

Bio 217 Pathophysiology Class Notes
Professor Linda Falkow

- Unit 1: Introduction to Pathophysiology
 - Chapter 1: Cellular Biology
 - Chapter 2: Genes & Genetic Diseases
 - Chapter 3: Altered Cellular & Tissue Biology
 - Chapter 4: Fluids & Electrolytes, Acids & Bases

Cellular Biology

Chapter 1

Cellular Functions

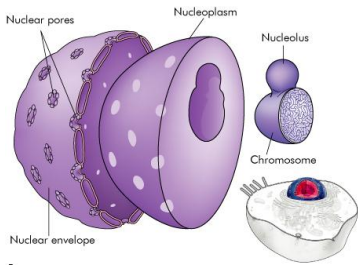
- Movement
- Conductivity
- Metabolic absorption
- Secretion
- Excretion
- Respiration
- Reproduction
- Communication

Cell Structure & Function

- Nucleus
 - DNA
 - DNA replication _____
 - Cell division
- Cytoplasm
 - Cytosol
 - Cytoplasmic organelles

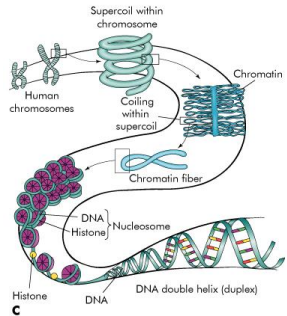
Eukaryotic Cell

- Nucleus



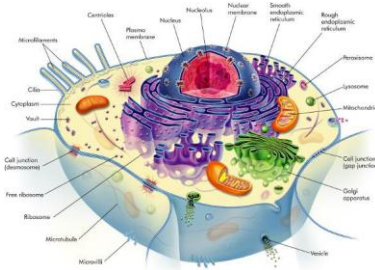
Eukaryotic Cell

- Nucleus



Eukaryotic Cell

- Cytoplasm



Organelles

- _____
 - Protein synthesis
- _____
 - Rough ER – site of protein synthesis
 - Smooth ER - site of lipid synthesis
- _____
 - Proteins from the endoplasmic reticulum are packaged in the _____

Eukaryotic Organelles

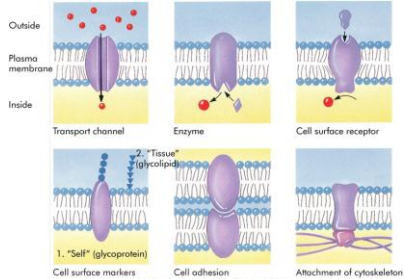
- Lysosomes
 - Contain enzymes
 - Role in autodigestion as a result of cellular injury
- Peroxisomes
 - Contain oxidative enzymes
 - Produce H₂O₂
- _____
 - Participates in oxidative phosphorylation (ATP production)
- Cytoskeleton
 - “Bones and muscles” of the cell
 - Microtubules and Microfilaments

Plasma Membrane

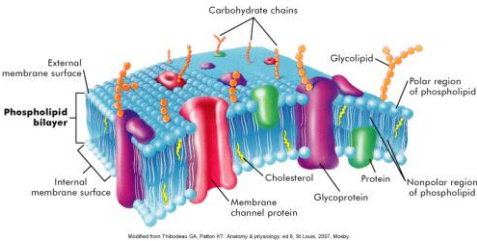
- Lipids
 - Hydrophilic and hydrophobic
 - Phospholipids, glycolipids, and cholesterol
- Carbohydrates
 - Glycoproteins
- Proteins
 - Integral, peripheral, transmembrane
 - Functions

Plasma Membrane

- Plasma membrane protein functions



Membrane Fluidity

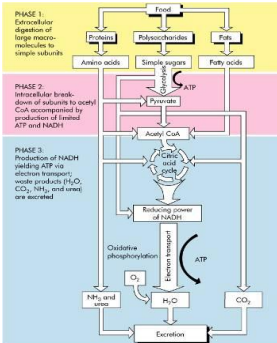


Adenosine Triphosphate

- Created from the chemical energy contained in organic molecules
- Used in synthesis of organic molecules, muscle contraction, and active transport
- Stores and transfers energy

