Diagnosing and managing mitochondrial dysfunction in disease – and what to do about it!

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AONM

Academy of Nutritional Medicine

Feb 2025

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NHS GP (1981-2000)
Independent General Practice 2000-2021
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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"
"The Underactive Thyroid" – do it yourself because your doctor won't"

Life is not a battle but a war

It is a war that we fight for life. It is a war we know we are going to lose, what if I lose my war age 102 then I will settle for that!

Start fighting now.

We have to put in place all interventions that are biologically plausible, affordable and sustainable so that they can be readily integrated into normal life.

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

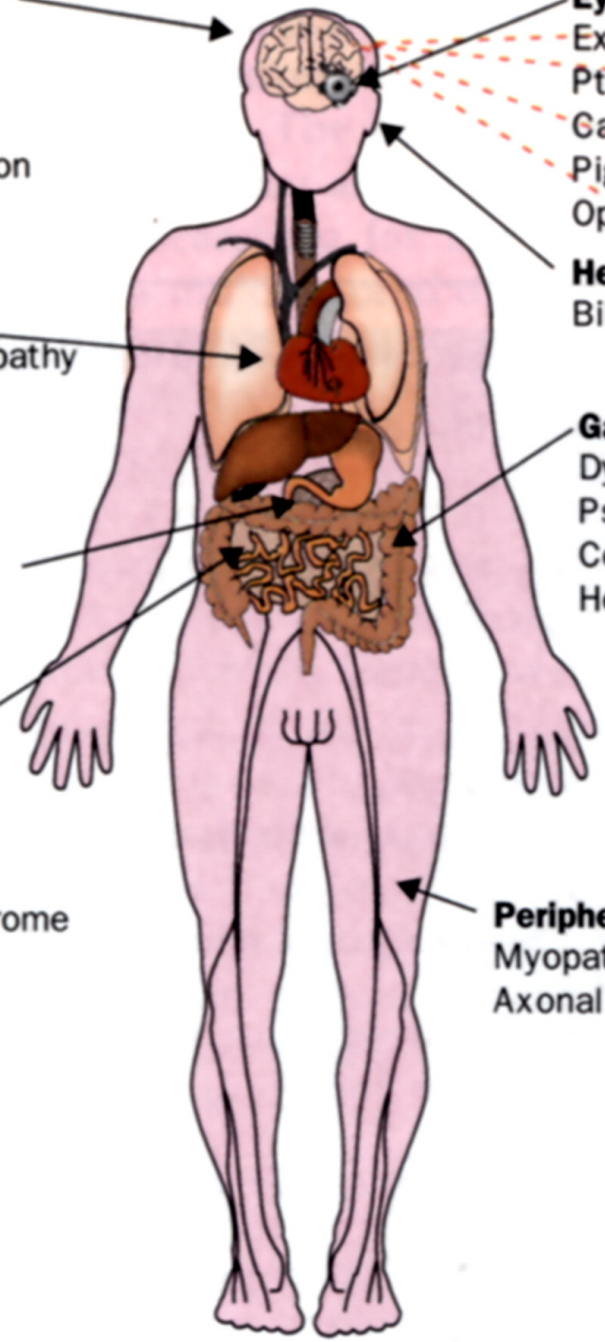
Renal
Renal tubular defects
Toni-Fanconi-Debre syndrome

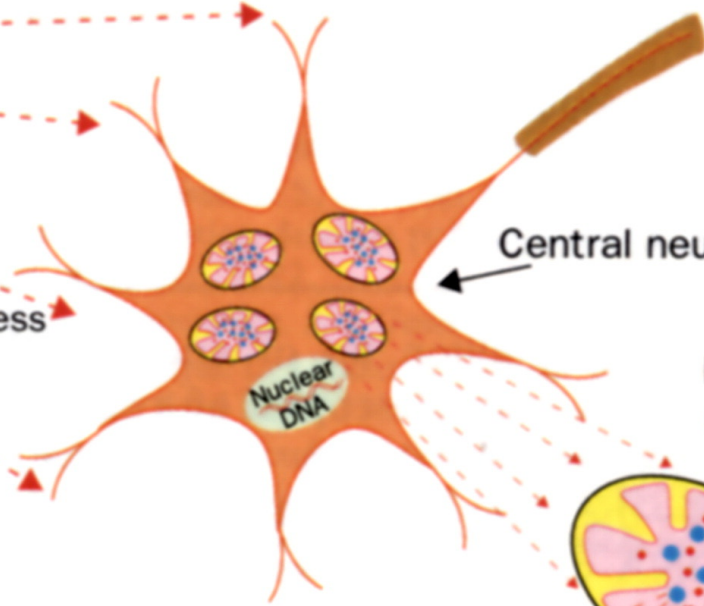
Eye
External ophthalmoplegia
Ptosis
Cataract
Pigmentary retinopathy
Optic atrophy

