Chapter 8, The Muscular System
Outline of class notes
Objectives:
After studying this chapter you should be able to:
1. Briefly describe the three types of muscle tissue and their distinguishing characteristics.
2. Describe the functions and properties of muscle tissue.
3. Explain the connective tissue components of muscle.
4. Describe the anatomy of a skeletal myofiber.
5. Describe the components of a sarcomere and the Sliding Filament Model of a muscle contraction.
6. Describe how skeletal muscles are innervated and the structures of the neuromuscular junction.
7. Explain the steps involved in the contraction and relaxation of a skeletal muscle fiber.
8. Discuss how contractile force is regulated
9. Describe the difference between a twitch, wave summation, and tetany in muscle contraction.
10. Describe the difference between isometric and isotonic contractions.
11. Describe the energy requirements of skeletal muscle and the creatine phosphate system.
12. What is meant by oxygen dept?
13. Explain the process of muscle fatigue.
14. Discuss the causes of muscle hypertrophy and muscle atrophy.
15. Discuss the following conditions: Duchenne Muscular Dystrophy, Rigor Mortis, Myasthenia gravis, botulism, BOTOX, and Fibromyalgia.

Muscular System Overview
• Muscle identification
• Muscle Tissue Types
• Functions of Muscular Tissue
• Skeletal Muscle Anatomy
  – Myofiber (muscle cell)
  – Neuromuscular junction
• Events of a muscle contraction/relaxation
• Metabolism of skeletal muscle
  – Fatigue
  – Oxygen dept
• Control of Muscle Tension

Muscles
• Accounts for 40-50% of total body mass
• A Muscle is an organ
  – Contains nerves, blood vessels, various connective tissues, and muscle cells (muscle fibers).
• There are
List of muscles that you need to know – use reference from book (figure 8.13) to fill in names.

Biceps brachii
Calcaneal (achilles) tendon
Deltoid
External oblique
Frontalis
Gluteus maximus
Gluteus medius
Gastrocnemius
Gracilis
Hamstring muscles
  Biceps Femoris
  Semitendinosus
  Semimembranosus
Latissimus dorsi
Masseter
Occipitalis
Orbicularis oris
Orbicularis oculi
Pectoralis major
Platysma
Rectus abdominis
Rectus femoris
Sartorius
Serratus anterior
Soleus
Sternocleidomastoid
Temporalis
Tibialis anterior
Triceps brachii
Trapezius
Vastus lateralis
Vastus medialis
Zygomaticus
Three Types of Muscle Tissue
1. Skeletal Muscle
2. Smooth Muscle
3. Cardiac Muscle

Skeletal Muscle
- **Skeletal muscle**
  - Location: Attached to bones – provides
  - Consist of long, cylindrical cells that are **striated** and **multinucleate**
    - Striations (light and dark bands) gives a banded appearance.
  - Under **voluntary control** and can grade (vary) its contraction strength.

Cardiac Muscle
- **Cardiac muscle**
  - Predominant tissue within
  - Consists of **striated**, cylinder-shaped branching cells connected by **intercalated discs**
  - Involuntary muscle – intrinsic pacemaker (sinoatrial node) that sets pace at ~75 beats/minute.
  - Cells contain 1-2 nuclei; single nucleus in most cells.

Smooth Muscle
- **Smooth muscle**
  - Located primarily in the walls of hollow organs (stomach, blood vessels, uterus, bladder, airways to lungs, etc.)
  - Consists of **non-striated (smooth)** spindle-shaped cells
  - Involuntary muscle

Functions of Muscles
1. **Movement**: Contraction may be voluntary (skeletal muscle) or involuntary (cardiac and smooth muscle)
   - Movement of:
     - Body parts such as arms, legs, hands, etc.
     - Food (and, subsequently, food waste) through the GI tract
     - Urine through the urinary tract
     - Heart pumps blood through
2. **Maintenance of posture**
   - Ex:
3. Thermogenesis
   - Muscle contractions generate heat.
   - Shivering – an involuntary contraction of skeletal muscle.