Cellular Energy

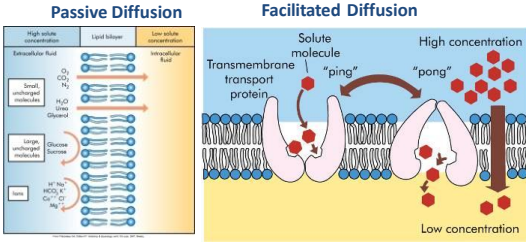
1. Digestion
2. Glycolysis & oxidation
3. Citric Acid Cycle



Membrane Transport

- Passive transport
 - Diffusion (simple and facilitated)
 - Concentration gradient [high → low]
 - Filtration
 - Hydrostatic pressure
 - Osmosis
 - Movement of water
 - Tonicity
 - Isotonic, hypertonic, and hypotonic

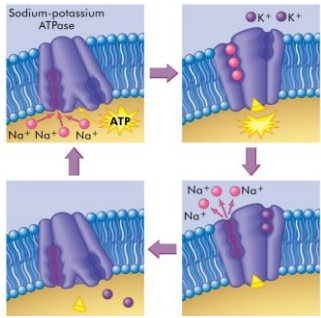
Membrane Transport



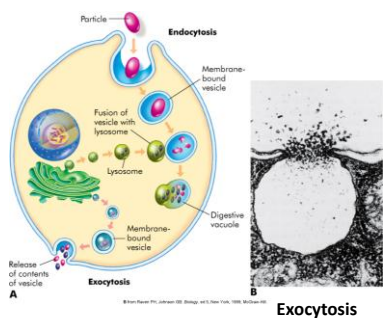
Membrane Transport

- Active transport
 - Active transport pumps (Na/K Pump)
 - Transport by vesicle formation
 - Endocytosis
 - Pinocytosis
 - Phagocytosis
 - Receptor mediated
 - Exocytosis

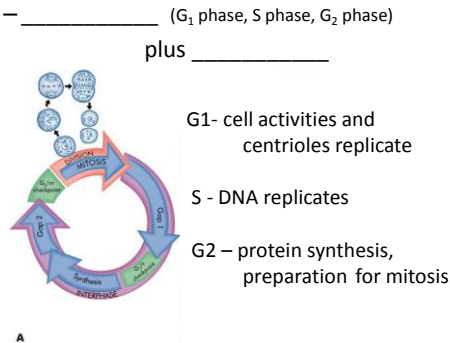
Active Transport (Na-K Pump)



Membrane Transport



The Cell Cycle



Influences on the Cell Cycle

- Cellular division rates
 - Complete cell cycle 12-24 hours
 - Mitosis 1 hour
- Growth factors (cytokines)
 - PDGF
 - EGF
 - IGF-I

Types of Tissue

- **Epithelial tissue**
 - Simple vs. stratified squamous
 - Transitional
 - Cuboidal
 - Simple vs. stratified columnar
 - Pseudostratified ciliated
- **Connective tissue**
 - Dense regular or irregular
 - Loose and dense connective tissue
 - Elastic and reticular connective
 - Cartilage, bone, vascular, and adipose

Types of Tissue

- **Muscle tissue**
 - Smooth
 - Striated (skeletal)
 - Cardiac
- **Nerve tissue**
 - Neurons conduct nerve impulses
 - Neuroglia provide support activities

Concept Check

- 1. What are the main parts of the eukaryotic cell?
 - A. Lipids, CHO, proteins
 - B. Minerals and water
 - C. Organelles
 - D. Cytoplasm and membrane-bound nucleus

2. Which of the following cellular functions does NOT occur in all cell types?

- A. Respiration
- B. Excretion
- C. Metabolic absorption
- D. Secretion

3. Which of the following statements regarding transport across membranes is TRUE?

- A. Diffusion requires a significant energy input.
- B. Mediated transport involves a receptor with a high degree of specificity.
- C. Active transport moves molecules down a concentration gradient.
- D. Facilitated transport expends energy.

• 4. Which can transport substances against the concentration gradient?

