

Muscles and Muscle Tissue

9

Overview of Muscle Tissues (pp. 280–281)

1. Compare and contrast the basic types of muscle tissue.
2. List four important functions of muscle tissue.

Skeletal Muscle (pp. 281–309)

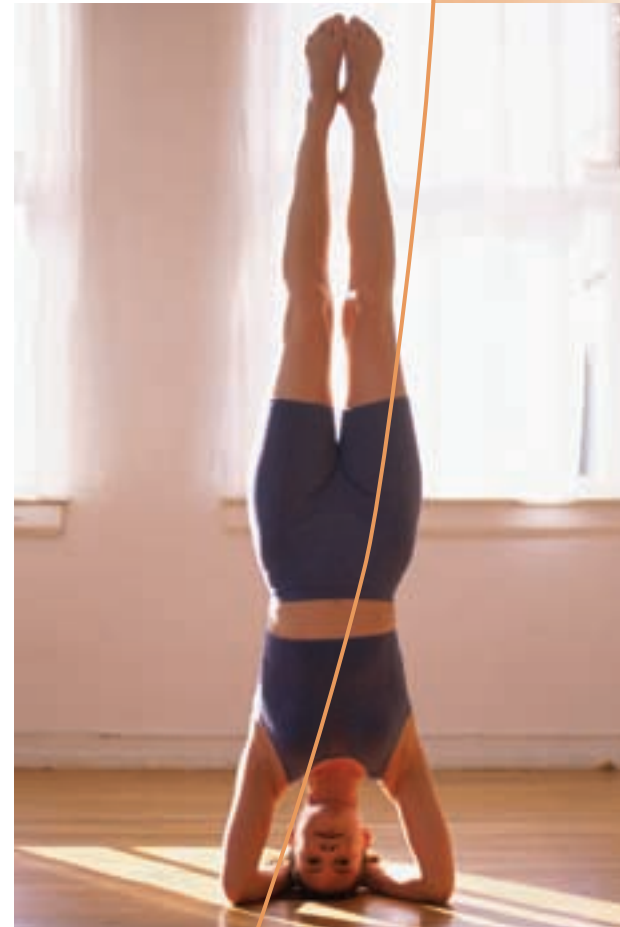
3. Describe the gross structure of a skeletal muscle.
4. Describe the microscopic structure and functional roles of the myofibrils, sarcoplasmic reticulum, and T tubules of muscle fibers (cells).
5. Explain the sliding filament mechanism.
6. Define motor unit and explain how muscle fibers are stimulated to contract.
7. Define muscle twitch and describe the events occurring during its three phases.
8. Explain how smooth, graded contractions of a skeletal muscle are produced.
9. Differentiate between isometric and isotonic contractions.
10. Describe three ways in which ATP is regenerated during skeletal muscle contraction.
11. Define oxygen debt and muscle fatigue. List possible causes of muscle fatigue.
12. Describe factors that influence the force, velocity, and duration of skeletal muscle contraction.
13. Describe three types of skeletal muscle fibers and explain the relative value of each type.
14. Compare and contrast the effects of aerobic and resistance exercise on skeletal muscles and on other body systems.

Smooth Muscle (pp. 309–315)

15. Compare the gross and microscopic anatomy of smooth muscle cells to that of skeletal muscle cells.
16. Compare and contrast the contractile mechanisms and the means of activation of skeletal and smooth muscles.
17. Distinguish between single-unit and multiunit smooth muscle structurally and functionally.

Developmental Aspects of Muscles (pp. 318–319)

18. Describe embryonic development of muscle tissues and the changes that occur in skeletal muscles with age.



Because flexing muscles look like mice scurrying beneath the skin, some scientist long ago dubbed them *muscles*, from the Latin *mus* meaning “little mouse.” Indeed, the rippling muscles of professional boxers or weight lifters are often the first thing that comes to mind when one hears the word *muscle*. But muscle is also the dominant tissue in the heart and in the walls of other hollow organs. In all its forms, muscle tissue makes up nearly half the body’s mass. The most distinguishing functional characteristic of muscles is their ability to transform chemical energy (ATP) into directed mechanical energy. In so doing, they become capable of exerting force.

Overview of Muscle Tissues

Types of Muscle Tissue

The three types of muscle tissue are *skeletal*, *cardiac*, and *smooth*. Before exploring their characteristics, however, let us introduce some terminology. First, skeletal and smooth muscle cells (but not cardiac muscle cells) are elongated and, for this reason, are called **muscle fibers**. Second, muscle contraction depends on two kinds of **myofilaments**, which are the muscle equivalents of the actin- or myosin-containing microfilaments described in Chapter 3. As you will recall, these two proteins play a role in motility and shape changes in virtually every cell in the body, but this property reaches its highest development in the contractile muscle fibers. Third, whenever you see the prefixes **myo** or **mys** (both are word roots meaning “muscle”) and **sarco** (flesh), the reference is to muscle. For example, the plasma membrane of muscle fibers is called the *sarcolemma* (sar’ko-lem’ah), literally “muscle” (sarco) “husk” (lemma), and muscle fiber cytoplasm is called *sarcoplasm*. Now we are ready to describe the three types of muscle tissue.

Skeletal muscle tissue is packaged into the *skeletal muscles*, organs that attach to and cover the bony skeleton. Skeletal muscle fibers are the longest muscle cells; they have obvious stripes called **striations** and can be controlled voluntarily. Although it is often activated by reflexes, skeletal muscle is called **voluntary muscle** because it is the *only type subject to* conscious control. Therefore, when you think of skeletal muscle tissue, the key words to keep in mind are *skeletal*, *striated*, and *voluntary*. Skeletal muscle is responsible for overall body mobility. It can contract rapidly, but it tires easily and must rest after short periods of activity. Nevertheless, it can exert tremendous power, a fact revealed by reports of people lifting cars to save their loved ones. Skeletal muscle is also remarkably adaptable. For example, your hand muscles can exert a force of a fraction of an ounce to pick up a dropped paper clip

and the same muscles can exert a force of about 70 pounds to pick up this book!

Cardiac muscle tissue occurs only in the heart (the body’s blood pump), where it constitutes the bulk of the heart walls. Like skeletal muscle cells, cardiac muscle cells are striated, but cardiac muscle is not voluntary. Most of us have no conscious control over how fast our heart beats. Key words to remember for this muscle type are *cardiac*, *striated*, and *involuntary*. Cardiac muscle usually contracts at a fairly steady rate set by the heart’s pacemaker, but neural controls allow the heart to “shift into high gear” for brief periods, as when you race across the tennis court to make that overhead smash.

Smooth muscle tissue is found in the walls of hollow visceral organs, such as the stomach, urinary bladder, and respiratory passages. Its role is to force fluids and other substances through internal body channels. It has no striations, and like cardiac muscle, it is not subject to voluntary control. We can describe smooth muscle tissue most precisely as *visceral*, *nonstriated*, and *involuntary*. Contractions of smooth muscle fibers are slow and sustained.

Skeletal and smooth muscles are discussed in this chapter. Cardiac muscle is discussed in Chapter 18 (The Heart). Table 9.3 on pp. 314–315 summarizes the most important characteristics of each type of muscle tissue.

Functional Characteristics of Muscle Tissue

Muscle tissue is endowed with some special functional properties that enable it to perform its duties.

Excitability, or **irritability**, is the ability to receive and respond to a stimulus, that is, any change in the environment whether inside or outside the body. In the case of muscle, the stimulus is usually a chemical—for example, a neurotransmitter released by a nerve cell, or a local change in pH. The response is generation of an electrical impulse that passes along the sarcolemma (plasma membrane) of the muscle cell and causes the cell to contract.

Contractility is the ability to shorten forcibly when adequately stimulated. This property sets muscle apart from all other tissue types.

Extensibility is the ability to be stretched or extended. Muscle fibers shorten when contracting, but they can be stretched, even beyond their resting length, when relaxed.

Elasticity is the ability of a muscle fiber to recoil and resume its resting length after being stretched.

Muscle Functions

Muscle performs four important functions for the body: It produces movement, maintains posture, stabilizes joints, and generates heat.

Producing Movement

Just about all movements of the human body and its parts are a result of muscle contraction. Skeletal muscles are responsible for all locomotion and manipulation. They enable you to respond quickly to changes in the external environment, for example, by jumping out of the way of a runaway car, directing your eyeballs, and smiling or frowning.

The coursing of blood through your body is evidence of the work of the rhythmically beating cardiac muscle of your heart and the smooth muscle in the walls of your blood vessels, which helps maintain blood pressure. Smooth muscle in organs of the digestive, urinary, and reproductive tracts propels, or squeezes, substances (foodstuffs, urine, a baby) through the organs and along the tract.

Maintaining Posture

We are rarely aware of the workings of the skeletal muscles that maintain body posture. Yet these muscles function almost continuously, making one tiny adjustment after another that enables us to maintain an erect or seated posture despite the never-ending downward pull of gravity.

Stabilizing Joints

Even as muscles pull on bones to cause movements, they stabilize and strengthen the joints of the skeleton (Chapter 8).

Generating Heat

Finally, muscles generate heat as they contract. This heat is vitally important in maintaining normal body temperature. Because skeletal muscle accounts for at least 40% of body mass, it is the muscle type most responsible for generating heat.

* * *

In the following section, we examine the structure and functioning of skeletal muscle in detail. Then we consider smooth muscle more briefly, largely by comparing it with skeletal muscle. Because cardiac muscle is described in Chapter 18, its treatment in this chapter is limited to the summary of its characteristics provided in Table 9.3.

Skeletal Muscle

The levels of skeletal muscle organization, gross to microscopic, are summarized in Table 9.1.

Gross Anatomy of a Skeletal Muscle

Each **skeletal muscle** is a discrete organ, made up of several kinds of tissues. Although skeletal muscle fibers predominate, blood vessels, nerve fibers, and substantial amounts of connective tissue are also

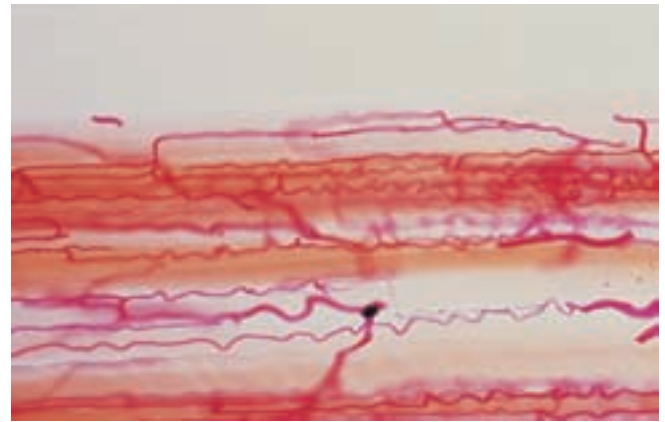


FIGURE 9.1 Photomicrograph of the capillary network surrounding skeletal muscle fibers. The arterial supply was injected with dark red gelatin to demonstrate the capillary bed. The long muscle fibers are stained orange (30 $\times$).

present. A skeletal muscle's shape and its attachments in the body can be examined easily without the help of a microscope.

Nerve and Blood Supply

In general, each muscle is served by one nerve, an artery, and by one or more veins, all of which enter or exit near the central part of the muscle and branch profusely through its connective tissue sheaths (described below). Unlike cells of cardiac and smooth muscle tissues, which can contract in the absence of nerve stimulation, each skeletal muscle fiber is supplied with a nerve ending that controls its activity.

Contracting muscle fibers use huge amounts of energy, a situation that requires more or less continuous delivery of oxygen and nutrients via the arteries. Muscle cells also give off large amounts of metabolic wastes that must be removed through veins if contraction is to remain efficient. Muscle capillaries, the smallest of the body's blood vessels, are long and winding and have numerous cross-links, features that accommodate changes in muscle length (Figure 9.1). They straighten when the muscle is stretched and contort when the muscle contracts.

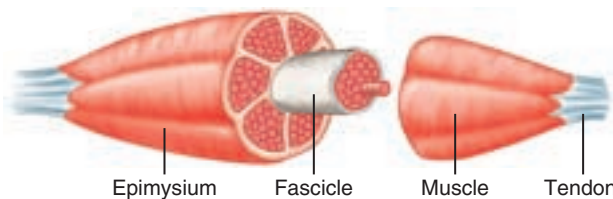
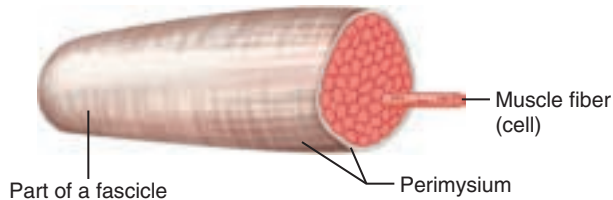
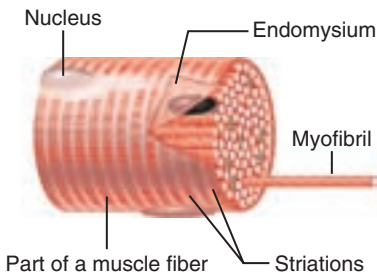
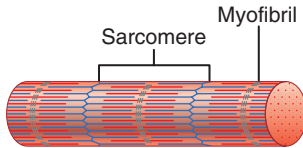
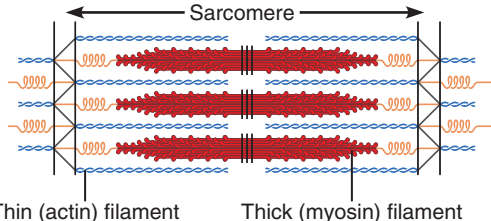
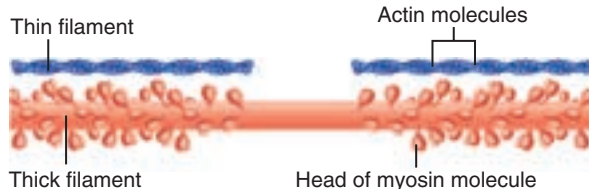
Connective Tissue Sheaths

In an intact muscle, the individual muscle fibers are wrapped and held together by several different connective tissue sheaths. Together these connective tissue sheaths support each cell and reinforce the muscle as a whole. We will consider these from internal to external (Figure 9.2).

1. Endomysium. Each individual muscle fiber is surrounded by a fine sheath of connective tissue consisting mostly of reticular fibers. This is the endomysium (en"do-mis'e-um; "within the muscle").

TABLE 9.1

Structure and Organizational Levels of Skeletal Muscle

Structure and Organizational Level	Description	Connective Tissue Wrappings
Muscle (organ) 	Consists of hundreds to thousands of muscle cells, plus connective tissue wrappings, blood vessels, and nerve fibers	Covered externally by the epimysium
Fascicle (a portion of the muscle) 	Discrete bundle of muscle cells, segregated from the rest of the muscle by a connective tissue sheath	Surrounded by a perimysium
Muscle fiber (cell) 	Elongated multinucleate cell; has a banded (striated) appearance	Surrounded by the endomysium
Myofibril or fibril (complex organelle composed of bundles of myofilaments) 	Rodlike contractile element; myofibrils occupy most of the muscle cell volume; appear banded, and bands of adjacent myofibrils are aligned; composed of sarcomeres arranged end to end	
Sarcomere (a segment of a myofibril) 	The contractile unit, composed of myofilaments made up of contractile proteins	
Myofilament or filament (extended macromolecular structure) 	Contractile myofilaments are of two types—thick and thin: the thick filaments contain bundled myosin molecules; the thin filaments contain actin molecules (plus other proteins); the sliding of the thin filaments past the thick filaments produces muscle shortening. Elastic filaments (not shown here) maintain the organization of the A band and provide for elastic recoil when muscle contraction ends	



Consider the term epimysium. What is the meaning of epi? Of mys? How do these word stems relate to the role and position of this connective tissue sheath?

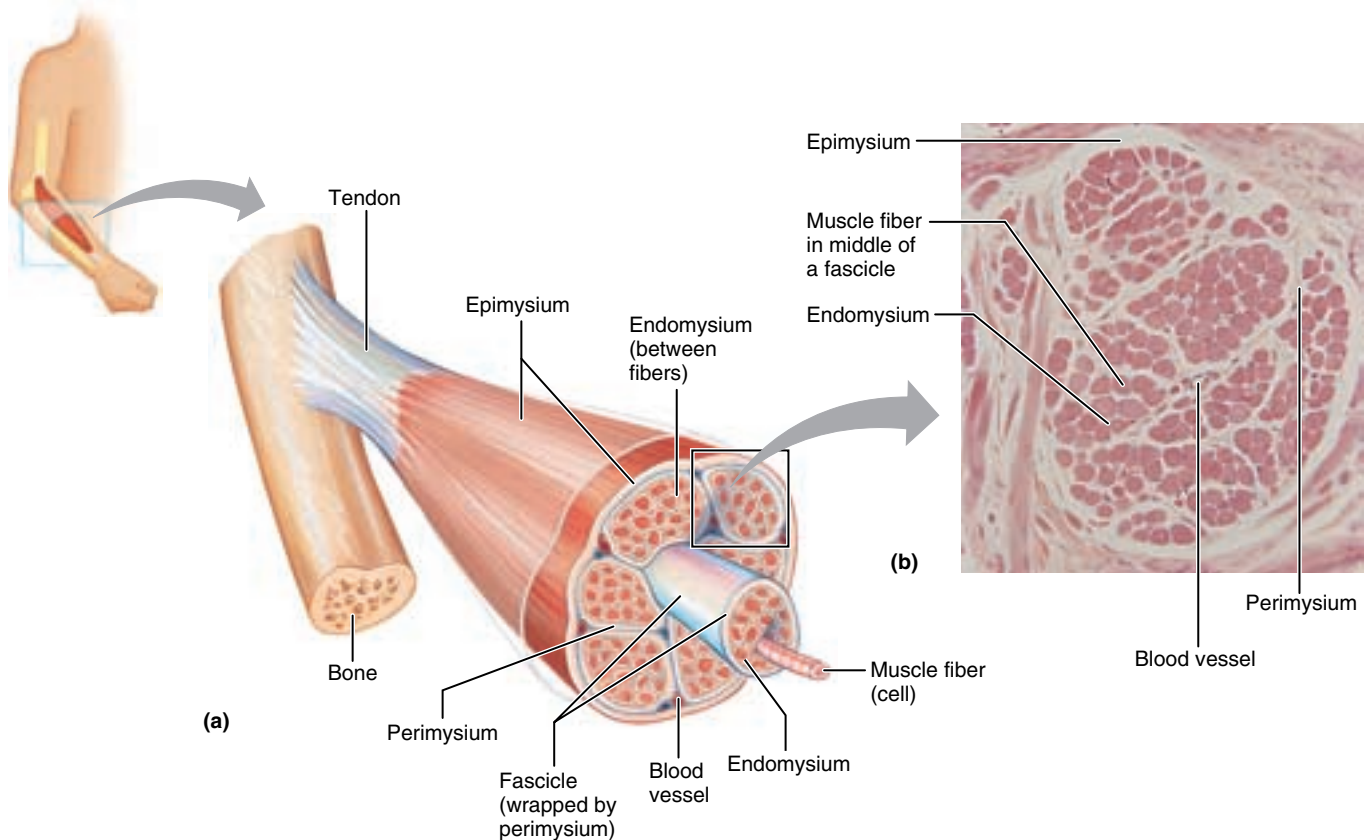


FIGURE 9.2 Connective tissue sheaths of skeletal muscle. (a) Each muscle fiber is wrapped with a delicate connective tissue sheath, the endomysium. Bundles, or fascicles, of muscle fibers are bound by a collagenic sheath called a perimysium. The entire muscle is strengthened and wrapped by a coarse epimysium sheath. (b) Photomicrograph of a cross section of part of a skeletal muscle (90 $\times$).

2. Perimysium and fascicles. Within each skeletal muscle, the endomysium-wrapped muscle fibers are grouped into fascicles (fas'i-klz; "bundles") that resemble bundles of sticks. Surrounding each fascicle is a layer of fibrous connective tissue called perimysium [per'i-mis'e-um; "around the muscle (fascicles)"].

3. Epimysium. An "overcoat" of dense irregular connective tissue surrounds the whole muscle. This coat is the epimysium (ep'i-mis'e-um), a name that means "outside the muscle." Sometimes the epimysium blends with the deep fascia that lies between neighboring muscles or the superficial fascia deep to the skin.

As shown in Figure 9.2, all of these connective tissue sheaths are continuous with one another as

well as with the tendons that join muscles to bones. Therefore, when muscle fibers contract, they pull on these sheaths, which in turn transmit the pulling force to the bone to be moved. They also contribute to the natural elasticity of muscle tissue, and for this reason these elements are sometimes referred to collectively as the *series elastic components*. The wrappings also provide entry and exit routes for the blood vessels and nerve fibers that serve the muscle.

Attachments

Recall from Chapter 8 that (1) most skeletal muscles span joints and are attached to bones (or other structures) in at least two places and (2) when a muscle contracts, the movable bone, the muscle's **insertion**, moves toward the immovable or less movable bone, the muscle's **origin**. In the muscles of the limbs, the origin typically lies proximal to the insertion.

epi = outer; mys = muscle. The epimysium covers the external surface of the muscle.

Muscle attachments, whether origin or insertion, may be direct or indirect. In **direct**, or **fleshy attachments**, the epimysium of the muscle is fused to the periosteum of a bone or perichondrium of a cartilage. In **indirect attachments**, the muscle's connective tissue wrappings extend beyond the muscle either as a ropelike tendon or as a sheetlike **aponeurosis** (ap"o-nu-ro'sis). The tendon or aponeurosis anchors the muscle to the connective tissue covering of a skeletal element (bone or cartilage) or to the fascia of other muscles.

Of the two, indirect attachments are much more common because of their durability and small size. Because tendons are mostly tough collagenic fibers, they can cross rough bony projections that would tear apart the more delicate muscle tissues. Because of their relatively small size, more tendons than fleshy muscles can pass over a joint—thus, tendons also conserve space.

Microscopic Anatomy of a Skeletal Muscle Fiber

Each skeletal muscle fiber is a long cylindrical cell with multiple oval nuclei arranged just beneath its **sarcolemma** surface (see Figure 9.3a). Skeletal muscle fibers are huge cells. Their diameter typically ranges from 10 to 100 μm —up to ten times that of an average body cell—and their length is phenomenal, some up to 30 cm long. Their large size and the fact that they are multinucleate are not surprising once you learn that each fiber is actually a *syncytium* (sin-sish'e-um; "fused cells") produced by the fusion of hundreds of embryonic cells.

The **sarcoplasm** of a muscle fiber is similar to the cytoplasm of other cells, but it contains unusually large amounts of *glycosomes* (granules of stored glycogen) and substantial amounts of an oxygen-binding protein called *myoglobin*. **Myoglobin**, a red pigment that stores oxygen, is similar to hemoglobin, the pigment that transports oxygen in blood. The usual organelles are present, along with some that are highly modified in muscle fibers: myofibrils and the sarcoplasmic reticulum. T tubules are unique modifications of the sarcolemma. Let's look at these special structures more closely.

Myofibrils

Each muscle fiber contains a large number of rodlike **myofibrils** that run parallel to its length (see Figure 9.3b). With a diameter of 1–2 μm each, the myofibrils are so densely packed in the fiber that mitochondria and other organelles appear to be squeezed between them. Hundreds to thousands of myofibrils are in a single muscle fiber, depending on its size, and they account for about 80% of cellular volume. The myofibrils contain the contractile elements of skeletal muscle cells.

Striations, Sarcomeres, and Myofilaments

Striations, a repeating series of dark **A bands** and light **I bands**, are evident along the length of each myofibril. In an intact muscle fiber, the A and I bands are nearly perfectly aligned with one another, giving the cell as a whole its striped (striated) appearance.

As illustrated in Figure 9.3c, each A band has a lighter stripe in its midsection called the **H zone** (*H* for *helle*; "bright"). The H zones are visible only in relaxed muscle fibers for reasons that will soon become obvious. Each H zone is bisected vertically by a dark line called the **M line**. The I bands also have a midline interruption, a darker area called the **Z disc** (or Z line). A **sarcomere** (sar'ko-mër; literally, "muscle segment") is the region of a myofibril between two successive Z discs, that is, it contains an A band flanked by half an I band at each end (see Figure 9.3c). Averaging 2 μm long, the sarcomere is the smallest contractile unit of a muscle fiber. Thus, the *functional units* of skeletal muscle are sarcomeres aligned end-to-end like boxcars in a myofibril "train."

