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2024 ANNUAL CONVENTION



Understanding and Addressing Drug-Induced Nutrient Depletion

NCPA 2024 Annual Convention and Expo
Columbus, Ohio

Speaker



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Owner

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Pharmacist Learning Objectives

1. Recall medications that can cause vitamin B12, vitamin D, and calcium depletion.
2. Discuss the relationship between HMG-COA reductase inhibitors and Coenzyme Q10.
3. Summarize strategies for implementing clinical nutrition into everyday education within the community pharmacy setting.



Technician Learning Objectives

1. Recall medications that can cause vitamin B12, vitamin D, and calcium depletion.
2. Identify the relationship between HMG-COA reductase inhibitors and Coenzyme Q10
3. Summarize strategies for implementing clinical nutrition into everyday education within the community pharmacy setting.



Populations Vulnerable to Nutrient Deficiencies

- 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



Drug-Induced Nutrient Depletion



Patient presents with symptoms and is started on a medication



Medication helps with original symptoms



DIND starts to have effect on the patient's body



Patient develops another set of symptoms or disease



Patient returns to physician and started on another drug



Process starts all over again

Drug-Induced Nutrient Depletion

Mechanism of Action

- Inhibition of nutrient absorption – **PPI's**
- Inhibition of nutrient synthesis – **Statins**
- Alterations in transport of nutrients across membranes – **Metformin**
- Increase or decrease in metabolism of nutrients – **Estrogens**
- Increase or decrease in excretion of nutrients – **ACE Inhibitors**
- Alteration in the body's ability to store nutrients – **Caffeine, Alcohol**

Examples of Drug-Induced Nutrient Depletion

Drug of Class	Uses	Nutrient(s) Depleted
Proton Pump Inhibitor	Heartburn/acid reflux	Magnesium & B12 Deficiencies may lead to muscle cramps, fatigue, and neurological issues
Statins	Lower cholesterol	CoQ10 Deficiencies may lead to muscle pain and fatigue
Metformin	Diabetes	B12 & Folate (B9) Deficiencies may lead to anemia and peripheral neuropathy
ACE Inhibitors	Lower blood pressure	Zinc Deficiencies may delay wound healing and increase susceptibility to infections.

MCO



Slide 10

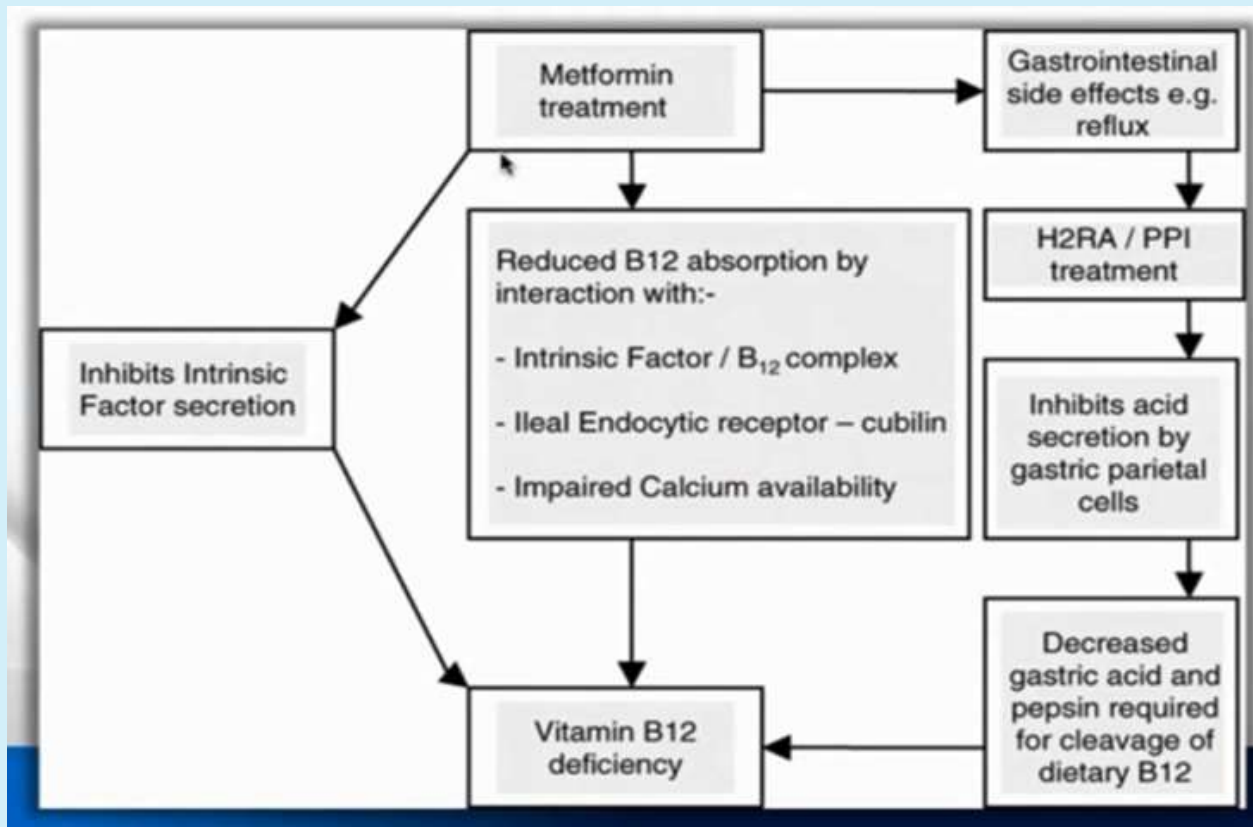
MCO Consider adding calcium and vit. D to better align with learning objective #1
Maria Cho, 2024-10-10T20:01:37.985