- A. Active transport
- B. Osmosis
- C. Facilitated diffusion
- D. Dialysis

___ 5. Anaphase a. centrioles separate

___ 6. Chromatin b. single stranded DNA in non-dividing cell

___ 7. Metaphase c. site of protein synthesis

___ 8. Mitochondria d. chromatids separate

___ 9. Ribosome e. powerhouse of cell

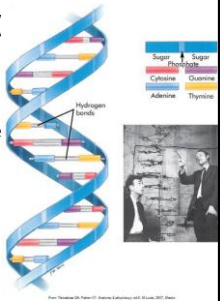
___ 10. Prophase f. chromatid pairs align

Genes and Genetic Diseases

Chapter 2

DNA

- Pentose sugar (_____)
- Phosphate molecule
- Four _____ bases
 - Pyrimidines: Cytosine and Thymine
 - Purines: Guanine and Adenine
- Double helix model
- _____



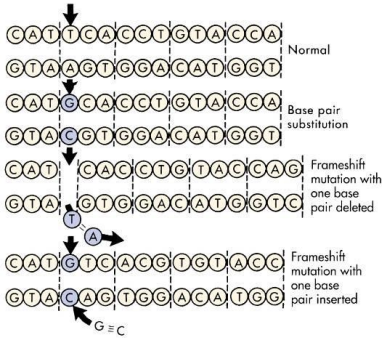
Proteins

- One or more polypeptides
- Composed of amino acids
 - _____ amino acids
 - Directed by sequence of bases (codons)

Mutation

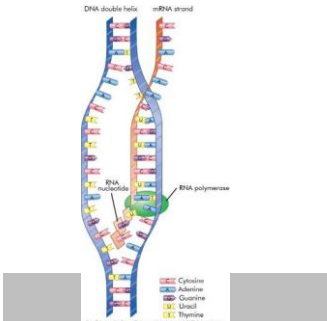
- Any inherited alteration of genetic material
 - Chromosome aberrations
 - Base pair substitution
 - One base pair is substituted for another
- Frameshift mutation
 - Insertion or deletion of one or more base pairs
 - Causes a change in the entire “reading frame”
- Mutagens
 - Increase frequency of mutations
 - Radiation and chemicals

Mutation



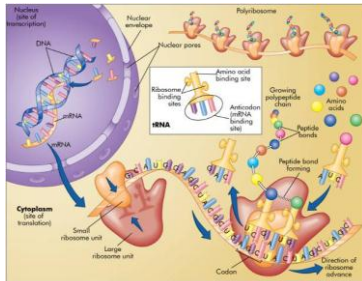
Transcription

- DNA serves as template for formation of _____



Translation

- Process by which RNA directs the synthesis of a _____



Chromosomes

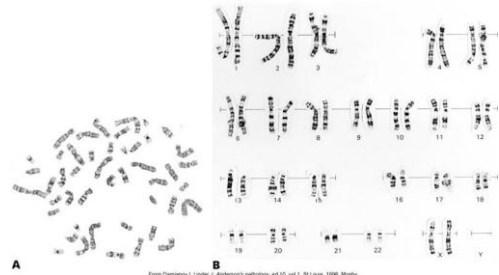
- Somatic cells (____)
 - Contain 46 chromosomes (23 pairs)
- Gametes (____)
 - Contain 23 chromosomes
- Meiosis
 - Formation of haploid cells from diploid cells
- Mitosis
 - Forms _____ cells

Chromosomes

- Autosomes
 - The first 22 of the 23 pairs of chromosomes in males and females
- Sex chromosomes
 - Remaining pair of chromosomes
 - In females (____)
 - In males (____)

Karyotype

- Ordered display of chromosomes (metaphase)



Chromosome Aberrations

- **Euploid** cells have a multiple of the normal number of chromosomes ("eu" Gk. = good)
 - n and $2n$ cells are euploid forms
- **Polyploid** - when a euploid cell has more than the diploid number
 - Triploidy - three copies of each chromosome ($3n=69$)
 - Tetraploidy: - four copies of each ($4n=92$ total)
- Triploid or tetraploid fetuses never survive

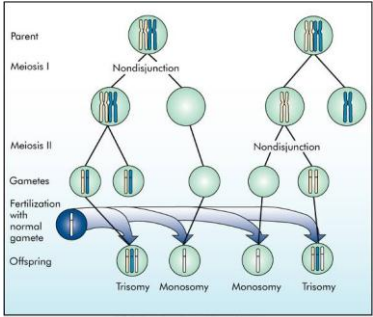
Chromosome Aberrations

- **Aneuploidy**
 - Somatic cell that does not contain a multiple of 23 chromosomes
 - Cell containing three copies of one chromosome is trisomic (trisomy)
 - Monosomy is one copy of any chromosome, often lethal
- "It is better to have extra than less"

Chromosome Aberrations

- Disjunction
 - Normal separation of _____ during cell division
- Nondisjunction
 - Usually the cause of aneuploidy
 - Failure of homologous chromosomes to separate normally during cell division

