

ANP 1105 – Midterm # 1 Study Notes

Section I: Structural Organization of the Human Body

1.1 - Structural Organization: pg 1-8

Atom: building block of an element

Molecule: a combination of two or more atoms of the same element held together by chemical bonds → oxygen gas

Compound: a combination of two or more different atoms (H₂O)

Organic compound: unique to living systems → carbohydrates, proteins, lipids, nucleic acids

Cell: fundamental structural & functional unit of a living thing

Tissue: groups of similar cells that have a common function

Organ: structure composed of at least 2 (usually 4) → tissue types that performs a specific function for the body

Organ system: organs that work closely with one another to accomplish a common purpose

Levels of Organization:

- 1) Chemical level: atoms combine to form molecules
- 2) Cellular level: cells are made up of molecules
- 3) Tissue level: consists of similar types of cells
- 4) Organ level: organs are made up of different types of tissues
- 5) Organ system level: consist of different organs that work together
- 6) Organismal level: human is made up of many organ systems

Organ systems: (that will be studying)

-Endocrine

-Cardiovascular

-Lymphatic/immunity

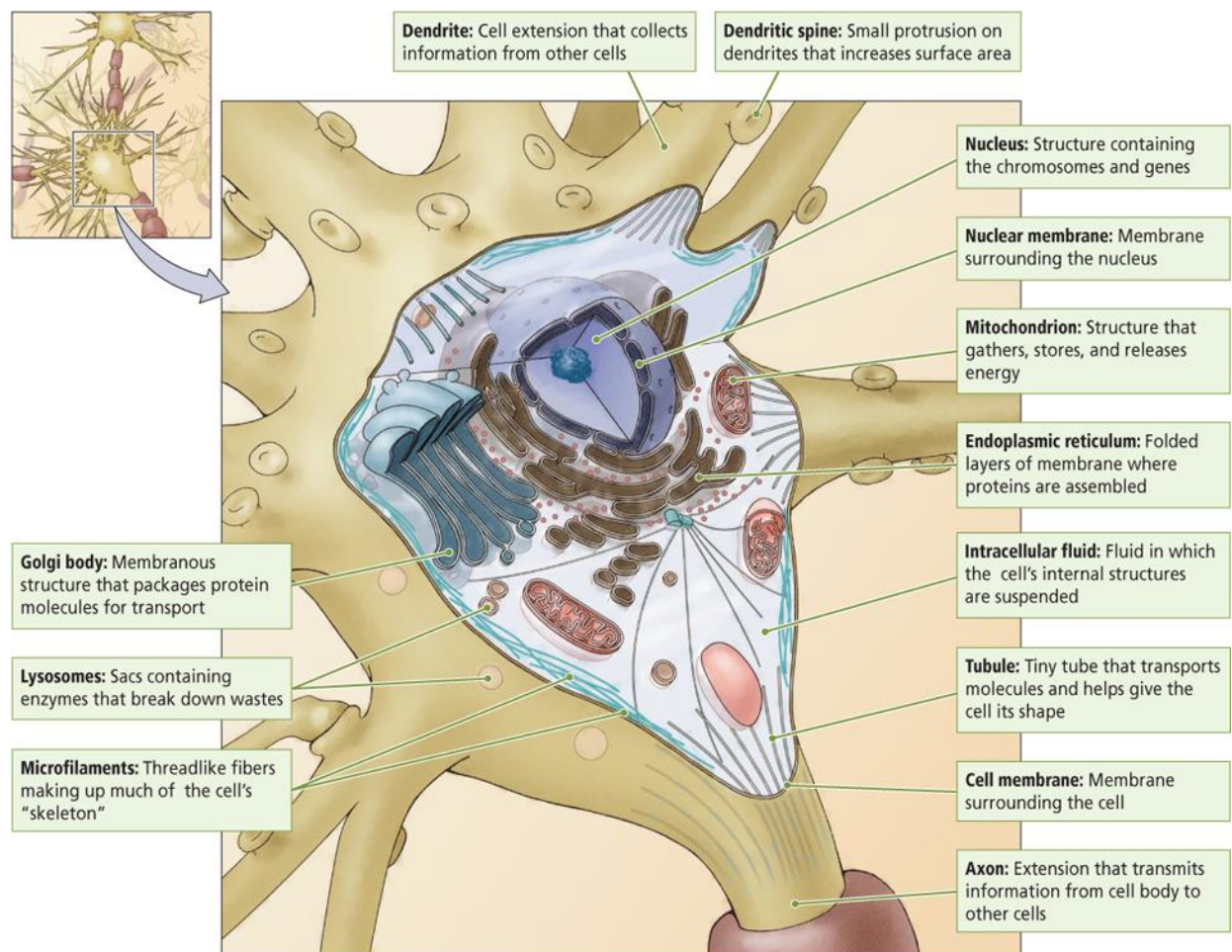
-Respiratory

Necessary Life Functions:

Maintaining boundaries: cell membranes, the integumentary system

Movement: muscles (actin and myosin), cilia, flagella
 Responsiveness: nervous system,
 Digestion:
 Metabolism:
 Excretion: feces, urine, CO₂
 Reproduction:
 Growth:

1.2 - Cells: summarize the major organelles and structures found in body cells
pg 61-96



Cell Diversity: cells differ in shape size and function

(a) Cells that connect body parts, form linings and transport gases
 -fibroblasts – erythrocytes – epithelial cells

(b) Cells that move organs and body parts

(c) Cells that store nutrients

-fat cells

(d) Cells that fight disease

-macrophage

(e) Cells that gather information and controls body function

(f) Cell of reproduction

3 Main Structures:

PLASMA MEMBRANE

CYTOPLASM

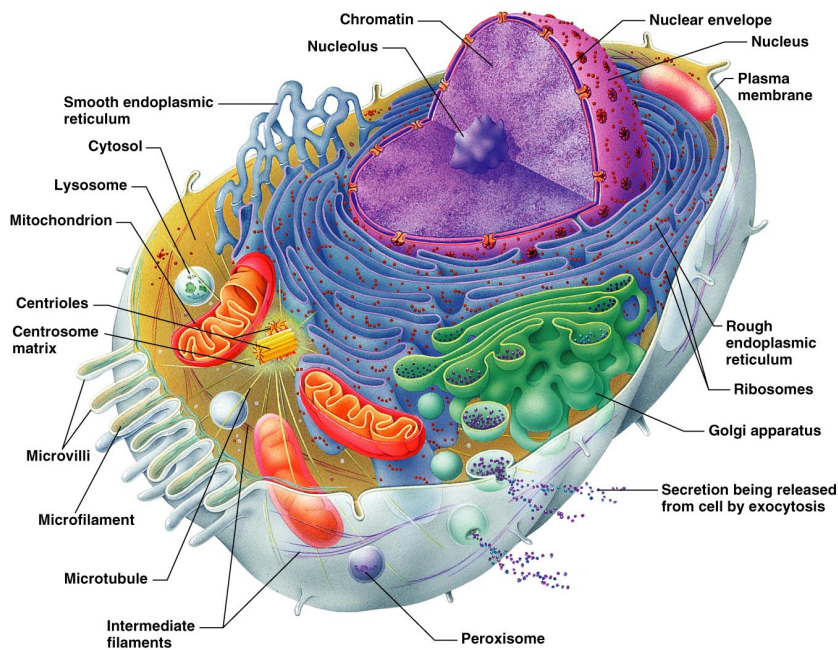
-Cytosol

-Organelles – membrane/ non membrane

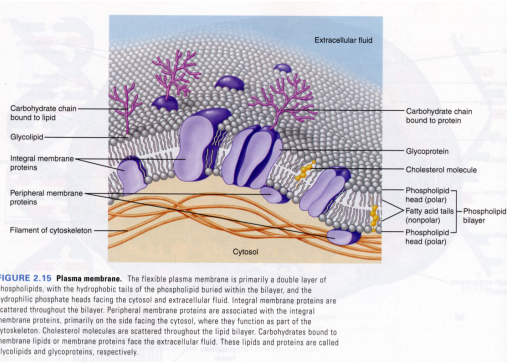
-Inclusions

NUCLEUS

-nucleoli



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PLASMA MEMBRANE:

- flexible
- double layer of phospholipids –bilayer
- hydrophobic tail
- hydrophilic phosphate head – facing cytosol and extra cellular fluid
- separates intracellular fluid and extracellular fluid
- membrane proteins in bilayer
- Fluid Mosaic Model
- Phospholipid bilayer forms a barrier to large polar molecules

Fluid Mosaic Model: lipid bilayer forms the basic structure of the membrane

-proteins involved in membrane functions → membrane transport, catalysis and cell to cell recognition

Membrane Lipids:

Phospholipids: two fatty acids and phosphate containing groups

Lipid Rafts: saturated phospholipids

- stable, less fluid, cell signaling
- 20% of outer membrane surface

Glycolipids: attached sugar groups

Cholesterol: 20% of membrane lipids

Membrane Proteins:

Integral Membrane proteins: embedded within lipid bilayer

- transmembrane proteins (entire width of membrane)
- transport: channels, carriers

Peripheral membrane proteins: loosely attached to integral proteins or membrane lipids

-mechanical functions

Functions of Membrane Proteins:

- i) Transport
- ii) Enzymatic activity
- iii) Receptor for signal transduction
- iv) Intercellular joining
- 5) Cell to cell recognition
- 5) Attachment to the cytoskeleton and extracellular matrix

Carbohydrates (CHO): located on membrane outer surface

- bound to plasma lipid or proteins
- i) glycolipids or ii) glycoproteins
- forms fuzzy and sticky GLYCOCALYX

Fx:

- 1) protective layers that holds cells together
- 2) Role in cell recognition

CYTOPLASM:

