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: Review of Ch 6 & 4!

<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>
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<tr>
<td>Receptor = _______</td>
<td>Receptor = _______</td>
<td>Epinephrine with B2 &amp; α-adrenergic receptors</td>
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<tr>
<td>&amp; also</td>
<td>&amp; also</td>
<td></td>
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<tr>
<td>Glycine &amp; GABA with</td>
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<tr>
<td>muscarinic receptors (Ch 4)</td>
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<tr>
<td>(for IPSPs – muscle relax)</td>
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<td></td>
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<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 (↓HR) &amp; epinephrine (↑HR)</td>
<td>ACh or epinephrine</td>
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<tr>
<td>(not “autorhythmic”)</td>
<td></td>
<td></td>
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<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>
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</tbody>
</table>

QUES:
Epineph. binding to β2-adrenergic receptors causes ______________________________

Epineph. binding to α-adrenergic receptors causes ________________________________
Cardiac muscle versus smooth muscle: Review Ch 6 & 7!

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

BUT:

<table>
<thead>
<tr>
<th>REVIEW!!!</th>
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<tbody>
<tr>
<td>1. Cardiac Muscle:</td>
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<tr>
<td>- AP starts in SA node (pacemaker cells)</td>
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<tr>
<td>- Rate of contraction influenced sympathetic vs parasympathetic stim.</td>
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<tr>
<td>- ↑ heart rate by epinephrine &amp; (\beta_1)-adrenergic receptors</td>
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<tr>
<td>- ↓ heart rate by ACh &amp; muscarinic cholinergic receptors</td>
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</table>

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.

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

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.
3. **Sliding Filament Theory of Muscle Contraction**: the sequence of action.

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**)

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.

Click [HERE](#) for YouTube video
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).

4. The Energetics of Muscle Contraction (Muscle Fatigue)

Muscle Fatigue

<table>
<thead>
<tr>
<th>Depletion of:</th>
<th>Accumulation of:</th>
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<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>
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</tbody>
</table>
Creatine phosphate = 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). Tissues that burn energy quickly need this molecule!

Creatine phosphokinase (CK or CPK) = is a blood test that can detect stressed (or damaged) tissues (skeletal muscle, cardiac muscle, and brain tissue)

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 =

B) Isometric contraction =
5. Factors Influencing Muscle Contractile Force:

**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).

5. Factors Influencing Muscle Contractile Force:

**Tradeoff:**

<table>
<thead>
<tr>
<th>Muscle Precision</th>
<th>vs</th>
<th>Muscle Power?</th>
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<tbody>
<tr>
<td>- one motor neuron innervates few muscle fibers.</td>
<td></td>
<td>- one motor neuron innervates many muscle fibers</td>
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![Diagram of muscle unit and fibers]
Muscle Contractile Force 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.

Fig. 9.6

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)

- Most common form of MD.
- Leads to muscle wasting (atrophy)
- Sex-linked recessive genetic disorder (found more in males)
- Early onset in children = walking & balance problems.
- 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

**REVIEW!**

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

![Diagram of normal neuromuscular junction and myasthenia gravis](image)
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)
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**

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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)

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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***
9. 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

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III. Reciprocal Innervation

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.
<table>
<thead>
<tr>
<th>Review</th>
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<tbody>
<tr>
<td><strong>Muscle sensory organs:</strong></td>
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<tr>
<td>- Golgi tendon organ</td>
</tr>
<tr>
<td>- Spindle apparatus (intrafusal fibers &amp; extrafusal fibers)</td>
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<tr>
<td><strong>Neural control of skeletal muscles</strong></td>
</tr>
<tr>
<td>- Upper motor neurons (in brain’s motor cortex)</td>
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<tr>
<td>- Lower motor neurons (brainstem, spinal cord to spinal nerves of PNS)</td>
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<td></td>
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<tr>
<td><strong>Voluntary reflex</strong></td>
</tr>
<tr>
<td>- Involves sensory neurons, spinal cord, brain, and motor neurons (longer, slower pathway)</td>
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<tr>
<td><strong>Spinal reflex</strong></td>
</tr>
<tr>
<td>- Involves sensory neurons, spinal cord, and motor neurons</td>
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<tr>
<td>- Shorter, faster pathway under autonomic control</td>
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<tr>
<td>Ex. Knee jerk reflex (monosynaptic)</td>
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