CHAPTER
12 Nutrients Involved in Blood Health and Immunity

Chapter Summary

Blood is the only fluid tissue in our bodies. It has four components: erythrocytes, or red blood cells; leukocytes, or white blood cells; platelets; and plasma. Blood is critical for transporting oxygen and nutrients to our cells and for removing waste products from our cells. Iron is a trace mineral found in hemoglobin, the oxygen-carrying protein in our blood. Iron assists with the transportation of oxygen in our blood, is a cofactor for many enzymes involved in metabolism, and is part of the superoxide dismutase antioxidant enzyme system that fights free radicals. Zinc acts as a cofactor in the production of hemoglobin, in the superoxide dismutase antioxidant enzyme system, in energy metabolism, and in activating vitamin A in the retina. Zinc is also critical for cell reproduction, growth, and proper development and functioning of the immune system. Copper functions as a cofactor in energy metabolism, in the production of collagen and elastin, as part of the superoxide dismutase antioxidant enzyme system, and in the proper transport of iron. Vitamin K acts as a coenzyme assisting in the coagulation of blood and in the synthesis of proteins that maintain bone density. The B-vitamins primarily involved in blood health are folate and vitamin B_{12}. Neural tube defects can result from inadequate folate intake during the first weeks of pregnancy. Severe iron deficiency, the most common nutrient deficiency in the world, results in microcytic anemia, in which healthy red blood cells and hemoglobin levels are inadequate. Macrocytic anemia results from folate or B_{12} deficiency and causes the formation of excessively large red blood cells that have reduced hemoglobin. Symptoms are similar to those of iron-deficiency anemia, with the added potential for nerve damage and disorders. Pernicious anemia is caused by a deficit of intrinsic factor, which in turn results in vitamin B_{12} deficiency.

A healthy immune system is a network of cells and tissues that protects us from harmful agents. The body has both nonspecific and specific immune function. The two primary types of cells involved in specific immunity are: B cells that produce antibodies and mark antigens for destruction; and T cells that destroy body cells harboring foreign agents and signal other immune cells to respond. In active immunity, the body has memory cells sensitized to a given antigen after experiencing an infection or being vaccinated. In passive immunity the body acquires antibodies from another organism, such as a mother. Malfunctions of the immune system include allergies, autoimmune diseases, chronic inflammation, and immunodeficiencies. Protein/energy malnutrition and obesity can impair immune responses. A balanced intake of essential fatty acids is important for controlling inflammation. Immune function relies on vitamins A, C, and E and the minerals zinc, copper, iron, and selenium; both deficiency and excess of these micronutrients can impair immune response.

Nutrition Myth or Fact addresses the question: Do zinc lozenges help fight the common cold?

Learning Objectives

After studying this chapter, the student should be able to:

1. Identify the functions and components of blood and the micronutrients most critical to blood health (pp. 464-465).

2 Discuss the role that iron plays in maintaining blood health overall, and specifically in oxygen transport (pp. 466–467).

3. Explain how the body absorbs, transports, and stores iron (pp. 467-470).

4. Discuss the progression of iron deficiency from depletion to microcytic anemia (pp. 474–475).

5. Discuss the functions, RDA, and food sources of zinc (pp. 476–480).

6. Discuss the functions, RDA, and food sources of copper (pp. 480-482).

5. Discuss the functions and sources of vitamin K (pp. 482–484).

6. Describe the contributions of vitamin B_6, folate, and vitamin B_{12} to blood health (pp. 481–485).

7. Compare and contrast nonspecific and specific immunity (pp. 486–487).

8. Describe the role of protein-energy malnutrition, obesity, essential fatty acids, and key micronutrients in immune function (pp. 488-490).

