Chapter 12 Muscle Physiology - Important Questions

3 kinds of muscle fibers

1. Name 3 kinds of muscle fibers and their location inside body.
   a. Skeletal m.f. – attached by tendons to bones.
   b. Smooth m.f. – found in walls of hollow organs and vessels.
   c. Cardiac m.f. – found in walls of heart.

2. Give at least 2 characteristics of 3 kinds of muscle fibers.
   a. Skeletal muscles are multinucleate and have striations (light and dark bands arrangement).
   b. Cardiac muscles are uninucleate, have striations, branching and intercalated discs with gap junctions.
   c. Smooth muscles are uninucleate, no striations, spindle shaped and may have gap junctions.

Structure of Skeletal Muscle fiber

3. Explain bundle within bundle organization of a muscle.
   a. Thick and thin filaments → myofibril → muscle fiber = cell (covered by endomysium) → fascicle (covered by perimysium) → muscle (covered by epimysium). All connective tissue coverings are continuous with tendon.

4. How many thin filaments surround a thick filament?
   6 thin filaments surround each thick filament.

5. How many fibers surround a thin filament? Name them.
   3 thin and 3 thick alternating filaments surround each thin filament.

6. **Mechanism of Muscle Contraction**

   What is the role of tropomyosin in muscle contraction?
   a. In a relaxed muscle it covers the binding sites of actin for cross-bridges of myosin.

7. What is the role of troponin?
   a. Troponin has a binding site for Ca^{2+}. When Ca^{2+} joins troponin undergoes conformational change and pulls the tropomyosin away and exposes the binding sites.


   A motor neuron has many terminal branches ending in knobs. A terminal knob neuron and motor end plate of sarcolemma lie very close across synaptic cleft and form a neuromuscular junction. Motor end plate has receptors for acetylcholine secreted by terminal knob.
9. How does nervous stimulus pass through synaptic cleft? List the main events.
   a. Depolarization of presynaptic membrane opens Ca$^{2+}$ channels.
   b. Influx of Ca$^{2+}$ causes exocytosis of vesicles releasing Acetylcholine in synapse.
   c. Acetylcholine binds to receptors in postsynaptic membrane = motor end plate and opens Na$^{+}$ channels.
   d. Influx of Na$^{+}$ depolarizes the motor end plate.

10. How many action potentials of neuron needed to cause action potential of motor end plate?
    a. 1 action potential of neuron is sufficient to produce action potential of motor end plate.

11. What breaks the continuity of depolarization once the motor end plate gets depolarized?
    a. Acetylcholine detaches from receptors when the motor end plate gets depolarized. Enzyme cholinesterase present in the synapse breaks acetylcholine $\rightarrow$ acetate + choline. Terminal knob reabsorbs the choline.

12. What is the role of t-tubules?
    a. Depolarization wave travels from motor end plate to sarcolemma and enters t-tubules = invaginations of sarcolemma. Depolarization wave travels deep into muscle fiber through t-tubules.

13. How Ca$^{2+}$ is released into cytosol of muscle fiber?
    a. Depolarization of t-tubules causes depolarization of terminal cisternae that lie on each side of t-tubule. The fall in voltage activates Dihydropyridine receptors; that open Ryanodine receptors and Ca$^{2+}$ ions move out in cytosol.

14. Explain the 4 steps of cross-bridge cycle. (A = actin, M = myosin, M.ADP = period represents a bond between myosin and ADP) Also study fig 12.9.
    a. Cross bridge binds to actin. In this stage cross bridge is already in cocked up position due to energy provided by earlier cycle. ADP + P$_i$ are attached to the binding site of cross-bridge.
       i. $A + M$.ADP.P$_i$ $\rightarrow$ A.M .ADP. P$_i$
    b. Cross bridge moves to pull actin by using the provided by release of ADP + P$_i$
       i. A.M .ADP. P$_i$ $\rightarrow$ A.M + ADP + P$_i$
    c. ATP binds to the cross bridge and provides energy for detachment of cross bridge.
       i. A.M + ATP $\rightarrow$ A + M.ATP
    d. ATP breaks into ADP + P$_i$ and cross bridge returns to original cocked up position by using this energy.
       i. A + M.ATP $\rightarrow$ A + M.ADP.P$_i$

15. What keeps the muscle contracted continuously and what ends the contraction?
a. A series of action potentials from neuron keeps the muscle contracted by keeping $\text{Ca}^{2+}$ in cytosol. When action potentials of neuron stop motor end plate – sarcolemma – t-tubule – terminal cisternae get repolarized. $\text{Ca}^{2+}$ are actively pumped by $\text{Ca}^{2+}$ ATPase. The fall in $\text{Ca}^{2+}$ in cytosol brings the change in conformation of troponin-tropomyosin and covers the binding sites of actin.

