Chapter 1 - The Human Body: An Orientation

Levels of Structural Organization

1. Chemical
2. Cellular
3. Tissue
4. Organ
5. Organ System
6. Organismal

- Difference between one cell and another is the genome
    - Cells have the same exact genetic material

Homeostasis: maintenance of relatively stable internal conditions > dynamic state of equilibrium

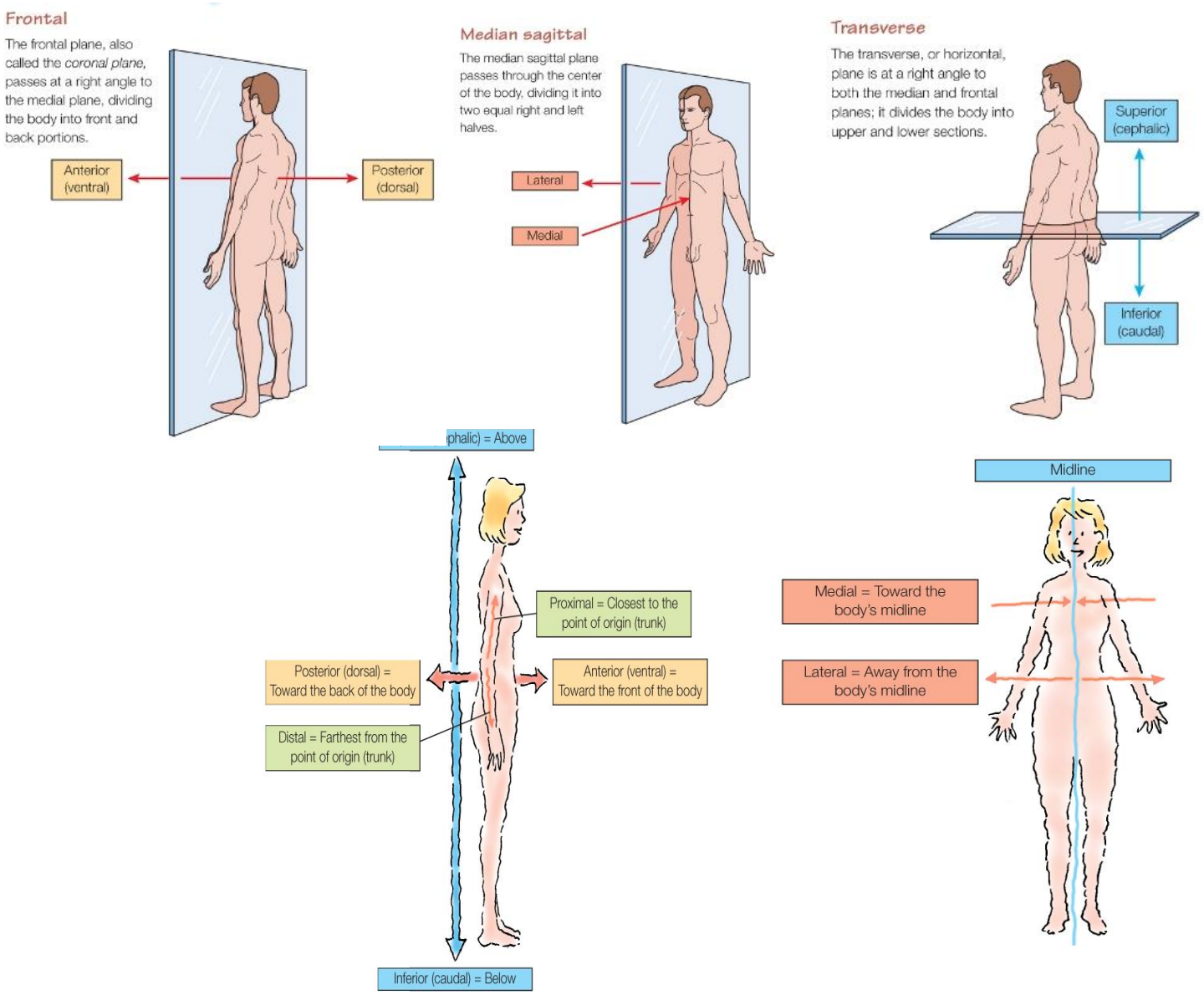
Elements of Homeostatic Control

1. Stimulus: change in variable
2. Receptor: detects change
3. Input: info sent along pathway to control centre
4. Output: info sent along efferent pathway to effector
5. Response: feeds back to reduce effect of stimulus and returns variable to homeostatic level

Negative Feedback: shuts off / reduces original effect of the stimulus > variable changes in opposite direction

Positive Feedback: enhances the effect of the stimulus > variable is exaggerated

Directional Terms

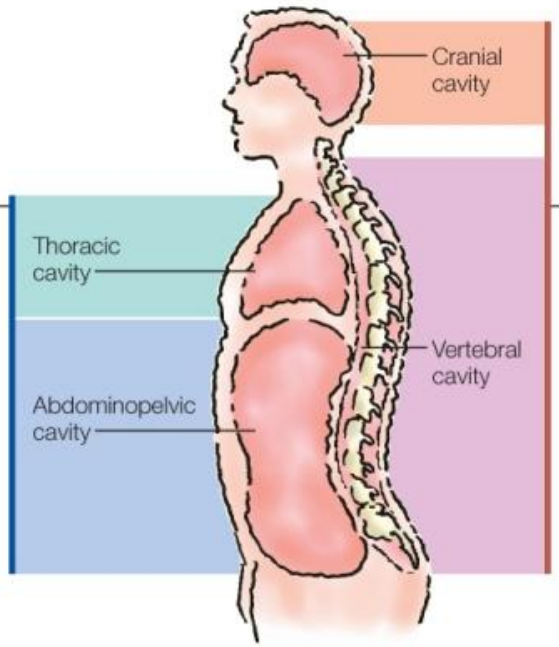


Ventral cavity

Subdivided into the thoracic cavity and the abdominopelvic cavity

Thoracic cavity

- Surrounded by the ribs and chest muscles
- Subdivided into the pleural cavities and the mediastinum
  - Two pleural cavities each contain a lung
  - Mediastinum contains the heart, large vessels of the heart, trachea, esophagus, thymus, lymph nodes, and other blood vessels and nerves



Dorsal cavity

Subdivided into the cranial cavity and the vertebral cavity

Cranial cavity

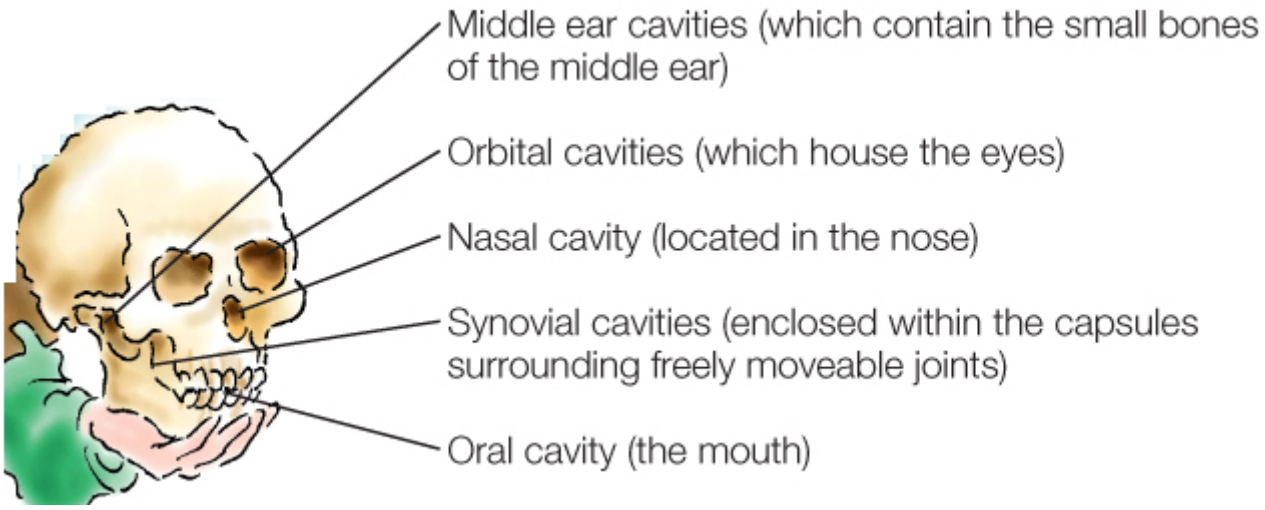
- Also called the *calvaria*
- Encases the brain

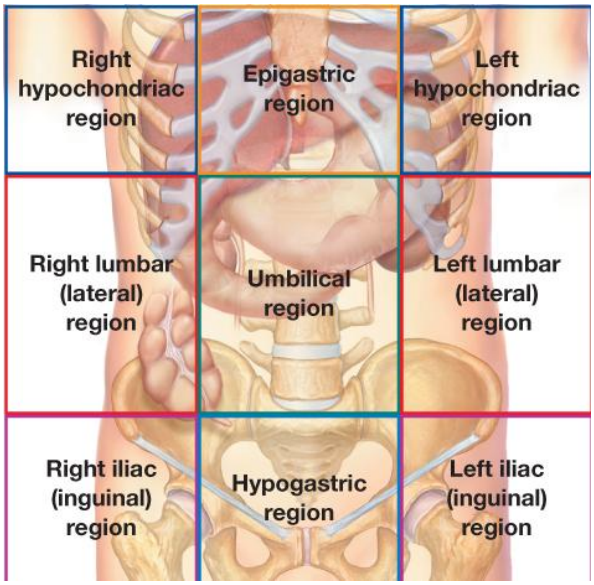
Vertebral canal

- Also called the *spinal cavity* or *vertebral canal*
- Formed by the vertebrae
- Encloses the spinal cord