Key Terms

antigens
antiserum
B cells
ceruloplasmin
cytotoxic T cells
erythrocytes
ferritin
ferroportin
helper T cells
heme
heme iron
hemoglobin
hemosiderin
hephaestin
immunocompetence
iron-deficiency anemia (stage III)
iron-deficiency erythropoiesis (stage II)
iron depletion (stage I)
leukocytes
macrocytic anemia
meat factor
memory cells
metallothionein
microcytic anemia
myoglobin
non-heme iron
nonspecific immune function
pernicious anemia
plasma
plasma cells
platelets
specific immune function
T cells
transferrin
vaccination

Chapter Outline

I. What Are the Functions and Components of Blood?

A. Blood transports nutrients, oxygen, and waste products.

B. Blood is important for body defenses and heat transfer.

C. Blood is comprised of four components, which depend on a healthful diet and adequate fluid intake.

1. Erythrocytes transport oxygen.

2. Leukocytes (white blood cells) are the key to the immune system.
3. Platelets assist in formation of blood clots.
4. Plasma is the fluid portion of the blood.

Key Terms: erythrocytes, leukocytes, platelets, plasma

Figure and Table:

Figure 12.1: Blood has four components

Table 12.1: Overview of Nutrients Essential to Blood Health.

II. Why is Iron Essential to Blood Health?

A. Iron is a trace mineral, but iron deficiency is the most common nutrient deficiency in the world.

1. Iron functions as a component of many proteins.
   - **a.** The body relies on the iron in the heme groups of hemoglobin to bind and release oxygen transported through blood.
   - **b.** Iron is a component of myoglobin, which transports and stores oxygen within the muscles.
   - **c.** Iron is a component of cytochromes within the metabolic pathways, which produce energy.
   - **d.** Iron is part of key enzymes in the TCA cycle, in amino acid and lipid metabolism, and in the antioxidant enzyme system.
   - **e.** Iron is involved in DNA synthesis, cognitive development, and immune health.

B. Iron is necessary for life, yet too much iron is toxic; thus, iron homeostasis is extremely important.

1. Homeostasis is regulated by iron digestion, absorption, and transport.
2. The body's ability to absorb dietary iron is influenced by a number of factors: a person's iron status, the level of dietary iron consumption, the type of iron present in the foods consumed, amount of stomach acid present to digest the foods, and presence of dietary factors that can enhance or inhibit absorption.
   - **a.** Iron absorption is low in healthy individuals and rises with higher demand.
   - **b.** More iron is absorbed when dietary intake is low.
3. The type of iron in foods is another major factor influencing iron absorption.
   - **a.** Heme iron, found only in animal-based foods, is part of hemoglobin and myoglobin and is the best absorbed form of iron.
   - **b.** A special meat factor further enhances non-heme iron absorption from meat, fish, and poultry.
   - **c.** Non-heme iron from both plants and animals requires adequate amounts of stomach acid or vitamin C for absorption.
4. Iron absorption is impaired by phytates, polyphenols, vegetable proteins, fiber, and calcium.
5. Iron is taken into the enterocytes to be stored there or to be transported by ferroportin into the interstitial fluid and circulation.
   - **a.** In the interstitial fluid, iron is converted to ferric iron, bound to transferrin, and transported to cells.
   - **b.** Transferrin receptors on the cells regulate the amount of iron the cell takes in.

6. The body stores iron in two storage forms: ferritin and hemosiderin.

a. Iron is stored in the enterocytes, liver, bone marrow, and spleen

b. Hemosiderin storage occurs predominately with iron overload, a condition that may damage the heart and liver.

c. The amount of iron stored varies dramatically between men and women.

7. Regulation of total body iron is accomplished through three mechanisms.

a. Iron absorption is reliant on consumption, need, and dietary factors.

b. The body regulates iron intake through iron loss from turnover of gut enterocytes, blood, sweat, semen, and cells that are shed from the skin and urinary tract.

c. As old red blood cells are broken down, iron is recycled and returned to the body's iron pool, accounting for approximately 20 times more storage than absorbed iron.

8. How much iron should we consume?

a. The RDA for men is 8 mg per day, and for women 18 mg per day until age 50.

b. After age 50, the RDA for women decreases to 8 mg per day.

c. During pregnancy, RDA for iron rises to 27 mg per day.

d. The UL for iron is 45 mg per day, which seldom occurs with dietary intake.

9. Good food sources of heme iron are meat, poultry, and fish; sources of non-heme iron include fortified grains, some vegetables, and legumes.