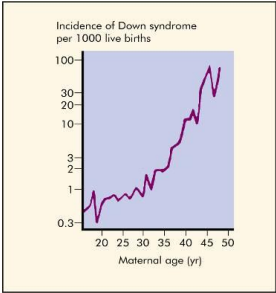
Nondisjunction



Autosomal Aneuploidy

- Down syndrome (_____)
 - Best known example of aneuploidy
 - 1:800 live births
 - Mentally retarded, low nasal bridge, epicanthal folds (eyes), protruding tongue, poor muscle tone
 - Risk increases with maternal age >35

Down Syndrome



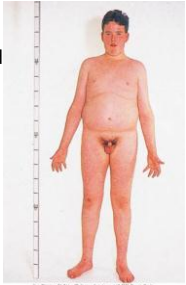
Sex Chromosome Aneuploidy

- Turner syndrome (45, X)
 - Females with only one _____
 - Characteristics
 - Absence of ovaries (sterile)
 - Short stature (~ 4'7")
 - Webbing of the neck
 - Edema
 - Underdeveloped breasts; wide nipples
 - High number of aborted fetuses have this karyotype
 - X is usually inherited from mother



Sex Chromosome Aneuploidy

- Klinefelter syndrome (47, XXY)
 - Individuals with at least two Xs and one Y chromosome
 - Characteristics
 - Male appearance
 - Develop female-like breasts
 - Small testes
 - Sparse body hair
 - Long limbs



- Chromosome breakage
 - If breakage does occur, physiologic mechanisms usually repair the break, but often heals so that chromosome structure is altered
 - Clastogens - harmful agents such as:
 - ionizing radiation
 - chemicals
 - viruses

- Breakage or loss of DNA
- **Cri du chat syndrome**
 - “Cry of the cat”
 - Deletion of short arm of chromosome 5
 - Low birthweight, mental retardation, and microcephaly

- **Homozygous**
 - Loci on a pair of chromosomes have identical genes
 - Example
 - O blood type (OO)
- **Heterozygous**
 - Loci on a pair of chromosomes have different genes
 - Example
 - AB blood type (A and B genes on pair of loci)

- Genotype (“what they have”)
 - The genetic makeup of an organism
- Phenotype (“what they demonstrate”)
 - The observable, detectable, or outward appearance
- Example
 - Individual with the A blood type could be AA or AO.
 - Genotype = _____
 - Phenotype = _____

- If two alleles are found together, the allele that is observable is dominant, and the one whose effects are hidden is recessive
- ____ = homozygous
- ____ = heterozygous
- ____ = homozygous
- Alleles can be codominant

- Carrier
 - A carrier is one that has a disease gene but is phenotypically normal
 - For a person to demonstrate a recessive disease, the pair of recessive genes must be inherited
 - Example
 - Ss = sickle cell anemia carrier
 - ss = demonstrates sickle cell disease

Single-Gene Disorders

- Autosomal dominant disorder
 - Abnormal allele is dominant, normal allele is recessive, and the genes exist on a pair of autosomes
- Huntington's disease (Hh)
 - Dementia, uncontrollable movements
 - Evident after age 40
 - results in death

Expressivity

- variation in phenotype

- Examples:
 - von Recklinghausen's disease (Neurofibromatosis type 1)
 - Autosomal dominant
 - Long arm of chromosome 17
 - Disease varies from spots (caf-au-lait) on the skin to malignant neurofibromas, scoliosis, gliomas, neuromas, etc.

Autosomal Recessive

- Cystic fibrosis
 - Defect on Ch 7
 - Cl⁻ ion transport defect → salt imbalance → thick mucus
 - Affect respiratory and digestive systems
 - Individuals live to ~ age 30

Consanguinity

- Mating of two related individuals → inbred offspring
- Dramatically increases the recurrence risk of recessive disorders

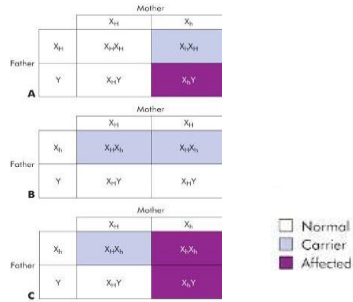
Sex-Linked Disorders

- The Y chromosome contains only a few dozen genes, so most sex-linked traits are located on the X chromosome (X-linked)
- Sex-linked (X-linked) disorders are usually expressed by males because females have another X chromosome to mask the abnormal gene

Sex-Linked Disorders

- Male-pattern baldness
 - Occurs mostly in men (autosomal dominant)
 - Can occur in women (autosomal recessive)
- Color-blindness
 - Affects 8% of males; 0.5% females
 - Unable to distinguish red from green

Sex-Linked Disorders



Concept Check

1. Which of the following statements is TRUE?
- A. Protein synthesis takes place in the cytoplasm.
 - B. DNA is replicated in the cytoplasm.
 - C. RNA is double-stranded.
 - D. RNA contains the same bases as DNA.

