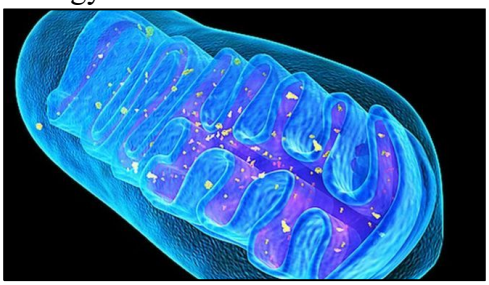
Methylene Blue & Metabolic Medicine

The "Magic Bullet" & Futuristic Medicine.

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

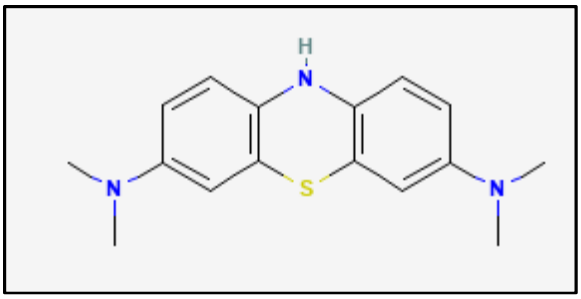
Metabolic Medicine, the Future of Medicine.

Metabolic medicine is the future of medicine as the most *"upstream"* aspect of health. Cellular energy 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 diseases here in the USA even though we possess most of the medicines, yet we are much sicker than most countries with far less "modern" pharmaceutical-based health care. The 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 organism with the divine intelligence which contains all it needs to be healthy and repair. It's not about chasing genes either because your genes fail due to a poor stress response which is generally

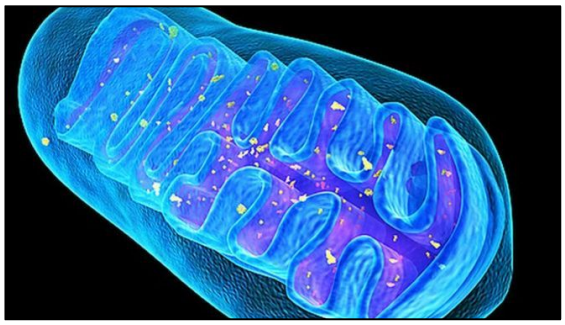


Your body is a self-healing, self-regulating and intelligent organism with contains all it needs to be healthy and repair itself.

Many human diseases involve abnormal metabolic states that interrupt normal physiology and lead to tissue and cellular disruption.



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 newfound spark of life. Not only does this medicine work but it 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. To fully understand how metabolic medicine works you need to have a base of knowledge of the mitochondria.

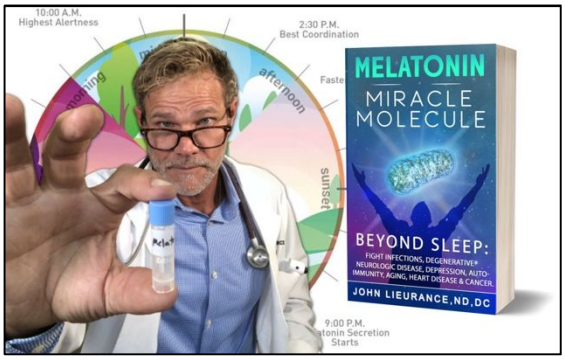


Mitochondria & Cellular Wellness

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 is called an exothermic reaction. Moving electrons creates energy your cells utilize to do work, like keeping up with all 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 that 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

Melatonin is produced by every mitochondria and is the primary way that the mitochondria neutralize the stress of oxidation.

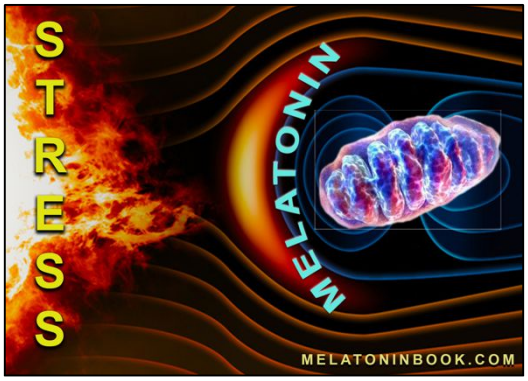
systems and require a high total energy supply. When that starts to run low, both your heart and your brain, being very “metabolically sensitive” organs, will begin to show signs of stress such as being fatigued and developing disease. Making your mitochondria more efficient is the name of the game to 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.



Methylene blue was first synthesized in 1876 by the German chemist Heinrich Caro (1834-1911) as an aniline-based dye for cotton dyeing.[1] Methylene blue (chemical name: tetramethylthionine chloride) is a cationic dye and belongs to the class of compounds known as phenothiazines (neuroleptic drug group). [2]

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



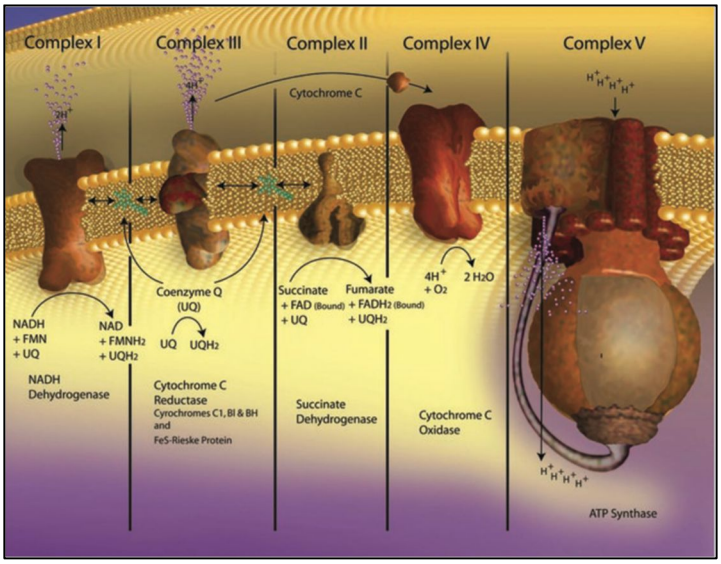
chain. This is what chokes off the energy reserves with COVID-19 causing a patient to go into a cytokine storm that typically leads to death from acute respiratory distress syndrome. Melatonin is the molecule that is the primary antioxidant within all your cells that neutralizes this oxidation and can 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 is 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. Stressors act on your genes, your body responds, and you have a net gain in

health. They call the zone that you benefit most from the hormetic 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 border. 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 hormetic zone before hitting the danger zone.



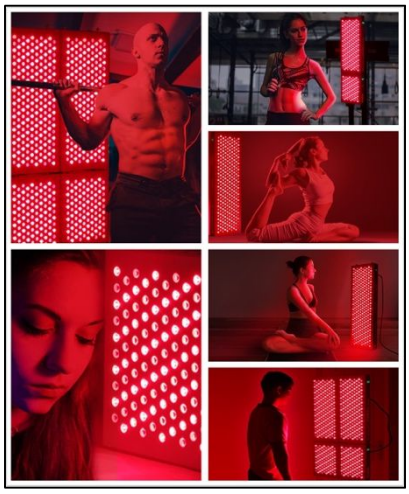
The Cytochrome Complex. What is it & why would you want to know about it?

The word cytochrome comes from cyto /cell and chrome/light. It is a way your cells can use the energy in light to convert it into energy in the body. The cytochrome complex consists of cytochrome I-VI and consists of small "hemeproteins" found associated with all 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 can modulate to support themselves to be stronger and more resilient. Photo-bio-modulation therapy relies on the use of specific light parameters to promote tissue repair. This has been demonstrated in different cell models and tissues. Studies suggest that cellular healing and repair are enhanced by both red and near-infrared light. Photobiomodulation involves the activation of the mitochondrial respiratory chain using the cytochrome complex. The healing effect 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 [3],[4], reduce pain [5],[6], 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 [7],[8] chronic traumatic brain injuries [9],[10], and depression [11],[12]. 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 [13],[14],[15]. 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 human cells and can directly and specifically affect and improve mitochondria function through the CCO. [16] 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). [17]
A case study at UCSF found light therapy had positive effects for a pro hockey player with persistent post-concussive symptoms, [18] 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. [19] 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 Lumostem. The use of this type of therapy into the ears holds promise. 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 (MB) was first used as a dye. It is now known that MB improves mitochondria respiration and could be the "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. What they found was that MB could inactivate certain microbes. It's an anti-microbial that leaves cells and tissues virtually unharmed! That's right, it's a powerful antimicrobial! It gets even more impressive, so

stay with me. MB was one of the first chemotherapeutic medications ever tested in humans. In 1891, it was used to treat malaria. It was replaced by antibiotics when they first came on the scene, even though MB is superior to them. With heavy marketing to doctors by big pharma, a shift was made to these new "superior" anti-microbials. Are they really superior? We know that antibiotics can have negative effects on our health by 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 they have created resistant strains which makes them useless. Unlike with antibiotics, micro-organisms have no resistance to MB. Your microbiome is an incredibly important, diverse group of bacteria that coexist in your body, mostly in your gut. The malarial parasite, *Plasmodium falciparum*, is now showing an increased resistance to common antimalarial drugs. As a result, methylene blue is being considered as a better option.

