

Vitamins and Minerals

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Objectives

- Fat-soluble and Water soluble vitamins
- Trace minerals (zinc, selenium, copper, chromium, and more)
- Deficiency and Toxicity
- Sources and Recommendations
- Clinical implication

Which food has the most vitamin A?



Sweet potatoes



Beef liver



Cantaloupe

Vitamin A

The benefits of vitamin A:



maintains health of specialized tissues such as the retina

aids in growth and health of skin and mucous membranes

promotes normal development of teeth, soft and skeletal tissue

Adult RDA: 1000 μg RE

Fat-soluble

ADAM.

Vitamin A Deficiency

- Main feature (nyctalopia)
Night blindness, Corneal, conjunctiva
- Dermatitis, keratomalacia
- Phrynoderma (follicular hyperkeratosis):
Blockage of hair follicles with plugs of keratin, Dry, scaly skin on face and thighs



GI patients at risk of Vitamin A deficiency

- Crohn's (small bowel)
- Celiac sprue
- Cholestatic liver disease
- Pancreatic deficiency
- Short gut
- Cystic fibrosis

Vitamin A toxicity

- Arctic explorers who feasted on polar bear liver (10 million IU/lb) - acute overdose.



Vitamin A toxicity: 3 syndromes

- Acute (>660,000 units): n/v; vertigo; blurry vision; drowsiness, malaise
- Chronic (higher than 10X daily values): ataxia; alopecia; hyperlipidemia; hepatotoxicity, bone and msk pain; visual impairments; increase risk osteoporotic fractures (need to avoid >5000 units)
- Teratogenic: first trimester; spontaneous abortion; fetal anomalies

Vitamin B1 (thiamine)

- Antiberiberi factor
- Absorption is in the small intestine
- Catalyst for conversion of pyruvate to acetyl CoA
- Involved in initiation of nerve impulse
- Transketolation of the pentose phosphate pathway



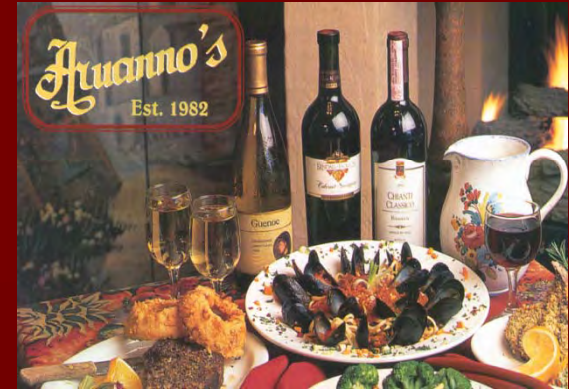
Vitamin B₁



Vitamin B₁ (Thiamine)
is found in fortified breads
and cereals, fish, lean meats and milk

ADAM.

Thiamine Deficiency



- Main features

Beriberi (peripheral neuropathy, CHF, muscle weakness)

Wernicke's Encephalopathy (ataxia, nystagmus, confusion)

Korsakoff's Syndrome (loss of memory, confabulation)

- Treatment - Intravenous, intramuscular, then oral

Often empiric. Need 0.5 mg per 1000 Kcal

Wet Berberi

- Precipitated by a high carbohydrate intake along with strenuous physical exertion with edema due to biventricular heart failure and pulmonary congestion
- Tense calf muscles, fast pulse, distended neck veins, increased BP, decrease UOP
- Administration of glucose in TPN with less than the requirement of thiamine can result in the rapid development of wet beriberi

Dry Beriberi

- Worsening of polyneuritis of early stage
- Loss of function or paralysis of lower extremities
- Wernicke-Korsakoff (need 50 mg per day to treat)
- To treat beriberi (50-100 mg IV per day for 7-14 days) or po 10 mg per day

What is Leigh's syndrome?

- Condition seen in thiamine deficiency
- Subacute necrotizing encephalomyopathy
- Sporadic mitochondrial disorder
- Ataxia, dysarthria, movement disorders, areflexia, muscle atrophy, and weakness

Vitamin B₂

Food sources of Riboflavin (vitamin B₂):