Hearing
Bilateral sensorineural deafness

Gastrointestinal
Dysphagia
Pseudo-obstruction
Constipation
Hepatic failure

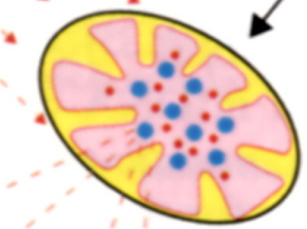
Peripheral nervous system
Myopathy
Axonal sensorimotor neuropathy

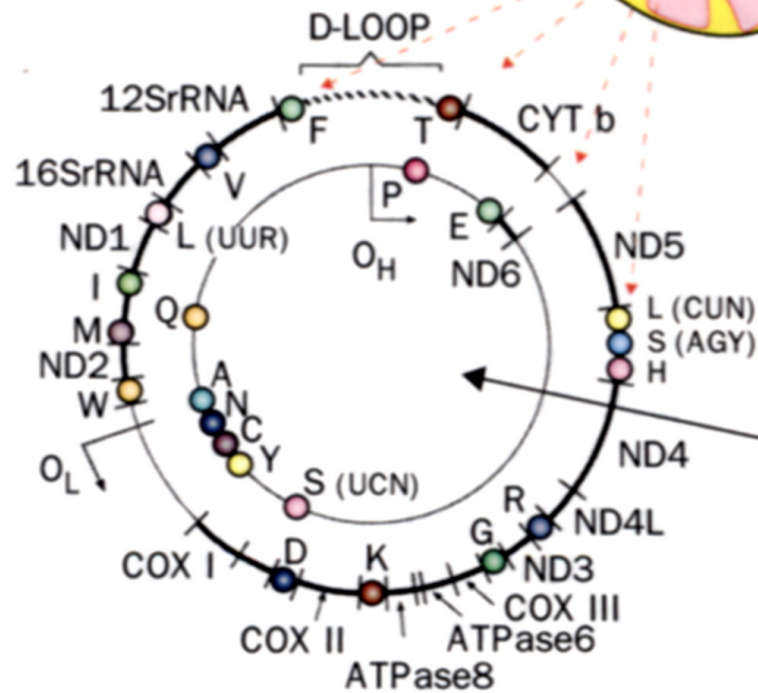




Central neuron

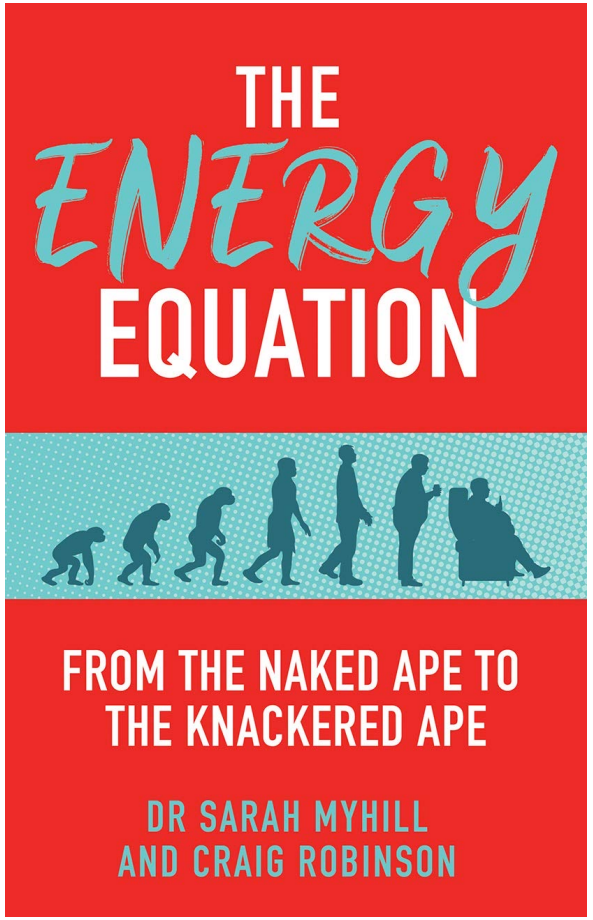
Heteroplasmic mitochondrion





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 or damaged by some toxin