4. Stabilization of joints
   - Muscles keep the

Connective Tissue and Muscle
   - Fibrous Connective tissue:
     - Forms tendons which attach
   - Fibrous CT (fascia) forms three layers within and around skeletal muscle:
     - Epimysium: Outer most layer that
     - Perimysium:
       - Fascicle: A bundle of skeletal muscle cells (muscle fibers),
       - Fascicles may contain bundles of 10 to over 100 muscle cells.
     - Endomysium:

Skeletal Muscle Attachments
   - Tendons: Fibrous connective tissue that
   - Tendons are continuous with the connective tissue that surrounds and contained within skeletal muscle.

Skeletal Myofiber Anatomy
   - Sarcolemma:

   - Sarcoplasm: Cytoplasm of a muscle cell
     - Sarcoplasm has lots of mitochondria, lots of glycogen granules (to provide glucose for energy needs) as well as myofibrils and sarcoplasmic reticuli.
   - T (transverse) tubules: Tubular invaginations of the sarcolemma that extend through the cell.
     - Function to carry an action potential deep into the myofiber cytoplasm
   - Sarcoplasmic reticulum: Muscle endoplasmic reticulum that surrounds the myofibrils.
     - Functions as a
       - Terminal cisternae are dilated end sacs of the sarcoplasmic reticulum that lie near the T tubules.
• **Triads**: Complex consisting of a **central T tubule** flanked on each side by **terminal cisternae**
• **Myofibrils**: Rodlike structures that
  
  - Composed of cylindrical bundles of **thick** and **thin myofilaments** arranged in repeating units called **sarcomeres**
  - The interaction of these proteins allow for muscle contraction.

**Thick Myofilaments**

• **Thick myofilaments**:  
  
  - A single myosin protein resembles 2 golf clubs whose shafts have been twisted about one another.
  - About 300 of these myosin molecules are joined together to form a single thick filament.
  - The myosin heads (cross bridges) extend out toward the thin filaments.
  - Each myosin head contains an **ATP-binding site** and an **actin-binding site**

**Thin Myofilaments**

• **Thin myofilament**: Composed of 3 different types of proteins: **actin** (main component), **troponin** and **tropomyosin**.
• **Actin filament**: A polymer formed of 300 – 400 gobular subunits, arranged as a double row of proteins twisted to from a helix.
  
  - On each actin subunit, there
  
  - Under resting conditions, myosin binding is prevented by the **troponin-tropomyosin** complex.
- **Tropomyosin:** Long strands of protein molecules that are located in the groves of the actin helix.
  - Covers the myosin binding sites and
- **Troponin** binds to tropomyosin forming a **troponin-tropomyosin complex**.
  - **Troponin** has a receptor for a **calcium ion**. In resting muscle, intracellular calcium concentrations are low and the calcium binding site is empty.

**Sarcomeres**
- **Sarcomere:** The contractile unit in a striated muscle cell extending from
  - Each myofibril is made up 1000’s of repeating units known as **sarcomeres**
  - The portion of the sarcomere which contains the thick filament is known as the **A band**.
  - The portion of the sarcomere which does not contain any thick filaments is known as the “**I**” band.
  - Banding pattern of sarcomere gives

**Muscle Contraction: The Sliding Filament Model**
- Model describes the movement of thick (myosin) and thin (actin) filaments during contraction
  - During a contraction, thick and thin filaments do not
  - Thin filaments slide past thick filaments as **Z disks** are drawn closer together.
  - Sarcomere represents area between successive Z disks, therefore **the sarcomere gets smaller during a contraction**
- When all the sarcomeres in a fiber do this the entire fiber gets shorter which pulls on the attached tendon and then pulls on the bone. Voila, we have movement.
Muscle Innervation

- Each muscle is
  - **Nerve**: A bundle of **axons** and/or dendrites carrying signals to or from the spinal cord to the muscle or other structure.
  - **Motor unit**: A motor neuron and all the
    - Muscles that control small precise movements have many motor units with few muscle fibers.
      - Ex. Muscles of fingers, eyes
    - Muscles that cause large, powerful movements have few motor units with many muscle fibers per motor unit.
      - Ex. Gastrocnemius
    - Within the muscle, each axon will eventually end in a bulbous swelling known as the **synaptic end bulb**.
  - **Synapse**: The functional junction (site of interaction) between