Cereal, nuts, milk,
eggs, green leafy
vegetables
and lean meat



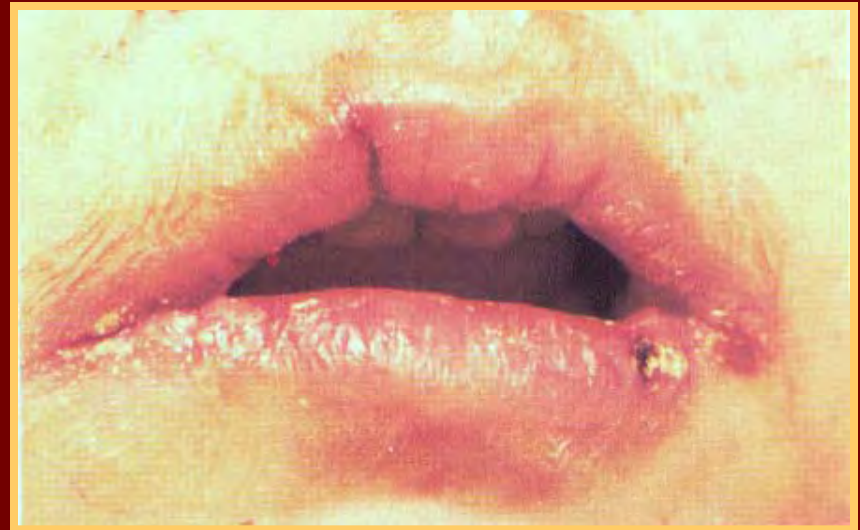
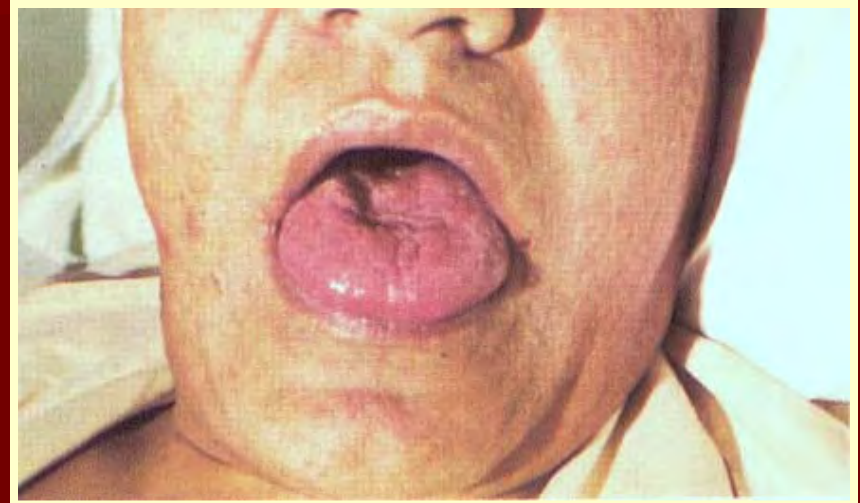
ADAM.

Vitamin B2 (Riboflavin)

- Primarily as a component of coenzymes flavin adenine dinucleotide (FAD) and flavin adenine mononucleotide (FMN)
- Catalyze oxidation-reduction reactions in cells and are hydrogen carriers in the mitochondrial system
- Actively absorbed from the proximal small intestine; absorption increased by the presence of food

Vitamin B2 Riboflavin deficiency

- Intake must be low for several months to develop
- Photophobia, lacrimation, eye irritation, loss of visual acuity, sore lips, mouth, tongue
- Seborrheic dermatitis
- Angular stomatitis; cheilosis (may be in niacin, folic acid, thiamine, B6, B12 deficiency)



Riboflavin deficiency

- More common than generally appreciated
- Urinary riboflavin excretion and the erythrocyte glutathione reductase assay are better functional indices of riboflavin deficiency
- At risk: anorexia; lactose intolerant, celiac sprue, short bowel, rare inborn errors of metabolism, long term use of phenobarbital and other barbiturates (these oxidate riboflavin and impair function)

Riboflavin and HIV

- Patients with HIV who develop lactic acidosis (zidovudine or stavudine) may be treated with riboflavin.
- Some intramitochondrial beta-oxidation defects may respond to riboflavin therapy

Vitamin B3 (Niacin)

- Two forms: nicotinic acid and nicotinamide
- NAD and NADP hydrolyzed in the intestinal lumen to nicotinamide. Nicotinamide converted to nicotinic acid
- Crucial in oxidation of fatty acids and synthesis and metabolism of CHO, fatty acids and proteins

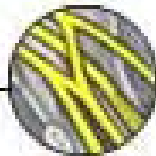
Vitamin B₃



Food sources of Niacin (vitamin B₃) include dairy, poultry, fish, lean meat, nuts and eggs

Vitamin B₃

Niacin (vitamin B₃) works with other B vitamins to help release energy from carbohydrates



Healthy nerves

Healthy skin

Healthy digestive system

Adult RDA: 19 mg

Water-soluble

ADAM.

Vitamin B₃



An inability to absorb niacin (vitamin B₃) or the amino acid tryptophan may cause pellagra, a disease characterized by scaly sores, mucosal changes and mental symptoms

 ADAM.

