

A Burning Question: Can Niacin Help Mitochondrial & Blood Vessel Issues in ME/CFS, FM and long COVID?

by Cort Johnson | Apr 9, 2022 | Cardiovascular, Endothelial Cells, Energy Enhancers, Energy Production, Homepage, Supplements | 57 comments



I tried to lay as still as possible. It felt like I'd swallowed a stick of dynamite that was slowly detonating. Any movement at all would send what seemed like waves of molten lava cascading inside me. As the burning sensations slowly eased, though, I felt an unusual state of clarity and calmness. My rushing mind and brain fog were gone. I was at peace.

That was my introduction to niacin (vitamin B3) – at the 500 mg level, no less – something I would not recommend as a starter dose. Over the past five years, I've used niacin intermittently and the effects have varied. Sometimes it does nothing at all. Other times, though, it produces 30 minutes or more of astounding calmness and clarity.

I have the idea that niacin's flushing action – which leaves you with a burning sensation and your skin reddened for a period of time – may be needed for me to have positive effects but am not sure. Sometimes the flush occurs quickly; other times it can pop up unexpectedly half an hour or more later.

Something is definitely going on. I rarely respond so quickly and well to anything. I had never heard of niacin being used in chronic fatigue syndrome (ME/CFS) or fibromyalgia (FM) until I learned that Dr. Kerr in Toronto recommended it for some of her ME/CFS patients – presumably for its detoxification purposes.

Niacin, though, is a fascinating compound that intersects with several issues found in ME/CFS. The niacin blog is part 6 in a series of possible mitochondrial enhancers for ME/CFS, FM, and long COVID.

The Mitochondrial Enhancers for Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia and Long COVID Series



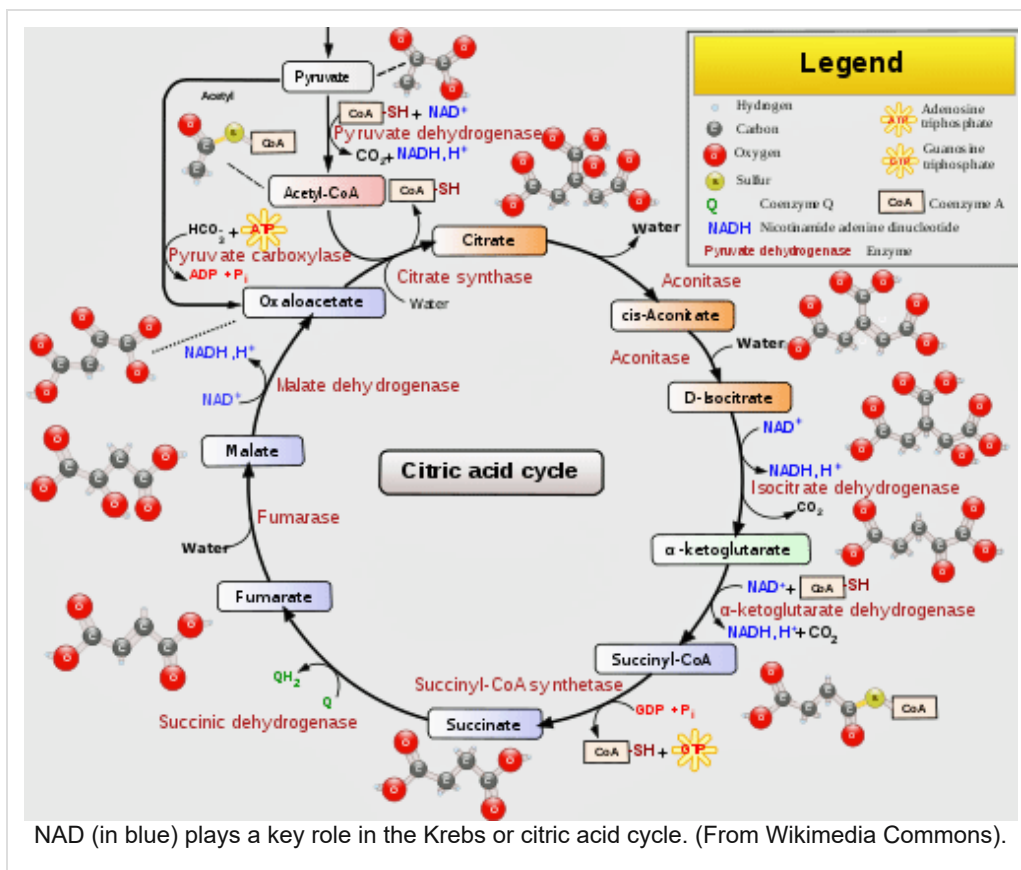
It felt like I'd swallowed a stick of dynamite.