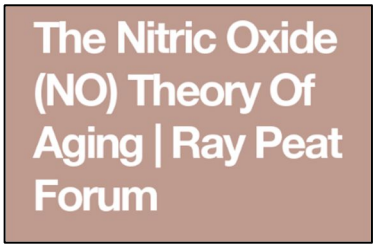
Methylene Blue & Nitric Oxide

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

MB is a powerful inhibitor of nitric oxide (NO). There is a lot of hype around the benefits of NO and its ability for open blood vessels to improve circulation. Viagra works on NO and has been hugely successful to improve the male and female erection. But is it as safe as is generally thought? There are 3 types of nitric oxide synthase enzymes (NOS) which generate NO. They are named according to their activity or the tissue type in which they were first described. They are neuronal NOS (nNOS), endothelial NOS (eNOS) and inducible NOS (iNOS). NO is released in short and brief moments of stress exposure, and it is a vital molecule to support us. NO is also a free radical and is a powerful oxidant that the body needs to neutralize. Too much NO is associated with tissue damage and is an aging accelerant. It is also present in air pollution. In 1990, a multitude of scientific research was released claiming NO to be a safe and powerful molecule to treat many diseases such as erectile dysfunction, improve heart function and as a stroke preventative. In 1992, NO was proclaimed "the molecule of the year". NO went from a toxic free radical to Miracle Drug.

.

NO is Part of the Body's Stress Response!



NO 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 NO is a signaling molecule and signals stress in the body that can enroll a hormetic response if its dosage is within the hormetic zone and not into the danger zone. Chronically elevated NO or ozone would NOT be beneficial to the body for the same reasons.

NO is commonly taken by body builders and men with ED on a daily basis. L-arginine and citrulline are both precursors to NO that are in many body building and endurance supplements. NO can give you a pump through an enhanced inflammatory response within the muscles but may not be the healthiest strategy long term.

Anyone looking to maximize fitness might consider this 2015 study in which a scientist found that NO powerfully inhibits testosterone. Using an NO inhibitor like MB might negate these effects as in the above study. "Warning to men: Erection drugs might kill you!" This is an article written by Michael Castleman. [20] Since its approval in 1998, Viagra has been implicated in 1,828 deaths, Cialis 236 deaths, and Levitra 221 deaths. These three ED medications alone account for 2,500 deaths and 25,000 other side effects such as mini stroke, vision loss and hearing loss.

The dirty secret with these studies is that they only look at a few thousand people. If a drug kills 1 in 100,000, that side effect may not show up in the study. Millions of men are now taking Viagra, and as a result, thousands have died due to this fact. The most common problem that leads to death is when there is a co-administration of nitroglycerine. The person ends up getting a double dose of NO.

Chronically elevated NO levels can cause cardiovascular disease, MS, Alzheimer's, Dementia, and other degenerative neurological diseases. A recent study showed a dramatic increase in skin cancer after Viagra use, with an 84% increase in melanoma. [21]

Just because NO 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 by inhibiting CCO. NO in high amounts causes the opposite and you will have vasoconstriction. NO is also involved in the inflammatory response. [22]

In the paper called "The NO Hypothesis of Aging", the author presents the causes of aging, suggesting one of the prominent theories is the free radical theory. According to this theory, free radicals generated through mitochondrial metabolism can 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. [23] Aging of the anterior pituitary and pineal will result in decreased secretion of pituitary hormones and the pineal hormone, melatonin. The induction of iNOS from infections, in the temperature-regulating centers, may cause a decreased febrile response in the elderly due to loss of thermosensitive neurons. NO may play a role in the progression of Alzheimer's disease and Parkinsonism.[24] Activation of cytokine and iNOS production in the cardiovascular system leads to coronary heart disease. [25] Antioxidants, such as MB, melatonin, vitamin C, and vitamin E, play important roles in reducing or eliminating the oxidant damage produced by NO. [26]

Regarding NO and Angiogenesis, in the short term, such as post-injury, elevated levels of NO to increase angiogenesis might be helpful. However, chronic activation of angiogenesis might put you at a higher risk for cancer.

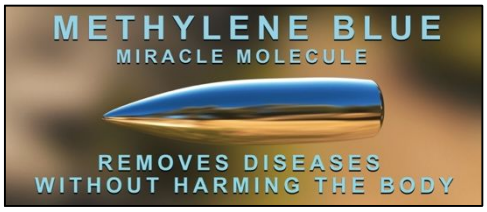
It's not the virus that kills; it's the cytokine storm. NO is the primary molecule that causes the cytokine storm. The cytokines then signal a shift in the cellular energy away from the electron transport chain to aerobic glycolysis. This cuts down available energy by 90%, causing the immune system to literally starve and be 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. MB's inhibition of NO is one way it supports recovery from infection, in addition to its anti-viral properties.

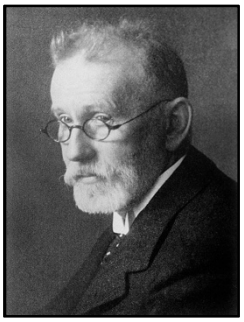
At first glance, NO is an enhancement to circulation. However, step back and look at things more holistically. It's clear that it's not the right approach, and its likely to cause more harm than good. MB, as a powerful inhibitor of NO, supports the body fully**.**

Methylene Blue: Magic Bullet

The term **magic bullet** is a scientific concept developed by the German Nobel laureate, Paul



Ehrlich, in 1900.[27] Ehrlich had the idea that we could kill specific disease-causing microbes, such as bacteria, without harming the body itself. He named this agent *Zauberkugel*, or "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 body the energy reserves it needs to work, it will correct disease much better than any man-made chemicals such as pharmaceuticals.



Methylene Blue & Mitochondria

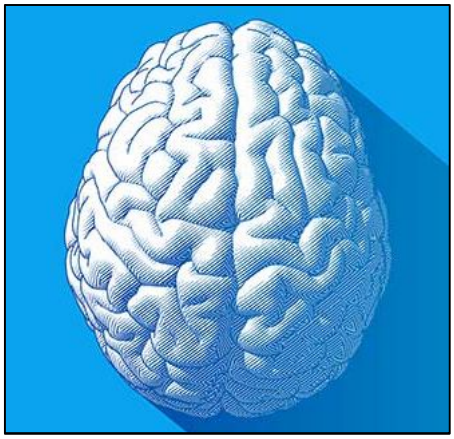
Methylene blue is anti-inflammatory and neuroprotective, showing promise in treatment of diseases such as stroke, Alzheimer's disease, and Parkinson's disease. [28]

Remember your mitochondria works through the electron transport chain where it shuffles electrons. They release chemical energy that the body uses to make ATP, the energy currency in our cells. Methylene blue is an electron carrier and even recycles electrons, which allows it to improve mitochondrial function. It 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 very efficient energy production.

Methylene Blue & The Brain

Studies show methylene blue enhances memory and is metabolically neuroprotective for the brain. MB has been associated with improvement of memory consolidation. In addition, low doses of methylene blue have been used for neuroprotection against mitochondrial dysfunction in human disease. There are neurometabolic mechanisms for memory enhancement and neuroprotection from methylene blue. [29] Another study showed that MB could enhance memory through an increase in brain cytochrome oxidase activity. Yet another study titled, Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain, showed impressive brain support. [30]



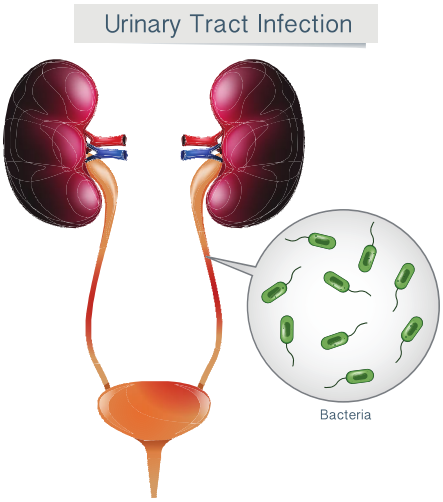
In a study titled, Extinction Memory Improvement by the Metabolic Enhancer Methylene Blue, MB may also function as a cholinesterase inhibitor, [31] increasing the amount of acetylcholine available, a neurotransmitter in the brain responsible for arousal, attention, memory and motivation. [32]

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. [33] A 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. [34] 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. It also calms down the inflammation that occurs after a head trauma that is associated with microglial cells becoming overactivated. "Methylene blue exerts a neuroprotective effect against traumatic brain injury by promoting autophagy and inhibiting microglial activation." [35]

Methylene Blue Use for Chronic Urinary Tract Infection

The use of MB to treat chronic urinary tract infection was an old indication for MB until antibiotic therapy was introduced. This therapy was forgotten about as antibiotics were the new sexy treatment. This is common in medicine where new drugs are advertised and promoted by pharma companies and the doctors are taught about these new drugs. The Pharma companies also have an influence as to what our medical books contain so they sway our doctor to think in line with the agenda they would like promoted. In a case like MB, where the patent has expired, pharma companies do not have any incentive to promote. Therefore, many doctors do not even know about using MB for chronic urinary tract infection even though there is zero negative impact to one's health, only positive health benefits. Antibiotics, on the other hand, have led to resistant super bugs and obliteration of the microbiome. It can take up to 2 years to recover from just one round of antibiotic therapy.



