Nutritional Disease  
September 23, 2010

I. Malnutrition  
A. Marasmus - calorie malnutrition  
B. Kwashiorkor - protein malnutrition - importance of protein quality as well as quantity  
C. Most cases of severe malnutrition are a combination of A and B usually characterized by:
   - Failure of growth  
   - Behavioral changes  
   - Edema (kwashiorkor)  
   - Dermatosis  
   - Changes in hair  
   - Loss of appetite  
   - Liver enlargement  
   - Anemia  
   - Osteoporosis

II. Primary vs. secondary disorders - Most nutritional disorders in developed countries are not due to simple dietary deficiencies but are rather a secondary manifestation of an underlying primary condition or disorder.
   - Chronic alcoholism  
   - Pregnancy and lactation  
   - Renal dialysis  
   - Eating disorders  
   - Prolonged use of diuretics  
   - Malabsorption syndromes  
   - Neoplasms  
   - Food fads  
   - Vegans  
   - AIDS

III. Anemia (Disorder of Hematopoietic System) - Probably the most common effect of nutritional deficiency. Any factor that decreases hematopoiesis can cause an anemia.
   A. Iron deficiency - Widely recognized as the most important cause of anemia, in the U.S. some estimates have indicated that ½ of all pregnant women and infants are affected, as are ~13% of all adult women.
      1. Dietary factors - Availability of iron from different food sources and mixtures.  
      2. Malabsorption – One third of patients with inflammatory bowel disease (IBD) have recurrent anemia and 30% or more of patients who have had partial gastrectomy will develop iron deficiency anemia.  
      3. Blood loss - Menses, gastrointestinal bleeding
4. Increased demand - Pregnancy, growth in children.
5. Congenital - Atransferrinemia
6. Importance of multiple factors.
7. Pathophysiology - Initially iron is mobilized from reticuloendothelial stores and increased intestinal absorption occurs. Total iron stores are depleted, serum iron levels fall. In severe cases in peripheral blood, the red cells become smaller (microcytic) and their hemoglobin content is reduced (hypochromic).

B. Megaloblastic anemias- Characterized by the presence of abnormal WBCs and RBCs. In severe cases, megaloblasts (abnormal red cell precursors) may be present. These anemias are a consequence of disordered DNA synthesis.
    1. Folate deficiency - Can be caused by:
        a. Dietary deficiency
        b. Malabsorption (celiac disease)
        c. Increased demand (pregnancy & lactation)
        d. Drugs - methotrexate, anticonvulsants, oral contraceptives, alcoholism.
        e. Liver disease
    2. Cobalamin (vitamin B₁₂) deficiency - Almost always a secondary disorder that can be caused by:
        a. Intrinsic factor deficiency (pernicious anemia due to autoimmune destruction of the gastric mucosa)
        b. Malabsorption (see section IV.-G.)
    3. Pyridoxine (vitamin B₆) deficiency - most commonly associated with alcoholism.

C. Other factors known to be frequently associated with anemia would include protein-calorie malnutrition, vitamin C deficiency, and pyridoxine deficiency (usually associated with alcoholism).

D. Other anemias not particularly associated with nutritional disease would include hemolytic anemia (decreased red cell life span) and aplastic anemia (failure of marrow to produce new cells).

IV. Avitaminoses - In developed countries acute or primary dietary vitamin deficiencies are rare and probably over diagnosed. Vitamin deficiencies are more commonly secondary disorders associated with malabsorption conditions and chronic alcoholism.

A. Vitamin A - (retinoids, fat soluble compounds derived from β-carotene) The best-known effect of deficiency is an inability to see in weak light (night blindness due to decreased rhodopsin). The pathology is also characterized by skin lesions (rash on the extremities with punctate erythematous lesions). In malnourished children, vitamin A supplements reduce the incidence of infections such as measles, even in children without signs of preexisting deficiency.

B. Vitamin D - (1, 25 OH₂ D₃) Deficiency produces osteomalacia (called rickets in children). Many of the effects of osteomalacia overlap with the more common osteoporosis, but the two disorders are significantly different. The specific alteration in osteomalacia and rickets is a failure of mineralization of the osteoid matrix resulting in decreased appositional bone growth. There is also epidemiological data that suggests that vitamin D deficiency may be linked to an increased
incidence of prostate cancer.

