Nutrient Depletions, Medications, and the Immune System

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Partners

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Disclosures

- Paid education consultant for Young Living Essential Oils, a company that also distributes dietary supplements.

Objectives

- By the end of this presentation, you will be able to:
  - Describe the impact of nutrient depletions and medication-related nutrient depletions on immune function.
  - Recommend proper doses to mitigate the risk of side effects related to drug induced nutrient depletions.
  - Discuss micronutrient testing
  - Define a nutrient and how each nutrient interacts with the immune system
  - Describe common nutrient depletions caused by medications

What are nutrients?

- Nutrients are substances that provides nourishment essential for growth and the maintenance of life
- There are six major nutrients:
  - Carbohydrates
  - Fats
  - Proteins
  - Vitamins
  - Minerals
  - Water

Carbohydrates and the Immune System

- In humans, healthy carb intake stabilizes blood sugar, decreases stress response, and enhances immunity
- Pathogens pick up pieces of carb from the host, bind carb receptors and mimic endogenous carbs
- Low carb diets increase stress on the immune system because of lack of fiber and resultant changes in microbiome

Gardner CD, Hauser ME. Food Revolution. *Am J Lifestyle Med*. 2017;11(5):387-396. Published 2017 Mar 8. doi:10.1177/1559827617696289

Fats and the Immune System

- High fat diets increase the risk of *Listeria* infection by increasing the number of goblet cells, a known binding site for the pathogen, and induces profound changes to the microbiota and promotes a pro-inflammatory gene expression

Institute of Medicine (US) Committee on Military Nutrition Research. Military Strategies for Sustainment of Nutrition and Immune Function in the Field. Washington (DC): National Academies Press (US); 1999. 14, Fatty Acids and Immune Functions. Available from: https://www.ncbi.nlm.nih.gov/books/NBK230960/

Proteins and the Immune System

- Amino acids are used as fuel by the immune system either directly, or following their conversion to other amino acids (e.g., glutamine) or to glucose

Phillip C. Calder, Branched-Chain Amino Acids and Immunity, The Journal of Nutrition,
136, Issue 1, January 2006, Pages 288S–293S, https://doi.org/10.1093/jn/136

Water and the Immune System

- Water carries oxygen to blood cells
- Removes toxins from the body
- Cleans the mouth and eyes
- Helps digest food
- Critical in the production of melatonin, and sleep is critical to immune function

Diuretics and the Immune System

- Dehydration caused by diuretic use is an excellent example of the complexity of today's discussion

Vitamins and the Immune System

- Vitamin C
- Vitamin D
- Vitamin B12/B9
- Beta Carotene

Vitamin C and the Immune System

- Vitamin C
  - Electron donor, potent antioxidant, cofactor for gene regulation
  - Contributes to immune defense by supporting various cellular functions of both the innate and adaptive immune system.
    - Supports epithelial barrier function against pathogens
    - Promotes oxidant scavenging activity of the skin, thereby potentially protecting against environmental oxidative stress
    - Accumulates in phagocytic cells, and can enhance chemotaxis, phagocytosis, generation of reactive oxygen species, and ultimately microbial killing
    - Clears spent neutrophils from sites of infection by macrophages, decreasing necrosis and tissue damage
    - Enhances differentiation and proliferation of B- and T-cells

Carr AC, Maggini S. Vitamin C and Immune Function. Nutrients. 2017;9(11):1211. Published 2017 Nov 3. doi:10.3390/nu9111211

Vitamin C and the Immune System

- Deficiency results in impaired immunity and higher susceptibility to infections.
- Infections significantly impact vitamin C levels due to enhanced inflammation and metabolic requirements
- Supplementation prevents and treats respiratory and systemic infections.
  - Prevention of infection requires dietary vitamin C intakes of 100–200 mg/day
  - Treatment requires higher doses of >1 gram

Nutrients. 2017;9(11):1211. Published 2017 Nov 3.
doi:10.3390/nu9111211

Vitamin D

- Vitamin D deficiency is very common in people with autoimmune disorders.
- Vitamin D has numerous effects on cells within the immune system.
  - Inhibits monocyte production of inflammatory cytokines such as IL-1, IL-6, IL-8, IL-12 and TNFα.

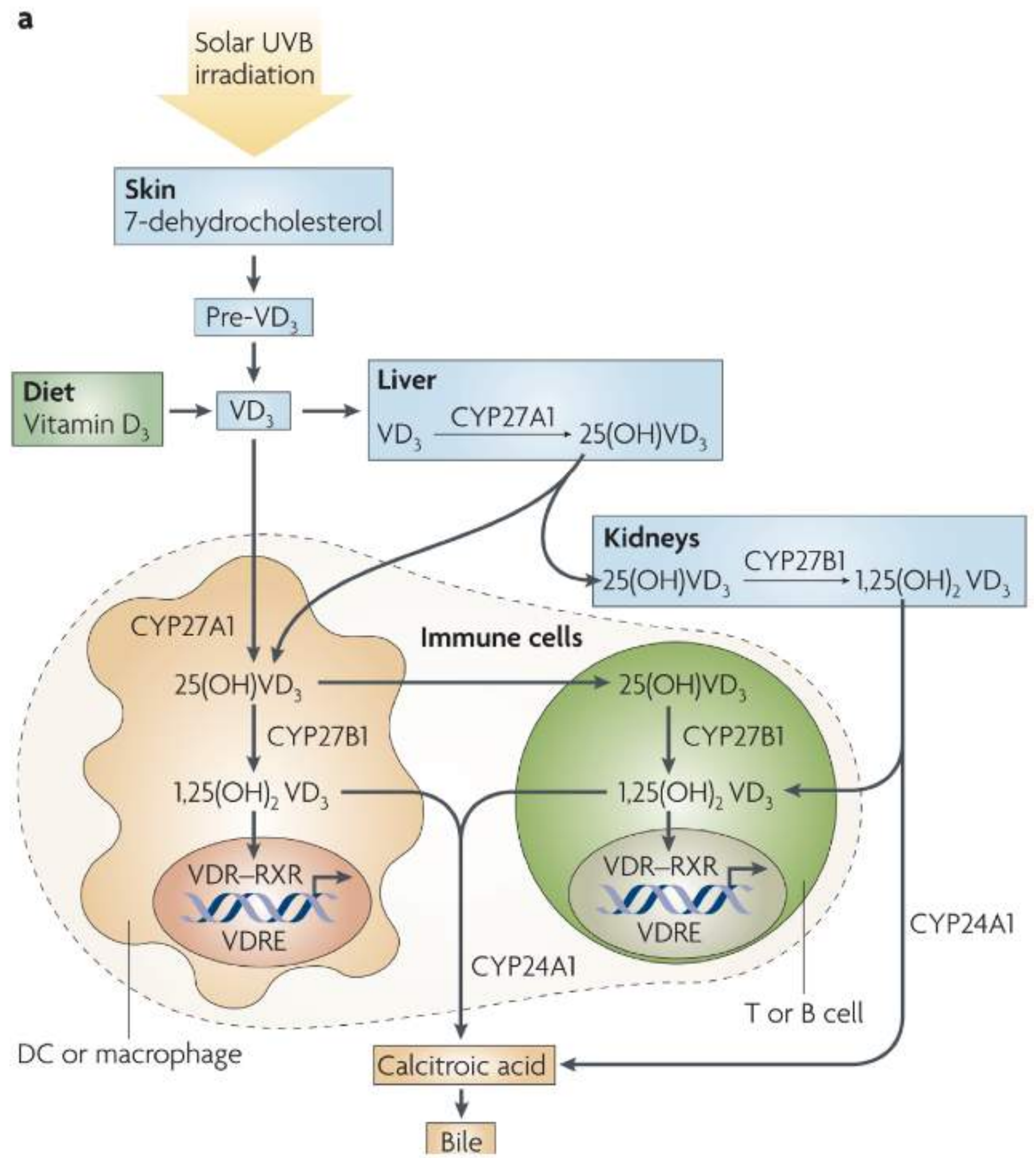
Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20. doi:10.3390/pharmaceutics10010036