Mechanics of single-fiber contraction

16. What is contraction of a muscle?
   a. Contraction means turning on of Cross-Bridge-Cycle. It may or may not result in shortening of a muscle.

17. Name and explain 3 types of contractions of muscle fibers.
   a. **Isometric Contraction** – muscle generates tension (force) but maintains length. For example holding a weight in hand without moving the arm or trying to push immovable weight.
   b. **Isotonic Contraction** – muscle changes length but maintains tension. For example after lifting a weight in hands, flexing your arm; tension remains same but muscle shortens (a concentric contraction).
   c. A lengthening (eccentric) contraction – tension generated by cross bridges of muscle is less than the load (weight) carried by muscle. It increases the length of muscle though the cross bridge cycle is on. For example the lengthening of quadriceps muscles in femur allows you to lower yourself to a seat. Fig 9.18

18. What is the relationship between frequency of stimulation and tension?
   a. Slow frequencies allow individual contraction – relaxations = Twitches.

19. What is summation?
   a. When a 2\textsuperscript{nd} stimulus is applied before the completion of 1\textsuperscript{st} twitch, it results in a greater contraction called summation because it sums the 2 contraction.

20. What is tetanus?
   a. A fast series of stimulations resulting in a continued contraction at maximum level is called tetanus. It can by unfused tetanus if you can see individual contractions. A very fast series of stimulations causes a fused tetanus when we cannot see individual contractions.

21. What is the relationship between length of muscle fiber and isometric tension?
   a. Maximum isometric tension is produced at optimal sarcomere length ($L_0$) due to optimal overlap of actin and myosin filaments. Both increase and decrease in sarcomere length decrease the isometric tension.

22. What is the effect of load on velocity of shortening of muscle fiber?
   a. The increase in load decreases the velocity of shortening of muscle fiber.

Skeletal muscle energy metabolism

23. Name 3 processes performed by ATP in muscle contraction.
   a. Detachment of cross-bridge from actin.
b. Cocking up of cross bridge.

c. Power stroke – the bending of cross-bridge to pull actin toward center of sarcomere.

24. Write briefly about 3-ways how ATP can be generated in a muscle fiber?

a. ADP + C-P → ATP + C, by transferring a phosphate from creatine phosphate to ADP.

b. By oxidative phosphorylation of glucose (glycolysis → Kreb’s cycle → Electron Transport Chain) by mitochondria using O₂. (36 ATP/glucose).

c. By substrate-level phosphorylation in glycolytic pathway in cytosol without using O₂. (2 ATP/glucose). It starts above 70% of maximal activity of a muscle. It generates lactate.

25. Name at least 3 causes of muscle fatigue.

A muscle is fatigued when it fails to contract in the presence of neural stimulus. Main 3 causes are:

a. Extended submaximal exertion can deplete stored glycogen in muscle.

b. Accumulation of inorganic phosphates in cytosol of muscle cell during short term maximal exertion.

c. Ionic imbalances also play role in fatigue

Give characteristics of 3 types of skeletal muscle fibers. Table 12.2

<table>
<thead>
<tr>
<th>Slow Oxidative fibers = Type - 1</th>
<th>Fast Oxidative-Glycolytic = Type 2</th>
<th>Glycolytic Fibers = Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Many capillaries, many mitochondria</td>
<td>• Many capillaries, many mitochondria</td>
<td>• Few capillaries/mitochondria</td>
</tr>
<tr>
<td>• High myoglobin – red muscle fiber</td>
<td>• High myoglobin – red muscle fiber</td>
<td>• Low – white muscle fiber</td>
</tr>
<tr>
<td>• Glycolytic enzyme activity low</td>
<td>• intermediate</td>
<td>• high</td>
</tr>
<tr>
<td>• Fiber diameter and motor unit small</td>
<td>• Both intermediate</td>
<td>• Both large</td>
</tr>
<tr>
<td>• Contraction velocity slow</td>
<td>• fast</td>
<td>• fast</td>
</tr>
</tbody>
</table>

26. Explain muscle contraction and all or none principle.

a. Muscle fiber and motor units obey all or none principle but muscles do not. CNS can make a muscle generate greater tension by activating a greater number of motor units.

27. What is the order of recruitment of 3 kinds of muscle fibers?


b. This is why called type 1 or 2 or 3.

