Chapter 10: Muscle

3 Types of Muscle

--Skeletal Muscle
  * attaches to bone, skin, or fascia
  * striated with light and dark bands visible with scope
  * voluntary control of contraction and relaxation
  * multinucleated

--Cardiac Muscle
  * striated in appearance
  * involuntary control
  * branches
  * autorhythmic because of built in pacemaker--if loses inn. it can still contract
  * uninucleated

--Smooth Muscle
  * attached to hair follicles in skin
  * in walls of hollow organs (blood vessels, GI, viscera)
  * nonstriated in appearance
  * involuntary
  * autorhythmic (d/n need inn.)

Functions of Muscle Tissue

-- producing body movements
-- stabilizing body positions
-- regulating organ volumes (bands of smooth muscle called sphincters)
-- movement of substances w/l the body (smooth and cardiac)
  * blood, lymph, urine, air, food and fluids, sperm
-- producing heat (skeletal)
  * involuntary contractions of skeletal muscle (shivering)

Properties of Muscle Tissue

-- Excitability: respond to chemicals released from nerve cells (nervous and muscle)
-- Conductivity: ability to propagate electrical signals over membrane (similar to nervous tissue)
-- Contractility: ability to shorten and generate force (only muscle)
  * 2 types of shortening: isometric and isotonic
-- Extensibility: ability to be stretched without being damaged
-- Elasticity: ability to return to original shape after being stretched
Skeletal Muscle

Connective Tissues

--Superficial Fascia: loose CT and fat underlying skin, path for blood vessels and nerves
--Deep Fascia: dense irregular CT around muscles with similar functions, isolates muscles from body allowing movement
--CT components of the muscle (all extend beyond muscle belly to form tendon)
  *epimysium: surrounds the whole muscle
  *perimysium: surrounds bundles/fascicles of 10-100 muscle cells
  *endomysium: separates individual muscle cells (some cells can contract while others d/n, prevent cross excitation)

Nerve and Blood Supply

--Each skeletal muscle supplied by a nerve, artery, vein, and capillary bed
--Each motor neuron supplies multiple muscle cells (NEUROMUSCULAR JUNCTION)
--Each muscle cell is supplied by one motor neuron
--Each muscle cell is in contact with one or two capillaries
--Nerve fibers and capillaries found in the endomysium b/w individual cells

Formation/Growth of Muscle Fibers

--Every mature muscle cell develops from 100 myoblasts that fuse together in the fetus (hence multinucleated → too big to be controlled by one nucleus)
--Mature muscle cells c/n divide → in Go, no mitosis or meiosis (no hyperplasia)
  *muscle growth result of cellular enlargement (HYPERTROPHY)
--Satellite cells retain the ability to regenerate new muscle fibers
--Atrophy
  *wasting away of muscle
  *caused by disuse (disuse atrophy) or severing of the nerve supply (denervation atrophy)
  *transition to CT cannot be reversed
--Hypertrophy
  *increase in the diameter of muscle fibers, not number
  *resulting from forceful, repetitive muscular activity and an increased in myofibrils, SR, and mitochondria

Anatomy of the Skeletal Muscle

--Myofiber/Muscle Fiber
  *muscle cells are long, cylindrical, and multinucleated
  *Sarcolemma: muscle cell cell membrane
*Sarcoplasm: filled with myofibrils and myoglobin (protein that binds oxygen in muscles, where oxygen is stored, if in blood shows damage to skeletal muscle, 1 myoglobin can bind 1 oxygen)

--Transverse Tubules
  *Invaginations of the sarcolemma into the center of the cell
  *filled with extracellular fluid
  *carry muscle APs down into the cell
--Mitochondria
  *lie in rows throughout the cell, near the muscle proteins that use ATP during contraction
--Myofibrils
  *Threads of muscle fibers, encircled by sarcoplasmic reticulum (SR)
--Myofilaments (thick and thin filaments)
  *Contractile proteins of muscle
--Sarcoplasmic Reticulum (SR)
  *system of tubular sacs similar to SER in nonmuscle cells
  *Stores Ca++ in a relaxed muscle
  *Release of Ca++ triggers muscle contraction
  *Forms TRIAD with T-tubules (1 tubule b/w 2 terminal cisternae)

