9. BONE PHYSIOLOGY

Hershel Raff, Ph.D., and Joseph L. Shaker, M.D.

1. Describe the general composition of bone.

Bone is composed of an organic matrix (primarily type 1 collagen fibers) into which calcium and phosphate are deposited and precipitate to form the salt hydroxyapatite crystals. Other ions are also present within the bone, and the organic matrix is also composed of proteoglycans and glycoproteins. The process of deposition of calcium and phosphate in bone is called **mineralization.** Collagen is the primary source of tensile strength, whereas the deposited minerals are the primary source of the ability to withstand compression. Bone is the main storage site for calcium and phosphate in the body. These minerals are in a constant state of flux with the plasma compartment.

2. What are the general types of bone?

Cortical bone (~ 80% of bone mass)—e.g., long bones
Trabecular bone (~ 20% of bone mass)—e.g., skull, ribs, vertebrae, pelvis

3. Compare and contrast cortical and trabecular bone.

Cortical bone provides the external surface of bones and is dense. Trabecular bone is composed of a network of thin calcified trabeculae. In cortical bone, about 80–90% of the volume of bone is calcified; in trabecular bone, 15–25% of the bone is calcified. The remainder of trabecular bone is marrow, blood vessels, and connective tissue. Cortical bone serves a mechanical and protective function. Trabecular bone is more metabolically active than cortical bone.

4. Is bone mass constant?

No. Bone minerals are constantly being renewed by the coupling of bone formation and bone resorption. This coupling is tightly regulated and occurs in basic multicellular units (BMUs). Bone mass increases in childhood and teenage years and probably reaches a peak in the third decade of life. As described in Chapter 8, bone growth occurs at the growth (epiphyseal) plates.

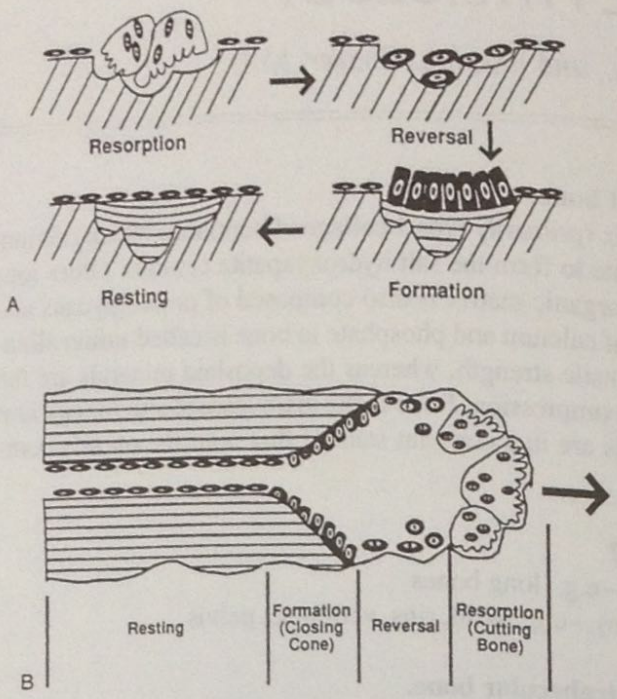
5. What cell types are involved in bone remodeling.

- **Osteoblasts** are responsible for bone formation (arise from stromal mesenchymal cells).
- **Osteoclasts** are responsible for bone resorption (arise from hematopoietic stem cells).
- **Osteocytes** are mature osteoblasts that have been trapped in mineralized bone. They may serve a mechanosensory function.

6. Describe the process of bone remodeling.

Bone remodeling helps repair fatigue damage and occurs at the level of the BMU. Approximately 20% of the trabecular surface is undergoing remodeling at any given time. The process is as follows (see figure, next page):

- Local and circulating hormones, cytokines, and growth factors influence the origination of BMUs.
- Activation is followed by osteoclastic bone resorption. The osteoclasts tunnel into bone by release of enzymes (e.g., collagenase) and hydrogen ions (acid).
- After resorption has occurred, there is a reversal phase followed by bone matrix formation. Osteoblasts synthesize osteoid (unmineralized bone matrix).
- Mineralization, the process of deposition of calcium phosphate into unmineralized matrix, occurs next. Mineralization is completed with the deposition of hydroxide and bicarbonate to form hydroxyapatite crystals.
- The osteoblasts surrounded by mineralized bone transform into osteocytes.



Principal phases of the adult bone remodeling cycle in trabecular (cancellous) bone (*A*) and cortical bone (*B*). Large multinucleated cells are osteoclasts; small, mononucleated cells are osteoblasts. (From Dempster DW: Bone remodeling. In Coe FL, Favus MJ (eds): Disorders of Bone and Mineral Metabolism. New York, Raven Press, 1992, with permission.)