- Pt. I: D-Ribose, CoQ10 and PQQ
- Pt. II: L-carnitine and Acetylcarnitine
- Pt. III: Magnesium
- Pt. IV: N-acetyl cysteine (NAC)
- Pt. V: Oxaloacetate
- Pt. VI: Niacin, Nicotinamide, and Nicotinamide riboside

Electron Transfer Maestros

Nicotinamide adenine dinucleotide (NAD) and its phosphorylated form, NADP, are **electron transfer maestros** that are able to readily and easily form oxidized and reduced forms of themselves. In its oxidized form (NAD⁺), NAD accepts electrons from other molecules, which results in it becoming reduced and forming NADH.

If, for instance, you look at the Krebs or citric acid (or tricarboxylic acid cycle (TCA)) – all names for the same thing – you'll see NAD⁺ or NADH again and again – because they are major outputs of the cycle. The NADH produced in the TCA cycle then kicks off electron transport chain activity by donating electrons to Complex #1. The upshot is that NAD's nimble redox activities allow it to play a key role in energy generation.



NAD also acts as a **coenzyme in redox** (reduction/oxidation) reactions and plays a role in the ubiquitous **ADP-ribosylation** reactions that are involved in many cellular processes (cell signaling, DNA repair, gene regulation, apoptosis.) NAD⁺'s regulation of two enzyme families (PARPs, sirtuins)

also allows it to coordinate the strength of the **inflammatory response** and fight off pathogens. Some believe NAD+ boosters may function as anti-inflammatories and pathogen fighters.

Plus reduced NAD+ levels may prevent a cell from producing an effective response to a pathogen. Several viruses (HIV-1, herpes simplex virus 1, hepatitis C, and the SARS-CoV-2) have been associated with lower NAD+ concentration in immune or muscle cells. Other studies suggest that the metabolic pathways associated with NAD+ get highly upregulated during coronavirus infections.

Mitochondrial Supplement?

A small Finnish study found that NAD+ supplementation helped people with mitochondrial myopathies. That was intriguing as both **mitochondrial myopathies** and ME/CFS share the unusual characteristic of exercise intolerance as well as muscle fatigue and weakness. The symptoms in mitochondrial myopathies are often first noticed around the age of 20 when a person develops exercise intolerance or muscle weakness. The National Institutes of Neurological Disorders and Stroke (NINDS) description of “**exertional fatigue**” sounds uncannily like ME/CFS/FM.

“Exercise intolerance, also called exertional fatigue, refers to unusual feelings of exhaustion brought on by physical exertion. The degree of exercise intolerance varies greatly among individuals. Some people might have trouble only with athletic activities like jogging, while others might experience problems with everyday activities such as walking to the mailbox or lifting a milk carton.”

Symptoms can vary widely and can include some not often found in ME/CFS such as stroke-like episodes, problems with eye mobility, droopy eyelids, hearing loss, and others. Depending on the tissues affected, mitochondrial myopathies can cause a multitude of symptoms.

Different forms of mitochondrial myopathies exist, but in general, they’re described as “neuromuscular diseases caused by damage to the mitochondria”. Because nerve cells in the brain and muscles require the most energy, they’re the most likely to be affected.

Several case reports suggest that mitochondrial myopathies may, at times, be masquerading as FM or ME/CFS. In 1999, an Italian group described a case of **mitochondrial myopathy misdiagnosed as fibromyalgia**. Dr. Ambrus described a woman with **mitochondrial myopathy and fibromyalgia** who responded to mitochondrial supplements (which did not include NAD). Similarly, in 2015, a Spanish group described a 30-year-old Ph.D. student with ME/CFS who was found to have **mitochondrial myopathy**.