**Sarcomere**

--Z discs: sarcomere runs Z disk to Z disc
--I band: light band with only thin filaments
  *2 ½ I bands/sarcomere
--A band: dark band with thick and thin filaments
  *6 thin filaments surround each thick filament
  *1 A band/sarcomere
--M line: anchors thick filaments
--H zone: area within A band that only contains thick filaments (heavy chains only)
--Zone of overlap: where there are thick and thin filaments

**Exercise Induced Muscle Damage**

--Intense exercise does cause muscle damage
  *torn sarcolemmas, damaged myofibrils, disrupted Z discs
  *increased blood levels of myoglobin and creatine-P found only inside of muscle cells
--Delayed onset muscle soreness
  *12 to 48 hours after strenuous exercise
  *stiffness, tenderness and swelling due to microscopic cell damage

**Proteins of Muscle**
--Contractile Proteins
  a. Myosin
     *thick filaments
     *each molecule resembles two golf clubs with twisted together handles
     *head toward z disc, tail attached to M line (held by myomesin)
     *myosin heads (crossbridges) extend toward the thin filaments (6 thin filaments surround a myosin—made of 3 strands)
     *made up of 2 heavy chains and 4 light chains (head)
  b. Actin (F actin made of G-actin)
     *thin filaments (with 2 regulatory proteins)
     *myosin binding site on each actin is covered by tropomyosin in relaxed muscle
     *thin filaments are held in place by Z lines (attached to z disk and point towards M line)
     *thin filament is made of 2 chains of F-actin, 2 chains tropomyosin, Troponin

--Regulatory Proteins (turn contraction on and off)
  a. Troponin
     *3 Domains: C (binds calcium), T (binds tropomyosin), I (binds actin)
     *conformational change when Ca++ is present to open active site for myosin
  b. Tropomyosin
     *cover active sites for myosin heads therefore c/n form crossbridges

--Structural Proteins (provide proper alignment, elasticity, and extensibility)
  a. Titin
     *anchors thick filament to M line and extends to Z disc
     *filamentous, springy; maintains side by side orientation of sliding filaments
     *portion of the molecule b/w the Z disc and the end of the thick filament can stretch to 4x its resting length and spring back unharmed
     *role in recovery of the muscle from being stretched, prevents overextension, maintains the position of A band in the center of the sarcomere
  b. Myomesin
     *connects to titin and adjacent thick filaments
  c. Nebulin
     *inelastic protein that helps align the thin filaments
  d. Dystrophin
     *links thin filaments to integral sarcolemmal proteins and transmits the tension generated to the tendon
Sliding Filament Model

--Actin myofilaments sliding over myosin to shorten sarcomeres
  *actin and myosin d/n change length
  *sarcomere shortening is responsible for skeletal muscle contraction
    (sarcomeres lead to fiber to muscle length shortening)
  *Shortening: I band shortens by sliding toward M line, H zone disappears, zone of overlap inc., z discs come toward each other

--During relaxation, sarcomeres lengthen
  *Lengthening: I band inc., H zone inc., zone of overlap dec.
  *Resting: I and H bands are at maximum width

Beginning of Contraction

--Nerve impulse (from motor neuron) reaches axon terminal → synaptic vesicles release Ach → Ach diffuses to receptors on sarcolemma and ligand gated Na+ channels open → Na+ rushes into cell → muscle AP spreads over sarcolemma and into t-tubules → voltage gated Ca++ channels in SR open → SR released Ca++ into sarcoplasm → Ca++ binds to troponin and causes troponin-tropomyosin complex to move and reveal myosin binding sites on actin → begins contraction cycle

--Contraction cycle (4 steps)
  *myosin heads hydrolyze ATP → attachment of myosin to actin to form crossbridges (release P) → power stroke (release of ADP) → detachment of myosin from actin due to ATP binding in the site where ADP use to be → repeat

--Cycle keeps repeating as long as there is ATP available and high Ca++ level near thin filament

