3.Muscle contraction:

About 40% of the body mass is skeletal muscle, and perhaps another 10% is smooth muscle and cardiac muscle. Many of the principles of contraction apply to all three types of muscle. In this chapter, the function of skeletal muscle is considered. The func- tions of smooth muscle are discussed in Chapter 8, and the functions of cardiac muscle are discussed in Chapter 9.

Physiologic Anatomy of Skeletal Muscle (p. 71)

Skeletal Muscle Fiber Figure 6–1 shows the organization of skeletal muscle. In most muscles the fibers extend the entire length of the muscle. Each fiber is innervated by only one nerve ending.

Myofibrils Are Composed of Actin and Myosin Filaments. Each muscle fiber contains hundreds to thousands of myofibrils, and, in turn, each myofibril (see Fig. 6–1D) is composed of about 1500 myosin filaments and 3000 actin filaments lying side by side. These filaments are large polymerized protein molecules that are responsible for muscle contraction. In Figure 6–1 the thick filaments are myosin, and the thin filaments are actin; note the following features:

• Light and dark bands. The myosin and actin fila- ments partially interdigitate and thus cause the myofibrils to have alternate light and dark bands. The light bands contain only actin filaments and are called I bands. The dark bands called A bands con- tain myosin filaments as well as the ends of the actin filaments. The length of the A band is the length of the myosin filament.

• Cross-bridges. The small projections from the sides of the myosin filaments are cross-bridges. They protrude from the surfaces of the myosin filament along its entire length except in the center. Myosin cross-bridges interact with actin filaments causing contraction.

• Z disc. The ends of the actin filaments are attached to Z discs (see Fig. 6–1E). The Z disc passes across the myofibril and from one to another, attaching and aligning the myofibrils across the muscle fiber.

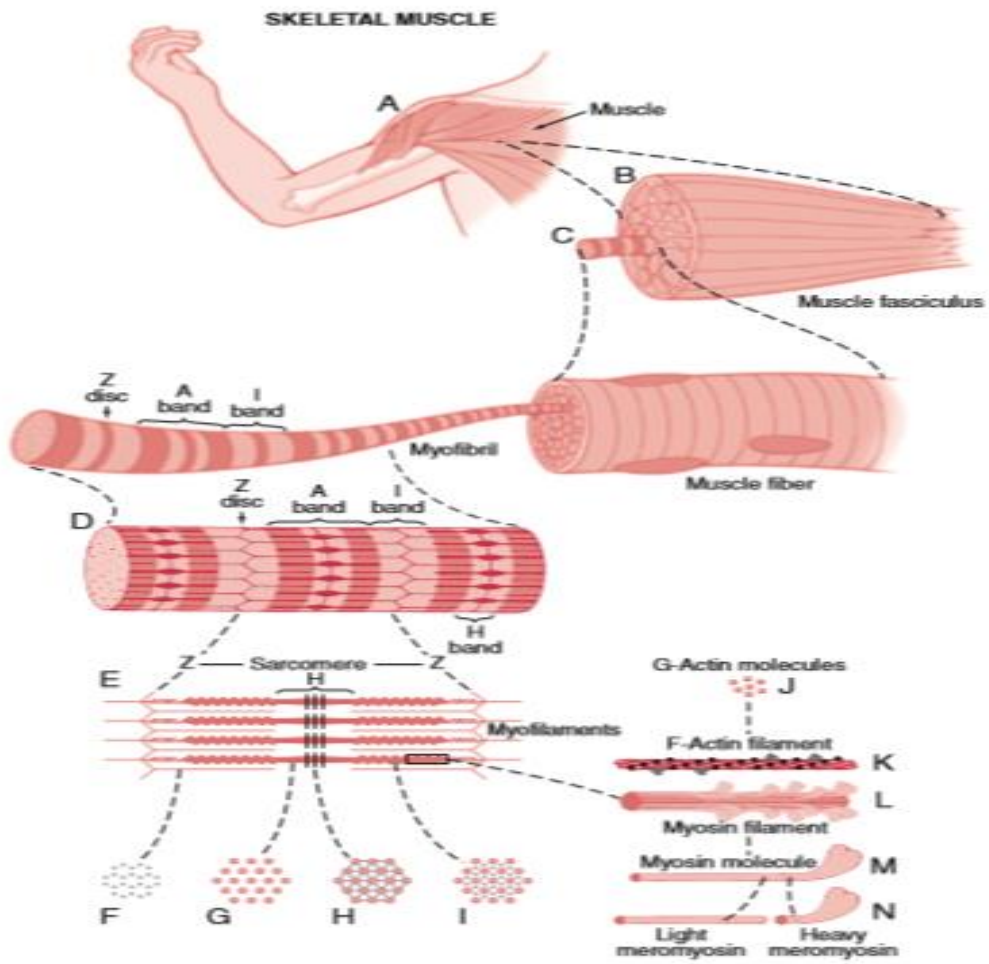

Figure 6–1. Organization of skeletal muscle, from the gross to the molecular level. *F, G, H,* and *I* are cross sections at the levels indicated.

