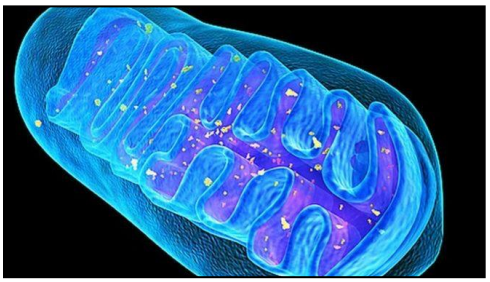
Methylene Blue & Metabolic Medicine

The "Magic Bullet" & Futuristic Medicine.

Many of the suggestions in this chapter are not meant to be performed without consulting your healthcare provider first.

Metabolic Medicine, the Future of Medicine.



Metabolic medicine is the future of medicine as the most *"upstream"* aspect of health and is at the root of most all diseases. Our current pharmaceutical-based medical system is a broken system. It has failed miserably as we have more disease than many countries here in the USA while we possess most of the medicines, yet we are much sicker than most countries with far less "modern" pharmaceutical-based health care. Bottom line is our drugs are killing us. The idea that we can "cure" disease by giving a certain molecule (drug) for a certain condition has shown to be like painting over rust leaving the patient as the victim to only need more drugs for side effects of the first drug and so on. Your body is a self-healing, self-regulating and intelligent organism with contains all it needs to be healthy and repair itself. It's not about chasing genes either because your

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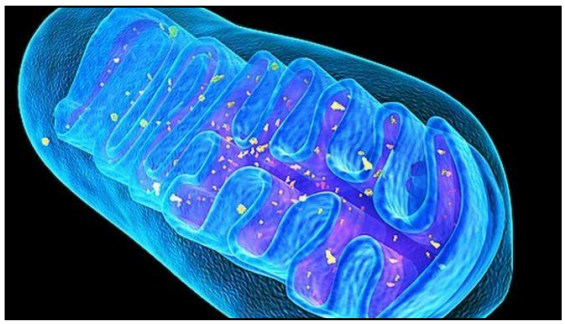
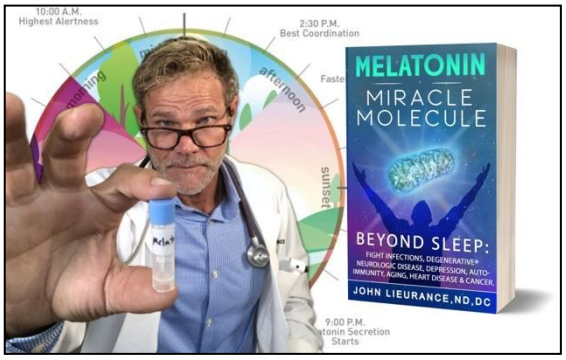
genes fail due to a poor stress response which is generally caused by a poor metabolic capacity of your cells. Any human diseases involve abnormal metabolic states that interrupt normal physiology and lead to tissue and cellular disruption. When you get to the top of the mountain where the stream begins you have *metabolism* and the ability to make adequate energy with as little waste as possible. This is a new health paradigm for treating disease which will allow the body with its innate wisdom to figure the complexities out with its new found spark of life. Not only does this medicine work but it actually addresses the cause of many conditions. In this article we will dive into how to use the science of metabolic medicine to gain better health and vitality. In order to fully understand how metabolic medicine works you need to have a base of knowledge of the mitochondria.



Mitochondria & Cellular Wellness

The mitochondria are where you convert glucose and oxygen into energy through something called the electron transport chain. This is where electrons are moved through a chain of chemical reactions to produce what's called an exothermic reaction. Moving electrons creates energy your cells utilize to do work, like keeping up with all of their functions. Just like a train which burns coal to produce energy that drives the train down the tracks, your cells burn sugar. And just like the train produces toxins that are released when the coal is burned in the form of smoke, your cells also produce a toxic by product called oxidation. The ability of the mitochondria to stay healthy and continue to efficiently make energy hinges on its ability to neutralize these harmful byproducts. Antioxidants are the primary method the mitochondria use to do this. Consider your brain is 2% of your bodyweight however it consumes 20% of the overall energy. Your brain and your heart are the two most energy demanding systems and require a high total energy supply. When that starts to run low, both your heart and your brain being very “metabolically sensitive” organs will begin to show signs of stress such as being

