1 Biology

Wednesday, January 02, 2008
4:35 PM

Fatty Acids - building blocks for most, but not all, complex lipids
- Long chains of carbon truncated at one end by a COOH
- Can be saturated or unsaturated

Triacylglycerols
- Store metabolic energy, provide insulation and padding
- Sometimes called triglycerides or simple fats and oils
- Constructed from a three carbon backbone called glycerol

Adipocytes
- Fat cells that are specialized cells where the cytoplasm contains nothing but triglycerides

Phospholipids
- Serve as a structural component of membranes
- Built from a glycerol backbone but a polar phosphate group replaces one of the fatty acids
- Amphipathic - have two charges on two different sides of the molecule

Steroids
- Four ringed structures including hormones, *vitamin D*, and cholesterol(an important membrane component)
- Regulate metabolic activities

Lipoproteins
- Transfer lipids that are insoluble in aqueous solution
- Contains a lipid core surrounded by phospholipids and apoproteins
- Classified by their density: VLDL, LDL, HDL

Proteins(Polypeptides)
- Built from a chain of amino acids held together by peptide bonds

Amino Acids
- Proline - disrupts α-helix
- Alanine - a methyl group
- Glycine - just a hydrogen
- Cysteine/Methionine - have sulfur
- Both α-helices and β-pleated sheets are reinforced by hydrogen bonds between the carbonyl oxygen and the hydrogen on the amino group

Five Forces Create Tertiary Structure

i. Covalent disulfide bonds between two cysteine amino acids on different pars of the chain
ii. Electrostatic(ionic) interactions mostly between acidic and basic side chains
iii. Hydrogen bonds
iv. Van der Waals forces
v. Hydrophobic side chains pushed away from water towards center of protein

- When you see nitrogen THINK protein

Glycoproteins - proteins with carbohydrate groups attached

Proteoglycans - mixture of proteins and carbohydrates

Anomers
- Alpha - When the hydroxyl group on the first carbon and the methoxy group on the 6-carbon are on opposite sides

Glycogen
- Found in all animal cells, large amounts found in muscle and liver
- Liver regulates blood glucose levels so they are one of the few cell types capable of reforming glucose from glycogen and releasing it back into the blood stream
- Only certain epithelial cells in the digestive tract and the proximal tubule of the kidney are capable of absorbing glucose against a concentration gradient. This is done via secondary transport down the sodium concentration gradient.

- Insulin increases the rate of facilitated diffusion for glucose and other monosaccharides.
    - In the absence of insulin only neural and hepatic cells are capable of absorbing sufficient amounts of glucose via the facilitated transport system

Minerals

- dissolved inorganic ions inside and outside the cell. By creating electrochemical gradients they assist in the transport of stuff into and out of the cell

Enzyme Models

Lock and Key - the active site of the enzyme has a specific shape that only binds the specific substrate

Induced Fit Model - the shape of both the enzyme and the substrate are altered upon binding

Enzyme Kinetics

- V_{max} is proportional to enzyme concentration
- K_m does not vary with enzyme concentration and therefore is a good indicator of an enzyme's affinity for its substrate

Cofactor - non-protein component required by an enzyme to reach the optimal activity; either mineral or coenzyme

Apoenzyme - an enzyme without its cofactor

Coenzymes - cosubstrates and prosthetic groups

Cosubstrates - reversibly bind to a specific enzyme and transfer some chemical group to another substrate. The cosubstrate is then changed back to its original form by another enzymatic reaction

Prosthetic groups - remain covalently bound to the enzyme throughout the reaction

Competitive Inhibition

- Raise the apparent K_m but do not change the V_{max}
- Can be overcome by excess substrate

Noncompetitive Inhibition

- Can't be overcome by excess substrate
- V_{max} is lowered but since enzyme affinity is the same K_m remains the same

Feedback inhibitors do not resemble the substrate of enzymes that they inhibit

Allosteric Regulation - come back and bind to a different site of the enzyme causing a conformational change, many alter affinity of substrate for enzyme(K_m) but not V_{max}

- Can be either positive or negative regulation
- At low substrate concentrations, small increases in substrate concentration increase enzyme efficiency as well as reaction rate

- A lyase catalyzes addition of one substrate to a double bond while a ligase governs an addition reaction using ATP

1 Krebs Cycle

Wednesday, January 02, 2008
6:33 PM

Metabolism

- 1.) macromolecules are broken down into their constituent parts releasing little or no energy
- 2.) constituent parts are oxidized to acetyl CoA, pyruvate, or other metabolites forming ATP and reduced coenzymes (NADH and $FADH_2$)
- 3.) If oxygen is available and the cell is capable of using oxygen these metabolites go into the citric acid cycle and oxidative phosphorylation to form large amounts of energy(more NADH, FADH2, or ATP); otherwise the coenzyme NAD^+ and other byproducts are either recycled or expelled as waste

Glycolysis - first step of anaerobic and aerobic respiration

- Products: 2 molecules of ATP from ADP/water , 2 pyruvate molecules from 1 glucose, 2 molecules of NADH from reduction of NAD^+
- In the 3rd step the molecule is committed to glycolysis

Substrate Level Phosphorylation

- The formation of ATP from ADP using energy released from the decay of high energy phosphorylated compounds as opposed to using energy from diffusion(oxidative phosphorylation)
- 2 ATPs are spent, 4 ATPs are produced

- Much of the fructose and galactose ingested by humans is converted into glucose in the liver enterocytes; however fructose can enter as fructose-6-phosphate or G3P; galactose can be converted to G6P to enter glycolysis

Fermentation - anaerobic respiration

- Includes glycolysis, reduction of pyruvate to ethanol or lactic acid, and oxidation of NADH back to NAD^+
- Takes place when a cell or organism is either unable to assimilate the energy from NADH and pyruvate, or has no oxygen available to do so
- Recycles NADH back to NAD^+

Aerobic Respiration

- Products of glycolysis move into the matrix of the mitochondrion
- Once inside the matrix pyruvate is converted to acetyl CoA in a reaction that produces NADH and CO2

Krebs Cycle

- Acetyl CoA transfer two carbons from pyruvate to 4-carbon oxaloacetic acid
- Each turn produces 1 ATP, 3 NADH, and 1 $FADH_2$
- ATP production in the krebs cycle is substrate-level phosphorylation
- Triglycerides can also be catabolized for ATP. Fatty acids are converted into acyl CoA along the outer membrane of the mitochondrion and endoplasmic reticulum at the expense of 1 ATP
  - The reaction also produces $FADH_2$ and NADH for every two carbons taken from the original fatty acid
  - The glycerol backbone is converted to PGAL
- Amino acids are deaminated in the liver. The deaminated product is either chemically converted to pyruvic acid or acetyl CoA, or it may enter the Krebs cycle at various stages depending upon which amino acid was deaminated

Electron Transport Chain

- A series of proteins on the inner membrane of the mitochondrion
- The first protein complex in the series oxidizes NADH by accepting high energy electrons that it will then pass to O2
- As electrons are passed along, protons are pumped into the intermembrane space for each NADH

- The protons then diffuse back to the mitochondrial matrix turning ADP into ATP through the pump, ATP synthase
    - Oxidative phosphorylation - production of ATP through diffusion/oxidation of NADH, like this
    - Intermembrane space has lower pH than matrix

Important Facts

- Aerobic respiration produces about 36 net ATPs
- 1 NADH brings back 2 to 3 ATPs
- 1 $FADH_2$ brings back 2 ATPs
- Glucose + O_2 -> CO_2 + H_2O (not balanced here, its a combustion reaction)

2 Genes

Wednesday, January 02, 2008
6:56 PM

<u>Gene</u> - series of nucleotides that code for the production of a single polypeptide or mRNA, rRNA, tRNA

- Eukaryotes can have multiple copies of a gene but prokaryotes only have one copy of each gene
- Eukaryotic genes that are being actively transcribed by a cell are associated with regions called <u>euchromatin</u>
- Genes not being actively transcribed are associated with tightly packed regions called <u>heterochromatin</u>
- <u>Genome</u> - entire sequence of DNA of an organism

<u>Central Dogma</u> - DNA is transcribed to RNA, which is translated to amino acids forming a protein

<u>DNA</u>

- Sugar-phosphate backbone
- Phosphodiester bond
- 3' end is attached to an -OH group and 5' end is attached to a phosphate group
- A2T hydrogen bonds, C3G hydrogen bonds

<u>DNA replication</u>

- <u>Semi-conservative</u> - when a new strand is created one strand from the original DNA goes to the new strand
- Governed by a group of proteins called a <u>replisome</u>
- Two replisomes proceed in opposite directions along the chromosome making replication a <u>bidirectional</u> process
- The point where a replisome is attached to the chromosome is called the replication fork
- <u>Replicons</u> - replication units - each chromosome of eukaryotic DNA is replicated in many discrete segments called replicons
- <u>DNA helicase</u> - unwinds double helix
- <u>DNA polymerase</u> - enzyme that builds the new DNA strand, can't initiate a strand from two nucleotides ,needs primer
  - Reads from 3' -> 5'(upstream) direction, writes 5' to 3'(downstream)
- <u>Primase</u> - an RNA polymerase, creates an RNA primer 10 ribonucleotides long to initiate the strand
- <u>Lagging strand</u> - interrupted strand
  - Made up from Okazaki fragments
- <u>Leading strand</u> - written continuously
  - <u>DNA ligase</u> - moves along the lagging strand and ties the Okazaki fragments together
- Since the formation of one strand is continuous and the other fragmented the process of replication is called <u>semidiscontinuous</u>
- <u>Exonuclease</u> - removes nucleotides from center of a strand, exonuclease on DNA polymerase

  <u>Telomeres</u> - repeated six nucleotide units that protect the chromosomes from being eroded through repeated rounds of replication

  - *Telomerase* - catalyzes the lengthening of telomeres

  <u>Differences between DNA and RNA</u>

  - RNA is produced by <u>transcription</u> - RNA is manufactured from a DNA template in this process
  - DNA is produced by replication

  <u>rRNA (ribosomal RNA)</u> - combines with proteins to form ribosomes

  <u>1.) Initiation</u> - beginning of transcription

  - An *initiation factor* finds a promoter on the DNA strand
  - Promoter - sequence of DNA nucleotides that designates a beginning point for transcription

- In prokaryotes its located upstream
- Most commonly found sequence is the consensus sequence
  - Variations from the *consensus sequence* causes RNA polymerase to bond less tightly and less often leading to those genes being transcribed less often

- After binding to the promoter RNA polymerase unzips the double helix creating a transcription bubble, next the complex switches to elongation mode

2.) Elongation - RNA polymerase transcribes only one strand of the DNA nucleotide sequence into a complementary RNA nucleotide sequence. Only one strand of DNA is transcribed.

