Instructor's Answer Key

Chapter 12: Muscle: Mechanisms of Contraction and Neural Control

Answers to Test Your Understanding of Concepts and Principles

1. Graded and sustained skeletal muscle contractions are produced by the asynchronous activity of somatic motor neurons innervating groups of muscle fibers (motor unit). The brain selects some motor units to contract before others in response to voluntary control. At lower levels of effort fewer muscle fibers are stimulated to contract because smaller motor units are activated within the muscle. At greater levels of effort larger motor units are recruited and activated resulting in stimulation of a greater number of muscle fibers and producing a stronger contraction. Sustained muscle contraction *in vivo* occurs when all the motor units are used and the rate of neural firing is maximal – such as lifting an extremely heavy weight. This exertion will result in muscle fatigue and is thought to be due to an accumulation of extracellular K^+. [Note: This question is also answered in the Student Study Guide.]

2. When fewer and smaller motor units are stimulated and the load is sufficiently heavy, the contraction strength may not be sufficient to shorten the muscle; the muscle thus contracts isometrically. As more and larger motor units are stimulated, or recruited to move the load, the contraction strength increases. At the start of the contraction, this tension must first stretch the series elastic component of the muscle and then must overcome any opposing forces on the muscle (such as gravity). Once this has occurred, the muscle tension is sufficient to shorten the muscle and move a load; this contraction becomes isotonic.

3. The cross bridges cannot attach to the actin subunits when a muscle is relaxed because they are physically prevented from doing so by the troponin-tropomyosin complex. When a somatic motor nerve stimulates a muscle, ACh is released and binds to nicotinic cholinergic receptors on the motor end plate. The subsequent depolarizations are end plate potentials (EPPs) that result in the formation of new action potentials on the sarcolemma and the release of Ca^{2+} from the sarcoplasmic reticulum. The Ca^{2+} attaches to troponin, which causes the troponin-tropomyosin complex to change its position on the thin filament. This exposes binding sites on the actin for the cross bridges in the head of the myosin, so that contraction can occur.

4. According to the *length-tension relationship*, the contraction strength of a muscle is influenced by the initial length of its resting muscle fibers. Experiments demonstrate that the "ideal" resting length for skeletal muscle fibers or the length at which they can generate maximum force is when muscles are at 100% of their normal resting length. In the sarcomere, this force is maximal when the thin filaments only partially overlap at the edges of the thick filaments. If the muscle length is greater than about 2.2 μm the filaments do not overlap optimally, the myosin cross bridges cannot attach to actin maximally, and contraction force is diminished. If the muscle length is decreased shorter than 2.0 μm, so that the Z lines are close to the edges of the thick filaments, the muscle cannot shorten much more because the thick filaments will abut on the Z lines and the force generated by the muscle contraction declines.

5. The maintenance of muscle tone requires the contraction activity of *gamma* motoneurons, which stimulate isometric contraction of the intrafusal fibers of muscle spindles. This keeps the spindles taut, so that stretch of the extrafusal muscles will stimulate a monosynaptic reflex involving the activation of alpha motoneurons. Stimulation of alpha motoneurons causes the extrafusal muscle fibers to contract. In this way, a basal level of muscle contraction, which is called muscle tone, opposes the relaxation and lengthening of a muscle. When descending motor tracts are damaged, the tonic level of activity of gamma motoneurons is at first abolished, and muscle tone decreases. After some time, however, the absence of inhibitory influences from the basal ganglia causes the muscle stretch reflexes to become hyperexcitable and, as a result, muscle tone becomes greater than normal (clonus). Muscle tone therefore is maintained by normal feedback between the muscle spindles sensitive to stretch and the gamma loop stimulation from upper motor neurons.

6. Hydrolysis of ATP is required for activation of the myosin head of the cross bridges, an event that must precede binding of the cross bridges to actin and the swiveling action that occurs in the contraction cycle. In addition, the binding of a new ATP by the myosin head is required for the detachment of the cross bridge from actin and the continuation of the contraction cycle. Thirdly, in order for muscle relaxation to occur, Ca^{2+} must be transported out of the sarcoplasm and pumped into the sarcoplasmic reticulum. This requires active transport, and thus relaxation—like contraction—also requires the hydrolysis of ATP.