Cytoplasm: is a cellular material between the plasma membrane and the nucleus

-cellular activities happen

i)Cytosol: gel-like fluid containing water + salts + carbohydrates + proteins

- site of production and storage of molecules
- contains enzymes catalyzing specific reactions

ii)Cytoplasmic Organelles: structures made up of a variety of biomolecules

-carry out specific functions in the body

iii)Inclusions: substances stored in cytosol

-glycogen (liver) – triglycerides –pigment (melanin)

Non-membranous Organelles:

- ribosomes
- vaults
- cytoskeleton
- centrioles

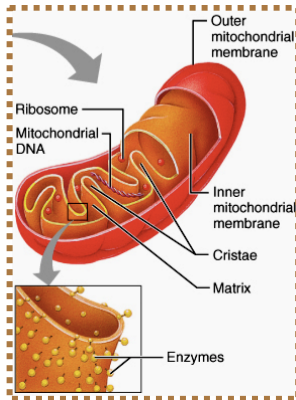
Membranous organelles:

Mitochondria: Powerhouse

- rod shaped
- double membrane
- smooth outer and folded inner membrane (cristae)

- matrix granules
- self replicating (own DNA, RNA and ribosomes)

Fx: POWER HOUSE of cells → aerobic metabolism of glucose and fatty acids → ATP



Endoplasmic Reticulum: system of interconnected tubes and parallel membranes enclosing fluid filled cavities (CISTERNAE)

Smooth ER:

- smooth tubules, no ribosomes

Fx:

- synthesis of cholesterol, steroids, lipid components of lipoproteins
- absorption, synthesis and transport of lipids in the intestine
- detox of drugs
- breakdown of glycogen to glucose
- synthesis of steroid base hormones (sex)
- storing calcium

Rough ER:

- flatten sacks with ribosomes containing RNA and proteins
- continuous with outer membrane of nuclear envelope
- secretory cells, antibody producing cells, liver cells

Fx:

- ribosomes manufacture all proteins secreted from cells
- membrane factory – creates proteins and phospholipids

Golgi Apparatus:

- stacks of flattened sacks – CISTERNEA

Fx:

-packages, modifies and concentrates proteins → secretion from cell (that are made from R ER)
-lysosomes and plasma membrane

Secretory Vesicles/ granules: proteins destined for export pinch off the trans face – migrate to plasma membrane and discharge their contents from the cell → exocytosis

Lysosomes: spherical structures surrounded by single membrane
-digestive enzymes
-membrane = hydrogen ion pump

Fx:

- 1) Endocytosis – digestion of bacteria, viruses, toxins
- 2) Breakdown of non useful tissue
- 3) Metabolic functions
- 4) Organelle replacement
- 5) Break down bone – calcium blood -

Peroxisomes:

-liver and kidney cells
-formed by budding off of ER
-single membrane
-contain enzymes (important)
-self replicate

Fx:

-degradation of molecules (fatty acids, amino acids, toxic foreign matter)
-Neutralize FREE RADICALS (reactive chemicals with unpaired electrons)
-oxidase enzymes convert FR into H₂O₂
-catalase enzymes then convert H₂O₂ to H₂O

Non-membranous organelles:

Ribosomes:

-small granuels of PROTEIN and rRNA

Fx: -site of protein synthesis

Free ribosomes → produce soluble proteins

Membrane-bound ribosomes (ER) → produce proteins primary for membrane or export

Vaults:

Cytoskeleton: provides the cell with support and enabled some degree of motility and contractility

- allows for cell movement
- three rods – smallest to biggest

i) Microtubulus: -made of tubulin
-shape of cell, distribution of cell organelles
-motor proteins
-hollow tubes

ii) Microfilaments: -protein – actin
-cell shape and motility

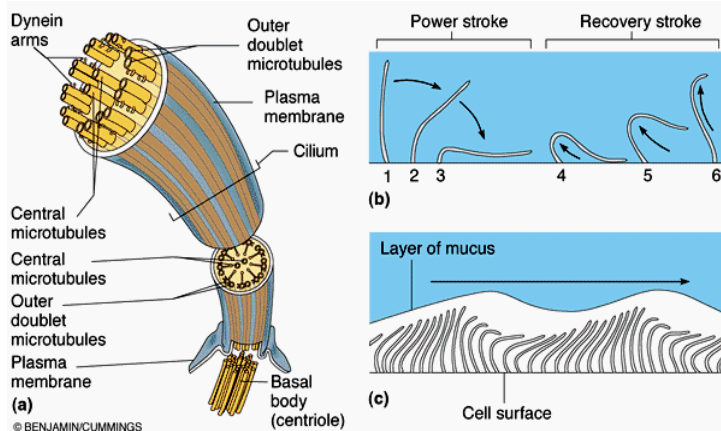
iii) Intermediate filaments:
-tough, insoluable
-high tensile strength ex keratin, myosin

Microtubules: part of cytoskeleton –
-provide strength to the cytoskeleton
-form spindle fibres during cell division
-assist with directional movement of vesicles
-part of cilia and flagella

Centrioles: basal bodies
-9 triplets of microtubules
-source of microtubules
-formation of mitotic spindle, base of cilia, flagella

Cilia: Cilia are slender protuberances that project from cell body
-sensory
-propel substances across cell surface

Flagellum: only in sperm – propels the cell



Centrosome: acts as a microtubule organizing center
 -microtubules are anchored at one end to the centrosome

Centrioles: organize mitotic spindle,
 -role in cytokinesis
 -form basis for cilia and flagella

THE NUCLEUS

Nucleus: cell's largest organelle
 -control center → genetic material
 -instructions for protein synthesis
 -forms to shape of cell

-one nucleus or multinucleate
 -anucleate (no nucleus; cannot reproduce)

Main Structures:

Nucleus envelope:
 -double membrane with large pores
 -separates the nucleoplasm from cytoplasm

Nucleoplasm: jelly like fluid – keeps structures suspended

Nucleolus/ nucleoli:
 -spherical structures composed of RNA and protein
 -nucleolar organizer regions → DNA with instructions for ribosomal RNA synthesis
 -ribosomes assembly

Chromatin: threads of 30% DNA combined with 60% histone proteins 10% rna

- made of nucleosomes
- site of genetic information

Nucleosomes: physical means of packing DNA
-gene regulation

SECTION II:

PLASMA MEMBRANE & CELLULAR TRANSPORT

Cell Membrane: Specialization & Transport

Functions of Plasma Membrane:

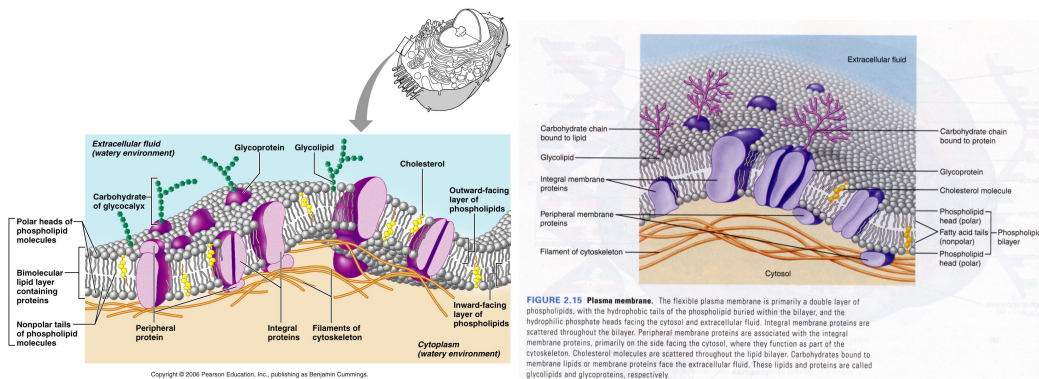
- external cell barrier
- cellular joining, attachment communication
- transport (in and out of cell)
- maintenance of membrane potential that is essential for functioning of excitable cells
- signal transduction → receptors + associated proteins
- cell to cell recognition

Plasma Membrane: -defines cells

- selective/ semi permeable barrier
- phospholipid bilayer embedded with proteins
- forms a barrier to large polar molecules

Fluid Mosaic Model:

- lipid bilayers form two dimensional liquids
- considered a fluid
- can move around laterally – mosaic pattern
- proteins not attached
- lots of proteins → structure



Phospholipids: glycerol backbone – 2 fatty acids + phosphate
-polyunsaturated fatty acids → increase membrane fluidity

-Saturated fatty acids (SFA) → lipid rafts → more stable, less fluid, involved in cell signaling

Cholesterol: 20% of membrane lipids
→ form lipid rafts

Lipid rafts: saturated FA, cholesterol
→ receptor mediated signal transduction

Membrane Fluidity Index:

Proteins:

-proteins in lipid bilayer – change position

2 membrane proteins

1) integral membrane proteins – in lipid bilayer → trans membrane protein

-receptors, channels, carry proteins

2) peripheral membrane proteins

-loosely attached to integral proteins or membrane lipids

Plasma Membrane → Function

1) Transport

2) Enzymatic activity

3) Receptors for signal transduction

4) Intercellular joining

5) cell to cell recognition

6) attachment to cytoskeleton and extra cellular matrix

Carbohydrates (CHO)

-membrane outer surface

-bound to plasma lipids or proteins → glycolipids + glycoproteins

CHO Fx → form fuzzy and sticky glycocalyx

1) Protective layer that holds cells together

2) role in cell recognition

-important for immune response, reproduction, cancer

Microvilli: -extension of plasma membrane

-increase plasma membrane surface area

-absorptive cells

Membrane Junctions:

-many epithelial cells are knit into tight communities

3 Factors that bind cells together

- 1) Glycoproteins in the glycocalyx act as an adhesive
- 2) Wavy contours of the membrane of adjacent cells fit together in a tongue and groove fashion
- 3) Special membrane junctions are formed