The entire muscle fiber therefore has light and dark bands, giving skeletal and cardiac muscle a striated appearance.

• Sarcomere. The portion of a myofibril that lies between two successive Z discs is called a sarcomere. During rest, the actin filaments overlap the myosin filaments with an optimal amount of interdigitation in skeletal muscle and slightly shorter than optimal interdigitation in cardiac muscle.

General Mechanism of Muscle Contraction (p. 73) The initiation and execution of muscle contraction occur in the following sequential steps:

1. An action potential travels along a motor nerve to its endings on muscle fibers, and each nerve ending secretes a small amount of the neurotransmitter substance acetylcholine.

2. The acetylcholine acts on a local area of the muscle membrane to open acetylcholine-gated cation channels, which allows mainly sodium ions but also calcium ions to flow into the muscle fiber causing a local depolarization. The local depolarization in turn leads to opening of voltage-gated sodium channels resulting in an action potential.

3. The action potential travels along the muscle fiber membrane, causing the sarcoplasmic reticulum to release calcium ions into the myofibrils that have been stored in the sarcoplasmic reticulum.

4. The calcium ions initiate attractive forces between the actin and myosin filaments, causing them to slide together; this is the contractile process.

5. The calcium ions are continually pumped back into the sarcoplasmic reticulum, where they remain stored until a muscle action potential arrives; this removal of the calcium ions from the myofibrils causes muscle contraction to cease.

Molecular Mechanism of Muscle Contraction (p. 74)

Muscle Contraction Occurs by a Sliding Filament Mechanism. Mechanical forces generated by the interaction of myosin cross-bridges with actin filaments cause the actin filaments to slide inward among the myosin filaments. Under resting conditions, these forces are inhibited, but when an action potential travels over the muscle fiber membrane, the sarcoplasmic reticulum releases large quantities of calcium ions, which activate the forces between the myosin and actin filaments, and contraction begins.

The Myosin Filament Is Composed of Multiple Myosin Molecules. The tails of myosin molecules bundle together to form the body of the filament, whereas the myosin heads and part of each myosin molecule hang outward to the sides of the body, providing an arm that extends the head outward from the body. The protruding arms and heads together are called cross-bridges. An important feature of the myosin head is that it functions as an adenosine triphosphatase (ATPase) enzyme, which allows it to cleave adenosine triphosphate (ATP) and thus energize the contraction process.

The Actin Filament Is Composed of Actin, Tropo- myosin, and Troponin. Each actin filament is about 1 mm long. The bases of the actin filaments are inserted strongly into the Z discs, whereas the other ends pro- trude in both directions into the adjacent sarcomeres where they lie in the spaces between the myosin molecules.

Interaction of One Myosin Filament, Two Actin Filaments, and Calcium Ions to Cause Contraction The actin filament is inhibited by the troponin- tropomyosin complex: activation is stimulated by calcium ions.

• Inhibition by the troponin-tropomyosin complex. The active sites on the normal actin filament of the relaxed muscle are inhibited or physically covered by the troponin-tropomyosin complex. Consequently, the sites cannot attach to the heads of the myosin filaments to cause contraction until the inhibitory effect of the troponin-tropomyosin complex is itself inhibited.

• Activation by calcium ions. The inhibitory effect of the troponin-tropomyosin complex on the actin fila- ments is inhibited in the presence of calcium ions. Calcium ions combine with troponin C, causing the troponin complex to tug on the tropomyosin molecule. This “uncovers” the active sites of the actin, allowing contraction to proceed.

A “Walk Along” Theory Can Explain How the Activated Actin Filament and the Myosin Cross-Bridges Interact to Cause Contraction. When a myosin head attaches to an active site, the head tilts automatically toward the arm that is dragging along the actin filament. This tilt of the head is called the power stroke. Immediately after tilting, the head automatically breaks away from the active site. The head then returns to its normal perpendicular direction. In this position, it combines with a new active site farther along the

actin filament. Thus, the heads of the cross-bridges bend back and forth and, step by step, walk along the actin filament, pulling the ends of the actin filaments toward the center of the myosin filament.

The Amount of Actin and Myosin Filament Overlap Dictates Tension Development by the Contracting Muscle (p. 77)

The Strength of Contraction Is Maximal When There Is Maximal Overlap between Actin Filaments and the Cross-Bridges of the Myosin Filaments. A muscle cannot develop tension at very long sarcomere lengths because there is no overlap between actin and myosin filaments. As the sarcomere shortens and actin and myosin filaments begin to overlap, the tension increases progressively. Full tension is maintained at a sarcomere length of about 2.0 mm because the actin filament has overlapped all of the cross-bridges of the myosin filament. On further shortening, the ends of the two actin filaments begin to overlap (in addition to overlapping the myosin filaments), causing muscle tension to decrease. When the sarcomere length decreases to about 1.65 mm, the two Z discs of the sarcomere abut the ends of the myosin filaments, and the strength of contraction decreases precipitously.

