Artesunate, Lipoic Acid Mineral Complex & Phosphatidylcholine

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Under Accreditation Council for Continuing Medical Education guideline disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

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Received an educational grant from ImprimixRX

Unless otherwise stated, the level of evidence is C and based on clinical experience.

Intravenous Artesunate

Case 1

46 year old female referred to me for difficult EBV

- Symptoms of fatigue and exercise resistance
- Onset presented 3-4 months after double mastectomy (prevention due to BRACA)
- Tried oral protocols with lysine, monolaurin, vitamin A
- Started oral Artemesinin + once every other week IV Mega C (25-50 grams Vitamin C, nutrients and lysine) + IV Artesunate
- Usually would to once weekly but due to finances

Case 1

46 year old female referred to me for difficult EBV

2/2016: Initial labs EBV Early Antigen 36.7 U/ml
3/2016: 38.4 U/ml
4/2016: 37.3 U/ml
7/2016: 29.3 U/ml

Drastic improvement in energy and able to return to exercise without extreme exhaustion 3 months into treatment. Patient discontinued treatment due to feeling well and another practitioner told her to let her body handle the EBV.

Case 2

41 year old female referred to me for chronic fatigue

- Initial work up suggested past exposure with EBV high VCA and Nuclear Antigen
- Further workup shows Lyme WB borderline positive confirmed positive with Ispot lyme test.

History of not tolerating Artemesinin orally. Feeling unwell.

Case 2

41 year old female referred to me for chronic fatigue

Test dosage of 30 mg Artesunate IV to start and tolerated well without issues. Able to work up to therapeutic dosage 120 mg without issues.

IV Mega C + Artesunate once per week for 4-5 months. Initial month ups and downs. Currenlty seeing improvement in symptoms and lyme titers showing resolution of p23 band.

Case 3

68 year old male initially came in early 2014 with metastatic non small cell lung cancer with metastasis to brain and bone.

- Environmental hx. Mill work, asphalt, smoking history, lumber worker, asbestos exposure and high red meat intake.
- On oral erlotinib
- Only abnormal lab finding was CMV IgG 8.30 U/ml (2014)

Worked up to 100 gram IVC + DMSO + Artesunate given once every other week due to finances and travel distance. Also on oral 1 tsp 5 days per week liposomal Artemesinin.

Case 3

68 year old male

- After 3 months infusions patient PET and MRI showed improvements:

-Lung mass, brain and bone mets.

- 6 months

Lung nodule stable to resolved

Bone mets resolved

Brain still present but stable

Currently August 2017. No lung nodules, no bone mets, stable but present brain lesion.

CMV is now at 6.6 IgG

ART and CMV Virus

From the Abstract:

"This is the first report of treatment of cytomegalovirus infection with artesunate, for a stem cell transplant recipient with a newly identified foscarnet-resistant and ganciclovir resistant DNA polymerase L776M mutation. Artesunate treatment resulted in a 1.7–2.1-log reduction in viral load by treatment day 7, with a viral half-life of 0.9–1.9 days, indicating a highly effective block in viral replication."

Shapira MY, et. Al. Artesunate as a Potent Antiviral Agent in a Patient with Late Drug-Resistant Cytomegalovirus Infection after Hematopoietic Stem Cell Transplantation. Clinical Infectious Diseases 2008; 46:1455–7

ART and CMV Virus

And a cell line study bore out the superiority of Artesunate over other Artemesia compoinds in CMV:

Flobinus A. Stability and antiviral activity against human cytomegalovirus of artemisinin derivatives. J. Antimicrob. Chemother. (2014) 69 (1): 34-40. doi: 10.1093/jac/dkt346

ART and Bacteria

"Artemisinin and nine of its semisynthetic derivatives were tested for antibacterial activity against anaerobic, facultative anaerobic, microaerophilic and aerobic bacteria. Only anaerobic bacteria and gonococci showed sensitivity to artemisinin derivatives."

Shoeb HA, Tawfik AF, Shibl AM, el-Feraly FS. Antimicrobial activity of artemisinin and its derivatives against anaerobic bacteria. Journal of Chemotherapy (Florence, Italy) [1990, 2(6):362-367] (PMID:2128751)

ART Pharmacokinetics

Abstract

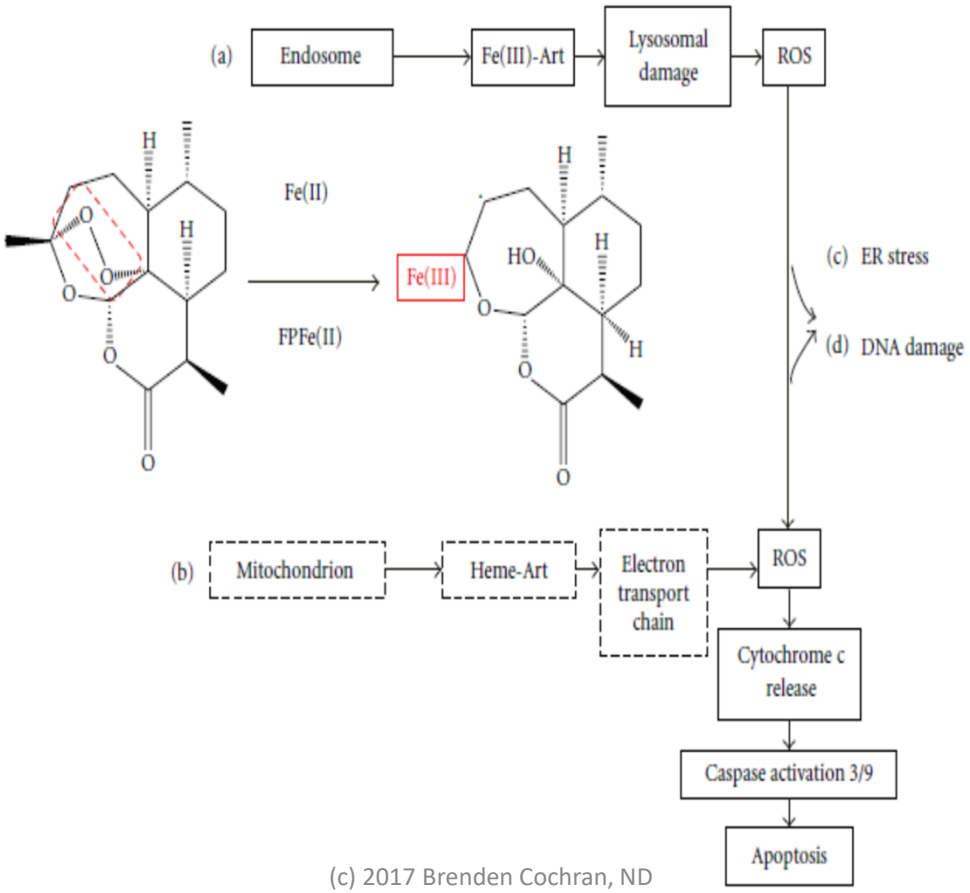
- The pharmacokinetics of good manufacturing process injection of artesunate (AS) were evaluated after single doses at 0.5, 1, 2, 4, and 8 mg/kg with a 2-minute infusion in 40 healthy subjects. Drug concentrations were analyzed by validated liquid chromatography and mass spectrometry system (LC-MS/MS) procedures. The drug was immediately converted to dihydroartemisinin (DHA), with elimination half-lives ranging 0.12-0.24 and 1.15-2.37 hours for AS and DHA, respectively. Pharmacokinetic model-dependent analysis is suitable for AS, whereas DHA fits both model-dependent and -independent methods. Although DHA concentration was superior to that of AS with a 1.12-1.87 ratio of area under the curve (AUC)(DHA/AS), peak concentration of AS was much higher than that of DHA, with a 2.80- to 4.51-fold ratio of peak concentration (C(max AS/DHA)). Therefore, AS effectiveness has been attributed not only to its rapid hydrolysis to DHA, but also to itself high initial C(max).
- Li Q, Cantilena LR, Leary KJ, Saviolakis GA, Miller RS, Melendez V, Weina PJ. Pharmacokinetic profiles of artesunate after single intravenous doses at 0.5, 1, 2, 4, and 8 mg/kg in healthy volunteers: a phase I study.Am J Trop Med Hyg. 2009 Oct;81(4):615-21. PMID: 19815876

