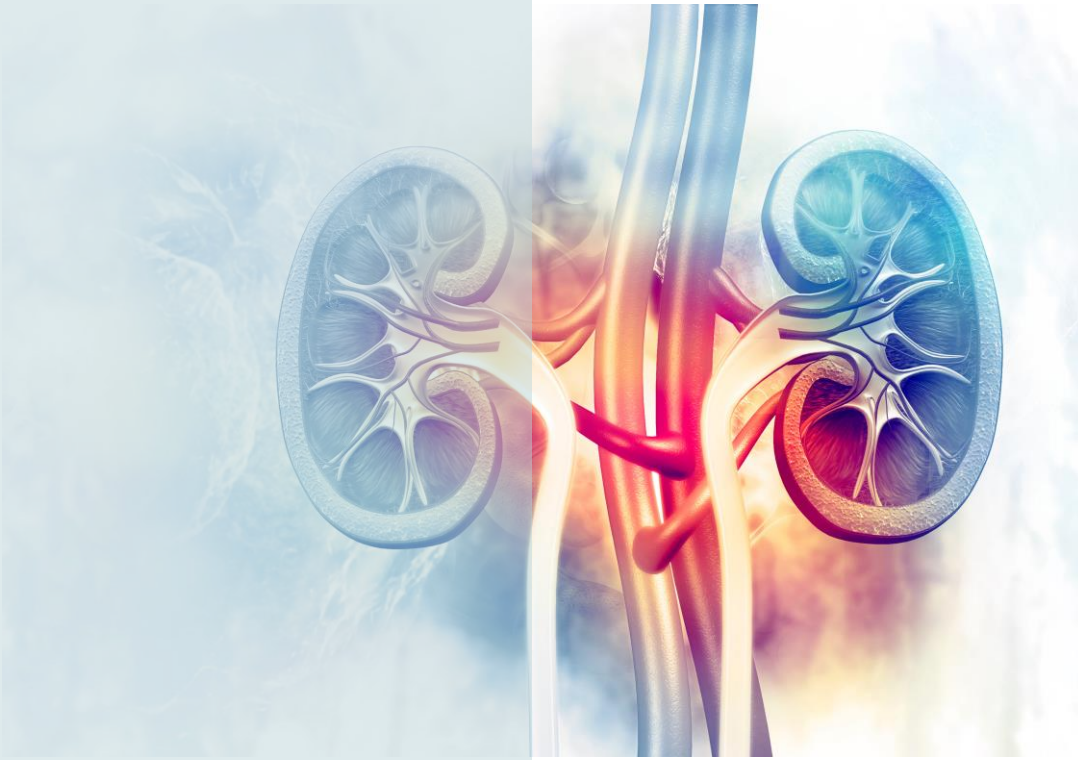
VITAMINS AND MINERALS IN CKD

Lindsey Zirker, MS RD



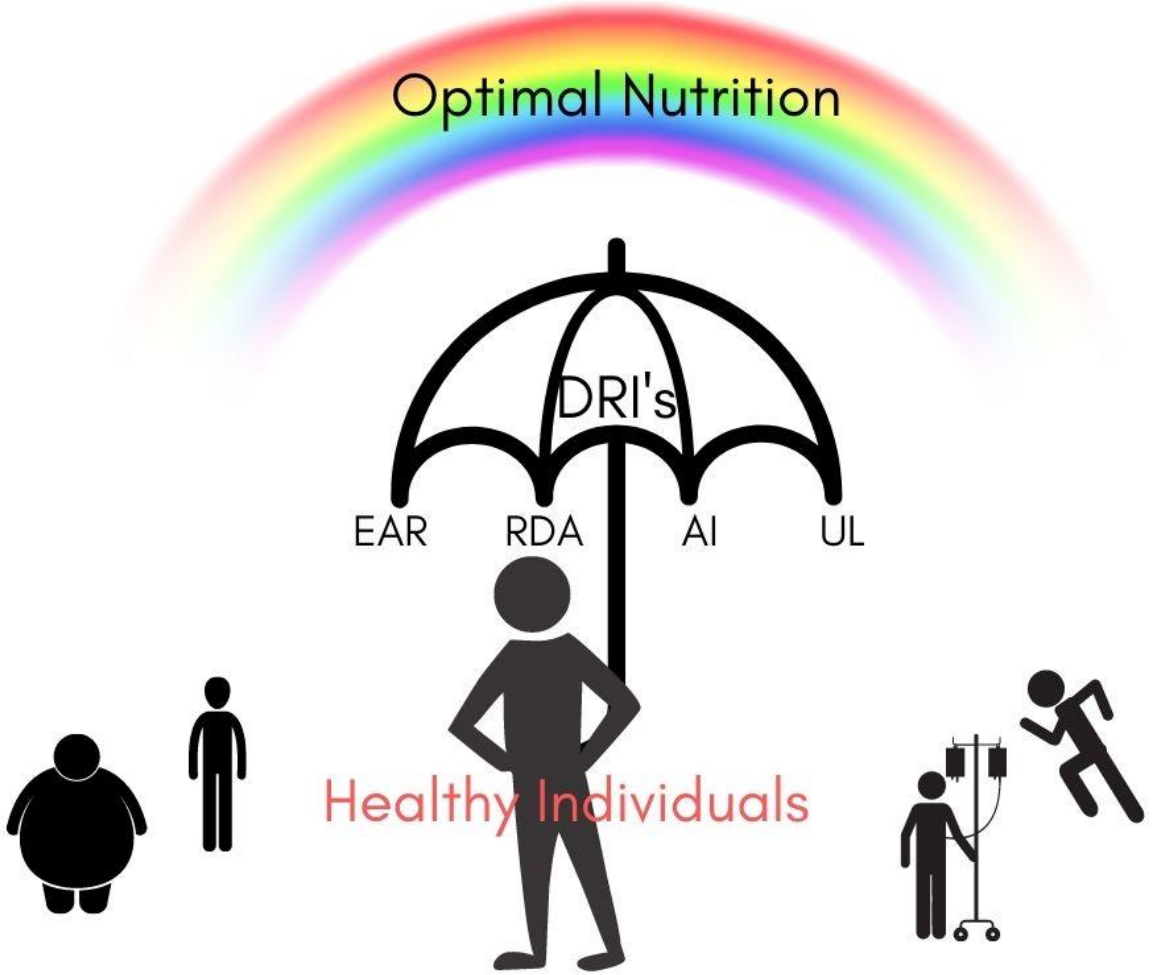
Disclosures

- Kidney Nutrition Institute
- RD2RD

Objectives

- Understand DRIs in context of CKD
- Assess and analyze vitamin and mineral needs in context of CKD
- Assess nutrient need, implement intervention and monitor for effectiveness

Dietary Reference intakes[1]



DRI assumptions

- DRIs are generally from 1998 and based on height, weight, age/ life stage and gender[1]
- Height and weight tables from 1988-1994 NHANES III data[1]
- "…there is no evidence that weight should change as adults age if activity is maintained…"[1]
- Lack of evidence to support using BMI for health recommendations[2]

KDOQI guidelines on vitamins[3]

- 5.0.1 In adults with CKD 3-5D or posttransplantation, it is reasonable for the registered dietitian nutritionist (RDN) or international equivalent to encourage eating a diet that meets the recommended dietary allowance (RDA) for adequate intake for all vitamins and minerals (OPINION).
- 5.0.2 In adults with CKD 3-5D or posttransplantation, it is reasonable for the registered dietitian nutritionist (RDN) or international equivalent, in close collaboration with a physician or physician assistant, to assess dietary vitamin intake periodically and to consider multivitamin supplementation for individuals with inadequate vitamin intake (OPINION).
- 5.0.3 In adults with CKD 5D who exhibit inadequate dietary intake for sustained periods of time, it is reasonable to consider supplementation with multivitamins, including all the water-soluble vitamins, and essential trace elements to prevent or treat micronutrient deficiencies (OPINION).