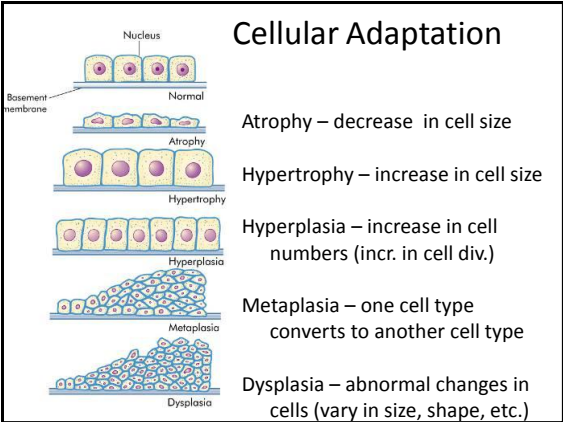
2. Which term best describes an allele with an observable effect?
- A. Homozygous
 - B. Heterozygous
 - C. Dominant
 - D. Recessive

Altered Cellular and Tissue Biology

Chapter 3

Cellular Adaptation

- Physiologic (normal) vs. pathogenic (diseased states)
 - Atrophy
 - Hypertrophy
 - Hyperplasia
 - Metaplasia
 - Dysplasia



Cellular Adaptation

Normal ciliated epithelium

Metaplasia
Chronic injury or irritation

Dysplasia
Persistent severe injury or irritation

Cellular Injury

- Reversible
- Irreversible

Cellular Injury (Hypoxic Injury due to ischemia)

Reversible Cell Injury

Obstruction or cessation of blood flow

Ischemia

Membrane damage

Severe vacuolization of mitochondria

↓ Mitochondrial oxygenation

↓ ATP

↓ Na⁺ pump

↑ Intracellular Na⁺

↑ Extracellular K⁺

↑ Intracellular Ca²⁺

↑ H₂O

↑ Acute cellular swelling

Dilation of endoplasmic reticulum

Detachment of ribosomes

↓ Protein synthesis

Lipid

↑ Glycolysis

↓ Glycogen

↑ Lactate

↓ pH

Nuclear chromatin clumping

↑ Swelling of lysosomes

Irreversible injury (cell death)

Loss of phospholipids

Alterations of cytoskeleton

Activation of inflammation (complement, cytokines, and leukocytes)

↑ Free radicals

Lipid breakdown

Release of enzymes (CPK, LDH) (see Table 3-9)

↑ Ca²⁺ influx

↑ Ca²⁺ in mitochondria

↑ Release of lysosomal enzymes (hydrolases)

Cellular digestion (autodigestion)

Cellular Injury Mechanisms

- Hypoxic injury
 - Ischemia - _____
 - Anoxia - lack of _____ (due to blood clot)
 - Cellular responses
 - Decrease in ATP, causing failure of Na-K pump and sodium-calcium exchange
 - Cellular swelling
 - Vacuolation (formation of vacuoles)
 - If O₂ restored → Reperfusion injury → ↑ free radicals

Cellular Injury

Anoxia

Thrombus

Blood vessel

Swollen cell

Reperfusion

Radicals

O₂⁻, H₂O₂, OH⁻

Reprinted from Damjanov I. Pathology for the health professions, 4th ed. St Louis, 2008. Saunders.

