

UC San Diego

Independent Study Projects

Title

Supplemental Study Resources and Assessment Questions for MS1 Nutrition Thread

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<https://escholarship.org/uc/item/7hk9b4fs>

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Publication Date

2016

Micronutrient Index

Overview of supplemental modules provided for additional study

The Behavioral and Social Science Foundations for Future Physicians reports, “Over 50 percent of premature morbidity and mortality is caused by behavioral and social determinants of health such as smoking, diet, exercise, and socioeconomic status.” Schlair and colleagues (2012) share another statistic that 70% of adults in America are overweight or obese. What people eat plays a major role in their predicted health outcomes. Doctors have an obligation to educate their patients on lifestyle changes, even if it is only a few words or suggestions each visit. Unfortunately, many physicians today do not offer advice on nutrition to patients because they either do not have the know-how or they are not confident to do so (Schlair et al, 2012). In a survey that Schlair and colleagues conducted, doctors felt more confident counseling their patients on nutrition once they were offered an education course about the basics of diet improvement.

Studies have also shown that improving one’s own health and habits improves counseling to a patient (Schlair et al, 2012). Certainly, doctors should practice what they preach (Kushner et al, 2013). If they live the healthy lifestyles that they tell their patients to endorse, physicians will undoubtedly gain more credibility in the eyes of their patients and strengthen their relationships with them.

The study modules that follow were designed to enhance medical student learning in the first year Nutrition Thread. As expressed above, nutrition education is integral to creating well-rounded physicians especially with the obesity epidemic running rampant in this nation. These modules provide a condensed overview of the most valuable vitamins and minerals that the human body requires to function adequately and thrive. They should serve as supplemental study resources to the course material taught in lectures throughout the Nutrition Thread. Salient points listed in these modules will also appear on assessments (both weekly quizzes and exams), so it is recommended that students use them as a reference throughout the year.

Listed below is an abbreviated outline of the vitamins and minerals included in the modules.

Vitamins	Minerals
= essential, organic substances needed in small amounts in the diet; they are not a source of energy, but instead aid in growth, development, and maintenance of body tissues	= inorganic substances critical to many body functions, including cell metabolism, nerve impulse transmission, growth and development
<i>Fat soluble vitamins:</i> So named because they dissolve in organic solvents <ul style="list-style-type: none">• Vitamins A, D, E, K	<i>Major minerals:</i> reasonably large quantities in food, present in large amounts in body <ul style="list-style-type: none">• Electrolytes: sodium, chloride, potassium• Calcium, phosphorus, magnesium
<i>Water soluble vitamins:</i> So named because they dissolve in water <ul style="list-style-type: none">• Vitamin C, thiamin, folate, vitamin B12, vitamin B6, niacin, biotin, pantothenic acid, riboflavin	<i>Trace minerals:</i> small quantities in food, minute stores in body <ul style="list-style-type: none">• Iron, copper, zinc, iodine, manganese, selenium, fluoride, chromium, molybdenum

Other helpful definitions when studying from these modules:

- Recommended Dietary Allowance (RDA): average daily level of intake sufficient to meet the nutrient requirements of nearly all (97-98%) healthy individuals
- Adequate intake (AI): established when evidence is insufficient to develop an RDA and is set at a level assumed to ensure nutritional adequacy
- Upper Limit (UL): maximum daily intake unlikely to cause adverse health effects

Resources

ods.od.nih.gov

The NIH provides a comprehensive database of major vitamins and minerals. Much of the information provided in the study modules was drawn from this resource.

“Report of the Behavioral and Social Science Expert Panel.” Behavioral and Social Science Foundations for Future Physicians. Association of American Medical Colleges. 2011.

www.aamc.org/socialsciencesfoundation

Schlair S, Hanley K, Gillespie C, Disney L, Kalet A, Darby P, Frank E, Spencer E, Harris J, Jay M. Medical students' behaviors and attitudes affect the impact of a brief curriculum on nutrition counseling. *J Nutr Educ and Behav*; 2012; 44 (6); 633-637.

Kushner RF, Van Horn L, Rock CL, Edwards M, Bales CW, Kohlmeier M, Akabas SR. Nutrition education in medical school: A time of opportunity. *American Journal of Clinical Nutrition*, in press.

Nutrient Summary Sheet

***Disclaimer—The facts on this page are by no means comprehensive as compared to the Supplemental Study Materials from which they originate. You may be tested on material presented in the complete modules that is not found within the summary pages of this document.*

FAT SOLUBLE VITAMINS

Nutrient	Major function	RDA in adult	UL in adult	Clinical significance
Vitamin A	Vision and regulation of cell proliferation and differentiation	700-900 mcg	3000 mcg	-Main source of retinoic acid and retinaldehyde, active forms of the vitamin -Deficiency causes corneal ulceration (keratomalacia), Bitot's spots, follicular hyperkeratosis, impaired immune function, and night blindness
Vitamin D	Calcium absorption and resorption	15 mcg or 600 IU	100 mcg or 1500 IU	-UV rays from sun help convert precursor to vitamin D in skin, but exogenous source is also necessary to meet requirements -It should be supplemented to breastfeeding infants and is added as a fortificant to infant formula -Deficiency causes rickets in children and osteomalacia in adults
Vitamin E	Antioxidant	15 mg	1000 mg	-Deficiency causes hemolytic anemia and impaired immune function
Vitamin K	Coagulation and bone health	75 mcg	N/A	-Newborns at risk of deficiency and consequently hemorrhagic disease of the newborn, so AAP recommends all neonates receive parenteral supplement at birth -Deficiency causes impaired coagulation, resulting in bruising, mucosal bleeding, splinter hemorrhages, melena, and hematuria

WATER SOLUBLE VITAMINS

Nutrient	Major functions	RDA in adult	UL in adult	Clinical significance
Vitamin C	Collagen synthesis, protein and fatty acid metabolism, immunity, non-heme iron absorption	75-90 mg	2000 mg	-Deficiency results in clinical syndrome of scurvy – starts as gum inflammation and progresses to petechiae, ecchymosis, purpura, joint pain, poor wound healing
Thiamin	Branched chain amino acid and carbohydrate metabolism	1.1-1.2 mg	N/A	Clinical deficiency can manifest as: 1. Beriberi syndrome: peripheral polyneuropathy sometimes involving development of heart failure 2. Wernicke-Korsakoff syndrome: triad of ophthalmoplegia/nystagmus, ataxia with wide base, and mental status disturbances – usually

				alcoholics 3. Leigh syndrome: rare, causes infant encephalopathy
Folate	Nucleic acid synthesis	400 mcg	1000 mcg	-Deficiency results in megaloblastic anemia, which is clinically similar to vitamin B12 deficiency; however, folate stores are depleted within months while B12 deficiency takes years to develop -Folate supplementation during pregnancy reduces the risk of preterm delivery and neural tube defects
Vitamin B12	Nucleic acid synthesis and neurologic function	2.4 mcg	N/A	-Good stores in liver and small requirements, so takes years to deplete (vs. folate) -Vegans at risk of deficiency due to lack of animal products in diet -Clinical deficiency manifests as megaloblastic anemia; more severely, subacute combined degeneration -Patients taking long term PPI's should have periodic B12 monitoring
Vitamin B6	100s of coenzyme reactions	1.3 mg	100 mg	-Deficiency usually occurs with other vitamin deficiencies, including B12 and folate; symptoms include neuropathy, seizure, dermatitis, anemia -Toxicity can occur from excess supplementation; results in irreversible nervous system damage
Niacin	Oxidation/reduction reactions involved in energy metabolism	14-16 mg	35 mg	-Deficiency causes pellagra, a clinically syndrome involving the triad of dementia, dermatitis, and diarrhea -Toxicity causes flushing, GI upset, liver damage
Biotin	Coenzyme for carboxylation reactions in energy metabolism	30 mcg	N/A	-Excessive consumption of raw eggs can lead to deficiency; symptoms include rash, alopecia, and neurologic deficits -Inherited biotinidase deficiency occurs in 1 in 100,000 infants, which subsequently causes biotin deficiency
Pantothenic acid	Energy and fatty acid metabolism	5 mg	N/A	-Ubiquitous in foods, so deficiency very rare
Riboflavin	Coenzyme in energy metabolism	1.1-1.3	N/A	-Deficiency usually occurs with other vitamin deficiencies; clinically manifests as ariboflavinosis, which causes mouth and skin lesions, anemia, and constitutional symptoms

ELECTROLYTES

Nutrient	Major functions	RDA in adult	UL in adult	Clinical significance
Sodium	Body water balance, muscle contraction and nerve	1500 mg	2300	-Hyponatremia: caused by volume loss or overload and SIADH; asymptomatic if slow developing; rapid development causes nausea/vomiting then delirium, seizure, coma

	conduction			-Hypernatremia: caused by diabetes insipidus or states where patient cannot express thirst; patient's experience symptom of thirst; progression causes altered mental status, seizure, other movement disorder
Chloride	Body water balance, acid base balance in lungs, acid component in stomach	Adequate intake: 2300 mg	3600 mg	-Hypochloremia: common in vomiting; severe depletion causes weakness, anorexia, lethargy
Potassium	Body water balance, muscle contraction and nerve conduction	Adequate intake: 4700 mg	18 g	-Hypokalemia: causes include gastrointestinal loss, renal disease, drugs; symptoms include weakness and muscle cramps progressing to arrhythmia and paralysis -Hyperkalemia: causes include metabolic acidosis, drugs, rhabdomyolysis; most serious effect is arrhythmia, which can progress to ventricular fibrillation, which is fatal

MAJOR MINERALS

Nutrient	Major functions	RDA in adult	UL in adult	Clinical significance
Calcium	Bone integrity, nerve conduction, hormonal secretion, enzymatic regulation, blood coagulation	1000-1200 mg	2500 mg	-Vitamin D enables absorption in small intestine -Deficiency: at risk groups include postmenopausal women, lactose intolerant, vegan diet, chronic glucocorticoid use; chronic depletion leads to osteopenia and osteoporosis -Toxicity: renal stones, polydipsia; bone abnormalities; constipation; altered mental status
Phosphorus	Cellular energy, cell membrane structure, bone homeostasis	700 mg	4000 mg	-Deficiency: diabetics recovering from DKA and patients with refeeding syndromes at risk; symptoms include appetite loss, weakness, bone fragility, numbness -Toxicity: caused by CKD, hypoparathyroidism, alcohol abuse; symptoms manifested as those in hypocalcemia
Magnesium	Cellular energy, nerve conduction, muscle contraction, bone homeostasis	320-420 mg	N/A	-Magnesium sulfate prescribed to pregnant women with preeclampsia to prevent or treat seizures -Deficiency: at risk groups include excessive gastrointestinal loss, alcohol abuse, insulin-resistant diabetics, chronic loop diuretic or PPI use; symptoms include neuromuscular dysfunction, arrhythmia, hypokalemia, hypoparathyroidism, hypocalcemia

				-Toxicity: progression from gastrointestinal upset and mild neurological deficit to altered mental status and autonomic nervous system dysregulation to respiratory failure and cardiac arrest
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TRACE MINERALS

Nutrient	Major functions	RDA in adult	UL in adult	Clinical significance
Iron	Aerobic respiration, growth and development	8-18 mg	45 mg	-Deficiency causes anemia; corresponding lab values usually reveal low serum iron, low serum ferritin, high total iron binding capacity, and low percent transferrin saturation -Hereditary hemochromatosis causes iron overload, which manifests as liver cirrhosis and carcinoma, heart disease, and endocrinopathy -Acute ingestion of excess supplements causes gastrointestinal upset; overdose is leading cause of poisoning in young children
Copper	Oxidation-reduction reactions	900 mcg	10 mg	-Adequate iron metabolism requires normal copper absorption -Deficiency causes pancytopenia -Patient's with Wilson's disease have decreased copper excretion and complex with ceruloplasmin, which results in excessive organ deposition
Zinc	Immunity, growth and development, wound healing, taste and smell	8-11 mg	40 mg	-Developing countries use zinc supplements in children with diarrhea to reduce symptoms and duration -Deficiency causes poor growth, diarrhea, dermatitis, impaired immunity, sexual dysfunction and delayed adolescent sexual development -Toxicity causes gastrointestinal upset and reduced copper absorption
Iodine	Thyroid hormone synthesis	150 mcg	1100 mcg	-Goitrogen compounds found in abundance in raw vegetables inhibit bioavailability of iodine; this makes patients in developing countries with high consumption of uncooked vegetables at particular risk for deficiency -Deficiency causes neonatal cretinism and thyroid goiter -Toxicity causes either hypothyroidism or hyperthyroidism depending on iodine status at time of excessive intake -Pregnant women should consume adequate amounts to ensure they maintain normal TSH levels and thus help prevent sequela of abnormal thyroid hormone levels
Manganese	Oxidation-reduction reactions	Adequate intake 1.8-	11 mg	-Toxicity more concerning than deficiency; at risk individuals include children on long term TPN and industrial workers with long term

		2.3 mg		pollutant inhalation; chronically produces parkinsonism, pulmonary fibrosis, psychosis
Selenium	Enzymatic reactions, antioxidant defense, peripheral thyroid hormone conversion	55 mcg	400 mcg	-Deficiency is rare due to abundance in food; when deficiency manifests, it is often associated with Keshan's disease, a severe cardiomyopathy that occurs in China -Inadequate intake is linked to increased risk for cancer -Toxicity causes gastrointestinal upset, hair loss, brittle nails, skin rash
Fluoride	Reduces occurrences of dental caries	3-4 mg	10 mg	-Fortified in water supply to help prevent dental caries -Excess intake causes fluorosis, which manifests as tooth mottling -Children can become poisoned from excess ingestion of mouthwash, which results in gastrointestinal upset, seizure, and coma
Chromium	Energy metabolism, enhances insulin	Adequate intake 25-35 mcg	N/A	-Little known about the specific health and functions of this trace mineral -Deficiency and toxicity are not well characterized
Molybdenum	Coenzyme in oxidation reduction reactions	45 mcg	2 mg	-Deficiency and toxicity are not well characterized

ASSESSMENT QUESTIONS

FAT SOLUBLE VITAMINS

1.) You are rotating at a pediatric clinic that specializes in newborn care. Your first newborn patient is a 1.5 week old crying male with evidence of active bleeding from his umbilicus. On your differential includes which of the following vitamin deficiencies?