KDOQI rational for no vitamin guidelines[3]

Many studies did not report baseline status of micronutrients

Outcome variation

Dose of supplement variation

Serum levels often used as a marker for outcomes

Most studies in HD population, not many in CKD, PD or transplant

"there is insufficient evidence to support or oppose supplementation and more good quality trials are needed to help clarify evidence in this area."

Risk for Deficiencies[3,4]

Pregnant women	Gastric bypass	Poor appetite	Wasting syndromes	Malabsorption conditions
Vegetarians	Taking certain medications- diuretics	Restricted diet	Uremia altering metabolic pathways	Intradialytic losses

KDOQI Implementation Considerations[3]

- Gather information on micronutrient supplements
- Suggested vitamin intake should be based on recommendations for the general population (RDA) unless there are specific considerations requiring modification
- Assess dietary intake
- Review if patients may be at risk for deficiency
- Supplementation dose individualized based on each patient's needs and risk profile

HOW THE BODY USES MICRONUTRIENTS

Make sense of nutrient need, symptoms and root issues

Deficiency risks associated with the GI tract[6]

- Medications- binders, antibiotics, PPis
- Dysbiosis
- CKD
- Malnutrition
- Reduced stomach acid
- Conditions: inflammatory bowel, celiac, autoimmune
- GI surgery: bypass, gallbladder removal

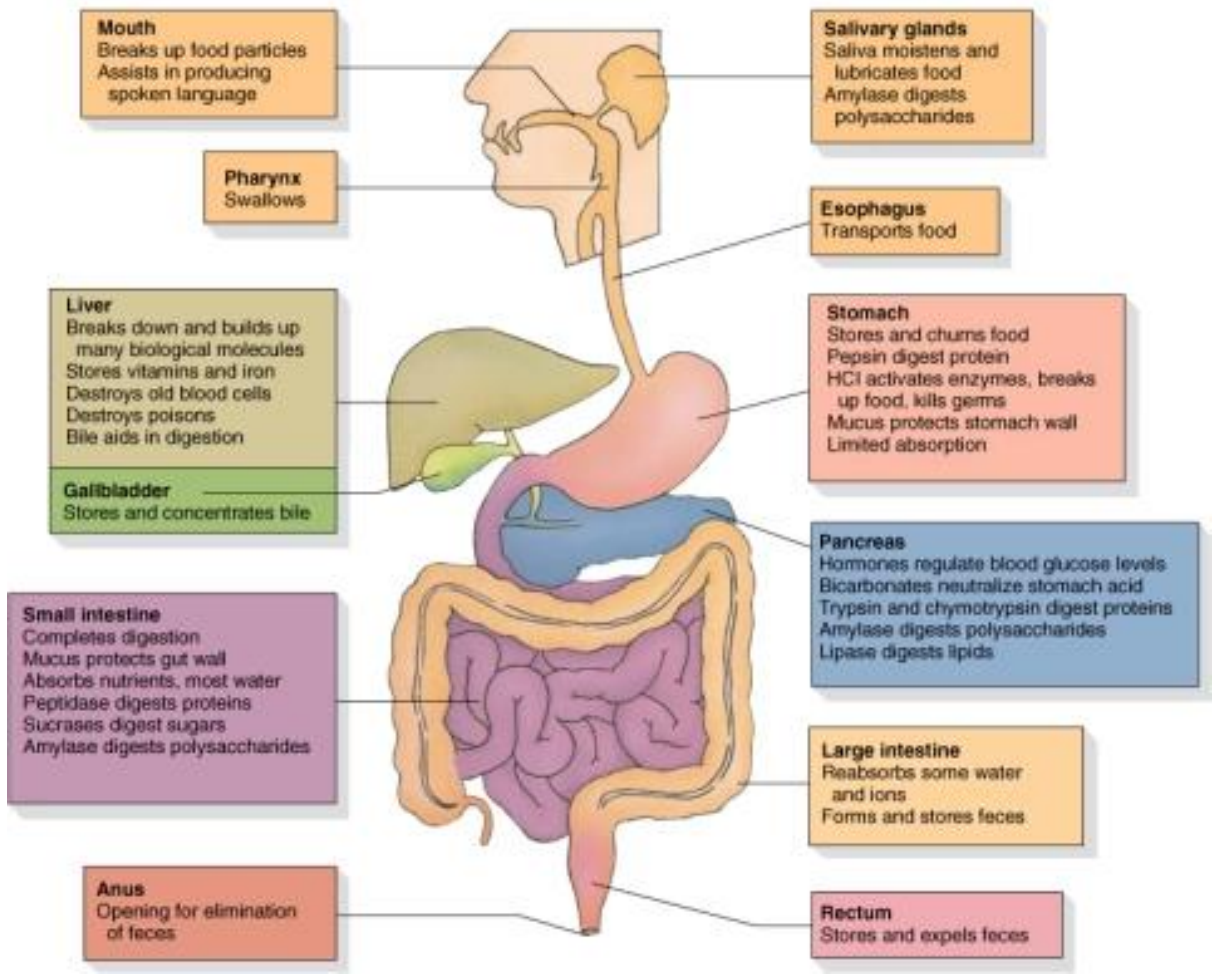


Figure 1. The Digestive System[6]