Metformin Drug-Induced Nutrient Depletion

- **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

Bjorke Monsen AL, Ueland PM. Homocysteine and methylmalonic acid in diagnosis and risk assessment from infancy to adolescence. *AM J Clin Nutr.* 2003;78(1):7-21.

Metformin Drug-Induced Nutrient Depletion



Metformin and Vitamin B12 deficiency. Dr Hiren Patt D.M.
(Endocrinologist) Satellite, A'bad.

Clinical Studies

Study of Vitamin B₁₂ deficiency and peripheral neuropathy in metformin-treated early Type 2 diabetes mellitus

Indian J Endocrinol Metab. 2016 Sep-Oct;20(5):631-637

Objective: The aim of this study is to define the prevalence of Vitamin B₁₂ deficiency in early Type 2 diabetic patients (duration ≤5 years or drug treatment ≤3 years) and the relationship among metformin exposure and levels of cobalamin (Cbl), folic acid, and homocysteine (Hcy) with severity of peripheral neuropathy.

Conclusion: Even short-term treatment with metformin causes a decrease in serum Cbl folic acid and increase in Hcy, which leads to peripheral neuropathy in Type 2 diabetes patients. A multicenter study with heterogeneous population would have increased the power of the study. We suggest prophylactic Vitamin B₁₂ and folic acid supplementation or periodical assay in metformin user.

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

Common Drugs & Dietary Choices

that Deplete Vitamin B12

MCO

- Acid Blockers
- Antacids
- Antibiotics
- Diabetes medications
- Hormone Replacement Therapies
- SERMs
- Alcohol
- Vegan or Vegetarian diet

Slide 15

MCO Consider changing word "drug" as alcohol and vegan/vegetarian diet is not considered a drug/medication

Maria Cho, 2024-10-10T19:31:15.026

0 0 Gold call out - updated title to reflect!

Elise Damman, 2024-10-15T22:35:57.323

Adding Vitamin B12 to Your Plate



- Primarily animal foods; beef liver, liverwurst, snapper, venison, shrimp (cooked), scallops, salmon, beef, lamb, cod, oysters, sardines, clams, flounder, halibut, yogurt, cow's milk, blue cheese, and eggs
- Vegetarian options: spirulina, brewer's yeast, tempeh, miso, and tofu

Cohen, S. (2011). Drug muggers: Which medications are robbing your body of essential nutrients and natural ways to restore them. Rodale. 2011.

Calcium

- 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

Calcium Deficiency

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

Calcium Depleting Medications

- Corticosteroids
 - Calcium absorption is decreased due to inhibition of vitamin-D-dependent intestinal calcium absorption and increased calcium efflux
- Acid Blockers and Antacids
- Anticonvulsants
- Blood pressure agents
- Hormone Replacement Therapy

Mitchell Bebel Stargrove JT, Dwight L. McKee. *Herb, Nutrient, and Drug Interactions: Clinical Implications and Therapeutic Strategies*. Mosby Elsevier; 2008.