AP and Muscle Contraction

--AP along T-tubules → open voltage gated Ca++ channels on SR → T-tubules and SR are physically linked by a membrane protein (RYANODINE RECEPTOR) functions as a Ca channel → ryanodine receptor comes in contact with t-tubule membrane protein (DIHYDROPYRIDINE/DHP RECEPTORS) → DHP is a voltage sensors → voltage changes alters DHP conformation that opens ryanodine receptors → Ca++ diffuses from SR to cytosol

Relaxation

--Muscle AP ceases → Achesterase breaks down Ach within synaptic cleft → Ca++ release channels on SR close → Active transport pumps Ca++ back into storage in SR → Ca++ binding protein (CALSEQUESTRIN) in the SR helps hold Ca++ (10,000 times higher in SR than cytosol) → tropomyosin-troponin complex recovers binding site on actin
NMJ/Synapse

--End of axon nears surface of muscle fiber at its motor end plate region (remain separated by synaptic cleft)
--Synapse or NMJ
  *presynaptic terminal: synaptic end bulbs are swellings of axon terminals that contain synaptic vesicles filled with Ach (voltage gated Ca++ channels open Ca++ enters synaptic end bulb to promote fusion of NT to membrane so that NT is released into synaptic cleft)

  *synaptic cleft: Ach released here where it attaches to receptor molecule on motor end plate//AChE breaks down ACh in synaptic cleft → choline is reuptaked by neuron and acetic acid released
  *postsynaptic membrane or MOTOR END PLATE: contains 30 million Ach receptors

--Synaptic Vesicles
  *Ach: neurotransmitter
  *AChE: degrading enzyme in synaptic cleft

--Pharmacology of NMJ
  *Botulinum toxin: blocks release of NT at NMJ so muscle contraction c/n occur (bacteria found in improperly canned food, death occurs from paralysis of the diaphragm)
  *Curare: plant poison from poison arrows, causes muscle paralysis by blocking ACh receptors, used to relax muscles during surgery
  *Neostigmine: anti-cholinesterase agent, blocks removal of ACh from receptors → strengthens weak muscle contractions (as in myasthenia gravis), also an antidote for curare after surgery is finished

Ion Channels

--Ligand-gated: opened via NT
--voltage-gated: open and close in response to small voltage changes across plasma mem.

Excitation-Contraction Coupling

--All the steps that occur from muscle AO reaching the T tubule to contraction of the muscle fiber

Length of Muscle Fibers

--Optimal overlap of thick and thin filaments
  *produces greatest number of crossbridges and the greatest amount of tension
--Overstretching muscle (past optimal length)
*fewer crossbridges exist and less force is produced
--Muscle is overly shortened (less then optimal)
  *fewer crossbridges exist and less force is produce
  *thick filaments crumpled by Z discs
--Normally
  *resting muscle length remains between 70-130% of the optimum

**Muscle Metabolism**

--Production of ATP in Muscle fibers
  *Muscle uses ATP at a great rate when active
  *Sarcoplasmic ATP only lasts a few seconds

--3 sources of ATP
  a. Creatine Phosphate
    *excess ATP w/I resting muscle used to form creatine-P
    *Creatine-P is 3-6x more plentiful than ATP w/I muscle
    *quick breakdown provides energy for creation of ATP
    *sustains contraction for 15 sec
    *athletes tried creatine supplementation (gain muscle mass but shut down body’s own synthesis—safe?)
  b. Anaerobic Cellular Respiration
    *occurs in absence of oxygen and results in breakdown of glucose to yield ATP and lactic acid (sent to liver to be converted back to glucose)
    *glycolysis can continue anaerobically for 30-40 seconds of maximal activity
    *glycogen storage in skeletal muscle used (75% of total glycogen storage in muscle, other 25% in liver)
  c. Aerobic Cellular Respiration
    *requires oxygen and breaks down glucose to produce ATP, CO2, and H2O
    *more efficient than anaerobic
    *ATP for any activity lasting over 30 sec (if sufficient oxygen available, pyruvic acid enters the mitochondria to generate ATP, water, and heat//fatty acids and amino acids can also be used by mitochondria)
    *provides 90% of ATP energy if activity lasts more than 10 minutes

