CHAPTER 9

Musculoskeletal System Disorders

CHAPTER OUTLINE

LEARNING OBJECTIVES

After studying this chapter, the student is expected to:

1. Describe the general structure and function of bone and joints.
2. Describe the general structure and function of skeletal muscle.
3. Describe the types of fractures, the healing process in bone, and potential complications.
4. Compare dislocations, sprains, and strains.
5. Describe the pathophysiology of osteoporosis, the predisposing factors, and possible complications.
6. Compare the causes and effects of rickets, osteomalacia, and Paget's disease.
7. Describe the common bone tumors.
8. Describe the characteristics of Duchenne's muscular dystrophy.
9. Describe the effects of fibromyalgia.
10. Compare osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis with regard to pathophysiology, etiology, manifestations, and possible complications.
11. Describe the distinguishing features of infectious (septic) arthritis.
12. State the etiology and common signs of gout.

KEY TERMS

anabolic steroids
ankylosis
arthroscopy
articulation
crepitus
diaphysis
electromyograms
endosteum
epiphysis
fascia
hyperuricemia
kyphosis
lordosis
medullary cavity
metaphysis
motor unit
neuromuscular junction
osteoblasts
osteoclast
osteocytes
periosteum
pseudohypertrophic
scoliosis
uveitis

Review of the Musculoskeletal System

Bone

The skeletal system provides rigid support for the body, particularly when it is in an upright position or is in motion. The skeletal framework determines the basic size and proportions of the body. Protection is provided for the viscera, such as the heart and lungs, and for fragile structures such as the spinal cord and brain. Bone also has important metabolic functions related to calcium metabolism and storage and the bone marrow, which serves as the area where new blood cells are produced by a process called hematopoiesis.

Bones may be classified by *shape*:

- Long bones, such as the humerus and femur, consist of a long, hollow shaft with two bulbous ends.
- Short bones are generally square-like in shape and are found in the wrist and ankle.
- Flat bones occur in the skull and are relatively thin and often curved.
- Irregular bones, which have many projections and vary in shape, are represented by the vertebrae and the mandible.

Individual bones have unique markings, which may be lines, ridges, processes, or holes. Such landmarks provide for attachment of tendons or passage of nerves and blood vessels.

Bone is special connective tissue consisting of an intercellular matrix and bone cells. The matrix is organized in microscopic structural units called *Haversian systems* or osteons, in which rings of matrix (lamellae) surround a Haversian canal containing blood vessels (Fig. 9-1). The matrix is composed of collagen fibers and calcium phosphate salts (e.g., hydroxyapatite crystals), which provide a very strong and rigid structure. Mature bone cells, or **osteocytes**, lie between the rings of matrix in spaces called *lacunae*. Small passages termed canaliculi provide communication between the Haversian canals and the lacunae.

- A dynamic equilibrium is maintained between new bone, which is constantly being produced by **osteoblasts**, and the resorption of bone by **osteoclast** activity, in accordance with the various hormonal levels and the degree of stress imposed on the bone substance. Osteoblast and osteoclast activity provide the homeostasis of bone. Osteoprogenitor cells differentiate into osteoblasts.
  - Osteoprogenitor cells are derived from embryonic mesenchymal cells.
- Osteoblasts are responsible for secreting the matrix of bone.
- Osteoclasts are derivatives of macrophage progenitor cells.
- Osteoblast and osteoclast activity depend on two hormones: calcitonin and parathyroid hormone.
  - Calcitonin stimulates osteoblasts.
  - Parathyroid hormone stimulates osteoclasts.

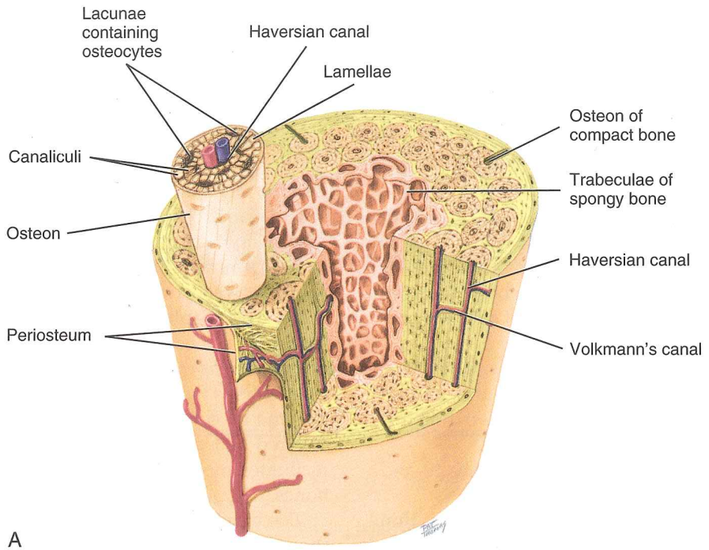
Bone tissue consists of two types, which differ in density. *Compact* bone is formed when many Haversian systems are tightly packed together, producing a very strong, rigid structure that forms the outer covering of bones. *Cancellous* or *spongy* bone is less dense and forms the interior structure of bones. Spongy bone lacks Haversian systems but is made up of plates of bone bordering cavities that contain marrow.

A typical long bone consists of the **diaphysis**, a thin shaft, between two larger ends or epiphyses (see Fig. 9-1*B*). The diaphysis is formed of compact bone surrounding a medullary cavity containing marrow. The **metaphysis** is the area where the shaft broadens into the **epiphysis**. The epiphysis is made up of spongy bone covered by compact bone. The end of each epiphysis is covered by hyaline cartilage (articular cartilage), which facilitates movement at points of **articulation** between bones.

The epiphyseal cartilage or plate ("growth" plate) is the site of longitudinal bone growth in children and adolescents, such growth being promoted by growth hormone and sex hormones. Longitudinal bone growth ceases when the epiphyseal plate ossifies during adolescence or early adulthood depending on the specific bone. The epiphyseal plate is referred to as the epiphyseal line following ossification or closure. No bone growth in length occurs after the epiphyseal plate becomes the epiphyseal line.

However, bone may change in density or thickness at any time under the influence of hormones such as growth hormone, parathyroid hormone, or cortisol. The stress (weight-bearing or muscle tension) placed on the bone also affects the balance between osteoblastic and osteoclastic activity. With aging, bone loss is accentuated, resulting in decreased bone mass and density. *Osteoporosis, loss of bone density due to loss of calcium salts,* is common in older people, particularly women (see Chapter 24). Except for the surface of the bone covered by articular cartilage, the bone is covered by **periosteum**, a fibrous connective tissue. The periosteum contains osteoblasts, blood vessels, nerves, and lymphatics, some of which penetrate into the canals in the bone. When the periosteum is stretched or torn, severe pain results.

The **medullary cavity** is lined with **endosteum**, also containing osteoblasts. These osteoblasts are required for bone repair and remodeling as needed. At birth the medullary cavity in most bones contains red bone marrow in which *hematopoiesis* takes place. Gradually, yellow (fatty) bone marrow replaces red bone marrow in the long bones. In adults, red bone marrow is found in the cranium, bodies of the vertebrae, ribs, sternum, and ilia, the last two being the usual sites of bone marrow aspiration used in the diagnosis and monitoring of leukemias and blood dyscrasias.



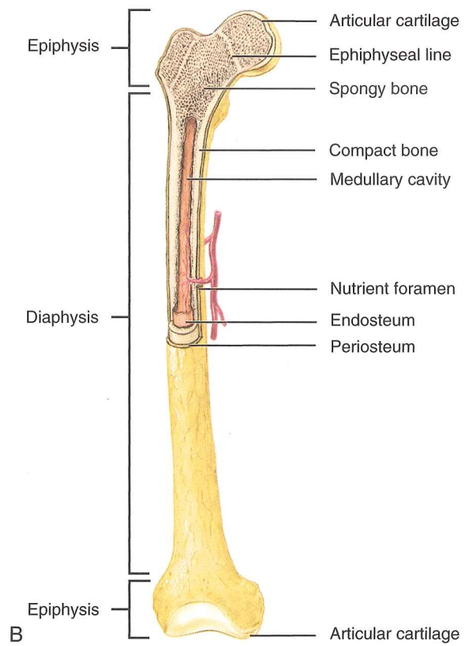


FIGURE 9-1 **A**, Structure of a bone. **B**, Structure of a long bone. *(From Applegate EJ:* The Anatomy and Physiology Learning System, *Philadelphia, 2000, Saunders.)*

THINK ABOUT 9-1

a. Describe the functions of bone.
b. Differentiate compact bone from cancellous bone in terms of structure and function.
c. Describe the characteristics of the: (1) periosteum; (2) epiphyseal plate; and (3) metaphysis.

Skeletal Muscle

Skeletal muscle has four basic functions:

1. To facilitate body movement by muscle contraction
2. To maintain body position by continuing *muscle tone*
3. To stabilize the joints and prevent excessive movement
4. To maintain body temperature by producing heat through muscle contraction

Skeletal muscle is considered to be under voluntary control, although some muscle activities occur without deliberate intent, such as respiratory movements, postural reflexes, blinking, shivering, or certain facial expressions.

Skeletal is *striated* muscle that consists of bundles of muscle fibers (cells) covered by connective tissue. The striated or striped appearance results from the arrangement of the actin and myosin filaments within the muscle fibers.

Connective tissue coverings of skeletal muscles are:

- Epimysium—surrounding the entire muscle
- Perimysium—surrounding the fascicles
- Endomysium—surrounding the individual muscles fibers (cells)

Muscle tissue is well supplied with nerves and blood vessels, necessary to fulfill its function. Each muscle fiber is an elongated muscle multinucleated cell containing many mitochondria that supply energy for the contraction process. A muscle is stimulated to contract when an efferent impulse is conducted along a motor neuron to a muscle. The axon of the motor nerve branches as it penetrates a muscle so that each muscle fiber in the muscle receives a stimulus to contract at the same time. The motor neuron of the spinal cord and all the muscle fibers it stimulates are referred to as the **motor unit**. At the **neuromuscular junction**, where the synapse between the end of the motor nerve and the receptor site in the muscle fiber is located, the chemical transmitter *acetylcholine* is released (Fig. 9-2). Following its release and the subsequent muscle contraction, acetylcholine is inactivated by the enzyme acetylcholinesterase (AChE). Skeletal muscle relaxing drugs may act by blocking acetylcholine at the muscle receptor sites,

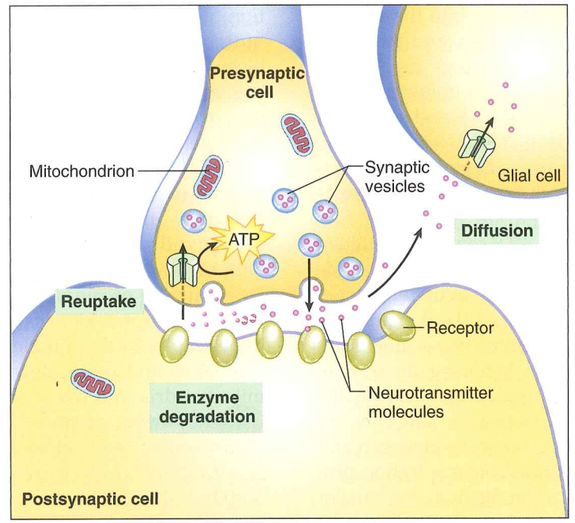


FIGURE 9-2 Fate of neurotransmitters. After synaptic transmission, the signal must be stopped by removing neurotransmitters from the synaptic cleft. Many neurotransmitters are immediately transported back into the presynaptic neuron in a process called reuptake. Some neurotransmitters are broken down by enzymes in the synaptic cleft, and the resulting molecules are transported back into the presynaptic neuron for recycling. Some neurotransmitter molecules may diffuse out of the synapse and be transported into a nearby glial cell (which may return an altered form of the molecule to the presynaptic neuron). *(From Patton KT, Thibodeau GA:* Anatomy & Physiology, *ed 8, St. Louis, 2013, Mosby.)*

whereas muscle activity may be promoted by drugs that interfere with cholinesterase activity.