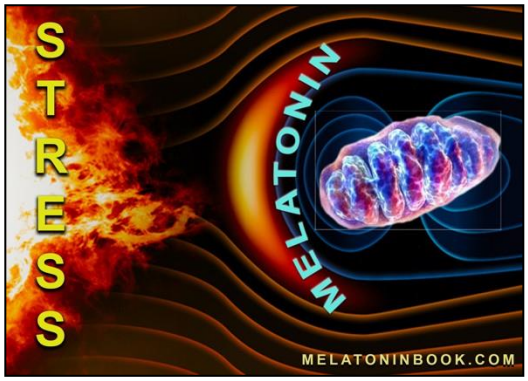
> *Melatonin is produced by every mitochondria and is the primary way that the mitochondria neutralizes the stress of oxidation.*



fatigued and developing disease. Making your mitochondria more efficient is the name of the game to improve all aspects of health, vitality and lifespan. The good news is there are some great ways to do this through something called the cytochrome pathway. There are 4 complexes in the cytochrome pathway and I will reveal a way to access all 4 cytochrome pathways later. I will also be discussing strategies to greatly improve mitochondrial function through something called autophagy and mitophagy. First it is important to fully understand how stress and cytokines work at the cellular level to appreciate some of my methods that I will share.

Stress, Cytokines & Melatonin.

All stressors lead to one outcome which is inflammation. Whether it's a sunburn, an infection or even intense exercise there is a specific set of cytokines that are responsible for the inflammation that occurs, which in essence is cellular stress. When that inflammation or the cytokines become too overwhelming for the cell to deal with, it switches its energy production method from moving electrons in the mitochondria to a very primitive way of making energy called aerobic glycolysis. The problem with aerobic glycolysis is that it only produces 10% of the energy that is otherwise created through the electron transport chain. This is what chokes off the energy reserves with COVID-19 when a patient goes into a cytokine storm that typically leads to death due to acute respiratory distress syndrome. Melatonin is the molecule that is the primary antioxidant within all of your cells that neutralizes this oxidation and can return the energy production back to its proper 100% functioning through the electron transport chain. I wrote a book called Melatonin: Miracle Molecule. You can find information on this at melatoninbook.com. In that book, we discussed how melatonin has been shown to enhance the health of virtually every system in your body.



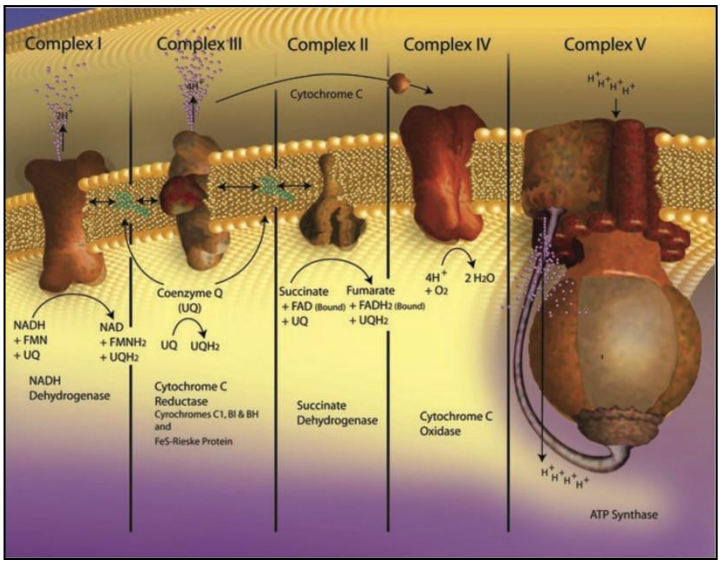
There is a large body of research that supports the use of high dose melatonin for a variety of different diseases. When you consider that the brain and the heart are the two most metabolically sensitive organs in the body it is easy to understand that melatonin may improve the function of the central nervous system and support many people looking to improve the health of their brain.