1) Tight Junctions:

- proteins fused together in plasma membrane
- impermeable junction that encircles the cell
- preventing ion passage increases exponentially with the number of strands
- strand → row of transmembrane proteins embedded in both plasma membrane – extracellular domains joining one another directly
- junctional proteins: claudins and occludins → like hooks
- ex: digestive tract – keep digestive enzymes in intestine from getting into the blood

Fx:

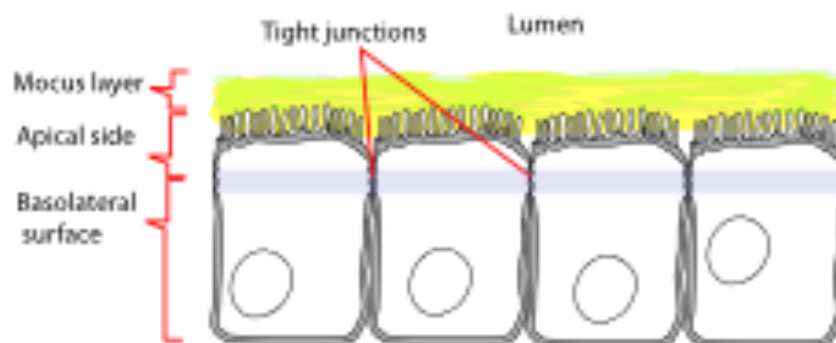
- they hold cells together (join together the cytoskeleton of adjacent cells)
- They prevent the passage of molecules and ions through the space between adjacent cells → control what substances are allowed in
→ help maintain blood barrier
- they block the movement of integral membrane proteins between the apical and basolateral surfaces of the cell → allowing specialized function of each surface to be preserved

Apical surface: receptor mediate → endocytosis

-faces inwards

Basolateral surface: → exocytosis

-faces outwards



Adherens junctions: are located below the region of the tight junctions

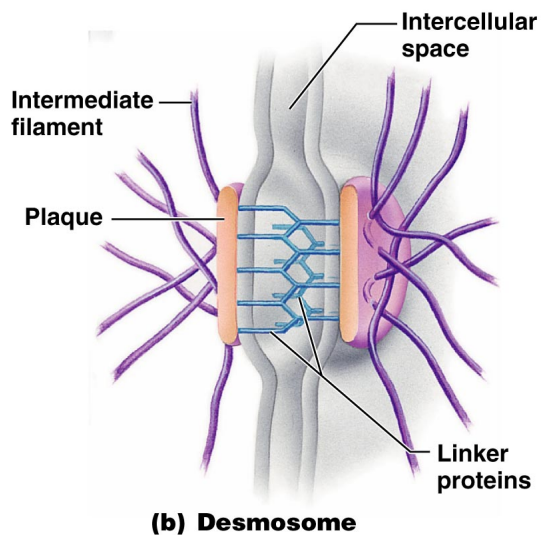
-help epithelial surfaces resist separation

2) Desmosomes: anchoring junction

- cells are held together by thin linker protein filaments (CADHERINS)
- plaque on the cytosolic side of the cell → button like thickening
- cadherins extend from plaque and fit together like teeth of a zipper in the intercellular space
- keratin extend from the cytoplasmic side of the plaque across the width of the cell to anchor to the plaque on the cells opposite side
- continuous internal network
- work against pulling forces

Fx:

- binding neighboring cells together
- providing stability of cells and tissues
- prevent separation of cells under tension or contraction



3) Gap Junction

- a communication junction between adjacent cells
- plasma membranes are very close – cells are connected by cylinders called CONNEXONS (transmembrane proteins)

Fx:

- passage of small molecules (sugars, AA, ions) from one cell to another
- Helps with synchronized cells (tissue activity) – in heart and smooth muscle tissue
- muscle contraction

Cell's internal environment:
=3 fluid compartments

Extracellular Fluid (ECF):

- i) Interstitial fluid → fluid surrounding the cell
- ii) blood plasma → liquid portion of blood

Intracellular Fluid (ICF): the fluid inside the cell

- Continuous traffic across plasma membrane including →
- nutrients (CHO AA FA vitamins and minerals)
- gases
- electrolytes
- hormones (some)
- neurotransmitters
- water
- waste products

Plasma membrane transport

- membrane is selective (differentially permeable) barrier → allows substances to pass while restricting others
- when membrane is damaged – becomes permeable

Two main transport:

1) Passive processes

- a) simple diffusion
- b) facilitated diffusion – carrier + channels
- c) osmosis
- d) filtration

2) Active Transport:

- a) Active transport
 - primary
 - secondary
- b) Vesicular transport
 - endocytosis, vesicular trafficking
 - phagocytosis
 - transcytosis
 - exocytosis

PASSIVE PROCESSES:

a) Diffusion

- molecules or ions to move from an area where they are in HIGHER concentration to an area of LOWER concentration → moves down CONCENTRATION GRADIENT
- a substance diffuses down a concentration gradients until it reaches an equilibrium
- molecules and ions are dispersed (due to collisions)
- more collision → faster diffusion of particles
- driving force → kinetic energy of molecules
- speed of diffusion influence by
 - size of molecule (smaller, faster)
 - temperature (warmer, faster)

-hydrophobic core is a physical barrier to free diffusion

Molecules will diffuse through membrane if:

- lipid soluble
- small enough to pass through membrane channels
- assisted by a carrier molecules

Factors affecting diffusion:

- 1) Steepness of concentration gradient – the greater the difference in concentration between the two sides – the higher rate of diffusion
- 2) Temperature – the higher the temp → higher diffusion gradient
- 3) Mass of diffusing substance – the larger the mass of diffusing particle → the slower its diffusion rate
- 4) Surface area – the larger the area available for diffusion → faster
- 5) Diffusion distance – the greater the distance → longer it takes

i) Simple Diffusion

- unassisted diffusion of lipid soluble/ small particles
- osmosis – unassisted diffusion of a solvent (water) through a membrane
- includes: nonpolar hydrophobic solute, fatty acids, steroids, fat soluble vitamins, glycerol and small alcohols

Pores: for small, polar molecules (Na⁺ Cl⁻) → water filled, narrow, selective
-some open, some closed – need chemical or electrical signals

ii) Facilitated Diffusion

- cannot pass through lipid bilayer (too large or insoluble)
- 1) binds to protein carriers in the membrane (change shape when binding the substance)
- 2) moves through water filled protein channels

-glucose sugars AA ions...

*transport may be limited by availability of transporters and channels

Features:

- 1) specific
- 2) no ATP required
- 3) limited by carrier saturation
- 4) movement DOWN concentration gradient

i) Carriers: transmembrane integral proteins show specificity for molecules of a certain POLAR substance

-envelope and then release

-moves down its concentration gradient

ii) Channels: transmembrane proteins that transport substances through aqueous channels

-binding or association sites exist within the channels

-selective (pore size)

-leakage channels

c) Osmosis: is a passive movement of a solvent through a selectively permeable membrane

-solvent = water in living organisms

-water moves from an area of higher water concentration to a lower water concentration (from lower solute concentration to its higher concentration)

-water is highly polar but still passes through lipid bilayer

-occurs whenever the water concentration differs on two sides of the membrane

-if solute concentration on the two sides of the membrane differ, water concentration differs as well

Water moves:

1) through the gaps in the lipid bilayer (water is polar but small enough)

2) by moving through aquaporins

Aquaporin's: water specific channels constructed by transmembrane proteins

Osmolality: total concentration of solute particles in solution (number is important, not type) → one molecule displaces one molecule of water

*when equal volumes of aqueous solutions of different osmolality are separated by permeable to all molecules in the system – net diffusion of both solute and water occurs each moving DOWN its concentration gradient

*impermeable to solute molecules → water quickly diffuses from left to right and continues to do so until its concentration is the same on the two sides of the membrane

-equilibrium is from water alone (solutes are prevented from moving)

-movement of water leads to dramatic changes in the volumes of two different sides

-osmosis continues until osmotic and hydrostatic pressures acting at the membrane are equal

-osmotic pressure of a solution → indirect measure of its solute concentration

→ the higher the solute concentration – the higher the osmotic pressure

Hydrostatic pressure: the back pressure exerted by water against the membrane

Osmotic pressure: the tendency of water to move into cell by osmosis

Tonicity: the ability of a solution to change the shape of ton of cells by altering their internal water volume

-measure of effective osmotic pressure gradient (water potential of two solutions) or two solutions separated by a semi permeable membrane

-relative concentration of solutions that determine the direction and extent of diffusion

A) Isotonic – solutions with the same concentration of nonpenetrating solutes as those found inside cells

-effective osmole concentration is the same as the solute concentration of a cell

-neither swells nor shrinks

-no concentration gradient for water across cell membrane

B) Hypotonic – solutions that are more dilute than other inside cells

-lower concentration of solutes outside the cell than inside the cell

-water will rush into the cell, causing it to swell and maybe burst

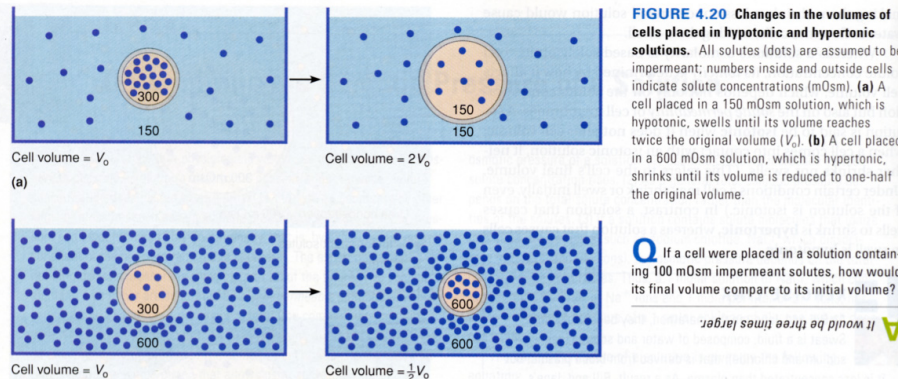
-rehydrate dehydrated patients

C) Hypertonic – solutions with a higher concentration of non penetrating solutions than those inside cells