Cellular Injury Mechanisms

- Chemical injury (poisons)
 - Carbon tetrachloride (CCl₄) - forms free radicals by liver
 - Lead -- environmental or occupational sources
 - affects nervous system, hemopoiesis, kidneys
 - Carbon monoxide (CO)-- causes hypoxic injury due to increased affinity for Hb
 - Ethanol (C₂H₅OH)→nutritional deficiencies & liver disorders
 - conversion to acetaldehyde → fat deposits, liver enlargement and necrosis, CNS depressant
 - Mercury (Hg) -- dental amalgams, fish, vaccines
 - controversy over health effects
 - Social or street drugs - THC, C₁₀H₁₅N (meth), cocaine, opiates

Unintentional and Intentional Injuries

- Blunt force injuries
 - Application of mechanical energy to the body resulting in the tearing, shearing, or crushing of tissues
 - Contusion (bruise) vs. hematoma (collection of blood)
 - Abrasion (scrape)
 - Laceration (tear in skin or tissue)
 - Fractures (bones break)

Unintentional and Intentional Injuries

- Sharp injuries
 - Incised wounds
 - Stab wounds
 - Puncture wounds
 - Chopping wounds

Unintentional and Intentional Injuries



Patterned Abrasion



Avulsed Laceration

Unintentional and Intentional Injuries

Stab Wounds



Unintentional and Intentional Injuries

- Asphyxial injuries
 - Caused by failure of cells to receive or use oxygen
 - Suffocation
 - Choking asphyxiation
 - Strangulation
 - Hanging, ligature, and manual strangulation
 - Chemical asphyxiants
 - Cyanide and hydrogen sulfide
 - Drowning
 - Cerebral hypoxia → unconsciousness

Infectious Injury

- Pathogenicity of a microorganism
- Disease-producing potential
 - Invasion and destruction
 - Toxin production
 - Production of hypersensitivity reactions

Immunologic and Inflammatory Injury

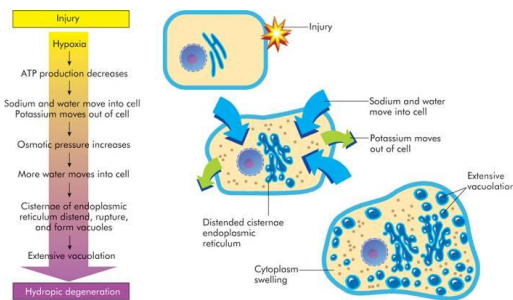
- Phagocytic cells
- Immune and inflammatory substances
 - Histamine, antibodies, lymphokines, complement, and proteases
- Membrane alterations
 - K⁺ leakage from cell

Manifestations of Cellular Injury

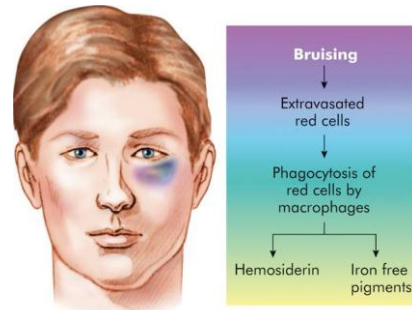
- Cellular accumulations (infiltrations)
 - Water
 - Lipids and carbohydrates
 - Glycogen
 - Proteins
 - Pigments
 - Melanin, hemoproteins, bilirubin
 - Calcium
 - Urate

Oncosis (Hydropic Degeneration)

- swelling (degeneration by water)



Manifestations of Cellular Injury

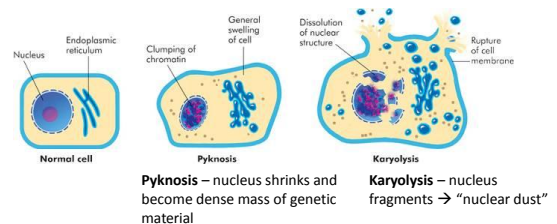


Cellular Death

- Necrosis
 - Cellular changes after local cell death and the process of cellular autodigestion (self-digestion)
- 4 types of Necrosis:
- Coagulative
 - Liquefactive
 - Caseous
 - Fatty
- Gangrenous necrosis is large area of tissue death, not a separate type of cell death.

Cellular Death

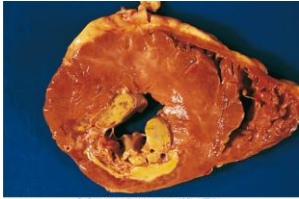
Stages of Necrosis



Necrosis

- Coagulative necrosis – result of hypoxia due to ischemia
 - Kidneys, heart, and adrenal glands
 - Proteins denature → coagulation

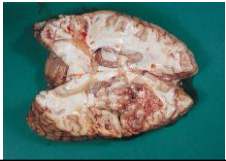
Coagulative Necrosis of Myocardium of LV (heart): note anemic infarct and necrosis of papillary muscle