Structures of the Neuromuscular Junction

- **Neuromuscular Junction**:
  - The **axon terminal** and **motor endplate** constitute the neuromuscular junction.
  - The minute space between the axon terminal and the sarcolemma is known as the **synaptic cleft**.
  - **Motor end plate**: Region (depression) of the sarcolemma that is adjacent to the synaptic end bulbs.
  - The nerve terminal is filled with vesicles that
    - The motor end plate has folds that contain a number of **acetylcholine receptors**
    - **Acetylcholinesterase** is an enzyme located in the **junctional folds**, it degrades acetylcholine.
Contraction of Skeletal Myofibers

- **Steps involved:**
  1. Excitation of the Neuron Terminal
  2. Excitation of the Myofiber
  3. Relaxation of the Myofiber

**Excitation of Neuron Terminal**

- A nerve signal (action potential) arrives at
  - Triggers the synaptic vesicles to release **acetylcholine** from the synaptic endbulbs into the synaptic cleft by exocytosis.
  - **Acetylcholine (ACh)** diffuses across the synaptic cleft and binds to the ACh receptors and causes them to open.
    - Na+ will rush into the cell stimulating an action potential to be produced along the sarcolemma.

**Excitation: Myofiber**

- The **action potential** travels along the sarcolemma and into the **T tubules**.
- The **T tubules** stimulate the release of **calcium ions** from the **sarcoplasmic reticulum**.

- The Ca2+ interacts with the **troponin** causing a confirmational change in the **troponin-tropomyosin** complex, that exposes attachment sites for the **myosin head**.

- The **myosin head** (cross-bridges), previously activated by the hydrolysis of ATP, attaches to actin.
  - ATP hydrolysis provides the
• Once attached to actin, the myosin head undergoes a **power stroke** and pulls the thin filaments over the thick filament.
  
  – This results in the thin filament sliding along the thick filament.
• Myosin then remains bound to actin until it binds to another ATP. Attachment of fresh ATP provides the energy to “cock” the myosin head back and detach it from the actin molecule. The cycle can repeat as long a calcium remains attached to troponin and ATP is available.

**Relaxation of the Myofiber**

• Cessation of action potentials stops the release of ACh
  
  – The **sarcoplasmic reticulum**
  
  – Without calcium, **Tropomysosin** moves over the **myosin binding site** on the actin filament preventing attachment of the **myosin crossbridge**.
• **Acetylcholine** is broken down by the enzyme **acetylcholinesterase** which exists as part of the sarcolemma and free within the synaptic cleft.
Summary of the Steps of a Muscle Contraction
1. An action potential travels along an axon membrane to a neuromuscular junction.
2. ACh is released from the synaptic vesicles in the presynaptic terminal of the neuron by exocytosis.
3. ACh diffuses across the synaptic cleft and binds ACh receptors located on the motor endplates of the sarcolemma, and stimulates the opening of sodium channels which stimulates an action potential.
4. The action potential travels along the sarcolemma and into the T tubules which carry the wave of depolarization into the muscle cell.
5. The action potentials of the T tubules stimulate the release of calcium from the sarcoplasmic reticulum.
6. Calcium released into the sarcoplasm binds to troponin molecules, causing a change in its structure that results in the attached tropomyosin to shift position on the actin filament, which exposes attachment sites for the myosin head.
7. The myosin head (cross-bridges), previously activated by the hydrolysis of ATP to ADP and P, attaches to actin.
8. Once attached to actin, the myosin head undergoes a power stroke and pulls the thin filaments over the thick filament. The ADP and P molecules are released.
9. Fresh ATP binds to the myosin head and energizes the myosin head allowing the cross-bridge to detach from actin. The myosin head bends back to its resting position and will repeat the contraction cycle as long as calcium remains attached to troponin.
10. When action potentials stop being produced, the sarcoplasmic reticulum actively retrieves calcium via and tropomyosin moves over the myosin binding site on the actin filament preventing attachment of the myosin crossbridge.

Rigor Mortis
• Upon death, muscle cells are unable to prevent calcium entry.
  – Since there is no ATP made postmortem, the myosin cannot unbind and the body remains in a state of muscular rigidity for a couple days.