Niacin Deficiency

- Main features - 4 "D's"

Diarrhea

Dermatitis

Dementia

Death

- Carcinoid syndrome because

tryptophan is metabolized to 5-OH tryptophan and serotonin rather than to nicotinic acid

- Prolonged use of **isoniazid** since isoniazid depletes stores of pyridoxal phosphate, which enhances the production of tryptophan, a precursor of niacin



Niacin Deficiency



Pellagra
Casal's Necklace

Hartnup disease

- Autosomal recessive congenital disorder
- Defect in transport of tryptophan
- Diagnosis by detecting a number of neutral amino acids in the urine (not seen with dietary pellagra)

Niacin toxicity

- Flushing, n/v/pruritus, hives, elevation in serum aminotranferases and constipation; myopathy (doses of 1000-3000 mg/day)
- Hyperglycemia, hyperuricemia (caution in those with gout)
- 60 mg tryptophan = 1 mg niacin

Vitamin B5 (Pantothenic Acid)

- Coenzyme A (CoA)
- Essential in first step of the tricarboxylic acid cycle, crucial role in the synthesis of many molecules (A,D, cholesterol, steroids, heme A, FA, AA, and proteins)
- No known toxicity

Vitamin B6 (pyridoxine)

- Three interchangeable forms. (pyridoxal phosphate (PLP) and pyridosamine phosphate (PMP) are critical coenzymes for transamination; upper small intestine absorbs and phosphorylates
- Involved in decarboxylation of amino acids, gluconeogenesis, conversion of tryptophan to niacin, sphingolipid biosynthesis, neurotransmitter synthesis, immune function, and steroid hormone modulation

Vitamin B6



Vitamin B6 (pyridoxine) is important for maintaining healthy brain function, the formation of red blood cells, the breakdown of protein and the synthesis of antibodies in support of the immune system

Adult RDA: 2 mg

Water-soluble

 ADAM.

Not found in typical MVI (centrum)

Vitamin B6

Food sources of vitamin B6 (pyridoxine) include beans, legumes, nuts, eggs, meats, fish breads and cereals



Vitamin B6 deficiency

- Nonspecific stomatitis, glossitis, cheilosis, irritability, confusion, and depression
- Genetic syndromes affecting PLP dependent enzyme mimic deficiency (homocystinuria, cystathionuria)

Vitamin B6 toxicity

- Requires long term megadoses 250 mg/day
- Peripheral neuropathy
- Dermatoses
- Photosensitivity
- Dizziness
- Nausea

Biotin (Vitamin B7)

- Biotin acts as CO₂ carrier on the surface of enzymes (carboxylases); essential role in protein in DNA synthesis and cell replication
- Gut bacteria produces it; mostly absorbed in small intestine

Biotin Deficiency

- May occur in patients on Chronic TPN
- Conjunctivitis, Dermatitis around the eyes, nose and mouth, alopecia with loss of normal hair coloring, skin infections, and neurologic symptoms such as ataxia, hypotonia, increase cholesterol, and severe lethargy, depression, and possibly parasthesia and hallucinations



Before

After

Vitamin B₁₂

Food sources of
vitamin B₁₂:

Eggs, meat, poultry,
shellfish, milk and
milk products



ADAM.

Vitamin B12

- Required for DNA synthesis (transfers methyl group)
- Meat and dairy products are the only source for humans

Vitamin B12 absorption

- Gastric acid/pepsin releases it from food protein
- B12 binds to R protein (from salivary gland and gastric mucosa)
- B12-R requires pancreatic proteases to release B12; need acid environment
- B12 then binds to intrinsic factor (parietal cells) to facilitate absorption in the ileum

Causes of B12 deficiency

- Gastric abnormalities (gastrectomy)
- Pernicious anemia (autoimmune attack on IF)
- H.Pylori infection, *Diphyllobothrium Latum*
- Small bowel disease (ileal resection/bypass; crohn's)
- Pancreatitis (pancreatic insufficiency)
- Diet (vegan, chronic alcoholism)
- Agents that block absorption
 - Neomycin
 - Biguanides (eg, metformin)
 - PPI
 - N2O anesthesia inhibits methionine synthase

Vitamin B12 deficiency

- Megaloblastic anemia
- Neurologic abnormalities
- Demyelinating disorder
- Painful paresthesias and loss of proprioception (symmetrical Legs > arms)
- Hypospermia
- Glossitis

Vitamin C

- Ascorbic acid absorbed in the distal small intestine
- Provides electrons needed to reduce molecular oxygen
- Greatest concentrations are found in the pituitary, adrenal, brain, leukocytes, and the eye