Stress & The Metabolic Ceiling.

In the image above factors that dictate metabolic capacity or the ceiling are factors that affect mitochondrial function. Poor mitochondrial function will become limiting when there becomes more stress than you are able to adapt or compensate for and you hit the ceiling!

Whenever we want to create strength or activate a healing response in the body it is always through stressors acting on your genes where your body responds and you have a net gain in health. They call the zone that you benefit most from the hormesis zone. The familiar zone is when there is too little to activate any changes and the danger zone is when it's too much activation or stimulation. The metabolic ceiling is what limits the hormetic zone's outer boarder. Using metabolic medicine to support the mitochondrial function, you get stronger autonomics and better fuel delivery and utilization. This way you have a positive effect on how far you can push into the hermetic zone before hitting the danger zone.

The Cytochrome Complex. What is it & why would you want to know about it?



The word cytochrome when you break it down is cyto /cell and chrome/light. It is a way your cells can use the energy in light to convert it into energy. The cytochrome complex consists of cytochrome I-VI and consist of small "hemeproteins" found associated with all of your mitochondria. The complex belongs to the cytochrome c family of proteins and plays a major role in cell apoptosis and is an essential component of the electron transport chain, where it actually carries an electron. It primarily transfers electrons between Complexes III (Coenzyme Q) and IV (CCO). The cytochrome complex helps your mitochondria shuffle electrons which allows your cells to make energy. Next, I will get into red light therapy and how your mitochondria convert red light into ATP and later how methylene blue can supercharge this system.

Red Light Therapy & Photo-Bio-Modulation.

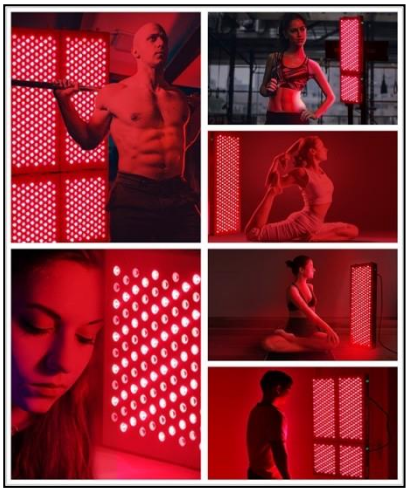


Photo-bio-modulation refers to Photo/light, Bio/Your Body. Cells then, of course, have the ability to modulate them to support them to be stronger and more resilient. Photo-bio-modulation therapy relies on the use of specific light parameters to promote tissue repair. Although demonstrated in different cell models and tissues. Studies suggested that cellular healing and repair is enhanced by both red and near-infrared light. Photobiomodulation involves the activation of the mitochondrial respiratory chain using the cytochrome

complex. The healing effects of light therapy was first used in the late 1800s to treat skin tuberculosis (TB), and NASA used it in the 1980s to grow plants in outer space.

Low-level laser/light therapy or photobiomodulation, refers to the use of red-to-near-infrared range (620–1100 nm) to stimulate cellular functions for physiological or clinical benefits. Photobiomodulation has been used to improve wound healing 1,2, reduce pain 3,4, and many other healing and regenerative applications. The light can be supplied by lasers or light-emitting diodes (LEDs). Transcranial LLLT has amazing therapeutic
uses in various neurological and psychological conditions, including ischemic stroke 5,6, chronic traumatic brain injuries 7,8, and depression 9,10. Using endo-nasal along with transcranial LLLT is a promising upgrade. A Study using a LLLT to the forehead, Barrett and Gonzalez-Lima demonstrating that LLLT to the forehead benefits cognition in healthy humans, including enhanced attention, working memory, and executive functions 11,12,13. Remember though the red light only works on the one cytochrome oxidase (CCO) complex IV. What if we can get all 4 complexes to activate? We will discuss ways to further enhance this to the max for even greater benefit.
Red light as a treatment is considered bio-active in humans cells and can directly and specifically affect and improve mitochondria function through the CCO.[14] Red light photons are absorbed by our cells and converted to energy. This energy produced can then stimulate the production of collagen, elastin, and adenosine triphosphate (ATP), which is great for skin however it goes much deeper and can have diverse positive effects on all aspects of health and vitality due to its mitochondrial enhancing properties.

In the study “Interplay between up-regulation of CCO and hemoglobin oxygenation induced by laser”, the author describes how this process using red-to-near-infrared light can stimulate cellular functions for physiological or clinical benefits. The mechanism of LLLT is assumed to rely on photon absorption by cytochrome c oxidase (CCO). [15]
A case study at UCSF found light therapy had positive effects for a pro hockey player with persistent post-concussive symptoms, [16] and several VA Boston case studies showed good outcomes of light therapy for former pro football players with symptoms due to repetitive head impacts. In addition, researchers are studying light therapy for PTSD, Parkinson’s Disease (see

also Dr. John Mitrofanis' book Running in the Light), Alzheimer's Disease, and dementia. The effects include increased cerebral blood flow, increased (ATP) energy production, increased neuroprotection and brain repair, and reduced inflammation. A 2019 study found that using light therapy applied to the head (transcranial) and intra-nasally has a positive effect on brain wave patterns in just one treatment; read more about the study here. [17] I wish I could place lasers on my balloons when I treat patients! Using red light therapy may enhance any endo-nasal release program. We use it intravenously as well with Lumestem. The use of this type of therapy into the ears holds promise. Read more about this in chapter 11. Red light therapy is best done for NO more than 10 minutes per day. I personally stand between eight panels every morning. Next, we dive into how you can enhance all 4 cytochrome subunits to really drive healing and regeneration.

Introduction to Methylene Blue. A Key to Cellular Wellness

A brilliant blue salt, methylene blue or MB was first used as a dye. It is now known that MB improves mitochondria respiration and might be a magic bullet within metabolic medicine. In 1870, MB was discovered and used as an industrial dye. Soon after MB was found to be a great way to stain human tissues and microbes for microscope examination. They found that MB would even inactivate certain microbes. An anti-microbial that leaves cells and tissues virtually unharmed. That's right, a powerful antimicrobial! It gets even more impressive so stay with me. MB was one of the first chemotherapeutic medications ever tested in humans. It was used to treat malaria, in 1891. Of course, it was replaced by antibiotics when they first came on the scene even though MB is superior to them. With heavy marketing by big pharma to doctors a shift was made to these new "superior" anti-microbials. Are they really superior? We have now found that antibiotics can have negative effects to our health through killing our microbiome and that many bugs can become resistant to the antibiotics. The treatment of malaria with antibiotics has proven that this is not the best way as many of the antibiotics have created resistant strains thus making them useless. With MB there has been NO detection that the micro-organism have resistance to MB unlike antibiotics. Your micro biome is an incredibly important diverse group of bacteria that coexist in your body, mostly your gut. The malarial parasites, *Plasmodium*

falciparum, is now showing an increased resistance to common antimalarial drugs. As a result, methylene blue is being considered a better option.

Methylene Blue & Nitric Oxide

MB is a powerful inhibitor of nitric oxide or N0. There is a lot of hype around the benefits of NOS and its ability for open up blood vessels to improve circulation. Viagra works on NOS and has been hugely successful to improve the male and female erection. But is it really as safe as is generally thought? There are 3 types of NOS named according to their activity or the tissue type in which they were first described. They are neuronal NOS (or nNOS), endothelial NOS (or eNOS) and inducible NOS (or iNOS). NOS is released in short and brief moments of stress exposure and it is a vital and important molecule to support us. NOS is also a free radical and is a powerful oxidant that the body needs to neutralize. Too much NOS is associated with tissue damage and is an aging accelerate. It is also part of the toxic air pollutant. In 1990, droves of scientific research were released claiming NOS to be safe as well as a powerful molecule to treat many diseases such as erectile dysfunction, heart function and as a stroke preventative. In 1992, NOS was pro-claimed molecule of the year. NOS went overnight from toxic free radical to miracle drug.

NOS is a signaling molecule and assists us in stress responses.

NOS is Part of the Bodies Stress Response!

NOS is a signaling molecule and is best used in short and measured dosage. We use Ozone in our clinic with great success and it is also a powerful free radical. Why is ozone helpful? Ozone like NOS is a signaling molecule and signals stress in the body that can enroll a hermetic response as long as its dosage is within the hermetic zone and not into the danger zone. Chronically elevated NOS or ozone would NOT be beneficial to the body for the same reasons.

NOS is taken commonly by body builders and men with ED on a daily basis. l-arginine and citrulline are both precursors to NOS that are in many body building and endurance supplements.

NOS can give you a pump through an enhanced inflammatory response within the muscles but may not be the healthiest strategies long term.

Also, anyone looking at maximizing fitness might consider this study in 2015 where a scientist found that NOS powerfully inhibits testosterone. Using a NOS inhibitor like MB might negate these effects as in the above study. "Warning to men: Erection drugs might kill you!" In this article by Michael Castlemen. [18] Since its approval in 1998, Viagra has been implicated in 1,828 deaths and Cialis 236 and Levetra 221. Between the 3, that accounts for 2500 deaths and 25,000 other side effects such as mini stroke, vision loss and hearing loss.

The dirty secret with these studies is that the studies look at only a few thousand and if a drug kills say 1 in say 100,000 that side effect may not show up in the study. The problem is that millions of men are now taking Viagra and the results are that thousands have died due to this fact. The most common problem that leads to dearth is when there is a co-administration of nitroglycerine so the person would get a double dose of NOS in that case.

Chronic elevated NOS levels can cause cardiovascular disease, MS, Alzheimer's, Dementia and other degenerative neurological diseases. Recent study showed a dramatic increase in skin cancer after Viagra use with an 84% increase in melanoma. [19]

Just because NOS dilates blood vessels doesn't mean it's good for you long term. It will help the tissues receive more blood flow however due to the cytokine elevation it will inhibit the oxygen utilization through the electron transport chain through inhibition of CCO. NOS in high amounts cause the opposite and you will have vasoconstriction. NOS is also involved in the inflammatory response. [20]

In the paper called "The NOS Hypothesis of Aging" the author presents the causes of aging, suggesting one of the prominent theories of aging is the free radical theory. According to this theory, free radicals generated through mitochondrial metabolism can act to cause abnormal

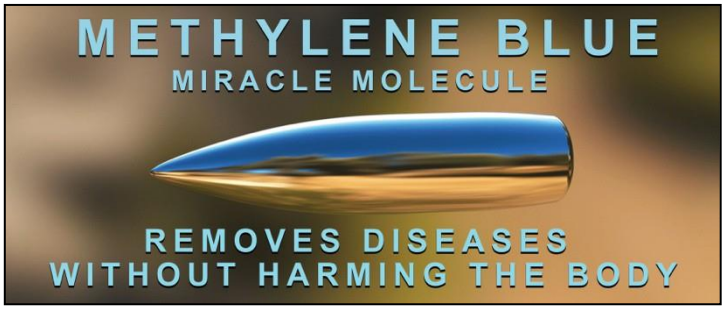
function and cell death. Various toxins in the environment can injure mitochondrial enzymes, leading to increased generation of free radicals that, over the life span, eventually play a major part in aging. [21] Aging of the anterior pituitary and pineal will result in decreased secretion of pituitary hormones and the pineal hormone melatonin. The induction of iNOS in the temperature- regulating centers by infections may cause the decreased febrile response in the elderly by loss of thermosensitive neurons. NOS may play a role in the progression of Alzheimer's disease and Parkinsonism.[22] Activation of cytokine and iNOS production in the cardiovascular system leads to coronary heart disease. [23] Antioxidants, such as MB, melatonin, vitamin C, and vitamin E play important roles in reducing or eliminating the oxidant damage produced by NOS. [24]

NOS and angiogenesis. In the short term, like following an injury, elevated levels of NOS to increase angiogenesis might be helpful, however, chronic activation of angiogenesis might put you as a higher risk of cancer.

It's not the virus that kills, it's the cytokine storm. NOS is the primary molecule that causes the cytokine storm. The cytokines then signal a shift in the cellular energy away from the electron transport chain to aerobic glycolysis. This cuts down available energy by 90% causing the immune system to literally starve and become taken over by the infection. This is, in essence, the cytokine storm with COVID-19 and any other viral infection. We will dive deeper into how MB supports recovery from infection later. Its inhibition of NOS is one way besides its anti-viral properties.

Looking close up one see's NOS as an enhancement of circulation however step back and look at things more wholistically it's clear that it's not the right approach and its likely to cause more harm than good. MB as a powerful inhibitor of NOS and this is one of the ways MB supports the body.

Methylene Blue: Magic Bullet.



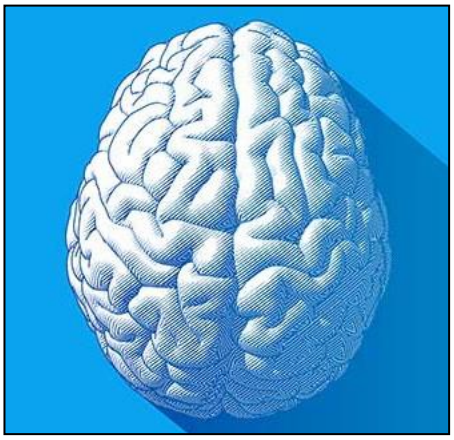
The term **magic bullet** is a scientific concept developed by a German Nobel laureate Paul Ehrlich in 1900.[25] Ehrlich formed an idea that it could be possible to kill specific microbes (such as bacteria), which cause diseases in the body, without harming the body itself. He named this agent as *Zauberkugel*, the "magic bullet." This magic bullet was methylene blue! Methylene blue does seem to have very little negative effects and is extremely safe to consume. Since it works on an upstream aspect of health which is the energy production or metabolism, it supports the body in a wide range of conditions. If you give the energy reserves the body needs to work, it will correct disease much better than any man-made chemical such as with virtually all pharmaceutical approaches to health and disease.

Methylene Blue & Mitochondria

Methylene blue is anti-inflammatory and neuroprotective showing promise in treatment of diseases such as stroke, Alzheimer's disease and Parkinson's disease. [26]

Remember your mitochondria works through the electron transport chain where it shuffles electrons, which releases chemical energy that the body uses to make ATP, which is the energy currency in our cells. Methylene blue is an electron carrier and even recycles electrons, which allows it to improve mitochondrial function. It basically turns your mitochondria into super mitochondria! It is highly beneficial in toxic situations in the brain as it encourages cellular oxygen consumption and decreases anaerobic glycolysis. This fits into the melatonin conversation where stress induces cytokines (inflammation) and causes the cell to switch to the inefficient, anaerobic glycolysis. We will dive into melatonin in another section. Where methylene blue really shines is that it improves the electron transport chain in the mitochondria such that it recycles electrons. This shifts your cells into a very efficient energy producing quality.

Methylene Blue & The Brain



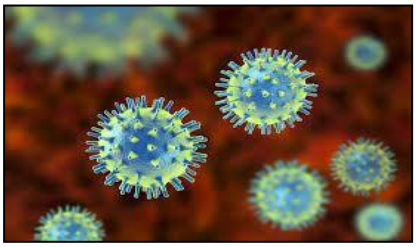
Studies show a memory-enhancing and neuroprotective metabolic mechanisms of action of methylene blue for the brain. The memory-enhancing effects have been associated with improvement of memory consolidation. In addition, low doses of methylene blue have also been used for neuroprotection against mitochondrial dysfunction in human disease. There are neurometabolic mechanisms for memory enhancement and neuroprotection from methylene blue. [27] Another study showed that MB administered could enhance memory through an increase in brain cytochrome oxidase activity. Another study using brain MRI's showed impressive brain support. Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain. [28]

Extinction Memory Improvement by the Metabolic Enhancer Methylene Blue. Ref MB may also function as a cholinesterase inhibitor, [29] increasing the amount of acetylcholine available, a neurotransmitter in the brain responsible for arousal, attention, memory and motivation. [30]

The relationship between methylene blue (MB) and Alzheimer's disease (AD) has recently attracted increasing scientific attention since it has been suggested that MB may slow down the progression of this disease. MB has been shown to reverse the formations of amyloid plaques and neurofibrillary tangles responsible for AD, and to partially repair impairments in mitochondrial function and cellular metabolism. [31] This pharmaceutical drug derived from MB

has also shown benefit in both Alzheimer's disease and frontal temporal dementia (Lewy Body Disease) and is currently in late phase trials. [32] I'm sure these types of trials may place MB at risk of becoming too expensive for many of us. MB has also been shown to assist healing in traumatic brain injuries by promoting a self-cleaning mechanism called Autophagy and calming down the inflammation that occurs after a head trauma that is associated with microglial cells becoming over activated. "Methylene blue exerts a neuroprotective effect against traumatic brain injury by promoting autophagy and inhibiting microglial activation." [33]

Methylene Blue is Anti-Viral.



Besides improving mitochondrial function, methylene blue also has antiviral properties. It displays broad-spectrum virucidal activity in the presence of UV light and has been shown to be effective in inactivating various viruses in blood products prior to transfusions. [34] Methylene blue displays virucidal preventive and therapeutic activity against influenza virus H1N1 and SARS-CoV-2. [35]

A recent French publication on a cohort of 2500 end stage cancer patients treated with MB during the first wave of CoviD-19 mentions a possible protective role of MB against respiratory viruses, as this study group showed no reported cases of influenza or SARS-CoV-2 infections. [36] It makes sense that immune cells with stronger energy reserves work better to keep you safe from infections. The “inner mask” is more powerful than an outer mask. Experts that have looked into the efficacy of wearing a mask find them to be ineffective anyway. [37]

The body will not become sick or warn out prematurely for no reason. Having treated many diseases over the years, I've come to the conclusion that it's either toxins or infections that are at the root of the disease. New science is demonstrating that many of the proteins such as beta amyloid and alpha synuclein are the immune system's response to these toxins and or infections and most often there are both involved. I have found virtually all of the patients that have come to me test positive for at least one but typically two different viruses. I often test for Epstein Barr, cytomegalovirus, and HHV6 as well as an immune marker called CD57. A lab called Cyrex runs an array 12 that tests about 25 different microbes. Things like ozone & methylene blue have qualities to both improve mitochondrial status as well as having an antiviral/anti-microbial effect making them great therapeutic substances for any brain-based conditions.

Methylene Blue is an Anti-depressant

In higher doses, methylene blue seems to be a powerful anti-depressant. Keep in mind that in higher doses, MB acts as an MAO inhibitor. This is why it can be dangerous to take

antidepressants along with higher doses of MB. In this study, methylene blue at 15 mg/day, was compared with placebo in treatment of severe depressive illness. The 3-week trial showed that the improvement in patients receiving methylene blue was significantly greater than in those receiving placebo. Methylene blue at a dose of 15 mg/day appears to be a potent antidepressant, and further clinical evaluation is essential. [38]

Methylene blue increases autophagy which is cellular cleaning and recycling. This study showed MB induced neuroprotection by enhancing autophagy. [39] Due to this, methylene blue might be considered something helpful during fasting. We will get into fasting a little later. In order fully understand fasting and how it works to enhance your mitochondria, we need to review some concepts on how the body clears out old cells and mitochondria recycling them into brand new cells and mitochondria.

