



Utilizing Nutritional Testing in Pain Management

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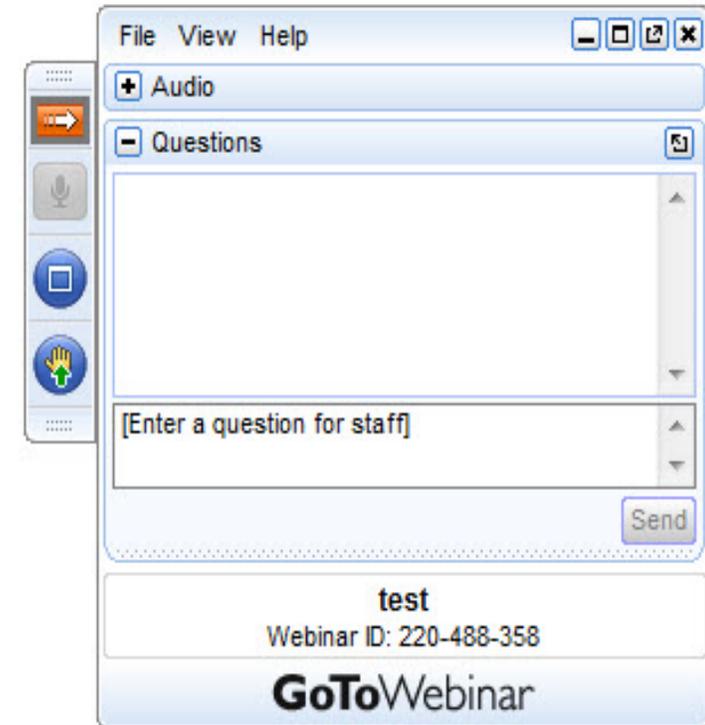
Atlanta Functional Medicine, Founder



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We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.



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The screenshot shows the Genova Diagnostics website. At the top, there are social media icons (Twitter, LinkedIn, YouTube, Facebook) and navigation links (Payments, About, Contact, Search, myGDX, Region). The main header includes the Genova Diagnostics logo and navigation tabs for HOME, CLINICIANS, and PATIENTS. The breadcrumb trail reads: Home / Clinicians / Medical Education.

Medical Education

Genova Diagnostics is an internationally renowned medical testing facility committed to the highest professional standards. The Medical Affairs Team provides educational support in a broad array of formats, including complementary phone consultations to healthcare professionals with Genova Diagnostic accounts. Supplemental educational materials are available for assistance in clinical application and interpretation of Genova Diagnostics tests throughout the site.

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At the bottom of the page, there are logos for GLfx, NutrEval, and DON (Division of Optimal Nutrition), along with a quote: "Providing comprehensive and innovative clinical laboratory services for the prevention, diagnosis and treatment of complex chronic disease..." attributed to Genova Diagnostics.



Objectives for This Presentation

- Identify specific nutrients which benefit common pain conditions
- Discuss how pre-emptive nutrient assessments and repletion of nutrient deficiencies can protect at-risk patients from future pain conditions
- Review current medical research regarding the impact of specific nutrients improving pain and/or augmenting established pain relief strategies

OBJECTIVE





Why Assess Nutrients in Pain Patients?

- More than 70,200 Americans died from illicit and prescription drug overdoses in 2017
- National Institute for Drug Abuse reported that 1 of 3 Americans used opiates for pain in 2015
- From 2007 – 2014 pregnancy drug dependence rose 511%
- A large percentage of accidents are related to opioid impaired driving
- There is pressure to shift from reliance on opiates toward comprehensive pain management that involves evidence based, medication free options
- Low back pain, knee osteoarthritis, and headache are among the most common and most costly
- Nutrient studies as treatment for pain conditions are sparse

Man's ability to handle pain is grossly underrated

- Acute and chronic pain have been present since time began
- The interaction of what resides *within us* and what impacts us *from the natural world* must have allowed us to manage and conquer acute and chronic pain
- Evaluating nutrients for their positive effects becomes MORE INTERESTING



Why Assess Nutrients in Pain Patients?

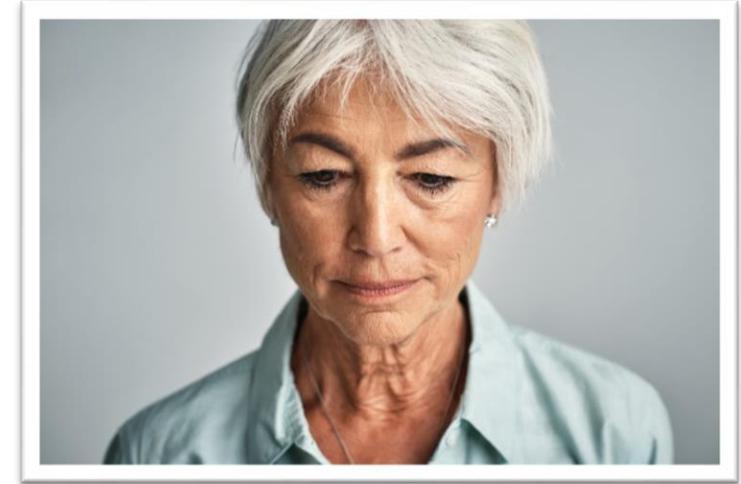
- The NIH cites the following environmental factors as causes of epigenetic changes:
 - Exercise
 - Diet
 - Nicotine
 - Alcohol
 - Chemical exposures
 - Medications
 - Stress
 - **Micronutrient deficiency**





Case Study #1: 70 Female with Cervicalgia

- CC: chronic cervicalgia after two falls
 - Underwent cortisone injections without benefit
 - Neurosurgeon diagnosed her with rheumatoid arthritis; however, all rheumatologic studies are negative
- Treated with multiple antibiotics 5 years ago for staph infection
- Diet: organic and minimal meat
- Lifestyle: exercises regularly
- Supplements:
 - Ashwagandha, Holy Basil, and Rhodiola Rosea
 - Glucosamine and MSM
 - 4000IU D3
 - Methylated B12 sublingual
 - Ca⁺⁺/Mag
 - Raw Zinc
 - Bioidentical hormones





Case Study #1: 70 Female with Cervicalgia

Stay tuned

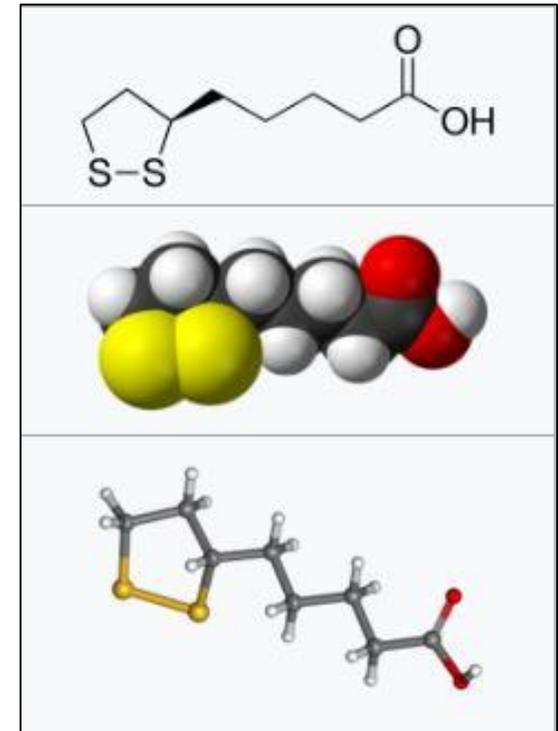
- Plan
 - Anti-inflammatory diet
 - Routine Labs
 - HS CRP: 2.3
 - Vit D: 58ng/ml
 - CoQ10: 1.15
 - MTHFR: 1298 homozygous CC
 - Ferritin: 60
- Is this enough information?
- Is she at risk for nutrient deficiencies?
- Which nutrients have efficacy for pain conditions?





Specific Nutrients: Alpha Lipoic Acid

- **Lipoic acid (LA)**, also known as **α -lipoic acid**, **alpha lipoic acid (ALA)**, and **thioctic acid** is an organosulfur compound derived from octanoic acid
- ALA is made in animals normally, and is essential for aerobic metabolism
- Manufactured and available as a dietary supplement and marketed as an antioxidant, also available as a pharmaceutical drug in other countries
- Although the body can synthesize LA, it can also be absorbed from the diet
- Dietary supplementation in doses from 200–600 mg are likely to provide up to 1000 times the amount available from a regular diet
- It is therefore recommended that dietary LA be taken 30–60 minutes before or at least 120 minutes after a meal
- Maximum blood levels of LA are achieved 30–60 minutes after dietary supplementation, and it is thought to be largely metabolized in the liver





Specific Nutrients: Alpha Lipoic Acid

- ALA plus epalrestat (aldose reductase inhibitor) combination therapy was superior to ALA and epalrestat monotherapies for clinical efficacy and nerve conduction velocities in patients with **diabetic peripheral neuropathy**
- Results of a study re: pain from **diabetic peripheral neuropathy**: methylcobalamine, alpha lipoic acid, and pregabalin combination provides pain relief and improves sleep interference. Addition of methylcobalamin and ALA to pregabalin improves the nerve function. Due to small sample size, most of the efficacy parameters could not reach significant difference between groups...
- Low **back pain** with **Sciatic neuropathy** benefited by alpha lipoic acid as part of a multimodal approach
- Women with **endometriosis** ..treated with a preparation containing N-acetyl cysteine, alpha lipoic acid and bromelain: significant improvement in endometriosis-associated pelvic pain and required lower intake of rescue analgesics
- Alpha Lipoic Acid and Omega-3 Fatty Acids added to amitriptyline treatment in patients with **Vestibulodynia associated With Painful Bladder Syndrome** appears to improve outcomes and may allow for a lower dosage of amitriptyline
- Alpha lipoic acid and PEA improved **endometriosis** at 6 and 9mo

Zhao M, et al. *Neural Reg Res*. 2018;13(6):1087-95.

Vasudevan D, et al. *Ann Indian Acad Neurol*. 2014;17(1):19–24.

Checchia GA, et al. *Eur Rev Med Pharmacol Sci*. 2017;21(7):1653-64.

Lete I, et al. *Eu J Obstete Gynecol Reprod Biol*. 2018;228:221-24.

Murina F, et al. *J Obstet Gynaecol Can*. 2017;39(3):131-37.

Caruso S, et al. *Minerva Ginecol*. 2015;67(5):413-19.



Specific Nutrients: Omega 3 FAs

- Omega 3 (Polyunsaturated Fatty Acids - PUFAs)
- Associated with reduced pro-inflammatory prostaglandins.
- Doses over 2.7gm/day reduced NSAID use in **Rheumatoid Arthritis** patients





Specific Nutrients: Omega 3 FAs

- Improved **osteoarthritis knee** pain in patients with low omega6:omega3 ratio
- Use of Marine fish oils resulted in significant effect was found in patients with **rheumatoid arthritis** (22 trials; -0.21; 95% CI, -0.42 to -0.004) and other or mixed diagnoses, less with osteoarthritis
- Polyunsaturated omega 3 fatty acids used with Elavil are useful for prophylaxis of **migraine** attacks
- Ratio of omega6:omega3 was directly related to unacceptable pain and refractory pain in **Rheumatoid Arthritis** patients on methotrexate
 - Omega 3 PUFAs was inversely related to refractory pain
- Increasing omega 3 and reducing omega 6 fatty acids reduced **chronic headache pain**, altered antinociceptive mediators, and improved QOL

Sibille, KT, et al. *Clin J Pain*. 2018;34(2):182-89.

