Ch 6: Muscle Physiology

Objectives:
1. Review 3 muscle types and how they are regulated.
2. Review muscle anatomy.
3. Slow vs fast twitch muscle fibers
4. Sliding filament theory of how muscles contract and relax.
5. Types of muscle contraction.
6. Factors that influence muscle contractile strength.
7. Energetics of muscle use
8. Muscle growth & repair
10. Muscle sensory organs

1. Differences in function of the 3 muscle types:

<table>
<thead>
<tr>
<th>a) Skeletal Muscle</th>
<th>b) Cardiac Muscle</th>
<th>c) Smooth Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voluntary (somatic motor)</td>
<td>Involuntary (autonomic motor)</td>
<td>Involuntary (autonomic motor)</td>
</tr>
</tbody>
</table>

QUEST:
Epineph. binding to β2-adrenergic receptors causes ____________
Epineph. binding to α-adrenergic receptors causes ____________
2. Review Anatomy of Skeletal Muscle:

**muscle organ** = whole muscle group, made of muscle fascicles
(e.g. biceps brachii, triceps brachii)

**fascicle** = bundle of muscle fibers that make up muscle organ.

**fiber** = single muscle cell that a somatic motor neuron stimulates. Many fibers make up a muscle fascicle. Each fiber made of many muscle myofibrils.

**myofibril** = A fiber is made of many myofibrils. Each myofibril contains thousands of sarcomeres.

**sarcomere** = functional unit of muscle contraction. Has “myofilaments” actin and myosin.
### 3. Slow vs Fast Twitch Muscle Fibers: Pg 109

<table>
<thead>
<tr>
<th>Red (slow twitch) fibers</th>
<th>White (fast twitch) fibers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dark fibers – have more myoglobin &amp; capillaries</td>
<td>Have less myoglobin, fewer capillaries</td>
</tr>
<tr>
<td>Many mitochondria for ATP (for aerobic metabolism)</td>
<td>Fewer mitochondria – more likely to resort to anaerobic metabolism</td>
</tr>
<tr>
<td>Steady but little power</td>
<td>Short bursts of high power</td>
</tr>
<tr>
<td>For endurance aerobic activity</td>
<td>For short duration intense activity</td>
</tr>
<tr>
<td>Fatigues slowly</td>
<td>Fatigues quickly</td>
</tr>
<tr>
<td>Find in legs, postural, &amp; core muscles</td>
<td>Ex. arm muscles</td>
</tr>
</tbody>
</table>

### 4. Sliding Filament Theory of Muscle Contraction: Pg 109 - 110

![Sliding Filament Theory Diagram](image)
Review of Neuromuscular Junction (*review from Ch 4*)

Neuromuscular junction = between a single motor neuron and the muscle fiber it innervates.

If it’s a somatic motor neuron stimulating a skeletal muscle cell the following happens:

- **Acetylcholine** released by presynaptic motor neuron crossed the synapse
- binds to **nicotinic cholinergic** receptors on skeletal muscle fibers.
- Binding of receptor opens **Na⁺** ion channels
- **Na⁺** enters muscle cell & causes AP (or EPSP),
- AP causes **Ca⁺** release from sarcoplasmic reticulum.

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Sarcomere contains myofilaments Actin & Myosin:

A) **Actin** = thin filament with active sites, and proteins troponin & tropomyosin.
   > **active sites** = where myosin heads want to bind to create a “crossbridge”

   > **troponin** = protein that Ca⁺ binds to.

   > **tropomyosin** = protein that normally blocks active sites. It moves out of the way when troponin binds to Ca⁺2.

B) **Myosin** = thick filament with “heads” that bind to active sites on actin
Announcement

Update to syllabus:

Exam 4, scheduled for Nov 25\textsuperscript{th}.

FINAL Exam (a 5\textsuperscript{th} exam) scheduled for Fri Dec 4\textsuperscript{th} at 8:30 am.
> is cumulative, and chance to drop lowest exam grade
> is optional

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4. Sliding Filament Theory of Muscle Contraction

- ACh binds to nicotinic receptor
- Opens Na\textsuperscript{+} channels
- AP formed, goes down transverse tubules
- Causes Ca\textsuperscript{2+} release from sarcoplasmic reticulum
3. **Sliding Filament Theory of Muscle Contraction: the sequence of action.**

1. **Somatic motor neuron** releases **ACh** into synapse at neuromuscular junction with skeletal muscles.