Abdominopelvic cavity

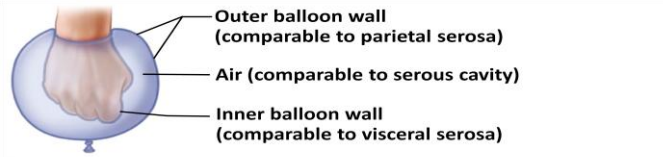
- Subdivided into the abdominal cavity and the pelvic cavity
  - Abdominal cavity contains the stomach, intestines, spleen, liver, and other organs
  - Pelvic cavity, inferior to the abdominal cavity, contains the bladder, some of the reproductive organs, and the rectum



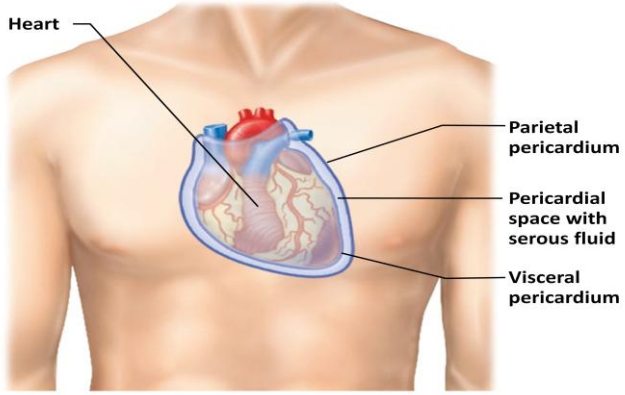


Right and left hypochondriac: diaphragm, portions of kidneys, right side of the liver, spleen and part of pancreas
Epigastric: most of pancreas, portions of stomach, liver, inferior vena cava, abdominal aorta, duodenum
Right and Left Lumbar (Lateral): portions of small and large intestines and portions of the kidney
Umbilical: sections of the small and large intestines, inferior vena cava and abdominal aorta
Right and Left Iliac (inguinal): portions of small and large intestines
Hypogastric (pubic): portion of sigmoid colon, urinary bladder and ureters, and portions of the small intestine

Serous Membrane
1. Visceral Pericardium
2. Pericardial Space w/ serous fluid
3. Parietial Pericardium



(a) A fist thrust into a flaccid balloon demonstrates the relationship between the parietal and visceral serous membrane layers.



(b) The serosae associated with the heart.

Chapter 2 - Chemistry Comes Alive

Matter: anything that has a mass or occupies space

Forms of Energy
1. Chemical
2. Electrical
3. Mechanical
4. Radiant/Electromagnetic

Atoms: building blocks for elements –smallest particle
- Protons and neutrons have the same weight
- Electrons have negligible weight
- Atomic number = Proton number
- Atomic mass = proton + neutron

Isotopes: elements with similar # of protons but different # of neutrons

Molecules: 2+ atoms bonded together

Compound: 2+ molecules bonded together

Chemical Bonds: energy relationships b/w electrons of reacting atoms

Valence Shell: have most potential energy

Anion: gains electron = negatively charged

Cation: loses electron = positively charged

Covalent: sharing of 2+ valence electrons

Ionic: not sharing

Hydrogen Bonds: attractive force between electropositive H and electronegative H

Anabolic: synthesis

Catabolic: breaks down > adds water in the bond

Organic Compounds
1. Carbs: main source of energy
2. Lipids: source of energy
3. Proteins: building blocks
4. Nucleic Acids: genetic material found in cell

5 Classes of Lipids
1. Fatty Acids
2. Eicosanoids: derived from fatty acids found in all cell membranes
3. Glycerides
4. Steroids: have 4 ring structure: basis of steroid hormones
5. Phospholipids: main form of fats found in membrane...head is polar

Proteins
- Assembled by dehydration synthesis where water molecule is removed from COOH group of first amino acid and NH_3 group of 2^{nd} amino acid
- Encoded in DNA as genes

Hydrolysis: peptide bonds linking amino acids together are broken when water is added

Dehydration Synthesis: acid group of one amino acid is bonded to the amine group of next > loss of water

Levels of Protein Structure
1. Primary: sequence of amino acids that forms polypeptide chains
2. Secondary: primary chain forms spirals
3. Tertiary: superimposed on secondary structure

4. Quaternary: 2+ polypeptide chains

Rates of Chemical Rxns

- Increase temp, increase rate
- Increase concentration of reactant, increase rate
- Decrease particle size, increase rate
- Catalysts increase rate without being part of product/being chemically changed

Mechanisms of Enzyme Action

1. Substrate binds at active site –temporarily forming an enzyme-substrate complex
2. E-S complex undergoes internal rearrangements that form the product
3. Enzyme releases product of the reaction

Nucleic Acids

- Contains deoxyribose sugar, phosphate backbone
- RNA is messenger material in cell
- RNA is single stranded

Chapter 3 – Cells: The Living Unit

Prokaryotic: include bacteria > do not have a membrane enclosed nucleus –has DNA genome

Eukaryotic: have membrane enclosed nucleus and a DNA genome

- Every cell in body (except RBC, sperm and eggs) has he same genome which consists of two copies of 23 chromosomes

Basic Parts of Cell

1. Plasma Membrane: flexible outer boundary
2. Cytoplasm: intracellular fluid containing organelles
3. Nucleus: control centre containing the DNA genome

Phospholipids: main component of membrane

Plasma Membrane: fluid mosaic model

- Phosphate heads: polar and hydrophilic
- Phosphate tails: non-polar and hydrophobic
- Sugars provide signalling from one cell to another
- Cholesterol affects melting temperature of membrane

Membral Proteins

1. Integral: firmly inserted into membrane + have hydrophobic/phillic regions + functions as transport proteins
2. Peripheral: loosely attached to integral + has filaments on intracellular surface for membrane support + functions as enzymes; motor proteins for shape change during cell division + muscle contraction + cell-to-cell connections

6 Functions of Membrane Proteins

1. Transport
    - Facilitated Diffusion: substance goes down on concentration gradient
    - Active Transport: substance goes against concentration gradient > requires ATP
2. Receptors for Signal Transduction
    - Membrane protein exposed to the outside of cell may have binding site that fits shape of specific chemical messenger
    - When bound, chemical messenger may cause a change in shape in protein that initiates chain of chemical rxns in cell
3. Attachment to the Cytoskeleton and Extracellular Matrix
    - Cytoskeleton is cell's internal support
    - Extracellular Matrix: substances ma anchor to membrane proteins which helps cell maintain shape and fix location of certain membrane proteins
4. Enzymatic Activity

- Membrane protein may be an enzyme with active site exposed to substances in the adjacent solution
- Team of several enzymes in a membrane may catalyze sequential step of metabolic pathway

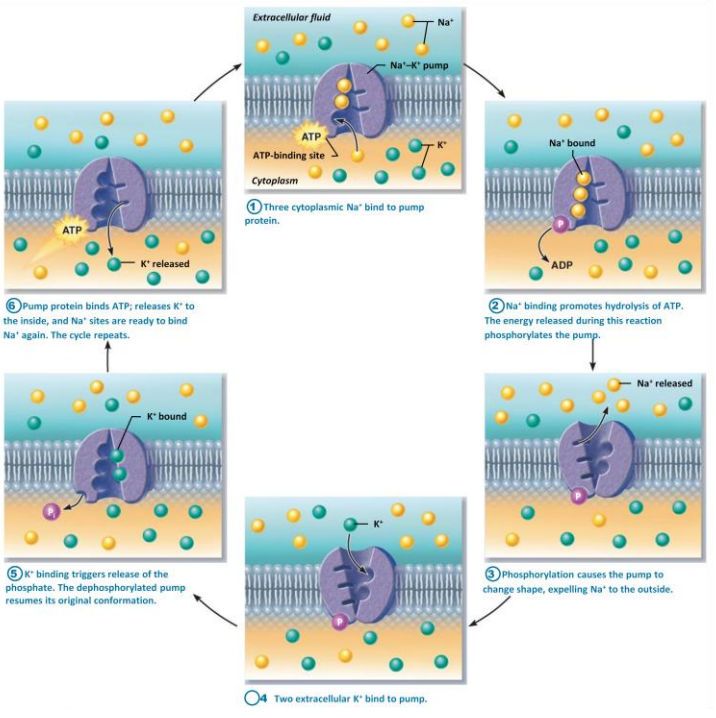
5. Intercellular Joining
    - Membrane of proteins of adjacent cells may be hooked together in various kinds of intercellular junctions
    - Some membrane proteins provide temporary binding sites that guide cell migration and other cell-to-cell interactions
6. Cell-to-Cell Recognition
    - Some glycoproteins serve as identification tags that are specifically recognized by other cells