Senftleber NK, et al. *Nutrients*. 2017;9(1).pii: E42.

Soares AA, *Nutr Neurosci*. 2017;9(1).pii: E42.

Lourdudoss C, et al. *Arthritis Care Res (Hoboken)*. 2018;70(2):205–12.

Ramsden C, et al. *Pain* 2013 Nov 154(11):2441-51.



Specific Nutrients: Vitamin C

- Vitamin C is a safe and effective adjunctive therapy for acute and chronic pain
- Scurvy: sore arms and legs plus muscle and joint aches
- Humans lack an enzyme that enables the liver to make Vit C
- Present in raw meat





Specific Nutrients: Vitamin C

- 3 grams intravenous Vit C reduced **postop pain** in uvulopalatopharyngoplasty with tonsillectomy without increased side effects
- Vitamin C in combination with ruscus and hesperidin methyl chalcone improves pain, heaviness, feeling of swelling, tingling, ankle circumference, and global symptoms in **Chronic Venous Disease**
- Lower plasma concentrations of Vit C were noted in patients with **post-herpetic neuropathy** and reduction in spontaneous post-herpetic neuropathy pain after high-dose vitamin C treatment
- Reductions in development of **post surgical CRPS** after wrist and ankle surgery with Vitamin C
- Oral vit C reduced **osteoarthritis** related hip and knee pain = ½ dose of NSAID
- Vitamin C improves QOL parameters in **cancer-related pain** (nausea, vomiting, pain, fatigue, and insomnia), but does not appear to lower opiate requirements



Specific Nutrients: Vitamin C



Antioxidant

Radical oxygen scavenger protecting cells from oxidative stress

Steroid- and catecholamine synthesis

Cofactor in catecholamine, vasopressin and steroid synthesis
Improves hemodynamics; may accelerate resolution of shock

Immune cell function

Increases neutrophil phagocytosis and chemotaxis
Affects macrophage migration
Enhances T and NK cell proliferation, modulates their function
May increase antibody formation

Endothelial cell function

Decreases endothelial ICAM expression and leukocyte adhesion
Improves endothelial barrier function
Decreases fluid requirements in burn patients
Improves microcirculation

Carnitine production

Modulates fatty acid metabolism
May improve microcirculation and cardiac function

Wound healing

Cofactor of collagen production
Mitogen for fibroblasts



Specific Nutrients: Vitamin D

- Vitamin D deficiency is often found in chronic pain sufferers and correlates with muscle fatigue risk factors
- A rapid dose of vitamin D3 attenuates inflammation, epidermal structure damage and redness from **sunburn**
- High dose Vit D reduces prevalence of PMS and **dysmenorrhea**: 50,000 iu a week followed for 9 weeks
- Serum vitamin D concentration is important for the prevalence and severity of pain in the **neck and thoracic spine, knees and hands or wrists**, but not for the lumbar spine, shoulders and elbows of postmenopausal agriculture workers
- D3-Vitamin was superior to placebo in reducing **migraine** days in migraine patients
- **Burning mouth syndrome**
- 2016 meta-analysis of 19 RCTs significantly greater mean decrease in pain score (primary outcome) was observed with vitamin D supplementation compared with placebo in people with **chronic pain**

Tick H, et al. *Explore (NY)*. 2018;14(3):177-211.

Bahrami A, et al. *Gynecol Endocrinol*. 2018;34(8):659-63.

Raczkiewicz D, et al. *Ann Agric Environ Med*. 2017;24(1):151-55.

Gazerani P, et al. *Curr Med Res Opin*. 2019;35(4):715-23.

Morr Verenzuela CS, et al. *Int J Dermatol*. 2017;56(9):952-56.

Wu Z, et al. *Pain Physician*. 2016;19(7):415-27.



Specific Nutrients: Vitamin D

- A 2017 meta-analysis re: chronic widespread pain (including **fibromyalgia**), revealed that vitamin D supplementation is able to decrease pain scores and improve pain despite no significant change in VAS after increasing serum vitamin D serum level
- Vitamin D has been inversely correlated with painful manifestations, such as fibromyalgia and **rheumatic diseases**
 - Studies have demonstrated a possible action of vitamin D in the regulatory mechanisms of both sleep and pain
 - The supplementation of vitamin D associated with good sleep hygiene may have a therapeutic role, not only in sleep disorders but also in the prevention and treatment of chronic pain conditions
- Brief case example – 48 yo male with chronic widespread pain
 - Had been treated with elimination diet
 - Serum Vit D was 15
 - Started 10,000 IU daily for two weeks then 5,000 IU thereafter
 - Placed on Low Dose Naltrexone (LDN).
 - Returns in 2 months: ALL of his pain resolved.
 - Will begin weaning the LDN due to side effects.



Specific Nutrients: Magnesium

- Magnesium has also been studied as an **NMDA** (N-methyl-D-aspartate) receptor blocker in the treatment of **neuropathic pain**
 - A review of the concomitant use of magnesium with opioids in animals suggests that magnesium may potentiate opioid analgesia while also mitigating some of the adverse effects of opioids including the development of hyperalgesia
- **Migraines:** Results suggest that the proprietary supplement containing feverfew, coenzyme Q10, and magnesium could be beneficial and safe for the prevention of migraine in adult patients and merits further study
- **Menstrual migraines** benefit in short term from magnesium
- Intra-articular injection improved **knee arthroscopy** improved pain relief & chondrocyte protection
- IV magnesium improved **CRPS** pain peri-partum
- Intra-op magnesium sulfate **reduces post-op pain** requirements, agitation and PACU stay

Maasumi K, et al. *Headache*. 2017;57(2):194-208.

Moscano, F, et al. *Ital J Pediatr*. 2019;45:36-42.

Zeng C , et al. *Sci Rep*. 2016;6:38024.

Niconchuk JA, et al. *Reg Anesth Pain Med*. 2019;pii:rapm-2018-100142.

Elsersy HE, et al. *Eur J Anaesthesiol*. 2017;34(10):658-64.



Specific Nutrients: Zinc and Selenium

- Individuals with **chronic myofascial pain**
 - Exhibited low concentrations of Zn²⁺ and Se
 - Had a greater likelihood of inadequate intake of selenium as well as lower intake of zinc
 - These results suggest that the inflammatory state increases the need for mobilizing bodily reserves of these nutrients to meet antioxidant demand
- A combination product was evaluated to treat **chronic prostatitis**:
 - lycopene, epigallocatechin gallate, ellagic acid, selenium and zinc
 - Results showed a statistically significant reduction in inflammatory parameters (leucocytes in seminal fluid and EPS), progressive sperm motility, and sperm morphology
 - Improvements were also seen in the pain score of the NIH-Chronic Prostatitis Symptom Index (CPSI) confirming that the reduced inflammation also resulted in a reduction in pain



Specific Nutrients: B Vitamins

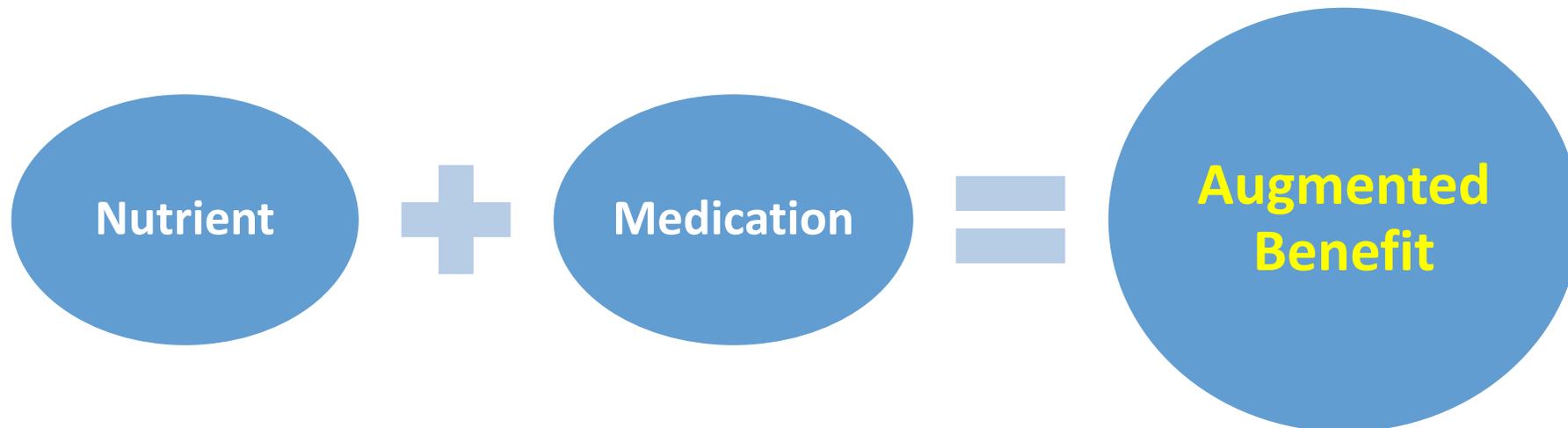
- B vitamins are water soluble and lack toxicity except for B6.
 - Niacin can create symptoms such as flushing, itching, liver toxicity and glucose dysregulation.
- B vitamins are particularly concentrated in meat such as turkey, tuna, and liver
 - Good sources for B vitamins include legumes, whole grains, potatoes, bananas, chili peppers, tempeh, nutritional yeast, brewer's yeast and molasses.
- Increased consumption of beer and other alcoholic beverages results in a net deficit of most B vitamins

B1	Thiamin
B2	Riboflavin
B3	Niacin
B5	Pantothenic Acid
B6	Pyridoxine
B7	Biotin
B9	Folate
B12	Cobalamins



Specific Nutrients: B Vitamins

- Many Examples of Nutrients Augmenting Pain Relief
 - **Oral B vitamin** with Diclofenac improved VAS and total pain beyond Diclofenac alone or Diclofenac and vit E in patients with osteoarthritis of the knee
 - “Animal studies have demonstrated synergistic benefits of **vitamin B12** combined with other pain medications, including NSAIDs and opiates. Clinical trials provide evidence for the effectiveness of vitamin B12 for the treatment of low back pain and neuralgia...”