Artesunate

- Artesunate (ART), a derivative of artemisinin, can be a potent and selective antitumor agent as well as antimicrobial agent.
- Importantly, ART has produced a dose-dependent tumor regression in an in vivo pancreatic cancer xenografts model.
- **The in vivo antitumor activity of ART was similar to that of gemcitabine.**
- ART is considered to produce a ROS burst which may alter cancer cell activity.
- Additionally ART appears to be a synergist with oxidative therapies such as high dose ascorbic acid.
- Potential COX-2 inhibitor
  - **Artesunate inhibits the growth and induces apoptosis of human gastric cancer cells by downregulating COX-2. (Onco Targets Ther 2015 Apr 16;8:845-54)**

https://www.academia.edu/20316500/Artesunate_Monograph

Maria P. Crespo-Ortiz and Ming Q.Wei. Antitumor Activity of Artemisinin and Its Derivatives: From aWell-Known Antimalarial Agent to a Potential Anticancer Drug .Journal of Biomedicine and Biotechnology. Volume 2012, Article ID 247597, 18 pages. doi:10.1155/2012/247597



J. Biol Chem. Artesunate induces cell death in human cancer in human cancer cells via enhancing lysosomal function and lysosomal degradation of ferritin. 2014 Nov. 28;289(48):33425-41. doi: 10.1074/jbc.M114.564567. Epub 2014 Oct 10
Yang ND, Tan SH, Shi Y, et al

In summary, our study demonstrates that ART treatment activates lysosomal function and **then promotes ferritin degradation, subsequently leading to the increase of lysosomal iron that is utilized by ART for its cytotoxic effect on cancer cells.**

Protocol for Artesunate

- **D5W or NS**
  - **100 mL bag**
- **Infuse directly prior or after HDIVC (High Dose IVC)**
- **Infuse 60mg on the first occasion as a test dose**
- **120mg IV Artesunate on subsequent doses**
- **Frequency: Once to twice weekly as directed;**
  - **Re-evaluate after 10-15 treatments.**
- **Short half life: oxidant within 20 min (not after 2 hours or less)**
- **Oxidative treatment**
  - **Compatible with IVC and other oxidants**

Uses include infections (especially viral) and oncology

Oral Artesunate

Artesunate

- 200 mg per day oral Artesunate

Artemesinin

- 300 mg three times per day x 3-5 days on 9-11 days off. (Pulsed dosage due to GI absorption issues).
  Best to take with food, preferably fat.

Liposomal Artemesinin (more effective than oil)

- 1 tsp once to twice daily. Improved absorption.

Dosage: How high could you go?

Zhou X, Sun WJ, Wang WM, Chen K, Zheng JH, Lu MD, Li PH, Zheng ZQ . Artesunate inhibits the growth of gastric cancer cells through the mechanism of promoting oncosis both in vitro and in vivo. Anticancer Drugs. 2013 Oct;24(9):920-7. doi:10.1097/CAD.0b013e328364a109 Epub 2013.

This study aims to investigate the significance and mechanism of artesunate involved in suppressing the proliferation of gastric cancer in vitro and in vivo. In the in-vitro experiments, artesunate inhibited the growth of gastric cancer cell lines (SGC-7901, BGC-823, and AGS) with concentration-dependent activity, with no significant effect on GES-1 cells. BGC-823 cells treated with artesunate showed the typical morphologic features of oncosis rather than apoptosis. Meanwhile, we observed calcium overload, downregulation of vascular endothelial growth factor expression, and upregulation of calpain-2 expression in the artesunate-treated BGC-823 cells. In addition, the in-vivo study showed that artesunate produced a dose-dependent tumor regression in **nude mice**. **The antitumor activity of 240 mg/kg artesunate was similar to that of 10 mg/kg docetaxel.** Furthermore, compared with the control group, no significant difference was observed in the body weight of artesunate-treated nude mice other than docetaxel-treated nude mice. These observations show that artesunate has concentration-dependent inhibitory activities against gastric cancer in vitro and in vivo by promoting cell oncosis through an impact of calcium, vascular endothelial growth factor, and calpain-2 expression.

Toxicity

- Oral Toxicity

No toxicity in dogs using oral 45 mg/kg q6 hours x 3 weeks. Most common side effect was anorexia. Bioavailability wasn't high enough.

- Minimal AST, ALT elevations
- No neutropenia
- No anemia

- 556 mg/kg Artemether per day no toxicity in beagles
- No toxicity in monkeys which received 292 mg/kg (642 mg/pound) of Artemether over 1-3 months

Artesunate References

Stockwin LH. et. al. Artemisinin dimer anti-cancer activity correlates with hemecatalyzed ROS generation and ER stress induction. Int J Cancer. 2009 September 15; 125(6): 1266–1275. doi:10.1002/ijc.24496.