Each muscle cell contains myofibrils, which in turn are made up of smaller myofilaments consisting of the proteins actin and myosin. Actin and myosin filaments are the contractile elements of the muscle fiber.

The mechanism of muscle contraction starts at the neuromuscular junction and ends with the actual contraction of the skeletal muscle fibers.

- An action potential from the motor neuron arrives at the presynaptic terminal.
- The arrival of the action potential results in the depolarization of the presynaptic terminal.
- The depolarization is followed by a calcium influx into the presynaptic terminal.
- The calcium influx results in the exocytosis of the neurotransmitter (Ach) into the synaptic cleft.
- Diffusion of the neurotransmitter to the postsynaptic receptor results in a muscle action potential.
- The muscle action potential travels down the t-tubules to cause a second messenger activation.
- Calcium is released from the sarcoplasmic reticulum and causes the power stroke—contraction of the muscle fiber.
- During muscle relaxation calcium is transported back into the sarcoplasmic reticulum.
- Both muscle contraction and relaxation require cellular energy (adenosine triphosphate, ATP).

During exercise, the blood vessels in the muscles are dilated to promote greater blood flow into the muscle, thus increasing the supply of oxygen and nutrients (glucose and fatty acids) to provide energy for the contraction and remove metabolic wastes. Limited amounts of oxygen can be bound to *myoglobin* and stored in muscle fibers. Myoglobin is a red oxygen-binding protein, similar in structure to hemoglobin, which is present in muscle cells. *Glycogen*, a source of glucose, is also stored in muscle.

Aerobic respiration to produce ATP can be maintained in muscle fibers as long as adequate oxygen is made available from the myoglobin and the circulating blood. If the supply of oxygen does not meet the demand, the process of *anaerobic respiration* begins, using glucose as the primary energy source and incurring an oxygen debt (the amount of oxygen required to restore the muscle cell to its normal resting state, including converting lactic acid to pyruvic acid, glucose, or glycogen and replenishing stores of ATP). Anaerobic respiration produces lactic acid rather than carbon dioxide, and smaller amounts of ATP. This state of acidosis leads to the increased respirations commonly observed during exercise. These respirations operate as a compensatory mechanism to reduce acidosis by decreasing carbon dioxide levels in the blood (see Chapter 2).

The accumulated lactic acid may cause local muscle pain and cramping during and immediately after exercise. A muscle *cramp* is pain resulting from a strong muscle contraction or spasm, usually caused by local irritation from metabolic wastes. Muscle spasm reduces blood flow, thus leading to ischemic pain. Muscle soreness and pain that appear a day or so after strenuous exercise are often due to minor damage to muscle cells and subsequent inflammation. Also, during periods of strenuous physical activity and anaerobic metabolism, excessive lactic acid diffuses into the blood, lowering serum pH and causing metabolic acidosis.

A muscle may be attached directly to the periosteum of a bone, but more often the connective tissue covering the muscle (perimysium) extends to form a cordlike structure or *tendon*, which attaches each end of the muscle to the two bones that articulate at a joint. At a joint, one bone remains fixed, forming the *origin* of the muscle. The other bone attached to the same muscle is moved by the muscle contraction and is called the *insertion*. *Ligaments* form a direct attachment between two bones. Tendons and ligaments are composed of collagen fibers arranged in bundles, a structure that can withstand considerable stress. At the insertion point of tendons or ligaments there is a gradual transition from the connective tissue to the bone or cartilage. Tendons and ligaments have little blood supply; therefore healing of these structures is difficult and slow.

Muscles may work singly or in groups to perform a specific movement. Also, muscles at a site may be designated as *antagonists* because one muscle opposes the action of another, allowing movement in either direction. For example, at the elbow, the triceps brachii muscle functions as an extensor muscle, whereas the biceps brachii is a flexor muscle. Antagonistic muscles prevent excessive movement and provide better control of movements.

Skeletal muscle cells do not undergo mitosis; therefore that process cannot be used to enhance muscle activity or replace damaged muscle. However, muscle cells may undergo *hypertrophy* (increased size of the muscle cell) when the demands are increased, such as with regular exercise. *Aerobic* or *endurance* exercise, such as swimming or running, increases the muscle's capacity to work for a longer time without causing marked hypertrophy of the muscle. Such exercise increases the capillaries and blood flow in a muscle as well as the mitochondria and myoglobin content, thus improving efficiency and endurance. This type of exercise also promotes general respiratory and cardiovascular function. *Anaerobic* or resistance exercise, such as weight lifting or bodybuilding, focuses on increasing muscle strength by increasing muscle mass (hypertrophy). It is helpful for those persons interested in developing strong muscles to incorporate some aerobic exercise into the training program to improve cardiopulmonary fitness as well as strength.

Anabolic steroids are synthetic hormones similar to testosterone, the male sex hormone. They are used by some athletes, bodybuilders, and others interested in changing the body image to *build up* muscle strength and mass. Speed and endurance do not appear to be affected. These synthetic hormones (e.g., methenolone [Primobolan]) have been developed to increase the anabolic effects, or protein synthesis, and decrease the androgenic or male characteristics produced by these chemicals. Serious and sometimes life-threatening side effects are associated with the use of these substances, such as liver damage, cardiovascular disease, personality changes, emotional lability, and sterility. Unfortunately, this type of steroid is abused by many adolescents and young adults, including those involved in sports, those with eating disorders, and those with psychological problems related to body image and poor self-esteem. The use of anabolic steroids by participants in athletic competition has been banned by many organizations.

Skeletal muscle also may *atrophy*, in which muscle cell size is decreased, when the muscle is not used (see Chapter 1). Atrophied muscle becomes weak and flaccid. Atrophy may occur within a short period of time when a fractured limb is placed in a cast or the pain of arthritis limits movement. Such *disuse atrophy* is also associated with immobilization and chronic illness (see Chapter 25). Atrophy may be secondary to nerve injury, with resultant flaccid paralysis. Also, nutritional deficiencies, particularly protein, secondary to disorders such as anorexia or Crohn's disease, lead to atrophy. Skeletal muscle may also become weak owing to degenerative changes involving accumulations of fatty or fibrous tissue. With aging, muscle mass decreases owing to both a decrease in number of muscle cells and a decrease in size (diameter) of the fibers. Muscle strength generally diminishes as well, although this may vary with the individual's degree of activity and general health status.

Muscle twitch or *tetany* usually results from increased irritability of the motor nerves supplying the muscle. For example, hypocalcemia causes increased permeability of the nerve membrane and therefore increased or spontaneous stimulation of the skeletal muscle fibers, causing a contraction or spasm of the muscle. Note that sufficient calcium is stored and returned to storage in the skeletal muscle cell following contraction, and therefore hypocalcemia does not directly affect skeletal muscle function, but rather its innervation.

THINK ABOUT 9-2

a. Explain why skeletal muscle cells contain many mitochondria.
b. Explain the purpose of shivering when one is cold.
c. What electrolyte is required for skeletal muscle contraction and what is its source?
d. Differentiate muscle hypertrophy from atrophy and give a cause of each.
e. Explain how an anticholinesterase drug affects skeletal muscle function.
f. When does anaerobic metabolism occur in skeletal muscle and what are the effects of this?

Joints

Joints, or articulations between bones vary in the degree of movement allowed:

- *Synarthroses*, represented by the sutures in the skull, are immovable joints.
- *Amphiarthroses*, slightly movable joints, are joints in which the bones are connected by fibrocartilage or hyaline cartilage. Examples of this type of joint include the junction of the ribs and sternum and the symphysis pubis.
- *Diarthroses* or *synovial* joints are freely movable joints and are the most common type of joint in the body.

Different types of diarthroses allow a variety of movements. For example, a hinge joint, providing flexion and extension, is found at the elbow, whereas a ball-and-socket joint at the shoulder provides a wide range of motion, including rotation. Both hinge and gliding movements are found in the temporomandibular joint (TMJ), controlling the opening of the mouth. Common body movements are illustrated in Ready Reference 1 (see Fig. RR 1-6).

In a synovial joint, the ends of the bone are covered with *articular* (hyaline) *cartilage*, providing a smooth surface and a slight cushion during movement (see Fig. 9-13*A*). With aging, the cartilage in joints tends to degenerate and become thin, leading to difficulty with movement and potential changes in the alignment of bones.

The joint cavity or space between the articulating ends of the bones is filled with a small amount of *synovial fluid*, which facilitates movement. The synovial fluid prevents the articular cartilage on the two surfaces from damaging each other and also provides nutrients to the articular cartilage. The synovial fluid is produced by the *synovial membrane* (synovium), which lines the joint capsule to the edge of the articular cartilages. The synovial membrane is well supplied with blood vessels.

The *articular capsule* is composed of the synovial membrane and its outer covering, the *fibrous capsule*, a tough protective material that extends into the periosteum of each articulating bone (Sharpey's fibers). The capsule is reinforced by *ligaments*, straps across the joint that link the two bones, which support the joint and prevent excessive movement of the bones.

In a few joints there are some variations in structure. The knee has additional moon-shaped fibrocartilage pads, termed lateral and medial *menisci*, which act to stabilize the joint. *Bursae* are fluid-filled sacs composed of synovial membrane and located between structures such as tendons and ligaments; they act as additional cushions in the joint. The TMJ, the only movable joint in the skull and face, has two synovial cavities and a central articular cartilage of dense collagen tissue.

APPLY YOUR KNOWLEDGE 9-1

Explain how blood doping—taking extra concentrated doses of red blood cells—can help an athlete.

The *nerves* supplying a joint are those supplying the muscles controlling the joint. These motor fibers are accompanied by sensory fibers from *proprioceptors* in the tendons and ligaments that respond to the changing tensions related to movement and posture. The joint capsule and ligaments are supplied with pain receptors.

THINK ABOUT 9-3

a. Name and describe the type of joint found in the skull.
b. Describe two structures in a joint that facilitate movement.
c. Describe the location and purpose of the synovial membrane.

Diagnostic Tests

In persons in whom trauma, tumors, or metabolic disease are suspected, bone abnormalities may be evaluated using x-rays (radiographs) and bone scans.

Electromyograms (EMGs) measure the electrical charge associated with muscle contraction and are helpful in differentiating muscle disorders from neurologic disease. Also, the strength of individual muscle groups can be determined. Muscle biopsy is required to confirm the presence of some muscular disorders, such as muscular dystrophy. Joints may be visualized by **arthroscopy** (insertion of a lens directly into the joint) or by magnetic resonance imaging (MRI), a noninvasive imaging procedure. Synovial fluid may be aspirated and analyzed to ascertain whether inflammation, bleeding, or infection is present.

Serum calcium, phosphate, and parathyroid hormone levels may indicate metabolic changes, perhaps secondary to renal disease or parathyroid hormone imbalance. Muscle disorders may be checked by determining levels of components such as serum creatine kinase (CK), which is elevated in persons with many muscle diseases. Creatine kinase, an enzyme with an essential role in energy storage, leaks out of damaged muscle cells into body fluids.