Inflammation

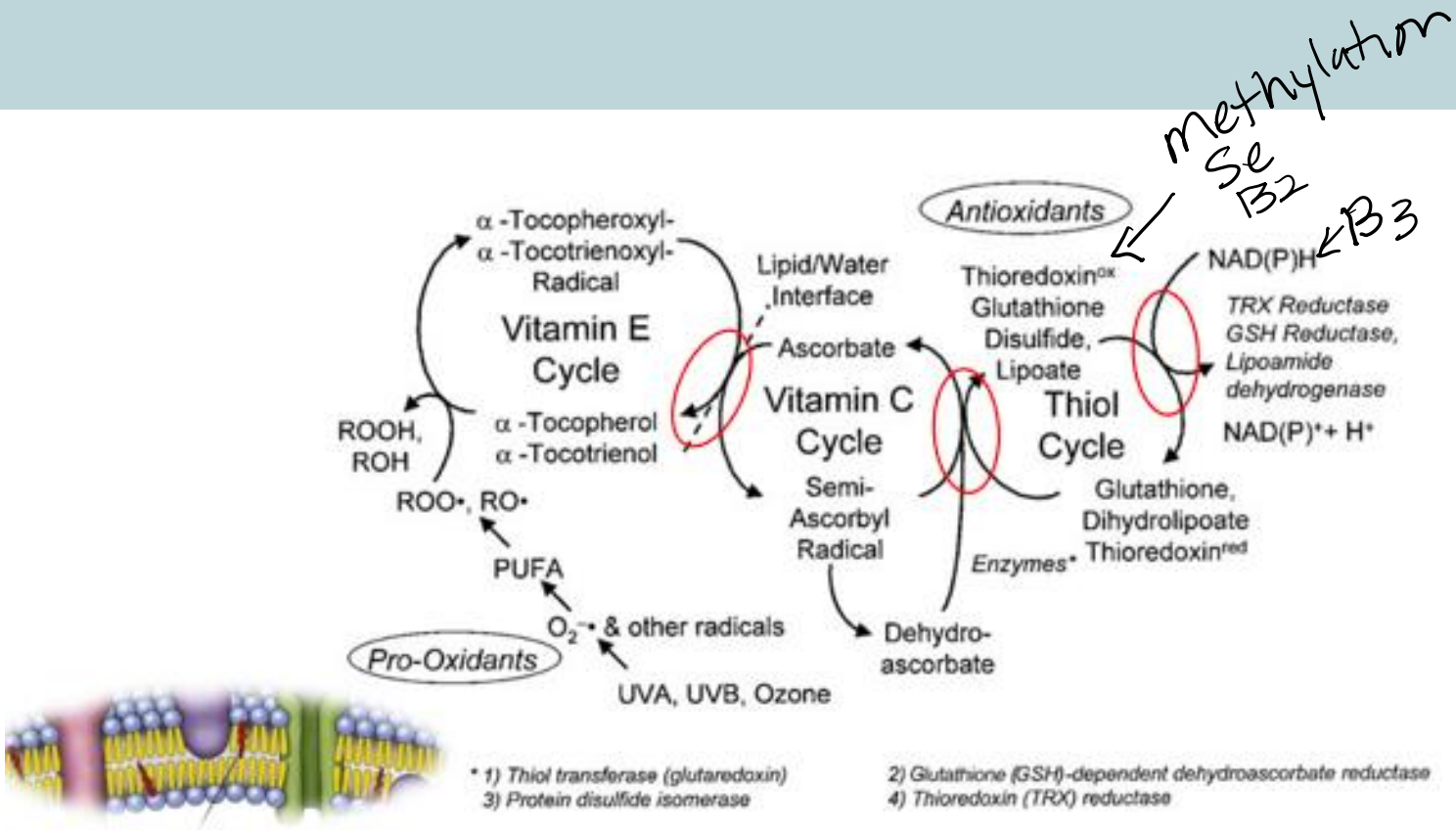
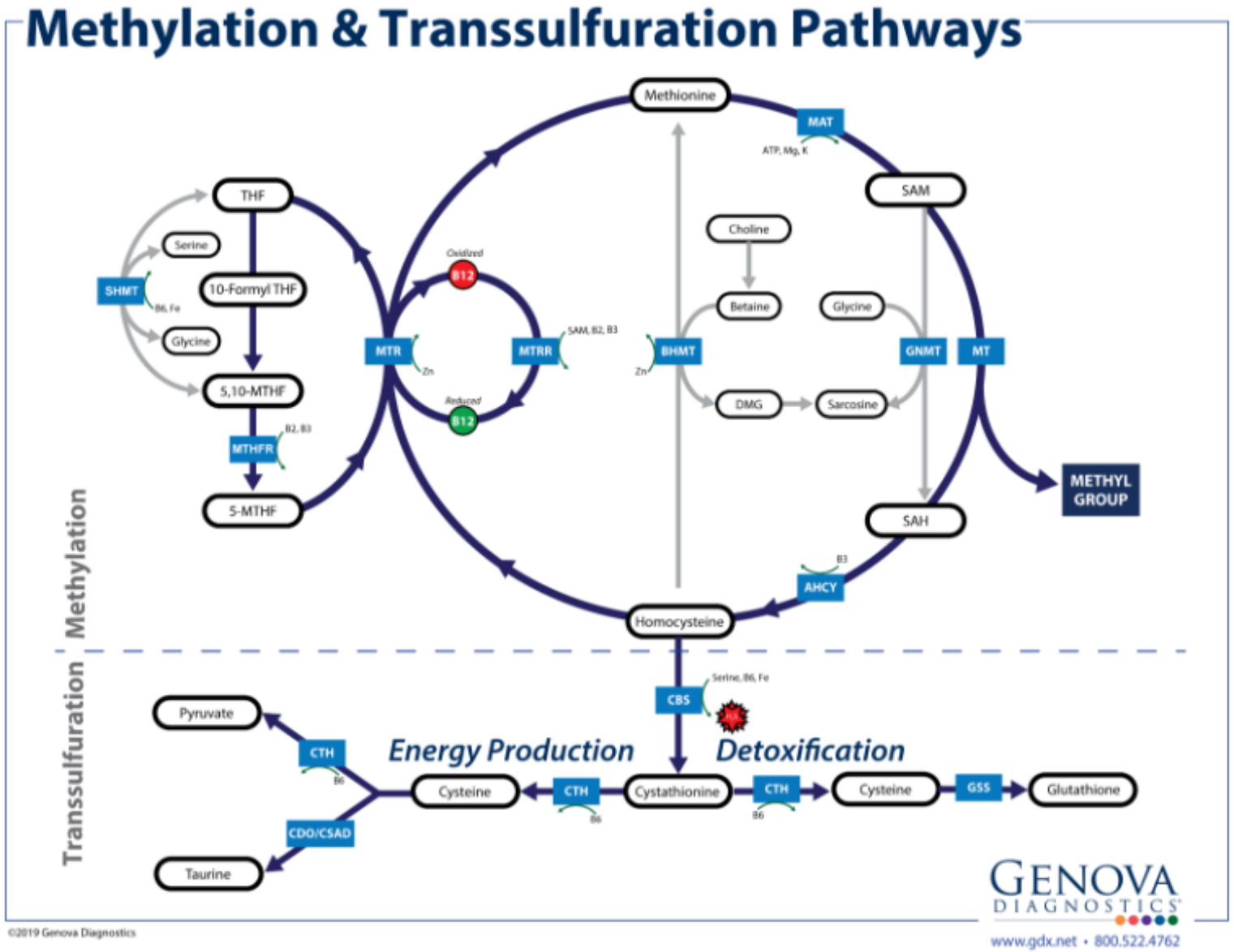


Figure 2: Antioxidant Regeneration[7]

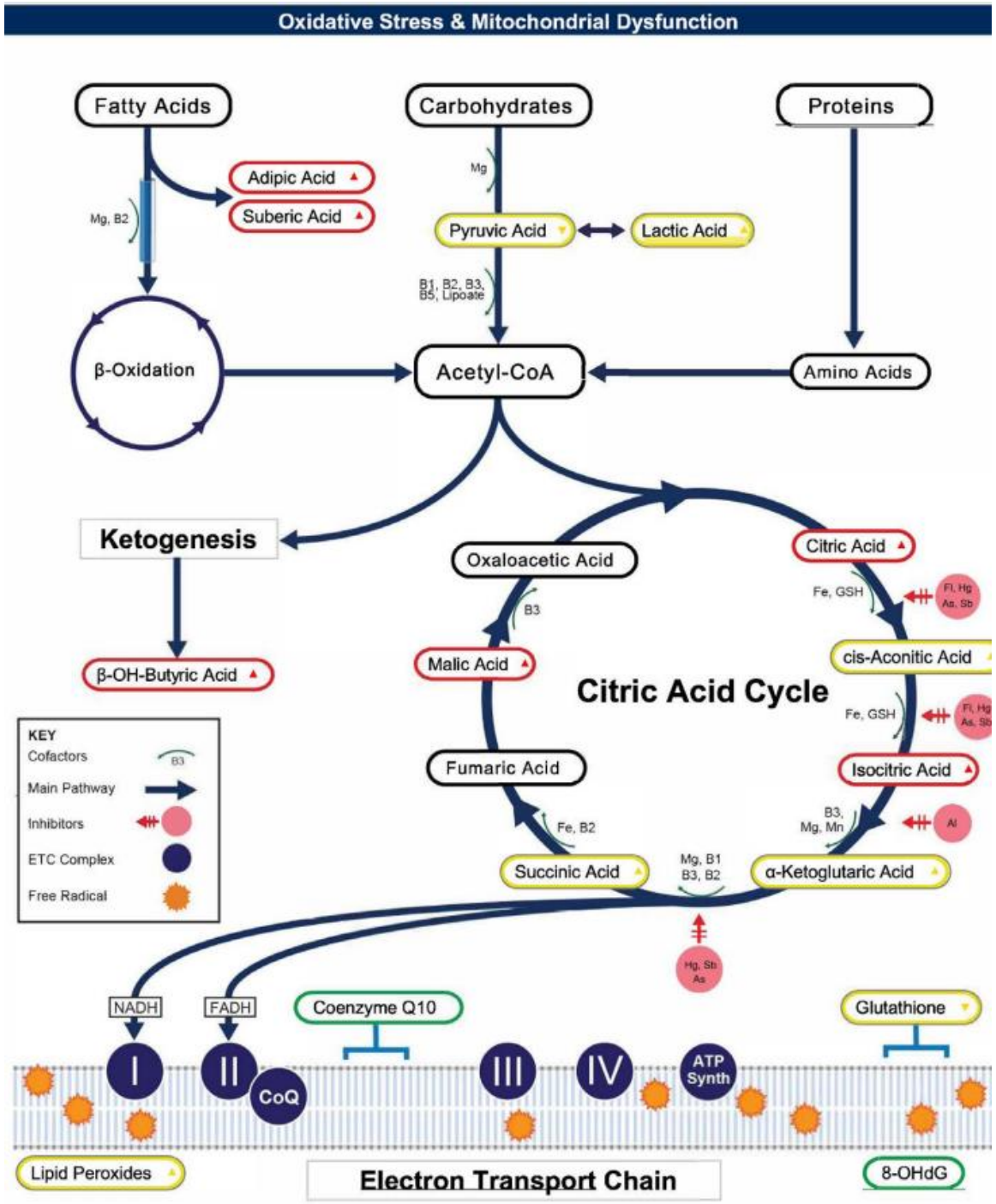


WHAT IS METHYLATION?

