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5 Common Drug-Induced Nutrient Depletions and Supplement Recommendations Every Pharmacy Can Tackle

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Disclosure Statement

There are no relevant financial relationships with ACPE defined commercial interests for anyone who was in control of the content of the activity.

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Pharmacist and Technician Learning Objectives

1. Describe five common classes of prescription medications associated with nutrient depletion and the specific nutrients they deplete.
2. Discuss the appropriate use of dietary supplements for drug-induced nutrient depletions.
3. Review effective communication strategies for integrating supplement recommendations into the patient care process.

Speaker

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Populations Vulnerable to Nutrient Deficiencies[1]

- Eating the Standard American Diet
- Vegetarians and Vegans
- Gluten-Free Diet
- Carbohydrate-Restricted Diet
- Eating Disorders
- Alcohol Abuse
- Exercise-Induced Nutrient Depletion
- Drug-Induced Nutrient Depletion

How Drug-Induced Nutrient Deficiencies Develop[1]

- Inhibition of nutrient absorption
- Inhibition of nutrient synthesis
- Alterations in transport of nutrients across membranes
- Increase or decrease in metabolism of nutrients
- Increase or decrease in excretion of nutrients
- Alteration in the body's ability to store nutrients

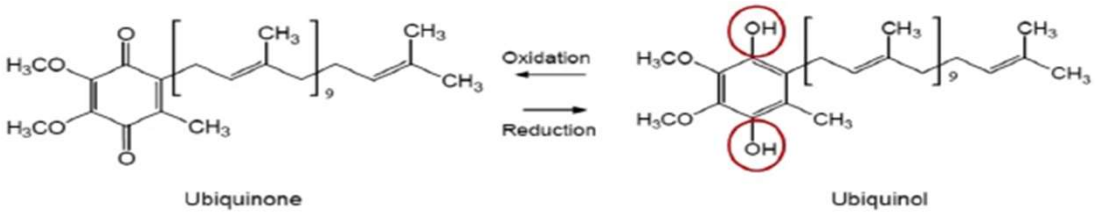
Deficiencies We Will Discuss

1. CoEnzyme Q10
2. Vitamin B12
3. Calcium
4. Iron
5. Magnesium

CoEnzyme Q10[1]

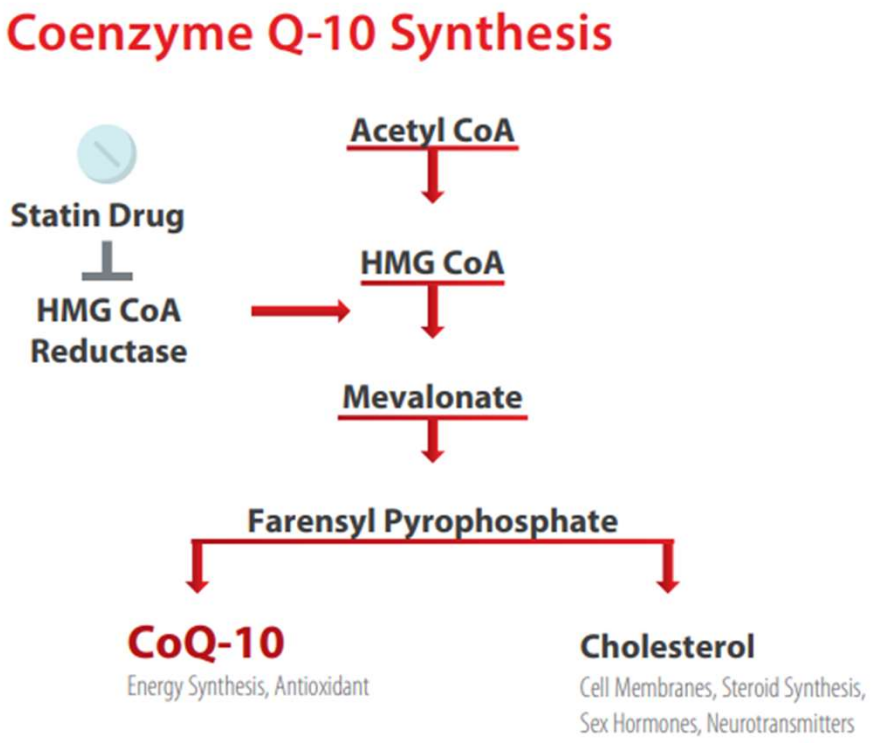
Statins deplete CoEnzyme Q10

- CoQ-10 is a powerful fat-soluble, vitamin-like substance
- Main functions
  - Energy production
  - Antioxidant recycling
- Two main forms
  - Ubiquinone-oxidized form
  - Ubiquinol-reduced form