-higher concentration of solutes outside the cell than inside the cell

-water to flow out of the cell in order to balance the concentration of solutes

-pull water out of swollen tissues



d) Filtration

- movement of solvents (such as water) and solutes (such as glucose) across a selectively permeable membrane as a result of gravity or hydrostatic water pressure from one area of higher to lower pressure
- continuous as long as there is a pressure gradient
- not selective

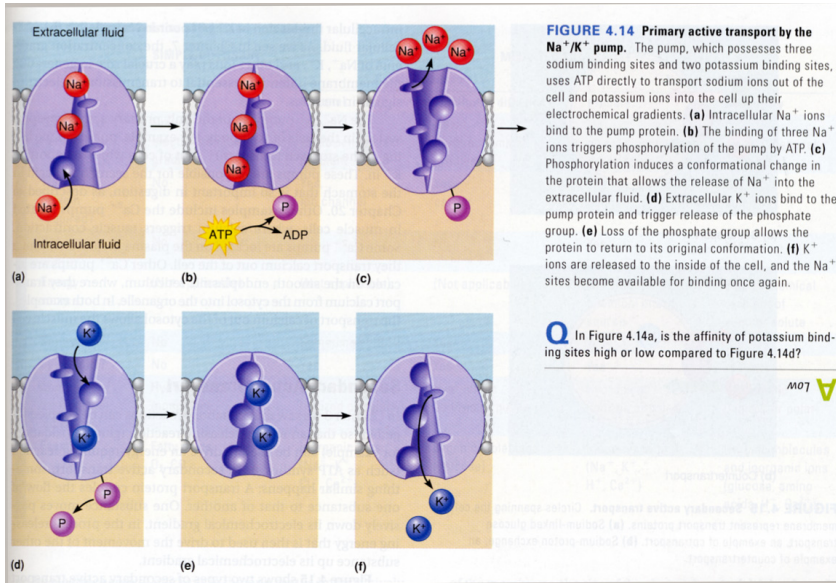
ACTIVE TRANSPORT

a) Active Transport

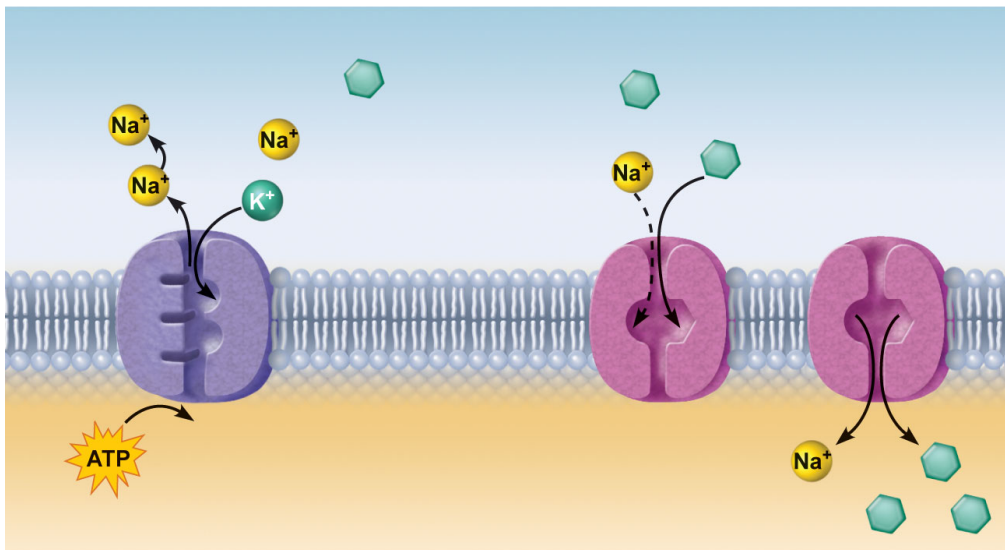
- requires carrier proteins that combine specifically and reversibly with transported substances
- solute pumps move solutes(ions) UPHILL **AGAINST** the concentration gradient → ATP

- i) Primary: to move substances across the plasma membrane against concentration gradient it requires energy from splitting ATP
- primary active transport → sodium potassium pump
- ex:

- 1) Cytoplasmic Na binds to pump protein
 - 2) Binding of Na promotes phosphorylation of the protein by ATP
 - 3) Phosphorylation causes the protein to change shape expelling Na to the outside
 - 4) Extracellular K binds to pump protein
 - 5) K binding triggers release of the phosphate. Pump proteins return to its original conformation
 - 6) K is released from the pump protein and Na sites are ready to bind Na again
- Repeat



- ii) **Secondary:** involves simultaneous movement of two substances or more (coupled system) across plasma membrane
- the different in concentration gradient (created by primary transport) builds up a DIFFUSION energy \rightarrow can pull substances along through the cell membrane
 - one is usually Na^+
 - uses potential energy present in Na^+ concentration gradient, which is maintained by primary active transport
 - secondary active transport – indirectly uses energy from the splitting of ATP



1) The ATP-driven Na⁺-K⁺ pump stores energy by creating a steep concentration gradient for Na⁺ entry into the cell.

2) As Na⁺ diffuses back across the membrane through a membrane cotransporter protein, it drives glucose against its concentration gradient into the cell. (ECF = extracellular fluid)

Symport system: transported substances move in the same direction

Antiport: opposite directions

VESICULAR TRANSPORT

-requires energy

-fluids containing large particles and macromolecules are transported across cellular membrane inside membranous sacs called VESICLES

i) Endocytosis

-cell ingests small patches of plasma membrane and moves substances from the cell exterior to the cell interior

1) substance to be taken into the cell by endocytosis is progressively enclosed in a folding portion of the plasma membrane called a coated pit (clathrin)

Clathrin: coated vesicles provide main route for endo and trans of bulk solids

2) Vesicle detaches

3) the coat proteins are recycled back to the plasma membrane

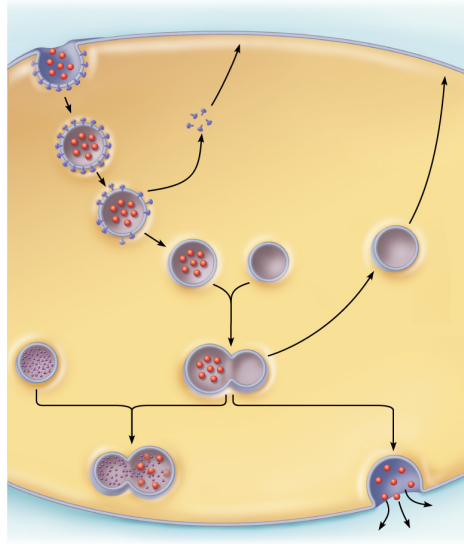
4) uncoated vesicle then typically fuses with a processing and sorting vesicle called ENDOSOME

5) some membrane components and receptors of the fused vesicle may be recycled back to the plasma membrane in a transport vesicle

6) the remaining contents of the vesicle

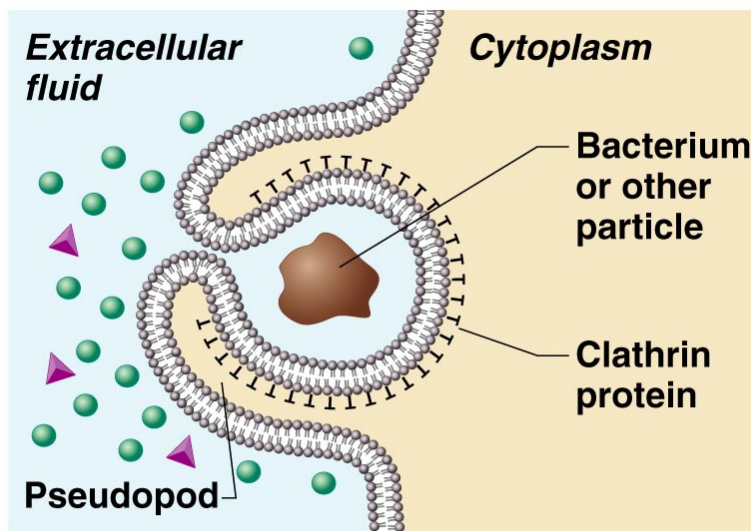
→ combine with a lysosome - degraded or released

→ transported completely across the cell and released by exocytosis



Phagocytosis: Cell eating

- type of endocytosis
- engulf large solid material
- particle binds to receptors
- pseudopods engulf the solids and bring them into cells interior
- lysosome then digest
- extra waste is ejected from cell by exocytosis



Pinocytosis: Cell drinking

- fluid phase endocytosis
- plasma membrane surrounds extracellular fluid with dissolved molecules
- enters the cells and fuses with an endosome

Transcytosis:

Receptors mediated endocytosis:

Exocytosis:

-stimulated by cell surface signal

-secretion or ejection of substances from a cell: the substance is enclosed in a membranous vesicle → fuses with plasma membrane and ruptures, releasing the substance to the exterior

-hormone secretion, neurotransmitter release, mucus secretion, ejection of waste

2.3 Muscles

Muscles Tissue:

- 50% of bodys mass
- transforms chemical energy (ATP) to directed mechanical energy → exert force

Three Types: Skeletal, muscle, cardiac

- myo, mys, sarco – prefixes for muscles

Muscles fibers: skeletal and smooth muscles (but not cardiac muscles) are elongated