Trauma

Fractures

A fracture is a break in the rigid structure and continuity of a bone (Fig. 9-3). Fractures can be classified in several ways:

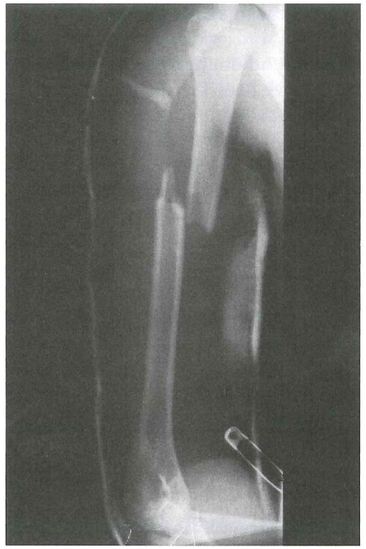


FIGURE 9-3 Fracture of the midshaft of the humerus. *(Courtesy of Dr. Mercer Rang, The Hospital for Sick Children, Toronto, Ontario, Canada.)*

- Complete-incomplete. A *complete fracture* occurs when the bone is broken to form two or more separate pieces, whereas in an *incomplete fracture* the bone is only partially broken. An example of the latter is a *greenstick* fracture, common in the softer bones of children, in which the shaft of the bone is bent, tearing the cortical bone (outer layer of compact bone) on one side but not extending all the way through the bone.
- Open-closed. An *open* or compound fracture results when the skin is broken (Fig. 9-4). The bone fragments may be angled and protrude through the skin. In open fractures there is more damage to soft tissue, including the blood vessels and nerves, and there is also a much higher risk of infection. In a *closed* fracture the skin is not broken at the fracture site.
- Number of fracture lines:
  - *Simple* fracture, a single break in the bone in which the bone ends maintain their alignment and position
  - *Comminuted* fracture, in which there are multiple fracture lines and bone fragments
  - *Compression* fracture, common in the vertebrae, occurring when a bone is crushed or collapses into small pieces
- Other types:
  - *Impacted* fracture occurs when one end of the bone is forced or telescoped into the adjacent bone; for example, the neck of the femur is crushed against the pelvis.

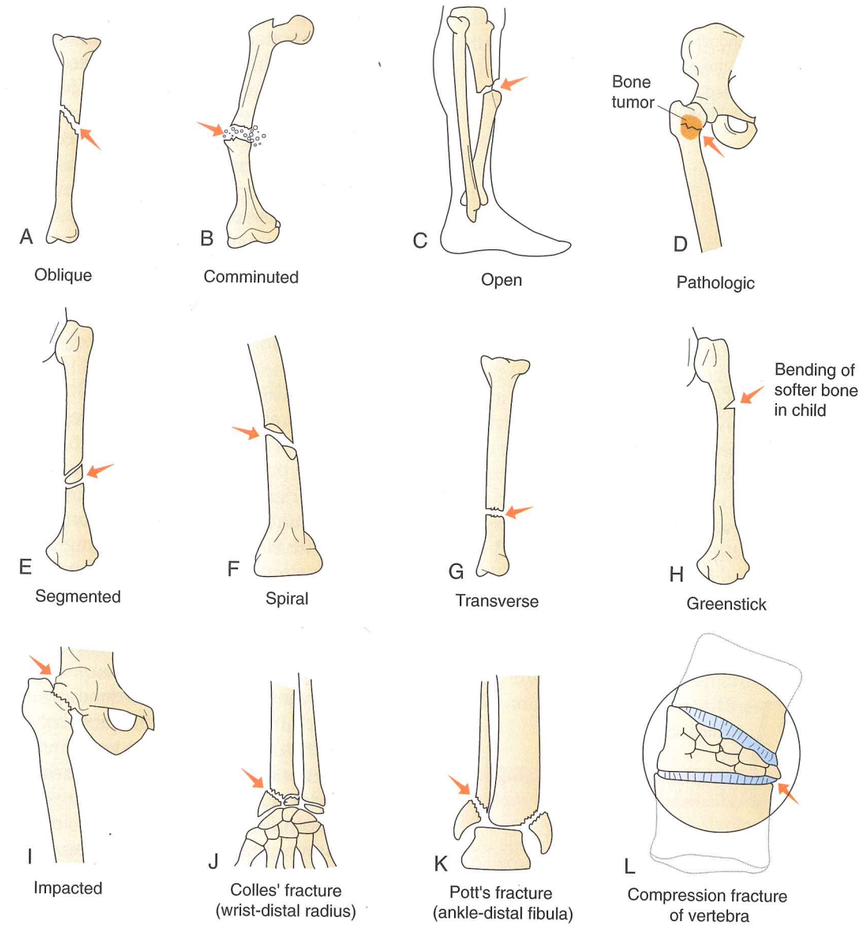


FIGURE 9-4 Types of fractures.

- *Pathologic* fracture results from a weakness in the bone structure due to conditions such as a tumor or osteoporosis. The break occurs spontaneously or with very little stress on the bone.
- *Stress* fractures (fatigue fractures) result from repeated excessive stress, commonly in the tibia, femur, or second and third metatarsals.
- *Depressed* fracture occurs in the skull when the broken section is forced inward on the brain.
- Direction of the fracture line; for example:
  - A fracture across the bone is a *transverse* fracture.
  - A break along the axis of the bone is a *linear* fracture.
  - A break at an angle to the diaphysis of the bone is an *oblique* fracture.
  - A break that angles around the bone, usually due to a twisting injury, is a *spiral* fracture.
- Unique names for certain types of fractures; for example:
  - Colles' fracture is a break in the distal radius at the wrist, commonly occurring when a person attempts to break a fall by extending the arm and open hand. Sometimes the ulna is also damaged.
  - Pott's fracture refers to a fracture of the lower fibula due to excessive stress on the ankle; for example, when stepping down with force. The tibia may be damaged as well.

Pathophysiology

When a bone breaks, bleeding occurs from the blood vessels in the bone and periosteum. Bleeding and inflammation also develop around the bone because of soft tissue damage. This *hematoma* or clot forms in the medullary canal, under the periosteum, and between

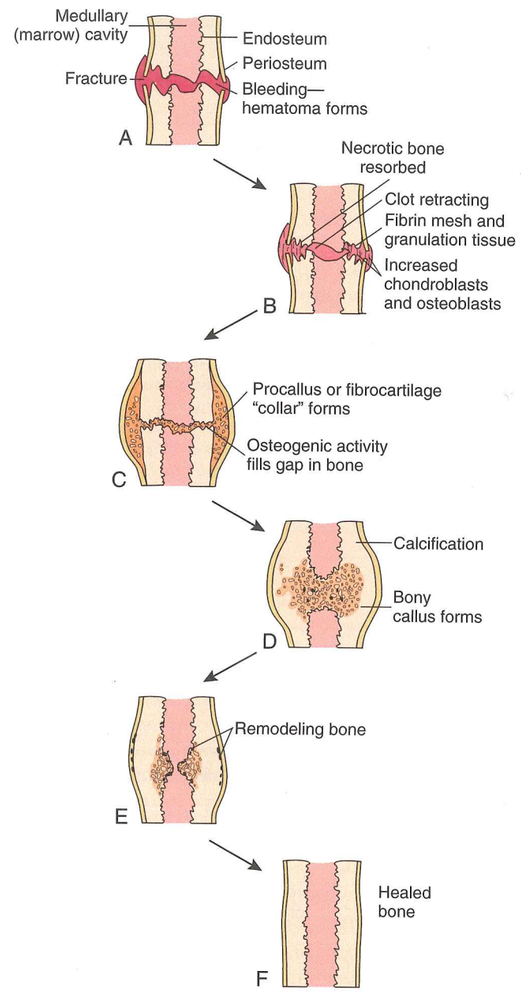


FIGURE 9-5 Healing of a fracture.

the ends of the bone fragments (Fig. 9-5). Necrosis occurs at the ends of the broken bone because the torn blood vessels are unable to continue delivery of nutrients. An inflammatory response develops as a reaction to the trauma and the presence of debris at the site.

At fracture sites, the hematoma serves as the basis for a fibrin network into which granulation tissue grows. Many new capillaries extend into this tissue, and phagocytic cells (for removing debris) and fibroblasts (for laying down new collagen fibers) migrate to it. Also, chondroblasts begin to form cartilage. Thus, the two bone ends become splinted together by a *procallus* or *fibrocartilaginous callus* (collar). This structure is *not* strong enough to bear weight, but constitutes the preliminary bridge repair in the bone.

Osteoblasts from the periosteum and endosteum begin to generate new bone to fill in the gap. Gradually the fibrocartilaginous callus is replaced by bone through extensive osteogenic activity, which forms a *bony callus*. Note that damaged bone is repaired by new bone formation, not by scar tissue. During subsequent months the repaired bone is *remodeled* by osteoblastic and osteoclastic activity in response to mechanical stresses on the bone. The excessive bone in the callus is removed, more compact bone is laid down, and eventually the bone assumes a normal appearance.

To summarize, the five stages of bone healing are hematoma, granulation tissue, procallus (fibrocartilage), bony callus, and remodeling.

Factors Affecting the Healing of Bone

Many factors affect the *healing process* in bone. In children fractures usually heal in approximately 1 month; in adults the process requires 2 or more months. A fracture in an elderly person may require many months.

- The amount of local damage done to the bone and soft tissue is a major determining factor. Prolonged inflammation or extensive damage to the periosteum or blood vessels impairs healing.
- The more closely approximated the ends of the bone are, the smaller the gap to be filled and the faster the healing process. When necessary to promote healing and prevent deformity, the bones must be realigned (reduced) in the proper position before healing can begin. It is most important to maintain immobilization of the bones to prevent disturbance or damage to the developing fragile bridge of tissue.
- Any secondary problem such as foreign material or infection at the site delays healing.
- Numerous systemic factors also affect the healing process in bone. For example, fracture repair is delayed in older persons and individuals with circulatory problems, anemias, diabetes mellitus, or nutritional deficits as well as in those taking drugs such as glucocorticoids (see Chapter 5).

Complications may affect healing in patients who sustain severe injuries:

1. Muscle spasm may occur as local pain and irritation cause strong muscle contractions at the fracture site. This muscle spasm pulls the bone fragments further out of position, causing angulation (deformity), rotation of a bone, or overriding of the bone pieces. Such abnormal movement of the bone causes more soft tissue damage, bleeding, and inflammation.
2. *Infections* such as tetanus or osteomyelitis (see Chapters 6 and 23) are a threat in persons with compound fractures or when surgical intervention is required. In such cases, precautions include wound débridement, application of a windowed cast, tetanus booster shots, and prophylactic antimicrobial therapy.
3. *Ischemia* is a complication that develops in a limb following treatment as edema increases during the first 48 hours after the trauma and casting. If the peripheral area (e.g., the toes or fingers) becomes pale or cold and numb or if the peripheral pulse has decreased or is absent, it is likely that the cast has become too tight and is compromising the circulation in the limb. The cast must be released quickly to prevent secondary tissue damage. During the later stages of healing it is also important that the cast not become too loose as edema decreases and muscle atrophies because the newly formed procallus may break down if there is any bone movement.
4. *Compartment syndrome* may develop shortly after the fracture occurs when there is more extensive inflammation, such as with crush injuries. Increased pressure of fluid within the **fascia**, the nonelastic covering of the muscle, compresses the nerves and blood vessels, causing severe pain and ischemia or necrosis of the muscle. The pressure effects may be aggravated by a cast.
5. *Fat emboli* are a risk when fatty marrow escapes from the bone marrow into a vein within the first week after injury. Fat emboli are more common in patients with fractures of the pelvis or long bones such as the femur, particularly when the fracture site has not been well immobilized during transportation immediately after the injury.

   Fat emboli travel to the lungs (see Chapter 13), where they cause obstruction, extensive inflammation, and respiratory distress syndrome, and they may disseminate into the systemic circulation as well. Frequently the first indications of a fat embolus are behavioral changes, confusion, and disorientation associated with cerebral emboli, in combination with respiratory distress and severe hypoxia.
6. Nerve damage may occur with severe trauma or tearing of the periosteum.
7. Failure to heal (nonunion) or healing with deformity (malunion) may result if the bone is not stabilized with ends closely approximated and aligned.
8. Fractures in or near the joint may have long-term residual effects, such as osteoarthritis or stunted growth if the epiphyseal plate is damaged in a child.