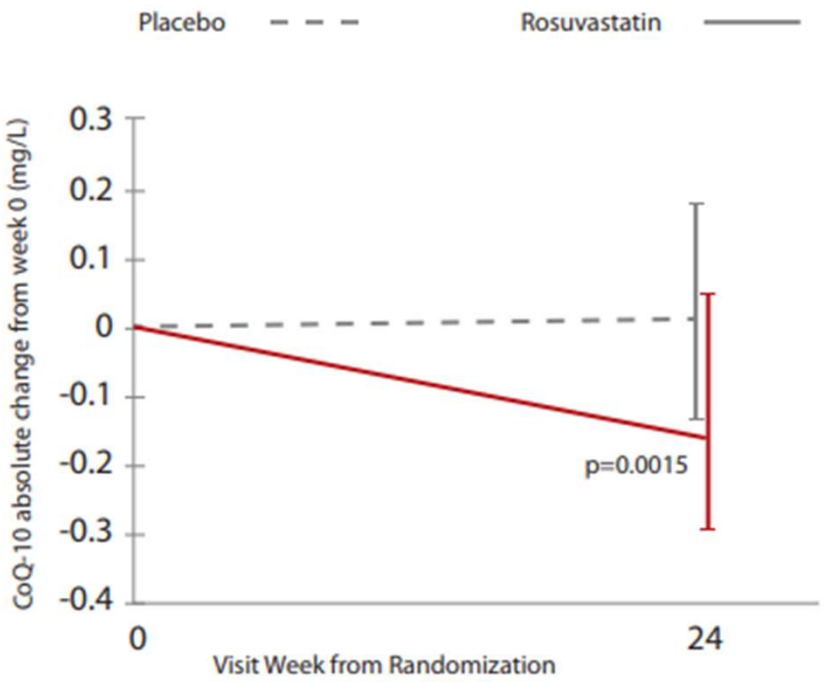
Picture citation: Zhang, Y.; Liu, J.; Chen, X.-q.; Oliver Chen, C. Y., Ubiquinol is superior to ubiquinone to enhance Coenzyme Q10 status in older men. Food & Function 2018, 9 (11), 5653-5659.

Statin Mechanism of Action



https://www.q10facts.com/coenzyme-q10-red-yeast-rice-heart-disease/

Rosuvastatin Depletes CoEnzyme Q10



In a 24 week RCT, 124 patients taking rosuvastatin showed significantly reduced plasma CoQ-10 levels when compared to placebo.[1]

Morrison, Justin T et al. "Effect of rosuvastatin on plasma coenzyme Q10 in HIV-infected individuals on antiretroviral therapy." *HIV clinical trials* vol. 17,4 (2016): 140-6. doi:10.1080/15284336.2016.1184863

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Side effects associated with statins are identical to symptoms of CoEnzyme Q10 deficiency

- Memory loss and confusion
- Muscle pain, weakness, and permanent nerve damage
- Fatigue, headache and difficulty sleeping
- Nausea, vomiting, diarrhea and constipation
- Liver and kidney problems
- Infertility
- Increased risk of heart failure
- Increases risk of type 2 diabetes

Drugs and Other Factors that Deplete CoEnzyme Q10

Antidiabetic Medications	Cardiovascular Medications	Lifestyle Choices
1. Sulfonylureas	1. Statins 2. Beta blockers 3. Thiazide diuretics 4. Vasodilators	1. Strenuous exercise 2. High sugar intake 3. High caffeine intake 4. High carbohydrate intake 5. High alcohol intake

Vitamin B12[2]

Metformin depletes Vitamin B12

- Metformin reduces folate and vitamin B12 absorption
  - Elevated homocysteine levels associated with long-term metformin administration
- Folic Acid
  - Folic-Megaloblastic anemia, birth defects, cervical dysplasia, elevated homocysteine, headache, fatigue, hair loss, increased infections
- Vitamin B12
  - B-12 fatigue, peripheral neuropathy, tongue and mouth irregularities, macrocytic anemia, depression, confusion, memory loss, easy bruising, dermatitis, loss of appetite

Vitamin B12 Deficiency

- Vitamin B12 deficiencies can lead to complex neurological symptoms
- Peripheral nerves usually affected first
  - Patients complain of paresthesia
- Posterior columns may become impaired
  - Patients complain of difficulty with balance
- Megaloblastic anemia

Drugs and Other Factors that Deplete B12

Medications	Lifestyle Choices
1. Acid blockers 2. Antacids 3. Antibiotics 4. Anticonvulsants 5. Diabetes medications 6. Hormone Replacement Therapies 7. Selective Estrogen Receptor Modulators	1. Alcohol 2. Vegan or vegetarian diet

Calcium[1]

- Most abundant mineral in human body
  - Primarily located in skeletal system
- Secondary messenger
  - Key to smooth muscle and skeletal muscle relaxation and contraction
- Tightly regulated by hormones
  - Parathyroid hormone and Calcitonin