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Paik IH, Xie S, Shapiro TA, Labonte T, Narducci Sarjeant AA, Baege AC, Posner GH. Second generation, orally active, antimalarial, artemisinin-derived trioxane dimers with high stability, efficacy, and anticancer activity. J Med Chem. 2006; 49:2731–4. [PubMed: 16640333]

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Chen HH. et. al. Inhibitory Effects of Artesunate on Angiogenesis and on Expressions of Vascular Endothelial Growth Factor and VEGF Receptor KDR/flk-1 Pharmacology 2004;71:1–9 DOI: 10.1159/000076256

Efferth T, et. al. The anti-malarial artesunate is also effective against cancer. International journal of Oncology. 2001. 18; 767-773

Yang J, et. al. Dihydroartemisinin is an inhibitor of ovarian cancer cell growth. Acta Pharmacol Sin 2007 Jul; 28 (7): 1045–1056. doi: 10.1111/j.1745-7254.2007.00612.x

Yan Yang, Xiaomin Zhang, Xiofen Wang, et. Enhanced delivery of artemisinin and its analogues to cancer cells by their adducts with human serum transferrin. International Journal of Pharmaceutics. 2014, March 2014, 467 (1-2):113-122 doi:10.1016/j.ijpharm.2014.03.044

Lipoic Acid Mineral Complex

Case 1

- 21 year old female presented to me initially in March 2016 with chronic GI problems, POTS and chronic nerve and joint pain.
  - GI problems onset December 2014
  - POTS diagnosed Oct-November 2014
  - Chronic nerve and joint pains onset April 2011
- Chronic pain/Fatigue started after taking 1 pill of levofloxacin for a sinus infection. Next morning woke up very weak, severe joint pain, swelling, cold, burning in leg muscles with weakness. Was put on gabapentin 600 mg daily for managing the pain.
- Patient able to work off gabapentin by November 2016 using intravenous nutrients + Glutathione + LAMC.
  - Initially was only getting Nutrients + Glutathione which showed improvement but after adding LAMC within a month of initial IV's this really allowed her to speed recover.

Case 1

- Was also getting many URI at the time.
- After going off the gabapentin noticed URI reduced frequency, GI issues resolved, POTS became more controlled, nerve and joint pain completely resolved by end of 2016.
- March 2017 IV once a week. May 2017 transitioned to IV once a month and using oral LAMC.
- April-May I diagnosed her with mast cell activation syndrome due to symptoms of unusual swelling, respiratory SOB, high histamines and response with anti-histamines.
- May 2017 on IV's once per month and oral LAMC. Fatigue completely resolved.
- Currently working on the mast cell activation syndrome.

Strauchman, M et al. Fluoroquinolone toxicity symptoms in a patient presenting with low back pain. Case Study. Natural Wellness & Pain Relief Centers, Grand Blanc, MI

Case 2

- 55 year old female inherited from another physician who retired. Symptoms of chronic infections, lead toxicity resistant to chelation, hypothyroid, mitochondrial dysfunction, chronic fatigue at times needing to collapse for a 10 minute nap, hypertension, chemical sensitivity, SNP profile indicates very poor detoxification genetics.
- Initially was treated for lead toxicity but developed stage II uterine cancer. This was treated with conventional oncological treatments and integrative oncology support.
- 30-50 chelation infusions before my care.
- Post chemotherapy neuropathy and worsening chronic fatigue.
- Multiple allergies. Very allergic to corn.

Case 2

- Comes into my care with very high liver enzymes and ferritin, multiple infections, fatigue pattern and metal toxicity. Has been getting nutrient IV's + Glutathione for 2-3 years. Months before seeing me started on Lipoic Acid Mineral Complex.
- 5 ml Lipoic Acid Mineral Complex caused massive reaction and extreme rollercoaster of fatigue. Reduced dosage better.
- After 3-4 months of LAMC patient improves to tolerating 10-15 ml. Reporting increased energy, sulfur dumping every time dosage increased. Neuropathy resolved. Energy has improved 60%
- Increased dosage to 25 ml beginning of this year which has increase energy more.

Case 2

- Other issues managed include hormones
- Heavy metals starting to move
- Energy more stable less rollercoaster
- Currently continuing once weekly nutrient + LAMC+glutathione
- Will be starting IVIgG soon for infections.
  - C. pneumonia
  - M. pneumonia
  - EBV, HHV6 (tx. with valcyte recently)
  - Low IgG (low to mid 500's) and subclass Igg
- Ferritin has reduced from 650 to 222 ng/ml with nutrient support and has had 2-3 therapeutic phlebotomies to get it down to 122 ng/ml