Vitamin D and the Immune System

- Vitamin D has numerous effects on cells within the immune system.
  - Inhibits B cell proliferation, blocks B cell differentiation and immunoglobulin secretion.
  - Suppresses T cell proliferation and results in a shift from a Th1 to a Th2 phenotype.
  - Affects T cell maturation with a skewing away from the inflammatory Th17 phenotype and facilitates the induction of T regulatory cells.
    - These effects result in decreased production of inflammatory cytokines (IL-17, IL-21) with increased production of anti-inflammatory cytokines such as IL-10.
    - Inhibits dendritic cell differentiation and maturation with preservation of an immature phenotype with decreased expression of MHC class II molecules, co-stimulatory molecules and IL-12.

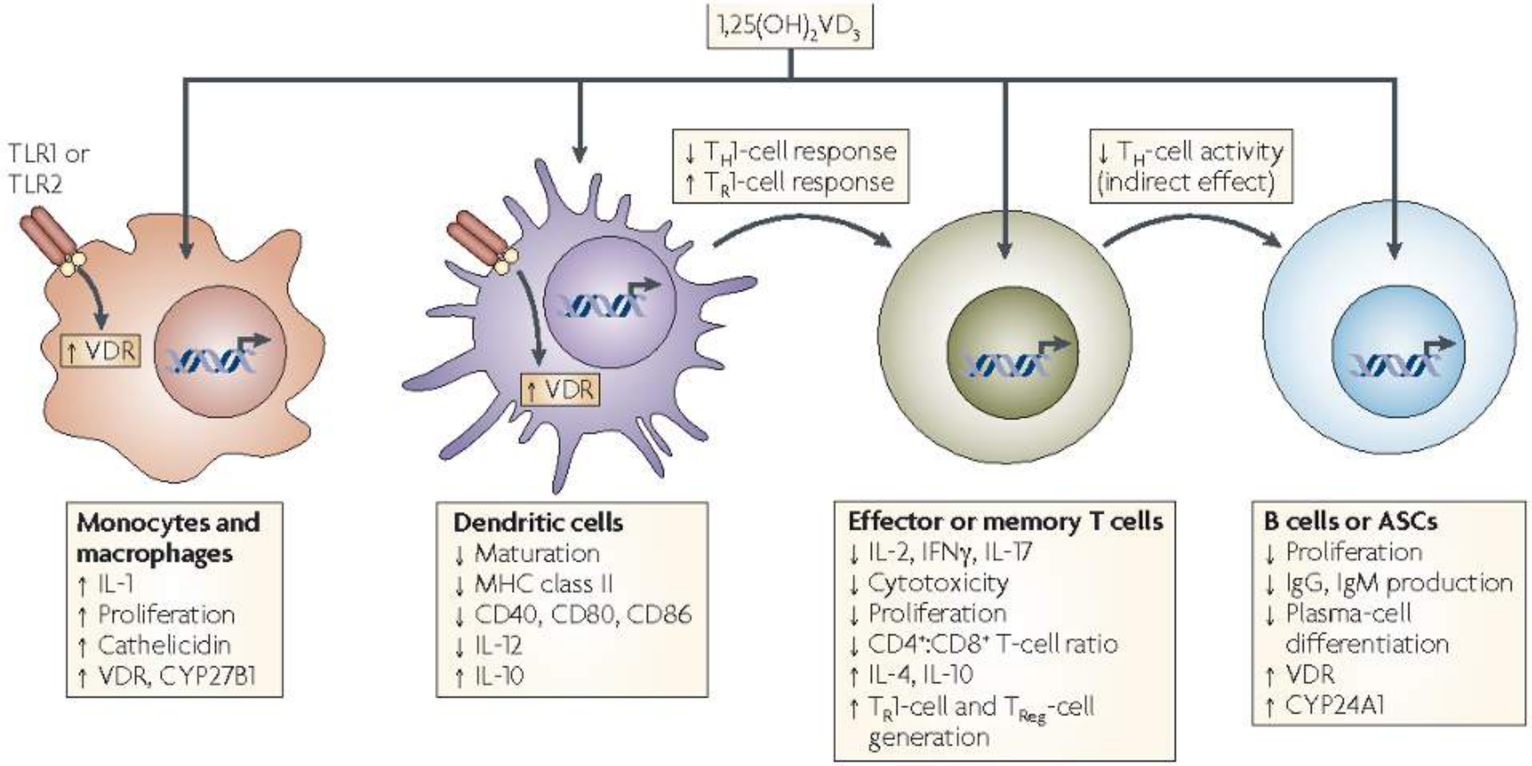
J Investig Med. 2011;59(6):881-886. doi:10.2310/JIM.0b013e31821b8755

Vitamin D and the Immune System



Nature Reviews Immunology 8 (2008): 685-698.