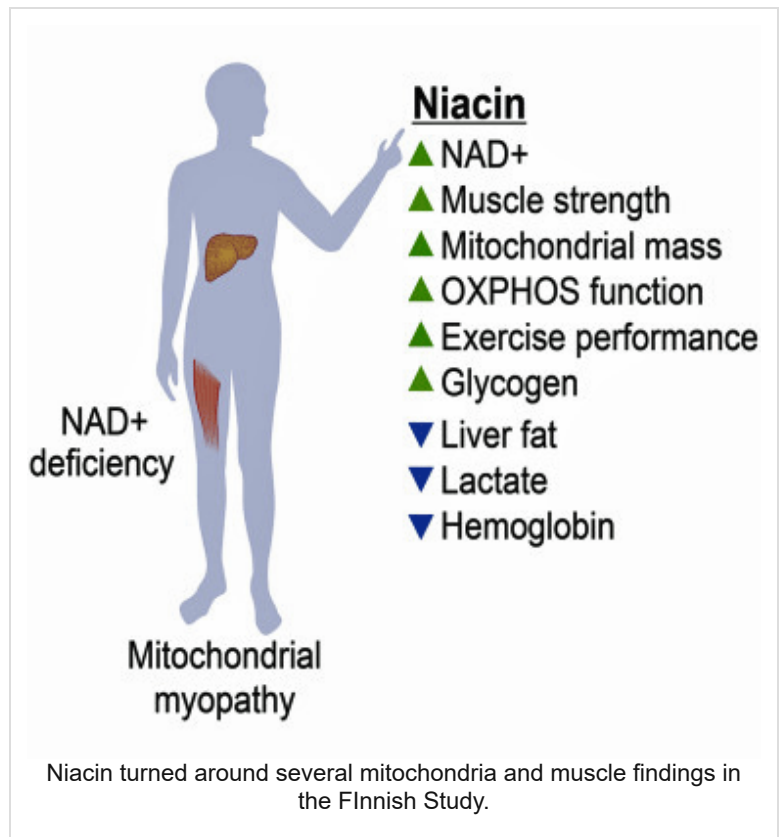
The tests needed to ferret out these issues are rarely done in either of these diseases.

The Finnish Study

Niacin isn’t often thought of as a mitochondrial supplement, but mouse models suggest that mitochondrial myopathies are associated with reduced cellular NAD+ levels. The recent Finnish study, “**Niacin Cures Systemic NAD + Deficiency and Improves Muscle Performance in Adult-Onset Mitochondrial Myopathy**”, appears to have been the first study to assess niacin in mitochondrial myopathy – but will surely not be the last. Biopsies revealed 2fold lower levels of NAD+ in the muscles of mitochondrial myopathy patients.

The participants started off with 250 mg/day of niacin a day and ramped up to 750 (for the smallest participant) or 1,000 mg/day for 4 months. They were asked to take the niacin with a light meal in the evening. The healthy controls were monitored for 4 months and the mitochondrial myopathy patients for up to 10 months.

A slow-release form of niacin was used to avoid flushing, but upon reaching 500 mg/day, everyone in the trial experienced flushing. Over time, though, the incidence of flushing declined. A few people reported flatulence, gastrointestinal irritation, and skin drying.



Health Rising's End of the Year Fundraising Drive

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The study found that 750-1,000 mg/day of niacin over 10 months in people with mitochondrial myopathy, and for 4 months for 10 healthy controls, raised blood NAD+ levels dramatically (7-fold for patients and 5-fold for healthy controls).

Over that period of time, the muscle NAD+ levels of the mitochondrial patients reached those of the healthy controls. (That the muscle NAD+ levels did not increase in healthy controls indicated they already had optimal NAD+ levels). Muscle mass, however, was increased in both groups without any weight gain.

Interestingly, niacin also significantly reduced the “unhealthy” fat deposits in the liver and the body by 50% and 25%, respectively, in the patients. Niacin supplementation didn’t decrease total cholesterol

levels but did decrease levels of the unhealthy LDL cholesterol in the mitochondrial myopathy patients.