LAMC

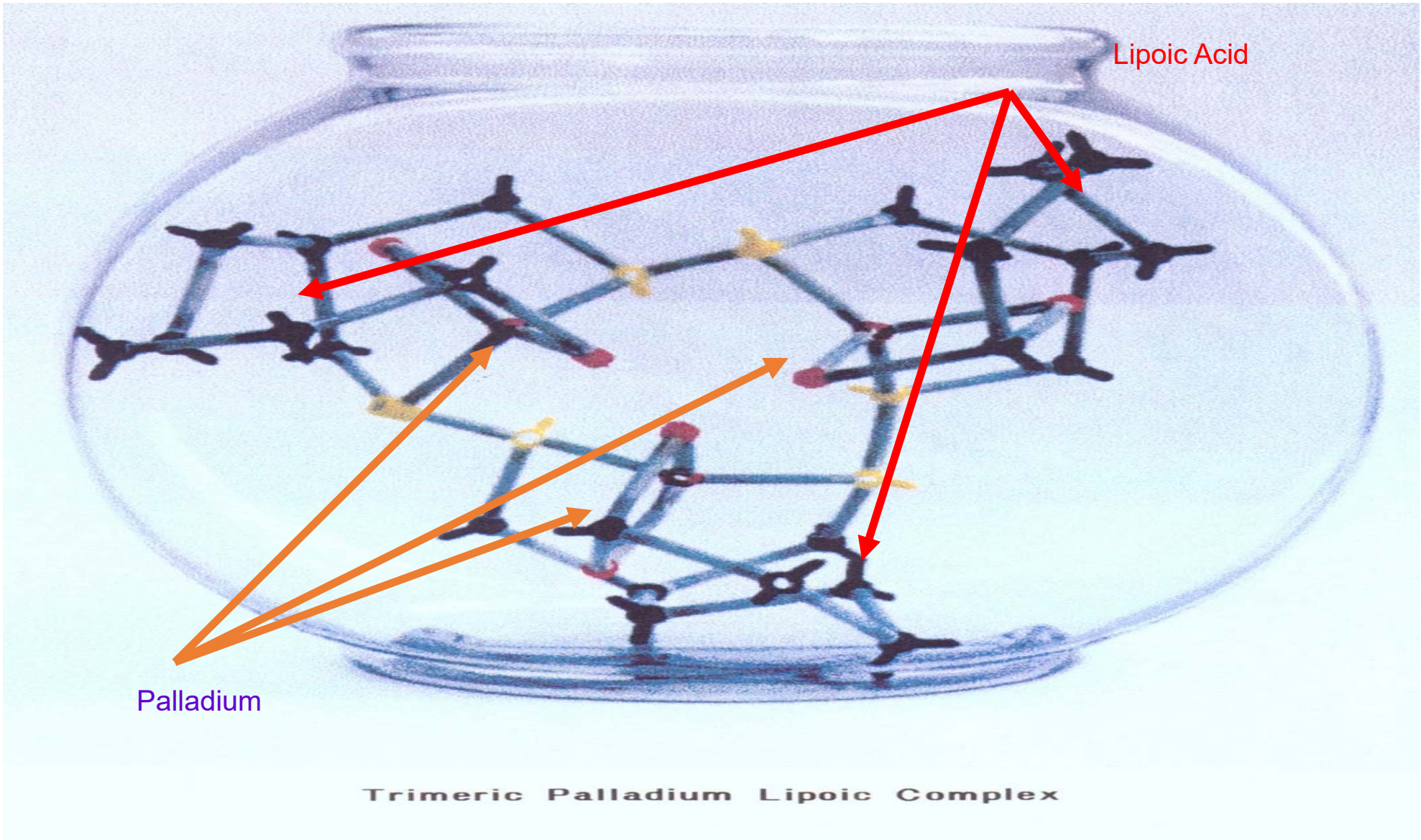
Composition of POLY-MVA*.

Palladium α-lipoic acid complex (1:1)	3.72×10^{-2} mmol/L
Thiamine	2.17×10^{-3} mmol/L
N-acetyl cysteine	1.13×10^{-3} mmol/L
Riboflavin	4.62×10^{-4} mmol/L
N-formyl methionine	1.46×10^{-4} mmol/L
Cyanocobalamin (Vitamin B12)	1.37×10^{-4} mmol/L
Rhodium	1.34×10^{-4} mmol/L
Molybdenum	4.63×10^{-4} mmol/L
Ruthenium	1.42×10^{-5} mmol/L
Sodium chloride	2.64×10^{-1} mmol/L

* Data supplied by manufacturer of POLY-MVA, El-Gen LLC, 7 Shirley Street, Bohemia, NY 11716-1735, USA.

Overview of actions

- Anti-oxidant
- DNA protection and repair
- Red Blood Cell protection
- Increases spleen colony formation
- Attenuation of radiation-induced weight loss
- Enhanced radiotherapy
- Strong mitochondrial supporting agent
- Improves chronic fatigue
- Support mitochondrial detoxification



Trimeric Palladium Lipoic Complex

LAMC

- Notice no free palladium and no free alpha lipoic acid. This enhances solubility in fat and water.
- Palladium bound is non toxic and a novel way of using a transition mineral to serve as a very efficient catalyst in aerobic respiration.
- More efficient redox since it is a polymer, rather than a single molecule.
- LAMC provides cellular energy by facilitating aerobic metabolism