Figure 3. Methylation Cycle[8]

VITAMINS AND MINERALS IN ENERGY PRODUCTION

Figure 4: The Citric Acid Cycle[9]



VITAMINS IN CKD

Reviewing common concerns and questions

B Vitamins and CKD

Common current practices:

- Supplement with renal vitamin, esp for those on dialysis due to dialysis losses
- Maybe folate and B12 will be checked if patient anemia is not responding to typical treatment
- Recommend DRI, although there are some sources that have slightly higher recommendations

	Folic acid	B12	B6	B1	B2	B3	B5	Biotin
DRI/RDA[1]	400mcg	2.4-2.8mcg	1.3-1.7mg	1.1-1.2mg	1.1-1.3mg	14-16mg	5mg	20mcg
CKD[10]	>1000mg	2-3mcg	>5mg	1.5mg	1.8mg	14-20mg	5mg	30-100mcg
Dialysis[10]	1000mg	2.4mcg	10mg	1.2mg[7]	1.3mg	16mg	5mg	30mcg

What about this study?

Effect of B-Vitamin Therapy on Progression of Diabetic Nephropathy

A Randomized Controlled Trial

Andrew A. House, MD; Misha Eliasziw, PhD; Daniel C. Cattran, MD; et al

» Author Affiliations | Article Information

JAMA. 2010;303(16):1603-1609. doi:10.1001/jama.2010.490

"Given the recent large-scale clinical trials showing no treatment benefit, and our trial demonstrating harm, it would be prudent to discourage the use of high-dose B vitamins as a homocysteine-lowering strategy outside the framework of properly conducted clinical research."[11]

VITAMINS ARE HARMFUL IN PATIENTS WITH CHRONIC KIDNEY DISEASE

General nephrology · Jordan Weinstein · Monday, 10 May 2010 · 97208 Hits · **0 Comments**

"The study shows that people with diabetes and kidney damage should not take high doses of vitamin B and folic acid. This does not mean you should stop taking a prescribed daily multivitamin. Multivitamins have much lower doses and there may be other benefits for you."[12]

Division of Nephrology, St. Michael's Hospital, Assistant Professor of Medicine, University of Toronto Director, UKidney.com

Dialysis losses of water-soluble vitamins[13]

Vitamin	Effects	RDA	Clearance	Supplementation
Thiamin/B_1	• Conduction of nerve impulses • Muscle function • Stimulation of appetite	M: 1.2 mg F: 1.1 mg	• HD: 6%9 • Low flux= high flux10 • PD< urine11	0.6–1.5 mg/d8
Riboflavin/B_2	• Release of energy from nutrients • Supports normal vision • Healthy skin	M: 1.3 mg F: 1.1 mg	• HD: 7%10	20 mg post-HD 3/w17
Nicotinamide/B_3	• NAD+/NADP+: oxidation-reduction reactions • Improve lipid profile • Hyperphospatemia19,20	M: 16 mg F: 14 mg	• Rapid metabolic clearance • Not cleared by dialysis	
Biotin/B_8	• Energy metabolism: tricarboxylic acid cycle • Gluconeogensis • Metabolism of fatty acids • Breakdown of amino acids	30 mcg	• Partially cleared in high flux HD	30 mcg/d
Pantothenic acid	• Synthesis of lipid, neurotransmitters, steroid hormones and haemoglobin • Part of Coenzyme A	5 mg		5 mg/
Pyridoxine/B_6	• Metabolism of amino acids and fatty acids cognitive development immune function • Steroid synthesis erythropoietic activity • Peripheral neuropathy	1.3 mg	• PD<HD • Clearance 28–48% High eff/cy HD > 50%24,25	50–300 mg i.v. post-HD 60–100 mg/d per os26–29,32
Folate	• DNA synthesis/cell division • B_{12} conversion • Interconversion of aminoacids	400 mcg Pregnancy: 600 mcg	• HD=PD11,33,34 • Clearance 37%10,17,24	5–10 mg/d for hyperhomocysteinaemia 1 mg/d in dialysis
Cobalamin/B_{12}	• DNA and RNA synthesis • Homocystein reduction	2.4 mcg	• Not cleared in HD and PD	<1000 mg/d i.v.26,28,29,48,49
Ascorbic Acid/vit C	• Antioxidant • Formation of collagen • Matrix to form teeth and bone • Wound healing • Production of Norepinephrine and Thyroxine • Iron absorption • Resistance to infections	M: 90 mg F: 75 mg	• Clearance: 30–53% • Losses: 80–280 mg per session8,55,56 Diffusion: 2/3 of loss • Convection 1/3 of loss56	60 mg/d per os

Considerations for thiamin in CKD

HD patients with lower body weight= increased thiamin loss during dialysis[14]
Uremia down regulates thiamin transporters[15]
2.5x higher risk of thiamin deficiency in patients with heart failure[10 linus]
Removed by dialysis[13]
Medications that deplete thiamin: loop diuretics, antibiotics[17]
Large glucose loads may increase need (for all b vitamins)[5]

Niacin and CKD

1

Lowering phosphorus- up to 500-1500mg BID (nicotinaminde)

- Niacin can inhibit the sodium phosphorus transporters decreasing phosphorus absorption in the intestine and phosphorus reabsorption in the kidneys.[18]
- Also found: improved renal tissue lipid metabolism, renal function and structure, HTN, proteinuria, histological changes (animal study)[19]
- Mitigates upregulation of oxidative stress and inflammation in the kidney[19]

2

Lowering LDL, VLDL and TG, increasing HDL – 500mg TID (nicotinic acid)[20]

- High levels recommended may cause negative side effects

Biotin

Does it really help with hair loss?	• "although hair loss is a symptom of severe biotin deficiency, there are no published scientific studies that support the claim that high-dose biotin supplements are effective in preventing or treating hair loss in men or women"[21]
Other interventions for hair loss	• Consider Iron, vitamin D, oxidative stress, protein malnutrition, thyroid condition, autoimmune disease, hormone imbalance[22]
How much is too much with regards to interference with labs (like PTH)?	• Intakes greater than 5,000-10,000mcg/ day[23] • Biotin half life is about 2 hours- avoid supplement for about 8 hours[23]

Vitamin A

Usually avoided r/t concerns about toxicity[17]

Zinc deficiency= reduced retinol binding protien= reduced vitamin A[24]

Many CKD patients have high vitamin A plasma levels (3-4x) but do not show toxicity[17]

HD patients with the lowest vitamin A levels (although still above normal concentrations) had increased mortaility[17]

High levels of vitamin A can increase calcium levels[17]