Muscle Hypertrophy
  • Hypertrophy:
    – **Muscle Hypertrophy**: Enlargement of existing myofibers due to increased numbers of:
      • myofibrils, mitochondria, sarcoplasmic reticulum, and nutrient storage (glycogen)
    – **Hyperplasia**: An increase in the number of fibers.
      • Rare to contribute to muscle hypertrophy after birth

Muscle Atrophy
  • Atrophy
    – Reduction in size of a
      • In muscles, it’s often caused by disuse or denervation.
      • Muscle fibers become smaller and weaker due to a decrease in the number of myofibrils within a muscle fiber.
Control of Muscle Contractile Force
- The force of a contraction is increased in two ways: **Motor unit recruitment** and by **frequency of muscle fiber stimulation**.
- **Motor Unit Recruitment (Summation):**
  - Recruitment is one factor responsible for producing smooth movements.
  - **Frequency of stimulation:** Increasing the frequency of stimulation of
    - Frequency refers to the number of times a motor neuron is stimulating its muscle fibers and can be divided into incomplete and complete tetany.
    - **Incomplete (Unfused) tetanus:** Muscle fibers are stimulated at a rate where they don't completely relax before the next stimulus.
      - Have partial relaxation between twitches.
      - **Twitch:** A single rapid contraction and relaxation of a muscle fiber or group of muscle fibers.
    - **Complete (Fused) tetanus:** High rate of stimulation where the muscle fibers do not relax between stimuli.

Types of Contractions
- Contractions can be classified as **isometric** or **isotonic**:
  1. **Isometric** (Iso= same, metr=measure)
     - Contraction in which there is no appreciable shortening of the muscle.
     - Example: Pushing on a brick wall
  2. **Isotonic** (Iso= same, ton=tension)
     - The force of contraction remains constant throughout the shortening process
     - Example: Picking up something that you can lift through the complete motion such as curling your physiology textbook

Muscle Contraction and ATP
- ATP is necessary for muscle contraction.
- ATP is supplied to muscles from three sources:
  1. **Aerobic Respiration**
  2. **Aerobic Respiration**
    - ATP production without oxygen
  3. **Creatine phosphate**
Creatine Phosphate
- Quick way to replenish ATP during the initial phase (~15 seconds) of heavy exercise.
  - **Creatine phosphate** adds a high energy phosphate group to ADP forming ATP.
  - Creatine phosphate provides for short bursts of energy
    - Ex:

- **Creatine**: Produced by the liver, kidneys and pancreas and
  - **Creatine monohydrate** dietary supplements can increase muscle phosphocreatine by 15% – 40%
    - Found to increase muscle mass, strength, and performance of high-intensity exercise.
    - High doses can damage liver and kidneys.

Oxygen Debt
- **Oxygen dept**: The amount of oxygen needed (heavy breathing) to restore normal conditions after exercise has stopped.
- **Restoration includes**:
  - Replenish the oxygen withdrawn from myoglobin in muscle and hemoglobin in blood cells.
  - Aerobic metabolism to make ATP which is used to:
    - Replenish the Creatine phosphate (phosphagen) system
    - Power the Na+/K+ pump so as to restore resting ionic conditions within the cell.
    - Replenish the glycogen stores

Muscle Fatigue
- **Muscle fatigue**: The inability of the muscle to contract forcefully after long periods of activity.
  - Results from:
    - Depletion of ATP, glycogen, and/or creatine phosphate
    - Reduced release of Ca2+ ions from sarcoplasmic reticulum.
    - Insufficient oxygen to make ATP
    - Failure of nerve impulses to release enough acetylcholine.

Clinical Perspectives
Myasthenia Gravis
- **Autoimmune disease**: Antibodies block and destroy
  - Results in progressive weakening of the skeletal muscles. Why?
  - Treated with anticholinesterases such as neostigmine or physostigmine. These decrease the activity of acetylcholinesterase.
    - *Why would this help someone with myasthenia gravis?*
Botulism/Botox

- **Botulism:** A form of food poisoning
  - Caused by *botulinum toxin*, produced by the bacterium *Clostridium botulinum*.
  - Toxin inhibits acetylcholine release at
    - Marked by muscle paralysis, vomiting, visual disorders, and death (asphyxiation) if untreated and/or the poison amount is too great
- **Botox** is used medically for:
  - Facial wrinkles
  - Severe underarm sweating
  - **Cervical dystonia** - a neurological disorder that causes severe neck and shoulder muscle contractions
  - **Blepharospasm** - uncontrollable blinking

Nerve Gas

- A number of pesticides and nerve gases work by
  - If acetylcholine degradation is blocked, the muscle continues to contract and paralysis ensues.