The patients also showed remarkable increases in muscle strength (10-fold in abdominal muscles, 2-fold in back muscles, 2.5-fold in upper extremities (shoulder and elbow flexion strength) but just a slight improvement in the 6-min walking test. While maximum oxygen or exercise capacity did not improve during a cardiopulmonary exercise test (CPET), lactate levels after exercise were reduced. While some patients reported they were able to exercise better, most did not.

Niacin supplementation also increased most of the amino acids in the patients' muscles, and levels of creatine reached normal levels over time. Gene expression revealed a widespread downregulation of the mammalian target of rapamycin (mTOR) – a mitochondrial inhibitor.

Slight reductions in hemoglobin concentrations, and decreased red blood cells, suggested that niacin “suppressed slightly erythropoiesis or iron metabolism”. Vit B12 decreased and then rebounded over time. The authors underscored the need for “special attention to hemoglobin concentration and blood counts”.

Endothelial Cell and Blood Vessel Support

Given the possibility that damage to the endothelial cells may be contributing to ME/CFS, fibromyalgia, and long COVID, niacin's ability to vasodilate the blood vessels could be producing the increase in energy and clarity I sometimes experience.

Some evidence suggests it might. A **higher dietary intake of niacin** was associated with greater endothelial functioning among healthy middle-aged and older adults. A **2014 review** found niacin therapy significantly improved endothelial functioning (flow-mediated dilation) and that higher doses of niacin (≥ 2000 mg/day) were the more effective. A **2019 review** asserted that niacin and nicotinamide riboside should be considered “critical components of combination therapies to slow the vascular aging process and increase cardiovascular health span.” One study highlighted the improvement seen in the “microcapillary network”.

Longevity

The discovery that NAD⁺ levels decline as we age has sparked considerable interest in using NAD precursors like niacin to increase longevity, combat neurodegenerative diseases, etc. NAD⁺ declines have been associated with **numerous neurological diseases**, including dementia and Alzheimer's, and studies are underway to assess the effects of NAD⁺ boosters.

It appears that an NAD⁺ decline locks in a “**pseudohypoxic state**” that disrupts oxidative phosphorylation; e.g. energy production. Interestingly, this pseudohypoxic state occurs *even in the midst of normal oxygen levels*.

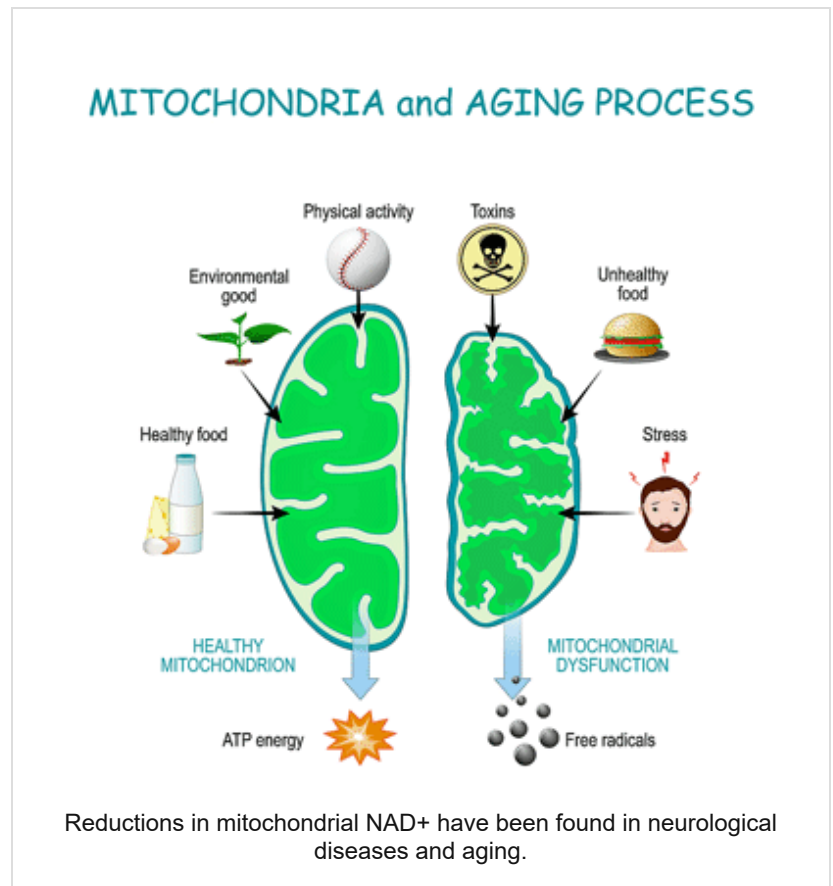
In 2013, a Harvard NMN (nicotinamide mononucleotide) study that was able to return the mitochondria in the muscles of older mice to a younger state really got the ball rolling. **The authors reported:**