2. ACh binds to **nicotinic cholinergic** receptors.

3. Opens **Na+** channels, **Na+** enters cell, an **AP (or EPSP)** forms.

4. AP moves to T-tubules of cell.

5. AP causes **Ca^{2+}** release from **sarcoplasmic reticulum** of muscle cell.

6. **Ca^{2+}** binds to **troponin** (protein on actin).

7. This causes **tropomyosin** to move off **active sites** on actin.

8. **Myosin heads** “grip” active sites (forms **crossbridges**)

How ATP and ADP is used during muscle contraction

Myosin heads “pulling” on actin involves: “Grip & Re-grip” Action

1) Myosin has ADP – forms crossbridge
2) ADP released = Power Stroke (myosin pulls on actin)
3) ATP binds
   - myosin breaks crossbridge
   - ATP pumps Ca^{2+} into sarcoplasmic retic.
4) ATP converted to ADP
   - Ready to bind again.

Click HERE for YouTube video

ATP and Rigor Mortis

= sustained whole body muscle tetany 12-18 hrs post-mortem due to lack of ATP in muscle cells at death (No ATP – no breaking of crossbridges between actin & myosin).

At 24 – 36 hrs post-mortem body relaxes because actin & myosin degradation (necrosis).
5. Factors Influencing Muscle Contractile Force:

Types of muscle contractions

A) Isotonic contraction = muscle shortens

B) Isometric contraction = muscle generates tension but doesn’t shorten

Review

- Contrast how 3 muscle types function
- Muscle anatomy
  - organ, fascicles, fibers, myofibrils, and sarcomere arrangement of myofilaments (actin and myosin)
- Slow twitch vs fast twitch muscle fibers
- Neuromuscular junction
- Sliding filament theory of muscle contraction
- The use of ATP and ADP in muscle contraction
- Types of muscle contraction (isotonic vs isometric)
**6. Factors Influencing Muscle Contractile Strength:**

**Motor unit** = motor neuron and all the muscle fibers (cells) it innervates.

- There can be as many as 150 muscle fibers innervated by 1 motor neuron. It depends on the “Power versus Precision” principle (see later).

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**Table:**

<table>
<thead>
<tr>
<th>Muscle Precision</th>
<th>vs</th>
<th>Muscle Power?</th>
</tr>
</thead>
<tbody>
<tr>
<td>- one motor neuron innervates few muscle fibers.</td>
<td>- one motor neuron innervates many muscle fibers</td>
<td></td>
</tr>
</tbody>
</table>
Muscle Contractile Strength Depends On:

1. The number of fibers responding:
   > If more fibers respond = more force produced
   > If fewer fibers respond = less force produced

2. Strength of stimulus: (for 1 motor neuron)
   > If stimulus strong = more force produced
     (a lot of ACh)
   > If stimulus weak = less force produced
     (a little ACh)
     “Graded potential”
   > If stimulus VERY strong – get “Recruitment”
     - more than one motor neuron involved & all its muscle fibers.
     - produced greater force than with 1 motor neuron.

Muscle Contractile Strength Depends On:

3. Frequency of stimulus:
   A) Muscle Twitch = Single stimulus produces single muscle fiber contraction

B) Treppe = muscle “warm up”. After repeated low frequency stimuli each muscle contractile force increases until reaches max. force. Muscle can relax in between stimuli (force goes back to baseline).

C) Summation = repeated high frequency stimuli
   Result is each contraction has cumulative increase in force, BUT so rapid muscle cannot relax (don’t go to baseline).

D) Muscle Tetanus = repeated highest frequency stimuli produces greatest possible contractile force BUT comes at cost. Sustained muscle contraction leads to muscle fatigue and failure.
Sleep Twitches

**Sleep Twitch** - myoclonus or myoclonic jerk (a.k.a. hypnagogic massive jerk)

= involuntary muscle movement as enter REM sleep.

Might be due to change in muscles as go from conscious to unconscious – involves GABA inhibition of muscles.

Review

- Motor unit
- Muscle precision Vs power
- Factors influencing muscle contractile strength
  - # muscle fibers responding
  - Strength of the stimulus
  - Frequency of stimulus
    (muscle twitch, treppe, summation, & tetanus)
Muscle Fatigue

**Depletion of:**
- O2
- ATP
- Glycogen
- Myoglobin

**Accumulation of:**
- CO2
- ADP
- Lactic acid
- Phosphate (from using creatine phosphate)

**QUEST:**
How is lactic acid removed from the bloodstream?

**Phosphocreatine =**
natural molecule stored in large supply in resting muscle, is needed to convert ADP back into ATP. (donates a phosphate to ADP to make ATP)

**Creatine phosphokinase (CK or CPK) =**
enzyme (in skeletal muscle, brain, and heart), which is needed to convert creatine into phosphocreatine.