Specific Nutrients: Vitamin B1 (Thiamine)

- High-dose thiamine improves symptoms of **fibromyalgia** (levels were checked)
- Clinically significant reduction in pain and improved functional mobility in patients with **chronic joint, back, and muscle pain** using vitamin B1 and 5-herb blend
- Oral High-Dose Thiamine Improves the symptoms of **chronic cluster headache**:
 - Thiamine treatment started with an oral dose of 250 mg in the morning
 - Every 3 days the dose was increased by 250 mg up to the dose of 750 mg
 - Within 10 days the 41 yo patient with a 26y hx of CH was symptom free
- A 66-year-old female patient with diagnosis of vertebrobasilar dolichectasia, right **trigeminal neuralgia**, and vestibular paroxysmia - treated with Vitamin B1 (10 mg), methylcobalamin (0.5 mg), and carbamazepine (0.1 g) given orally 3 times a day to relieve the symptoms successfully
- **Burning Mouth Syndrome**

Costantini A, et al. *BMJ Case Rep.* 2013;2013:bcr2013009019.

Hedaya R. *Altern Ther Health Med.* 2017;23(1):14-19.

Antonio C, et al. *Case Report Neuro Med.* 2018;2018:3901619.

Han J, et al. *Medicine (Baltimore).* 2018;97(25):e11192.

Morr-Verenzuela CS, et al. *Int J Dermatol.* 2017;56(9):952-56.



Specific Nutrients: Vitamin B2 (Riboflavin)

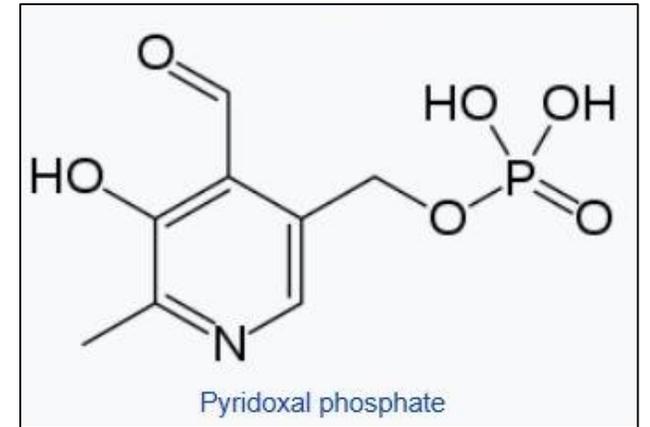
- **Migraines:** Treatment with a proprietary supplement containing magnesium, riboflavin, and Q10 (Migravent[®] in Germany, Dolovent[®] in USA) had an impact on migraine frequency which showed a trend towards statistical significance
- 659 patients with **Burning Mouth Syndrome**, the most common decreased values or deficiencies were vitamin D₃ (15%), vitamin B₂ (15%), vitamin B₆ (5.7%), zinc (5.7%), vitamin B₁ (5.3%)...





Specific Nutrients: Vitamin B6 (Pyridoxine)

- Vitamin B6 also plays a role in cognitive development through the biosynthesis of neurotransmitters
- Inactive form pyridoxine competitively inhibits the active pyridoxal-5'-phosphate
- Consequently, symptoms of vitamin B6 supplementation are similar to those of vitamin B6 deficiency
- Recommend dosages below less than 100mg to prevent peripheral neurotoxicity
- The richest sources of vitamin B6 include fish, organ meats such as beef liver, starchy vegetables including potatoes, and fruit (other than citrus).
- In the United States, adults obtain most of their dietary vitamin B6 from fortified cereals, beef, poultry, starchy vegetables, and some non-citrus fruits.
 - About 75% of vitamin B6 from a mixed diet is bioavailable.





Specific Nutrients: Vitamin B12 (Cobalamine)

- Vitamin B12 has a proclivity for neural tissue; animal models suggest that B12 helps to regenerate nerves by **inducing axonal growth** and **Schwann cell** differentiation, which improves functional recovery in difficult-to-treat nerve crush injuries.
- In addition, B12 upregulates brain-derived neurotrophic factor (BDNF) and **increases nerve conduction velocity**, which may reflect part of the regeneration process
- Vitamin B12 is normally acquired through food; it is typically bound to protein and **requires stomach acid** and the **digestive enzyme pepsin** to release it in free form
- Nerve damage related to vitamin B12 deficiency appears to be a direct result of the body being unable to keep myelin basic protein methylated, leading to degeneration of the **myelin sheath**



Specific Nutrients: Vitamin B12 (Cobalamine)

Author	Condition Treated	Intervention	Significant Outcomes
Goldberg	Compressive Neuralgia	PO 2000 µg HCB* 3x/day for 1 month	Pain decreased 60%
Han	Chemotherapy-Induced Peripheral Neuropathy	IM 500 µg MCB* every other day x10, then PO MCB 500 µg 3x/day for 2 months	Pain decreased 23%
Devathasan	Diabetic Neuropathy	PO 1500 µg MCB* daily for 3 months	Pain decreased 70%, cramps decreased 85%, and 2-point discrimination improved 33%
Yaqub	Diabetic Neuropathy	PO 500 µg MCB* 3x/day for 4 months	Improvement of somatic symptoms by 32%, autonomic symptoms by 36%, and the signs of diabetic neuropathy by 11%
Shindo	Diabetic Neuropathy	PO 500 µg MCB* 3x/day for 4 weeks	Somatosensory symptoms improved 50%
Xu	Herpetic Neuralgia	SubQ 500 µg MCB* x4 locations daily for 4 weeks	Pain decreased 54%
Mauro	Low Back Pain	IM 1000 µg CCB* daily for 2 weeks	Pain decreased 87%, disability by 82%
Chiu	Low Back Pain	IM 500 µg MCB* 3x/week for 2 weeks	Pain decreased 31%, disability by 27%
Liu	Aphthous Stomatitis	Topical MCB* and steroid 4x/day for 2 days	Pain decreased 94% (control using steroid, 65%)

*HCB = Hydroxycobalamin, MCB = methylcobalamin, CCB = cyanocobalamin



Specific Nutrients: Vitamin B12 (Cobalamine)

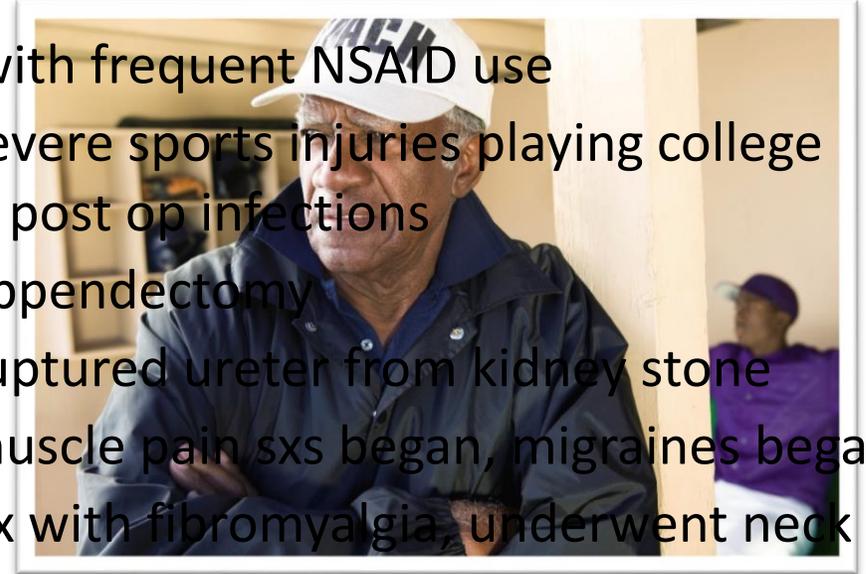
- 20 different genetic abnormalities affecting cobalamin transport proteins required for intracellular delivery of B12 to tissue targets including mitochondria
- Methyl-B12 alleviated pain behaviors in **diabetic neuropathy, low back pain and neuralgia**, plus it improved nerve conduction, promoted the regeneration of injured nerves, and inhibited ectopic spontaneous discharges of injured primary sensory neurons
- **Small fiber neuropathy** associations with B12 deficiency
- Treatment of **chemo induced peripheral neuropathy**
- **Low back pain and neuralgia**
- **Herpetic neuralgia**: decreased analgesics and improved QOL
- **Apthous Ulcers**

Zhang M, et al. *Neural Plast.* 2013;2013:424651
Gunes HN, et al. *Acta Neurol Belg.* 2018;118(3):405-10.
Soloman LR. *Support Care Cancer.* 2016;24(8):3489-494.
Buesing S, et al. *Pain Physician.* 2019;22(1):E45-E52.
Wang JY, et al. *Complement Ther Med.* 2018;41:277-82.
Liu H-L, et al. *Pain Manag Nurs.* 2015;16:182-87.



60 y/o College Baseball Coach with Fibromyalgia

- Migraines
 - Fibromyalgia
 - Insomnia
 - Peripheral neuropathy
 - Takes Ambien, Tramadol, Relpax, Phenergan, and Gabapentin
 - ROS: fatigue, constipation, decreased strength and sex drive
 - Diet: SAD with sugar binges
- Athlete with frequent NSAID use
 - 18 yo - severe sports injuries playing college baseball, post op infections
 - 31 yo - appendectomy
 - 40 yo - ruptured ureter from kidney stone
 - 44 yo - muscle pain sxs began, migraines began
 - 47 yo - dx with fibromyalgia, underwent neck surgery
 - 56 yo - Right shoulder joint replacement
 - 58 yo - Back surgery
 - 6 months ago migraines worsen
 - Has been on multiple antibiotics, steroids, NSAIDS, opiates (now Tramadol 100mg TID), and medial branch blocks worsened pain





60 y/o College Baseball Coach with Fibromyalgia

• Lab Results:

- CRP: 1.2
- **Vit D: 23**
- Homocysteine: **13**
- **B12: 388**
- CoQ10: 0.96
- Fasting glucose: 106
- Omega 3 index: **5.1**
 - EPA: 0.4 % (0.1 – 2.5%)
- Stool Test: low diversity and SCFAs plus dysbiosis

Normal	Borderline	High Need	Supplementation for High Need
Antioxidants			
Vitamin A / Carotenoids			
Vitamin C			
Vitamin E / Tocopherols			
α-Lipoic Acid			
CoQ10			
B-Vitamins			
	Thiamin - B1		
Riboflavin - B2			
Niacin - B3			
Pyridoxine - B6			
	Biotin - B7		
		Folic Acid - B9	Folic Acid - B9 - Dose = 1,200 mcg
	Cobalamin - B12		
Minerals			
Magnesium			
Manganese			
Molybdenum			
Zinc			



60 y/o College Baseball Coach with Fibromyalgia

- Initial Plan:
 - Anti-Inflammatory/ Elimination diet: No sugar, gluten, dairy, soy, eggs, processed meat or carbs, corn, peanuts, alcohol, night shades,
 - INCREASE COLORS
 - Medical shake containing turmeric and low allergenic rice based protein
 - EPA fish oil
 - Vit D3
 - CoQ10
 - Magnesium (up to bowel tolerance)qhs
 - B vitamins with B12
 - Consult w/ Health Coach





