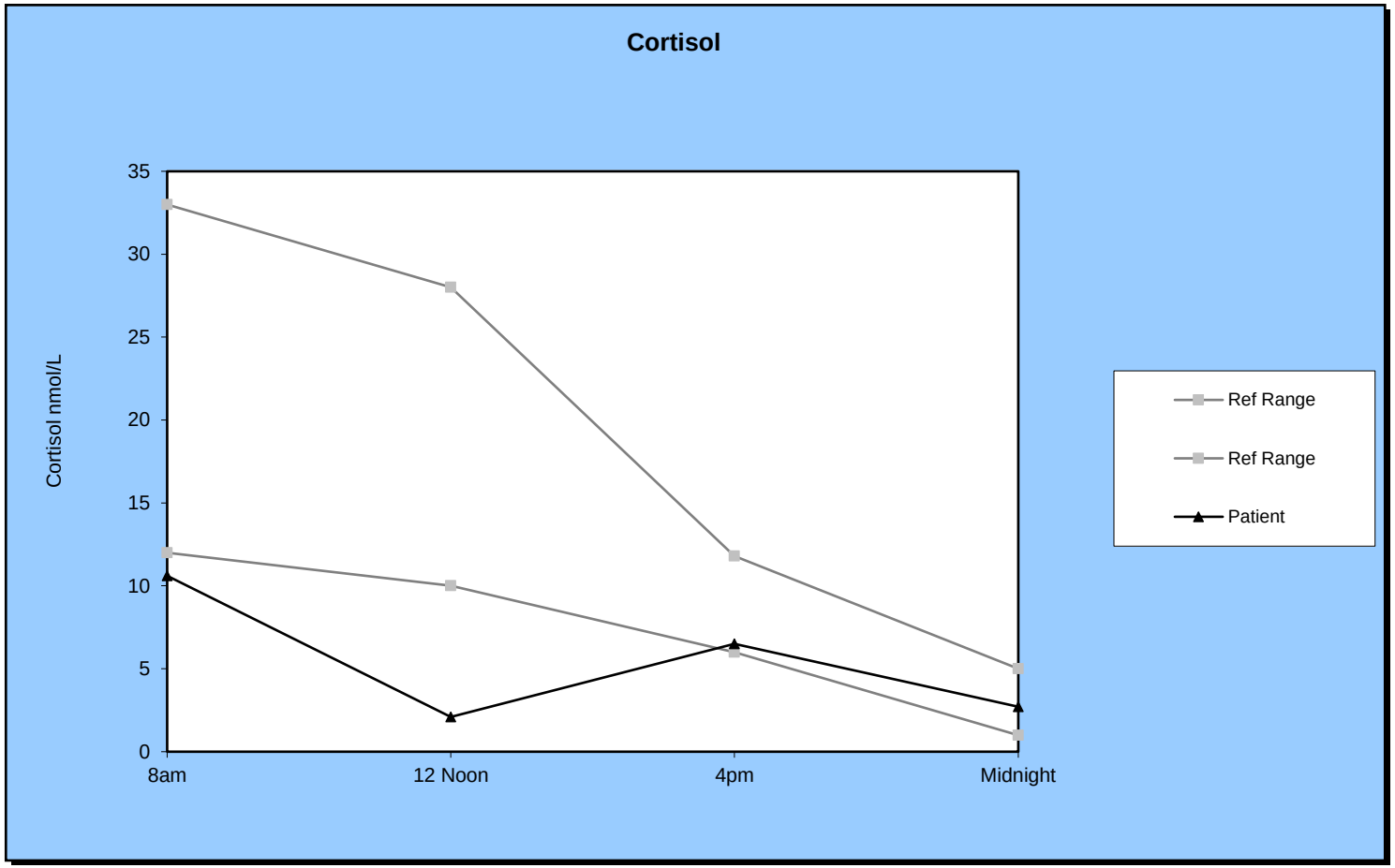
Eg Armour thyroid, Thyroid S, Naturthroid,

The final dose is also weight related

Typical daily doses are

- up to 9 stone – 1-1 ½ grains
- up to 12 stone – 1 ½ to 2 grains
- up to 15 stone – 2- 2 ½ grains
- Above 15 stone – 3 grains

A typical CFS/ME adrenal stress profile test result showing low levels of cortisol and DHEA.



Treatment of adrenal fatigue

There is a two pronged approach:

- Identify the cause of the unremitting stressor: metabolic syndrome (carbs and deficiencies), immunological (infection, allergy, auto-immunity), mental, emotional (PTSD), social (families!), financial etc
- Use adrenal support such as pregnenolone (25-100mgs) DHEA (25-100mgs) adrenal glandulars. Take subling on rising.
- Adjust the dose using core temperatures – we can use this to “fine tune”.

Conclusion

To improve mitochondrial function you have to do it all and you have to do it in the right order:

1	**MUST start with the PK diet** **Ensure you are in ketosis using a ketone breath meter**	**If you are eating carbohydrates you will have a fermenting gut. Taking supplements will feed the fermenting gut!**	**Chapter 6 and 17**
2	**Then take vitamin C, at least 5 grams daily, probably more, little and often through the day** **Lugol's iodine 15 % 3 drops at night**	**This helps kill upper gut fermenters, facilitates the absorption of minerals, protects you from infection, helps detox and improves anti-oxidant status**	**P 235**
3	**Then take the Basic Package of supplements**	**Now you will absorb these well**	**Chapter 18**
4	**Then take the mitochondrial package of supplements**	**Now you will absorb these well**	**Chapter 4**
5	**Then balance up the adrenal gear box and thyroid accelerator pedals**	**These glands work by kicking mitochondria into action. You need mitochondria in a fit state to respond**	**Chapter 5**
6	**If you suspect a toxicity problem**	**Put in place detox regimes**	**Chapter 20**
7	**If you suspect an immunological hole in the energy bucket**	**Consider tests to identify what?**	**Chapters 9, 10, 11, 12 and 13**
8	**If you suspect an emotional hole in the energy bucket**		**Chapter 21**
	REMEMBER – you must pace throughout so you do not suffer post-exertional malaise	**Chronic production of lactic acid inhibits mitochondria and slows recovery**	
	EXPECT - to have a bumpy ride	**All the above may cause short term worsening because of diet, detox and die off reactions.** **See https://www.drmyhill.co.uk/wiki/Diet,_Detox_and_Die-off_Reactions_-_expect_to_get_worse.**	
	BE SATISFIED with gentle progress in the right direction	**It takes six months for the body to heal and repair and this demands energy too**	
	IF YOU GET STUCK join a workshop	**https://drmyhill.co.uk/wiki/Workshops_for_Ecologi**	