Glycocalyx: "sugar covering" at cell surface + allows immune system to recognize "self" and "non-self" + special biological markers for cell to cell recognition
Cell Junction: some cells are free > some cells are bound into communities
Tight Junction: impermeable, prevents molecules from passing through intercellular space
Desmosomes: anchor cells together, forms internal tension reducing network of fibres
Gap Junction: communication allows ions and small molecules to pass intercellular space

<u>Types of Membrane Transport</u>

1. Passive
    - No ATP needed
    - Substances move down concentration gradient
        - Diffusion: carrier and channel mediated facilitated diffusion + osmosis
        - Filtration: usually across capillary walls
2. Active Processes
    - ATP required
    - Occurs only in living cell membranes

Simple Diffusion: fat soluble molecules directly pass through phospholipid bilayer
Carrier-Mediated Facilitated Diffusion: via protein carrier > specific for one chemical + binding of substrate causes transport protein to change shape
Osmosis: diffusion of solvents such as water through a specific channel protein (aquaporin) or through lipid bilayer + concept is important when patients are treated with isotonic solutions when transfusions or drips are used > could suffer severe damage (Normal Saline) > solution of 0.90% of NaCl
Freely Permeable Membrane: both solute and water
Selectively Permeable Membrane: impermeable to solute, water can pass



<u>Active Transport</u>

- Important in nerve/kidney function because substances are carried against concentration gradient
- Uses ATP

Primary Active Transport: ATP driven + K^+ pump stores energy by creating a steep concentration gradient for Na^+ entry into cell
Secondary Active Transport: As Na^+ diffuses back across membrane through a membrane cotransporter protein, it drives glucose against concentration gradient into the cell

<u>Vescular Transport Functions</u>

1. Exocytosis: transport out of cell
2. Endocytosis: transport in cell
3. Transcytosis: transport into cell
4. Vescular Trafficking: Transport from one area/organelle in cell to another

Cytoplasm: located between plasma membrane and nucleus

Composition of Cytoplasm

1. Cytosol: water with solutes
2. Organelles: metabolic machinery of cell; each with specialised function + either membranous or nonmembranous
3. Inclusions: vary with cell type

Cytoplasmic Organelles

Membranes allows crucial compartmentalization

Membranous

1. Mitochondria
    - Aeriobic respiration
    - Provides most cells ATP
    - Contains DNA, RNA and ribosomes
    - Can do cell division via fission
2. Peroxisomes
    - Membranous sacs containing oxidases and catalases
        - Oxidases: use oxygen to convert free radicals (high reactive chemicals with unpaired electrons) to hydrogen peroxide + detoxifies alcohol and formaldehyde
        - Catalases: converts hydrogen peroxide into water and oxygen
    - Detoxifies harmful chemicals/substances
3. Lysosomes
4. Endoplasmic Reticulum
    - Interconnected tissues and parallel membranes enclosing cisterns and continuous with outer nuclear membrane
    - Rough ER: have many ribosomes close to the surface > site of protein modification made on surface and proteins are then shipped to Golgi apparatus for further modification
    - Smooth ER: metabolize lipids and make steroid hormones + detoxifies drugs and breaks down stored glycogen to give glucose
5. Golgi Apparatus
    - 3 types of vesicles from concave transface
        - Secretory (granules): to transface; release proteins by exocytosis
        - Vesicles of Lipids and transmembrane proteins for plasma membrane / organelles
        - Lysosomes: containing digestive enzymes, remains in cell

Nonmembranous

1. Cytoskeleton
    - Elaborate series of rods throughout cytosol + protein links rods to other cells
    - Microfilaments: made of actin, included in terminal web attached to plasma membrane + involved in cell motility, exocytosis, endocytosis and cytokenesis
    - Intermediate Filaments: made of keratin filaments and joins to desmosomes
    - Microtubules: made of tubulin, radiates from centrosome and act as railroad tracks inside the cell
2. Centriole
    - "cell center" near nucleus + generate microtubules
    - Forms basis of cilia and flagella
        - Whip-like, motile extensions on surfaces of certain cells
        - Contains microtubules/motor molecules
        - Cilia moves substances across cell surfaces
        - Longer flagella propel whole cells (tail of sperm)
    - Made of pinwheel array of 9 triplets of microtubules
3. Ribosomes

- Granules containing protein and rRNA
- Free ribosomes: synthesize soluble proteins that function in cytosol or other organelles
- Membrane-bound ribosomes: forming rough ER > synthesize proteins to be incorporated into membranes, lysosomes, exported from other cells

Nucleus

- Largest organelle
- Contains DNA
- Responds to signals; dictates kinds and amount of proteins synthesized
- Uninucleate:
- Multinucleate:
- Anucleate:

Nuclear Envelope: double membrane barrier' encloses nucleoplasm
Nuclear Pore Complex: regulates transport of large molecules in and out of cell
Nucleoli: involved in rRNA synthesis and ribosome subunit assembly + associated with nuclear organizer regions+ contains DNA coding for rRNA
Nucleosomes: threadlike strands of DNA
Chromosomes: barlike bodies of histone DNA molecules when cells divide

The Cell Cycle

1. Growth (G1)
2. Growth and DNA synthesis (S)
3. Growth and final preparations for division (G2)
4. Mitotic Phase
    - Prophase
    - Metaphase
    - Anaphase
    - Telophase
    - Cytokinesis: division of cytoplasm cleave furrow

To replicate DNA and enter mitosis:

- Cyclins: regulatory proteins
- Cyclin-Dependent-Kinases: bind to cyclins
- Cyclin destroyed after mitotic division

DNA Replication

1. DNA helicase separate replication bubbles with replication forks at each end
2. DNA polymerase begins adding nucleotides at RNA primer
    - Synthesis one leading/lagging strand
        - Leading: synthesized continuously
        - Lagging: synthesized discontinuously in segments
3. DNA ligase splices short segments of discontinuous strand together

Result: 2 identical DNA molecules from original
Semi-conservative Replication: each DNA is made up of one new strand and one old strand

Cell Division

1. Meiosis: cell division producing gametes
2. Mitotic: produces clones + essential for body and tissue repair + occurs continuously in some cells (skin, intestinal lining) + not found in nervous tissue, skeletal/cardiac muscle > repairs with fibrous tissue

Protein Synthesis

- DNA is a master blueprint
- Gene: segment of DNA with blueprint for one polypeptide
- Bases: A G T C
- Each triplet specifies coding for #, kind, and order of amino acids in polypeptide

Transcription

- Transfers DNA base sequence to complementary base sequence of mRNA
- Factors: gene activators
    - Loosens histones from DNA area to be transcribed
    - Bind to promoter > DNA sequence specifying start site of gene on template strand
    - Mediates binding of RNA polymerase (enzyme synthesizing mRNA) to promoter

1. Initiation: RNA polymerase separates DNA strands
2. Elongation: RNA polymerase adds complementary nucleotides
3. Termination: signalled to stop

Translation

- Converts base sequence of nucleic acid into amino acid sequence of proteins
- Involves mRNA, tRNA, rRNA
- Uses a triplet code following codons on mRNA with no spaces and proceeds continuously from start to finish of open reading frame
- Starts at ATG > inserts methionine

1. Initiation
2. Elongation
    a. Codon recognition: tRNA binds complementary codon in A site
    b. Peptide Bond Formation: amino acid of tRNA in P site bond to amino acid of tRNA to A site
    c. Translocation: tRNAs move one position A > P, P > E
3. Termination
    a. Stop codon enters A site to signal end
    b. Protein release factor binds to stop codon > water is added to chain + release of polypeptide chain + separation of ribosome subunits + degradation of mRNA + protein processed into functional 3D structure

Role of tRNA

- 45 different types
- Binds specific amino acid to one end
- Anticodon at other end (head) binds mRNA codon at ribosome by Hydrogen bonds
- Ribosomes coordinates coupling of mRNA and tRNA > Aminoacyl Peptidyl, Exit sites

Role of Endoplasmic Reticulum in Protein Synthesis

- mRNA-ribosome complex directed to rough ER by signal-recognition particle
- Forming protein enters ER
- Sugar groups may be added to protein, shape may be altered
- Protein enclosed in vesicle for transport to golgi apparatus

Chapter 4 – Tissue: The Living Fabric

Types of Primary Tissues

1. Epithelial: covers inside and outside the body
2. Connective: supports
3. Muscle: produces movement
4. Nerve: controls everything: muscle, release of hormones

Functions of Epithelial Tissue

- Lines body surface and cavities
- Forms the glands of body
- Protection: from outside environment, prevents organ damage
- Absorption: kidneys, digestive system, intestines
- Filtration: kidneys
- Excretion: kidneys
- Secretion: secretion of hormones, juice, enzymes
- Sensory Reception: sensitivity of skin

Characteristics of Epithelial Tissue

- Exhibit polarity: distinct surfaces giving apical and basal surfaces
- Specialized contacts: tight junctions and demosomes
- Supported by connective tissue: all rest on a basement membrane or basal lamina of extracellular material
- Avascular but not innervated
- Can regenerate due to stem cells

Classification of Epithelia

Simple: one cell layer thick –places where there needs to be exchange (ex: alveoli of lung, kidney, and capillaries)