60 y/o College Baseball Coach with Fibromyalgia

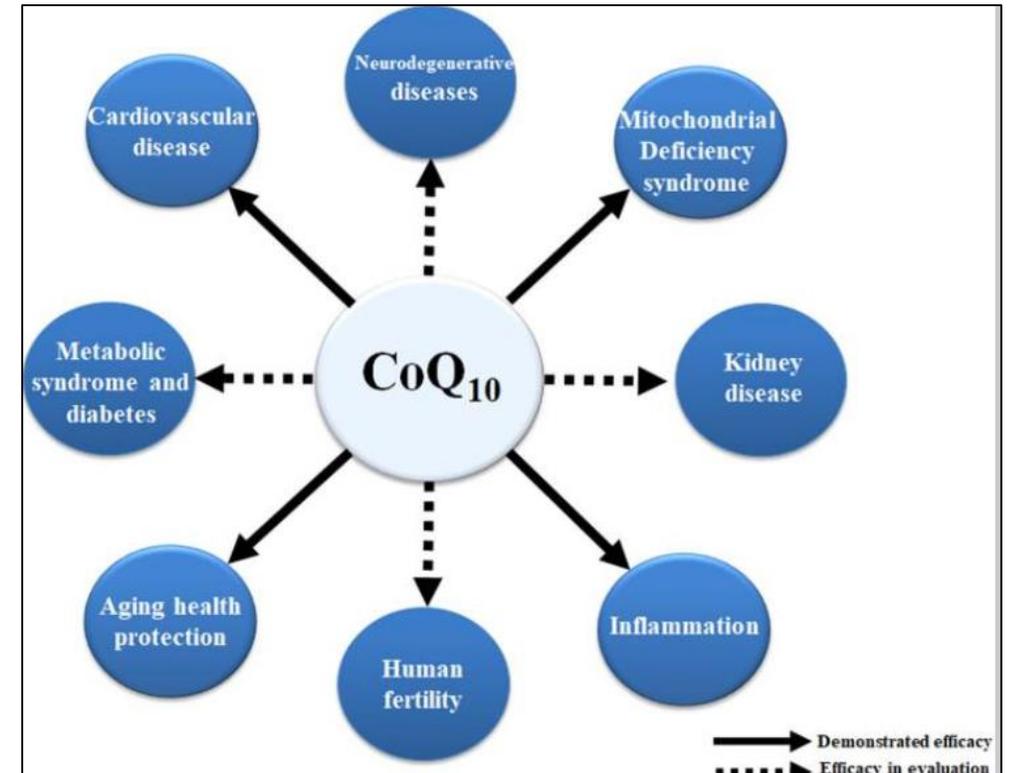
- 3 week follow up
 - Has decreased his Tramadol
 - Sleeping through the night off of Ambien
 - Increased energy
 - Regular bowel movements
 - 1 migraine since last visit
 - Family reports better mood
 - Lost 11 pounds
 - Pain only when throwing pitches





Specific Nutrients: Coenzyme Q10

- **Migraine** as a mitochondrial disorder: CoQ10 and riboflavin pharmaceutical doses
- Statin induced myopathy: no improvement meta-analysis 2015
- **Fibromyalgia** patients are candidates for Coenzyme Q10 benefit





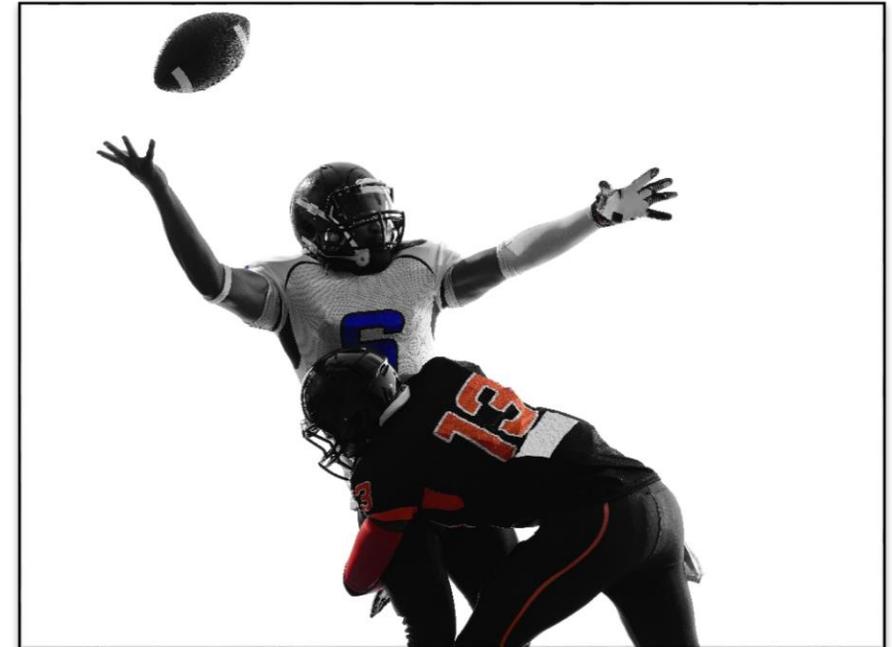
Specific Nutrients: Acetyl L Carnitine

- L-Carnitine supplementation improved clinical status without changing oxidative stress and lipid profile in women with **knee osteoarthritis**
- The current evidence suggests that acetyl L carnitine has a moderate effect in reducing pain measured on VAS in **Peripheral neuropathic Pain** patients with acceptable safety
 - Larger trials with longer follow-up, however, are warranted to establish the effects
- L-carnitine improves **muscle pain recovery** in athletes. (25% made endogenously, 75% must be consumed, major source is meat: need for supplementation)



Specific Nutrients: Branched Chain Amino Acids (BCAA)

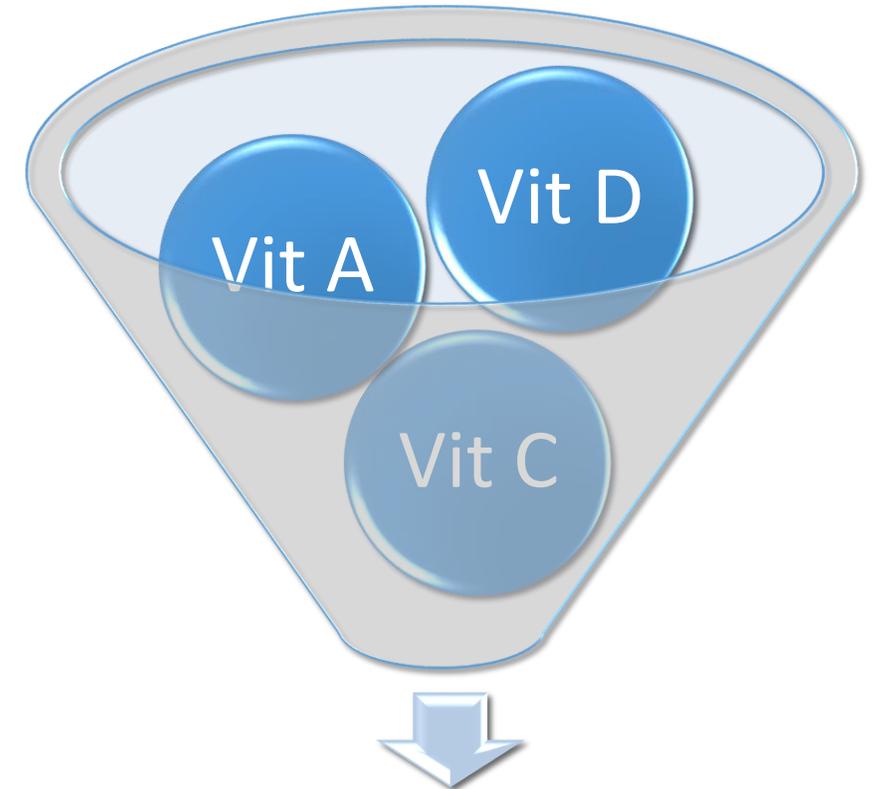
- Mixed results for muscle damage and recovery in athletes





Specific Nutrients: Antioxidants

- **Chronic pancreatitis:** Vit A
- **Endometriosis** pain benefits from Vit D and Vit. A
- 2 months of antioxidants (vitamins E and C) not only lowered peritoneal inflammatory markers, but also resulted in reduced **chronic pelvic pain** in women with **endometriosis**.



Decreased Oxidative Stress



Pain Patients at Risk for Nutrient Deficiencies

- Gut Dysfunction
- Malabsorption and pancreatitis (think PPIs)
- TMJ
- Alcoholism:
 - acute painful nutritional axonal neuropathy
 - Vitamin C supplementation and carnitine improved muscle aching and weakness
- Chronic kidney disease
- Bariatric surgery and anorexia: acute nutritional axonal neuropathy, painful
- Vegan, lack of dietary meat



Pain Patients at Risk for Nutrient Deficiencies

- Patients with chronic liver and kidney disease do not produce adequate amounts of L-carnitine
- Athletes with spinal cord injuries are deficient in nutrients
- Patients on long term prescription medications that can deplete nutrients
 - Proton Pump inhibitors: B12, Vit C, Fe, Ca, Mag, Zinc, and B-carotene
 - NSAIDS: Vit C and Fe
 - Diuretics: Ca, Mag, B1, Zinc, and Potassium
 - Anti-Hypertensives: B9, Potassium, and Fe
 - Statins: CoQ10, Vit D, Vit E, and B-carotene
 - Diabetic Drugs: B12, Ca, and Vit D
 - Steroids: Ca, Vit D, sodium, potassium, and chromium
 - Bronchodilators: Ca and Vit D
 - Anti-depressants: Ca, Vit D, and B9
 - Oral contraceptives: B6, B9, B12, Ca, Mag, Vit C, and Vit E



Medications *rob* us of at least one nutrient

Anti Depressants:	Coenzyme Q10, B2, B9, Ca, Vit D
Anti-Hypertensives:	Coenzyme Q10, B1, B6, B9, Zinc, Fe
Anti-Virals:	B12, Cu, Carnitine, Zinc, Ca, Mag, K+
Anti-Inflammatories:	Ca, B9, Vit C, Fe, B5, Vit D, Zinc, Se, Chromium, Mag
Anti-Convulsants:	B1, B7, B9, B12, Ca, Copper, Carnitine, Zinc, Vit D, Vit K
Antibiotics:	B vitamins, Vit K, Ca, Mag, Fe, Zinc
Antacids, PPIs:	Ca, Fe, Zinc, B9, B12, Vit D, Vit C, EFAs, Mag, B-carotene
Diuretics:	Coenzyme Q10, B1, B6, B9, Vit C, Ca, Mag, Zinc, Na, K+
Beta Blockers:	Coenzyme Q10, Melatonin
Diabetic Drugs:	Coenzyme Q10, B9, B12
Hormones and BCPs:	B Vitamins, Mag, Se, Zinc, Vit C, Vit E, Ca
Statin:	Carnitine, Cu, CoQ10, EFAs, Se, Vit D, Vit E, Zinc, B-carotene
Steroids:	Ca, Vit D



Specific Pain Conditions Benefited by Nutrients





Chronic Postpartum Pain Treatment

- Supplementation of **lipoic acid** in association with **omega-3** seems effective and safe for the treatment of chronic postpartum pain, allowing a pathogenetic approach to neuroinflammation, thus reducing the consumption of analgesic drugs, often contraindicated during breast-feeding.





