The Original Magic Bullet

Methylene Blue: History, Mechanisms, Dosing, and Clinical Applications

Dr. Scott Sherr, MD

Lecture Outline

- Methylene Blue (MB) History
- MB → Mitochondria
- MB → Inflammation
- MB → Antioxidant / Capacity
- MB → Ischemia
- MB → Infections & Biofilms
- MB → Alzheimer's Disease
- MB → Mental Illness
- MB → Cognitive Optimization
- Dosing
- Quality
- Contraindications

Methylene Blue History

- Synthesized in late 1800's at a textile dye
- First medical indication: Malaria
- Used extensively as an antifungal, antibacterial, and antiviral agent before prescription antimicrobials became available in the 1950's
- In the mid 20th century, MB was discovered to have antipsychotic and mood enhancing properties (as an MAO-I). It was also added to other drugs to ensure medication compliance. Blue urine? You've been taking your drugs!
- The first antipsychotic chlorpromazine was derived from it
- Since the early 20th century, MB has been regularly used as a bacteriologic stain, a cellular stain, as an indicator dye, and for surgical and medical marking.

https://pubmed.ncbi.nlm.nih.gov/27576224/

Methylene Blue History (Cont.)

- Remains on the World Health Organizations list of Essential Medications
- It is used methemoglobinemia and cyanide poisoning
- Re-emerging use as a Malaria treatment as drugs are becoming more resistant
- Prescribed PO at compounding pharmacies
- Available DTC via online retailers
- USP is key for human consumption and additional testing also recommended, even on USP.
- And yes, it's used in fish tank cleaner (but impurities abound)

Howland RH. Methylene Blue: The Long and Winding Road from Stain to Brain: Part 1. J Psychosoc Nurs Ment Health Serv. 2016 Sep 1;54(9):21-4. doi: 10.3928/02793695-20160818-01. PMID: 27576224.

MB: Hormetic Dose Response Curve

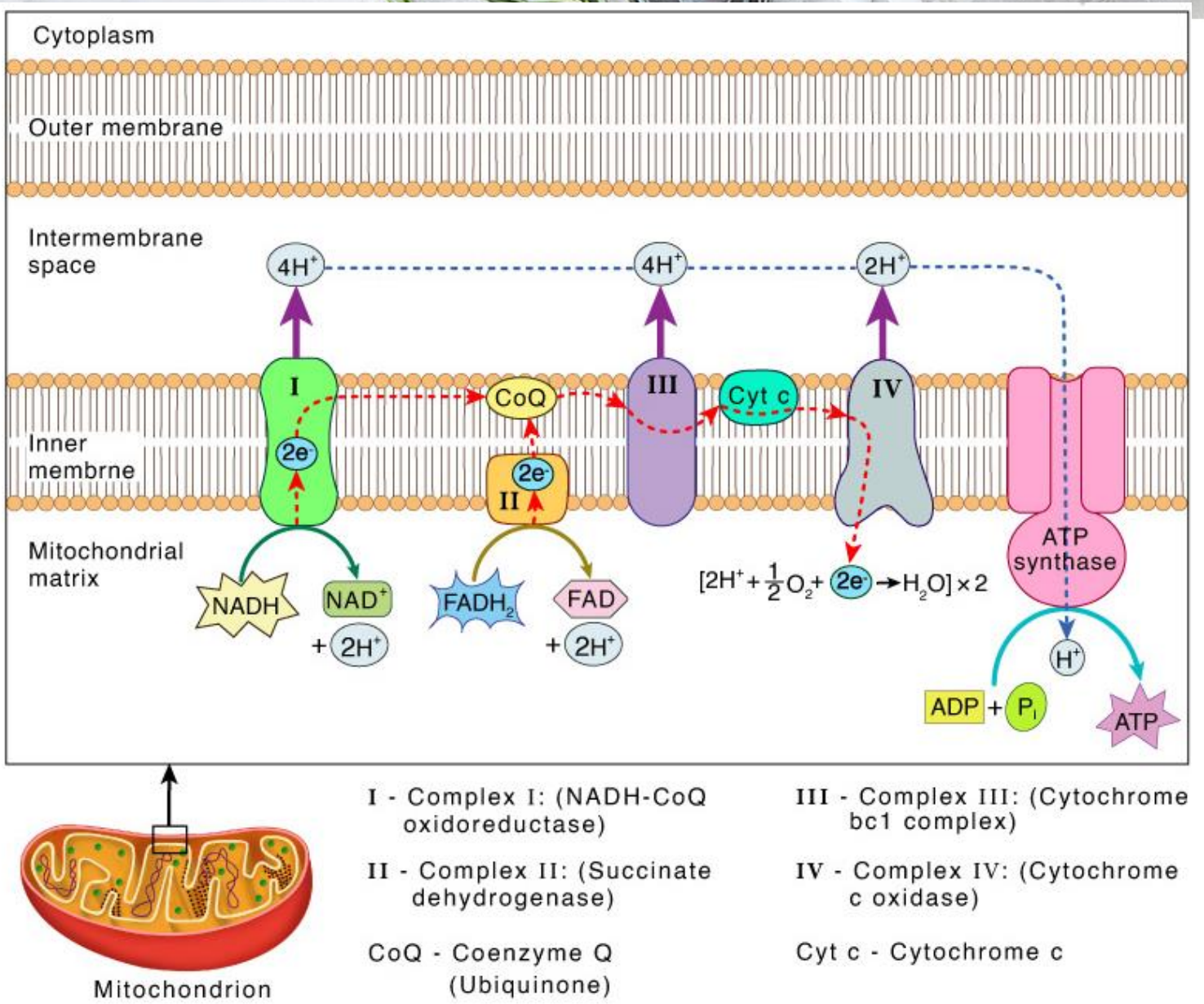
- Low dose Methylene Blue (<3 mg/kg) is an electron cycler both donating and accepting electrons.
- High dose MB (>3mg/kg) becomes pro-oxidant
- After absorption in the buccal mucosa (e.g. in a troche), oral ingestion, or IV administration, MB concentrates in tissues with the most mitochondria (e.g. the brain, heart, liver, kidneys, and muscle).
- It is just about 100% bioavailable, no matter the delivery method, but concentrations in various tissues depends on the delivery method e.g. IV gets to the brain the fastest.

http://dose-response.org/wp-content/uploads/2014/06/Gonzalez-Lima.pdf
Walter-Sack I, Rengelshausen J, Oberwittler H, Burhenne J, Mueller O, Meissner P, Mikus G. High absolute bioavailability of methylene blue given as an aqueous oral formulation. Eur J Clin Pharmacol. 2009 Feb;65(2):179-89. doi: 10.1007/s00228-008-0563-x. Epub 2008 Sep 23. PMID: 18810398.

Methylene Blue "Low" Dosing (Proposed)

Acute & Severe Conditions: 0.5mg to 3mg/kg	• Acute/severe mitochondrial complex dysfunction, trauma, ischemia, acute/severe inflammation, infection • Short term dosing or close monitoring for LT dosing
Chronic Brain Condition/Health Optimization Dosing: < 0.5mg/kg to 1mg/kg	• Gently enhancing mitochondrial function, nootropic benefit, post-infectious recovery • Neurodegeneration, Mental Health d/o • Low dose for daily / regular dosing