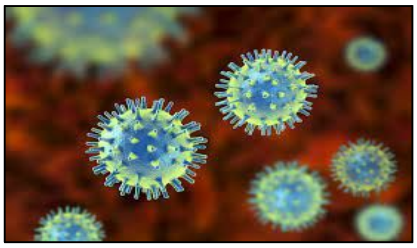
In the study 'Treatment of Recurrent Urinary Tract Infection Symptoms with Urinary Antiseptics Containing Methenamine and Methylene Blue: Analysis of Etiology and Treatment Outcomes.' The scientists found a total of 144 subjects were randomized per group and 272 completed the study.[36] Primary endpoint analysis demonstrates homogeneity between treatment groups, with 69.4% and 72.2% subjects, respectively, showing improvement in the score of the urinary regularity UTISA domain after 3 days of treatment (p= 0.87). At Visit 2, incidence of treatment-related adverse events was higher in Group B. The A group was the one

where they kept the MB at 20mg, and the B was the one where they increased the methenamine. This is a typical strategy pharmaceutical companies will take. This is similar to the study they did with lithium for depression and methylene blue. Methylene blue by itself is amazing and these companies are trying to create something they can patent because they cannot just market methylene blue by itself even though it works better. There are so many examples of this in medicine. For example, red yeast rice extract is by far the most advanced statin drug. In fact, the entire family of statins is based on red yeast rice but many if not all the studies do not show as much efficacy as simply taking red yeast rice extract. The bottom line is it is best to just take MB by itself for this indication.

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. [37] Methylene blue displays virucidal preventive and therapeutic activity against influenza virus H1N1 and SARS-CoV-2. [38]

A recent French publication on a cohort of 2,500 end-stage cancer patients treated with MB during the first wave of COVID-19 mentions a possible protective role of MB against respiratory viruses. This study group showed no reported cases of influenza or SARS-CoV-2 infections. [39] 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 investigated the efficacy of wearing a mask find them to be ineffective anyway. [40]



The body will not become sick or worn out prematurely without cause. Having treated many diseases over the years, I have come to the conclusion that it is either toxins or infections that are the root cause. 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 they are both involved. I have found virtually all the patients that have come to me test positive for at least one, but typically two viruses. I often test for Epstein Barr, cytomegalovirus, and HHV6, as well as an immune marker called CD57. Cyrex Labs 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/antimicrobial effect making them great therapeutic substances for any brain-based conditions.

Methylene Blue for Lyme & Bartonella

In the initial stages of infection, bacteria are in a growth phase where they divide rapidly to increase the number of bacteria to establish an infection. Bacteria then enter a stationary phase where bacterial growth slows down. The current antibiotic treatments for acute and chronic Lyme disease and Bartonella primarily work in the bacterial growth phase. However, these antibiotics are ineffective once the bacteria enter the stationary phase. In recent years, researchers have conducted screening studies of drugs and natural compounds to identify effective treatments for Lyme disease and bartonella in a stationary phase. Surprisingly, a medication called methylene blue proved to be an effective treatment for stationary phase Lyme disease and Bartonella. Stationary phase of the Lyme spirochete causes more severe symptoms. In 2018 researchers from John Hopkins University published a study that looked at the severity of arthritis when the bacteria that causes Lyme disease was in the growth phase, the stationary phase, and biofilm colonies. The research discovered the arthritis was more severe earlier in an infection (in the stationary phase and biofilm groups) than in the growth phase group. The researchers also concluded that currently used antibiotic regimens are less effective against the stationary and biofilm bacteria.

In 2014, researchers from Johns Hopkins University screened an FDA drug library for activity against borrelia burgdorferi (the bacteria that causes Lyme disease). They identified 165 hits (drugs) with higher activity against Lyme disease than doxycycline and amoxicillin. The following year the same researchers narrowed the results down to the top 52 drugs that can be used in humans and effectively killed at last 65% of stationary phase bacteria.

The researchers discovered that various drugs used to treat other infections – including antibiotics, antivirals, antifungals, and antiparasitics – were effective at killing stationary

phase *Borrelia*. One of the top hits was a medication called methylene blue. Methylene blue was originally an antimalarial medication currently used to treat a condition called methemoglobinemia and urinary tract infections. Methylene blue was almost as effective as daptomycin – a drug that has received attention for its ability to treat persistent Lyme disease.

Researchers published the first study to evaluate drug combinations against Bartonella in the stationary phase and biofilms in 2020. Again, a team of researchers led by Ying Zhang, MD from Johns Hopkins University, expanded upon the single drug screen study from 2019. This research study evaluated the top-performing drugs from the 2019 trial and created 25 two-antibiotic combinations to test their efficacy against Bartonella in the stationary phase and biofilms.

Of the 25 combinations of antibiotics, four were able to completely eradicate stationary phase Bartonella in 24 hours – azithromycin/ciprofloxacin, azithromycin/methylene blue, rifampin/ciprofloxacin, and rifampin/methylene blue. Methylene blue was almost as effective as daptomycin – a drug that has received attention for its ability to treat persistent Lyme disease in a recent study.

I have been using MB with many biotoxin cases and Lyme disease cases with good success. I have been using an oral or suppository version of MB called Lumetol Blue. It comes in a 60mg and a 300mg. The 300 mg is meant to be broken into quarters (4 pieces) and taken by mouth once daily for those seeking to take 75mg daily. The 60mg suppository can be broken into halves for 30mg dosing as well.

Methylene Blue is an Anti-depressant

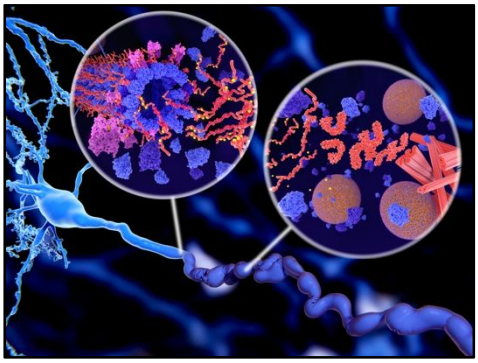
In higher doses, methylene blue seems to be a powerful antidepressant. Keep in mind that in higher doses, MB acts as an MAO inhibitor. Therefore, it can be dangerous to take antidepressants along with higher doses of MB. In this study, methylene blue at 15 mg/day, was compared with placebo in treatment 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. [41]

In this study 'Effects of Post-Session Administration of Methylene Blue on Fear Extinction and Contextual Memory in Adults with Claustrophobia", the scientists concluded: Methylene blue enhances memory and the retention of fear extinction when administered after a successful exposure session but may have a deleterious effect on extinction when administered after an unsuccessful exposure session. [42]

In this study, methylene blue was tested for the treatment of manic depression. **'**A two-year double-blind crossover trial of the prophylactic effect of methylene blue in manic-depressive psychosis.'

During the year, the patients were treated with methylene blue at 300 mg/day, and they were significantly less depressed than during the year on 15 mg/day. [43]
Another study 'Methylene blue treatment for residual symptoms of bipolar disorder:



Randomized crossover study' they used 195mg/day. This is what they concluded: **"**We conducted a double-blind crossover study of a low dose (15 mg, 'placebo') and an active dose (195 mg) of methylene blue in patients with bipolar disorder treated with lamotrigine." [44]

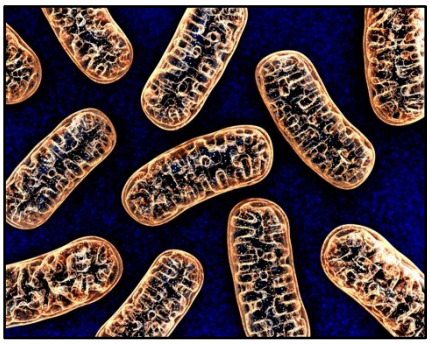
Forming memory to extinguish fear such as with a phobia. Research in extension learning, where memory consolidation and the energy for the brain is boosted allows for less fear experienced, and less PTSD and anxiety disorder, and all show benefit from the use of methylene blue. MB is used for memory consolidation where one dose is given during the integration phase of the therapy. The results are alarming as to how well this works synergistically with the right therapy to dig deep

into the conscious and unconscious mind. We discover that many of the stories that we have stuck in our mind are telling us our true nature is anything less than love. [45] In this study methylene blue was tested for manic depression. ‘A two-year double-blind crossover trial of the prophylactic effect of methylene blue in manic-depressive psychosis.’ [46]

Methylene Blue & Degenerative Neurological Disorders.

Let’s consider the massive need nerves have for a high and constant energy source. There are 100 trillion mitochondria in the average human body. The number of mitochondria in a cell can vary widely by organism, tissue, and cell type. A mature red blood cell has no mitochondria, [47] whereas a liver cell has 1000-2000 mitochondria. [48][49] There are about 5000 mitochondria in the average heart muscle cell, however the brain can have an estimated population of 1-2 million mitochondria per cell.[50] This is due to the incredible demand nerves have for lots of energy. The brain has 2% of the weight of the body yet consumes 20% of the total energy produced by the body.

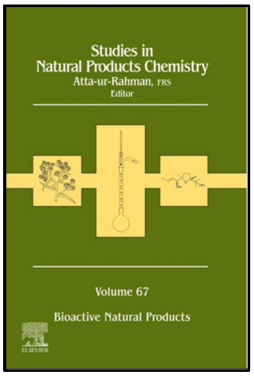
Due to this huge energy demand, cures for degenerative neurological disorders have been eluding doctors for decades due to the complexities with supporting cellular energy. Because these disorders are classically associated with the accumulation of various proteins in the brain such as tau, beta amyloid plaque, and alpha synuclein, scientists have been myopically perusing ways to clear these proteins and ignoring energy and metabolism. There are two re



ports on the effects of MB on tau aggregation.

In one study, MB did not alter abnormal tau phosphorylation, and failed to inhibit tau-dependent neuronal cell toxicity in zebrafish [51]

The failure of this study could be due to the use of toxic methylene blue. This is a common practice with animal studies, where no regard is placed on the impact heavy metals and industrial chemicals may have on mitochondrial function, which is the key to methylene blue's effect and benefit.



