Ch. 6: Muscle Physiology (updated Feb 21, 2025)

1. Review 3 muscle types and how they are regulated.
2. Review muscle anatomy.
3. The neuromuscular junction
4. The sarcomere
5. Sliding filament theory of how muscles contract and relax.
6. Energetics of muscle contraction (ATP & ADP)
7. Types of muscle contraction.
8. Factors that influence muscle contractile strength.
9. Energetics of muscle use
10. Muscle growth & repair
11. Common muscle injuries & disorders.
Might cover - Muscle sensory organs, Voluntary movement VS reflex muscle movements

1. Types of Muscle: *[Review from Ch 4]*

a) Skeletal Muscle	b) Cardiac Muscle	c) Smooth Muscle
Voluntary (somatic motor)	Involuntary (autonomic motor)	Involuntary (autonomic motor)
Neurotransmitter = ACh **Receptor = nicotinic cholinergic (for EPSPs)** & also Glycine & GABA with muscarinic receptors (Ch 4) **(for IPSPs – muscle relax)**	**Parasymp. Neurotrans.** = **ACh** **Receptor = muscarinic cholinergic** effect = ↓ heart rate **Sympath. Neurotrans. = epinephrine** **receptor = β1-adrenergic** Effect = ↑ heart rate	**ACh with muscarinic cholinergic receptors,** **Epinephrine with B2 & α-adrenergic receptors**
Requires somatic motor neuron stimulus to contract (not "autorhythmic")	Is "autorhythmic", but HR influenced by ACh (↓HR) & epinephrine (↑HR)	Is "autorhythmic" – influenced by ACh or epinephrine
Fastest contraction speed	Intermediate contraction speed	Slowest contraction speed
Prone to fatigue	Fatigue resistant	Fatigue resistant

QUES: Ask students What happens to bronchiole smooth muscle when epinephrine binds to **β2-adrenergic receptors?**

Ans = bronchodilation

What happens to artery smooth muscle when when epinephrine binds to **β2-adrenergic receptors?**

Ans = vasodilation

What happens to GI smooth muscle when epinephrine binds to α-adrenergic receptors?

ANS = ↓ peristalsis (muscles inhibited) What about to GI gland secretions? ANS = ↓

What about artery smooth muscle that leads to GI tract? **ANS = vasoconstriction** (muscle contracts) to divert blood away.

Compare cardiac vs smooth muscle ***[review from Ch 4]***

Cardiac muscle

> Action potential starts in sino-atrial (SA) node – heart's pacemaker muscle cells

> heart rate influenced by sympathetic vs parasympathetic regulation *[review from Ch 6]*

- ↑ heart rate with epinephrine binding to β1-adrenergic receptors on pacemaker cells
- ↓ heart rate with ACh binding to muscarinic cholinergic receptors on pacemaker cells

Smooth muscle (depends on what neurotransmitter involved)

> ↑ GI smooth muscle peristalsis with ACh binding to muscarinic cholinergic receptors

> ↓ GI peristalsis with epinephrine binding to α-adrenergic receptors

> Bronchoconstriction with ACh binding to muscarinic cholinergic receptors

> Bronchodilation with epinephrine binding to β2-adrenergic receptors

> skeletal muscle arteriole smooth muscle vasodilation with epinephrine binding to β2-adrenergic receptors

> GI arteriole smooth muscle vasoconstriction w/epinephrine binding to α-adrenergic receptors

2. Anatomy & Physiology of Skeletal Muscle [*Review from anatomy! Go over QUICKLY!]*

> **muscle organ** = whole muscle group, made of fascicles (ex. biceps brachii)

> **fascicle** = bundle of muscle muscle fibers

> **fiber** = Single muscle cell. What motor neuron innervates. Contains bundle of muscle myofibrils.

> **myofibril** = contains thousands of sarcomeres

> **sarcomere** = functional unit of muscle contraction. Made up of actin and myosin myofilaments.

3. Review of neuromuscular junction (review from Ch 4)

Neuromuscular junction = between single motor neuron and muscle cell it innervates.

