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 influences 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>
<tr>
<td>Neurotransmitter = _______</td>
<td>Parasymp. Neurotrans. = _______</td>
<td>ACh with muscarinic cholinergic receptors,</td>
</tr>
<tr>
<td>Receptor = _______</td>
<td>Receptor = _______</td>
<td>Epinephrine with B2 &amp; ( \alpha )-adrenergic receptors</td>
</tr>
<tr>
<td>&amp; also Glycine &amp; GABA with</td>
<td>Sympath. Neurotrans= _______</td>
<td></td>
</tr>
<tr>
<td>muscarinic receptors (Ch 4)</td>
<td>receptor = _______</td>
<td></td>
</tr>
<tr>
<td>(for IPSPs – muscle relax)</td>
<td>Effect = ______________</td>
<td></td>
</tr>
<tr>
<td>Requires somatic motor</td>
<td>Is “autorhythmic”, but HR influenced</td>
<td>Is “autorhythmic” – influenced by</td>
</tr>
<tr>
<td>neuron stimulus to contract</td>
<td>by ACh (( \downarrow )HR) &amp; epinephrine (( \uparrow )HR)</td>
<td>ACh or epinephrine</td>
</tr>
<tr>
<td>Fastest contraction speed</td>
<td>Intermediate contraction speed</td>
<td>Slowest contraction speed</td>
</tr>
<tr>
<td>Prone to fatigue</td>
<td>Fatigue resistant</td>
<td>Fatigue resistant</td>
</tr>
</tbody>
</table>

QUEST:
Epineph. binding to \( \beta 2 \)-adrenergic receptors causes ________________________________

Epineph. binding to \( \alpha \)-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.

**fiber** = single muscle cell that a somatic motor neuron stimulates. Contains muscle myofibrils.

**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>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></td>
</tr>
</tbody>
</table>

**Review of Neuromuscular Junction (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:**

- ________ released by presynaptic motor neuron crossed the synapse
- binds to _____________________________ receptors on skeletal muscle fibers.
- Binding of receptor opens _____________ ion channels
- _____ enters muscle cell & causes AP (or EPSP), which causes Ca+ release from sarcoplasmic reticulum.

**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

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

2. ACh binds to ______________________ receptors.

3. Opens _______channels, _______ enters cell, an AP (or EPSP) forms.

4. AP moves to T-tubules of cell.

5. AP causes ________ release from sarcoplasmic reticulum of muscle cell.

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

7. This causes ______________________ to move off active sites on actin.

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


4. Sliding Filament Theory of Muscle Contraction

1. ACh binds to nicotinic receptor

2. Opens Na+ channels

3. AP formed, goes down transverse tubules

4. Causes Ca^{+2} release from sarcoplasmic reticulum

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ACh binds to nicotinic receptor

Opens Na+ channels

AP formed, goes down transverse tubules

Ca^{+2} release from sarcoplasmic reticulum

---

1. Somatic motor neuron

2. ACh

3. Na+ channels

4. AP

5. Ca^{+2}

6. Actin-binding protein

7. Myosin heads

8. Crossbridges

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

1 & 2) Myosin has ADP – forms crossbridge

3 & 4) ADP released = Power Stroke
(myosin pulls on actin)

5) ATP binds
-myosin breaks crossbridge
-ATP pumps Ca^{2+} into sarcoplasmic retic.

6) ATP converted to ADP
- Ready to bind again.

Click HERE for YouTube video
How ATP and ADP is used during muscle contraction

“Grip & Re-grip” Action of Myosin with Actin requires ADP & ATP

- **ADP** is needed for myosin head to grip active site and to pull on actin.

- **ATP** is needed for myosin head to release active site (break crossbridge) and to pump Ca\(^{2+}\) back into sarcoplasmic reticulum.

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**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).
Types of muscle contractions

A) Isotonic contraction =

B) Isometric contraction =

5. Factors Influencing Muscle Contractile Force:

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** =

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

![Diagram of motor units and muscle fibers]

**Tradeoff:**

**Muscle Precision** vs **Muscle Power**

![Images of surgical procedure and patient]
**Muscle Contractile Strength Depends On:**

1. **The number of fibers responding:**
   - If more fibers respond = ______________
   - If fewer fibers respond = ______________

2. **Strength of stimulus:** (for 1 motor neuron)
   - If stimulus strong = ______________
   - If stimulus weak = ______________
   - If stimulus VERY strong – get “Recruitment”
     - more than one motor neuron involved & all its muscle fibers.
     - produced greater force than with 1 motor neuron.