If we examine the *banding pattern* of a myofibril at the molecular level, we see that it arises from an orderly arrangement of two types of even smaller structures, called **myofilaments** or **filaments**, within the sarcomeres (Figure 9.3d). The central **thick filaments** extend the entire length of the A band. The more lateral **thin filaments** extend across the I band and partway into the A band. The Z disc is a coin-shaped sheet composed of the protein *nebulin*. It anchors the thin filaments and connects each myofibril to the next throughout the width of the muscle cell. The H zone of the A band appears less dense because the thin filaments do not extend into this region. The M line in the center of the H zone is slightly darker because of the presence of fine protein strands that hold adjacent thick filaments together in that area. The third type of myofilament illustrated in Figure 9.3d, the *elastic filament*, is described in the next section.

A longitudinal view of the myofilaments, such as that in Figure 9.3d, is a bit misleading because it gives the impression that each thick filament interdigitates with only four thin filaments. In areas where thick and thin filaments overlap, each thick filament is actually surrounded by a hexagonal arrangement of six thin filaments.

Ultrastructure and Molecular Composition of the Myofilaments

Thick filaments (about 16 nm in diameter) are composed primarily of the protein **myosin** (Figure 9.4a). Each myosin molecule has a rodlike *tail* terminating in two globular *heads*. The tail consists of two interwoven *heavy* polypeptide chains. Its globular heads are the ends of the heavy chains, and the "business end" of myosin. The heads link the thick and thin filaments together (form **cross bridges**) during contraction. As

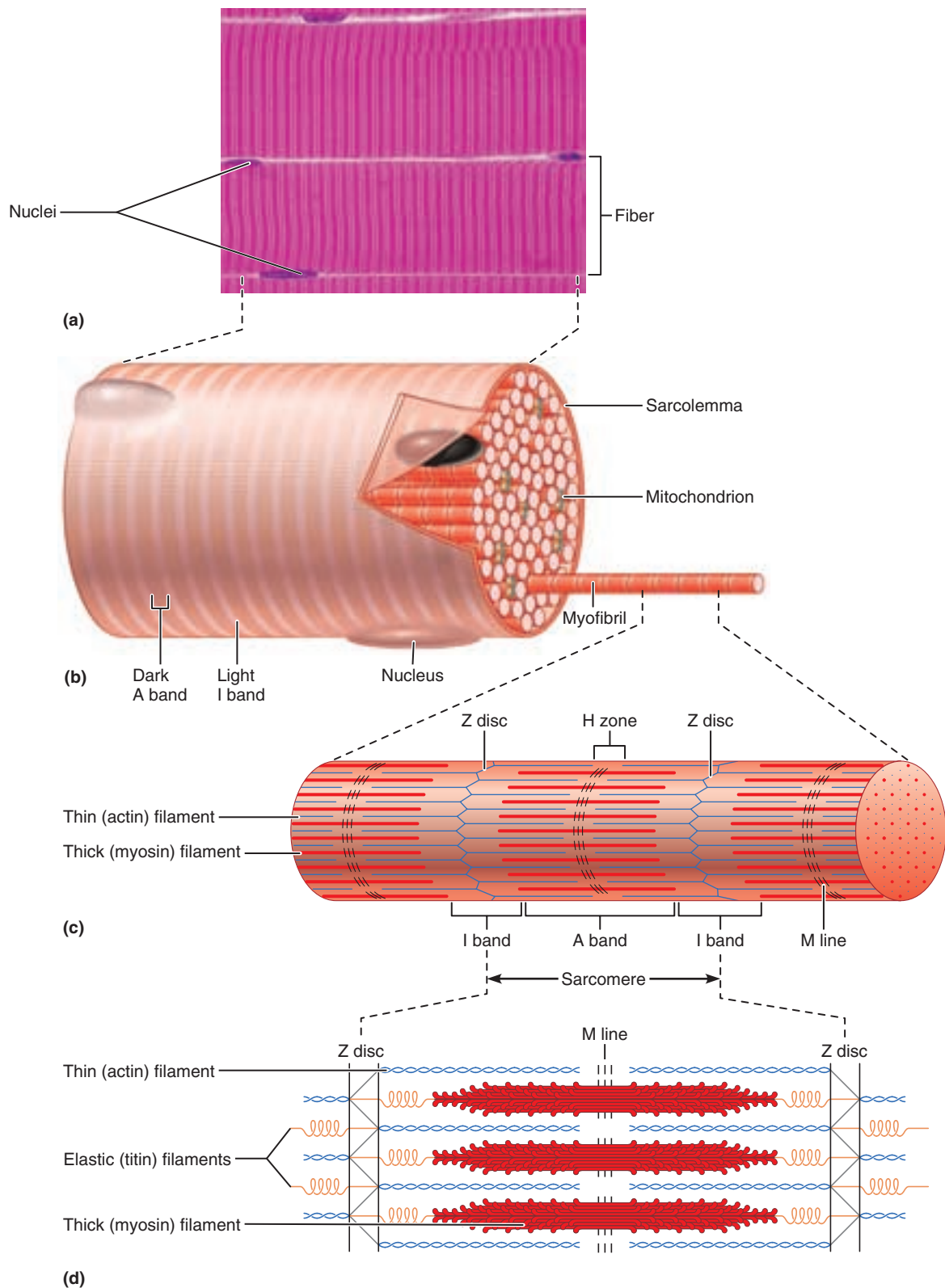
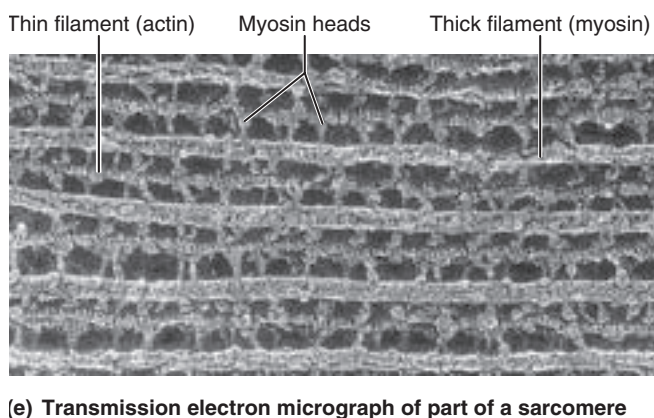
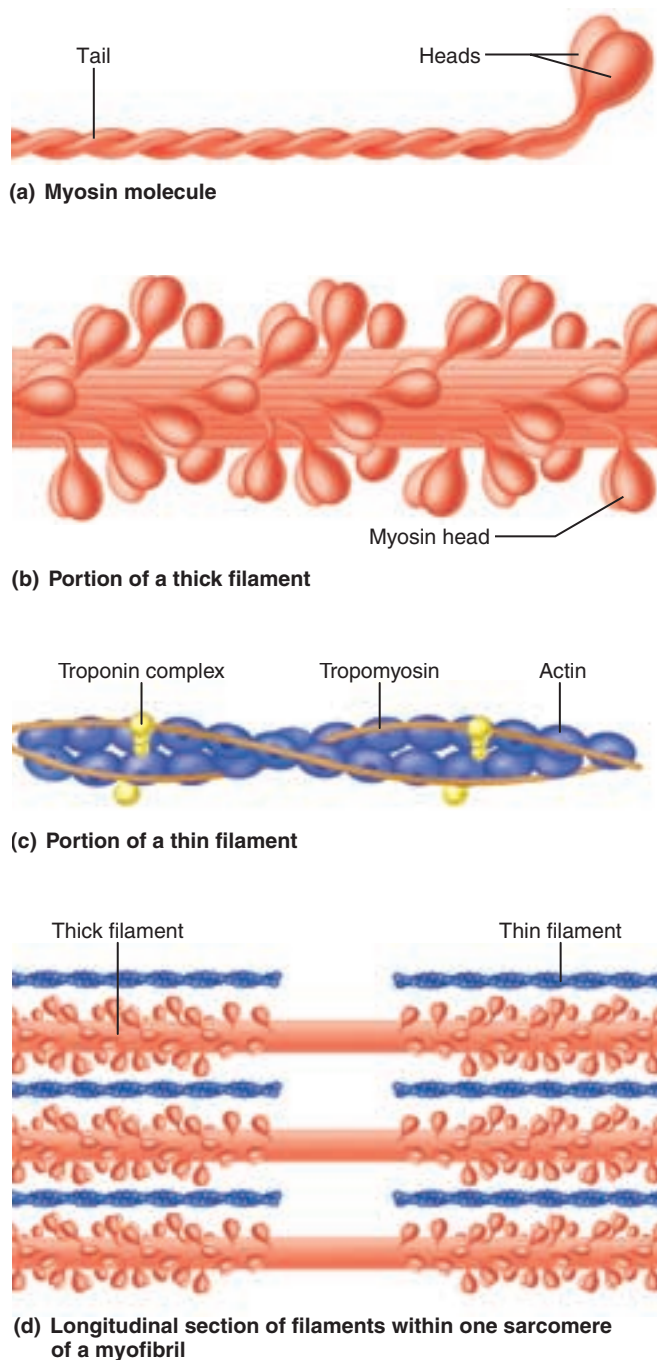


FIGURE 9.3 Microscopic anatomy of a skeletal muscle fiber. (a) Photomicrograph of portions of two isolated muscle fibers (700 $\times$). Notice the obvious striations (alternating light and dark bands). (b) Diagram of part of a muscle

fiber showing the myofibrils. One myofibril extends from the cut end of the fiber. (c) A small portion of one myofibril enlarged to show the myofilaments responsible for the banding pattern. Each sarcomere

extends from one Z disc to the next. (d) Enlargement of one sarcomere (sectioned lengthwise). Notice the myosin heads on the thick filaments.



explained shortly, these cross bridges act as motors to generate the tension developed by a contracting muscle cell. Each thick filament contains about 200 myosin molecules bundled together with their tails forming the central part of the thick filament and their heads facing outward and in opposite directions at each end (Figure 9.4b and d). As a result, the central portion of a thick filament is smooth, but its ends are studded with a staggered array of myosin heads. Besides bearing actin binding sites, the heads contain ATP binding sites and ATPase enzymes that split ATP to generate energy for muscle contraction.

The thin filaments (7–8 nm thick) are composed chiefly of the protein **actin** (Figure 9.4c). The kidney-shaped polypeptide subunits of actin, called *globular actin* or *G actin*, bear the active sites to which the myosin heads attach during contraction. G actin monomers are polymerized into long actin filaments called *fibrous*, or *F actin*. The backbone of each thin filament appears to be formed by an actin filament that coils back on itself, forming a helical structure that looks like a twisted double strand of pearls.

Several regulatory proteins are also present in the thin filament. Two strands of **tropomyosin** (tro'po-mi'o-sin), a rod-shaped protein, spiral about the actin core and help stiffen it. Successive tropomyosin molecules are arranged end-to-end along the actin filaments, and in a relaxed muscle fiber, they block actin's active sites so that the myosin heads cannot bind to the thin filaments. The other major protein in the thin filament, **troponin** (tro'po-nin), is a three-polypeptide complex. One of these polypeptides (TnI) is an inhibitory subunit that binds to actin; another (TnT) binds to tropomyosin and helps position it on actin. The third (TnC) binds calcium ions. Both troponin and tropomyosin help control the myosin-actin interactions involved in contraction.

The discoveries of additional types of muscle filaments during the past decade or so demand that the established view of striated muscle as a two-filament

FIGURE 9.4 Composition of thick and thin filaments.

(a) An individual myosin molecule has a rodlike tail, from which two "heads" protrude. (b) Each thick filament consists of many myosin molecules, whose heads protrude at opposite ends of the filament, as shown in (d). (c) A thin filament contains a strand of actin twisted into a helix. Each strand is made up of actin subunits. Tropomyosin molecules coil around the actin filaments, helping to reinforce them. A troponin complex is attached to each tropomyosin molecule. (d) Arrangement of the filaments in a sarcomere (longitudinal view). In the center of the sarcomere, the thick filaments are devoid of myosin heads, but at points of thick and thin filament overlap, the heads extend toward the actin, with which they interact during contraction. (e) Transmission electron micrograph of part of a sarcomere clearly showing the myosin heads that generate the contractile force.

? Which of the following structures shown in this diagram would contain the highest concentration of Ca^{2+} in a resting muscle cell: T tubule, mitochondrion, or SR?

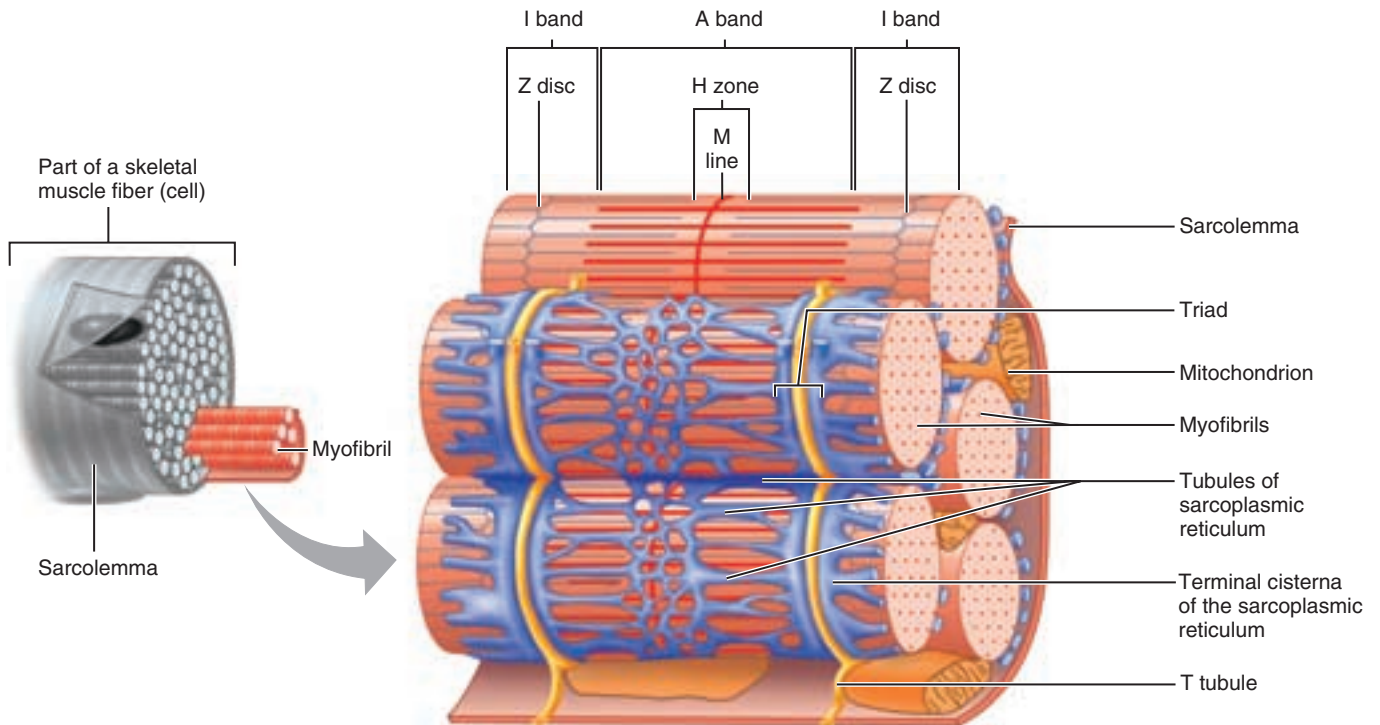


FIGURE 9.5 Relationship of the sarcoplasmic reticulum and T tubules to myofibrils of skeletal muscle. The tubules of the SR encircle each myofibril like a “holey” sleeve. The tubules fuse to form communicating

channels at the level of the H zone and abutting the A-I junctions, where the saclike elements called terminal cisternae are formed. The T tubules, inward invaginations of the sarcolemma, run deep into the cell between the

terminal cisternae. Sites of close contact of these three elements (terminal cisterna, T tubule, and terminal cisterna) are called triads.

system be rewritten. One of these newly discovered filament types, the **elastic filament** referred to earlier, is composed of the giant protein **titin**, which extends from the Z disc to the thick filament, and then runs within the latter to attach to the M line. It has two basic functions: (1) holding the thick filaments in place, thus maintaining the organization of the A band, and (2) assisting the muscle cell to spring back into shape after being stretched. It can perform the second task because the part of the titin that spans the I bands is extensible, unfolding when the muscle is stretched and recoiling when the tension is released. Titin does not resist stretching in the ordinary range of extension, but it stiffens as it uncoils, helping the muscle to resist excessive stretching, which might pull the sarcomeres apart.

Sarcoplasmic Reticulum and T Tubules

Skeletal muscle fibers (cells) contain two sets of intracellular tubules that participate in regulation of muscle contraction: (1) the sarcoplasmic reticulum and (2) the T tubules (Figure 9.5).

Sarcoplasmic Reticulum The **sarcoplasmic reticulum (SR)** is an elaborate smooth endoplasmic reticulum (see pp. 87–88). Its interconnecting tubules surround each myofibril the way the sleeve of a loosely crocheted sweater surrounds your arm. Most of these tubules run longitudinally along the myofibril. Others form larger, perpendicular cross channels at the A band–I band junctions. These channels are called **terminal cisternae** (“end sacs”) and they always occur in pairs.

The major role of the SR is to regulate intracellular levels of ionic calcium: It stores calcium and releases it on demand when the muscle fiber is stimulated to contract. As you will see, calcium provides the final “go” signal for contraction.

■ The SR, which is a calcium storage depot.

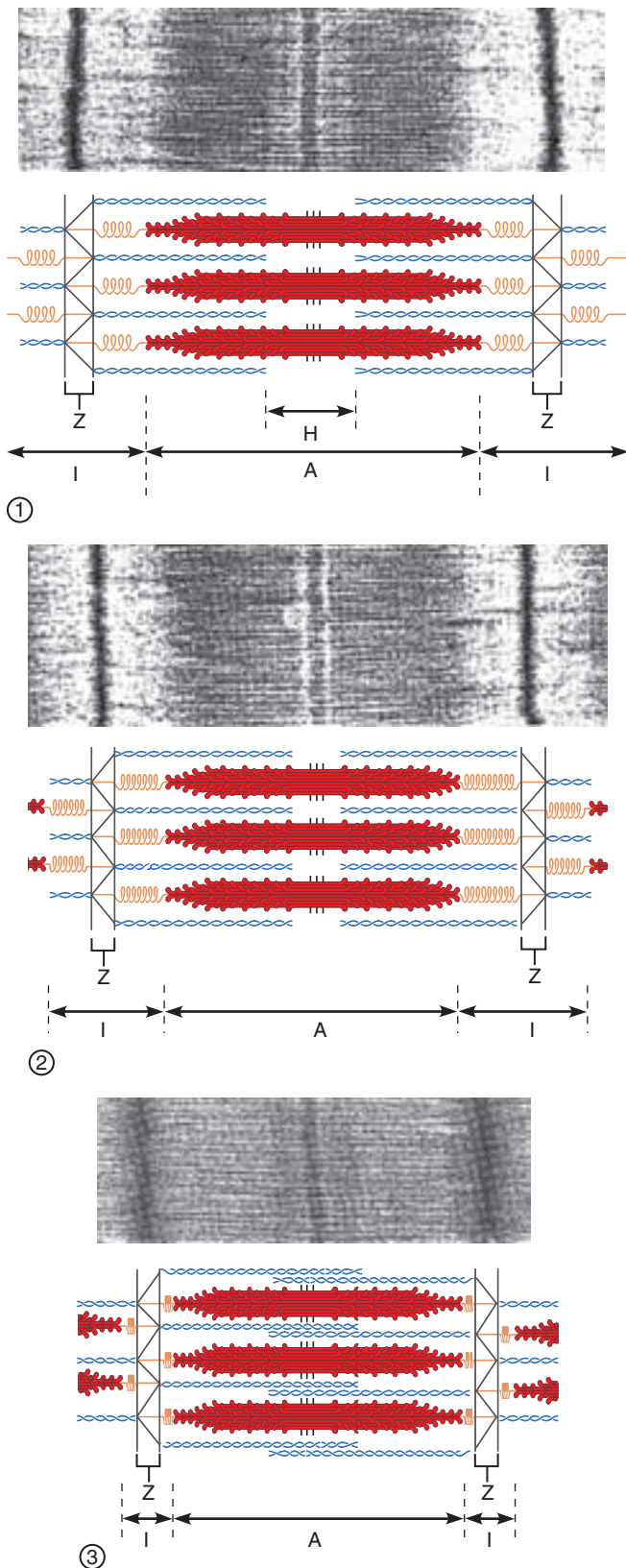


FIGURE 9.6 Sliding filament model of contraction.

The numbers indicate the sequence of events, with ① being relaxed and ③ fully contracted. At full contraction, the Z discs abut the thick filaments and the thin filaments overlap each other. The photomicrographs (top view in each case) show enlargements of 25,000 $\times$.

T Tubules At each A band–I band junction, the sarcolemma of the muscle cell penetrates into the cell interior to form an elongated tube called the **T tubule** (T for “transverse”). Believed by some to be the result of fusing tubelike caveoli, the lumen of the T tubule is continuous with the extracellular space. As each T tubule protrudes deep into the cell, it runs between the paired terminal cisternae of the SR so that **triads**, successive groupings of the three membranous structures (terminal cisterna, T tubule, and terminal cisterna), are formed (Figure 9.5). As they pass from one myofibril to the next, the T tubules also encircle each sarcomere.

Muscle contraction is ultimately controlled by nerve-initiated electrical impulses that travel along the sarcolemma. Because T tubules are continuations of the sarcolemma, they can conduct impulses to the deepest regions of the muscle cell and to every sarcomere. These impulses signal for the release of calcium from the adjacent terminal cisternae. Thus, the T tubules can be thought of as a rapid telegraphy system that ensures that every myofibril in the muscle fiber contracts at virtually the same time.

Triad Relationships The roles of the T tubules and SR in providing signals for contraction are tightly linked. At the triads, where these organelles come into closest contact, something that resembles a *double zipper* of integral proteins protrudes into the intermembrane spaces. The protruding integral proteins of the T tubule act as voltage sensors; and those of the SR, called *foot proteins*, are receptors that regulate the release of Ca^{2+} from the SR cisternae. We will return to consider their interaction shortly.

Sliding Filament Model of Contraction

Although we almost always think “shortening” when we hear the word **contraction**, to physiologists the term refers only to the activation of myosin’s cross bridges, which are the force-generating sites. Shortening occurs when the tension generated by the cross bridges on the thin filaments exceeds the forces opposing shortening. Contraction ends when the cross bridges become inactive and the tension generated declines, inducing **relaxation** of the muscle fiber. Proposed in 1954 by Hugh Huxley, the **sliding filament theory of contraction** states that during contraction the thin filaments slide past the thick ones so that the actin and myosin filaments overlap to a greater degree (Figure 9.6). In a relaxed muscle fiber, the thick and thin filaments overlap only slightly. But when muscle fibers are stimulated by the nervous system, the cross bridges latch on to myosin binding sites on actin in the thin filaments, and the sliding begins. Each cross bridge attaches and detaches several times during a contraction, act-

ing like a tiny ratchet to generate tension and propel the thin filaments toward the center of the sarcomere. As this event occurs simultaneously in sarcomeres throughout the cell, the muscle cell shortens. Notice that as the thin filaments slide centrally, the Z discs to which they are attached are pulled *toward* the thick filaments. Overall, the distance between successive Z discs is reduced, the I bands shorten, the H zones disappear, and the contiguous A bands move closer together but do not change in length.

Physiology of a Skeletal Muscle Fiber

For a skeletal muscle fiber to contract, it must be stimulated by a nerve ending and must propagate an electrical current, or **action potential**, along its sarcolemma. This electrical event causes the short-lived rise in intracellular calcium ion levels that is the final trigger for contraction. The series of events

linking the electrical signal to contraction is called *excitation-contraction coupling*. Let's consider these events in order.

The Neuromuscular Junction and the Nerve Stimulus

Skeletal muscle cells are stimulated by *motor neurons** of the somatic nervous system. Although these motor neurons “reside” in the brain or spinal cord, their long threadlike extensions called *axons* travel, bundled within nerves, to the muscle cells they serve. The axon of each motor neuron divides profusely as it enters the muscle, and each axonal ending forms a branching **neuromuscular junction** with a single muscle fiber (Figure 9.7). As a rule, each muscle fiber has only one neuromuscular junction,

*Somatic motor neurons are nerve cells that activate skeletal muscle cells.