7. The muscle fiber type is determined by the motor neuron that innervates it, so that all of the muscle fibers of a given motor neuron are of the same type. Motor neurons that innervate fewer muscle fibers (smaller motor units) have a smaller cell body and is stimulated by lower levels of excitatory input than a larger neuron that innervates a greater number of muscle fibers. The smaller motor units thus are more easily depolarized to threshold than larger motor units, and so are activated more frequently. Since smaller motor neurons tend to innervate slow-twitch muscle fibers, and larger motor neurons tend to innervate fast-twitch muscle fibers, slow-twitch fibers will be stimulated more frequently than fast-twitch fibers.

8. Endurance training (steady increase in the intensity of exercise) results in the improved ability to obtain ATP from oxidative phosphorylation, increased size and number of mitochondria, less lactic acid production, increased myoglobin content, increased lipoprotein lipase, increased proportion of energy derived from fat, lower rate of glycogen depletion during exercise, improved efficiency in extracting oxygen from blood, and a decrease in the size of type IIB fibers. By contrast, anaerobic respiration and the production of lactic acid contribute to muscle fatigue by depleting muscle glycogen, interfering with excitation-contraction coupling, and by shifting K^+ from intracellular to extracellular compartments. When exercise is performed at greater than 60% of the maximal oxygen uptake, anaerobic respiration contributes a proportionate share of energy requirements. Since endurance training increases the maximal oxygen uptake of a muscle, a given level of exercise in an endurance-trained muscle will result in a lower percentage of its maximal oxygen uptake and thus in a lower contribution of anaerobic respiration to the energy requirements. Less lactic acid will thus be produced at that level of exercise. Put another way, a greater level of exercise will be required in an endurance-trained muscle to reach a given percentage of its maximal oxygen uptake than would be the case in an untrained muscle.

9. In striated muscle, EPPs at a one neuromuscular junction produce all-or-none action potentials that result in all-or-none contractions of the muscle cells. In smooth muscle, the entire surface of smooth muscle cells contains neurotransmitter receptor proteins. Release of neurotransmitters from autonomic bulges, or varicosities provides the stimulus for a graded depolarization and subsequent contraction of a number of smooth muscle cells. The graded depolarization results in a graded opening of voltage-sensitive Ca^{2+} gates in the plasma membrane of smooth muscle cells. Unlike the case in striated muscle, the sarcoplasmic reticulum is poorly developed in smooth muscle cells, and most of the Ca^{2+} required for contraction passes into the cell through the plasma membrane. In striated muscle, Ca^{2+} released from the sarcoplasmic reticulum combines with troponin. In smooth muscle cells, the Ca^{2+} combines with calmodulin. The complex thus formed activates myosin light chain kinase, which phosphorylates the myosin cross bridges. Unlike the case in striated muscle, such phosphorylation is required before the cross bridges of smooth muscles can attach to actin. In this way, the number of cross bridges that participate in the contraction of a smooth muscle cell can be graded by the amount of Ca^{2+} that enters the cell.

10. Electrical synapses, or gap junctions join cardiac muscle cells and single-unit smooth muscle fibers. Since all cells are electrically joined, a myocardium contracts to its full extent each time because all of its cells contribute to the contraction. Single-unit smooth muscles have numerous gap junctions (electrical synapses); thus they behave as a single unit and display pacemaker activity, much like cardiac muscle. Both cardiac muscle and single-unit smooth muscles also display intrinsic, or myogenic electrical activity and contraction in response to stretch. Multiunit smooth muscles such as the arrector pili muscles and ciliary muscle attached to the lens of the eye, by contrast, require nerve stimulation for contraction. There are few, if any, gap junctions, so each individual cell must be stimulated separately by neurotransmitters released from autonomic nerve bulges, or varicosities that form synapses known as synapses en passant.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. Yes and no. Running marathons requires endurance training. He is right because carbohydrates are stored as glycogen in skeletal muscle and the liver to a limited extent and because depletion of muscle glycogen places a limit on exercise, leading to fatigue. In addition, during heavy exercise (above the lactate threshold) glucose from muscle glycogen and from blood plasma supplies about two-thirds of the energy requirement. However, “carbo loading” is no longer recommended nor practiced by elite long distance runners. Even if depleted of muscle glycogen by serious, vigorous training, glycogen stores are replenished rapidly, usually within hours of a meal and any extra carbohydrate calories are shuttled along alternative pathways including those leading to fatty acid synthesis. Other suggestions to improve performance include increased training of all muscle fiber types so that endurance training is mixed with shorter, more intense regimens, maintaining proper fluid, and balanced nutrition intake with adequate rest.