Signs and Symptoms

In some cases a fracture is clearly present, as in patients with compound fractures or an obvious deformity. Swelling, tenderness at the site, or altered sensation is present but may occur with any type of injury. Inability to move the broken limb is apparent. **Crepitus**, a grating sound, may be heard if the ends of the bone fragments move over each other. (The limb should *not* be moved to test for this!)

Pain usually occurs immediately after the injury. In some cases, particularly with compound or multiple fractures, pain is delayed when nerve function at the site is lost temporarily. Pain results from direct damage to the nerves by the trauma and from pressure and irritation due to the accumulated blood and inflammatory response. Severe pain may cause shock with pallor, diaphoresis, hypotension, and tachycardia. Nausea and vomiting sometimes occur.

Diagnostic Tests

X-ray films are used to confirm the presence of a fracture.

Treatment

Immediate splinting and immobilization of the fracture site is essential to minimize the risk of complications.

If necessary, *reduction* of the fracture is performed to restore the bones to their normal position. *Closed* reduction is accomplished by exerting pressure and traction; *open* reduction requires surgery. During surgery, devices such as pins, plates, rods, or screws may be placed to fix the fragments in position; any necrotic or foreign material is removed, and the bone ends are aligned and closely approximated. Immobilization is attained by applying a cast or splints or by using traction.

Traction involves the application of a force or weight pulling on a limb that is opposed by body weight. This force maintains the alignment of the bones, prevents muscle spasm, and immobilizes the limb. During the healing period, exercises are helpful to limit muscle atrophy in the immobilized area, maintain good circulation, and minimize joint stiffness or contractures.

EMERGENCY TREATMENT FOR FRACTURES

1. Cover open wounds with sterile or clean dressing material.
2. Splint for support and immobilize for transport, including joints above and below the fracture.
3. Elevate the limb slightly and apply cold if possible. Check pulse and sensory function distal to the fracture.
4. Keep patient warm. Check for signs of shock.

Dislocations

A dislocation is the separation of two bones at a joint with loss of contact between the articulating bone surfaces (Fig. 9-6). Usually one bone is out of position, while the other remains in its normal location. For example, the humerus is displaced from the shoulder joint. If the bone is only partially displaced, with partial loss of contact between the surfaces, the injury is termed *subluxation*.

Trauma, such as a fall, is usually the cause of dislocations. In some cases, a fracture is associated with a dislocation, whereas in others, an underlying disorder such as a muscular disease or rheumatoid arthritis, or other damage such as torn ligaments, may predispose the individual to dislocation.

Dislocations cause considerable soft tissue damage, including damage to the ligaments, nerves, and blood

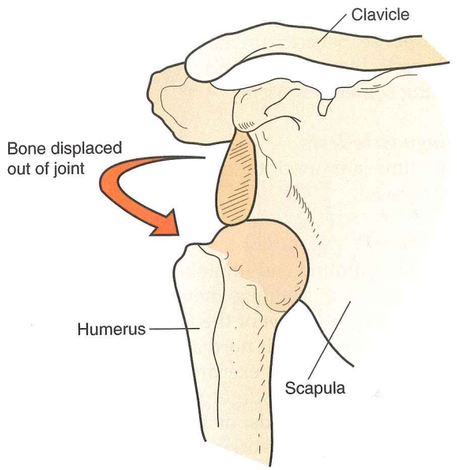


FIGURE 9-6 Dislocation.

vessels as the bone is pulled away from the joint. Bleeding and inflammation result. Severe pain, swelling, and tenderness develop. Deformity and limited movement are usually evident. The diagnosis is confirmed by x-rays. Treatment consists of reduction to return the dislocated bone to its normal position, immobilization during healing, and therapy to maintain joint mobility. Healing is slow if the ligaments and soft tissue are extensively damaged.

Sprains and Strains

A tear in a *ligament* is called a *sprain*, and a tear in a *tendon* is referred to as a *strain*. Ligaments and tendons support the bones in a joint and can easily be torn when excessive force is exerted on a joint. In some cases, the ligaments or tendons can be completely separated from their bony attachments, a problem known as *avulsion*. Sprains and strains are quite painful and are accompanied by tenderness, marked swelling, and often discoloration due to hematoma formation. Bleeding into the joint capsule delays healing. Strength and range of movement in the joint are limited. Diagnosis requires x-rays and other tests to rule out the presence of a fracture and determine the extent of the damage.

After a tear occurs, inflammation and then granulation tissue develop at the site. Collagen fibers are formed that create links with the remaining tendon or ligament, and eventually the healing mass is bound together with fibrous tissue. A tendon or ligament requires approximately 6 weeks before it is strong again. Stress on a tendon in the early stage will reopen the tear and lead to the development of excessive fibrous tissue in the tendon and thus less strength, shortening, and decreased flexibility at the joint. With severe damage to the tendons and ligaments, surgical repair may be necessary.

Other Injuries

The number of traumatic and overuse injuries has been increasing with the rising numbers of adults and children participating in fitness and recreational activities. Some of the predisposing factors include inappropriate or inadequate equipment, training, or warm-up techniques; more aggressive approaches to sports (e.g., skiing); and failure to allow minor injuries to heal completely before resuming activity. Minor injuries resulting from excessive use or abuse, particularly of joints, are also increasing; for example, tennis elbow, in which inflammation develops at the junction of the forearm muscles with the humerus. Muscle tears are more common, leading to hematoma and scar tissue formation.

Muscle Tears

Muscle tears are tears along the muscle itself or at points of attachment. They can occur as a result of a direct trauma or overexertion/overstressing of the muscle. There are three degrees of muscle tears:

- First degree—usually involves only a small percentage of the muscle. Pain is usually mild and does not result in any appreciable loss in strength or range of motion.
- Second degree—a larger tear than involves much of the muscle but stops short of being a complete tear. Pain is usually severe and the muscle can be partially contracted with a substantial loss of strength and range of motion.
- Third degree—a complete tear across the width of the muscle. The muscle will be unable to contract, there will be a great deal of internal bleeding and may require surgery for proper healing.

As soon as a tear occurs, activity involving the use of the muscle should stop, cold should be applied to help reduce internal bleeding, a compression bandage should be applied, and the limb or affected area should be elevated. In third-degree tears surgery may be necessary to repair the tear. An example of a third degree requiring surgery may be tearing of the gastrocnemius (the "hamstring"). In all cases, any scar tissue that forms will reduce the flexibility and strength of the muscle

Repeated injuries eventually result in fibrous scar tissue replacing normal structures, hindering mobility, as well as permanent joint damage and development of osteoarthritis. For example, repeated tears in the knee ligaments appear to cause early development of osteoarthritis. Shoulder pain and damage to the rotator cuff can result from excessive swinging motions, particularly with force (as in golf, tennis, hockey, and painting walls and ceilings), leading to tendinitis.

Repetitive Strain Injury

Repetitive strain injury (RSI) is a term referring to disorders affecting muscles, tendons, and nerves that develops over a period of time. The cause seems to be repeated forceful or precision movements, many of which are associated with work-related activities, although sports such as golf and certain exercises are also common causes. It appears that rapid repetition of certain movements interferes with circulation to the area and damages soft tissues, with cumulative effects. Most injuries affect the upper body. Higher stress levels increase the risk. Those affected are primarily in the 30 to 50 year range, and the incidence is increasing. Work such as repetitive lifting of merchandise, pivoting on an assembly line, or retrieving and shelving library materials are examples that are associated with a higher risk of RSI. The result is pain, weakness, and numbness, causing disability and interference with sleep. Examples include tendinitis, inflammation or injury of the tendon and sheath, or compression of a peripheral nerve, seen in carpal tunnel syndrome. In the latter, the median nerve is compressed at the wrist between tendons and the transverse carpal ligament.

Diagnosis requires a history, x-rays, and perhaps arthroscopic examination. Common treatment includes rest, applications of cold or heat, use of nonsteroidal anti-inflammatory drugs, and physiotherapy. Occupational therapy is helpful in identifying ergonomic changes in work that will lessen damage or reduce strain and pain. Surgery may be required to repair tears, remove damaged tissue, or replace joints. Sports medicine clinics can provide evaluation, education and preventive measures, assistive devices, and rehabilitation programs.

THINK ABOUT 9-4

a. Define each type of fracture: (1) compound; (2) comminuted; and (3) transverse.
b. List the three degrees of muscle tears and the steps in the treatment of a third-degree tear.
c. Differentiate a dislocation from a sprain.

Bone Disorders

Osteoporosis

Osteoporosis is a common metabolic bone disorder characterized by a decrease in bone mass and density, combined with loss of bone matrix and mineralization (see Fig. 24-1). Estimates for prevalence run as high as 10 million in the United States, with many more having low bone mass, and therefore increased risk. Although women have a higher risk of osteoporosis, a significant number of men also have been diagnosed. Osteoporosis is a factor in an estimated 1.5 million fractures annually, of which 300,000 involve the hip. Regular bone mass density tests are recommended for all individuals more than 50 years of age. This procedure requires resting on the scanner table for 10 to 15 minutes and is noninvasive.

Osteoporosis occurs in two forms: primary, including postmenopausal, senile, or idiopathic osteoporosis, and secondary, affecting men and women, following a specific primary disorder such as Cushing's syndrome.

Pathophysiology

During the continuous bone remodeling process, bone resorption exceeds bone formation, leading to thin, fragile bones that are subject to spontaneous fracture, particularly in the vertebrae (see Fig. 24-2). Although bone density and mass are reduced, the remaining bones are normal. Osteoporosis affects the bones consisting of higher proportions of cancellous bone, such as the vertebrae and femoral neck. The early stages of the condition are asymptomatic, but can be diagnosed using various bone density scans and x-rays to demonstrate the bone changes.

Etiology

Bone mass normally peaks in young adults, and then gradually declines, depending on genetic factors (such as vitamin D receptors), nutrition, weight-bearing activity, and hormonal levels. It appears that calcium intake in the child and young adult is critical to maintenance of bone mass later in life. A number of factors predispose people to osteoporosis. These include:

- Aging:
  - Osteoporosis is common in older individuals, particularly postmenopausal women with estrogen deficiency (see Chapter 24).
  - Osteoblastic activity is less effective with advancing age.
- Decreased mobility or a sedentary lifestyle:
  - Mechanical stress on bone by muscle activity is essential for osteoblastic activity. Decreased mobility is a factor with aging, but also if a patient is on bed rest for a prolonged time with a chronic illness, or has limited activity due to rheumatoid arthritis.
  - One limb or area of the body may be affected by osteoporosis when it is immobilized because of conditions such as a fracture (disuse osteoporosis).
- Hormonal factors such as hyperparathyroidism, Cushing's syndrome, or continued intake of catabolic glucocorticoids such as prednisone
- Deficits of calcium, vitamin D, or protein related to diet or history of deficits in childhood or malabsorption disorders
- Cigarette smoking

- Small, light bone structure, as in Asian and Caucasian persons
- Excessive caffeine intake

Signs and Symptoms

Compression fractures of the vertebrae have several obvious effects. Back pain is a common sign of osteoporosis, associated with the altered vertebrae causing pressure on the nerves. **Kyphosis** and **scoliosis**, abnormal curvatures of the spine with accompanying loss of height, are characteristic of the spinal changes seen with osteoporosis (see Figs. 23-2 and 23-3). Spontaneous fractures involving the head of the femur or pelvis are frequent occurrences. Healing of the fractures is slow.