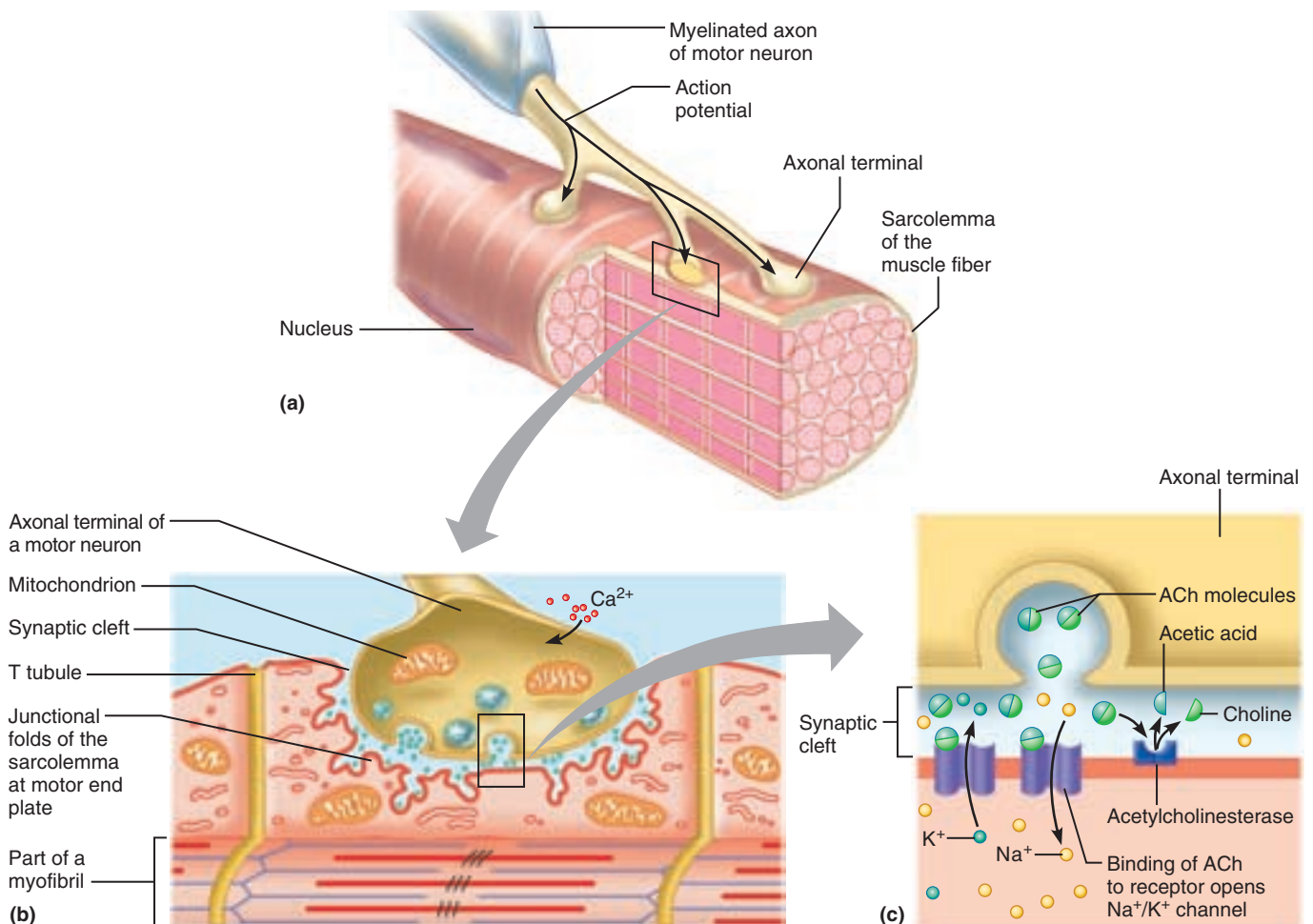


FIGURE 9.7 The neuromuscular junction. (a) Axonal ending of a motor neuron forming a neuromuscular junction with a muscle fiber. (b) Each axonal terminal contains vesicles filled with the neurotransmitter acetylcholine

(ACh), which is released when the action potential reaches the axonal terminal. The sarcolemma is highly folded adjacent to the synaptic cleft, and ACh receptors are present in these junctional folds. (c) ACh diffuses across the

synaptic cleft and attaches to receptors on the sarcolemma, opening ion channels and initiating depolarization of the sarcolemma.

located approximately midway along the fiber's length. Although the axonal ending and the muscle fiber are exceedingly close (1–2 nm apart), they remain separated by a space, the **synaptic cleft**, filled with a gel-like extracellular substance rich in glycoproteins. Within the flattened moundlike axonal ending are **synaptic vesicles**, small membranous sacs containing the neurotransmitter **acetylcholine** (as"ě-til-ko'lēn), or **ACh**. The **motor end plate**, the troughlike part of the muscle fiber's sarcolemma that helps form the neuromuscular junction, is highly folded. These *junctional folds* provide a large surface area for the millions of **ACh receptors** located there.

When a nerve impulse reaches the end of an axon, voltage-gated calcium channels in its membrane open, allowing Ca^{2+} to flow in from the extracellular fluid. The presence of calcium inside the axon terminal causes some of the synaptic vesicles to fuse with the axonal membrane and release ACh into the synaptic cleft by *exocytosis*. ACh diffuses across the cleft and attaches to the flowerlike ACh receptors on the sarcolemma. The electrical events triggered in a sarcolemma when ACh binds are similar to those that take place in excited nerve cell membranes (see Chapter 11).

After ACh binds to the ACh receptors, it is swiftly broken down to its building blocks, acetic acid and choline, by **acetylcholinesterase** (as"ě-til-ko"lin-es'ter-ās), an enzyme located on the sarcolemma at the neuromuscular junction and in the synaptic cleft (Figure 9.7c). This destruction of ACh prevents continued muscle fiber contraction in the absence of additional nervous system stimulation.

HOMEOSTATIC IMBALANCE

Many toxins, drugs, and diseases interfere with events at the neuromuscular junction. For example, *myasthenia gravis* (*asthen* = weakness; *gravi* = heavy), a disease characterized by drooping of the upper eyelids, difficulty swallowing and talking, and generalized muscle weakness, involves a shortage of ACh receptors. Serum analysis reveals antibodies to ACh receptors, suggesting that myasthenia gravis is an autoimmune disease. Although normal numbers of receptors are initially present, they appear to be destroyed as the disease progresses. ●

Generation of an Action Potential Across the Sarcolemma

Like the plasma membranes of all cells, a resting sarcolemma is *polarized*. That is, a voltmeter would show there is a potential difference (voltage) across the membrane and the inside is negative relative to the outer membrane face. (The resting membrane potential is described on pp. 82–83.) Binding of ACh

molecules to ACh receptors at the motor end plate opens chemically (ligand) gated ion channels housed in the ACh receptors that allow both Na^+ and K^+ to pass (Figure 9.7). Because more Na^+ diffuses in than K^+ diffuses out, a transient change in membrane potential occurs such that the interior of the sarcolemma becomes slightly less negative, an event called **depolarization**.

Initially, depolarization is a local electrical event called an *end plate potential*, but it ignites the action potential that spreads in all directions from the neuromuscular junction across the sarcolemma, just as ripples move away from pebbles dropped into a stream.

The action potential (AP) is the result of a predictable sequence of electrical changes that once initiated occurs along the entire length of the sarcolemma (Figure 9.8). Essentially three steps are involved.

1. First the membrane areas adjacent to the depolarized motor end plate are depolarized by local currents that spread to them from the neuromuscular junction. This opens voltage-gated sodium channels there, so Na^+ enters, following its electrochemical gradient, and initiates the action potential.
2. During step 2, the action potential is propagated (moves along the length of the sarcolemma) as the local depolarization wave spreads to adjacent areas of the sarcolemma and opens voltage-gated sodium channels there (see Figure 9.8c). Again, sodium ions, normally restricted from entering, diffuse into the cell following their electrochemical gradient.
3. Step 3 is **repolarization**, which restores the sarcolemma to its initial polarized state. The repolarization wave, which quickly follows the depolarization wave, is a consequence of Na^+ channels closing and voltage-gated K^+ channels opening. Since the potassium ion concentration is substantially higher inside the cell than in the extracellular fluid, K^+ diffuses rapidly out of the muscle fiber (Figure 9.8d).

During repolarization, a muscle fiber is said to be in a **refractory period**, because the cell cannot be stimulated again until repolarization is complete. Notice that repolarization restores only the *electrical conditions* of the resting (polarized) state. The ATP-dependent Na^+/K^+ pump restores the ionic conditions of the resting state, but several contractions can occur before ionic imbalances interfere with contractile activity.

Once initiated, the action potential is unstoppable and ultimately results in contraction of the muscle cell. Although the action potential itself is very brief [1–2 milliseconds (ms)], the contraction phase of a muscle fiber may persist for 100 ms or more and far outlasts the electrical event that triggers it because active transport of Ca^{2+} back into the SR takes substantially longer than its release.

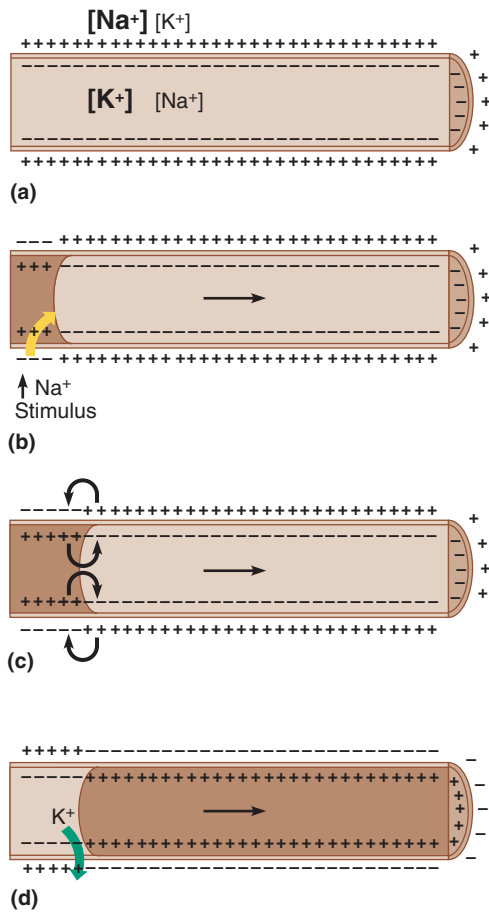


FIGURE 9.8 Summary of events in the generation and propagation of an action potential in a skeletal muscle fiber.

Excitation-Contraction Coupling

Excitation-contraction (E-C) coupling is the sequence of events by which transmission of an action potential along the sarcolemma leads to the sliding of myofilaments. The action potential is brief and ends well before any signs of contraction are obvious. During the *latent period* (*laten* = hidden), between action potential initiation and the beginning of mechanical activity (shortening), the events of excitation-contraction coupling occur. As you will see, the electrical signal does not act directly on the myofilaments; rather, it causes the rise in intracellular calcium ion concentration that allows the filaments to slide (Figure 9.9).

Excitation-contraction coupling consists of the following steps:

- ① The action potential propagates along the sarcolemma and down the T tubules.
- ② Transmission of the action potential past the triads causes the terminal cisternae of the SR to release Ca^{2+} into the sarcoplasm, where it becomes avail-

able to the myofilaments. The “double zippers” (p. 288) at the T-SR junctions of the triads are involved in this action as follows: The T tubule proteins are sensitive to voltage and change shape in response to the arrival of the action potential. This voltage-regulated change is communicated to the SR foot proteins, which in turn undergo shape changes that open their calcium channels (and perhaps other mechanically linked Ca^{2+} channels nearby). Because these events occur at every triad in the cell, within 1 ms massive amounts of Ca^{2+} flood into the sarcoplasm from the SR cisternae.

③ Some of this calcium binds to troponin, which changes shape and removes the blocking action of tropomyosin.

④ When the intracellular calcium is about 10^{-5} M, the myosin heads attach and pull the thin filaments toward the center of the sarcomere.

⑤ The short-lived Ca^{2+} signal ends, usually within 30 ms after the action potential is over. The fall in Ca^{2+} levels reflects the operation of a continuously

? (1) Why is Ca^{2+} called the final trigger for contraction? (2) What constitutes the initial trigger?

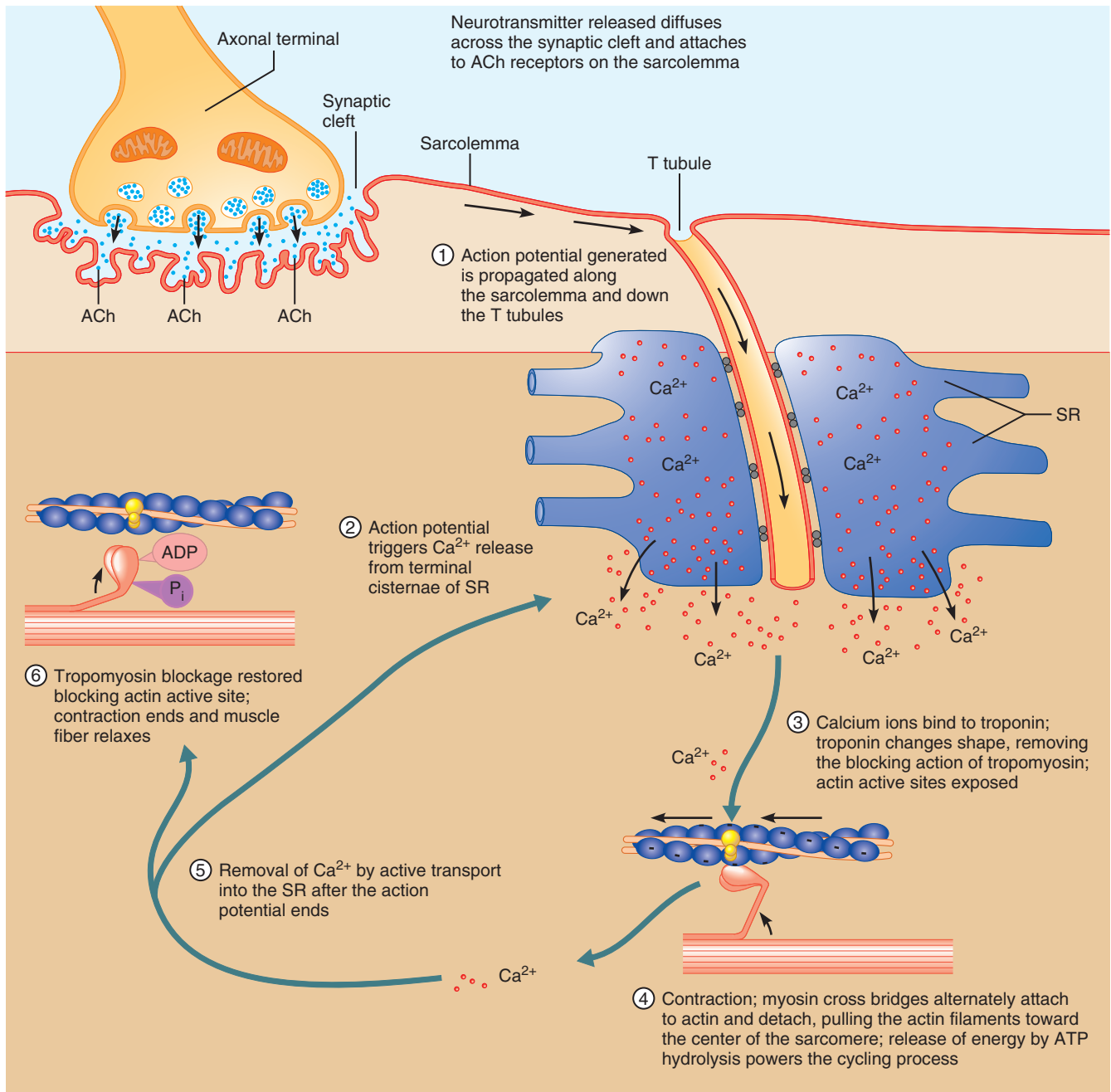


FIGURE 9.9 Excitation-contraction coupling. Events ① through ⑤ indicate the sequence of events in the coupling process. Contraction continues until the calcium signal ends ⑥.

(1) Because calcium binding to troponin frees the actin active sites to bind with myosin cross bridges. (2) The initial trigger is neurotransmitter binding, which initiates generation of an action potential along the sarcolemma.

active, ATP-dependent calcium pump that moves Ca^{2+} back into the SR to be stored once again.

⑥ When intracellular Ca^{2+} levels drop too low to allow contraction, the tropomyosin blockade is reestablished and myosin ATPases are inhibited. Cross bridge activity ends and relaxation occurs.

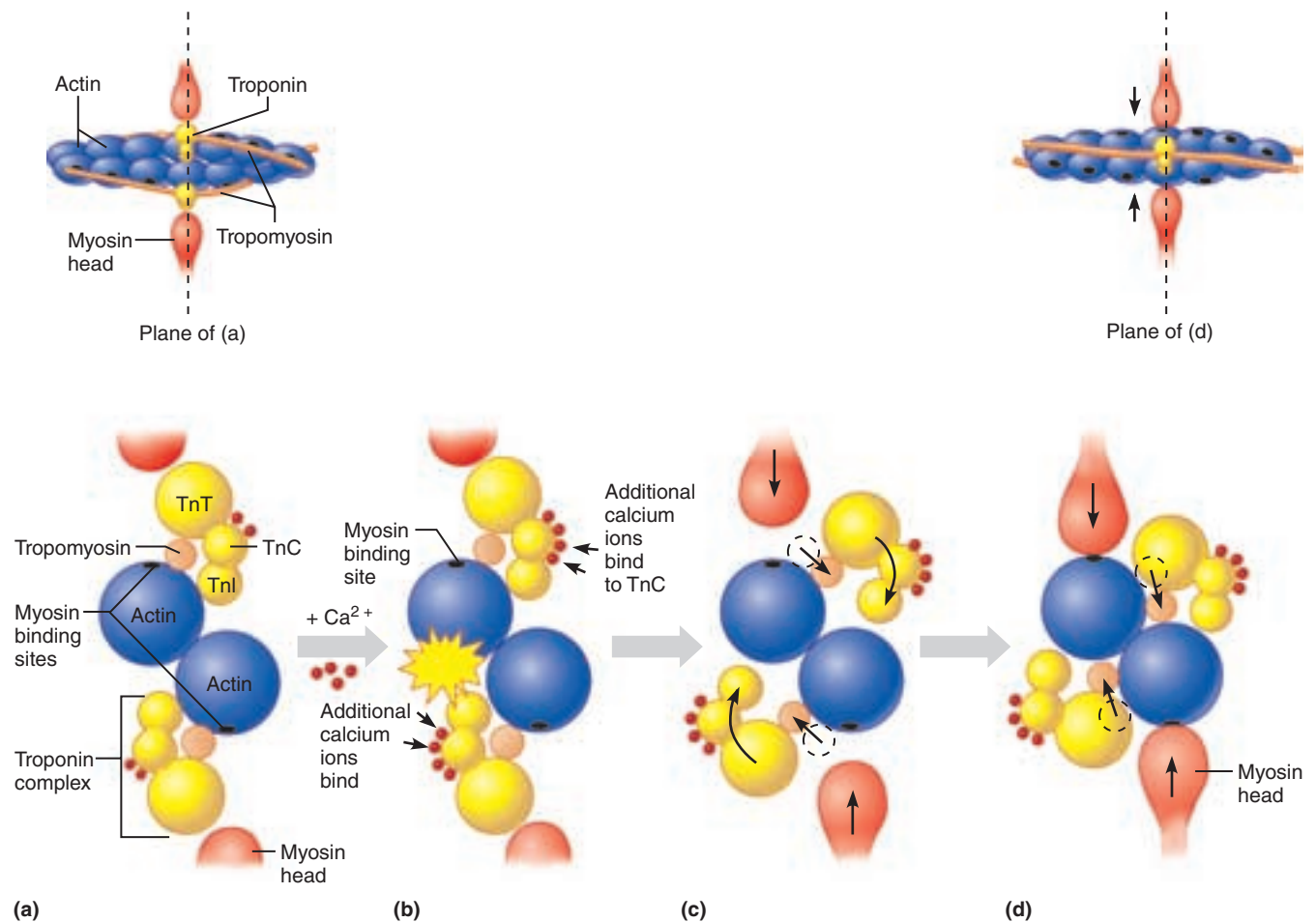


FIGURE 9.10 Role of ionic calcium in the contraction mechanism. Views (a–d) are cross-sectional views of the thin (actin) filament. (a) At low intracellular Ca^{2+} concentration, tropomyosin blocks the binding sites on actin,

preventing attachment of myosin cross bridges and enforcing the relaxed muscle state. (b) At higher intracellular Ca^{2+} concentrations, additional calcium binds to (TnC) of troponin. (c) Calcium-activated troponin undergoes a

conformational change that moves the tropomyosin away from actin's binding sites. (d) This displacement allows the myosin heads to bind and cycle, and contraction (sliding of the thin filaments by the myosin cross bridges) begins.

This sequence of events is repeated when another nerve impulse arrives at the neuromuscular junction. When the impulses are delivered rapidly, intracellular Ca^{2+} levels increase greatly due to successive “puffs” or rounds of Ca^{2+} release from the SR. In such cases, the muscle cells do not completely relax between successive stimuli and contraction is stronger and more sustained (within limits) until nervous stimulation ceases.

Summary of Roles of Ionic Calcium in Muscle Contraction

Except for the brief period following muscle cell excitation, calcium ion concentrations in the sarcoplasm are kept almost undetectably low. There is a reason for this: ATP provides the cell's energy source and its hydrolysis yields inorganic phosphates (P_i). If the intracellular level of Ca^{2+} were always high, calcium and phosphate ions would combine to form

hydroxyapatite crystals, the stony-hard salts found in bone matrix. Such calcified cells would die. Also, because calcium's physiological roles are so vital (i.e., besides triggering neurotransmitter secretion, release of Ca^{2+} from the SR, and sliding of the myofilaments, it promotes breakdown of glycogen and ATP synthesis), its cytoplasmic concentration is exquisitely regulated by intracellular proteins. These include **calsequestrin** (found within the SR cisternae) and **calmodulin**, which can alternately bind and release calcium to provide a metabolic signal.

Muscle Fiber Contraction

As noted, cross bridge attachment to actin requires Ca^{2+} . When intracellular calcium levels are low, the muscle cell is relaxed, and the active (myosin binding) sites on actin are physically blocked by tropomyosin molecules (Figure 9.10a). As Ca^{2+} levels rise, the ions bind to regulatory sites on troponin



What would be the result if the muscle fiber suddenly ran out of ATP when the sarcomeres had only partially contracted?

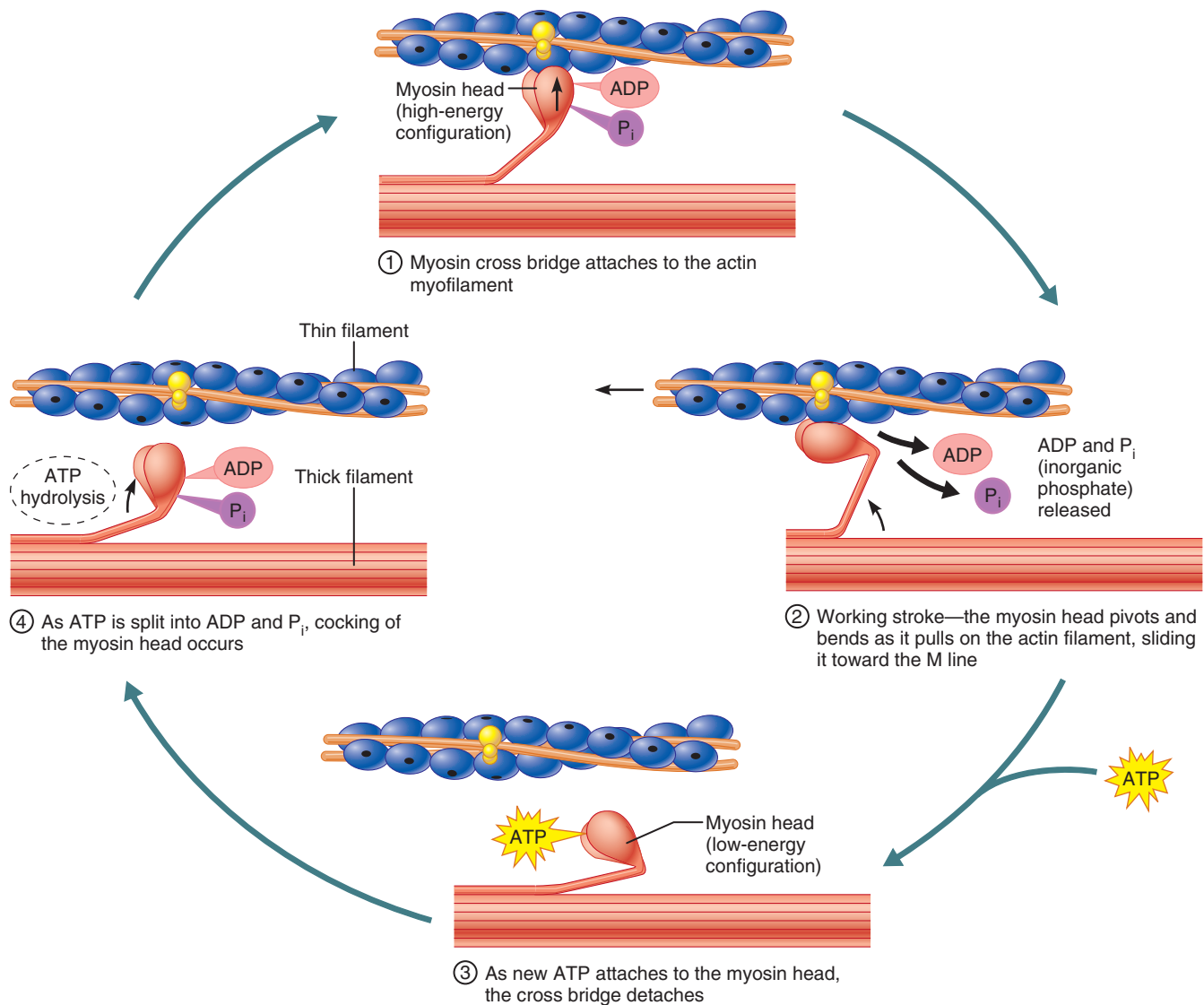


FIGURE 9.11 Sequence of events involved in the sliding of the thin filaments during contraction. A small section of adjacent thick and thin filaments is used to illustrate the interactions that occur between the two types of myofilaments. These events occur only in the presence of ionic calcium (Ca^{2+}), which releases tropomyosin's blockade of actin's active sites.