Oxalate, kidney stones, and vitamin C

- Oxalate- Vitamin C doses of >500mg /day have been found to increase serum oxalate levels.[3,5]
- Secondary oxalate nephropathy- rare but >50% of cases require dialysis. Most common causes: Fat malabsorption (88%), Excessive oxalate consumption (20%)[25]
- Vitamin C intakes of greater than 1000mg/ day may increase risk of kidney stones[26]
- Dialysis previously didn’t remove oxalate well, newer technology is much more efficient[27]

VITAMIN D ENDOCRINE & AUTOCRINE FUNCTIONS[28]

Autocrine Function

Immune Modulation

Endothelial function

Secretion of insulin

Cell differentiation

Epigenetic signaling

Endocrine Function

Parathyroid hormone

Increased intestinal absorption of calcium and phosphorus

Renal reabsorption of calcium

FGF 23

Recommendation

Vitamin D, 25 hydroxy >30nmol/L

Higher levels may be recommended to achieve more optimal health outcomes

2000 IU/ day often recommended to maintain levels

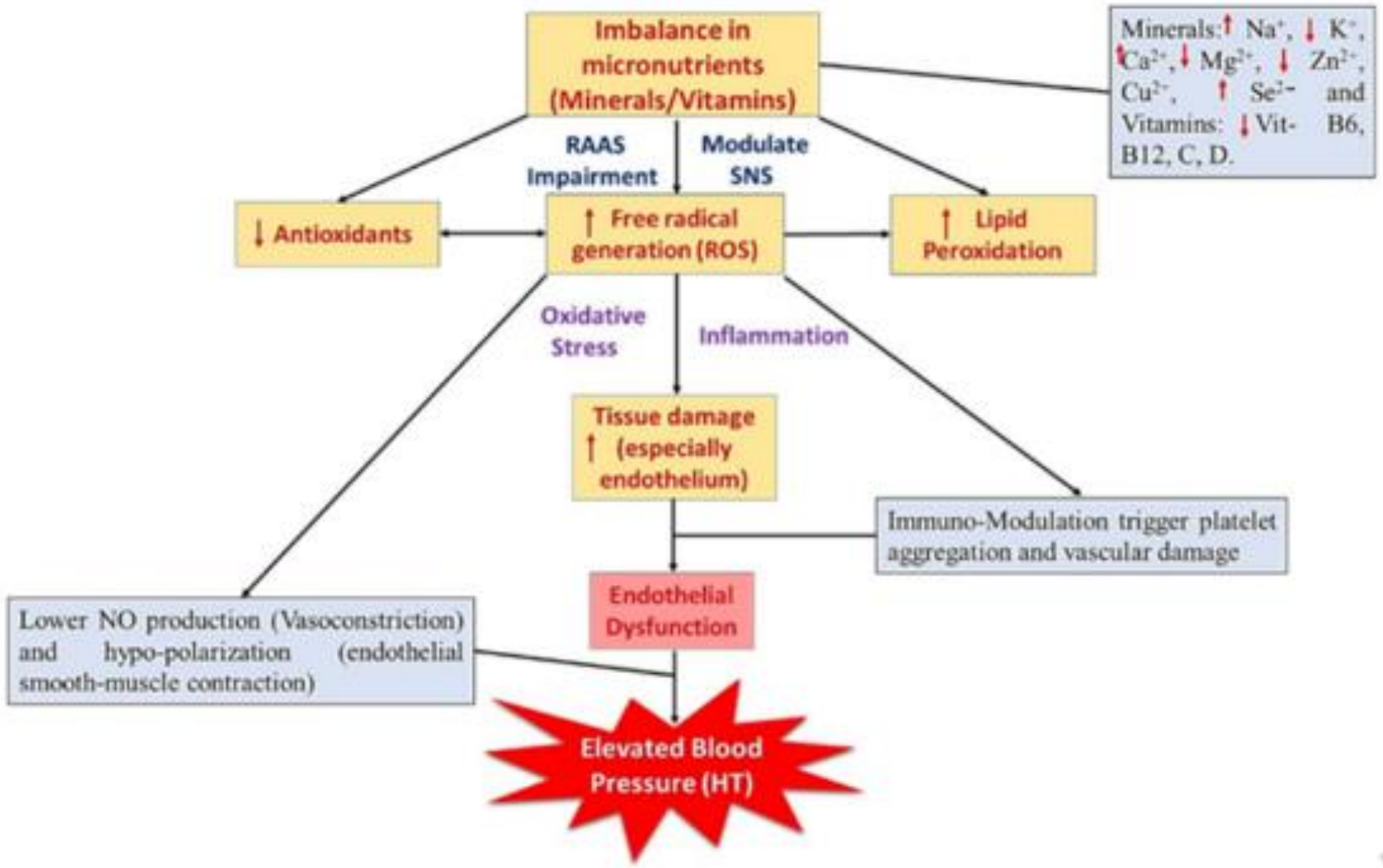
Fat malabsorption, body weight may increase nutrient need

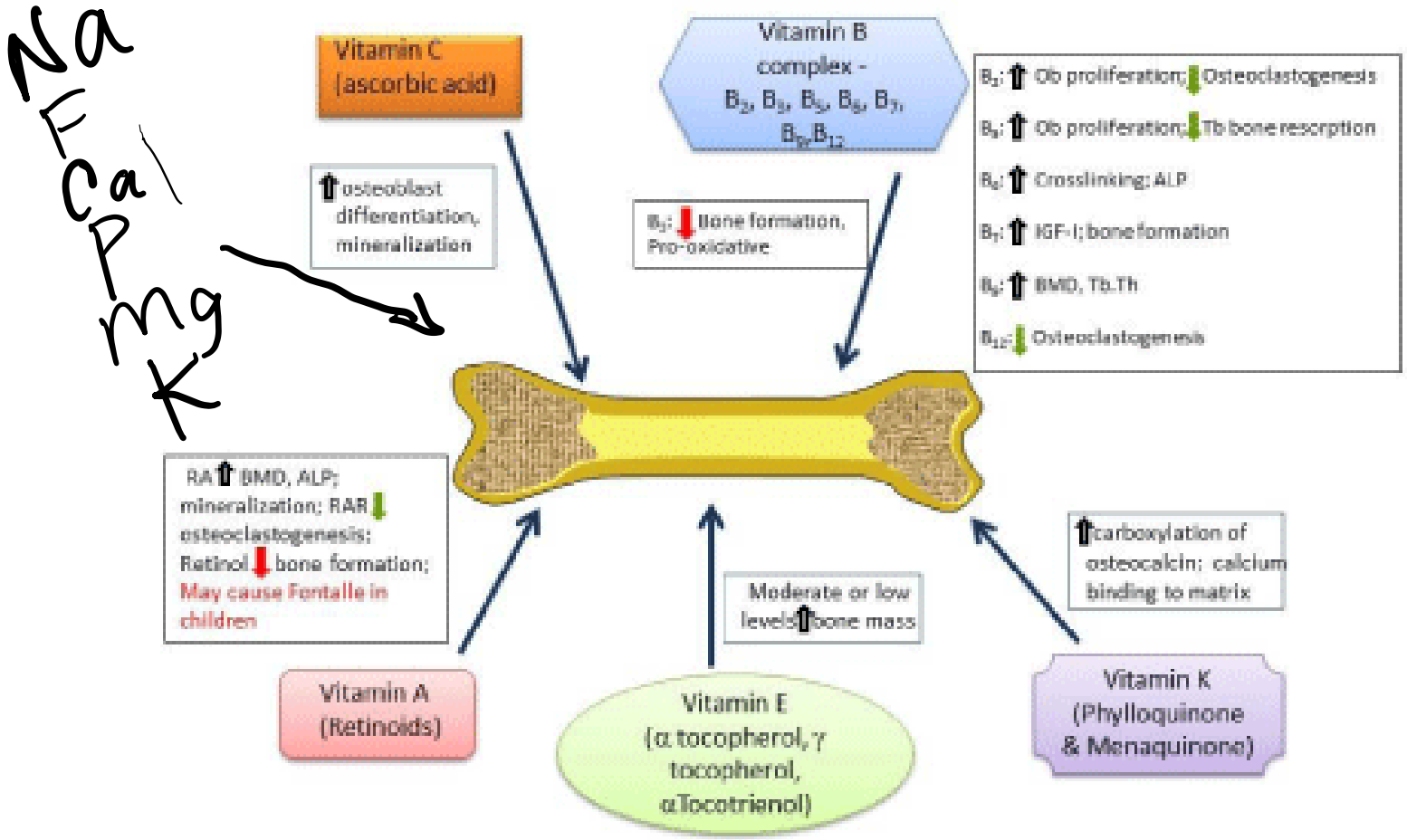
MINERALS

Clarifying common questions

BLOOD PRESSURE

Figure 5. Vitamins and minerals in blood pressure control[29]