Treatment

Usually bone cannot be restored to normal structural levels, but therapy can retard further bone loss. In addition to treating any underlying problem, therapeutic measures may include:

- Dietary supplements of calcium and vitamin D or protein. It is currently recommended that premenopausal women need at least 1000 mg of calcium, whereas postmenopausal women require more than 1500 mg. Intake of vitamin D should be 400 to 800 IU daily.
- Fluoride supplements to promote bone deposition
- Bisphosphonates such as alendronate (Fosamax) can be used as a short-term option to inhibit osteoclast activity and bone resorption.
- Calcitonin (Miacalcin nasal spray)
- Injected human parathyroid hormone to decrease bone resorption (helpful for some individuals)
- Regular weight-bearing exercise program such as walking or weight lifting
- Raloxifene (Evista) or tamoxifen, classed as selective estrogen receptor modulator drugs; recommended in specific cases because there is less effect on uterine and breast tissue. (The use of estrogen replacement therapy for osteoporosis has been questioned because of the possible risk of cancer.)
- Other newer medications under investigation, including strontium ranelate that appears to decrease bone resorption and increase bone formation as well as antibody preparations that bind to osteoclasts, preventing bone resorption
- Surgery to reduce kyphosis and realign the vertebral column

Research continues into new methods to stabilize bones and prevent fractures.

Rickets and Osteomalacia

These conditions result from a deficit of vitamin D and phosphates required for bone mineralization. They occur with dietary deficits, malabsorption, prolonged intake of phenobarbital (for seizures), or lack of sun exposure. The result is soft bone and rickets in children. Vitamin D is required for the absorption of calcium, and the lack of calcification of the cartilage forming at the epiphyseal plate leads to weak bones, often deformities, and the typical "bow legs" (rickets). The child's height is usually below normal. Osteomalacia occurs in adults in whom poor absorption of vitamin D or sometimes calcium causes soft bones and resulting compression fractures. "Renal rickets" refers to osteomalacia associated with severe renal disease (see Chapter 18).

Paget's Disease (Osteitis Deformans)

Paget's disease is a progressive bone disease that occurs in adults older than 40 years. The cause has not yet been established; however, childhood infection with a virus has been implicated and there is evidence of a genetic factor. Excessive bone destruction occurs, with replacement of bone by fibrous tissue and abnormal bone. Structural abnormalities, evident on x-rays, and enlargement (or thickening) are apparent in the long bones, vertebrae, pelvis, and skull. In some cases, the disease is asymptomatic. Pathologic fractures are common. When the vertebrae are affected, compression fractures and kyphosis result. Skull involvement leads to signs of increased pressure such as headache and compression of cranial nerves. Paget's disease also causes cardiovascular disease and heart failure. Treatment goals are to reduce the risk of fractures and deformity.

Osteomyelitis

Pathophysiology and Etiology

Osteomyelitis is a bone infection usually caused by bacteria and sometimes fungi. The microorganisms can enter the blood from an infection anywhere in the body and spread to the bones. An infection can also occur as result of surgery, particularly when a pin or structural insert is involved.

Signs and Symptoms

As with most infections there can be both local and systemic manifestations. These may include:

- Local inflammation and bone pain
- Fever and excessive sweating
- Chills
- General malaise

Treatment

As with other infections, use of antibiotics are the primary treatment used to eliminate the infection. If the infection is prolonged and significant damage has occurred in the bone tissue, surgery may be required to remove and repair the damaged tissue. If an insert or mechanical implant is involved, surgery may also be necessary to remove the device.

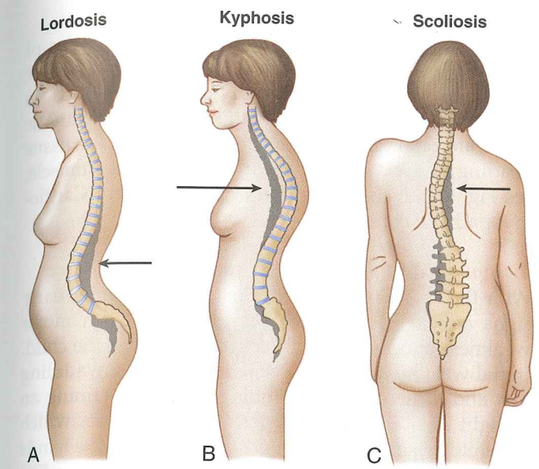


FIGURE 9-7 Abnormal spine curvatures. **A**, Lordosis. **B**, Kyphosis. **C**, Scoliosis. Black arrows highlight areas of abnormal curvature. *(From Patton KT, Thibodeau GA:* Anatomy & Physiology, *ed 8, St. Louis, 2013, Mosby.)*

Abnormal Curvatures of the Spine

The curves formed by the vertebrae help the spine absorb the stress of body movement and the action of gravity. When abnormalities occur, the curves may become misaligned or exaggerated, resulting in three main types of curvature disorders: lordosis, kyphosis, and scoliosis (Fig. 9-7).

Pathophysiology and Etiology

The three types share some common causes such as osteoporosis or arthritis, but other causes are specific to the disorder. These abnormalities can also develop during adolescence and are covered in Chapter 23.

Lordosis, also referred to as *swayback*, is characterized by the spine curving significantly inward at the lower back. Some of the specific causes of lordosis include:

- Achondroplasia
- Obesity
- Discitis
- Slipping forward of the vertebrae

Kyphosis, also referred to as *hunchback* or *humpback*, is characterized by an abnormally rounded upper back. Some specific causes of kyphosis include:

- Poor posture
- Spina bifida
- Congenital defects
- Spinal tumors or infections
- Scheuermann's disease

Scoliosis is characterized by either an S- or C-shaped sideways curve to the spine. The specific causes of the most common form of this abnormality are generally not known; however, scoliosis tends to run in families, and some more general causes such as disease, trauma, or congenital defects are also believed to be implicated.

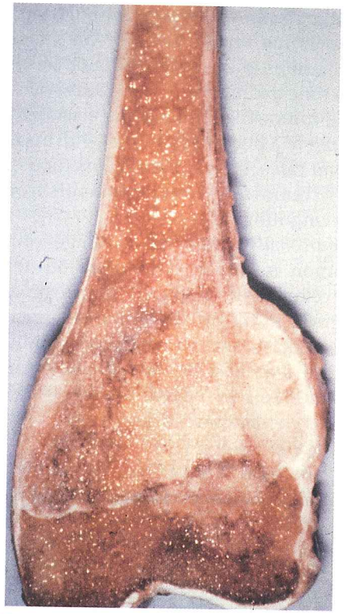


FIGURE 9-8 Osteosarcoma. The tumor (*white area*) has grown through the cortex of the bone and elevated the periosteum. *(From Kumar V, Cotran RS, Robbins SL:* Basic Pathology, *ed 8, Philadelphia, 1997, WB Saunders.)*

Bone Tumors

The majority of primary bone tumors are malignant. Bone is also a common site of secondary tumors, particularly in the spine and pelvis. Metastatic bone tumors usually are secondary to malignant tumors in the breast, lung, or prostate.

Osteosarcoma (osteogenic sarcoma) is a primary malignant neoplasm that usually develops in the metaphysis of the femur, tibia, or fibula in children or young adults, particularly males (Fig. 9-8). *Ewing's* sarcoma is another malignant neoplasm common in adolescents that occurs in the diaphysis of long bones.

Both types of tumor grow quickly and metastasize to the lungs in the early stages of tumor development. Sometimes the tumor is revealed by pathologic fracture. Bone pain is the common symptom, a constant steady pain at rest as well as with activity that gradually increases in severity. An individual often feels the increased pain at night. Treatment involves surgical amputation or excision of the tumor, followed by chemotherapy. Some clinics have used adjuvant chemotherapy before localized surgery without the need for amputation. Adjuvant chemotherapy appears to increase

the survival rates in most patients. Survival rates vary greatly depending on the stage of the cancer and the histologic features of the tumor. Tumors localized to the bone at the time of diagnosis have a survival rate of 70%. Many bone tumors have already metastasized at diagnosis, leading to a poorer prognosis, with approximately 30% survival rates. Newer surgical methods have been successful in removing secondary tumors from the lung and preserving lung tissue.

Chondrosarcomas arise from cartilage cells and are more common in adults older than 30 years. These tumors develop more gradually in the pelvic bone or shoulder girdle at the points of muscle attachment and eventually metastasize to the lung. Pain does not develop until late, and the tumors may remain silent until they are well advanced. Surgery is the primary treatment for chondrosarcomas.

THINK ABOUT 9-5

a. Describe four contributing factors to osteoporosis in older women.
b. Explain how osteoporosis leads to loss of height.

Disorders of Muscle, Tendons, and Ligaments

Muscular Dystrophy

Muscular dystrophy (MD) is a group of inherited disorders characterized by degeneration of skeletal muscle. The disorders differ in type of inheritance, area affected, age at onset, and rate of progression. Common types are summarized in Table 9-1.

Duchenne's or **pseudohypertrophic** muscular dystrophy is the most common type, affecting young boys, with a prevalence of about 3/100,000 males. X-linked inheritance has been demonstrated in most cases of Duchenne's muscular dystrophy. Some cases appear to be spontaneous gene mutations. Serum CK is elevated in many but not all carriers of the abnormal gene and appears before the first signs.

Pathophysiology

The basic pathophysiology is the same in all types of muscular dystrophy. A metabolic defect, a deficit of dystrophin (a muscle cell membrane protein) leads to degeneration and necrosis of the cell. Skeletal muscle fibers are replaced by fat and fibrous connective tissue (leading to the hypertrophic appearance of the muscle; see Fig. 9-9). Muscle function is gradually lost. Cardiomyopathy is common.

Signs and Symptoms

With the Duchenne type of muscular dystrophy, early signs appear at around 3 years of age, when motor weakness and regression become apparent in the child. Initial weakness in the pelvic girdle causes a waddling gait and difficulty with climbing stairs or attaining an upright position. The "Gower's maneuver," in which the child pushes to an erect position by using the hands to climb up the legs, is a typical manifestation (see Fig. 9-9). The weakness spreads to other muscle groups and eventually to the shoulder girdle. Tendon reflexes are reduced. Vertebral deformities such as kyphoscoliosis and various contractures develop. Respiratory insufficiency and infections are common. The majority of patients with muscular dystrophy develop cardiac abnormalities and mental retardation.

Diagnostic Tests

Diagnosis is based on identification of common genetic abnormalities, elevated creatine kinase levels (which are raised before clinical signs appear), electromyography, and muscle biopsy. Female carriers in a family can be identified by the presence of defective dystrophin in the blood. Chorionic villus testing can be performed on the fetus at 12 weeks' gestation.