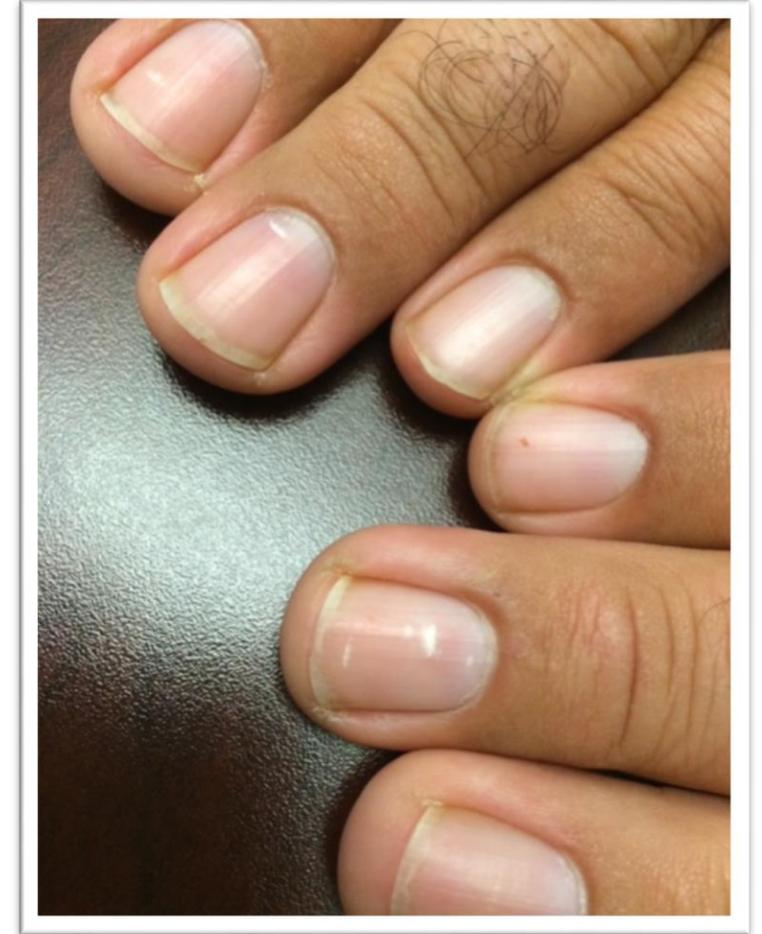
Chronic Pelvic Pain

- Endometriosis associated pelvic pain: 300 mg of palmitoylethanolamide (PEA) and 300mg twice daily **α-lipoic acid** (LA) given to 56 women
 - By the 6th and 9th month, pain symptoms ($P < 0.001$) and all categories of the QOL ($P < 0.001$) improved
- RPCT: antioxidant vitamins **Vit C** and **vit E** women with pelvic pain and endometriosis: 43% improved pain, 37% improved dysmenorrhea, 24% dyspareunia improvement



Chronic Myofascial Pain

- Assessment of intake, serum and intracellular levels of **selenium** and **zinc**
 - Chronic Myofascial pain patients had a lower RBC zinc and selenium
- Piriformis syndrome (PS) is an entrapment of the sciatic nerve by the piriformis muscle, or myofascial pain from the piriformis muscle
 - Mannitol plus **B Vitamins** is effective in the management of piriformis syndrome and it could be an alternative regime in treatment of PS





Burning Mouth Syndrome

- Among 659 patients with BMS, the most common decreased values or deficiencies were **vitamin D₃** (15%), **vitamin B₂** (15%), **vitamin B₆** (5.7%), **zinc** (5.7%), **vitamin B₁** (5.3%), thyrotropin (TSH) (3.2%), vitamin B₁₂ (0.8%), and folic acid (0.7%)
 - Laboratory values for fasting blood glucose and TSH were increased in 23.7% and 5.2%, respectively
 - Our results suggest it is reasonable to screen for fasting blood glucose, vitamin D (D₂ and D₃), vitamin B₆, zinc, vitamin B₁, and TSH
- **Gabapentin** may boost the efficacy of **alpha lipoic acid** in therapy for burning mouth syndrome



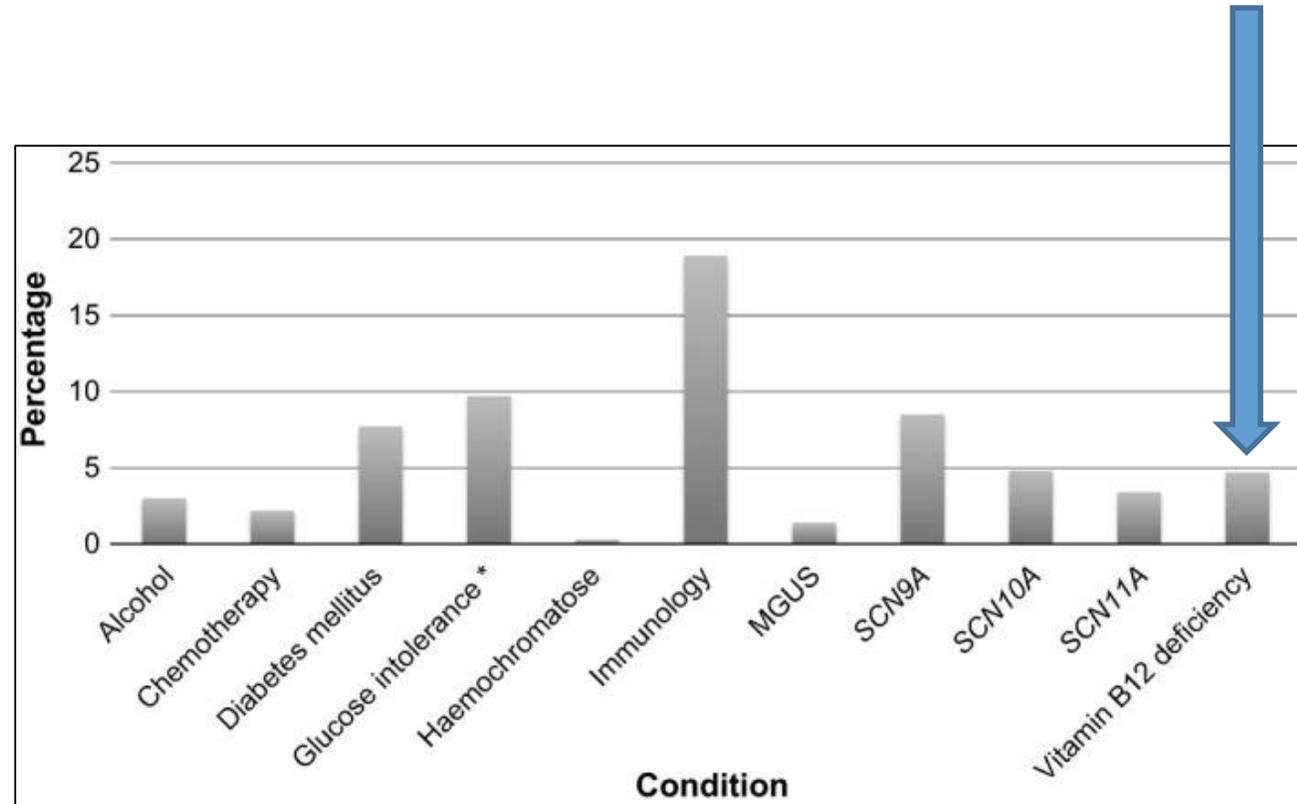
Fibromyalgia

- Administration of **Coenzyme Q10** improves hyperalgesia and quality of life in patients with fibromyalgia (decreases oxidative stress and protects mitochondria)
- Our results show, compared to a control group, administration of **CoQ10** significantly improved most pain-related outcomes by 24-37%, including fatigue (by ~22%) and sleep disturbance (by ~33%)
 - These results confirm the considerable role played by CoQ10 in reducing pain, fatigue, and sleep disturbance in subjects affected by fibromyalgia
- High dose **thiamine B1** improves the symptoms of fibromyalgia
- Muscle pain has been associated with deficiencies in **amino acids, magnesium, selenium, vitamins B and D**, as well as with the harmful effects of heavy metals, such as mercury, cadmium, and lead
 - Research indicates that patients deficient in certain essential nutrients may develop dysfunction of pain inhibitory mechanisms together with fatigue and other FM symptoms
 - Mercury and other toxic elements may interfere with the bioavailability of essential nutrients
 - When optimal levels of nutrition are achieved, pain levels are usually lowered



Small Fiber Neuropathy

- Patients with pure SFN are screened at least for autoimmune diseases, sodium channel gene mutations, diabetes mellitus including glucose intolerance, and **vitamin B12** deficiency, even when they already have a potential underlying condition at referral
- Pilot study showed that **vitamin B12** deficiency causes symptomatic as well as asymptomatic small fiber loss like diabetes mellitus





Tendon Injuries

- Preliminary evidence suggests that various nutrients such as proteins, **amino acids (leucine, arginine, glutamine)**, **vitamins C and D**, **manganese, copper, zinc**, and **phytochemicals** may be useful in improving tendon growth and healing
- **Eggplant: Vitamin K, Thiamin, Vitamin B6, Folate, Potassium and Manganese**, and a very good source of **Dietary Fiber** and rich in **phytonutrients**.

Looks a little like
MITOCHONDRIA





Temporal Mandibular Joint Pain

- 23 women avg age 40.6y with chronic TMJ, post surgical:
- **Iron, vitamin C, and vitamin B6** were the most common deficiencies seen
 - Depleted **iron** stores (evaluated by serum ferritin levels) were found in 70% (16/23) of the patients, while 48% (11/23) of the patients had low serum iron levels. A laboratory diagnosis of anemia was made on the basis of serum iron values obtained
 - A high incidence of vitamin deficiencies was seen in patients for **beta-carotene** (48%, 11/23); **vitamin B1** (52%, 12/23), **vitamin B6** (57%, 13/23), **vitamin B12** (35%, 8/23); **folate** (26%, 6/23); and **vitamin C** (57%, 13/23)
 - Other deficiencies included **zinc** (26%, 6/23) and **magnesium** (22%, 5/23)
 - The occurrence of excessively high values of the micronutrients tested was seen in an insignificant number of patients ($\leq 6\%$), except zinc (16%)
- Some other clinical and laboratory findings suggestive of deficiencies in this group of patients were as follows: glossitis, 48% (11/23); anemia, 48% (11/23); cheilosis, 26% (6/23); poor skin healing, 48% (11/23); and hair loss, 52% (12/23)



Prophylactic treatments: Migraine

- **Riboflavin** is well tolerated, inexpensive and has demonstrated efficacy in the reduction of adult patient's **migraine headache** frequency
 - Additional data are needed, however, to resolve questions involving pharmacokinetic issues and pharmacogenomic implications of therapy
 - Mild if any side effects
- **Migraine Prevention:** butterbur, riboflavin, coenzyme Q10, and magnesium citrate received a strong recommendation for use from the Canadian Headache Society
- Evidences indicate that supplementation with **magnesium, carnitine, riboflavin, niacin, CoQ10, vitamin D, Vitamin B₁₂** and **alpha lipoic acid** have prophylactic and therapeutic effects on **migraine** patients



Chronic Tension: Type Headache

- Low serum **Vit D** (<20 ng/ml) may be related to migraine and tension-type headache
- Case reports of children with **Vit D** less than 10 with musculoskeletal pain and tension headaches which resolved after increasing vit D
- Randomized, placebo-controlled, double-blind, cross-over trial included 14 children suffering from tension-type headache
 - A significant reduction of mean frequency of headaches with a tension-type phenotype was found in favor of the **riboflavin** 50mg treatment (P = 0.04).