10. Iron overdose results in toxicity and is the leading cause of poisoning deaths in U.S. children under age 6.

a. Acute iron toxicity may cause nausea, vomiting, diarrhea, dizziness, confusion, and rapid heartbeat.

b. Untreated iron toxicity damages the heart, central nervous system, liver, and kidneys, resulting in death.

c. Hemochromatosis, a hereditary disorder, is characterized by excessive absorption of dietary iron.

11. What happens if we don't consume enough iron?

a. Iron-deficiency anemia is the most common nutrient deficiency in the world.

b. Factors that contribute to iron deficiency include poor dietary intake or absorption of iron, loss through blood or sweat, and heavy menstrual loss.

c. Iron deficiency progresses through three stages:

i. Iron depletion is the stage I. A decrease in iron stores reduces the level of ferritin circulating in the blood.

ii. Iron-deficiency erythropoiesis is stage II. There is a decrease in the transport of iron. A reduction of the saturation of transferrin with iron occurs.

iii. Iron-deficiency anemia is stage III. Production of normal, healthy red cells decreases cell size decreases by a third and hemoglobin levels are inadequate.

d. Iron deficiency anemia is a microcytic anemia, which is characterized by red blood cells that are smaller than normal.

e. Symptoms of oxygen and energy deprivation are present in iron-deficiency anemia and include: general fatigue, pale skin, depressed immune function, pregnancy complications, and impaired cognitive and nerve function, work performance, and memory.

Key Terms: hemoglobin, myoglobin, heme, heme iron, nonheme iron, meat factor, ferroportin, hephaestin, ceruloplasmin, transferrin, ferritin, hemosiderin, iron depletion (stage I), iron deficiency erythropoiesis (stage II), iron-deficiency anemia (stage III), microcytic anemia

Figures and Table:

Figure 12.2: Iron is contained in the hem portion of hemoglobin and myoglobin.

Figure 12.3: Overview of iron absorption and transport.

Figure 12.4: Common food sources of iron.

Figure 12.5: Iron deficiency passes through three stages.

Table 12.2: Special Circumstances Affecting Iron Status

III. How Does Zinc Support Blood Health?

A. Zinc is a trace mineral that is found in muscle and bone.

- **1.** A small exchangeable pool of zinc is found in the bone, liver, and blood. Zinc has no dedicated storage sites in the body.

B. Functions of zinc are divided into three categories.

- **1.** Zinc is required by more than 300 different enzymes to properly function.
  - **a.** Functions include alcohol metabolism, hemoglobin production, generating energy, and digestion.
- **2.** In helping proteins maintain their biologically active shape, zinc helps regulate gene expression, stabilize vitamin A receptors in the retina, and maintain integrity of enzymes.
- **3.** Zinc regulates gene expression, in turn regulating cell replication, blood glucose levels, and many other hormones.

C. Several factors influence zinc absorption and transport.

- **1.** Zinc is absorbed from the intestine into the enterocytes through both active transport and simple diffusion.
  - **a.** Zinc is then released into the interstitial fluid or bound to metallothionein, which prevents zinc from moving into the system.
  - **b.** Once zinc is absorbed from the intestine into the enterocytes, it crosses the basolateral enterocyte membrane to reach the interstitial fluid.
  - **c.** Albumin picks up zinc and carries it to the liver.
  - **d.** Zinc is repackaged in the liver and delivered to cells via the blood.
  - **2.** Non-heme iron, phytates, and fiber inhibit zinc absorption.
  - **3.** Dietary protein enhances zinc absorption.
- **4.** How much zinc should we consume?
  - **a.** The RDA for men and women 19 years of age and older 11 mg per day and 8 mg per day, respectively, and the UL for adults 19 years of age and older is 40 mg per day.
  - **b.** Good food sources include red meat, some seafood, and whole and enriched grains.
- **5.** What happens if we consume too much zinc?
  - **a.** Toxicity from supplemental zinc can cause intestinal pain, nausea, loss of appetite, vomiting, diarrhea, and headaches.

b. Excessive supplemental intake can depress the immune system, decrease HDL, and interfere with iron and copper absorption.