Dystrophin muscle protein

- **Dystrophin:** A cytoskeleton protein that links thin filaments of the sarcomere to integral membrane proteins of the sarcolemma.
  - In connection with associated proteins, functions to reinforce the sarcolemma and help transmit the tension generated by the sarcomeres to the tendons.

Muscular Dystrophy

- Refers to a group of inherited muscle-destroying diseases that cause progressive degeneration of skeletal muscle.
  - Characterized by the replacement of degenerating skeletal muscle by
    - **Duchenne muscular dystrophy** is most common form
      - Little to no dystrophin protein made - sarcolemma lacks support
      - Results: Sarcolemma tears during muscle contraction and myofibers slowly rupture and die.
      - Disorder apparent between ages of 2-5 years
        - By age 12, are usually in a wheelchair
        - By age 20 – 30, death due to respiratory or cardiac failure
Muscle Fiber Types

• Every muscle in the body is composed of a mixture of slow and fast muscle fibers, with other fiber types gradated between these two extremes. The types of muscle fibers is based on their contraction speed and major pathways for forming ATP.
  - **Speed of Contraction**: Slow and fast fibers are based on how fast their myosin ATPases split ATP resulting in filaments sliding over each other.
  - **Major pathways for forming ATP**: Oxidative fibers rely mostly on aerobic pathways; glycolytic fibers rely more on anaerobic glycolysis.

Slow Fibers (Type I or Red or Slow Twitch)

• **Slow fibers**: Specialized for endurance; high fatigue resistance –
  - Contract slowly because its myosin ATPases splits ATP at a slow rate.
  - Depends on oxygen for aerobic pathways to make ATP.
  - **Abundant capillaries, mitochondria, and myoglobin content** to support increased blood flow and high levels of oxidative metabolism.
    - **Myoglobin**: Pigment in muscle specialized for oxygen storage until needed and gives the muscle cell a reddish color thus called red fibers.
  - Example: soleus muscle contains more slow fibers than fast fibers.

Fast Fibers (Type II or White or Fast Twitch)

• **Fast twitch**: Split ATP at a rapid rate and thus have a fast contraction velocity after stimulation, but fatigue rapidly.
  - Contain densely packed myofibrils, large glycogen reserves, and relatively few mitochondria and myoglobin.
  - **Anaerobic metabolism** – Less extensive blood supply and fewer mitochondria because oxidative metabolism is of secondary importance, most ATP production is without oxygen.
  - Does not contain a lot of myoglobin and appear white, thus called white fibers.
  - Best suited for short term, power activities such as
  - Example: Most arm muscles have more fast fibers than slow fibers.

White vs Dark Meat

• Chicken’s breast is composed mainly of fast-twitch fibers giving the characteristic white meat appearance.
  - Relatively little blood supply and less myoglobin than dark meat
  - Muscles adapted to contract rapidly for

• Chicken’s leg muscles are composed of slow-twitch fibers - meat is dark.
  - Muscles adapted for endurance – running
  - Darker appearance is partly due to a richer blood supply and presence of myoglobin.
  - **Myoglobin** is an oxygen-carrying pigment of muscle tissue – it stores oxygen temporarily until the muscle needs it.
Muscle Response to Exercise
- Exercise can induce two types of changes in muscle fibers: Changes in their oxidative ATP synthesizing capacity and muscle size.
  - **Improvement in Oxidative Capacity (ATP production)**
    - Regular aerobic endurance exercise increases a number of factors including the quantity of mitochondria, number of capillaries supplying blood to these fibers, and myoglobin content.
    - Muscles can use oxygen more efficiently and therefore
      - Targets slow oxidative fibers.
  - **Muscle Hypertrophy**
    - Regular anaerobic, short duration, high intensity resistance training, such as weight lifting cases muscle hypertrophy.
    - Most of the fiber thickening results from increased synthesis of myosin and actin filaments, which permits a greater opportunity for cross-bridge interaction and consequently increases muscles’ contractile strength.
    - Targets fast fibers