- The transcribed strand is called the template strand or antisense strand
- The other strand, the sense strand(coding strand) protects its partner against degradation

- RNA polymerase moves along the DNA strand from 3' -> 5' building the new RNA 5' -> 3'
  - No proofreading, 10x slower than replication

3.) Termination - requires special termination sequence to tell RNA polymerase to detach

- Replication makes no distinction between genes, transcription does through activators and repressors
- Most genetic regulation occurs at transcription when regulatory proteins bind DNA and activate or inactivate its transcription. Thus,
  - Activators and repressors - bind to DNA close to the promoter and either activate or repress the activity of RNA polymerase(activators before the promoter sequence, repressor after)
  - Primary function of gene regulation in prokaryotes is to respond to environmental changes
    - Changes in gene activity are a response to the concentration of specific nutrients in and around the cell
  - Primary function of gene regulation in multi-cellular organisms is to control the intracellular and extracellular environments
- Polycistronic - prokaryotic mRNA typically includes several genes in a single transcript
- Monocistronic - eukaryotic mRNA includes one gene per transcript
- Operon - genetic unit of prokaryotic DNA consisting of the operator, promoter, and all other genes that contribute to a single mRNA

Post-Transcriptional Processing - occurs in both eukaryotes and prokaryotes

- In prokaryotes rRNA and tRNA go through post-transcriptional processing but mRNA usually doesn't, in eukaryotes mRNA goes through post-transcriptional processing too
- Primary transcript - initial mRNA nucleotide, also known as pre-mRNA
  - Processed in three ways
    1) Addition of nucleotides
    2) Deletion of nucleotides
    3) Modification of nitrogenous bases
  - In eukaryotic mRNA the 5' cap is added as protection against degradation by exonucleases
  - The 3' end is *polyadenylated* with a poly A tail to protect it from exonucleases
- Introns - before leaving the nucleus introns are removed from the pre-mRNA
  - Do not code for protein and are degraded in the nucleus
- Exons - parts of pre-mRNA that survive post-transcriptional processing
  - Can be spliced together in different ways to code for different proteins
- snRNPs - recognize nucleotide sequences at the ends of the introns
  - Several snRNPs form a complex called a spliceosome
  - Spliceosome - inside the spliceosome introns are looped bringing exons together

Denatured - when heated or immersed in high concentration salt solution or high pH solution

- Melting temperature T_m is higher for G-C because they make more hydrogen bonds than A-T

- Denatured DNA is less viscous, denser, and more able to absorb UV light

Nucleic acid hybridization

- Separated strands like to spontaneously associate with their original partner: DNA-DNA, DNA-RNA, RNA-RNA

Restriction Enzymes(endonucleases)

- Digest(cut) nucleic acid sequences
- bacteria defend themselves from viruses by cutting the viral DNA into fragments
- Bacteria protect their own DNA with *methylation*(adding $-CH_3$)
- Typically a restriction site is palindromic

Recombinant DNA

- DNA that is reformed from restriction endonuclease cuts(remember sticky ends)
- Reconnected by DNA ligase
- Can be made long enough for bacteria to replicate and then placed within the bacteria using a vector, typically a plasmid or sometimes a virus
    - The bacteria can then be grown in large quantity forming a clone of cells containing the vector with the recombinant DNA. The clones can be saved in a library
- By including in the vector a gene for resistance to a certain antibiotic and the lacZ gene which enables the bacteria to metabolize the sugar X-Gal
    - When you apply the antibiotic those without the vector die
    - You use an endonuclease that cuts at the lacZ gene to insert the new DNA so if the bacteria metabolizes X-Gal you know its not the right bacteria. Clones with the active lacZ gene turn blue

Complementary DNA (cDNA) - DNA reverse transcribed from mRNA

- It's useful to clone DNA with no introns so you use reverse transcriptase

Polymerase Chain Reaction - (PCR)

- The double strand to be cloned(amplified) is placed in a mixture with primers, polymerase
- Heated to 95°C to denature it, cooled to 60°C, the primers hybridize(anneal) to their complementary ends of the DNA strands
- Heat resistant polymerase is added and is activated when the temperature hits 72°C

Southern Blotting

- technique to identify target fragments of known DNA sequence in large populations
- DNA is cleaved into restriction fragments which are then resolved by gel electrophoresis
    - Large fragments move slower than small fragments
- Next, the gel is made alkaline to denature the DNA and a sheet of nitrocellulose is used to blot the gel which transfers the resolved single stranded DNA fragments onto the membrane
- A radio-labeled probe with a nucleotide sequence complementary to the target fragment hybridizes with and marks the target fragment…this reveals the location of the probe and the target fragment

Northern Blotting

- Just like southern blot except it identifies RNA

Western Blot

- Can detect a particular protein in a mix of proteins
- First the mixture of proteins is resolved by size through electrophoresis
- Next they are blotted onto a nitrocellulose membrane
- An antibody(the primary antibody) specific to the protein in question is then added and binds to that protein. Next, a secondary antibody-enzyme conjugate is added and binds to that protein
- The secondary antibody recognizes and binds to the primary antibody and marks it with the enzyme for subsequent visualization. The reaction catalyzed by the enzyme attached to the secondary antibody can produce a colored, fluorescent or radioactive reaction product which can be visualized with an x-ray film
- Probably not on MCAT

Restriction Fragment Length Polymorphisms (RFLP)

    - Identifies individuals as opposed to specific genes
    - People possess different restriction sites and varying distances between them
  DNA is *degenerative*, *unambiguous*, and *almost universal*
    - Start codon - AUG
    - Stop codon - UAA, UAG, UGA
- By convention, RNA is written 5' -> 3'
  Translation - process of protein synthesis directed by mRNA
    - Ribosome
        - Prokaryote 30S and 50S form 70S
        - Eukaryote 40S and 60S form 80S
        - Formed in a special organelle called the nucleolus(prokaryotes don't have these)
    - After post-transcriptional processing mRNA leaves the nucleus through the nuclear pores and enters the cytosol
    - The 5' end of mRNA attaches to the small subunit of a ribosome
    - A tRNA with 5'-CAU-3'(AUG start codon) gets methionine and puts it in the P site
        - This signals the large subunit to attach and form the initiation complex
        - This is called 1.)initiation
    - 2.) Elongation
        - A tRNA with its corresponding AA attaches to the A site at the expense of 2 GTP's
        - The C-terminus of the methionine attaches to the N-terminus of the amino acid
    - 3.) Translocation
        - The term for the ribosome shift 3 nucleotides closer to the 3' end
    - The tRNA carrying methionine moves to the E site where it can exit the ribosome and the dipeptide moves to the P site so the A site is free for the next tRNA
        - Ends when a stop(*nonsense*) codon reaches the A site, then an H_2O is added to the end of the polypeptide chain
        - Even as the polypeptide is being synthesized it begins folding, assisted by *chaperones*
    - 4.) Post-translational Modifications
        - Sugars, lipids, or phosphate groups can be added to amino acids
        - Polypeptide can be cleaved in many places
    - Translation - takes place on a free floating ribosome in the cytosol or it may attach itself to the rough ER during translation to to inject proteins in the ER lumen
        - Proteins injected into the ER lumen become membrane bound proteins of the nuclear envelope, ER, golgi, lysosomes, plasma membrane, or will be secreted from the cell
        - The growing polypeptide itself may or may not cause the ribosome to attach to the ER depending upon the polypeptide
        - Signal peptide - 20 amino acid sequence that is recognized by a protein-RNA signal-recognition particle(SRP)
            - SRP - carries the entire ribosome complex to a receptor protein on the ER where it is removed by an enzyme
            - Can also attach to polypeptides to target them to mitochondria, nucleus, or other organelles

Mutations

Gene mutation - mutation to a single gene

Chromosomal mutation - occurs when the structure of the chromosome is changed

Mutagen - chemical agents that causes mutations

Base-pair mutations

Point mutation - mutation that changes a single base-pair of nucleotides in a double strand of DNA

Base-pair substitution- where one base-pair is replaced by another

Missense mutation - base-pair mutation that occurs in the amino acid coding sequence of a protein; may or may not alter the amino acid sequence of the protein(degeneracy)

- May or may not alter the AA sequence of the protein

- If no change in function it’s a *neutral mutation*, if an AA isn't changed it’s a *silent mutation*

Insertion of Deletion - may or may not result in a frameshift mutation

Frameshift mutation - results when insertions or deletions occur in groups of 3

Nonsense mutation - when an insertion or deletion results in a stop codon

Chromosomal Mutations

- May occur to a chromosome in the form of deletions, duplications, translocations, and inversions
- Deletions - occur when a portion of the chromosome breaks off or is lost during recombination/crossing over
- Duplications - when a DNA fragment breaks free of one chromosome and incorporates a into homologous chromosome

Translocation - when a segment of DNA from one chromosome is inserted into another chromosome

Inversion - when a section of DNA is reversed

Transposable Elements/Transposons - can excise themselves from a chromosome and reinsert themselves at another location

- Will be flanked by identical sequences
- One way an organism can modify its genetic makeup without meiosis

Wild type - original state

Proto-oncogenes - stimulate normal growth of cells; can be converted to oncogenes that cause cancer by mutagens

Histones - sections of DNA that are not in use are wrapped around proteins called histones

- 8 histones wrapped in DNA form a nucleosomes which wrap ino coils called solenoids, which wrap into supercoils
- Basicity of histones gives them a net positive charge at the normal pH of the cell

Chromatin - the total DNA/protein complex

Constitutive Heterochromatin - chromatin that is permanently coiled

Euchromatin - only coiled during nuclear division

How many chromosomes are there?

- In the nucleus of a human somatic cell there are 46 double stranded DNA molecules
- There are 46 chromosomes before replication, and 46 chromosomes after replications
- That means 23 pairs
- Duplicates can be referred to separately as sister chromatids
- Figure this shit out

- Homologues - Each chromosome possesses a partner that codes for the same traits as itself
- Diploid - any cell that contains homologous pairs
- Haploid - any cell that does not contain homologous pairs

2 Cell Life Cycle

Thursday, January 03, 2008
1:11 PM

Four Stages

a. G_1 - first growth phase
b. S - synthesis
c. G_2 - second growth phase
d. M - mitosis or meiosis
e. C - cytokinesis

Interphase - G_1, S, and G_2

G_1 - the cell has just split and begins to grow in size making new organelles and proteins

- Regions of chromatin have been unwound and decondensed into euchromatin
- RNA and protein synthesis is very active
- The cell has to reach a certain size and synthesize sufficient protein to continue to the next stage
- Cell growth is assessed at the G_1 checkpoint near the end of G_1
    - G_1 Checkpoint - if conditions are favorable the cell enters the S phase; otherwise it enters the G_0 phase
        - Main factor in triggering the beginning of S is cell size based upon ratio of cytoplasm to DNA
- Normally the longest phase

G_0 - the nongrowing phase distinct from interphase

- Allows for the differences in length of the cell cycle

S - in this phase the cell devotes most of its energy to replicating DNA

- Organelles and proteins are produced more slowly
- Each chromosome is exactly duplicated but, by convention, the cell is still considered to have the same number of chromosomes just now each chromosome is *made of two identical sister chromatids*

G_2 - the cell prepares to divide

- Organelles continue to duplicate
- RNA and protein(especially tubulin for microtubules) are actively synthesized
- Occupies 10-20% of the cell cycle
- Near the end of G_2 is the G_2 Checkpoint
    - G2 Checkpoint - checks for the mitosis promoting factor(MPF). If enough MPF mitosis is triggered

Mitosis

- nuclear division WITHOUT genetic change
- 4 stages: PMAT

Prophase

- condensation of chromatin into chromosomes
- Centrioles move to opposite ends of the cell
- First the nucleolus and then the nucleus disappears; the spindle apparatus begins to form consisting of aster(microtubules radiating from the centrioles), *kinetochore microtubules* growing from the centromeres(a group of proteins near the center of the chromosome), and spindle microtubules connecting the two centrioles
- Kinetochore - the structure of protein and DNA located a the centromere of the joined chromatids of each chromosome

Metaphase

- Chromosomes line up along the equator of the cell

Anaphase

- Begins when sister chromatids split at their attaching centromeres and move towards opposite ends of the cell(disjunction)

- Cytokinesis - actual separation of the cytoplasm due to constriction of the microfilaments about the center of the cell; indicates the end of anaphase

Telophase - nuclear membrane reforms followed by reformation of the nucleolus. Chromosomes decondense and become difficult to see under the light microscope

Meiosis

- Double nuclear division which produces four haploid gametes(germ cells)
- In humans only the *spermatogonium* and the *oogonium* undergo meiosis
- After replication happens in the S phase of interphase the cell is called a primary spermatocyte or primary oocyte
    - In females replication takes place before birth and the life cycle of all gametes are arrested at the primary oocyte stage until puberty
    - Just before ovulation a primary oocyte undergoes the first meiotic division to become a secondary oocyte
    - The secondary oocyte is released upon ovulation and the penetration of the secondary oocyte by the sperm stimulates anaphase II of the second meiotic division in the oocyte
- Meiosis is two rounds of cell division called meiosis I and meiosis II