Necrosis

- Liquefactive necrosis
 - Due to ischemic injury to brain cells (neurons and neuroglia)
 - Hydrolytic enzymes digest cells
 - Caused by bacterial infection
 - Staphylococci, streptococci, and *Escherichia coli*

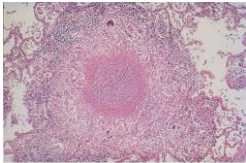
Liquefactive necrosis of brain



Necrosis

- Caseous necrosis
 - Tuberculous pulmonary infection
 - Combination of coagulative and liquefactive necrosis

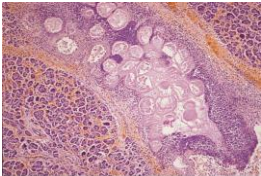
Granuloma with Central Caseous Necrosis: typical of pulmonary TB



Necrosis

- Fat necrosis
 - Breast, pancreas, and other abdominal organs
 - Due to action of lipases

Fat Necrosis of Pancreas - note necrotic adipocytes



Necrosis

- Gangrenous necrosis
 - Death of tissue from severe hypoxic injury
 - Dry vs. wet gangrene
 - Gas gangrene
 - Clostridium

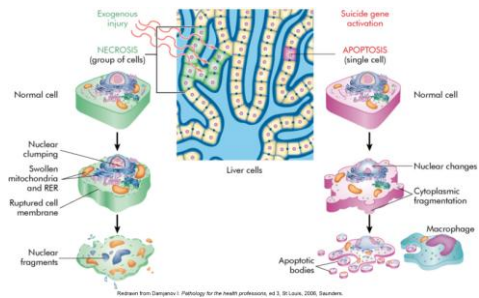
Gangrenous Necrosis



Apoptosis

- Programmed cellular death
- Physiologic (normal tissue turnover)
vs. pathologic (exogenous injury)

Necrosis vs. Apoptosis



Concept Check

- Which of the following is the most common cause of cellular injury?
 - Free radical-induced injury
 - Chemical injury
 - Hypoxia
 - Dysplasia
- Which cell adaptation is observed in the cervix?
 - Hyperplasia
 - Hypertrophy
 - Dysplasia
 - Metaplasia

- Which of the following terms best describes death of a cell from hypoxia, generally as a result of ischemia in the lower extremities?
 - Coagulative necrosis
 - Liquefactive necrosis
 - Fat necrosis
 - Gangrenous necrosis
- Cellular swelling is:
 - Irreversible
 - Occurs early in all cell injuries
 - Low intracellular Na is common
 - None of the above

Match the manifestation with the characteristic:

- | | |
|---|-----------------|
| ___ 5. Necrosis due to Clostridia | a. Rigor mortis |
| ___ 6. Rigidity of muscles after death | b. Gas gangrene |
| ___ 7. Increased cell number | c. Hyperplasia |
| ___ 8. Necrosis from lysosomal release | d. Metaplasia |
| ___ 9. Replacement of one cell with another | e. Liquefaction |
| ___ 10. Normal & pathologic cell self-destruction | f. Apoptosis |

Fluids and Electrolytes, Acids and Bases

Chapter 4

Distribution of Body Fluids

- Total body water (TBW) ~60% of body wt.
 - Intracellular fluid (ICF) ~2/3 of TBW
 - Fluid within cells
 - Extracellular fluid (ECF) ~1/3 of TBW
 - Interstitial fluid - intercellular and not in vessels
 - Intravascular fluid - plasma
 - Other ECF: Lymph, synovial, intestinal, CSF, sweat, urine, pleural, peritoneal, pericardial, and intraocular fluids

Net Filtration

- Forces favoring filtration
 - Capillary hydrostatic pressure (blood pressure)
 - Interstitial colloid osmotic pressure (water-pulling)
- Forces favoring reabsorption
 - Plasma oncotic pressure (water-pulling)
 - Blood colloid osmotic pressure
 - Interstitial hydrostatic pressure

Edema

- Accumulation of _____ within the interstitial spaces
- Causes:
 - Increase in capillary hydrostatic pressure due to venous obstruction or salt & water retention (thrombophlebitis, CHF)
 - Decrease in plasma colloid osmotic pressure due to decreased plasma proteins (kidney disease, hemorrhage, cirrhosis of liver)
 - Increases in capillary permeability due to trauma
 - Lymph obstruction due to removal of lymph nodes