TnC (Figure 9.10b), causing it to change shape. This event moves tropomyosin deeper into the groove of the actin helix and away from the myosin binding sites (Figure 9.10c and d). Thus, the tropomyosin "blockade" is removed when sufficient calcium is present.

Once binding sites on actin are exposed, the following events occur in rapid succession (Figure 9.11).

① Cross bridge formation. The activated myosin heads are strongly attracted to the exposed binding sites on actin and cross bridges form.

② The working (power) stroke. As a myosin head binds, it pivots (moves through an angle of about 70°) changing from its high-energy configuration to its bent, low-energy shape, which pulls on the thin

The sarcomeres would remain in their partially contracted state.

filament, sliding it toward the center of the sarcomere. At the same time, inorganic phosphate (P_i) and ADP generated during the *prior* contraction cycle are released sequentially from the myosin head. Each working stroke of myosin produces a movement or step of 5–15 nm.

③ **Cross bridge detachment.** As a new ATP molecule binds to the myosin head, myosin's hold on actin loosens and the cross bridge detaches from actin.

④ **“Cocking” of the myosin head.** The ATPase in the myosin head hydrolyzes ATP to ADP and P_i which provides the energy needed to return the myosin head to its prestroke high-energy, or “cocked,” position. This provides the potential energy needed for its *next* sequence of attachment and working stroke. (The ADP and P_i remain attached to the myosin head during this phase.)

At this point, the cycle is back where it started. The myosin head is in its upright high-energy configuration, ready to take another “step” and attach to an actin site farther along the thin filament. This “walking” of the myosin heads along the adjacent thin filaments during muscle shortening is much like a centipede's gait. Because some myosin heads (“legs”) are always in contact with actin (the “ground”), the thin filaments cannot slide backward as the cycle is repeated again and again.

A single working stroke of all the cross bridges in a muscle results in a shortening of only about 1%. Because contracting muscles routinely shorten 30 to 35% of their total resting length, each myosin cross bridge must attach and detach many times during a single contraction. It is likely that only half of the myosin heads of a thick filament are exerting a pulling force at the same instant; the balance are randomly seeking their next binding site. Sliding of thin filaments continues as long as the calcium signal and adequate ATP are present. As the Ca^{2+} pumps of the SR reclaim calcium ions from the sarcoplasm and troponin again changes shape, the actin active sites are covered by tropomyosin, the contraction ends, and the muscle fiber relaxes.

HOMEOSTATIC IMBALANCE

Rigor mortis (death rigor) illustrates the fact that cross bridge detachment is ATP driven. Most muscles begin to stiffen 3 to 4 hours after death. Peak rigidity occurs at 12 hours and then gradually dissipates over the next 48 to 60 hours. Dying cells are unable to exclude calcium (which is in higher concentration in the extracellular fluid), and the calcium influx into muscle cells promotes formation of myosin cross bridges. Shortly after breathing stops, however, ATP synthesis ceases, and cross bridge de-

tachment is impossible. Actin and myosin become irreversibly cross-linked, producing the stiffness of rigor mortis, which then disappears as muscle proteins break down several hours after death. ●

Contraction of a Skeletal Muscle

In its relaxed state, a muscle is soft and unimpressive; not at all what you would expect of a prime mover of the body. However, within a few milliseconds, it can contract to become a hard elastic structure with dynamic characteristics that intrigue not only biologists but engineers and physicists as well.

Before we consider muscle contraction on the organ level, let's review a few principles of muscle mechanics.

1. The principles governing contraction of a muscle fiber (cell) and of a skeletal muscle consisting of a huge number of cells are pretty much the same.
2. The force exerted by a contracting muscle on an object is called **muscle tension**, and the opposing force exerted on the muscle by the weight of the object to be moved is called the **load**.
3. A contracting muscle does not always shorten and move the load. If muscle tension develops but the load is not moved, the contraction is called *isometric* (“same measure”). If the muscle tension developed overcomes the load and muscle shortening occurs, the contraction is *isotonic*. These major types of contraction will be described in detail shortly, but for now the important thing to remember when reading the accompanying graphs is that *increasing muscle tension* is measured in isometric contractions, whereas the *amount of shortening* (distance in millimeters) is measured in isotonic contractions.
4. A skeletal muscle contracts with varying force and for different periods of time in response to stimuli of varying frequencies and intensities. To understand how this occurs, we must first look at the nerve-muscle functional unit called a *motor unit*. This is our next topic.

The Motor Unit

Each muscle is served by at least one motor nerve, which contains axons (fibrous extensions) of hundreds of motor neurons. As an axon enters a muscle, it branches into a number of terminals, each of which forms a neuromuscular junction with a single muscle fiber. A motor neuron and all the muscle fibers it supplies is called a **motor unit** (Figure 9.12). When a motor neuron fires (transmits an electrical impulse), all the muscle fibers it innervates contract. The number of muscle fibers per motor unit may be as high as several hundred or as few as four. Muscles that exert very fine control (such as those controlling

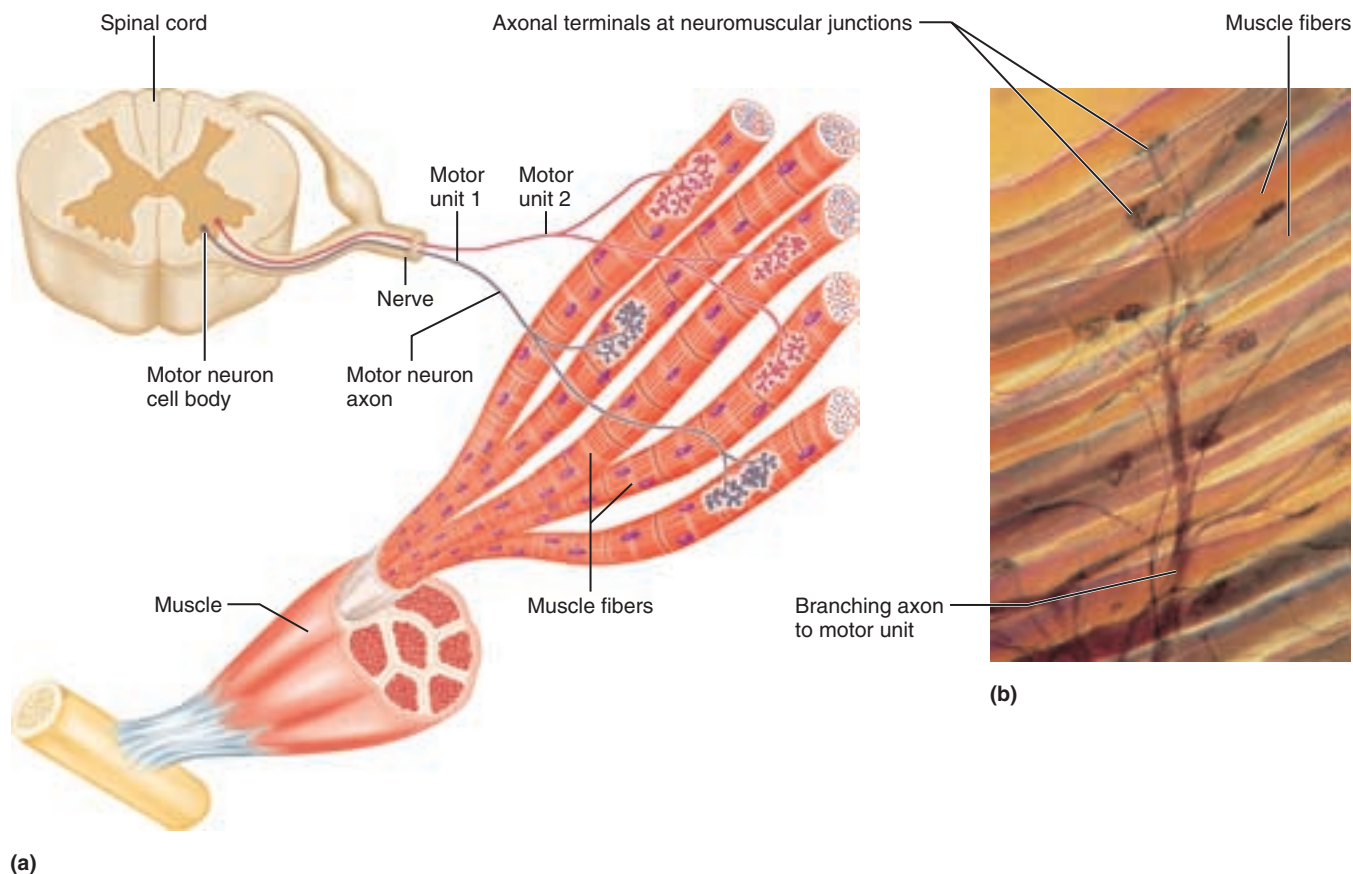


FIGURE 9.12 A motor unit consists of a motor neuron and all the muscle fibers it innervates.

(a) Schematic view of portions of two motor units. The cell bodies of the motor neurons reside in the spinal cord,

and their axons extend to the muscle. In the muscle, each axon divides into a number of axonal terminals that are distributed to muscle fibers scattered throughout the muscle. (b) Photo-

micrograph of a portion of a motor unit (80X). Notice the diverging axonal terminals and the neuromuscular junctions formed by the terminals and muscle fibers.

the fingers and eyes) have small motor units. By contrast, large, weight-bearing muscles, whose movements are less precise (such as the hip muscles), have large motor units. The muscle fibers in a single motor unit are not clustered together but are spread throughout the muscle. As a result, stimulation of a single motor unit causes a weak contraction of the *entire* muscle.

The Muscle Twitch

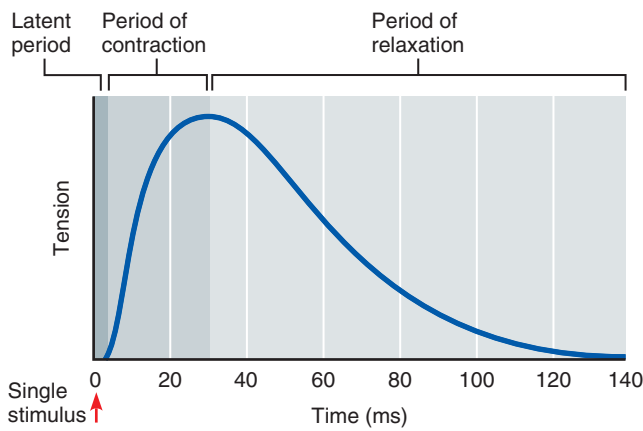
Muscle contraction is easily investigated in the laboratory using an isolated muscle. The muscle is attached to an apparatus that produces a **myogram**, a graphic recording of contractile activity. (The line recording the activity is called a *tracing*.)

The response of a motor unit to a single action potential of its motor neuron is called a **muscle twitch**. The muscle fibers contract quickly and then relax. Every twitch myogram has three distinct phases (Figure 9.13a).

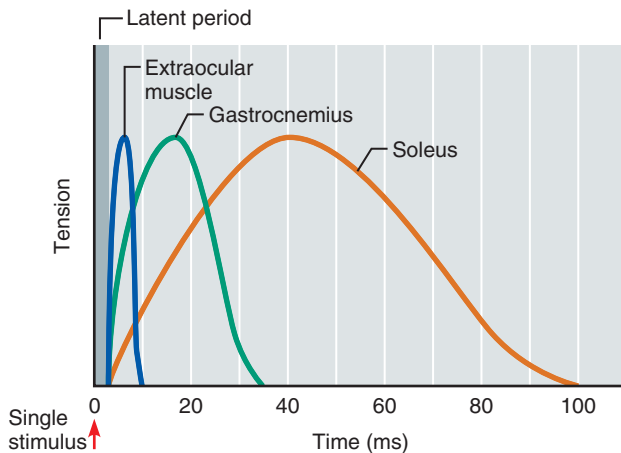
1. Latent period. The latent period is the first few milliseconds following stimulation when excitation-contraction coupling is occurring. During this period, muscle tension is beginning to increase but no response is seen on the myogram.

2. Period of contraction. The period of contraction is when cross bridges are active, from the onset to the peak of tension development, and the myogram tracing rises to a peak. This period lasts 10–100 ms. If the tension (pull) becomes great enough to overcome the resistance of a load, the muscle shortens.

3. Period of relaxation. The period of contraction is followed by the period of relaxation. This final phase, lasting 10–100 ms, is initiated by reentry of Ca^{2+} into the SR. Because contractile force is no longer being generated, muscle tension decreases to zero and the tracing returns to the baseline. If the muscle shortened during contraction, it now returns to its initial length.



(a)



(b)

FIGURE 9.13 The muscle twitch. (a) Myogram of an isometric twitch contraction, showing its three phases: the latent period, the period of contraction, and the period of relaxation. (b) Comparison of the twitch responses of extraocular, gastrocnemius, and soleus muscles.

As you can see in Figure 9.13b, twitch contractions of some muscles are rapid and brief, as with the muscles controlling eye movements. In contrast, the fibers of fleshy calf muscles (gastrocnemius and soleus) contract more slowly and remain contracted for much longer periods. These differences between muscles reflect metabolic properties of the myofibrils and enzyme variations.

Graded Muscle Responses

Although *muscle twitches*—like those single, jerky contractions provoked in a laboratory—may occur as a result of certain neuromuscular problems, this is *not* the way our muscles normally operate. Instead, healthy muscle contractions are relatively smooth and vary in strength as different demands are placed on them. These variations (an obvious requirement for proper control of skeletal movement) are referred to as **graded muscle responses**. In general, muscle contraction can be graded in two ways: (1) by changing the frequency of stimulation and (2) by changing the strength of the stimulus.

Muscle Response to Changes in Stimulation Frequency

If two identical stimuli (electrical shocks or nerve impulses) are delivered to a muscle in rapid succession, the second twitch will be stronger than the first. On a myogram the second twitch will appear to ride on the shoulders of the first (Figure 9.14). This phenomenon, called **wave summation**, occurs because the second contraction occurs before the muscle has completely relaxed. Because the muscle is already partially contracted when the next stimulus arrives and more calcium is being released to replace that being reclaimed by the SR, muscle tension produced during the second contraction causes more shortening than the first. In other words, the contractions are summed. (However, the

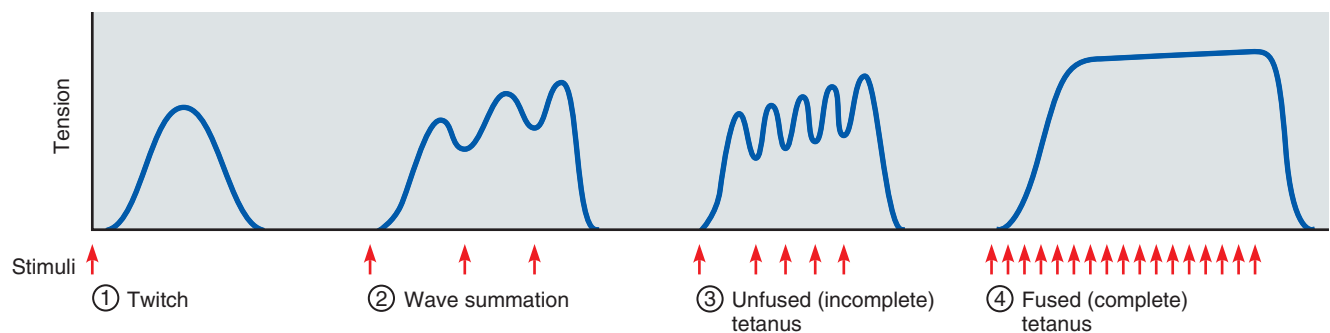


FIGURE 9.14 Wave summation and tetanus in a whole muscle. In ① a single stimulus is delivered, and the muscle contracts and relaxes (twitch contraction). In ② stimuli are delivered

more frequently, so that the muscle does not have adequate time to relax completely, and contraction force increases (wave summation). In ③ more complete twitch fusion (unfused or

incomplete tetanus) occurs as stimuli are delivered more rapidly. In ④, fused or complete tetanus, a smooth, continuous contraction without any evidence of relaxation occurs.

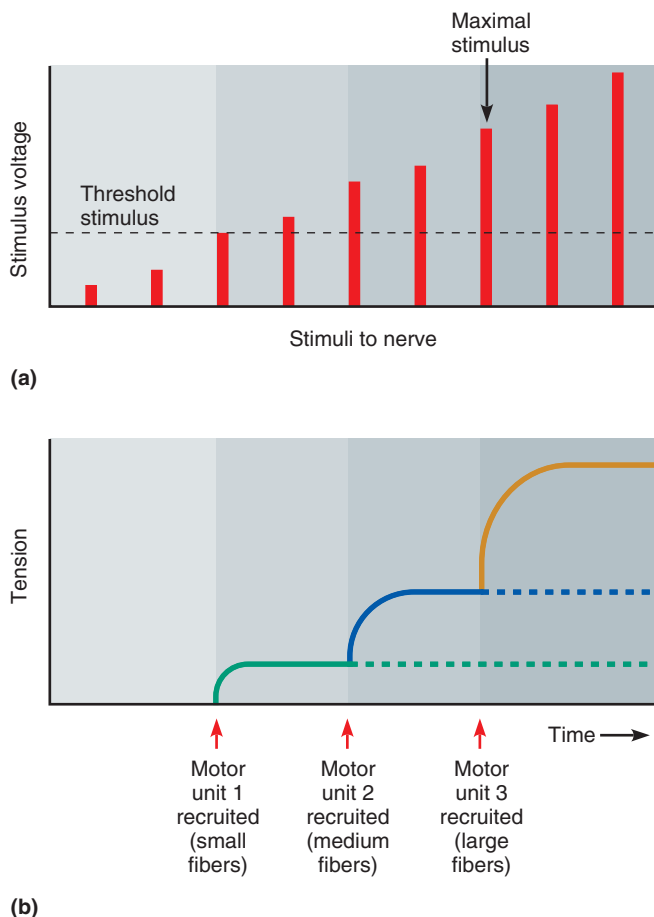


FIGURE 9.15 Relationship between stimulus intensity and muscle tension. (a) Below threshold voltage, no muscle response is seen on the tracing. Once threshold is reached, increases in voltage excite (recruit) more and more motor units until the maximal stimulus is reached. (b) At lower voltages, small motor neurons controlling motor units containing small-diameter muscle fibers are recruited. As the voltage is increased, recruitment proceeds to larger and larger motor neurons, which in turn stimulate increasingly larger diameter muscle fibers. Consequently, the contractions get stronger and stronger.

refractory period is *always* honored. Thus, if a second stimulus is delivered before repolarization is complete, no summation occurs.) If the stimulus strength is held constant and the muscle is stimulated at an increasingly faster rate, the relaxation time between the twitches becomes shorter and shorter, the concentration of Ca^{2+} in the sarcoplasm higher and higher, and the degree of summation greater and greater, progressing to a sustained but quivering contraction referred to as **unfused** or **incomplete tetanus**. Finally, all evidence of muscle relaxation disappears and the contractions fuse into a smooth, sustained contraction called **fused** or **complete tetanus** (tet'ah-nus; *tetan* = rigid, tense). (Tetanus is often confused with the bacterial disease

of the same name that causes severe involuntary contractions.)

Vigorous muscle activity cannot continue indefinitely. Prolonged tetanus inevitably leads to *muscle fatigue*, a situation in which the muscle is unable to contract and its tension drops to zero.

Muscle Response to Stronger Stimuli Although wave summation contributes to contractile force, its primary function is to produce smooth, continuous muscle contractions by rapidly stimulating a specific number of muscle cells. The force of contraction is controlled more precisely by **multiple motor unit summation** (Figure 9.15). In the laboratory this phenomenon, also called **recruitment**, is achieved by delivering shocks of increasing voltage to the muscle, calling more and more muscle fibers into play. The stimulus at which the first observable contraction occurs is called the **threshold stimulus**. Beyond this point, the muscle contracts more and more vigorously as the stimulus strength is increased (Figure 9.15a). The **maximal stimulus** is the strongest stimulus that produces increased contractile force. It represents the point at which all the muscle's motor units are recruited. Increasing the stimulus intensity beyond the maximal stimulus does not produce a stronger contraction. In the body, the same phenomenon is caused by neural activation of an increasingly large number of motor units serving the muscle.

In weak and precise muscle contractions, relatively small motor units are stimulated. Conversely, when larger forces are needed, the larger motor units are activated. This explains how the same hand that pats your cheek can deliver a stinging slap. In any muscle, the smallest motor units (those with the fewest and smallest muscle fibers) are controlled by small, highly excitable motor neurons and these motor units tend to be activated first. The larger motor units, containing large coarse muscle fibers, are controlled by larger, less excitable neurons and are activated only when a stronger contraction is necessary and frequency of stimulation is much greater (Figure 9.15b).

Although *all* the motor units of a muscle may be recruited simultaneously to produce an exceptionally strong contraction, motor units are more commonly activated asynchronously in the body. At a given instant, some are in tetanus (usually unfused tetanus) while others are resting and recovering. This technique helps prolong a strong contraction by preventing or delaying fatigue. It also explains how weak contractions promoted by infrequent stimuli can remain smooth.

Treppe: The Staircase Effect When a muscle begins to contract, its contractions may be only half as strong as those that occur later in response to

stimuli of the same strength. During these periods, a tracing shows a staircase pattern called **treppe** (trep'è) (Figure 9.16). Treppe probably reflects the increasing availability of Ca^{2+} in the sarcoplasm; more Ca^{2+} ions expose more active sites on the thin filaments for cross bridge attachment. Additionally, as the muscle begins to work and liberates heat, its enzymes become more efficient and the muscle becomes more pliable. Together, these factors produce a slightly stronger contraction with each successive stimulus during the initial phase of muscle activity. This is the basis of the warm-up period required of athletes.

Muscle Tone

Skeletal muscles are described as “being voluntary,” but even relaxed muscles are almost always slightly contracted, a phenomenon called **muscle tone**. This is due to spinal reflexes that activate first one group of motor units and then another in response to activation of stretch receptors in the muscles and tendons. Muscle tone does not produce active movements, but it keeps the muscles firm, healthy, and ready to respond to stimulation. Skeletal muscle tone also helps stabilize joints and maintain posture.

Isotonic and Isometric Contractions

As noted earlier, there are two main categories of contractions—*isotonic* and *isometric*. In **isotonic contractions** (*iso* = same; *ton* = tension), muscle length changes (decreasing the angle at the joint) and moves the load. Once sufficient tension has developed to move the load, the tension remains rela-

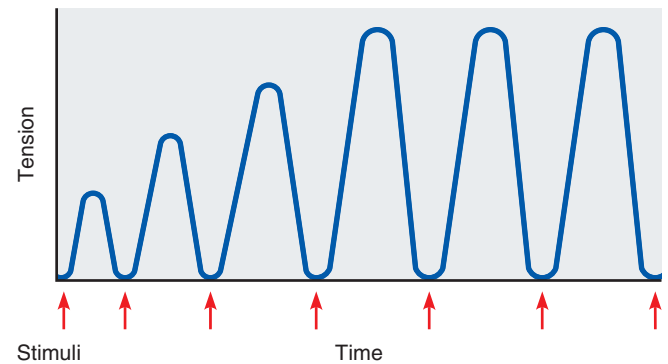


FIGURE 9.16 Myogram of treppe. Notice that although the stimuli are of the same intensity and the muscle is not being stimulated rapidly, the first few contractile responses get stronger and stronger.

tively constant through the rest of the contractile period (Figure 9.17a).