ETC

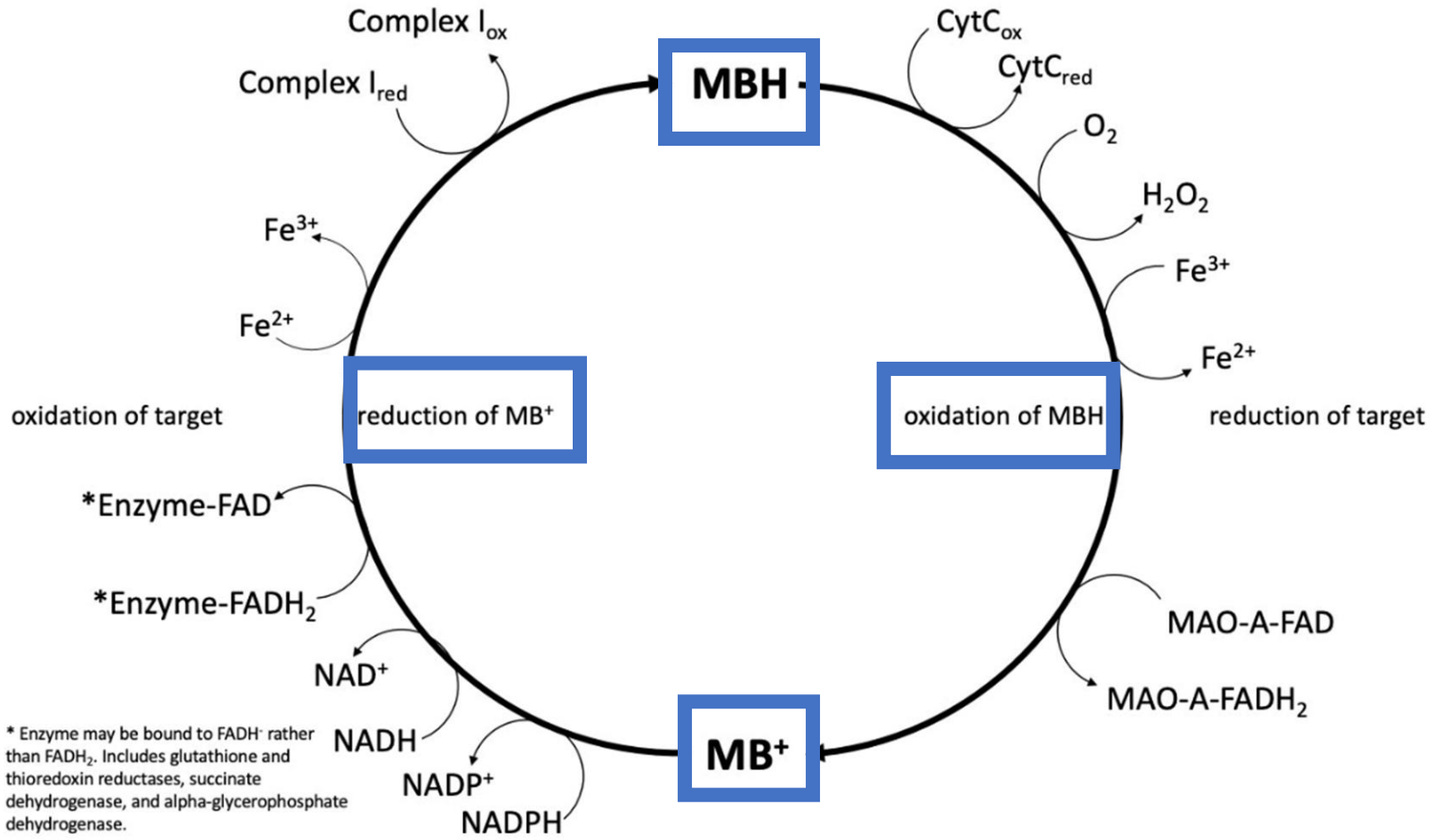


https://www.sciencefacts.net/electron-transport-chain.html

Mitochondrial Dysfunction

- Mitochondrial Diseases, rare
- Mitochondrial Dysfunction, very common
- 6% of the US population metabolically healthy
- Metabolic dysfunction due to: Infection, drugs, toxins, metabolic syndrome/insulin resistance, and more
- Metabolic dysfunction → Mitochondrial dysfunction
- Methylene Blue to support and/or potentially rescue (+)

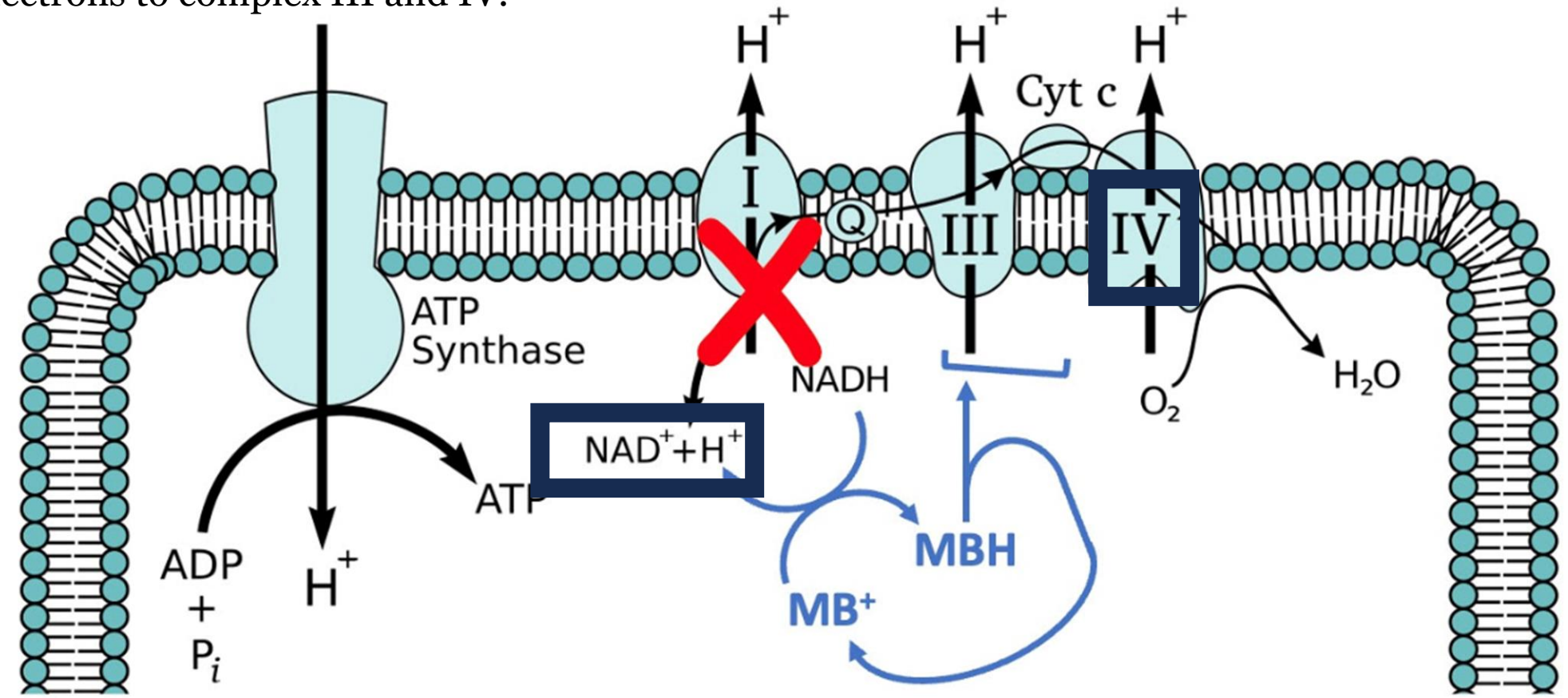
https://peakheart.com/only-6-8-of-americans-are-in-optimal-cardiometabolic-health/#:~:text=Fewer%20than%201%20out%20of,the%20American%20College%20of%20Cardiology.



red, reduced; ox, oxidized; CytC, cytochrome C, MAO-A, monoamine oxidase-A

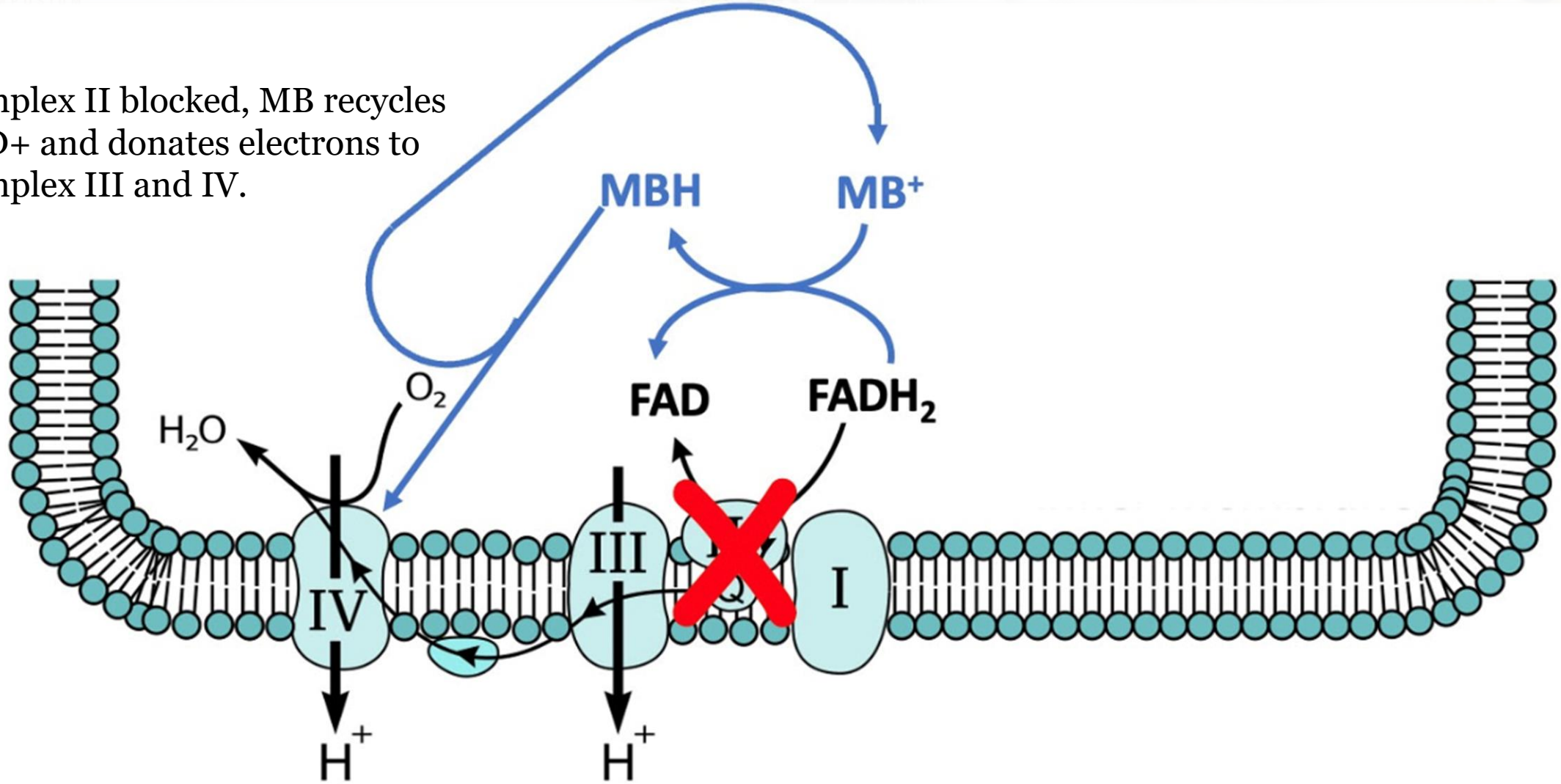
https://rb.gy/p9vajh

Complex I blocked, MB recycles NAD+ and donates electrons to complex III and IV.