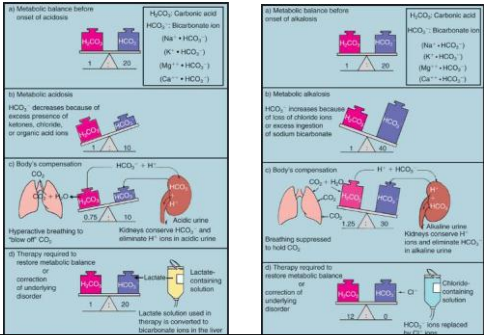
Acidosis and Alkalosis

- Four categories of acid-base imbalances
 - Respiratory acidosis—elevation of pCO₂ as a result of ventilation depression
 - Respiratory alkalosis—depression of pCO₂ as a result of alveolar hyperventilation

Acidosis and Alkalosis

- Metabolic acidosis—depression of HCO₃⁻ or an increase in noncarbonic acids
- Metabolic alkalosis—elevation of HCO₃⁻ usually caused by an excessive loss of metabolic acids

Metabolic Acidosis and Alkalosis



Respiratory
Acidosis Alkalosis

a) Metabolic balance before onset of acidosis

H_2CO_3 : Carbonic acid
 HCO_3^- : Bicarbonate ion
 $(\text{Na}^+ + \text{HCO}_3^-)$
 $(\text{K}^+ + \text{HCO}_3^-)$
 $(\text{Mg}^{++} + \text{HCO}_3^-)$
 $(\text{Ca}^{++} + \text{HCO}_3^-)$

1 20

b) Respiratory acidosis

Respirating is suppressed, holding CO_2 in body

25 0

c) Body's compensation

Acidic urine
Kidneys conserve HCO_3^- ions and eliminate H^+ ions in acidic urine

25 0

d) Therapy required to restore metabolic balance or correction of underlying disorder

Lactate solution used in therapy is converted to HCO_3^-

25 0

a) Metabolic balance before onset of alkalosis

H_2CO_3 : Carbonic acid
 HCO_3^- : Bicarbonate ion
 $(\text{Na}^+ + \text{HCO}_3^-)$
 $(\text{K}^+ + \text{HCO}_3^-)$
 $(\text{Mg}^{++} + \text{HCO}_3^-)$
 $(\text{Ca}^{++} + \text{HCO}_3^-)$

1 20

b) Respiratory alkalosis

Hyperventilative breathing blows off CO_2

0.5 20

c) Body's compensation

Alkaline urine
Kidneys conserve H^+ ions and eliminate HCO_3^-

0.5 15

d) Therapy required to restore metabolic balance or correction of underlying disorder

Chloride-containing solution
 HCO_3^- ions are replaced by Cl^- ions

0.5 10

Concept Check

1. Which of the statements is TRUE regarding water balance?

A. Isotonic fluids cause increased cellular swelling.

B. Hypertonic fluid causes increased cellular swelling.

C. Hypotonic fluid causes cellular swelling.

D. Hypernatremia causes cellular swelling.

2. Of the 60% of TBW made up of water, about 2/3 is _____.
– A. ECF
– B. ICF
– C. Intravascular fluid
– D. interstitial water

3. Total water loss per day by an adult is about:
– A. 0.8 L
– B. 1.2 L
– C. 2.2 L
– D. 2.8 L

4. Aldosterone controls ECF volume by:
A. CHO, fat, and protein catabolism
B. Na reabsorption
C. K reabsorption
D. H_2O reabsorption
E. B and D are correct

5. The release of ADH is NOT stimulated by:
A. Stress
B. Hyponatremia
C. Hypernatremia
D. Increase in plasma osmolality

6. The pH of saliva is about 7 and the pH of gastric juice is about 2. How many times more concentrated is the $[\text{H}^+]$ in gastric juice than in saliva?
A. 5
B. 50
C. 10,000
D. 100,000

Match the acid base with the probable cause:
____7. Respiratory acidosis a. Excessive baking soda
____8. Respiratory alkalosis b. Severe anxiety (hyperventilation)
____9. Metabolic alkalosis c. Emphysema

Match the imbalance with the appropriate compensatory mechanism:

10. Respiratory acidosis a. Kidneys excrete H^+ , retain HCO_3

11. Respiratory alkalosis b. Kidneys excrete HCO_3 , retain H^+

12. Metabolic acidosis c. Hyperventilation (blow off CO_2)