The other study was on mice where they received a 2 to 3-week treatment with oral MB. In this latter study, MB acted as a tau aggregation inhibitor. [52]

They concluded, "Methylene blue may have potential as a drug candidate for the treatment of tauopathy. Based on these results, tau aggregation inhibitors are strong candidates for the treatment of tauopathy." [53]

The researchers, scientist and doctors are chasing the wrong outcome. To understand this, you should first consider this scenario. Imagine you have a rat infestation problem in your home. Let's say that you are very sloppy, and you don't take your trash out and, as a result, your food and trash accumulate in the house. This attracts the rats that are hungry and just looking for food to eat. If you were to take an approach to try and trap the rats to solve the problem, you would be chasing a downstream consequence of an upstream cause. In this example, it is all the food and trash that is attracting the rats into the house. You could further argue that you also need to address all the ways the rats are gaining entry into the home. But for the purposes of this explanation, if we focus just on the food that the rats are being attracted to and we resolve this

problem giving the rats zero reason to come into the house, this would be a much better solution to the problem. Now let's transfer that to the issue with these proteins that are accumulating in the brain. Many of these proteins are associated with the immune system and they are there to protect us and the central nervous system from toxins and infections that find themselves in the central nervous system. The proteins are designed to wrap around these invaders to protect the brain from being exposed to them. Therefore, these proteins are healthy, and they are a consequence of a normal protection mechanism that the brain uses to protect itself from invading substances and microbes. If the focus to resolve these issues is simply to find substances that dissolve these proteins, we would really be missing the boat. This is why all these substances that are being studied by the big pharmaceutical companies wind up having no benefit or demonstration of improvement in the participants in the study. We do not see improvement in their brain function or slowing of the degenerative neurologic disorder. In fact, once these protein tangles form, these nerves are no longer functional and can never be resuscitated into a normal functioning neuron. Therefore, this is an insanely idiotic approach. However, this is the main approach that the pharmaceutical companies are taking right now. There is a lot of controversy in the scientific field. We are trying to wake these people up to get them on a different track of thought process within this area of science. Methylene blue has been shown to decrease the level of tau in a recent study.[54] In a book called Studies in Natural Products Chemistry" they reference "Besides reducing the tau aggregation process it also shows a significant impact on cognitive performance in the stages of AD." [55]

Methylene Blue also supports synapsis protection and the improvement of protein clearance through autophagy. [56]. We will dive more into autophagy in the next section. This is exciting; however, these researchers are ignoring the real miracle of methylene blue and its ability to enhance the metabolism and mitochondrial function of the nerves.

I also wrote a book on melatonin called Melatonin: Miracle Molecule. Along with MB, I feel melatonin holds much promise in the treatment and prevention of brain degeneration. This was a study on Tau and Melatonin called "Effect of Melatonin on Tau aggregation and Tau-mediated cell surface morphology" and the study concluded that melatonin can reduce the formation of Tau. Melatonin also modulates and helps to maintain membrane morphology. Melatonin administration shows mild anti-aggregation and cytoprotective effects.[57] In the book, we dive deep into how melatonin is the greatest resilient molecule and protects us from stress in many

ways. It is worth a read as I use both of these molecules regularly in practice with great success. Here is a link to find the book on amazon. They both work at the core of many, if not all diseases. They are metabolic disorders, and all disease starts with energy deficits. The body then cannot keep up with maintenance and adaption to environmental stressors, toxins, and infections.

Ways MB supports the brain and nerves:

- Supports autophagy and removal of senescent cells
- Upregulates energy production through mitochondrial health and strength
- Calms down oxidation thus lowering inflammation
- Acts to support immune system to remove and kill infection in the body and brain.
- Supports detoxification of the brain
- Lowers mental and emotional stress; thus, improving health and brain function through its antidepressant effects

Methylene Blue for Inner Ear Rejuvenation

Many doctors have been seeking out the best options for treatments aimed to regenerate the inner ear for conditions such as tinnitus, hearing loss, hyperacusis and even balance disorders which can all be due to inner ear damage. Besides our loud modern environment, we also have stresses such as Covid and vaccine injury that are contributing to inner ear conditions. At Advanced Rejuvenation, we brought LumoMed laser treatment to the USA almost a decade ago and are currently the only providers for LumoMed in the USA. Our clinic became certified in ShimSpot in 2022, and we are currently offering the combination of both techniques which we call SunaVae. It comes at the perfect time to support all who suffer damage to the inner ear.

Stem cells are fragile, and there is a risk called senescence where they can go into a permanent state of sleep. This is the major focus of many studies on improving stem cell results by scientists working in the field of regenerative medicine. Methylene Blue, which helps optimize cellular energy and autophagy, also aides in stem cell activation.

Laser in the spectrum of 660nm with a high power of 25,000 mv is the technology used at Advanced Rejuvenation and through LumoMed. Methylene Blue is used to further improve the activation of the stem cells by the laser, through a process called PhotBioModulation.

At Advanced Rejuvenation, we have been working to put together the most cutting-edge protocol for inner ear health we call the “Sensory Rejuvenation Protocol”. This protocol focuses on specific lifestyle modifications, nutritional support and removing all triggers causing inflammation in the nervous system and/or the inner ear. This protocol utilizes methylene blue to

further promote cellular energy as well as the removal of senescent cells. Read Dr John's Article on Sensory Rejuvenation HERE.

MB, Fasting, Autophagy & Mitochondria

Methylene blue increases autophagy, which is cellular cleaning and recycling. This study showed MB induced neuroprotection by enhancing autophagy. [58] Due to this, methylene blue might be considered helpful during fasting. We will get into fasting a little later. To 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.

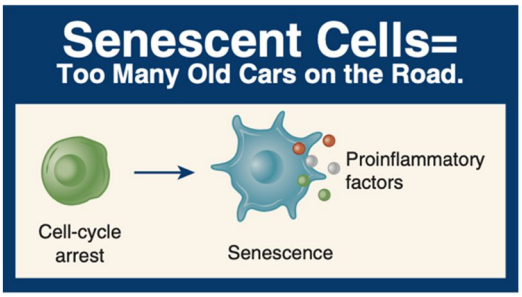
Mitochondrial dysfunction is a hallmark of metabolic decline (vitality) during aging. [59]. We are constantly replacing our old, dysfunctional mitochondria with new, healthy, fresh mitochondria or "mito." The population of all the mito of a given cell constitutes your *Chondriome*. Like your microbiome, we have a healthy pool of mitochondria and an unhealthy pool. This will dictate how functional they are. The average cell in your body has between 1,000-2,000 mito. As cells get old, they are recycled, through the gene modulation process ruled by **mTOR.**

The **mTOR** pathway is a central regulator of metabolism (vitality) and physiology (function). 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 to regenerate newer, healthier cells. [60]

Mitophagy is the selective degradation of mitochondria by autophagy. It often occurs in defective mitochondria following damage or stress. [61] Remember all the types of stress? These ALL have an impact on the demand for Mitophagy to be activated through mTOR![62] 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. [63] 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, spewing inflammation and sucking the life out of your body. They defer vital energy that would normally be going to healthy cells.

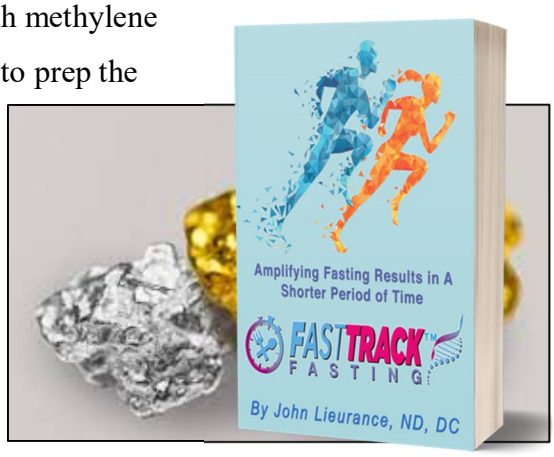
We discussed ozone as a signaling molecule when we discussed NO. Ozone works through hormetic activation in the body, which results in a powerful autophagy and mitophagy response. NO, on the other hand, inhibits autophagy. [64] I will often have my patients do ozone and MB during their fasting phase. There are home units you can purchase and do rectal insufflation that is very powerful. There are also saunas that deliver ozone quite efficiently. As stated, methylene blue, such as in Lumetol Blue, activates autophagy and can be taken during fasting. [65]

In my clinic I use the Fast Tract Fast from MitoZen.com to increase and improve the signaling associated with the healing qualities of fasting. This is a fasting protocol where there is a preparation phase followed by the fast which is enhanced with various nutraceuticals and plant extracts to increase clearance of cells as well as the deep recycling created by autophagy.

Following the fast (Phase 3) is where it is important to stimulate and activate growth and repair. This is the portion of fasting many people miss. It is just as important to heighten the signaling during fasting as it is during the post fast or feeding phase. It all involves MTOR either being inhibited or being activated. This was the theory behind creating the Fast Track Fast protocol.

Check out the e-book on Fast Track Fast at FastTrackFast.com for a deeper dive into this subject and the protocol.

This protocol can be done in as little as a 24 hour fast or as long of a fast as one wants to perform. It can even be done as a one meal a day program which I have been gravitating towards with my patients. I have them do two days in a row where they just consume one meal on both of those days. Two days prior, I will have them load with methylene blue and or NAD+ to enhance cellular resilience and to prep the cells in the body for the stressor of the fast. The Phase 2 products are taken in the morning if someone is only having dinner or lunch. You would take the Phase 2 product when you are in a fasting state to enhance autophagy and senescent clearing. This product is called a senolytic. Senolytics such as pterostilbene, fisetin and resveratrol are very powerful senolytics. They are in the product, Lucitol, which is the Phase 2 product that can be used either as a suppository or there is a liquid version in a liposomal delivery.



Silver & Gold Enhance MB

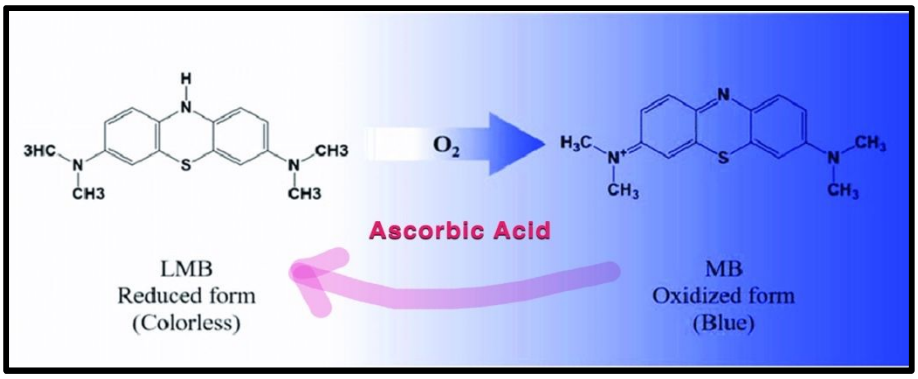
Using nano silver and gold mixed with MB can greatly enhance its photobiomodulation abilities. These precious metals work by enhancing the cytochrome complex when combined with MB, which allows more electrons to flow through the chain within the mitochondria.

According to a 2015 study, silver nanoparticles decorated with methylene blue potentiated the photodynamic inactivation of *pseudomonas aeruginosa* and *staphylococcus aureus*. [66] In addition, this study shows the synergistic reaction of silver nitrate, silver nanoparticles, and methylene blue against bacteria. [67]

A 2009 study discussed the antimicrobial properties of light-activated polymers containing methylene blue and gold nanoparticles. [68] Gold nanoparticles have been studied in

combination with MB for cancer with great promise as it supports photodynamic therapy (PDT). [69]

I have developed a special medical protocol called LumeBlue, combining nano gold, nano silver, and MB together in an infusion. Once the IV is dripping into the patient, a Laser IV is started using 660nm wavelength to photoactivate the mixture. The IV lasts about 45 minutes to 1 hour. Oxygen therapy following the IV has great benefit. In my clinic, we use both hyperbaric oxygen therapy and the CVAC chamber. Oxygen therapy enhances the LumeBlue protocol, as it drives more oxygen into the cells to further support the electron transport chain within the mitochondria.



Methylene Blue & Leuco-Methylene Blue

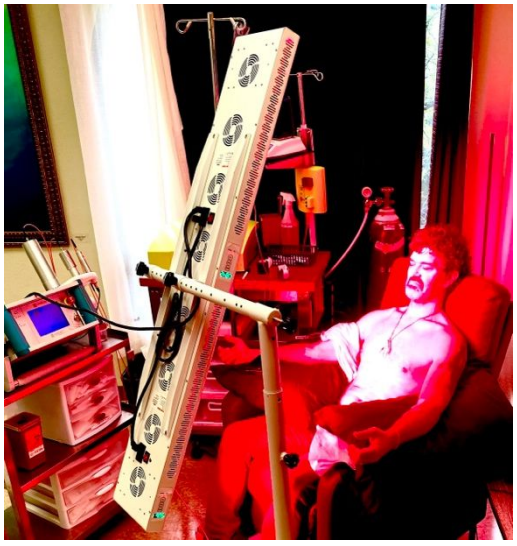
Adding a reducing agent, such as ascorbic acid, can transform the MB to its reduced form which is a less brilliant blue color and can even become white; thus, the name “Leuco” (like Leucocyte or white blood cell).

Color-switching materials have attracted a great deal of attention due to their application prospects in rewritable paper, sensors, optical data storage and

security feature technologies.[70] Significant efforts were previously devoted to developing various systems with improved stability to enhance switching rates. Color switching of organic redox dyes over various catalysts are strongly influenced by the pH of the solution or the type of reducing agent contained in the system.[71] There are several ways to reduce MB into its redox, Leuco MB form, as seen in the research. Methylene blue (MB), a *positively charged heterocyclic aromatic thiazine dye*, has long been used as a staining agent in industry.[72] In a reducing environment, methylene blue can be reduced to colorless leuco-methylene blue (LMB) through a hydrogenation reaction. It can switch back to initial blue color by oxidative dehydrogenation upon exposure to an oxidizing environment. The most viable and practical is the combination of MB with ascorbic acid. [73]

The redox reactions of methylene blue (MB^+) often occur on a time scale of a few seconds to minutes. *Leuco*-Methylene Blue is very reactive once mixed with ascorbic acid and since it is also in a UV-driven triplet state photochemically, it undergoes photo-oxidative quenching with dissolved oxygen. This means after its redox reaction with ascorbic acid, it can be reversed when it is exposed to oxygen. [74]

Lumostem with Red light at 660nm. Part of the LumeBlue protocol at Advanced Rejuvenation.



Guidelines to Methylene Blue Use

According to experts, the proper dosage for methylene blue is between ½ - 4 mg per kilogram each day. Half-life is 12 1/2 hours for methylene blue. MB is released through the urine, so be prepared for a blue or green urine for a day or two after a higher dose. If an intervention is desired, such as in the case of poisoning or toxicity, a higher one-time dose of 4mg/kilo is given. This would apply with methemoglobinemia, when such a higher dose might be given orally. ½ -1 mg per kilogram can be given every day safely. Lower doses may be taken if nano silver and gold are combined with the MB for greater effects. Much higher doses can be used in special circumstances, however, there can be a diminishment in effect with doses higher for

mitochondrial support. It is important that higher doses be monitored through a healthcare practitioner.

Methylene Blue & SSRIs

One of the concerns with methylene blue consumption is a serotonin storm when methylene blue is taken with SSRIs, SNRIs or drugs that increase serotonin levels, such as anti-depressants and other MAOI inhibitors. The contraindications for methylene blue and SSRIs are based on a handful of cases (x5) where extremely high doses of methylene blue were used to stain the parathyroid gland during a surgical procedure to remove part or all this gland due to disease. The patients that were on SSRIs experienced a serotonin storm and did not do as well. The doses used during this procedure where much higher than the therapeutic doses discussed in this book. This concern was rescinded by Mayo Clinic, and the FDA in Canada does not have this warning associated with methylene blue except as it relates to this surgical procedure. The FDA in the United States has not removed this contraindication to date. To my knowledge, there have never been any issues with methylene blue and SSRIs besides these 5 cases. If you research methylene blue, you will find a lot of negative and scary articles and papers saying it is, a dangerous substance to take when, in fact, it is amazingly safe. In fact, methylene blue has been around since before the FDA was formed. It was grandfathered in due to its safety record; therefore, it did not need to go through any studies to prove itself safety. Taking SSRIs and or serotonin-based medicines like Ayahuasca, Psilocybin, MDA, MDMA or LSD are considered risky. I think these concerns are exaggerated and I personally know of many people who take MB in the space of medicine journeys. Microdosing these psychedelics is also completely safe, in my opinion, when done alongside methylene blue. In fact, I think it is an upgrade that may become more widely recognized for its synergistic powers. Due to the neuroprotective aspects of methylene blue, and the ability to have stronger mitochondrial function when doing deep spiritual work or work on their subconscious and unconscious, methylene blue can be a powerful addition. Much research has been done on methylene blue for

memory consolidation where one dose is given during the integration phase of the psychotherapy. This can be a great upgrade with plant medicine work such as with ketamine, MDMA, psilocybin and even ayahuasca experiences. In our clinic at Advanced Rejuvenation, we often address mental emotional and even spiritual headwinds to optimal health and vitality with ketamine journeys. Using methylene blue before, during, and after is part of our protocol.

Do not take MB if you are pregnant or breastfeeding as it is contraindicated. This study demonstrated a 31% death rate with mothers who took MB during the third trimester. [75]

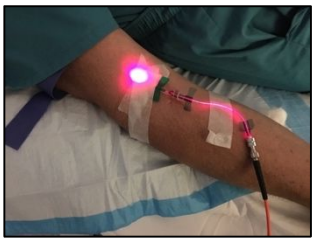
At high doses (>10mg/kg or about 6-700mg), methylene blue may cause some potential side effects including hypertension, methemoglobinemia, dizziness, GI distress, altered pulse oximeter readings, and it can induce hemolytic anemia in people with a genetic condition called G6PD.

It is important that your source of methylene blue is pharmaceutical grade, as other sources may carry significant heavy metals and other toxins. In the USA, this is labeled as USP and is a higher purity than that produced in Europe and other countries.

MitoZen.com carries a few different products that contain clean MB. You can find sublingual methylene blue in drops or troches; however, this will turn your mouth completely blue which may look strange. MB is safest and best absorbed when it is slowly released into your body. MitoZen.com has created a suppository called Lumetol Blue which may provide better absorption due to the sustained release. This product can also be taken orally and will not leave any blue stain in your mouth. You would break up the 300 mg suppository or bullet into quarters and place the ¼ suppository toward the back of your throat and swallow it down with a drink. It's very popular right now for people to take sublingual methylene blue in a delivery called a troche. The experts suggest this is a poor idea as methylene blue fares much better when it is mixed with stomach acid. Unlike a lot of other substances where the stomach acid would be harmful, methylene blue prefers this route versus anything sublingual. Therefore, I feel that the suspension of methylene

blue in palm oil, which is how it is supplied with the methylene blue bullet, is a superior delivery system. By the time you are reading this book, Mike Tyson may have the palm oil suspension of methylene blue in small bars that can be broken into pieces. These pieces are then thrown in the back of the throat and consumed with fluid so that there is no blue left in the mouth. Taking methylene blue in a suppository is also very effective and extremely safe to do it slow absorption into the bloodstream overtime. The only concern I would bring up is staining of the toilet. I have found that cleaning right afterwards prevents the staining. Leaving it to sit over a period of time makes it much more difficult to clean. I also have found putting toilet paper or a paper towel inside the toilet bowl and then flushing immediately afterwards works very well.