**Fatigue**

--decreased capacity to work and reduced efficiency of performance
--3 Types
  a. psychological: depends on emotional state of individual
b. muscular: results from ATP depletion  
c. synaptic: occurs in NMJ due to lack of ACh  

--Muscle Fatigue  
  a. inability to contract after prolonged activity  
     *central fatigue is feeling of tiredness and a desire to stop (protective mechanism), depletion of creatine-P, decline of Ca++ w/i the sarcoplasm  
  b. Factors that contribute to muscle fatigue  
     *insufficient oxygen or glycogen  
     *buildup of lactic acid and ADP, decrease in pH  
     *insufficient release of ACh from motor neurons, lack of Ca++  

Oxygen Consumption after Exercise (OXYGEN DEBT)  

--Muscle has 2 sources of oxygen  
  *diffuses in from blood  
  *released by myoglobin inside muscle fibers  
--aerobic system requires oxygen to produce ATP needed for prolonged activity  
  *increased breathing effort during exercise  
--recovery oxygen uptake  
  *elevated oxygen use after exercise (OXYGEN DEBT)  
  *lactic acid is converted back to pyruvic acid  
  *elevated body temp increases rates of all metabolic reactions  

Motor Unit  

--motor unit = 1 somatic motor neuron and all the skeletal muscle cells/fibers it stimulates  
  *muscle fibers normally scattered throughout belly of muscle  
  *one nerve cell supplies on average 150 cells that all contract in unison  
--total strength of a contraction depends on how many motor units are activated and how large the motor units are  
--ALL OR NONE LAW: for muscle fibers and motor unit, contraction of equal force in response to each AP (sub-threshold, threshold, and suprathreshold stimuli)  
  *graded response for whole muscles (based on number of motor units activated): strength of contraction ranges from weak to strong depending on stimulus strength  
--SMALLEST motor units are always recruited first and proceeds with successively larger motor units as more force is needed  
  *fired first b/c have smallest neuronal somas which require less stimulation to fire AP  
  *have smaller muscle fibers, which generate the least amount of force  

Types of Contraction
--Twitch/Single Muscle Contraction
  * brief contraction of all fibers in a motor unit in response to a single AP in its motor neuron and/or electrical stimulation of a neuron or muscle fibers
  * Myogram: graph of twitch contraction (AP 1-2msec, twitch contraction lasts 20-200msec)
  * Parts of a Twitch Contraction
    a. latent period (2-5msec): Ca++ released from SR, slack removed from elastic components
    b. Contraction period (10-100 msec): filaments slide past each other
    c. Relaxation period (10-100 msec): active transport of Ca++ into SR
    d. Refractory period (very short): muscle c/n respond and has lost its excitability, 5msec for skeletal and 300msec for cardiac

**TABLE 9.2**
--Wave/Temporal Summation
  * 2nd stimulus applied after refractory period but before complete muscle relaxation leads to second contraction b/c already have some Ca++ \(\rightarrow\) add more Ca++ \(\rightarrow\) more active sites exposed \(\rightarrow\) more binding
  * 2nd contraction is easily added to first b/c elastic elements remain partially contracted and d/n delay the beginning of next contraction

--Unfused Tetanus
  * if stimulated at 20-30 times/second there will be only partial relaxation b/w stimuli (inc. frequency, not strength of AP)

--Fused tetanus
  * if stimulated at 80-100 times/second, a sustained contraction with no relaxation b/w stimuli will result (Inc frequency, not strength of AP)
  * hits a plateau with max active sites open and max cross bridge formation

--Spatial Summation (motor unit recruitment)
  * motor units in a whole muscle fire asynchronously (some fibers are active others are relaxed, delays muscle fatigue so contraction can be sustained)
  * produces smooth muscular contraction (not series of jerky movements)
  * precise movements require smaller contractions (motor units must be smaller—fewer fibers/nerve)
  * large motor units are active when greater tension is needed
  * Whole muscle contracts with a small or large force depending on number of motor units stimulated to contract
    a. subthreshold: no motor units respond
    b. threshold: one motor unit responds
    c. submaximal: increasing numbers of motor units respond
    d. maximal: all motor units respond
    e. supramaximal: all motor units respond (at plateau)