“Our data show that 1 week of treatment with a compound that boosts NAD⁺ levels is sufficient to *restore the mitochondrial homeostasis and key biochemical markers of muscle health* in a 22-month-old mouse to levels similar to a 6-month-old mouse.”

Five years later Sinclair linked **NAD+ depletion** with a reduction in capillary formation and was able, using nicotinamide mononucleotide (NMN), to restore blood vessel growth, muscle functioning and endurance to mice.

Age-related changes in blood vessels could mirror the changes that occur more rapidly in ME/CFS and long COVID. Several findings, after all, suggest that people with ME/CFS or **post-COVID-19** are **aging more rapidly than expected**.

Age-related blood vessel changes result in increased coagulation (a possibility in ME/CFS and long COVID), damage to the microvascular barrier (possibly promoting the leakage, aka Systrom's work), and the reduced release of vasodilators from the small blood vessels – thus possibly reducing blood flows (Wirth and Scheibenbogen) to the mitochondria in the skeletal muscle, heart, and central nervous system.



One form of niacin quickly reversed **age-related declines in muscle functioning** in older mice by restoring endothelial functioning, increasing blood vessel elasticity, increasing mitochondrial activity, and ATP production, and reducing inflammation. A 2022 review "**NAD+ in COVID-19 and viral infections**" proposed that the decline in NAD+ levels seen body-wide during aging may be one reason older people are more susceptible to serious coronavirus infections.

Niacin, it appears, is being studied in **many clinical trials** including one to determine if it can improve recovery from exercise (reduced lactate levels among others.) At least 9 trials are assessing niacin in COVID-19 patients, including one that's combining **low dose naltrexone with niacin**.

Treatment

Diet

Enriched flours are fortified with niacin (Vit. B3). Meat (chicken, liver), fish (tuna, sardines, salmon), poultry, enriched and whole-grain bread, fortified cereals, edamame, avocado, and broccoli have been reported to be particularly high in niacin.

Supplementation

Niacin

Niacin or nicotinic acid is actually an oxidized form of nicotine but has vastly different functions (and is not addictive). The word niacin was created out of the words nicotinic acid and vitamin in order to differentiate it from nicotine. The goal in taking niacin is for it to be converted into nicotinamide adenosine dinucleotide or NAD – an essential “energy enzyme” which plays a role in many biological processes.

Niacinamide

Niacinamide is structurally closer to NAD – the compound we want to increase in the body – and is more easily converted to it. Nicotinamide also does not cause flushing, which some find disturbing.