Phosphocreatine is needed to make ATP in tissues requiring high ATP.
Different isoforms of CPK for different organs can be elevated due to death of tissues:

1. **CPK isoform MM** = elevated form associated with diseased skeletal muscle, like in muscular dystrophy. Clinical App ONLINE

2. **CPK isoform BB** = elevated form associated with damaged brain.

3. **CPK isoform MB** = elevated form associated with damaged heart.
8. Muscle Growth & Repair

Muscle growth & repair:

Myostatin

= muscle stem cells that are activated with muscle injury. Makes new muscle fibers

Myostatin

= inhibits muscle growth & repair by inhibiting satellite cells.

Elderly people with muscle atrophy have high myostatin levels.

When myostatin is inhibited - get excessive muscle growth!

9. Muscle Disorders

Muscle atrophy = shrinking of muscle tissue.

Due to many possible factors:

- Lack of use (couch potatoes)
- Broken bone healing
- Injury or disease of muscle (e.g. MD, myasthenia gravis)
- Injury to nerves (e.g. ALS)

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9. Muscle Disorders

Muscle cramp = painful cramp from strenuous activity, lactic acid buildup. (Could also be due to dehydration & loss of electrolytes).

Muscle spasms = muscle seizure or convulsion.

Muscle sprain = joint injury involving a stretched or torn ligament

Tx for sprain = RICE
- Rest
- Ice
- Compression
- Elevate

Muscle strain (pulled muscle) = a muscle, or its tendon, is overstretched or torn.
**9. Muscle Disorders**

**Muscle clonus** = when nerve cells that control the muscles are damaged, causing involuntary muscle contractions or spasms.

Usually caused by lesions on motor neurons. Could also be problem in CNS like multiple sclerosis, cerebral palsy, Huntington disease, brain and spinal cord injuries, and stroke.

**Dermatomyositis** = (pronounce “dur-muh-tow-mai-uh-sai-tuhs“ = disorder of muscle inflammation (or myopathy).

> 1 / 100,000
> women predominantly

**Presentation:**
- Muscle weakness that progresses
- Affects muscles close to trunk (hip, shoulder, neck)
- Skin rashes

**TX:**
- anti-inflammatory
  - steroids (prednisone)
  - NSAIDs
  - sunscreen to protect rashes.

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9. Muscle Disorders

2) Muscular Dystrophy (Duchenne’s)

- Most common form of MD.
- Sex-linked recessive genetic disorder (found more in males)
- Early onset in children = walking & balance problems. Muscle atrophy leads to loss of muscle function.
- Loss of dystrophin thought to influence.

“dystrophin” = protein needed for muscle function.

3) ALS (Amyotrophic Lateral Sclerosis)

a.k.a. Lou Gherig’s disease

= loss of motor neurons, leads to muscle atrophy, eventual paralysis.

> Tends to start in motor neurons to hands and feet
> Eventually affects respiratory muscles.
> Life expectancy after diagnosis < 5 yrs.
> Reason?
- Loss of superoxide dismutase (an antioxidant that prevents cell death)
- Glutamate toxicity = excess brain stimulation
  > glutamate supposed to be taken up by astrocytes. (astrocyte problem?)
  > excess glutamate also thought to play role in Parkinson’s & Alzheimer’s disease) Clinical App
4) **Myasthenia gravis** = autoimmune attack on nicotinic ACh receptors of skeletal muscles. Loss of motor control & tone = hypotonia and muscle atrophy.

> Loss of motor neuron stimulation = muscle atrophy.

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5) **Tetanus** = buildup of tetanus toxin from Clostridium tetani bacteria. Toxin acts as an ACh agonist, promoting ACh stimulation of skeletal muscle contraction. Causes spastic paralysis or hypertonia.