C. Vitamin E - Very rare. Occurs as a secondary disorder in conditions associated with fat maladsorption such as cystic fibrosis, pancreatitis, and cholestasis (bile-flow obstruction). Vitamin E deficiency causes a neurological disorder characterized by sensory loss, ataxia and retinitis pigmentosa due to free radical mediated neuronal damage.

D. Vitamin K - Present in most leafy plants and also synthesized by intestinal bacteria. Vitamin K is required for the production of specific clotting factors and a deficiency is characterized by impaired coagulation (elevated clotting times). Although this can occur in newborns that are given breast milk low in vitamin K, the deficiency is almost always secondarily associated with the use of certain anti-coagulants or disorders such as obstructive jaundice, celiac, or pancreatic disease.

E. Thiamine - The classic deficiency is known as beriberi. Thiamine deficiency is characterized by a peripheral neuropathy that affects sensation particularly in the legs (associated with demyelination of peripheral nerves), in more severe cases Korsakoff syndrome (neuropathy characterized by impaired ocular motility, ataxia, and mental confusion) and cardiomyopathy can occur.

F. Nicotinamide (niacin) - The classic deficiency is known as pellagra. Primary deficiencies are associated with diets that consist primarily of a single low quality protein source (i.e. corn). As a practical matter in developed countries, pellagra is very rare but occasionally associated with multivitamin deficiencies of the B group, most commonly as a complication of alcoholism. The pathology is characterized by hyperkeratosis and vesiculation of skin, atrophy of the tongue epithelium, and a neuropathy that can affect cortex and peripheral neurons. Initial symptoms include a smooth, red tongue, a sore mouth, and ulceration of the inside of the cheeks. The skin on the neck, chest, and back of the hands may become brown and scaly. Often there is nausea, vomiting, and diarrhea. There may also be insomnia, depression, confusion, and rapid changes of mood. Long-standing pellagra can result in dementia and death.

G. Vitamin B12 - Because cobalamin is synthesized by intestinal bacteria and is widely available in many foods, deficiencies are almost always secondary disorders associated with gastric atrophy (and decreased uptake via intrinsic factor), microbial proliferation (AIDS), long-term antacids, chronic alcoholism, idiopathic (age-related). A recent study indicated that ~20% of elderly people exhibit cobalamin deficiency. See section II-B2 on pernicious anemia. In addition to anemia, the primary clinical symptoms include a sensory neuropathy (polyneuropathy), sclerosis of the spinal cord and atrophy of some mucous tissues.

H. Vitamin C - The classic deficiency is known as scurvy. The essential pathology involves an inability to produce mature collagen and hence affects connective tissue. This is characterized by an inability to synthesize osteoid and dentin (and results in decreased wound healing) and a loss of integrity of blood vessel walls. Oral lesions are only a feature of the advanced form of the disease; early signs include fatigue, dermatitis, and purpura. There can be abnormalities in the growing bones of infants.
I. Vitamin B<sub>6</sub> (Pyridoxine) A deficiency can lead to peripheral neuropathy, most commonly associated with multivitamin B deficiencies in malnutrition and alcoholism.

J. Other vitamins, such as B<sub>3</sub>, and biotin are associated with deficiencies in experimental conditions, but it is doubtful that they have important roles in clinical deficiency syndromes.

V. Major Minerals - Sodium, potassium, chlorine, and magnesium are required for life but dietary deficiencies do not develop.
   A. Iodine - Essential for the synthesis of thyroid hormones, and severe iodine deficiency is associated with hypothyroidism. The compensatory activity of the thyroid gland causes a characteristic enlargement called goiter.

B. Calcium - Required for bone mineralization, the RDA for adults is 800 mg/day. Clinical trials have shown that 1000-2000 mg/day can delay the bone loss observed in the elderly and decrease the risk of osteoporosis. See also section IV B.