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

Poor quality exclusion zone water – which need background EM radiation (heat) for its structure

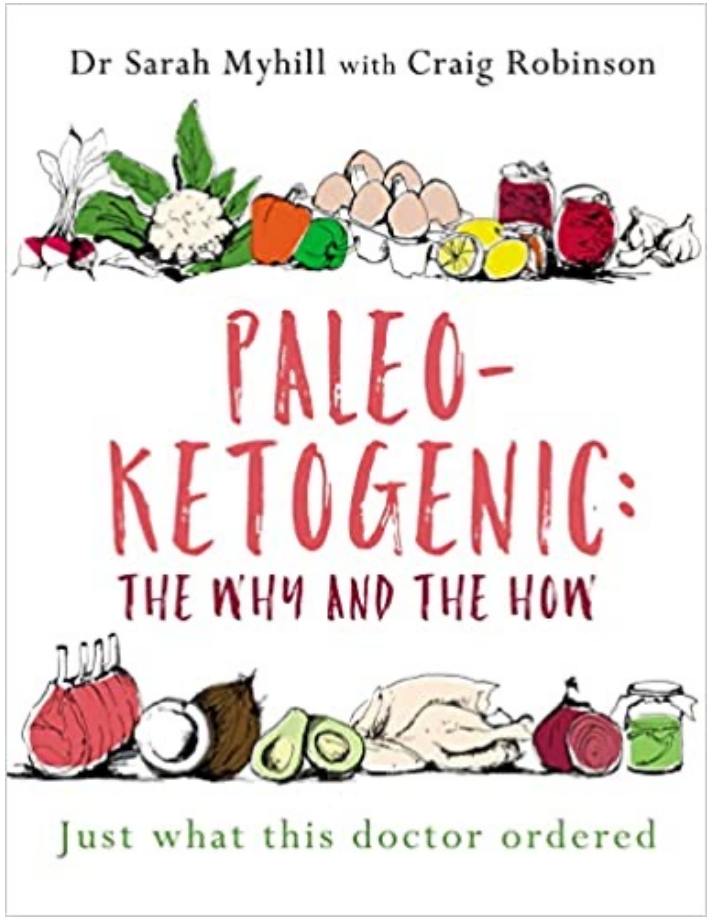
How the body generates energy for life. FIRST the fuel in the tank

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!



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

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.