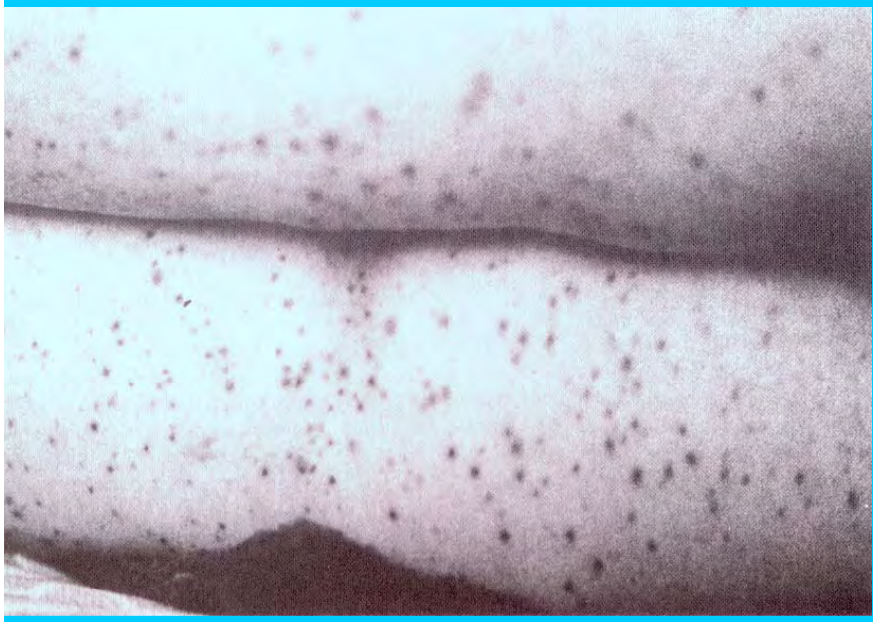
Vitamin C

- Fatty acid transport (long chain fatty acids)
- Collagen synthesis
- Neurotransmitters
- Prostaglandin metabolism

Scurvy

- Impaired collagen synthesis
- Occur as early as three months
- Ecchymoses
- Bleeding gums
- Petechiae
- Hyperkeratosis
- Sjogren's syndrome
- Arthralgias
- Impaired wound healing
- Weakness
- Joint swelling
- Coiled hair
- Neuropathy
- Vasomotor instability
- Need 10 mg to prevent

Scurvy



Vitamin C deficiency

- Drug and alcohol abusers
- Low intake associated with gastric cancer; but supplementation has not been studied
- Note breast milk provides ADEQUATE source
- Elderly, institutionalized, or chronically ill patients at risk

Vitamin C Toxicity

- Requires one gram quantities
- False negative stool guaiac
- Diarrhea and abdominal bloating
- Fatal cardiac arrhythmias in patients with iron overload (due to oxidative injury)
- Controversy: risk factor for calcium oxalate stones (patients who predisposition or on hemodialysis should avoid excessive)



Vitamin D (calciferol)

- Role in calcium homeostasis and bone metabolism
- May have a role in inhibiting the carcinogenic effects of bile acids through calcium binding in the bowel lumen

Vitamin D



The body itself makes vitamin D when it is exposed to the sun

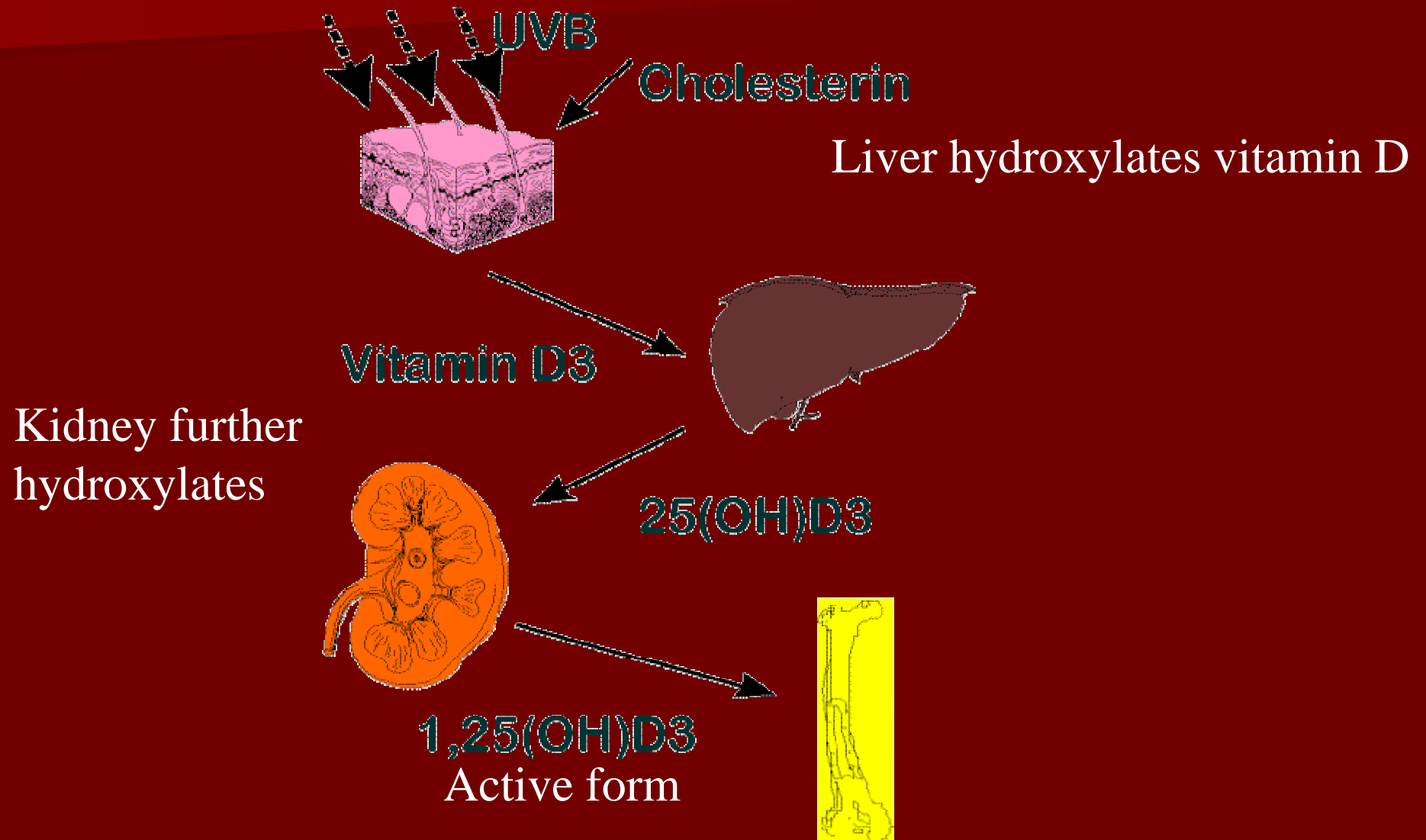
Cheese, butter, margarine, fortified milk, fish and fortified cereals are food sources of vitamin D