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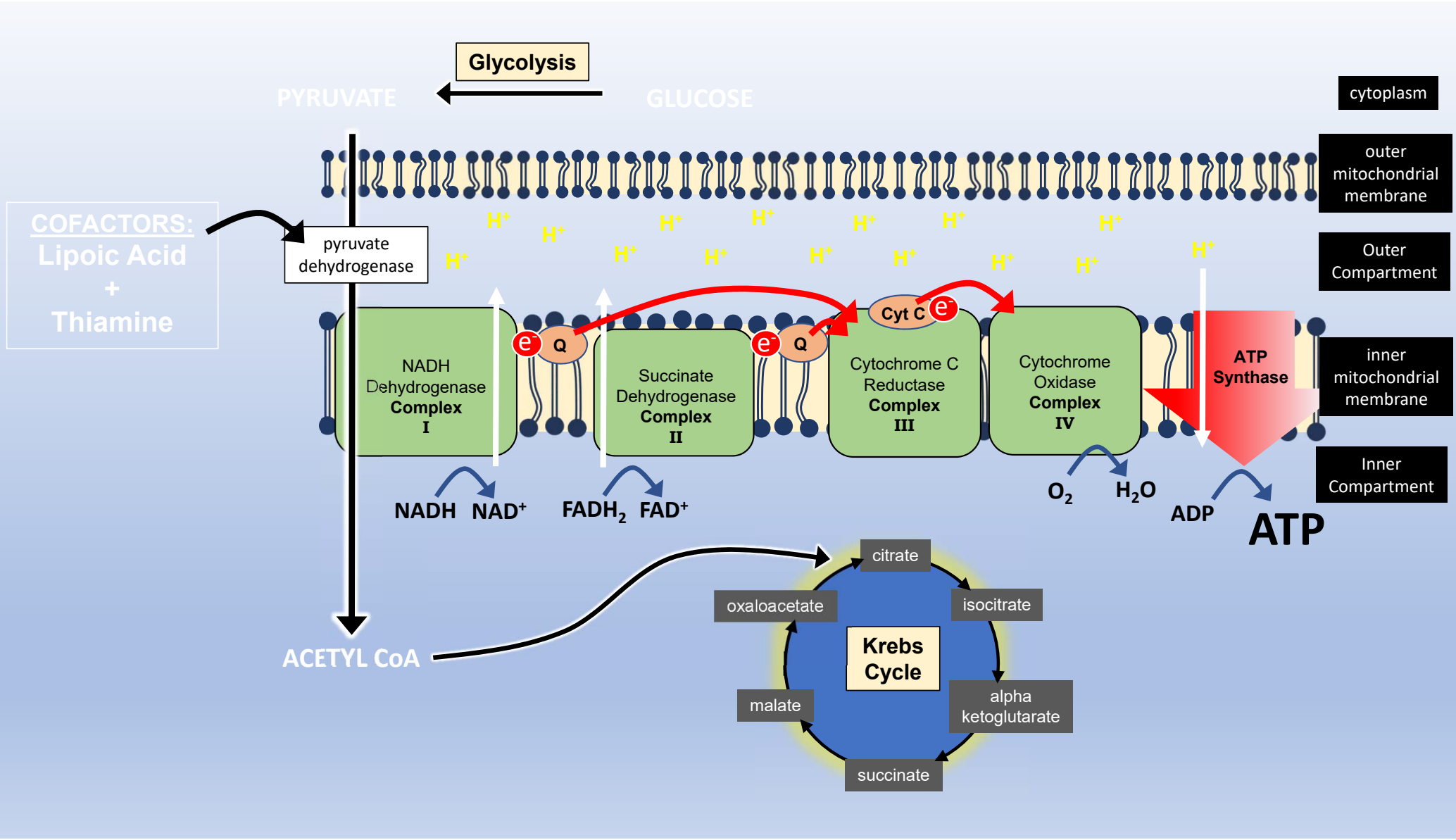
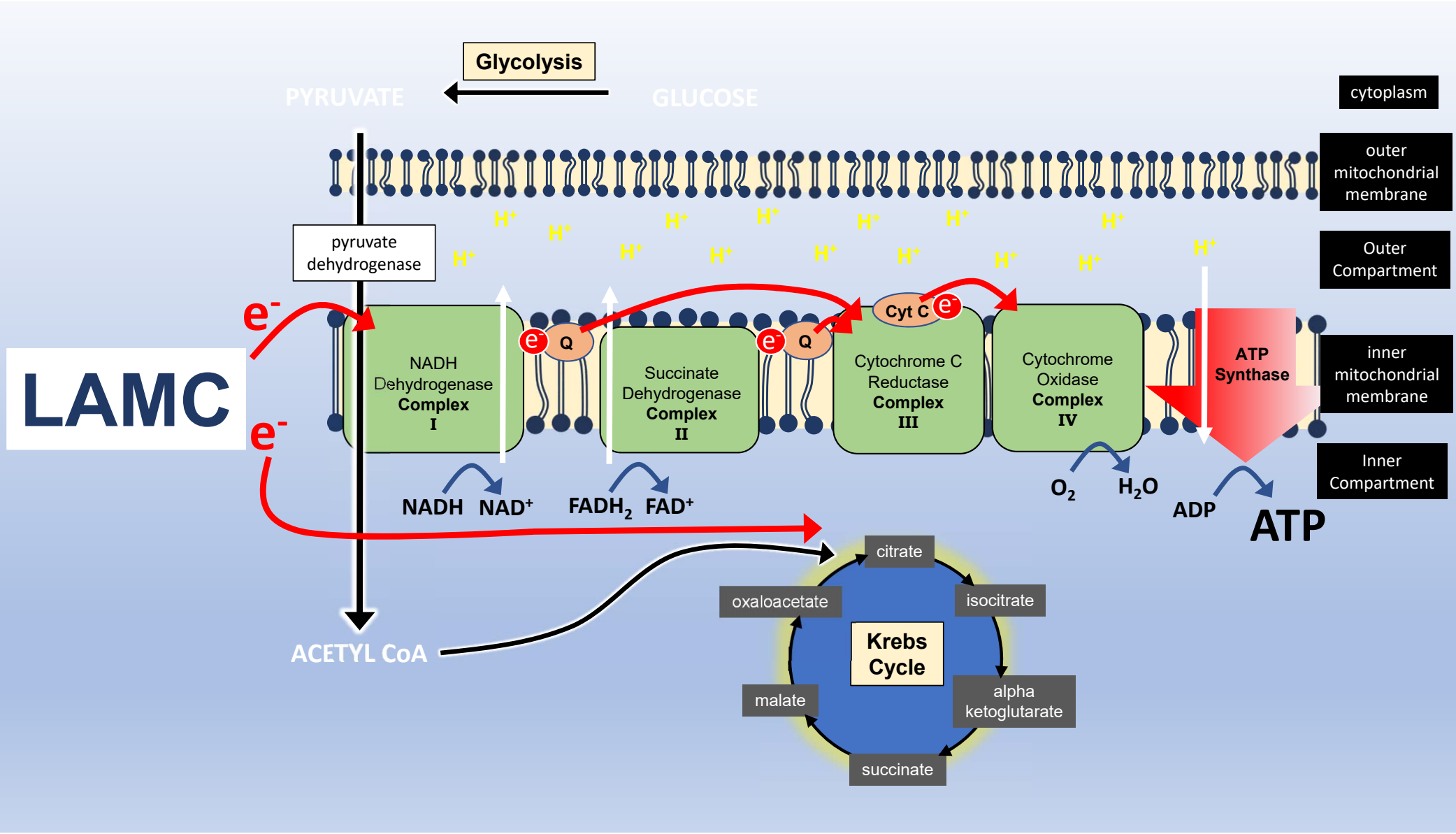
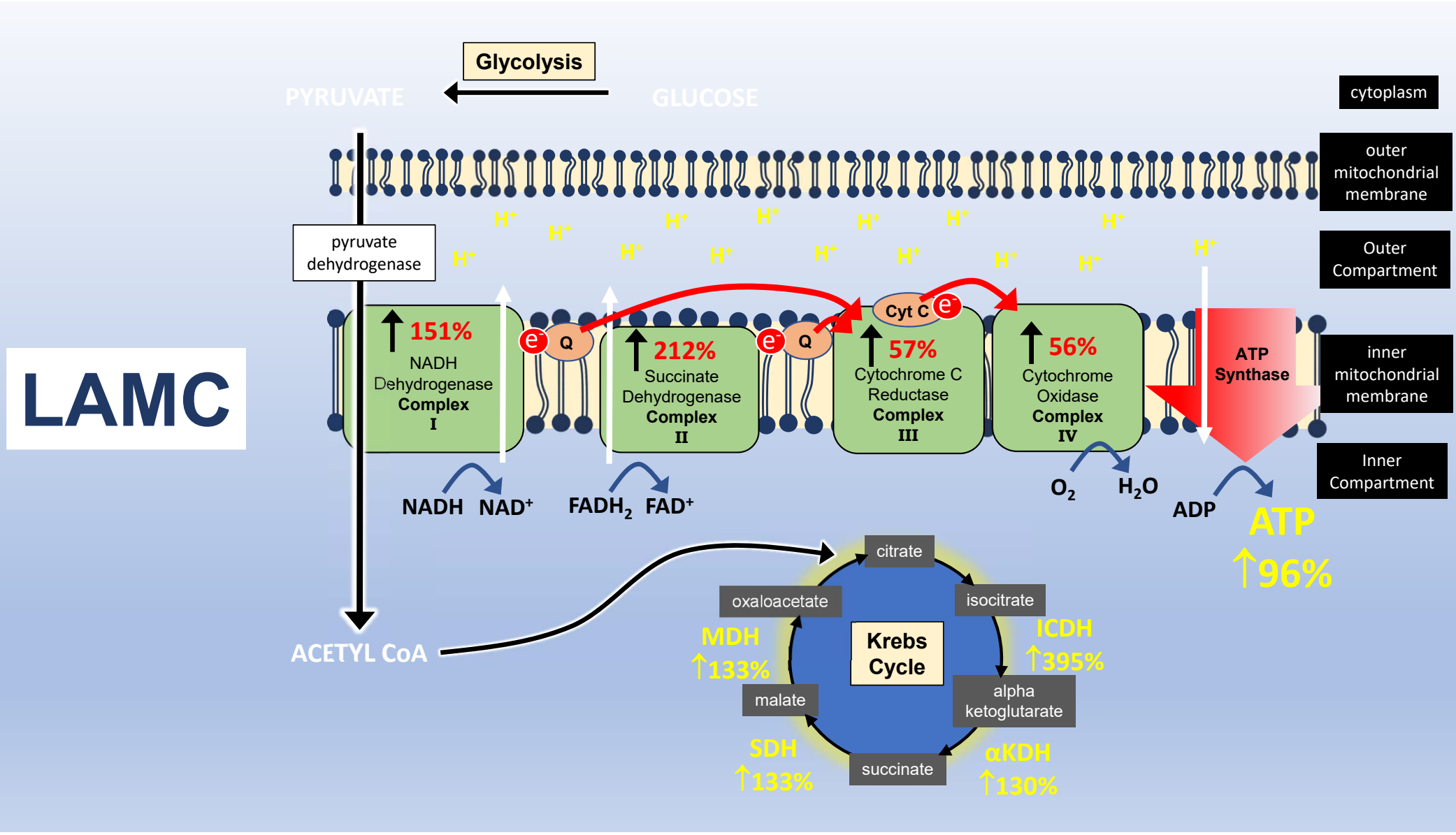