Isotonic contractions come in two “flavors”—*concentric* and *eccentric*. **Concentric contractions** in which the muscle *shortens* and does work—picking up a book or kicking a ball, for instance—are probably more familiar. However, **eccentric contractions**, in which the muscle contracts as it *lengthens*, are equally important for coordination and purposeful movements. Eccentric contractions occur in your calf muscle, for example, as you walk up a steep hill. Eccentric contractions are about 50% more forceful than concentric ones at the same load and more often cause delayed-onset muscle soreness. (Consider

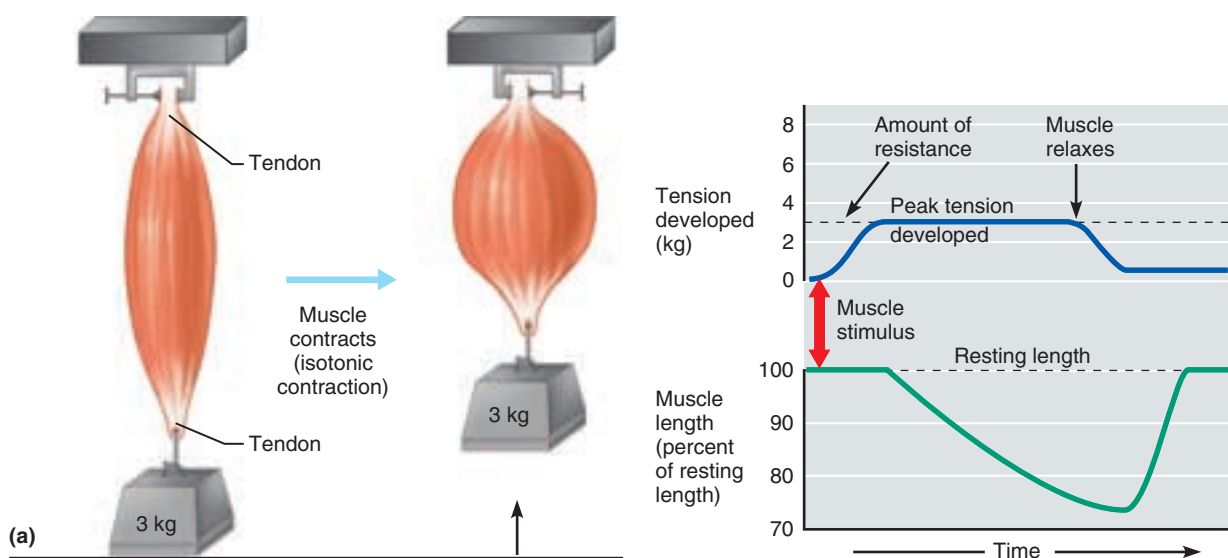


FIGURE 9.17 Isotonic (concentric) and isometric contractions. (a) On stimulation, this muscle develops

enough tension (force) to lift the load (weight). Once the resistance is overcome, tension remains constant for

the rest of the contraction and the muscle shortens. This is a concentric isotonic contraction.

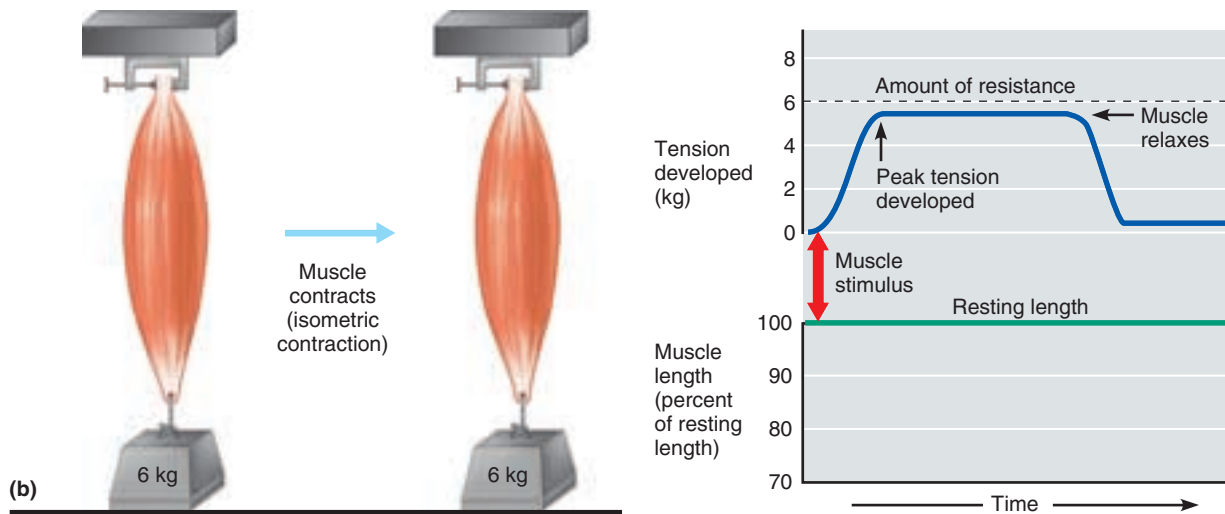


FIGURE 9.17 Isotonic (concentric) and isometric contractions. (continued) (b) This muscle is attached to a

weight that exceeds the muscle's peak tension-developing capabilities. When stimulated, the tension increases to the

muscle's peak tension-developing capability, but the muscle does not shorten. This is an isometric contraction.

how your calf muscles *feel* the day after hiking up that hill.) Just why this is so is unclear, but it may be that the muscle stretching that occurs during such contractions causes microtears in the muscles.

Squats, or deep knee bends, provide a simple example of how concentric and eccentric contractions work together in our everyday activities. As the knees flex, the powerful quadriceps muscles of the anterior thigh lengthen (are stretched), but at the same time they also contract (eccentrically) to counteract the force of gravity and control the descent of the torso ("muscle braking") and prevent joint injury. Raising the body back to its starting position requires that the same muscles contract concentrically as they shorten to extend the knees again. As you can see, eccentric contractions put the body in position to contract concentrically. All jumping and throwing activities involve both types of contraction.

In **isometric contractions** (*metric* = measure), tension builds to the muscle's peak tension-producing capacity, but the muscle *neither shortens nor lengthens* (Figure 9.17b). Isometric contractions occur when a muscle attempts to move a load that is greater than the force (tension) the muscle is able to develop—think of trying to lift a piano singlehandedly. Muscles that act primarily to maintain upright posture or to hold joints in stationary positions while movements occur at other joints are contracting isometrically. In our knee bend example, the quadriceps muscles contract isometrically when the squat position is held for a few seconds to hold the knee in the flexed position. They also contract isometrically when we begin to rise to the upright position until their tension exceeds the load (weight of the upper body). At that point muscle shortening

(concentric contraction) begins. So the quadriceps contractile sequence for a deep knee bend from start to finish is (1) knee flex (eccentric), (2) hold squat position (isometric), (3) knee extend (isometric, then concentric). Of course, this does not even begin to consider the isometric contractions of the posterior thigh muscles or of the trunk muscles that maintain a relatively erect trunk posture during the movement.

Electrochemical and mechanical events occurring within a muscle are identical in both isotonic and isometric contractions. However, the result is different. In isotonic contractions, the thin filaments are sliding; in isometric contractions, the cross bridges are generating force but are not moving the thin filaments. (You could say that they are "spinning their wheels" on the same actin binding site.)

Muscle Metabolism

Providing Energy for Contraction

Now let's look at the mechanisms by which the body provides the energy needed for contraction.

Stored ATP As a muscle contracts, ATP provides the energy for cross bridge movement and detachment and for operation of the calcium pump. Surprisingly, muscles store very limited reserves of ATP—4 to 6 seconds' worth at most, just enough to get you going.

Because ATP is the *only* energy source used directly for contractile activities, it must be regenerated as fast as it is broken down if contraction is to continue. Fortunately, after ATP is hydrolyzed to ADP and inorganic phosphate, it is regenerated within a fraction of a second by three pathways



Which of these energy-producing pathways would predominate in the leg muscles of a long-distance cyclist?

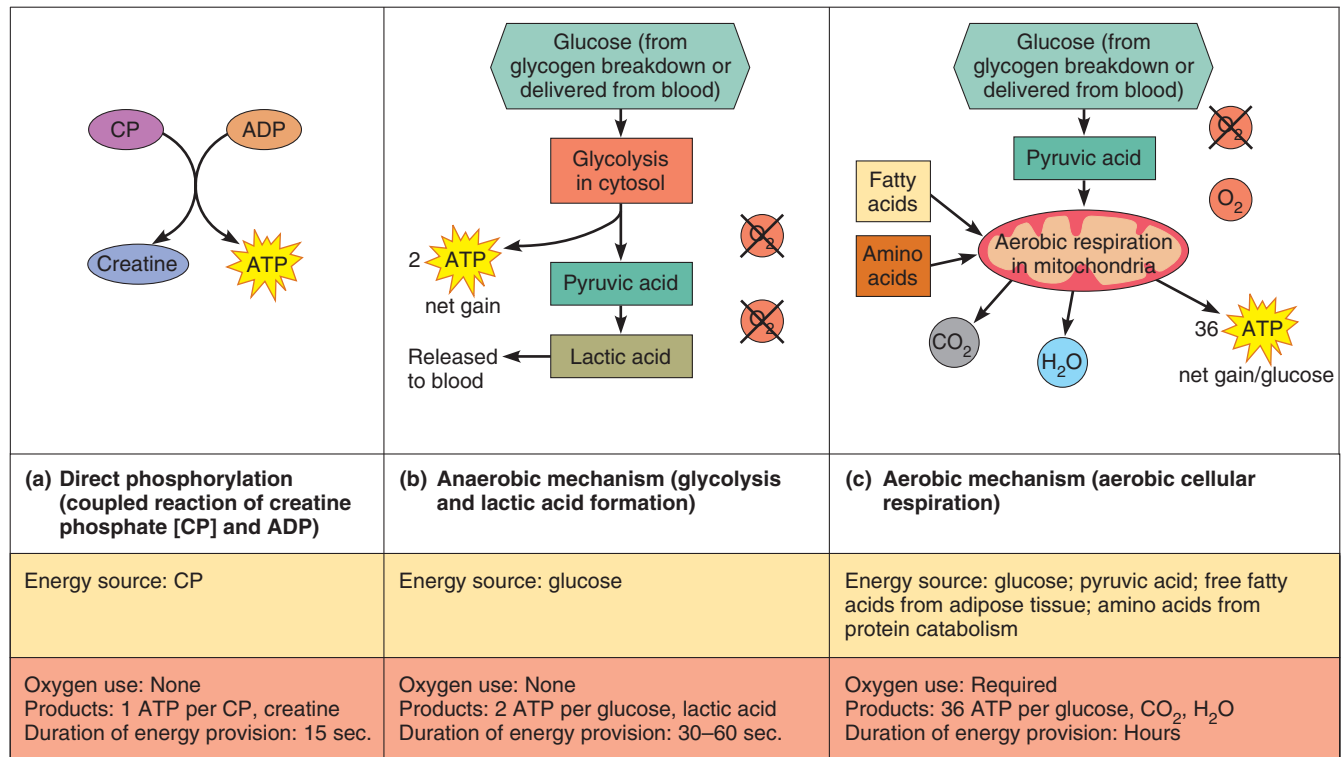


FIGURE 9.18 Methods of regenerating ATP during muscle activity. The fastest mechanism is direct phosphorylation (a); the slowest is the aerobic mechanism (c).

(Figure 9.18): (1) by interaction of ADP with creatine phosphate, (2) from stored glycogen via the anaerobic pathway called glycolysis, and (3) by aerobic respiration. The second and third of these metabolic pathways, which are used to produce ATP in all body cells, are just touched on here, as they are described in detail in Chapter 24.

Direct Phosphorylation of ADP by Creatine Phosphate

As we begin to exercise vigorously, ATP stored in working muscles is consumed within a few twitches. Then **creatine phosphate (CP)** (kre'ah-tin), a unique high-energy molecule stored in muscles, is tapped to regenerate ATP while the metabolic pathways are adjusting to the suddenly higher demands for ATP. The result of coupling CP with ADP is almost instant transfer of energy and a phosphate group from CP to ADP to form ATP:



Muscle cells store much more CP than ATP, and the CP-ADP reaction, catalyzed by the enzyme **creatine kinase**, is so efficient that the amount of ATP in

muscle cells changes very little during the initial period of contraction.

Together, stored ATP and CP provide for maximum muscle power for 10 to 15 seconds—long enough to energize a 100-meter dash. The coupled reaction is readily reversible, and to keep CP “on tap,” CP reserves are replenished during periods of inactivity.

Anaerobic Mechanism: Glycolysis and Lactic Acid Formation

As stored ATP and CP are used, more ATP is generated by catabolism of glucose obtained from the blood or by breakdown of glycogen stored in the muscle. The initial phase of glucose respiration is **glycolysis** (gli-kol'ī-sis; “sugar splitting”). This pathway occurs in both the presence and the absence of oxygen, but because it does not use oxygen, it is an **anaerobic** (an-a'er-ob-ik; “without oxygen”) pathway (see Figure 9.18b). During glycolysis, glucose is broken down to two **pyruvic acid** molecules, releasing enough energy to form small amounts of ATP (2 ATPs per glucose).

Ordinarily, pyruvic acid produced in glycolysis then enters the mitochondria and reacts with oxygen to produce still more ATP in the oxygen-using

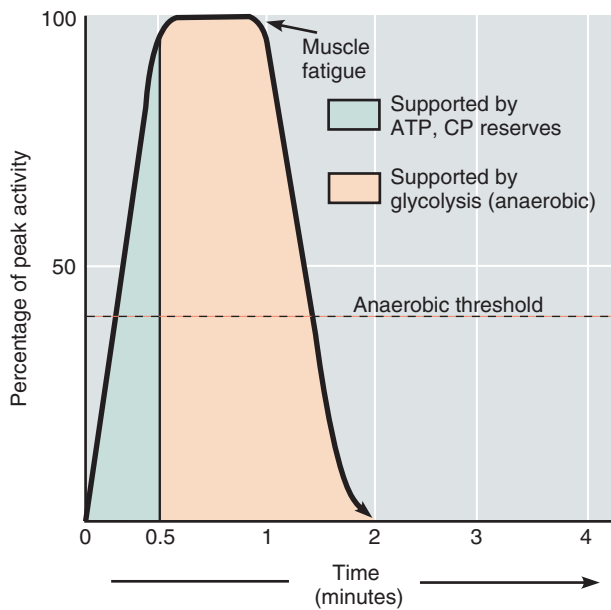


FIGURE 9.19 Energy system used during sports at peak activity levels. Skeletal muscles rely largely on glycolysis (anaerobic respiration) for ATP synthesis. The initial activity burst is energized by ATP and CP reserves. Muscles operating at peak levels fatigue rapidly as lactic acid accumulates.

pathway called aerobic respiration, described shortly. But when muscles contract vigorously and contractile activity reaches about 70% of the maximum possible (e.g., running 600 meters with maximal effort), the bulging muscles compress the blood vessels within them, impairing blood flow and hence oxygen delivery. Under these anaerobic conditions, most of the pyruvic acid produced during glycolysis is converted into **lactic acid**, and the overall process is referred to as **anaerobic glycolysis**. Thus, during oxygen deficit, lactic acid is the end product of cellular metabolism of glucose. Most of the lactic acid diffuses out of the muscles into the bloodstream and is completely gone from the muscle tissue within 30 minutes after exercise stops. Subsequently, the lactic acid is picked up by liver, heart, or kidney cells, which can use it as an energy source. Additionally, liver cells can reconvert it to pyruvic acid or glucose and release it back into the bloodstream for muscle use, or convert it to glycogen for storage.

The anaerobic pathway harvests only about 5% as much ATP from each glucose molecule as the aerobic pathway; however, it produces ATP about $2\frac{1}{2}$ times faster. Thus, when large amounts of ATP are needed for moderate periods (30–40 seconds) of strenuous muscle activity, glycolysis can provide most of the ATP needed as long as the required fuels

and enzymes are available. Together, stored ATP and CP and the glycolysis–lactic acid system can support strenuous muscle activity for nearly a minute.

Although anaerobic glycolysis is very effective in providing the energy to sustain spurts of vigorous exercise, it has shortcomings. Huge amounts of glucose are used to produce relatively small harvests of ATP, and the accumulating lactic acid contributes to muscle fatigue and is partially responsible for the muscle soreness resulting from intense exercise.

Aerobic Respiration During rest and light to moderate exercise, even if prolonged, 95% of the ATP used for muscle activity comes from aerobic respiration. **Aerobic respiration** occurs in the mitochondria, requires oxygen, and involves a sequence of chemical reactions in which the bonds of fuel molecules are broken and the energy released is used to make ATP.

During aerobic respiration, which includes glycolysis and the reactions that take place in the mitochondria, glucose is broken down entirely, yielding water, carbon dioxide, and large amounts of ATP as the final products (Figure 9.18c).



The carbon dioxide released diffuses out of the muscle tissue into the blood and is removed from the body by the lungs.

As exercise begins, muscle glycogen provides most of the fuel. After that, bloodborne glucose, pyruvic acid from glycolysis, free fatty acids, and in some cases even amino acids are the major sources of fuels for oxidation. Aerobic respiration provides a high yield of ATP (about 36 ATPs per glucose), but it is relatively sluggish because of its many steps and it requires continuous delivery of oxygen and nutrient fuels to keep it going.

Energy Systems Used During Sports Activities

As long as it has enough oxygen, a muscle cell will form ATP by aerobic reactions. When ATP demands are within the capacity of the aerobic pathway, light to moderate muscular activity can continue for several hours in well-conditioned individuals. However, when exercise demands begin to exceed the ability of the muscle cells to carry out the necessary reactions quickly enough, glycolysis begins to contribute more and more of the total ATP generated (Figure 9.19). The length of time a muscle can continue to contract using aerobic pathways is called **aerobic endurance**, and the point at which muscle metabolism converts to anaerobic glycolysis is called **anaerobic threshold**.

Exercise physiologists have been able to estimate the relative importance of each energy-producing system to athletic performance. Activities that re-

quire a surge of power but last only a few seconds, such as weight lifting, diving, and sprinting, rely entirely on ATP and CP stores. The more on-and-off or burstlike activities of tennis, soccer, and a 100-meter swim appear to be fueled almost entirely by anaerobic glycolysis. Prolonged activities such as marathon runs and jogging, where endurance rather than power is the goal, depend mainly on aerobic respiration.

Muscle Fatigue

The relatively large amounts of glycogen stored in muscle cells provide some independence from blood-delivered glucose, but with continued exertion even those reserves are exhausted. When oxygen is limited and ATP production fails to keep pace with ATP use, muscles contract less and less effectively and ultimately muscle fatigue sets in. **Muscle fatigue** is a state of *physiological inability to contract* even though the muscle still may be receiving stimuli. This is quite different from psychological fatigue, in which the flesh is still able to perform but we feel tired. It is the will to win in the face of psychological fatigue that sets athletes apart from the rest of us. Note that muscle fatigue results from a *relative deficit* of ATP, not its total absence. When no ATP is available, **contractures**, which are states of continuous contraction, result because the cross bridges are unable to detach (not unlike what happens in rigor mortis). Writer's cramp is a familiar example of temporary contractures.

Excessive intracellular accumulation of lactic acid (which causes the muscles to ache and raises H^+) and other ionic imbalances also contribute to muscle fatigue. The drop in muscle pH limits the usefulness of anaerobic ATP production. As action potentials are transmitted, potassium is lost from the muscle cells, and excess sodium enters. So long as ATP is available to energize the Na^+-K^+ pump, these slight ionic imbalances are corrected. However, fatigued muscle cells seem to lose more K^+ than can be explained by normal action potential generation, and the Na^+-K^+ pumps are insufficient to reverse the ionic imbalances. In general, intense exercise of short duration produces fatigue rapidly via ionic disturbances that alter E-C coupling, but recovery is also rapid. By contrast the slow-developing fatigue of prolonged low-intensity exercise may require several hours for complete recovery. It appears that this type of exercise damages the SR, interfering with Ca^{2+} regulation and release, and therefore with muscle activation.

Oxygen Debt

Whether or not fatigue occurs, vigorous exercise causes a muscle's chemistry to change dramatically.

For a muscle to return to its resting state, its oxygen reserves must be replenished, the accumulated lactic acid must be reconverted to pyruvic acid, glycogen stores must be replaced, and ATP and creatine phosphate reserves must be resynthesized. Additionally, the liver must convert any lactic acid persisting in blood to glucose or glycogen. During anaerobic muscle contraction, all of these oxygen-requiring activities occur more slowly and are (at least partially) deferred until oxygen is again available. Thus, we say an *oxygen debt* is incurred, which must be repaid. **Oxygen debt** is defined as the extra amount of oxygen that the body must take in for these restorative processes. It represents the difference between the amount of oxygen needed for totally aerobic muscle activity and the amount actually used. All nonaerobic sources of ATP used during muscle activity contribute to this debt.

A simple example will help illustrate oxygen debt. If you ran the 100-yard dash in 12 seconds, your body would require about 6 L of oxygen for totally aerobic respiration. However, the VO_2 max (the amount of oxygen that can be delivered to and used by your muscles) during that 12-second interval is only about 1.2 L, far short of the required amount. Thus, you would have incurred an oxygen debt of 4.8 L, which you would repay by breathing rapidly and deeply once you stopped running. This heavy breathing is triggered primarily by high levels of H^+ in the blood, which indirectly stimulates the respiratory center of the brain. The amount of oxygen used during exertion depends on several factors, including age, size, athletic training, and health. In general, the more exercise to which a person is accustomed, the higher his or her oxygen delivery (and anaerobic threshold) during exercise and the lower the oxygen debt incurred. For example, the VO_2 max of most athletes is at least 10% greater than that of a sedentary person, and that of a trained marathon runner may be as much as 50% greater.

Heat Production During Muscle Activity

Only about 40% of the energy released during muscle contraction is converted to useful work. The rest is given off as heat, which has to be dealt with if body homeostasis is to be maintained. When you exercise vigorously, you start to feel hot as your blood is warmed by the liberated heat. Ordinarily, heat buildup is prevented from reaching dangerous levels by several homeostatic mechanisms, including sweating and radiation of heat from the skin surface. Shivering represents the opposite end of homeostatic balance, in which muscle contractions are used to produce more heat.

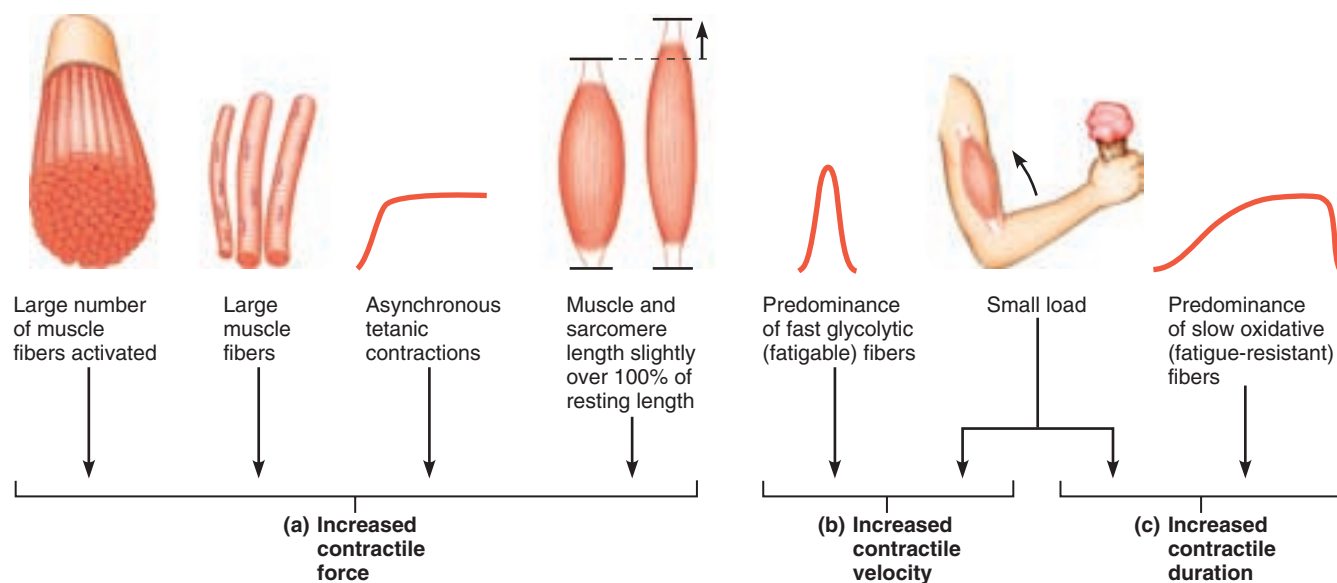


FIGURE 9.20 Factors influencing force, velocity, and duration of skeletal muscle contraction.