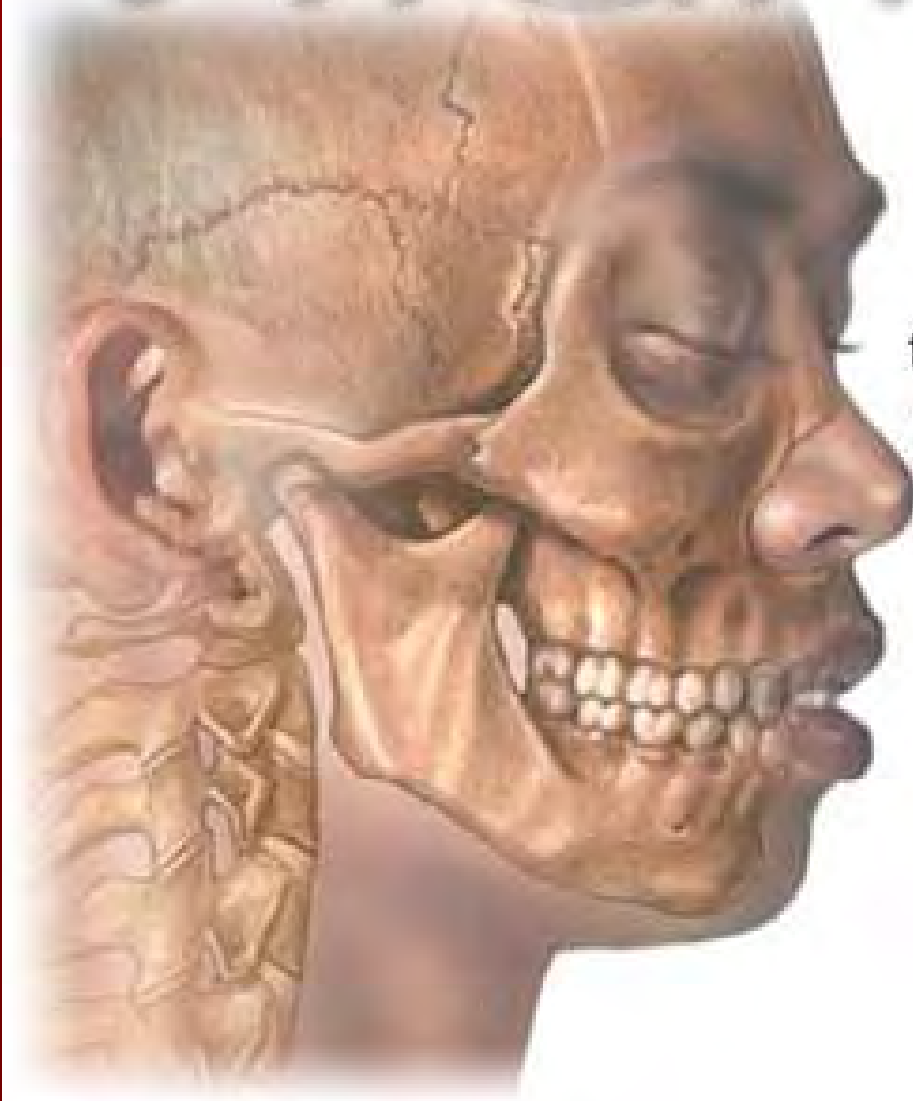
ADAM.