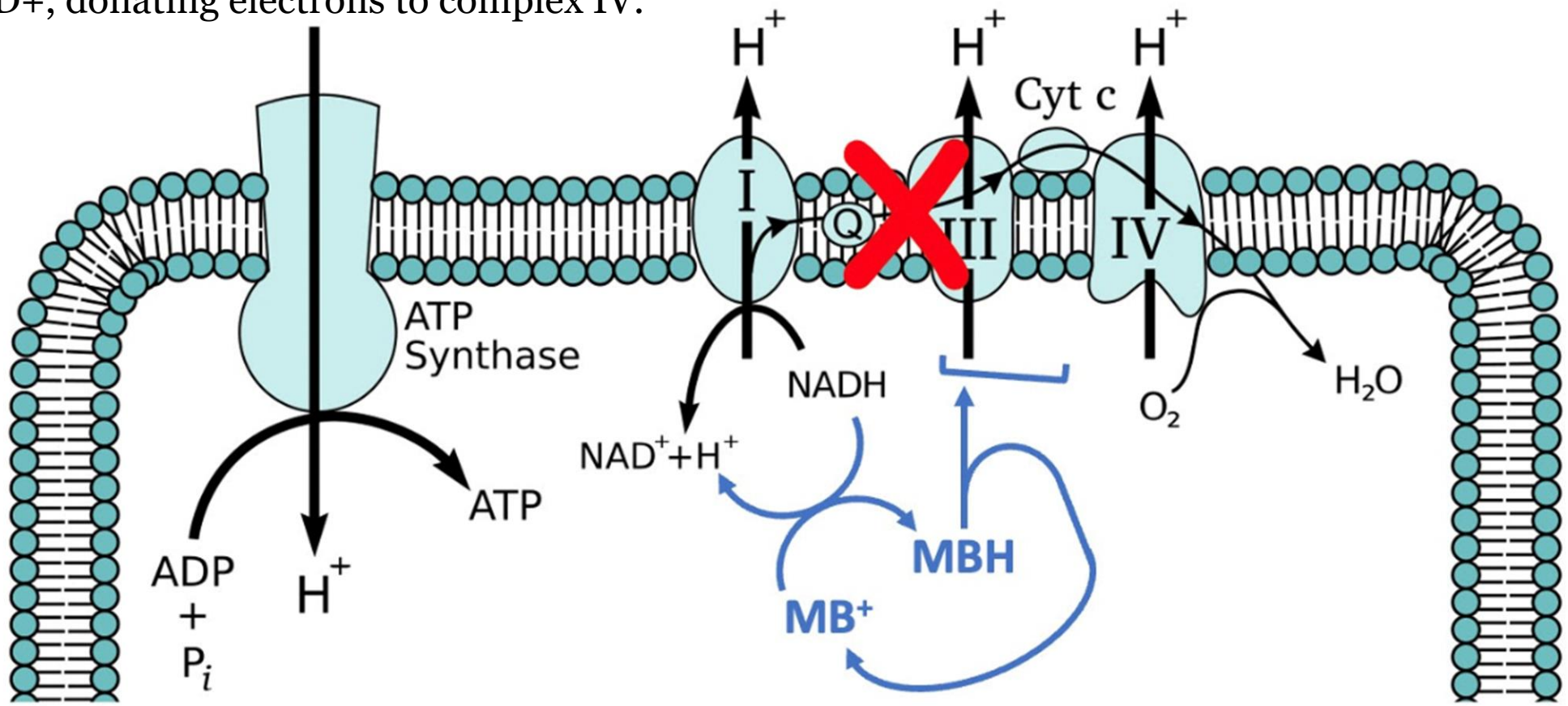
https://rb.gy/p9vajh

Complex II blocked, MB recycles FAD+ and donates electrons to Complex III and IV.



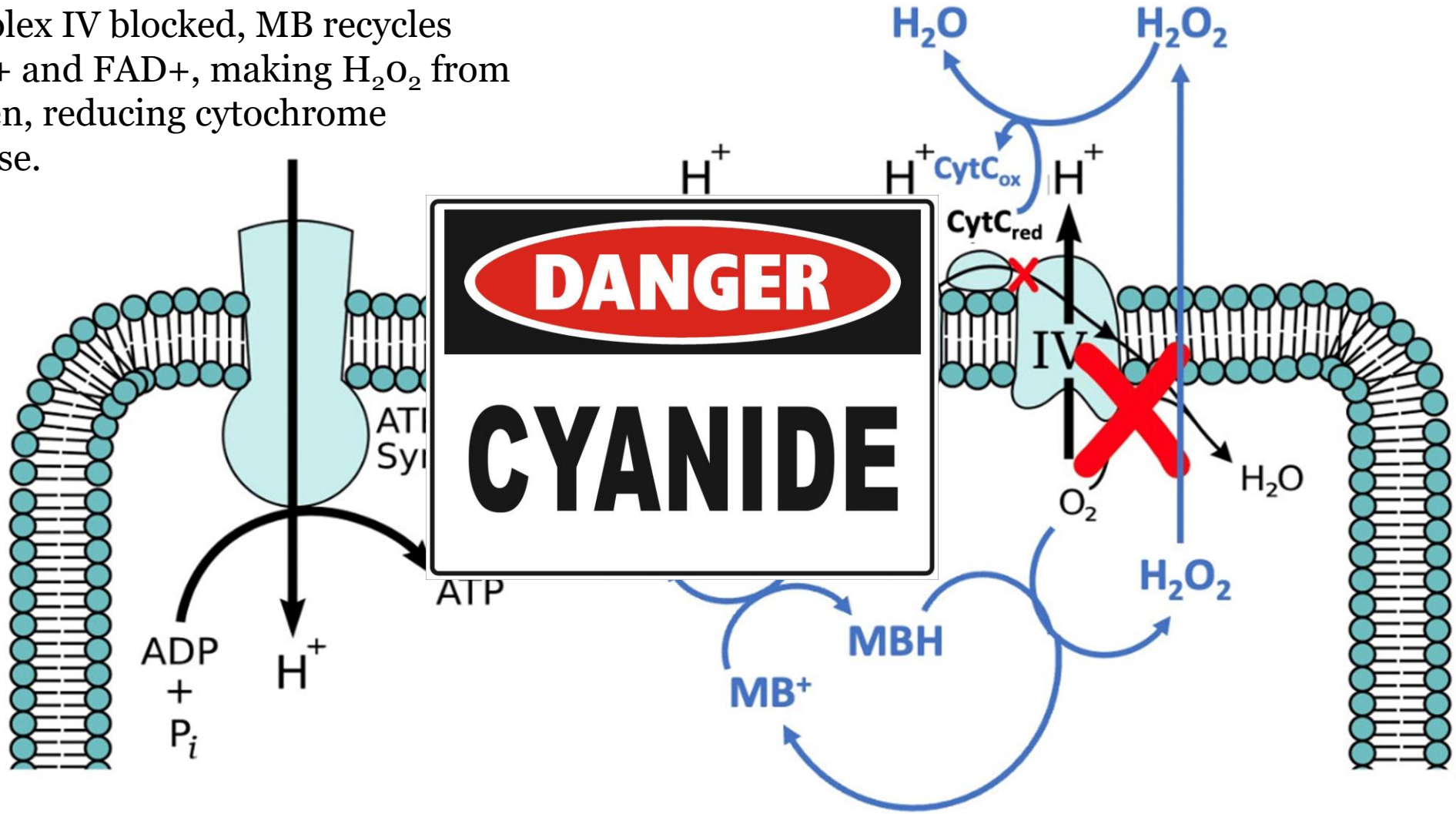
https://rb.gy/p9vajh

Complex III blocked, MB recycles NAD+ and FAD+, donating electrons to complex IV.



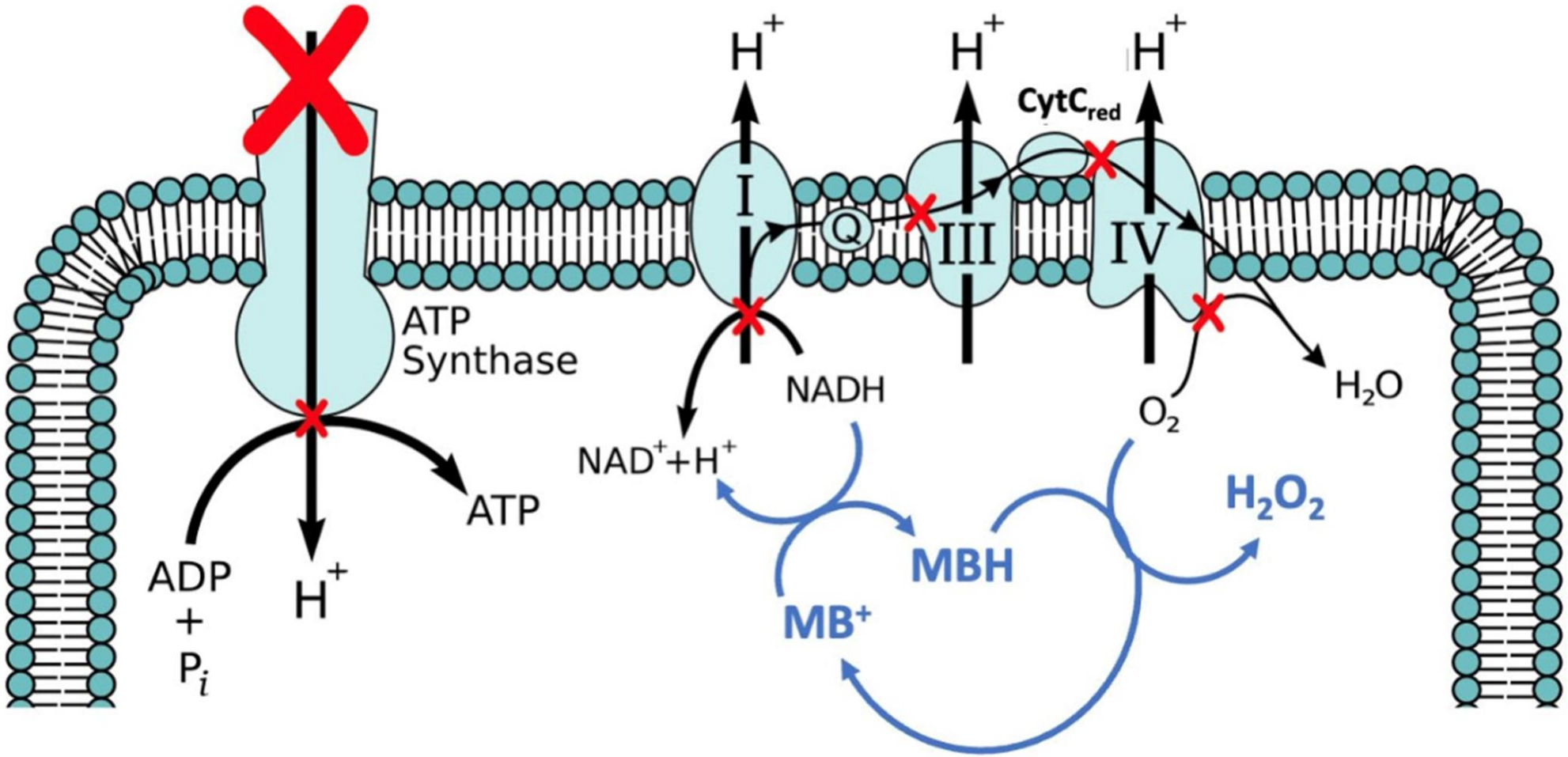
https://rb.gy/p9vajh

Complex IV blocked, MB recycles NAD+ and FAD+, making H_2O_2 from oxygen, reducing cytochrome oxidase.