Force of Muscle Contraction

The force of muscle contraction is affected by (1) the number of muscle fibers stimulated, (2) the relative size of the fibers, (3) frequency of stimulation, and (4) the degree of muscle stretch (Figure 9.20a). Let's briefly examine the role of each of these factors.

Number of Muscle Fibers Stimulated

As already discussed, the more motor units that are recruited, the greater the muscle force will be.

Size of the Muscle Fibers Stimulated

The bulkier the muscle (the greater its cross-sectional area), the more tension it can develop and the greater its strength, but there is more to it than this. As noted earlier, the large fibers of large motor units are very effective in producing the most powerful movements. Regular exercise increases muscle force by causing muscle cells to *hypertrophy* (hi-per'tro-fe) or increase in size.

Frequency of Stimulation

As a muscle begins to contract, the force generated by the cross bridges (myofibrils)—the **internal tension**—stretches the series elastic (noncontractile) components. These in turn become taut and transfer their tension, called the **external tension**, to the load (muscle insertion), and when the contraction ends, their recoil helps to return the muscle to its resting length.

The point is that time is required to take up slack and stretch the series elastic components, and

while this is happening, the internal tension is already declining. So, in brief twitch contractions, the external tension is always less than the internal tension (Figure 9.21a). However, when a muscle is stimulated rapidly, contractions are summed up, becoming stronger and more vigorous and ultimately producing tetanus. During tetanic contractions more time is available to stretch the series elastic components, and external tension approaches the internal tension (Figure 9.21b). So, the more rapidly a muscle is stimulated, the greater the force it exerts.

Degree of Muscle Stretch

The optimal resting length for muscle fibers is the length at which they can generate maximum force (Figures 9.20a and 9.22). Within a sarcomere, the ideal **length-tension relationship** occurs when a muscle is slightly stretched and the thin and thick filaments barely overlap, because this permits sliding along nearly the entire length of the thin filaments. If a muscle fiber is stretched to the extent that the filaments do not overlap (Figure 9.22c), the cross bridges have nothing to attach to and cannot generate tension. Alternatively, if the sarcomeres are so compressed and cramped that the Z discs abut the thick myofilaments and the thin filaments touch and interfere with one another (Figure 9.22a), little or no further shortening can occur.

Identical relationships exist in a whole muscle. A severely stretched muscle (say one at 180% of its optimal length) cannot develop tension. Likewise, once a muscle contracts to 75% of its resting length, further shortening is limited. Muscles, like muscle

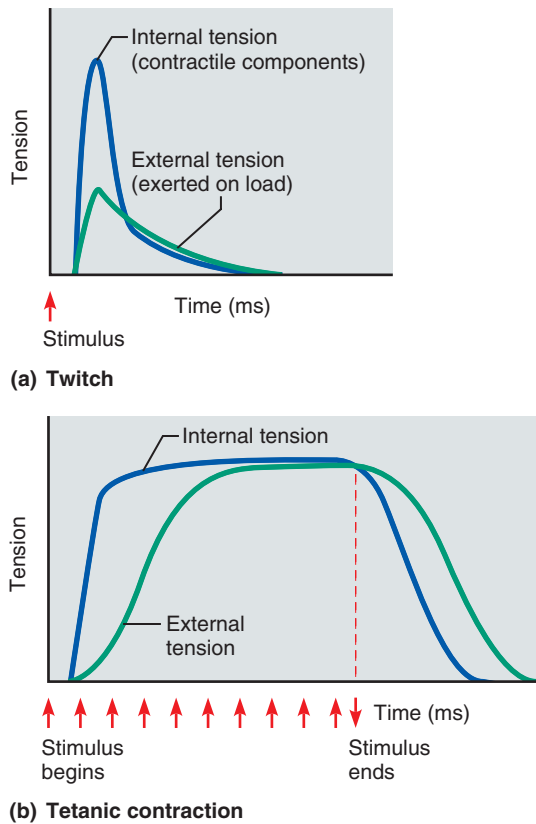


FIGURE 9.21 Relationship between stimulus frequency and external tension. (a) During a single-twitch contraction, the internal tension developed by the cross bridges peaks and begins to drop well before the series elastic components are stretched to equal tension. As a result, the external tension exerted on the load is always less than the internal tension. (b) When the muscle is stimulated tetanically, the internal tension lasts long enough for the series elastic components to be stretched to similar tension, so that external tension approaches and finally equals the internal tension.

fibers, are at optimal operational length from about 80% to about 120% of their normal resting length. In the body, skeletal muscles are maintained near that optimum by the way they are attached to bones; that is, the joints normally prevent bone movements that would stretch attached muscles beyond their optimal range.

Velocity and Duration of Contraction

Muscles vary in how fast they can contract and in how long they can continue to contract before they fatigue. These characteristics are influenced by muscle fiber type, load, and recruitment.

Muscle Fiber Type

There are several ways of classifying muscle fibers, but learning about these classes will be easier if you

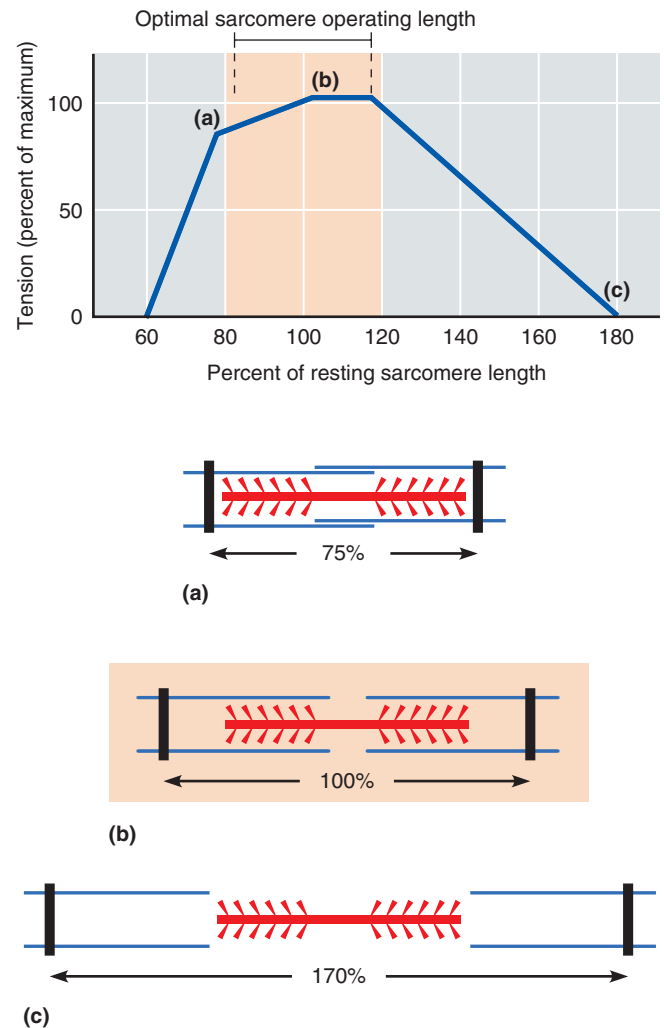


FIGURE 9.22 Length-tension relationships in skeletal muscles. Maximum force is generated when the muscle is between 80 and 120% of its resting length. Increases and decreases beyond this optimal range result in decreased force and inability to generate tension. Depicted here is the relative sarcomere length in a muscle that is (a) strongly contracted, (b) at normal resting length, and (c) excessively stretched.

initially pay attention to just two major functional characteristics:

- **Speed of contraction.** On the basis of speed of shortening or contraction, there are **slow fibers** and **fast fibers**. The difference in speed of these fibers reflects how fast their myosin ATPases split ATP.
- **The major pathways for forming ATP.** The cells that rely mostly on the oxygen-using aerobic pathways for ATP generation are **oxidative fibers**; those that rely more on anaerobic glycolysis are **glycolytic fibers**.

On the basis of these two criteria, we can classify skeletal muscle cells as being **slow oxidative fibers**,

TABLE 9.2

Structural and Functional Characteristics of the Three Types of Skeletal Muscle Fibers

	Slow Oxidative Fibers	Fast Oxidative Fibers	Fast Glycolytic Fibers
Metabolic Characteristics			
Speed of contraction	Slow	Fast	Fast
Myosin ATPase activity	Slow	Fast	Fast
Primary pathway for ATP synthesis	Aerobic	Aerobic (some anaerobic glycolysis)	Anaerobic glycolysis
Myoglobin content	High	High	Low
Glycogen stores	Low	Intermediate	High
Recruitment order	First	Second	Third
Rate of fatigue	Slow (fatigue-resistant)	Intermediate (moderately fatigue-resistant)	Fast (fatigable)
Activities Best Suited For			
	Endurance-type activities—e.g., running a marathon; maintaining posture (antigravity muscles)	Sprinting, walking	Short-term intense or powerful movements, e.g., hitting a baseball
Structural Characteristics			
Color	Red	Red to pink	White (pale)
Fiber diameter	Small	Intermediate	Large
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few

fast oxidative fibers, or **fast glycolytic fibers**. Details about each group are given in Table 9.2, but a word to the wise: Do not approach this information by rote memorization—you’ll just get frustrated. Instead, start with what you know for any category and see how the characteristics listed support that. For example, a *slow oxidative fiber*

- Contracts relatively slowly because its myosin ATPases are slow (a criterion)
- Depends on oxygen delivery and aerobic mechanisms (high oxidative capacity—a criterion)
- Is fatigue resistant and has high endurance (typical of fibers that depend on aerobic metabolism)
- Is thin (a large amount of cytoplasm impedes diffusion of O₂ and nutrients from the blood)
- Has relatively little power (a thin cell can contain only a limited number of myofibrils)
- Has many mitochondria (actual sites of oxygen use)
- Has a rich capillary supply (the better to deliver bloodborne O₂)
- Is red (its color stems from an abundant supply of myoglobin, muscle’s oxygen-binding pigment that

stores O₂ reserves in the cell and aids diffusion of O₂ through the cell)

Conversely, a *fast glycolytic fiber* contracts rapidly (Figure 9.20b), depends on plentiful glycogen reserves for fuel rather than on a blood-delivered supply, and does not use oxygen (Table 9.2). Consequently, compared with an oxidative cell, it has few mitochondria, little myoglobin and low capillary density (and so is white), and tends to be a much larger cell (because it doesn’t depend on continuous oxygen and nutrient diffusion from the blood). Because glycogen reserves are short-lived and lactic acid accumulates quickly in these cells, they tire quickly and hence are fatigable fibers. However, their large diameter reflects their plentiful contractile myofilaments that allow them to contract powerfully before they “poop out.” Thus, the fast glycolytic fibers are best suited for short-term, rapid, intense movements (moving furniture across the room, for example). Details about the intermediate muscle fiber type, called the fast oxidative fiber, are listed in Table 9.2.

Although some muscles have a predominance of one fiber type, most contain a mixture of fiber types, which gives them a range of contractile speeds and fa-

tigue resistance. For example, a calf muscle can propel us in a sprint (using mostly its white fast glycolytic fibers), or a long-distance race (making good use of its intermediate fast oxidative fibers), or may simply help maintain our standing posture (using slow oxidative fibers). As might be expected, all muscle fibers in a particular motor unit are of the same type.

Although everyone's muscles contain mixtures of the three fiber types, some people have relatively more of one variety. These differences are genetically controlled and no doubt determine athletic capabilities to a large extent. For example, muscles of marathon runners have a high percentage of slow oxidative fibers (about 80%), while those of sprinters contain a higher percentage (about 60%) of fast oxidative fibers. Weight lifters appear to have approximately equal amounts of both.

Load Because muscles are attached to bones, they are always pitted against some resistance, or load, when they contract. As you might expect, they contract fastest when there is no added load on them. The greater the load, the longer the latent period, the slower the contraction, and the shorter the duration of contraction (Figure 9.23). If the load exceeds the muscle's maximum tension, the speed of shortening is zero and the contraction is isometric.

Recruitment Just as many hands on a project can get a job done more quickly and also can keep working longer, the more motor units that are contracting, the faster and more prolonged the contraction.

Effect of Exercise on Muscles

The amount of work a muscle does is reflected in changes in the muscle itself. When used actively or strenuously, muscles may increase in size or strength or become more efficient and fatigue resistant. Muscle inactivity, on the other hand, *always* leads to muscle weakness and wasting.

Adaptations to Exercise

Aerobic, or endurance, exercise such as swimming, jogging, fast walking, and biking results in several recognizable changes in skeletal muscles. There is an increase in the number of capillaries surrounding the muscle fibers, and in the number of mitochondria within them, and the fibers synthesize more myoglobin. These changes occur in all fiber types, but are most dramatic in slow oxidative fibers, which depend primarily on aerobic pathways. The changes result in more efficient muscle metabolism and in greater endurance, strength, and resistance to fatigue.

The moderately weak but sustained muscle activity required for endurance exercise does not pro-

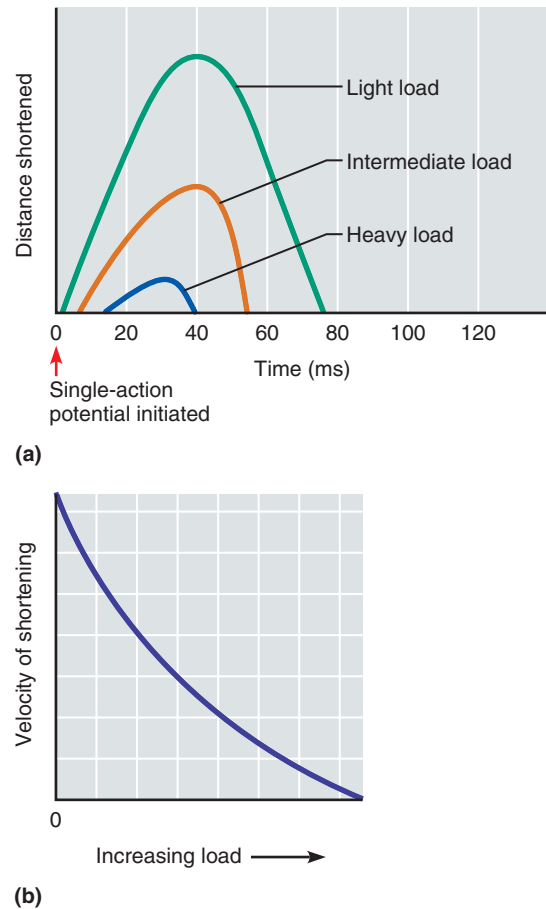


FIGURE 9.23 Influence of load on contraction velocity and duration. (a) Relationship of load to degree and duration of contraction (shortening). (b) Relationship of load to velocity of shortening. As the load increases, the speed of contraction decreases.

more significant skeletal muscle hypertrophy, even though the exercise may go on for hours. Muscle hypertrophy, illustrated by the bulging biceps and chest muscles of a professional weight lifter, results mainly from high-intensity **resistance exercise** (typically under anaerobic conditions) such as weight lifting or isometric exercise, in which the muscles are pitted against high-resistance or immovable forces. Here strength, not stamina, is important; a few minutes every other day is sufficient to allow even a proverbial weakling to put on 50% more muscle within a year. The increased muscle bulk largely reflects increases in the size of individual muscle fibers (particularly the fast glycolytic variety) rather than an increased number of muscle fibers. [However, some of the increased muscle size may result either from longitudinal splitting or tearing of the fibers and subsequent growth of these “split” cells, or from the proliferation and fusion of satellite cells (see p. 318). The controversy is still raging.] Vigorously stressed muscle fibers contain more mitochondria,



A CLOSER LOOK Athletes Looking Good and Doing Better with Anabolic Steroids?

Society loves a winner and top athletes reap large social and monetary rewards. Thus, it is not surprising that some will grasp at anything that might increase their performance—including anabolic steroids. Anabolic steroids, variants of the male sex hormone testosterone engineered by pharmaceutical companies, were introduced in the 1950s to treat victims of anemia and certain muscle-wasting diseases and to prevent muscle atrophy in patients immobilized after surgery. Testosterone is responsible for the increase in muscle and bone mass and other physical changes that occur during puberty and converts boys into men. Convinced that megadoses of steroids could produce enhanced masculinizing effects in grown men, many athletes and bodybuilders were using them by the early 1960s. Today, steroid use is no longer confined to athletes. Indeed, it is estimated that nearly one in every ten young men has tried them, and the practice is also growing rapidly among young women.

It is difficult to determine the extent of anabolic steroid use because most international competitions ban the use of drugs, and users (and prescribing physicians or drug dealers) are naturally reluctant to talk about it. Nonetheless, there is little question that many professional bodybuilders and athletes competing in events that require muscle strength (e.g., shot put, discus throwing, and weight lifting) are heavy users. Sports figures such as football players have also admitted to using steroids as an adjunct to training, diet, and psychological preparation for games. These athletes claim that anabolic steroids enhance muscle mass and strength, and raise oxygen-carrying capability owing to greater red blood cell volume.

Typically, bodybuilders who use steroids combine high doses (up to 200 mg/day) with heavy resistance

training. Intermittent use begins several months before an event, and commonly entails the use of many anabolic steroid supplements (a method called stacking). Injected or transdermal (taken via a skin patch) steroid doses are increased gradually as the competition nears.

Do the drugs do all that is claimed? Research studies report increased isometric strength and body weight in steroid users. While these are results weight lifters dream about, there is a hot dispute over whether this actually translates into athletic performance requiring fine muscle coordination and endurance needed by runners, etc. The “jury is still out” on this question.

Do the alleged advantages of steroids outweigh their risks? Absolutely not. Physicians say they cause bloated faces (Cushingoid sign of steroid excess); acne and hair loss; shriveled testes and infertility; damage to the liver that promotes liver cancer; and changes in blood cholesterol levels that may predispose users to coronary heart disease. In addition, females can develop masculine characteristics such as smaller breasts, enlarged clitoris, excess body hair, and thinning scalp hair. The psychiatric hazards of anabolic steroid use may be equally threatening: Recent studies indicate that one-third of users suffer serious mental problems. Depression, delusions, and manic behavior—in which users undergo Jekyll-and-Hyde personality swings and become extremely violent (termed ‘roid rage’)—are all common.

A recent arrival on the scene, sold over the counter as a “nutritional performance-enhancer,” is androstenedione, which is converted to testosterone in the body. Though it is taken orally (and much of it is destroyed by the liver soon after ingestion), the few milligrams that survive temporarily boost testosterone levels.

Reports of its use by baseball great Mark McGwire before he retired, and of athletic wanna-bes from the fifth grade up sweeping the supplement off the drugstore shelves, are troubling, particularly since it is not regulated by the U.S. Food and Drug Administration



(FDA) and its long-term effects are unpredictable and untested. A study at Massachusetts General Hospital found that males who took androstenedione developed higher levels of the female hormone estrogen as well as testosterone, raising their risk of feminizing effects such as enlarged breasts. Youths with elevated levels of estrogen or testosterone may enter puberty early, stunting bone growth and leading to shorter-than-normal adult height.

Some people admit to a willingness to try almost anything to win, short of killing themselves. Are they unwittingly doing this as well?

form more myofilaments and myofibrils, and store more glycogen. The amount of connective tissue between the cells also increases. Collectively these changes promote significant increases in muscle strength and size.

Resistance training can produce magnificently bulging muscles, but if done unwisely, some muscles may develop more than others. Because muscles work in antagonistic pairs (or groups), opposing muscles must be equally strong to work together smoothly. When muscle training is not balanced, individuals can become *muscle-bound*, which means they lack flexibility, have a generally awkward stance, and are unable to make full use of their muscles.

Endurance and resistance exercises produce different patterns of muscular response, so it is important to know what your exercise goals are. Lifting weights will not improve your endurance for a triathlon. By the same token, jogging will do little to improve your muscle definition, nor will it enhance your strength for moving furniture. A program that alternates aerobic activities with anaerobic ones provides the best program for optimal health.



HOMEOSTATIC IMBALANCE

To remain healthy, muscles must be active. Complete immobilization due to enforced bed rest or loss of neural stimulation results in *disuse atrophy* (degeneration and loss of mass), which begins almost as soon as the muscles are immobilized. Under such conditions, muscle strength can decrease at the rate of 5% per day!

Even at rest, muscles receive weak intermittent stimuli from the nervous system. When totally deprived of neural stimulation, a paralyzed muscle may atrophy to one-quarter of its initial size. Lost muscle tissue is replaced by fibrous connective tissue, making muscle rehabilitation impossible. Atrophy of a denervated muscle may be delayed by electrically stimulating the muscle periodically while waiting to see whether the damaged nerve fibers regenerate. ●

Training Smart to Prevent Overuse Injuries

Don't expect to get in shape by playing a sport; you've *got to get in shape to play* the sport. Regardless of your choice—running, lifting weights, or tennis, for example—exercise stresses muscles. Muscle fibers tear, tendons stretch, and accumulation of lactic acid in the muscle causes pain.

Effective training walks a fine line between working hard enough to improve and preventing overuse injuries. Whatever the activity, exercise gains adhere to the *overload principle*. Forcing a

muscle to work hard promotes increased muscle strength and endurance, and as muscles adapt to the increased demands, they must be overloaded even more to produce further gains. To become faster, you must train at an increasingly fast pace. A heavy-workout day should be followed by one of rest or an easy workout to allow the muscles to recover and repair themselves. Doing too much too soon, or ignoring the warning signs of muscle or joint pain, increases the risk of **overuse injuries** that may prevent future sports activities, or even lead to lifetime disability. Changing or restricting activity, using ice packs to prevent or reduce inflammation, and taking nonsteroidal anti-inflammatory drugs (aspirin, ibuprofen, acetaminophen) to reduce pain are the main treatment modes for virtually all overuse injuries.

Smooth Muscle

Except for the heart, which is made of cardiac muscle, the muscle in the walls of all the body's hollow organs is almost entirely smooth muscle. Although the chemical and mechanical events of contraction are essentially the same in all muscle tissues, smooth muscle is distinctive in several ways (see Table 9.3).

Microscopic Structure of Smooth Muscle Fibers

Smooth muscle fibers are spindle-shaped cells, each with one centrally located nucleus (Figure 9.24). Typically, they have a diameter of 2–5 μm and are 100 to 400 μm in length. Skeletal muscle fibers are some 20 times wider and thousands of times longer.

Smooth muscle lacks the coarse connective tissue sheaths seen in skeletal muscle. However, a small amount of fine connective tissue (endomysium), secreted by the smooth muscles themselves and containing blood vessels and nerves, is found between smooth muscle fibers. Most smooth muscle is organized into sheets of closely apposed fibers. These sheets occur in the walls of all but the smallest blood vessels and in the walls of hollow organs of the respiratory, digestive, urinary, and reproductive tracts. In most cases, two sheets of smooth muscle are present, with their fibers oriented at right angles to each other (Figure 9.24). In the *longitudinal layer*, the muscle fibers run parallel to the long axis of the organ. Consequently, when the muscle contracts, the organ dilates and shortens. In the *circular layer*, the fibers run around the circumference of the organ. Contraction of this layer constricts the lumen (cavity) of the organ and causes the organ to elongate.

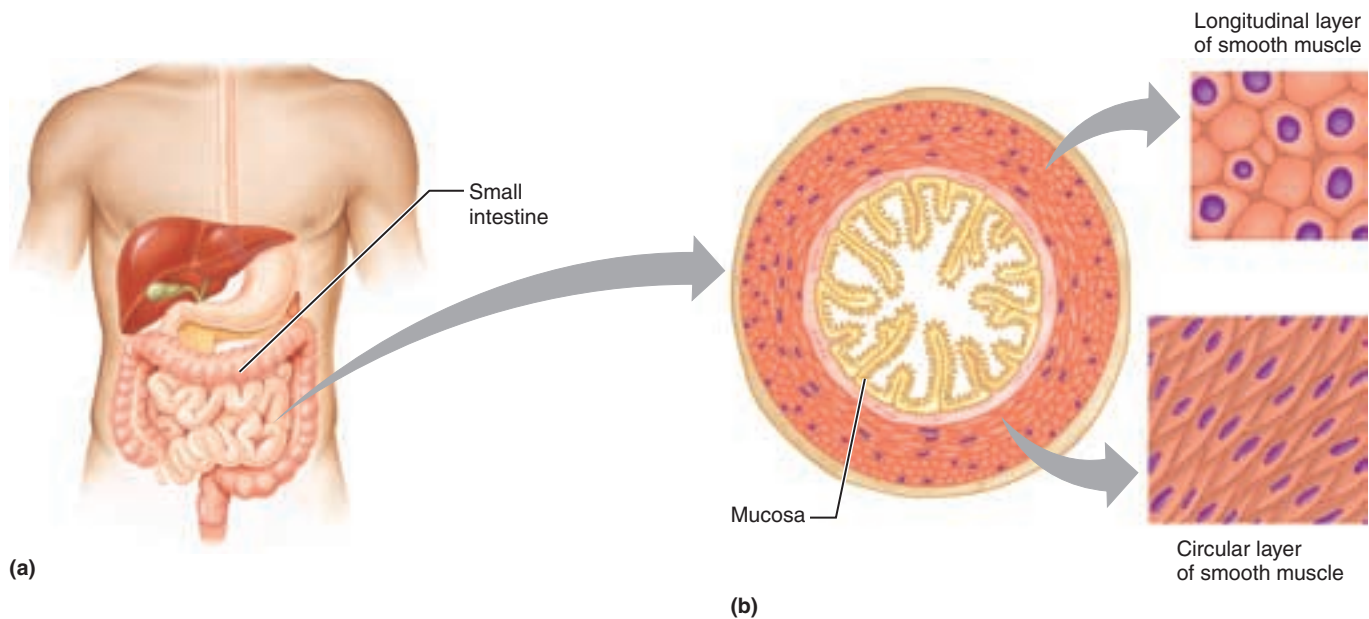


FIGURE 9.24 Arrangement of smooth muscle in the walls of hollow organs. Simplified cross-sectional view of the intestine showing two smooth muscle layers (one circular and the other longitudinal) running at right angles to each other.