Metabolism

Skin photoisomerization from D to D3



Vitamin D



Vitamin D promotes the body's absorption of calcium, essential to development of healthy bones and teeth

DRI: 5 μg

Fat-soluble

 ADAM.

Causes of Vitamin D deficiency

- Decreased intake/ Insufficiency sunlight
- Fat malabsorption (celiac disease, pancreatic insufficiency, IBD, cystic fibrosis, post-gastrectomy states, and small bowel resection)
- Impaired liver/kidney
- Symptoms: Rickets, osteomalacia, hypophosphatemia (more than hypocalcemia), muscle weakness, phosphaturia

Bone Mineral Abnormalities in IBD

Diet

rich in calcium as simple, effective means of prophylaxis against osteopenia/porosis

- Encourage 1.5g dietary calcium per day

- Supplement with calcium/vitamin D

 - Adequate po Ca/vit D doesn't improve bone density in patients on steroids¹

 - Vit D supplementation does prevent bone loss²

 - Bisphosphonate to build bone while on steroids

- Dietary supplementation important in overall in preventing and treating bone loss in IBD patients

1. Bernstein Aliment Pharm Ther 1996; 10: 777-86

2. Vogelsang Eur J Gastro 1995; 7: 609-14

Vitamin D Toxicity

- Minimum 200 IU/day; Pregnancy 400 IU/day; Must be with calcium to prevent fracture
- If children $>1,800$ IU or adults $>2,000$ IU toxic
- Excessive calcification of bone, kidney stones, metastatic calcification of soft tissues (kidney and lung) headache, weakness, n/v, constipation, polyuria, polydipsia

Vitamin E (Tocopherol)

- Eight naturally occurring compounds (alpha, beta, gamma, and delta)
- Free radical scavenger, protecting polyunsaturated fatty acids (PUFA), a major structural component of cell membranes from peroxidation

Vitamin E

Tocopherol



Vitamin E is found in corn, nuts, olives, green, leafy vegetables, vegetable oils and wheat germ, but food alone cannot provide a beneficial amount of vitamin E, and supplements may be helpful

ADAM.

Vitamin E metabolism

- Dependent on breakdown of fatty acids and uptake via enterocytes to the enterohepatic circulation
- Synthesis of chylomicrons are required for transport of vitamin E via the lymphatic system to the liver
- Within hepatocytes chylomicron remnants are broken down by lysosomes, and RRR- α -tocopherol is preferentially secreted into the bloodstream, packaged within VLDL

Vitamin E

- Reduced plasma and hepatic vitamin E levels have been reported in liver disease
- Vitamin E has antioxidant/anti-inflammatory properties

Vitamin E deficiency: RARE

- At risk: cirrhosis, cholestatic liver disease, cystic fibrosis, small bowel bacterial overgrowth, pancreatic insufficiency, gluten sensitive enteropathy, regional enteritis
- Deficiency proportional to magnitude and duration of steatorrhea
- Skeletal myopathy, spinocerebellar ataxia, pigmented retinopathy; hemolytic anemia (G-6-PD) deficiency; areflexia

Vitamin E toxicity: Unusual

- May interfere with vitamin K, arachidonic acid metabolism
- Large oral supplements associated with necrotizing enterocolitis in infants
- Headache, Myopathy
- Vitamin E supplementation with a dose \geq 400 IU/day was associated with a significantly increased risk of all-cause mortality

Vitamin K: 3 forms

- Phylloquinone: green plants
- Menaquinone: formed as the results of bacterial action in the intestinal tract
- Water-soluble form (K1 and K2)
- None of the forms are stored in appreciable amounts
- Destroyed by alkali and light

Vitamin K metabolism

- Requires pancreatic and biliary function for intact absorption
- Protein bound and requires pancreatic enzymes in the small intestine for liberation

Vitamin K function

- Cofactor for carboxylase
- Vitamin K essential for activity of clotting factors 7,9,10 prothrombin, and anticoagulant protein C and S

Vitamin K deficiency

- Risk: TPN, long term antibiotics
- Easy bruisability, mucosal bleeding, splinter hemorrhages, melena, hematuria
- Hemorrhagic disease of the newborn: develops within the first week of life

Vitamin K Toxicity

- Infants: hemolytic anemia; hyperbilirubinemia, jaundice, and kernicterus
- With rapid IV infusion possible flushing and cardiovascular collapse

Folic acid

- Established as essential in 1946
- Nurses' Health Study found that women who consumed folate-containing supplements daily for 15 years were 75% less likely to develop colorectal cancer
- The Health Professionals Follow-up study showed a moderate risk reduction in men receiving folate for more than 10 years

Vitamin B9 Folate

Food sources of folate include beans and legumes, citrus fruits and juices, whole grains, dark green leafy vegetables, poultry, pork, shellfish and liver



ADAM.