1,25(OH)$_2$-Vitamin D$_3$



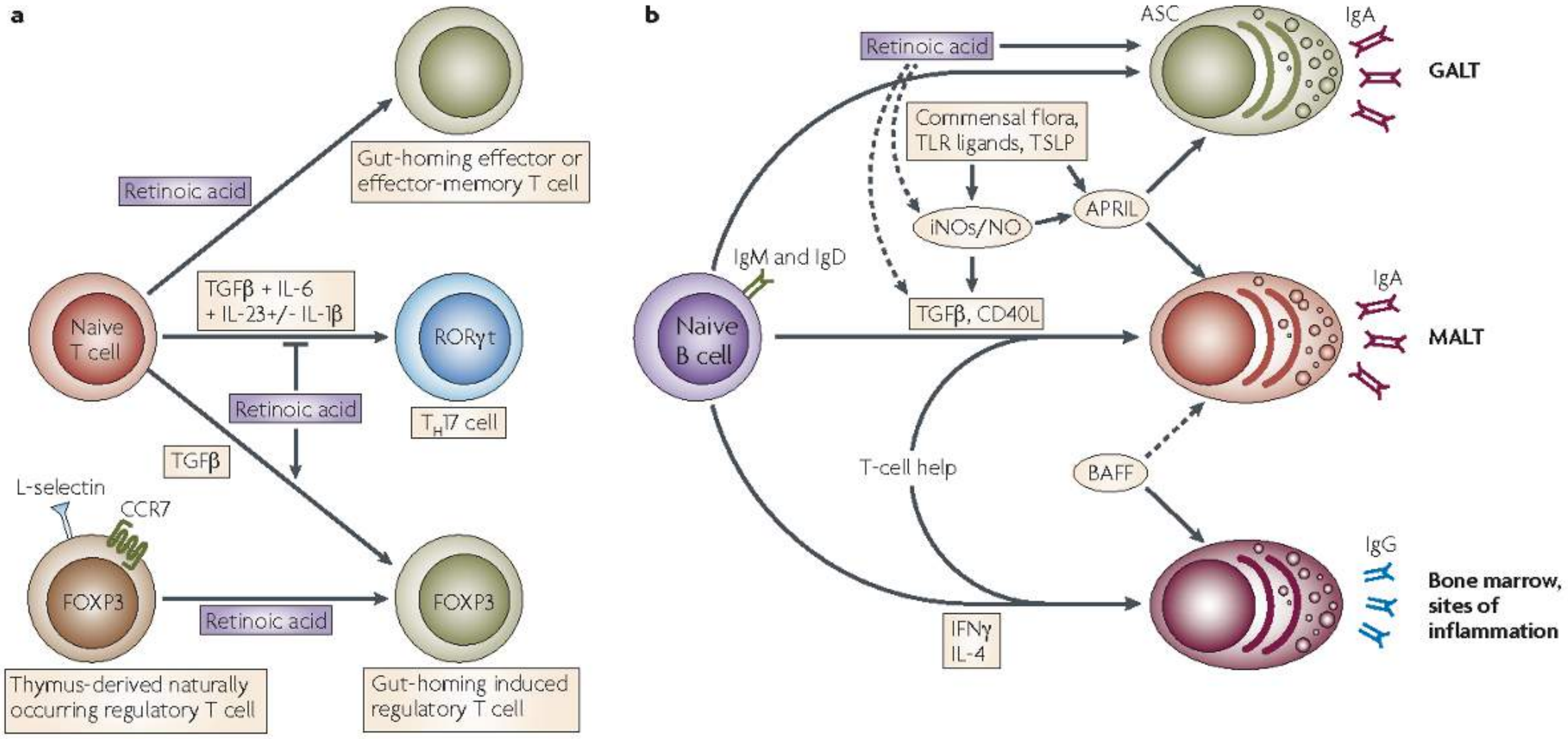
Nature Reviews Immunology 8 (2008): 685-698.

Vitamin A and the Immune System

- Vitamin A is an anti-inflammation vitamin because of its critical role in enhancing immune function.
  - Vitamin A exists in the form of retinol, retinal, and retinoic acid (RA), among which RA shows the most biological activity.
- Vitamin A affects cell differentiation, maturity, and immunological function in innate immunity
- RA induces T-cell migration, control T-reg cells, and manages T-cell homeostasis, promotes Th17 cell differentiation
- RA acts directly on B-cells and affects the synthesis and secretion of IgA

J Clin Med. 2018;7(9):258. doi:10.3390/jcm7090258

Vitamin A and the Immune System



Nature Reviews Immunology 8 (2008): 685-698.

Vitamin B12/B9 and the Immune System

- Immunomodulator for cellular immunity.
- Inadequate levels of B9/B12 drastically alter immune responses by:
  - Affecting the production of nucleic acid
  - Protein synthesis
  - Inhibiting the activity of immune cells
  - Interfering with metabolic processes, including methylation and serine, glycine, and purine cycles.

Nutrition and Immunity. Springer, Cham. https://doi.org/10.1007/978-3-030-16073-9_6
Clin Exp Immunol. 1999;116(1):28-32. doi:10.1046/j.1365-2249.1999.00870.x

Vitamin B12/B9 and the Immune System

- B12 plays an important role in white blood cell production, and white blood cells are essential for proper immune system functioning
- Lack of B12 lowers immunity, and some autoimmune system disorders can increase deficiency.
- Pernicious anemia attacks cells in the gut that product intrinsic factor, reducing absorption of B12.

Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20.
doi:10.3390/pharmaceutics10010036

Minerals and the Immune System

- Zinc
- Magnesium
- Iron
- Calcium

Zinc and the Immune System

- Zinc affects multiple aspects of the immune system.
  - Crucial for normal development and function of cells mediating innate immunity, neutrophils, and NK cells.
  - Macrophage phagocytosis, intracellular killing, and cytokine production all are affected by zinc deficiency.
  - Deficiency adversely affects the growth and function of T and B cells.
  - Functions as an anti-oxidant and stabilize membranes
  - Has a role in the prevention of free radical-induced injury during inflammatory processes.

Mol Med. 2008;14(5-6):353-357. doi:10.2119/2008-00033.

Magnesium and the Immune System

- Mg deficiency increases proinflammatory cytokines (IL-6, TNF-α)
- Increased plasma substance P during the first week of Mg deficiency.
  - SP increases IL-2, IL-4, IL-5, IL-10, IL-12, IL-13 and IFN-γ
    - Maximal at either 5 days (IL-4 and IL-5) or 7 days (IL-2, IL-10 and INF-γ) after Mg deficiency.
  - SP might play a key role in regulating T lymphocyte cytokine production during Mg deficiency
    - Especially cytokines regulating mast cells and the immunopathological response.
- Mg deficiencies may contribute to atherosclerosis by modification of lipoprotein metabolism, and by the release of growth factors that induce cell migration and proliferation

Eur J Clin Nutr **57,** 1193–1197 (2003). https://doi.org/10.1038/sj.ejcn.1601689

Iron and the Immune System

- Iron homoeostasis plays a vital role in controlling iron fluxes such that bacteria are prevented from utilizing iron for growth; secondly, cells of the innate immune system, monocytes, macrophages, microglia and lymphocytes, are able to combat bacterial insults by carefully controlling their iron fluxes, which are mediated by hepcidin and ferroportin.
- Lymphocytes play an important role in adaptive immunity.
- Toll-like receptors, NF-κB, hypoxia factor-1, heme oxygenase, will orchestrate the inflammatory response by mobilizing cytokines, neurotrophic factors, chemokines, and reactive oxygen and nitrogen species.

Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20.
doi:10.3390/pharmaceutics10010036

Calcium and the Immune System

- Calcium acts as a second messenger in many cell types, including lymphocytes.
  - Resting lymphocytes maintain a low concentration of Ca.
  - Engagement of antigen receptors induces Ca influx from the extracellular space, activatin lymphocytes.
- Store-operated channels allow entry of Ca.
  - Two components of SOC channels, CRACM1 (the pore-forming subunit) and STIM1 (the sensor of stored calcium) present targets for medications and gene therapy.