Bone Health

Figure 6. Vitamins and minerals in bone metabolism[30,31]

Potassium

- KDOQI guidelines 6.4.1 and 6.4.2 potassium restriction for ***all*** CKD no longer recommended[3]
- "We found no clinical trials on how modifying diet can influence serum potassium levels in patients with CKD"[3]

- Other factors influencing potassium:[3]
  - Medications
  - Hydration status
  - Acid-base balance
  - Glycemic control
  - Constipation
  - Catabolic state
  - Lab error

Potassium interventions

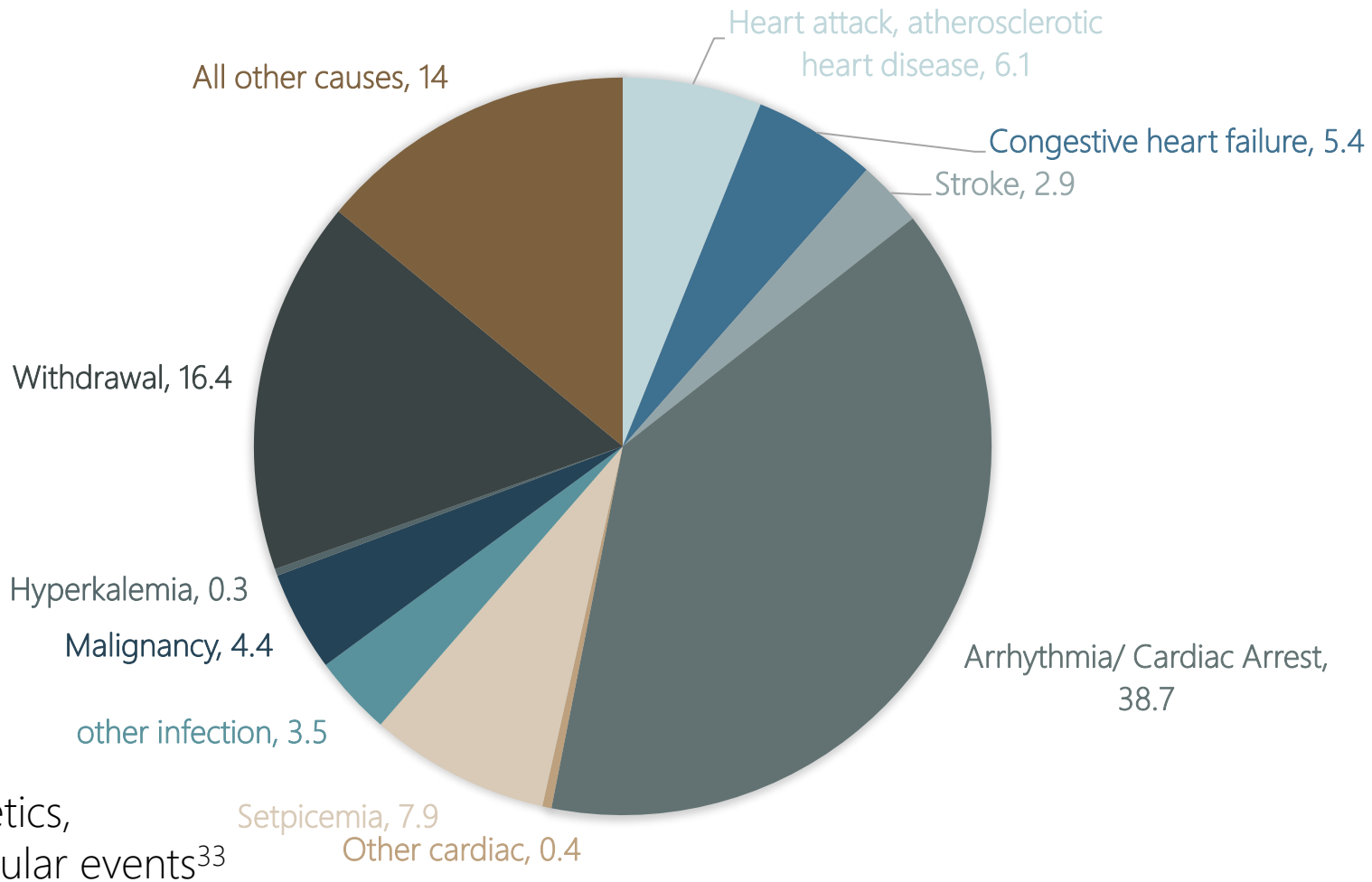
Constipation

- Fiber
- Probiotics
- Physical activity
- Stress management- Vagus nerve

Acid-base balance

- Sodium bicarb
- Increase intake of fruits and vegetables
- - PRAL (if tracking food intake)
- Alkalizing supplements (calcium, magnesium and potassium citrate)

Causes of death in ESRD patients 2012-2014[32]



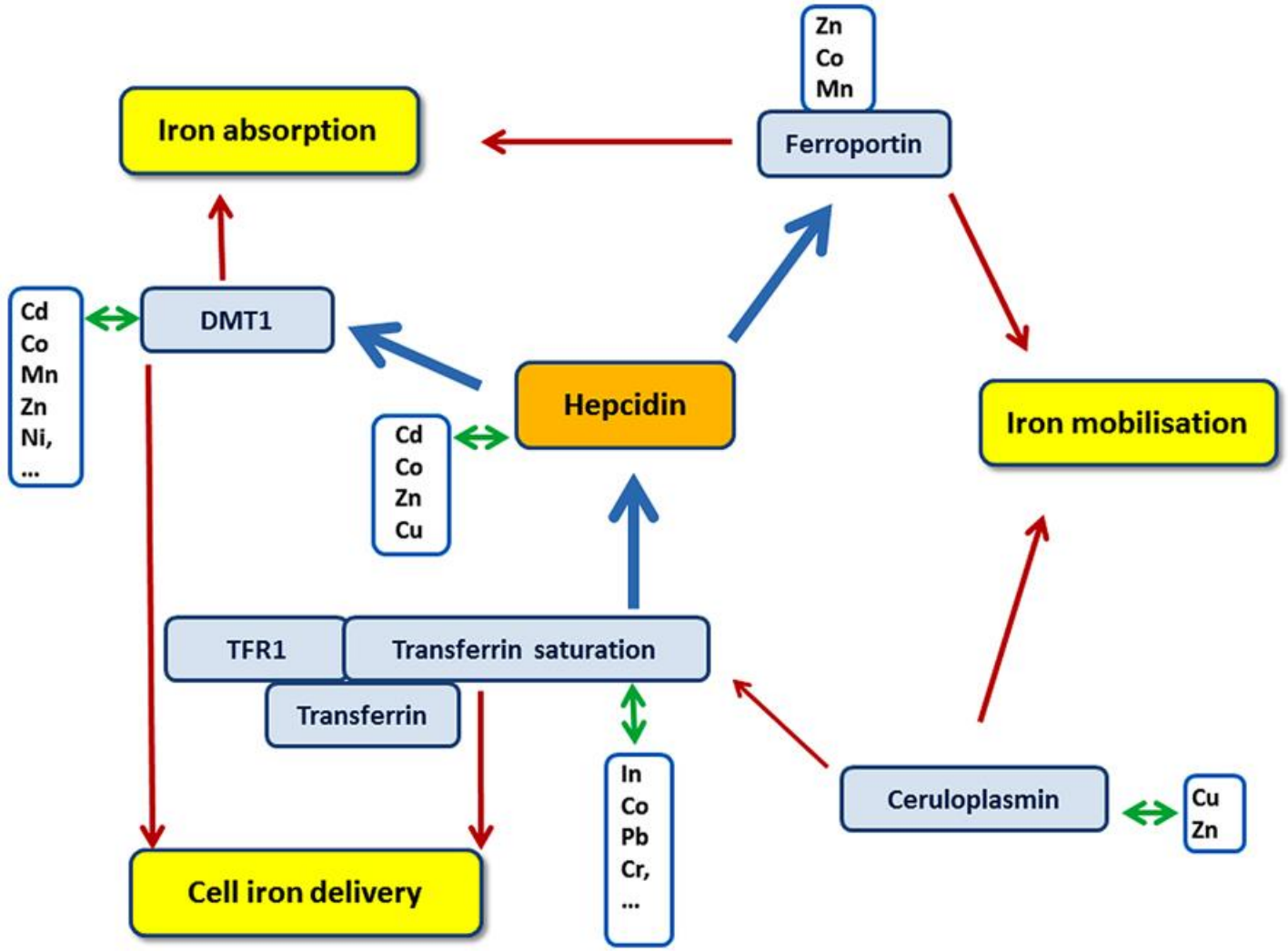
Study referenced on diuretics, potassium and cardiovascular events[33]