Meiosis I - is the same as mitosis except for the following differences

- Prophase I - homologous chromosomes line up alongside each other matching genes exactly; at this time they can exchange DNA by crossing over
    - Genetic recombination occurs during crossing over
    - Each duplicated chromosome in prophase I appears as an 'x'; the side by side homologues exhibit a total of four chromatids known as tetrads
    - If crossing over does occur, the two chromosomes are "zipped" along each other where nucleotides are exchanged forming the *synaptonemal complex*
        - Synaptonemal complex is the single point where the two chromosomes attach creating the 'x' shape known as the chiasma
        - Genes that are located next to eachother are said to be linked
- INSERT TABLE FROM PAGE 49

Chromosome counts

46 two sets of 2 chromatid w/ centromere connecting	Spermatogonium	Oogonium
46 chiasma	Primary Spermatocyte	Primary Oocyte
23 chiasma	Secondary Spermatocytes(2 of them)	Secondary Oocyte(the other 'n' turned into a body) gets hit by spermatozoa so has 2n in next step
23 single set of 2 chromatid w/ centromere connecting	spermatids	46 chromosomes: zygote
	Spermatozoa with 'n'	

- Meiosis is like mitosis except that in meiosis there are two rounds, the daughter cells are haploid, and genetic recombination occurs. Must know names of cells at different stages and whether they are haploid or diploid. Recognize that metaphase in mitosis would appear like metaphase II in meiosis and not like metaphase I.
- Metaphase I
    - In metaphase I the homologues remain attached and move to the metaphase plate
    - Instead of single chromosomes aligned along the plate in mitosis tetrads align in meiosis

- Anaphase I
    - Separates homologues from their partners
- Telophase I
    - A nuclear membrane may or may not reform and cytokinesis may or may not occur
    - In humans the nuclear membrane does not reform and cytokinesis doesn't happen
    - If cytokinesis occurs, the new cells are haploid with 23 replicated chromosomes and are called secondary spermatocytes or secondary oocytes. For the female one of the oocytes, called the first polar body, is much smaller and degenerates. This is to conserve cytoplasm which is only contributed by the ovum. The first polar body may or may not go through meiosis II producing two polar bodies.

- Meiosis I is reduction division

Meiosis II

- Proceeds with prophase II, metaphase II, anaphase II, and telophase II and appears under the microscope to be similar to mitosis
- Final products are haploid gametes with 23 chromosomes
- For the spermatocyte 4 sperm cells are formed, for the oocyte a single ovum is formed.
    - In females telophase II produces one gamete and a second polar body

Nondisjunction

- if during anaphase I or II the centromere of any chromosome doesn't split.
- Nondisjunction in anaphase I results in one of the cells will have two extra chromatids(a complete extra chromosome) and the other will be missing a chromosome. The extra chromosome will line up along the metaphase plate and behave normally in metaphase II.
- Nondisjunction in anaphase II will result in one cell having one extra chromatid and one lacking one chromatid.
- Can also occur in mitosis but ramifications are less severe because genetic information in new cells isn't passed over to new cells

3 Microbiology, Viruses

Thursday, January 03, 2008
4:14 PM

Viruses - capsid, nucleic acid, and lipid-rich protein envelope
For some viruses: tail, base plate, and tail fibers for most bacteriophages

Capsid - protein coat of a virus
- one to several hundred genes in the form of DNA or RNA inside the capsid inside--viruses contain either DNA or RNA exclusively

Envelope
- Most viruses surround themselves with a lipid rich envelope either borrowed from the membrane of the host cell or synthesized in the host cell cytoplasm
- Contains virus-specific proteins

Virion - mature virus outside the cell

Why viruses aren't alive…

a. Can reproduce but always need the host cell's reproductive machinery
b. Don't metabolize organic nutrients; use ATP of host cell
c. In their active form they aren't separated from their external environment by a barrier like a cell wall or membrane
d. Possess either DNA or RNA--all other living organisms contain both

- ○ Can be crystallized without losing their ability to infect

- Infection begins when virus adsorbs to a specific chemical receptor site on the host(usually a specific glycoprotein)
- Next, the nucleic acid of the virus penetrates into the cell

Bacteriophage - a virus that infects bacteria
- Nucleic acid is normally injected through the tail after viral enzymes have digested a hole in the cell wall
  - This means viruses have digestive enzymes

Endocytotic - most viruses that infect eukaryotes are engulfed like this

Lytic Infection
- When a the virus takes over the cell's machinery to reproduce new viruses
- Eclipse period - the brief period before the first fully formed virion appears
- Latent period - period from infection to lysis
- Virulent virus - a virus that follows the lytic cycle

Lysogenic Infection
- Viral DNA is incorporated into host genome
- Reverse transcriptase - if the virus is an RNA virus and it possesses this enzyme DNA is reverse transcribed. When the host replicates this DNA does as well
- Temperate virus - virus in the lysogenic phase
- Provirus - when a virus is dormant or latent
  - A prophage if the host cell is a bacterium
- Dormant viruses can become active when there is a stress on the cell such as UV radiation or carcinogens

Virus Classification by Type of Nucleic Acid Enclosed
- Plus-strand RNA - indicates that protein can be directly translated from the RNA
  - Retrovirus - carries the enzyme reverse transcriptase to create DNA from RNA
- Minus-strand RNA - minus-strand RNA is the complement to mRNA and must be transcribed to plus-RNA before being translated
- There are double stranded RNA viruses and double stranded DNA viruses

Viroids - small rings of naked RNA without capsids; only infect plants

Prions - reproduce without DNA or RNA

Defenses against Viral Infections

- Humans fight viral infections with antibodies that bind to the protein and with cytotoxic T cells which destroy infected cells
- Although the envelope is borrowed from the host cell spike proteins encoded from viral nucleic acids protrude from the envelope
    - These proteins bind to receptors on a new host cell causing the virus to be infectious
    - Spike proteins also allow human antibodies to recognize them when fighting infection
    - Since RNA polymerase has no proofreading mechanism the spike proteins change
- Vaccine - injection of antibodies or an injection of a nonpathogenic virus with the same capsid or envelope
    - The latter allows the immune system to make its own antibodies

Carrier Population - even if all viral infections of a certain type were eliminated in humans the virus could still live in another animal until it mutates again

3 Prokaryotes

Thursday, January 03, 2008
5:14 PM

Prokaryotes

- do not have a membrane bound nucleus
- Instead of a nucleus they have a single, circular double stranded DNA molecule that is twisted into supercoils and associated with histones in Archaea and other proteins in bacteria
- Nucleoid - the RNA and protein complex in prokaryotes; called the chromatin body, nuclear region, or nuclear body.
    - Not enclosed by a membrane
- Have no complex, membrane-bound organelles(key words complex, membrane-bound)
- Split into two domains: Archaea and Bacteria
- Found in salty lakes and boiling hot springs
- Cell walls of Archaea are not made from peptidoglycan

- To some degree all microorganisms are capable of fixing CO2(reducing it and using the carbon to create organic molecules through the Calvin Cycle)
    - However, reduction of CO2 is energy expensive and most can't use it exclusively

Autotrophs - organisms that are capable of using CO2 as their sole source of carbon

Heterotrophs - use preformed, organic molecules as source of carbon

- This carbon comes from other organisms--living or dead

All organisms acquire energy from one of two sources:

a. Light
b. Oxidation of organic or inorganic matter

Phototrophs - organisms that use light as their energy source

Chemotrophs - those that use oxidation of organic or inorganic matter

- MCAT expects you to know two classifications: carbon source and energy source
    - Only prokaryotes can acquire energy from an inorganic source other than light

Nitrogen Fixation - some bacteria are capable of fixing nitrogen

- Process by which N_2 is converted to ammonia
- Most plants can't use ammonia and wait for bacteria to process it through nitrification

Nitrification

- Two step process that creates nitrates
- Requires two genera of chemoautotrophic prokaryotes
    - $NH_4^+ + 1.5O_2 \rightarrow NO_2^- + H_2O + 2H^+$
    - $NO_2^- + 0.5O_2 \rightarrow NO_3^-$

- Chemoautotropy is an inefficient mechanism for acquiring energy so chemoautotrophs require large amounts of substrate
- Two shapes of bacteria:
    - Cocci - round
    - Bacilli - rod shaped
    - Helically shaped bacteria are called spirilla if they are rigid or otherwise are called spirochetes

Mesosome

- Invaginations of the plasma membrane

3 Membranes

Thursday, January 03, 2008
5:47 PM

<u>Plasma membrane</u> - phospholipid bilayer that surrounds the cytosol
  Phospholipid bilayer - composed to phosphate group, two fatty acid chains, and a glycerol backbone

<u>Micelle</u> - spherical structure that's formed when amphipathic proteins are placed in a liquid…hydrophobic parts inside

- Unlike eukaryotic membranes prokaryotic plasma membranes don't contain steroids such as cholesterol
- Membrane proteins act as transporters, receptors, attachment sites, and enzymes
- <u>Integral/Intrinsic Proteins</u> - Amphipathic proteins that transverse the membrane from the inside to out the outside
- <u>Peripheral/Extrinsic Proteins</u> - situated entirely on surface of membrane
  - Ionically bonded to integral proteins or the polar group of a lipid
- Both integral and peripheral proteins can contain carbohydrate chains making them glycoproteins
  - Carbohydrate portion obviously always protrudes
- <u>Lipoproteins</u> - lipid anchored proteins exist in some plasma membranes with the lipid portions embedded in the membrane and protein portions at the surfaces

<u>Fluid Mosaic Model</u>
- Membranes are fluid; parts can move laterally but it can't separate
- In eukaryotes cholesterol moderates membrane fluidity

<u>Membrane</u> - not only a barrier but actually creates the different compositions

<u>Electrical Gradient</u> - points in the direction a positively charged particle will tend to move

<u>Semi-permeability</u> - what you call a membrane that slows diffusion
- Two factors that affect it: size and polarity
  - Larger the molecule the less permeable the membrane is and the more polar the particle the less permeable

<u>Facilitated Diffusion</u>
- When transport or carrier proteins help highly charged or large size molecules across the membrane
- Makes the membrane selectively permeable

<u>Active Transport</u>
- Movement of a compound against its electrochemical gradient
- Uses energy; either ATP directly or can use ATP to create an electrochemical gradient and then using the energy of the gradient to acquire or expel a molecule…this is *secondary active transport*

<u>Bacterial Envelope</u>
- Surrounds the protoplast--the bacterial plasma membrane and everything inside of it

- Most bacteria are <u>hypertonic</u> to their environment meaning the aqueous solution inside contains more particles
- When hydrostatic pressure equals osmotic pressure(remember, this is a pulling force of water to concentrated solute areas) the filling of the cell stops; the strong cell wall protects from rupture

<u>Peptidoglycan</u>
- cell wall is made of it; it's porous
- Series of disaccharide polymer chains with amino acids
- Lysozyme attacks the linkage in humans causing the cell to lyse

<u>Gram Staining</u>
  <u>Gram-Positive</u> -shows up purple; thick peptidoglycan cell wall prevents the gram stain from leaking out
  - Periplasmic space is area between cell wall and internal membrane

  <u>Gram-Negative</u> - shows up pink

    - Outside the cell wall gram-negative bacteria have a phospholipid bilayer
    - This second membrane is more permeable than the first and resembles the plasma membrane
    - Lipopolysaccharides - the polysaccharide is a long chain of carbohydrates which protrudes outward from the cell and can form a protective barrier from antibiotics and antibodies
    - The periplasmic space in gram-negative bacteria is between this membrane and the cell wall

  Capsule or Slime Layer - capsules proect bacterium from phagocytosis, dessication, some viruses, and immune responses of host