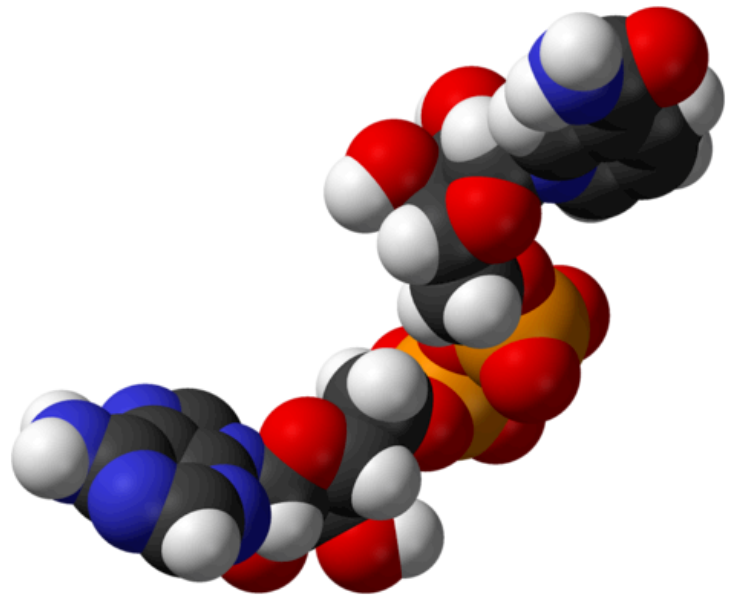
Studies suggest that [niacinamide](#) can help reduce acne, help prevent some non-melanoma skin cancers, improve joint flexibility, and reduce inflammation in people with osteoarthritis. One [naturopath reported](#) that niacinamide in doses ranging from 500 mg twice a day to 1,000 mg 3 times per day helps some patients with anxiety – which fits my experience of it as a calming agent. (This could be due to its ability to increase blood flows). This is a plus in many doctors’ books but a minus in some others.

One [alternative health website](#) reported that using nicotinamide or niacinamide instead of niacin does not open blood vessels wider nor provide a cholesterol-lowering effect. It’s believed the flushing effect allows the toxins stored in these fatty tissues to spill into the bloodstream and get processed out of the body.

Nicotinamide mononucleotide

[Nicotinamide mononucleotide](#) is the form of niacin most associated with longevity and anti-aging. It’s what Sinclair twice used to turn back the clock in his animal studies and appears to have neuroprotective properties. A 2021 clinical trial found that NMN actually *improved muscular insulin sensitivity* in prediabetic women. Studies are underway to assess its effectiveness and safety in humans.

Nicotinamide riboside



Niacin comes in 4 forms – each of which produce the crucial element – NAD (seen above) – in the body.

The Gist

- I have intermittently experienced significant periods of mental clarity and energy improvement while using niacin (Vit B3). (Those episodes may (or may not) be associated with the flushing that some forms of niacin produce.)
- Niacin in its various forms produces NAD in the body – a key compound that plays a role in numerous processes including energy production. NAD exists in various forms depending on whether it’s been oxidized or reduced. Its ability to easily pick up and discard electrons has made it a central player in Complex 1 in the mitochondria.

Nicotinamide riboside (NR) is a synthetic form of nicotinamide that may be able to increase coenzyme **NAD+** levels more efficiently than either niacin or nicotinamide. It may also be helpful in preserving the telomeres. It's also quite a bit more expensive. Dr. Ambrus reported that he uses NR in his metabolic myopathy patients.

Takeaways

If you're using niacin to vasodilate the blood vessels, use niacin. If you're using it to enhance mitochondrial production, to support skin health, or for other reasons, try niacinamide or nicotinic riboside.

Dosage

Verywell Health recommends taking 3 grams daily (divided up into small doses) for 12 weeks for osteoarthritis. For acne, take supplements containing 750 mg of niacinamide combined with 25 mg of zinc, 1.5 mg of copper, and 500 mcg of folic acid once or twice daily.

RxList reports that 3 grams per day of niacinamide can result in liver problems or high blood sugar. A naturopath recommended taking 500-3,000 mg/day broken up into at least 3 sessions a day. (Niacin has a short half-life in the body.)

The **National Institutes of Health**, on the other hand, asserts that taking 1,000 mg/day can lead to low blood pressure, tiredness, high blood sugar levels, nausea, heartburn, and abdominal pain, and blurred vision:

- Extreme tiredness
- High **blood sugar** levels
- **Nausea**, heartburn, and abdominal pain
- Blurred or impaired vision and fluid buildup in the eyes.

Several websites recommend getting periodic liver function tests (serum aminotransferase levels) when taking high doses of niacin (1,500 mg/day or more).