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.
     [see tension go back to baseline between stimuli!]
   - **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

<table>
<thead>
<tr>
<th>Depletion of:</th>
<th>Accumulation of:</th>
</tr>
</thead>
<tbody>
<tr>
<td>O2</td>
<td>CO2</td>
</tr>
<tr>
<td>ATP</td>
<td>ADP</td>
</tr>
<tr>
<td>Glycogen</td>
<td>Lactic acid</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>Phosphate (from using creatine phosphate)</td>
</tr>
</tbody>
</table>

QUES:
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.

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**Different isoforms of CPK for damage in different organs: Clinical App** [ONLINE]

1. **CPK isoform MM** =

2. **CPK isoform BB** =

3. **CPK isoform MB** =
8. Muscle Growth & Repair

Muscle growth & repair:
= 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 =

Due to many possible factors:

➢ .
➢ .
➢ .
➢ .

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9. Muscle Disorders

Muscle spasms =

Muscle cramp =

Pg 112-113

9. Muscle Disorders

Muscle sprain =

Tx for sprain = RICE

Muscle strain (pulled muscle) =

Pg 112-113
Dermatomyositis = 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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A) 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.

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B) **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 & Alzheimers disease) **Clinical App**

C) **Myasthenia gravis** =

> Loss of motor neuron stimulation = muscle atrophy.
REVIEW!

**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.

**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)
2 types of Muscle Sensory Organs:

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

2. Muscle spindle apparatus:
   - Sense amount of muscle Stretch

2 Muscle Sensory Receptors:

1. Golgi Tendon organs:
   - Senses muscle pull (Tension) 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 isometric contraction (muscle shortening)
B) Intrafusal fibers – thin stretch fibers, slower, thinner, weaker, less numerous. Involved in isotonic contraction (muscle tone, no shortening)
Neural control of skeletal muscle

2 types of muscle motor neurons:
1) Upper motor neurons (“interneurons”)
   - In primary motor cortex
   - Communicate w/lower motor neurons

2) Lower motor neurons = “somatic motor neurons”
   - In brainstem & ventral spinal cord.
   - Extend into major nerves of body
     2 types of lower motor neurons:
     1. alpha
     2. gamma

Activity of lower motor neurons of brainstem & spinal cord regulated by feedback from:
   A. upper motor neurons in primary motor cortex.
   B. feedback from muscle “sensory organs”
      (golgi tendon & muscle spindle apparatus)

2 types of Lower Motor Neurons (in brainstem & spinal cord):
1) Alpha motor neurons:
   - Innervate extrafusal (contracting) muscle fibers of muscle spindle
   - Result in muscle isotonic contraction (muscle shortens)

2) Gamma motor neurons:
   - Innervate intrafusal (stretch) muscle fibers of muscle spindle
   - Result in muscle isometric contraction (doesn’t shorten)
   - Provides muscle “tone”, more sensitive to stretch.

***Stimulation of both alpha & gamma lower motor neurons, by upper motor neurons in primary cortex at the same time, called co-activation
11. Voluntary vs Spinal Reflex Muscle Movement

Somatic Motor Neurons (voluntary!) & 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):

1. 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

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 (spans distance between dorsal horn to ventral horn)

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

4) Effect = 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

1) Stretch of primary muscle & tendon stimulates 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.

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**IV. Crossed Extensor Reflex or double reciprocal innervation**

1. About to step with right leg
2. Right foot steps on tack
3. Right leg begins to flex, while left leg begins to extend
4. Right leg is flexed, left leg is extended
5. Only afterward do you notice the pain!
## Review

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

- **Neural control of skeletal muscles**
  - Upper motor neurons (in brain’s motor cortex)
  - Lower motor neurons (brainstem, spinal cord to spinal nerves of PNS)
    - Alpha and gamma lower motor neurons

- **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)