Glycolysis
PYRUVATE
GLUCOSE
cytoplasm
outer mitochondrial membrane
COFACTORS:
Lipoic Acid
+
Thiamine
pyruvate dehydrogenase
Outer Compartment
NADH Dehydrogenase Complex I
Succinate Dehydrogenase Complex II
Cytochrome C Reductase Complex III
Cytochrome Oxidase Complex IV
ATP Synthase
inner mitochondrial membrane
Q
Cyt C
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
Inner Compartment
ACETYL CoA
citrate
isocitrate
alpha ketoglutarate
succinate
malate
oxaloacetate
Krebs Cycle


Glycolysis
PYRUVATE
GLUCOSE
cytoplasm
outer mitochondrial membrane
pyruvate dehydrogenase
Outer Compartment
LAMC
e-
e-
NADH Dehydrogenase Complex I
Q
Succinate Dehydrogenase Complex II
Q
Cyt C
e-
Cytochrome C Reductase Complex III
Cytochrome Oxidase Complex IV
ATP Synthase
inner mitochondrial membrane
Inner Compartment
H+
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
ACETYL CoA
citrate
isocitrate
alpha ketoglutarate
succinate
malate
oxaloacetate
Krebs Cycle


LAMC
Glycolysis
PYRUVATE
GLUCOSE
cytoplasm
outer mitochondrial membrane
Outer Compartment
inner mitochondrial membrane
Inner Compartment
pyruvate dehydrogenase
H+
151%
NADH Dehydrogenase Complex I
212%
Succinate Dehydrogenase Complex II
Cyt C
57%
Cytochrome C Reductase Complex III
56%
Cytochrome Oxidase Complex IV
ATP Synthase
e-
Q
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
↑96%
ACETYL CoA
citrate
isocitrate
ICDH
↑395%
alpha ketoglutarate
αKDH
↑130%
succinate
SDH
↑133%
malate
MDH
↑133%
oxaloacetate
Krebs Cycle

LAMC: Research Areas

- Chronic Neurological Disease
  - Mitochondrial support
  - Cell support
- Fatigue States
  - Mitochondrial energy / repair support
- Adjunctive Cancer Care
  - Quality of life
  - Potential for antimetabolic supporrt

LAMC / MOA

Is LAMC's proposed mechanism of action directly related to its structural formulation?

LAMC's unique electronic and redox properties appear to be the key to its physiological effectiveness. When glucose enters a cell, it is broken down under anaerobic conditions (absence of oxygen) into pyruvate. Pyruvate subsequently enters the mitochondria, via complex I, and is quickly oxidized, in the presence of alpha-lipoic acid, to acetyl-CoA. In aerobic respiration, acetyl-CoA is then channeled into the Krebs/Citric Acid Cycle to create the reduced forms of nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide (FADH2). NADH and FADH2 donate their electrons to the electron transport chain to make the high energy molecule ATP.

Studies in India (Sudheesh et al., 2009) have demonstrated Palladium Lipoic Acid Complex's ability to facilitate aerobic metabolism, which is responsible for ATP production in healthy cells. The energy needs of the body are supplied by splitting ATP into adenosine diphosphate (ADP) and a free phosphate (Griffin et al. 2006).

LAMC / MOA

Studies have demonstrated that LAMC provides electrons to DNA, via the mitochondria. Electrons are lost in normal cells as a result of oxidative damage from radiation and chemotherapy (Garnett and Garnett 1996).

LAMC electron transfer provides an additional energy source to normal cells. However, cancer cells are metabolically challenged, and function in a hypoxic environment. Since there is less oxygen and more free electrons in the cancer cell, generation of free radicals occurs at the tumor mitochondrial membrane (Antonawich et al. 2004).

This activates apoptosis by facilitating the release of cytochrome C from the inner mitochondrial membrane, allowing the formation of an apoptotic complex in the cytoplasm. This complex, results in the subsequent activation of the caspase cascade of enzymes that destroy the malignant cells.