Vulnerable Populations

- Vegetarians
 - Certain components in plants have been shown to inhibit calcium absorption leading to increased susceptibility to calcium deficiency
 - Oxalates and phytates
 - Decreased calcium consumption relative to omnivores
- Lactose Intolerance
 - Estimated effect of $\frac{2}{3}$ of the world's population
 - Need to consume calcium-fortified foods or ensure adequate intake with calcium supplementation

Vulnerable Populations

- Postmenopausal Women
 - Estrogen production and utilization is sharply decreased
 - Can lead to substantial bone and calcium loss
 - Can lead to osteoporotic fractures

Adding Calcium to Your Plate

- Turnip greens
- Spinach
- Mustard greens
- Collard greens
- Basil
- Thyme
- Cinnamon
- Blackstrap molasses
- Kale
- Celery
- Fennel
- Green beans
- Garlic
- Tofu
- Figs
- Quinoa
- Mozzarella cheese
- Cow's milk
- Sardines
- Yogurt



Cohen, S. (2011). Drug muggers: Which medications are robbing your body of essential nutrients and natural ways to restore them. Rodale. 2011.

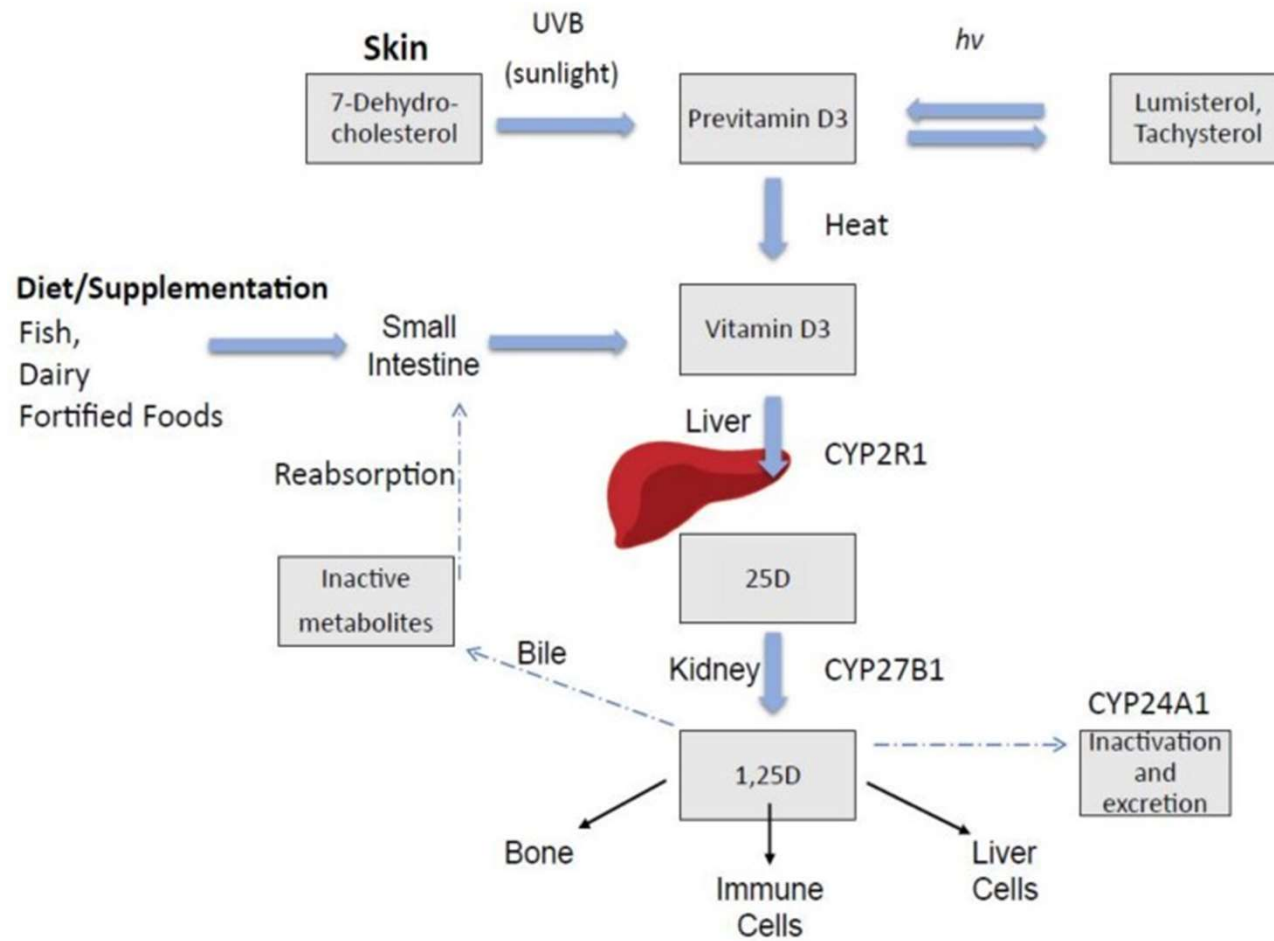
Vitamin D

Essential functions: Fat soluble compound converted in the body to its active form 1,25 Dihydroxyvitamin D

Vitamin D acts via regulation of gene expression facilitated by the action of the vitamin D receptor (Vdr)

Important for normal bone development and maintenance

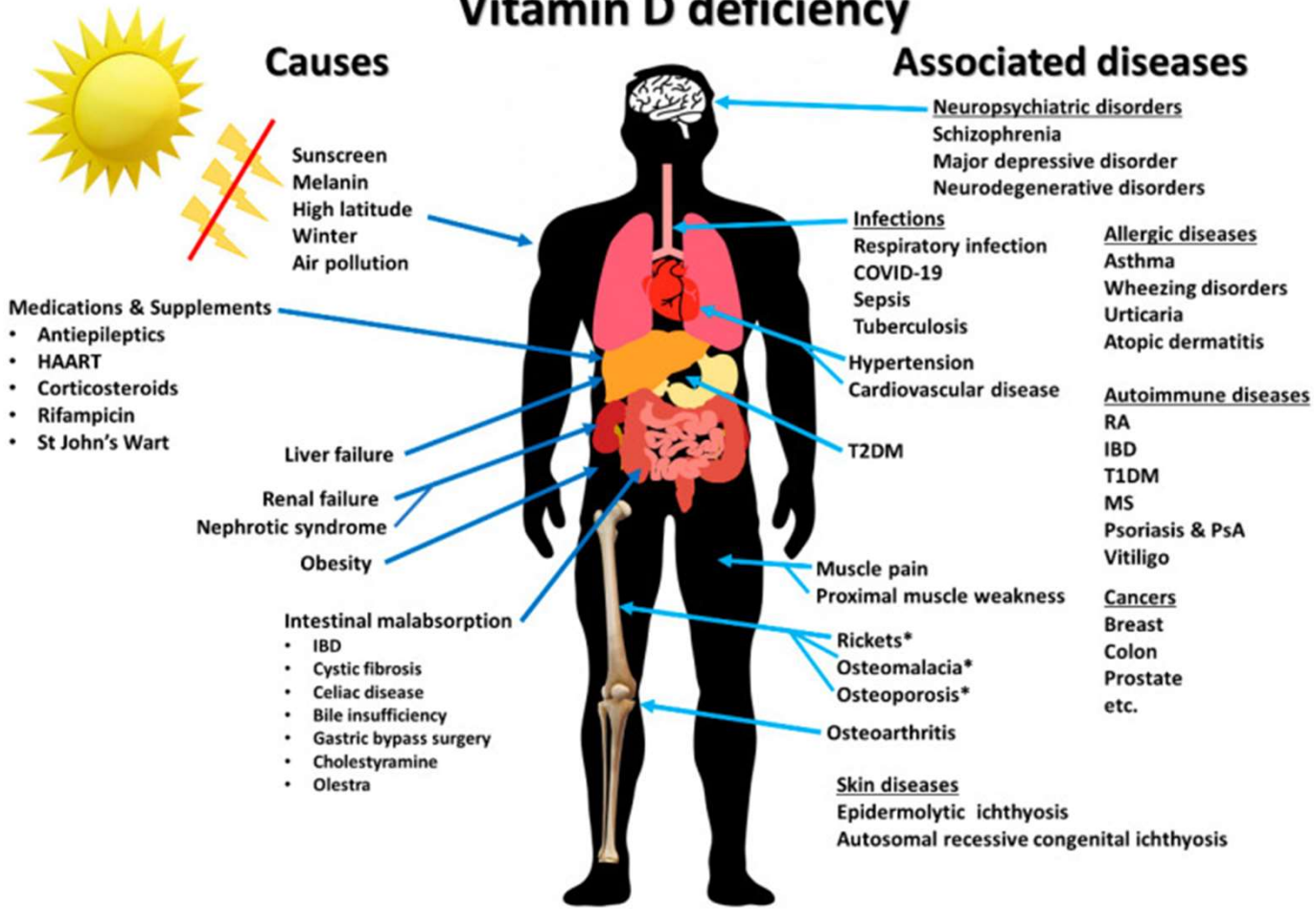
- Regulation of calcium and phosphorus homeostasis