IF it's a somatic motor neuron and a skeletal muscle cell:

ASK "What would be the neurotransmitter?" **ANS = ACh**

ASK "What would be the receptor on the muscle?" **ANS = nicotinic cholinergic**

ASK "Binding of receptors opens what ion channels on cell?" **ANS = Na+ channels**

ASK "What ion enters muscle cell causing an EPSP?" **ANS = Na+**

4. Sarcomere contains myofilaments:

a) **actin** = ***thin*** filament w/ active sites, troponin, tropomyosin. ***("If you stay ACTIVE you stay thin")***

- actin has ***troponin*** = protein that will bind with Ca++
- actin has ***tropomyosin*** = filament attached to troponin & it normally blocks active sites on actin.

b) **myosin** = ***thick*** filament w/globular head that "pulls" on actin when cross bridges form.

> ***Z-lines*** = end**Z** of each sarcomere. These move closer during contraction.

> ***M-line*** = **M**iddle of sarcomere

> ***A-bands*** = where actin & myosin filaments overlap.

5. Go over, step-by-step of sequence of events from release of neurotransmitter from somatic motor neuron to muscle contraction (sliding filament theory of muscle contraction)

1. Somatic motor neuron releases ACh into synapse with skeletal muscle cell (fiber)
2. ACh binds to nicotinic cholinergic receptor on muscle cell
3. Na+ channels open in muscle cells

4. Action potential forms in muscle cells
5. AP travels down t-tubules in muscle
6. This causes Ca+2 release from muscle sarcoplasmic reticulum
7. Ca+2 binds to troponin
8. This causes tropomyosin to lift off active sites on actin
9. Myosin heads can now bind to active sites (form crossbridges)
10. The sarcomeres shorten, muscle cells shorten = muscle contraction

6. Energetics of muscle contraction with ATP & ADP

> Steps 1 & 2 = myosin uses ADP to "grip" active sites (forms cross bridge with actin) and pull on actin (power stroke). But now all of ADP used up and myosin can't release its crossbridge.

> Steps 3 & 4 = ATP allows myosin to break crossbridge (let go of actin) and then it becomes ADP, and is ready for next cycle.

> process repeats in a grip, pull, break grip, go back to "cocked and ready position"

7. Types of muscle contractions:

> **Isotonic contraction** = force generated is enough to move an object (muscle shortens)

> **Isometric contraction** = muscle produces tension but doesn't shorten.

"Iso" means "same and metric is for measure, so remember as "same measure"

8. Factors influencing muscle contractile strength (force)

> How is the motor unit arranged?

Motor Unit = a motor neuron and all the muscle fibers it innervates (can be up to 150 fibers innervated by 1 neuron). [*Many muscle fibers can be innervated by one motor neuron.]

Concept of Muscle Precision vs Muscle Power

> for parts of body needing fine motor control – tend to have one motor neuron innervating few fibers (produces less power, but more control)

> for parts of body needing great power, less precision (core muscles, and leg muscles) – tend to have one motor neuron innervating many muscle fibers.

Muscle Contractile Force Modified by:

A) # of muscle fibers responding & # crossbridges formed

> if more fibers respond = greater force produced

> if less fibers = less force

B) **Strength of stimulus (for one motor neuron) –** depends on how much neurotransmitter released

> if stimulus strong (lots of neurotrans) = greater force produced

> if stimulus weak (little neurotrans) = less force

> If stimulus VERY strong – can get recruitment = more than one motor neuron (and all the muscle fibers it innervated) become involved, which produces greater force than 1 motor neuron alone.

(A great analogy for students is to them imagine one student trying to lift the professor. It would be difficult to generate enough force to do it alone. If couple other students help, together they could generate enough force to do it.

C) Frequency of stimulus affects force:

a) **Muscle Twitch** = single stimulation produces a single muscle contraction (twitch) followed by relaxation

b) **Muscle Treppe** = repeated neuron stim at LOW frequency causes increasing force (builds up like steps) in muscle, but they have time in between stim to relax and force goes back to baseline.

c) **Muscle Summation** = repeated high frequency stim causes increasing strength of contaction w/each stim but stim so rapid that muscle cannot relax (force does not go back to baseline) in between contractions. Produces high force, but leads to muscle fatigue.

d) **Muscle Tetany** = neuron stim muscle at highest frequency possible, produces greatest forces possible (force immediately goes to max), but leads to muscle fatigue and "giving out" **(like muscle failure seen at the gym when people lifting weight – why they need spotter)**

D) Recruitment of different types of muscle fibers involving multiple motor units

- more than one motor neuron involved & all its muscle fibers
- recruit different types of muscle fibers depending on the need
- produced greater force than with 1 motor unit alone.