  Bacterial Flagella
  - Made of long, hollow, rigid, helical cylinders made from a globular protein called flagellin
  - Rotate counterclockwise to move the bacteria in a single direction
  - When they rotate clockwise the bacteria tumbles and changes direction
  - NOT to be confused with eukaryotic flagella which are made of microtubules
  - Flagellum propelled using energy from a proton gradient rather than by ATP
- Sexual reproduction requires meiosis; bacteria don't undergo meiosis or mitosis and can't reproduce sexually. However, they have alternative forms of genetic recombination: conjugation, transformation, transduction
- Binary Fission - a type of asexual reproduction
  - Circular DNA is replicated
  - Two DNA polymerases begin at the same point(origin of replication) and move in opposite directions making complementary single strands that combine with their template strands to form two complete DNA double stranded circles
  - Then the cell divides leaving one circular chromosome in each daughter cell
  - The two daughter cells are genetically identical
- Conjugation
  - Requires that one bacterium have a plasmid that codes for a sex pilus
  - Plasmid - small circle of DNA that exist and replicate independently of the bacterial chromosome
    - Not essential to the bacteria that carry them
    - If the plasmid can integrate into the chromosome its called an episome
  - Sex pilus - hollow protein tube that connects two bacterium allowing for DNA transfer
  - Passage of DNA is ALWAYS from cell containing the conjugative plasmid to the cell that doesn't
  - The plasmid replicates differently than the circular chromosome
    - One strand is nicked, and one end of this strand begins to separate from its complement as its replacement is replicated
    - The loose strand is then replicated and fed through the pilus
  - F Plasmid - fertility factor, a plasmid with the F factor is F+
    - If in the form of an episome and if the pilus is made while the F factor is integrated into the chromosome some or all of the rest of the chromosome may be replicated and transferred
  - R Plasmid - donates resistance to antibiotics
- Transformation
  - The process by which bacteria may incorporate DNA from their external environment into their genome
- Transduction
  - Sometimes the capsid of a bacteriophage will mistakenly encapsulate a DNA fragment of the host cell. When these virions infect a new bacterium they inject harmless bacterial DNA fragments instead of virulent viral DNA fragments
  - The virus that mediates transduction is called the vector

  Endospores
  - Some gram-positive material form spores that can lie dormant for hundreds of years

- Resistant to heat, UV, dessication, chemical agents
- Formation is usually triggered by a lack of nutrients
- In endospore formation the bacterium divides within its own cell wall, then one side engulfs the other
- The cell wall of the engulfed bacterium changes slightly to form the cortex of the endospore
- Several protein layers lie over the cortex to form the resistant structure called the spore coat
- The outer cell then lyses releasing the dormant endospore
- The endospore must be *activated* before it can *germinate* and grow
    - Activation involves heating, germination is triggered by nutrients

Fungi

- Separated into divisions, not phyla
- All are eukaryotic heterotrophs that obtain their food by absorption instead of digestion
- Secrete digestive enzymes outside their bodies and then absorb the products
- Saprophytic - feed on the dead; most fungii
    - However, some aren't, and they are potent pathogens
- Septa - cell walls made of a polysaccharide chitin
    - Perforated to allow exchange of cytoplasm between cells, called cytoplasmic streaming
    - Cytoplasmic streaming - allows for rapid growth
- Chitin - more resistant to microbial attack than cellulose
- Spend most of their lives in a haploid state
- With the exception of yeast they are multicellular
- Lack centrioles
- Mitosis takes place only in the nucleus
- Cells can contain many nucleuses which may not be identical
- Mycelium - in their growth state they exist as a tangled mass of hyphae
- Hyphae - multiply thread-like structures
    - Can form reproductive structures that give off haploid spores that give rise to new mycelia through asexual reproduction

Fungal Reproduction

- Fungi alternate between haploid and diploid but are mostly diploid
- Hyphae are haploid
- Yeast - don't give off spores; reproduce by budding
- Budding(cell fission) - smaller cell pinches off from the single parent
- When sexual reproduction occurs it is between mycelia from two different mating types, + and -
    - Forms a diploid zygospore that then undergoes meiosis to form haploid mycelium colony

Important

- Asexual reproduction normally happens when conditions are good so that the offspring has a good chance of surviving
- Sexual reproduction normally occurs when conditions are tough; the hope is that mutations might make the offspring more fit for the environment

4 Eukaryotes

Thursday, January 03, 2008
5:14 PM

Eukaryotes - have nucleus
Nucleus - wrapped in a double phospholipid bilayer called the nuclear envelope or membrane

- Nuclear pores - nuclear envelope is perforated with large holes that allows RNA to exit but not DNA
- Nucleolus - area where rRNA is transcribed and subunits of the ribosome are assembled; not separated by a membrane

Endocytosis

- Phagocytosis - the cell membrane protrudes outward to envelope and engulf matter
  - Only a few cells are capable of this and the impetus is the binding of proteins on the particulate matter to protein receptors on the phagocytotic cell
  - Ex. Antibodies or complement proteins
- Pinocytosis - extracellular fluid is engulfed by small invaginations
  - Performed in a random fashion by most cells; nonselective
- Receptor mediated endocytosis - refers to specific uptake of macromolecules such as hormones, nutrients; ligand binds to a receptor protein on the cell membrane and then moves to a *clathrin coated pit* that invaginates to form a coated vesicle
  - Purpose is to absorb the ligands and that's how it differs from phagocytosis

Phospholipid bilayer of eukaryotic membrane

- Similar to prokaryotic plasma membrane except in eukaryotes the membrane invaginates and separates to form individual, membrane bound compartments and organelles

endoplasmic reticulum

- a thick maze of membranous walls separating the cytosol from the ER lumen(cisternal space)
- Contiguous with the cell membrane and nuclear membrane
- Contiguous in places with the space between the double bilayer of the nuclear envelope

Rough/Granular ER - ER near the nucleus has many ribosomes attached to it on the cytosolic side

- Translation on the rough ER propels proteins into the ER lumen as they are created
- These proteins are tagged with a signal sequence of amino acids and sometimes glycosylated(carbohydrate chains attached)
- Proteins move through the lumen towards the Golgi apparatus

Golgi Apparatus - series of flattened, membrane bound sacs

- Organizes and concentrates the proteins
- Proteins without signal sequences are put in secretory vesicles and sent out of the cell
- Can modify proteins by removing amino acids or glycosylating them
- Some polysaccharide formation takes place in the golgi apparatus
- End product is a vesicle filled with proteins that can be released from the Golgi to mature into lysosomes or transported to other parts of the cell such as the mitochondria or even the ER

Secretory Vesicles

- Supply the membrane with its proteins and also act in membrane expansion
- Endocytotic vesicles from the membrane are transferred to the Golgi for recycling of the cell membrane

Lysosomes - contain acid hydrolases(hydrolytic enzymes that function best in an acid environment) such as proteases, lipases, nucleases, and glycosidases

- These enzymes are capable of breaking down everything
- pH 5 interior
- Fuse with endocytotic vesicles and digest their contents; anything not digested is ejected from the cell
- Sometimes they autolyse to kill the cell

Smooth ER

- Hydrolyzes G6P to glucose; an important step in making glucose from glycogen
- Shares in role of cholesterol formation and subsequent change into steroids with cytosol
- Most of the phospholipids in the cell membrane are synthesized in the smooth ER
- Oxidizes foreign substances, detoxifying drugs, pesticides, toxins, and pollutants

Adipocytes

- Contain mainly fat droplets
- Important in storage and body temperature regulation

Peroxisomes

- Vesicles in the cytosol
- Grow by incorporating lipidsand proteins from the cytosol
- Rather than budding off membranes like lysosomes peroxisomes self-replicate
- Involved in the production and breakdown of hydrogen peroxide
- Inactivate toxic substances such as alcohol, regulate oxygen concentration, play a role in the synthesis and breakdown of lipids and in the metabolism of nitrogenous bases and carbohydrates

Important

- Cell can be divided into cytosol and ER lumen

- Stuff can reach the ER lumen by endocytosis without ever transporting across a membrane
- Rough ER has ribosomes attached to its cytosol

Cytoskeleton
- Structure and motility of a cell is determined by a network of filaments
- Anchors some membrane proteins and other cellular components, moves components within the cell, and moves the cell itself

Microtubules
- Larger than microfilaments and are involved in flagella and cilia construction, and the spindle apparatus
- Rigid hollow tubes made from a protein called tubulin
    - Tubulin - Globular protein that polymerizes into long straight filaments under certain conditions
- Makes up the mitotic spindle
- Axoneme - major portion of the flagellum and cilium contains 9 pairs of microtubules forming a circle around two lone microtubules in a 9+2 arrangement
- Cross bridges made from dynein that connects each outer pair of microtubules to its neighbor
- Have a + and - end, - end attaches to microtubule-organizing center
    - Microtubules grow away from the MTOC at its + end
    - Major MTOC is the centrosome; centrioles function in production of flagella and cilia

Microfilaments
- Smaller than microtubules
- Actin forms a major component of microfilaments
- Produce the contracting force in muscle and are involved in cytoplasmic streaming, phagocytosis, and microvilli movement

Tight Junctions
- Form a watertight seal from cell to cell that can block water, ions, and other molecules from moving around or past cells
- Epithelial tissue of organs are held together by tight junctions to prevent waste from flowing

Desmosomes
- Join two cells at a single point by attaching directly to the cytoskeleton of each cell

Gap Junctions
- Small tunnels connecting cells allowing molecules and ions to move between cells
- In cardiac muscle provide for the spread of the action potential

Mitochondria
- Krebs cycle happens here
- DNA replicates independently; contains no histones or nucleosomes
- Have their own ribosomes
- Inner membrane invaginates to form cristae
    - Holds the electron transport chain
- Area between inner and outer membrane is intermembrane space

Tissue - cells that form groups of similar cells that work together for a common purpose

Extracellular matrix - some cells called fibrolasts secrete fibrous proteins such as elastin and collagen to form a molecular network that holds tissue cells in place
- Can provide structural support, help to determine shape and motility, and affect cell growth

Tissues
- Epithelial tissue, muscle tissue, connective tissue, and nervous tissue
- Epithelial - separates free body surfaces from their surroundings
- Connective tissue - characterized by extensive matrix
    - Ex. Blood, lymph, bone, cartilage, etc.

4 Nervous System

Friday, January 04, 2008
2:20 AM

Neuronal Communication - tends to be rapid, direct, and specific
Hormonal Communication - tends to be slower, spreads throughout the body, and affects many cells and tissues in different ways
Neurons - rely on glucose for energy; don't need insulin; depend on aerobic respiration efficiency
- Rely on blood because they don't have sufficient glycogen or oxygen

Electrical synapses
- Transmit in both directions unlike chemical synapses and with more speed

White matter
- Myelinated axons

Grey matter
- Neuronal cell bodies

Saltatory Conduction - jumping nodes of ranvier
CNS
- Integrates nervous signals between sensory and motor neurons

PNS
- Somatic and autonomic nervous system
- Somatic - Designed to respond primarily to external environment; sensory and motor functions; uses AcH

ANS
- involuntary
- Sympathetic and Parasympathetic
- Most internal organs innervate by both

  Sympathetic
  - Dilates pupils
  - Increases heart beat rate and stroke volume
  - Constricts blood vessels around digestive and excretory systems to increase blood flow to muscles
  - Postganglionic neurons are adrenergic

Lower Brain
- Medulla, hypothalamus, cerebellum
- Integrates subconscious activities such as respiration, arterial pressure, salivation, emotions, reactions to pain and pleasure

Higher Brain
- Cerebral cortex - stores memories and processes thoughts

4 Visual & Auditory Systems

Friday, January 04, 2008
2:49 AM

Cornea - nonvascular
Lens - flattened by zonule fibers; when ciliary muscles contract the zonule fibers relax and the lens becomes spherical to see close up
Cones - distinguish colors

Three Parts of the Ear

- Outer ear
- Middle ear
    - Malleus
    - Incus
    - stapes
- Inner ear
    - Wave in inner ear moves through cochlea
    - Movement is detected by hair cells and organ of Corti
    - Semicircular canals - detect orientation