Skeletal Muscle Tissue: is packaged into skeletal muscles organ that attach to and cover the bony skeleton




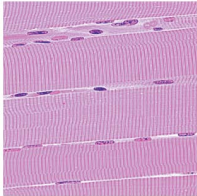

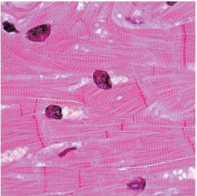

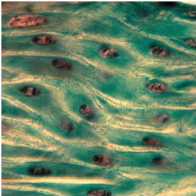

- longest muscles
- stripes called STRIATIONS
- voluntary muscles
- overall body movement
- adaptable

Cardiac Muscle Tissue: heart

- heart walls
- striated
- not voluntary
- cardiac, striated, involuntary

Smooth Muscle tissue: walls of hollow visceral organs

- stomach urinary bladder and respiratory passages
- force fluid and other substances through internal body channels
- elongated fibers but not striated
- visceral, non-striated, and involuntary

Table 9.3 Comparison of Skeletal, Cardiac, and Smooth Muscle			
CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Body location	Attached to bones or (some facial muscles) to skin	Walls of the heart	Unitary muscle in walls of hollow visceral organs (other than the heart); multi unit muscle in intrinsic eye muscles, airways, large arteries
			
Cell shape and appearance	Single, very long, cylindrical, multinucleate cells with obvious striations	Branching chains of cells; uni- or binucleate; striations	Single, fusiform, uninucleate; no striations
	 	 	 

Special Characteristics:

- i) **Excitability:** responsiveness and irritability
-receive and respond to a stimulus
- ii) **Contractibility:** ability to shorten forcibly when stimulated
-ability sets muscles apart from all other tissue types
- iii) **Extensibility:** the ability to be stretched or extended
-muscle cells shorten when contracting, but they be stretched even beyond their resting length when relaxed
- iv) **Elasticity:** is the ability of s muscles cell to recoil and resume its resting length after being stretched

SKELETAL MUSCLES:

- attached to bones and skin
- elongated cells called MUSCLE FIBERS
- striated (striped)
- voluntary
- contract rapidly; tire easily; powerful
- require nerve stimulation

Muscles Functions:

- Producing movement
- Maintaining posture anybody position
- stabilizing joints
- generating heat
- product fragile internal organs (viscera)

Anatomy of Skeletal Muscles

- skeletal muscle fibers

- nerve and blood supply
- connective tissue sheath

Connective Tissue Sheath:

External to internal

- **Epimysium:** dense irregular connective tissue surrounding entire muscle; may blend with fascia
- **Perimysium:** fibrous connective tissue surrounding **fascicles** (groups of muscle fibers)
- **Endomysium:** fine areolar connective tissue surrounding each muscle fiber

Attachments:

-Attach in at least two places

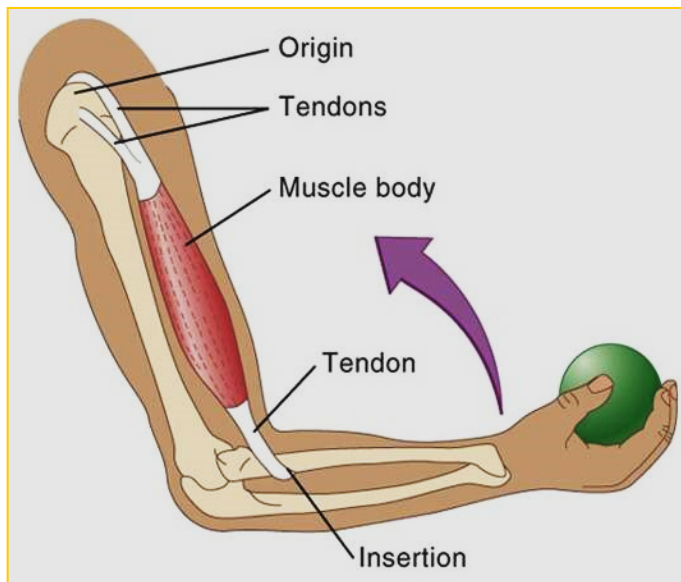
→ Insertion – moveable bone

→ Origin – immovable (less moveable) bone

-Direct or indirect attachment

→ Direct – epimysium fused to periosteum or bone or perichondrium of cartilage

→ Indirect – connective tissue wrapping extend beyond muscle as rope like tendon or sheet like aponeurosis



-each muscles served by one artery one nerve and one or more viens

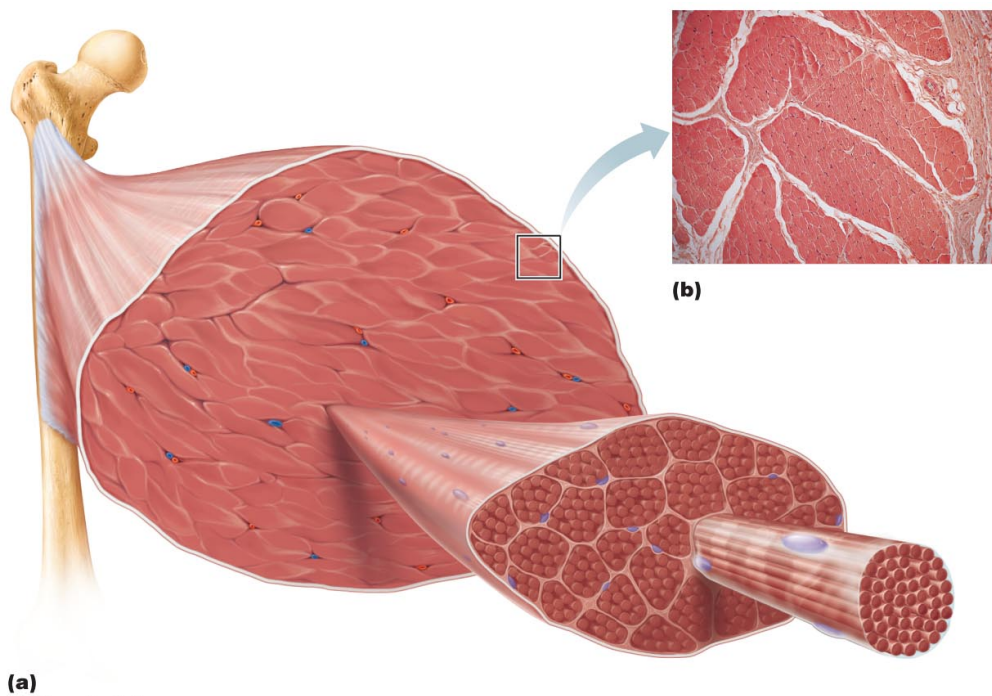
→ enter/exit near central part and branch through connective tissue sheaths

→ every skeletal muscles fiber supplied by nerve ending that control its activity

→ huge nutrient and oxygen need; generates large amount of waste

Structure and Organization Level	Description	Connective Tissue Wrappings
Muscle	A muscle consist of hundreds to thousand of muscles cells plus connective tissue wrappings, blood vessels and nerve fibers	Covered exxternally by epimysium
Fascicle (portion of the muscle)	A fascicle is a discrete bundle of muscle cells, segregated from the rest of the muscle by a connective tissue sheath	Surrounded by a perimysium
Muscle fiber (cell)	A muscle fiber is an elongated multinucleate cell; it has a banded (striated) appearance	Surrounded by endomysium
Myofibril/ Fibril (complex organelle composed of bundles of myofilaments)	Myofibrils are rodlike contractile elements that occupy most of the muscles cell volume. Composed of sarcomeres arranged end to end, they appear banded and bands of adjacent myofibrils are aligned	
Sarcomere (a segment of a myofibril)	-A sarcomere is a contractile unit, composed of myofilaments made up of contractile proteins -smallest contractile unit of muscle fiber – the functional unit of skeletal muscles	
Myofilament or filament (extended macromolecular structure)	- Contract myofilaments are two types → thick and thin - Thick filaments contain bundled myosin molecules -Thin filaments contain actin molecules (plus other proteins)	

	<p>-The sliding of the thin filaments past the thick filaments produce muscle shortening</p> <p>-Elastic filaments maintain the organization of the A band and provide for elastic recoil when muscle contraction ends</p>	



Skeletal Muscle Fibers:

- long cylindrical
- 10-11 um in diameter
- multiple peripheral nuclei

2 sets of intracellular tubules that participate in regulation of muscle contraction:
 (1) the sarcoplasmic reticulum (2) t tubules

Sarcolemma: plasma membrane

Sarcoplasm: cytoplasm

-glycosomes for glycogen storage, myoglobin for oxygen storage

Sarcoplasmic Reticulum: its interconnecting tubules surround each myofibril loosely

-large number of mitochondria and glycogen granules both involved in producing the energy used during contraction

T tubules: at each A band and I band junction, the sarcolemma of the muscle protrudes deep into the cell interior → forming elongated tube

-increase muscle fibers surface area

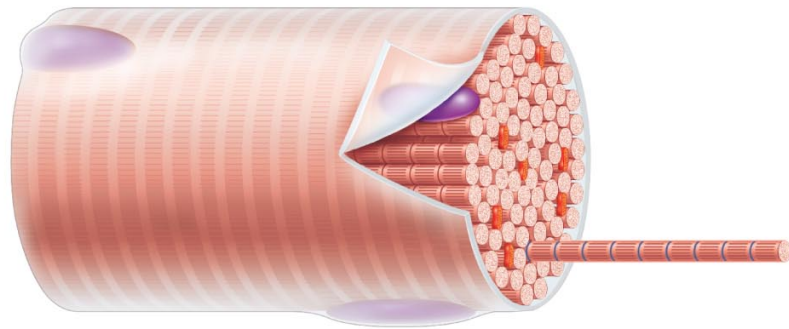
-runs between terminal cisternae forming TRIADS – successive groupings of the three membranous structures (terminal cisterna, t tubule and terminal cisterna)