Nat Immunol. 2009;10(1):21-27. doi:10.1038/ni.f.220

Of Special Note: Coenzyme-Q-10

- CoQ10 is a naturally occurring, fat-soluble, vitamin-like compound obtained from the diet and, to a lesser extent, from endogenous synthesis.
- CoQ10 functions in the electron transport chain in the mitochondria and, thus, plays an important role in energy metabolism.
- CoQ10 improves energy, augments the immune system, and acts as an antioxidant.
- CoQ10 plays a significant role in boosting the immune system and physical performance, as tissues and cells involved with immune function are highly energy-dependent and therefore require an adequate supply of CoQ10 for optimal function.

Saini R. Coenzyme Q10: The essential nutrient. *J Pharm Bioallied Sci*. 2011;3(3):466-467. doi:10.4103/0975-7406.84471

Medications that Increase Risk of Nutrient Depletions

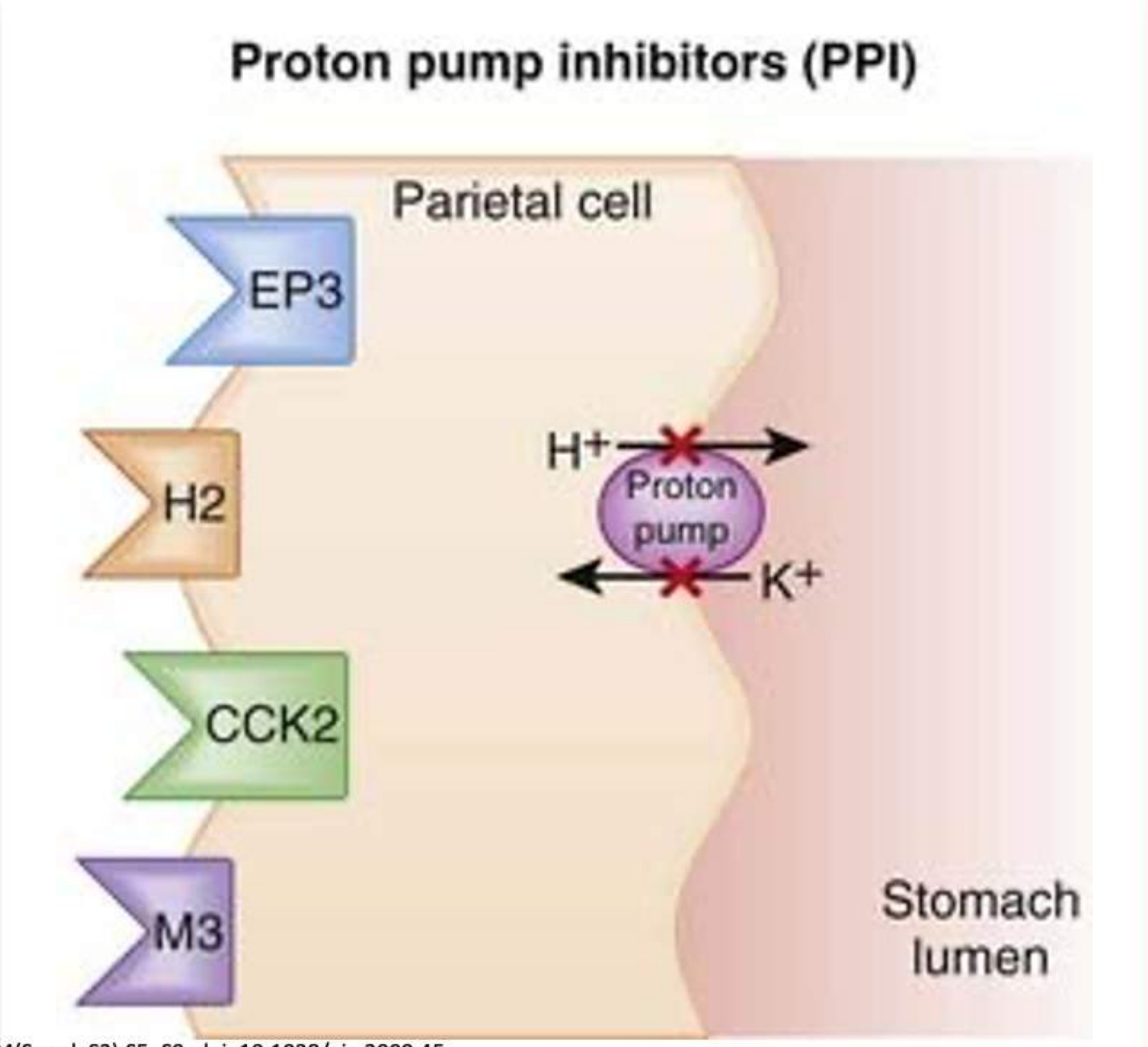
Medications Most Likely to Impact Nutrition Status

- Proton Pump Inhibitors
- Aspirin
- Diuretics
- ACE Inhibitors
- Calcium Channel Blockers
- Statins
- Metformin
- Thiazolidinediones
- Oral Corticosteroids
- Inhaled Beta2-Agonists
- Inhaled Corticosteroids
- Antidepressants
- Oral Contraceptives

Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. *Pharmaceutics*. 2018;10(1):36. Published 2018 Mar 20. doi:10.3390/pharmaceutics10010036

Proton Pump Inhibitors

- MOI: Reduces gastric acid production, limiting the absorption of micronutrients that depends on low pH for uptake



Am. J. Gastroenterol. 2009;104(Suppl. S2):S5–S9. doi: 10.1038/ajg.2009.45.

Nutrition. 2013;29:605–610. doi: 10.1016/j.nut.2012.11.011.

Eur. J. Gastroenterol. Hepatol. 2001;13:233–237. doi: 10.1097/00042737-200103000-00003.

Gastroenterology. 1999;116:813–822. doi: 10.1016/S0016-5085(99)70064-8.

Proton Pump Inhibitors

- Vitamin B12
  - Gastric acid is needed to remove B12 from proteins in food (but not for absorption from fortified foods and supplements)
  - Decreases protein-bound B12 absorption
  - American Gastroenterology Association recommends routine B12 screening or routine supplementation in patients
  - Increased risk of deficiency is seen in people with atrophic gastritis and/or H. pylori infection, and slow metabolizers of omeprazole

Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20.
doi:10.3390/pharmaceutics10010036

Proton Pump Inhibitors

- Vitamin C
  - Vit C is highly concentrated in gastric juice where it is activated to ascorbic acid which helps to kill carcinogenic nitrates from saliva.
  - Treatment with 40 mg/day omeprazole for 4 weeks in patients without *H. pylori* infection reduced the proportion of ascorbic acid to total vitamin C in gastric juice
  - May also reduce serum vitamin C, especially in patients with *H. pylori* infection
  - Chicken and Egg: Observational study detected 30% less vitamin C in the plasma in patients with *H. pylori*
- Iron
  - Non-heme iron in plant foods must be reduced prior to absorption in the small intestine
  - Omeprazole induced achlorhydria may impair the response to iron.

Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20. doi:10.3390/pharmaceutics10010036

Proton Pump Inhibitors

- Package Insert Warnings
  - Bone Fracture
    - Calcium absorption in the gut is influenced by gastric pH
    - PPI use increases risk of fracture and necessitate anti-osteoporosis therapy
    - Many discrepancies exist: food vs supplement, fasted vs fed, age
    - Highest risk may be in people with existing risks according to N Osteo Found
    - AGA does not recommend routine testing of BMD in pts on chronic PPI

Osteoporos. Int. 2014;25:2359–2381. doi: 10.1007/s00198-014-2794-2.
Gastroenterology. 2017;152:706–715. doi: 10.1053/j.gastro.2017.01.031.
World J. Nephrol. 2016;5:152–157. doi: 10.5527/wjn.v5.i2.152
Clin. Endocrinol. 2008;69:338–341. doi: 10.1111/j.1365-2265.2008.03194.x.

Proton Pump Inhibitors

- Package Insert Warnings
  - Hypomagnesemia
    - Case reports are widely documented
    - Magnesium supplementation alone is not always successful in reversing hypomagnesemia
    - No well-designed studies give mechanistic description of why this may occur

https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/020987s045lbl.pdf

Aspirin

- MOA: blocks prostaglandin synthesis.
- Non-selective for COX-1 and COX-2 enzymes.
- Platelet aggregation inhibition for about 7-10 days.
- Well established that aspirin causes mucosal damage, gastric ulcers, and increase the risk of GI bleed

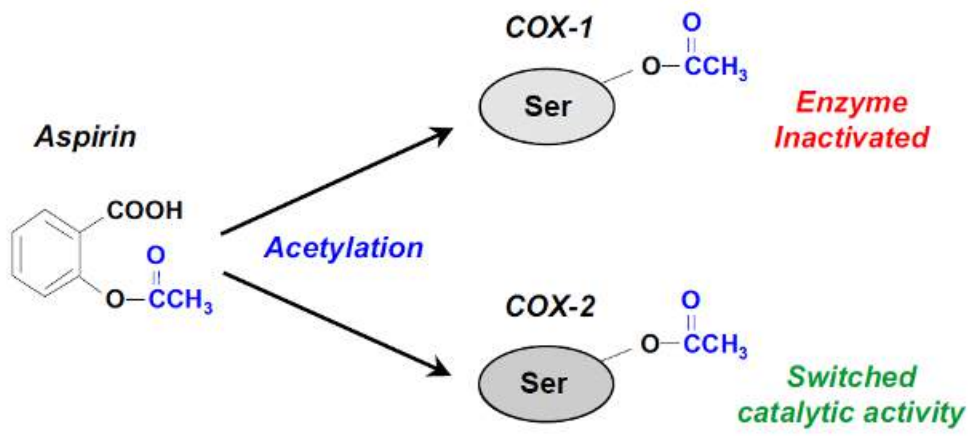


Figure 1. Aspirin mechanism of action -- acetylation of cyclooxygenase (COX). Aspirin acetylates a serine (Ser) residue of COX and irreversibly inactivates COX-1. In the case of COX-2, aspirin "turns off" its ability to generate prostaglandins, but "switches on" its capacity to produce novel protective lipid mediators.

https://go.drugbank.com/drugs/DB00945

Aspirin and Vitamin C Depletions

- Studies dating back to the 1970 conclude that high aspirin doses deplete vitamin C
- Ascorbic acid levels are abnormally low in patients with Rheumatoid arthritis
- Aspirin completely inhibits the uptake of ascorbic acid into leukocytes following a 600 mg dose

Lancet. 1971;1:937–938. doi: 10.1016/S0140-6736(71)91441-3.
J. Clin. Pharmacol. 1975;15:36–45. doi: 10.1002/j.1552-4604.1975.tb01426.x.

Aspirin and Vitamin C Depletions

- 2400 mg reduces vitamin C concentrations in the urine, plastic, and gastric mucosa
- Decreases in gastric mucosa may be due to antioxidant activity of vitamin C aiming to repair damage from aspirin
- Though somewhat counterintuitive, patients suffering from gastric mucosal injury due to aspirin may benefit from vitamin C supplementation
- Given the high dose of aspirin in publication, unclear how this relates to prophylactic dosing

Int. J. Clin. Pharmacol. Ther. 2004;42:481–487. doi: 10.5414/CPP42481.
Pain Pract. 2012;12:476–484. doi: 10.1111/j.1533-2500.2011.00517.x

Aspirin and Iron

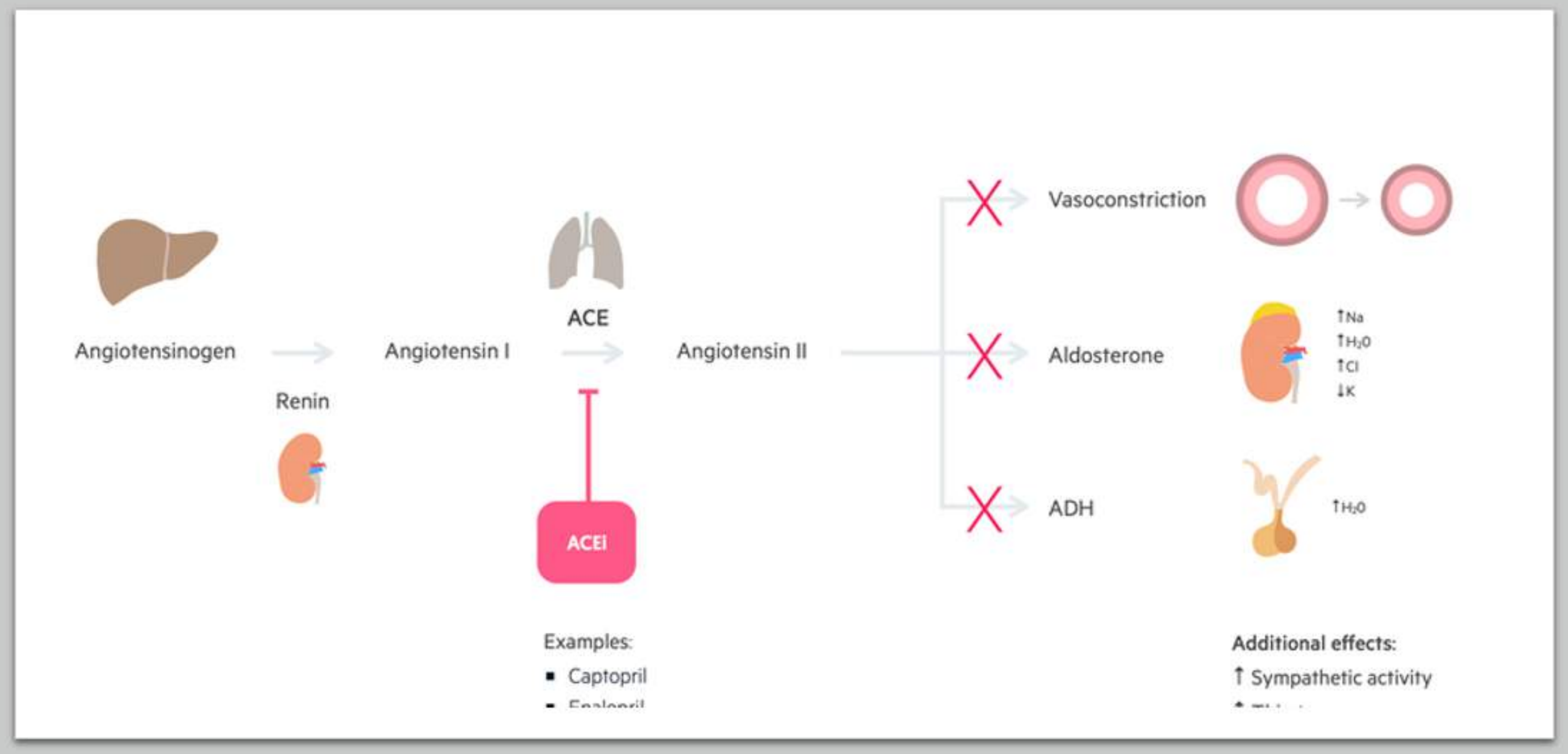
- Because of the impact of aspirin on the gut, and the increased risk of bleeding, iron deficiency anemia may result.
- A retrospective study of elderly patients (mean age 82) found that prevalence of anemia in aspirin users was double that of the control group (24% vs 11%, p-val not stated)
- A controlled trial of patients >70 years were randomized to take 100 mg aspirin/day or placebo
  - Aspirin treated patients had significant reductions in hemoglobin levels, though still WNL
  - But, Hb is typically the last marker of anemic measures to change, and measures of iron stores may be more effective than Hb