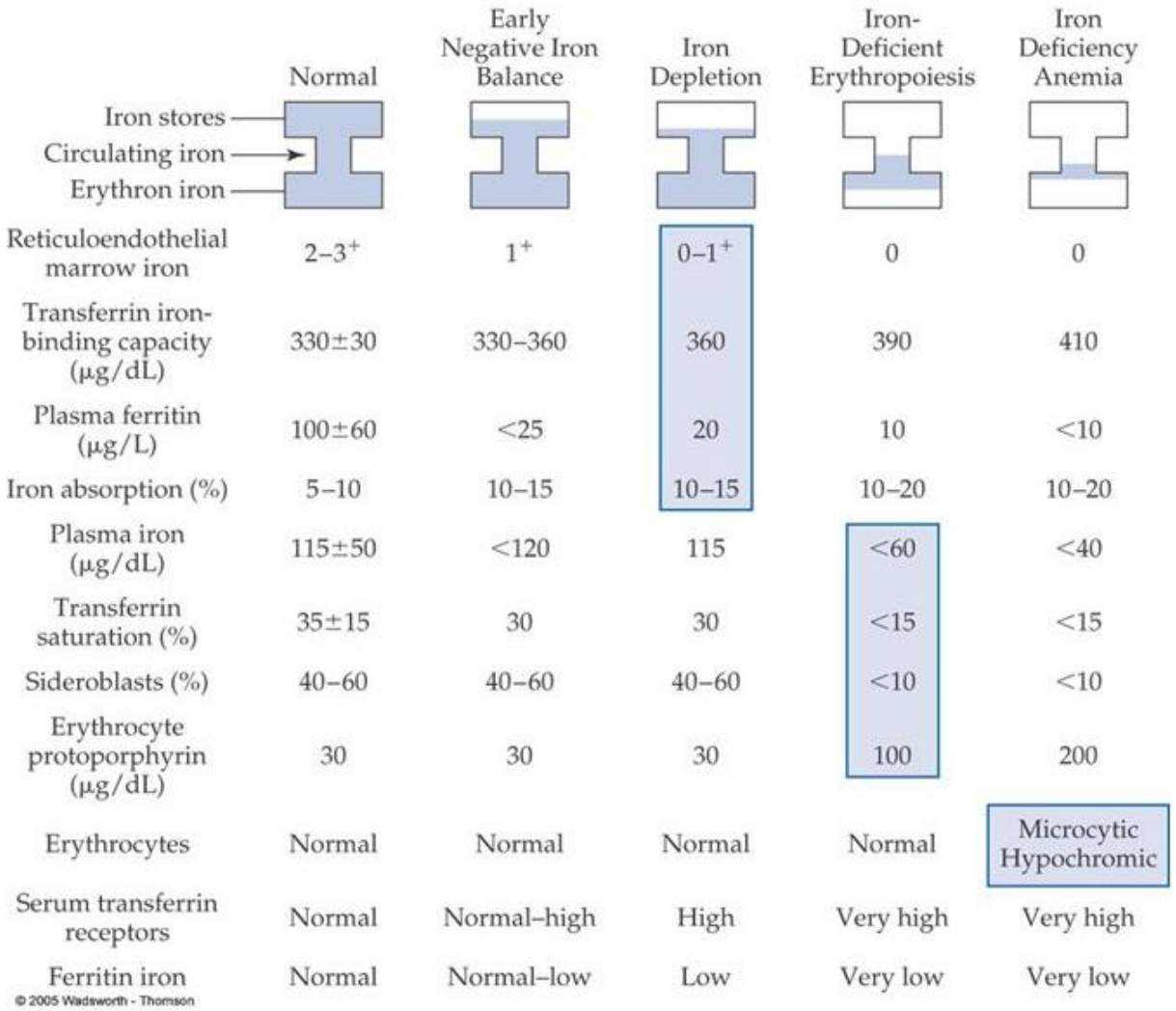
Magnesium[17]

Improved survival with higher magnesium levels, increased cardiovascular events and increased mortality with low levels.
Proteinuria increases renal wasting magnesium
Only 2% of magnesium is in the extracellular space- meaning it is difficult to assess and deficiency is only noticeable in later stages
RBC magnesium (in non anemic patients) may be an acceptable measure to assess

IRON

Figure 6. Minerals in involved in iron metabolism[34]





ASSESSING IRON DEFICIENCY

Figure 7. Iron status assessed by lab results[35]

Zinc[17]

Deficiency may increase progression of CKD

Increased losses through kidney as CKD progresses

May help to correct anemia and reduce EPO need in HD patients

Optimal zinc copper ratio 9:1[36]

Tools for assessing

- Physical assessment
- Symptoms
- Estimated intake
- Risk factors
- Medications
- Lab tests

INTERVENTION/ RECOMMENDATIONS

Nutrient Need Overview

	Nutrient Need (0 1 2 3 4 5 6 7 8 9 10)	DRI	Suggested Recommendations	Provider Recommendations
Antioxidants				
Vitamin A		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	
Glutathione				
Plant-based Antioxidants				
B-Vitamins				
Thiamin - B1		1.1 mg	10 mg	
Riboflavin - B2		1.1 mg	10 mg	
Niacin - B3		14 mg	20 mg	
Pyridoxine - B6		1.5 mg	10 mg	
Biotin - B7		30 mcg	100 mcg	
Folate - B9		400 mcg	400 mcg	
Cobalamin - B12		2.4 mcg	100 mcg	
Minerals				
Magnesium		320 mg	600 mg	
Manganese		1.8 mg	3.0 mg	
Molybdenum		45 mcg	75 mcg	
Zinc		8 mg	20 mg	
Essential Fatty Acids				
Omega-3 Fatty Acids		500 mg	1,000 mg	
GI Support				
Digestive Support/Enzymes			0 IU	
Microbiome Support/Probiotics			10 billion CFU	

Amino Acids (mg/day)

Arginine	NR	Methionine	NR
Asparagine	NR	Phenylalanine	NR
Cysteine	NR	Serine	NR
Glutamine	NR	Taurine	NR
Glycine	NR	Threonine	NR
Histidine	NR	Tryptophan	NR
Isoleucine	NR	Tyrosine	NR
Leucine	NR	Valine	NR
Lysine	NR		

Recommendations for age and gender-specific supplementation are set by comparing levels of nutrient functional need to optimal levels as described in the peer-reviewed literature. They are provided as guidance for short-term support of nutritional deficiencies only.