6. What happens if we don't consume enough zinc?

a. Zinc deficiency can cause growth retardation, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, hair loss, impaired appetite, and impaired immunity.

b. Until deficiency symptoms occur, there is no way of assessing poor zinc status.

Key Term: metallothionein

Figures and Table:

Figure 12.6: Overview of zinc and absorption and transport.

Figure 12.7: Common food sources of zinc.

IV. What is the Role of Copper in Blood Health?

A. Copper is a trace mineral widely distributed in foods.

B. Copper has several important functions.

1. Copper is a component of ceruloplasmin, which oxidizes iron so that it can be transported to plasma.
2. Copper is a cofactor in many metabolic pathways.
3. Copper is involved in the regulation of some neurotransmitters.

C. Copper absorption is dependent on the amount in the diet, and excretion is through feces.

D. How much copper should we consume?

1. The RDA for men and women is 900 µg per day, with a UL for adults of 10 mg per day.
2. Good food sources include organ meats, seafood, nuts, seeds, and whole grains.
3. Toxicity symptoms include abdominal pain, nausea, diarrhea, and vomiting.
   - **a.** Liver damage can occur in extreme cases.
   - **b.** In Wilson's disease, copper accumulates in the liver, causing toxicity.
4. Copper deficiency is rare.

Figure:

Figure 12.8: Common food sources of copper.

V. What Vitamins Help Maintain Blood Health?

A. Vitamin K is a fat-soluble vitamin important to blood and bone health.

1. Vitamin K functions as a coenzyme for proteins involved in blood clotting.
2. What factors alter vitamin K absorption and balance?
   - **a.** Any factor that reduces bacterial production of vitamin K in the large intestine reduces vitamin K status.
   - **b.** Any factor that disrupts fat absorption adversely impacts vitamin K absorption.
   - **c.** Vitamin K is not stored in the liver, as are other fat-soluble vitamins.
3. How much vitamin K should we consume?
   - **a.** Vitamin K is produced in varying amounts by bacteria in the large intestine.

b. The AI is 120 µg per day for men and 90 µg per day for women. There is no established UL for this nutrient.
c. Good sources include green leafy vegetables and soybean and canola oil.

4. There are no known side effects of consuming too much vitamin K.
5. People who suffer from diseases that cause fat malabsorption are most likely to suffer from vitamin K deficiency.
   a. Vitamin K deficiency inhibits the ability to form blood clots, resulting in excessive bleeding.

B. Vitamin B_6 is essential for the synthesis of heme.

1. A deficiency of vitamin B_6 can cause microcytic anemia, although iron deficiency is a more common cause of that ailment.
   a. The RDA for men and women aged 19 to 50 is 1.3 mg per day. In adults over age 50 it increases to 1.5 mg for women and 1.7 mg for men. The UL is 100 mg per day.
   b. Vitamin B_6 is abundant in meats, poultry, fish, and soy-based products.

C. Folate is essential for the production of red blood cells.

1. Folate is a water-soluble B-vitamin known as folic acid in the supplemental form.
2. Folate is important for synthesis of DNA and amino acids; deficiency impairs the normal production of red blood cells.
   a. Folate is critical to the proper development of the embryo.
3. How much folate should we consume?
   a. The RDA for adults over 19 years old is 400 µg/day, with 600 µg/day required for pregnant women. The UL is 1,000 µg/day.
      i. Adequate folate intake is essential to prevent birth defects.
   b. In 1998 the USDA mandated fortification of many foods with folic acid.
   c. Good sources include fortified grain products, liver, spinach, lentils, oatmeal, asparagus, and romaine lettuce.
4. Folate deficiency progresses in stages similar to those seen with iron.
   a. Stage I, or negative folate balance: serum levels of folate begin to decline.
   b. Stage II, or folate depletion: low serum and red blood cell folate; elevated homocysteine concentrations.
   c. Stage III, or folate-deficiency erythropoiesis: the ability to synthesize new blood cells is inhibited.
   d. Stage IV, folate-deficiency anemia: the number of red blood cells has dropped and macrocytic anemia develops.
      i. Macrocytic anemia is characterized by the production of larger-than-normal red blood cells that contain insufficient hemoglobin.
      ii. Symptoms include weakness, fatigue, difficulty concentrating, irritability, headache, shortness of breath, and reduced work tolerance.