The alternating contraction and relaxation of these opposing layers mixes substances in the lumen and squeezes them through the organ's internal pathway. This phenomenon is called **peristalsis** (per"i-stal'sis; "around contraction"). Contraction of smooth muscle in the rectum, urinary bladder, and uterus helps those organs to expel their contents. Smooth muscle contraction also accounts for the constricted breathing of asthma and for stomach cramps.

Smooth muscle lacks the highly structured neuromuscular junctions of skeletal muscle. Instead, the innervating nerve fibers, which are part of the autonomic nervous system, have numerous bulbous swellings, called **varicosities** (Figure 9.25). The varicosities release neurotransmitter into a wide synaptic cleft in the general area of the smooth muscle cells. Such junctions are called **diffuse junctions**.

The sarcoplasmic reticulum of smooth muscle fibers is less developed than that of skeletal muscle and lacks a specific pattern relative to the myofilaments. Some SR tubules of smooth muscle touch the sarcolemma at several sites, forming what resembles half-triads that may couple the action potential to calcium release from the SR. T tubules are notably absent, but the sarcolemma of the smooth muscle fiber has multiple caveoli, pouchlike infoldings that enclose bits of extracellular fluid and allow a high concentration of Ca^{2+} to be sequestered close to the membrane. Consequently, when calcium

channels open, Ca^{2+} influx occurs rapidly. Although the SR *does* release some of the calcium ions that trigger contraction, most gain entry via calcium channels directly from the extracellular space. Contraction ends when calcium is actively transported into the SR and out of the cell.

There are no striations, as the name *smooth muscle* indicates, and no sarcomeres. Smooth muscle fibers *do* contain interdigitating thick and thin filaments, but the thick filaments are much longer than those in skeletal muscle. The proportion and organization of the myofilaments are also different:

1. The ratio of thick to thin filaments is much lower in smooth muscle than in skeletal muscle (1:13 compared to 1:2). However, thick filaments of smooth muscle contain actin-gripping heads along their *entire length*, a feature that allows smooth muscle to be as powerful as a skeletal muscle of the same size.
2. As with skeletal muscle, tropomyosin is associated with the thin filament of smooth muscle, but no troponin complex is present.
3. Smooth muscle thick and thin filaments are arranged diagonally within the cell so that they spiral down the long axis of the cell like the stripes on a barber pole. Because of this arrangement, the smooth muscle cells contract in a twisting way so that they look like tiny corkscrews (Figure 9.26b).

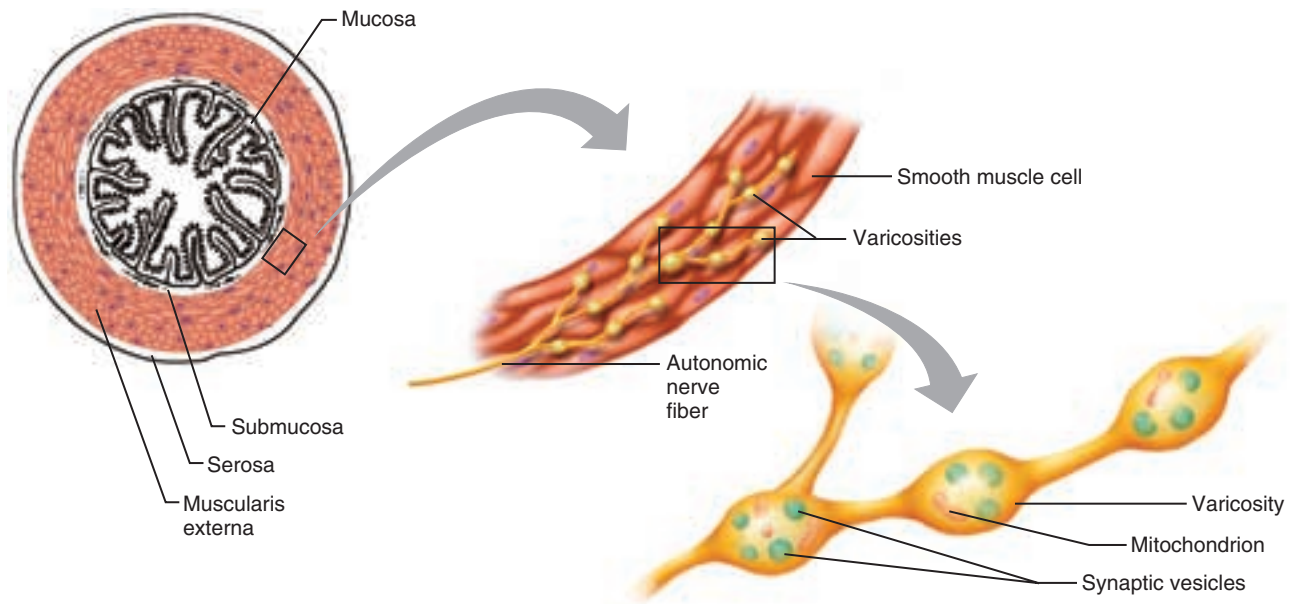


FIGURE 9.25 Innervation of smooth muscle. Most smooth muscle cells are innervated by autonomic nervous system fibers that release their neurotransmitters from varicosities into a wide synaptic cleft (a diffuse junction).

4. Smooth muscle fibers contain longitudinal bundles of noncontractile *intermediate filaments* that resist tension. These attach at regular intervals to structures called **dense bodies**. The dense bodies, which are also tethered to the sarcolemma, act as anchoring points for thin filaments and therefore correspond to Z discs of skeletal muscle. The intermediate filament–dense body network forms a strong, cable-like intracellular cytoskeleton that harnesses the pull generated by the sliding of the thick and thin filaments (Figure 9.26). During contraction, areas of the sarcolemma between the dense bodies bulge outward, giving the cell a puffy appearance (see Figure 9.26b). Dense bodies at the sarcolemma surface also bind the muscle cell to the connective tissue fibers outside the cell (endomysium) and to adjacent cells, an arrangement that transmits the pulling force to the surrounding connective tissue and that partly accounts for the synchronous contraction of most smooth muscle.

Contraction of Smooth Muscle

Mechanism and Characteristics of Contraction

In most cases, adjacent smooth muscle fibers exhibit slow, synchronized contractions, the whole sheet responding to a stimulus in unison. This phenomenon reflects electrical coupling of smooth muscle cells by *gap junctions*, specialized cell connections described in Chapter 3. Skeletal muscle fibers are

electrically isolated from one another, each stimulated to contract by its own neuromuscular junction. By contrast, gap junctions allow smooth muscles to transmit action potentials from fiber to fiber. Some smooth muscle fibers in the stomach and small intestine are *pacemaker cells* and, once excited, act as “drummers” to set the contractile pace for the entire

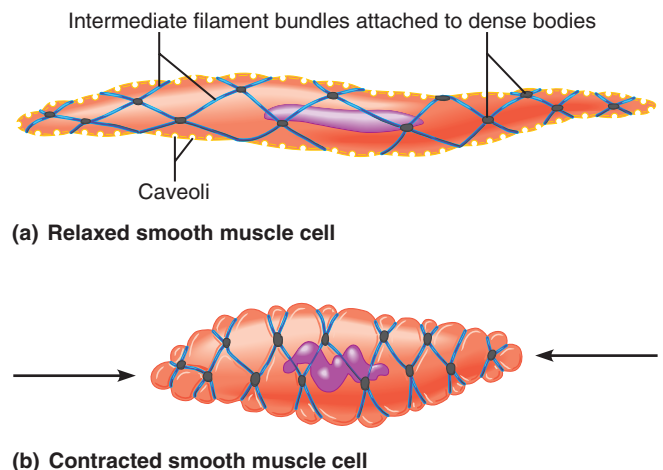


FIGURE 9.26 Intermediate filaments and dense bodies of smooth muscle fibers harness the pull generated by the activity of myosin cross bridges. Intermediate filaments attach to dense bodies scattered throughout the sarcoplasm and occasionally anchor to the sarcolemma. (a) A relaxed smooth muscle cell. (b) A contracted smooth muscle cell. [Caveoli are not illustrated in (b).]

muscle sheet. Additionally, some of these pace-makers are self-excitatory, that is, they depolarize spontaneously in the absence of external stimuli. However, both the rate and the intensity of smooth muscle contraction may be modified by neural and chemical stimuli.

The contraction mechanism in smooth muscle is like that in skeletal muscle in the following ways: (1) actin and myosin interact by the sliding filament mechanism; (2) the final trigger for contraction is a rise in the intracellular calcium ion level; and (3) the sliding process is energized by ATP.

During excitation-contraction coupling, Ca^{2+} is released by the tubules of the SR, but, as mentioned above, it also moves into the cell from the extracellular space. Calcium ions have the same triggering role in all muscle types, but in smooth muscle, they activate myosin by interacting with two regulatory molecules: **calmodulin**, a cytoplasmic calcium-binding protein, and a kinase enzyme called **myosin light chain kinase**. The thin filaments lack troponin and so are always ready for contraction. Apparently the sequence of events is:

1. Ca^{2+} binds to calmodulin, activating it.
2. Activated calmodulin activates the kinase enzyme.
3. The activated kinase catalyzes transfer of phosphate from ATP to myosin cross bridges.
4. Phosphorylated cross bridges interact with actin of the thin filaments, shortening the fiber. As with the other muscle types, ATP powers the cross bridge cycle.
5. The muscle relaxes when intracellular Ca^{2+} levels drop.

Smooth muscle takes 30 times longer to contract and relax than does skeletal muscle and can maintain the same contractile tension for prolonged periods at less than 1% of the energy cost. If skeletal muscle is like a speedy windup car that quickly runs down, then smooth muscle is like a steady, heavy-duty engine that lumbers along tirelessly. Part of the striking energy economy of smooth muscle is the sluggishness of its ATPases (the myosin light chain kinases) compared to those in skeletal muscle. Moreover, smooth muscle myofilaments may latch together during prolonged contractions, saving energy in that way as well.

The ATP-efficient contraction of smooth muscle is extremely important to overall body homeostasis. The smooth muscle in small arterioles and other visceral organs routinely maintains a moderate degree of contraction, called *smooth muscle tone*, day in and day out without fatiguing. Smooth muscle has low energy requirements. Typically, enough ATP is made via aerobic pathways to keep up with the demand.

Regulation of Contraction

Neural Regulation In some cases, the activation of smooth muscle by a neural stimulus is identical to that in skeletal muscle: An action potential is generated by neurotransmitter binding, and is coupled to a rise in calcium ions in the sarcoplasm. However, some types of smooth muscle respond to neural stimulation with graded potentials (local electrical signals) only.

All somatic nerve endings, that is, nerve endings that serve skeletal muscle, release acetylcholine, which excites the skeletal muscle. However, different autonomic nerves serving the smooth muscle of visceral organs release different neurotransmitters, each of which may excite or inhibit a particular group of smooth muscle cells. The effect of a specific neurotransmitter on a given smooth muscle cell depends on the type of receptor molecules on its sarcolemma. For example, when acetylcholine binds to ACh receptors on smooth muscle in the bronchioles (small air passageways of the lungs), the muscle contracts strongly, narrowing the bronchioles. When norepinephrine, released by a different type of autonomic nerve fiber, binds to norepinephrine receptors on the *same* smooth muscle cells, the effect is inhibitory; the muscle relaxes, dilating the air passageways. However, when norepinephrine binds to smooth muscle in the walls of most blood vessels, it stimulates the smooth muscle cells to contract and constrict the vessel.

Hormones and Local Factors Not all smooth muscle activation results from neural signals. Some smooth muscle layers have no nerve supply at all; instead they depolarize spontaneously or in response to chemical stimuli that bind to G protein-linked receptors. Others respond to both neural and chemical stimuli. Chemical factors that cause smooth muscle contraction or relaxation without an action potential (by enhancing or inhibiting Ca^{2+} entry into the sarcoplasm) include certain hormones, lack of oxygen, histamine, excess carbon dioxide, and low pH. The direct response to these chemical stimuli alters smooth muscle activity according to local tissue needs and probably is most responsible for smooth muscle tone. For example, the hormone gastrin stimulates contraction of stomach smooth muscle so that it can churn foodstuffs more efficiently. We will consider how the smooth muscle of specific organs is activated as we discuss each organ in subsequent chapters.

Special Features of Smooth Muscle Contraction

Smooth muscle is intimately involved in the functioning of most hollow organs and has a number of unique characteristics. Some of these—smooth

muscle tone; slow, prolonged contractile activity; and low energy requirements—have already been considered. But smooth muscle also responds differently to stretch and can shorten more than other muscle types. Let's take a look.

Response to Stretch When cardiac muscle is stretched, it responds with more vigorous contractions. So does skeletal muscle up to a point (about 120% of resting length). Stretching of smooth muscle also provokes contraction, which automatically moves substances along an internal tract. However, the increased tension persists only briefly; soon the muscle adapts to its new length and relaxes, while still retaining the ability to contract on demand. This **stress-relaxation response** allows a hollow organ to fill or expand slowly (within certain limits) to accommodate a greater volume without promoting strong contractions that would expel their contents. This is an important attribute, because organs such as the stomach and intestines must be able to store their contents temporarily to provide sufficient time for digestion and absorption of the nutrients. Likewise, your urinary bladder must be able to store the continuously made urine until it is convenient to empty your bladder or you would spend all your time in the bathroom.

Length and Tension Changes Smooth muscle stretches much more than skeletal muscle and generates more tension than skeletal muscles stretched to a comparable extent. As Figure 9.22c shows, precise, highly organized sarcomeres limit how far a skeletal muscle can be stretched before it is unable to generate force. In contrast, the lack of sarcomeres and the irregular, overlapping arrangement of smooth muscle filaments allow them to generate considerable force, even when they are substantially stretched. The total length change that skeletal muscles can undergo and still function efficiently is about 60% (from 30% shorter to 30% longer than resting length), but smooth muscle can contract from twice to half its resting length—a total length change of 150%. This allows hollow organs to tolerate tremendous changes in volume without becoming flabby when they empty.

Hyperplasia Besides the ability to hypertrophy (increase in cell size), which is common to all muscle cells, certain smooth muscle fibers can divide to increase their numbers, that is, they undergo *hyperplasia* (hi"per-pla'ze-ah). One example is the response of the uterus to estrogen. At puberty, girls' plasma estrogen levels rise. As estrogen binds to

uterine smooth muscle receptors, it stimulates the synthesis of more uterine smooth muscle, causing the uterus to grow to adult size. During pregnancy, high blood levels of estrogen stimulate uterine hyperplasia to accommodate the growing fetus.

Types of Smooth Muscle

The smooth muscle in different body organs varies substantially in its (1) fiber arrangement and organization, (2) responsiveness to various stimuli, and (3) innervation. For simplicity, however, smooth muscle is usually categorized into two major types: *single-unit* and *multiunit*.

Single-Unit Smooth Muscle

Single-unit smooth muscle, commonly called **visceral muscle**, is far more common. Its cells (1) contract rhythmically and as a unit, (2) are electrically coupled to one another by *gap junctions*, and (3) often exhibit spontaneous action potentials. All the smooth muscle characteristics described so far pertain to single-unit smooth muscle. Thus, the cells of single-unit smooth muscle are arranged in opposing sheets, exhibit the stress-relaxation response, and so on.

Multiunit Smooth Muscle

The smooth muscles in the large airways to the lungs and in large arteries, the arrector pili muscles attached to hair follicles, and the internal eye muscles that adjust pupil size and allow the eye to focus visually are all examples of **multiunit smooth muscle**.

In contrast to what we see in single-unit muscle, gap junctions are rare, and spontaneous synchronous depolarizations are infrequent. Like skeletal muscle, multiunit smooth muscle:

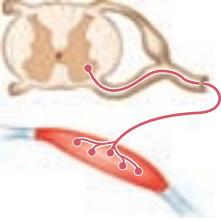
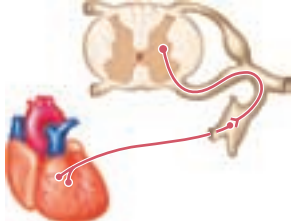
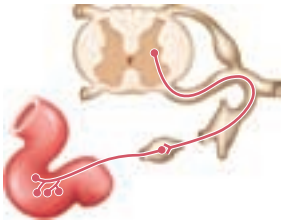
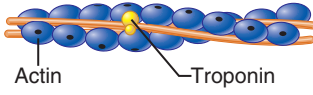
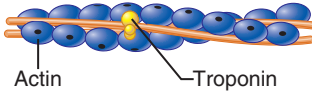
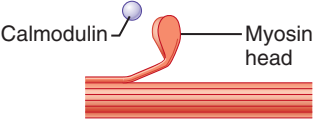
1. Consists of muscle fibers that are structurally independent of one another
2. Is richly supplied with nerve endings, each of which forms a motor unit with a number of muscle fibers
3. Responds to neural stimulation with graded contractions

However, while skeletal muscle is served by the somatic (voluntary) division of the nervous system, multiunit smooth muscle (like single-unit smooth muscle) is innervated by the autonomic (involuntary) division and is also responsive to hormonal controls. (*Text continues on p. 318.*)

TABLE 9.3 Comparison of Skeletal, Cardiac, and Smooth Muscle

Characteristic	Skeletal	Cardiac	Smooth
Body location	Attached to bones or (some facial muscles) to skin	Walls of the heart	Single-unit muscle in walls of hollow visceral organs (other than the heart); multiunit muscle in intrinsic eye muscles
Cell shape and appearance	Single, very long, cylindrical, multinucleate cells with very obvious striations	Branching chains of cells; uni- or binucleate; striations	Single, fusiform, uninucleate; no striations
Connective tissue components	Epimysium, perimysium, and endomysium	Endomysium attached to fibrous skeleton of heart	Endomysium
Presence of myofibrils composed of sarcomeres	Yes	Yes, but myofibrils are of irregular thickness	No, but actin and myosin filaments are present throughout; dense bodies anchor actin filaments
Presence of T tubules and site of invagination	Yes; two in each sarcomere at A-I junctions	Yes; one in each sarcomere at Z disc; larger diameter than those of skeletal muscle	No; only caveoli
Elaborate sarcoplasmic reticulum	Yes	Less than skeletal muscle (1–8% of cell volume); scant terminal cisternae	Equivalent to cardiac muscle (1–8% of cell volume); some SR contacts the sarcolemma

TABLE 9.3 (continued)

Characteristic	Skeletal	Cardiac	Smooth
Presence of gap junctions	No	Yes; at intercalated discs	Yes; in single-unit muscle
Cells exhibit individual neuromuscular junctions	Yes	No	Not in single-unit muscle; yes in multiunit muscle
			
Regulation of contraction	Voluntary via axonal endings of the somatic nervous system	Involuntary; intrinsic system regulation; also autonomic nervous system controls; hormones; stretch	Involuntary; autonomic nerves, hormones, local chemicals; stretch
			
Source of Ca^{2+} for calcium pulse	Sarcoplasmic reticulum (SR)	SR and from extracellular fluid	SR and from extracellular fluid
Site of calcium regulation	Troponin on actin-containing thin filaments	Troponin on actin-containing thin filaments	Calmodulin in the sarcoplasm
			
Presence of pacemaker(s)	No	Yes	Yes (in single-unit muscle only)
Effect of nervous system stimulation	Excitation	Excitation or inhibition	Excitation or inhibition
Speed of contraction	Slow to fast	Slow	Very slow
			
Rhythmic contraction	No	Yes	Yes in single-unit muscle
Response to stretch	Contractile strength increases with degree of stretch (to a point)	Contractile strength increases with degree of stretch	Stress-relaxation response
Respiration	Aerobic and anaerobic	Aerobic	Mainly aerobic

MAKING CONNECTIONS**SYSTEM CONNECTIONS: Homeostatic Interrelationships Between the Muscular System and Other Body Systems****Integumentary System**

- Muscular exercise enhances circulation to skin and improves skin health; exercise also increases body heat, which the skin helps dissipate
- Skin protects the muscles by external enclosure

Skeletal System

- Skeletal muscle activity maintains bone health and strength
- Bones provide levers for muscle activity

Nervous System

- Facial muscle activity allows emotions to be expressed
- Nervous system stimulates and regulates muscle activity

Endocrine System

- Growth hormone and androgens influence skeletal muscle strength and mass; other hormones help regulate cardiac and smooth muscle activity

Cardiovascular System

- Skeletal muscle activity increases efficiency of cardiovascular functioning; helps prevent atherosclerosis and causes cardiac hypertrophy
- Cardiovascular system delivers needed oxygen and nutrients to muscles

Lymphatic System/Immunity

- Physical exercise may enhance or depress immunity depending on its intensity
- Lymphatic vessels drain leaked tissue fluids; immune system protects muscles from disease

Respiratory System

- Muscular exercise increases respiratory capacity and efficiency of gas exchange
- Respiratory system provides oxygen and disposes of carbon dioxide

Digestive System

- Physical activity increases gastrointestinal mobility and elimination when at rest
- Digestive system provides nutrients needed for muscle health; liver metabolizes lactic acid

Urinary System

- Physical activity promotes normal voiding behavior; skeletal muscle forms the voluntary sphincter of the urethra
- Urinary system disposes of nitrogenous wastes

Reproductive System

- Skeletal muscle helps support pelvic organs (e.g., uterus); assists erection of penis and clitoris
- Testicular androgen promotes increased skeletal muscle size

Our skeletal muscles are a marvel. In the well conditioned, they ripple with energy. In those of us who are less athletic, they still allow us to perform the rather remarkable tasks of moving and getting around. No one would argue that the nervous system is indispensable for activating muscles to contract and for keeping them healthy via tone. Let's look at how skeletal muscle activity affects other body systems from the vantage point of overall health and disease prevention.

Cardiovascular System

The single most important barometer of how "well" we age is the health of our cardiovascular system. More than any other factor, regular exercise helps to maintain that health. Anything that gets you huffing and puffing on a regular basis, be it racquetball or a vigorous walk, helps to keep heart muscle healthy and strong. It also keeps blood vessels clear, delaying atherosclerosis and helping to prevent the most common type of high blood pressure and hypertensive heart disease—ailments that can lead to the deterioration of heart muscle and the kidneys. Uncluttered blood vessels also stave off painful or disabling intermittent claudication in which muscle pain due to ischemia hinders walking. Furthermore, regular exercise boosts blood levels of clot-busting enzymes, helping to ward off heart attacks and strokes, other scourges of old age.

Endocrine System

Muscle has a high rate of metabolism, and even at rest it uses much more energy than does fat. Consequently, exercise that builds moderate muscle mass helps to keep weight down and prevents obesity. Obesity is one of the risk factors for development of age-related diabetes mellitus—the metabolic disorder in which body

cells are unresponsive to insulin (secreted by the pancreas) and, hence, unable to utilize glucose normally. Additionally, exercise helps to maintain normal cellular responses to insulin. On the other hand, several hormones, including growth hormone, thyroid hormone, and sex hormones, are essential for normal development and maturation of the skeletal muscles.

Lymphatic System/Immunity

Physical exercise has a marked effect on immunity. Moderate or mild exercise causes a temporary rise in the number of phagocytes, T cells (a particular group of white blood cells), and antibodies, all of which populate lymphatic organs and mount the attack against infectious disease. By contrast, strenuous exercise depresses the immune system. The way in which exercise affects immunity—including these seemingly contradictory observations—is still a mystery, but the so-called stress hormones are definitely involved. Like major stressors such as surgery and serious burns, strenuous exercise increases blood levels of stress hormones such as epinephrine and glucocorticoids. These hormones depress the immune system during severe stress. This is thought to be a protective mechanism—a way of preventing large numbers of slightly damaged cells from being rejected.