Folate

- Coenzyme in transport of single-carbon fragments in amino acid metabolism and nucleic acid synthesis
- Usually present in polyglutamate form requires folyl conjugase from pancreas and mucosal conjugase from small intestine for absorption

Causes of Folate Deficiency

- Nutritional deficiency (substance abuse, etoh, poor diet, overcooked foods, depressed patient, nursing home)
- Malabsorption (sprue, IBD, infiltrative bowel disease, short bowel syndrome)
- Drugs (methotrexate, trimethoprim, ethanol, phenytoin, sulfasalazine)
- Increased requirements (pregnancy, lactation, chronic hemolysis, exfoliative dermatitis)
- Need: 200-400 micrograms/day

Folate deficiency

- Alcohol abuse on low folate intake can develop megaloblastosis within 5 to 10 weeks (impairs enterohepatic cycle and inhibits its absorption)
- Glossitis, intestinal mucosal dysfunction, megaloblastic anemia (no neurologic abnormalities)

Selected Trace Microminerals

Zinc, Copper, Selenium,
Chromium, Manganese,
Molybdenum

Zinc

- Required for zinc metalloenzymes and zinc finger proteins
- 1/3 of ingested zinc absorbed
- Acrodermatitis enteropathica: hereditary disease of impaired zinc absorption

The acute phase response is thought to be a beneficial reaction for the host. The two most widely accepted reasons for altered zinc metabolism following stress are:

- “Withholding” zinc makes an unfavorable environment for bacterial growth
- Increased hepatic zinc facilitates increased hepatic priority protein synthesis

Conditions that alter Zinc Metabolism

■ Intestinal Processes

- IBD
- Short bowel
- Jejunioileal bypass
- Sprue
- Diarrhea

■ Pancreatic disease

- Schwachman's syndrome
- CF

■ Liver disease

- ETOH
- PBC
- Viral hepatitis

■ TPN

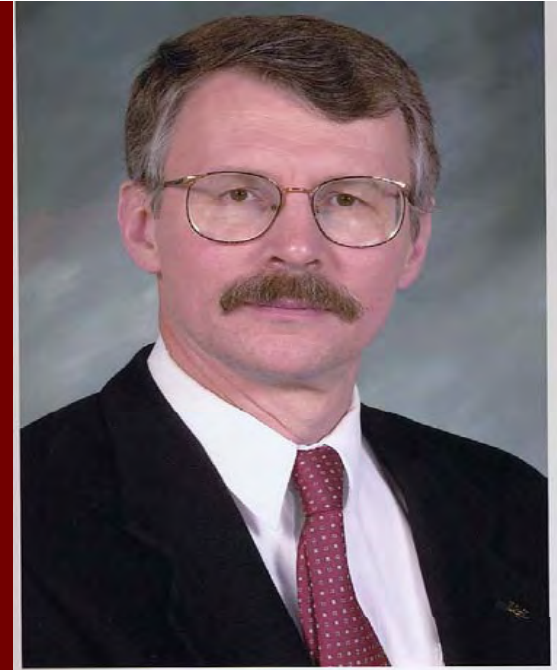
■ Sepsis/trauma

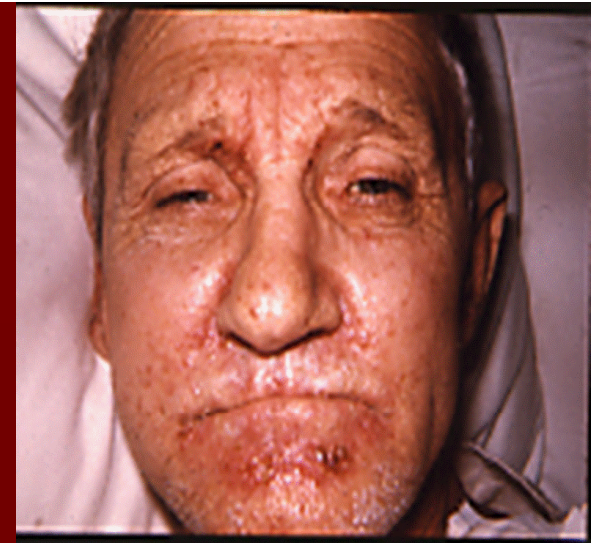
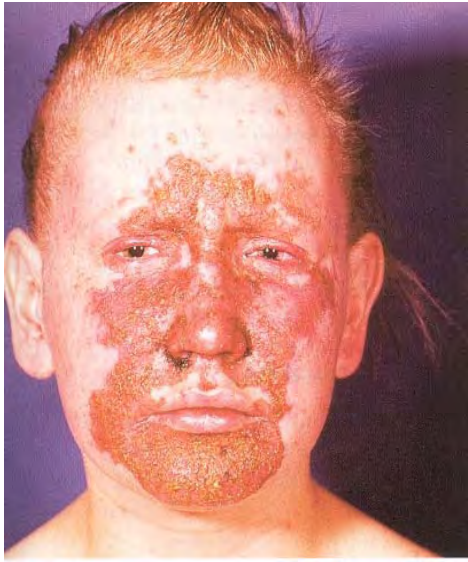
■ Eating disorders