6) **Botulism** = buildup of botulism toxin from Clostridium botulinum bacteria. Prevents ACh release from motor neurons. Muscles not get stimulus to contract. Causes flaccid paralysis or hypotonia.
Review

• Energetics of muscle contraction
  – ATP & ADP
  – Muscle fatigue and depletion vs accumulations of metabolic products
  – Creatine
  – CPK (CPK-BB, CPK-MB, CPK-MM)

• Muscle Growth & Repair
  – Satellite cells vs Myostatin

• Muscle Disorders:
  > muscle spasm, cramp, sprain, strain
  > Dermatomyositis
  > Duchenne’s MD
  > ALS
  > Myasthenia gravis
  > Toxins (tetanus & botulism)

10. Muscle Sensory Organs Provide Sensory Feedback to Brain for Regulating Muscle Tone & Contraction.

2 types of Muscle Sensory Organs:

1. Golgi tendon organs:
   - Sense Tension (pull) a muscle puts on a tendon.
10. Muscle Sensory Organs Provide Sensory Feedback to Brain for Regulating Muscle Tone & Contraction.

2 types of Muscle Sensory Organs:

1. Golgi tendon organs:
   - Sense Tension (pull) a muscle puts on a tendon.

2. Muscle Spindle apparatus:
   - Senses muscle Stretch
     > Sudden rapid stretch = more contractile force
     > Slow stretch = less contractile force

Spindle Contains:

A) Extrafusal fibers — thick contracting fibers, faster, thicker, stronger, more numerous.
   - Involved in *isotonic* contraction (muscle shortening)

B) Intrafusal fibers — thin stretch fibers, slower, thinner, weaker, less numerous.
   - Involved in *isometric* contraction (muscle tone, no shortening)

11. Voluntary vs Spinal Reflex Muscle Movement

**Somatic Motor Neurons & Skeletal Muscle**

- **Somatic neurons** synapse with **skeletal muscle fibers** at neuromuscular junctions for **VOLUNTARY movement**.

If someone tells you to contract your quadriceps muscles after they are touched:

- First, touch receptors on leg stimulated, send ascending info to sensory cortex.
- Sensory info shared with motor cortex. Motor command from motor neurons descends spinal cord.
- Somatic motor neurons (of spinal nerves) release ACh
  - Binds to nicotinic ACh receptors on skeletal muscles
  - Evokes EPSPs by opening Na+ channels
  - Causes contraction
### 4 Spinal reflexes (Involuntary Movement):

#### I. Knee-jerk reflex

1) Tapping patellar tendon stretches tendon & quadriceps muscle - stimulates **spindle fiber** (stretch receptor) in muscle

2) Stimulating spindle fiber **evokes action potentials in sensory neuron**

3) Sensory neuron synapses **directly** with alpha somatic motor neuron in spinal cord.

4) Alpha motor neuron stimulates contractile muscle fibers

This is ex. of **monosynaptic reflex**

> Only one synapse is crossed (in spinal cord)
II. Inhibitory Stretch Reflex (protects tendon from excessive muscle contractile force)

1) Muscle is stretched, muscle tendon is stretched, which stimulates AP in Golgi tendon organ (a sensory organ)

2) Sensory neuron goes into spinal cord & stimulates (+) an interneuron

3) Interneuron stimulates inhibitory (-) neurotransmitter to alpha motor neuron

4) Effect = motor neuron inhibited to

5) Muscle relaxes to reduces tension in tendon to prevent damage from excessive stretching

This is ex. of disynaptic stretch reflex = Two synapses are crossed in spinal cord

III. Reciprocal Innervation

How all our muscles work. Primary muscle is stimulated to contract while, simultaneously, the antagonist muscle is inhibited.

1) Stretch of primary muscle & tendon stim. sensory neuron. Sensory info enters dorsal spinal cord, crosses over to ventral horn & does two things:

2) Positive (+) stim. of primary muscle to contract.

3) Inhibition (-) of antagonist muscle (stays relaxed).
IV. Crossed Extensor Reflex or double reciprocal innervation

Ex. Painful stimulus on right foot stim sensory neuron, goes into dorsal horn spinal cord. Crosses to ventral horn on left and right sides of cord and does two things:

1) Right leg Flexors contract (+) and extensors relax (-) to withdraw injured foot on R.
2) Left leg, Extensors contract (+) and flexors relax (-) to put leg down & support body weight.
Review

- **Muscle sensory organs:**
  - Golgi tendon organ
  - Spindle apparatus (intrafusal fibers & extrafusal fibers)

- **Voluntary reflex**
  - Involves sensory neurons, spinal cord, brain, and motor neurons
    (longer, slower pathway)

- **Spinal reflex**
  - involves sensory neurons, spinal cord, and motor neurons
  - shorter, faster pathway under autonomic control

  Ex. Knee jerk reflex (monosynaptic)
      Inhibitory stretch reflex (disynaptic)
      Reciprocal innervation (contract one muscle & inhibit its antagonist)
      Crossed extensor reflex (usually in limbs supporting body)