Symptoms of Deficiency

- In children, severe vitamin D deficiency can cause rickets
 - Incomplete bone mineralization which results in skeletal deformities and soft bones
- In adults, weak bones due to osteomalacia
- Muscle weakness
- Bone pain

Vitamin D deficiency



Vulnerable Populations

- Breastfed infants, elderly
- Limited sun exposure/heavily pigmented skin, gastric bypass patients
- Inflammatory bowel disease, liver disease, cystic fibrosis, obesity, victims of severe burns, kidney disease
- Drug-induced depletion (weight loss medications, antiepileptic medications)

Blumberg JB, Frei B, Fulgoni VL, Weaver CM, Zeisel SH. Contribution of Dietary Supplements to Nutritional Adequacy in Various Adult Age Groups. *Nutrients*. 2017;9(12).

Vitamin D Depleting Medications

- Weight loss drugs
 - Orlistat (Alli, Xenical)
 - These drugs inhibit fat absorption and consequently impact absorption of fat-soluble vitamins, like vitamin D
- Antiepileptic Medications
 - Phenobarbital, Phenytoin
 - Increased CYP24A expression, the enzyme that breaks down vitamin D, results in low serum 25(OH)D levels

Robein K, Oppeneer SJ, Kelly JA, Hamilton-Reeves JM, Drug-vitamin D interactions; a systematic review of the literature. *Nutr Clin Pract.* 2013;28(2):194-208

McDuffie JR, Calis KA, Booth SL, Uwaifo GI, Yanovski JA, Effects of orlistat on fat-soluble vitamins in obese adolescents. *Pharmacotherapy.* 2002;22(7):814-822

James WP, Avenella, Broom J, Whitehead J. A one-year trial to assess the value of orlistat in the management of obesity. *Int J Obes Relat Metab Disord.* 1997;21 Suppl 3:S24-30.

Adding Vitamin D to Your Plate

- Wild cold-water seafood, including salmon, mackerel, tuna, sardines, cod, and halibut
- Milk
- Liver
- Egg yolks
- Fortified cereal
- 30 minutes of sunshine daily provides about 10,000 to 20,000 IU Vitamin D

Robein K, Oppeneer SJ, Cohen, S. (2011). Drug muggers: Which medications are robbing your body of essential nutrients and natural ways to restore them. Rodale. 2011.

Coenzyme Q10

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a proenzyme produced naturally within the body

Main Functions

- Energy Production (Enhances cellular energy production)
- Boosts Antioxidant Activity/antioxidant recycling (Vitamin E, Vitamin C, Lipoic Acid)
- Supports Cardiovascular health
- Helps maintain healthy blood sugars
- Promotes neurological health

What depletes our bodies of CoQ-10?

Drugs

- Statins
- Antidepressants
- Sulfonylureas Drugs
- Beta Blockers/ Cardio Medications

Age

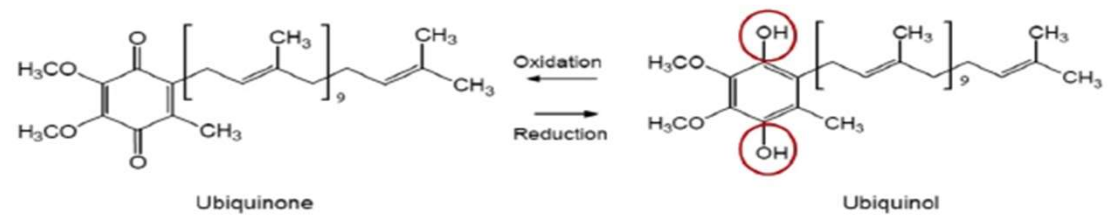
After the age of 35 to 40 years, endogenous synthesis of CoQ10 begins to decline.