You can now get very similar tests

Through AONM

https://aonm.org/mitochondrial-testing-with-aonm-prof-dr-brigitte-konig/

The tests available include

https://aonm.org/summary-of-mitochondrial-tests/

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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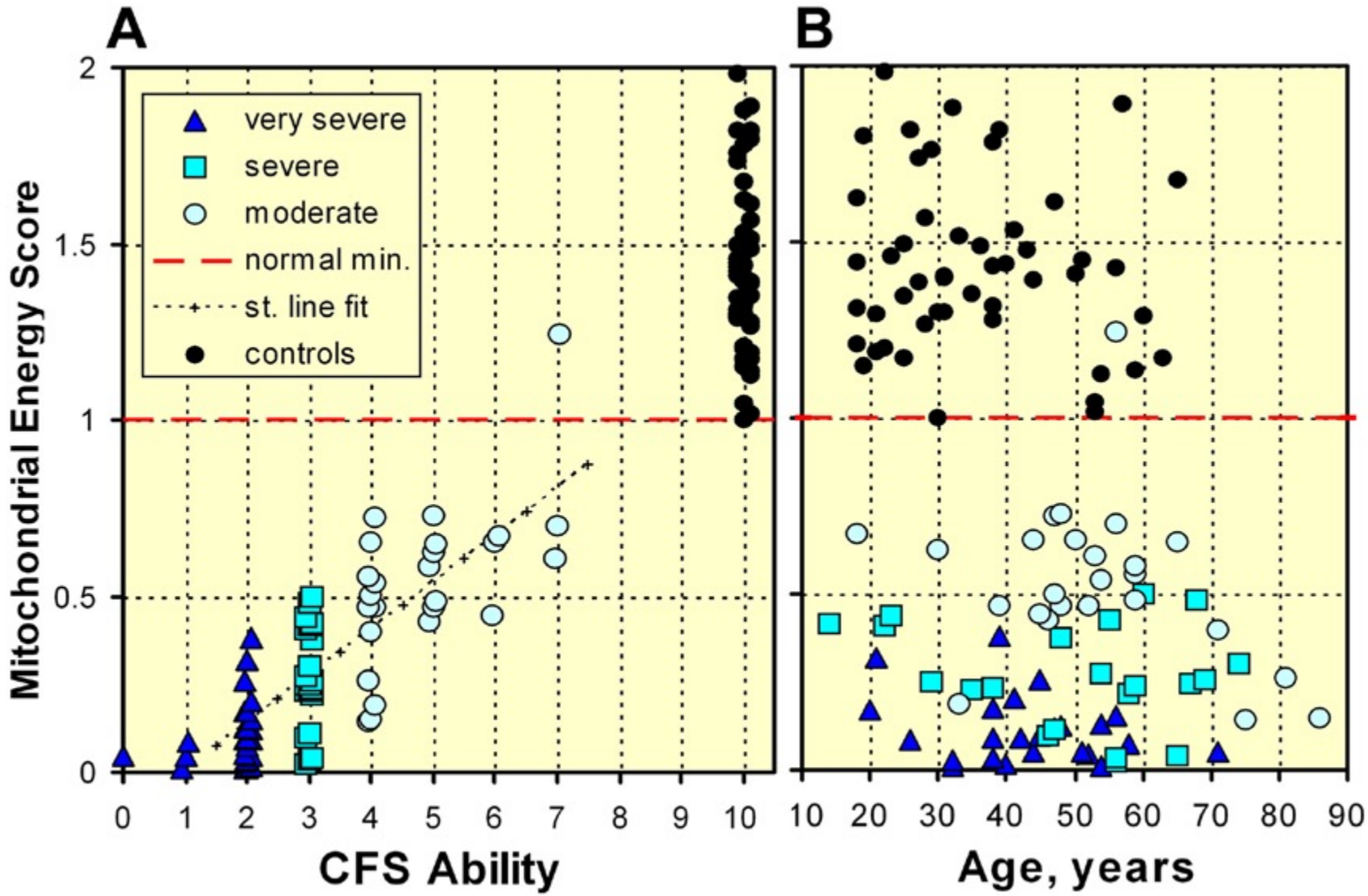
Received December 2, 2008; accepted January 12, 2009; available online January 15, 2009

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
2
1.5
1
0.5
0
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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Received July 10, 2012; Accepted October 11, 2012; Epub November 20, 2012; Published January 1, 2013