Can. Fam. Physician. 1995;41:64–68.
Clin. Pharmacol. Ther. 1993;54:84–89. doi: 10.1038/clpt.1993.115

Aspirin and Iron

- To make things more complicated, ferritin is related to inflammation
- Studies that conclude that aspirin therapy can reduce ferritin have failed to determine whether this is a measure of the desired anti-inflammatory action of aspirin or a predictor of the pathology of anemia

J. Gastroenterol. Hepatol. 2003;18:1024–1028. doi: 10.1046/j.1440-1746.2003.03089.x.



ACE Inhibitors

MOA: ACE inhibitors produce vasodilation by inhibiting the formation of angiotensin II.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019777s054lbl.pdf

ACE Inhibitors and Zinc

- Long term ACE treatment, especially with captopril, can cause hypogeusia.
  - Loss of taste is a symptom of Zn deficiency, and patients on long-term, high-dose captopril may have higher taste and recognition thresholds, lower plasma zinc levels, and high urinary zinc compared to controls.
  - Lower doses lower zinc status in people with kidney disease and heart failure. Other at-risk groups include older age, malabsorption, and diarrhea
- Other ACE-I are varied
  - Captopril=benazepril>enalapril perhaps because the thiol-radical group on captopril binds Zn
- Major limitation: zinc plasma levels ≠ tissue levels

Heart Fail. Rev. 2006;11:19–24. doi: 10.1007/s10741-006-9189-1.
J. Clin. Hypertens. 1987;3:405–408. J. Clin. Hypertens. 1987;3:405–408.
J. Trace Elem. Med. Biol. 2007;21(Suppl. S1):53–55. doi: 10.1016/j.jtemb.2007.09.018.
Nephron. 1983;34:195–197. doi: 10.1159/000183009.
Metabolism. 1990;39:665–667. doi: 10.1016/0026-0495(90)90098-W.
J. Am. Coll. Nutr. 1998;17:75–78. doi: 10.1080/07315724.1998.10720459.

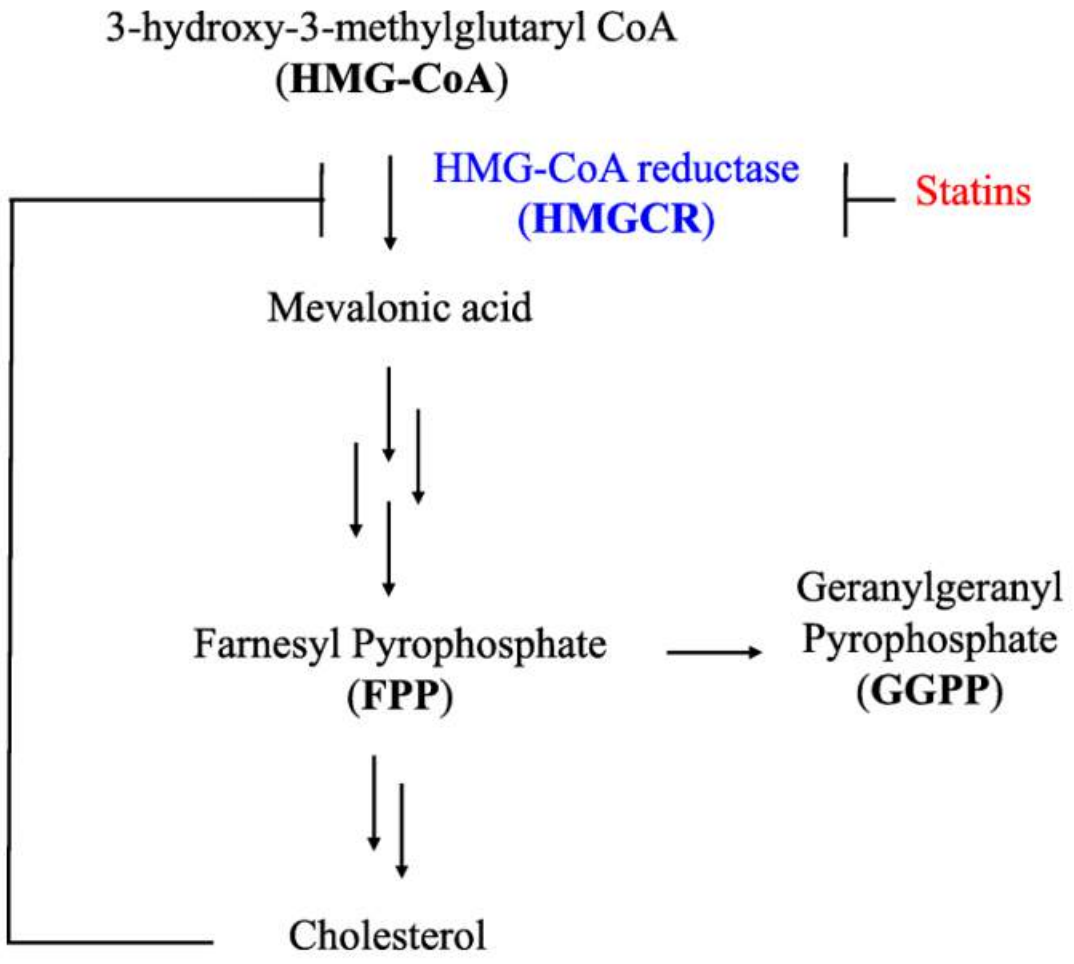
ACE Inhibitors and Potassium

- Well know that ACE-I increase risk of hyperkalemia, especially in patients with older age, renal disease, diabetes, heart failure, concomitant use of potassium-sparing diuretics, potassium supplements or consumption of potassium rich diets