Because no specific treatment is available, the goal is to maintain motor function as much as possible with moderate exercise and the use of supportive appliances. Occupational therapists play a significant role in support, assessment, and provision of appropriate assistive devices as the client's status and needs change. Death usually results by age 20 from respiratory or cardiac failure. If the patient chooses to use a ventilator

TABLE 9-1 Types of Muscular Dystrophy

Type	Inheritance	Age of Onset	Distribution	Progress
Duchenne's (variant-Becker type)	X-linked recessive (affects males)	2-3 years	Hips, legs, shoulder girdle (ascending)	Rapid
Fascioscapulohumeral (Landouzy)	Autosomal dominant	Before age 20	Shoulder, neck, face	Slow to moderate
Myotonic	Autosomal dominant (chromosome 19)	Birth to 50 years	Face, hands	Slow
Limb girdle	Autosomal recessive	All ages	Shoulders, pelvis	Varies

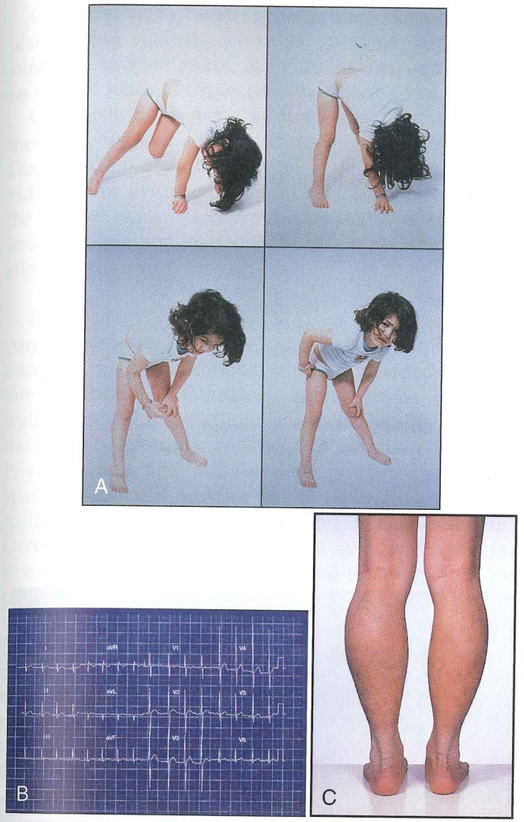


FIGURE 9-9 **A**, Gower's maneuver. **B**, Electrocardiogram in Duchenne's muscular dystrophy. **C**, Calf hypertrophy in Becker's muscular dystrophy. *(From Perkin GD:* Mosby's Color Atlas and Text of Neurology, *ed 2, London, 2002, Mosby.)*

in the event of respiratory failure, the lifespan can be prolonged substantially. Research on muscular dystrophy in mice has identified genetic therapies that alter the expression of MD genes and prevent dystrophic changes in young mice. This research is promising, but human applications will not be available for at least a decade.

THINK ABOUT 9-6

a. Describe the pathophysiologic changes in muscular dystrophy.
b. Explain how vertebral deformities develop in muscular dystrophy.

Primary Fibromyalgia Syndrome

Primary fibromyalgia syndrome is a group of disorders characterized by pain and stiffness affecting muscles, tendons, and surrounding soft tissues (not joints). Eighteen specific tender or trigger points, where pain and tenderness may be stimulated, have been identified in tendons and ligaments in the neck and shoulder area, trunk, and limbs, and these trigger points may be used in diagnosis. There are no obvious signs of inflammation or degeneration in the tissues. The cause is not known, but it appears to be related to altered central neurotransmission, resulting in increased soft tissue sensitivity to substance P, a neurotransmitter involved in pain sensation.

The incidence is higher in women 20 to 50 years of age. There is often a history of prior trauma or osteoarthritis. Aggravating factors include sleep deprivation, stress, and fatigue. Generalized aching pain is accompanied by marked fatigue, sleep disturbances, and depression. In some individuals, irritable bowel syndrome or urinary symptoms due to interstitial cystitis may accompany the chronic pain. Men tend to have localized fibromyalgia, including jaw pain or headache. Treatment includes stress reduction, regular early morning exercise, rest as needed, local applications of heat or massage as needed, and low doses of antidepressants, such as the tricyclic antidepressants or selective serotonin-norepinephrine reuptake inhibitors (SSNRIs). A new drug, Lyrica (pregabalin), has been approved for fibromyalgia and mediates the pain pathway. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been helpful to some individuals. Massage therapy is helpful as is occupational therapy to identify strategies to deal with pain and fatigue.

Joint Disorders

Arthritis occurs in many forms that impair joint function, leading to various types of disability in all age groups.

Osteoarthritis

Osteoarthritis (OA) may be called a degenerative, or "wear and tear," joint disease. The incidence of osteoarthritis is increasing. It is estimated that one in three adults in the United States has some degree of osteoarthritis. Men are affected more often than women. It is a major cause of disability and absence from the workplace.

Pathophysiology

In this condition:

1. The articular cartilage, of weight-bearing joints in particular (e.g., hips, knees), is damaged and lost through structural fissures and erosion resulting from excessive mechanical stress (Fig. 9-10), or breaks down for unknown reasons.
2. The surface of the cartilage becomes rough and worn, interfering with easy joint movement.

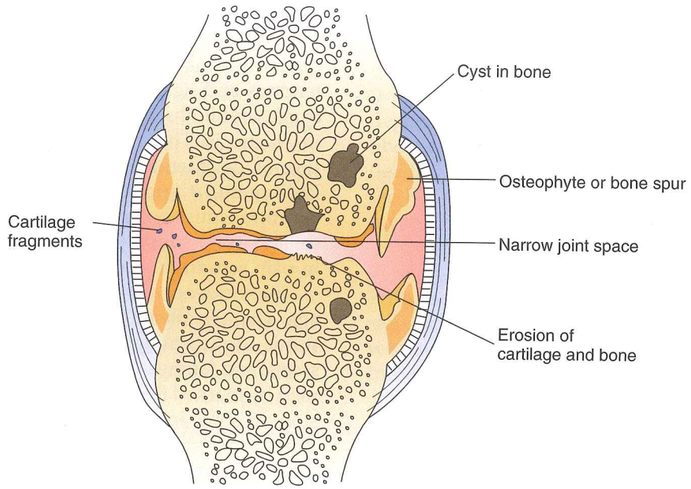


FIGURE 9-10 Pathologic changes with osteoarthritis.

3. Tissue damage appears to cause release of enzymes from the cells, which accelerates the disintegration of the cartilage.
4. Eventually the subchondral bone may be exposed and damaged, and cysts and *osteophytes* or new bone spurs develop around the margin of the bone.
5. Pieces of the osteophytes and cartilage break off into the synovial cavity, causing further irritation.
6. The joint space becomes narrower (easily seen on x-rays).
7. There may be secondary inflammation of the surrounding tissues in response to altered movement and stress on the joint. No systemic effects are present with osteoarthritis.

Etiology

The primary form of osteoarthritis is associated with obesity and aging, whereas the secondary type follows injury or abuse. Genetic changes in joint cartilage have been identified in research studies now underway. These genetic changes result in accelerated breakdown of articular cartilage.

Osteoarthritis often develops in specific joints because of injury or excessive wear and tear on a joint. This is a common consequence of participation in sports and certain occupations. Congenital anomalies of the musculoskeletal system may also predispose a patient to osteoarthritis. Once the cartilage is damaged, joint alignment or the frictionless surface of the articular cartilage is lost. A vicious cycle ensues, because uneven mechanical stress is then applied to other parts of the joint and to other joints. The large weight-bearing joints (e.g., the knees and hips) that are subject to injury or occupational stress are frequently affected.

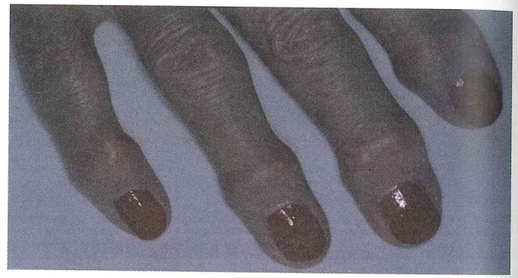


FIGURE 9-11 Heberden's node. *(From Lemmi FO, Lemmi CAE: Physical Assessment Findings CD-ROM, Philadelphia, 2000, Saunders).*

Signs and Symptoms

The pain of osteoarthritis, which is often mild and insidious initially, is an aching that occurs with weight bearing and movement. Pain becomes more severe as the degenerative process advances. It may be unilateral in some cases.

Joint movement is limited. Frequently the joint appears enlarged and hard as osteophytes develop. Walking becomes difficult if the joint is unstable, and the muscles atrophy, causing a predisposition to falls, particularly in older individuals. When the temporomandibular joint (TMJ) is involved, mastication becomes difficult, there is difficulty opening the mouth to speak or yawn, and preauricular pain may be quite severe. In some cases, the hands are involved with bony enlargement of the distal interphalangeal joints (Heberden's nodes; Fig. 9-11). Usually little soft tissue swelling is seen.

Crepitus may be heard as the cartilages become irregular, grating against each other. In some cases, other joints are affected as the individual exerts more stress on normal joints to protect the damaged joints.

Osteoarthritis is not a systemic disorder; therefore there are no systemic signs or changes in serum levels. Diagnosis is based on exclusion of other disorders and radiographic evidence of joint changes consistent with the clinical signs. Radiographic evidence often shows lesser progression of joint changes than the clinical effects of disease.

Treatment

Any undue stress on the joint should be minimized and adequate rest and additional support provided to facilitate movement. Ambulatory aids such as canes or walkers are helpful. Orthotic inserts in the shoes reduce the risk of deformity and help to maintain function. Physiotherapy and massage therapy help to reduce spasm in adjacent muscles due to pain. This results in maintenance of joint function and muscle strength. Occupational therapy is important in providing assistive devices such as joint splints and teaching alternate practices to reduce pain and deal with stiffness. Individuals with early OA may find pain relief and improved flexibility with the use of glucosamine-chondroitin compounds. Research studies on the use of static magnets to reduce pain have not shown significant results in rigorous double-blinded studies. Intra-articular injection of synthetic synovial fluid may reduce pain and facilitate movement. Glucocorticoids may be helpful. Analgesics or NSAIDs may be required for pain. Surgery is available to repair or replace joints such as the knee or hip with prostheses (Fig. 9-12). Success of such arthroplasty also depends on full participation in a rehabilitation program following surgery.

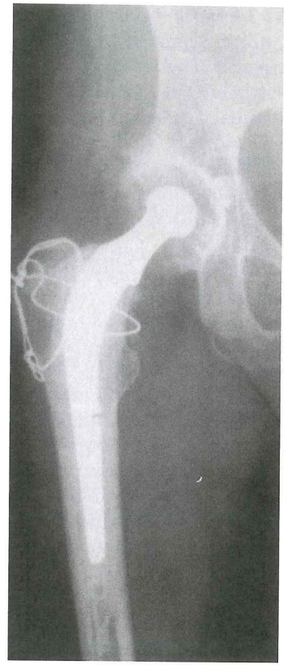


FIGURE 9-12 Hip arthroplasty. Radiograph shows hip after Charnley total hip arthroplasty (replacement of the femoral head and acetabulum with prosthesis cemented into bone). *(From Petty W: Total Joint Replacement, Philadelphia, 1991, Saunders.)*

Rheumatoid Arthritis

Rheumatoid arthritis (RA) is considered an autoimmune disorder causing chronic systemic inflammatory disease. It affects more than 1% of the population, and is a major cause of disability. Rheumatoid arthritis has a higher incidence in women than men and increases in older individuals.

Pathophysiology

Remissions and exacerbations lead to progressive damage to the joints. The disease often commences rather insidiously with symmetric involvement of the small joints such as the fingers, followed by inflammation and destruction of additional joints (e.g., wrists, elbows, knees). Many individuals also have involvement of the upper cervical vertebrae and TMJ. The severity of the condition varies from mild to severe, reflecting the number of joints affected, the degree of inflammation, and the rapidity of progression.

In the affected joints, the first step in the development of rheumatoid arthritis is an abnormal immune response, causing inflammation of the synovial membrane with vasodilation, increased permeability, and formation of exudate, causing the typical red, swollen, and painful joint. This *synovitis* appears to result from the immune abnormality. *Rheumatoid factor (RF)*, an antibody against immunoglobulin G, as well as other immunologic factors, is present in the blood in the majority of persons with rheumatoid arthritis. Rheumatoid factor is also present in synovial fluid. After the first period of acute inflammation, the joint may appear to recover completely.