- Simple Squamous Epithelium: flattened cells with disc shaped central nuclei and sparse cytoplasm + allows materials to pass by diffusion and filtration in sites + secretes lubricating substances in serosae + found in air sacs of lungs, blood vessels
- Simple Cuboidal Epithelium: single layer of cubelike cells with large, spherical central nuclei + found in kidney tubules for secretion and absorption
- Simple Columnar Epithelium: single layer of tall cells with round to oval nuclei + some cells bear cilia + layer may contain mucus-secreting unicellular glands + found in most of the digestive tract + used for aborption, secretion of mucus, enzymes and other substances

Stratified: more than one cell layer thick: exchange isn't important, epidermis must be stronger (ex: skin)

- Pseudostratified Columnar Epithelium: single layer of cells of different heights, some not reaching the free surface + nuclei seen at different levels + may contain mucus-secreting cells and bear cilia + found in upper respiratory tract + used to secrete substances
- Stratified Squamus Epithelium: thick membrane composed of seceral cell layers + basal cells are cuboidal or columnar and metabolically active + protects underlying tissues in areas subjected to abrasion + located in the esophagus, vagina, mouth
- -Transitional Epithelium: resembles both stratified squamus and stratified cuboidal + surface cells dome shaped or squamous like, depending on degree of organ stretch + stretches readily, permits stored urine to distend urinary organ + located in the ureters, bladder and part of urethra

Glandular Epithelia

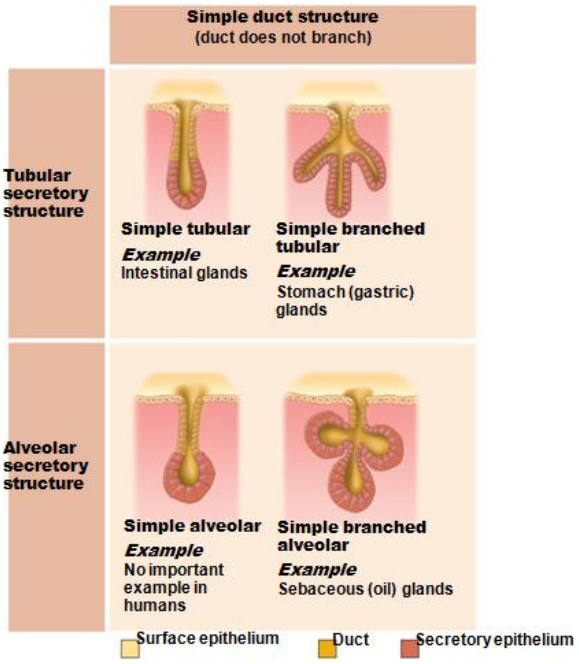
Gland: one or more cells that makes and secretes an aqueous fluid called a secretion

Endocrine: if substance is released directly into the bloodstream

Exocrine: if substance is released onto the surface or into an internal organ through a duct

Endocrine

- Ductless: secretions not released into a duct
- Secrete (by exocytosis) hormones that travel through lymph or blood to their specific target regions
- Target organs respond in some way but only if target cells express appropriate receptor
- Hormones will not work unless there is a receptor of that cell that is combined to that hormones and allows cells to respond



Exocrine Glands

- Secretions released onto body surfaces or into body cavities
- More numerous than endocrine
- Secrete
- Mucus, sweat, oil, digestive and salivary glands

Classification of Multicellular Glands

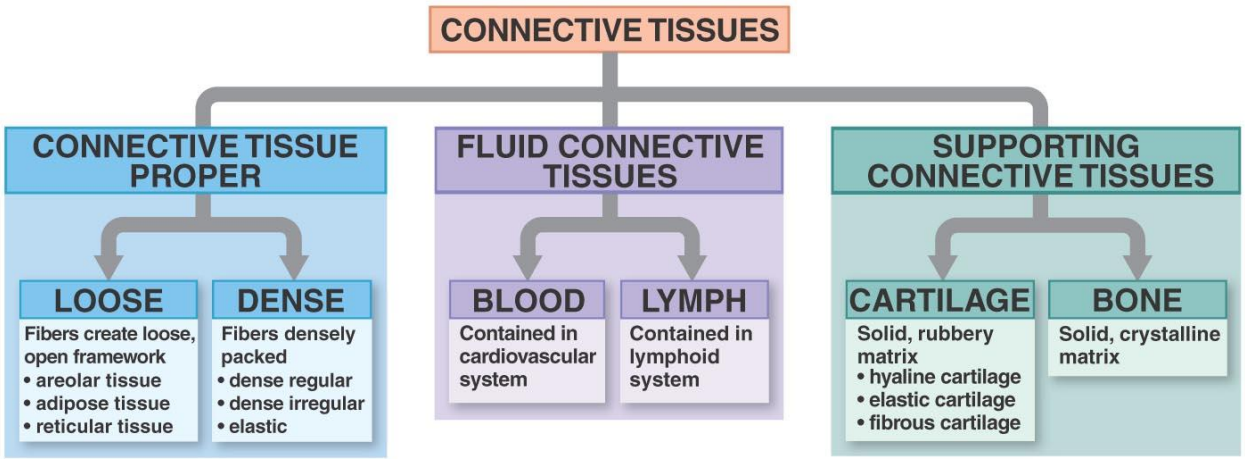
- Structure
  - Simple glands (unbranched duct) or compound glands (branched duct)
  - Cells, tubuluar, alveolar, or tubuloalveolal
- Types of secretion

- Merocrine: most secrete producs by excocytosis (pancreas and salivary glands)
- Holocrine: accumulate products within then rupture (sebaceous glands)
- Apocrine: accumulates products within but only apex ruptures (apocrine sweat glands)

Characteristics of Connective Tissue

- Derived from mesenchyme
- Degrees of vascularity
- Extracellular matrix

Dense: found in tendons and ligaments
Lymph: contained in lymphoid system



Fibroblast: able to make fibers
Lymphocyte: mainly found in the lymph system
Mast Cell: part of the inflammatory response; histamine

Ground Substance of Connective Tissue

- Interstitial fluid
- Cell adhesion proteins such as laminin and fibronectin
- Proteoglycans such as glycosaminoglycans, chondroitin, sulphate and hyaluronic acid

Structural Elements of Connectiev Tissue

1. Collagen Fibers: composed of collagen which is made up of tought, cross-linked, fibril protein. Collagen fivers have high tensile strength
2. Elastic Fibers: long thin fibers that form branching networks composed of elastin that is stretchy
3. Reticular Fibers: short fine collagenous fibers that are continuous with the collagenous fibers and that branch extensively

Cells of Connective Tissue

- Immature forum; mitotically active; secrete ground substance and fibers
- Fibroblasts in connective tissue
- Chondroblasts in cartilage
- Osteoblasts in bone
- Hematopoietic stem cells in bone marrow
- "Cyte" cells
- Mature form; maintain matrix

Types of Connective Tissues

- All connective tissues except bone, cartilage and blood
- Loose connective tissues
    - Areolar: gel like matrix with fibroblasts, macrophages, mast cells and some white blood cells + wraps and cushions organs, plays important role in inflammation + widely distributed under epithelia of body, surrounds capillaries and packages organs

    - Adipose: matrix as in, very sparse + closely packed adipocytes/fat cells, have nucleus pushed to the side by large fat droplet + provides reserve food fuel, insulates against heat loss, supports and protects organ + found under skin in subcutaneous tissue, around kidneys and eyeballs, within abdomen and in breasts
    - Reticular: network of reticular fibers in typical loose ground substance; lie on the network + form a soft internal skeleton (stroma) that supports other cell types including white blood cells, mast cells and macrophages + found in lymphoid organs (lymph nodes, bone marrow, and spleen)
- Dense connective tissues (aka fibrous connective tissues)
    - Dense regular: closely packed bundkes of collagen fibers parallel to direction of pull; few elastic fibers; major cell type is fibroblast + attaches muscle to bones or to muscles, bones to bones + withstands tensile stress when pulling force is applied in one direction + found in tendons, most ligaments and aponeuroses > poorly ascularized
    - Dense irregular: bundles of collagen thicker and irregularly arranged; major cell type is fibroblast + withstands tension exerted in many directions, provides structural strength + found in gibrous capsules of organs and joints, dermis of skin, submucosa of digestive tract
    - Elastic: dense regular connective tissue containing high proportion of elastic fibers + allows tissues to recoil after stretching, aids passive recoil of lungs following inspiration + found in walls of large arteries, bronchial tubes

<u>Cartilage</u>

- Chondroblasts make new cartilage
- Chondrocytes maintains cartilage and resides in lacunae
- Tough but flexible
- Lack nerve fibers
- Up to 80% water, can rebound after compression
- Avascular: receives nutrients from membrane surrounding it
    - Hyaline Cartilage: amorphous but firm matrix, collagen fibers form an imperceptible network, chondroblasts produce matrix and when mature they lie in lacunae + supports and reinforces, serves as resilient cushions, resists compressive stress + found in most embryonic skeleton, covers end of long bones in joint cavities, forms costal cartilage of ribs, nose, trachea, larynx
    - Elastic: similar to hyaline cartilage, but more elastic fibers in matrix + maintains shape of a structure while allowing great flexibility + found in external ear (pinna) and epiglottis
    - Fibrocartilage: matrix similar to hyaline but less firm, thick collagen fibers predominate + tensile strength allows to absorb comprehensive shock + found in intervertebral discs