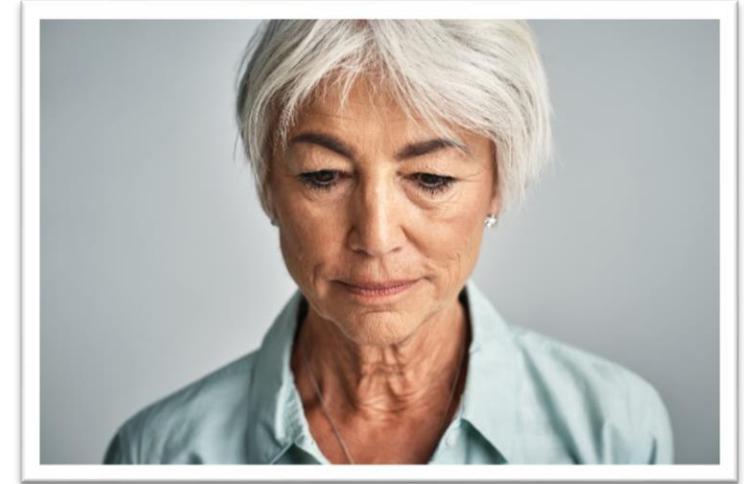
Treatment Framework Chronic Pain Patient

- Could this patient be at risk or be missing nutrients?
 - Vegan
 - SAD
 - TMJ, mouth pain, dental pain or loss
 - Eating disorder, anorexia
 - Medication thievery
- Could repletion of missing nutrients improve the patient's pain?
- What needs to be removed?
- Nutrients as adjuvants for current pain therapies
- NutrEval as a road map or guide



Case Study #1: 70 Female with Cervicalgia

- Plan
 - Anti-inflammatory diet
 - Routine Labs
 - HS CRP: 2.3
 - Vit D: 58ng/ml
 - CoQ10: 1.15
 - MTHFR: 1298 homozygous CC
 - Ferritin: 60
- Is this enough information?
- Is she at risk for nutrient deficiencies?
- Which nutrients have efficacy for pain conditions?





Case Study #1: 70 Female with Cervicalgia

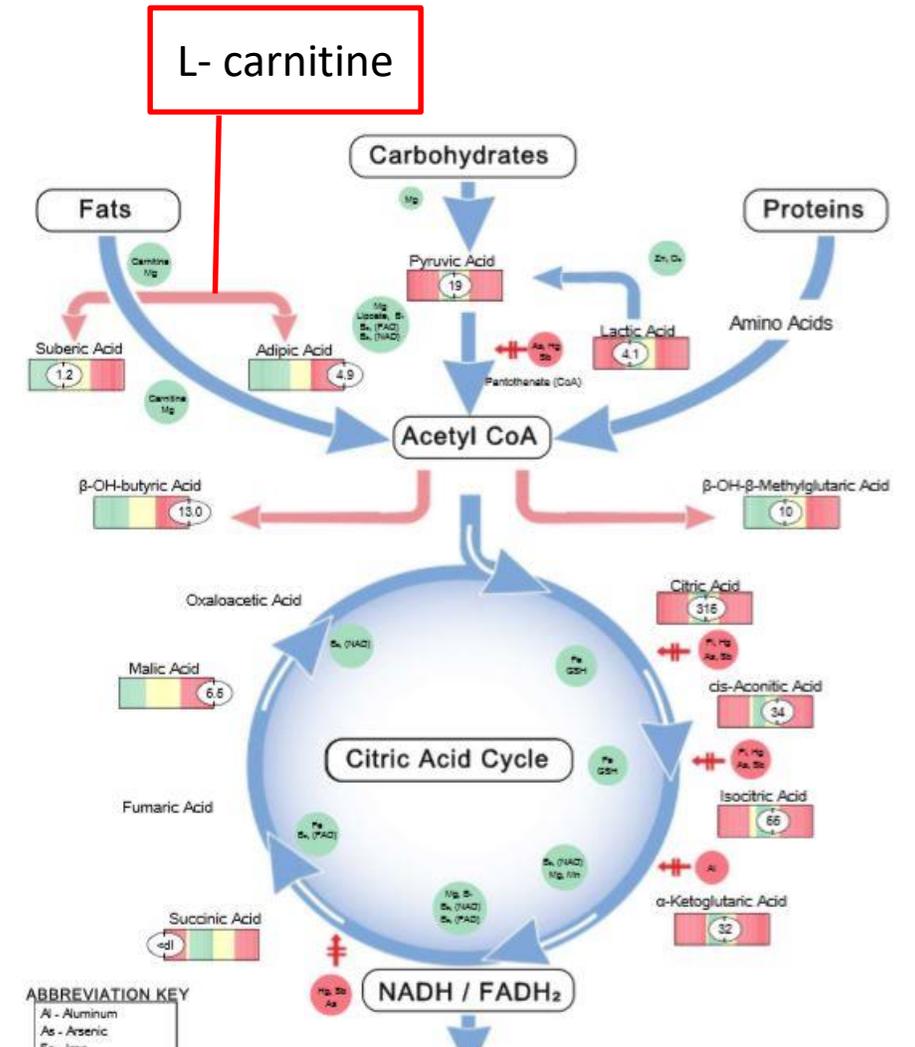
- Plan
 - Anti-inflammatory diet
 - Routine Labs
 - HS CRP: 2.3
 - Vit D: 58ng/ml
 - CoQ10: 1.15
 - MTHFR: 1298 homozygous CC
 - Ferritin: 60

Normal	Borderline	High Need	Supplementation for High Need
Antioxidants			
Vitamin A / Carotenoids		Vitamin C	Vitamin C - Dose = 1,000 mg
Vitamin E / Tocopherols		α-Lipoic Acid	α-Lipoic Acid - Dose = 200 mg
CoQ10			
B-Vitamins			
Biotin - B7	Niacin - B3 Pyridoxine - B6 Folic Acid - B9 Cobalamin - B12	Thiamin - B1 Riboflavin - B2	Thiamin - B1 - Dose = 60 mg Riboflavin - B2 - Dose = 60 mg
Minerals			
Zinc	Magnesium Manganese Molybdenum		



Case Study #1: 70 Female with Cervicalgia

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	3,000 IU	
Vitamin C	75 mg	1,000 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		200 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	50 mg	
Riboflavin - B2	1.1 mg	50 mg	
Niacin - B3	14 mg	30 mg	
Pyridoxine - B6	1.5 mg	25 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	800 mcg	
Cobalamin - B12	2.4 mcg	500 mcg	
Minerals			
Magnesium	320 mg	800 mg	
Manganese	1.8 mg	5.0 mg	
Molybdenum	45 mcg	150 mcg	
Zinc	8 mg	10 mg	
Essential Fatty Acids			
Omega-3 Oils	500 mg	500 mg	
Digestive Support			
Probiotics		25 billion CFU	
Pancreatic Enzymes		10,000 IU	
Other Vitamins			
Vitamin D	800 IU		
Amino Acid			
Amino Acid	mg/day	Amino Acid	mg/day
Arginine	45	Methionine	0
Asparagine	324	Phenylalanine	0
Cysteine	0	Serine	98
Glutamine	905	Taurine	725
Glycine	1,503	Threonine	0
Histidine	1,180	Tryptophan	0
Isoleucine	158	Tyrosine	429
Leucine	0	Valine	410
Lysine	818		





Case Study #1: 70 Female with Cervicalgia

- Treatment Plan
 - Treated her malabsorption; stressing importance of protein
 - Increased coenzyme Q10
 - Increased magnesium
 - Increased the omega 3s
 - Multi-vitamin to support mitochondria
 - B-Vitamins (methylated B12 and B9), acetyl-L carnitine, alpha lipoic acid, and anti-oxidants
- 2-Month Follow Up
 - Patient asked “Where is my neck pain? It is gone!”



Care & Feeding of Mitochondria

LOTS

- Oxygen
- B vitamins
- Magnesium
- Coenzyme Q10
- Moderate Exercise
- Anti-Oxidants
- Vitamin C
- L Carnitine

SOME

- Copper
- Zinc
- Iron (Fe)
- Manganese

AVOID

- Toxicants
- Heavy Metals
- Hg, Al, Sb, As, Fl
- Reactive Oxygen species
- Infections
- Oxidative Stress
- Medications





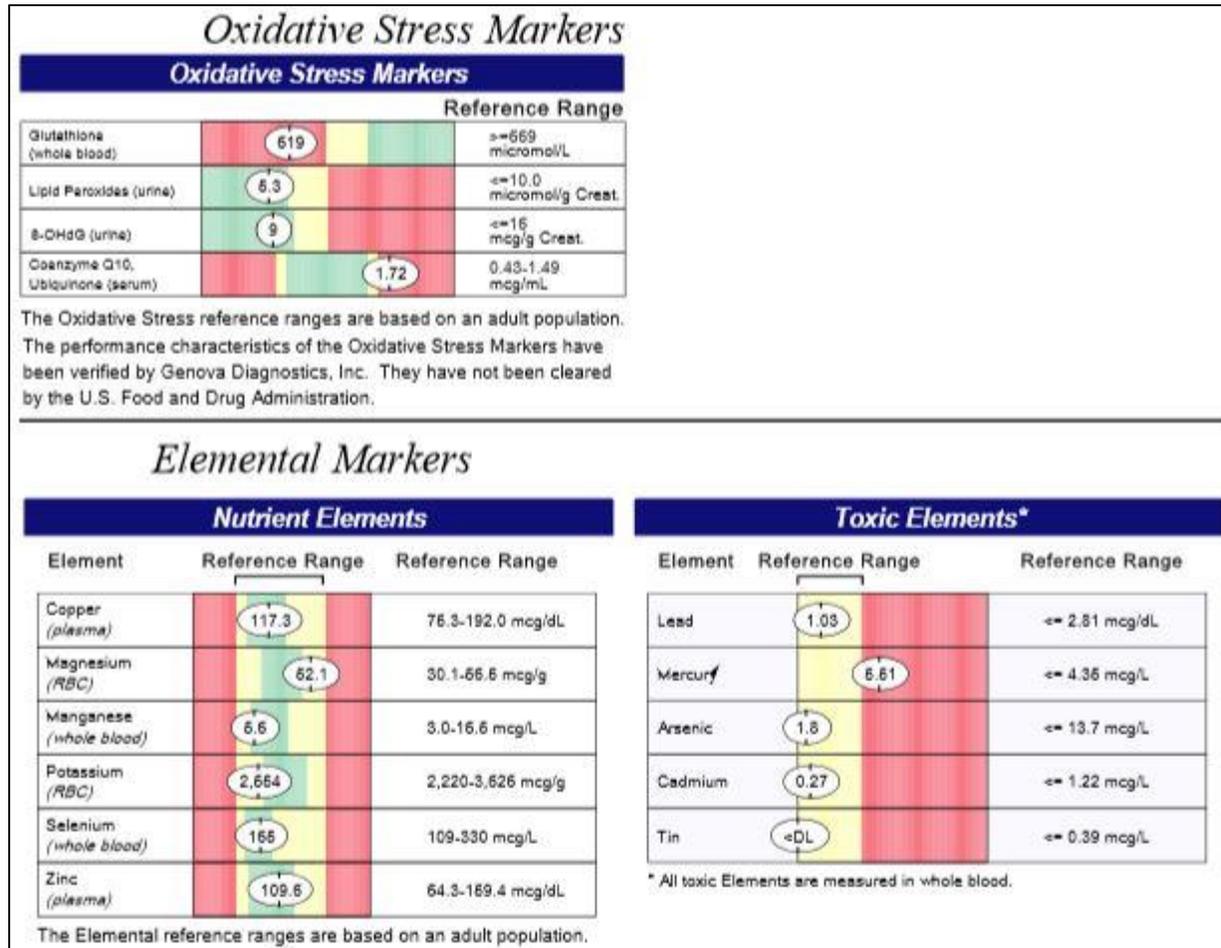
Case Study #2: 63 y/o Female with Arthritis