- a. Vitamin K
- b. Iron
- c. Vitamin C
- d. Folate

Answer: a. Vitamin K plays an integral role in the coagulation cascade. Newborns are at particular risk of deficiency within the first week of life. This is because their still underdeveloped livers have poor utilization of vitamin K, they have sterile guts that do not yet have bacteria producing vitamin K, and breast milk has limited vitamin K. As a result, the American Academy of Pediatrics recommends that all newborns be given parenteral vitamin K at birth. Iron deficiency (b) causes microcytic anemia. Vitamin C deficiency (c) causes scurvy, which can involve evidence of bleeding (mucosal gum bleeding, poor wound healing, easy bruising), but is not common in the newborn. Folate deficiency (d) causes a macrocytic megaloblastic anemia commonly seen in alcoholics.

2.) Which fat soluble vitamin is known for its antioxidant properties and sunflower and cereals are rich sources?

- a. Vitamin A
- b. Vitamin D
- c. Vitamin E
- d. Vitamin K

Answer: c. Both vitamins D and E have antioxidant properties. Oils are a rich source of vitamin E, whereas vitamin D is found in fortified foods, due to its more limited availability in foods naturally.

3.) A patient presents with complaint of worsening vision while driving home from work at night. On you differential is vitamin deficiency. Which vitamin could be the likely culprit?

- a. Vitamin A
- b. Vitamin D
- c. Vitamin E
- d. Vitamin K

Answer: a. Vitamin A plays an integral role in vision by interacting with rods and cones to ultimately send signals to the brain for processing and then output of vision. One of the earliest signs of vitamin A deficiency in an individual is the onset of night blindness, or decreased ability to see in low light conditions. If the deficiency progresses untreated, xerophthalmia ensues, which is a collection of abnormal eye changes that ultimately results in irreversible blindness.

4.) Which vitamin listed below would be most likely to become deficient in a person with persistent cholestasis?

- a. Vitamin B12
- b. Thiamin
- c. Folate
- d. Vitamin E
- e. Calcium
- f. Zinc

Answer: d. Vitamin E is a fat soluble vitamin along with vitamins A, D, and K. All of these require the adequate function of bile salts in order to be absorbed from the gut. If a patient is cholestatic, they are unable to release bile into the small intestine, and over time would likely develop steatorrhea and possible fat soluble vitamin deficiency.

5.) A woman of reproductive age presents with severe cystic acne. On exam of the face you notice several red papules that are tender to palpation as well as a few indented scars. She is interested in pursuing treatment with isotretinoin (Accutane) and would like to know about the risks and benefits of starting this medication. What is the best counseling option you should give her?

- a. Accutane's key ingredient is vitamin D, so the patient must be aware of concerning symptoms of toxicity, including weight loss, increased urinary frequency, and palpitations.
- b. Accutane's key ingredient is a form of vitamin A, which is teratogenic. The patient must be on a reliable contraception method to prevent pregnancy and possible birth defects.
- c. Accutane causes vitamin B6 deficiency, so the patient should watch for symptoms of hand and foot numbness and tingling. It is recommended that the patient also take Vitamin B6 while on this medication.
- d. Accutane cause macrocytic anemia, so the patient should supplement folate and vitamin B12 while on this medication.

Answer: b. Accutane's key ingredient is a form of vitamin A, which is teratogenic. Reproductively aged females should be taking a reliable birth control method to prevent pregnancy and teratogenic effects in the fetus. Vitamin D toxicity could cause weight loss, polyuria, or palpitations, but it is not an ingredient in Accutane. Isoniazid (INH) used to treat tuberculosis can cause vitamin B6 deficiency, but Accutane is not known to do this. Accutane does not cause anemia.

6.) Which vitamin is referred to as the sunshine vitamin because the exposure to UV rays causes it to be synthesized endogenously?

- a. Vitamin A
- b. Vitamin D
- c. Vitamin E
- d. Vitamin K

Answer: b. Exposure to UV rays from the sun starts a chemical reaction within the body that allows it to synthesize vitamin D endogenously. The other fat soluble vitamins listed are only obtained from food products.

7.) Vitamin D has to undergo two hydroxylation reactions within which locations in the body before it becomes biologically active?

- a. Skin and liver
- b. Skin and kidney
- c. Liver and kidney
- d. Bone and kidney

Answer: c. Inactive vitamin D gets converted to 25-hydroxyvitamin D in the liver by 25-hydroxylase. The kidney then converts the intermediate product to 1,25-dihydroxyvitamin D by 1-alpha-hydroxylase. UV rays absorbed through the skin can start the process of the body endogenously synthesizing vitamin D, but this is biologically inactive until both the liver and kidney process it. Bone remodeling relies on the interplay between several biologic products, including vitamin D, calcium, PTH, and calcitonin; however, it has no direct role in activating vitamin D.

8.) Vitamin D deficiency in children causes what clinical syndrome?

- a. Pellagra, which includes a triad of diarrhea, dermatitis, and dementia
- b. Scurvy, which causes gum bleeding, tooth loss, and iron deficiency anemia
- c. Wernicke-Korsakoff syndrome, which involves the triad of ophthalmoplegia, ataxia, and altered mental status.
- d. Rickets, which involves failure of bone mineralization, and subsequent bowing and fractures

Answer: d. Pellagra is caused by niacin deficiency, which is now largely uncommon in the US . Scurvy is caused by vitamin C deficiency, which occurs in smokers and individuals with malabsorption syndromes. Wernicke-Korsakoff syndrome is caused by thiamin deficiency and is most common in alcoholics.

9.) A mother brings her 2 day old newborn to the emergency department when she saw him start to seize uncontrollably. The neonate is found to have severe intracranial hemorrhage. No hospital records for the mother are available and she reports having a home birth two days ago with limited prenatal care. No neonatal prophylaxis measures were given to her child at birth. What vitamin deficiency could be causing the bleeding in the newborn's head?

- a. Vitamin A
- b. Vitamin D
- c. Vitamin E
- d. Vitamin K

Answer: d. Vitamin K is routinely administered to all newborns shortly after birth to prevent hemorrhagic disease of the newborn. The mother had limited prenatal care and gave birth at home. It is unclear what her gestational age was at time of delivery, and it is thus possible that the child may be premature, which would increase his risk of intraventricular hemorrhage. The seizures are a classic symptom. The question stem further discloses that the child likely did not get a vitamin K intramuscular injection.

10.) What is a major function of vitamin D?

- a. Hemostasis
- b. Vision
- c. Antioxidant
- d. Calcium homeostasis

Answer: d, calcium homeostasis. Vitamin D is called the 'sunshine vitamin,' because UV rays enable the body to synthesize it endogenously. However, it is still considered an essential vitamin because endogenous synthesis alone does not provide sufficient amounts to meet requirements for most people. It is heavily involved in the regulation of calcium. Deficiency of vitamin D causes Rickets in children and osteomalacia in adults. Vitamin K is required for adequate blood clotting or hemostasis. Vitamin A is necessary for vision. Vitamin E is required for its antioxidant properties.

WATER SOLUBLE VITAMINS

1.) An immigrant child presents to your office for medical evaluation. You immediately notice that he is in the 5th% on the growth curve charts. When you look in his mouth during your exam, you see that his gums are swollen and friable and several missing teeth. Among managing his other health needs, which vitamin(s) will you be sure to prescribe as supplementation?

- a. Vitamin A
- b. Riboflavin, thiamin, and folate
- c. Vitamin C
- d. Vitamin D

Answer: c. Vitamin C causes a clinical syndrome called scurvy, which starts as gum inflammation. As deficiency progresses, patients develop weaknesses in their connective tissue, manifested as bleeding disorders, joint pain, tooth loss. Vitamin A deficiency is classically known for causing night blindness. Deficiencies of riboflavin, thiamin, and folate have many clinical manifestations. Vitamin D classically causes rickets in children and osteomalacia in adults when deficient.

2.) Thiamin deficiency clinically manifests as:

- a. Polyneuropathy, gaze and gait disturbances, and sometimes encephalopathy
- b. Macrocytic megaloblastic anemia and neural tube defects in utero
- c. Sub-acute combined degeneration, resulting in impaired sensation and motor deficits
- d. Dermatitis, diarrhea, and dementia

Answer: a. Thiamin deficiency causes beriberi syndrome involving the peripheral nervous system; Wernicke-Korsakoff syndrome involving ophthalmoplegia, gait disturbance, and altered mental status; and rarely, Leigh syndrome, involving encephalopathy. Folate deficiency causes the anemia listed in b. Vitamin B12 deficiency causes sub-acute combined degeneration. Niacin deficiency causes the triad listed in d.

3.) Vitamin B12 and folate deficiencies can present with macrocytic megaloblastic anemia, which can make them clinically indistinguishable. What is one key difference between their bioavailability in the body?

- a. Folate requires specific proteins found in the stomach in order to be absorbed, whereas B12 is freely absorbed in the small intestine
- b. Vitamin B12 is stored in mass quantities in the bone, whereas folate is stored in mass quantities in the liver
- c. Only half of the body's folate is stored in the liver so it's much easier to deplete these than B12
- d. The best source of folate is in animal products, whereas B12 is ubiquitous in foods

Answer: c. It is much easier to deplete folate, because only half of the stores are in the liver. On the contrary, vitamin B12 is mainly stored in the liver, so it takes years to deplete it. Vitamin B12 requires intrinsic factor protein found in the stomach's parietal cells in order to be absorbed. Neither vitamin is stored in the bone. The best sources of vitamin B12 are animal products, while folate is found in many foods, including fortified cereals and grains.

4.) Why would autoimmune destruction of parietal cells in the stomach as seen in pernicious anemia be detrimental for adequate vitamin B12 absorption?

- a. The parietal cells of the stomach directly absorb vitamin B12
- b. Stomach parietal cells secrete intrinsic factor, which binds vitamin B12 and enables its absorption in the small intestine
- c. When the stomach parietal cells get destroyed, they leak enzymes that break down vitamin B12 before it can get absorbed
- d. The antibodies that cause destruction of stomach parietal cells also destroy vitamin B12 when it enters the GI tract

Answer: b. The parietal cells of the stomach secrete a necessary protein, called intrinsic factor, which binds vitamin B12 and enables its absorption in the distal ileum. If the cells get destroyed, a patient is at risk for developing anemia caused by vitamin B12 deficiency. None of the other answers are true.

5.) What one vitamin in pregnancy is absolutely recommended as part of the prenatal care regimen and why?

- a. B12, because it helps prevent fetal neural tube defects
- b. Folate, because it helps prevent fetal neural tube defects

- c. Calcium, because it helps prevent fetal bone deformities
- d. Iron, because it helps prevent fetal anemia

Answer: b. Folate has been empirically shown to reduce the incidence of neural tube defects in pregnancy. It is thus highly recommended for pregnant women as part of their prenatal regimen. Many physicians would also recommend daily folate supplementation in reproductively aged females in case they were to get pregnant.

- 6.) Which water soluble vitamin is also used as a cholesterol lowering agent?
- a. Vitamin B12
 - b. Pantothenic acid
 - c. Riboflavin
 - d. Niacin

Answer: d. Physicians may prescribe 1-2 grams/day niacin for patients with difficulty to manage hypercholesterolemia. Adverse effects include skin flushing, GI upset, and liver damage. Prescription niacin is prepared very differently from supplemental niacin, such that the supplement cannot be a replacement to help lower cholesterol.

- 7.) Which biochemical reactions does thiamin help facilitate by acting as a coenzyme?
- a. Conversion of pyruvate to acetyl CoA, an oxidative decarboxylation reaction mediated by pyruvate dehydrogenase
 - b. Conversion of alpha-ketoglutarate to succinyl CoA, a tricarboxylic acid cycle (TCA cycle) reaction mediated by alpha-ketoglutarate dehydrogenase
 - c. Transketolation of the pentose phosphate pathway
 - d. All of the above

Answer: d. Vitamin B1 plays a vital role as coenzyme in all of the above listed biochemical reactions. More generally, it plays a role in branched chain amino acid and carbohydrate metabolism.

- 8.) What is the best food source for vitamin B12?
- a. Animal products
 - b. Gluten products
 - c. Vegetables and fruits
 - d. Grain products

Answer: a. Animal products, including fish, meat, poultry, eggs, and milk, are the best sources of vitamin B12. It can also be fortified into breakfast cereals, which makes it available for vegetarians. Vegans should take vitamin B12 supplementation.

- 9.) An adolescent teen presents with several weeks of cough, night sweats, and weight loss. Laboratory, imaging, and microbiologic studies confirm diagnosis of tuberculosis. The patient will be treated with quadruple therapy, including isoniazid. Which vitamin would be reasonable to supplement in this patient during his treatment?
- a. Vitamin B6
 - b. Vitamin B12
 - c. Thiamin
 - d. Niacin

Answer: a. Vitamin B6 can easily become depleted with prolonged isoniazid therapy. It is reasonable to supplement when patients are using this medication. Proton pump inhibitors like pantoprazole or omeprazole may interact with Vitamin B12, but the data are conflicting. It has not been shown that thiamin and niacin become depleted with any specific medications. Niacin at prescribed high doses can be used as a cholesterol-lowering agent.