<u>Bones</u>

- Aka osseous tissue
- Supports and protects body structures
- Stores fat and synthesizes blood cells in cavities
- More collagen than cartilage
- Has inorganic calcium salts
- Osteoblasts produce matrix
- Osteocytes maintain matrix
- Osteoclasts break down boneand release calcium
- Osteons are structural units
- Richly vascularised

<u>Blood</u>

- Most atypical connective tissue
- Fluid that functions in transport of oxygen, carbon dioxide, nutrients, hormones, etc
- RBC/Erythrocytes: carry oxygen

- WBC/leukocytes: part of immune system
- Platelets: part of clotting system
- Fibers: soluble proteins that precipitate during blood clotting

Muscle Tissue

- Highly vascularised
- Responsible for most types of movements
- Skeletal Muscle Tissue
    - Found in skeletal muscle
    - Striated (striped)
    - Long, multinucleated cells with peripheral nuclei
    - Voluntary
- Cardiac Muscle Tissue
    - Found in walls of heart
    - Striated
    - Often single cells, branched, central nucleus, connected by intercalated discs
    - Involuntary
- Smooth Muscle Tissue
    - Mainly in walls of hollow organs other than heart
    - Not striated
    - Involuntary
- Stripes in skeletal muscle are caused by common proteins such as myecin, actin

Nervous Tissue

- Neurons
    - Electrically excitable
    - Have voltage gated channels
    - Transmits information
- Neuroglia
    - Supports neural tissue
    - Help supply nutrients to neurons
    - More abundant that neurons

Dendrites: chemically gated channels that bind to neurotransmitters and bring info to cell body
Axon: bring info away from cell body, contains voltage gated ion channels
Myelin Sheath: insulating wires

Tissue Repair

- Necessary when barriers are penetrated
- Cells must divide and migrate
- Regeneration
    - Same kind of tissue replaces old destroyed tissue
    - Original function stored
- Fibrosis
    - Connective tissue replaces destroyed tissue
    - Original function lost

1. Inflammation sets the stage
    - Severed blood vessels bleed
    - Inflammatory chemicals released
    - Local blood vessels become more permeable, allowing WBC, fluid, clotting proteins, and other plasma proteins to seep into injured area
    - Clotting occurs
2. Organization restores the blood supply
    - Clot is replaced with granulation tissue, which restoresvascular supply

- Fibroblasts produce collagen fibers that bridge the gap
- Macrophages phagocytise dead and dying cells and other debris
- Surface epithelial cells multiply and migrate over the granulation tissue

3. Regeneration and fibrosis effect permanent repair
    - Fibrosed area matures and contracts, epithelium thickens
    - Fully regenerated epithelium with an underlying area of scar tissue results

Developmental Aspects

- Primary germ layers
    - Superficial to Deep: ectoderm, mesoderm, endoderm
- Formed early in embryonic development
- Specialize to form the four primary tissues
    - Nerve tissue arises from ectoderm
    - Muscle and connective tissues arise from mesoderm
    - Epithelial tissue arise from all three germ layers

Aging Tissues

- Normally function through youth and middle age if adequate diet, circulation, and infrequent wounds and infections
- Epithelia thin with increase of age, more easily breached
- Tissue repair is less efficient
- Bone, muscle, and nervous tissues begin to atrophy
- DNA mutations possible > increased cancer risk

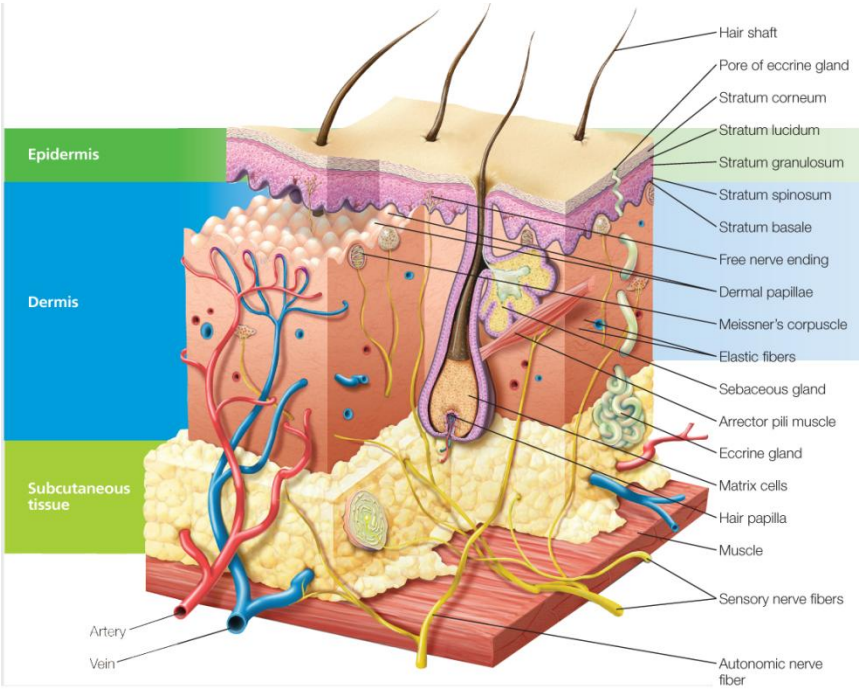
Cancer

- Malignant neoplasms that can undergo metastasis
- Oncogenes: implicated in causing cancer + usually mutated forms of regular genes called proto-oncogenes involved in cell division, signalling and migration
- Oncogenes: ras, rac
- Caused by mutation of tumour suppression genes
- Clonal origin which means if cancer has metastasized, it has the same type of cell that came from some original site

Chapter 5 – The Integumentary System

Skin

Epidermis: superficial region (epithelial tissue)
Dermis: underlies epidermis (mostly fibrous connective tissue)
Hypodermis (superficial fascia): subcutaneous layer deep to skin + not part of skin but shares some functions + mostly adipose tissue that absorbs shock and insulates + anchors skin to underlying structures –mostly muscle



Skin Structure

- Upper layer of skin is epidermis
- Basal cells are dividing cells
- Dermis has a thin papillary layer which has capillaries, which provides sensation
- Reticular layer = veins, arteries, sends up smaller arteries which eventually break up into capillaries, hair follicle, nerve structures, sensorty receptors, sensitive to pressure

- Hair contains oil which helps prevent infection in follicle
- Arrector Pill Muscle: helps hair stand up straight

Four Types of Cells in Epidermis

1. Keratinocytes
    - Produce fibrous protein called keratin
        - Tough, fibrous, structural
        - Matrix of epidermis > makes it water-resistant
        - Built up if skin is rubbed (callus)
        - Main component of hair, skin cells, and nails
    - Most numerous cells f epidermis
    - Tightly connected by desmosomes
    - Journey from the bottom to the top of epidermis takes 25-45 days
2. Melanocytes
    - 10-25% of cells in deepest epidermis
    - Produe pigment called melanin –packaged into melanosomes + protects apical surface of keratinocyte nucleus from UV damage + melahnocytes numbers are approximately the same regardless of skin colour
3. Dendric (langerhans) cells
    - Macrophages –key activators of immune system
4. Tactile (merkel cells)
    - Sensory touch receptors

Gap Junctions: there's fastest connection

Epidermis

- Keratinized stratified squamous epithelium
- Has 4/5 distinct layers

1. Stratum Corneum: most superficial + 20-30 layers of dead cells + essentially flat membranous sacs filled with keratin + glycolipids in extracellular space
2. Stratum Lucidum (in thick skin): layer of clear dead cells
3. Stratum Granulosum: 5 layers of flattened cells + organelles deteriorating + cytoplasm full of lamellar granules (release lipids) and keratohyaline granules
4. Stratum Spinosum: several layers of keratinocytes unified by desmosomes + cells contain thick bundles of intermediate filaments made of pre-keratin
5. Stratum Basale: deepest epidermal layer + one row of actively mitotic stem cells + some newly formed cells become part of the more superficial layers + see occasional melanocytes and dendritic cells

- Cells change from stratum basale to stratum corneum

Apoptosis: type of cell death in which cell uses specialized cellular machinery to kill itself; cell suicide

- Controlled cell suicide
- Nucleus and organelles break down
- Plasma membrane thickens
- Allows cells to slough off as dandruff and dander
- Shed ~50, 000 cells every minute
- Reduce blood count when people are feeling tired after finishing radiation > rapidly dividing cells

Dermis

- Strong, flexible connective tissue
- Cells: fibroblasts, macrophages, occasionally mast cells and WBC
- Fibers in matrix bind body together
- Contains nerve fibers; blood and lymphatic vessels
- Contains epidermal hair follicles; oil and sweat glands
- Papillary Layer
    - Areolar connective tissue with collagen and elastic fibers and blood vessels

    - Loose tissue (phagocytes can patrol for microorganisms
    - Dermal papillae: superficial peglike projections
- Reticular Layer
    - ~80% of dermal thickness
    - Coarse, irregularly arranged, dense fibrous, connective tissue
    - Elastic fibers provide stretch-recoil properties
    - Collagen fibers: provide strength and resiliency + run in all directions but mostly parallel to skin surface + bind water
    - Cleavage lines: most collagen fibers parallel to skin surface > externally invisible, important to surgeons, incision parallel to cleavage line gap less and heal more readily