Lifestyle Choices

- Oxidative Stress
- Strenuous exercise
- High Sugar Intake
- High Caffeine intake
- High carbohydrate intake
- High Alcohol intake

Statins Deplete Coenzyme Q10

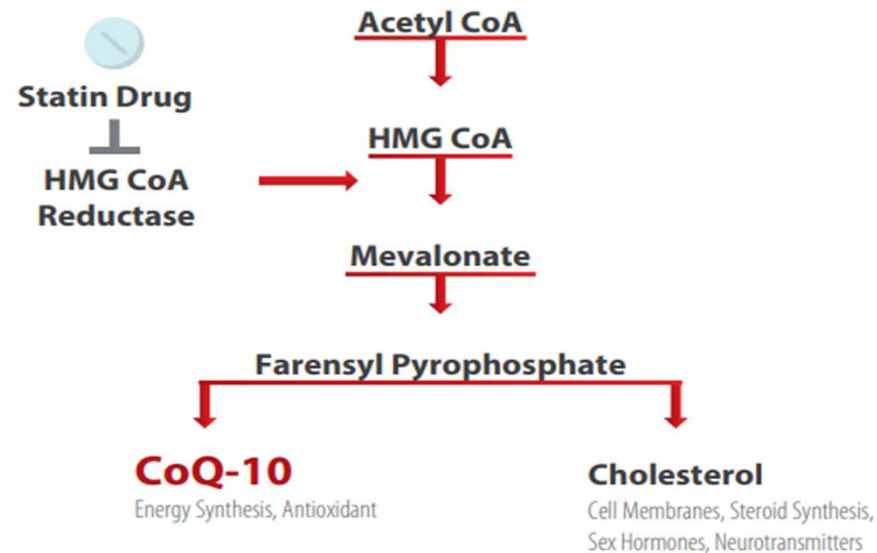
- CoQ-10 is a powerful fat-soluble, vitamin-like substance
- Main functions
 - Energy production
 - & antioxidant recycling
- Two main forms
 - Ubiquinone-oxidized form
 - Ubiquinol-reduced form



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.

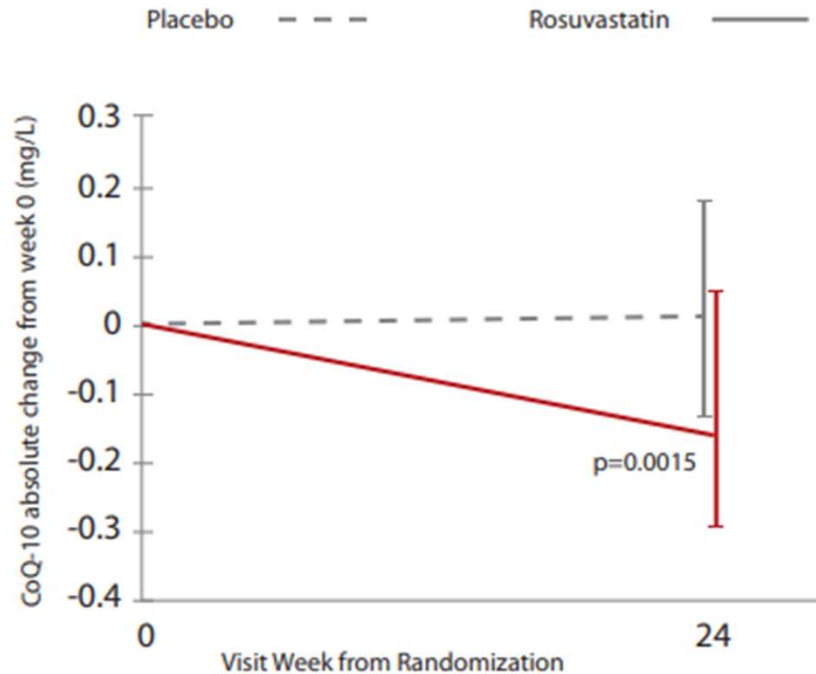
Statin Drug Mechanism of Action

Coenzyme Q-10 Synthesis



Brendan Tan, Franklin Rosenfeldt, Ruchong Ou & Con Stough (2019) Evidence and mechanisms for statin-induced cognitive decline, *Expert Review of Clinical Pharmacology*, 12:5, 397-406, D