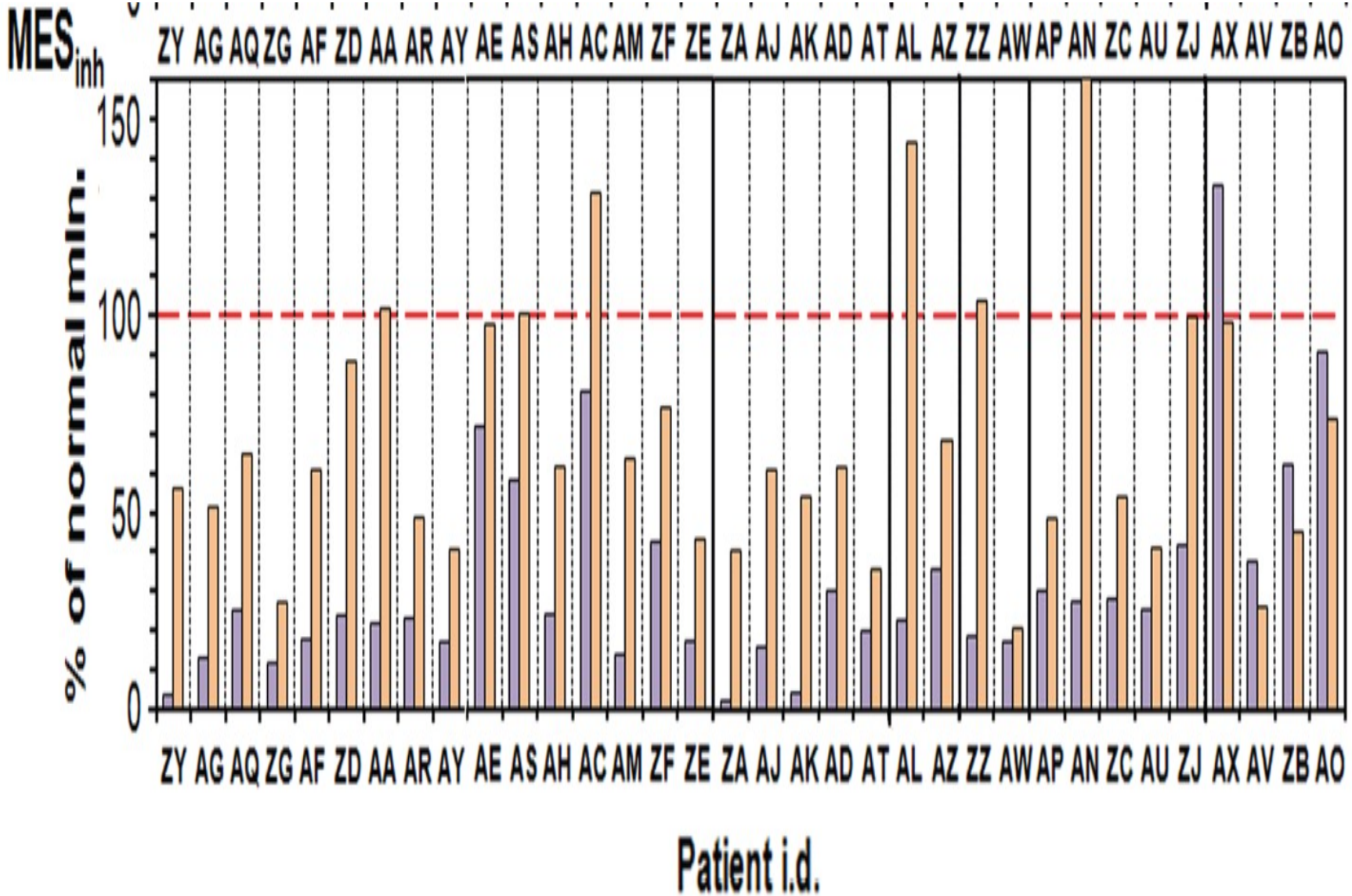
Abstract: We report on an audit of 34 ME/CFS patients who attended a private practice and took the ATP Profile biomedical test. The results revealed that all of these patients had measurable mitochondrial dysfunction. A basic treatment regime, based on

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 however Professor Koenig is offering very similar tests through AONM.
However we have the clinical experience to know what works from the above papers further borne out by 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
- Take melatonin (the major anti-oxidant within mitos responsible for mopping up free radicals) – up to 50mgs at night

https://pipingrock.com/en-gb/products/melatonin-10-mg-120-tablets-4231

- Sort the control mechanisms – both thyroid and adrenal hormones
- Heat (Sunshine, FIR sauna, warm baths etc)
- You need to put these interventions in place in the correct order