During subsequent exacerbations, the process continues:

1. Synovitis—Inflammation recurs, synovial cells proliferate.
2. Pannus formation—Granulation tissue from the synovium spreads over the articular cartilage. This granulation tissue, called *pannus*, releases enzymes and inflammatory mediators, destroying the cartilage (Fig. 9-13).
3. Cartilage erosion—Cartilage is *eroded* by enzymes from the pannus, and in addition, nutrients that are normally supplied by the synovial fluid to the

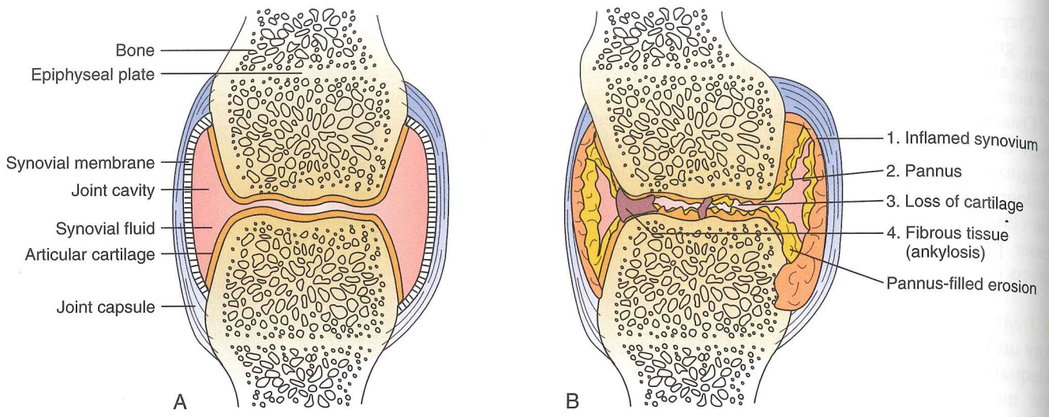


FIGURE 9-13 Pathologic changes with rheumatoid arthritis.

cartilage are cut off by the pannus. Erosion of the cartilage creates an unstable joint.

4. Fibrosis—In time, the pannus between the bone ends becomes fibrotic, limiting movement. This calcifies and the joint space is obliterated.
5. Ankylosis—Joint fixation and deformity develop.

During each exacerbation or acute period, inflammation and further damage occur in joints previously affected, and additional joints become affected by synovitis.

During this process, other changes frequently occur around the joint:

- Atrophy of muscles—The acute inflammation leads to disuse atrophy of the muscles and stretching of the tendons and ligaments, thus decreasing the supportive structures in the unstable joint.
- The alignment of the bones in the joint shifts, depending on how much cartilage has been eroded and the balance achieved between muscles.
- Inflammation and pain may cause muscle spasm, further drawing the bones out of normal alignment.
- Contractures and deformity with subluxation develop. Various contractures and deformities, such as ulnar deviation, swan neck deformity, or boutonniere deformity, may occur in the hands (Fig. 9-14), depending on the degree of flexion and hyperextension in the joints.

Mobility is greatly impaired as the various joints become damaged and deformed. Walking becomes very difficult when the knees or ankles are affected.

The inflammatory process has other effects on the body. Rheumatoid or subcutaneous nodules may form on the extensor surfaces of the ulna. Nodules also may form on the pleura, heart valves, or eyes. These are small granulomas on blood vessels.

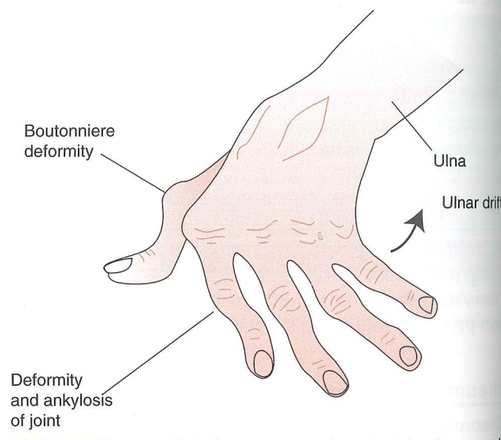


FIGURE 9-14 Typical deformity in a hand with rheumatoid arthritis.

Systemic effects are thought to arise from the circulating immune factors, causing marked fatigue, depression and malaise, anorexia, and low-grade fever. Iron deficiency anemia with low serum iron levels is common; when it results from rheumatoid arthritis, this anemia is resistant to iron therapy.

Etiology

Although rheumatoid arthritis is considered an autoimmune disorder, the exact nature of the abnormality has not been fully determined. A genetic factor is present, with familial predisposition. The abnormality seems to be linked to several viral infections. Rheumatoid factor is not present in all patients with rheumatoid arthritis, yet it may be present in certain other disorders as well. Rheumatoid arthritis is more common in women than men, and the incidence increases with aging.

Signs and Symptoms

Rheumatoid arthritis is insidious at onset, often becoming manifest as mild general aching and stiffness.

Inflammation may be apparent first in the fingers or wrists. It affects joints in a symmetric (bilateral) fashion, and usually more than one pair of joints is involved.

The joints appear red and swollen and often are very sensitive to touch as well as painful. Joint stiffness occurs following rest, which then eases with mild activity as circulation through the joint improves.

Joint movement is impaired by the swelling and pain. Frequently, daily activities become difficult, including dressing, food preparation, and oral hygiene. Malocclusion of the teeth may develop from TMJ involvement as the condyle is damaged.

With each exacerbation of disease, the function of the affected joints is further impaired as joint damage progresses. Eventually the joint is no longer inflamed but is fixed and deformed ("burned out").

The College of Rheumatology has established criteria for diagnosis based on four out of seven of the manifestations on their list, for example, swelling of three joints for a minimum of 6 weeks.

Systemic signs are marked during exacerbations and include fatigue, anorexia, mild fever, generalized lymphadenopathy, and generalized aching.

Diagnostic Tests

Synovial fluid analysis demonstrates the inflammatory process. Rheumatoid factor may be present in serum but is not specific for diagnosis.

Treatment

- A balance between rest and moderate activity is suggested to maintain mobility and muscle strength while preventing additional damage to the joints. Physical therapy and occupational therapy are important parts of any treatment regimen. Both assist in reducing pain and maintaining function. Occupational therapy also teaches adaptive practices to reduce effort and fatigue.
- For pain control, relatively high doses of the anti-inflammatory analgesic aspirin (ASA) or NSAIDs may be required (see Chapter 4). In more severe cases, glucocorticoids may be prescribed, and administered either orally or as intra-articular injections. Patients like the effects of glucocorticoids because the drug does promote a feeling of well-being and improves the appetite. However, there are a number of potential complications with long-term use of these drugs, so they should be used only during acute episodes or taken on alternate days at the lowest effective dose (see Chapter 4). Other drugs, such as gold compounds and immunosuppressants (methotrexate), are used in more resistant cases.

A newer group of NSAIDs, the COX-2 (cyclooxygenase-2) inhibitors, such as celecoxib (Celebrex) act to inhibit prostaglandins during inflammation. They appear to be quite effective in rheumatoid arthritis; at this time they are under further investigation because of the increased incidence of heart attacks and strokes associated with their use.

Disease-modifying antirheumatic drugs (DMARDs), including gold salts, methotrexate, and hydroxychloroquine have proved useful in some cases.

Newer biologic response modifying agents (such as infliximab [Remicade]) block tumor necrosis factor an inflammatory cytokine present in RA. Beta cell–depleting agents (rituximab [Rituxan]) and Interleukin-1 antagonists (anakinra [Kineret]) seem to be effective in cases of severe pain and improving joint function.

- The use of heat and cold modalities can be very effective when they are used correctly.
- During acute episodes, joints may require splinting to prevent excessive movement and maintain alignment. Appropriate body positioning and body mechanics when walking or moving also help to maintain function.
- Assistive devices such as wrist supports or padded handles with straps are available to help the patient cope with daily activities and reduce contractures.
- Surgical intervention to remove pannus, replace damaged tendons, reduce contractures, or replace joints may be necessary to improve function. This is particularly important in the treatment of RA in the hands.

Most individuals are subject to periodic exacerbations. If the number and severity of recurrences can be minimized, mobility can be maintained. About 10% of individuals incur severe disability.

Juvenile Rheumatoid Arthritis

Juvenile rheumatoid arthritis (JRA) occurs in several different types. In some respects, JRA differs from the adult form of rheumatoid arthritis (see Chapter 23). For example, the onset is usually more acute than the adult form. Systemic effects are more marked, but rheumatoid nodules are absent. The large joints are frequently affected. Rheumatoid factor is not usually present, but other abnormal antibodies such as antinuclear antibodies (ANAs) may be present. The systemic form, sometimes referred to as Still's disease, develops with fever, rash, lymphadenopathy, and hepatomegaly as well as joint involvement. A second form of JRA causes polyarticular inflammation similar to that seen in the adult form. A third form of JRA involves four or fewer joints but causes uveitis, inflammation of the iris, ciliary body, and choroid (uveal tract) in the eye.

Infectious (Septic) Arthritis

Infectious or septic arthritis usually develops in a *single* joint. The joint is red, swollen, and painful, with decreased range of movement. The synovium is swollen, and a purulent exudate forms. Aspiration of synovial fluid followed by culture and sensitivity tests confirms the diagnosis. Blood-borne bacteria such as gonococcus or staphylococcus are the source of infection in many cases, although anaerobic bacteria are becoming increasingly common. In some cases there is a history of trauma, surgery, or spread from a nearby infection such as osteomyelitis (see Chapter 23).

Lyme disease, caused by a spirochete and transmitted by ticks, is characterized by a migratory arthritis and rash developing several weeks to months after the tick bite. The knee and other large joints are most often involved. A vaccine for Lyme disease is now available.

In cases of infectious arthritis, immediate, aggressive antimicrobial treatment is necessary to prevent excessive cartilage destruction and fibrosis of the joint.

Gout (Gouty Arthritis)

This form of joint disease is common in men older than 40 years. Gout results from deposits of uric acid and urate crystals in the joint that then cause an acute inflammatory response (Fig. 9-15). Uric acid is a waste product of purine metabolism, normally excreted through the kidneys. **Hyperuricemia** may develop if renal excretion is not adequate or a metabolic abnormality, often a genetic factor such as a deficit of the enzyme uricase, leading to elevated levels of uric acid (primary gout) is present.

A sudden increase in serum uric acid levels usually precipitates an attack of gout. Gout often affects a single joint, such as in the big toe. When acute inflammation develops from uric acid deposits, the articular cartilage is damaged. The inflammation causes redness and swelling of the joint and severe pain. Attacks occur intermittently. Diagnosis is confirmed by examination of synovial fluid and blood tests.

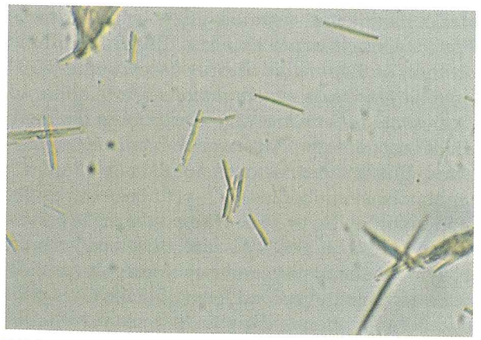


FIGURE 9-15 Gout. Urate crystals in synovial fluid cause inflammation in the joint. *(From Stevens ML:* Fundamentals of Clinical Hematology, *Philadelphia, 1997, Saunders.)*

A *tophus* is a large, hard nodule consisting of urate crystals that have been precipitated in soft tissue or bone, causing a local inflammatory reaction. Tophi usually occur a few years after the first attack of gout and may develop at joint bursae, on the extensor surfaces of the forearm, or on the pinnae of the ear.

