Ch 9: Muscle Physiology

Objectives:
1. Review 3 muscle types and how they are regulated.
2. Review muscle anatomy.
4. Energetics of muscle contraction.
5. Factors that influence muscle contractile strength.
6. Muscle growth & repair
7. Common muscle disorders.
8. 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 = ( \text{ACH} )</td>
<td>Parasymp. Neurotrans. = ( \text{ACH} )</td>
<td>ACh with muscarinic cholinergic receptors,</td>
</tr>
<tr>
<td>Receptor = ( \text{nicotinic} ) (for EPSPs) &amp; also Glycine &amp; GABA with muscarinic receptors (Ch 4) (for IPSPs – muscle relax)</td>
<td>Receptor = ( \text{muscarinic} ) cholinergic</td>
<td>Epinephrine with B2 &amp; ( \alpha )-adrenergic receptors</td>
</tr>
<tr>
<td>Requires somatic motor neuron stimulus to contract (not “autorhythmic”)</td>
<td>Is “autorhythmic”, but HR influenced by ACh (( \downarrow ) HR) &amp; epinephrine (( \uparrow ) HR)</td>
<td>Is “autorhythmic” – influenced by 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>

QUES:
Epineph. binding to \( \beta_2 \)-adrenergic receptors causes **bronchodilation & vasodilation** of arterioles of skeletal muscle

Epineph. binding to \( \alpha \)-adrenergic receptors causes **GI activity**
Cardiac muscle versus smooth muscle:

BOTH are:
- **autorhythmic** (stimulus for contraction initiated from within)
- regulated by autonomic motor N.S.
- involve Ca\(^{2+}\) release BUT:

**REVIEW!!!**

1. **Cardiac Muscle:**
   - AP starts in SA node (pacemaker cells)
   - Rate of contraction influenced sympathetic vs parasympathetic stim.
     - ↑ heart rate by epinephrine & \(\beta\)1-adrenergic receptors
     - ↓ heart rate by ACh & muscarinic cholinergic receptors

2. **Smooth Muscle:** Stimulated by a variety of hormones (ACh, epinephrine)
   - ↑ GI activity through ACh and muscarinic cholinergic receptors
   - ↓ GI activity through epineph & \(\alpha\)-adrenergic receptors.
   - bronchodilation through epineph & \(\beta\)2-adrenergic receptors.
   - bronchoconstriction through ACh & muscarinic cholinergic receptors.
   - Muscle arteriole smooth muscle **vasodilation** to skeletal muscle through epineph & \(\beta\)2-adrenergic receptors.
   - GI arteriole smooth muscle **vasoconstriction** through epineph & \(\alpha\)-adrenergic receptors.

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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.
**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

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**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:

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

1. **Somatic motor neuron** releases \( \text{ACh} \) into synapse at neuromuscular junction with skeletal muscles.

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

3. Opens \( \text{Na}^+ \) channels, \( \text{Na}^+ \) enters cell, an **AP (or EPSP)** forms.

4. AP moves to T-tubules of cell.

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

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

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

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


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*Fig. 9.15*
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.
“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.
**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).

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**4. The Energetics of Muscle Contraction (Muscle Fatigue)**

**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>

Cori Cycle =
**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.

\[
\text{Creatine} \xrightarrow{\text{CPK}} \text{Phosphocreatine}
\]

Phosphocreatine is needed to make ATP in tissues requiring high ATP.

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**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 Pg 239 and ONLINE

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

3. **CPK isoform MB** = elevated form associated with damaged heart.
Review

• Contrast how 3 muscle types function
• Muscle anatomy
  – organ, fascicles, fibers, myofibrils, and sarcomere
  arrangement of myofilaments (actin and myosin)
• Neuromuscular junction
• Sliding filament theory of muscle contraction
• Energetics of muscle contraction
  – ATP & ADP
  – Muscle fatigue and depletion vs accumulations of metabolic products

5. Factors Influencing Muscle Contractile Force:

Types of muscle contractions

A) Isotonic contraction =
  • muscle shortens (move object)

B) Isometric contraction =
  • muscle doesn’t shorten (stays same size)
5. Factors Influencing Muscle Contractile Force:

Motor unit = One motor neuron & all muscle fibers it connects to.

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

5. Factors Influencing Muscle Contractile Force:

Tradeoff:

Muscle Precision vs Muscle Power?

- one motor neuron innervates few muscle fibers.
- one motor neuron innervates many muscle fibers
Muscle Contractile Force Depends On:

1. The number of fibers responding:
   > If more fibers respond = More Force
   > If fewer fibers respond = Less Force

2. Strength of stimulus: (for 1 motor neuron)
   > If stimulus strong = more Force
     (lots of neurotransmitter)
   > If stimulus weak = less Force
     only 1 motor neuron involved
   > 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.

Review

Factor influencing muscle contractile force:

- Types of muscle contraction
  - Isotonic (concentric, eccentric), isometric
- Motor unit
- Muscle precision Vs power
- Contractile force depends on
  - # muscle fibers responding
  - Strength of the stimulus
  - Frequency of stimulus
    (muscle twitch, treppe, summation, & tetanus)
6. Muscle Growth & Repair (read *Physiology in Health & Disease*)

**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!

7. Muscle Disorders

A) Muscular Dystrophy (Duchenne’s)

Clinical App Pg 229

- 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.
7. Muscle Disorders

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

7. Muscle Disorders

C) Myasthenia gravis = autoimmune attack on nicotinic ACh receptors of skeletal muscles. Loss of motor control & tone = hypotonia and muscle atrophy.

Figure 11.14
7. Muscle Disorders

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.

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**Review**

- **Muscle Growth & Repair**
  - Satellite cells vs Myostatin
- **Muscle Disorders:**
  - Duchenne’s MD
  - ALS
  - Myasthenia gravis
  - Toxins (tetanus & botulism)