10.) A mother brings her teenage daughter into clinic because she is concerned that the teen appears more fatigued lately and that her grades have started to fall over the past six months. The mother notes that the teens diet has changed over the last year. A lab workup reveals macrocytic anemia. Which deficiency of vitamins listed below could be contributing to her anemia and subsequent fatigue?

- a. Vitamin A and Vitamin C
- b. Folate and Vitamin B12
- c. Thiamin and niacin
- d. Vitamin B6 and riboflavin

Answer: b. This teen is likely of child-bearing age, which already puts her at risk of folate deficiency, which can occur over months. The fact that her diet has changed and fatigue later ensued makes both folate and B12 deficiencies possible. Vitamin B12 deficiency classically occurs in vegans due to the lack of animal product ingestion, the key source of B12. However, B12 deficiency usually takes years to become depleted. It would be reasonable to test her blood for these deficiencies, especially if the specific type of anemia was macrocytic.

11.) What is the single best food source of B12 vitamin?

- a. Animal products (meat, poultry, fish)
- b. Legume products (peas, beans, lentils)
- c. Cereal products (wheat and rye)
- d. Ubiquitous, so available in most foods

Answer: a. Animal products are the only source of naturally-occurring vitamin B12 (although some cereal products may be fortified with this vitamin), which is why strict vegetarians and vegans are so susceptible to deficiency.

12.) A chronic alcoholic presents with chronic diarrhea. During his visit, he also states that he has been feeling out of sorts for the past several months. He continues to drink alcohol despite all of your attempts to help him quit. On exam, you notice his skin has patches of erythema and scaling with occasional desquamation. You know thiamin deficiency is the most common deficiency in alcoholics, but wonder if his clinical symptoms fit better with deficiency of another micronutrient. On your differential would include deficiency of which of the following vitamins?

- a. Pantothenic acid
- b. Vitamin C
- c. Vitamin A
- d. Niacin

Answer: d. Niacin deficiency classically causes the clinical syndrome of pellagra, which includes diarrhea, dementia, and dermatitis; all of these symptoms are listed in the question stem. This patient's chronic alcoholism puts him at a high risk of multiple vitamin deficiencies. It would be reasonable to assess for additional B vitamin deficiencies in his work-up; including (but not limited to), thiamin, folate, vitamin B12, vitamin B6, and riboflavin.

13.) A young man seeking to enter a body building competition in 6 months starts researching online nutrition blogs to help prepare his body. He reads from multiple forums that consuming raw eggs is a surefire way to get his body in tiptop shape. After several weeks of eating up to 10 raw eggs per day in shakes, he starts to feel weaker at the gym and notices that he his hair seems to be falling out in the shower. Which vitamin deficiency could this young man be suffering from?

- a. Biotin
- b. Niacin
- c. Molybdenum
- d. Riboflavin

Answer: a, biotin. Raw eggs classically cause biotin deficiency if a patient consumes up to 12/day. The symptoms of biotin deficiency include rash, hair loss, and neurologic deficit. Niacin deficiency causes pellagra, with tetrad of symptoms of diarrhea, dermatitis, dementia, and even death. Molybdenum is an ultra-trace mineral that has been poorly characterized in the literature. Riboflavin deficiency causes ariboflavinosis, which is characterized by multiple mucosal symptoms (mouth, skin) and mental status changes.

ELECTROLYTES

- 1.) Which of the following is true regarding sodium in the body?
- It regulates plasma volume and thus regulates water balance in the body
 - It is most abundant in raw foods
 - It is absorbed by passive transport in the intestines
 - Most Americans eat less than the adequate intake of 1500 mg/day

Answer: a. One of sodium's largest roles is to regulate plasma volume and thus control water balance in the body. It is most abundant in processed foods. It is absorbed via active transport. Up to 95% Americans exceed the adequate intake every day.

- 2.) Which of the following medical conditions can cause hyponatremia?
- Vomiting or diarrhea
 - Heart failure and liver cirrhosis
 - Syndrome of inappropriate antidiuretic hormone (SIADH)
 - All of the above

Answer: d. Either volume depletion or overload as well as SIADH can all cause a state of hyponatremia. If it develops quickly or is left untreated, it can cause delirium, seizure, and coma.

- 3.) Which of the following nutrients plays an integral role in plasma volume and water balance in the body?
- Calcium and phosphorus
 - Sodium and potassium
 - Chloride and magnesium
 - Copper and iodine

Answer: b. Sodium and potassium are the major cations in the body that play a vital role in plasma volume and water balance. Sodium is the major extracellular cation while potassium is the major intracellular cation. They both also play a role in nerve impulses and muscle contraction by their movement across cell membranes.

- 4.) Which hormone acts as a major player in the kidneys to help regulate both sodium and potassium balance?
- Erythropoietin
 - Atrial natriuretic peptide
 - Aldosterone
 - Antidiuretic hormone

Answer: c. Aldosterone acts on both sodium and potassium transporters in the distal portion of the kidney to retain or excrete ions depending on the body's water needs. ADH also works in the kidney, but primarily on the aquaporin water channels and sodium channels. Erythropoietin is a hormone produced by the kidney that increased erythrocyte production. ANP is produced by the heart and plays a less active role in water balance in the body.

- 5.) What EKG findings are characteristic of hyperkalemia, or excess potassium ions in the blood?
- Flutter waves
 - Peaked T waves
 - Delta waves
 - Deep s waves

Answer: b. The classic EKG finding in hyperkalemia is a peaked T wave. Flutter waves are characteristic of atrial flutter, which occurs when electricity abnormally conducts around the tricuspid valve. Delta waves occur in Wolff Parkinson White syndrome, characterized by an accessory pathway in the heart that conducts irregularly. Deep s waves can be seen in hypertrophy of the heart.

- 6.) A child comes into the emergency department with intractable vomiting. What is one vitamin is likely depleted as a result?
- Sodium
 - Chloride
 - Phosphorous
 - Calcium

Answer: b. Chloride complexes with hydrogen ions in the stomach to create an acidic environment that helps break down food products. With intractable vomiting, the patient becomes hypochloremic.

- 7.) Which major minerals below work in unison to help maintain water balance in the body?
- Sodium and hydrogen (NaH)
 - Potassium and chloride (KCl)
 - Sodium and chloride (NaCl)
 - Potassium and bromide (KBr)

Answer: c, sodium and chloride. Essential to the body's homeostasis is adequate water balance, which is mainly regulated by the main extracellular cation, sodium, and the main extracellular anion, chloride. Alternatively, potassium is the body's major intracellular cation. Movement of all of these ions across membranes can generate electrical current, necessary for nerve conduction and muscle contraction. Bromide is not considered a major mineral or electrolyte.

- 8.) Excretion of which electrolyte in the distal colon helps facilitate water excretion from the body?
- Sodium
 - Chloride
 - Potassium

Answer: b, chloride. Although all of the listed electrolytes are excreted by the kidney, chloride can also be excreted in the distal colon to help facilitate water excretion from the body.

MAJOR MINERALS

- 1.) Which of the following regulators decreases calcium levels in the blood?
- PTH
 - Phosphate
 - Vitamin D
 - Calcitonin
 - Both a and c
 - Both b and d

Answer: f. Calcitonin and phosphate decreases serum calcium levels, while PTH and vitamin D increase levels.

2.) A 47 year old male with end stage renal disease from chronic diabetes mellitus type 2 complains of polydipsia (excessive urination), joint pain, and mental slowing. Included in your work up is assessment for vitamin deficiency. If this were the case, which vitamin would likely be deficient?

- a. Calcium
- b. Iron
- c. Folate
- d. Zinc

Answer: a. Calcium deficiency can be remembered with phrase, “stones, bones, groans, and psychiatric moans.” All of the above listed symptoms could encompass the presentation of calcium deficiency. Iron deficiency results in anemia. Folate deficiency is rare, but could present in alcoholics as megaloblastic, macrocytic anemia. Zinc deficiency would present with non-specific symptoms of loss of appetite and impaired immunity.

3.) You are completing an Emergency Department night shift. At approximately 2 am, the police bring in a middle-aged man who was arrested for indecent exposure. He has slurred speech and gait disturbances. Among vitamin B12 and folate deficiencies, which of the following macrominerals do you worry about this patient lacking?

- a. Potassium
- b. Sodium
- c. Chloride
- d. Calcium
- e. Phosphorus
- f. Magnesium
- g. Sulfur

Answer: f. Magnesium can become deficient with chronic alcohol abuse, which is the presentation that should be inferred from the question stem (middle age, indecent exposure, slurred speech, gait disturbance, possible vitamin B12 and folate deficiencies). One might suspect low potassium if the patient was vomiting, but no mention of this is made. The other macrominerals listed are not typically associated with chronic alcohol abuse.

4.) Which vitamin enhances calcium absorption in the small intestine?

- a. Vitamin A
- b. Vitamin D
- c. Vitamin E
- d. Vitamin K

Answer: b. Vitamin D enhances calcium absorption in the small intestine. Other major regulators of calcium homeostasis are PTH (increase Ca serum levels) and calcitonin (decreases Ca serum levels). The other vitamins listed are also fat soluble vitamins, but they do not play a role in calcium homeostasis.

5.) A 42 year old overweight gentleman is diagnosed with hypertension. You want to start a diuretic, but will run some screening labs beforehand. Which vitamin listed below would be valuable to check given its interactions with diuretics?

- a. Folate
- b. Iron
- c. Calcium
- d. Vitamin B12

Answer: c. Diuretics can affect calcium balance in the body. Loop diuretics cause hypocalcemia whereas thiazide diuretics cause hypercalcemia. The rest of the vitamins listed would not be affected by diuretic use.

- 6.) Long-term glucocorticoid (eg: prednisone) use can adversely deplete stores of which vitamin?
- Calcium
 - Chloride
 - Copper
 - Manganese

Answer: a. Calcium stores get depleted with long-term glucocorticoid use, which can result in osteopenia and osteoporosis.

- 7.) You are managing a patient's advanced chronic kidney disease and you notice that the patient has a low calcium level on screening labs. He is complaining of numbness and uncontrollable muscle contractions in his extremities. You plan to add a new medication that will affect the levels of which vitamin listed?
- Phosphorous
 - Iron
 - Riboflavin
 - Vitamin A

Answer: a. The patient has hyperphosphatemia caused by chronic kidney disease. This excess phosphorous is binding calcium in the blood and depleting its stores, thereby causing symptoms of hypocalcemia. Providing the patient with phosphate binders would help alleviate some of these symptoms. He should also be on a low phosphorous diet.

- 8.) Which vitamin enhances calcium absorption in the small intestine?
- Vitamin A
 - Vitamin C
 - Vitamin B12
 - Vitamin D

Answer: d. Vitamin D is a fat soluble vitamin that plays a major role in calcium homeostasis in the body. Other hormones that regulate serum calcium levels include parathyroid hormone (increase levels) and calcitonin (decrease levels). Vitamin A is a fat soluble vitamin that aids in vision, immunity, and cell growth. Vitamin C is a water soluble vitamin that helps synthesize collagen, serves as an antioxidant and immune system booster, and plays a role in energy metabolism. Vitamin B12 is a water soluble vitamin involved in erythrocyte production and DNA synthesis.

- 9.) Which anti-hypertensive that works primarily in the kidney can cause hypocalcemia (calcium loss from the body)?
- Carbonic anhydrase inhibitors
 - Loop diuretics
 - Thiazide diuretics
 - Potassium sparing diuretics

Answer: b. Loop diuretics inhibit NKCC channel in the thick ascending loop. This subsequently decreases sodium reabsorption primarily, but also calcium and magnesium paracellular reabsorption. As a result, loop diuretics can be used in settings of symptomatic acute hypercalcemia to help the body excrete calcium. On the contrary, thiazide diuretics can cause hypercalcemia. Carbonic anhydrase inhibitors and potassium sparing diuretics do not have a meaningful effect on calcium excretion or reabsorption in the kidney.

- 10.) Which nutrient deficiency is one of the hallmarks of refeeding syndrome?
- Calcium
 - Magnesium

- c. Phosphorous
- d. Iron

Answer: c. Deficiency of phosphorus is a hallmark feature of refeeding syndrome, which occurs when malnourished patients are aggressively fed with enteral or parenteral nutritional support. Symptoms would include loss of appetite, muscle weakness, bone fragility, extremity numbness.

11.) Which mineral would you consider prescribing to a near term pregnant female who presents with headache and is later found to have a blood pressure of 195/100 and hyperreflexia on exam?

- a. Calcium
- b. Magnesium
- c. Phosphorous
- d. Iron

Answer: b. Magnesium is often given to pregnant females in labor and delivery triage when they present with preeclampsia. Symptoms of preeclampsia include headache, vision changes, altered mental status, right upper quadrant pain, and shortness of breath. The goal of magnesium is to prevent development of seizures, which would qualify the disease as eclampsia. The ultimate cure of either syndrome is delivery of the fetus.

TRACE MINERALS

1.) Which of the following is an example of a source of organic heme iron?

- a. Prunes
- b. Bran muffin
- c. Oysters
- d. Tofu

Answer: c. Prunes (a), bran muffin (b) and tofu (d) are all examples of inorganic non-heme sources of iron. Oysters (c) are considered organic heme sources, which confer greater bioavailability due to their higher levels of absorption.