--Treppe: complete relaxation in b/w contractions
  * graded response
*occurs in whole muscle rested for prolonged period
*each subsequent contraction is stronger than previous until all equal after
few stimuli
*each individual muscle fiber and each motor unit respond in all or non
fashion, the muscle as a whole responds in graded fashion

**Types of Muscle Contractions**

--Isometric (static): no change in length while tension may change (postural muscles
of body)
  *no movement
  *tension is generated w/o muscle shortening
  *maintaining posture and supporting objects in a fixed position
--Isotonic (dynamic): change in length with constant tension
  *concentric: overcomes opposing resistance and muscle shortens (muscle
  shortens to produce force and movement)
  *eccentric: tension maintained but muscle lengthens (muscle lengthens while
  maintaining force)
  *isokinetic: maximal tension during contraction at constant speed over full
  range of motion

--Muscle tone: constant tension by muscles for long periods of time
  *involuntary contraction of a small number of motor units (alternately active
  and inactive in a constantly shifting pattern)
  *keep muscles firm even though relaxed
  *does not produce movement
  *essential for maintaining posture (head upright)
  *important for maintaining blood pressure (tone of smooth muscles in walls
  of blood vessels)

--Active VS Passive Tension
  *Active: tension developed due to the contraction
  *Passive: tension in muscle present before contraction

--Velocity of muscle shortening DECREASES with increased load: at maximal load
  the velocity =0 therefore isometric contraction
--Sarcomeres are organized in “series” and in “parallel”
  *Series: increase tension
  *Parallel: increase power and diameter

**Variations in Skeletal Muscle Fibers**

--Myoglobin, mitochondria, and capillaries
  *red muscle fibers: more myoglobin, an oxygen storing reddish pigment,
  more capillaries and mitochondria
*White muscle fibers: less myoglobin ad fewer capillaries give fibers their pale color
--Contraction and relaxation speeds vary
  *how fast myosin ATPase hydrolyzes ATP
--Resistance to fatigue
  *different metabolic reactions used to generate ATP
--Slow twitch
  *contract more slowly, smaller in diameter, better blood supply, more mitochondria, more fatigue-resistant than fast twitch
--Fast twitch
  *respond rapidly to nervous stimulation, contain myosin to break down ATP more rapidly, less blood supply, fewer and smaller mitochondria than slow twitch
--Distribution: most muscles have both, but proportion varies for each muscle
--Effects of exercise
  *Hypertrophies: increases in muscle size
  *Atrophies: decreases in muscle size

Classification of Muscle Fibers

--Type I: slow oxidative (slow twitch)
  *red in color (lots of mitochondria, myoglobin and blood vessels)
  *prolonged, sustained contractions for maintaining posture

--type IIb: fast oxidative-glycolytic (fast-twitch)
  *"pink" in color (lots of mitochondria, myoglobin and blood vessels)
  *split ATP at very fast rate; used for walking and sprinting
--Type IIa: fast glycolytic (fast-twitch)
  *white in color (few mitochondria and blood vessels, low myoglobin)
  *anaerobic movements for short duration; used for weight lifting

--Most muscles contain all 3 fibers
--Proportions vary with usual action of the muscle
  *neck, back, leg have higher proportion of postural, slow oxidative fibers
  *shoulder, arm higher proportion of fast glycolitic fibers
--All fibers of any one motor unit are same