5 Endocrine System

Friday, January 04, 2008
2:54 AM

<u>Endocrine glands</u> - release hormones directly into the blood
<u>Exocrine glands</u> - release enzymes to the external environment through ducts
  - Ex. Sweat, oil, mucous

- Effects of endocrine system tend to be slower and longer lasting than nervous system
- All hormones need a receptor--either on the membrane or in the cell

<u>Hormone Types</u>

a. <u>Peptide Hormones</u> - derived from peptides
    - May be large or small and often attached to carbohydrates
    - ALL are synthesized in the rough ER as a preprohormone where it is sent to the Golgi
    - Are water soluble
b. <u>Steroid Hormones</u>
    - Derived from cholesterol
    - Formed in the smooth ER and mitochondria since they are lipids
    - Require a protein transport molecule through the blood but diffuse across the membrane on their own
    - Hit receptors in the cytosol where they are transported to the nucleus and act at the transcription level
    - Typical effect is to increase certain membrane or cellular proteins
    - Important ones are
        - the glucocorticoids and mineral corticocoids of the adrenal cortex
        - Gonadal hormones: estrogen, progesterone, testosterone
c. <u>Tyrosine Derivatives</u>
    - T_3, T_4, and catecholamines(formed in the adrenal medulla)
        - Epinephrine and norepinephrine are water soluble
    - Formed by enzymes in the cytosol or on the rough ER
    - Thyroid hormones are lipid soluble and must be carried in blood by plasma protein carriers
        - Their high affinity to their binding proteins in the plasma and in the nucleus create a latent period in their response and increase the duration of the effect of the thyroid hormones
        - Increase the transcription of large numbers of genes in nearly all cells of the body

- Endocrine glands tend to over secrete their hormones
    - The gland lags behind the effector; respond to the condition instead of creating it
        - Ex. High insulin levels do NOT create low blood glucose, they are a response to high blood glucose
        - Ex. If you have high blood pressure and decreased urine output you have low ADH levels because ADH is responding to the condition

5 Hormones

Friday, January 04, 2008
3:20 AM

Anterior Pituitary (FLATPEG!)

- Releases ONLY peptide hormones

a. hGH
    - increases growth in almost all cells of the body
    - Increases episodes of mitosis, cell size, rates of protein synthesis, mobilizing fat stores, use of fatty acids for energy, decreasing use of glucose
    - Increases AA transport across membrane, translation and transcription, and decreases breakdown of protein and AA

b. Adrenocorticotropic hormone(ACTH)
    - Stimulated by stress
    - Stimulates the adrenal cortex to release glucocorticoids(stress hormones)

c. Thyroid-stimulating hormone(TSH)
    - Stimulates thyroid to release T_3 and T_4
    - Increases thyroid cell size, number
    - T_3 and T_4 concentrations have a negative feedback effect on TSH release

d. FSH and LH

e. Prolactin
    - Promotes lacation
    - Although hypothalamus has a stimulatory effect on the release of all other anterior pituitary hormones it has an inhibitory effect on the release of prolactin
    - Release stimulated by suckling

Posterior Pituitary

- Oxytocin and ADH are synthesized in the neural cell bodies of the hypothalamus

a. Oxytocin
    - a peptide hormone that increases uterine contractions and causes milk to be ejected from the breasts

b. ADH(vasopressin)
    - Peptide hormone that causes the collecting ducts of the kidney to become permeable to water reducing the amount of urine and concentrating it
    - Since fluid is reabsorbed it also increases blood pressure

Adrenal Glands

- Cortex - secretes ONLY steroids; mineral corticoids and glucocorticoids
- Mineral Corticoids - affect electrolyte balance in the bloodstream
- Glucocorticoids - increase blood glucose concentration and have an even greater effect on fat and protein metabolism

Adrenal Cortex

a. Aldosterone - a steroid is a mineral corticoid that acts in the distal tube and collecting duct to increase Na^+ and Cl^- reabsorption and K^+ and H^+ secretion. Causes an increase in blood pressure.

b. Cortisol - a steroid glucocorticoid that increases blood glucose levels by stimulating gluconeogenesis(creation of glucose and glycogen from amino acids, glycerol, lactic acid) in the liver
    - degrades adipose tissue to fatty acids to be used for cellular energy;
    - Stress hormone
    - Diminishes capacity of immune system to fight infection
    - Degradation of nonhepatic proteins and amino acids and an increase in hepatic amino acids and proteins

c. Catecholamines
    - Tyrosine derivatives synthesized in the adrenal medulla
    - Epinephrine and norepinephrine - vasoconstrictors of most internal organs and skins,

but are vasodilators of skeletal muscles

Thyroid Hormones

a. T_3 and T_4 - lipid soluble tyrosine derivatives that diffuse through the lipid bilayer and act in the nucleus of the cells of their effector
   - Increase resting metabolic rate
   - Secretion is regulated by TSH
b. Calcitonin
   - Large peptide hormone that slightly decreases blood calcium level by decreasing osteoclast activity and number

Pancreas

a. Insulin -a peptide hormone released when blood levels of carbohydrates or proteins are high
   - Carbohydrates are stored as glycogen in the liver and muscles, fat is stored in adipose tissue, and amino acids are taken up and turned into proteins
   - Permeability of membrane to AA is increased
   - Intracellular metabolic enzymes are activated and even translation and transcription rates are affected
   - Effect is to lower blood glucose levels
b. Glucagon - a peptide hormone that stimulates glycogenolysis and gluconeogenesis in the liver
   - Breaks down adipose tissue increasing the fatty acid level in the blood
   - Net effect is to raise blood glucose levels

Parathyroid Hormone

- a peptide that increases blood calcium
- Increases osteocyte absorption of calcium and phosphate from the bone and stimulates proliferation of osteoclasts
- Increases renal calcium reabsorption and renal phosphate excretion
- Regulated by calcium ion plasma concentration

5 Reproduction

Friday, January 04, 2008
7:43 PM

- Except for FSH, LH, HCG, andinhibin, which are peptides, the reproductive hormones below are steroids released from the testes, ovaries and placenta.

Male Reproductive System
  - Production of sperm happens in the seminiferous tubules
  - Spermatogonia located in the seminiferous tubules arise from epithelial tissue to become spermatocytes, spermatids, and then spermatozoa
  - Sertoli cells stimulated by FSH surround and nurture the spermatocyte and spermatids
  - Leydig cells release testosterone when stimulated by LH
  - Sertoli cells secrete inhibin, a peptide hormone that acts on the pituitary gland to inhibit FSH secretion

Testosterone is the primary androgen(male sex hormone) and stimulates germ cells to become sperm
  - Responsible for secondary sex characteristics such as enlargement of the larynx, growth of seminal vesicles
  - Stimulates growth spurt at puberty and closure of the epiphyses of the long bones ending growth

Spermatid
  - As it becomes a spermatozoan it loses its cytoplasm and forms the head, midpiece, and tail
  - Head of sperm has nuclear material and acrosome that contains lysosome-like enzymes to penetrate the egg

- Once freed in the tubule lumen the spermatozoon is carried to the epididymus. On ejaculation it travels through the vas deferens into the urethra. Semen is the mixture of spermatozoa and fluid from the seminal vesicles, prostrate, and the bulbourethral(Cowper's) glands.
- Spermatozoa becomes active for fertilization in a process called capacitation in the vagina

Female Reproductive System
  - Oogenesis begins in the ovaries of the fetus
  - All the eggs are arrested as primary oocytes at birth

Menstrual Cycle
  - At puberty, FSH stimulates growth of granulosa cells around the primary oocyte. Granulosa cells secrete a viscous substance around the egg called the zona pellucida. This structure is called the primary follicle.
  - Next, theca cells differentiate from the interstitial tissues and grow around the follicle to for a secondary follicle
  - Upon stimulation by LH, theca cells secrete androgen, which is converted to estradiol(a type of estrogen) by the granulosa cells in the presence of FSH and secreted into the blood
  - Estradiol is a steroid hormone that prepares the uterine wall for pregnancy
  - The follicle grows and bulges from the ovary
  - Typically, estradiol inhibits LH secretion by the anterior pituitary
  - Luteal Surge - However, just before ovulation(bursting of the follicle) the estradiol levels rise rapidly causing a dramatic increase in LH
    - Results from a positive feedback loop of rising estrogen levels which increase LH levels, which increase estrogen
    - Causes the follicle to burst, releasing the egg(now a secondary oocyte) into the body cavity
      - Then the egg is swept up into the fallopian tube or oviduct
      - Remaining portion of follicle becomes the corpus luteum
    - Corpus luteum - secretes estradiol and progesterone throughout pregnancy, or in the case of no pregnancy, for about two weeks until it turns into the corpus albicans

- Cycle is divided into three phases
  i. Follicular phase - begins with the development of follicle and ends at ovulation
  ii. Luteal phase - begins with ovulation and ends with the degeneration of the corpus luteum
  iii. Flow - shedding of uterine lining lasting about 5 days
- LOOK AT GRAPH ON PAGE 114

Fertilization
- Once in the fallopian tube the egg is swept towards the uterus by cilia
- Fertilization takes place in the fallopian tube
- Entry of the sperm activates the cortical reaction which prevents other sperm from fertilizing the same egg
- Now the oocyte goes through the second meiotic division to become an ovum and release a second polar body
- Occurs when the nuclei of the ovum and sperm fuse to form the zygote

Cleavage
- Begins while the zygote is still in the fallopian tube
- Zygote goes through many cycles of mitosis--when it is 8 cells its called a morula

Blastocyst -fluid filled ball that forms the morula continues to divide

Implantation - when the blastocyst lodges in the uterus on the 5th to 7th day after ovulation

Human Chorionic Gonadotropin (HCG)
- A peptide hormone that is released by the egg upon implantation that prevents degradation of corpus luteum and maintains its secretion of estrogen and progesterone

Placenta
- Formed from the tissue of the egg and the mother and takes over the job of hormone secretion
- At 3 mothns begins secreting its own estrogen and progesterone while lowering the secretion of HCG

Determination
- Process where a cell becomes committed to a specialized developmental path(a certain tissue)

Differentiation
- The specialization that occurs at the end of development forming a specialized tissue cell

Gastrula
- Formation begins in the second week and is called gastrulation
- Cells begin to slowly move about the embryo for the first time
  - Three primary layers are formed: ectoderm, endoderm(lining of digestive tracts, liver, and pancreas), mesoderm(stuff that lies between the inner and outer covering of the body--muscle, bone, etc.)
- In the third week the gastrula develops into the neurula in a process called neurulation
  - Notochord - induces ectoderm to form neural plate

Apoptosis - regulated by proteins

6 Digestive, Excretory System

Friday, January 04, 2008
8:37 PM

Digestive Tract- mouth; esophagus; stomach, small intestine(duodenum, ileum, jejunum); large intestine(ascending, transverse, descending, sigmoid colon); rectum; anus

Digestion begins with α-amylase in the saliva
- α-amylase begins breaking down the long straight chains of starch into polysaccharides
- Starch is the major carbohydrate in the human diet

Peristaltic action - moves the bolus down the esophagus by swallowing; smooth muscle
- Wave motion

- Saliva lubricates food to help it move down esophagus

Stomach
- Chyme - stomach mixes and stores food reducing it to a semi-fluid mass
- Exocrine glands - have gastic pits(?)
- Begins protein digestion with the enzyme pepsin
- Low pH of 2 in stomach assists protein digestion by denaturing proteins; kills bacteria
- Four major cell types:
  i. Mucous cells - line stomach walls to protect cells from acidic environment; mucous is mainly sticky glycoproteins; some secrete small amount of pepsinogen
  ii. Chief(peptic) cells - secrete pepsinogen deep in the exocrine gland; pepsinogen activated by low pH
  iii. Parietal(oxyntic) cells - secrete HCl; lowers pH of stomach and raises pH of blood
     - Bicarbonate released outside cell, hydrogen from carbonic acid released into cell
  iv. G cells - secrete gastrin, a large peptide hormone, into the blood and stimulates parietal cells to secrete HCl