Circulation. 1998;97:1411–1420. doi: 10.1161/01.CIR.97.14.1411.
Cardiovasc. Ther. 2012;30:e156–e166. doi: 10.1111/j.1755-5922.2010.00258.x.
Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. *Pharmaceutics*. 2018;10(1):36. Published 2018 Mar 20. doi:10.3390/pharmaceutics10010036

Statins

- MOA: competitively block the active site of the first and key rate-limiting enzyme in the mevalonate pathway, HMG-CoA reductase



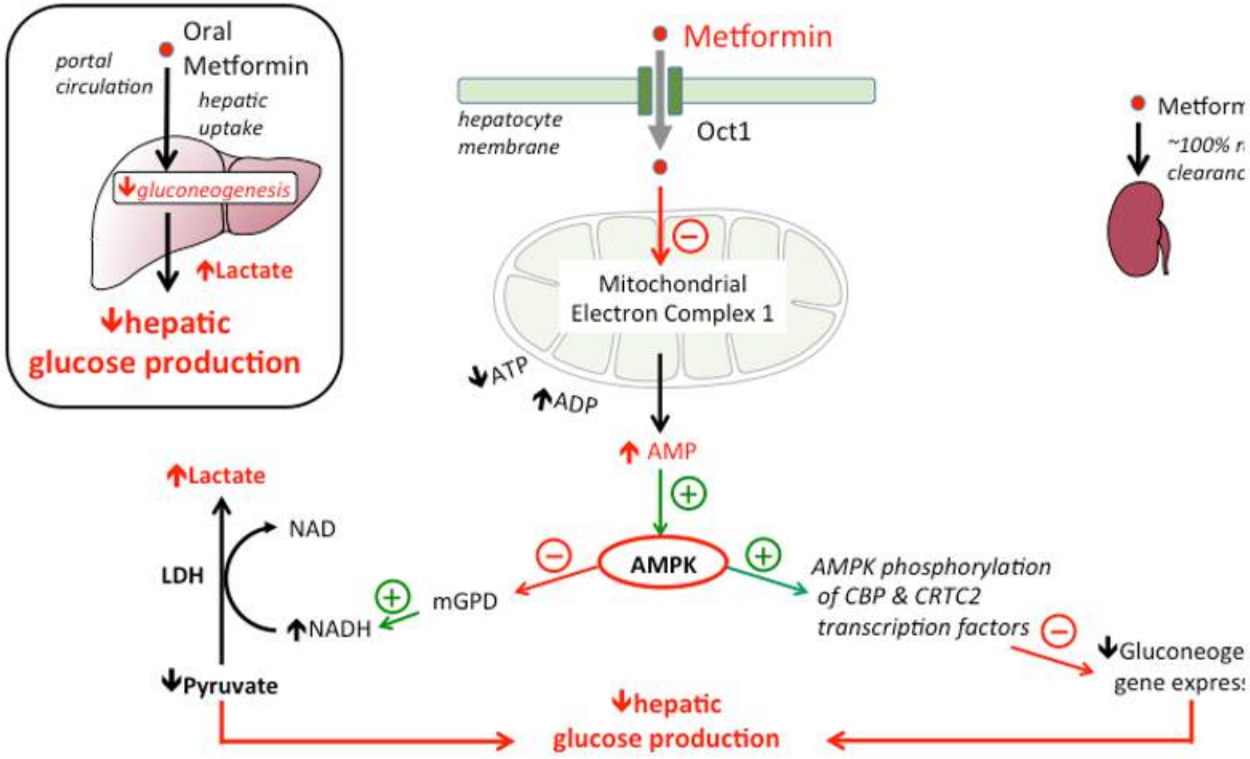
https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/019766s078lbl.pdf

Statins and CoQ10

- CoQ10 is an intermediate in the mevalonate pathway, which is inhibited by statins.
- A number of studies report that statins lower CoQ10, especially the elderly
- Changes may be dose dependent, and supplementation effectively increases blood CoQ10
- In addition to harm to the energetics of the immune system, CoQ10 depletion may also lead to myopathies

Antioxidants (Basel). 2020 Apr 22;9(4):341.
Am J Health Syst Pharm. 1999 Mar 15; 56(6):519-21.
J. Clin. Pathol. 1993;46:1055–1057. doi: 10.1136/jcp.46.11.1055.
BioFactors. 2003;18:113–124. doi: 10.1002/biof.5520180213
Mol. Asp. Med. 1997;18:137–144. doi: 10.1016/S0098-2997(97)00014-9.

Metformin



- MOA: decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/020357s037s039,021202s021s023lbl.pdf

Metformin and Vitamin B12 Depletion

- Metformin may decrease vitamin B12 in a duration- and dose-dependent manner through impaired intestinal absorption.
- Individuals already at risk of low B12 status, including the elderly and vegetarians, may be at greater risk during drug therapy.
- Current evidence is sufficient to recommend periodic assessment of vitamin B12 in patients taking metformin

Pharmaceutics. 2018;10(1):36. Published 2018 Mar 20. doi:10.3390/pharmaceutics10010036

Nutrient Tests

- Increased access to at home testing for wide array of hormone (including cortisol), nutrients, infections, inflammatory toxins, inflammatory mediators, food sensitivities
- Many companies exist including SpectraCell, Everywell, NutraEval
- Easy to incorporate into telepharmacist practice

Repleting Lost Nutrients

- No great data on how to replete, when to test, or how much to dose and how often for most vitamins, minerals
- Sometimes, in the case of magnesium, vitamin C, and B12, supplementation is generally well tolerated and aggressive doses have been documented with minimal side effects
- However GI disturbances may occur include constipation with calcium and iron, and diarrhea with zinc
- Additional caution is warranted with fat soluble vitamins, in patients with autoimmune disorders, underlying conditions, and with fat soluble vitamins that may accumulate

Reference Levels

Nutrient	Serum Reference Levels
Vitamin A	30 – 95 µg/dL
Vitamin B12	200 - 800 pg/mL
Vitamin C (plasma)	0.2 - 2.0 mg/dL
1,25-Dihydroxy-vitamin D	24 - 65 pg/mL
Vitamin E	5 – 20 µg/mL
Iron	25 - 170 µg/dL
Magnesium	1.5 - 2.4 mEq/L Critical value: <1.0 mEq/L and >4.7 mEq/L
Calcium	0-6 months: 8.9-11.0 mg/dL 7 mon to adults: 8.5-10.6 mg/dL 8.5 - 10.3 mg/dL
Zinc (plasma)	60 - 130 µg/dL