The use of methylene blue intravenously in my clinic (along with red light & oxygen therapy) has shown to be of benefit in most of the cases in which I have used it. Because supporting mitochondria and overall cellular energy is such an "upstream" therapeutic, it has benefited many of my patients with a variety of conditions. I have used this protocol on neurological cases such as Parkinson's & brain injuries, Lyme & mold cases, viral infections, autoimmune conditions, and general wellness/longevity programs. Methylene blue is considered photo dynamic, meaning it has a response to light. Red light in the 660 nm range is the sweet spot for methylene blue. We use a system called Lumostem which is an intravenous laser along with the methylene blue. We also use red light panels where are you stand in front of them and receive the light therapy through the skin after a MB infusion. We will then use either hyperbaric oxygen therapy or the CVAC pod. Flooding the body with oxygen after MB further drives ATP production after receiving MB. We call this protocol LumeBlue. This protocol can also be combined with fasting to allow for proper autophagy and mitophagy to create new strong mitochondria. I have been working with a protocol that can be done at home using methylene blue and red-light panels. Using a suppository called Lumetol Blue along with red light panels set to 660 nm called MitoLights. It is also great to go out and get some sun after receiving MB to gain even more photobiomodulation activity.



CVAC Pod at Advanced Rejuvenation. Cyclic Variations in Adaptive Conditioning is what CVAC stands for.

“At home” example of a MB program

If you are unable to get to a clinic that provides MB IV, then I have designed a program for those that would like to effectively use MB at home. Since there are only a handful of clinics that are properly trained in the use of MB this might be your best option. You can find MB as an oral tincture, nasal spray, and suppository through *MitoZen.com*. This is the *Lumetol Blue* line of products. The Lumetol Blue suppository comes in a 60 and 300 mg dose. The 60 mg is recommended for rectal delivery and is well tolerated. The 300mg is not well tolerated rectally and it is better for orally delivery and will not leave any blue stain in your mouth if you consume it correctly. First break up the 300 mg suppository into quarters and place the ¼ suppository toward the back of your throat and swallow it down with a drink. Its best to give yourself 15 minutes between each ¼ as to not cause nausea. I find that having my patients pulse the MB 2-4 times a week seems to work best. On days you choose to take MB, you might consider your dose per day you would like to be at. Of course, it’s best to find a health care provider that can advise you. However, if you need support, then you could reach out to my team about my coaching programs.

Let’s say you wanted to dose 200 mg per day for 3 days. You could take one 60mg suppository and ½ of the 300 mg *Lumetol Blue* (two ¼ pieces or 150mg). You would take the 60 mg suppository in the am after your morning bowel movement, and at the same time the two ¼ pieces. After 30 minutes to an hour, if possible, get in front of a red-light panel that is set to 660 nm. *MitoLights* are panels set to work with MB and are also available through *MitoZen.com*. It is suggested to do only 10 minutes a day with red light therapy, however on MB days, I often suggest that my patients do 2 or even 3 sessions spread out though out the day. I also suggest as much direct sunlight as you can on MB days. I will also suggest my patients consume one tablespoon of Argentyn 23 or Sovereign colloidal silver 3 times throughout that day as well. If you have a hyperbaric soft chamber at home or a clinic that has one you might consider doing that on your MB days within 1-2 hours of consuming the MB.

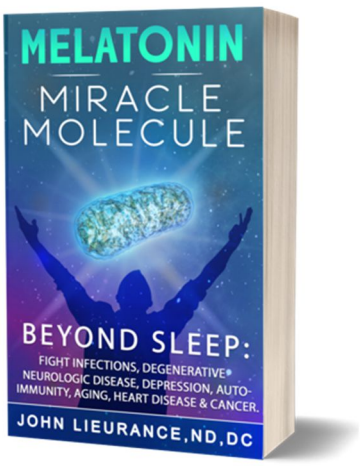
Keep in mind, MB is also a good supplement to take along with fasting as it promotes autophagy. Timing is best if you take it in the morning if you are doing intermittent fasting and

skipping breakfast. This protocol can be done for a month to boost cellular energy or for multiple months, as MB is safe to take long term, such as in cases of degenerative neurologic disease. Lower dosing, such as 10-20 mg per day of MB, may be considered in many cases, and the Lumetol Blue tincture or nasal spray might be a consideration. These lower doses should also be used with red light, silver, and an oxygen therapy if available. Also be prepared to see blue to green urine for up to 2 days following an MB Day.

Keep in mind, many animal studies have been done with poor quality MB and not the higher pure grades of MB. Just like with the SSRI contraindication, which has most medical professionals fearful of rx MB, especially with patients on SSRIs for depression, these have been flawed studies where higher doses have been used in animal research and the side effects shown are due to high levels of heavy metals and other contaminants.

Methylene Blue, Sleep Hygiene and "Upstream Therapies"

The positive effects of methylene blue are even greater when sleep is optimized. I suggest that you track your sleep and make sure you are getting enough REM sleep and deep sleep. Sleep will support your stress adaptation response and metabolic status. Another tool to enhance metabolic pathways, and which pair well with MB, is fasting. I have designed a fasting protocol called Fast Track Fast™. Along with MB and red-light therapy, fasting with Fast Track Fast™ is a great option to enhance your health through metabolic pathways. I call these "upstream therapies." These are therapies which address metabolic conditions through enhancement of the mitochondria. There are also "downstream" treatments which address genes, enzymes, and other chemical reactions in the body. In my clinical practice, I prefer upstream therapies that get to the core of what is disturbing the health and vitality of the cell. The body is an amazing machine which self-regulates and self-heals through its innate intelligence.



Conclusion

Metabolic medicine addressing the mitochondria and the energy reserves in the body is the most powerful medicine available, restoring health at its core.

There are few things more important than a strong metabolic status. Keeping your cells energized allows the full expression of life force through your body, particularly important to your brain and heart. suggest that you track your sleep and make sure you are getting When considering MB, consider all the stressors that we have in today's world which makes it more important for us to take some extra precautionary steps. It's as easy as integrating some rituals into your daily routine. 10 minutes of red-light therapy in the morning with a device like the *MitoLight* should be considered along with methylene blue such as *Lumetol Blue*. I have designed a fasting protocol called Fast Track Fast. Red light therapy along with fasting with Fast Track Fast are great options to enhance your health through metabolic pathways… what I call "*upstream therapies*". These are therapies which address metabolic conditions through enhancement of the mitochondria. Many types of treatments and modalities are what I called downstream where it addresses genes or enzymes or various chemical reactions in the body. In my clinical practice I prefer to go as upstream to the core of what's disturbing the health and vitality of the cell. Remember the body is an amazing machine with self-regulating, self-healing through the innate intelligence within the body. When your cells are given the right energy, that wisdom can do a much better job than throwing chemistry at a specific system. When you address the function of the mitochondria through metabolic medicine you have what I consider to be the ultimate situation to recover from a condition or simply be at your functional best. I always recommend people work with a healthcare provider whenever they start any type of

FASTTRACK FAST.COM

program using MB. For more information on melatonin go to the website **melatoninbook.com** to find my book *Melatonin: Miracle Molecule*.

References

1. Oz, M., Lorke, D., Hasan, M., Petroianu, G., (2010) Cellular and Molecular Actions of Methylene Blue in the Nervous System. *Medical Research Reviews.* Vol. 31:1, 93-117. https://doi.org/10.1002/med.20177
2. Kayabasi, Y., Erbas, O. (2020) Methylene Blue and its Importance in Medicine. *The Archives of Rheumatology in Demiroglu Science University Florence Nightingale Journal of Medicine.* 2020, Vol. 6, Iss. 3, 136-145. https://doi.org/10.5606/fng.btd.2020.25035
3. Eells, J. T. et al. Mitochondrial signal transduction in accelerated wound and retinal healing by near-infrared light therapy. Mitochondrion 4, 559–567, doi: 10.1016/j.mito.2004.07.033 (2004).
4. Wong-Riley, M. T. et al. Photobiomodulation directly benefits primary neurons functionally inactivated by toxins: role of cytochrome c oxidase. J Biol Chem 280, 4761–4771, doi: 10.1074/jbc.M409650200 (2005).
5. Chow, R. T., Johnson, M. I., Lopes-Martins, R. A. & Bjordal, J. M. Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. Lancet 374, 1897–1908, doi: 10.1016/S0140-6736(09)61522-1 (2009).
6. Kingsley, J. D., Demchak, T. & Mathis, R. Low-level laser therapy as a treatment for chronic pain. Front Physiol 5, 306, doi: 10.3389/ fphys.2014.00306 (2014).
7. Lampl, Y. et al. Infrared laser therapy for ischemic stroke: a new treatment strategy: results of the NeuroThera Effectiveness and Safety Trial-1 (NEST-1). Stroke; a journal of cerebral circulation 38, 1843–1849, doi: 10.1161/STROKEAHA.106.478230 (2007).
8. Zivin, J. A. et al. Effectiveness and safety of transcranial laser therapy for acute ischemic stroke. Stroke 40, 1359–1364, doi: 10.1161/ STROKEAHA.109.547547 (2009).
9. Naeser, M. A., Saltmarche, A., Krengel, M. H., Hamblin, M. R. & Knight, J. A. Improved cognitive function after transcranial, lightemitting diode treatments in chronic, traumatic brain injury: two case reports. Photomed Laser Surg 29, 351–358, doi: 10.1089/ pho.2010.2814 (2011).
10. Naeser, M. A. et al. Significant improvements in cognitive performance post-transcranial, red/near-infrared light-emitting diode treatments in chronic, mild traumatic brain injury: open-protocol study. J Neurotrauma 31, 1008–1017, doi: 10.1089/neu.2013.3244 (2014).
11. Schiffer, F. et al. psychological benefits 2 and 4 weeks after a single treatment with near infrared light to the forehead: a pilot study of 10 patients with major depression and anxiety. Behavioral and brain functions: BBF 5, 46, doi: 10.1186/1744-9081-5-46 (2009).
12. Disner, S. G., Beevers, C. G. & Gonzalez-Lima, F. Transcranial Laser Stimulation as Neuroenhancement for Attention Bias Modification in Adults with Elevated Depression Symptoms. Brain Stimul, doi: 10.1016/j.brs.2016.05.009 (2016).
13. Barrett, D. W. & Gonzalez-Lima, F. Transcranial infrared laser stimulation produces beneficial cognitive and emotional effects in humans. Neuroscience 230, 13–23, doi: 10.1016/j.neuroscience.2012.11.016 (2013).