Consequences of Calcium Deficiency

- Risk of osteoporosis
- Tooth decay
- High blood pressure
- Heart disease
- Insomnia
- Acid reflux
- Digestive problems
- Obesity
- Diabetes
- Cancer

Calcium Depleting Medications

1. Corticosteroids
    a. Calcium absorption is decreased due to inhibition of vitamin-D-dependent intestinal calcium absorption and increased calcium efflux
2. Acid Blockers and Antacids
3. Anticonvulsants
4. Blood Pressure Agents
5. Hormone Replacement Therapy

Vulnerable Populations

1. Postmenopausal Women
    a. Estrogen production and utilization is sharply decreased
        i. Can lead to substantial bone and calcium loss
        ii. Can lead to osteoporotic fractures
2. Vegetarians
    a. Certain components in plants have shown to inhibit calcium absorption leading to increased susceptibility of calcium deficiency
        i. Oxalates and phytates
    b. Decreased calcium consumption relative to omnivores
3. Lactose Intolerance
    a. Estimated effect of ⅔ of the world's population
    b. Need to consume calcium-fortified foods or ensure adequate intake with calcium supplementation

Iron Deficiency[3,4,5,6,7]

- Essential for oxygen transport and storage, electron transfer, energy production, DNA replication/repair and more
- Over two-thirds of the body's iron stores are attached to hemoglobin
- Over 100 different enzymes and proteins use iron as a cofactor

Consequences of Iron Deficiency

- Fatigue
- Cranky
- Depressed
- Trouble concentrating
- Pale skin
- Pale or sore tongue
- Brittle nails
- Weakened immune system

Iron Depleting Medications

1. Acid blockers
    a. An acidic environment is required to promote efficient non-heme iron absorption; it helps to reduce the less soluble ferric iron form (Fe 3+) to more soluble ferrous form (Fe 2+)
2. Analgesics
3. Antacids
4. NSAIDs
5. Bisphosphonates

Vulnerable Populations

1. Pregnancy
    a. Higher recommended intake than non-pregnant premenopausal women
2. Vegetarians
    a. Plants provide non-heme sources of iron
        i. Not well absorbed form
    b. Recommended 1.8x increased intake
3. Gastrointestinal Disorders
    a. Inflammatory bowel disease, Celiac disease
4. Obesity
    a. Decreased absorption due to increased hepcidin related to adiposity-related inflammation

Magnesium[1,8,9,10,11]

- One of most abundant and important minerals in body
  - ~90% is stored in skeletal and muscle tissues
  - Over 300 different enzymatic reactions rely on magnesium as a cofactor
    - Energy production, cell signaling, cell migration, synthesis of essential molecules, ion transport
- Magnesium deficiency is one of the most common nutrient deficiencies in Western countries

Consequences of Magnesium Deficiency

- Muscle weakness
- Tremor
- Muscle spasm
- Arrhythmias
- Atrial fibrillation
- Irregular contraction
- Rapid heart rate
- Migraines
- Insomnia
- Anxiety
- Brain fog
- Depression

Magnesium Depleting Medications

- Oral contraceptives
  - Oral contraceptives reduce serum magnesium by impacting uptake into tissues
- PPIs
  - Impair magnesium absorption, inhibit transporters for active Mg uptake in intestines and distal convoluted tubules of kidneys
- Antibiotics
  - Interfere with the absorption of magnesium
- Corticosteroids
  - Mineralocorticoid receptor interactions

Vulnerable Populations

1. Elderly
    a. Malabsorption, increased urinary excretion, bone loss
    b. Increased likelihood of taking medications for chronic diseases
2. Exercise
    a. Energy production depends on magnesium status, increased metabolism and leads to increased demand
3. Gastrointestinal disorders
    a. IBD, Celiac, Chronic diarrhea
4. Alcohol abuse
    a. Increased loss from frequent urination and inadequate nutrition intake
5. Cardiometabolic conditions
    a. Increased renal wasting of magnesium

Benefits of Replenishing Deficiencies

- Usually have a slow onset (can show up 2 to 3 years later)
- Physicians, nurses and pharmacists not always trained to look for these
- Providers often think these symptoms are new indications of a different disease state
- Patients often started on new drugs for the supposed new disease state
- New drug might cause another nutritional depletion, starting the process over again

Nutrients Can Be Replenished Through the Diet[12]

CoEnzyme Q10	Vitamin B12	Calcium	Iron	Magnesium
• Beef • Chicken • Peanuts • Sesame Seeds • Pistachios • Broccoli • Cauliflower • Whole grains • Sesame oil • Spinach	• Primarily animal foods • Vegetarian options: spirulina, brewer's yeast, tempeh, miso, and tofu	• Cows milk • Yogurt • Turnip greens • Spinach • Collard greens • Basil • Kale • Celery • Green beans • Garlic • Tofu • Quinoa	• Meat/poultry /fish • Swiss chard • Spinach • Turmeric • Parsely • Mustard Greens • Green beans • Mushrooms • Asparagus • Chickpeas • Tofu • Olives	• Swiss chard • Spinach • Oatmeal • Whole grains • Squash • Pumpkin seeds • Broccoli • Halibut • Flax seed • Quinoa • Tomatoes