- CC: to improve the outcome of her recent PRP injections
- Eats a varied diet
- Meds: Ramipril, HCTZ, Premarin, and Zantac
- NutrEval: Which nutrients might we expect to be low?

Normal	Borderline	High Need	Supplementation for High Need
Antioxidants			
Vitamin A / Carotenoids		Vitamin C	Vitamin C - Dose = 1,000 mg
Vitamin E / Tocopherols		α-Lipoic Acid	α-Lipoic Acid - Dose = 200 mg
CoQ10			
B-Vitamins			
Niacin - B3	Thiamin - B1	Riboflavin - B2	Riboflavin - B2 - Dose = 50 mg
	Pyridoxine - B6		
	Biotin - B7		
	Folic Acid - B9		
	Cobalamin - B12		
Minerals			
Magnesium	Manganese		
Molybdenum			
Zinc			



Case Study #2: 63 y/o Female with Arthritis



SUGGESTED SUPPLEMENT SCHEDULE			
Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	3,000 IU	
Vitamin C	75 mg	1,000 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		200 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	26 mg	
Riboflavin - B2	1.1 mg	60 mg	
Niacin - B3	14 mg	20 mg	
Pyridoxine - B6	1.6 mg	26 mg	
Biotin - B7	30 mcg	200 mcg	
Folic Acid - B9	400 mcg	800 mcg	
Cobalamin - B12	2.4 mcg	600 mcg	
Minerals			
Magnesium	320 mg	400 mg	
Manganese	1.8 mg	6.0 mg	
Molybdenum	45 mcg	76 mcg	
Zinc	8 mg	10 mg	
Essential Fatty Acids			
Omega-3 Oils	600 mg	1,000 mg	
Digestive Support			
Probiotics		60 billion CFU	
Pancreatic Enzymes		6,000 IU	
Other Vitamins			
Vitamin D	600 IU		
Amino Acid			
Arginine	0 mg/day	Methionine	0 mg/day
Asparagine	13	Phenylalanine	0
Cysteine	0	Serine	0
Glutamine	220	Taurine	0
Glycine	0	Threonine	0
Histidine	0	Tryptophan	0
Isoleucine	0	Tyrosine	0
Leucine	0	Valine	0
Lysine	0		



Case Study #2: 63 y/o Female with Arthritis

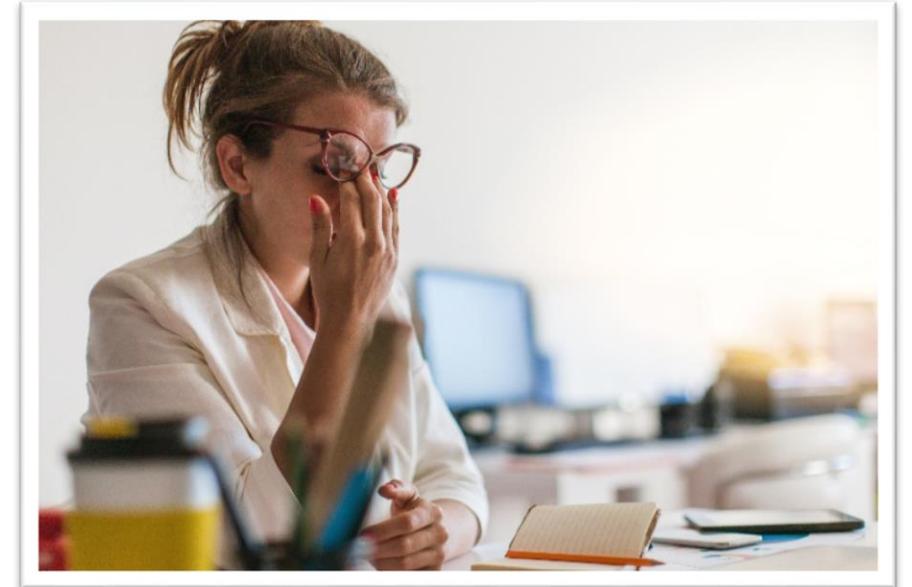
- Treatment and outcome
 - Repletion of nutrients led to full recovery and satisfaction of her orthopedic surgeon
 - B vitamins and mitochondrial support
 - Increased Selenium
 - Elimination of high mercury fish
 - Glutathione precursors
 - Increased vit c foods
 - Patient requires no NSAIDS nor opiates for sustained pain relief





Case Study #3: 42 y/o Female with Lumbar Pain and Headaches

- CC: Family h/o Alzheimer's Disease, seeking prevention
- Chronic lumbar pain and chronic migraine headaches
- Past h/o of antibiotics and Ritalin
- Eats organic
- Supplements:
 - Mag
- Current Labs:
 - Vit D: 39
 - CoQ10: 0.89
 - Homocysteine: 6
 - Ferritin: 20





Case Study #3: 42 y/o Female with Lumbar Pain and Headaches

Normal	Borderline	High Need
Antioxidants		
Vitamin A / Carotenoids		
Vitamin C		
Vitamin E / Tocopherols		
	α-Lipoic Acid	
CoQ10		
B-Vitamins		
	Thiamin - B1	
Riboflavin - B2		
	Niacin - B3	
Pyridoxine - B6		
Biotin - B7		
Folic Acid - B9		
	Cobalamin - B12	
Minerals		
	Magnesium	
	Manganese	
Molybdenum		
	Zinc	

Supplements	Daily Recommended Intake (DRI)	Patient's Daily Recommendations	Provider Daily Recommendations
Antioxidants			
Vitamin A / Carotenoids	2,333 IU	3,000 IU	
Vitamin C	75 mg	260 mg	
Vitamin E / Tocopherols	22 IU	100 IU	
α-Lipoic Acid		100 mg	
CoQ10		30 mg	
B-Vitamins			
Thiamin - B1	1.1 mg	26 mg	
Riboflavin - B2	1.1 mg	10 mg	
Niacin - B3	14 mg	30 mg	
Pyridoxine - B6	1.3 mg	10 mg	
Biotin - B7	30 mcg	100 mcg	
Folic Acid - B9	400 mcg	400 mcg	
Cobalamin - B12	2.4 mcg	600 mcg	
Minerals			
Magnesium	320 mg	600 mg	
Manganese	1.8 mg	5.0 mg	
Molybdenum	45 mcg	75 mcg	
Zinc	8 mg	20 mg	
Essential Fatty Acids			
Omega-3 Oils	600 mg	1,000 mg	
Digestive Support			
Probiotics		10 billion CFU	
Pancreatic Enzymes		0 IU	
Other Vitamins			
Vitamin D	600 IU	Not ordered	
Amino Acid		Amino Acid	
	mg/day		mg/day
Arginine	618	Methionine	237
Asparagine	114	Phenylalanine	126
Cysteine	67	Serine	0
Glutamine	619	Taurine	0
Glycine	0	Threonine	219
Histidine	16	Tryptophan	0
Isoleucine	390	Tyrosine	343
Leucine	360	Valine	0
Lysine	134		



Case Study #3: 42 y/o Female with Lumbar Pain and Headaches

Elemental Markers

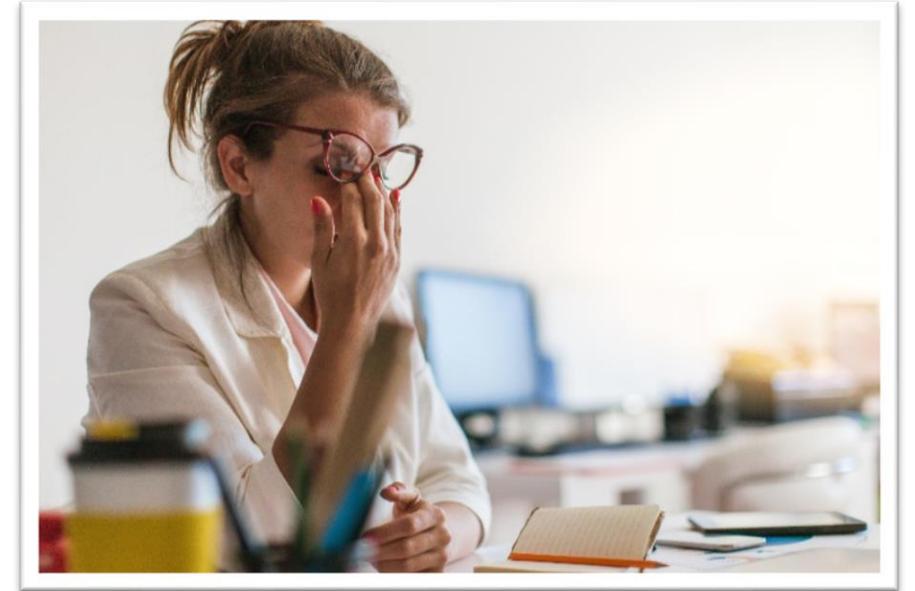
Nutrient Elements		
Element	Reference Range	Reference Range
Copper (plasma)	91.7	76.3-192.0 mcg/dL
Magnesium (RBC)	37.4	30.1-66.6 mcg/g
Manganese (whole blood)	6.6	3.0-16.6 mcg/L
Potassium (RBC)	2,416	2,220-3,626 mcg/g
Selenium (whole blood)	163	109-330 mcg/L
Zinc (plasma)	103.6	64.3-169.4 mcg/dL

- Magnesium
- B Vitamins
- Alpha lipoic acid
- Zinc
- HCl and Pepsin
- Vitamin D
- Reacted Fe



Case Study #3: 42 y/o Female with Lumbar Pain and Headaches

- First follow up
 - Taking 2-4 HCl tablets with meals
- 6 week follow up
 - Headaches completely resolved
 - Sleeping well
 - Energy had improved
 - Exercising without back pain
- 10 weeks follow up
 - Remains headache free