D. Vitamin B_{12} is necessary for the proper formation of red blood cells.

1. Vitamin B_{12} is part of coenzymes that assist with DNA synthesis necessary for red blood cell formation.
2. Stages of B_{12} deficiency are 1) negative B_{12} balance, a decline in the blood level, 2) vitamin B_{12} depletion, 3) vitamin B_{12}-deficiency erythropoiesis, decreasing red

blood cell synthesis, and 4) vitamin B_{12}-deficiency anemia, number of red blood cells has declined, vitamin B_{12} not available for DNA synthesis, and macrocytic anemia develops.

   a. Can develop in those who follow a vegan diet or those with malabsorption disorders.

3. Pernicious anemia is associated with vitamin B_{12} deficiency. It occurs at the end stage of an autoimmune disorder that causes loss of stomach cells, including the parietal cells that produce intrinsic factor.

3. The RDA for vitamin B_{12} for adults aged 19 and older is 2.4 µg/day.

4. Only animal foods contain B_{12}, so vegans must eat foods fortified with B_{12} or supplement with it.

5. Vitamin B_{12}-deficiency can also cause neurological deficits arising from the destruction of the myelin sheath covering nerve cells, which facilitate nerve impulse transmission.

Key Terms: macrocytic anemias, pernicious anemia

Nutrition Animation: Vitamin B_{12} Absorption (located in IR-DVD folder).

Figure:

Figure 12.9: Prevalence of spina bifida in the years following mandatory folate fortification.

VI. What Is the Immune System, and How Does It Function?

A. Nonspecific immune function protects against all potential invaders.

1. Skin and mucous membranes block invaders from entering organs and deeper tissues.
2. Coughing, sneezing, vomiting, and diarrhea prevent microbes from entering tissues, and stomach acid destroys some microbes.
3. Immune cells kill a wide variety of harmful microorganisms.
4. Release of inflammatory chemicals inhibits growth of microorganisms by changing the environment in the body.

B. Specific immune function protects against identified antigens.

1. The first time the immune system encounters an antigen, it produces a primary immune response and memory cells.
2. Two main types of lymphocytes provide specific immunity.
   - **a.** B cells produce memory cells and plasma cells that produce thousands of antibodies.
   - **b.** T cells differentiate into cytotoxic T cells, which kill cells harboring non-self-substances, and helper T cells.
3. Specific immunity can be acquired in a variety of ways.
   - **a.** Active immunity is acquired through having a disease once or vaccination.
   - **b.** Immunity can be acquired naturally from mother to infant or artificially through antiserum.
4. Immune system malfunction can cause chronic inflammation and infection.
   - **a.** During allergic reactions, harmless proteins in the environment or in food are mistaken for pathogens.
   - **b.** In autoimmune diseases the body’s own proteins are mistaken for pathogens.

c. Chronic infection can occur in malnourished individuals and people with immune deficiency diseases.

Key Terms: nonspecific immune function, specific immune function, antigens, memory cells, B cells, plasma cells, T cells, cytotoxic T cells, helper T cells, vaccination, antiserum

VII. How Does Nutrition Affect the Immune System?

A. Protein/energy malnutrition impairs immune function.

1. Since immune response requires energy and amino acids, malnutrition diminishes the immune response.

2. Moderate nutrient deficiencies impair immune function; hence, immunocompetence is an indicator of reduced nutritional status.

B. Obesity increases incidence and severity of infections.

1. Mechanisms underlying lower immune function in obese individuals are most likely related to lower B and T cells.

2. Obesity is related to a low-grade inflammatory response.

3. The low-grade inflammatory state present in obese individuals may increase the risk of developing asthma, hypertension, cardiovascular disease, and type 2 diabetes.

C. Essential fatty acids make signaling molecules for the immune system.

1. The essential fatty acids are precursors for important signaling molecules called eicosanoids, which the immune system needs to respond to threatening agents.

2. Supplementation with EPA and DHA reduces inflammation and may be useful in treating some chronic inflammatory conditions.