28. List 4 factors that determine muscle tension

a. Frequency of action potentials – a minimal fast series of action potentials to generate maximal fused tetanus contraction.
b. Length of fiber – optimal length of sarcomeres needed to produce maximum tension

c. Fiber diameter – thicker fibers result in higher tension

d. Fatigue

e. # of fibers in motor unit

f. # of motor units activated

29. Why do many poisons like arrowhead poison cause paralysis of muscles?

a. They inhibit neuromuscular junctions by strongly binding to Ach binding sites without opening Na⁺ channels.

30. Name a sex linked genetic disease of progressive muscle degeneration.

a. Duchenne muscular dystrophy. It is due to a mutation of a gene on X-chromosome which alters the structure of protein Dystrophin needed for attachment of cytoskeletal muscles to membrane and integrity of membrane.

31. Name an autoimmune disorder of muscles leading to chronic muscle fatigue and weakness.

a. Myasthenia gravis – is a collection of neuromuscular disorders. It is more common in women. Main cause is destruction of nicotinic ACh receptor proteins.

32. Name the involuntary contraction of skeletal muscles (may occur due to excessive muscle activity).

a. Muscle Cramps – reasons not fully understood yet but may be due to electrolyte imbalance.

Smooth and Cardiac Muscles Section-B

33. Name with examples 2 types of smooth muscle fibers.

a. Single-unit smooth muscle fibers lie in vessels and hollow organs and multi-unit smooth muscle fibers – example is hair arrector pili muscles of integument.

34. What is the arrangement of thick and thin filaments in smooth muscle fibers?

a. They do not form striations of dark and light bands. Thin fibers lack troponin. Thin fibers are attached to either cell membrane or Dense bodies present in cytosol. In function dense bodies are similar to Z-lines. Contraction is due to sliding of thin filaments over thick filaments.

35. What is the source of Ca²⁺ in smooth muscle contraction?

a. Sarcoplasmic Reticulum and extracellular (come in by opening of channels).

36. Which muscle fiber is likely to have spontaneously generated action potential s by pace-makers (no impulse needed from CNS)?

a. Single unit smooth muscle fiber and some cardiac muscle fibers (SA node of heart).
37. What is the site of Ca\textsuperscript{2+} regulation in smooth and skeletal muscle fibers?
   a. Myosin in smooth muscle fibers and Troponin in skeletal muscle fibers.

38. List main steps of activation of smooth muscle fiber by Ca\textsuperscript{2+}?
   a. Cytosolic Ca\textsuperscript{2+} level gets high due to its release by varicosities of SR and its entry through membrane channels.
   b. Ca\textsuperscript{2+} binds to protein Calmodulin in cytosol.
   c. Ca\textsuperscript{2+}-Calmodulin complex binds to protein ‘light-chain kinase’ = LCK
   d. Myosin-light-chain kinase uses ATP to phosphorylate (add phosphate) to myosin cross bridges.
   e. Phosphorylated cross bridges bind to actin filaments.
   f. Cross bridge cycle produces tension and shortening. (it operates similar to a skeletal muscle fiber).

39. Comment about innervations of smooth muscle fibers.
   Smooth muscle fibers are stimulated by autonomic nerve fibers. Instead of ending into terminal knobs the axon branch into beaded branches and neurotransmitters are released by beads = varicosities. In addition single unit smooth muscle fibers have gap junctions over most cells. Therefore if a few cells are depolarized the action potentials pass through gap junctions to next cells, making all cells in group to contract simultaneously = single unit.

40. What are pace-maker potentials? How do they change to action potentials?
   Smooth muscle fibers of GI tract and some cardiac muscle fibers continuously generate graded potentials less than threshold stimulus. When an excitatory input, like entry of food to a segment, is added these potentials cross threshold and change to action potentials. GI tract, heart and some neurons in CNS can contract rhythmically in absence of neural stimulation.

Cardiac Muscle fibers

41. Give 2 unique features of cardiac muscle fibers.
   They are branched and have special end plates = intercalated discs with gap junctions.

42. Name similarities between skeletal and cardiac muscle fibers.
   a. Both have striations of dark and light bands due to similar arrangement of thin and thick filaments in sarcomeres.
   b. Both use troponin-Ca\textsuperscript{2+} for activating cross-bridge cycle.

43. Why are skeletal muscle fibers fast contracting and cardiac smooth muscle fibers slow contractors?
   a. Action potential of skeletal muscle fibers is like a spike. It persists only for 1-2 milliseconds. It develops a faster contraction which also relaxes at a fast rate.
b. Action potential of cardiac muscle fibers develops rapidly but remains high for about 250 milliseconds. The cardiac muscle contraction develops slowly and starts declining only after about 200 milliseconds. This suits the working of heart because heart muscle needs to pump blood but then relax to allow filling of the atria and ventricles.