Sauna Therapy

- A small Finnish study found low NAD+ levels in patients with mitochondrial myopathy – a disease that shares several features with ME/CFS/FM including exercise intolerance. Several case studies have described FM and ME/CFS patients with mitochondrial myopathy who benefitted from mitochondrial therapy involving niacin and/or other supplements.
- While exercise intolerance was not improved in some patients, increases in blood and muscle NAD+, muscle strength, muscle mass, and amino acids, and reductions in unhealthy fatty deposits and lactate during exercise were seen.
- Other studies suggest that niacin may be able to help with endothelial functioning; i.e. increase blood flows through the small capillaries that provide nutrients and remove toxins from the tissues.
- “Niacin” comes in four forms: niacin, niacinamide (NMN), nicotinamide ribose (NR), and nicotinamide mononucleotide. The first form, niacin, can produce a hot flushing sensation that usually declines over time. It may be the most helpful blood vessel enhancer. The second form, niacinamide, is more efficiently metabolized into NAD and does not produce flushing. The third form, nicotinamide riboside, may be the most effective mitochondrial enhancer but is

Niacin is often used in combination **with sauna** to support detox. One **sauna detox site** recommends slowly (50-100 mg implements at first) working your way up to *2,500 – 5,000 (!)* mg of niacin per detox session so as to keep the flush going.

Decades ago, I did a 6-week sauna detox program at Dr. Rea's **Environmental Health Center** in Dallas. I don't remember if they used niacin, but everything else was similar. Supplements to support detox were given, and a 25-30 minute bout on an exercise cycle – which I tried but had to give up – got the toxins flowing, which the sauna session was designed to flush out. Even doing the minimum amount – 1 sauna session a day – was grueling. (This was before infrared saunas). Six weeks of that left me in considerable pain, but a couple of days later while driving back to the West Coast, I felt an unusual sense of clarity and well-being.

Risks

Although niacin is often described as being completely safe, there are some warnings associated with long-term use, particularly at higher levels. Long-term use of niacin led to increased insulin resistance in a rodent given a high-fat diet. (In contrast, in 2017, a **delayed-release form of niacin** improved markers of insulin resistance and metabolic inflammation.)

The **Mayo Clinic** warns people with liver disease, peptic ulcer, or severe low blood pressure about taking *large amounts of niacin* (2-6,000 mg daily). People with allergies, gallbladder disease, symptoms of certain thyroid disorders, diabetes, and gout (niacin can increase uric acid) could also find their symptoms exacerbated.

A naturopath recommended that the dose be lowered if nausea occurs and that people taking large doses of niacinamide ($\geq 1,500$ mg/day) should have periodic liver function tests (serum aminotransferase levels) done.

Conclusion

Niacin is not a godsend but it presents an intriguing possibility for those going the mitochondrial supplementation route. It's considered safe at moderate doses, helped people with mitochondrial myopathy in a small trial, is engaged in a wide variety of important processes, may be able to help with blood vessel flows, and has been linked with longevity. It's also quite cheap (in its niacin/niacinamide form).

Those using the non-flushing form may not receive the blood vessel and detoxification effects while those going with other forms might receive better mitochondrial effects. Nicotinamide mononucleotide

more expensive. The fourth form, nicotinamide mononucleotide has been most associated with longevity research.

- Still, other studies indicate that NAD⁺ declines occur as we age and NAD⁺ precursors such as niacin may be helpful in reversing some of the aging processes. This is an active area of research.
- Niacin appears to be mostly safe but at higher levels and over longer terms may cause side effects in some and liver tests should be done. (See blog)
- All in all, with its good safety profile, its ability to affect the mitochondria and open the blood vessels, and possibly affect longevity, niacin presents an intriguing possibility for those trying to enhance the activity of their mitochondria.

is most associated with anti-aging and studies are underway to assess its effectiveness and safety.

The Mitochondrial Enhancers for Chronic Fatigue Syndrome (ME/CFS) and Fibromyalgia Series

- **Pt. I: D-Ribose, CoQ10 and PQQ**
- **Pt. II: L-carnitine and Acetylcarnitine**
- **Pt. III: Magnesium**
- **Pt. IV: N-acetyl cysteine (NAC)**
- **Pt V: Oxaloacetate**
- **Pt. VI: Niacin, Nicotinamide, and Nicotinamide riboside**
- Coming up Metformin, Rapamycin and ?