Treatment consists of reducing serum uric acid levels by drugs and dietary changes, depending on the underlying cause. Increasing fluid intake and increasing the pH of the urine promotes excretion of excess uric acid. Colchicine may be used during an acute episode, and allopurinol is used as a preventive maintenance treatment. Normalization of serum uric acid levels is important because uric acid kidney stones are a threat in anyone with chronic hyperuricemia. Also, relief of the inflammation and pain associated with acute attacks by NSAIDs should be achieved as soon as possible.

Ankylosing Spondylitis

Ankylosing spondylitis is a chronic progressive inflammatory condition that affects the sacroiliac joints, intervertebral spaces, and costovertebral joints of the axial skeleton. Women tend to have peripheral joint involvement to a greater extent than men, although the disorder is more common in men. It usually develops in persons 20 to 30 years of age and varies in severity. Remissions and exacerbations mark the course.

The cause has not been fully determined, but it is deemed an autoimmune disorder with a genetic basis, given the presence of HLA-B27 antigen in the serum of most patients.

Pathophysiology

In patients with ankylosing spondylitis:

1. The vertebral joints first become inflamed.
2. Fibrosis and calcification or fusion of the joints follows. The result is ankylosis or fixation of the joints and loss of mobility (Fig. 9-16).
3. Inflammation begins in the lower back at the sacroiliac joints and progresses up the spine, eventually causing a typical "poker back."
4. Kyphosis develops as a result of postural changes necessitated by the rigidity and loss of the normal spinal curvature.
5. Osteoporosis is common and may contribute to kyphosis because of pathologic compression fractures of the vertebrae.
6. Lung expansion may be limited at this stage, as calcification of the costovertebral joints reduces rib movement.

Signs and Symptoms

Initially low back pain and morning stiffness are evident. Pain is often more marked when lying down, and may radiate to the legs similar to sciatic pain. The discomfort is relieved by walking or mild exercise.

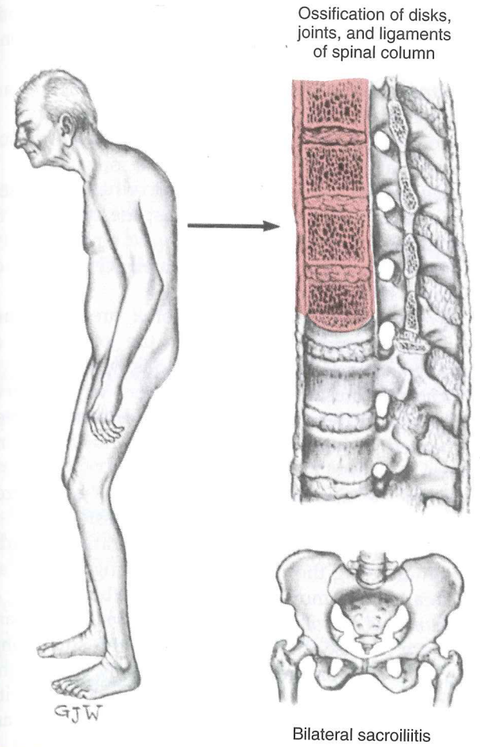


FIGURE 9-16 Characteristic posture and sites of ankylosing spondylitis. *(From Mourad L:* Orthopedic Disorders, *St. Louis, 1991, Mosby).*

As calcification develops, the spine becomes more rigid, and flexion, extension, and rotation of the spine are impaired.

Some individuals (about one third of patients) develop systemic signs such as fatigue, fever, and weight loss. Uveitis, particularly iritis (inflammation in the eye), is a common additional problem.

Treatment is directed at relief of pain and maintenance of mobility. Sleeping in a supine position reduces the tendency to flexion, and an appropriate daily exercise program promotes muscle support and proper posture. Anti-inflammatory drugs, as described, are useful during exacerbations of disease.

THINK ABOUT 9-7

a. Compare osteoarthritis and rheumatoid arthritis with respect to pathophysiology, common joints affected, and characteristics of pain.
b. Describe two unique characteristics of septic arthritis.
c. Explain how the pathophysiologic changes in ankylosing spondylitis differ from those of rheumatoid arthritis.

Other Inflammatory Joint Disorders

Bursitis is an inflammation of the bursae associated with bones, muscles, tendons, and ligaments of various joints. The bursae are small fluid-filled sacs that act as cushions at or near the structures of the joint. The most common causes of this inflammation are repetitive motions or positions that physically irritate the bursae at a specific joint. These include actions such as throwing a baseball repeatedly or washing floors frequently on hands and knees. Bursitis is primarily diagnosed by physical examination in which the joint appears swollen, red, achy, or stiff and pain with joint motion. Other methods for diagnosis may include imaging such as ultrasound or MRI and analysis of the fluid in the bursae to detect underlying problems such as an infection. The first step in treatment involves rest, application of cold compresses, and pain relievers. If the condition persists or worsens treatments include anti-inflammatory drugs, physical therapy, antibiotics in cases in which an infection is a cause, and in severe cases the bursae can be surgically drained.

Synovitis is an inflammation of the synovial membrane lining the joint. Movement of the joint is restricted and painful due to swelling as the synovial sac fills with fluid. The joint becomes swollen, red, and warm and can also be diagnosed by analyzing the synovial fluid for signs of infection or crystals indicating gout. Treatment includes use of anti-inflammatory drugs and treatment for underlying causes such as in cases of infection.

Tendinitis is the irritation or inflammation of the tendon. It is usually characterized by a dull ache at the site of tendon attachment, tenderness, and mild swelling. Although tendinitis can be caused by a single, sudden trauma, it is more likely the result of repetitive motions/actions. Diagnosis is done by physical examination. The first line of treatment involves rest, application of ice, and pain relievers. If the condition persists or worsens, treatments include anti-inflammatory drugs and physical therapy. In cases in which there has been significant injury to the tendon, surgery may be required.

CASE STUDY A

Fracture

J.R., age 17, has a compound fracture of the femur and is undergoing surgical repair.

1. Describe a compound fracture.
2. Give several reasons why it is important in this case to have immobilized the femur well before transporting J.R. to the hospital.
3. Explain why there is an increased risk of osteomyelitis in this case.
4. Explain why there is severe pain with this type of fracture.

The day after surgery J.R.'s toes are numb and cold.

5. Explain the possible causes of the cold, numb toes.
6. Explain why appropriate exercise is important during healing of the fracture.
7. List four factors that would promote healing of this fracture.
8. Explain why the leg should be elevated during recovery.
9. Explain why, following the removal of the cast, J.R. can expect to feel some weakness and stiffness in the leg.

CASE STUDY B

Rheumatoid Arthritis

Ms. W.P. is 42 years old and has had rheumatoid arthritis for 6 years. Her fingers are stiff and show slight ulnar deviation. She is now experiencing an exacerbation, and her wrists are red and swollen. She finds clothing or a touch on the skin over her wrists very painful. Her elbows and knees are also stiff and painful, especially after she has been resting. She is feeling extremely tired and depressed and has not been eating well.

1. Explain the reasons for the appearance and the pain occurring at her wrists.
2. Describe the factors contributing to the stiff, deformed fingers.
3. Explain why some activity relieves the pain and stiffness of rheumatoid arthritis.
4. Describe several factors contributing to the systemic symptoms noted in Ms. W.P.
5. Explain how each of the following drugs acts in the treatment of rheumatoid arthritis (see Chapter 5): (1) NSAIDs; (2) glucocorticoids; (3) disease-modifying agents; and (4) biologic agents.
6. Predict the possible course of this disease in Ms. W.P.

CHAPTER SUMMARY

Muscles, bones, and joints form the framework of the body, providing support and protection as well as a mechanism for movement. Any damage to the parts of this system is likely to impair mobility.

- The type of *fracture*, such as open, closed, or comminuted, is defined by the characteristics of the bone fragments.
- Fractures heal in four stages, the hematoma, fibrocartilaginous callus, bony callus, and remodeling.
- Dislocations, sprains, and strains cause soft tissue damage at joints.
- *Osteoporosis* is a common disorder, in which decreased bone mass and density predispose patients to fractures.
- *Rickets* and *osteomalacia* are caused by deficits of vitamin D and phosphate.
- *Osteosarcoma* and *Ewing's* sarcoma are malignant tumors, commonly occurring in the long bones of young adults. Constant bone pain is typical.
- *Duchenne's* muscular dystrophy is one of a group of progressive degenerative muscle disorders, often inherited as an X-linked recessive trait, affecting boys.
- *Primary fibromyalgia syndrome* causes generalized aching pain, severe fatigue, and depression.
- *Osteoarthritis* is a progressive degenerative disorder often affecting the large weight-bearing joints. Pain increases with movement and weight bearing.
- *Rheumatoid arthritis* is a progressive systemic inflammatory disease that usually affects the small joints initially and progresses symmetrically. The pathologic process in an affected joint includes synovitis, pannus formation, cartilage erosion, fibrosis, and ankylosis, leading to contractures and loss of function.
- *Infectious* or *septic arthritis* usually involves a single joint. Early treatment is required to prevent permanent damage.
- *Gout* is a form of inflammatory arthritis caused by deposits of uric acid and urates in a joint.
- *Ankylosing spondylitis* is a progressive inflammatory disorder of the vertebral joints that leads to a rigid spine.

STUDY QUESTIONS

1. Describe each of the following structures in a bone:
   a. endosteum
   b. medullary cavity
   c. diaphysis of a long bone
2. Define an irregular bone and give an example.
3. Where is red bone marrow found in adults? What is the purpose of red marrow?
4. a. Describe the sources of energy for skeletal muscle contraction.
   b. Explain the effect of a cholinergic blocking agent on skeletal muscle contraction (see Chapter 14).
   c. Explain how anabolic steroid drugs affect skeletal muscle.
   d. Describe the purpose and structure of a tendon.
   e. Describe the outcome after part of a muscle has died.
5. a. Describe the structures that stabilize and support a joint.
   b. What type of joint is needed for the articulation between the ribs and sternum? What kind of mobility does it have?
   c. Explain the meaning of the term *origin* as related to muscles at a joint.

6. a. Describe each type of fracture: (1) compression fracture, (2) pathologic fracture, and (3) spiral fracture.
   b. Differentiate the procallus from the bony callus in the healing of a fracture.
7. Compare the changes and effects of a strain and a subluxation.
8. Compare the pathophysiology of osteoporosis, osteomalacia, and Paget's disease.
9. a. Explain why the muscles of the legs of a child with Duchenne's muscular dystrophy appear large.
   b. Explain why only boys are affected by Duchenne's muscular dystrophy.
   c. Explain why a child with muscular dystrophy pulls himself up a flight of stairs.
10. Describe the characteristics of synovial fluid in:
    a. rheumatoid arthritis
    b. gout
    c. septic arthritis
    d. osteoarthritis
11. Explain why eating and coughing may be difficult in a person with severe ankylosing spondylitis.

ADDITIONAL RESOURCES

Applegate EJ: *The Anatomy and Physiology Learning System Textbook*, ed 3, Philadelphia, 2006, Saunders.
Beers MH, Berkow R, editors: *The Merck Manual of Diagnosis and Therapy*, ed 18, Rahway, NJ, 2006, Merck Research Laboratories.
Kumar V, Abbas AK, Fausto M: *Robbins and Cotran Pathologic Basis of Disease*, ed 8, Philadelphia, 2007, Saunders.

Web Sites

http://www.arthritis.org *Arthritis Foundation*
http://www.niams.nih.gov *National Institute of Arthritis and Musculoskeletal and Skin Diseases*
http://www.ninds.nih.gov/disorders/md/md.htm *National Institute of Neurological Disorders and Stroke*
http://www.nof.org *National Osteoporosis Foundation*
http://www.osteo.org *The NIH Osteoporosis and Related Bone Diseases—National Resource Center*
http://www.rheumatology.org *American College of Rheumatology*