- Major hormones that affect secretion of stomach juices are AcH, gastin, and histamine
  - AcH increases secretion of all cell types

Small Intestine
- 90% of digestion and absorption occurs here
- Digestion happens in duodenum; absorption in jejunum and ileum

Small Intestinal Wall
- Villi - finger-like projections in outer layer
  - Increase surface area of the wall allowing for greater digestion and absorption
  - within each villus is a capillary network and a lymph vessel called a lacteal
- Nutrients absorbed through the wall of the small intestine pass into the capillary network and the lacteal
- Microvilli - smaller finger-like projections on each villus
  - Appear as a fuzzy covering called the brush border
- Brush Border
  - Contains membrane bound digestive enzymes that are carbohydrate digesting
  - Contains protein-digesting enzymes called peptidases
  - Contains nucleotide-digesting enzymes called nucleosidases
  - Enterocytes - cells of the brush border that reduce di/tri-peptides to AAs
- Goblet cells
  - Epithelial cells that secrete mucus to lubricate the intestine and protect the brush border from mechanical and chemical damage
- Lysozyme
  - Regulates bacteria within the intestine

Pancreas
- Duodenum
  - Has a pH of 6 due to bicarbonate ion secreted by the pancreas

- Major enzymes secreted(Need to know!)
  i. Trypsin - degrades proteins into small polypeptides; most proteins reach the brush border as small polypeptides where they are reduced to AAs before they are absorbed by enterocytes
  ii. Chymotrypsin - same as above
  iii. Pancreatic Amylase - hydrolyzes polysaccharides to disaccharides; degrades nearly all carbohydrates from the chyme into small glucose polymers
  iv. Lipase - degrades fat(triglycerides)
  v. Ribonuclease
  vi. Deoxyribonuclease
- Bile
  - produced in the liver and stored in the gall bladder
  - weakens bonds between fat(emulsifies) to increase surface area so lipase can break it down
  - Reabsorbed by small intestine and sent back to the liver

- Hormones in the small intestine cause increased blood insulin levels after the meal

Large Intestine
- Major functions are water absorption and electrolyte absorption
  - When this fails diarrhea results
- Contains E. Coli
  - Produces vitamin K, B_{12}, thiamin, and riboflavin

Carbohydrates
- Sodium is pumped out of the enterocyte
- Glucose is dragged into the enterocyte by sodium(secondary active transport)
- One of the jobs of the liver is to maintain a fairly constant blood glucose level
- Glycogenesis - formation of glycogen
- Glycogenolysis - takes place in the liver when the blood glucose level decreases
- In all cells except enterocytes and the cells of the renal tubule glucose is transported from high concentration to low concentration

Proteins
- Protein digestion results in amino acids, dipeptides, and tripeptides
- Absorption of many of these products occurs via a cotransport mechanism down the concentration gradient of sodium
- All dietary protein is broken down to its amino acids before being absorbed into the blood
- All polypeptides absorbed into an enterocyte are hydrolyzed to their AA components by enzymes within the enterocytes
- Then they are absorbed quickly into the blood and taken up by all cells of the body; especially liver
- Transport may be facilitated or active--never passive because of polarity, size
- Cell immediately creates proteins from AAs to keep concentration low
- When AAs reach their upper limit for protein storage AAs can be burned for energy or converted to fat for storage
- Easily broken down and returned to blood when needed
- Ammonia - nitrogen containing compound produced as a by-product of gluconeogenesis
  - Nearly all ammonia converted to urea

Fats
- Most of dietary fat consists of triglycerides which are broken down to monoglycerides and fatty acids before they are shuttled to the brush border by bile micelles and diffuse to the enterocyte membrane
- Once inside the enterocyte monoglycerides/fatty acids are turned back into triglycerides at the smooth ER
- Newly synthesized triglycerides aggregate within the smooth ER lumen
- Move to Golgi apparatus and are released via exocytosis(chylomicrons!)
- Major absorption of fat occurs in the liver and adipose tissue

- The first stop for most of the digested fat is the liver
    - Albumin - most fatty acids are transported in the blood with albumin
- Lipoproteins
    - made from triglycerides, cholesterol, phospholipids, and proteins
    - Most are made in the liver
    - VLDL transport triglycerides from the liver to adipose tissue
    - Intermediate and LDL transport cholesterol and phospholipids to the cells of the body
- Vena Cava - All blood received by the liver moves to the hepatic vein and leads to the vena cava

Liver Functions

a. Blood Storage - liver can expand to store blood for the body
b. Blood Filtration - Kupfer cells phagocytize bacteria picked up from the intestines
c. Carbohydrate Metabolism - liver maintains normal blood glucose levels through gluconeogenesis, glycogenesis, and storage of glycogen
d. Fat Metabolism - liver synthesizes bile from cholesterol and converts carbohydrates and proteins into fat; oxidizes fatty acids for energy and forms most lipoproteins
e. Protein Metabolism - liver deaminates amino acids; forms urea from ammonia in the blood; synthesizes fibrinogen, prothrombin, albumin, nonessential amino acids
f. Detoxification - detoxified chemicals are excreted by the liver as part of bile or polarized so they maybe excreted by the kidney
g. Erythrocyte destruction - destroy irregular erythrocytes
h. Vitamin Storage - liver stores vitamins A, D, and B12

Prothrombin and Fibrinogen - two important clotting factors
Albumin - major osmoregulatory protein in the blood

Ketosis/Acidosis - when the liver mobilizes fat or protein for energy blood acidity increases

6 Kidney

Friday, January 04, 2008
11:42 PM

- You have two kidneys. They are made up of an <u>outer cortex</u> and an inner <u>medulla</u>

  Kidney Functions(obviously important)
  a. Excretes waste products such as urea, uric acid, ammonia, and phosphate
  b. Maintains homeostasis of body fluid volume and solute composition
  c. Controls plasma pH

- Urine is created by the kidney and emptied into the renal pelvis
- Renal pelvis is emptied by the ureter, which carries urine to the bladder, which is then drained by the urethra
- Nephron - functional unit of the kidney
- Blood flows into the first capillary bed called the glomerulus
- Renal Corpuscle - made up by Bowman's capsule and the glomerulus
  - Fenestrations - hydrostatic pressure forces plasma through fenestrations of the glomerular endothelium and into Bowman's capsule
    - Act as a sieve filtering blood cells and large proteins entering bowman's capsule
- Proximal tubule
  - Where most reabsorption occurs; filtrate from bowman's capsule flows here
  - Reabsorption of nearly all glucose, most proteins, and other solutes
  - Water is reabsorbed here
  - Drugs, toxins, and other solutes are secreted into the filtrate by the cells here
    - Hydrogen ions are secreted through an antiport system with sodium
  - Net result is to reduce the amount of filtrate in the nephron while changing the solute composition without changing the osmolarity
- Loop of Henle
  - Dips into the medulla
  - Function is to increase the solute concentration and thus the osmotic pressure
  - As filtrate descends into the medulla water passively diffuses out of the loop andinto the medulla; this area of the medulla has low permeability to salt so filtrate osmolarity goes up
  - As filtrate rises out salt diffuses out(passively then actively)
  - Ascending loop is permeable to salt but impermeable to water
- Distal Tubule
  - Reabsorbs Na^+ and Ca^{2+} while secreting K^+, H^+, and HCO_3^-
  - Aldosterone increases sodium and potassium membrane proteins
  - Net effect is to lower the filtrate osmolarity
  - ADH increases the permeability of the cells to water so in the presence of ADH water flows from the tubule concentrating the filtrate
- Collecting Tube
  - At the end of the distal tube
  - Carries the filtrate to the highly osmotic medulla
  - Impermeable to water but sensitive to ADH
  - When ADH is around water exits into the medulla concentrating the urine
- Juxtaglomerular Apparatus
  - Monitors filtrate pressure in the distal tube
  - Specialized cells secrete renin which ultimately stimulates the adrenal cortex to secrete aldosterone

  Overview

- Filtration occurs in the renal corpuscle; reabsorption and secretion mostly in the proximal tubule; the loop of Henle concentrates solute in the medulla; distal tubule empties into the collecting duct; collecting duct concentrates the urine
- Amount of filtrate is related to the hydrostatic pressure of the glomerulus
- Ascending loop of Henle actively transports sodium into the kidney

7 Cardiovascular System

Saturday, January 05, 2008
12:14 AM

Circulatory Path of Blood

Systemic Circulation
- Beginning with the left ventricle, blood is pumped through the aorta.
- From the aorta branch many smaller arteries which branch into smaller arterioles and then capillaries
- Blood from the capillaries is collected into venules which then collect into larger veins
- These larger veins collect again into the superior and inferior vena cava
- Vena cava empties into the right atrium of the heart

Pulmonary Circulation
- From the right atrium blood is squeezed into the right ventricle
- The right ventricle pumps blood through the pulmonary arteries, to the arterioles, and then to the capillaries of the lungs
- From the capillaries of the lungs blood collects in venules, then veins, and finally in the pulmonary veins leading to the heart
- Pulmonary veins empty into the left atrium which fills the left ventricle

Systole
- Occurs when ventricles contract

Diastole
- Occurs during relaxation of the entire heart and then contraction of the atria

- The rate of these contractions is controlled by the autonomic nervous system but the autonomic nervous system doesn't initiate these contractions

Sinoatrial Node(SA node)
- The heart contracts automatically paced by a specialized group of muscle cells called the sinoatrial node(SA node) in the right atrium
- Contracts by itself rhythmically spreading its contractions to the surrounding cardiac muscles via electrical synapses made from gap junctions
- Pace of the SA node is faster than heartbeats but its innervated by the vagus nerve slowing contractions
- Spreads around both atria causing them to contract and at the same time spreads to the atrioventricular node(AV node)

Atrioventricular Node(AV node)
- Slower to contract, creating a delay which allows the atria to finish their contraction and to squeeze their contents into the ventricles before the ventricles begin to contract
- From the AV node the AP moves down conductive fibers called the bundle of His
- Bundle of His
  - Located in the walls separating the ventricles
  - The AP branches out through the ventricular walls via conductive fibers called Purkinje fibers where the AP is then spread through gap junctions from one cardiac muscle to the next
  - Purkinje fibers - fibers in the ventricles allow for a more unified and stronger contraction

Arteries
- elastic, and stretch as they fill with blood
- Wrapped in smooth muscle that is typically innervated by the sympathetic nervous system
- Epinephrine is a vasoconstrictor that causes arteries to narrow
- Larger arteries have less smooth muscle and are thus less affected by sympathetic innervation

Arterioles

- Very small, wrapped by smooth muscle
- Constriction and dilation can be used to regulate blood pressure and reroute blood

Capillaries

- Microscopic blood vessels
- Nutrient and gas exchange takes place here
- Four methods of crossing capillary walls
    i. Pinocytosis
    ii. Diffusion or transport through capillary cell membranes
    iii. Movement through pores called fenestrations
    iv. Movement through the space between the cells
- As blood flows in hydrostatic pressure is greater than osmotic pressure and net flow is out of the capillary and into the interstitium
- Although osmotic pressure is constant through the capillary towards the end hydrostatic pressure drops so net fluid flow is into the capillary

Venules and Veins

- Similar to arterioles and arteries
- Lumen is larger than the lumen of comparable arteries and veins contain a far greater volume of blood
- Veins, venules, and venus sinuses in the systemic circulation hold about 64% of the blood in a body at rest and act as a reservoir
- Arteries, arterioles, and capillaries in the systemic circulation carry about 20%

- Blood volume flow rate is approximately constant
- MEMORIZE FIGURE 7-7 ON PAGE 143
- Veins have a valve system that prevents back flow to compensate for the lower pressure in the veins

Important Stuff

- An artery carries blood away from the heart
- A vein carries blood towards the heart
- Don't confuse oxygenated blood with the definition of arteries; the pulmonary arteries contain the most deoxygenated blood in the body