<u>Skin Colour</u>

- Carotene: yellow/orange + accumulates in stratum corneum of epidermis + can be converted to vitamin A
- Melanin: brown/yellow-brown/black + located in stratum germinativum + absorbs UV radiation (prevents skin damage) + albino when defected
- Pink colour in pale skin is due to hemoglobin

<u>Skin Colour Diagnosis</u>

- Cyanosis: blue –low oxygenation of hemoglobin
- Erythma (redness): fever, hypertension, inflammation, allergy
- Pallor (blanching): anemia, low blood pressure, fear, anger
- Jaundice (yellow cast): liver disorder
- Bronzing: inadequate steroid hormone in Addison's disease
- Bruises: clotted blood beneath skin

<u>Appendages of the Skin</u>

- Hair and hair follicles
    - Non-living, keratinized
    - Originates in follicle
    - Composed of root and shaft
    - Root base (hair papilla) surrounded by hair bulb and root hair plexus
    - Soft medulla, hard cortex
    - Cuticle: superficial dead protective layer > vellus: peach fuzz > terminal (heavy): shed and grow in cycle
    - Alopecia: hair thinning in both sexes
    - True baldness: genetically determined and sex-influenced condition, male patterns baldness casued by follicular response to DHT
        - Treatment: minoxidil (rogaine) and finasteride (propecia)
- Nails
    - Nail body covers nail bed
    - Nail production occurs at the nail root
    - Eponychium (cuticle) overlies root
    - Free edge of nail extends over hyponychium
    - Nails contain hard keratin
    - Nail matrix contains stem cells
        - Holocrine secretion: whole cell bursts, whole cell is present in seabum, seabum goes to surface of hairs, serves as protective, prevents hair from becoming extremely dry
- Sweat glands (sudiferous)
    - present all over skin except nipples and some external genitalia
    - Apocrine: odorous secretion into hair follicles (axillae, nipples, groin)
    - Merocrine: secretion directly onto skin surface + more numerous than apocrine + sensible perspiration: clear secretion + functions as thermoregulation, excretion, protection

- Sebaceous (oil) glands

Functions of Integumentary System

- Protection: chemical, physical, and biological barrier
- Skin = body temperature regulation = homeostasis
- Cutaneous sensation = nerves
- Metabolic functions
- Blood reservoir
- Excretion

Chemical Barriers of Skin

- Skin secretions: low pH retards bacterial multiplication + sebum and defensins kill bacteria
- Melanin: defense against UV radiation damage

Physical Barriers of Skin

- Flat, dead cells of stratum corneum surrounded by lipids
- Keratin and glycolipids block most water and water soluble substances
- Limited penetration of skin
    - Lipid-soluble substances
    - Plant oleoresins
    - Organic solvents
    - Salt of heavy metals
    - Some drugs
    - Drug agents

Biological Barriers of Skin

- Dendric cells of epidermis: present foreign antigens to WBC
- Macrophages of dermis: present foreigN antigens to WBC
- DNA: electrons absorb UV radiation + radiation converted to heat > gamma radiation causes fouble stranded DNA breaks

Skin Cancer

1. Basal Cell Carcinoma
    - Least malignant, most common
    - Stratum basale cells proliferate and slowly invade dermis and hypodermis
2. Squamous Cell Carcinoma
    - Cured by surgical excision
    - Keratinocytes of stratum spinosum
    - Usually scaly reddened papule on scalp, ears, lower lip, and hands
    - Does metastasize
    - Good prognosis if treated by radiation therapy or removed surgically
3. Melanoma
    - Cancer of melanocytes
    - Highly metastatic and resistant to chemotherapy
    - Treated by wide surgical excision accompanied by immunotherapy

Burns

1. First degree: epidermal damage > localized, redness, edema (swelling), and pain
2. Second degree: epidermal and upper dermal damage > blisters
3. Third degree: entire thickness of skin involved, skin gray-white, cherry red, or blackened + not painful + skin grafting is necessary

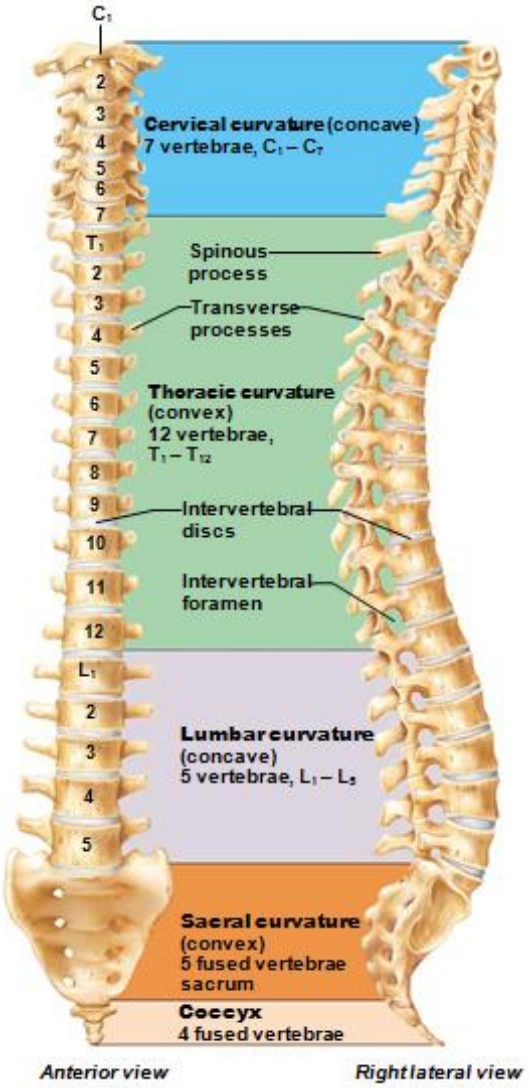
Issues: fluid loss + patients require extra calorie intake + infection after first 24 hours + complicated by immune system deficiency after 24 hours

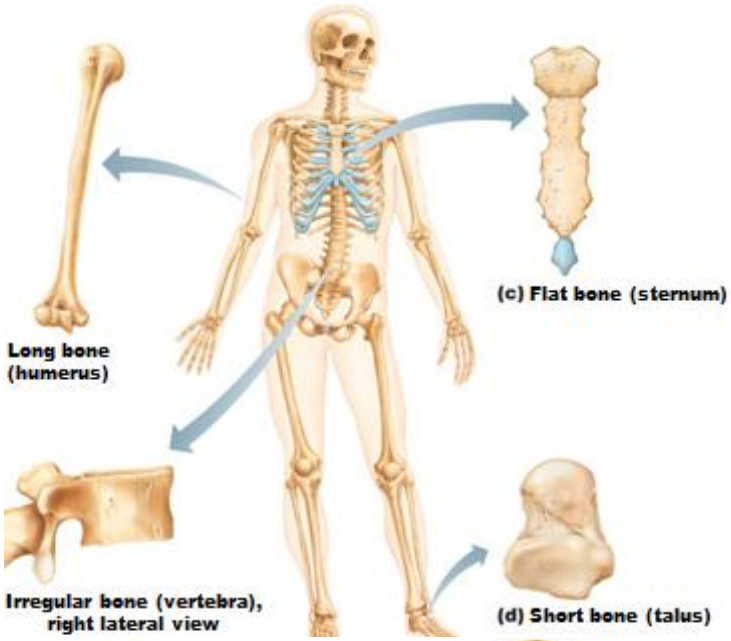
Treatment: debridement (removal) of burned skin + antibiotics + temporary covering + skin grafts

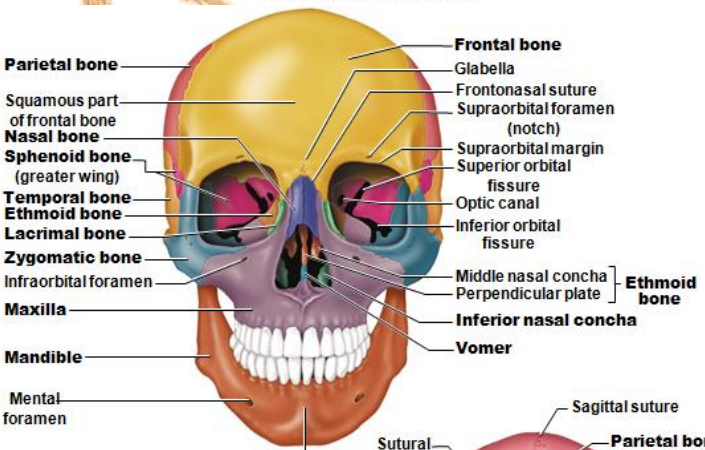
Developmental Aspects

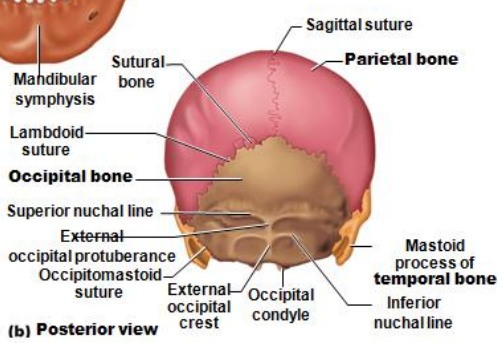
- Fetal
    - Ectoderm > epidermis; Mesoderm > dermis and hypodermis
    - Lanugo Coat: delicate hairs
    - Vernix Caseosa: sebaceous gland secretion; protects skin of fetus
- Infancy to Adulthood
    - Skin thickens, accumulates more subcutaneous fat
    - Sweat and sebaceous gland activity increases
    - Effects of cumulative environmental assaults show after 30
    - Scaling and dermatitis become more common
- Aging Skin
    - Epidermal replacement slows, skin becomes thing, dry and itchy (decreased sebaceous gland activity)
    - Subcutaneous fat and elasticity decrease, leading to cold intolerances and wrinkle
    - Increased risk of cancer due to decreased numbers of melanocytes and dendric cells
    - Hair thinning