7. List the steps in the development and growth of long bone.

1. Initial (fetal) step is cartilage deposition after which the shaft of the bone is ossified (endochondral bone formation).
2. Epiphyses (end of long bones) are separated from the shaft by epiphyseal (growth) plates.
3. Bone length increases as the epiphyseal plate lays down new bone at the end of the shaft of the bone. Bone growth is accelerated by a variety of endocrine and local growth factors stimulated by growth hormone (including insulin-like growth factor 1 [IGF-1], as described in Chapter 8, Endocrine Physiology).
4. Long bones stop growing when the epiphyses are closed, usually after puberty. The closure of the growth plates is mediated by gonadal steroids (see Chapter 8).

8. How are calcium and phosphates readily exchanged between the interior bone and extracellular fluid?

Fluid-filled channels called **canaliculi** provide a large surface area and path for exchange of ions.

9. Describe the coupling of bone formation and resorption in more detail.

- Bone resorption and formation are normally coupled in the remodeling process.
- The factors that are responsible for this coupling are not completely understood.
- If resorption exceeds formation, bone mass will decrease.

10. What are lamellae and haversian canals?

Orientation of collagen fibrils in bone alternates from layer to layer, resulting in a lamellar structure. Lamellae may be parallel to each other on a flat surface (trabecular and periosteum) or concentric if around a channel for blood vessels (haversian canal).

11. When does bone mineral mass usually reach its peak?

After puberty and the closure of epiphyseal plates, bone width increases by addition to the surfaces of cortical bone (periosteum). Bone mass continues to increase and usually reaches its peak toward the end of the third decade of life.

12. What controls the attainment of peak bone mass?

Many factors are involved in the achievement of peak bone mass. One important factor is **genetics.** Genes are important in determining the maximal predicted peak bone mass, although the

specific genes involved are not yet understood. Another major factor is **weight-bearing,** which increases bone mass. This is one reason why weight-bearing exercise is often recommended to prevent bone loss. Many **humoral factors** are also involved. Gonadal steroids (estrogen and testosterone) inhibit bone resorption and encourage an increase in bone mass. This is why hypogonadism in men and women can lead to loss of bone mass.

13. Does bone mass decline with aging?

Yes. After the peak in bone mass, resorption exceeds accretion, and bone mass decreases. This process accelerates with menopause in women because of the decline in estrogen (an antiresorptive hormone). Osteoporosis also occurs in men but is less common and occurs on average at an older age. A moderate decrease in bone mass is called **osteopenia,** or low bone mass. A more severe decrease in bone mass is called **osteoporosis.**

14. Other than osteoporosis, name one other metabolic bone disease.

Osteomalacia is a softening of bone due to failure to mineralize osteoid adequately. It may be due to vitamin D deficiency caused by inadequate intake or malabsorption. Conditions that result in phosphate wasting in the kidney or inability to properly metabolize vitamin D also may cause osteomalacia. When it occurs in children, osteomalacia is called **rickets.**

15. How is bone mineral mass assessed clinically?

The most common method of assessment of bone mineral density (BMD) is by **dual energy x-ray absorptiometry (DEXA).** It is a simple painless technique that exposes the patient to very low levels of radiation.

16. How can osteoporosis be prevented?

An important factor is to attain maximal genetically determined peak bone mass. In general, adequate calcium and vitamin D intake and weight-bearing exercise are useful. Avoidance of tobacco and excess alcohol is also recommended. Antiresorptive drugs (see question 17) also may be used to prevent bone loss after menopause. Eating disorders (e.g., anorexia or bulimia) may prevent attainment of optimal peak bone mass.

17. How can osteoporosis be treated?

As in prevention, adequate calcium and vitamin D are important. Avoidance of tobacco and excess alcohol is advisable. Currently, several drugs that decrease bone resorption are used, including estrogen, selective estrogen receptor modulators (SERMs), bisphosphonates, and calcitonin. In the future, drugs that directly stimulate bone formation may be used (e.g., intermittent exposure to parathyroid hormone).

BIBLIOGRAPHY

1. Bilezikian JP, Raisz LG, Rodan GA (eds): Principles of Bone Biology, 2nd ed. San Diego, Academic Press, 2002.
2. Favus MJ (ed): Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 4th ed. Philadelphia, Lippincott Williams & Williams, 1999.
3. Ganong WF: Review of Medical Physiology, 20th ed. New York, McGraw-Hill, 2001.
4. Genuth SM: Endocrine regulation of calcium and phosphate metabolism. In Berne RM, Levy MN (eds): Physiology, 4th ed. St. Louis, Mosby, 1998, pp 848–871.
5. Guyton AC, Hall JE (eds): Textbook of Medical Physiology, 10th ed. Philadelphia, W.B. Saunders, 2000.