https://rb.gy/p9vajh

Complex V blocked, MB recycles NAD+ and FAD+, making H_2O_2, leaving some ATP production possible via glycolysis only. MB can also act as a final electron acceptor at complex IV if needed.



https://rb.gy/p9vajh

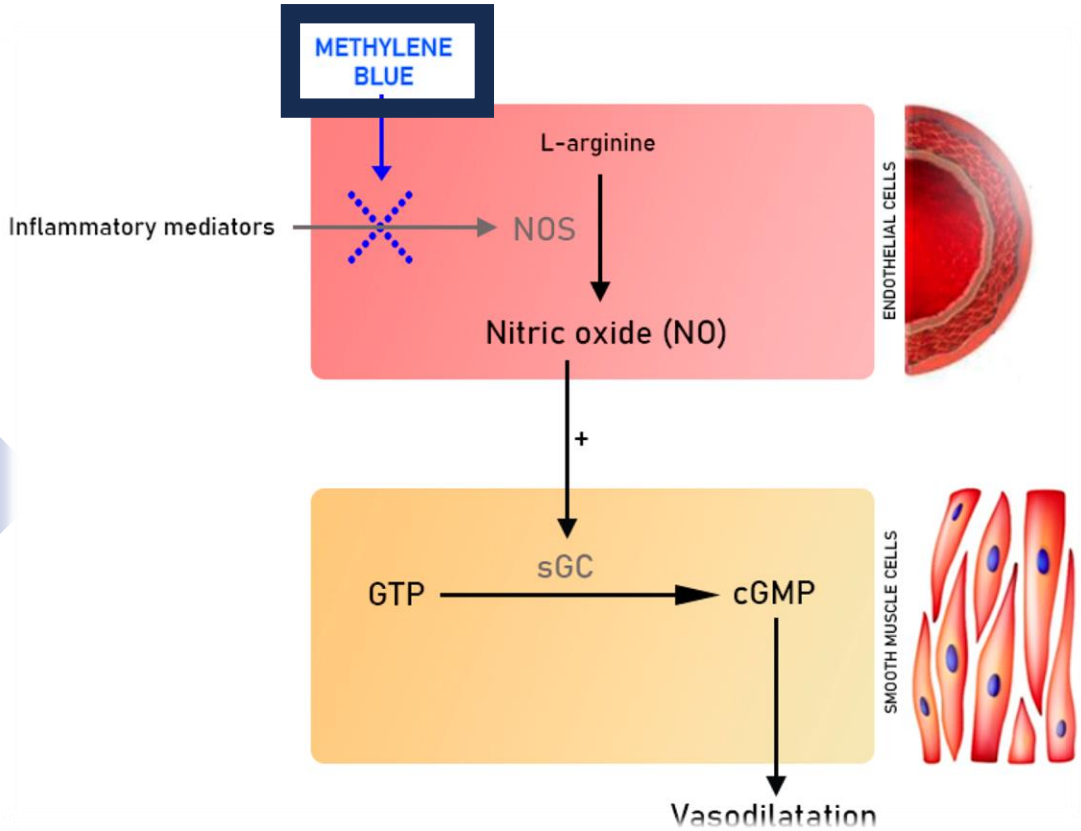
Methylene Blue → Inflammation: iNO

MB at doses of >1mg/kg inhibit inducible nitric oxide that occurs due to stress

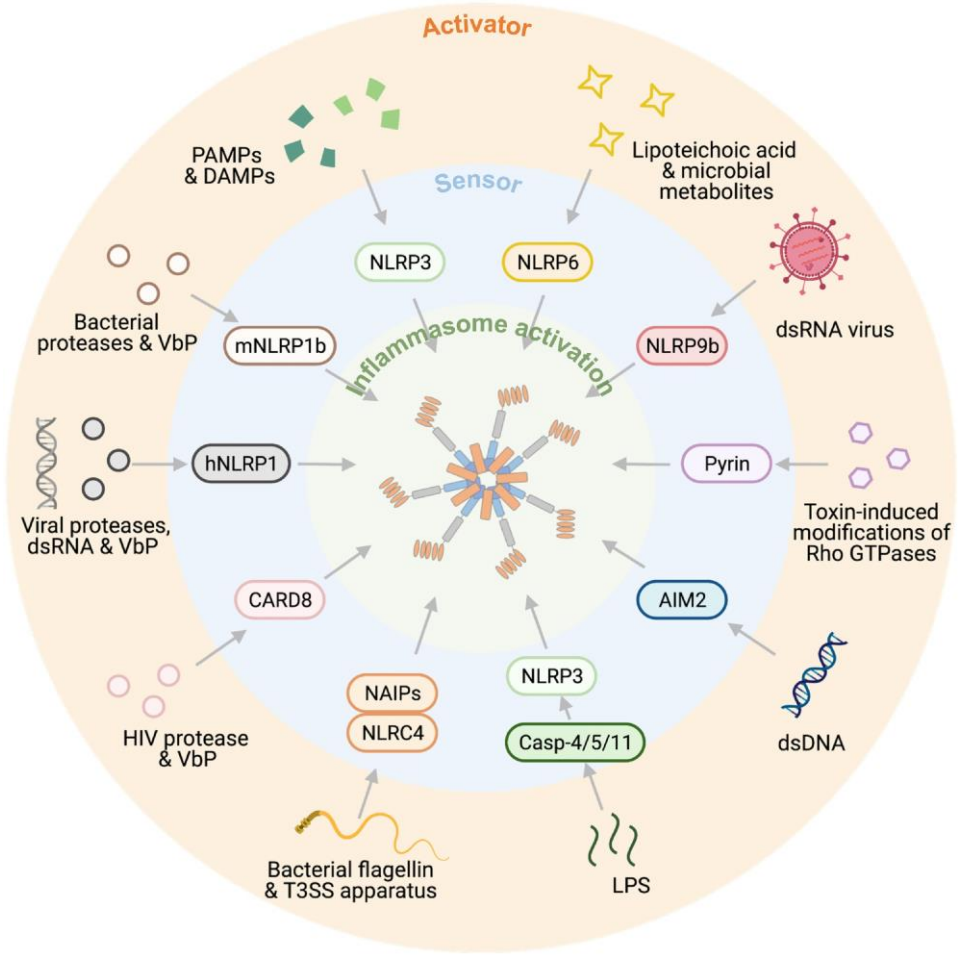
This can be stress related to trauma, ischemia, toxicity, infection, or just about any etiology that causes acute inflammation.

Our basal supply of nitric oxide synthase is in cell membranes and thus protected from MB.

Decreased iNO also associated with decreased pain



Pluta, M.P.; Putowski, Z.; Czempik, P.F.; Krzych, Ł.J. Successful Use of Methylene Blue in Catecholamine-Resistant Septic Shock: A Case Report and Short Literature Review. *Int. J. Mol. Sci.* **2023**, *24*, 10772. https://doi.org/10.3390/ijms241310772



Trends in Cell Biology

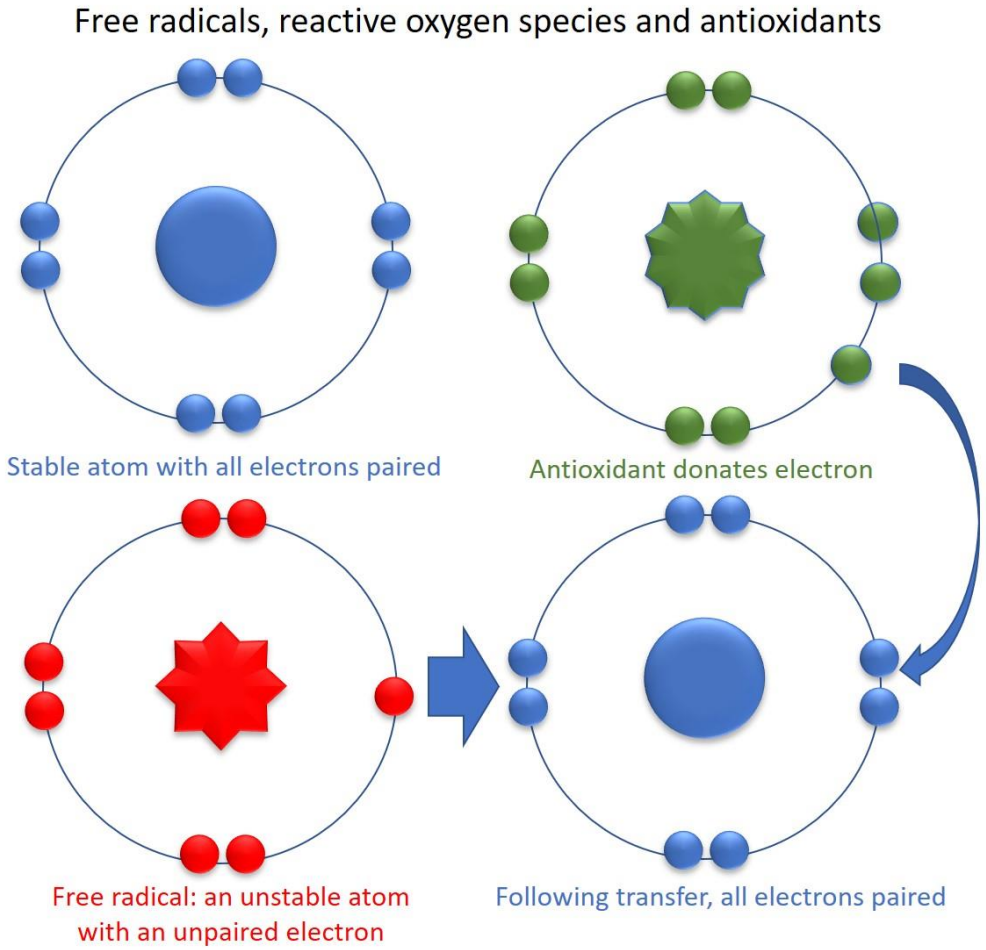
Methylene Blue → Inflammation

- MB doses 0.5mg to 3mg/kg downregulates the production of inflammatory cytokines including IL6 and STAT3
- Downregulates Inflammasome activation and NFKb activation
- MB rescues dysfunctional ETC complexes and maintains ATP production
- Induction of a robust antioxidant response, especially via the NFRF2 pathway and glutathione production