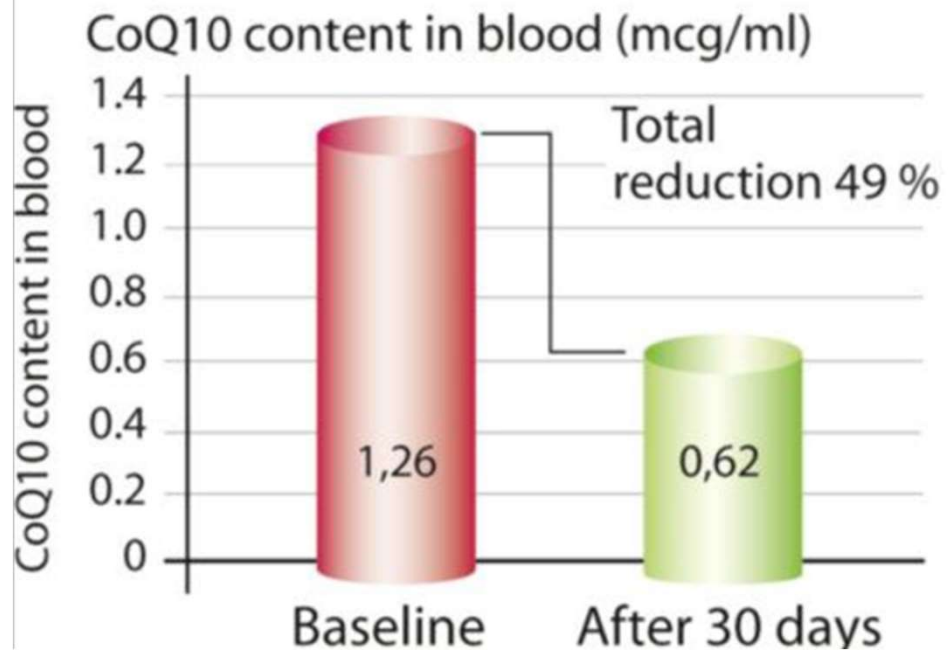
Rosuvastatin depletes plasma CoQ10



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

CoQ10 reduction and statin use



Side effects associated with statins are identical to symptoms of CoQ10 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 CoQ10

Antidiabetic Medications

- Sulfonylureas

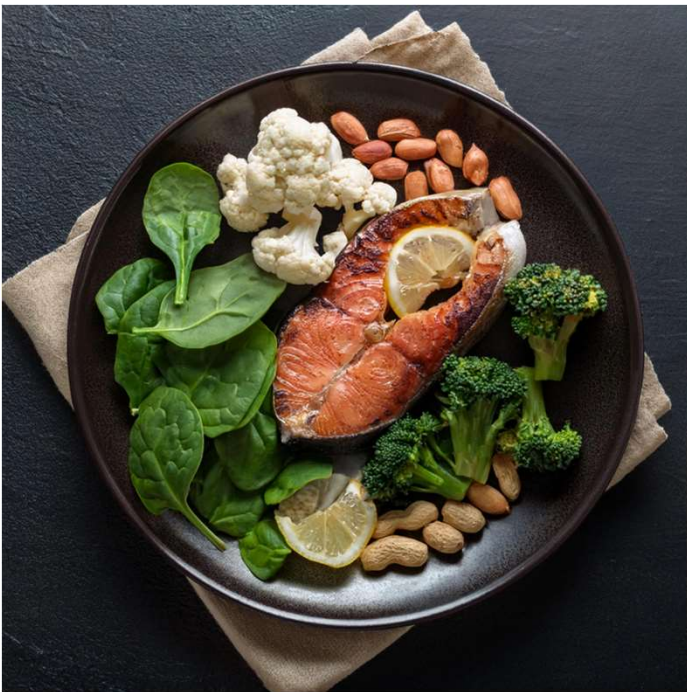
Cardiovascular Medications

- Statin Drugs
- Beta Blockers
- Thiazide Diuretics
- Vasodilators

Lifestyle Choices- Oxidative Stress

- Strenuous exercise
- High sugar intake
- High caffeine intake
- High carbohydrate intake
- High alcohol intake

Adding CoQ10 to Your Plate



- Beef
- Chicken
- Soybean oil
- Rainbow trout
- Peanuts
- Sesame Seeds
- Pistachios
- Broccoli
- Cauliflower
- Organ meats
- Fish (tuna, herring, mackerel, sardines, and salmon)
- Whole grains
- Sesame oil
- Spinach

Cohen, S. (2011). Drug muggers: Which medications are robbing your body of essential nutrients and natural ways to restore them. Rodale. 2011.