-muscle contraction is controlled by nerve initiated electrical impulses that travel along the sarcolemma

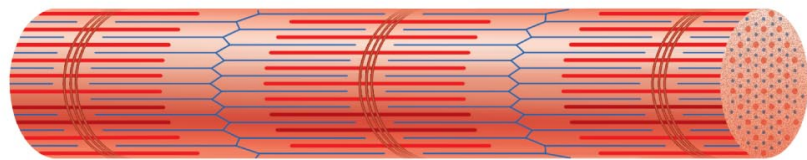
-tubules conduct impulses to the deepest region of the muscle cell and to every sarcomere

-signals released → calcium

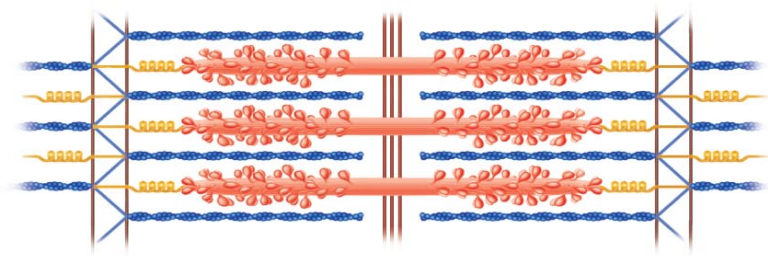
(b)



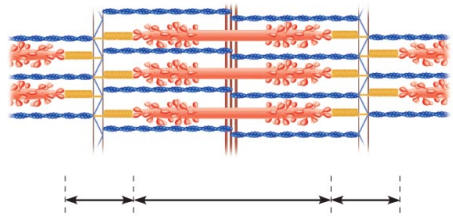
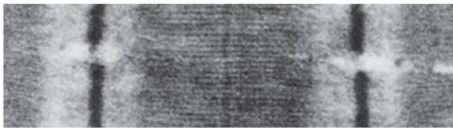
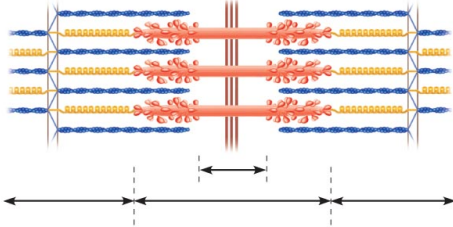
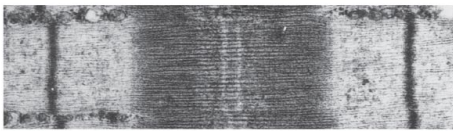
(c)



(d)



Z disc (line): coin shaped sheet of proteins on midline light I band that anchors thin filaments and connects myofibrils to one another



PHYSIOLOGY OF SKELETAL MUSCLE

For skeletal muscles to contract:

i) Requires Activation

- stimulation of neuromuscular junction
- must generate action potential in sarcolemma

ii) Excitation-contraction coupling:

- AP propagated along sarcolemma
- intracellular CA levels must rise briefly

Steps:

- 1) it must be activated/ stimulated by a nerve ending so that a change in membrane potential occurs
- 2) must generate and propagate an electrical current called an action potential along its sarcolemma
- 3) then a short lived rise in intracellular calcium ions levels that is the final trigger for contraction must occur

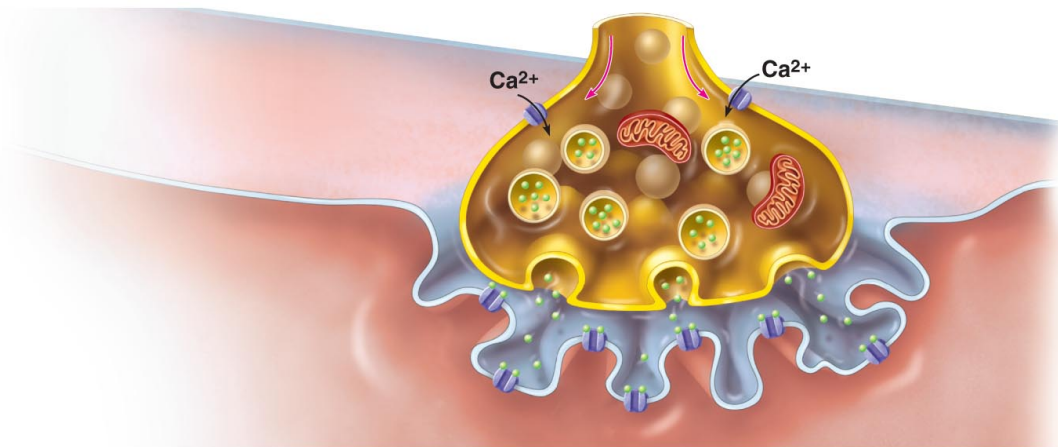
- skeletal muscles are stimulated by motor neurons called **MOTOR NEURONS OF THE SOMATIC (VOLUNTARY) NERVOUS SYSTEM**
- in the brain or spinal cord but they have long axons

Neuromuscular junction: each axon ending forms this with a single muscle fiber
-each muscle fiber has only one junction
-includes axon endings, synaptic cleft, and the junctional folds of the sarcolemma (plasma membrane)

Synaptic cleft: axon terminal and muscle fiber are exceedingly close

Synaptic vesicle: small membrane sacs containing the neurotransmitters acetylcholine (Ach)

-junctional folds – provide large surface area for the millions of Ach receptors (on sarcolemma)



Events at Neuromuscular Junction:

- 1) AP arrives at the axon terminal of a motor neuron
- 2) voltage gated Ca channels open. Ca enters the axon terminal moving down its electrochemical gradient
- 3) Ca entry causes Ach to be released by exocytosis
- 4) Ach diffuses across the synaptic cleft and binds to its receptors on the sarcolemma
- 5) Ach binding opens ion channels that allow simultaneous passage of Na into the muscle fiber and K out of the muscle fiber. More Na ions enter the K ions leave and this produced a local change in the membrane potential (DEPOLARIZATION)
- 6) Ach effects are terminated by its enzymatic breakdown in the synaptic cleft by acetylcholinesterase.

Generation and propagation of an action potential:

- 1) Local depolarization: generation of the end of plate potential on the sarcolemma
-binding of Ach to Ach receptors opens the chemically gated ion channels housed in the Ach receptors → allowing Na and K to pass
-More Na diffuses in than K diffuses out → depolarization
-interior of the sarcolemma is slightly less negative
-called End Plate Potential

2) Generation and propagation of the action potential

- local current is spread and sarcolemma membrane are depolarized
- opens voltage gated sodium channels there so Na enters, following its electrochemical gradient and initiates AP
- AP is propagated as the local depolarization wave spread to adjacent area of the sarcolemma and open more channels
- sodium ions (normally restricted from entering) diffuse into the cell following their electrochemical gradient

3) Repolarization

- Na channels close and voltage gated K channels open
- K diffuses rapidly out of the muscle fiber down its concentration gradient → as K concentration is substantially higher inside the cell → restoring negative conditions inside the cell

Excitation-contraction (E-C): pg 290

Is the sequence of events by which transmission of an action potential along the sarcolemma leads to the sliding of myofilaments

- released Ach binds to receptor proteins on the sarcolemma and triggers an action potential in muscle fibers

-provides excitation

- 1) Action potential is propagated along the sarcolemma and down the T tubules
- 2) Calcium ions are released

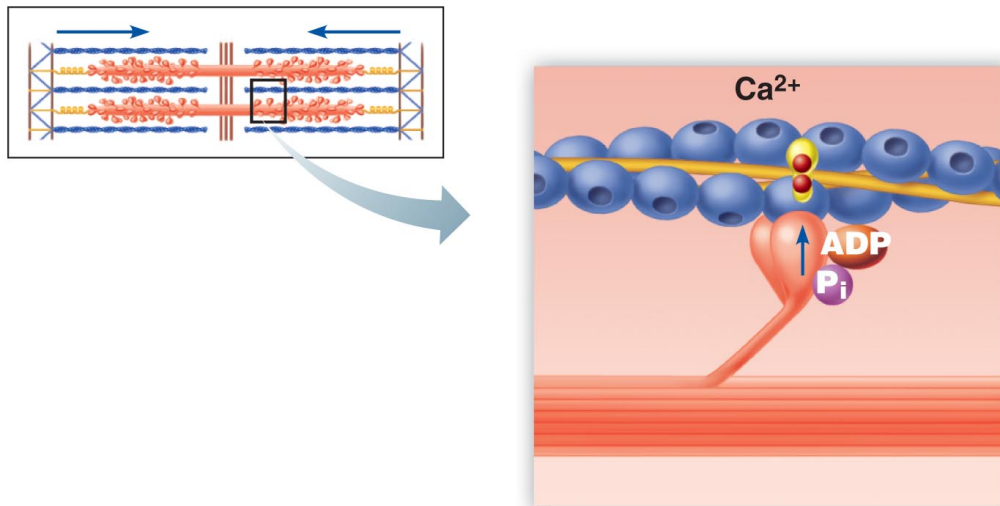
- AP travels along t tubules → causing voltage sensitive tubule proteins to change shape
- opens the Ca release channels in terminal cisternae of the sarcoplasmic reticulum
- allowing massive amounts of CA to flow into cytosol

Contraction:

- 3) Calcium binds to troponin and removes the blocking action of tropomyosin
 - exposes binding sites for myosin (active sites) on the thin filaments
- 4) Contraction begins: myosin binding to actin forms cross bridges and contraction (cross bridge cycling) begins
 - E-C coupling is over