Chapter 6 – Bones and Skeletal Tissues









Skeletal Cartilages

- All contain chondrocytes in lacunae and extracellular matrix
- Hyaline Cartilage
    - Provides support, flexibility, and resilience
    - Collagen fibers only' most abundant type
    - Articular, costal, respiratory, nasal cartilage
- Elastic Cartilage
    - Similar to hyaline cartilage, but contains elastic fibers
    - External ear and epiglottis
- Fibrocartilage
    - Thick collagen fibers: has great tensile strength
    - Menisci of knee; vertebral discs

Growth of Cartilage

- Appositional Growth : cells secrete matrix against external face of existing cartilage
- Interstitial Growth: chondrocytes divide and secrete new matrix, expanding cartilage from within
- Calcification: occurs during normal bone growth > hardens but calcified is not bone

Classification of Bones

- Axial Skeleton: long axis of body, skull, vertebral column, rib cage
- Appendicular Skeleton: bones of upper and lower limbs, girdles

Bone Functions

1. Support: for body and soft organs
2. Protection: for brain, spinal cord, and vital organs
3. Movement: levers for muscle action
4. Mineral and Growth Factor Storage: calcium and phosphorus, and growth factors reservoir
5. Blood cell formation (hematopoiesis): red marrow cavities of certain bones
6. Triglyceride (fat): storage in bone cavities + energy source
7. Hormone Production: osteocalcin –regulates bone formation + protects against obesity, glucose intolerance, diabetes

Bones

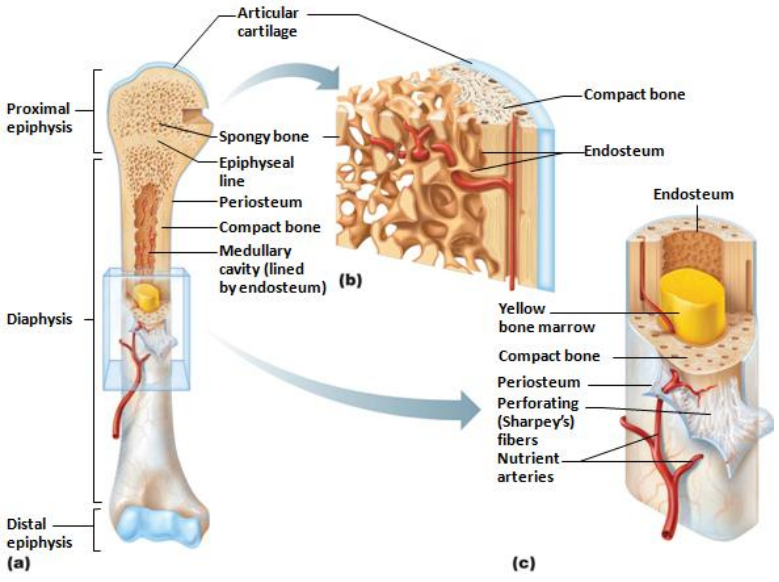
- Organs
- Contain different types of tissues
- Bone (osseus) tissue, nervous tissue, cartilage, fibrous connective tissue, muscle and epithelial cells in its blood vessels
- Three levels of structure: gross anatomy, cellular, chemical
- Two types of bone textures: compact and spongy

Flat bones: consist of a layer of spongy bone sandwiched between two thin layers of compact bone

- Thin plates of spongy bone covered by compact bone
- Plates sandwiched between connective tissue membranes: periosteum (outer) and endosteum
- No shaft or epiphyses
- Bone marrow throughout spongy bone; no marrow cavity
- Hyaline cartilage covers articular surfaces

Structural of Typical Long Bone

- Diaphysis
    - Tubular shaft forms long axis
    - Compact bone surrounding medullary cavity



- Epophyses
    - Bone ends
    - External compact bone; internal spongy bone
    - Articular cartilage
    - Between is epiphyseal line: remnant of childhood bone growth at epiphyseal plate

Hematopoietic Tissue in Bones

- Red Marrow
    - Found within trabecular cavities of spongy bones and diploe of flat bones
    - In medullary cavities and spongy bone of newborns
    - Adult long bones have little red marrow > heads of femur and humerus only
    - Red marrow in diploe and some irregular bones is most active
    - Yellow marrow can convert to red, if necessary

Cells of Bone Tissue

1. Osteogenic Cells or Osteoprogenitor Cells
    - Mitotically active stem cells in periosteum and endosteum
    - When stimulated differentiate into osteoblasts or bone lining cells
    - Somes osteogenic cells
2. Osteoblasts
    - Bone-forming cells that are mitotically active and secrete in mineralized bone matrix or osteoid
    - Includes collagen = 90% of bone protein
3. Osteocytes
    - Mature bone cells in lcunae that monitor and maintain bone matrix
4. Bone Lining Cells
    - Believed to maintain matrix in flat bones
5. Osteoclasts
    - Derived from hematopoietic stem cells that become macrophages
    - Giant, multinucleate cells for bone resorption
    - Ruffled border increases surface area for enzyme degradation of bone and seals off area from surrounding matrix

Table 6.1 Bone Markings

NAME OF BONE MARKING	DESCRIPTION	ILLUSTRATIONS
Projections That Are Sites of Muscle and Ligament Attachment		
Tuberosity (too"bĕ-ros'ĭ-te)	Large rounded projection; may be roughened	
Crest	Narrow ridge of bone; usually prominent	
Trochanter (tro-kan'ter)	Very large, blunt, irregularly shaped process (the only examples are on the femur)	
Line	Narrow ridge of bone; less prominent than a crest	
Tubercle (too'ber-kl)	Small rounded projection or process	
Epicondyle (ep"ĭ-kon'dīl)	Raised area on or above a condyle	
Spine	Sharp, slender, often pointed projection	
Process	Any bony prominence	

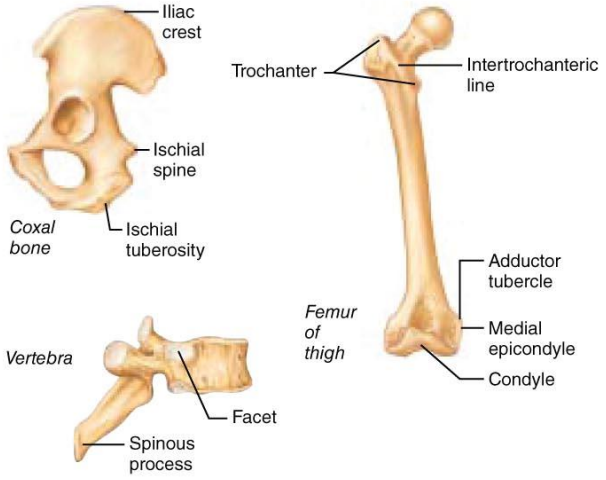
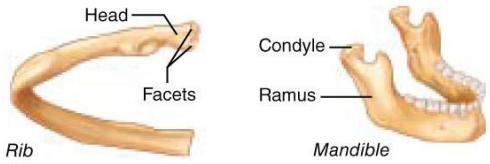
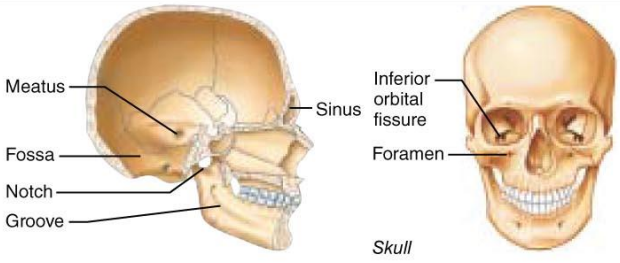


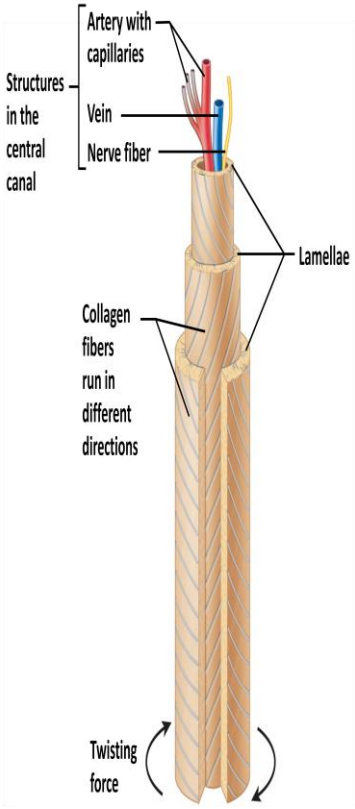
Table 6.1 Bone Markings (*continued*)