7 Respiratory System

Saturday, January 05, 2008
1:00 AM

- Provides for gas exchange between the external environment and the blood
- Air enters through the nose, moves through the pharynx, larynx, trachea, bonchi, bronchioles, and into the alveoli where oxygen is exchanged for CO_2 with blood

<u>Diaphragm</u>
  - when this contracts air is inhaled
  - Is a skeletal muscle innervated by the phrenic nerve

<u>Nasal Cavity</u>
  - Space inside he nose that <u>filters, moistens, and warms</u> incoming air
  - <u>Coarse Hair</u> - at the front of the cavity traps large dust particles
  - <u>Mucus</u> - secreted by goblet cells traps smaller dust particles and moistens the air
  - <u>Cilia</u> - moves the mucus and dust back toward the pharynx so that it may be removed by spitting or swallowing
  - <u>Pharynx</u> - functions as a passageway for food and air
  - <u>Larynx</u> - contains vocal cords, sits behind epiglottis
    - When nongaseous material enters coughing occurs to force the material out
  - <u>Epiglottis</u> - cartilaginous member that prevents food from entering the trachea when swallowing
  - <u>Trachea(windpipe)</u> - lies in front of the esophagus
    - Mucus and cilia collect dust in the trachea and move it towards the pharynx
  - <u>Bronchi</u> - there is a right and left bronchi that air from the trachea splits into before it enters the lungs
  - <u>Bronchioles</u> - each bronchus branches many more times and ends in tiny bronchioles
  - <u>Alveoli</u> - bronchioles terminate in grape-like clusters called alveolar sac composed of tiny alveoli
    - From each alveolus oxygen diffuses into a capillary where it is picked up by red blood cells
    - The red bloods release CO_2 which diffuses into the alveolus and expelled upon exhalation

<u>Important</u>
- Since microtubules are found in cilia and ciliated cells are found in the respiratory tract(and the Fallopian tubes and ependymal cells of the spinal cord), a problem in microtubule production in breating(or fertility or circulation of cerebrospinal fluid)

7 Gas Exchange

Saturday, January 05, 2008
1:39 PM

- Oxygen diffuses into the capillaries and carbon dioxide diffuses into the alveoli
- 98% of the oxygen in the blood binds rapidly and reversibly with the protein hemoglobin inside the erythrocytes forming oxyhemoglobin
- Hemoglobin - heme cofactor is an organic molecule with an atom of iron at its center
    - Each of the 4 iron atoms in hemoglobin bind one O_2 molecule increasing the likelihood of a second molecule binding
- As O_2 pressure increases, the O_2 saturation of hemoglobin increases sigmoidally

Oxygen Dissociation Curve

- Is shifted to the right by an increase in carbon dioxide pressure, hydrogen ion concentration, or a temperature
- A shift to the right indicates a lowering of hemoglobin's affinity for oxygen
- Carbon monoxide has more than 200 times greater affinity for hemoglobin than does oxygen but shifts the curve to the left

Carbon Dioxide

- Carried by the blood in three forms; physical solution, bicarbonate ion, in carboamino compounds(compounds with hemoglobin, etc.)

Carbonic Anhydrase

- An enzyme that catalyzes this reversible reaction
- $CO_2 + H_2O \rightarrow HCO_3^- + H^+$

- Because carbonic anhydrase is inside the red blood cell and not in the plasma, when carbon dioxide is absorbed in the lungs, bicarbonate ion diffuses into the cell. To balance the electrostatic forces, chlorine moves out of the cell in a phenomenon called the chloride shift
- Haldane Effect - when hemoglobin becomes saturated with oxygen, its capacity to hold CO_2 is reduced. Facilitates the transfer of carbon dioxide from blood to lungs, and from tissues to blood.
    - Reduced hemoglobin(Hb, hemoglobin without oxygen) *acts as a blood buffer by accepting protons*
    - It is the greater capacity of reduced hemoglobin to form carbamino hemoglobin that explains the Haldane effect
- In the case of acidosis(too much acid in the blood), the body compensates by increasing the breathing rate thereby expelling carbon dioxide and raising the pH of the blood
- Central and peripheral chemoreceptors monitor CO_2 concentration in the blood and increase breathing when levels get too high

7 Lymphatic, Blood, Immune System

Saturday, January 05, 2008
2:41 PM

<u>Lymphatic system</u>

- collects interstitial fluid and returns it to the blood. Proteins and large particles that can't be taken up by the capillaries are removed by the lymph system.
- Reroutes low soluble fat digestates around the small capillaries of the intestine and into the large veins of the neck
- Most tissues are drained by lymphatic channels
- Lymph system is an open system
- Lymph capillaries are like tiny fingers protruding into the tissues
- To enter the lymph system, interstitial fluid flows between overlapping endothelium cells
- Interstitial fluid is slightly fluid
- As the interstitial pressure rises toward zero, lymph flow increases
- Factors that affect interstitial pressure include: blood pressure, plasma osmotic pressure, interstitial pressure(from proteins, infectious response, etc.), permeability of capillaries
- Lymph vessels are constructed with intermittent valves, which allow fluid to flow in only one direction
- Smooth muscle in the walls of larger lymph vessels contracts when stretched
- Lymph from the right arm and heads enters the blood through the *lymphatic duct*. The rest of the body is drained by the *thoracic duct*.
- Throughout the lymphatic system are many lymph nodes, containing large quantities of lymphocytes.

<u>Blood</u>

- Blood is connective tissue
- Like any connective tissue it contains cells and a matrix
- Blood regulates the extracellular environment of the body by transporting nutrients, waste products, hormones, and even heat
- Plasma contains the matrix of the blood, which includes water, ions, urea, ammonia, proteins, and other organic and inorganic compounds
- <u>Albumin</u>, <u>Immunoglobulins</u> - clotting factors
    - <u>Albumin</u> - transports fatty acids and steroids and regulates the osmotic pressure of blood
- Plasma in which the clotting protein fibrinogen is removed is called serum
- An important function of plasma proteins is to act as a source of amino acids for tissue protein replacement

- All blood cells differentiate from stem cells in the bone marrow

<u>Erythrocytes(red blood cells)</u>

- No organelles, not even a nucleus--so no mitosis
- like bags of hemoglobin and have no nucleus or organelles
- Know the main function is to transport O_2 and CO_2

<u>Leukocyte(white blood cells)</u>

- No nucleus; don't undergo mitosis
- Don't have hemoglobin
- Protect body from foreign invaders
- Granulocytes - live a short time(multiply quickly to fight an infection); function nonspecifically towards all infectious agents
- Agranulocytes - work against specific agents of infection

<u>Platelets</u>

- Small portions of membrane-bound cytoplasm torn from megakaryocytes

- Tiny cells without a nucleus
- Contain actin and myosin, residuals of the Golgi and the ER, mitochondria
- Its membrane is designed to avoid adherence to healthy endothelium while adhering to injured endothelium
- When platelets come across injured endothelium they become sticky and adhere releasing various chemicals and activating other platelets

Coagulation - a process involving many factors that starts with platelets includes the plasma proteins prothrombin and fibrin

Immune System

Inflammation

- dilation of blood vessels, increased permeability of capillaries, swelling of tissue cells, and migration of granulocytes and macrophages in response to injury to tissue cells
- Part of the effect is to wall off the effected tissue and local lymph vessels from the rest of the body to impede the spread of the infection

Macrophages

- Infectious agents that are able to pass through the skin or the digestive defenses and enter the body are first attacked by macrophages
- They engulf the bacteria

Neutrophils

- Next on the scene after macrophages
- Move toward infected or injured areas drawn by chemicals released from damaged tissue or by the infectious agents themselves
- Engulf bacteria

- When neutrophils and macrophages engulf necrotic tissue and bacteria they die. These dead leukocytes along with tissue fluid and necrotic tissue form pus

Two Types of Acquired Immunity: humoral or β-cell immunity and cell-mediated or T-cell immunity

- Humoral Immunity
  - Is promoted by B lymphocytes
    - B lymphocytes differentiate and mature in the bone marrow and liver
    - Each B lymphocyte is capable ofmaking a single type of antibody or (immunoglobulin), which it displays in the membrane
    - Antigen - an antibody recognizes a foreign particle called an antigen
  - If the B lymphocyte antibody contacts a match antigen(presented by a macrophage), the B lymphocyte, assisted by a helper T cell, differentiates into plasma cells and memory B cells.
  - Plasma cells - begin synthesizing free antibodies releasing them into the blood
  - Free antibodies may attach their base to mast cells
  - When an antibody whose base is bound to a mast cell also binds to an antigen, the mast cell releases histamine and other chemicals
  - Antibodies
    - Once bound, antibodies may begin a cascade of reactions involving blood proteins that cause the antigen bearing cell to be perforated
    - The antibodies may mark the antigen for phagocytosis by macrophages and natural killer cells
    - Antibodies may cause the antigenic substance to agglutinate
  - Primary response
    - the first time the immune system is exposed to an antigen
    - Requires 20 days to reach its full potential
  - Secondary response
    - Memory B cells proliferate and remain in the body. In the case of reinfection each of these cells can be called upon to synthesize antibodies resulting in a faster acting and

more potent affect called the secondary response
    - Requires 5 days to reach full potential
- Cell-mediated Immunity
  - Involves T-lymphocytes
  - T-lymphocytes
    - Mature in the thymus
    - Have an antibody-like protein at their surface that recognizes antigens
    - Tested against self-antigens. If it binds to a self-antigen the T lymphocyte is destroyed
    - T-lymphocytes that are not destroyed differentiate into helper T cells, memory T cells, suppressor T cells, and killer T cells
  - Helper T Cells
    - Assist in activating B lymphocytes as well as killer and suppressor T cells
  - Memory T cells
    - Have a similar function to Memory B cells
  - Suppressor T Cells
    - Play a negative feedback role in the immune system
  - Killer T Cells
    - Bind to the antigen-carrying cell and release perforin, a protein which punctures the antigen-carry cell
    - Can attack many cells because they don't phagocytize their victims
    - Responsible for fighting some forms of cancer and attacking transplanted tissue

- Overview
  - Bacteria enters and is engulfed by macrophages and neutrophils. Then the interstitial fluid is flushed into the lymphatic system where lymphocytes wait in the lymph nodes. Macrophages process and present the bacterial antigens to B lymphocytes. With the help of Helter T cells, B lymphocytes differentiate into memory cells and plasma cells The memory cells are preparation in the event that the same bacteria ever attacks again(the secondary response). The plasma cells produce antibodies which are released into the blood to attack the bacteria.
  - A single antibody is specific for a single antigen. A single B lymphocyte produces only one antibody type.