2. Duchenne's muscular dystrophy is inherited as an X-linked recessive trait that involves progressive muscular wasting. The defective gene produces an abnormal form of a protein called *dystrophin*, which is associated with the support of skeletal muscle fibers. Dystrophin bridges the cytoskeleton and myofibrils in the fiber with the extracellular matrix. When dystrophin is defective, muscle wasting occurs. This type of muscular dystrophy usually results in confinement to a wheelchair by age 12, and many die in their 20s. The serum level of the isoenzyme creatine kinase, or creatine phosphokinase, is elevated in these patients. Amyotrophic lateral sclerosis (ALS), by contrast, is caused by a defect in a gene (not X-linked) that codes for a specific enzyme – *superoxide dismutase*. With this defective gene, ALS patients lack this enzyme resulting in the accumulation of highly toxic superoxide free radicals that damage the lower motor neurons innervating skeletal muscle fibers. As motor neuron innervation ceases, skeletal muscle fibers progressively atrophy and eventually become paralyzed.

3. Stored high-energy phosphates in the form of phosphocreatine, or creatine phosphate (CP) are present in skeletal muscle in more than three times the concentration of ATP. CP therefore is a ready reserve of high-energy phosphate that can be directly donated to ADP to reform ATP during sustained muscle activity. This ATP production is so efficient that muscle concentrations of ATP barely change when the rate of ATP breakdown rapidly increases from rest to heavy exercise. During the recovery from exercise, the muscle enzyme called creatine kinase, or creatine phosphokinase, can reform ATP and restore the levels of CP within the muscle fibers. If the body ever ran out of ATP one might expect a transient rigor mortis where muscle fibers contract and are temporarily unable to disengage the myosin head from actin myofilaments. Without relaxation, the muscles would become stiff; but without ATP, cross bridge cycling would stop. As time passes, the sarcoplasmic reticulum would no longer be able to restore calcium and the excitation of action potentials along the sarcolemma would eventually cease, leading to a muscle paralysis. Death would be imminent.

4. Excitation-contraction coupling occurs when a skeletal muscle fiber is stimulated to contract by somatic motor neuron action potentials. By way of motor end plate potentials (EPPs) the new action potentials travel along the sarcolemma and into the transverse tubules. Transverse tubules contain voltage-gated calcium channels (dihydropyridine or DHP receptors) that respond to the arriving action potentials by directly causing the calcium release channels (also called ryanodine receptors) to open. This results in the release of Ca^{+2} by passive diffusion into the sarcoplasm and stimulating contraction. In addition to the ryanodine receptors, the sarcoplasmic reticulum membrane contains a Ca^{+2}-induced Ca^{+2} release mechanism channel that opens in response to the raised Ca^{+2} concentration of the cytoplasm. The net release of Ca^{+2} by all mechanisms results in binding to troponin and stimulating the sliding of actin over myosin with muscle shortening. Part of the reason this coupling has been a mystery for so long involves the fact that the transverse tubules that conduct electrical action potentials are not physically continuous with the sarcoplasmic reticulum that stores and releases the Ca^{+2}. Even now the details of this electromechanical release mechanism are theoretical and more experimental evidence is needed.

5. A rise in extracellular Ca^{+2} available to the beating heart would lead to a positive inotropic response (increased force of contraction). The higher flow of Ca^{+2} through calcium channels in the sarcoplasmic reticulum may stimulate other calcium channels to open, resulting in a Ca^{+2}-induced Ca^{+2} release mechanism. The increase in intracellular Ca^{+2} binds to troponin and increases the force of contraction in cardiac muscle. This also occurs in response to epinephrine or to stretch of the myocardial walls. Lowering of blood Ca^{+2} causes skeletal muscle spasms because an abnormally low concentration increases the permeability of the plasma membranes to Na^{+} and other ions. The subsequent spontaneous depolarization of isolated muscle fiber membranes causes random firing of action potentials and muscle contractions (spasms).