C. Iron - see section III A.

VI. Trace Elements - At least 10 elements (examples: Co, Mn, Si) are required in minute amounts for normal development and metabolism, but overt human deficiency syndromes for most have not been reported.
   A. Zinc - A deficiency can result from inadequate amounts given during total parenteral nutrition or as a secondary effect of acrodermatitis enteropathica (autosomal recessive trait characterized by alopecia, dermatitis, and diarrhea - the disease responds to administration of zinc).

B. Copper - Deficiencies are rare and primarily associated with malabsorption syndromes and total parenteral nutrition. Copper is required for normal hematopoiesis and bone growth. A deficiency resembles iron deficiency anemia and osteoporosis.

C. Fluoride - Levels in drinking water greater than 1 ppm cause mottling of teeth and in areas with chronic naturally induced fluorosis there is abnormal calcification of ligaments and tendons.

VII. Nutritional Deficiencies in U.S. Individuals - Acute deficiencies of micronutrients are rare, but sub-optimal nutrient intake (less than the RDA) can be widespread. The relationship between sub-optimal intake of micronutrients and chronic disorders is less clear. Examples:
   A. Minerals
      • Iron- ~75% of women 20-30 yrs consume less than the RDA (18 mg), 25% consume less than half the RDA.
      • Zinc- ~50% of men/women over the age of 50 consume less than the RDA (8/11 mg), 10% consume less than half of the RDA.
   B. Vitamins
      • Folate- before US fortification in 1998, ~75% of adults (20+ yrs) consumed less than the RDA (400 μg).
      • B6 - ~50% of adults consume less than the RDA (1.5-1.7 mg).
      • B12- ~25% of adults consume less than the RDA (2.4 μg).
      • C- ~50% of adult women/men consume less than the RDA (75/90 mg), 25% consume
less than half.

VIII. **Hypervitaminosis** - High doses of some vitamins, usually associated with megavitamin dietary regimes can produce toxic effects.

A. Vitamin A - Toxicity results in liver damage (hepatotoxicity), headache (elevated intracranial pressure) and skin and vision changes. In addition, high doses of vitamin A and some of its analogs appear to be teratogenic. Acute toxicity results from 25,000 IU/kg and chronic toxicity results from 4,000 IU/kg/day. for 6-15 months.

B. Vitamin D - In adults, taking 50,000 IU/day over a prolonged period can produce toxicity. The main symptoms result from hypercalcemia. Anorexia, nausea, and vomiting can develop, often followed by polyuria, polydipsia, weakness, nervousness, pruritus, and eventually renal failure. Proteinuria, urinary casts, azotemia, and metastatic calcifications (particularly in the kidneys) can develop.

C. Vitamin E - Daily doses over 800 IU can produce hypertriglyceridemia and depressed thyroxine levels.

D. Water Soluble Vitamins - It was long thought that because water-soluble vitamins are rapidly cleared by the kidneys, toxicity was not a significant problem. However, a variety of disorders have now been described that are associated with megadoses of some water-soluble vitamins.

1. Nicotinic acid - Used in large doses (500-2,500 mg/day) to treat hypercholesterolemia (see X, D.), niacin produces skin flushing, itching and sometimes rashes. Rare instances of abnormal liver function have also been reported (RDA=20 mg).

2. Thiamine - Can cause hypersensitivity reactions when given by injection.

3. Vitamin C - Although uncommon, gastrointestinal disturbances and skin rashes have been reported in some individuals taking gm amounts/day. Individuals with pre-existing conditions such as cystinuria, oxalosis, or hyperuricemia can develop kidney stones (RDA=75-90 mg).

4. Folic acid - doses above 5000 μg/day can cause birth defects (RDA=400 μg)

5. Pyridoxine - high doses (500 mg/day) cause a sensory neuropathy (RDA=2 mg)

**For additional information**

A good website with a lot of both general info and specific recommendations on dietary constituents:
http://www.hsph.harvard.edu/nutritionsource/

A website that lists many good sources of reliable nutritional information:
http://hnrc.tufts.edu/resources/nutrition.shtml

A short reading list of books available for everything from sports nutrition to recommendations for children:
http://www.eatsmart.org/client_images/gd20051201139111.pdf