Case Study #4: 45 y/o Female CC: Migraines, Insomnia, Excessive Thirst

- Conventional Labs:
 - Myeloperoxidase 3555
 - Vit D: >120 ng/ml
 - Homocysteine 19
 - CoQ10: 0.66
 - Cystatin 1.11

Normal	Borderline	High Need	Supplementation for High Need
Antioxidants			
CoQ10	Vitamin A / Carotenoids Vitamin C Vitamin E / Tocopherols α-Lipoic Acid		
B-Vitamins			
Biotin - B7	Niacin - B3 Pyridoxine - B6 Folic Acid - B9 Cobalamin - B12	Thiamin - B1 Riboflavin - B2	Thiamin - B1 - Dose = 60 mg Riboflavin - B2 - Dose = 60 mg
Minerals			
Molybdenum	Magnesium Manganese Zinc		



Case Study #4: 45 y/o Female CC: Migraines, Insomnia, Excessive Thirst

Nutrient Elements			Toxic Elements*		
Element	Reference Range	Reference Range	Element	Reference Range	Reference Range
Copper (plasma)	113.6	75.3-192.0 mcg/dL	Lead	1.24	<= 2.81 mcg/dL
Magnesium (RBC)	41.2	30.1-56.5 mcg/g	Mercury	33.37	<= 4.35 mcg/L
Manganese (whole blood)	9.4	3.0-16.5 mcg/L	Arsenic	3.1	<= 13.7 mcg/L
Potassium (RBC)	2,977	2,220-3,626 mcg/g	Cadmium	0.51	<= 1.22 mcg/L
Selenium (whole blood)	144	109-330 mcg/L	Tin	<DL	<= 0.39 mcg/L
Zinc (plasma)	82.6	64.3-159.4 mcg/dL			

* All toxic Elements are measured in whole blood.

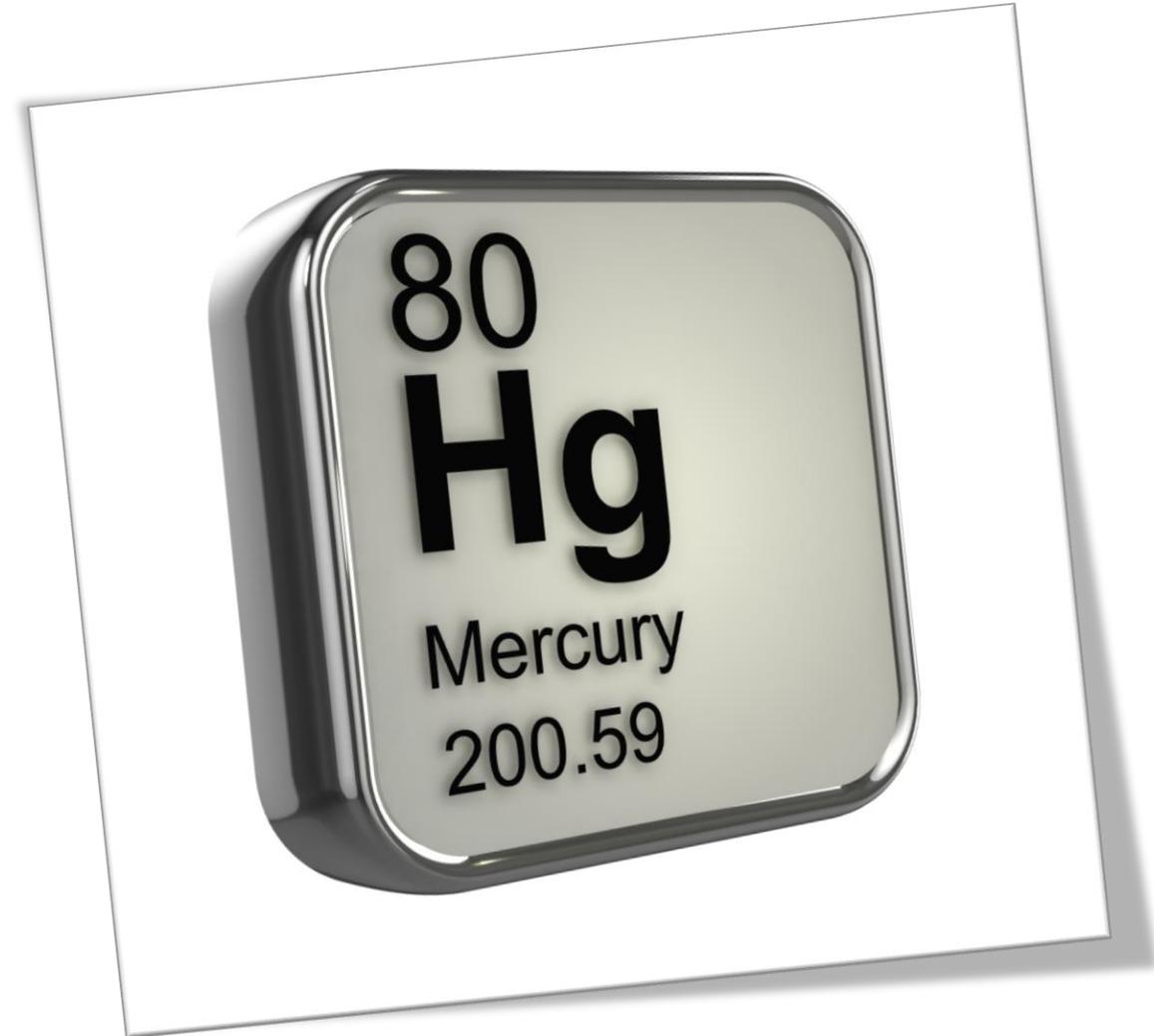
- Low Selenium
- High Mercury



Mercury Toxicity

Possible pain related symptoms include:

- Chest, local pharyngeal, abdominal, allergic contact dermatitis, and headache pain

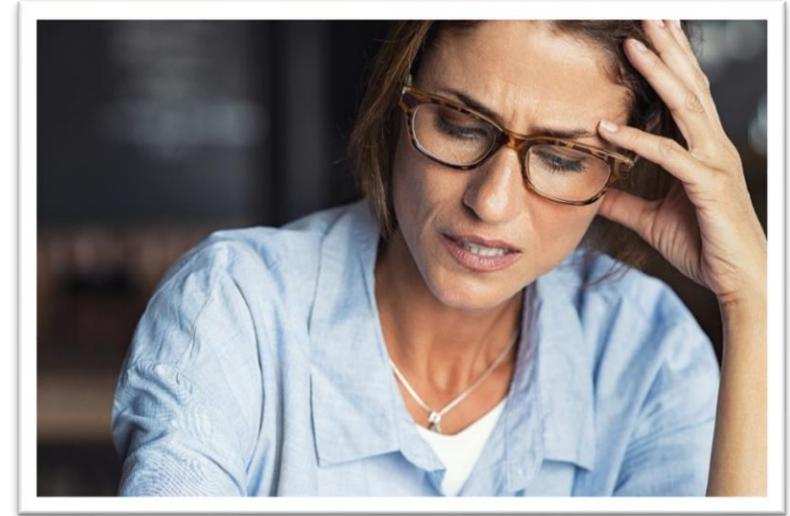




Case Study #4: 45 y/o Female CC: Migraines, Insomnia, Excessive Thirst

Initial Plan

- Organic unprocessed food
- CoQ10 300mg
- Magnesium up to bowel tolerance
- Methylated B complex
- Selenium
- EPA omegas
- Detoxification medical food (remove mercury)
- Stopped all herbals, no high Hg source foods
- Daily exercise
- Daily bowel movements



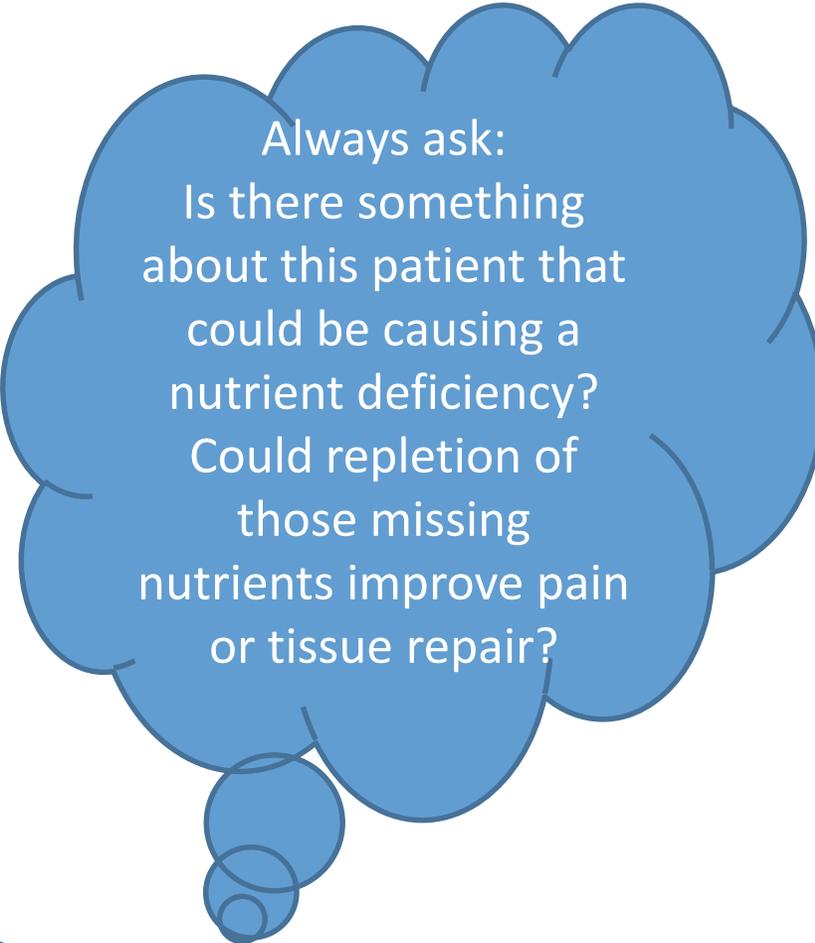
6-Week Follow Up

- Has been having no more headaches and has good sleep
- Exercise does not bother her as much anymore



Summary points

- Nutrient testing can improve pain relief by identifying deficient nutrients necessary for:
 - Quenching inflammation and/or oxidative stress
 - Providing essential ingredients for repair of nerves
 - Decreasing pain signaling
- Identifying nutrient deficiencies early on can increase compliance whether the therapy is diet or supplement based.
- Nutrient repletion can be done:
 - Alone
 - In combination with other synergistic nutrients
 - In combination with medications to augment
- More research is needed; until then, the risk benefit ratio is far more favorable given the increase in opiate related deaths.



Always ask:
Is there something about this patient that could be causing a nutrient deficiency?
Could repletion of those missing nutrients improve pain or tissue repair?



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***We look forward to
hearing from you!***

Questions?



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Christine Stubbe, ND, FABNO

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