NAME OF BONE MARKING	DESCRIPTION	ILLUSTRATIONS
Projections That Help to Form Joints		
Head	Bony expansion carried on a narrow neck	
Facet	Smooth, nearly flat articular surface	
Condyle (kon'dīl)	Rounded articular projection	
Ramus (ra'mus)	Armlike bar of bone	
Depressions and Openings		
For Passage of Blood Vessels and Nerves		
Groove	Furrow	
Fissure	Narrow, slitlike opening	
Foramen (fo-ra'men)	Round or oval opening through a bone	
Notch	Indentation at the edge of a structure	
Others		
Meatus (me-a'tus)	Canal-like passageway	
Sinus	Cavity within a bone, filled with air and lined with mucous membrane	
Fossa (fos'ah)	Shallow, basinlike depression in a bone, often serving as an articular surface	



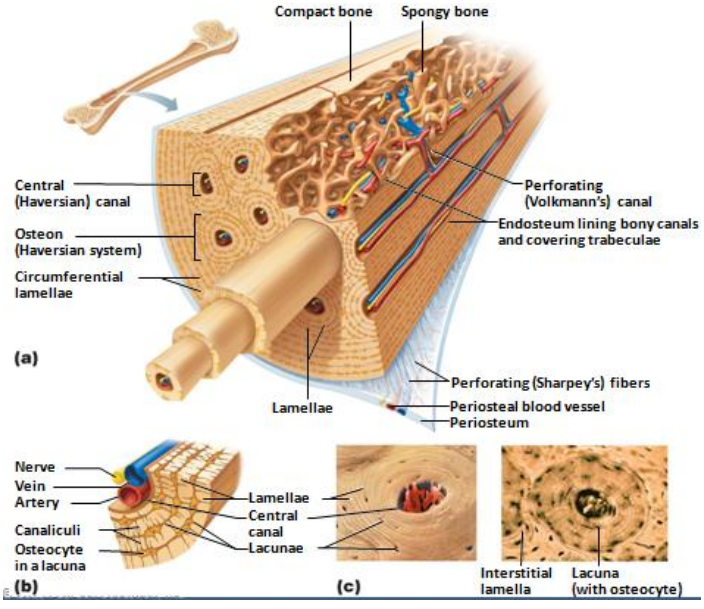


Single Osteon



<u>Microscopic Anatomy of Bone: Compact Bone</u>

- Aka lamellar bone
- Osteon or haversian system
  - Structural unit of compound bone
  - Elongated cylinder parallel to long axis of bone
  - Hollow tubes of bone matrix called lamellae
    - Collagen fibers in adjacent rings run in different directions
    - Withstands stress
- Canals and canaliculi
  - Central (haversian) canal: runs through core of osteon
  - Contains blood vessels and nerve fibers
- Preforating (volkmann's) canals
  - Canals lined with endosteum at right angles to central canal
  - Connect blood vessels and nerves of periosteum, medullary cavity, and central canal
- Lacunae: small cavities that contain osteocytes
- Canaliculi: hairlike canals that connect lacunae to each other



Osseus Tissue

- Osteoid: orgnic bone matrix is secreted by osteoblasts and makes up 33% of bone
    - Made up of ground substance (proteoglycans and glycoproteins)
    - Collagen fibers (most abundant protein)
    - Contributes to structure; provides tensile strength and flexibility
- Resilience of bond due to sacrificial bonds in or between collagen molecules
- Approx. 66% of bone is inorganic
- Mainly hydroxyapatite and other calcium salts with sodium, magnesium, and chloride that are composed of tiny calcium crystals embedded in collagenous matrix
- Bone is covered by periosteum

Ossification

1. Endochondral
    - Bone forms by replacing hyaline cartilage
    - Bones called cartilage (endochondral) bones
    - Forms most of skeleton
    - Forms most all bones inferior to base of skull except clavicles
    - Begins late in 2nd month of development
    - Requires breakdown of hyaline cartilage prior to ossification
    - Uses hyaline cartilage, converting it to a vascularised periosteum + results into change in nutrition, underlying mesenchyma cels specialize into osteoblasts
        - Begins at primary ossification center in centre shaft: blood vessels infiltration of perichondrium converts it to periosteum > underlying cells change to osteoblasts
        - Bone collar forms around diaphysis of cartilage model
        - Central cartilage in diaphsis calcifies, then develops cavities
        - Periosteal bud invades cavities > formation of spongy bone
        - Diaphysis elongates and medullary cavity forms
        - Epiphyses ossify
2. Intramembranous
    - Bones develops from fibrous membrane
    - Bones called membrane bones
    - Forms flat bones (ex: clavicles and cranial bones)
        - Ossification centers appear in fibrous connective tissue
        - Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming ossification center that produces the first trabeculae of spongy bone
        - Osteoid is secreted within fiberous membrane and calcifies
        - Osteoblasts bein to secrete osteoid, which calcifies for a few days
        - Trapped osteoblasts become osteocytes
        - Woven bone and periosteum form
        - Accumulating osteoid is laid down between embryonic blood vessels in a manner that results in a network of trabeculae called woven bone
        - Vascularised mesechyme condenses on the external face of the woven bone and beomes periosteum
        - Lamellar bone replaces woven bone, just deep to periosteum + red marrow appears
        - Trabeculae just deep to the periosteum thicken, mature lamellar bone replaces them, forming compact bone plates
        - Spongy bone (diploe) consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow

Bone Development and Growth

1. Long bones develop by endochondral ossification where a hyaline cartilage precursor is remodelled at the metaphysic by ossification

    - Occurs gradually throughout childhood
    - Causes increasing bone length
    - Timing of epiphyseal closure differs
2. Thickness of a long bone is increased by appositional growth
3. Flat bones develop by intramembranous ossification where a mesenchyme or fibrous connective tissue turns to bone

Postal Bone Growth

- Interstitial (longitudinal) Growth: increase in length of long bones
- Appositional Growth: increase in bone thickness

Hormonal Regulation of Bone Growth

- Growth Hormone
    - Most important in stimulating epophyseal plate activity in infancy and childhood
    - Produced by anterior pituitary
- Thyroid Hormone
    - Modulates activity of growth hormone
    - Ensures proper proportions
- Testosterone and Estrogens at puberty
    - Promote adolescent growth spurts
    - End growth by inducing epiphyseal plate closure
- Excesses or deficits of any cause abnormal skeletal growth

Bone Homeostasis

- Spongy bone replaced every 3-4 years
- Compact bone replaced every 10 years
- Older bones become more brittle
- Calcium salts crystallize
- Fractures more easily
- Consists of bone remodelling and bone repair
- Consists of both bone deposit and bone resorption*
- Occurs at surfaces of both periosteum and endosteum
- Remodelling units: adjacent osteoblasts and osteoclasts

Bone Homestasis: Response to Mechanical Stress

- Bones reflect stresses they encounter
    - Long bones thickest midway along diaphysis where bending stresses is greatest
- Bones stressed when weight bears on them or muscle pulls on them
    - Usually off center so tends to bend bones
    - Bending compresses on one side

Hormonal Control of Blood Ca^{2+}

- Parathyroid Hormone (PTH)
    - Produced by parathyroid glands
    - Removes calcium from bone regardless of bone integrity
- Calcitonin
    - Oduced by parafollicular cells of thyroid gland
    - In high doses, lowers blood calcium levels temporarily

Stages in Healing of a Bone Fracture

1. Torn blood vessels hemorrhage
    - Clot (hematoma) forms
    - Site is swollen, painful and inflamed
2. Capillaries grow into hematoma and phagocytic cells clear debris
    - Fibroblasts secrete collagen fibers and fibroblasts, cartilage, and osteogenic cells begin reconstruction of bone

        - Create cartilage matrix of repair tissue
        - Osteoblasts from spongy bone within matrix
    - Mass of repair tissue called fibrocartilaginous callus
3. Within a week new trabeculae appear in fibrocartilaginous callus
    - Callus converted to bony (hard) callus of spongybone
    - ~2 months later firm unions form
4. Beings during body callus formation
    - Continues for several months
    - Excess material on diaphysis exterior and within medullary cavity removed
    - Compact bone laid down o reconstruct shaft walls
    - Final structure resembles original because responds to same mechanical stressors

<u>Homeostatic Imbalances</u>

- Osteomalacia
    - Bones poorly mineralized as Calcium salts not adequate
    - Soft, weak bones
    - Pain upon bearing weight
- Rickets (osteomalcia of children)
    - Bowed legs and other bone deformities
    - Bones ends enlarged and abnormally long
    - Cause: Vitamin D deficiency or insufficient dietary calcium
- Osteoporosis
    - Group of diseases
    - Bone resorption outspaces deposit
    - Spongy bone of spin and neck of femur most susceptible
        - Vertebral and hip fractures common
    - Risk factors: postmenopausal women, men to lesser degree, sex hormones maintain normal bone health and density > as secretion wanes with age, osteoporosis can develop

<u>Age-related Changes in Bone</u>

- Children and adolescents: bone formation exceeds resorption
- Young adults: both in balance; males greater mass
- Bone density changes over lifetime largely determined by genetics: gene for Vitamin D"s cellular docking determines mass early in life and osteoporosis risk age
- Bone mass, mineralization, and healing ability decrease with age, beginning in 4th decade: except bones of skull, bone loss of greater in whites and females, electro stimulation' daily ultrasound treatment hasten repair