Cross Bridge Cycle: is the series of events during which myosin heads pull thin filaments toward the center of the sarcomere

- 1) Cross Bridge formation: energized myosin head attaches to actin myofilament forming a cross bridge
- 2) Power (working) stroke: ADP and Pi are released and the myosin heads pivots and bends changing to its bent low energy shape
 - pulls on the actin filament sliding it toward the M line
- 3) Cross bridge detachment:
 - ATP attached to myosin
 - link between myosin and actin weakens → myosin head detaches
- 4) Cocking of myosin head
 - ATP is hydrolyzed to ADP and P
 - myosin head returns to its prestrike high energy/ cocked position



-cycle continues as long as ATP is available and Ca is bound to troponin

Contraction of a Skeletal Muscle:

Muscle tension: force exerted contracting muscle on an object

Load: opposing force exerted on the muscle by weight of the object to be moved

Isometric: if muscle tension develops but the load is not moved

- lifting car
- same measure

Isotonic: if muscle tension developed overcomes the load and muscle shortening occurs

- same tension

*increasing muscle tension is measured for isometric contractions

* amount of muscle shortening (distance in mm) is measured for isotonic contractions

Motor Unit: nerve muscle functional unit

-each muscle is served by at least one motor nerve → each motor nerve contains axons (fibrous extensions)

-when axon enters a muscle – branches into many axon terminals which form neuromuscular junctions

→ A motor unit consists: of a motor neuron and all the muscle fibers it supplies

-when a motor neuron (transmits AP) → muscle fibers contract

-stimulation of single motor neuron will cause a weak contraction of the entire muscle → spread throughout the muscle

Muscle Twitch: the response of a motor unit to a single action potential of its motor neuron

Three stages:

1) latent period: muscle tension begins to increase, no response

2) period of contraction: cross bridges are active

-tension development

3) period of relaxation : reentry of Ca into SR

-muscle tension decreases to 0

-muscle returns to initial length

Graded Muscle Responses: healthy muscle contractions are relatively smooth and vary in strength as different demands are placed on them

-these variations are needed for proper control of skeletal movements

Muscle contractions can be graded in two ways:

1) changing the frequency of stimulation

2) changing the strength of stimulation

Muscle Response to changes in Stimulus Frequency:

-increase firing rate of motor neurons

Temporal/ Wave Summation: occurs because second contraction occurs before the muscle has completely relaxed

-two stimuli are delivered to muscle in rapid succession – second twitch will be stronger –

-muscle is already partially contracted when the next stimulus arrives and more calcium is brought into cytosol – more muscle shortening than the first

-contractions are summed

→ can lead to unfused or incomplete tetanus (when it keeps going)

→ fused/ complete tetanus: muscle relaxation disappears → like when people lift up a car

-each contraction builds on the previous one

Tetanus: fused contractions – inter-stimulus interval too short to allow inter twitch muscle relaxation – eventually followed by muscle fatigue

→ allows smooth continuous contractions

Muscle Responses to Changes in Stimulus Strength:

Multiple Motor unit summation:

-force of contraction is controlled by this

Threshold stimulus: first observable response (contraction)

→ muscle contracts more and more as stimulus strength is increased

Maximal Stimulus: strongest stimulus that produces an increase in contractile force (more motor units recruited)

-all muscle motor units are recruited

-increasing stimulus intensity beyond max does not produce stronger contractions

-smaller motor units controlled by most excitable neurons

-more intense stimulation recruits larger motor units

Muscle tone:

-relaxed muscle are slightly contracted (tone) due to spinal reflexes activated by stretch receptors

-does not produce active movements → keeps muscles firm and healthy

Two main categories on contraction:

-Isotonic + isometric

1) **ISOTONIC:** iso = same ton = tension

-muscle length changes and moves the load

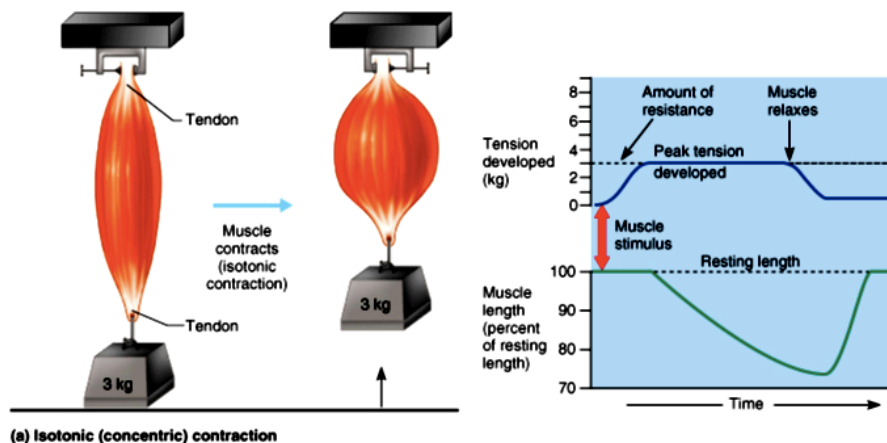
-once enough tension has developed to move the load → tension remains relatively CONSTANT through the rest of the contractile period

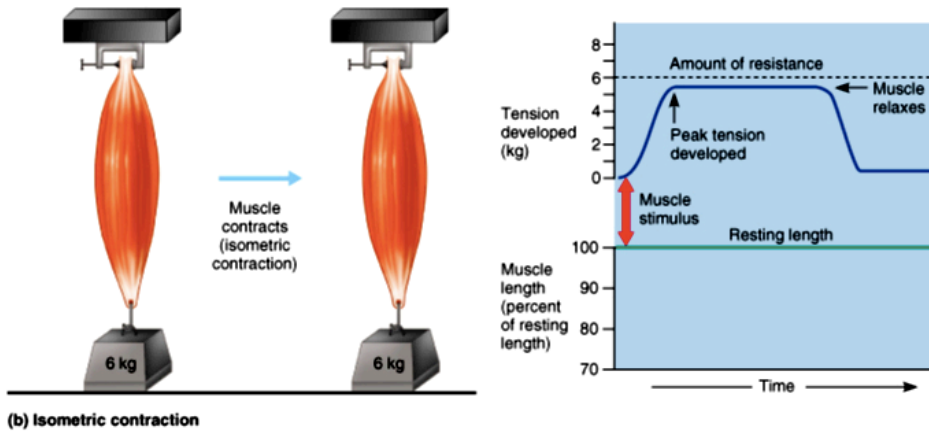
Concentric contraction: muscle SHORTENS and does work
-ex picking up a book

Eccentric contraction: muscle generates force as it LENGTHS
-coordination and purposefully movements
-50 % more forceful than concentric contractions
-use less ATP and oxygen
-fewer muscle fibers
-delayed on set soreness (microtears in muscle)
-walking up a hill

2) ISOMETRIC: tension increase but muscle stays same length
-neither shortens or lengths even when at its peak muscle tension producing capacity
-occurs when a muscle attempts to move a load that is greater than the force (tension) the muscle is giving
-helps us to remain upright posture/ hold joints in stationary position while movements occurs at other joints

*most body movements are isotonic and isometric (mix)
-isotonic contraction, the thin filaments are sliding
-isometric contractions, cross bridges generating force, but do NOT move thing filaments

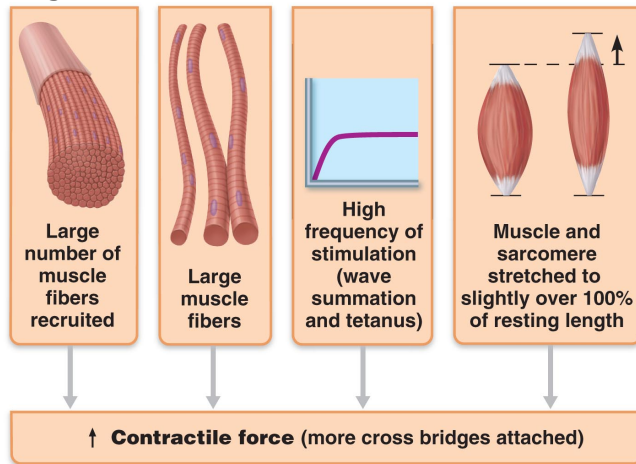




*ideal LENGTH-tension relationship when muscle slightly stretched
 → supported by attachment to bones

The force of muscle contraction is affected by

- number of muscle fibers stimulated
- size of the fibers
- frequency of stimulation
- degree of muscle stretch



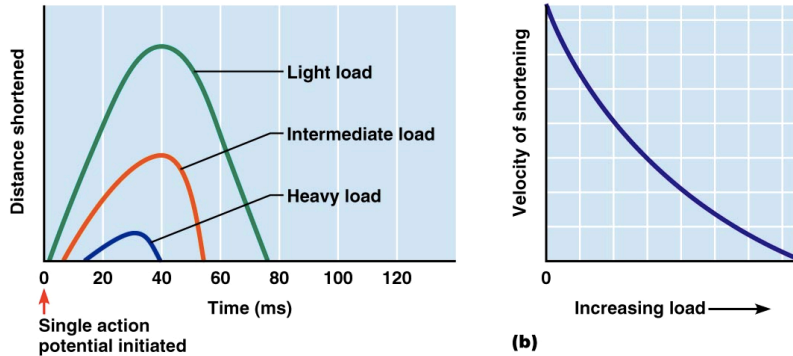
Velocity and Duration of Contraction:

- muscle vary in how fast they contract and how long they contract before they fatigue
- influenced by muscle fiber type, load and recruitment

Load --> the great the load, the longer latent period, slower contraction, short contraction duration

-if load exceeds the muscle maximum tension, the speed of shortening is zero and the contraction is isometric