Energetics of Muscle Contraction (p. 78)

Muscle Contraction Requires ATP to Perform Three Main Functions

• Most of the ATP is used to activate the walk-along mechanism of muscle contraction.

• Calcium is pumped back into the sarcoplasmic reticulum causing the contraction to terminate.

• Sodium and potassium ions are pumped through the muscle fiber membrane to maintain an appropriate ionic environment for the propagation of action potentials.

There Are Three Main Sources of Energy for Muscle Contraction. The concentration of ATP in the muscle fiber is sufficient to maintain full contraction for only 1 to 2 seconds. After the ATP is split into adenosine diphosphate (ADP), the ADP is rephosphorylated to form a new ATP. There are several sources of energy for this rephosphorylation.

- Phosphocreatine carries a high-energy bond similar to that of ATP but has more free energy. The energy released from this bond causes bonding of a new phosphate ion to ADP to reconstitute the ATP. The combined energy of ATP and phosphocreatine is capable of causing maximal muscle contraction for only 5 to 8 seconds.
- • The breakdown of glycogen to pyruvic acid and lactic acid liberates energy that is used to convert ADP to ATP. The glycolytic reactions can occur in the absence of oxygen. The rate of formation of ATP by the glycolytic process is about 2.5 times as rapid as ATP formation when the cellular foodstuffs react with oxygen. Glycolysis alone can sustain maximum muscle contraction for only about 1 minute.
- • Oxidative metabolism occurs when oxygen is com- bined with the various cellular foodstuffs to liberate ATP. More than 95% of all energy used by the mus- cles for sustained, long-term contraction is derived from this source. The foodstuffs consumed are car- bohydrates, fats, and proteins.

Characteristics of Whole Muscle Contraction (p. 79)

Isometric Contractions Do Not Shorten Muscle, Whereas Isotonic Contractions Do Shorten Muscle

• Isometric contraction occurs when the muscle does not shorten during contraction. True isometric contractions cannot be generated in the intact body because the so-called series elastic components stretch during the contraction, allowing some shortening of the muscle. These elastic elements include the tendons, sarcolemmal ends of muscle fibers, and perhaps the hinged arms of the myosin cross-bridges.

• Isotonic contraction occurs when the muscle shortens and the tension on the muscle remains constant. The characteristics of the isotonic contraction depend on the load against which the muscle contracts as well as on the inertia of the load.

Fast Fibers Are Adapted for Powerful Muscle Contractions, Whereas Slow Fibers Are Adapted for Prolonged Muscle Activity. Each muscle is composed of a mixture of so-called fast and slow muscle fibers, with still other fibers that are between these two extremes. However, a given muscle may have predominantly fast muscle fibers (e.g., anterior tibialis), whereas other muscles may have predominantly slow muscle fibers (e.g., soleus).

• Slow fibers (type I, red muscle) (1) are smaller muscle fibers, (2) have high capillarity and large numbers of mitochondria to support high levels of oxidative metabolism, and (3)contain large amounts of myoglobin, which gives the slow muscle a reddish appearance and the name “red muscle.” The deficit of red myoglobin in fast muscle provides the name white muscle.

• Fast fibers (type II, white muscle) (1) are larger for greater strength of contraction, (2) have extensive sarcoplasmic reticulum for rapid release of calcium ions, (3) have large amounts of glycolytic enzymes for rapid release of energy, and (4) have lower capillarity and fewer mitochondria because oxidative metabolism is of secondary importance.

Mechanics of Skeletal Muscle Contraction (p. 80)

Force Summation Is the Adding Together of Individual Twitch Contractions to Increase the Intensity of Overall Muscle Contraction. Summation occurs in two ways:

• Multiple motor unit summation. When the central nervous system sends a weak signal to contract a muscle, the motor units in the muscle that contain the smallest and fewest muscle fibers are stimulated in preference to the larger motor units. Then, as the strength of the signal increases, larger motor units also begin to be excited, with the largest motor units often having up to 50 times as much contractile force as the smallest units.

• Frequency summation and tetanization. As the frequency of muscle contraction increases, there comes a point at which each new contraction occurs before the preceding one ends. As a result ,the second contraction is added partially to the first, so the total strength of contraction rises progressively with increasing fre- quency. When the frequency reaches a critical level, the successive contractions fuse, and the action appears to be completely smooth; this is called tetanization.

Muscle Hypertrophy Is an Increase in the Total Mass of a Muscle; Muscle Atrophy Is a Decrease in the Mass

• Muscle hypertrophy results from an increase in the number of actin and myosin filaments in each muscle fiber. When the number of contractile proteins increases sufficiently, the myofibrils split within each muscle fiber to form new myofibrils. It is mainly this great increase in the number of additional myofibrils

that causes muscle fibers to hypertrophy; however, under special conditions, the total number of muscle fibers can also increase.

• Muscle atrophy. When a muscle remains unused for a long period, the rate of decay of the contractile proteins occurs more rapidly than the rate of replacement; therefore muscle atrophy occurs. Atrophy begins almost immediately when a muscle loses its nerve supply because it no longer receives the contractile signals that are required to maintain normal muscle size.