NIH ODS https://ods.od.nih.gov/HealthInformation/Dietary_Reference_Intakes.aspx

Recommended Daily Intake

Nutrient	RDA
Vitamin A	Adult Males <70 years: 900 mcg/day Adult Females <70 years: 700 mcg/day
Vitamin B12	2.4 mcg/day
Vitamin C	Adult Males: 90 mg/day Adult Females: 75 mg/day
Vitamin D	15 mcg/day
Vitamin E	15 mg/day
Iron	Adult Males: 8 mg/day Adult Females: 18 mg/day until menopause
Magnesium	Adult Males: 400-420 mg/day Adult Females: 310-320 mg/day
Calcium	Adult Males: 1000 mg/day Adult Females: 1000-1200 mg/day
Zinc	Adult Males: 11 mg/day Adult Females: 8 mg/day

NIH ODS
https://ods.od.nih.gov/HealthInformation/Dietary_Reference_Intakes.aspx

Repleting Lost Nutrients

- Ideally clinicians recommend patients get adequate nutrition from their diet
- A full spectrum multiple vitamin/mineral supplement may be sufficient
  - Adults who take a daily MVM are less likely than non-users to be deficient in any one nutrients
  - Helps fulfill micronutrient requirements and improve nutritional status even in healthy adults
- Physicians have been historically hesitant to recommend a MVM despite little risk of mortality or morbidity

JAMA Intern. Med. 2013;173:355–361. doi: 10.1001/jamainternmed.2013.2299.
J. Nutr. 2000;130:3090–3096. doi:
Nutr. J. 2014;13:72. doi: 10.1186/1475-2891-13-72.

Before We Go

- Vitamin D and Sars-CoV-2
  - Retrospective case-control study of 216 COVID patients and 197 population-based controls.
    - 19 were on vitamin D supplements and were analyzed separately.
  - In COVID patients, mean 25-OH-D levels were 13.8±7.2 ng/ml, compared to 20.9±7.4 ng/ml in controls ($p<0.0001$)
  - Vitamin D deficiency was found in 82.2% of COVID-19 cases and 47.2% of population-based controls ($p<0.0001$).
  - Vitamin D-deficient COVID patients had
    - More hypertension and CV diseases
    - Raised serum ferritin and troponin levels
    - Longer length of hospital stay than those with 25OHD levels ≥20 ng/ml.

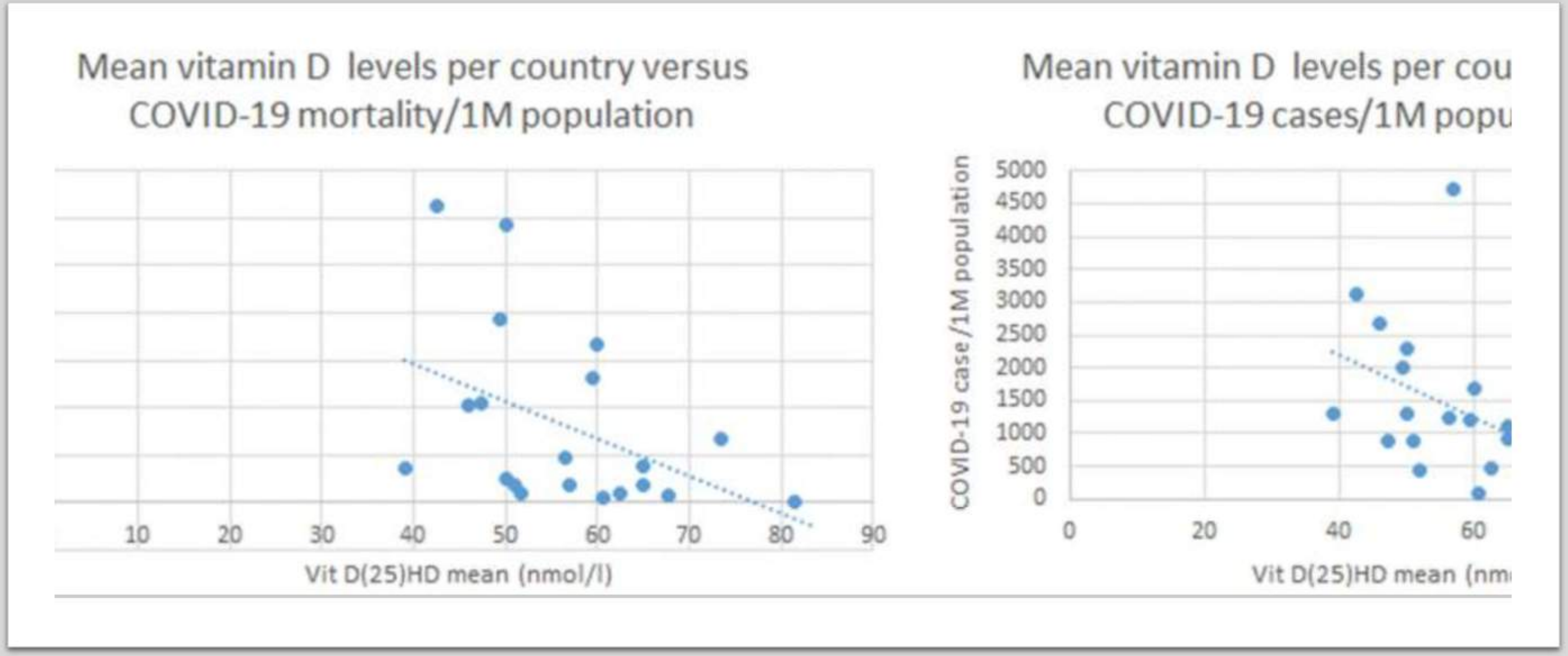
The Journal of Clinical Endocrinology & Metabolism, ,
dgaa733, https://doi.org/10.1210/clinem/dgaa733

Vitamin D and Sars-CoV-2

- Mean levels of vitamin D (average 22.44 ng/mL,) in 20 Europeans Countries
- Strongly associated with the number of cases/1M (mean 295.95 p=0.004
- Mortality/1M (mean 5.96, $p < 0.00001$).

Aging Clin Exp Res. 2020;32(7):1195-1198. doi:10.1007/s40520-020-01570-8

Vitamin D and Sars-CoV-2



Aging Clin Exp Res. 2020;32(7):1195-1198. doi:10.1007/s40520-020-01570-8

Vitamin D and Sars-CoV-2

- A total of 489 patients had a vitamin D level measured in the year before COVID-19 testing.
- Vit D status was categorized as likely deficient for 124 participants (25%), likely sufficient for 287 (59%), and uncertain for 78 (16%).
- 71 participants (15%) tested positive for COVID-19.
  - Testing positive for COVID-19 was associated with:
    - increasing age up to age 50 years (relative risk, 1.06; 95% CI, 1.01-1.09; *P* = .02)
    - non-White race (relative risk, 2.54; 95% CI, 1.26-5.12; *P* = .009),
    - deficient vitamin D status (relative risk, 1.77; 95% CI, 1.12-2.81; *P* = .02)
- COVID-19 rates in the deficient group were 21.6% (95% CI, 14.0%-29.2%) vs 12.2%(95% CI, 8.9%-15.4%) in the sufficient group.

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