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journal homepage: www.elsevier.com/locate/foodchemtox

Effect of POLY-MVA, a palladium α-lipoic acid complex formulation against declined mitochondrial antioxidant status in the myocardium of aged rats

N.P. Sudheesh [a], T.A. Ajith [b], K.K. Janardhanan [a], C.V. Krishnan [c,d,*]

Results of this study reveal that palladium α-lipoic acid formulation is an effective agent to protect the age-linked decline of myocardial mitochondrial antioxidant status and thus is capable to enhance the energy production of normal cell mitochondria.

LAMC

- Oral form available
  - Orally given 2-4 tsp/day often for fatigue, neurological, mitochondrial issues.
  - Up to 8 tsp per day in oncology support

- Intravenous form available
  - Given without other additives
  - Generally added to a small normal saline (NS) bag

  (See protocol section)

Lipoic-Mineral Complex

Nutrient	mg/ml	mL	mOsm/ml	mOsm*vol
1. LAMC		5 - 40		
2. D5W or 0.9% Saline		100 - 250		

Est. Treatment time: 0.5 – 1.5 hours **Desired drip rate: 3-4 mL/min**
Final osmolarity: Approx. Iso-osmolar

Technical notes:
1.DO NOT add any other nutrients or injectables to this solution.
2.Can be used in series with other nutrients
3.The **first treatment dose** should be 5 – 10 mL
4.LAMC may be increased to 40 mL with successive treatment if the first IV is well tolerated.

LAMC in Regeneration & Mitochondrial Dysfunction

- We have used oral and IV LAMC in the setting of mitochondrial damage and dysfunction – oncology radiation, chemotherapy, fluoroquinolone toxicity, fibromyalgia, etc.
- Doses in the Autoimmune - Fatigue – Mitochondrially injured – Neurodegenerative population need to be lower and ramped up more slowly than in the oncology patient.
  - Oral doses can be 5 to 15 mL BID
  - IV doses are given in 100 to 250 mL D5W or NS
    - 5 mL test dose
    - Ramp up to 20-25 mL
    - Give in series (as a separate bag) with other nutrients

Sequencing in Regenerative Cases:

- Often we will sequence IV's on the same day to increase synergy and speed healing. (see case in the PTC notes).
- Often this is some or all of the following:

1. Vitamin-Mineral IV
2. Glutathione
3. ALA or LAMC
4. Phospholipids (often added once the patient is past an acute phase)

LAMC

LAMC for IV Use:

1 – No oxidative therapies / HDIVC within 12 hours of Poly-MVA IV

2 – Infuse LAMC per protocol over 30-90 minutes

3- Infusion Frequency: Two IV's weekly for six weeks then re-evaluate

LAMC References

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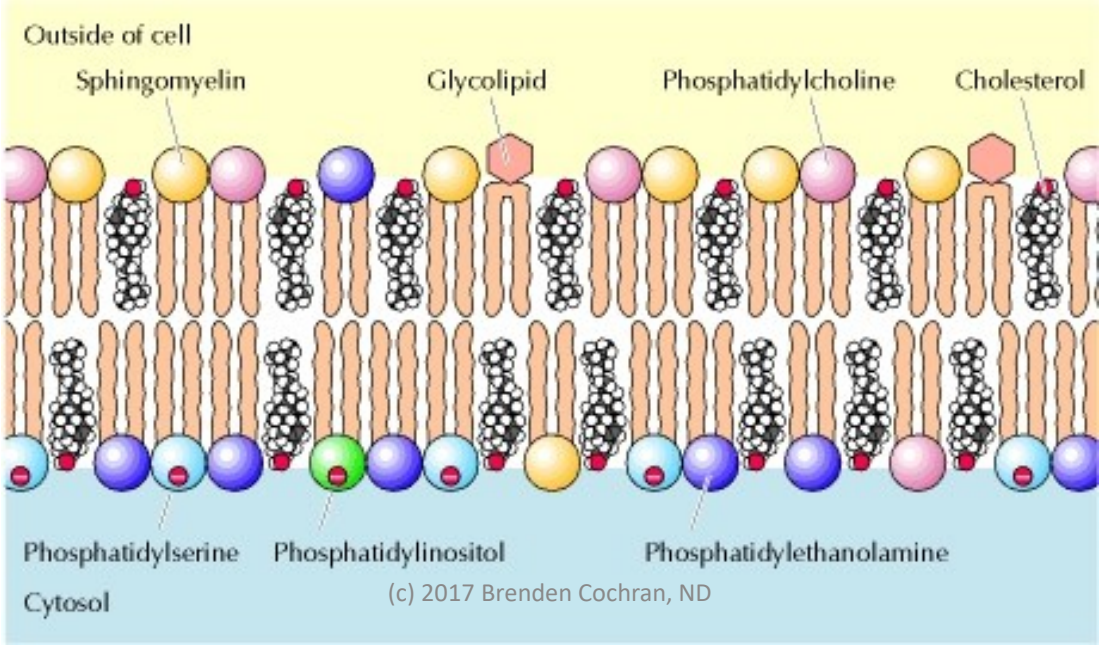
Phosphatidylcholine



Case

- 21 year old male with visual field disturbances, numbness and coordination issues. Diagnosed with multiple sclerosis treated with natalizumab as one of the more recent treatments which showed little to no benefit.
- Part of treatment included PTC + Nutrients which was helpful but more noticeable stabilization in symptoms using Nutrients, Glutathione, Poly-MVA, PTC.

Indications

- Liver
- Cardiovascular
- Post stroke recovery: Glycerophosphocholine
- Encephalopathy
- Memory, cognitive decline

Phosphatidylcholine (PTC)

- Methyl donor
- Cell Membrane structural support and maintenance
- Highly metabolic tissues
  - Brain / Heart / Kidney / GI
  - High concentration in brain CM's
    - May help with concentration
    - Donates Choline for ACh synthesis
      - Used for cognitive support
- Liver damage (Drug / ETOH / Hep - B,C)
  - Also appropriate in NASH

The ***Alt Med Rev*** Monograph is reprinted in your notes.