Skeletal System

Last, but not least, weight-bearing exercise of the skeletal muscles promotes skeletal strength and helps prevent osteoporosis. Since osteoporosis severely detracts from the quality of life by increasing risk of fractures, this is an extremely important interaction. But without their bony attachments, muscles would be ineffective in causing body movement.

**CLINICAL
CONNECTIONS**

Muscular System

Case study: Let's continue our tale of Mrs. DeStephano's medical problems, this time looking at the notes made detailing observations of her skeletal musculature.

- Severe lacerations of the muscles of the right leg and knee
- Damage to the blood vessels serving the right leg and knee
- Transection of the sciatic nerve (the large nerve serving most of the lower limb), just above the right knee

Her physician orders daily passive range-of-motion (ROM) exercise and electrical stimulation for her right leg and a diet high in protein, carbohydrates, and vitamin C.

1. Describe the step-by-step process of wound healing that will occur in her fleshy (muscle) wounds, and note the consequences of the specific restorative process that occurs.
2. What complications in healing can be anticipated owing to vascular (blood vessel) damage in the right leg?
3. What complications in muscle structure and function result from transection of the sciatic nerve? Why are passive ROM and electrical stimulation of her right leg muscles ordered?
4. Explain the reasoning behind the dietary recommendations.

(Answers in Appendix F)

Developmental Aspects of Muscles

With rare exceptions, all muscle tissues develop from embryonic mesoderm cells called **myoblasts**. Multinucleate skeletal muscle fibers form by the fusion of several myoblasts. Skeletal muscle fibers are contracting by week 7 when the embryo is only about 1 inch long. Initially, ACh receptors “sprout” over the entire surface of the developing myoblasts. But as spinal nerves invade the muscle masses, the nerve endings target individual myoblasts and release the growth factor *agrin*, which stimulates clustering and maintenance of ACh receptors at the newly forming motor end plate in each muscle fiber. Then, the nerve endings provide an independent chemical signal that disperses the receptor sites not innervated and stabilized by agrin. Electrical activity in the neurons serving the muscle fibers also plays a critical role in muscle fiber maturation. As the muscle fibers are brought under the control of the somatic nervous system, the number of fast and slow contractile fiber types is determined.

Myoblasts producing cardiac and smooth muscle cells do not fuse. However, both develop gap junctions at a very early embryonic stage. Cardiac muscle is pumping blood just 3 weeks after fertilization.

Specialized skeletal and cardiac muscle cells become amitotic early on but retain the ability to lengthen and thicken in a growing child and to hypertrophy in adults. However, *satellite cells*, myoblastlike cells associated with skeletal muscle, help repair injured fibers and allow *very limited* regeneration of dead skeletal muscle fibers. Cardiac muscle was thought to have no regenerative capability whatsoever, but recent studies suggest that cardiac cells do divide at a modest rate. Nonetheless, injured heart muscle is repaired mostly by scar tissue. Smooth muscles have a good ability to regenerate throughout life.

At birth, a baby’s movements are uncoordinated and largely reflexive. Muscular development reflects the level of neuromuscular coordination, which develops in a head-to-toe and proximal-to-distal direction. In other words, a baby can lift its head before it can walk, and gross movements precede fine ones. All through childhood, our control of our skeletal muscles becomes more and more sophisticated. By midadolescence, we reach the peak of our *natural* neural control of muscles, and can either accept that level of development or improve it by athletic or other types of training.

A frequently asked question is whether the difference in strength between women and men has a biological basis. It does. Individuals vary, but on av-

erage, women’s skeletal muscles make up approximately 36% of body mass, whereas men’s account for about 42%. Men’s greater muscular development is due primarily to the effects of testosterone on skeletal muscle, not to the effects of exercise. Body strength per unit muscle mass, however, is the same in both sexes. Strenuous muscle exercise causes more muscle enlargement in males than in females, again because of the influence of testosterone. Some athletes take large doses of synthetic male sex hormones (“steroids”) to increase their muscle mass. This illegal and physiologically dangerous practice is discussed in *A Closer Look* (p. 308).

Because of its rich blood supply, skeletal muscle is amazingly resistant to infection throughout life and, given good nutrition and moderate exercise, relatively few problems afflict skeletal muscles. However, muscular dystrophy is a serious condition that deserves more than a passing mention.



HOMEOSTATIC IMBALANCE

The term **muscular dystrophy** refers to a group of inherited muscle-destroying diseases that generally appear during childhood. The affected muscles enlarge due to fat and connective tissue deposit, but the muscle fibers atrophy and degenerate.

The most common and serious form is **Duchenne muscular dystrophy (DMD)**, which is inherited as a sex-linked recessive disease: Females carry and transmit the abnormal gene, but it is expressed almost exclusively in males (1 in every 3500 births). This tragic disease is usually diagnosed when the boy is between two and seven years old. Active, normal-appearing children become clumsy and fall frequently as their muscles weaken. The disease progresses relentlessly from the extremities upward, finally affecting the head and chest muscles. Victims rarely live beyond their early 20s, dying of respiratory failure.

Recent research has pinned down the cause of DMD: The diseased muscle fibers lack *dystrophin*, a cytoplasmic protein that links the cytoskeleton to the extracellular matrix and helps stabilize the sarcolemma. Although the precise defect is still unknown, problems in regulating calcium entry are suspect and the fragile sarcolemma tears during contraction.

There is still no cure for DMD, and thus far, the only medication that has improved muscle strength and function is the steroid prednisone. One promising new technique, *myoblast transfer therapy*, involves injecting diseased muscle with healthy myoblast cells that fuse with the unhealthy ones. Once inside a fiber, the normal gene provided allows the

fiber to produce dystrophin and so to grow normally. Clinical trials on humans are showing limited success. Another approach is to inject affected muscles with *plasmids*, tiny circlets of DNA containing a pared-down version of the dystrophin gene. In initial tests on mice, about 1% of the muscle cells took up the plasmids and made functional dystrophin protein. The large size of human muscles presents a huge challenge to both therapies. A different approach being tested is coaxing dystrophic muscles to produce more *utrophin*, a protein, in mice at least, that can compensate for dystrophin deficiency. ●

As we age, the amount of connective tissue in our skeletal muscles increases, the number of muscle fibers decreases, and the muscles become stringier, or more sinewy. Because skeletal muscles form so much of the body mass, body weight and muscle strength decline in tandem. Muscle strength has usually decreased by about 50% by the age of 80 years. This “flesh wasting” condition, called *sarcopenia* (sar’ko-pe’ne-ah) has serious health implications for the elderly, particularly because falling becomes a common event. But we don’t have to slow up during old age; muscle is responsive to exercise throughout life. Regular exercise helps reverse sarcopenia, and frail elders who begin to “pump iron” (lift leg and hand weights) can rebuild muscle mass and dramatically increase their strength. Performing those lifting exercises rapidly can improve one’s ability to carry out the “explosive” movements needed to rise from a chair or catch one’s balance.

Muscles can also suffer indirectly. Aging of the cardiovascular system affects nearly every organ in

the body, and muscles are no exception. As atherosclerosis takes its toll and begins to block distal arteries, a circulatory condition called *intermittent claudication* (klaw’dī-ka’shun; “limping”) occurs in some individuals. This condition restricts blood delivery to the legs, leading to excruciating pains in the leg muscles during walking, forcing the person to stop and rest to get relief.

Smooth muscle is remarkably trouble-free. The few problems that impair its functioning stem from external irritants. In the gastrointestinal tract, irritation might result from ingestion of excess alcohol, spicy foods, or bacterial infection. Under such conditions, smooth muscle mobility increases in an attempt to rid the body of irritating agents, and diarrhea or vomiting occurs.

* * *

The capacity for movement is a property of all cells but, with the exception of muscle, these movements are largely restricted to intracellular events. Skeletal muscles, the major focus of this chapter, permit us to interact with our external environment in an amazing number of ways, but they also contribute to our internal homeostasis as summarized in *Making Connections* (pp. 316–317). In this chapter we have covered muscle anatomy from the gross level to the molecular level and have considered muscle physiology in some detail. Chapter 10 continues from this point to explain how muscles interact with bones and with each other, and then describes the individual skeletal muscles that make up the muscular system of the body.

Related Clinical Terms

Fibromyositis (*fibro* = fiber; *itis* = inflammation) A group of conditions involving chronic inflammation of a muscle, its connective tissue coverings and tendons, and capsules of nearby joints. Symptoms are nonspecific and involve varying degrees of tenderness associated with specific trigger points.

Hernia Protrusion of an organ through its body cavity wall; may be congenital (owing to failure of muscle fusion during development), but most often is caused by heavy lifting or obesity and subsequent muscle weakening.

Myalgia (mi-al’je-ah; *algia* = pain) Muscle pain resulting from any muscle disorder.

Myofascial pain syndrome Pain caused by a tightened band of muscle fibers, which twitch when the skin over them is touched. Mostly associated with overused or strained postural muscles.

Myopathy (mi-op’ah-the; *path* = disease, suffering) Any disease of muscle.

Myotonic dystrophy A form of muscular dystrophy that is less common than DMD; in the U.S. it affects about 14 of 100,000 people. Symptoms include a gradual reduction in muscle mass and control of the skeletal muscles, abnormal heart rhythm, and diabetes mellitus. May appear at any time; not sex-linked. Underlying genetic defect is multiple repeats of a particular gene on chromosome 19. Because the number of repeats tends to increase from generation to generation, subsequent generations develop more severe symptoms. No effective treatment.

RICE Acronym for *rest*, *ice compression*, and *elevation*, the standard treatment for a pulled muscle, or excessively stretched tendons or ligaments.

Spasm A sudden, involuntary smooth or skeletal muscle twitch ranging in severity from merely irritating to very painful; may be due to chemical imbalances. In spasms of the eyelid or facial muscles, called tics, psychological factors have been implicated. Stretching and massaging the affected

area may help to end the spasm. A **cramp** is a prolonged spasm; usually occurs at night or after exercise.

Strain Commonly called a “pulled muscle,” a strain is excessive stretching and possible tearing of a muscle due to muscle overuse or abuse; the injured muscle becomes painfully inflamed (myositis), and adjacent joints are usually immobilized.

Chapter Summary

Media study tools that could provide you additional help in reviewing specific key topics of Chapter 9 are referenced below.

IP = Interactive Physiology.

Overview of Muscle Tissues (pp. 280–281)

Types of Muscle Tissue (p. 280)

1. Skeletal muscle is attached to the skeleton, is striated, and can be controlled voluntarily.
2. Cardiac muscle forms the heart, is striated, and is controlled involuntarily.
3. Smooth muscle, located chiefly in the walls of hollow organs, is controlled involuntarily. Its fibers are not striated.

Functional Characteristics of Muscle Tissue (p. 280)

4. Special functional characteristics of muscle include excitability, contractility, extensibility, and elasticity.

Muscle Functions (pp. 280–281)

5. Muscles move internal and external body parts, maintain posture, stabilize joints, and generate heat.

Skeletal Muscle (pp. 281–309)

Gross Anatomy of a Skeletal Muscle (pp. 281–284)

1. Skeletal muscle fibers (cells) are protected and strengthened by connective tissue coverings. Deep to superficial, these are endomysium, perimysium, and epimysium.
2. Skeletal muscle attachments (origins/insertions) may be direct or indirect via tendons or aponeuroses. Indirect attachments withstand friction better.

Microscopic Anatomy of a Skeletal Muscle Fiber (pp. 284–288)

3. Skeletal muscle fibers are long, striated, and multinucleate.
4. Myofibrils are contractile elements that occupy most of the cell volume. Their banded appearance results from a regular alternation of dark (A) and light (I) bands. Myofibrils are chains of sarcomeres; each sarcomere contains thick (myosin) and thin (actin) myofilaments arranged in a regular array. The heads of myosin molecules form cross bridges that interact with the thin filaments.
5. The sarcoplasmic reticulum (SR) is a system of membranous tubules surrounding each myofibril. Its function is to release and then sequester calcium ions.
6. T tubules are invaginations of the sarcolemma that run between the terminal cisternae of the SR. They allow the electrical stimulus to be delivered quickly to deep cell regions.

Sliding Filament Model of Contraction (pp. 288–289)

7. According to the sliding filament theory, the thin filaments are pulled toward the sarcomere centers by cross bridge (myosin head) activity of the thick filaments.

Tetanus (1) A state of sustained contraction of a muscle that is a normal aspect of skeletal muscle functioning. (2) An acute infectious disease caused by the anaerobic bacterium *Clostridium tetani* and resulting in persistent painful spasms of some of the skeletal muscles. Progresses to fixed rigidity of the jaws (lockjaw) and spasms of trunk and limb muscles; usually fatal due to respiratory failure.

Physiology of a Skeletal Muscle Fiber (pp. 289–295)

8. Regulation of skeletal muscle cell contraction involves (a) generation and transmission of an action potential along the sarcolemma and (b) excitation-contraction coupling.

9. An end plate potential is set up when acetylcholine released by a nerve ending binds to ACh receptors on the sarcolemma, causing changes in membrane permeability that allow ion flows that depolarize the membrane at the motor end plate. Once initiated, the action potential is self-propagating and unstoppable.

10. Current flows from the motor end plate depolarize the adjacent area of the sarcolemma, opening voltage-gated Na^+ channels which allow Na^+ influx. Then Na^+ gates close and K^+ voltage-gated channels open, repolarizing the membrane. These events generate the AP.

11. In excitation-contraction coupling, the action potential is propagated down the T tubules, causing calcium to be released from the SR into the cell interior.

12. Sliding of the filaments is triggered by a rise in intracellular calcium ion levels. Troponin binding of calcium moves tropomyosin away from myosin binding sites on actin, allowing cross bridge binding. Myosin ATPases split ATP, which energizes the working strokes and is necessary for cross bridge detachment. Cross bridge activity ends when calcium is pumped back into the SR.

IP Muscular System CD-ROM; Topic: Sliding Filament Theory, pages 18–29.

Contraction of a Skeletal Muscle (pp. 295–300)

13. A motor unit is one motor neuron and all the muscle cells it innervates. The neuron's axon has several branches, each of which forms a neuromuscular junction with one muscle cell.

14. A motor unit's response to a single brief threshold stimulus is a twitch. A twitch has three phases: the latent period (preparatory events occurring), the period of contraction (the muscle tenses and may shorten), and the period of relaxation (muscle tension declines and the muscle resumes its resting length).

15. Graded responses of muscles to rapid stimuli are wave summation and unfused and fused tetanus. A graded response to increasingly strong stimuli is multiple motor unit summation.

16. Isotonic contractions occur when the muscle shortens (concentric contraction) or lengthens (eccentric contraction) as the load is moved. Isometric contractions occur when muscle tension produces neither shortening nor lengthening.

IP Muscular System CD-ROM; Topic: Contraction of Motor Units, pages 1–11.

Muscle Metabolism (pp. 300–303)

17. The energy source for muscle contraction is ATP, obtained from a coupled reaction of creatine phosphate with ADP and from aerobic and anaerobic metabolism of glucose.

18. When ATP is produced by nonaerobic pathways, lactic acid accumulates and an oxygen debt occurs. To return the muscles to their resting state, ATP must be produced aerobically and used to regenerate creatine phosphate and glycogen reserves and to oxidize accumulated lactic acid.

19. Only about 40% of energy released during ATP hydrolysis powers contractile activity. The rest is liberated as heat.

IP Muscular System CD-ROM; Topic: Muscle Metabolism, pages 1–7.

Force of Muscle Contraction (pp. 304–305)

20. The force of muscle contraction is affected by the number and size of contracting muscle cells (the more and the larger the cells, the greater the force), the frequency of stimulation, and the degree of muscle stretch.

21. In twitch contractions, the external tension exerted on the load is always less than the internal tension. When a muscle is tetanized, the external tension equals the internal tension.

22. When the thick and thin filaments are slightly overlapping, the muscle can generate maximum force. With excessive increase or decrease in muscle length, force declines.

Velocity and Duration of Contraction (pp. 305–307)

23. Factors determining the velocity and duration of muscle contraction include the load (the greater the load, the slower the contraction) and muscle fiber types.

24. There are three types of muscle fibers: (1) fast glycolytic (fatigable) fibers, (2) slow oxidative (fatigue-resistant) fibers, and (3) intermediate fast oxidative (fatigue-resistant) fibers. Most muscles contain a mixture of fiber types.

Effect of Exercise on Muscles (pp. 307–309)

25. Regular aerobic exercise results in increased efficiency, endurance, strength, and resistance to fatigue of skeletal muscles.

26. Resistance exercises cause skeletal muscle hypertrophy and large gains in skeletal muscle strength.

27. Immobilization of muscles leads to muscle weakness and severe atrophy.

28. Improper training and excessive exercise result in overuse injuries, which may be disabling.

Smooth Muscle (pp. 309–315)**Microscopic Structure of Smooth Muscle Fibers (pp. 309–311)**

1. Smooth muscle fibers are spindle shaped and uninucleate; they display no striations.

2. Smooth muscle cells are most often arranged in sheets. They lack elaborate connective tissue coverings.

3. The SR is poorly developed; T tubules are absent. Actin and myosin filaments are present, but sarcomeres are not. Intermediate filaments and dense bodies form an intracellular network that harnesses the pull generated during cross bridge activity and transfers it to the extracellular matrix.

Contraction of Smooth Muscle (pp. 311–313)

4. Smooth muscle fibers may be electrically coupled by gap junctions, the pace of contraction may be set by pacemaker cells.

5. Smooth muscle contraction is energized by ATP and is activated by a calcium pulse. However, calcium binds to calmodulin rather than to troponin.

6. Smooth muscle contracts for extended periods at low energy cost and without fatigue.

7. Neurotransmitters of the autonomic nervous system may inhibit or stimulate smooth muscle fibers. Smooth muscle contraction may also be initiated by pacemaker cells, hormones, or other local chemical factors that influence intracellular calcium levels, and by mechanical stretch.

8. Special features of smooth muscle contraction include the stress-relaxation response, the ability to generate large amounts of force when extensively stretched, and hyperplasia under certain conditions.

Types of Smooth Muscle (pp. 313–315)

9. Single-unit smooth muscle has electrically coupled fibers that contract synchronously and often spontaneously.

10. Multiunit smooth muscle has independent, well-innervated fibers that lack gap junctions and pacemaker cells. Stimulation is via autonomic nerves (or hormones). Multiunit muscle contractions are rarely synchronous.

Developmental Aspects of Muscles (pp. 318–319)

1. Muscle tissue develops from embryonic mesoderm cells called myoblasts. Skeletal muscle fibers are formed by the fusion of several myoblasts. Smooth and cardiac cells develop from single myoblasts and display gap junctions.

2. For the most part, specialized skeletal and cardiac muscle cells lose their ability to divide but retain the ability to hypertrophy. Smooth muscle regenerates well and undergoes hyperplasia.

3. Skeletal muscle development reflects maturation of the nervous system and occurs in cephalocaudal and proximal-to-distal directions. Peak development of natural neuromuscular control is achieved in midadolescence.

4. Women's muscles account for about 36% of their total body weight and men's for about 42%, a difference due chiefly to the effects of male hormones on skeletal muscle growth.

5. Skeletal muscle is richly vascularized and quite resistant to infection, but in old age, skeletal muscles become fibrous, decline in strength, and atrophy unless an appropriate exercise regimen is followed.

Review Questions

Multiple Choice/Matching

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

- The connective tissue covering that encloses the sarcolemma of an individual muscle fiber is called the (a) epimysium, (b) perimysium, (c) endomysium, (d) perios-teum.
- A fascicle is a (a) muscle, (b) bundle of muscle fibers en-closed by a connective tissue sheath, (c) bundle of myofi-brils, (d) group of myofilaments.
- Thick and thin myofilaments have different composi-tions. For each descriptive phrase, indicate whether the fila-ment is (a) thick or (b) thin.
 ____ (1) contains actin
 ____ (2) contains ATPases
 ____ (3) attaches to the Z disc
 ____ (4) contains myosin
 ____ (5) contains troponin
 ____ (6) does not lie in the I band
- The function of the T tubules in muscle contraction is to (a) make and store glycogen, (b) release Ca^{2+} into the cell interior and then pick it up again, (c) transmit the action po-tential deep into the muscle cells, (d) form proteins.
- The sites where the motor nerve impulse is transmitted from the nerve endings to the skeletal muscle cell mem-branes are the (a) neuromuscular junctions, (b) sarcomeres, (c) myofilaments, (d) Z discs.
- Contraction elicited by a single brief stimulus is called (a) a twitch, (b) wave summation, (c) multiple motor unit summation, (d) tetanus.
- A smooth, sustained contraction resulting from very rapid stimulation of the muscle, in which no evidence of relaxation is seen, is called (a) a twitch, (b) wave summa-tion, (c) multiple motor unit summation, (d) fused tetanus.
- Characteristics of isometric contractions include all but (a) shortening, (b) increased muscle tension throughout, (c) absence of shortening, (d) use in resistance training.
- During muscle contraction, ATP is provided by (a) a coupled reaction of creatine phosphate with ADP, (b) aerobic respiration of glucose, and (c) anaerobic glycolysis.
 ____ (1) Which provides ATP fastest?
 ____ (2) Which does (do) not require that oxygen be avail-able?
 ____ (3) Which (aerobic or anaerobic pathway) provides the highest yield of ATP per glucose molecule?
 ____ (4) Which results in the formation of lactic acid?
 ____ (5) Which has carbon dioxide and water products?
 ____ (6) Which is most important in endurance sports?
- The neurotransmitter released by somatic motor neu-rons is (a) acetylcholine, (b) acetylcholinesterase, (c) norepi-nephine.
- The ions that enter the muscle cell during action poten-tial generation are (a) calcium ions, (b) chloride ions, (c) sodium ions, (d) potassium ions.
- Myoglobin has a special function in muscle tissue. It (a) breaks down glycogen, (b) is a contractile protein, (c) holds a reserve supply of oxygen in the muscle.

13. Aerobic exercise results in all of the following except (a) increased cardiovascular system efficiency, (b) more mito-chondria in the muscle cells, (c) increased size and strength of existing muscle cells, (d) increased neuromuscular system coordination.

14. The smooth muscle type found in the walls of digestive and urinary system organs and that exhibits gap junctions and pacemaker cells is (a) multiunit, (b) single-unit.

Short Answer Essay Questions

- Name and describe the four special functional charac-teristics of muscle that are the basis for muscle response.
- Distinguish between (a) direct and indirect muscle at-tachments and (b) a tendon and an aponeurosis.
- (a) Describe the structure of a sarcomere and indicate the relationship of the sarcomere to the myofilament. (b) Ex-plain the sliding filament theory of contraction using appro-priately labeled diagrams of a relaxed and a contracted sarcomere.
- What is the importance of acetylcholinesterase in mus-cle cell contraction?
- Explain how a slight (but smooth) contraction differs from a vigorous contraction of the same muscle using the understandings of multiple motor unit summation.
- Explain what is meant by the term excitation-contraction coupling.
- Define motor unit.
- Describe the three distinct types of skeletal muscle fibers.
- True or false: Most muscles contain a predominance of one skeletal muscle fiber type. Explain the reasoning behind your choice.
- Describe the cause(s) of muscle fatigue and define this term clearly.
- Define oxygen debt.
- Name four factors that influence contractile force and two that influence velocity and duration of contraction.
- Smooth muscle has some unique properties, such as low energy usage, ability to maintain contraction over long periods, and the stress-relaxation response. Tie these proper-ties to the function of smooth muscle in the body.



Critical Thinking and Clinical Application Questions

- Diego was seriously out of shape the day he joined his friends for a game of touch football. While he was running pell-mell for the ball, his left calf began to hurt. He went to the clinic the next day and was told he had a strain. Diego insisted that this must be wrong, because his joints did not hurt. Clearly, Diego was confusing a *strain* with a *sprain*. Explain the difference.
- Jim Fitch decided that his physique left much to be de-sired, so he joined a local health club and began to “pump iron” three times weekly. After three months of training, during which he was able to lift increasingly heavier weights, he noticed that his arm and chest muscles were substantially larger. Explain the structural and functional ba-sis of these changes.

3. When a suicide victim was found, the coroner was unable to remove the drug vial clutched in his hand. Explain the reasons for this. If the victim had been discovered three days later, would the coroner have had the same difficulty? Explain.
4. Kristin, a dedicated sprinter, knows that the best way to treat a muscle pull is through "RICE." What does this mean?
5. When Eric returned from jogging, he was breathing heavily, sweating profusely, and complained that his legs ached and felt weak. His wife poured him a sports drink and urged him to take it easy until he could "catch his breath." On the basis of what you have learned about muscle energy metabolism, respond to the following questions.
 - Why is Eric breathing heavily?
 - What ATP harvesting pathway have his working muscles been using that leads to such a breathing pattern?

- What metabolic product(s) might account for his sore muscles and his feeling of muscle weakness?

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