2.) Which of the following would result in increased absorption of iron from the gastrointestinal tract?

- a. High levels of iron bound to transferrin in the blood
- b. An inactivating mutation in ferroportin
- c. Sloughing of iron-containing enterocytes in the gastrointestinal tract
- d. A non-anemic pregnant woman who takes iron supplements
- e. High levels of calcium circulating in the blood

Answer: d. A non-anemic pregnant woman taking iron supplements likely does not have iron deficiency and since she is taking supplements, she is going to have increased levels of absorption from the gut (d). If there are high levels of iron bound to transferrin (a), less will be absorbed from the gut to prevent iron overload. An inactivating mutation in ferroportin would cause decreased ability of iron to be transported out of enterocytes and into the blood (b) If those enterocytes were then sloughed off in the gut (c), there would be decreased iron absorption. Finally, high calcium levels decrease iron bioavailability (e).

3.) What is the number one nutritional deficiency worldwide?

- a. Calcium
- b. Vitamin A
- c. Iron
- d. Folate
- e. Vitamin K

Answer: c. Iron deficiency is the most common nutritional deficiency in the world. Initially, patients are asymptomatic as stores of iron are being used up. Over time, deficiency causes a microcytic anemia.

4.) A 15 year old female is brought in by her mother for evaluation. Her mother complains that her daughter always looks tired – she is slow to wake up in the morning, struggling in school, and often needs to take naps in the afternoon to stay awake past dinner. On exam you notice that the patient has pale conjunctiva. Which of the following minerals is likely deficient in this patient?

- a. Zinc
- b. Copper
- c. Iron
- d. Iodine

Answer: c, iron. The mother is concerned about persistent fatigue in her adolescent daughter. Very common in teenage females is iron deficiency anemia from menstrual bleeding, which can manifest clinically as fatigue. Another factor hinting toward anemia is the finding of pale conjunctiva on exam. Zinc deficiency (a) causes poor growth, diarrhea, impaired immunity. Wilson disease, which is a genetic disease that involves impaired copper metabolism can result in *excess* copper in the body (b). Iodine deficiency (d) causes thyroid dysfunction and brain damage.

5.) Which of the following is the correct order for non-heme iron metabolism in the body?

- a. Reduced to Fe^{2+} → absorbed into enterocyte in duodenum → transported to blood by ferroportin → carried around blood bound to transferrin → stored as ferritin
- b. Absorbed into enterocyte in duodenum → reduced to Fe^{2+} → transported to blood by ferroportin → carried around blood bound to transferrin → stored as ferritin
- c. Reduced to Fe^{2+} → transported to blood by ferroportin → absorbed into enterocyte in duodenum → stored as ferritin → carried around blood bound to transferrin
- d. Stored as ferritin → carried around blood bound to transferrin → transported to blood by ferroportin → absorbed into enterocyte in duodenum → Reduced to Fe^{2+} `

Answer a. Iron metabolism starts as food ingestion. If it is non-heme, it must be reduced to Fe^{2+} . Iron then gets absorbed into a duodenal enterocyte then transferred onto ferroportin to be moved into blood. It then gets bound to transferrin in blood. Finally, it is stored as ferritin. Iron is never free in blood because it can generate free radicals, which are toxic.

6.) What is the most common nutritional deficiency in the world?

- a. Iron
- b. Calcium
- c. Vitamin C
- d. Fluoride

Answer: a. Iron is the most common nutritional deficiency worldwide. It manifests as microcytic anemia that can be detrimental when severe. Adequate dietary sources include animal products, fortified foods, as well as nuts, beans, and vegetables.

7.) Which trace mineral acts as a coenzyme in oxidation-reduction reactions, including reacting with ceruloplasmin, superoxide dismutase, and cytochrome C oxidase?

- a. Iron
- b. Copper
- c. Iodine
- d. Fluoride

Answer: b. Copper is a coenzyme for many oxidation-reduction reactions due to its ability to alternate between 2 oxidation states, Cu^{1+} and Cu^{2+} . One important role is its activity with ceruloplasmin, an

enzyme that is required in appropriate oxidation of iron, such that iron can be incorporated into transferrin. It is also part of superoxide dismutase enzymes, which eliminate superoxide free radicals that otherwise cause oxidative damage to cell membranes. Finally, it acts as a coenzyme for cytochrome C oxidase involved in catalysis of the electron transport chain in energy metabolism.

8.) Which mineral is necessary for adequate iron metabolism?

- a. Phosphorous
- b. Magnesium
- c. Zinc
- d. Copper

Answer: d. Copper complexes with ceruloplasmin. The latter is involved in oxidation reactions of iron, specifically allowing it to complex with transferrin.

9.) What is the leading cause of poisoning in children under the age of 6 years old?

- a. Lead
- b. Iron
- c. Copper
- d. Fluoride

Answer: b. Iron is the leading cause of poisoning in children under the age of 6 years old. Fluoride is another micronutrient that children can accidentally ingest in excess (ie when they swallow toothpaste), which can lead to fluorosis. Copper excess is typically seen in Wilson disease. Lead is not a micronutrient, but classically causes poisoning in older buildings with lead paint on the walls.

10.) Copper interacts with which enzyme to help iron become complexed to transferrin?

- a. Ceruloplasmin
- b. Cytochrome C oxidase
- c. Lysyl oxidase
- d. Superoxide dismutase

Answer: a. One important role of copper is its activity with ceruloplasmin, an enzyme that is required in appropriate oxidation of iron, such that iron can be incorporated into transferrin. Copper also interacts with the other enzymes listed above for various functions in the body. It is a coenzyme for cytochrome C oxidase (answer b) involved in catalysis of the electron transport chain in energy metabolism. It is also a component of lysyl oxidase (answer c), which cross-links collagen and elastin. These proteins give tensile strength to connective tissues in lungs, blood vessels, skin, teeth, and bones. Finally, it is part of superoxide dismutase enzymes (answer d), which eliminate superoxide free radicals that otherwise cause oxidative damage to cell membranes.

11.) What are classic symptoms of Wilson disease, which occurs when patients have decreased copper excretion?

- a. Tachycardia, profuse sweating, and altered mental status
- b. Wing-beating tremor and Kayser-Fleischer rings
- c. Fatigue, pale appearance, and shortness of breath
- d. Diarrhea, dermatitis, and dementia

Answer: b. Wilson disease classically causes a wing-beating tremor and Kayser-Fleischer rings in the eyes. The symptoms listed in answer choice a could manifest with hyperthyroidism, which could occur when patients have iodine toxicity. The symptoms in answer choice c would signify anemia, which could occur with vitamin B12 or folate deficiencies. The symptoms listed in choice d classically occur in the syndrome known as pellagra, which manifests when patients have niacin deficiency.

12.) Which micronutrient is necessary for adequate thyroid hormone synthesis?

- a. Chromium
- b. Iodine
- c. Selenium
- d. Magnesium

Answer: b. Iodine's only function in the body is synthesis of thyroid hormone. Adequate levels of hormone are vital for energy expenditure, macronutrient metabolism, brain development, growth and organ maturation.

13.) Phytates inhibit zinc absorption in the gastrointestinal tract; they are present in unleavened whole grain breads, cereals, and legumes. What is the name of the compound that inhibits bioavailability of iodine in the gastrointestinal tract?

- a. Phytates
- b. Intrinsic factor
- c. Biotinidase
- d. Goitrogens

Answer: d. Goitrogens decrease bioavailability of iodine. These compounds are abundant in raw vegetables, including turnips, cabbage, brussel sprouts, cauliflower, broccoli, and potatoes. Iodine deficiency is a particular problem in underdeveloped nations where consumption of raw vegetables is high. This is not a great problem in the US where many vegetables are cooked, and the goitrogens subsequently destroyed. Intrinsic factor (answer b) is required for adequate vitamin B12 absorption. Biotinidase (answer c) helps release biotin from biocytin so that free biotin can be absorbed.

14.) Which mineral can affect incidence of dental carries?

- a. Zinc
- b. Vitamin C
- c. Fluoride
- d. Iron

Answer: c. Sufficient fluoride intake is associated with decreased incidence of dental carries. This deficiency is relatively uncommon in the US however, because water is often fluoridated. Zinc deficiency (answer a) causes growth delay and impaired immunity. Vitamin C deficiency (answer b) causes the clinical syndrome of scurvy, which affects the gums primarily. Iron deficiency causes anemia.

FAT SOLUBLE VITAMINS

VITAMIN A

About
Vitamin A is a fat soluble vitamin. <u>Major functions:</u> -Necessary for vision and adequate immunity -Involved in intercellular communication via the connexin mechanisms -Helps regulate nuclear transcription via receptor coupling, which is necessary for cellular growth and differentiation
Food Sources
<u>Pre-formed Vit A:</u> meat (esp beef liver and other organ meats), poultry, fish (esp salmon), dairy <u>Pro-vitamin A:</u> fruits (mangos, cantaloupe, peaches, apricots), vegetables (carrots, spinach, winter squash, sweet potatoes)
Absorption and Metabolism
Pre-formed Vit A is directly converted to active compounds, retinaldehyde and retinoic acid, which are biologically active. Pro-vitamin A carotenoids are first enzymatically metabolized and then converted to active compounds.
Recommended Intakes
The recommended dietary allowance (RDA) in an adult female is 700 mcg/day and 900 mcg/day in an adult male. The upper limit (UL) for an adult to reduce the risk for toxicity is 3000 mcg/day.
Clinical Relevance
<u>Medicinal use:</u> One form of retinoic acid, 13-cis-retinoic acid, is synthetically synthesized as isotretinoin (brand: Accutane), which is used to treat acne vulgaris. Accutane has known teratogenic effects, and it is listed under pregnancy category X; thus, young women taking acne medication must use reliable birth control method. Synthetic retinoids are also used to treat psoriasis (examples: Acitretin, Bexarotene). <u>Deficiency:</u> -At risk: patients with cystic fibrosis -Deficiency is rare in the US -In developing countries, deficiency does occur and is associated with corneal ulceration (keratomalacia), Bitot's spots, follicular hyperkeratosis, impaired immune function, and night blindness (xerophthalmia) <u>Toxicity:</u> -From supplements or certain medicines -Symptoms: dizziness, nausea, bone pain and bone loss, headache, coma <u>Drug interactions:</u> Orlistat reduces absorption of vitamin A
Other
More information: http://ods.od.nih.gov/factsheets/VitaminA-QuickFacts/

VITAMIN D

About

Vitamin D is a fat soluble vitamin. Active forms include cholecalciferol (vitamin D3), ergocalciferol (vitamin D2), and calcitriol (1-25-dihydroxyD3).

Major functions:

- Calcium homeostasis: helps absorb it from the gut, also facilitates calcium release from bone → this is ultimately necessary for adequate bone growth and remodeling
- Cell growth and gene transcription, neuromuscular and immune function

Food Sources

- Present naturally in few food sources, the best of which include fatty fish (eg, salmon, tuna), fish liver oils
 - smaller amounts also present in beef liver and egg yolks
- Fortified in many foods, including milk, other dairy products like yogurt, cereals, orange juice
- Vitamin D can be synthesized endogenously; the required primary reaction involves absorption of UV rays through skin

Absorption and Metabolism

Vitamin D obtained from food or sun is biologically inactive. It undergoes two hydroxylation reactions in the liver then kidney to become activated...

<u>Liver</u>	<u>Kidney</u>
Inactive vitamin D → 25-hydroxyvitamin D or 25(OH)D <i>25-hydroxylase</i>	→ 1,25-dihydroxyvitamin D or 1,25(OH) ₂ D <i>1-alpha-hydroxylase</i>

Recommended Intakes

The recommended dietary allowance (RDA) for an adult male or female is 15 mcg, or 600 IU, per day. The upper limit (UL) for an adult to prevent toxicity is 100 mcg, or 1500 IU, per day.

Clinical Relevance

Medicinal use:

- Supplement to breast fed infants – of note, infant formulas have mandated vitamin D fortification
- Scientists are trying to elucidate direct links between deficiency and disease; several proposed diseases categories or states include cancer, infection, type 2 diabetes mellitus, and hypertension

Deficiency:

- At risk: African Americans and others with dark skin pigmentation; those who wear excessive amounts of sunscreen or those with head to toe coverings; patients with IBD who have poor fat soluble vitamin absorption
- Rickets in children:
 - Before the epiphyseal plates close, bone fails to mineralize resulting in softening and subsequent bowing and increased propensity to fracture
 - This has largely become a rare disease in the US due to vitamin D fortification of foods
 - If it occurs in adults after the epiphyseal plates have closed, called osteomalacia
- Contributes to development of osteoporosis

Toxicity:

- Intakes greater than the UL cause hypercalcemia, calcification of soft tissue, nausea and vomiting, loss of bone mineral density, joint pain
- Note that one cannot get toxicity from excess sun exposure alone

Drug interactions:

- Orlistat and cholestyramine both reduce absorption of fat soluble vitamins
- Barbituates increased vitamin D metabolism and reduce calcium absorption

Other

More information: <http://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/>

VITAMIN E

About

Vitamin E is a fat soluble vitamin. It functions as an antioxidant that protects cell membranes from oxidation and subsequent destruction

Food Sources

Vegetable oils (particularly olive and sunflower oil), seeds and nuts, and leafy vegetables

Absorption and Metabolism

The bioactive and best retained form of Vitamin E is alpha-tocopherol. Larger amounts of gamma-tocopherol are found in the diet, but a liver protein preferentially binds and retains the alpha-tocopherol form. Given that Vitamin E is fat soluble, it is absorbed and transported to the liver via chylomicrons, and then processed by hepatocytes into VLDL. Tocopherols are transported in the circulation non-specifically by cholesterol-containing lipoproteins.