Phosphatidylcholine (PTC)

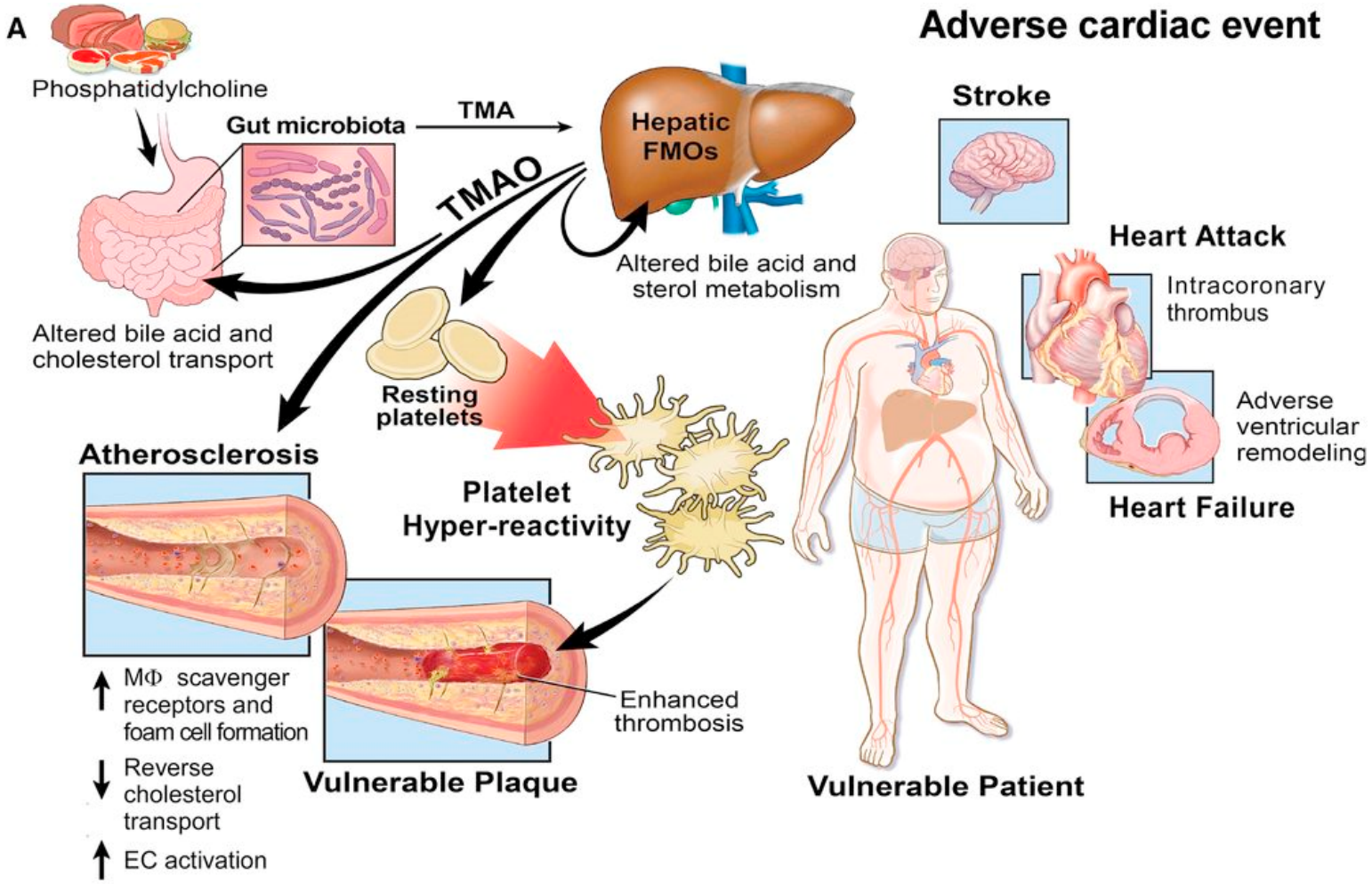
- Multiple IV protocols are published.
  - All appear to have their own merit based on clinical reports from physicians employing them in similar groups of patients.
  - The following is the protocol I feel is best to begin with, and has the least phlebitis and other side effect potential

Phosphatidylcholine (PTC)

- Protocol:
  - Infuse slowly (higher concentrations and faster administration will cause phlebitis) over 1 hour if tolerated.
  - No other additives are mixed with this infusion
  - You can follow or lead with a different nutrient bag.
  - **MUST FLUSH OR CHANGE LINE** between bags
  - Sensitive patients (MCS, Elderly, Multiple co-morbidities) may experience **GI distress** – RAMP Those patients doses up slowly from 10 mL starting dose.

IV PTC benefit to Oral

- **IV is best until you know your patient!**
- Cleveland clinic has found that choline can contact certain bacteria in the intestines which converts choline to TMA. In the liver there is an enzyme that makes TMAO (Trimethylamine-N-oxide)
- TMAO forms vascular inflammation and unstable plaques in the arterial walls.



http://dx.dol.org/10.1016/j.cell.2016.02.01101

PTC (Intravenous Protocol)

- PC 35mg/mL OR 50mg/ml, Sodium Deoxycholate 24mg/mL, Benzyl Alcohol 0.9% and Ethanol 0.2%.
- Basic protocol:
  - Increment dose and infuse over 90 minutes
  - 25 ml PTC (maximum 50 ml) in 250 mL D5W **(MUST BE IN NON-IONIC carrier)**
  - Optional: Follow with glutathione push
- Caution is can cause GI upset and diarrhea. Work up slow and consider fiber.

Rx: Phosphatidylcholine

		PTC (35-50 mg) (3-50 mls)			
		D5W (250-500 ml)			

Additions /Subtractions:

Glutathione + 0.9% Normal Saline

Total Volume: mL Osmolarity: mOsm/L

(The “Push Protocol”)

- Draw 5 to 10 ml Essentiale-N into a syringe at least twice the volume, leave 5 ml air in syringe
    - Some add 0.5 mL heparin, 1000 IU/mL
- Establish the IV using a 21 or 23 gauge butterfly set & draw an equal volume blood into syringe
- Mix the blood and Essentiale-N during and after drawing sufficient blood into the syringe
- Immediately inject the mixture over 2-3 minutes, keeping the air bubble uppermost in syringe to avoid injecting air
- Remove empty syringe and attach syringe for glutathione push, 600-2500 mg
- Injections are given 3-5 times weekly until liver tests normalize
- It may be more prudent to add the Essentiale-N to 250 mL D5W and infuse over 90 minutes
- Flush butterfly – administer glutathione IV push

Parenteral PC Caution

- Phosphatidylcholine is compounded by a number of pharmacies in the U.S. for use in Mesotherapy. This is commonly 100 mg/mL concentration. This formulation can not be used for intravenous applications.

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Thank You!