<table>
<thead>
<tr>
<th></th>
<th>Type I Slow Oxidative</th>
<th>Type IIa Fast Glycolytic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>Red</td>
<td>White</td>
</tr>
<tr>
<td>Speed on contraction</td>
<td>Slow</td>
<td>Fast</td>
</tr>
<tr>
<td>Max force generated</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Fiber diameter</td>
<td>Small</td>
<td>Large</td>
</tr>
<tr>
<td>Motor unit size</td>
<td>Small</td>
<td>Large</td>
</tr>
<tr>
<td>----------------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>Resistance to fatigue</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Capillaries</td>
<td>Many</td>
<td>Few</td>
</tr>
<tr>
<td>Mb content</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Mitochondria</td>
<td>Many</td>
<td>Few</td>
</tr>
<tr>
<td>Glycogen</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Myosin-ATPase</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Oxidative phosphorylation</td>
<td>High</td>
<td>How</td>
</tr>
<tr>
<td>Anaerobic glycolysis</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Sensitivity to hypoxia</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Anabolic Steroids**

--similar to testosterone
--increases muscle size, strength, and endurance
--many very serious side effects: liver cancer, kidney damage, heart disease, mood swings, facial hair and voice deepening in females, atrophy of testicles and baldness in males

**Regulation of Contraction**

--Regulation of contraction due to
  a. nerve signals from somatic and autonomic nervous system
  b. changes in local conditions (pH, O2, CO2, temp and ionic concentration)
  c. hormones (epinephrine—relaxes muscle in airways and some blood vessels)

--Stress-relaxation response
  a. when stretched, initially contracts and then tension decreases to what is needed
  b. stretch hollow organs as they fill and yet pressure remains fairly constant
  c. when emptied, muscle rebounds and walls firm up

**Regeneration of Muscle**

--Skeletal muscle fibers c/n divide after 1st year
  *growth is enlargement of existing cells
  *repair (satellite cells and bone marrow produce some new cells, if not enough numbers fibrosis occurs—most often)
--Cardiac muscle fibers c/n divide or regenerate (all healing done by fibrosis—scar
formation)
--Smooth muscle fibers (regeneration is possible)
  * cells can grow in size (hypertrophy)
  * some cells (uterus) can divide (hyperplasia)
  * new fibers can form from stem cells in BV walls

**Effects of Aging on Skeletal Muscle**

--reduced muscle mass
--increased time for muscle to contract in response to nervous stimuli
--reduced stamina
--increased recovery time
--loss of muscle fibers
--decreased density of capillaries in muscle
--skeletal muscle starts to be replaced by fat beginning at 30 “use it or lose it”
--slowing of reflexes and decrease in maximal strength
--change in fiber type to slow oxidative fibers may be due to lack of use or may be result of aging

**Myasthenia Gravis**

--progressive autoimmune disorder that blocks the ACh receptors at the NMJ
--more receptors are damaged the weaker the muscle
--more common in women 20-40 with possible link to thymus gland tumors
--begins with double vision and swallowing difficulties and progresses to paralysis of respiratory muscles
--Treatment: steroids that reduce antibodies that bind to ACh receptors and inhibitors of AChE

**Muscular Dystrophies**

--Inherited, muscle-destroying diseases
--Sarcolemma tears during muscle contraction
--Mutated gene is on X chromosome so problem is with males almost exclusively
--Appears by age 5 in males and by 12 may be unable to walk
--Degeneration of individual muscle fibers produce atrophy of the skeletal muscle
--Gene therapy is hoped for with the most common form = Duchenne muscular dystrophy

**Lever Systems and Leverage**

--First Class Lever
  * Force – Fulcrum – Load
  * Advantage: need small tension to balance weight
  * Disadvantages: limitations are how far a load can be moved and how heavy
a load can be
*Examples: head resting on vertebral column

--Second Class Lever
*Fulcrum – load – force/effort
*Advantages: always produce mechanical advantage
*Disadvantages: sacrifice speed and sacrifice distance
*Examples: raising up on your toes

--Third Class Lever
*Fulcrum – Force – Resistance
*Advantages: favors speed and range of motion
*Disadvantages: always produces a mechanical disadvantage
*Examples: flexor muscles at the elbow

**Coordination w/I Muscle Groups**

--most movement is result of several muscle working at the same time
--most muscles are arranged in opposing pairs at joints
  *prime mover/agonist: contracts to cause the desired action
  *antagonist: stretches and yields to prime mover
  *synergists: contract to stabilize nearby joints
  *fixators: stabilize the origin of the prime mover (scapula held steady so deltoid can raise arm)