The Nutrient Need Overview is provided at the request of the ordering practitioner. Any application of it as a therapeutic intervention is to be determined by the ordering practitioner.

Essential & Metabolic Fatty Acids (RBCs)

Omega-3 Fatty Acids

Analyte		Reference Range
α-Linolenic (ALA) 18:3 n3	(cold water fish, flax, walnut) 0.24	>= 0.09 wt %
Eicosapentaenoic (EPA) 20:5 n3	0.40	>= 0.16 wt %
Docosapentaenoic (DPA) 22:5 n3	1.24	>= 1.14 wt %
Docosahexaenoic (DHA) 22:6 n3	2.6	>= 2.1 wt %
% Omega-3s	4.5	>= 3.8

Omega-9 Fatty Acids

Analyte		Reference Range
Oleic 18:1 n9	(olive oil) 14	10-13 wt %
Nervonic 24:1 n9	2.5	2.1-3.5 wt %
% Omega-9s	16.4	13.3-16.6

Saturated Fatty Acids

Analyte		Reference Range
Palmitic C16:0	(meat, dairy, coconuts, palm oils) 20	18-23 wt %
Stearic C18:0	19	14-17 wt %
Arachidic C20:0	0.28	0.22-0.35 wt %
Behenic C22:0	0.86	0.92-1.68 wt %
Tricosanoic C23:0	0.20	0.12-0.18 wt %
Lignoceric C24:0	2.3	2.1-3.8 wt %
Pentadecanoic C15:0	0.10	0.07-0.15 wt %
Margaric C17:0	0.27	0.22-0.37 wt %
% Saturated Fats	43.2	39.8-43.6

Omega-6 Fatty Acids

Analyte		Reference Range
Linoleic (LA) 18:2 n6	(vegetable oil, grains, most meats, dairy) 14.1	10.5-16.9 wt %
γ-Linolenic (GLA) 18:3 n6	0.08	0.03-0.13 wt %
Dihomo-γ-linolenic (DGLA) 20:3 n6	0.79	>= 1.19 wt %
Arachidonic (AA) 20:4 n6	17	15-21 wt %
Docosatetraenoic (DTA) 22:4 n6	2.03	1.50-4.20 wt %
Eicosadienoic 20:2 n6	0.23	<= 0.26 wt %
% Omega-6s	34.6	30.5-39.7

Monounsaturated Fatty Acids

Omega-7 Fatty Acids

Analyte		Reference Range
Palmitoleic 16:1 n7	0.23	<= 0.84 wt %
Vaccenic 18:1 n7	0.87	<= 1.13 wt %

Trans Fats

Analyte		Reference Range
Elaidic 18:1 n9t	0.26	<= 0.59 wt %

Delta-6-Desaturase Activity

Analyte	Upregulated / Functional / Impaired	Reference Range
Linoleic / DGLA 18:2 n6 / 20:3 n6	17.7	6.0-12.3

Cardiovascular Risk

Analyte		Reference Range
Omega-6s / Omega-3s	7.6	3.4-10.7
AA / EPA 20:4 n6 / 20:5 n3	43	12-125
Omega-3 Index	3.0	>= 4.0

The Essential Fatty Acid reference ranges are based on an adult population.

Thought process: “Should I take…?”

Is that what they really need?

Consider root issue and symptoms

Is it safe?

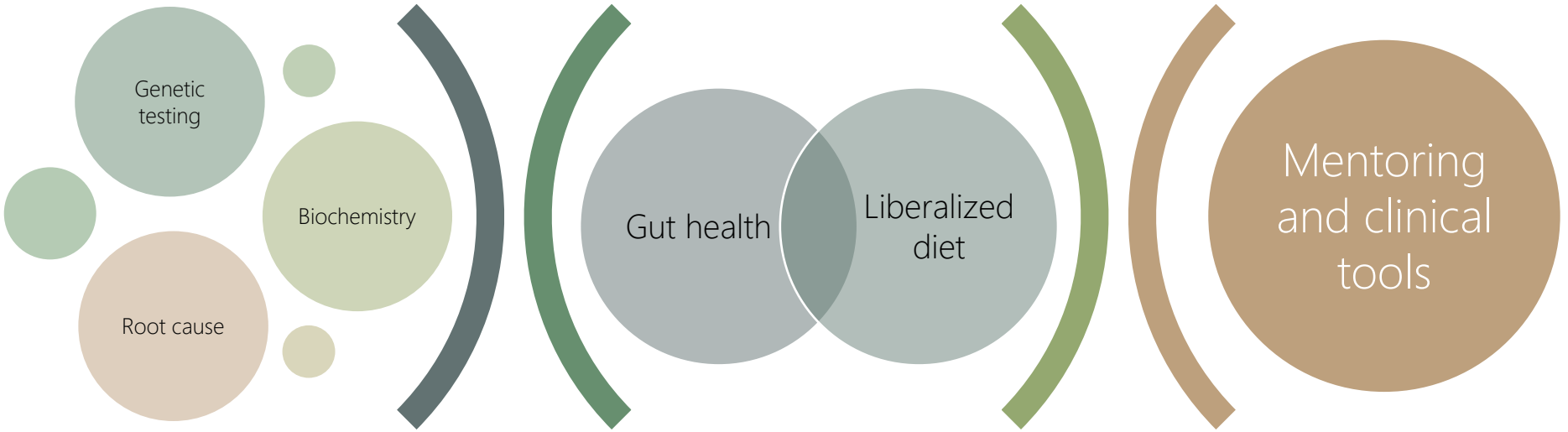
Is it going to be effective?

What dose or form?

Are there other considerations?

Follow up and monitor

Putting it all together



Big Picture

Nutrition strategy

Putting it all together

Resources: Vitamins and minerals

- CKD specific
  - KNI vitamins course: https://kidneynutritioninstitute.org/courses/vitamin-considerations-in-ckd-and-esrd/
  - Nutritional Management of Renal Disease 4th edition
- Vitamins and minerals
  - Labs- Genova Diagnostics, Vibrant America, Spectracell, 3x4
  - Advanced Nutrition and Human Metabolism- Gropper and Smith
  - Merck Manuals: https://www.merckmanuals.com/professional
  - Linus Pauling Institute- Micronutrient Center: https://lpi.oregonstate.edu/mic

Resources: Vitamins and minerals

- Evidence and how to use supplements
  - Natural Medicine Database
  - Integrative therapeutics interaction checker
  - Fullscript
- Handouts and clinical tools
  - Labs that do micronutrient testing
  - RD2RD- Guides, handouts, clinical tools made by other RDs
- Training
  - Nutrition focused physical exam: https://anhi.org/education/course-catalog/NFPE-1and2
  - Labs and supplement companies- lots of free webinar training

Gut Health

- CKD specific:
    - Kidney Nutrition Institute: https://kidneynutritioninstitute.org/courses/2021-ckd-deep-dive-supplements-and-root-cause-approach/
    - A clinical guide to nutrition care in kidney disease, 3rd edition- Chapter 22
- Digestive Health with Real Food- Aglaee Jacobs
- Advancing Medicine with Food and Nutrition- Ingrid Kohlstadt
- Labs- Genova Diagnostics, Diagnostic Solutions
- GERD
    - Kohlstadt book
    - Efficacy and safety of aloe vera syrup for the treatment of gastroesophageal reflux disease: a pilot randomized positive - controlled trial https://pubmed.ncbi.nlm.nih.gov/26742306/
    - What everybody ought to know but doesn't about heartburn/ gerd https://chriskresser.com/what-everybody-ought-to-know-but-doesnt-about-heartburn-gerd/
    - Omperazole use and risk of CKD evolution https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0229344

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THANK YOU!

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