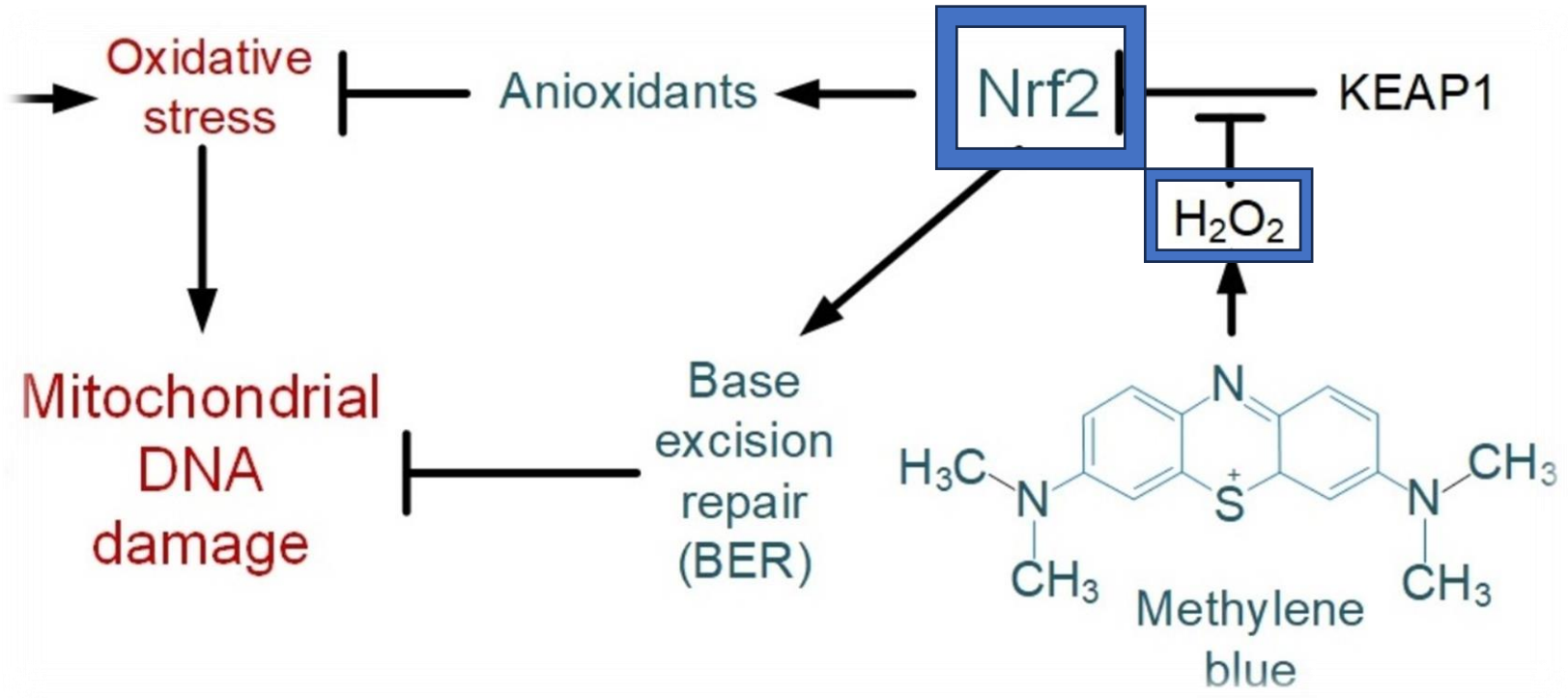
Li Y, Ying W. Methylene blue reduces the serum levels of interleukin-6 and inhibits STAT3 activation in the brain and the skin of lipopolysaccharide-administered mice. Front Immunol. 2023 May 30;14:1181932. doi: 10.3389/fimmu.2023.1181932. PMID: 37325623; PMCID: PMC10266349.
Kast RE. Inhibiting the NLRP3 Inflammasome With Methylene Blue as Treatment Adjunct in Myelodysplasia. Front Oncol. 2018 Jul 27;8:280. doi: 10.3389/fonc.2018.00280. PMID: 30101125; PMCID: PMC6072867.
Scigliano G, Scigliano GA. Methylene blue in covid-19. Med Hypotheses. 2021 Jan;146:110455. doi: 10.1016/j.mehy.2020.110455. Epub 2020 Dec 10. PMID: 33341032; PMCID: PMC7728423.

Methylene Blue → Antioxidant (Direct)

MB scavenges free electrons in the mitochondria and the cytosol, reducing (i.e. neutralizing) them > or = NAC, MitoQ, and Vitamin A at doses between 50 to 100mg in several studies.



https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.cellgs.com%2Fblog%2Ffree-radicals-vs-reactive-oxygen-species-whats-the-difference.html&psig=AOvVaw3tMTaex8xYKw7yzlp49m_L&ust=1695174155728000&source=images&cd=vfe&opi=89978449&ved=0CA8QjRxqFwoTCOD81v3FtYEDFQAAAAAdAAAAABAN



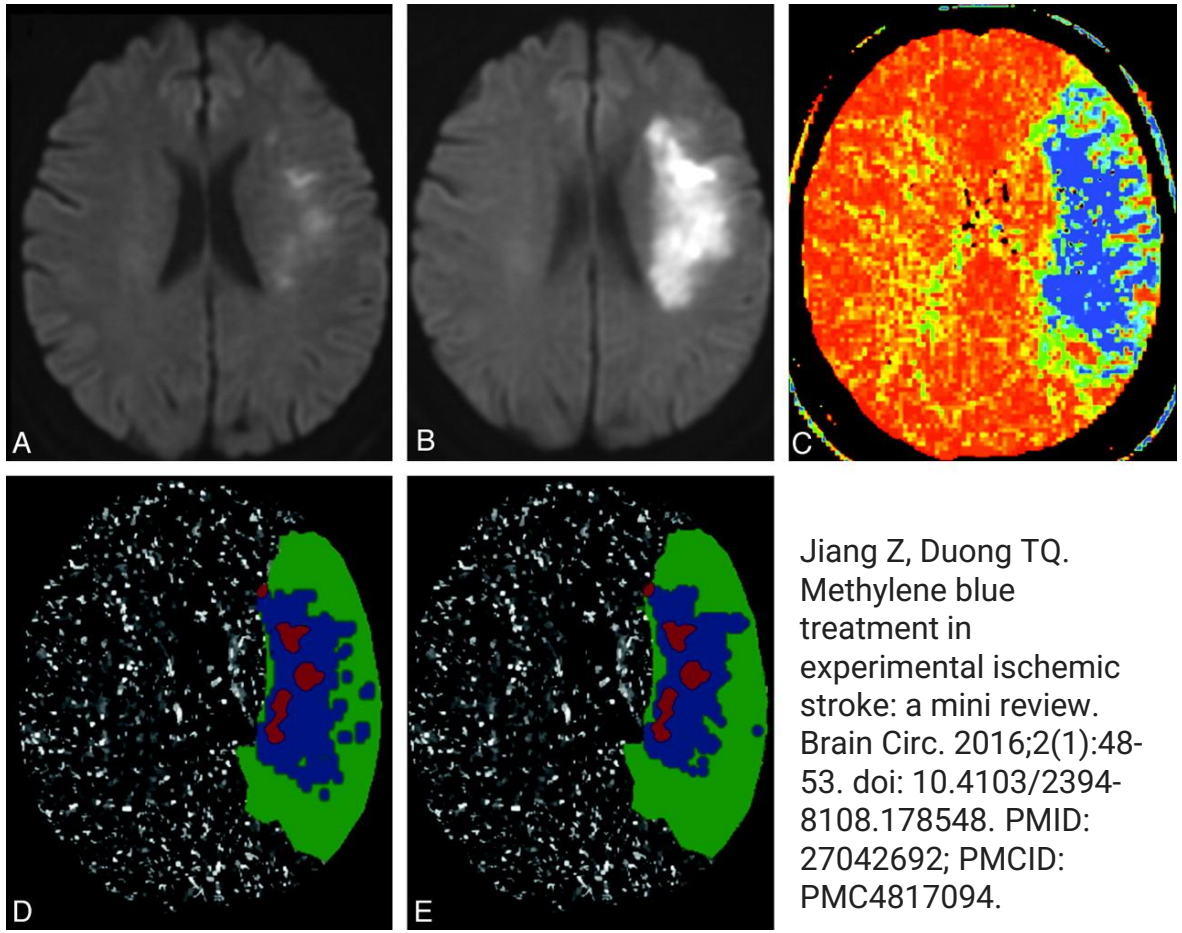
Methylene Blue as Antioxidant Booster (Indirect)

MB upregulates the NRF2 pathway via Hydrogen Peroxide (H_2O_2) production.