Supplementation is Often Needed

- Helpful if you know laboratory levels to make specific recommendations but not always necessary
- Supplement choice should take into consideration
  - Drug interactions
  - Dosing
  - Absorption
    - Salt forms
  - Lifestyle factors
  - Patient preferences
  - Potential side effects
  - Other potential benefits

Integrating Recommendations

Pharmacists should play a key role in bridging the gap between conventional care and evidence-based supplementation.

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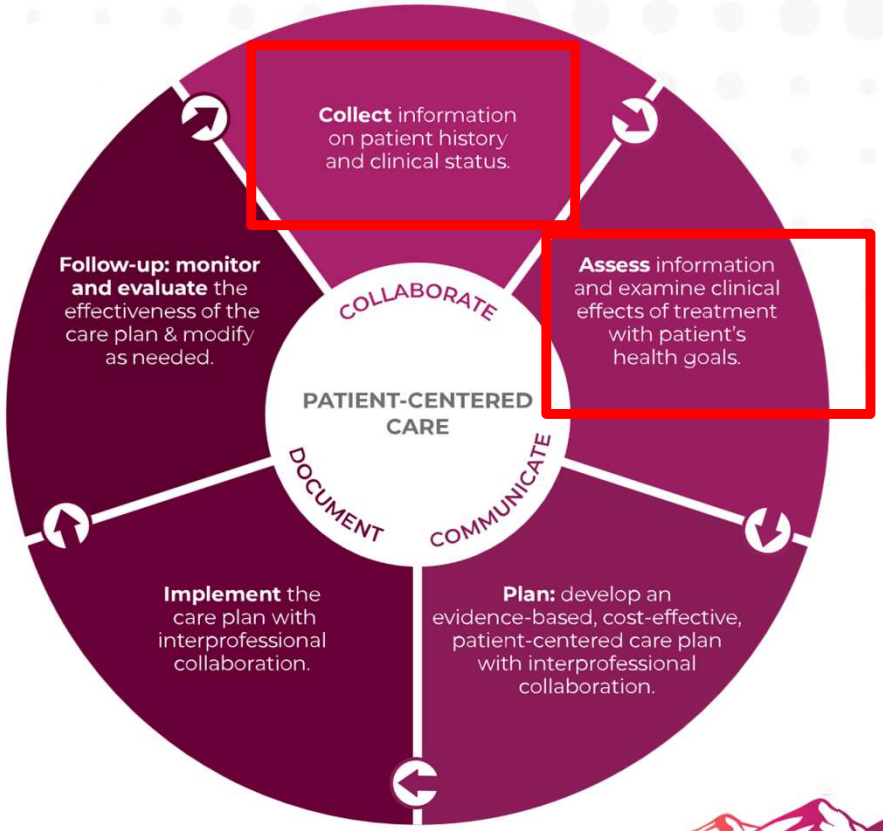
Integrating Supplement Recommendations

Start the conversation

"I noticed you're taking a medication often used for…"

"Did you know the medication you're taking…"

"Do you take any prescription medications?"



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Integrating Supplement Recommendations

Engage in a conversation

- Use this as a time to educate
- Ask questions
  - Age
  - Medical Conditions
  - Medications (prescription, over the counter and supplements)
  - Diet Habits
  - Allergies
  - Laboratory Measurements
- These conversations **build trust**, **promote safety**, and **empower** informed choices

Technician Tips

- As a tech, you can help identify opportunities by reviewing medication profiles or engaging patients during pickup or drop-off.
- Questions you can ask:
  - “Have you talked to the pharmacist about how this medication might affect your nutrient levels?”
  - “Have you noticed any side effects from your medication lately?”
  - “Would you like the pharmacist to check if there are any vitamins that could support your therapy?”
- Our role is critical in surfacing the right opportunities for the pharmacist to make personalized supplement recommendations. You’re the first line of contact—your questions can make all the difference.

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Meet Them at Their Level

- Supplement knowledge varies greatly from patient to patient
- All about educating individuals to make an informed decision

Summary

- Statins deplete CoEnzyme Q10
- Metformin depletes Vitamin B12
- Calcium, iron and magnesium can be depleted by a variety of medications
- Lifestyle choices can also lead to nutrient deficiencies
- Supplementation and diet changes can help replenish depleted nutrients
- Effective communication strategies include initiating the conversation, asking appropriate questions and meeting people at their level

Questions?

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