Recommended Intakes

The recommended dietary allowance (RDA) for adult men and women is 15 mg/day. The tolerable upper limit (UL) to prevent hemorrhagic effects is 1000 mg daily.

Clinical Relevance

Deficiency:

- Very rare in healthy individuals given its abundance in the diet in fat-containing foods.
- At risk groups:
 - Malabsorption diseases that result in steatorrhea – cholestasis, cirrhosis, pancreatic insufficiency, cystic fibrosis, Celiac, Crohn's disease
 - Congenital anemias, including thalassemia, sickle cell anemia, spherocytosis, glucose-6-phosphate dehydrogenase deficiency
- Causes neuropathy, hemolytic anemia (especially in newborns), impaired immunity

Toxicity: Animal studies have shown that exceeding tolerable upper limit in Vitamin E supplements (but not food sources) can cause hemorrhage secondary to breakdown of coagulation cascade. Studies in humans have revealed inhibition in platelet aggregation with excess supplementation.

Drug Interactions: excess vitamin E supplementation can interfere with vitamin K metabolism, which could have adverse implications in patients taking warfarin (brand: Coumadin) for anticoagulation.

Other

More information: http://www.uptodate.com/contents/overview-of-vitamin-e?source=search_result&search=vitamin+e&selectedTitle=5~150

VITAMIN K

About

Vitamin K is a fat soluble vitamin.

Major functions:

- Vitamin K is a crucial coenzyme involved in post-translational oxidation reaction of the hepatic carboxylase enzyme, gamma-glutamyl carboxylase, a reaction that facilitates the activation of coagulation factors, II, VII, XI, X
- Proteins C and S involved in anticoagulation also require Vitamin K
- Also important for bone and cardiovascular metabolism, cell proliferation, brain function, and energy metabolism

Food Sources

- Highest source in green vegetables
 - Highest source: spinach, brussels sprouts, greens (collard, turnip, mustard, beet), kale
 - Medium source: asparagus, green beans, broccoli, cabbage, carrots, celery, coleslaw, lettuce (butter lettuce, iceberg, romaine, green leaf), okra, peas, pickles
- Some: avocado, bananas, chickpeas, corn, olive oil, bell peppers, seaweed, tomatoes

Absorption and Metabolism

Vitamin K comes from both the diet in the form of K1, phylloquinone or phytonadione, and also from gut microbiota, in the form of K2, or menaquinones. Dietary Vitamin K gets processed like other fat soluble vitamins – incorporated into micelles then chylomicrons for absorption and transfer to liver. Gut microbiota also synthesize Vitamin K, which can be absorbed in the distal small intestine (although the bacteria-produced Vitamin K accounts for a very limited amount for humans).

Recommended Intakes

The recommended dietary allowance (RDA) for adult men and women is 75 mcg/day. No tolerable upper limit (UL) has been defined since toxicity is so rare.

Clinical Relevance

Deficiency:

- Very rare in an otherwise healthy adult because widely distributed and easily recycled
- At risk groups:
 - Fat malabsorption syndromes: cystic fibrosis, primary biliary cirrhosis, primary sclerosing cholangitis, celiac, inflammatory bowel disease
 - Newborns
 - Immature livers do not efficiently utilize Vitamin K, low Vitamin K stores in breast milk, sterile gut not producing Vitamin K
 - Clinically termed hemorrhagic disease of the newborn
 - American Academy of Pediatrics thus recommends all newborns be administered parenteral Vitamin K at birth as well as receive supplementation with Vitamin K-enriched formula to prevent disease

-Manifests clinically as impaired coagulation (easy bruising, mucosal bleeding, splinter hemorrhages, melena, hematuria)
-Lab abnormalities: prolonged PT/INR, in severe cases, PTT also prolonged

Other

More information: http://www.uptodate.com/contents/overview-of-vitamin-k?source=search_result&search=vitamin+K&selectedTitle=5~150

WATER SOLUBLE VITAMINS

VITAMIN C

About

Vitamin C is a water-soluble vitamin.

Major functions:

- Synthesis of collagen, which helps provide structure and strength of connective tissues (including bone, skin, tendon, cartilage, blood vessels, granulation tissue)
- Synthesis of L-carnitine, which is necessary for fatty acid metabolism
- Cofactor for conversion of dopamine to norepinephrine in protein metabolism
- Antioxidant and immune system booster
- Improves absorption of non-heme iron by keeping iron in reduced state

Food Sources

Fruits and vegetables:

- Best sources: citrus fruits, tomato, potato
- Other sources: bell peppers, kiwi, broccoli, strawberries, brussel sprouts, cantalope

Absorption and Metabolism

Once absorbed in the gut, it is reduced to ascorbic acid. Vitamin C is stored ubiquitously throughout the body, although not to any great extent. The body can prevent elevated blood levels and maintain homeostasis by excreting unmetabolized ascorbic acid through the kidney.

Recommended Intakes

The recommended dietary allowance (RDA) for an adult male is 90 mg/day and 75 mg/day for an adult female. The upper limit (UL) for an adult to reduce the risk for toxicity is 2,000 mg/day.

Clinical Relevance

Deficiency: results in the clinical syndrome called scurvy –

- Historical note: During 1700s, scurvy was brought to attention after many sailors on long voyages were dying. James Lind, a British Navy physician, discovered that providing citrus fruits could prevent scurvy.
- Begins as gum inflammation starting 1 month after cessation of ingestion
- More severe deficiency causes impaired collagen synthesis resulting in weak connective tissue, which is manifested by petechiae, ecchymosis, purpura, joint pain, poor wound healing, hyperkeratosis, corkscrew hairs
- Can also cause capillary fragility, which is manifested as bleeding gums and tooth loss, and iron deficiency anemia

Toxicity: Excess intake would particularly arise from supplementation. Symptoms include GI upset (diarrhea, nausea, abdominal cramps), increased risk of kidney stones, and excess iron absorption.

Other

Fun fact: most animals can synthesize vitamin C endogenously, but humans cannot

More information: <http://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/>

THIAMIN

About

Thiamin is a water-soluble vitamin.

Major functions: Thiamin is an important coenzyme for branched chain amino acid and carbohydrate metabolism. Some important examples include:

- Facilitates the conversion of pyruvate to acetyl CoA, an oxidative decarboxylation reaction mediated by pyruvate dehydrogenase
- Helps convert alpha-ketoglutarate to succinyl CoA, a tricarboxylic acid cycle (TCA cycle) reaction mediated by alpha-ketoglutarate dehydrogenase
- Finally, it is involved in the transketolation of the pentose phosphate pathway

Food Sources

- Found in small amounts in a wide variety of foods, especially sunflower seeds, pork products, and legumes
- Grains and cereal products are all fortified with thiamin, green peas, asparagus, liver, peanuts, mushrooms

Absorption and Metabolism

Thiamin is carried in the body either bound to albumin or inside red blood cells. Little amounts are stored (in liver and skeletal muscle), otherwise largely excreted by kidney.

Recommended Intakes

The recommended dietary intake (RDA) is 1.2 mg/day for adult males and 1.1 mg/day for adult females. Currently, no data exists to suggest an upper limit of thiamin to prevent toxicity.

Clinical Relevance

Deficiency: Clinical symptoms of deficient thiamin can manifest in any of the syndromes listed below.

1. Beriberi: peripheral polyneuropathy sometimes involving development of heart failure
2. Wernicke-Korsakoff: triad of ophthalmoplegia/nystagmus, ataxia with wide base, and mental status disturbances (confusion, delirium, amnesia, confabulation) – almost exclusively found in alcoholic patients
3. Leigh: rare syndrome of infants involving progressive sub-acute necrotizing encephalopathy

Other

More information: <http://www.uptodate.com/contents/overview-of-water-soluble-vitamins?source=machineLearning&search=vitamin+b1+thiamin&selectedTitle=6~150§ionRank=4&anchor=H3#H3>

FOLATE

About

Folate is a water-soluble vitamin.

Major functions:

- Acts as a coenzyme for single carbon transfers necessary for nucleic acid synthesis and amino acid metabolism (including homocysteine metabolism)
- Methylation of deoxyuridylate to thymidylate, necessary for DNA synthesis, and subsequent proper cell division – impairment of this in folate deficiency causes megaloblastic anemia

Food Sources

Ubiquitous in foods:

- Highest levels: spinach, asparagus, brussel sprouts, liver, yeast
- Mandated in US to be fortified into cereal and grain products
- Dark leafy green vegetables, fruit and fruit juices
- Nuts, beans, peas
- Limited amount in dairy, poultry, meat, eggs, seafood

Absorption and Metabolism

Ingested folate in foods gets hydrolyzed to monoglutamate form. Once absorbed, monoglutamate form of folate gets reduced into tetrahydrofolate (THF). Half of folate in body stored in liver, but stores can be depleted much more quickly than B12.

Recommended Intakes

The recommended dietary allowance (RDA) for folate in an adult is 400 mcg of dietary folate equivalents (DFE) daily, where 1 mcg DFE = 0.6 mcg folic acid from fortified foods or dietary supplements consumed with food. The tolerable upper limit (UL) to prevent toxicity is 1000 mcg/day in both adult males and females.

Clinical Relevance

Medicinal use:

- Many studies are ongoing to elucidate the role of folate in cancer progression, reduction in cardiovascular disease, and improvement of neurodegenerative diseases, including Alzheimer's and dementia; however, these have yet to find evidence of hard and fast associations or causative effects
- Folate supplementation is known to reduce the risk of preterm delivery, neural tube defects, and other congenital defects, as well as lengthen gestational age. Thus, many clinicians recommend that all women of child-bearing age achieve adequate folate intake during the periconceptual period.

Deficiency

- At risk groups: women of childbearing age, non-Hispanic black females, alcoholics
- Isolated deficiency rare – usually co-exists with deficiency of other nutrients where commonly affected groups include alcoholics, patients with poor diet, and patients with malabsorptive disorders
- Both folate and vitamin B12 deficiencies can present similarly as megaloblastic anemia; however, folate stores can become depleted over months, whereas vitamin B12 stores become depleted over years
- Clinical symptoms:
 - Megaloblastic anemia most common; This is clinically difficult to distinguish from B12 deficiency
 - Mucosal ulcerations
 - Teratogenicity: neural tube defects, preeclampsia, still births, impaired fetal growth

Drug interactions: the following impair folate action – methotrexate, certain anti-epileptics (phenytoin, carbamazepine, valproate), sulfasalazine

Other

More information: <http://ods.od.nih.gov/factsheets/Folate-HealthProfessional/>

VITAMIN B12

About

Vitamin B12 is a water-soluble vitamin.

Major functions:

- Facilitates red blood cell production
- Necessary for adequate neurological function
- Involved in DNA synthesis
- Involved in formation of methyl donors involved in cellular reactions

Food Sources

The only natural source of vitamin B12 is animal products, including fish, meat (especially liver), poultry, eggs, milk, and milk products. It can also be added as a fortificant to breakfast cereals, which can be important sources for vegetarians.

Absorption and Metabolism

When an animal product is ingested, vitamin B12 enters the GI tract bound to protein. These separate in the acidic stomach environment allowing free B12 to bind intrinsic factor released from parietal cells in stomach. This complex can be absorbed in distal ileum such that B12 can be used for bodily needs.

B12 is stored in reasonable quantities in the liver, so it takes years to deplete those stores should the body stop adequately obtaining or absorbing it from foods. Both vitamin B12 deficiency and folate deficiency present with a macrocytic, megaloblastic anemia.

Recommended Intakes

The recommended dietary allowance (RDA) for an adult is 2.4 mcg/day. This vitamin has a low potency for toxicity.

Clinical Relevance

Deficiency:

- Relatively common in the US – affects 1.5-15% of Americans
- Causes: malabsorption from foods, pernicious anemia, post-surgical malabsorption, strict vegetarian/vegan diet
- Pernicious anemia: autoimmune destruction of parietal cells in stomach causes lack of intrinsic factor to facilitate B12 absorption – the result is a macrocytic, megaloblastic anemia
- Sub-acute combined degeneration: degeneration of dorsal column and lateral corticospinal tracts causes impaired proprioception, vibration, and discriminative touch as well as upper motor neuron syndrome
- Other symptoms: loss of balance, depression, confusion, dementia, amnesia, mouth and tongue soreness

Drug interactions: proton pump inhibitors have been shown to interfere with B12 absorption, so patients on long term PPI's should have B12 levels monitored

Other

More information: <http://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/>

VITAMIN B6

About

Vitamin B6 is a water-soluble vitamin. The term is generic for a family of three compounds, including pyridoxine, pyridoxal, and pyridoxamine; these can all become phosphorylated to become active vitamin B6.

Major functions:

Vitamin B6 is involved in more than 100 coenzyme reactions, including transamination, amino acid metabolism, gluconeogenesis and glycogenolysis. Pyridoxal phosphate (PLP) is one of the most active forms of modified B6. Some important examples of its coenzymatic actions are listed below:

- Synthesis of non-essential amino acid groups. Without this coenzyme, every amino acid group would be essential, and thus have to be supplied by the diet.
- Release of glucose from glycogen
- Catalyzes a step in heme synthesis, a nitrogen ring necessary to hold iron in place (example: hemoglobin)
- Synthesis of neurotransmitters, including serotonin, dopamine, norepinephrine, histamine, and GABA

Vitamin B6 also plays a role in adequate immune function.