Samoylova, N.A.; Gureev, A.P.; Popov, V.N. Methylene Blue Induces Antioxidant Defense and Reparation of Mitochondrial DNA in a Nrf2-Dependent Manner during Cisplatin-Induced Renal Toxicity. *Int. J. Mol. Sci.* **2023**, *24*, 6118. https://doi.org/10.3390/ijms24076118

Methylene Blue → Ischemia

- MB has been studied in various models of stroke, TBI, and other ischemic insults using doses of 0.5mg/kg to 3mg/kg with significant benefits.
- In stroke models, MB improves cerebral blood flow, decreases mitochondrial destruction, decreases infarct size, and decreases reperfusion injury.
- Although there have been very few studies done in humans, **there is very likely a role of MB as an abortive at the first signs of an ischemic episode** (stroke, especially), of course alongside treatments that are well known to improve outcomes, like antiplatelet therapy.



Jiang Z, Duong TQ. Methylene blue treatment in experimental ischemic stroke: a mini review. Brain Circ. 2016;2(1):48-53. doi: 10.4103/2394-8108.178548. PMID: 27042692; PMCID: PMC4817094.

https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.ajnr.org%2Fcontent%2F33%2F3%2F545&psig=AOvVaw1SmB4XOpqZk1lTAKlUXmVS&ust=1694144138645000&source=images&cd=vfe&opi=89978449&ved=0CA8QjRxqFwoTCNiM6e7Il4EDFQAAAAAdAAAAABAI

Methylene Blue → Powerful Anti-infective

At doses of >0.5 mg/kg MB: production of hydrogen peroxide (donation of electrons to oxygen making superoxide and hydrogen peroxide free radicals). No evidence that low dose MB (<0.5mg) makes significant H_2O_2.

H_2O_2 kills organisms directly, especially enveloped viruses such as COVID and Zika, parasites like Malaria, and cell-wall-containing bacteria such as staph, strep, enterococcus, E. coli plus other gram-negative bacteria, and many others that do not have inherent protection. No resistance patterns for MB have ever been described.

MB is also immunomodulatory due to H_2O_2 production → enhancing the activity of macrophages and neutrophils, reducing excessive inflammation via stress-induced nitric oxide synthase production (iNOs), cytokine downregulation, and antioxidant production.

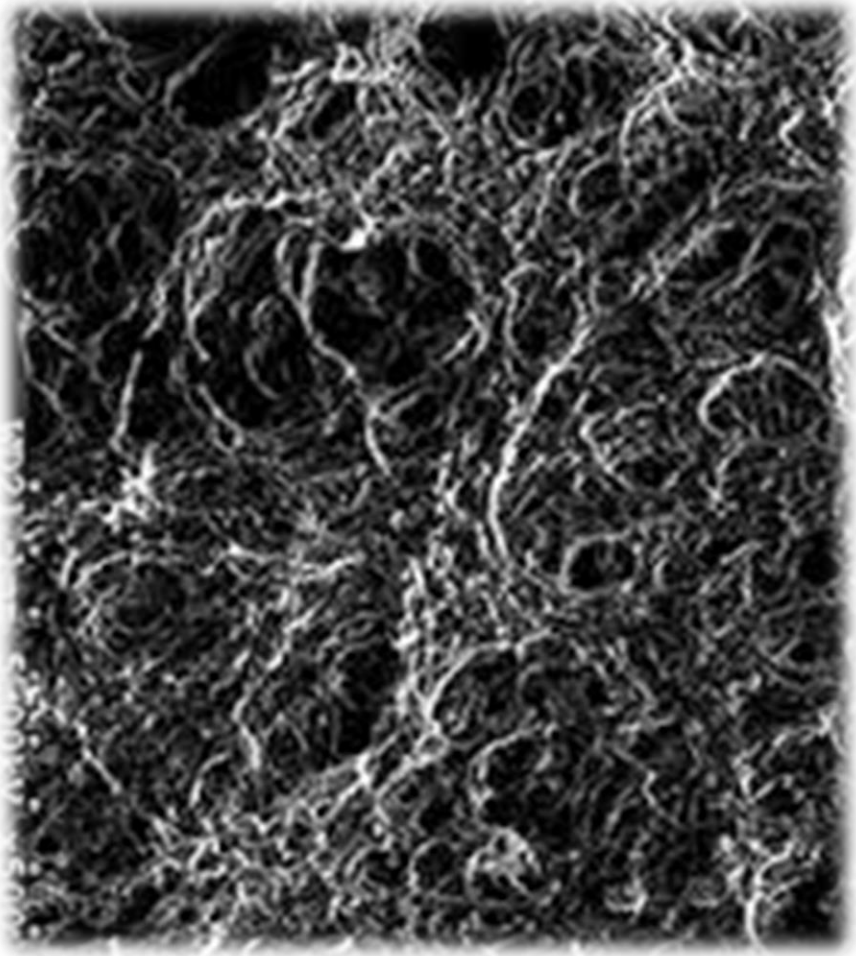
- L. Tretter, G. Horvath, A. Hölgyesi, F. Essek, V. Adam-Vizi, Enhanced hydrogen peroxide generation accompanies the beneficial bioenergetic effects of methylene blue in isolated brain mitochondria, Free Radical Biology and Medicine, Volume 77, 2014, Pages 317-330, ISSN 0891-5849, https://doi.org/10.1016/j.freeradbiomed.2014.09.024.
- Methylene Blue–Mediated Antimicrobial Photodynamic Therapy Against Clinical Isolates of Extensively Drug Resistant Gram-Negative Bacteria Causing Nosocomial Infections in Thailand, An In Vitro Study Frontiers in Cellular and Infection Microbiology VOLUME=12 YEAR=2022 URL=https://www.frontiersin.org/articles/10.3389/fcimb.2022.929242 DOI=10.3389/fcimb.2022.929242 ISSN=2235-2988
- 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

  Li Z, Lang Y, Sakamuru S, Samrat S, Trudeau N, Kuo L, Rugenstein N, Tharappel A, D'Brant L, Koetzner CA, Hu S, Zhang J, Huang R, Kramer LD, Butler D, Xia M, Li H. Methylene blue is a potent and broad-spectrum inhibitor against Zika virus *in vitro* and *in vivo*. Emerg Microbes Infect. 2020 Dec;9(1):2404-2416. doi: 10.1080/22221751.2020.1838954. PMID: 33078696; PMCID: PMC7646565.

  Zolfaghari PS, Packer S, Singer M, Nair SP, Bennett J, Street C, Wilson M. In vivo killing of Staphylococcus aureus using a light-activated antimicrobial agent. BMC Microbiol. 2009 Feb 4;9:27. doi: 10.1186/1471-2180-9-27. PMID: 19193212; PMCID: PMC2642833.
- Prinz, J.; Wink, M.; Neuhaus, S.; Grob, M.C.; Walt, H.; Bosshard, P.P.; Achermann, Y. Effective Biofilm Eradication on Orthopedic Implants with Methylene Blue Based Antimicrobial Photodynamic Therapy In Vitro. *Antibiotics* **2023**, *12*, 118. https://doi.org/10.3390/antibiotics12010118

Methylene Blue → Biofilm Buster

- A biofilm is a complex and organized community of microorganisms, primarily bacteria, that adhere to surfaces and are encased in a self-produced matrix of extracellular polymeric substances (EPS).
- This matrix is composed of various molecules such as polysaccharides, proteins, DNA, and other organic and inorganic materials. Biofilms can form on a wide range of surfaces, including medical devices, natural and industrial surfaces, pipes, and living tissues like the GI trace and teeth.



https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.cambridge.org%2Fcore%2Fservices%2Faop-cambridge-core%2Fcontent%2Fview%2F164461853AEE5CC443A125CF5FF83CC7%2FS1431927615001981a.pdf%2Fbartonella_henselae_biofilm_detected_on_catheter_of_patient_with_persistent_bartonellosis.pdf&psig=AOvVaw0TfsOJewRNT3UmPB4z3F0B&ust=1694146761981000&source=images&cd=vfe&opi=89978449&ved=0CA8QjRxqFwoTCOCV2anUl4EDFQAAAAAdAAAAABAL

MB → Biofilm Buster (cont.)

- Via H_2O_2 production, and at doses between 0.5 to 3mg/kg, MB works in several ways.

1. MB disrupts the extracellular matrix, a key component of biofilms, which provides structural support and protection to the microorganisms within

2. MB interferes with the ability of microorganisms to adhere to surfaces and form biofilms. By preventing initial adhesion, it reduces the formation of biofilms and limits their growth.

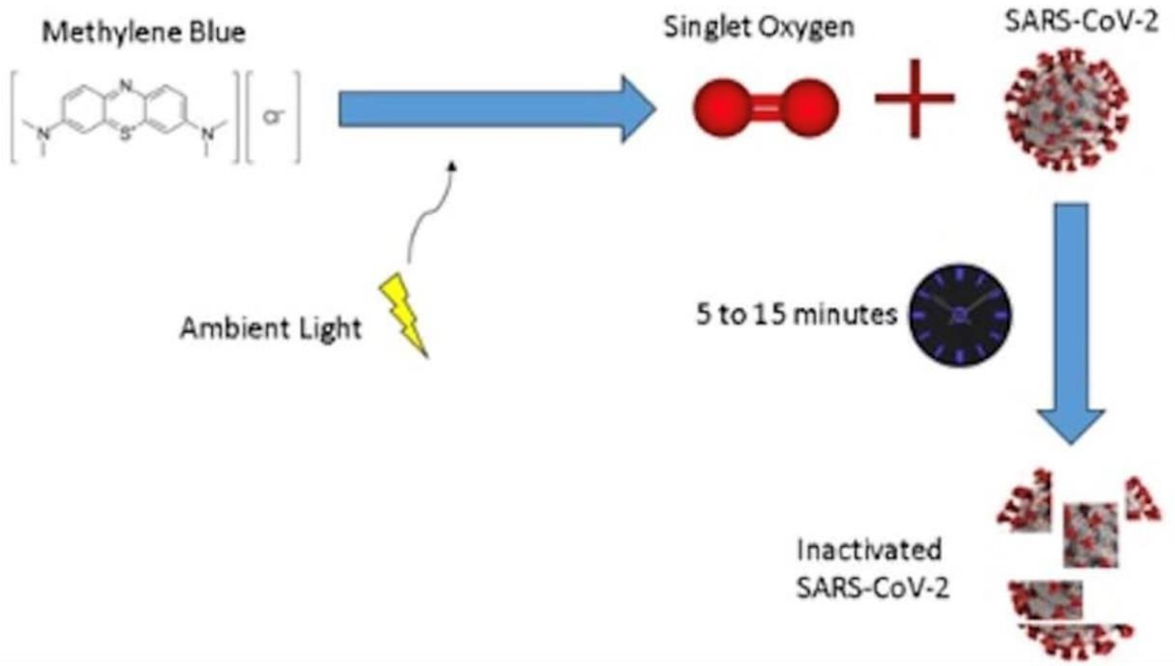
3. MB penetrates the biofilm and directly targets microorganisms, inhibiting their growth and causing their death.

Prinz, J.; Wink, M.; Neuhaus, S.; Grob, M.C.; Walt, H.; Bosshard, P.P.; Achermann, Y. Effective Biofilm Eradication on Orthopedic Implants with Methylene Blue Based Antimicrobial Photodynamic Therapy In Vitro. *Antibiotics* **2023**, *12*, 118. https://doi.org/10.3390/antibiotics12010118

Wu J, Xu H, Tang W, Kopelman R, Philbert MA, Xi C. Eradication of bacteria in suspension and biofilms using methylene blue-loaded dynamic nanoplatforms. Antimicrob Agents Chemother. 2009 Jul;53(7):3042-8. doi: 10.1128/AAC.01604-08. Epub 2009 May 4. PMID: 19414585; PMCID: PMC2704698.

MB + Photodynamic Therapy (high dose/high intensity)

Light in the 600 to 690 nm spectrum reacts with H_2O_2 creating singlet oxygen radicals which are highly reactive and can more easily kill microorganisms.



https://asm.org/Articles/2022/March/Methylene-Blue-The-Little-Known-Disinfectant

MB + Photodynamic Therapy (low dose/low intensity)

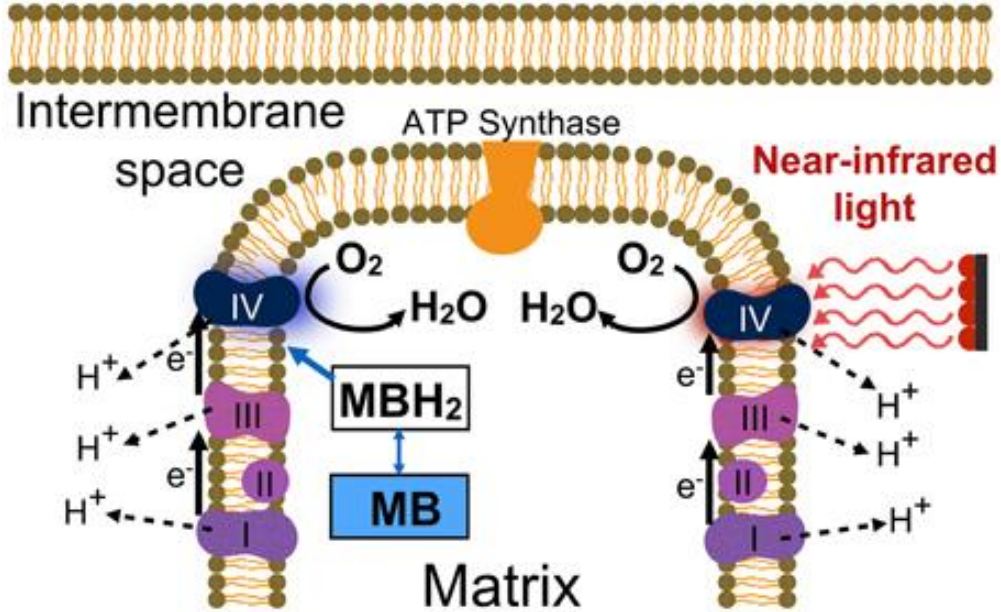
OPINION article

Front. Cell. Neurosci., 12 May 2015
Sec. Cellular Neuropathology
Volume 9 - 2015 | https://doi.org/10.3389/fncel.2015.00179

This article is part of the Research Topic
Neurodegeneration: from genetics to molecules
View all 23 Articles >

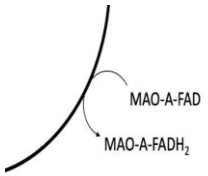
Protection against neurodegeneration with low-dose methylene blue and near-infrared light

F. Gonzalez-Lima* Allison Auchter

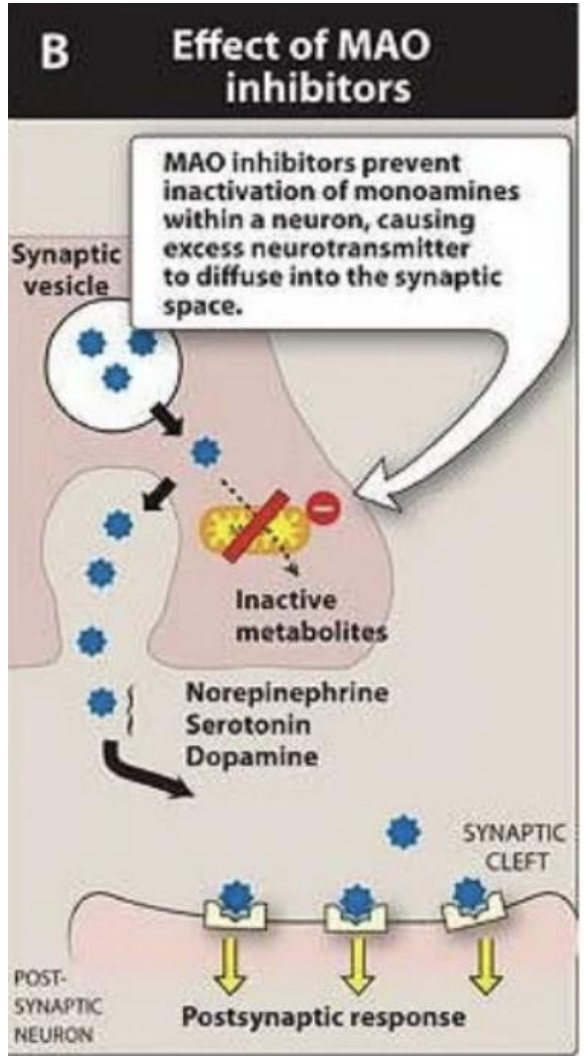


Gonzalez-Lima F and Auchter A (2015) Protection against neurodegeneration with low-dose methylene blue and near-infrared light. *Front. Cell. Neurosci*. **9**:179. doi: 10.3389/fncel.2015.00179

MB → MAO-I Inhibition + Ach



- MB prevents monoamine neurotransmitter breakdown (dopamine, melatonin, norepinephrine, and serotonin) which leads directly to increases in these neurotransmitters
- The higher dose, the more the MAO Inhibition
- MB may also function as a **cholinesterase inhibitor**, increasing the amount of acetylcholine available, a neurotransmitter in the brain responsible for arousal, attention, memory, and motivation



Delport A, Harvey BH, Petzer A, Petzer JP. The monoamine oxidase inhibition properties of selected structural analogues of methylene blue. Toxicol Appl Pharmacol. 2017 Jun 15;325:1-8. doi: 10.1016/j.taap.2017.03.026. Epub 2017 Apr 1. PMID: 28377303.

Pfaffendorf, M., Bruning, T.A., Batink, H.D. and Van Zwieten, P.A. (1997), The interaction between methylene blue and the cholinergic system. British Journal of Pharmacology, 122: 95-98. https://doi.org/10.1038/sj.bjp.0701355

MB → Alzheimer's

EXPERT OPINION ON PHARMACOTHERAPY
https://doi.org/10.1080/14656566.2020.1719066

Taylor & Francis
Taylor & Francis Group

DRUG EVALUATION

An evaluation of hydromethylthionine as a treatment option for Alzheimer's disease

Nader Nael Hashweh[a], Zachary Bartochowski[a], Rita Khoury [b,c] and George T. Grossberg[a]

[a]Department of Psychiatry and Behavioral Neuroscience, Saint Louis University School of Medicine, Saint Louis, MO, USA; [b]Department of Psychiatry & Clinical Psychology, St. George Hospital University Medical Center, Balamand University, Faculty of Medicine, Beirut, Lebanon; [c]Institute for Development, Research, Advocacy & Applied Care (IDRAAC), Beirut, Lebanon

ABSTRACT

Introduction: Alzheimer's disease (AD) is a major cause of morbidity worldwide and its prevalence is expected to rise. Previous studies involving compounds that target the accumulation of amyloid β protein have been unsuccessful, renewing interest in therapies directed against intracellular deposits of tau proteins. Derived from methylene blue, hydromethylthionine is a tau aggregation inhibitor that recently emerged as a promising disease-modifying treatment for AD.

Areas covered: Herein, the authors cover the chemistry, pharmacodynamics and pharmacokinetics of hydromethylthionine and its oxidized form methylthionine chloride (MTC) that was first studied, as well as clinical efficacy and safety of hydromethylthionine in the treatment of mild to moderate AD.

Expert opinion: Randomized clinical trials with hydromethylthionine failed to show any impact of the doses used on the disease course. Data analysis from a non-randomized cohort showed that a smaller dose of the drug previously thought to be ineffective and used as placebo, prescribed as monotherapy rather than as add-on to AD approved symptomatic therapies may slow cognitive decline. This finding was further confirmed by a pharmacokinetic analysis study showing a dose/response relationship with doses around 16 mg daily. Future trials need to study the pharmacological properties of hydromethylthionine and ascertain the optimal safe and effective dose to be used.