■ Aging

McClain's Top 10 Manifestations of Zinc deficiency

- Skin lesions (acrodermatitis)
- Growth retardation
- Anorexia
- Poor wound healing
- Decreased night vision
- Hypogonadism
- Impaired immune function
- Diarrhea
- Depressed mental function
- Teratogenesis





Copper

- Cofactor for several oxidoreductases
- Risk of deficiency: CF; Crohn's disease, malabsorptive disorders; patients taking excess zinc

Copper

- Zinc induces metallothionein and IMPAIRS copper absorption; excess zinc may lead to deficiency
- Copper deficiency results in anemia NOT responsive to iron supplementation, neutropenia, and less often hypopigmentation, immune dysfunction and skeletal abnormalities

Copper Deficiency

- Main feature
Iron deficiency anemia
- Issues
Coenzyme for oxidation
of ferrous → ferric iron
Impaired iron absorption,
marrow utilization
- Other features - leukopenia
ageusia (taste)
- Diagnosis - clinical suspicion, serum copper, ceruloplasmin
- Toxicity – hepatic necrosis, coma, ARF; hypotension



Selenium

- Selenomethionine
- Required cofactor for protein and DNA synthesis
- Deficiency was seen in chronic TPN users with cardiomyopathy and skeletal muscle dysfunction
- Keshan disease: endemic cardiomyopathy that affects children and women of childbearing age in areas of China

Selenium Deficiency

- Main features

- Congestive heart failure
(Keshan syndrome)

- Muscle weakness

- Issues

- Related to soil content (mainland)

- Not included in most MVI

- Key component of glutathione peroxidase
(anti-oxidant free radical scavenger)

- Complements anti-oxidant properties of Vit E

- Diagnosis - clinical suspicion only



Iodine

- Used for synthesis of triiodotyrosine (T3) and thyroxine (T4)
- Deficiency: Goiter and hypothyroidism
- Cretinism: mental deficiency, spastic diplegia or quadriplegia, deaf mutism, dysarthria, shuffling gait, shortened stature, and hypothyroidism
- Toxicity: Goiter, hypo or hyperthyroidism



Chromium

- 1957 extracted from pork kidney termed "glucose tolerance factor") corrected hyperglycemia in rats
- In patients with diabetes requiring TPN, chromium deficiency was indicated by increased insulin requirements
- Required for normal lipid and carbohydrate metabolism

Chromium Deficiency

- Main feature - Glucose intolerance
 - Insulin resistance
- Issues
 - Cofactor to insulin for cellular glucose absorption
 - Glucose Tolerance Factor (GTF)
- Other features
 - Poor wound healing
 - Neurologic - peripheral neuropathy, ataxia

Manganese

- Deficiency first reported 1972
- Component of several enzymes; requires bile for absorption
- Deficiency: weight loss, transient dermatitis, n/v; changes in color, and slow growth of hair; sterility
- Striking skeletal abnormalities and ataxia in offspring in deficient mothers

Manganese toxicity

- Miners
- Accumulates in liver
- Accumulates in CNS
- Parkinson-like symptoms
- Iron deficiency enhances absorption

Molybdenum

- Required for several enzymes (xanthine oxidase and flavoproteins)
- Deficiency in long term TPN: mental changes and abnormalities in sulfur and purine metabolism
- Toxicity: gout like syndrome

What vitamins are in TPN?

- Vitamin A, D, E
- Ascorbic acid, folate, niacin, riboflavin, thiamin, pyridoxine, B12, pantothenic acid, biotin
- Trace minerals: zinc, copper, chromium, and manganese
- Single minerals: selenium and molybdenum separate

Anemia Due to Nutrient Deficiencies

Macrocytic

B₁₂
Folate

Microcytic

Iron
Copper

Normocytic

Vit K
Early iron
Mixed

Neurologic Abnormalities Due to Nutrient Deficiencies

Muscle weakness

Selenium

Vit E

Thiamine (Beri Beri)

Hypophosphatemia

Dementia

Niacin

Thiamine (Wernicke's, Korsakoff)

Ataxia

B₁₂

Thiamine (Wernicke's)

Chromium

Visual impairment

Vit A (night blindness)

Thiamine (nystagmus)

Rash due to Nutrient Deficiencies

Perifolliculitis -

Vit C

Dry skin -

Zinc

Vit A

Protein

Essential fatty acid

Crusting exudative -

Niacin (pellagra)

Zinc

Ecchymoses -

Vit K

Chelosis -

Riboflavin, B series

Wound-Healing Power Pack



- Zinc
- Vitamin C

- Chromium
- Vitamin A

Thank You

Dr. McClain



Dr. McClave



Dr. Tiu