Blood Types
  - Identified by A and B surface antigens
  - Type A means the red blood membranes
  - Having a certain blood type means you DON'T make antibodies for those types
  - Type O has neither A nor B antigens so makes A and B antibodies
  - An individual may donate blood only to a donor whose body does not have antigens

Table shows '-' when blood is accepted, '+' when it is rejected

		Donor		
	A	B	AB	O
A	-	+	+	-
B	+	-	+	-
AB	-	-	-	-
O	+	+	+	-

  - A and B antigens are co-dominant

Blood Type	Genotype
A	I^AI^A or I^Ai

B	I^BI^B or I^Bi
AB	I^AI^B
O	ii

- Rh factors are surface proteins on red blood cells
- Individuals having genotypes that code for nonfunctioning proteins are Rh-negative
- Transfusion reactions involving the Rh are usually mild; more of a concern in mother child

8 Muscle

Saturday, January 05, 2008
4:51 PM

Three Types of Muscle Tissue

a. Skeletal muscle
b. Cardiac muscle
c. Smooth muscle

- Any muscle tissues generates a force only by contracting its cells. Four possible functions:
  a. Body movement
  b. Stabilization of body position
  c. Movement of substances through the body
  d. Generating heat of maintain body temperature
- Skeletal muscle is voluntary muscle tissue that can be consciously conrolled.
  - Connects one bone to another
- Tendon - connects muscle o bone
- Ligament - connects bone to bone
- Typically a muscle stretches across a joint and the smaller bone moves while the larger remains stationary
- Muscles work in groups: agonists contract and antagonist stretches
- Synergistic Muscles - assist the agonist by stabilizing the origin bone or by positioning the insertion bone during the movement. In this way skeletal muscle allows for movement and posture.
- Contraction of skeletal muscle may squeeze blood and lymph vessels aiding circulation.
- Shivering - creates heat by rapid contractions; stimulated by hypothalamus

Sarcomere -

- smallest functional unit of skeletal muscle
- Composed of thick and thin filaments, laid side by side to form a cylindrical element
- Positioned end to end to form a myofibril
  - Each myofibril is surrounded by a specialized endoplasmic reticulum called the sarcoplasmic reticulum
    - Lumen of the sarcoplasmic reticulum is filled with Ca^{2+} ions
  - Lodged between myofibrils are mitochondria and many nuclei; skeletal muscle is multinucleate
- Thick filament - made of the protein myosin; several long myosin molecules wrap around eachother to form one thick filament
- Thin filament - composed mainly of the polymer actin

- Myosin and actin work together sliding alongside each other to create the contractile force of skeletal muscle
- Each myosin head crawls along the actin in a 5 stage cycle
  a. First, tropomyosin covers an active site on the actin preventing the myosin head from binding. The myosin head remains cocked in a high energy position with an ADP and P attached
  b. Second, in the presence of Ca2+ troponin pulls the tropomyosin back exposing the active site allowing the myosin head to bind to the actin
  c. Third, the myosin head expels a phosphate and ADP bend into a low energy position dragging the actin along with it. This is the power stroke.
  d. Fourthly, ATP attaches to the myosin head releasing the myosin head from the active site which is covered immediately by tropomyosin.
  e. Fifthly, ATP splits to P and ADP causing the myosin head to cock into the high energy contraction.
- T-tubules
  - ACh released across the neuromuscular synapse; action potential moves deep into the

muscle cell via small tunnels in the membrane called T-tubules
  - Allow for uniform contraction of the muscle by allowing the action potential to spread more quickly
  - When the AP travels to the sarcoplasmic reticulum it suddenly becomes permeable to Ca^{2+} ions beginning the 5-stage cycle
- Myoglobin - oxygen storing protein similar to hemoglobin; stores oxygen inside muscle cells, can only store one molecule of oxygen
- Types of Muscle
  a. Slow Oxidative(type I)
     - red from large amounts of myoglobin
     - Lots of mitochondria
     - Split ATP at a slow rate so they are slow to fatigue but have slow contraction velocity
  b. Fast Oxidative(type IIA)
     - Red, but split ATP at a fast rate
     - Contract rapidly and are resistant to fatigue but not as resistant as type I
  c. Fast Glycolytic(type IIB)
     - Have low myoglobin content
     - Appear white
     - Contract rapidly and have a lot of glycogen

Cardiac Muscle
- Is striated meaning its composed of sarcomeres
- Each cardiac muscle cell contains only one nucleus and is separated from its neighbor by an intercalated disc
- Intercalated disc - contains gap junctions which allow an action potential to spread from one cardiac cell to the next via electrical synapses
- Involuntary
- Exhibits a plateau after depolarization that's created by slow voltage-gated calcium channels which allow calcium to enter and hold the inside of the membrane at a positive potential difference. The plateau lengthens the time of contraction

Smooth Muscle
- Involuntary, so it is innervated by the autonomic nervous system
- Contains only one nucleus
- Contains thick and thin filaments but they aren't organized into sarcomeres
- In addition, smooth muscle cells contain intermediate filaments, which are attached to dense bodies spread throughout the cell. The thick and thin filaments are attached to the intermediate filaments, and, when they contract, they cause the intermediate filaments to pull the dense bodies together. Upon contraction, the smooth muscle cell shrinks length-wise.
- Single-unit smooth muscle cells are connected by gap junctions spreading the AP from a single neuron through a large group of cells allowing the cells to contract as a single unit.
- Contracts or relaxes in response to hormones, neural stimulus, change in pH, O_2 and CO_2 levels, temperature, and ion concentrations

8 Bone

Saturday, January 05, 2008
5:47 PM

- Bone is living tissue
- It's functions are: support of soft tissue, protection of internal organs, assistance in movement of the body, mineral storage, blood cell production, and energy storage in the form of adipose cells in bone marrow
- Bone tissue contains three types of cells surrounded by an extensive matrix
  a. Osteoblasts
     - secrete collagen and organic compounds upon which bone is formed
     - Incapable of mitosis
     - As they release matrix materials around themselves they become enveloped by the matrix and differentiate into osteocytes
  b. Osteocytes
     - Incapable of mitosis
     - Exchange nutrients and waste minerals with the blood
  c. Osteoclasts
     - Resorb bone matrix, releasing minerals back into the blood
     - Develop from white blood cells called monocytes
- Spongy Bone
  - Contains red bone marrow
    - Site of red blood cell development
- Compact Bone
  - Contains yellow bone marrow
    - Contains adipose cells for fat storage
  - In a continuous remodeling process osteoclasts burrow tunnels, called Haversian (central) cannals, through compact bone
    - Lamellae - Osteoclasts are followed by osteoblasts that lay down a new matrix onto the tunnel walls forming concentric rings called lamellae
    - Canaliculi - Osteocytes trapped between the lamellae exchange nutrients via canaliculi
    - Volkmann's Canals - Haversian cannals contain blood and lymph vessels and are connected by crossing canals called Volkmann's canals
    - Osteon - entire system of lamellae and Haversian canals
- Bone Function in Mineral Homeostasis
  - Calcium salts are only slightly soluble so most calcium in the blood is not in the form of free calcium ions but is bound by phosphates(HPO_4^{2-}) and other anions. It is the concentration of free calcium ions(Ca^{2+}) in the blood that is important physiologically.
    - Too much Ca^{2+} makes membranes become hypo-excitable producing lethargy, fatigue, and memory loss
    - Too little produces cramps and convulsions
  - Most of the Ca^{2+} in the body is stored in the bone matrix as hydroxyapatite
    - Gives bones greater compressive strength
  - Bone acts as a storage site for both Ca^{2+} and HPO_4^{2-}
  - Bone helps maintain consistent concentration of these ions in blood
  - Bone also stores energy in the form of fat and is the site of blood cell formation

- Cartilage
  - Flexible, resilient connective tissue composed primarily of collagen
  - Has great tensile strength
- Joints
  - Synovial fluid provides lubrication and nourishment to the cartilage

- Important Functions of the Skin
    a. Thermoregulation - blood conducts heat from the core of the body to skin. Some of this heat can be dissipated by the endothermic process of evaporation
    b. Protection
    c. Environmental Sensory Input
    d. Excretion - water and salts
    e. Immunity - specialized epidermis cells are components of the immune system
    f. Blood Reservoir - vessels in the dermis hold up to 10% of the blood in a resting adult
    g. Vitamin D Synthesis - UV radiation activates a molecule in the skin that is a precursor to vitamin D

- Skin is divided into two principal parts: 1.) epidermis and 2.) dermis
    - 1.) 90% of the epidermis is composed of Keratinocytes which produce keratin that helps waterproof the skin
    - 2.) Melanocytes transfer melanin to keratinocytes
    - 3.) Langerhands cells interact with the helper T-cells of the immune system
    - 4.) Merkel cells attach to sensory neurons and function in the sensation of touch
- Dermis
    - connective tissue derived from mesodermal cells
    - Collagen and elastic fibers in the dermis provide skin with strength, extensibility, and elasticity
    - Embedded by blood vessels, nerves, glands, and hair follicles

9 Populations

Saturday, January 05, 2008
6:43 PM

- To test his hypothesis Mendel performed a test cross between the F_1 generation(purple) with the homozygous recessive parent(white). Since there were white offspring resulting from this cross of a purple F_1 plant and a white parent plant, Mendel proved the F_1 generation was heterozygous.
  F_1 Generation -
  - the first filial generation
  - When F_1 was self-pollinated F_2 expressed both the dominant and recessive traits in 3-to-1 Mendelian ratio

  F_2 Generation
  - When F_2 was self-pollinated 33% produced dominant traits and the rest were the mendelian ratio. The white flowered plants produced only white flowered plants. Thus, half the F_2 generation expressed the dominant trait with the recessive trait latent.

  Complete Dominance
  - A diploid individual will have two chromosomes each containing a separate gene that codes for a specific trait
  - Locus - the corresponding genes are located at the same locus, or position, on the respective chromosome

  Law of Segregation
  - States that alleles segregate independently of each other when forming gametes
  - Any gamete is equally likely to express any allele

  Inbreeding
  - Doesn't change the frequency of alleles but does increase the number of homozygous individuals within a population

  Law of Independent Assortment
  - Genes located on different chromosomes assort independently of each other
  - If two genes are located on the same chromosome the likelihood that they will remain together during gamete formation is indirection proportional to the distance separating them

- Phenotypic ratio of a dihybrid cross is 9:3:3:1
- 23rd pair of chromosome establishes the sex of the individual and each partner is called a sex chromosome. 23rd chromosome of a man is abbreviated as a Y instead of an X.
  - Generally the allele is carried on the X and not the Y. In the female who has two X chromosomes one will condense and become a Barr body rendering its genes inactive.
    - Barr bodies are formed at random so the active allele is split about evenly among cells
    - Carrier - Thus, the female may carry a recessive trait on her 23rd pair without expressing it(?). Such a trait has a large chance of being expressed in her male offspring regardless of the genotype of her mate.
- Karyotype - a map of the chromosomes
- Gene Pool - total of all alleles in a population
- Evolution - change in the gene pool

  Trivia
  Kingdom; Phylum; Class; Order; Family; Genus; Species
  - Plant and Fungi use division instead of Phylum

  Phylum Cordata - > Subphylum Vertebrata
- All mammals belong to the class Mammalia and the phylum Chordata
- Domains: Bacteria, Archaea, Eukarya
- Coacervates - lipid or protein bilayer bubbles; grow randomly from fat in water

Species - loosely limited to but not inclusive of all organisms that can reproduce fertile offspring with eachother

Niche - the way in which a species exploits its environment

- No two species can exploit a niche indefinitely

Survival of the Fittest - says one species will exploit the niche more efficienty

r-Selection

- Large number of offspring with little or no parental care; have a high brood mortality rate

K-Selection

- Sigmoidal growth curve that levels off at the carrying capacity

Speciation -

- process by which new species are formed
- When gene flow stops between two sections of a population speciation begins

Adaptive Radiation

- Occurs when several separate species arise from a single ancestral species

Evolutionary Bottleneck

- If a species faces a crisis so severe as to cause a shift in the allelic frequencies of the survivors of the crisis

Divergent Evolution

- When two or more species evolving from the same group maintain a similar structure from the common ancestor

Convergent Evolution

- When two species evolve similar structures with no common ancestry

Polymorphism

- Occurrence of distinct forms such as tall/short, flower color, etc.

Hardy-Weinberg Equilibrium

a. Large Population
b. Mutational Equilibrium - rate of forward mutations equal to rate of back mutations(not true)
c. Immigration or Emigration must not change the gene pool
d. Random Mating
e. No Selection for Fittest Organism

- $p^2 + 2pq + q^2$
- $P+Q = 1$
- P is dominant, Q is recessive
- Probability that two p's come together is p^2
- Probability that a 'p' and a 'q' come together is 2pq
- Probability that 2 q's come together is q^2

Chordata

- phylum containing humans;
- all chordates have bilateral symmetry
- At some stage in development they possess a notochord, pharyngeal slits, a dorsal, hollow nerve cord, and a tail

Deuterostomes - all chordates are these; anus develops from or near blastopore

Coelom - chordates have these; body cavity with mesodermal tissue

Vertebrata

- have their notochord replaced by a segmented cartilage and bone structure
- Have a distinct brain enclosed in a skull