Food Sources

Vitamin B6 is stored in muscle tissue of animals; the richest sources include fish, beef liver, and other organ meats. These also provide the greatest bioavailability. Other sources are plant foods, such as whole grains, carrots, potatoes, spinach, bananas, and avocados. Excessive heat during meal preparation can cause loss of vitamin B6 within the food.

Absorption and Metabolism

Vitamin B6 is the generic name for several related compounds; these include pyridoxine, pyridoxal, pyridoxamine, and their phosphorylated forms. The most biologically active form is pyridoxal phosphate (PLP). Dephosphorylated B6 gets absorbed passively. Once transported to the liver, it gets phosphorylated, which renders it biologically active. These forms are then carried in the blood stream by albumin to be delivered to muscle tissues for storage. Excess vitamin B6 gets secreted by the kidneys.

Recommended Intakes

The recommended dietary allowance (RDA) in a healthy middle-aged adult male or female is 1.3 mg/day. The upper limit (UL) to avoid toxicity is 100 mg/day.

Clinical Relevance

Deficiency:

-Isolated deficiency is rare – usually see deficiency in association with other vitamin deficiencies

-At risk:

- Renal disease: chronic insufficiency, ESRD, post-kidney transplantation
- Rheumatologic disease: Crohn's, ulcerative colitis, Celiac, rheumatoid arthritis,
- Alcoholism, because acetaldehyde (product of alcohol metabolism) decreases cell formation of LP

and reduces PLP's biologic activity

-Clinical manifestations:

- Peripheral neuropathy, seizures, depression
- Seborrhic dermatitis with cheilosis and glossitis, microcytic anemia

-Several medications also decrease serum PLP; these include L-DOPA for Parkinson's and isoniazid for tuberculosis

Toxicity:

-Occurs when individuals ingest 2-6 grams daily for at least 2 months

-Classically occurs in bodybuilders and women seeking to relieve PMS symptoms

-Clinical manifestations: irreversible nervous system deficits, including gait disturbance and extremity paresthesias

Medicinal use:

-Women often attempt to treat PMS with vitamin B6 supplementation, but most studies have shown only limited benefit

-Some physicians prescribe vitamin B6 to pregnant women with severe nausea

Other

More information: <https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/>

NIACIN

About

Niacin is a water-soluble vitamin. It acts as a coenzyme as NAD and NADP+, which are active participants in oxidative-reduction reactions necessary for energy metabolism.

Food Sources

-Poultry, meat, fish

-Enriched bread and cereal products, which is FDA mandated fortification

-Unlike many other water soluble vitamins, niacin is very heat stable, so little is lost in cooking

Absorption and Metabolism

Niacin exists as two forms, nicotinic acid and nicotinamide. Niacin can be obtained from foods or synthesized in the body from tryptophan. The bioavailability of niacin can be low in some grains, especially corn. In Latin America, indigenous groups soak their staple food of corn in an alkali solution containing calcium hydroxide dissolved in water. This helps release niacin from its protein binders, such that it can be better absorbed, and bioavailability increased.

Recommended Intakes

The recommended dietary allowance (RDA) for a healthy adult male is 16 mg/day and 14 mg/day for a healthy adult female. The upper level (UL) to prevent toxicity is 35 mg/day.

Clinical Relevance

Deficiency:

-Causes syndrome known as 'pellagra:'

- Dermatitis: rough red rash on sun-exposed areas of skin
- Diarrhea

- Dementia
- Death

-During the 1900s, pellagra was rampant in the southeastern US, where corn was the staple food. Today, pellagra is common in African countries, where famine occurs, or in refugee camps where rations are mostly maize.

-Alcoholics are at high risk of deficiency in US

Clinical use: Niacin may be prescribed by physicians as a cholesterol lowering agent. The dose of 1-2 g per day is 60 times the RDA. Adverse effects include skin flushing, GI upset, and liver damage. Prescription niacin is in a different formula than supplemental niacin, such that the supplement cannot be a replacement to help lower cholesterol.

Other

More information: <http://umm.edu/health/medical/altmed/supplement/vitamin-b3-niacin>

BIOTIN

About

Biotin is a water soluble vitamin. It serves as a coenzyme for several carboxylase enzymes that add carbon dioxide to compounds. Examples of reactions include

- Carboxylation of pyruvate to oxaloacetate in the citric acid cycle; when serum glucose stores are low, gluconeogenesis begins with oxaloacetate
- Breakdown of amino acids threonine, leucine, methionine, and isoleucine
- Carboxylation of acetyl-CoA to malonyl-CoA required in fatty acid synthesis

Food Sources

Whole grains, eggs, nuts, legumes

Absorption and Metabolism

There are two forms of biotin, the free vitamin and the protein-bound form, called biocytin. In the small intestine, biotinidase enzyme releases biotin from biocytin. Free biotin is then absorbed. It is stored in small amounts in the muscles, liver, and brain. Humans excrete more biotin than they consume via the kidneys and the bile to a lesser extent.

Recommended Intakes

The adequate intake for an adult is 30 mcg/day. There is no established upper limit.

Clinical Relevance

Deficiency:

Historically, biotin was discovered in the 1920s in rat experiments. They were fed large amounts of raw eggs and developed severe rashes, alopecia, and paralysis. These symptoms were reversed when they were subsequently fed yeast and liver, which contain biotin. Today, humans can develop similar clinical symptoms of deficiency after consuming >12 raw eggs per day. The raw eggs have avidin protein that binds biotin and limits its absorption. Cooking an egg denatures avidin, which thus renders it ineffective.

One in 112,000 infants is born with a genetic defect that results in low levels of biotinidase, and subsequently causes biotin deficiency. Clinical symptoms include skin rash, alopecia, convulsions and impaired growth; they manifest within weeks of birth.

Other

More information: <http://lpi.oregonstate.edu/mic/vitamins/biotin>

PANTOTHENIC ACID

About

Pantothenic acid is a water-soluble vitamin.

Major functions:

The name is derived from the Greek word, 'pantothen,' meaning 'from every side.' This vitamin is present in all cells of the body and can be found in a wide variety of foods. Pantothenic acid is a precursor to coenzyme A, which reacts with acyl groups to create derivatives like acetyl-CoA, succinyl-CoA, malonyl-CoA, HMG-CoA, enzymes all essential in generating energy for the body. This vitamin also forms part of a compound called the acyl carrier protein, which shuttles fatty acids through a synthesis pathway to lengthen and modify them.

Food Sources

It is ubiquitous in foods, especially meat, milk and yogurt, and vegetables (mushrooms, broccoli, legumes). Intake from fresh food sources is generally greater than from processed foods because the latter results in vitamin loss after milling, refining, freezing, heating, and canning.

Absorption and Metabolism

Once absorbed through the small intestine, it travels through the bloodstream bound to erythrocytes. It gets converted to coenzyme-A within individual cells. This vitamin is excreted through the kidneys.

Recommended Intakes

The recommended dietary allowance (RDA) in a healthy middle-aged adult is 5 mg/day. No upper limit has been set because there is no known toxicity.

Clinical Relevance

Deficiency is rare and has only been described during World War II in extremely malnourished prisoners of war. Symptoms included numbness and paresthesias in extremities.

Other

More information: <http://lpi.oregonstate.edu/mic/vitamins/pantothenic-acid>

RIBOFLAVIN

About

Riboflavin is a water-soluble vitamin. It acts as a coenzyme in energy metabolism and is particularly known for its activation of FAD and FMN. Glutathione reductase is FAD dependent. In states of riboflavin deficiency, serum glutathione reductase can be low.

Food Sources

- Dairy products: milk, eggs, cottage cheese, cheddar cheese
- Enriched bread, rolls, crackers, and other cereal grain products, which is FDA mandated fortification
- Mushrooms, spinach, broccoli, asparagus

Absorption and Metabolism
It is freed from proteins with help of HCl in stomach then absorbed in the small intestine. It is rapidly excreted by the kidneys.
Recommended Intakes
The recommended dietary allowance (RDA) is 1.3 mg/day in a health adult male and 1.1 mg/day in a health adult female. Generally, Americans ingest as much as double those values in a given day, but there are no adverse effects of consuming large amounts, so no upper limit (UL) has been set.
Clinical Relevance
<u>Deficiency:</u> -At risk: adolescent girls and elderly, malabsorption states (alcoholism, diabetes, malignancy), long term use of phenobarbital -Rarely occurs in isolation -Clinical syndrome is termed 'aribo flavinosis:' <ul style="list-style-type: none">• Mouth: stomatitis, glossitis, angular cheilitis• Skin: seborrheic dermatitis• Erythrocytes: anemia• Fatigue, confusion, headache -May impair iron absorption
Other
More information: <ul style="list-style-type: none">• http://www.nlm.nih.gov/medlineplus/ency/article/002411.htm• http://lpi.oregonstate.edu/mic/vitamins/riboflavin

ELECTROLYTES

SODIUM

About
Sodium (Na) is an electrolyte and major mineral. The most important source is salt, sodium chloride. <u>Major functions:</u> -Main solute in extracellular fluid (exists as cation), which means it regulates plasma volume and is involved in water balance in the body -Helps absorb glucose and amino acids in small intestine -Flows across cell membranes thereby creating electrical current, which is required for normal nerve impulses and muscle contraction
Food Sources
-Mostly obtained from prepared and processed foods as salt -Commonly eaten foods, such as: <ul style="list-style-type: none">• Bread and other cereal-grain products• Hot dogs and lunch meats• Cheese• Canned and frozen entrees and soups• Condiments, bottled sauces, gravies

- Restaurant foods
- Table salt (40% Na + 60% Cl; 1 tsp salt = 2300 mg of sodium)

Absorption and Metabolism

Sodium is absorbed by active transport (sodium-potassium pump) in both the small and large intestines. Most of the body's sodium exists as cations found in the extracellular fluid compartment. The kidney excretes excess amounts of sodium. When low levels exist, aldosterone hormone acts on the distal nephrons to retain sodium ions.

Recommended Intakes

The adequate intake for adults under 51 years of age is 1500 mg/day. That number decreases to 1300 mg/day for adults aged 51-70, and again down to 1200 mg/day for adults older than 70. The upper limit recommended is 2300 mg/day, but up to 95% of Americans exceed that level of intake.

Clinical Relevance

Deficiency:

-Very rare due to abundance in diet

-Hyponatremia:

- Defined as low serum sodium
- If it develops progressively, often asymptomatic; if serum sodium drops drastically, intracranial pressure can increase to cause nausea/vomiting and more severe effects of delirium, seizure, and coma
- Common causes include volume loss (excessive perspiration, vomiting, diarrhea, diuretics), volume overload (heart failure, cirrhosis, renal failure), SIADH

Toxicity:

-Most common health problems associated with high sodium intake: hypertension, cerebrovascular disease, stroke

-Currently, there is discrepancy in the data that reduced intake below 2300 mg/day actually reduces mortality. More recent data has also shown that reduction in salt intake in heart failure patients does not affect their all-cause mortality (previously, low salt diet was a core tenet of heart failure management).

-Hypernatremia:

- Defined as high serum sodium
- Patients experience increased thirst if capable; when thirst not satisfied, patients can develop impaired consciousness, seizures, asterixis, myoclonus
- Common causes include impairment in ability to sense thirst or express need for water (infancy, dementia, mentally impaired, anesthetized); diabetes insipidus; chronic kidney disease and heart failure

Other

More information:

- <http://www.nutri-facts.org/eng/minerals/sodium-and-chloride/at-a-glance/>
- <http://www.mayoclinic.org/healthy-living/nutrition-and-healthy-eating/in-depth/sodium/art-20045479>

CHLORIDE

About

Chloride (Cl) is a major mineral and electrolyte.

Major functions:

- Chloride exists as the major anion in the extracellular fluid to preserve electroneutrality with the major cation, sodium. It plays a vital role in the appropriate regulation of fluid volume and balance.
- It can move across cell membranes to create a current, which aids in transmission of nerve impulses
- Component of stomach acid, HCl, which is necessary for adequate digestion
- It helps maintain acid-base balance in the lungs by shifting into cells as bicarbonate exits to maintain electroneutrality. This promotes appropriate excretion of carbon dioxide via exhalation.

Food Sources

The majority of chloride in food comes from table salt, sodium chloride. Thus, the foods that provide sodium in the diet via salt also provide most of dietary chloride. Salted foods such as many processed foods, olives, and bread are the primary dietary sources.

Absorption and Metabolism

Chloride absorption accompanies sodium absorption to maintain electroneutrality of ions. It gets passively absorbed paracellularly. The movement of sodium and chloride ions across enterocytes in the gut allows passive flow of water paracellularly. Chloride can be excreted in the distal colon, which facilitates intestinal water excretion. Once absorbed into the body, it exists primarily in the extracellular fluid to balance the positively charged sodium. Its levels are regulated by renal excretion.

Recommended Intakes

The adequate intake (AI) for chloride in adults is 2300 mg/day. This is based on the ratio of sodium to chloride in table salt as 40:60. The AI of sodium is 1500 mg/day, so that of chloride is 2300 mg/day. The upper limit of daily chloride intake is 3600 mg, which also parallels the upper limit of sodium of 2300 mg/day using the 40:60 ratio of sodium to chloride in table salt.

Clinical Relevance

Deficiency:

- Dietary deficiency is very unlikely because salt intake is so high in the US
- Chloride can get depleted with frequent episodes of vomiting since it is the anion that complexes with hydrogen to create stomach acid, HCl. If this happens, clinical manifestations of hypochloremia include weakness, anorexia, and lethargy. Acid-base balance can also become disrupted.

Toxicity:

- Although not specifically related to chloride, excess ingestion of salt-containing foods predisposes to development of disease, including hypertension, cerebrovascular disease, and stroke.

Other

More information:

- <http://www.nlm.nih.gov/medlineplus/ency/article/002417.htm>
- <http://www.vitamins-nutrition.org/vitamins/chloride.html>

POTASSIUM

About

Potassium (K) is an electrolyte and major mineral.

Major functions:

- Main intracellular solute (exists as a cation) that helps regulate fluid balance
- Movement across cell membranes generates electrical current, which is required for adequate nerve impulses and muscle contraction
- High levels promotes calcium retention and reabsorption from the kidney

Food Sources

- Major contributors of potassium in the adult diet include dairy products, potatoes, tomatoes, orange juice
- Other good sources are fruits (banana, cantaloupe, orange, watermelon), vegetables (broccoli, artichoke, squash), beans, yogurt, salmon

Absorption and Metabolism

The body absorbs 90% of potassium consumed through the small and large intestine. Once in the circulation, it gets transported into the body's cells. Aldosterone hormone stimulates excretion by the kidneys.

Recommended Intakes

The adequate intake for potassium for a healthy adult is 4700 mg/day. This number is rarely achieved in the U.S. Daily intake should not exceed 18 grams to prevent acute development of hyperkalemia.

Clinical Relevance

Deficiency:

- Can be life-threatening
- Hypokalemia
 - Defined as low serum potassium
 - Clinically presents as weakness, fatigue, muscle cramps, which can progress to flaccid paralysis and arrhythmia
 - Common causes include GI loss (vomiting, diarrhea), metabolic alkalosis *and* metabolic acidosis, renal disease (hyperaldosteronism, renal artery stenosis, renal tubular acidosis), drugs (diuretics), heart failure, alcoholism

Toxicity:

- Can also be life-threatening
- Hyperkalemia
 - Defined as high serum potassium
 - Most serious clinical implication is arrhythmia (EKG shows peaked T waves, short QT interval, wide QRS, absent p waves), which can progress to ventricular fibrillation if not managed early
 - Common causes include metabolic acidosis, drugs (beta blockers, digoxin, ACE inhibitors/angiotensin receptor blockers), rhabdomyolysis

Other

More information: <http://www.nutri-facts.org/eng/minerals/potassium/at-a-glance/>
<http://lpi.oregonstate.edu/infocenter/minerals/potassium/>

MAJOR MINERALS

CALCIUM

About

Calcium is a major mineral and is the most abundant one in the body.

Major functions:

- Structural integrity to bones (house majority of stored calcium)
- Freely circulating ionized calcium is involved in neuromuscular excitability, blood coagulation, hormonal secretion, and enzymatic regulation

Food Sources

- The best source of calcium is from dairy products, such as milk, yogurt, and cheese
- Other sources include collard greens, kale, broccoli, canned sardines, salmon

Absorption and Metabolism

Vitamin D enables calcium absorption in the small intestine. Other major regulators of homeostasis are PTH (increase Ca serum levels) and calcitonin (decreases Ca serum levels). Calcium is excreted primarily by the kidney.

Recommended Intakes

The recommended dietary allowance (RDA) for a 30-50 year old patient is 1000 mg/day. This number increases to 1200 for females older than 50 and all elderly patients older than 70. The upper limit (UL) for an adult to reduce risk for toxicity is 2500 mg.

Clinical Relevance

Clinical use:

- Low intake associated with increased risk for hypertension; increased intake associated with reduced risk of colon cancer
- 2-3 servings/day of low fat dairy products is recommended in Dietary Approaches to Stop Hypertension (DASH) diet

Deficiency:

- At risk individuals include post-menopausal women, lactose intolerant patients, vegans, chronic glucocorticoid use
- Initially asymptomatic as body depletes stores in bone → long term progression to osteopenia and osteoporosis

Toxicity:

Symptoms:

- Renal stones, polydipsia, polyuria (easy mnemonic: "stones")
- Osteitis fibrosis ("bones")
- Constipation ("groans")
- Decreased mental status, lethargy/stupor/coma ("psychiatric moans")

Drug interactions:

- Reduces absorption of bisphosphonates, fluoroquinolones, tetracyclines, levothyroxine, phenytoin
- Loop diuretics cause hypocalcemia, but thiazide diuretics cause hypercalcemia

-Antacids cause hypocalcemia
-Long term glucocorticoid use can deplete bone calcium stores and induce osteoporosis

Other

More information: <http://ods.od.nih.gov/factsheets/Calcium-QuickFacts/>

PHOSPHORUS

About

Phosphorus is a major mineral. Its name is commonly interchanged with phosphate, which is a salt composed of phosphorus and oxygen.

Major functions: essential component of cell membrane structure; cellular energy metabolism; involved in phosphorylation reactions; bone formation (works closely with calcium)

Food Sources

-Ubiquitous in foods:

- Cereal products, dairy foods, eggs, nuts (peanuts, almonds)
- Meat (turkey, chicken, beef), fish (salmon, halibut)

-Also contributed by cola products

Absorption and Metabolism

The majority of phosphorus is found in bones and teeth. The remaining 30% exists as protein-bound, free phosphorus; or is complexed with circulating cations. The action of phosphorus is tightly regulated by parathyroid hormone (PTH), which serves to decrease phosphorus levels when intake is increased.

Recommended Intakes

The recommended dietary allowance (RDA) for a healthy adult male or female is 700 mg/day. The tolerable upper limit (UL) in a healthy adult per day is 4000 mg.

Clinical Relevance

Deficiency:

-Rare because kidney can reabsorb to compensate for decreased intake

-At risk groups: refeeding syndrome, alcoholics, diabetics recovering from diabetic ketoacidosis

-Symptoms include loss of appetite, muscle weakness, bone fragility, extremity numbness

-Deficiency of phosphorus is a hallmark feature of refeeding syndrome, which occurs when malnourished patients are aggressively fed with enteral or parenteral nutritional support

Toxicity:

-Largely asymptomatic, but if manifested, symptoms are those of hypocalcemia (commonly neuromuscular excitability – paresthesias, numbness, tetany)

-Causes

- Chronic kidney disease results in failure to excrete phosphate, which induces state of hyperphosphatemia – patients must take extra caution to reduce consumption of phosphorus and they should utilize phosphate binders
 - For more information about a low phosphorus diet: <http://www.mayoclinic.org/food-and-nutrition/expert-answers/faq-20058408>
- Alcohol abuse

- Hypoparathyroidism

Drug interactions:

- Aluminum-containing antacids can decrease absorption
- Proton pump inhibitors limit efficacy in patients with CKD
- Potassium and phosphorus supplements taken together can induce hyperkalemia

Other

More information:

- <http://umm.edu/health/medical/altmed/supplement/phosphorus>
- <http://lpi.oregonstate.edu/infocenter/minerals/phosphorus/>

MAGNESIUM

About

Magnesium is a major essential mineral.

Major functions:

- Glucose metabolism, ATP stability, DNA and RNA synthesis, antioxidant function of glutathione
- Helps facilitate bone mineralization
- Important role in active transport of potassium and calcium across cell membranes, needed for nerve transmission and striated (particularly heart) and smooth muscle contraction

Food Sources

It is abundant in chlorophyll, therefore rich in plant products. These include green leafy vegetables, broccoli, squash, beans, nuts, seeds, whole grains, and chocolate. Brazil nuts are one of the richest sources. Magnesium also typically occurs in high quantities in hard tap water.

Absorption and Metabolism

Vitamin D promotes magnesium absorption to some extent. Half of body stores are in bone; the other half is found in various soft tissues throughout body. Magnesium is excreted through the kidney.

Recommended Intakes

The recommended dietary allowance (RDA) for magnesium in a healthy middle-aged adult male is 420 mg/day and female is 320 mg/day. The upper level (UL) recommended for *supplemental* magnesium intake is 350 mg/day. No UL has been established for dietary magnesium alone.

Clinical Relevance

Clinical use:

- Primary ingredient in milk of magnesia laxatives, also present in some antacids, like Roloids
- Adequate intake each day may reduce the risk of developing diabetes
- Prescribed to pregnant women with preeclampsia to prevent or treat seizures
- Drug interactions: magnesium can decrease absorption of bisphosphonates, prevent appropriate function of antibiotics, including tetracyclines and quinolones

Deficiency:

-At risk individuals:

- Excessive gastrointestinal loss (prolonged episodes of diarrhea and vomiting, chronic disease such

as Crohn's or Celiac disease)

- Alcoholics
- Insulin-resistant diabetics (excess glycosuria induces magnesium loss)
- Chronic use of loop diuretics or proton pump inhibitors

-Symptoms

- Neuromuscular: paresthesias, hyperreflexia, muscle spasm, tetany (resembles calcium deficiency)
- Cardiac: EKG abnormalities, including prolonged QT and R, ST depression, flattened or inverted p waves, torsade de pointes; also coronary spasm (resembles calcium excess)
- Hypokalemia, hypoparathyroidism then hypocalcemia

-Unfortunately, the most commonly used laboratory test to assess magnesium status in the body is serum levels, but since most magnesium is stored in bone and tissues, this is not an accurate way of discerning body levels

Toxicity:

-At risk individuals: elderly with declining kidney function, excess supplementation

-Symptoms worsen with increased intake:

- Serum concentration between 4-6 mEq/L: nausea/vomiting, flushing, headache, drowsiness/lethargy, diminished deep tendon reflexes
- 6-10: somnolence, hypocalcemia, absent deep tendon reflexes, hypotension, bradycardia
- >10: muscle paralysis, respiratory failure, complete heart block, cardiac arrest

Other

More information: <http://ods.od.nih.gov/factsheets/Magnesium-HealthProfessional/>

TRACE MINERALS

IRON

About

Iron is a trace mineral.

Major functions:

-Incorporated into hemoglobin so that oxygen can be adequately transported from lungs to tissues; also incorporated into myoglobin, which binds oxygen and supplies it to skeletal muscle

-Growth, development, normal cellular functioning, synthesis of some hormones and connective tissues

Food Sources

Heme food sources: animal products like red meat, fish, poultry

Non-heme food sources: nuts, beans, vegetables; iron fortified foods including breakfast cereals, grains, bread, and other cereal grain products

Absorption and Metabolism

Heme is better absorbed in the small intestine, so has a higher bioavailability. Non-heme absorption can be enhanced with concomitant vitamin C-rich foods. Calcium may reduce bioavailability of both sources.

Free ionized iron can form radical compounds, so the body largely regulates absorption and excretion, with hepcidin protein playing the most important role. Excretion of iron largely occurs in small intestine,

which sheds the outer epithelial layer of enterocytes housing iron. These sloughed off cells are lost in the feces. Storage and transport proteins also play a huge role in regulating amount of free ionized iron available for use.

Recommended Intakes

The recommended dietary allowance (RDA) for a 30-50 year old non-vegetarian male is 8 mg/day. The RDA for a 30-50 year old non-vegetarian female is 18 mg/day. Vegetarians should consume almost double the listed RDA since non-heme has lower bioavailability. The upper limit (UL) of iron is 45 mg/day for both males and females of adult age.

Clinical Relevance

Deficiency:

- #1 nutritional deficiency worldwide
- At risk individuals include patients with renal failure and heart failure, pregnant and menstruating women, and patients with gastrointestinal autoimmune diseases, like Celiac or irritable bowel disease
- Symptoms initially largely asymptomatic as iron storage is depleted → progresses to iron deficiency anemia
- Iron studies reveal low serum iron, low serum ferritin, high total iron binding capacity, and low percent transferrin saturation

Toxicity:

- Hereditary hemochromatosis can cause iron overload. Symptoms manifest as liver cirrhosis and carcinoma, heart disease, and endocrinopathy.
- Acute ingestion of excess iron supplements can cause nausea, constipation, vomiting, abdominal pain
- Overdose in young children less than 6 years is the leading cause of poisoning
- Higher intakes are associated with increased risk for cardiovascular disease and some cancers

Drug interactions:

- Iron supplements decrease efficacy of Levodopa and Levothyroxine
- Proton pump inhibitors reduce iron absorption

Other

More information: <http://ods.od.nih.gov/factsheets/Iron-HealthProfessional/>

COPPER

About

Copper is a trace mineral.

Major functions: Copper is a coenzyme for many oxidation-reduction reactions due to its ability to alternate between 2 oxidation states, Cu^{1+} and Cu^{2+} . Some of those reactions are described below:

- One important role is its activity with ceruloplasmin, an enzyme that is required in appropriate oxidation of iron, such that iron can be incorporated into transferrin.
- Also part of superoxide dismutase enzymes, which eliminate superoxide free radicals that otherwise cause oxidative damage to cell membranes
- Coenzyme for cytochrome C oxidase involved in catalysis of the electron transport chain in energy metabolism
- Involved in neurotransmission

-Component of lysyl oxidase, which cross-links collagen and elastin – these proteins give tensile strength to connective tissues in lungs, blood vessels, skin, teeth, and bones

Food Sources

The richest sources of copper include lentils, oysters, beef liver, and lobster. Other more commonly consumed products that contain copper include nuts (pecans, walnuts), legumes (beans), mushrooms, soy products, and dark chocolate.

Absorption and Metabolism

Once absorbed, copper gets transported through the blood bound to albumin or other proteins and delivered to the liver, the main storage site, as well as the kidneys. It leaves the liver bound to ceruloplasmin, which is an enzyme required in the oxidation of iron so that it can be incorporated into transferrin. As such, adequate copper intake is necessary for normal iron metabolism. Copper gets excreted primarily through bile into GI tract for fecal elimination.

Recommended Intakes

The recommended dietary allowance (RDA) for copper in a healthy adult is 900 micrograms/day. The upper limit for daily intake is 10 mg/day to reduce risk of liver damage.

Clinical Relevance

Deficiency:

-At risk population: infants, patients with Menke's disease, patients with zinc toxicity
-Symptoms: anemia, leukopenia, neutropenia, osteopenia

Toxicity: Patients with inheritable Wilson Disease (usually autosomal recessive) have decreased copper excretion and decreased incorporation into ceruloplasmin. This results in copper build up and deposition into tissues. Symptoms manifest as:

- Basal ganglia deposition: extra-pyramidal symptoms, wing-beating tremor
- Eye deposition: Kayser-Fleischer rings
- Liver deposition: cirrhosis

Other

More information: <http://lpi.oregonstate.edu/infocenter/minerals/copper/>

ZINC

About

Zinc is a trace mineral.

Major functions:

-Adequate immune response – zinc develops and activates T lymphocytes
-Protein and DNA synthesis
-Growth and developments in utero and infancy
-Wound healing – helps maintain integrity of skin and mucosal membranes
-Taste and smell

Food Sources

Oysters are the best source; but common sources include beef, poultry, shellfish, and fortified cereals.

Absorption and Metabolism
Phytates inhibit zinc absorption in the gastrointestinal tract – they are present in unleavened whole grain breads, cereals, and legumes.
Recommended Intakes
The recommended dietary allowance (RDA) for an adult male is 11 mg/day and for an adult female is 8 mg/day. The upper limit (UL) for an adult to prevent toxicity is 40 mg/day.
Clinical Relevance
<u>Medicinal use:</u> In developing countries, supplementing zinc in children with diarrhea has been shown to reduce the symptoms and duration. Some studies have shown that zinc can slow progression of macular degeneration. Data conflicts regarding the efficacy of zinc in helping to cure the common cold – generally, intranasal zinc sprays should be avoided due to reports of them causing chronic or permanent anosmia.
<u>Deficiency:</u> -At risk: gastrointestinal surgery, irritable bowel disease, vegetarians, alcoholics, sickle cell -Effects: slow growth in infants, diarrhea, loss of appetite, impaired immune function → more severe cases involve delayed adolescent sexual development, impotence, hair loss, diarrhea, dermatitis
<u>Toxicity:</u> -Symptoms: nausea, vomiting, loss of appetite, stomach cramps, diarrhea, headaches -Excessive use of denture adhesive creams can cause zinc toxicity and subsequent copper deficiency and neurological dysfunction
<u>Drug interactions:</u> -Simultaneous ingestion of zinc supplement with quinolone or tetracycline antibiotic reduces absorption of both – separate time of ingestion to reduce effect -Thiazide diuretics increase urinary excretion of zinc
Other
More information: http://ods.od.nih.gov/factsheets/Zinc-QuickFacts/

IODINE

About
Iodine (I ₂) is a trace mineral. It is present in food as iodide (I ⁻). Its only function in the body is synthesis of thyroid hormone. Adequate levels of this hormone are vital for energy expenditure, macronutrient metabolism, brain development, growth and organ maturation.
Food Sources
The best sources are saltwater seafood, seaweed, iodized salt, molasses, and dairy products. With regard to dairy products, iodide is not a natural source, but the element is added to cattle feeds and sanitizing solutions used in dairy products. Given its limited quantity in various foods, most Americans obtain iodine from iodized salt at the dinner table. Note that iodized salt is not used in fast food, processed and restaurant foods.

Absorption and Metabolism

Goitrogens decrease bioavailability of iodine. These compounds are abundant in raw vegetables, including turnips, cabbage, brussel sprouts, cauliflower, broccoli, potatoes. Iodine deficiency is a particular problem in underdeveloped nations where consumption of raw vegetables is high. This is not a great problem in the US where many vegetables are cooked, and the goitrogens subsequently destroyed.

When iodine is absorbed, the majority gets transported to the thyroid gland and stored for later use in thyroid hormone synthesis. The kidney excretes excess.

Recommended Intakes

The recommended dietary allowance (RDA) to maintain adequate thyroid hormone production is 150 mcg/day in healthy adults. Pregnant women should consume 220 mcg/day. The upper limit (UL) to prevent toxicity is 1100 mcg/day in healthy adults.

Clinical Relevance

Disease management:

-Radioactive iodine exploits the thyroid's natural tendency to absorb all iodine ingested. In patients with thyroid cancer or hyperthyroidism, this modified iodine gets absorbed by the thyroid and concentrated. The radiation subsequently destroys the thyroid tissue in a very localized fashion.

-Patients are advised to have a low iodine diet for several weeks prior and to be in a state of excess TSH, which promotes increased iodine uptake by thyroid. If the patients have already had their malignant thyroid gland resected and are taking levothyroxine for thyroid replacement, they can stop taking the medication for several weeks prior to radiation. This will induce a temporary state of hypothyroidism, but will increase circulating levels of TSH.

Deficiency:

-1/3rd of world's population is at risk for iodine deficiency. South America, Asia, Africa, and the Middle East all have the highest incidence of deficiency.

-Disorders include endemic goiter and endemic cretinism

-Insufficient dietary intake of iodine results in inability to synthesis T4 thyroid hormone. The body responds by releasing more TSH, which results in enlargement of the thyroid gland, thereby creating a goiter.

-There is particular concern for maternal deficiency during pregnancy when the fetus initially relies solely on maternal thyroid hormone for growth and development. The result of maternal iodine deficiency and subsequently lower thyroid hormone levels is birth of babies with congenital abnormalities, low birth weight, neurological disorders, mental retardation, poor physical development, and even death. This is termed cretinism when deficiency in utero is very severe and all symptoms are manifested.

Toxicity:

-Excess iodine can cause either hypothyroidism or hyperthyroidism depending on iodine status of individual when they start supplementation.

Other

More information: <http://ods.od.nih.gov/factsheets/Iodine-HealthProfessional/>

MANGANESE

About
Manganese is a trace mineral. <u>Major functions:</u> Similar to other trace minerals, manganese plays a vital role as cofactor for enzymatic reactions. Its ability to alternate between different oxidation states (Mn^{2+} , Mn^{3+} , and Mn^{7+}) makes it a very dynamic mineral. Examples of reactions include: <ul style="list-style-type: none">• Carbohydrate, amino acid, and cholesterol metabolism• Antioxidant function as manganese superoxide dismutase inside mitochondria• Help facilitate proteoglycan synthesis, proteins needed for healthy bone and cartilage formation
Food Sources
Whole grains, nuts, legumes (especially lima beans), and tea
Absorption and Metabolism
Manganese absorption through the small intestine has not been fully elucidated, but it is clear that iron status influences absorption. Increased iron stores (measured as serum ferritin level) are associated with decreased levels of absorbed manganese and vice versa. It gets excreted in the bile and excreted via fecal elimination.
Recommended Intakes
The adequate intake (AI) for manganese is 2.3 mg/day for a healthy adult male and 1.8 mg/day for a healthy adult female. The upper level (UL) to prevent toxicity and subsequent neurologic damage in a healthy adult is 11 mg/day.
Clinical Relevance
<u>Deficiency:</u> Very few cases of manganese deficiency have been reported in the US. Symptoms included poor growth, skeletal abnormalities, impaired glucose metabolism, and abnormal reproductive function. <u>Toxicity:</u> <ul style="list-style-type: none">-Toxicity is much more of a concern than deficiency-At risk individuals: children receiving long-term parenteral nutrition, workers with long term excessive inhalation of airborne industrial and automotive emissions (smelters, welders)-Long term effects: parkinsonism, psychosis, pulmonary fibrosis
Other
More information: http://lpi.oregonstate.edu/infocenter/minerals/manganese/

SELENIUM

About
Selenium is a trace mineral. <u>Major functions:</u> <ul style="list-style-type: none">-Very important coenzyme in enzymatic reactions-Known for its role in antioxidant defense as part of glutathione peroxidase enzymes – it specifically helps prevent lipid peroxidation and subsequent cell membrane damage-Component of iodothyronine deiodinase enzyme, which converts T4 to T3 in the periphery

Food Sources
Selenium is found in an array of food sources, including seafood (tuna, yellowfin, sardines, shrimp), meat (beef, turkey, chicken), cereals, grains, nuts (especially Brazil nuts), and dairy products. Most Americans consume adequate amounts in their regular diets.
Absorption and Metabolism
It exists in both organic (selenomethionine, selenocysteine) and inorganic (selenite, selenite) forms, both of which are absorbed through the intestine. The major site of storage is skeletal muscle. Selenium is excreted through the kidney.
Recommended Intakes
The recommended dietary allowance (RDA) for selenium in a healthy adult is 55 micrograms. This is based on the amount required to maximize glutathione peroxidase activity. The upper limit (UL) to prevent toxicity in a healthy adult is 400 mcg/day.
Clinical Relevance
<u>Clinical use:</u> Research has shown that selenium plays a role in preventing DNA damage and mutations. Studies are underway to elucidate the role in prevention of colorectal and prostate cancers. <u>Deficiency:</u> -Not common in the US -Results in decreased circulating levels of T3 and is associated with Keshan disease, a type of cardiomyopathy prevalent in China <u>Toxicity:</u> -Occurs in parts of the world with high levels of selenium in the soil where plants are grown for consumers -Symptoms: nausea, diarrhea, fatigue, hair loss, nail brittleness, skin rash
Other
More information: http://ods.od.nih.gov/factsheets/Selenium-HealthProfessional/

FLUORIDE

About
Fluoride is a trace mineral. Humans can function without it, but its presence in the diet and water supply reduces occurrence of dental caries. During tooth and bone development, fluoride forms hydroxyfluorapatite crystals, which prevent against bacterial and acid erosion of tooth enamel. Throughout a person's life, remineralization of teeth with fluoride continues to help prevent cavities.
Food Sources
The major source in the US is fluoridated water. The regions with the most fluoridated water include southern states and the Great Lakes states. Other sources include tea, seafood, and seaweed. Non-dietary sources to protect teeth include fluoridated toothpastes and mouth rinses.
Absorption and Metabolism
Once absorbed, fluoride is stored in the teeth and bone. This deposition is greatest during childhood. Fluoride is excreted by the kidney and via calcified tissue deposition.

Recommended Intakes
The adequate intake for healthy adult males is 4 mg/day and 3 mg/day for healthy adult females. Children should consume 0.7-3 mg/day. These values are based on the amount needed to resist dental caries but not cause dental fluorosis (see below). The upper limit to prevent mottling in a child's teeth during development is 0.1 mg/kg/day. The upper limit in adults is 10 mg/day.
Clinical Relevance
Deficient fluoride is associated with increased incidence of dental carries. If fluoride is used in excess in toothpastes or mouthwashes, it can cause dental fluorosis. This is mottling of the tooth enamel, which causes a speckled yellow discoloration of teeth. Toothpastes and mouth washes should be kept out of reach of young children when not being used specifically for cavity protection, because ingestion of large quantities can cause nausea, vomiting, diarrhea, sweating, spasms, convulsions, and coma. Furthermore, parents should also supervise brushing with fluoridated toothpastes in children less than 6 years. They often inadvertently swallow toothpaste and subsequently have higher levels of fluoride, which can promote fluorosis. It is recommended that children of this age only use a very thin smear of toothpaste when brushing.
Other
More information: http://lpi.oregonstate.edu/infocenter/minerals/fluoride/

CHROMIUM

About
Chromium is a trace mineral. Its role in health and specific functions in the body are not well characterized. However, it is known that it enhances the action of insulin and it appears to be involved in energy metabolism.
Food Sources
It is very ubiquitous in foods, and thus daily requirements are easy to meet. However, quantities within these foods are low. Foods include meat, whole grains, fruits (juice, apples, bananas), vegetables (especially broccoli), and spices.
Absorption and Metabolism
The biologically active form is trivalent (Cr^{3+}), while the toxic form from pollution exists as a hexavalent molecule (Cr^{6+}). Very little trivalent chromium is actually absorbed from the small intestine, but vitamin C and niacin have been known to increase absorption.
Recommended Intakes
The adequate intake (AI) for chromium in a healthy adult male is 35 micrograms/day and 25 micrograms/day in a healthy adult female. No RDA has been established for chromium because too little research exists on this mineral. No tolerable upper limit (UL) has been established.
Clinical Relevance
Deficiencies and toxicities are not well characterized.
Other
More information: http://ods.od.nih.gov/factsheets/Chromium-HealthProfessional/

MOLYBDENUM

About
Molybdenum is an ultra-trace mineral, meaning that it exists in even more limited amounts in the body, but is still just as essential as some of the more well-known minerals. It acts as a co-factor for several enzymatic reactions in the body. The enzymes that require molybdenum include sulfite oxidase, xanthine oxidase, aldehyde oxidase, and mitochondrial amidoxime reducing component.
Food Sources
Legumes, such as beans, lentils, and peas, are the richest source. Other sources include grains and nuts. Like iodine and selenium, the quantity varies depending on the soil used to grow these plants – some soils have richer stores of molybdenum.
Absorption and Metabolism
Its absorption and metabolism are not well characterized.
Recommended Intakes
The recommended dietary allowance (RDA) in a healthy adult is 45 mcg/day. These levels are often exceeded. The upper limit (UL) to prevent toxicity is 2 mg/day. This level is based on studies in rats, because little evidence actually exists to suggest that exceeding this UL will cause extremely adverse health outcomes in humans.
Clinical Relevance
Deficiency and toxicity are very rare.
Other
More information: http://lpi.oregonstate.edu/infocenter/minerals/molybdenum/