14. Blanco, N. J., Maddox, W. T. & Gonzalez-Lima, F. Improving executive function using transcranial infrared laser stimulation. Journal of neuropsychology, doi: 10.1111/jnp.12074 (2015).
15. Hwang, J., Castelli, D. M. & Gonzalez-Lima, F. Cognitive enhancement by transcranial laser stimulation and acute aerobic exercise. Lasers Med Sci, doi: 10.1007/s10103-016-1962-3 (2016).
16. Pastore, D., Greco, M. & Passarella, S. Specific helium-neon laser sensitivity of the purified cytochrome c oxidase. Int J Radiat Biol 76, 863–870 (2000).
17. Wang X, Tian F, Soni SS, Gonzalez-Lima F, Liu H. Interplay between up-regulation of cytochrome-c-oxidase and hemoglobin oxygenation induced by near-infrared laser. Sci Rep. 2016 Aug 3; 6:30540. doi: 10.1038/srep30540. PMID: 27484673; PMCID: PMC4971496.
18. Chao, L., Barlow, C., Karimpoor, M., Lim, L. (2020). *Changes in Brain Function and Structure After Self-Administered Home Photobiomodulation Treatment in a Concussion. Case*. Frontiers in Neurology. 8 September 2020. https://doi.org/10.3389/fneur.2020.00952
19. Zomorrodi, R., Loheswaran, G., Pushparaj, A. *et al.* Pulsed Near Infrared Transcranial and Intranasal Photobiomodulation Significantly Modulates Neural Oscillations: a *pilot exploratory* study. *Sci Rep* **9,** 6309 (2019). https://doi.org/10.1038/s41598-019-42693-x
20. Warning to Men: Erection Drugs Just Might Kill You | Psychology Today Australia
21. Li W, Qureshi AA, Robinson KC, Han J. Sildenafil Use and Increased Risk of Incident Melanoma in US Men: A Prospective Cohort Study. *JAMA Intern Med.* 2014;174(6):964–970. doi:10.1001/jamainternmed.2014.594
22. Brown GC, Bal-Price A. Inflammatory neurodegeneration mediated by nitric oxide, glutamate, and mitochondria. Mol Neurobiol. 2003 Jun;27(3):325-55. doi: 10.1385/MN:27:3:325. PMID: 12845153.
23. Kirkwood TB, Kowald A. Network theory of aging. Exp Gerontol. 1997 Jul-Oct;32(4-5):395-9. doi: 10.1016/s0531-5565(96)00171-4. PMID: 9315444.
24. Kirkwood TB, Kowald A. Network theory of aging. Exp Gerontol. 1997 Jul-Oct;32(4-5):395-9. doi: 10.1016/s0531-5565(96)00171-4. PMID: 9315444.
25. Kirkwood TB, Kowald A. Network theory of aging. Exp Gerontol. 1997 Jul-Oct;32(4-5):395-9. doi: 10.1016/s0531-5565(96)00171-4. PMID: 9315444.
26. Kirkwood TB, Kowald A. Network theory of aging. Exp Gerontol. 1997 Jul-Oct;32(4-5):395-9. doi: 10.1016/s0531-5565(96)00171-4. PMID: 9315444.
27. Paul Ehrlich - Wikipedia
28. Tucker, D., Lu, Y., & Zhang, Q. (2018). From Mitochondrial Function to Neuroprotection-an Emerging Role for Methylene Blue. *Molecular neurobiology*, *55*(6), 5137–5153. https://doi.org/10.1007/s12035-017-0712-2
29. Rojas JC, Bruchey AK, Gonzalez-Lima F. Neurometabolic mechanisms for memory enhancement and neuroprotection of methylene blue. Prog Neurobiol. 2012 Jan;96(1):32-45. doi: 10.1016/j.pneurobio.2011.10.007. Epub 2011 Nov 3. PMID: 22067440; PMCID: PMC3265679.
30. Rodriguez, P., Zhou, W., Barrett, D. W., Altmeyer, W., Gutierrez, J. E., Li, J., Lancaster, J. L., Gonzalez-Lima, F., & Duong, T. Q. (2016). Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain. *Radiology*, *281*(2), 516–526. https://doi.org/10.1148/radiol.2016152893

31. Pfaffendorf M, Bruning TA, Batnik HD, van Zwieten PA. The interaction between methylene blue and the cholinergic system. Br J Pharmacol. 1997 Sep;122(1):95-8. doi: 10.1038/sj.bjp.0701355. PMID: 9298533; PMCID: PMC1564911.
32. Giocomo, L.M., Hasselmo, M.E. Neuromodulation by Glutamate and Acetylcholine can Change Circuit Dynamics by Regulating the Relative Influence of Afferent Input and Excitatory Feedback. *Mol Neurobiol* **36,** 184–200 (2007). https://doi.org/10.1007/s12035-007-0032-z
33. Oz M, Lorke DE, Petroianu GA. Methylene blue and Alzheimer's disease. Biochem Pharmacol. 2009 Oct 15;78(8):927-32. doi: 10.1016/j.bcp.2009.04.034. Epub 2009 May 9. PMID: 19433072.
34. Home Page | TauRx Pharmaceuticals
35. Zhao, M., Liang, F., Xu, H., Yan, W., & Zhang, J. (2016). Methylene blue exerts a neuroprotective effect against traumatic brain injury by promoting autophagy and inhibiting microglial activation. *Molecular medicine reports*, *13*(1), 13–20. https://doi.org/10.3892/mmr.2015.4551
36. Game, C., et al. Treatment of Recurrent Urinary Tract Infection Symptoms with Urinary Antiseptics Containing Methenamine and Methylene Blue: Analysis of Etiology and Treatment Outcome. *Research and Reports in Urology,* 2020, Dec. 12:634-639. https://doi.org/10.2147/RRU.S279060
37. Cagno, V., Medaglia, C., Cerny, A. *et al.* Methylene Blue has a potent antiviral activity against SARS-CoV-2 and H1N1 influenza virus in the absence of UV-activation in vitro. *Sci Rep* **11,** 14295 (2021). https://doi.org/10.1038/s41598-021-92481-9
38. Cagno, V., Medaglia, C., Cerny, A. *et al.* Methylene Blue has a potent antiviral activity against SARS-CoV-2 and H1N1 influenza virus in the absence of UV-activation in vitro. *Sci Rep* **11,** 14295 (2021). https://doi.org/10.1038/s41598-021-92481-9
39. Cagno, V., Medaglia, C., Cerny, A. *et al.* Methylene Blue has a potent antiviral activity against SARS-CoV-2 and H1N1 influenza virus in the absence of UV-activation in vitro. *Sci Rep* **11,** 14295 (2021). https://doi.org/10.1038/s41598-021-92481-9
40. Chua, M. H., Cheng, W., Goh, S. S., Kong, J., Li, B., Lim, J., Mao, L., Wang, S., Xue, K., Yang, L., Ye, E., Zhang, K., Cheong, W., Tan, B. H., Li, Z., Tan, B. H., & Loh, X. J. (2020). Face Masks in the New COVID-19 Normal: Materials, Testing, and Perspectives. *Research (Washington, D.C.)*, *2020*, 7286735. https://doi.org/10.34133/2020/7286735
41. Naylor, G.J., Smith, A.H., & Connelly, P. (1987). A controlled trial of methylene blue in severe depressive illness. *Biological Psychiatry, 22*, 657-659.
42. Telch, M., Bruchey, A., Rosenfield, D., Cobb, A., Smits, J., Pahl, S., Gonzalez-Lima, F. Effects of Post Session Administration of Methylene Blue on Fear Extinction and Contextual Memory in Adult with Claustrophobia. American Journal of Psychiatry. Oct. 2014, 1091-1098. https://doi.org/10.1176/appi.ajp.2014.13101407
43. Naylor, G. et al. A Two-Year Double-Blind Crossover Trial of the Prophylactic Effect of Methylene Blue in Manic-Depression Psychosis. *Biological Psychiatry*. Aug. 1986, 915-920. https://doi.org/10.1016/0006-3223(86)90265-9
44. Alda, M., McKinnon, M., Blagdon, R., Garnham, J., MacLellan, S., O'Donovan, C., Hajek, T., Nair, C., Dursun, S., MacQueen, G. (2017). *Methlyene Blue Treatment for Residual Symptoms of Bipolar Disorder: Randomised Crossover Study*. British Journal of Psychiatry. Jan. 2017, Vol 210, 1; 54-60. https://doi.org/10.1192/bjp.bp.115.173930

45. Rojas, J., Aleksandra, B., Gonzalez-Lima, F. (2012*) Neurometabolic Mechanisms for Memory Enhancement and Neuroprotection of Methylene Blue*. Progress in Neurobiology. Jan. 2012, Vol. 96, 1, 32-45. https://doi.org/10.1016/j.pneurobio.2011.10.007
46. Naylor, G., Martin, B., Hopwood, S., Watson, Y. (1986) *Methylene Blue in Manic Depressive Psychosis*. Biological Psychiatry. Aug. 1986, Vol 21:10, 915-920. https://doi.org/10.1016/0006-3223(86)90265-9
47. Nay, P. (2011). *Normal and Disordered Reticulocyte Maturation.* Current Opinion in Hematology. May 2011, Vol. 18(3), 152-157. https://doi.org/10.1097/MOH.0b013e328345213e
48. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P (2005). Molecular Biology of the Cell. New York: Garland Publishing Inc. ISBN 978-0-8153-4105-5.
49. Voet D, Voet JG, Pratt CW (2006). *Fundamentals of Biochemistry* (2nd ed.). John Wiley and Sons, Inc. pp. 547, 556. ISBN 978-0-471-21495-3.
50. Misgeld, T., Schwarz, T. (2017). *Mitostasis in Neurons: Maintaining Mitochondria in an Extended Cellular Architecture.* Neuron. November 2017, Vol.96(3). 651-666. https://doi.org/10.1016/j.neuron.2017.09.055
51. Van Bebber, F., Paquet, D., Hruscha, A., Schmid, B., Haass, C. *Methylene Blue Fails to Inhibit Tau and Polyglutamine Protein Dependent Toxicity in Zebrafish*. (2010) Neurobiol. Sept. 2010, Vol. 39(3), 265-271. https://doi.org/10.1016/j.nbd.2010.03.023
52. Harrington C, Rickard JE, Horsley D, Harrington KA, Hindley KP, et al. (2008) *Methylthioninium chloride (MTC) acts as a tau aggregation inhibitor (TAI) in a cellular model and reverses tau pathology in transgenic mouse models of Alzheimer's disease.* Alzheimer's & Dementia July 2008, 4: T120–T121. https://doi.org/10.1016/j.jalz.2008.05.259
53. Hosakawa, M., Arai, T., Masuda-Suzukake, M., Nonaka, T., Yamashita, M., Akiyama, H., Hasegawa, M. (2012) *Methylene Blue Reduced Abnormal Tau Accumulation in P301L Tau Transgenic*. Plos One. 7(12): e52389. https://doi.org/10.1371/journal.pone.0052389
54. Silva, M., Caro, V., Guzman, C., Perry, G., Areche, C., Cornejo, A. (2020) *Chapter 1 - α-Synuclein and tau, two targets for dementia.* Studies of Natural Products Chemistry. 2020, Vol. 67, 1-25. https://doi.org/10.1016/B978-0-12-819483-6.00001-1
55. Silva, M., et al. (2020) *Chapter 1 - α-Synuclein and tau, two targets for dementia.* Studies of Natural Products Chemistry. 2020, Vol. 67, 1-25. https://doi.org/10.1016/B978-0-12-819483-6.00001-1
56. Silva, M., et al. (2020) *Chapter 1 - α-Synuclein and tau, two targets for dementia.* Studies of Natural Products Chemistry. 2020, Vol. 67, 1-25. https://doi.org/10.1016/B978-0-12-819483-6.00001-1
57. Das, R., Ankur Balmik, A., Chinnathambi, S. (2020) *Effect of Melatonin on Tau aggregation and Tau-mediated cell surface morphology*. Int'l Journal of Biological Macromolecules. 2020 Jun 1; 152:30-39. https://doi.org/10.1016/j.ijbiomac.2020.01.296
58. Jiang, Z., Watts, L. T., Huang, S., Shen, Q., Rodriguez, P., Chen, C., Zhou, C., & Duong, T. Q. (2015). The Effects of Methylene Blue on Autophagy and Apoptosis in MRI-Defined Normal Tissue, Ischemic Penumbra and Ischemic Core. *PloS one*, *10*(6), e0131929. https://doi.org/10.1371/journal.pone.0131929
59. Srivastava S. (2017). The Mitochondrial Basis of Aging and Age-Related Disorders. *Genes*, *8*(12), 398. https://doi.org/10.3390/genes8120398

60. Srivastava S. (2017). The Mitochondrial Basis of Aging and Age-Related Disorders. *Genes*, *8*(12), 398. https://doi.org/10.3390/genes8120398
61. Mitophagy - Wikipedia Killackey, S. A., Philpott, D. J., & Girardin, S. E. (2020). Mitophagy pathways in health and disease. *The Journal of cell biology*, *219*(11), e202004029. https://doi.org/10.1083/jcb.202004029
62. 10,11 Mitophagy - Wikipedia Killackey, S. A., Philpott, D. J., & Girardin, S. E. (2020). Mitophagy pathways in health and disease. *The Journal of cell biology*, *219*(11), e202004029. https://doi.org/10.1083/jcb.202004029
63. Lee, S., & Lee, J. S. (2019). Cellular senescence: a promising strategy for cancer therapy. *BMB reports*, *52*(1), 35–41. https://doi.org/10.5483/BMBRep.2019.52.1.294
64. Sarkar, S., Korolchuk, V. I., Renna, M., Imarisio, S., Fleming, A., Williams, A., Garcia-Arencibia, M., Rose, C., Luo, S., Underwood, B. R., Kroemer, G., O'Kane, C. J., & Rubinsztein, D. C. (2011). Complex inhibitory effects of nitric oxide on autophagy. *Molecular cell*, *43*(1), 19–32. https://doi.org/10.1016/j.molcel.2011.04.029
65. Jiang, Z., Watts, L. T., Huang, S., Shen, Q., Rodriguez, P., Chen, C., Zhou, C., & Duong, T. Q. (2015). The Effects of Methylene Blue on Autophagy and Apoptosis in MRI-Defined Normal Tissue, Ischemic Penumbra and Ischemic Core. *PloS one*, *10*(6), e0131929. https://doi.org/10.1371/journal.pone.0131929
66. Parasuraman, P., R.Y., T., Shaji, C., Sharan, A., Bahkali, A., Al-Harthis, H., Syed, A., Anju, V., Dyavaiah, M., Siddhardha, B. (2020) Biogenic Silver Nanoparticles Decorated with Methylene Blue Potentiated the Photodynamic Inactivation of *Pseudomonas aeruginosa* and *Staphylococcus aureus.* 2020 Jul 29;12(8):709. https://doi.org/10.3390/pharmaceutics12080709
67. Runze Li, Jie Chen, Thomas C. Cesario, Xin Wang, Joshua S. Yuan, Peter M. Rentzepis, Synergistic reaction against bacteria,Proceedings of the National Academy of Sciences Nov 2016, 113 (48) 13612-13617; DOI: 10.1073/pnas.1611193113
68. Stefano Perni, Clara Piccirillo, Jonathan Pratten, Polina Prokopovich, Wojciech Chrzanowski, Ivan P. Parkin, Michael Wilson, The antimicrobial properties of light-activated polymers containing methylene blue and gold nanoparticles,Biomaterials,Volume 30, Issue 1,2009,Pages 89-93,ISSN 0142-9612,https://doi.org/10.1016/j.biomaterials.2008.09.020.
69. Junliang Lv, Gongqing Wu, Yang He, Lijuan Zhang, and Yunhong Yi, "Methylene blue-loaded gold nanobipyramids @SiO_2 enhanced singlet oxygen generation for phototherapy of cancer cells," Opt. Mater. Express 7, 409-414 (2017).
70. Wang, W., Xie, N., He, L., Yin, Y. (2014). *Photocatalytic colour switching of redox dyes for ink-free light-printable rewritable paper.* Nature Communications. 2 December 2014. https://doi.org/10.1038/ncomms6459.
71. Liu, Y., Zhou, X., Wang, X., Liang, K., Yang, Z., Shen, C., Imran, M., Sahar, S., Xu, A. (2017*) Color switching of organic redox dyes over various catalysts are strongly influenced by the pH of the solution or the type of reducing agent contained in the system.* Royal Society of Chemistry. 2017, **7**, 30080-30085. https://doi.org/10.1039/C7RA04498D.
72. Liu, Y, et al. (2017). *Hydrogenation/oxidation induced efficient reversible color switching between methylene blue and leuco-methylene blue.* Royal Society of Chemistry. 2017 Issue 48. https://doi.org/10.1039/C7RA04498D
73. Mowry, S., Ogren, P. (1999). *Kinetics of Methylene Blue Reduction by Ascorbic Acid.* J.Chem. Educ. 1999, 76, 7, 970. https://doi.org/10.1021/ed076p970

74. Lee, S., Mills, A. (2003). *Novel photochemistry of* leuco-*Methylene Blue.* Chemical Communications. 2003, Issue 18, 2366-2367. https://doi.org/10.1039/B307228B
75. Kidd, S., Lancaster, P., Anderson, J., Boogert, A., Fisher, C., Robertson, R., Wass, D. *Fetal death after exposure to methylene blue dye during mid-trimester amniocentesis in twin pregnancy*. Prenatal Diagnosis. 1996 January 16 (1): 39-47. https://doi.org/10.1002/(SICI)1097-0223(199601)16:1<39::AID-PD789>3.0.CO;2-P