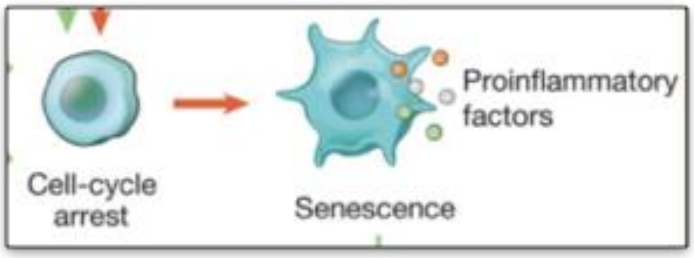
MB, Fasting, Autophagy & Mitochondria

Mitochondrial dysfunction is a hallmark of metabolic decline (vitality) during aging. [40]. You're constantly replacing your old, weak, dysfunctional mitochondria with new healthy fresh mitochondria or "mito". The population of all the mito of a given cell constitutes your *Chondriome*. Like your microbiome, we have a healthy pool of bacteria or an unhealthy pool. This will dictate how functional they are. The average cell in your body has between 1,000-2,000 mito. Again, they turn over as they get old. They are recycled, and it's a process medicated through a gene expression ruled by **mTOR.**

The **mTOR** pathway is a central regulator of metabolism (vitality) and physiology (function). Without getting too deep into mTOR, for now, let's just leave it at the fact that when mTOR is inhibited, we shift into a cleaning and recycling phase where we see Autophagy and Mitophagy. **Autophagy** is a Latin word that translates into "self-eating." **Autophagy** is the body's way of cleaning out damaged cells in order to regenerate newer, healthier cells. [41]

Mitophagy is the selective degradation of mitochondria by autophagy. It often occurs to defective mitochondria following damage or stress. [42] Remember all the types of stress? These ALL have an impact on the demand for Mitophagy to be activated through mTOR![43] So what activates mTOR and Autophagy? Fasting is the primary activator of this process and MB also activates it! We will revisit this soon, but first, we need to talk about senescent cells. What are senescent cells, and how do they have a detrimental effect on health and life span? As they accumulate, due to poor Autophagy (which normally removes and recycles them), they turn into fresh, healthy cells and fresh, healthy mito.

Cellular Senescence, Zombie Cells & How to Recycle to New Cells.

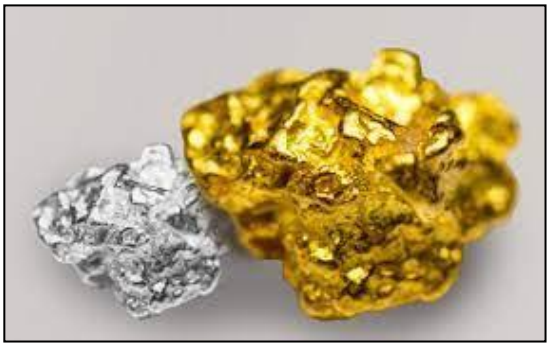


Cellular senescence is an irreversible cell-cycle arrest mechanism that acts to protect against cancer. [44] Basically, cellular senescence is a permanent state of sleep a cell goes into. This state is associated with a release of inflammatory products, and higher energy consumption, pulling it away from your healthy cells. They are zombies in the literal sense! Production of pro-inflammatory cytokines, is a common feature of senescent cells.

These “zombies” will float around your body spewing inflammation and sucking the life out of your body, by deferring vital energy that would normally be going to healthy cells.

We discussed ozone as a signaling molecule when we discussed NOS. Ozone works through hermetic activation in the body which results in a very powerful autophagy and mitophagy response. NOS, on the other hand, inhibits autophagy. [45] I will often have my patients do ozone and MB during their fasting phase. There are home units you can purchase and do rectal instillations that are very powerful. There are also saunas that can be purchased that deliver ozone quite efficiently. As stated, methylene blue such as in Lumotol Blue activates autophagy and can be taken during fasting. [46]

Silver & Gold Enhance MB.



Using nano silver and gold mixed with MB can greatly enhance its photobiomodulation abilities. The precious metals work by enhancing the cytochrome complex when combined with MB which allows more electrons to flow through the chain within the mitochondria.

Silver Nanoparticles Decorated with Methylene Blue Potentiated the Photodynamic Inactivation of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. [47] Synergistic reaction of silver nitrate, silver nanoparticles, and methylene blue against bacteria. [48]

The antimicrobial properties of light-activated polymers containing methylene blue and gold nanoparticles. [49] Gold nanoparticles has been studied in combination with MB for cancer with great promise as it supports photodynamic therapy (PDT). [50]

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