Recruitment of different muscle fiber types:

Type 1 = **slow twitch (S).** For endurance aerobic activities

Type 2 = **fast twitch fatigue resistant (FR).** For more strenuous, endurance aerobic & anaerobic activities. *(Intermediate between type 1 & 2 for speed, strength **and** stamina.)*

Type 3 = **fast twitch subject to fatigue (FF).** For maximum power short bursts of activities. Muscles fatigue when forced into anaerobic metabolism

[Types of Muscle Fibers (muscle cells):

> **Red (slow twitch fibers)** – have more myoglobin, capillaries, mitochondria for aerobic activity. Steady but little power, fatigues slowly. Find in core and posture muscles.

> **Whie (fast twitch) fibers**- have less myoglobin, capillaries, & mitochondria for short burst of high power over short time. Fatigues quickly.]

9. Energetics of muscle contraction – muscle fatigue

Muscle Fatigue due to:

Depletion of:	Accumulation of:
O2 & ATP	CO2 & ADP
Glycogen (storage form of glucose)	lactic acid (waste product of muscle activity)
Myoglobin (respiratory pigment in muscle)	phosphate (from using up creatine phosphate)

Phosphocreatine = natural chemical in muscle that is needed to convert ADP back to ATP

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

Diff isoforms CPK that are routinely used to test if organ damage:

1) **CPK MM** = elevated with diseased skeletal muscle ***(remember all M's = muscle)*** **Go to clinical app online**

2) **CPK BB** = elevated with brain damage (***remember all B's = brain)***

3) **CPK MB** = elevated with damaged heart (used to help confirm, along with EKG & other tests, heart attack)

10. Muscle growth & repair (for every action there is an equal and opposite reaction)

> Muscle growth and replacement involves muscle stem cells (**Satellite cells**)

> **Myostatin** = substance that inhibits muscle growth by inhibiting satellite cells.

(Elderly people often have high myostatin levels which contributes to muscle atrophy in old age)

11. Muscle Disorders:

Muscle Atrophy = loss of muscle (shrinks)

> due to malnutrition (starvation), lack of exercise (couch potato), muscle disorder, or nerve disorder.

Muscle spasm = sudden uncontrolled muscle contractions (seizures)

Muscle cramp = painful muscle contraction/muscle tension after strenuous activity. Cause – depletion of salts

Muscle sprain = injury to a joint from over-stretched or torn ligament.

Muscle strain (pulled muscle) = muscle, or its tendon, overstretched or torn.

Muscle clonus - nerve that control the muscles are damaged, causing involuntary muscle contractions or spasms.

Dermatomyositis = muscle inflammation (or myopathy). 1/100,000 – mostly women.

> muscle weakness that progresses

> muscles close to trunk (hip, shoulder, neck) affected first

> skin rashes

> treat with anti-inflamatories (steroids, NSAIDs), and sunscreen to protect skin.

Muscular dystrophy (specifically Duchenn's MD)

> most common form of MD

> sex-linked recessive disorder – seen more in males

> early onset in childhood w/walking & balance problems. Leads to muscle atrophy (muscle wasting)

> thought to be due to loss of protein dystrophin.

ALS (amyotrophic lateral sclerosis) = loss of motor neurons, muscles that go without stimulation atrophy, leads to paralysis (respiratory failure 5 yrs from diagnosis).

Thought to be due to :

> ***Loss of superoxide dismutase*** **-**antioxidant which gets rid of toxic free radicals & prevents cell death.

> ***Excess glutamate*** = excitatory neurotransmitter that stimulates motor neurons. "Riluteck" tx ↓ glutamate & extends life of ALS patients. ***Click Clinical App. to see online***

Myasthenia Gravis = autoimmune attack on ACh receptors of skeletal muscle cardiac, & smooth muscle. Loss of muscle stimulation leads to muscle atrophy. Eye droop, pharyngeal (swallowing & choking) problems, limb weakness.

Review tetanus & botulism muscle prob from Ch 4.) Clinical App online

Tetanus (*Clostridium tetani*) – blocks inhibitor Glycine, resulting in overstimulation (agonist) of ACh receptors of muscle. "Spastic paralysis". Also known as "**Hypertonia**"

Botulism (*Clostridium botulinum*) – prevents ACh release from presynaptic vesicles. No ACh stimulations (antagonist) of receptors on muscle = "flaccid paralysis". Also known as "**Hypotonia**"

Additional Optional Material:

Muscle Sensory Organs:

1) <u>Golgi Tendon organs</u>:

- sense **T**ension a muscle puts on a tendon ***(T in tendon for Tension)***

2) <u>Muscle spindle apparatus</u>: *(S in spindle for Stretch)*

- sense muscle **S**tretch (length)
- Stretching a muscle stretches the spindles
- More spindles = more precision
- <u>Spindle Contains</u>

"**extrafusal fibers**" contracting muscle fibers, contain contractile fibers along entire length,

"**intrafusal fibers**" thin stretch muscle fibers with nuclei (cells) in the center (noncontractile part) of fiber

Two types of <u>sensory cells</u> wrap around the intrafusal fibers:

A) Primary (annulospiral) = wrap around center of fiber, sense the start of muscle stretch

B) Secondary (flower-spray) = wrap around ends of fiber (near tendon), sense sustained stretch (tonic)

* Sudden, rapid muscle stretch activates both sensory cells and causes greater contractile response than gradual stretch.

Neurons of Skeletal Muscles:

<u>Two types of muscle motor neurons:</u>

1) Upper motor neurons (interneurons) = in the brain (motor cortex), communicate with lower motor neurons.

2) Lower motor neurons = somatic motor neurons w/cell bodies in brain stem and ventral horn of spinal cord.

-Travel with nerve plexuses to stimulate muscle contraction.

- Activity of these neurons regulated by feedback from:

> upper motor neurons

> "muscle sensory organs" (golgi tendon and muscle spindle apparatus)

<u>2 types of lower motor neurons</u>:

A) Alpha neurons: innervate extrafusal (contracting) muscle fibers

- Results in skeletal isotonic muscle contraction (muscle shortens)

B) Gamma: innervate intrafusal (stretch) muscle fibers

- Results in isometric contraction (no shortening)
- provides normal muscle "tone"
- Increase sensitivity to stretch.

***"coactivation"** = simultaneous stimulation of both alpha & gamma lower motor neurons by upper motor neurons in brain.

Voluntary vs Spinal Reflexes

Voluntary movement (if someone tells you to extend your knee) involves:

- sensory receptor sending info up spinal cord to brain, brain interpreting signal & sending motor command down spinal cord to muscles, and muscles contract. This takes longer time to happen than with spinal reflex.

4 Spinal Reflexes (there are more, but only covering these 4 here)

I. Monosynaptic Stretch Reflex = simplest type of reflex

Example = "Knee-Jerk" (Patellar tendon reflex)

<u>Mono</u>synaptic because there is only <u>one</u> synapse (between sensory neuron and motor neuron in spinal cord)

- strike patellar tendon (w/Taylor reflex hammer)
- stretches quadriceps muscle
- stretches the muscle spindles
- sensed by primary (annulospiral) cells of intrafusal fibers
- stimulates muscle alpha motor neurons to responds by causing strong contraction (muscle shortens, leg kicks out).

II. **Inhibitory Stretch Reflex** – functions to ↓ tension in tendon, prevent damage from excessive contractile force
Disynaptic Reflex = involves two synapses (one between sensory neuron in Golgi tendon organ & interneuron, and between interneuron & motor neuron in spinal cord)

- Golgi Tendon sensory organs which monitor muscle tension (from muscle contraction or stretching).
- golgi sensory neuron has "*excitatory synapses*" with interneurons (upper muscle motor neurons) in spinal cord.
- the interneurons have "*inhibitory synapse*" (IPSPs) with lower alpha motor neuron of muscle.

III. **Reciprocal Innervation** = simulataneous stimulation of agonist muscles & relaxation of antagonist muscles (within 1 limb only, one side of body only).

1. Muscle stretch activates spindle apparatus (intrafusal fibers)
Sensed by sensory neuron, to dorsal root ganglion spinal cord.

2. Response = **Agonist muscle contracts** (stimulated by EPSPs) in stretch reflex
(stimulated + thru Anterior root spinal cord to motor neuron)

3. Antagonist muscle is is inhibited – muscle remains relaxed because contraction inhibited by IPSPs.

IV. Crossed Extensor Reflex - double reciprocal innervation = reciprocal innervation involving multiple limbs.
- involves both limbs, on opposite (contralateral) body sides.
Ex. If you step on a tack with one foot, you reflexively lift that foot up while shifting weight & balance to opposite leg.

1. Flexor muscle contracts & extensor muscle relaxes to withdraw foot

2. Extensor muscle contracts & flexor muscle relaxes in contralateral leg to support leg.

[this works best if you act it out in front of class]

simpler diagram of cross extensor reflex

Review slide