ARTICLE HISTORY
Received 30 August 2019
Accepted 17 January 2020

KEYWORDS
Alzheimer's disease; tau aggregation inhibitor; methylene blue; leuco-methylthioninium; hydromethylthionine; disease-modifying therapy

Hashweh NN, Bartochowski Z, Khoury R, Grossberg GT. An evaluation of hydromethylthionine as a treatment option for Alzheimer's disease. Expert Opin Pharmacother. 2020 Apr;21(6):619-627. doi: 10.1080/14656566.2020.1719066. Epub 2020 Feb 8. PMID: 32037892.

MB → Alzheimer's

COMPLETED

Safety and Efficacy of TRx0237 in Subjects With Alzheimer's Disease Followed by Open-Label Treatment

ClinicalTrials.gov ID NCT03446001

Sponsor TauRx Therapeutics Ltd

Information provided by TauRx Therapeutics Ltd (Responsible Party)

Last Update Posted 2023-05-24

Study Arms ICMJE

- Experimental: TRx0237 16 mg/day
  Intervention: Drug: TRx0237 16 mg/day
- Placebo Comparator: Placebo
  Intervention: Drug: Placebo
- Experimental: TRx0237 8 mg/day
  Intervention: Drug: TRx0237 8 mg/day

https://clinicaltrials.gov/study/NCT01689233

MB → Depression

A controlled trial of methylene blue in severe depressive illness

G J Naylor, A H Smith, P Connelly

PMID: 3555627 DOI: 10.1016/0006-3223(87)90194-6

Abstract

Methylene blue, 15 mg/day, was compared with placebo in treatment of severe depressive illness. The 3-week trial was designed to avoid bias by placebo response and also to avoid observer bias. 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.

https://www.biologicalpsychiatryjournal.com/article/0006-3223(87)90194-6/pdf
Naylor GJ, Smith AH, Connelly P. A controlled trial of methylene blue in severe depressive illness. Biol Psychiatry. 1987 May;22(5):657-9. doi: 10.1016/0006-3223(87)90194-6. PMID: 3555627.

MB → "Healthy Adults"

Home > Radiology > VOL. 281, NO. 2

Original Research

Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain

Pavel Rodriguez, Wei Zhou, Douglas W. Barrett, Wilson Altmeyer, Juan E. Gutierrez, Jinqi Li, Jack L. Lancaster, Francisco Gonzalez-Lima, Timothy Q. Duong

Author Affiliations

Published Online: Jun 28 2016 | https://doi.org/10.1148/radiol.2016152893

Rodriguez P, Zhou W, Barrett DW, Altmeyer W, Gutierrez JE, Li J, Lancaster JL, Gonzalez-Lima F, Duong TQ. Multimodal Randomized Functional MR Imaging of the Effects of Methylene Blue in the Human Brain. Radiology. 2016 Nov;281(2):516-526. doi: 10.1148/radiol.2016152893. Epub 2016 Jun 28. PMID: 27351678; PMCID: PMC5084971.

MB Dosing Strategies (high dose)

- **Always use synergistic therapies. MB not a standalone treatment and still investigational.**
- Severe, Chronic conditions:
  - Start at 25mg QOD (every other day) for the first week, then increasing to daily, titrating up weekly from there to a max dose of up to 200mg per day. Most common dose: 25 to 50mg daily but may need to start lower
- Viral, bacterial, fungal illness:
  - Acute: 25 to 100mg BID X 5 days, consider photodynamic therapy. Higher dosing may be needed for some infections
  - Chronic: See above
- Acute Ischemia/Severe Acute Mitochondrial dysfunction:
  - 100 to 200mg X1 dose, repeat in 4 to 6 hours depending on severity, post event 25 to 50mg BID X 5 to 7 days

MB dosing Strategies (low dose)

- **Always use synergistic therapies. MB not a standalone treatment and still investigational.**
- Neurocognitive disorders
- Mental Health Disorders
- Possible in mild to moderate mitochondrial dysfunction (post infectious, medications, toxins, etc.)
- Dosing:
  - 4mg to 16mg daily, QOD, other? titrated dose.
  - If no improvements, increase to higher dose strategy
  - If mitochondrial function can be optimized, may not need it long term

MB Safety & Precautions (all doses)

- Pregnancy and breastfeeding
- MB contamination: Industrial-grade and chemical-grade MB sold as a dye or stain can consist of more than 8% or 11% of various contaminants. Even USP MB can have impurities.
- HTN
- Headaches
- Allergies to Thiazine dyes
- Blue Urine
- ”Detox Symptoms”

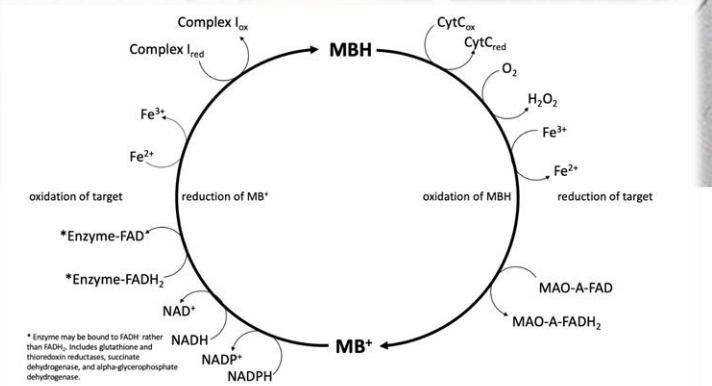
MB Precautions (higher doses)

Previous slide +

- Disruption of normal gut biofilms
- Build up of methylene blue due to ½ life
- Gastric ulceration
- Serotonin Syndrome (Unlikely, never demonstrated w/PO MB)
- G6PD deficiency (Unlikely, never demonstrated w/PO MB)
- >3mg/kg
  - Methemoglobinemia
  - Definite risk of SS, Hemolytic Anemia w/G6PD

GABAergic Alternatives

- Drugs
  - Zuranolone
- Supplements
  - Muscimol
  - Kava Kava
  - Valerian Root
  - Honokiol



red, reduced; ox, oxidized; CytC, cytochrome C, MAO-A, monoamine oxidase-A

Conclusion

- Methylene Blue is an extremely versatile compound and one of the few known to electron cycle.
- In the mitochondria, this means both energy *and* resilience with a wide range of dosing possible depending on severity and acuity.
- It is antimicrobial without known resistance patterns
- Consider use as a synergistic tool within a framework that optimizes health, rather than treats disease.
- Most data, although extremely compelling, is in animal models so it is still investigational (except for allopathic indications)

Thank you!

Email:

scott@snhlife.com
buccalup@troscriptions.com

References

- https://pubmed.ncbi.nlm.nih.gov/27576224/
- http://dose-response.org/wp-content/uploads/2014/06/Gonzalez-Lima.pdf
- https://pubmed.ncbi.nlm.nih.gov/18810398/
- https://www.sciencefacts.net/electron-transport-chain.html
- https://peakheart.com/only-6-8-of-americans-are-in-optimal-cardiometabolic-health/#:~:text=Fewer%20than%201%20out%20of,the%20American%20College%20of%20Cardiology.
- https://chrismasterjohnphd.substack.com/p/the-guide-to-methylene-blue
- https://www.jbc.org/article/S0021-9258(20)51465-8/fulltext?
- https://www.sciencedirect.com/science/article/pii/S0891584914004432
- https://www.caro.ca/wp-content/uploads/2016/07/D201_Cyanide.jpg
- https://pubmed.ncbi.nlm.nih.gov/30907955/
- https://pubmed.ncbi.nlm.nih.gov/28377303
- https://bpspubs.onlinelibrary.wiley.com/doi/full/10.1038/sj.bjp.0701355
- https://www.mdpi.com/1422-0067/24/13/10772

References (cont)

- https://www.mdpi.com/1422-0067/24/7/6118#
- https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.ajnr.org%2Fcontent%2F33%2F3%2F545&psig=AOvVaw1SmB4XOpqZk1ITAKIUXmVS&ust=1694144138645000&source=images&cd=vfe&opi=89978449&ved=0CA8QjRxqFwoTCNiM6e7I4EDFQAAAAAdAAAAABAI
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4817094/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10266349/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6072867/
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7728423/
- https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.cellgs.com%2Fblog%2Ffree-radicals-vs-reactive-oxygen-species-whats-the-difference.html&psig=AOvVaw3tMTaex8xYKw7yzlp49m_L&ust=1695174155728000&source=images&cd=vfe&opi=89978449&ved=0CA8QjRxqFwoTCOD81v3F
- https://www.sciencedirect.com/science/article/pii/S0891584914004432
- https://www.frontiersin.org/articles/10.3389/fcimb.2022.929242/full
- https://www.nature.com/articles/s41598-021-92481-9
- https://pubmed.ncbi.nlm.nih.gov/33078696/#:~:text=Overall%2C%20we%20have%20shown%20that,well%2Dtolerated%20for%20human%20use.
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2642833/

References

- https://www.mdpi.com/2079-6382/12/1/118
- https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.cambridge.org%2Fcore%2Fservices%2Faop-cambridge-core%2Fcontent%2Fview%2F164461853AEE5CC443A125CF5FF83CC7%2FS1431927615001981a.pdf%2Fbartonella_henselae_biofilm_detected_on_catheter_of_patient_with_pers
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2704698/
- https://asm.org/Articles/2022/March/Methylene-Blue-The-Little-Known-Disinfectant
- https://www.frontiersin.org/articles/10.3389/fncel.2015.00179/full
- https://pubmed.ncbi.nlm.nih.gov/32037892/
- https://clinicaltrials.gov/study/NCT01689233
- https://neurosciencenews.com/memory-methylene-blue-4586/

Thursday 1:30pm – 2:30pm

The Original Magic Bullet: Methylene Blue. History, Mechanisms, Dosing, and Clinical Applications

Please scan this QR code on you mobile

or tablet device to access the session feedback survey

The Original Magic Bullet: Methylene Blue. History Mechanisms Dosing and Clinical Applications