D. Certain vitamins and minerals are critical to a strong immune response.

1. Vitamin A is necessary to maintain mucosal surfaces and differentiate immune system cells.

2. Vitamin C and vitamin E provide antioxidant protection to immuno-defensive cells.

3. Zinc assists immune cell gene expression and enzyme activation for B and T cells.

4. Selenium is a required coenzyme for glutathione peroxidase, and an anti-oxidant enzyme in neutrophils and immune cells.

a. Selenium deficiency allows viruses to multiply.

5. Both iron and copper are part of two important antioxidant enzymes, superoxide catalase and dismutase.

a. Deficiency of these two nutrients have numerous effects on the body's immune system.

6. Infection can alter nutrition status in a variety of ways.

a. Reduced food intake can cause nutrient deficiency.

b. Increased nutrient loss, or malabsorption, can result from loss of fluid and electrolytes and decreased nutrient absorption due to gut inflammation.

c. Increased metabolic rate caused by fever increases energy expenditure when food intake is low.

d. Redistribution of energy and nutrients for the use of the immune response, which are then unavailable for important biological functions.

Key Terms: immunocompetence

Activities

1. Prior to the discussion of this chapter, ask students to make a list of their beliefs about anemia, including its causes, treatment, diagnosis, and prognosis. After they have read the chapter, ask them to review the list for changes in their beliefs.
2. Ask the class to develop a list of reasons why people would believe that dietary supplements prevent or cure disease. Once you have exhausted the possibilities, share some explanations posed by Quackwatch.com: "Why Bogus Therapies Often Seem To Work," www.quackwatch.com/01QuackeryRelatedTopics/altbelief.html, and Why Quackery Persists, www.quackwatch.com/01QuackeryRelatedTopics/persistance.html.
3. As a class, develop a list of cold remedies (excluding medications). Specific vitamins, minerals, foods, and herbal supplements are all possibilities. Divide students into small groups and assign each group one or two remedies. Have each group determine the validity and effectiveness of each cold remedy they are assigned. Students should note the cost of the remedy compared to its likely benefits. Then ask them to answer the following question: Does this remedy have any scientific basis?
4. To demonstrate how easy it would be for a child to mistake vitamin supplements for candy, bring in samples or pictures of children's multivitamin mineral supplements and the candies they resemble. Iron toxicity is the leading cause of poisoning in children under the age of 6. Individuals demonstrate signs of GI toxicity with ingestion of more than 20 mg/kg body weight but less than or equal to 40 mg/kg. Moderate-to-severe intoxication occurs when ingestion of elemental iron exceeds 40 mg/kg. Ingestion exceeding 60 mg/kg may be lethal. Children's multivitamins with iron contain about 18 mg per tablet. Have students calculate how many it would take to cause toxicity in a small child.

Diet Analysis Activities

5. Using the nutritional assessment previously completed, students should note the following.
   - **a.** What is your daily intake of:
     - folate?
     - iron?
     - zinc?
     - vitamin C?
   - **b.** How does your intake of these nutrients compare with recommendations?
   - **c.** What changes can you make in your diet to more closely meet recommendations and increase bioavailability of the nutrients?

Nutrition Debate Activity

6. Using a debate format, have students discuss the following questions:
   - **a.** Are multivitamin/mineral supplements truly "insurance in a bottle"?
   - **b.** Does vitamin C supplementation have any benefit in prevention or cure of viral infections? Of cancer?
   - **c.** Because folic acid is so effective in preventing defects in infancy, shouldn't fortification of processed foods increase?

Web Resources

Nutrient Data Laboratory Home Page
www.ars.usda.gov/ba/bhnrc/ndl
Web ME
www.webmd.com
http://www.webmd.com/a-to-z-guides/understanding-anemia-basics

UNICEF-Nutrition
www.unicef.org/nutrition
http://www.unicef.org/search/search.php?q=Micronutrients&type=Main

MEDLINE Plus, U.S. National Library of Medicine, National Institutes of Health
www.nlm.nih.gov/medlineplus
Kidshealth.org
www.kidshealth.org/parent

U.S. Food and Drug Administration
www.fda.gov

Office of Dietary Supplements
www.dietary-supplements.info.nih.gov