Benefit 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

Strategies for implementing DIND into practice

Quick Conversation

“Mrs. Jones, here is your atorvastatin prescription. Our clinical sources show that this medication can deplete an important nutrient from your body over time. This important nutrient is CoQ-10.”

- Offer them information about why the vitamin is important and the symptoms of depletion over time
- Provide valuable information
- Create bag stuffers

Conclusion

- Many populations vulnerable to nutrient deficiencies
- Statin side effects closely relate to Coenzyme Q10 deficiencies
- Vitamin B12 deficiencies can be caused by a few classes of prescription medications
- Calcium, iron, magnesium, vitamin C and D are other deficiencies caused by medications
- Vitamin D is a common nutrient deficiency that can be caused by medications, but is also common in a variety of populations



Question 1

Select the benefit of CoQ10 supplementation

- a. Replacement of statins
- b. Reduction of cholesterol
- c. Improve statin-associated muscle symptoms
- d. Increase statin-associated muscle symptoms



Question 1

Select the benefit of CoQ10 supplementation

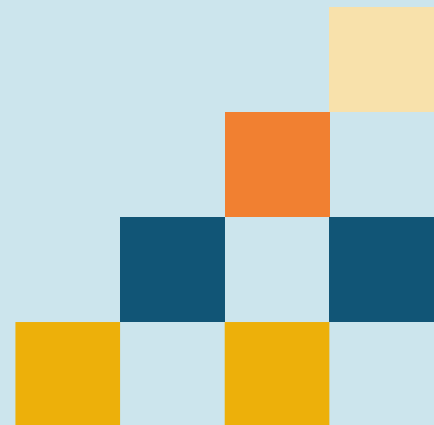
- a. Replacement of statins
- b. Reduction of cholesterol
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- d. Increase statin-associated muscle symptoms



Question 2

Which of the following nutrients do biguanides (metformin) deplete?

- a. Omega 3
- b. Vitamin B12
- c. Vitamin K
- d. Vitamin E



Question 2

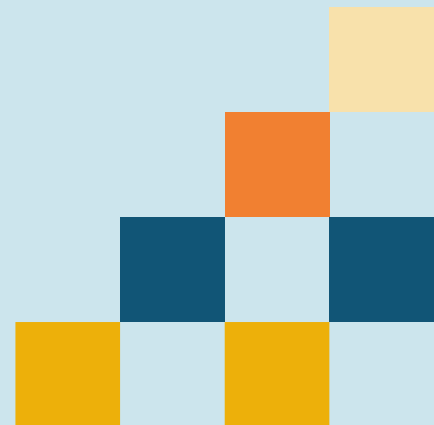
Which of the following nutrients do biguanides (metformin) deplete?

a. Omega 3

b. Vitamin B12

c. Vitamin K

d. Vitamin E



Question 3

Mrs. DeeDee stops by the pharmacy to pick up her Metformin and Atorvastatin. You are a technician ringing her up today. What is an appropriate conversation starter for recommending repletion supplements for her?

- a. The pharmacist recommends Vitamin B12 and CoQ10 since these medications you are taking can reduce your energy levels and cause muscle pain
- b. Looks like metformin is new for you. My pharmacist recommends taking Calcium as well because it will prevent your diabetes from getting worse
- c. These medications you are picking up deplete your Omega 3 fatty acids so it will be great to get started with my pharmacist recommendation today.

Question 3

Mrs. DeeDee stops by the pharmacy to pick up her Metformin and Atorvastatin. You are a technician ringing her up today. What is an appropriate conversation starter for recommending repletion supplements for her.

- a. Vitamin B12 My pharmacist recommends Vitamin B12 and CoQ10 since these medications you are taking can reduce your energy levels and cause muscle pain
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Citations

- Ann Clin Nutr Metab 2022;14(1):20-3
- J Pharm Technol 2018 Jun 20;34(5):216–230
- Brendan Tan, Franklin Rosenfeldt, Ruchong Ou & Con Stough (2019)
Evidence and mechanisms for statin-induced cognitive decline, Expert
Review of Clinical Pharmacology, 12:5, 397-406



Questions?

Thank You!



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