What are the 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

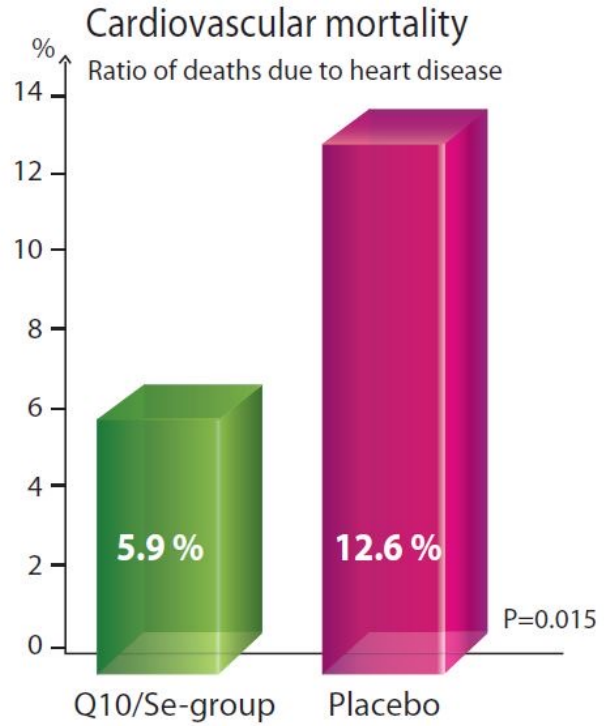
Genova, Great Plains

The importance of Co Q 10 in preventing cardiovascular disease

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 Dahlströmhttps://www.kisel-10.co.uk/

Selenium 200mcgms and Co Q 10 200mgs was the dose used

This halved the cardiovascular mortality



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

What may block mitochondria?
We know this from Acumen studies of the rate of oxidative phosphorylation and through translocator protein studies.

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, vitamin C 5grams daily with melatonin at night
Mycotoxins, viral proteins, immunogloblins	Look for an infectious cause. See “The Infection Game” Tests from Armin laboratories

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

TABLE 3. Symptom score and blood toxic chemical levels[a]

Description	Before sauna	After sauna	*P*-value
Sign and symptom scores	2100 units	210 units	<0.001
Blood toxic chemical levels	100%[b]	63% lower	<0.001
		18% higher	
		19% same	

[a]Pentachlorophenols, polychlorinated biphenyls, volatile aliphatic and aromatic chlorinated and non-chlorinated hydrocarbons and organochlorine pesticides.

[b]Above the detection limit.

TABLE 7. Complications of therapy in 210 patients

Symptoms	Number	Percentage
Hyperthermia	2	1.0
Initial exacerbation of original symptoms	200	95.2
Seizure[a]	1	0.5
Passing out	4	1.9
Gastrointestinal (bloating, gas, diarrhea, nausea/vomiting)	40	19.0
Increased liver enzymes	100	47.6
Cardiovascular (edema, tachycardia)	20	9.5
Muscular aches	80	38.1

[a]Patient discontinued Dilantin medication without notifying physician.

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 detoxes 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 Aim for 5 grams daily
	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 night (approx. 50mgs)
High fat diet. Eat organic	"Washes out" the polluted fats in the body and replaces with clean.	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.
	We should all know out homocysteine! Measure this at https://foodforthebrain.org/product/homocysteine-hcy/	If homocysteine low then correct with Methyl B12 as above, methyl B6 (pyridoxal 5 phosphate) 50mgs and methyltetrahydrofolate 800mcgms daily
High fibre diet	Mop up toxins in the gut	

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

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”.

When energy delivery mechanisms are working well the core temp should lie between 36.6 and 37.4 degrees centigrade

Use an infrared body thermometer. Cost approx. £12.

Take a deep breath, hold it for a few seconds so the inhaled air comes up to core temperature.

Breathe out slowly through an open mouth and point the thermometer at the back of the throat as you exhale. The sensor will be partly in the mouth cavity.

Press the button to activate the thermometer - -it will bleep in a couple of seconds to give you a true reading

(Do not do this whilst taking a hot drink or you may get a false high)

Conclusion

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

AND we should all b e doing as much of this stuff as is possible for a lnog an healthy life!