Recruitment → the more motor units that are contracting, the faster and more prolonged the contraction



- you increase the load – velocity goes down
- you increase the load – shortens less

Sources of Energy for muscle contraction:

- as muscle contracts – ATP supplies the energy for cross bridge movement and detachment and for operation of calcium pump in the SR
- store little reserves
- after ATP is hydrolyzed to ADP + phosphate in muscle fibers → regenerated by one or more of the pathways→
- uses glycolysis + aerobic respiration to produce ATP

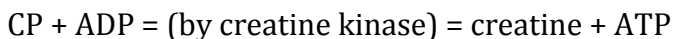
1) Stored ATP

- ATP for cross bridge movement and detachment; Ca pump
- only 4-6 second stored ATP: regenerated immediately and continuously

2) Direct Phosphorylation of ADP by creatine phosphate

- creatine phosphate tapped to regenerate ATP while the metabolic pathways are adjusting to the suddenly higher demands for ATP
- CP + ADP is an instant transfer of energy and a phosphate group from CP to ADP to form ATP
- catalyzed by enzyme creatine kinase
- CP replenished during periods of rest or inactivity
- enough for 14-16 seconds max muscle power

Creatine Phosphate: a unique high energy molecule stored in muscle



3) Aerobic Respiration:

- 95% of ATP used for muscle activity comes from this
- high ATP yields but slower, requires continuous O₂ and nutrients
- occurs in mitochondria, requires oxygen and involves a sequence of chemical reactions → bonds of fuel molecules are broken and the energy released is used to make ATP
- glucose is broken down→

glucose + oxygen → carbon dioxide + water + ATP

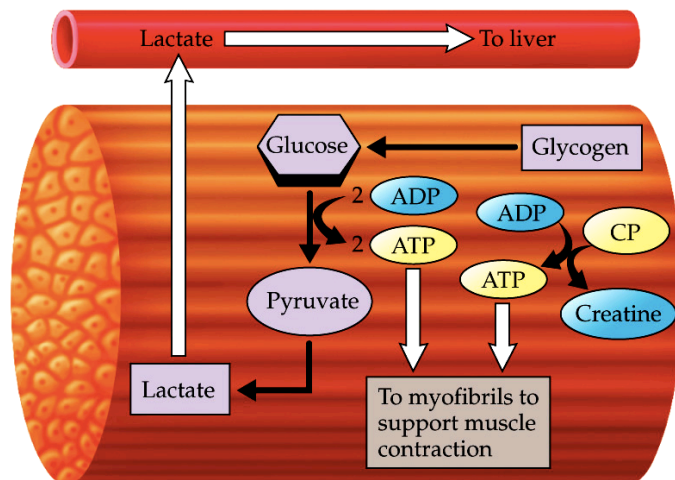
4) Anaerobic Pathway: Glycolysis and Lactic Acid Formation

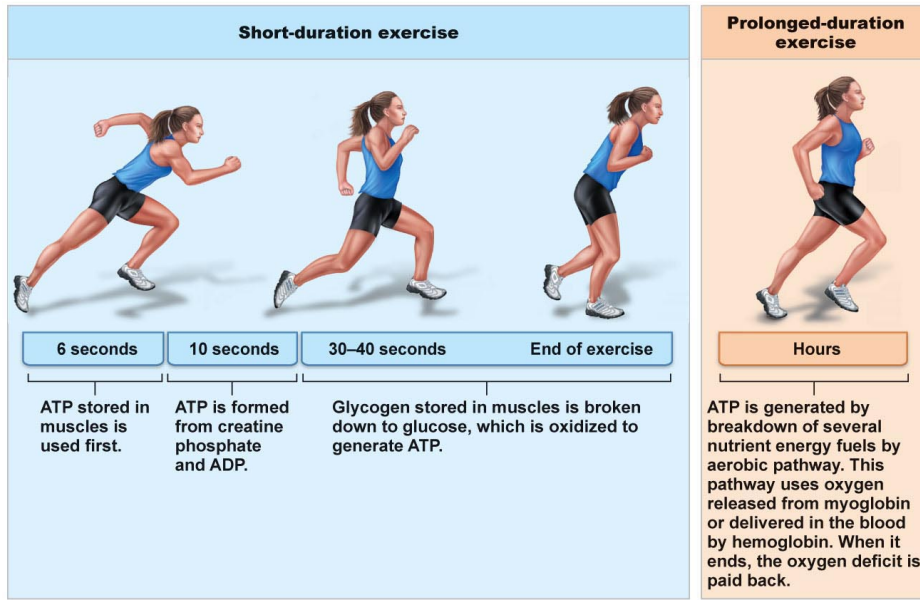
- does not use oxygen
- only 2 ATP/ glucose → fast
- ATP is generated by the breakdown (catabolism) of glucose obtained from the blood or glycogen stored in the muscle

- Glycolysis → sugar splitting → initial phase
- glucose breakdown
- glucose is broken down to two pyruvic acid molecules
- releasing energy to form small amounts of ATP (2 ATP per glucose)

- when muscle contract vigorously and contractile activity reaches about 70% maximum possible → bulging muscle compress the blood vessels within them → therefore impairing blood flow and oxygen delivery → no more oxygen

- pyruvic acid producing during glycolysis is then converted in LACTIC acid → this is anaerobic glycolysis → reconverted to lactic acid
- produces only about 5% the ATP that aerobic procures
- much faster
- for vigorous muscle activity





Energy Systems Used during Sport Activities:

Aerobic endurance: the length of time a muscle can continue to contract using aerobic pathways

Anaerobic threshold: muscle metabolism converts to anaerobic glycolysis

*Activities such as weight lifting, diving, and sprinting rely entirely on ATP and CP stores.

*on and off or burst activities like tennis, soccer, 100 meter swim appear to be fuel mostly by anaerobic glycolysis →

*marathon run, jogging → mainly aerobic but anaerobic may function until aerobic reaches full efficiency

Muscle Fatigue:

-physiological inability to contract; results from a relative deficit of ATP (total absence would cause contractures)

-Contractures: states of continuous contraction because the cross bridges are unable to detach → writers cramp

-problem in excitation- contraction coupling

-contributors build up of lactic acid, ion imbalance (Na/K pump requires ATP)

-intensive exercise of short duration produces fatigue rapidly via ionic disturbance that alter E-C coupling → recovery is rapid

- prolonged low intensity exercise may required several hours for complete recovery – exercise damages the SR, interfering with Ca regulation and released and therefore with muscle activation

Oxygen Debt: as the extra amount of oxygen that the body must take in for these restorative processes

-differences between the amount of oxygen needed for total aerobic muscle activity and the amount actually used

-all anaerobic sources of AP used during muscle activity contribute to this deficit

-For muscle to return to resting state: oxygen reserve must be replenished → lactic acid turns into pyruvic acid, glycogen stores must be replaced and ATP and creatine phosphate reserve must be resynthesized.

-liver converts additional lactic acid to glucose/ glycogen (cori cycle)

Excess post-exercise oxygen consumption (EPOC):

Heat Production during Muscle Activity:

-ATP driven muscle contraction 20-25% efficient; heat dissipated by body's cooling mechanisms

Muscle Fiber Type:

Two Major Functional Characteristics:

1) Speed of contraction → slow and faster fibers

-how fast ATPases split ATP and pattern of electrical activity of their motor neurons

-how quickly Ca is moved from cytosol to SR

2) Major Pathways for forming ATP

-cell mostly rely on oxygen using aerobic pathways for ATP generation are OXIDATIVE fibers and those that rely more on anaerobic glycolysis are GLYCOLYTIC FIBERS

a) Slow oxidative fibers: thin cells with slow acting myosin ATPases

-contract slowly (red = lots of myoglobin)

-primary energy fuel is fat

-lots of mitos, capillaries, aerobic enzymes, oxidative

-fatigue resistant, but not powerful thing

→ Endurance type activities

b) Fast glycolytic fibers: large pale white, little myoglobin

-fast acting myosin ATPases, contract quickly

-few mitochondria; lots of glycogen reserve: glycolytic

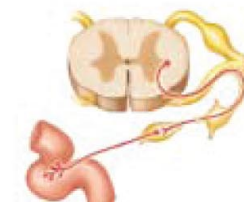
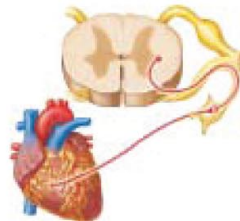
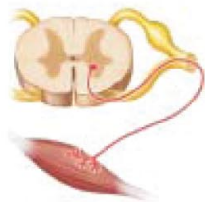
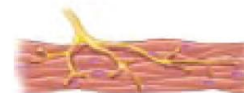
-will fatigue – powerful

→ Short term rapid intense movements

c) Fast oxidative fibers: red or pump, medium cell size

- fast acting myosin ATPases, contract quickly, high myoglobin content
- Oxygen dependent,
- some what fatigue resistant
- intermediate activities

Table 9.3 Comparison of Skeletal, Cardiac, and Smooth Muscle <i>(continued)</i>			
CHARACTERISTIC	SKELETAL	CARDIAC	SMOOTH
Elaborate sarcoplasmic reticulum	Yes	Less than skeletal muscle (1–8% of cell volume); scant terminal cisterns	Equivalent to cardiac muscle (1–8% of cell volume); some SR contacts the sarcolemma
Presence of gap junctions	No	Yes; at intercalated discs	Yes; in unitary muscle
Cells exhibit individual neuromuscular junctions	Yes	No	Not in unitary muscle; yes in multi unit muscle
Regulation of contraction	Voluntary via axon terminals of the somatic nervous system	Involuntary; intrinsic system regulation; also autonomic nervous system controls; hormones; stretch	Involuntary; autonomic nerves, hormones, local chemicals; stretch



Smooth Muscle: