2021

Integrated Systems Anatomy and Physiology **Notes**

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The Nervous System

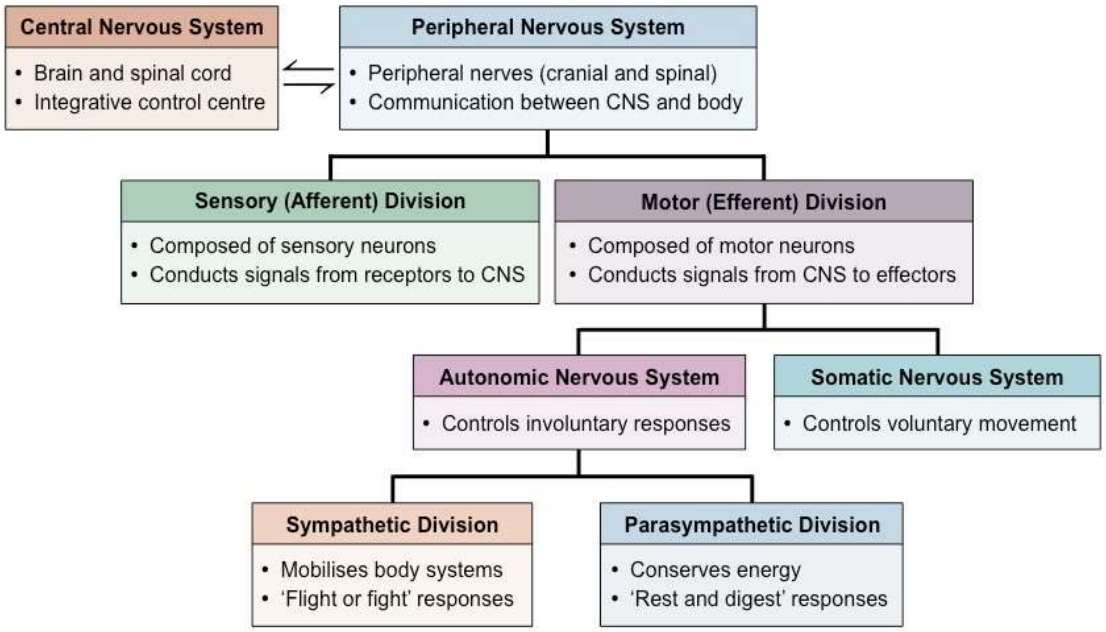
The Nervous system is one of the body's main control systems responsible for the regulation and maintenance of the body in coordination with the Endocrine system.
It is a communication network that primarily uses electrochemical signals called action potentials produced by neurons.

Structural divisions of the Nervous System

The Nervous system can be divided into two parts based on structure:

1. The **Central Nervous System (CNS)** consists of the brain and the spinal cord. The Central Nervous System (CNS) is responsible for the receiving and processing of sensory information and initiation of a motor response.
2. The **Peripheral Nervous System (PNS)** consists of the 31 pairs of spinal nerves and 12 pairs of cranial nerves. The Peripheral Nervous System (PNS) transmits sensory information to the CNS and the motor information from the CNS to the effectors.

Functional Divisions of the Nervous System



The Brain

The brain weighs about 1.2kg and is the most complex organ in the body and it is responsible for the integration of sensory information and initiation of motor information.

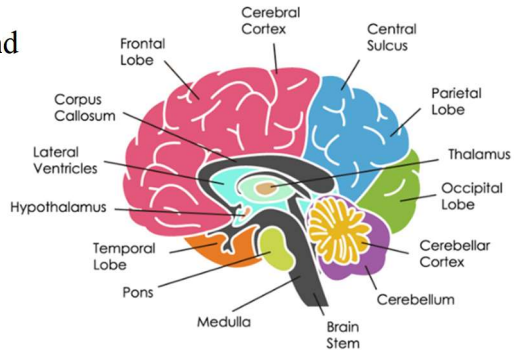
Brain Stem

The brain stem sits inferiorly to the diencephalon and connects the spinal cord to the brain.
The brain stem consists of the Midbrain, Pons, and Medulla Oblongata:

Medulla Oblongata

The Medulla Oblongata is the most inferior part of the brain stem and connects to the spinal cord at the foramen magnum. Grey matter in the medulla oblongata controls many homeostatic mechanisms with the following specialized centers;

- Cardiac Centre
  - Regulates heart rate
- Respiratory (Medullary Rhythmicity) Centre
  - Regulates rate and depth of breathing (via phrenic and intercostal nerves)



- Vasomotor Centre
  - Regulates the diameter of blood vessels
- Other reflex centers
  - E.g. coughing, sneezing, swallowing, and vomiting

Pons

The Pons is the bulging structure of the brain stem sitting between the Medulla Oblongata and the midbrain. White matter allows for connections between the cerebellum and other parts of the brain. The grey matter of the Pons in involved with the initiation of Rapid Eye Movement (REM) and includes a respiratory center that works in conjunction with the medullary rhythmicity center.

Midbrain

The most superior part of the brainstem is the Midbrain, which sits between the Pons and the Diencephalon. The nuclei in the midbrain have an important role in the stability of somatic movement. It also has grey matter responsible for the involuntary reflexes caused by visual, sensory and tactile input.

The Diencephalon

The diencephalon is superior to the brainstem and is made up of;

- Thalamus
  - The largest part of the diencephalon that relays sensory information to the different cerebral lobes
- Epithalamus
  - Includes the pineal gland and regulates emotions and rhythms
- Subthalamus
  - Involved in the control of motor functions
- Hypothalamus
  - The hypothalamus is inferior to the thalamus and it is very important in the control of many homeostatic mechanisms (e.g. body temperature and gas concentration)

Cerebrum

The Cerebrum is the largest and most superior part of the brain. It consists of an outer surface of grey matter, known as the Cerebral Cortex. Below that is white matter and deep in the Cerebrum is additional grey matter called the Basal Ganglia.

Folding of the Cerebral Cortex produces ridges called gyri. These gyri are separated by shallow grooves called sulci or deep grooves called fissures. The longitudinal fissure separates the Cerebrum into the left and right cerebral hemispheres. The 5 lobes of the cerebrum are:

- Frontal Lobe
  - The central sulcus separates the frontal and parietal lobes. The frontal lobe is responsible for voluntary motor functions, motivation, planning, aggression, olfaction, mood, and emotional behavior
- Parietal Lobe
  - The area of the cerebrum that receives the most sensory input
- Occipital Lobe
  - The part of the cerebrum that receives and processes visual input
- Temporal Lobe
  - Separated from the rest of the Cerebrum by the lateral fissure. Receives and processes smell (olfaction) and auditory sensory information. Also has a role in memory
- Insula
  - Receives and processes taste information

Cerebellum
The Cerebellum has a grey outer cortex and a white inner medulla. The Cerebellum controls locomotion in association with the cerebrum, fine motor control, posture, and balance
Corpus Callosum
The Corpus Callosum is the white matter that connects and allows communication between the left and right cerebral hemispheres

The Spinal Cord

The spinal cord starts at the Foramen Magnum (hole in the base of the skull) and extends inferiorly to the Lumbar vertebrae. It runs down the mid-sagittal posterior aspect of the body. The 31 pairs of spinal nerves are divided into 5 regions and are protected by 30 vertebrae

Region	Spinal Nerves	Vertebral Bones
Cervical	8 pairs	7 bones
Thoracic	12 pairs	12 bones
Lumbar	5 pairs	5 bones
Sacral	5 pairs	5 bones
Coccygeal	1 pair	1 bone
Total	31 pairs	30 bones

Structure
The spinal cord has enlargements in the cervical region and the lumbo-sacral regions, which corresponds to the nerves supplying the limbs. The cone-like end of the spinal cord at the lumbar region is called the Conus Medullaris. The Cauda Equina are the roots that extend from the Conus Medullaris.
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Reflexes

A reflex is a rapid, automatic response to stimulus. A reflex may either be somatic (activate skeletal muscle) or autonomic (activate smooth/cardiac muscle). Reflexes have the properties

- Involuntary
- Rapid
- Requires a stimulus
- Stereotyped

Reflex Arc
The Reflex Arc is the pathway an action potential follows in travelling from a sensory receptor to an effector organ. The Reflex Arc consists of the following components:

- Sensory Receptor
- Interneuron
- Effector Organ
- Sensory (Afferent) Neuron
- Motor (Efferent) Neuron

When a change is detected by a sensory receptor it triggers a nerve impulse. This nerve impulse travels up the sensory neuron through the dorsal root ganglion into the spinal cord via the dorsal root. In the spinal cord the neve impulse is transmitted from the sensory neuron to the motor neuron via the interneuron. The motor neuron transmits the nerve impulse to the effector organ via the somatic or autonomic route.
Types of Reflexes
Reflexes can be of three types;

- Stretch
- Golgi Tendon
- Withdrawal

The Endocrine System

The Endocrine system consists of several ductless glands that secrete chemical messengers called hormones into the bloodstream.

Types of Communication

- Autocrine
  - Releases chemicals that affect the same cell that released them
- Paracrine
  - Releases chemicals into the interstitial fluid to affect other nearby cells
- Endocrine
  - Chemicals secreted by endocrine glands into the bloodstream to affect distant cells

Types of Hormones

Amino Acid Based

- Made from amino acids, peptides, or proteins
- Water soluble
- Dissolve directly into plasma and travel as free hormones
- Indirect method of action;
  - Attaches to first receptor on the target cells membrane
  - Activates G protein complex
  - Adenyl-cyclase converts AMP to cAMP
  - cAMP acts as the secondary messenger and activates protein-kinases

Steroid Based

- Made from cholesterol or fatty acids
- Lipid soluble
- Bind to a binding protein when travelling through bloodstream
- Direct method of action;
  - Diffuses through cell membrane and attaches to receptor within cell
  - Hormone-receptor complex passes through nuclear envelope
  - Activates specific genes

Hormone Action

Hormones can alter the activities of a cell by:

- Changing the activities of the organelles
- Changing permeability of the cell membrane
- Activating a particular cell mechanism

Control of Hormone Release

Hormone secretion is regulated by multiple different stimuli.

- Humoral Stimuli
  - Response to changes in levels in the blood
- Neural Stimuli
  - Nerves directly stimulate an endocrine cell/tissue
- Hormonal Stimuli
  - Response to hormones secreted by other exocrine glands otherwise called 'Trophic' Hormones

Endocrine Glands

Pituitary Gland

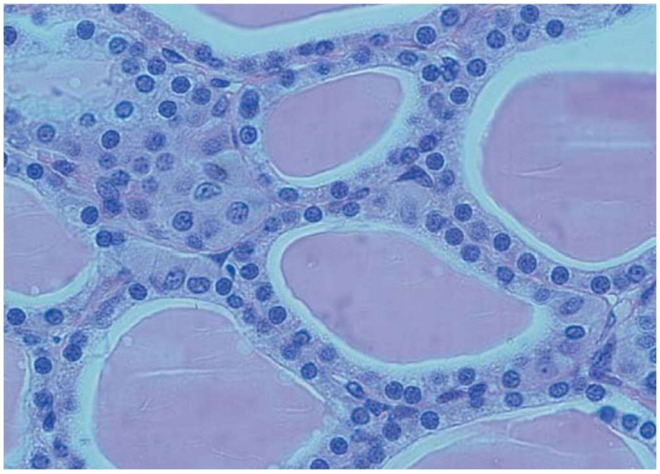
The pituitary gland is a small pea sized gland that sits inferiorly to the hypothalamus, connected by the infundibulum. It is divided into two parts;

- Anterior Pituitary (Adenohypophysis)

- Made of glandular tissue that originates from the pituitary diverticulum (oval cavity) during embryological development
- Constitutes 70-80% of the pituitary gland.
- Receives releasing or inhibiting factors from the hypothalamus via the Hypothalamohypophysial Portal System
- Responds to releasing factors by manufacturing hormones and secreting them into the bloodstream.

- Posterior Pituritary (Neurohypophysis)
  - Made of neural tissue that extended from the brain
  - Secretes Neurohormones it receives from the hypothalamus via the Hypothalamohypophysial Tract

Thyroid



The Thyroid is located anterior to the Trachea and consists of an Isthmus connecting the right and left lobes.
The thyroid gland is composed of units called thyroid follicles and cells between these unit called parafollicular cells. The thyroid follicles each consist of thyroglobulin surrounded by follicular cells. Thyroid follicles synthesize Tri-iodothyronine (T3) and Thyroxine (T4) whereas parafollicular cells produce calcitonin.

Parathyroid Glands

The Parathyroid glands are four pea sized bodies located on the posterior aspect of the thyroid gland.

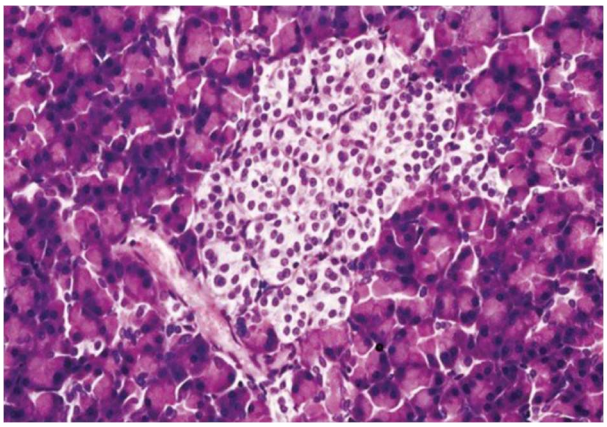
The Adrenal Glands

The adrenal glands are located superior to the kidneys and consist of an outer cortex and an inner medulla, surrounded by a connective tissue capsule.
The outer cortex of the Adrenal Glands is made up of three zones;

- The Zona Glomerulosa that produces Mineralocorticoids such as Aldosterone
- The Zona Fasciculata that produces Glucocorticoids such as Cortisol
- The Zona Reticularis that produces Androgens such as Testosterone

The Adrenal Medulla located deep within the adrenal glands is made up of nervous tissue, which when stimulated produces Adrenaline and Nor-Adrenaline

The Pancreas



The Pancreas is a long endocrine and exocrine gland located in the abdominal cavity consisting of three regions; a head, body and tail.
Most of the pancreas is made up of exocrine cells called acini cells. Throughout the pancreas are pancreatic islets (or Islets of Langerhans) which make up the endocrine component of the pancreas. There are multiple types of cells within the pancreas;

- Alpha cells produce Glucagon
- Beta cells produce Insulin
- Gamma cells produce pancreatic polypeptide
- Delta cells produce Somatostatin

Hormones

Gland	Hormone	Target Organ	Action
Posterior Pituitary	Antidiuretic Hormone (ADH)	Kidneys	Regulates water absorption
Posterior Pituitary	Oxytocin	Uterus	Stimulates contractions during labor and initiates lactation
Anterior Pituitary	Thyroid Stimulating (TSH)	Thyroid	Regulates Thyroid gland
Anterior Pituitary	Adrenocorticotropic Hormone (ACTH)	Adrenal Cortex	Regulates Adrenal Cortex
Anterior Pituitary	Follicle Stimulating (FSH)	Ovarian Follicle Testes	Regulates Gonads
Anterior Pituitary	Luteinising hormone (LH)	Ovarian Follicle Testes	Regulates Gonads
Anterior Pituitary	Growth Hormone (GH)	All Cells	Regulates growth in Children
Anterior Pituitary	Prolactin (PRL)	Mammary Glands	Regulates milk production
Anterior Pituitary	Melanocyte Stimulating Hormone (MSH)	Melanocytes	Stimulates melanocytes to produce more melanin
Thyroid Gland	Triiodothyronine (T3) Thyroxine (T4)	Most Cells	Stimulates an increase in metabolism to increase body temperature
Thyroid Gland	Calcitonin	Bones	Lowers Blood Calcium
Parathyroid Glands	Parathyroid Hormone	Bones	Raises Blood Calcium
Pancreas (Beta Cells)	Insulin	Liver & Muscle	Decreases blood glucose through Glycogenesis
Pancreas (Alpha Cells)	Glucagon	Liver & Fat	Increases blood glucose through Glycolysis and Gluconeogenesis
Pancreas (Delta Cells)	Somatostatin		Involved in inhibiting the production and secretion of other hormones
Adrenal Cortex	Aldosterone		Retention of Sodium in the Nephron
Adrenal Cortex	Cortisol		Stress Response
Adrenal Cortex	Testosterone		Triggers Spermatogenesis, maturation of sex organs, increases libido, and increases muscle mass
Adrenal Medulla	Adrenaline	Most Tissues	Fight or Flight Response
Adrenal Medulla	Noradrenaline	Most Tissues	Fight or Flight Response
Testes	Testosterone		Triggers Spermatogenesis, maturation of sex organs, increases libido, and increases muscle mass
Corpus Luteum (Ovaries)	Oestrogen	Endometrium	Endometrium Development
Corpus Luteum (Ovaries)	Progesterone	Endometrium	Maintains the Endometrium
Pineal	Melatonin		Regulates Sleep Patterns

Homeostasis

Homeostasis is the process of keeping the body's internal environment maintained in a steady state. homeostasis is also referred to as the ability to maintain the body's optimal working conditions. important aspects that must be regulated include:

- pH
- Blood Glucose levels
- Blood Pressure
- Body Temperature
- Gas concentrations
- Regulation of sleep cycles

The Skeletal System

The skeletal system is classified as connective tissue. The four primary components of the skeletal system are bones, cartilage, tendons, and ligaments.

Functions

1. Body Support – rigid structure allowing it to bear weight and support the body shape
2. Organ Protection – bones protect the underlying soft tissues and organs from physical damage
3. Body Movement – muscles connected to the bones (through tendons) allow movement
4. Storage of Minerals & Lipids – minerals such as calcium and phosphorus are stored in bones
5. Production of Blood Cells – bones marrow produces blood cells and platelets

Cartilage

Cartilage has no blood or nervous supply and is made up of two parts;

- A matrix – a noncellular substance consisting of non-fibrous proteins and proteoglycans
- A fluid produced by chondroblasts

Cartilage Cells

There are two types of cells within the cartilage, which are;

1. Chondroblasts
   - Originate from osteochondral progenitor cells in the perichondrium
   - Produce the matrix of the cartilage
2. Chondrocytes
   - Originate from differentiated Chondroblasts
   - Located in the spaces of matrix called the lacunae
   - Produce chemicals that maintain the matrix

Types of Cartilage

There are three types of Cartilage which include:

1. Hyaline Cartilage
   - Most associated with bones
   - Found where strong support and flexibility is needed
2. Fibrocartilage
   - Slightly compressible and very tough
   - Found where there is a lot of pressure
3. Elastic Cartilage
   - Somewhat flexible
   - Found where some rigidity is required

Bones

Bone is a type of connective tissue. The composition of the bones matrix is responsible for the characteristics of bone,

Bone Matrix

The bone matrix consists of 35% organic and 65% inorganic material. The organic component consists of collagen fibres and proteoglycans. The inorganic component consists of hydroxyapatite (calcium phosphate crystals).

Changing the bone matrix

Removal of minerals → bone is too flexible

Removal of collagen → bone is too brittle

Bone Cells

The three types of bone cells are:

1. Osteoblasts
   - Originate from the Osteochondral Progenitor cells
   - Collagen is produced by the Endoplasmic Reticulum (E.R.) and released by exocytosis
   - Release matrix vesicles with high concentrations of calcium (Ca^{2+}) and phosphate (PO_4^{3-}) ions
   - Process of forming bone is called ossification
2. Osteocytes
   - Originate from Osteoblasts
   - Occupy spaces in bone called lacunae
   - Retain connections to neighboring osteocytes through cell extensions
   - Maintain the bone's matrix
3. Osteoclasts
   - Originate from stem cells in the red bone marrow
   - Specialized for the breakdown of the bone matrix and reabsorption of Calcium (Ca^{2+}) and Phosphate (PO_4^{3-}) ions into the blood

Types of Bone Growth

Bone formation occurs through many stages of life, and there are two general types. Initially osteoblast's form relatively weak woven bone. In woven bone, collagen fibres are randomly orientated in many directions.

after this, osteoclasts breakdown woven bone and form a new matrix in a process called bone remodelling. Bone is reformed into thin sheets cold lamellae to form lamellar bone.

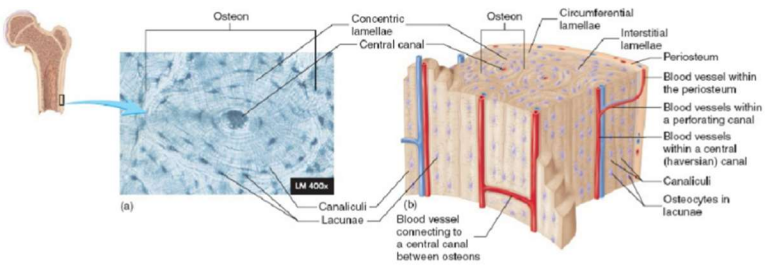
Types of Bone

Bones can be divided into two categories;

1. Spongy (cancellous) Bone
   - Appears porous (has more space and less matrix)
   - Contains columns of bone called trabeculae
   - Spaces contain bone marrow and blood vessels
2. Compact (cortical) Bone
   - Appears dense (more matrix and fewer pores)
   - Basic functional unit is the osteon

Compact Bone Structure

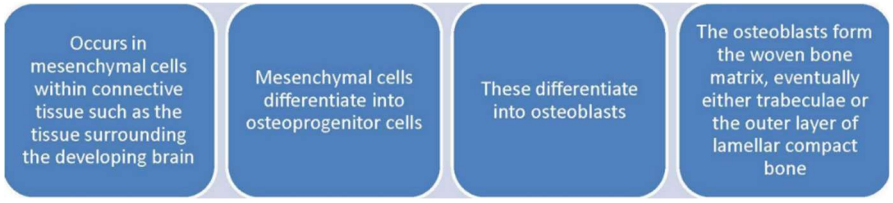
Perforating canals allow blood vessels from the periosteum to penetrate the compact bone and travel through the central canal. Nutrients and wastes travel to and from the osteocytes via interstitial fluid of the lacunae and canaliculi.



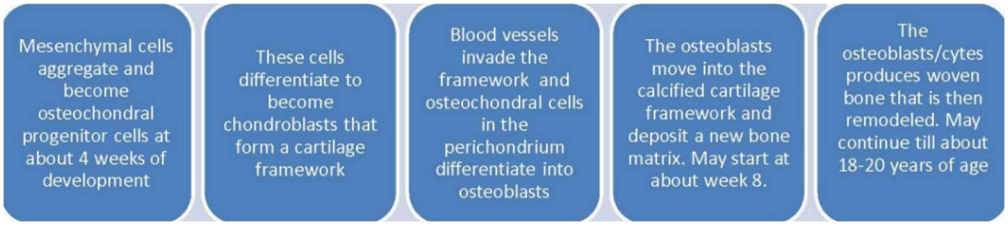
Foetal Bone Development

During Foetal Development, bones are formed in two patterns which are:

1. Intramembranous Ossification
   - Embryonic mesenchymal cells in the membrane differentiate into Osteoprogenitor cells
   - These cells specialize to form osteoblasts
   - The osteoblasts form internal spongy bone and external compact bone
   - This produces woven bone which is remodeled later in life to form lamellar bone

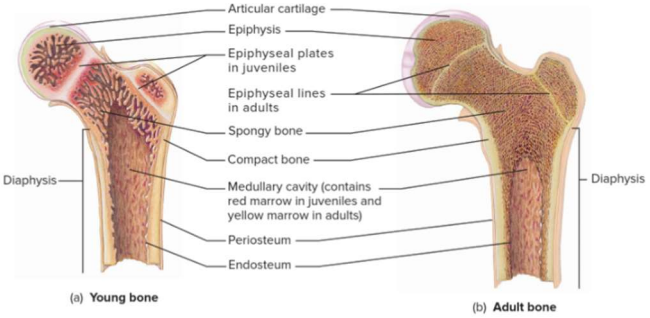


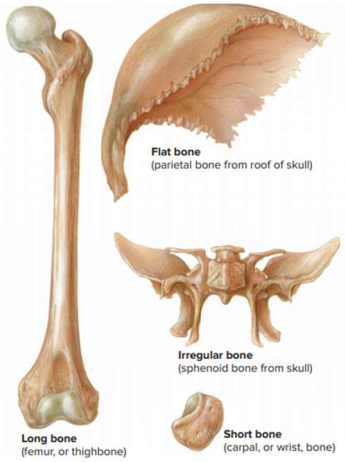
2. Endochondral Ossification
   - Mesenchymal cells aggregate and become Osteoprogenitor cells
   - These cells become chondroblasts and form a cartilage framework
   - Blood vessels invade the framework and produce osteoblasts
   - Osteoblasts move into the framework and produce the matrix.



Bone Structures

There are four general structures of bone which include flat short, irregular, and long.





Part	Description
Diaphysis	Shaft of the bone
Epiphysis	End of the bone; develops from its own center of ossification
Periosteum	Outer, double-layered connective tissue membrane with ligaments and tendons attached to bone through the periosteum; blood vessels and nerve pathways; the periosteum is where bone grows in diameter
Endosteum	Thin connective tissue membrane lining the inner cavities of bone
Articular cartilage	Thin layer of hyaline cartilage covering a bone where it forms a joint (articulation) with another bone
Epiphyseal plate	Hyaline cartilage between the diaphysis and epiphysis; its growth allows for growth in bone length
Spongy bone	Bone having many small spaces; found mainly in the epiphysis; arranged into trabeculae
Compact bone	Dense bone with few internal spaces organized into osteons; forms the diaphysis and covers the spongy bone of the epiphyses
Medullary cavity	Large cavity within the diaphysis
Red marrow	Connective tissue in the spaces of spongy bone or in the medullary cavity; the site of blood cell production
Yellow marrow	Fat stored within the medullary cavity or in the spaces of spongy bone

Term	Description	Example
Body	Main part	Body of femur
Head	Enlarged, often rounded end	Head of femur
Neck	Constriction between head and body	Neck of femur
Margin, border	Edge	Lateral border of scapula
Angle	Bend	Mandibular angle
Ramus	Branch off the body beyond the angle	Mandibular ramus
Condyle	Smooth, rounded articular surface	Lateral condyle of tibia
Facet	Small, flattened articular surface	Superior articular facet of atlas
Ridges		
Line, linea	Low ridge	Intertrochanteric line of femur
Crest, crista	Prominent ridge	Iliac crest
Spine	Very high ridge	Scapular spine
Projections		
Process	Prominent projection	Acromion process of scapula
Tubercle	Small, rounded projection	Greater tubercle of humerus
Tuberosity, tuber	Rounded projection; larger than a tubercle	Deltoid tuberosity of humerus
Trochanter	Tuberosity on the proximal femur	Greater trochanter of femur
Epicondyle	Upon a condyle	Lateral epicondyle of femur
Lingula	Flat, tongue-shaped process	Lingula of mandible
Hamulus	Hook-shaped process	Pterygoid hamulus of sphenoid bone
Horn	Horn-shaped process	Greater horn of hyoid bone
Openings		
Foramen	Hole	Foramen magnum of occipital bone
Canal, meatus	Tunnel	Hypoglossal canal of occipital bone
Fissure	Cleft	Superior orbital fissure of sphenoid bone
Sinus, labyrinth	Cavity	Ethmoid labyrinth

Bone Growth in Long Bones

There are two types of growth in long bones which are:

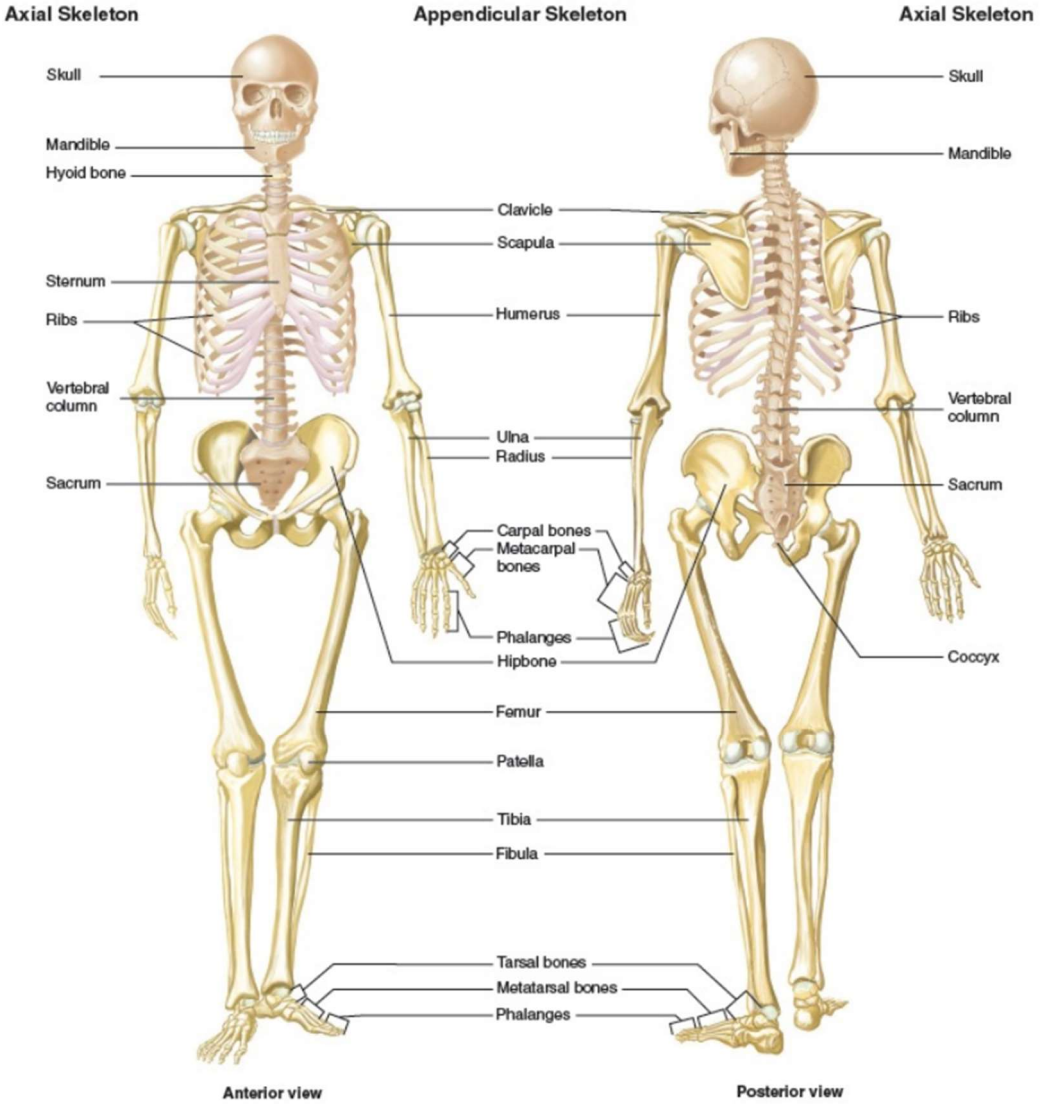
- Interstitial which is an increase in bone length
- Appositional which is an increase in bone width

Factors affecting Bone Growth

The size and shape of bones is determined genetically but may also be influenced by factors, including:

- Nutrition
  - Malnutrition affecting the proliferation of osteoblasts
  - Vitamin D deficiency causing decrease in calcium absorption
  - Vitamin C deficiency causing decrease in collagen synthesis
  - Excess Vitamin A
- Hormones
  - Growth Hormone (GH)
  - Triiodothyronine (T3) and Thyroxine (T4)
  - Calcitonin
  - Parathyroid Hormone
  - Reproductive Hormones (e.g. Testosterone)
- Exercise

The Skeleton



Joints

A joint, or articulation, is a place where two bones meet. Joints can be classified structurally into three different types: fibrous, cartilaginous, or synovial. They can also be classified into three groups functionally: synarthroses (non-moveable), amphiarthroses (slightly movable), and diarthroses (freely moveable).

Fibrous Joints

Bones united by fibrous connective tissue. They have no joint cavity an exhibit no movement. Subdivided into three groups;

- Gomphosis
  - Specialised joints consisting of pegs that fit into sockets, held in place by fine bundles of collagenous connective tissue.
  - Example. Periodontal ligaments that hold teeth in place
- Sutures
  - Opposing bones interdigitate where the periosteum of the two bones are continuous with each other. A sutural ligament is formed by the periosteum of both bones and fibrous connective tissue between.
  - Example. Bones of the skull
- Syndesmosis
  - Bones are further apart and joined by ligaments.
  - This joint allows for very slight movement.
  - Example. Radioulnar Joint

Cartilaginous Joints

Bones united by cartilage that produced very little movement. The connections can be either hyaline cartilage or fibrocartilage. Subdivided into two groups:

- Synchondroses
  - Consists of two bones joined together by hyaline cartilage
  - Most Synchondroses are temporary and later develop into Synchondrosis or synovial joints
- Symphyses
  - Consists of two bones joined by fibrocartilage which allows for slight movement
  - Example. Symphysis Pubis

Synovial Joints

Synovial Joints are complex joints that contain synovial fluid and allow considerable movement between bones.

- Hinge
  - Allows for movement on one axis
  - Allows flexion and extension
  - Example. Elbow and Knee
- Pivot
  - Allows for movement on one axis
  - Allows pronation and supination
  - Example. Arm
- Plane
  - Allows for gliding and rotation
  - Example. Carpals and Tarsals
- Ball and Socket
  - Allows for movement on all axis
  - Allows flexion, extension, abduction, adduction, rotation, and circumduction
  - Example. Shoulder (shallow) and Hips (deep)

Movement

The structure of a joint, determines the type and range of movement at the joint. Some joints can only perform one type of movement, whereas others can perform many. There are many different types of movement, which include:

Gliding Movements

A simple type of movement in which two flat surfaces slide over each other.

Angular Movements

- Flexion and Extension
  - Flexion is a bending movement in which the angle of a joint is decreased to bring two bones closer together
  - Extension is a straightening movement that increases the angle of a joint
  - Hypertension is defined as the extension of a joint beyond 180º
  - Examples. Elbow, Knee, Wrist, Head
- Adduction and Abduction
  - Abduction is movement away from the midline of the body
  - Adduction is movement towards to the midline of the body
  - Examples. Arms and Legs

Circular Movements

- Rotation
  - The turning of a structure around its long axis
- Pronation and Supination
  - Pronation is the palm of the hand facing posteriorly
  - Supination is the palm of the hand facing anteriorly
- Circumduction
  - Combination of flexion, extension, abduction, and adduction

Special Movements

- Elevation and Depression
  - Elevation is the movement of a structure superiorly
  - Depression is the movement of a structure inferiorly
  - Example. Shoulders
- Protraction and Retraction
  - Protraction is a gliding motion that moves a structure in an anterior direction
  - Retraction is a gliding motion that moves a structure in a posterior direction
- Excursion
  - Lateral excursion is movement of the mandible (jaw) to either side of the midline
- Opposition and Reposition
  - Opposition is the movement of the thumb, over the palm, to contact each of the other digits
  - Reposition is movement of the thumb back to its neutral position
- Inversion and Eversion
  - Inversion turns the ankle so that the plantar surface of the foot faces medially

The Muscular System

The muscular system is an organ system comprised of many different muscles. The major functions of the muscular system are:

- Movement of the body
- Maintenance of posture
- Respiration
- Production of body heat
- Allows for communication
- Constriction of organs and vessels
- Contractions of the heart and maintenance of blood flow

Types of Muscle Tissue

Skeletal Muscle

- Constitutes about 40% of body weight
- Generally attached to bone
- Controlled voluntarily by the somatic nervous system
- Responsible for locomotion, respiration, posture, mastication, and facial expressions
- Multiple nuclei located on the periphery

Smooth Muscle

- Most widely distributed type of muscle
- Found in hollow organs and tubes
- Controlled involuntarily by the autonomic nervous system
- Single, centrally located nucleus

Cardiac Muscle

- Specialised muscle, located only in the heart (myocardium)
- Produces contractions to pump blood around the body
- Controlled involuntarily by the autonomic nervous system

Properties of Muscle Tissue

Muscle tissue has four major functional properties

- Contractility - Ability of a muscle to shorten with force to produce tension
- Excitability - capacity of a muscle to respond to a nervous or hormonal stimulus
- Extensibility - a muscle can be stretched beyond its normal resting length to a degree
- Elasticity - ability of a muscle to return to its original position after being stretched

Skeletal Muscle Anatomy

Muscles are composed of fascicles, contained bundles of muscle fibres, surrounded by layers of connective tissue. Muscle tissue is also rich in blood and nervous supply.

Connective tissue coverings

- Epimysium - surrounds the entire muscle
- Perimysium - surrounds fascicles (groups of muscle fibres)
- Endomysium - surrounds individual muscle fibres

Skeletal Muscle Fibre Anatomy

Skeletal muscle cells are called muscle fibers and consist of:

- Plasma membrane called a sarcolemma
- Cytoplasm called sarcoplasm
- Multiple nuclei at the periphery
- Lots of mitochondria
- Myofibrils; very large cylindrical organelles in the sarcoplasm
- Sarcoplasmic Reticulum which is responsible for the storage of Calcium (Ca^{2+}) ions
- Transverse (T) Tubules; extensions of sarcolemma that run deep into the cell allowing the action potential to travel through the cell

Myofibrils

A myofibril contains two types of filaments called myofilaments:

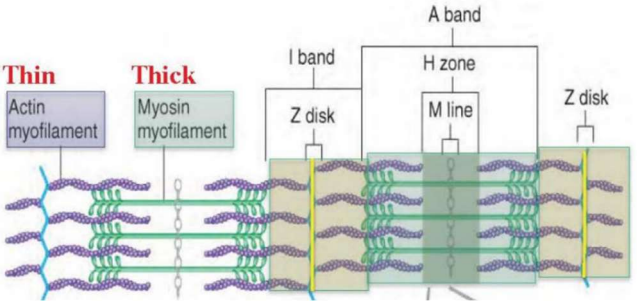
1. Thick (myosin)
2. Thin (Includes actin, troponin, and tropomyosin)

The myofilaments are arranged into units called sarcomeres.

Sarcomeres

The sarcomere is the basic structural and functional unit of the skeletal muscle. They are repeated units throughout the myofilaments separated by Z discs. The structure of a sarcomere gives the muscle a striated appearance.

- Z disc – separates two sarcomeres
- I band – located either side of the Z disc and only contains actin
- A band – extends the length of the myosin
- H zone – center of the myofilament, and only myosin is present
- M line – the middle point of the H zone



Myosin (Thick) Filament

- Composed of many elongated myosin filaments shaped like golf clubs
- Myosin heads can bend at the hinge region which allows binding to the active sites on the actin to form cross-bridges
- Myosin heads rest at about 45° towards the tail. The breakdown of ATP, releases energy, causing the myosin heads to stand erect, 90° to the tail.

Actin (Thin) Filament

- Globular (G) actin monomers form a double helix protein with active binding sites called actin
- Tropomyosin is a long protein that covers the binding sites on the actin
- Troponin is a molecule that attaches to both the actin and the tropomyosin
- Calcium ions (Ca^{2+}) attaches to troponin, causing it to change shape and expose the binding sites on the actin molecule

Sliding Filament Model

- Calcium ions bind to the troponin molecule. The troponin molecule changes shape in response. The tropomyosin is moved, exposing the active sites on the actin molecule
- Myosin heads breakdown ATP into ADP, causing the myosin heads to cock up
- The active site of the actin and the myosin heads bind to form cross-bridges
- The myosin heads release the energy and return to the original position (power stroke) causing the actin filaments to slide over the myosin filaments towards the M line\
- The sarcomere shortens causing a muscle contraction\
- ATP molecules bind to myosin heads causing it to detach from the actin

Activation of a Muscle Fibre

All muscles are served by motor neurons. As each nerve enters the muscle it branches and runs through the connective tissue layers. Neurons terminate at the muscle fibre at a point called the neuromuscular junction.

Neuromuscular junction

Calcium ions flood the neuron through the voltage gated channel when the nerve impulse reaches the end of the neuron. Synaptic vessels containing acetylcholine travel to the plasma membrane. Acetylcholine is exocytosed into the synaptic cleft where it diffuses across to the postsynaptic membrane. Acetylcholine attaches to a ligand gated channel.

Excitation – Contraction Coupling

The sarcolemma continues the action potential stated at the neuromuscular junction. The action potential causes the sarcoplasm to be filled with calcium allowing interaction between the actin binding sites and the myosin heads.

Muscle Movement

Isotonic Contraction

When the tension produced by muscles is greater than the load then movement occurs;

- Concentric
  - Overcomes the opposing resistance and the muscle contracts
- Eccentric
  - Tension is maintained but muscle lengthens

Isometric Contraction

When the tension produced by the muscle is not greater than the load then no movement occurs.

Muscle Tension

The presence of motor units allows for differing amounts of muscle contractions

Motor Units

One neuron may serve multiple different muscle fibres in a muscle. An action potential travelling down that motion neuron will only cause the muscle fibres in that unit to contract. Therefore, this creates a small amount of muscle tension.

Increasing the frequency of nerve impulses down one motor neuron and activating only the one motor unit is called Summation.

Multiple motor units exist within a muscle. With a greater number of motor units stimulated the muscular tension increases. The addition of more motor units is called Recruitment. Muscles that require more precision will have a greater number of motor units.

Muscles making a move

Muscles, tendons and bones act together as lever systems to move either parts of the body or the whole body. As a muscle contracts it creates tension on the tendons and pulls the bones closer together. Movement is determined by the relative positions of the bone, the joint and muscle.

Muscle Attachment

Muscles can attach to bones in several ways including:

- A tendon
  - Thick cord like structure
- An aponeurosis
  - Sheet like structure
- Directly attach to the periosteum of the bone

Although not all muscles attach to bones, some muscles attach to soft tissues such as the skin.

Assessing Muscle Movement

Assessing the joints crossed, position of a muscle in relation to a joint and the muscle's line of pull can help determine the movement caused by a muscle.

Joints Crossed

If a muscle does not cross a joint, it will not act upon it. Although if the muscle crosses the joint, it can move the bones limited to what the joint will allow.

Relative Placement

The placement of a muscle relative to the joint affects the type of movement that can occur;

- If the muscle crosses the *anteriorly* it will cause *flexion*
- If the muscle crosses the *posteriorly* it will cause *extension*
- If the muscle crosses the *medially* it will cause *adduction*
- If the muscle crosses the *laterally* it will cause *abduction*

Line of Pull

Muscles must shorten/contract across a joint to move a body part. The direction in which the muscle pulls is dictated by the arrangement of muscle fibers/fascicles.

Muscle Nomenclature

Muscles are named based on many factors, including:

Shape

- Deltoid (Triangular)
- Quadratus (4-sides)
- Trapezius (Trapezoid)
- Serratus (Finger-like)
- Rhomboid
- Orbicularis (circular)
- Gracilis (slender)
- Piriformis (Wedge-shaped)

Number of Heads

- Biceps – 2 muscle heads
- Triceps – 3 muscle heads
- Quadriceps – 4 muscle heads

Fascicle Direction

- External Oblique – diagonally facing outwards
- Internal Oblique – diagonally facing inwards
- Transverse – horizontal
- Rectus – vertical

Region

Muscles can be named based on their location:

- Infraspinatus
- Gluteals
- Brachii
- Iliacus
- Intercostals
- Femoris

Action

- Flexor
- Supinator
- Elevator
- Extensor
- Adductor

The Circulatory System

The Heart

Functions of the Heart

The heart carries out multiple functions including:

- Generating blood pressure to move blood through blood vessels
- Ensuring a one-way blood flow through two routes
- Regulating blood supply to match changing metabolic needs

Circulation Routes

- Pulmonary Circulation
  - Deoxygenated blood is pumped into the lungs to become re-oxygenated
  - It is a short loop and requires low pressure
- Systemic Circulation
  - Oxygenated blood is pumped throughout the body to supply the tissues with oxygen and other nutrients
  - It is a long loop and requires high pressure
- Coronary Circulation
  - The heart is a muscle and thus also requires a rich blood supply
  - Right and left coronary arteries branch off the aorta
  - Blood returns to the right atrium through the coronary sinus via the cardiac veins

Location of the Heart

The heart sits in the mediastinum. The heart is about the size of a closed fist and sits obliquely medial to the two lungs.

Pericardium

- Fibrous Pericardium
  - The outer layer of the pericardium surrounding the heart
  - It is tough and allows for anchorage and protection
- Serous Pericardium
  - Parietal layer (adheres to the fibrous pericardium)
  - Visceral layer (covers the heart surface)
  - Pericardial Cavity (space between layers filled with serous fluid)

Walls of the Heart

The heart consists of three distinct layers;

- Epicardium
  - Smooth epithelial outer surface of the heart
  - Also called the visceral layer
- Myocardium
  - Middle layer composed of cardiac muscle
  - Contacts to produce blood pressure
- Endocardium
  - Smooth epithelial inner surface of the heart
  - Lines the chambers and valves
  - In contact with the blood within the heart

Fibrous Skeleton of the Heart

There is a dense connective tissue that surrounds the four different valves. This provides anchorage, structural stability, and electrical insulation between the atria and ventricles.

Chambers and Valves of the Heart

Right Atrium

- Superior part of the heart
- Receives deoxygenated blood from the superior & inferior vena cava and coronary sinus

Right Atrioventricular (Tricuspid) Valve

- Connects the Right Atrium to the Right Ventricle
- Chordae Tendineae close the valve during the Systole

Right Ventricle

- Inferior part of the heart
- Deoxygenated blood is received from Right Atrium and pumped through the pulmonary semi-lunar valve into the pulmonary trunk

Pulmonary Semi-Lunar Valve

- Valve that prevents backflow between the Right Ventricle and the Pulmonary Trunk

Left Atrium

- Superior part of the heart
- Receives oxygenated blood from the four pulmonary veins

Left Atrioventricular (Bicuspid) Valve

- Connects the Left Atrium to the Left Ventricle

Left Ventricle

- Inferior part of the heart
- Receives oxygenated blood from the Left Atrium through the Bicuspid Valve
- Pumps oxygenated blood through the Aortic Semi-Lunar valve into the Aortic Arch

Septum

- The thick wall between the two ventricles

Specialized Cardiac Tissue

Some muscle fibers are non-contractile and form the specialized pacemaker/conduction system that regulates the heartbeat. The fast conduction system allows for fast spontaneous depolarization and autorhythmicity of the heart.

- Sino-Atrial (SA) Node
- Initiates the electrical signal that causes the contraction of the myocardium.
- Atrioventricular (AV) Node
- Sends conduction and results in the spontaneous polarization.
- Atrioventricular Bundle and Purkinjie Fibres
- Conducts the electrical impulse along the muscle to cause contraction.

The Cardiac Cycle

Cardiac Cycle

The Cardiac Cycle refers to one complete heartbeat, consistent of the systole and diastole. The cardiac muscle must depolarise before contraction and it must repolarise before it can relax.

Spread of impulse through the Heart

- Sino-Atrial (SA) Node generates an impulse and atrial excitation begins
- Impulse is delayed at the Atrioventricular (AV) Node
- Impulse travels down the Atrioventricular bundles to the apex of the heart and ventricular excitation begins
- Ventricular excitation is complete

The Sino-Atrial (SA) Node

The SA Node does not have a resting membrane potential (RMP). The membrane slowly depolarizes until it reaches a threshold at which an action potential is generated. The membrane repolarizes during the AV Node depolarization, and gradually depolarizes again.

Action potential along Cardiac Muscle

Cardiac muscle fibres have a stable resting membrane potential (RMP). An action potential is initiated when stimulated by an adjacent current flow. Fibres remain depolarized for a long period allowing ventricular contraction.

The muscle fibres return to the resting membrane potential (RMP) after repolarization.

Mechanical Phases of the Cardiac Cycle

1. Atrial depolarization followed by Atrial Systole
- Atrial systole pushes the remaining 20% of blood from the atrium to ventricle (most flowed through passively before this)

2. Ventricular depolarization followed by ventricular systole
- Atrioventricular (AV) valves close due to ventricular pressure increase
- Isovolumetric ventricular contraction
- Semilunar valves open as the blood is forced out of the ventricles.

3. Ventricular repolarization followed by ventricular diastole
- Semilunar valves close
- Isometric ventricular relaxation
- Atrioventricular (AV) valves open allowing for rapid passive ventricular filling (prior to the atria systole)

Cardiac Parameters

Heart Rate

- Speed of heartbeat measured by the number of contractions per minute
- Resting heart rate is approximately 75 bpm

Cardiac Volumes

- End Diastolic Volume (EDV)
- Volume of blood in the ventricle at the end of filling
- End Systolic Volume (ESV)
- Volume of blood remaining in the ventricle at the end of emptying
- Stroke Volume (SV)
- Volume of blood ejected per heartbeat
- Stroke Volume = End Diastolic Volume – End Systolic Volume

Cardiac Output

- A measure of heart performance
- Volume of blood ejected per ventricle per minute
- Cardiac Output = Heart Rate × Stroke Volume
- Cardiac Output is influenced by factors that alter the Heart Rate of Stroke Volume

ECG

Calculating Heart Rate

- Find the average number of mm squares between R and R points
- Multiply that average by 0.04 (each cube represents 0.04 seconds)
- Multiply by 60 (as there is 60sec per minute)

Types of Heart Rates

Bradycardia → slow

Normal

Tachycardia → fast

Factors affecting the Cardiac Output

Factors affecting the Heart Rate

Neural Factors

- SA and AV nodes are innervated by sympathetic and parasympathetic nerves which are controlled by the cardiovascular centre in the medulla oblongata
- Parasympathetic nerves reduce the heart rate and sympathetic nerves increase the heart rate

Hormones

- Hormones such as adrenaline, noradrenaline, and thyroxine all have an affect on the heart rate

Other Factors

- Body temperature
- Drugs
- Sleep

Factors affecting the Stroke Volume

Preload

- Defined as the “force” or “load” on the ventricular muscle prior to contraction
- Determined by the End Diastolic Volume (EDV)
- Venous return is the major determinant of End Diastolic Volume (EDV)
- Factors that affect the venous return include;
- Blood volume
- Venous pressure
- Venous tone

Contractility

- It is the “strength” of ventricular contraction at any given preload, which depends on the muscle fibres ability to contract
- The muscles ability to contract is dependent on the concentration of calcium in the muscle fibres.
- Myocardial contractility is increased by:
- Sympathetic stimulation
- Adrenaline and noradrenaline

Afterload

- The force against which the ventricles eject blood

Blood Vessels

Histology

Tunica Intima

- Inner layer of the blood vessels
- Endothelium attached to the basement membrane
- Lamina propria is the connective tissue layer attached to the basement membrane
- Internal elastic membrane

Tunica Media

- Consists of smooth muscle cells arranged circularly around the blood vessel
- Controls movements such as:
- Vasoconstriction: contraction of smooth muscle to decrease blood flow
- Vasodilation: relaxation of smooth muscle to increase blood flow

Tunica Externa (Adventitia)

- Connective tissue surrounding the vessels

Arteries

Elastic Arteries

- Characterised by having a great amount of elastic tissue
- Allows for the artery to expand and recoil
- Generally known as conducting arteries
- Examples: Aorta and the major branches of the Aorta

Muscular Arteries

- Have thick walls with many muscular layers
- Undergo vasoconstriction and vasodilation
- Generally known as distributing arteries

Arterioles

- Muscular arteries gradually decreasing in size down to the terminal arterioles

Veins

Veins

- Smooth muscle cells form a continuous layer
- Thin walls and large lumens
- Also contain valves to prevent the backflow of blood
- Generally called capacitance vessels due to how compliant they are (the extent to which they stretch)

Venules

- Small veins that drain the capillary network
- Endothelial cells attached to a basement membrane with a few muscular cells

Capillaries

- Very small vessels (<10 microns)
- Endothelial cells on a basement membrane with a delicate layer of loose connective tissue
- Designed for the rapid exchange of nutrients between blood and interstitial fluid

Types of Capillaries

- Continuous
- No gaps between endothelial cells
- Examples: muscle, skin
- Fenestrated
- Highly permeable
- Examples: kidney, endocrine glands
- Sinusoids
- Large fenestrae
- Examples: liver and bone marrow

Capillary beds

- Capillary beds are the functional areas of the circulation where the exchange of nutrients and wastes occurs between the blood and interstitial fluid
- Network of approximately 100 capillaries
- Blood supply through the capillary beds is variable and depends on the metabolic activity of the tissue
- Blood flow is controlled by the opening and closing of pre-capillary sphincters
- Excess fluid that flows out of the capillaries is collected by lymphatic vessels

Blood Flow

Types of Blood Flow

- Laminar Flow
  - Streamlined; smooth blood vessel walls and equal lumen diameter
  - Outermost layers of blood move slower than the centre
- Turbulent Flow
  - Flow is interrupted due to obstructions
  - Rate of flow exceeds critical velocity
  - Partially responsible for heart sounds
  - Sounds due to turbulence are not normal in blood vessels and may increase the chances of Thrombosis

Velocity of Blood Flow

- Velocity of blood flow relates to diameter, and is inversely proportional to the total cross-sectional area of a blood vessel category

Blood Flow Parameters

- Blood Flow (F) = volume of blood flow per unit time
  - Blood flow is directly proportional to pressure differences
  - Blood flow is inversely proportional to resistance
- Flow = $(P_1 – P_2) / R$
  - P_1 = pressure in the blood vessels at point 1
  - P_2 = pressure in the blood vessels at point 2
  - R = resistance to the blood flow
- Resistance = $128vl / \pi D^4$
  - v = viscosity
  - l = vessel length
  - D = vessel diameter

Blood Flow Control

Intrinsic (Local) Control

1. Local Metabolic Factors
   - When the tissue's metabolism increases, vasodilation occurs and the blood flow to that tissue increases
   - Vasodilation is caused by the increased production of metabolites such as CO_2, K^+, H^+
2. Local Vasoactive Substances
   - Vasodilators: histamine, bradykinins
   - Vasoconstrictors: endothelin – I, leukotrienes
3. Myogenic Control
   - Passive stretch of vessels causes vasoconstriction
   - Decreased stretch causes vasodilation

Extrinsic Control

1. Neural Control
   - The vasomotor centre in the medulla oblongata stimulates sympathetic adrenergic vasoconstrictor fibres resulting in either vasoconstriction or vasodilation
2. Hormonal Control
   - Adrenaline and Noradrenaline causes vasoconstriction in digestive organs and in the skin
   - Adrenaline also acts on B2 receptors to cause vasodilation in blood vessels supplying the skeletal muscles

- Antitensin II and Antidiuretic Hormone (ADH) are vasoconstrictors
- Atrial Naturetic Hormone (ANP) is a vasodilator

Blood Pressure

Blood pressure (BP) measures the:

- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)

Pulse pressure (PP) can be calculated by: SBP – DBP

Blood Pressure Regulation

Mean Atrial Pressure (MAP) is regulated by negative feedback control mechanisms. There are short term and long-term control mechanisms for Mean Atrial Pressure (MAP) regulation. The cardiovascular centre in the medulla oblongata is essential for overall MAP regulation.

Short Term MAP Control Mechanisms

1. The Baroreceptor Reflex
   - Baroreceptors are high pressure stretch receptors located in the Aortic Arch and the carotid sinus which are both connected to the cardiovascular centre in the medulla oblongata
   - Sensory impulses to the cardiovascular centre in the medulla oblongata change heart rate, stroke volume, and Total Peripheral Resistance (TPR).
2. Hormonal Influences
   - Adrenaline increases cardiac output (CO), total peripheral resistance (TPR), and Mean Atrial Pressure (MAP)
   - Angiotensin II and Antidiuretic Hormone (ADH) increase vasoconstriction, total peripheral resistance (TPR), and Mean Atrial Pressure (MAP)
3. Chemoreceptor reflexes
   - In emergencies in which CO_2 concentration increases and the pH decreases (acidity increase), Mean Atrial Pressure (MAP) may be affected
4. Higher Central Nervous System (CNS) centres
   - The brain may affect the cardiovascular system in the medulla oblongata in response to pain, stress and trauma
5. CNS ischaemic response
   - Decrease in oxygen, increase in CO_2, and a drop in pH cause changes to the MAP

Long Term MAP control mechanisms

1. Direct Renal Mechanisms
   - Increased blood volume → increased filtration results in decreased MAP
   - Decreased blood volume →decreased filtration results in increased MAP
2. Renin-Angiotensin-Aldoesterone (RAAS) System
   - Low blood volume or low Mean Atrial Pressure (MAP) causes the granular cells of the juxtaglomerular apparatus (JGA) in the kidney to secrete renin
   - Renin catalyses the formation of Angiotensin I in the blood from the protein Angiotensinogen
   - As the blood flows through the lungs the Angiotensin I is converted into Angiotensin II by the ACE enzyme
   - Angiotensin II causes vasoconstriction and the release of aldosterone. Aldosterone increases the absorption of water in the nephron of the kidneys causing the increase of blood volume. These two factors increase the Mean Atrial Pressure (MAP).

The Renal System

The Renal System composes of the two kidneys and the ureters which is part of the Urinary System also containing the urinary bladder and the urethra. Functions of the Renal System include:

- Excretion of waste products and excess ions
- Regulation of blood volume and blood pressure
- Regulation of body fluid composition
- Regulation of extracellular pH
- Stimulation of red blood cell synthesis
- Activation of vitamin D

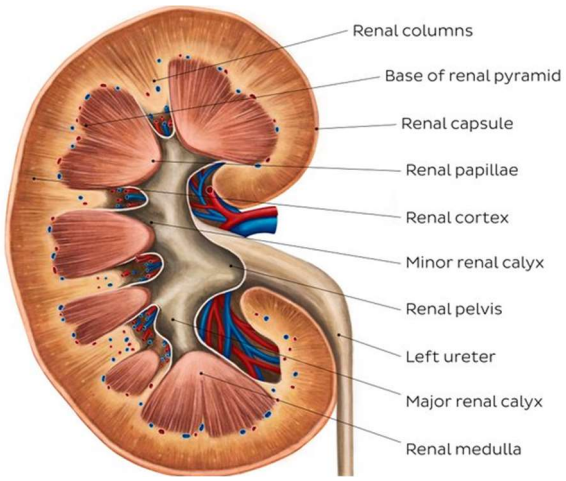
Kidney Anatomy and Histology

Location

The kidneys are retroperitoneal (behind the peritoneum) and are located on either side of the vertebral column. The liver causes the right kidney to be slightly lower than the left kidney. The kidneys are partially protected by the lumbar vertebrae and ribs.

External Anatomy

The renal capsule is the fibrous connective tissue surrounding each kidney. The renal capsule is surrounded by adipose tissue. A thin layer of connective tissue called the renal fascia surrounds the adipose tissue. The hilum is the indentation on the kidneys supplying the kidney with blood and nerves.



Internal Anatomy

The kidney is divided into the outer cortex and an inner medulla. The hilum is the surface at which the blood and nervous supply enter the kidneys. The hilum opens into the renal sinus filled with adipose tissue.

The medulla composes of multiple cone-shaped structures called renal pyramids separated by renal columns. The tips of the renal pyramids are called renal papillae and point towards the renal sinus. The minor calyces collect urine from the papillary ducts and empty into the major calyces. The major calyces empty into the renal pelvis which later becomes the ureter.

The Nephron

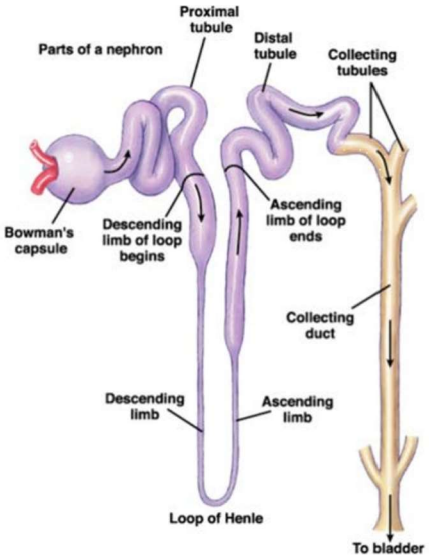
The nephron is the histological and functional unit of the kidney. The nephron is made up of the renal corpuscle (Glomerulus & Bowman's Capsule), proximal convoluted tubule, loop of Henle, distal convoluted tubule, and the collecting duct.

Types of Nephrons

There are approximately 1.3 million nephrons per kidney. The two types of Nephrons are:

1. Juxtamedullary
   - Long Loop of Henle that extends deep into the medulla
   - Accounts for approximately 15% of the nephrons
2. Cortical Nephron
   - Shorter Loop of Henle
   - Accounts for approximately 85% of the nephrons

Renal Corpuscle



The blood enters the nephron at the glomerulus through the afferent arteriole. The Bowman's capsule is the double walled structure surrounding the glomerulus. Together they form the renal corpuscle where the first stage of urine formation, filtration, occurs.
The Bowman's capsule has both a parietal and visceral layer. The visceral layer is made up of podocytes wrapping around the glomerulus. The filtration slits made up by the podocytes and the fenestrated epithelium allows for high filtration of the blood.

Proximal Convoluted Tubule (PCT)

The filtrate from the Bowman's capsule drains into the proximal convoluted tubule (PCT). The PCT is made up of simple cuboidal tissue with microvilli that allow for the active reabsorption of salt

Loop of Henle

The Loop of Henle is made up of the descending and ascending limb. Simple squamous tissue allows for osmosis and diffusion throughout the Loop of Henle.

Distal Convoluted Tubule (DCT)

The distal convoluted tubule (DCT) connects the Loop of Henle to the collecting ducts. Simple cuboidal tissue allows for diffusion.

Collecting Duct

Many nephrons drain the urine into collecting ducts that extend to the renal papillae and drain into the minor calyces.

Urine Formation

Filtration

Due to the pressure produced by afferent and efferent arterioles, fluid from the blood passes through the filtration membrane (podocytes and endothelium) in the glomerulus into the Bowman's capsule.
Filtration Pressure: $P_{eff} = GCP - (BCOP + CHP)$
The filtrate contains molecules mall enough to pass through the filtration membrane including water and many other useful ions (e.g., sodium & potassium) that should be reabsorbed.

Tubular Reabsorption

Transport proteins in cells throughout the nephron move water and other useful solutes out of renal tubules into the peritubular capillaries. The nephron reabsorbs approximately 99.5% of the filtrate. Most reabsorption occurs in the PCT and the Loop of Henle. Substances reabsorbed include amino acids, glucose, fructose, and ions such as Na^+, K^+, Cl^-, & Ca^{2-}.
The permeability of the DCT and the collecting duct is controlled by the Antidiuretic Hormone (ADH). The reabsorption of sodium in the DCT and collecting duct is controlled by the hormone Aldosterone.

Tubular Secretion

The transfer of solutes not filtered out of the blood across the DCT into the filtrate for excretion. Substances secreted into the DCT include toxic by-products of metabolism, drugs, or abnormal molecules.

Renal Effects on the Blood Pressure

The kidneys can influence the blood pressure because they have the ability to change the composition and volume of the blood plasma. The kidneys are therefore involved in blood pressure homeostatic mechanisms.

Mechanisms

A. Intrinsic Mechanisms
- *Autoregulation*: protects the kidneys from constant changes in blood pressure
- *RAA System*: juxtaglomerular cells detect the drop in blood pressure and secrete renin

B. Extrinsic Mechanisms

The Juxtaglomerular Apparatus (JGA)

The Juxtaglomerular Apparatus (JGA) consists of the juxtaglomerular cells of the afferent arteriole and the macula densa of the distal convoluted tubule (DCT). The Juxtaglomerular Apparatus (JGA) helps regulate glomerular blood pressure and the rate of blood filtration by the kidneys.

Autoregulation

$$P_{eff} = BHP - (BOP + CHP)$$

This equation shows how glomerular filtration is dependent on the blood pressure. Blood pressure varies throughout the day, therefore the blood flow to the glomerulus must vary to prevent kidney problems.

The JGA monitors blood flow and can regulate Glomerular Filtration Rate (GFR) by constricting or dilating the afferent arteriole to regulate renal blood flow.

The Renin-Angiotensin-Aldosterone (RAA) System

Juxtaglomerular cells monitor the blood pressure in the afferent arteriole. When a drop in the blood pressure is detected, the juxtaglomerular cells release renin.

Renin catalyzes the conversion of Angiotensinogen into Angiotensin I in the blood → Angiotensin I flows through the blood to the lungs where it is converted into Angiotensin II by the ACE enzyme → Angiotensin II causes vasoconstriction → aldosterone is release causing greater water reabsorption → cardiovascular centre in medulla oblongata increases heart rate → increase in blood volume → increase in blood pressure.

The Respiratory System

The respiratory system is an organ system serving multiple functions that include:
- Pulmonary ventilation and gaseous exchange
- Regulation of pH
- Voice production
- Olfaction
- Protection

Anatomy of the Respiratory System

The respiratory system is functionally divided into two parts

→ Conducting – nose, pharynx, larynx, trachea, bronchi, bronchioles, & terminal bronchioles

→ Respiratory – respiratory bronchioles, alveolar ducts, & alveoli

Lungs
Two cone shaped organs with a base and an apex located in the thoracic cavity. The left lung has two lobes and a cardiac notch, whereas the right lung has three lobes.
The lungs are held in the chest by the pleura. The parietal pleura lines the interior of the thoracic cavity and visual pleura covers the exterior of the lungs. Pleural fills the pleural cavity

Alveoli
The chambers at which gas exchange occurs. Approximately 300-500 million alveoli per lung contribute to the large surface area of the lungs. The alveoli are surrounded by a large network of capillaries which allow for gaseous exchange. Alveoli are made of different cells:

- Type I pneumocyte – simple squamous epithelium, involved in gaseous exchange
- Type II pneumocyte – cells involved in the secretion of surfactant
- Alveolar macrophage – involved in the ingestion and breakdown of invaders

Pulmonary Ventilation

Ventilation is the process of moving air in and out of the lungs.

Inhalation

- Diaphragm contracts and flattens, and the rib cage is elevated by the intercostal muscles
- Volume of the lungs increases
- Alveolar pressure decreases
- A pressure gradient is produced where the atmospheric pressure is higher than the alveolar pressure
- Air flows into the lungs to equilibrate

Expiration

- Diaphragm and intercostal muscles relax
- Volume of the lungs decrease
- Alveolar pressure increases
- A pressure gradient is produced in which the alveolar pressure is higher than the atmospheric pressure
- Air flows out of the lungs to equilibrate

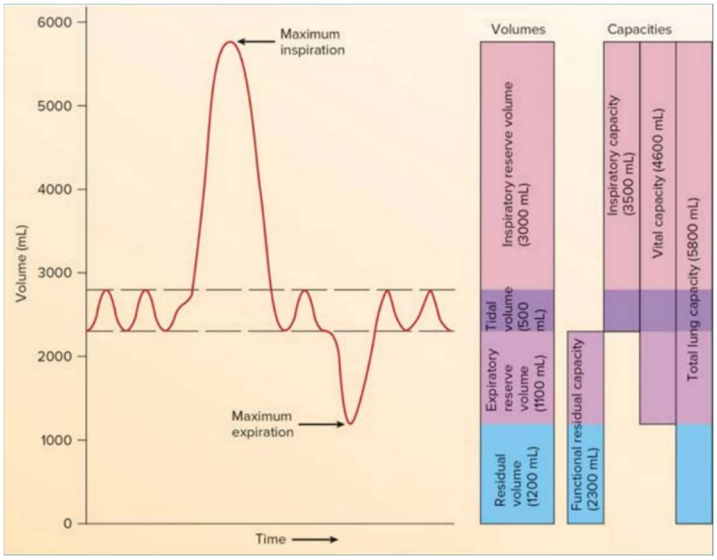
Forced Ventilation

- Accessory muscles, such as the sternocleidomastoid, scalenes, and pectoralis minor, assist in the elevation of the rib cage during inspiration
- Muscles assist the rebound of the lung muscles to forcefully expel air out.

Measurement of Lung Volumes

Spirometer
The volume of ventilation and total lung capacity can be measured using a spirometer. A spirogram is a graph that records inspiration and expiration.

Static Lung Volumes
During breathing at rest only a small proportion of the total lung volume is exchanged. Although it can change if breathing becomes more forceful



Dynamic Lung Volumes

Dynamic lung volumes are measured using a vitalograph.

- FVC (Forced Vital Capacity)
  - The volume of air forcefully expelled from the lungs during max expiration
- FEV_{1sec}
  - The volume of air that can be forcefully expelled from the lungs in the first second
  - This is a good indicator of airway obstruction
- $FEV_{1\%}$
  - The ratio of FEV_{1sec}/ FVC
  - This is a good indicator of restrictive versus obstructive respiratory dysfunction

Gaseous Exchange

Factors affecting the diffusion of gases

Gas diffusion rate across the respiratory membrane is influenced by several factors including:

- Gas partial pressure
- Temperature
- Surface area
- Diffusion distance

Respiratory Membrane

The respiratory membrane is made up of the capillary endothelial cell, fused basal lamina, alveolar epithelium, and the surfactant layer. It is adapted for the rapid transfer of gases due to factors such as:

- Thickness of 0.5µm
- Large surface area
- Reduced volume of blood
- Narrow capillaries

Gas exchange

Gases diffuse from areas of high concentration to areas of low concentration.

GAS	Atmos. Air (Sea Level)	Alveolar Air	DeO_2 Blood	O_2 Blood	Tissue Cells
PO_2	160 (21%)	105	40	105	40
PCO_2	0.3 (0.04%)	40	45	40	45
PN_2	597 (78%)	569	569	569	569
PH_2O	0.0 (0%)	47	-	-	-

At the lungs; oxygen gas moves from the alveoli to the blood and carbon dioxide moves from the blood to the alveoli. At the tissues; oxygen gas moves from the blood to the tissue and the carbon dioxide moves from the tissue to the blood.

Transport of Oxygen Gas

Oxygen is transported in the blood in two ways:

- Oxygen gas is very insoluble in solution, and only 1.5% is transported in the plasma
- Oxygen gas combines with the Haemoglobin pigment on the red blood cells

$$\text{Haemoglobin} + O_2 \leftrightarrow HbO_2 \text{ (Oxyheamoglobin)}$$

100ml of blood contains about 20ml of oxygen gas.

Haemoglobin

The Haemoglobin protein is a globular protein made from two alpha chains and two beta chains. 4 haem groups act as binding sites for the O_2 molecules.

Exchange of Oxygen

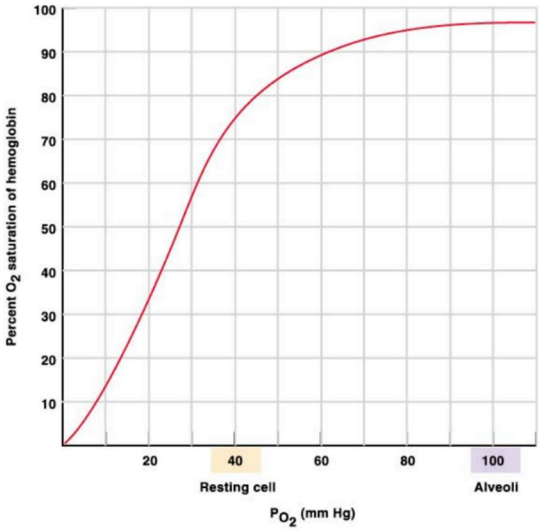
At the lungs;

- Oxygen moves from high pressure in the alveoli to low pressure in the blood
- The oxygen combines with the haemoglobin on the red blood cells]

At the tissues;

- Oxygen moves down its concentration gradient from the high pressure in the blood to the low pressure in the tissues
- High concentrations of O_2 on the Haemoglobin cause greater diffusion to the tissues

O_2 – Hb Dissociation Curve



The shape of the curve is significant. At low PO_2 values (0 – 40mmHg), small changes in the PO_2 represent large changes in the Hb% saturation. At high PO_2 values (40 – 104mmHg), large changes in PO_2 represent a small change in the Hb% saturation.

Factors affecting the affinity of Hb for O_2

Factors that affect the amount of O_2 gas that binds to haemoglobin include:

- PCO_2
- Temperature
- Acidity
- 2,3 – BPG

Transport of Carbon Dioxide

Carbon dioxide is transported in the blood by three methods:

- 7% is dissolved in the plasma
- 23% binds to haemoglobin to form carbaminohaemoglobin
- 70% as bicarbonate ions in the plasma

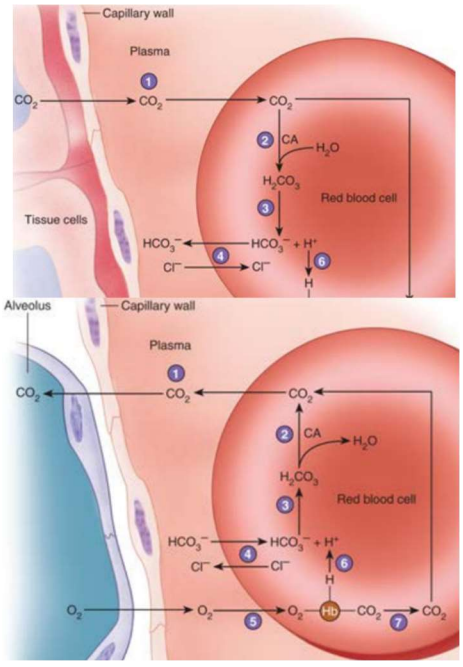
$$CO_{2\,(g)} + H_2O_{\,(l)} \leftrightarrow H_2CO_{3\,(aq)} \leftrightarrow H^+_{(aq)} + HCO_3^-{}_{(aq)}$$

Exchange of CO_2 at tissues

- PCO_2 is high in the tissues
- Carbon dioxide dissolves into the blood and enters the red blood cell
- Carbonic Anhydrase in the red blood cell catalyses the bicarbonate ion formation
- HCO_3^- exits the red blood cell in exchange for Cl^- ion from the plasma (Chlorine shift)

Exchange of CO_2 at the lungs

- PCO_2 is low in the lungs
- The reverse process occurs
- Carbon dioxide diffuses out of the blood and into the alveoli
- Cl^- ion exits the red blood cell in exchange for the HCO_3^- ion



Nervous (Central) Control of Respiration

3 groups of neurons (nuclei) in the brain control respiration.
Medulla Oblongata:

- Dorsal Respiratory Group (DRG)
- Ventral Respiratory Group (VRG)

Pons:

- Potine Respiratory Group (PRG)

Medulla Oblongata

The medulla rhythmicity centre provides the basic rhythm of breathing. Nuclei drive the muscles of inspiration and forced expiration via neurons.

1. Dorsal Respiratory Group (DRG)
    - Controls inspiratory muscles such as the diaphragm (via the phrenic nerve) and external intercostals (via the intercostal nerve)
    - Receives sensory input from the other areas of the brain
2. Ventral Respiratory Group (VRG)
    - Contains neurons only active during forced ventilation that stimulate intercostal and spinal nerves
    - Contains specialized neurons (pre-Botzinger complex) to establish the rhythm of respiration

Pons

The Pons has a major role in the process of breathing, by regulating responses to changing lung volumes and stretching airways.

1. Potine Respiratory Group (PRG)
    - Some neurons send inhibitory impulses to the Dorsal Respiratory Group (DRG) to stop inspiration
    - Some neurons send stimulatory signals to the DRG to prolong inspiration
    - The function of the PRG is to limit inspiration and facilitate expiration

Chemical Control

The concentration of Carbon Dioxide in the arterial blood is measured by chemoreceptors. The chemoreceptors send sensory information to the respiratory centers in the medulla oblongata and pons to adjust the rate of respiration.

Stimuli and Receptors

O_2, CO_2 and H_3O^+ concentrations in the blood are all monitored by chemoreceptors. There are two main groups of chemoreceptors:

- Peripheral – carotid and aortic bodies
- Central – bathed by Cerebrospinal Fluid (CSF) in the brainstem

CO_2 stimulation of Central Chemoreceptors

When CO_2 concentration increases it crosses the blood brain barrier and dissolves into the CSF. This causes the concentration of H_3O^+ to increase, which stimulates the central chemoreceptors. The respiratory centers in the medulla oblongata increase the rate and depth of breathing to lower the PCO_2 to normal levels.

CO_2 stimulation of Peripheral Chemoreceptors

The peripheral chemoreceptors are less sensitive to changes in PCO_2 but are strongly influenced by changes in H_3O^+ concentration.
They are also slightly sensitive to PO_2 changes, as they only respond to very large decreases in the pressure of oxygen gas. Therefore, O_2 concentration rarely causes changes to respiration.

The Digestive System

The digestive tract (alimentary canal) consists of many organs including the mouth, pharynx, esophagus, stomach, small intestines, large intestines, anus and accessory organs such as the teeth, tongue, salivary glands, liver, gall bladder and pancreas. These organs serve many functions, including:

1. Ingestion – introduction of food into the mouth
2. Mastication – mechanical digestion of food by chewing
3. Propulsion – movement of food through peristalsis
4. Secretion – lubrication and the release of catalysts for the chemical digestion of food
5. Digestion – breakdown of foods into nutrients
6. Absorption – movement of nutrients from the lumen of organs to the bloodstream
7. Elimination – removal of waste products through defecation

Histology of the Digestive Tract

The digestive tract is made up of multiple layers of tissue

Mucosa

The mucosa is made up of three sub layers;

- Epithelium
  - Non-keratinized stratified squamous (located in the mouth, esophagus, and anus)
  - Simple columnar (located in the remainder of the alimentary canal)
  - Specialized goblet cells secrete mucous
- Lamina Propia
  - Thin layer of connective tissue
  - Contains blood vessels, lymphatic vessels, and lymph nodes
- Muscularis mucosae
  - Thin layer of smooth muscle

Submucosa

Loose connective tissue containing blood vessels, lymphatic vessels, lymph nodes, submucosal glands, and nerves. Nerves control the blood flow, smooth muscle movement, and glandular secretions.

Muscularis Externa

Two layers of muscle: innermost circular and outermost longitudinal. Two types of muscle:

- Skeletal – voluntarily controlled (involved in swallowing)
- Smooth – involuntarily controlled (involved in peristalsis)

Serosa

Consists of loose connective tissue and simple squamous epithelium forming part of the visceral peritoneum.

Mesenteries

Mesenteries are folds of perioteneum between abdominal organs. They are two layers of peritoneum with connective tissue between, through which nerves and blood vessels travel. Some of the mesenteries are:

- Greater Omentum – connects the greater curve of the stomach to the transverse colon
- Lesser Omentum – connects the lesser curve of the stomach to the liver
- Transverse mesocolon – suspends the transverse colon from the posterior body wall
- Mesentery proper – suspends the jejunum and ileum from the posterior body wall

Anatomy

Oral Cavity

- The lips are anterior
- The fauces are the opening to the pharynx

- Lined with stratified squamous epithelium
- Contains 32 teeth; 8 incisors, 4 canines, 8 premolars, 12 molars
- Responsible for the ingestion of food

Lips and Cheeks

- The lips (labia) are made up of the Orbicularis Oris muscle
- Keratinized stratified squamous epithelium give the lip the colour
- Many muscles act to move the lips
- The cheeks are the lateral walls of the oral cavity made of the buccinator muscle
- Both the lips and the cheeks are involved in the process of mastication and speech

Palate

- Hard palate: anterior, supported by the maxilla
- Soft palate: posterior, consists of skeletal muscle
- Uvula: projection from the posterior of the soft palate

Palatine Tonsils

- The palatine tonsils make up the lateral wall of the fauces

Tongue

- Mostly muscle, intrinsic (changes the shape) and extrinsic (movement), with moist stratified squamous epithelium
- Lingual frenulum attaches the tongue to the inferior base of the oral cavity
- Some papillae (on the anterior) have tastebuds

Salivary glands

1. Parotid
    - Largest, secretes serous fluids
    - Anterior to the ear
2. Submandibular
    - Mixed, mostly serous and mucous secretions
    - Inferior border of the mandible
3. Sublingual
    - Smallest, mixed, more mucous than serous secretions
    - Inferior to the tongue

Pharynx

- Nasopharynx behind the nasal cavity
- Oropharynx behind the oral cavity
- Laryngopharynx superior to the larynx

Esophagus

- Transports food from the pharynx to the stomach
- Posterior to the trachea
- Passes through the esophageal hiatus (opening in the diaphragm)
- Lined with the moist stratified squamous epithelium

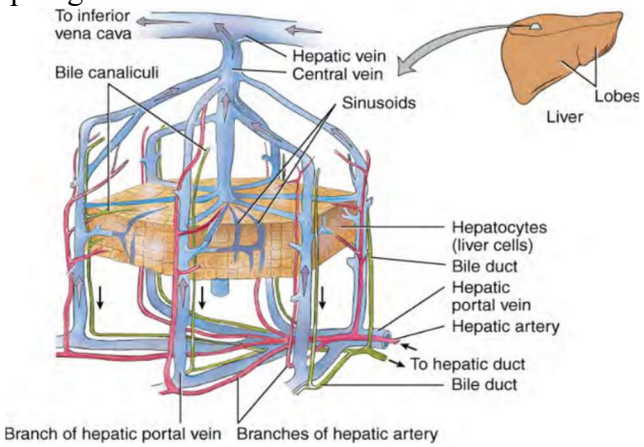
Stomach

- The cardiac sphincter is where the esophagus enters the stomach
- Fundus is the part of the stomach above the cardiac opening
- The cardiac part of the stomach is adjacent to the opening
- The body is the main part of the stomach
- Pyloric sphincter opens to the duodenum
- Greater and lesser curvatures attach to the omenta

- Stomach has a third muscularis layer: oblique
- Rugae are the folds in the stomach

Liver

- The liver has 2 major lobes, left & right, and 2 minor lobes, caudate & quadrate.
- Porta Hepatis is the inferior surface where the ducts, blood vessels, and nerves enter and exit the liver
- The falciform ligament connects the liver to the anterior body wall
- The coronary ligament connects the liver to the diaphragm
- Bile produced by the liver exits through either the left or right hepatic ducts which unite to form the common hepatic duct
- The bile either enters the duodenum through the common bile duct or enters the gall bladder through the cystic duct
- The liver is divided into about 100,000 lobules:
  - Central vein in the centre
  - Hepatic cords radiate from the central vein and are composed of hepatocytes
  - Hepatic sinusoids between hepatocytes

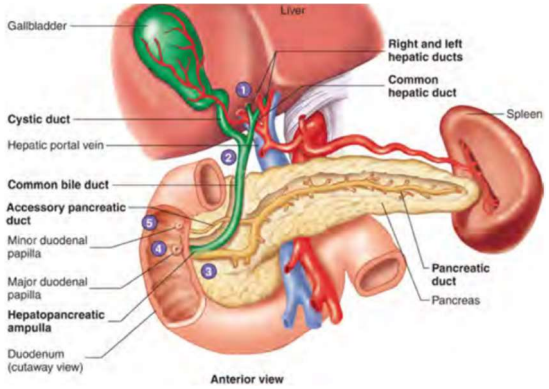


Gallbladder

- A sac located posterior to the liver
- Bile is constantly stored and concentrated
- Cholecystokinin and vagal nerves stimulate the gallbladder to secrete bile through the cystic and common bile ducts

Pancreas

- The pancreas has a head, body, and tail
- The pancreas has both an endocrine and exocrine function:
  - Endocrine: alpha and beta cells of the Islets of Langerhans produce glucagon and insulin
  - Exocrine: Acini groups from lobules and produce enzymes
- Enzymes exit the pancreas and enter the duodenum via:
  - Acinar cells → Intercalated ducts → Intralobular ducts → Interlobular ducts → Pancreatic duct → hepatopancreatic ampulla



Small Intestine

- The site of the greatest digestion and nutrient/water absorption
- Divisions of the small intestine
  - Duodenum (25cm)
  - Jejunum (2.5m)
  - Ileum (3.5m)
- Features that increase the surface area of the small intestine include; plicae circulares, villi, and microvilli
- There is a gradual decrease in the diameter, intestinal wall thickness, and number of villi as you continue through the small intestine

Large Intestine

- Starts at the Ileocecal junction and ends at the anus

- Consists of the caecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum, and anus
- Chyme is converted to faeces
- Functions of the large intestine include water absorption and mucous secretion

Rectum and Anus

- Straight muscular tube lined by non-keratinized stratified squamous epithelium
- Internal (smooth) sphincter and external (skeletal) sphincter

Mastication

Mastication is the process of chewing food and breaking it down into small digestible pieces with your teeth.

Muscles involved

- Elevation of the mandible
  - Temporalis, masseter, medial pterygoids
- Depression of the mandible
  - Lateral pterygoids
- Protraction and Excursion
  - Pterygoids and masseter
- Retraction
  - Temporalis

Mastication reflex

- Medulla Oblongata
- Cerebrum provides conscious control

Swallowing (Deglutition)

There are three phases to the swallowing of food:

1. Voluntary
   - Bolus of food is moved into the pharynx by the tongue
2. Pharyngeal Reflex
   - Controlled by the medulla oblongata
   - Soft palate elevates and esophageal sphincter relaxes
   - Food is pushed into the esophagus by the pharyngeal constrictors
   - Epiglottis is closed
   - Larynx elevates to prevent food entering the airway
3. Esophageal Reflex
   - Stretching of the esophagus causes the enteric nervous system to initiate peristalsis of muscles in the esophagus

Movement in the Small Intestine

Throughout the small intestine segmental contractions mix the chyme and peristalsis propels the chyme.

Gastro-ileal Reflex

- Gastrin is released when the activity of the stomach increases
- Results in the relaxation of the Ileocaecal sphincter and an increase of segmental contractions in the Ileum to empty the small intestine
- Peristaltic waves move the chyme from the ileum into the caecum
- Distention of the caecum causes a local reflex to constrict the ileocaecal sphincter, preventing more chyme from entering the caecum and preventing backflow

Mechanical Digestion in the Small Intestine

Haustral churning/contractions

- Relaxed haustrae are filled by muscular contractions

- Chyme is shuffled back and forth on 30minute intervals
- Controlled by local reflexes

Mass Movement

- Peristaltic waves continue along the length of the transverse colon
- Waves persist for about 10-30minutes
- Controlled by two reflexes
  - Gastro-colic reflex: mass movement initiated by contents of stomach
  - Duodeno-colic reflex: mass movement initiated by contents of duodenum

Defaecation Reflex

- Distention of the rectal walls by faeces stimulates the parasympathetic nervous system
- These reflexes cause the internal anal sphincter to relax and contractions of the colon to push the contents of the rectum toward the anus
- Accompanied by voluntary movements to expel the faeces

Regulation of the Digestive System

Nervous System

- Local: Enteric nervous system
  - Sensory, motor, and interneurons
  - Coordinates peristalsis and other local reflexes
- General
  - Coordinated by the central nervous system
  - May initiate long reflexes due to senses
- Parasympathetic
  - Stimulate muscle contractions and secretions
- Sympathetic
  - Inhibits muscle contraction and secretions
  - Reduces blood flow to the Gastro-intestinal Tract (GIT)\

Chemical Regulation

- Production of Hormones
  - e.g., gastrin, secretin, cholecystokinin (CCK)
  - 17 types of enteroendocrine cells in the Gastro-intestinal Tract (GIT)
- Paracrine chemicals
  - Secreted by cells into interstitial fluid to have a local effect on nearby cells (e.g., histamine)

Digestion in the Mouth

Mechanical digestion

- Breakdown of food into smaller pieces by mastication
- Mixes with the saliva to produce a bolus

Chemical digestion

- a-amylase begins digestion of starch into disaccharides
- Lingual lipase begins the breakdown of triglycerides

Salivary Glands

Extrinsic

- Parotid, submandibular, sublingual
- Produce 1 to 1.5 liters of saliva per day
- Responsible for serous and mucous secretions
- Saliva composition
  - 99.5% water

- 0.5% solutes; salt, mucin, lysosomes, amylase, lipase

Intrinsic

- Lingual and Buccal glands located on the tongue and oral cavity

Functions of the saliva

- Lubricates food to form the bolus (easier to swallow)
- Dissolves foods chemicals for the taste
- Buffers in saliva to neutralize acidic foods
- Chemical digestion by enzymes such as amylase and lipase
- Antimicrobial due to the presence of lysosomes and IgA proteins
- Contains minerals (e.g., calcium and phosphate) for teeth health

Digestion in the Stomach

Histology of the mucous membrane

- Simple columnar epithelium
- Several gastric glands located in the gastric pits
- Gastric gland cells include:
  - Mucous neck cells: secrete mucous
  - Parietal cells: secrete HCl and intrinsic factor
  - Chief cells: secretes pepsinogen and gastric lipase
  - Enteroendocrine (EE) cells: releases regulatory hormones

Chyme

The chyme is the food that was ingested plus the secretions of the stomach.

Secretions

- Mucous
  - Secreted by surface simple columnar cells
  - Viscous and alkaline
  - Protects cells from acidic chyme and pepsin
- Intrinsic Factor
  - Secreted by the parietal cells
  - Binds with vitamin B12 for increased absorption in the terminal Ileum
- HCl
  - Released by parietal cells
  - Kills bacteria
  - Inactivates salivary amylase therefore stopping the digestion of carbohydrates
  - Denatures proteins
- Pepsinogen
  - Secreted by chief cells (zymogen granules)
  - Pepsin breaks proteins down into amino acids
- Gastrin
  - Secreted by G-cells (type of EE cell)
  - Stimulates the release of stomach acid
- Histamine
  - Secreted by the Enterochromaffin cells
  - Stimulates the secretion of stomach acid

Stomach digestion

1. Cephalic phase
   - Sensory information stimulates the medulla oblongata
   - Impulse sent to the stomach via the vagus nerve
   - Stimulates secretion of HCl, pepsin, gastrin, and histamine
   - Gastrin and histamine cause further HCl secretions

2. Gastric phase
    - Distention of the stomach activates the parasympathetic reflex causing the medulla oblongata to stimulate stomach secretions
    - Distention also stimulates local (enteric) reflexes to amplify the stomach secretions
    - Gastrin and histamine also stimulate stomach secretions
3. Intestinal phase
    - Duodenum chemorecpetors send sensory input to the stomacg (via the vagus nerve) to stop stomach secretions
    - Secretin and cholecystokinin (CKK) decrease stomach secretions

Absorption of nutrients in the stomach

- Very minimal absorption in the stomach
- Water with electrolytes
- Some drugs (e.g., asprin and alcohol)

Digestion in the Small Intestine

Histology

- Villi are lined with simple columnar epithelium
- Columnar cells are modified to increase the surface area with microvilli
- Between columnar cells are goblet cells that secrete mucous
- Under the villi lies blood capillaries and lacteals

Secretions

- Intestinal juice (succus entericus)
    - Secreted into the crypts of Lieberkuhn
    - Consists of water, electrolytes, and mucous
    - Involved in dilution, lubrication, and protection
- Alkaline mucous
    - Secreted by Brunner's glands in the submucosa
    - Neutralize acidic chyme from the stomach
    - Stimulated by vagus nerve and secretin
- Digestive enzymes
    - Bound to the cell membrane of enterocytes
    - Composed of disaccharides, peptidases, and nucleosidases

Regulation of Intestinal Secretion and Mobility

- Enteric (local) reflexes; presence of chyme in the stomach
    - Increase the mobility of the intestine
    - Enterogastrones (CCK and Secretin) increase intestinal juices
    - Vasoactive intestinal peptide (VIP) stimulates intestinal juice production and capillary dilation
- Segmentation
    - Depends on the distention of the small intestine
    - Impulses are sent to the enteric plexus and central nervous system (CNS)

Pancreas

Secretions

1. Aqueous potion
    - Water containing ions such as Na^+, K^+, HCO_3^-
    - Has a pH of 8 to lower the duodenal pH and inhibit pepsin
2. Enzymatic portion

- Pancreatic amylase, pancreatic lipase, trypsinogen, chymotrypsinogen, and procarboxypeptidase

Control of the pancreatic secretions

- Vagus nerve
  - Stimulates secretions of enzymes
- Secretin
  - Acidity in the duodenum causes the release of secretin to act on the pancreas and increase HCO_3^- secretion
- Cholecystokinin (CKK)
  - Fats and proteins in the duodenum cause increased secretion of digestive enzymes from the pancreas
- Gastrin Inhibitory Peptide (GIP)
  - Increased blood glucose causes increased insulin release

Liver

Bile production

- Bile is a yellow-greenish solution produced by the liver
- Contains bile salts, bilirubin, cholesterol, fats, hormones, and lecithin
- Has a pH of 7.6-8.6, nutrilises and dilutes stomach acids
- Bile salts emulsify fats to be reabsorbed by the ileum
- Secretin (from the duodenum) stimulates the secretion of bile

Control of bile secretion

- Vagus nerve causes the gall bladder to contract and release bile into the duodenum
- Secretin and CCK from the duodenum causes the gallbladder to contract and hepatopancreatic sphincter to relax to release bile into the duodenum
- Bile salts stimulate the secretion of bile

Metabolic functions

- Gluconeogenisis: production of glucose from proteins
- Glycogenesis: formation of glycogen from glucose
- Glycogenolysis: breakdown of glycogen into glycose

Lipid Metabolism

- Synthesis of cholesterol
- Synthesis of lipoproteins
  - HDL and VLDL
- Stores tryglycerides
- Breaks down fatty acids into ATP

Protein metabolism

- Deamination: removes amine group from amino groups for gluconeogenesis
- Converts toxic ammonia into urea for excretion by the kidneys
- Synthesis of plasma proteins
- Converts amino acids (transaminations)

Other liver functions

- Detoxifies the blood by removing or altering drugs
- Removes waste products such as bilirubin from the haem
- Releases bile salts, helps digestion by emulsification
- Stores fat soluble vitamins including vitamin's A, D, E, & K
- Stores iron and copper
- Kupffer cells phagocytose worn out blood cells and bacteria
- Activates vitamin D

Digestion in the large intestine

Secretions

- No enzymes are secreted by the large intestines
- The parasympathetic nervous system (PNS) stimulates goblet cells to secrete mucous

Bacteria

- Ferment the undigested carbohydrates
- Conversion of undigested proteins into simpler substances
- Turn bilirubin into urobilinogen which produces the brown colour

The Immune System

The immune system is a collection of cells, tissues, proteins, and organs widely distributed throughout the body. Functions of the immune system include:

- Homeostatic mechanisms
- Detection of changes (surveillance)
- Discrimination between self and foreign
- Defense against attack from foreign substances

There are two categories to the immune system;

1. Innate
    - Non-specific immune response
    - Usually present at birth (does not require previous exposure to foreign antigen)
    - First line of defense are physical barriers
    - Second line of defense includes chemical mediators, white blood cells, inflammation, and fever
2. Adaptive
    - A immune response based on the ability to recognize a specific foreign antibody
    - Acquired during a person's lifetime depending on their exposure
    - Includes antibody mediated (humoral) and cell mediated responses

The innate immune system

Physical barriers

Mechanical barriers such as the skin and mucosa membranes prevent the invasion of foreign antigens. Competition with the natural flora (NF) prevents the colonization of foreign microbes. The secretions sebum, acids in gastric juices, spermine/zinc in semen, lysosomes in tears/saliva, and mucous in the respiratory/digestive tracts, that kill or remove microbes.

Chemical mediators

Chemical mediators are substances responsible for many aspects of innate immunity. Surface chemicals such as lysosomes, sebum, and mucus kill or prevent invasion of microbes. Histamine, complement, prostaglandins, and leukotrienes promote inflammation. Cytokines regulate the intensity and duration of an immune response.

White blood cells

White blood cells (leucocytes) are produced in the bone marrow and lymphatic tissue before they are released into the circulatory system. Chemicals are released by injured or infected areas which attract white blood cells. There are many different types of white blood cells;

Cell type	Function
Neutrophil	Circulate in the blood. First to arrive at the infected tissue. Provides phagocytotic protection and releases chemotactic factors to increase inflammation and attract other cells. Pus is the accumulation of dead neutrophils
Macrophages	Most effective phagocyte, derived from monocytes. Produce chemicals (prostaglandins) to enhance the immune response. Important in the later stages of an infection.
Basophils	Motile cells that exit the blood, enter the tissue, and release chemicals to promote inflammation
Eosinophils	Enter tissues from the blood and defend against parasites by secreting enzymes. Also involved in inflammation
Natural killer cells	Releases chemicals that cause the lysis of tumors and cells infected with a virus

Inflammation

A complex sequence of events that responds to the damage of tissues including trauma, burns, chemicals, and infection.

Inflammation can be local, confined to a particular area, or systemic, meaning it is spread throughout the body.

The purpose of inflammation is to:

- Reduce the spread of the pathogen
- Removal of damaged tissues and debris
- Repair of damaged tissue

The four cardinal signs of inflammation are pain, heat, swelling, and redness.

Chemical mediators such as histamine, kinins, and prostaglandins are released by the mast cells to product these effects:

- Increase in vasodilation
  - Increases the blood flow (nutrients and oxygen) to the affected area
  - Results in heat and redness
- Increase in capillary permeability
  - Fluid containing nutrients flows into the damaged area
  - Results in swelling and pain
- Chemotaxis
  - Attracts more white blood cells to the area

Fever

Fever is induced by the release of pyrogens by white blood cells. The pyrogens act directly on the thermoregulatory control centre of the hypothalamus to increase the body temperature.

The purpose of the fever is to:

- Increase the action of some antimicrobial substances
- Decrease the growth of microorganisms
- Increase the rate of tissue repair

Adaptive Immunity

Antigen

Antigens are large molecules that stimulate the adaptive immune response. Antigens can be one of two types:

- Foreign (non-self) – not produced by the body
- Self – produced by the body

Antibodies

Antibodies are proteins produced in the response to a foreign antigen during a humoral immune response. Antibodies are part of a group known as immunoglobulins. The antigen binding site of an antibody binds to the antigen and affects it by either interfering with the antigens ability to function or rendering the antigen ineffective. There are five classes of antibodies denoted as: IgG, IgM, IgA, IgD, IgE.

Humoral (Antibody Mediated) response

B-lymphocytes mediate humoral immunity by producing antibodies in the response to an infection. B-lymphocytes are developed from stem cells in the red bone marrow. Antigen presenting cells (APC) such as dendritic cells and macrophages phagocytose extracellular pathogens of foreign particles and present the antigen on its surface via MHCII. The antigen presenting cell (APC) travels to a local lymph node and presents the antigen to the T-helper cells using CD4. Each B-lymphocyte has a unique antibody on its surface; therefore the antigen and T-helper cells only stimulate one specific B-cell. That B-cell enlarges and divides, and each clone cell becomes either a plasma cell or memory B-cell. Plasma cells produce approximately 2000 of the specific antibodies per second. Effects of antibodies are:

- Inactivate the antigen
- Clump the antigens together (agglutination)
- Facilitate phagocytosis (opsonization)
- Activate complement

Cell Mediated Immunity

Cell mediated immunity is effective against intracellular antigens such as viruses, mycobacteria, and cancer cells. T-lymphocytes originate from the stem cells in the bone marrow that later migrate and mature in the thymus due to the hormone Thymosin. Antigen presenting cells (APC) present the antigen to T-helper cells in the lymphatic tissue through the use of MHCII and CD4. The T-helper cells stimulate B-cells and cytotoxic (killer) T-cells using CD8. Cytotoxic T-cells (T_C) bind to infected cells via CD8 that display the infectious antigen via MHCI, and kill the cell by releasing chemicals that cause lysis or apoptosis. Regulatory T-cells suppress the immune response when the antigen has been removed. Natural killer (NK) cells recognize when a cell s showing reduced MHCI and kills the cell using cytotoxic molecules.

Antibody responses

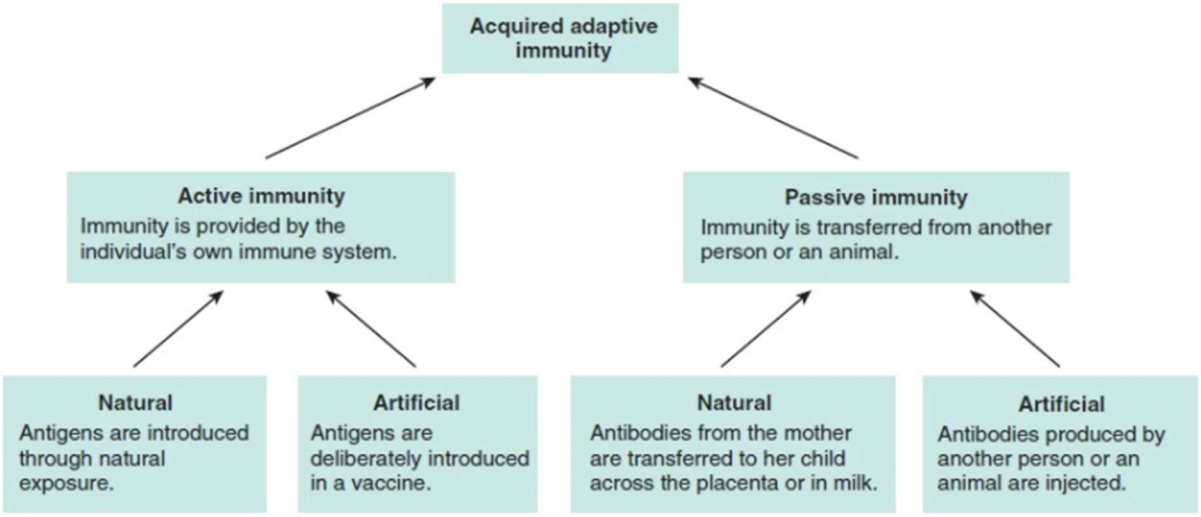
Primary response

The initial exposure to an antigen stimulates a primary humoral response. When a B-cell is first activated by an antigen it takes a few days for the B-cell to proliferate and produce plasma cells and memory cells.

Secondary response

The secondary response is the second or subsequent exposure to the same antigen. It is a much quicker response as memory cells divide much more rapidly to form plasma cells and additional memory cells.

Acquiring adaptive immunity



Vaccines

A vaccine is a biological preparation, usually administered by injection, that improves immunity to a specific disease by stimulating the production of antibodies.

The Male Reproductive System

Cell division

Mitosis

Mitosis is a process in which an exact genetic copy of a parent cell is created.

- For this to occur DNA replication must occur beforehand
- The parent cell produces two diploid cells
- Both diploid cells have the full 23 chromosomal pairs (46 chromosomes in total)
- Steps include: Interphase, Prophase, Metaphase, Anaphase, Telophase
- Used for replacement, repair, or proliferation

Meiosis

Meiosis is a process in which a parent cell divides to form 4 daughter cells with the haploid number of chromosomes

- Two consecutive cell divisions with only one DNA replication
- Produces 4 haploid cells each with 23 chromosomes
- Each of the 4 daughter cells is unique due to the recombination of genetic material caused by random assortment and crossing over
- The union of two haploid cells produces one diploid cells

Gametogenesis

The process in which we produce haploid cells called gametes

Oogenesis

- The gamete produced is called an ovum
- Oogenesis occurs before birth
- Ova are released between puberty and menopause
- Occurs in the ovaries of a female

Spermatogenesis

- The gametes produced are called spermatozoa
- Occurs in the seminiferous tubules of the testes in males

- Includes the process spermiogenesis
- Process begins at puberty (about 14 years) and continues throughout life
- Males produce about 400 million spermatozoa per day
- Each sperm cell contains both the persons maternal and paternal genes
- Spermatogenesis: production of spermatid from stem cells
- Spermiogenesis: transformation of spermatid into spermatozoa

Spermatogenesis

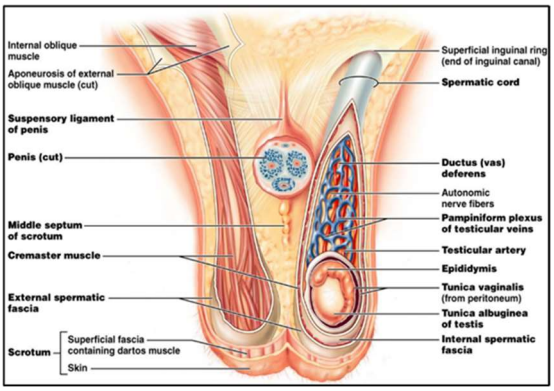
1. Stem cells, called Spermatogonia, in the seminiferous tubules divide to form two types of cells
   - Type A: remains as a spermatogonium in the germinal layer to produce more stem cells
   - Type B: becomes a primary spermatocyte and is pushed into the lumen
2. The primary spermatocyte divides by meiosis to form 2 secondary spermatocytes
3. The secondary spermatocytes divide again to form 2 spermatids each

   Each primary spermatocyte produces 4 spermatids

4. Each spermatid undergoes spermiogenesis to differentiate and form sperm (takes approximately 24 days)
   - Includes condensing nucleus, acrosome formation, body elongation, and tail formation
5. The resulting spermatozoon has a head, midpiece, and tail corresponding to genetic, metabolic, and locomotor regions

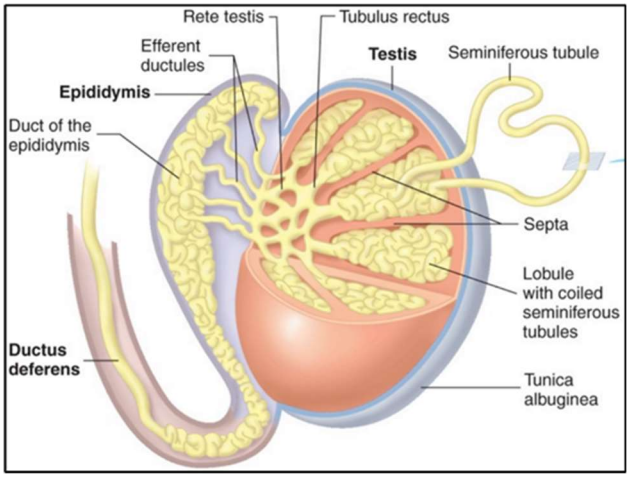
Anatomy of the male reproductive system

Scrotum



- Contains two testes in lateral pouches
  - Left testis is generally suspended lower than the right
- Has internal median septum to prevent testis movement
- Contains the dartos muscle, spermatic cord, and cremaster muscle
- Dartos muscle is responsible for folding of skin in the cold weather
- Cremaster muscle surrounds spermatic cord and contracts to pull testes up during cold weather
- The spermatic cord consists of the testicular artery, testicular vein, testicular nerves, ductus deferens, and pampiniform plexus
- The pampiniform plexus acts as a radiator to prevent excess heat from reaching the testes and impairing the production of sperm
- Therefore, the pampiniform plexus, dartos muscle, and cremaster muscle maintain a 2-3^{o}c cooler temperature for the scrotum

Testes



- The function of the testes is to produce sperm and testosterone
- Each testis is an oval shape about 4cm long and 2.5cm wide
- Each testis is surrounded by the tunica albuginea
- Septa divide the testes into about 250 lobules containing 1 to 4 seminiferous tubules
- Seminiferous tubules are each about 70cm long
- Seminiferous tubules from each lobe join to form tubulus rectus
- Tubulus rectus from rene testis which exit testis via the epididymis into the ductus (vans) deferens

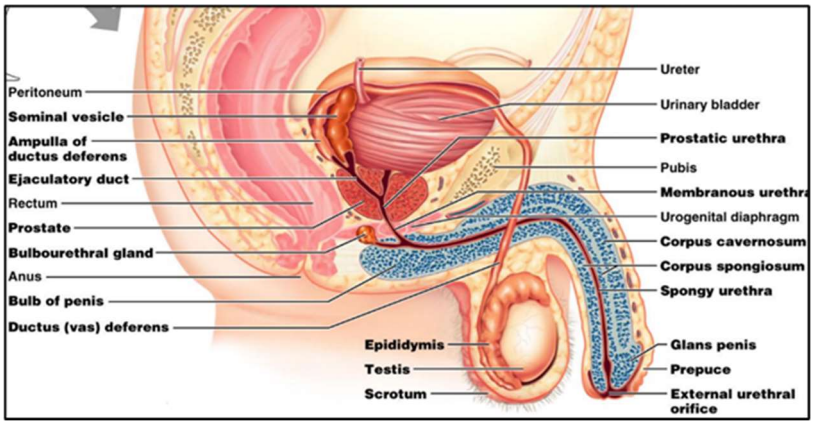
Seminiferous Tubules

- Between seminiferous tubules are clusters of interstitial cells (Leydig cells) responsible for producing testosterone
- Each seminiferous tubule is lined with:
  - Myoid cells (smooth muscle)
  - Lined by germinal epithelium
  - Sertoli cells

Epididymis

- The efferent ductules transport non-motile spermatozoa from the rene testis into the epididymis
- The epididymis is a highly coiled tube sitting on the posterior aspect of the testis lined with pseudostratified columnar epithelium
- Within the epididymis the sperm mature further, but remain non-motile and unfunctional

Ductus (Vans) Deferens



- The ductus deferens leaves the tail of the epididymis and travels up through the spermatic cord and inguinal canal to merge with the seminal vessel and form the ejaculatory duct
- At the ejaculatory duct sperm and seminal fluid is combined before moving into the urethra

Urethra

- The urethra is divided into three regions:
  - Prostatic urethra
  - Membranous urethra
  - Spongy urethra

Seminal Vesicles

- Small, coiled gland on the posterior of the bladder
- Produces 60% of the seminal fluid containing fructose, citric acid, prostaglandins, and fibrinogen

Prostate Gland

- Thick gland surrounding the urethra below the bladder

- Produces 30% of the seminal fluid containing enzymes that activate the sperm as well as clotting factors, and fibrinolysin

Bulbourethral (Cowper's) Gland

- Gland inferior to the prostate
- Secretes 5% of the seminal fluid containing mucous which lubricates and decreases the acidity of the urethra

Penis

- Output for both the urinary and male reproductive system
- Projects anteriorly and inferiorly to the pubic bone
- Contains erectile tissue for the erection response
- The penis is divided into three regions:
  - Two corpus cavernosum layers surrounded by the tunica albuginea
  - Corpus spongiosum forms the bulb of the penis and extends to form the glans penis
- Glans penis is covered by skin called the prepuce (foreskin)

Blood supply to the penis

- Pudendal artery supplies the external genitalia
  - Branches off the internal iliac artery
- Pudendal veins drain to the internal prostate veins
- Neuron innervation is from the pudendal nerve

Erection of the Penis

Erection

- Attained by a parasympathetic response
- Smooth muscle relaxation increases blood flow into the sinusoids of the cavernosum and spongiosum
- Parasympathetic nervous system (PNS) stimulates the bulbourethral gland to secrete mucous

Ejaculation

- Attained by a sympathetic response
- Blood flow to the corpus cavernosum decreases
- Seminal vesicle and prostate gland are stimulated to release their secretions

Hormonal Regulation

- Hormonal regulation occurs through the hypothalamic-pituitary-gonadal (HPG) axis
- The hypothalamus releases gonadotropin releasing hormone (GnRH) into the Hypothalamohypophysial portal system
  - Anterior pituitary secretes follicle stimulating hormone (FSH) and luteinizing hormone (LH) in response to GnRH
  - FSH stimulates spermatogenesis by causing Sertoli cells to release androgen binding protein (ABP)
  - LH binds to the interstitial (Leydig) cells producing testosterone
- Testosterone triggers spermatogenesis, maturation of sex organs, increases libido, and increases muscle mass
- Inhibin is a hormone released by Sertoli cells when the sperm count is too high to decrease the secretion of FSH from the anterior pituitary

The Female Reproductive System

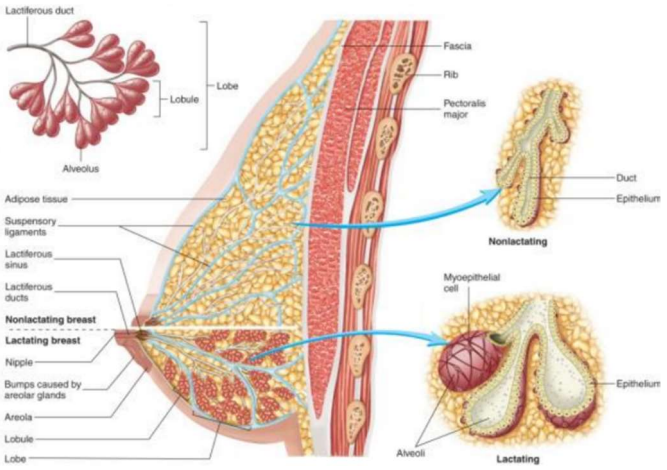
Functions

- Production of gametes (oocytes) through oogenesis
- Enhances fertilization by transporting the spermatozoa to the ovum
- Development and nourishment of future offspring
- Production of reproduction hormones

Anatomy of the Female reproductive system

The breasts

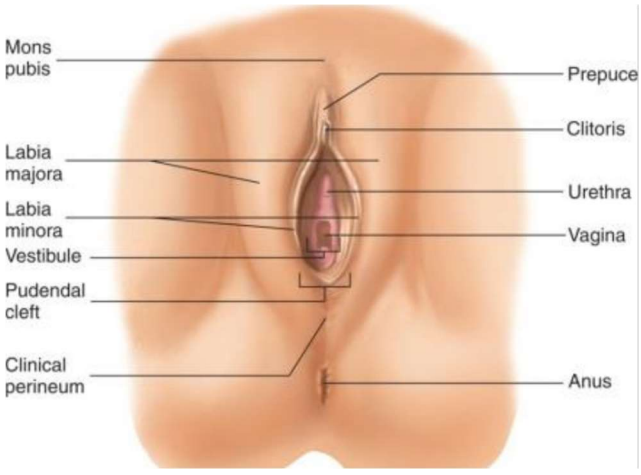
- Anterior to the pectoralis major muscle
- The nipple, pigmented projection, contains a series of lactiferous duct openings for milk release
- The region surrounding the nipple, the areola contains sebaceous glands which secrete sebum
- Strands of connective tissue called Cooper's (suspensory) ligaments support each breast by attaching to the pectoralis major
- Each breast contains mammary glands, modified sweat glands, that synthesize milk
- Each mammary gland is broken down into lobes separated by adipose tissue, divided into lobules containing alveoli
- Alveoli and lactiferous ducts develop during late pregnancy due to the hormone prolactin



- Myoepithelial cells contract to propel milk through the lactiferous ducts towards the nipple
- Oxytocin controls the letdown of milk through a positive feedback mechanism

External Genitalia

- Vulva
  - Vaginal vestibule and surrounding structures
- Vestibule
  - Extends from the vaginal opening to the clitoris, surrounded laterally by the labia minora
  - Glands that produce fluid include greater vestibule, lesser vestibule, and paraurethral glands
- Labia minora
  - Skin folds surrounding the vaginal opening, unites to form the prepuce
- Clitoris
  - Anterior border of vestibule, small mass or sensory and erectile tissue
- Labia majora
  - Rounded folds of skin on either side of the labia minora. Medial surfaces covered in numerous sebaceous and sweat glands
- Mons pubis
  - Labia majora merge anteriorly to the symphysis pubis to form the mons pubis

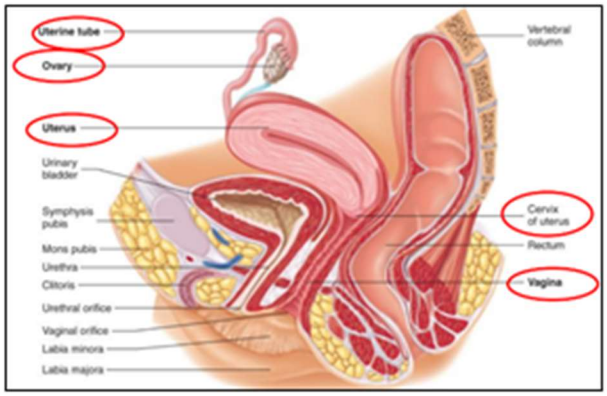


Perineum

- Diamond shaped region medial to the thighs and buttocks containing the external genitalia and the anus
- Clinical perineum (important role in childbirth) is between the vagina and the anus

Vagina

- Female organ of copulation, allows for menstrual flow and childbirth
- A tubular, fibromuscular structure, 10cm canal lined with mucous membrane extending from the exterior body to the uterine cervix
- The hymen covers the vaginal opening
- Fornix is the superior domed portion attached to the cervix
- The vagina is lined with non-keratinized stratified squamous epithelium
- Epithelial cells of the vaginal wall release glycogen for bacteria to metabolize and produce lactic acid, decreasing the pH, making it toxic for foreign pathogens
- The adventitia of the vagina connects to its surrounding structures such as the urethra and urinary bladder



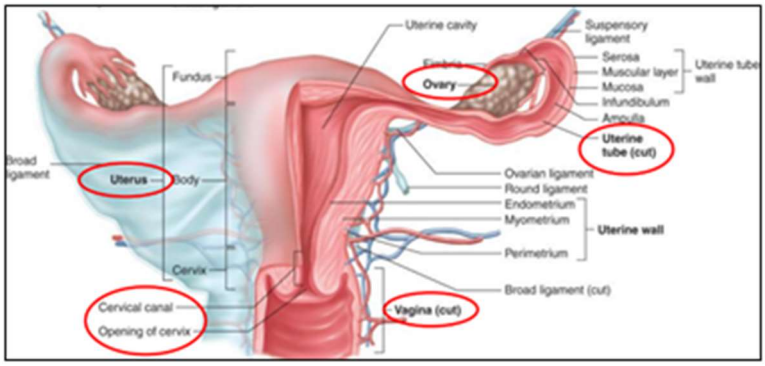
- Supplied by the internal vaginal artery, branching off the uterine artery

Cervix

- Portion projecting into the vagina is known as the ectocervix
- The opening of the ectocervix is called the external OS
- The narrow passage between the external OS and the uterine cavity is referred to as the cervical canal
- The cervical canal in lined with simple columnar epithelium continued from the uterine epithelium
- Mucosal glands in the cervical canal lubricate and increase the acidity of the vagina
- At ovulation, estrogen induces thinning of the mucosa, allowing sperm to get through the cervical canal into the uterus

Uterus

- Pathway for sperm, deposited into the vagina, to reach the uterine (fallopian) tubes
- Site of implantation for the fertilized ovum, development of fetus during pregnancy
- Source of menstrual shedding when implantation does not occur
- Supplied by the uterine artery
- There are three parts to the uterus; fundus, body, and cervix
- Supported by the broad, round, and uterosacral ligaments
- Layers of the uterine wall include:
  - Perimetrium: outer serous membrane
  - Myometrium: three layers of smooth muscle
  - Endometrium: innermost mucous membrane, with a functional and basal layer



Uterine (Fallopian) Tubes

- Two tubes extending laterally from the superior portion of the uterus
- Opens into the peritoneal cavity, fimbriae receive the oocyte from the ovaries
- 10cm route for sperm to fertilize the ovum
- There are three parts to the uterine tubes:
  - Infundibulum: closest to the ovary
  - Ampulla: widest part of the tube where fertilization occurs
  - Isthmus: short, thick walled, joins the uterus

Ovaries

- Size and shape of an almond
- Lateral to the uterus
- Connected to the broad ligaments by mesovarium
- Gonads – site of oogenesis and ovulation
- Produce estrogen and progesterone
- Ligaments holding ovaries in place include:
  - Mesovarium
  - Suspensory ligament
  - Ovarian ligament
- Histology of the ovary
  - Visceral peritoneum: simple columnar epithelium
  - Tunica albuginea: dense fibrous connective tissue
  - Ovary is made up of the cortex, medulla, and stroma

Gametogenesis

Gametogenesis is the process in males and females of producing gamete cells with the haploid number of chromosomes in the gonads. This is done through the process of meiosis.

Oogenesis

- Begins prior to birth and takes years to complete
- Germ cells arise in the embryo and form oogina in the gonadal ridges
- Oogina multiply rapidly by mitosis then enter the growth phase and produce nutrient reserves
- Primordial follicles develop as oogonia are transformed into primary oocytes
- At birth a female has her lifetime supply of oocytes, and by puberty they have 400,000 oocytes
- Primary oocyte begins meiosis I, and stopped in prophase I for 12-14 years
- Beginning of puberty, oocytes are recruited each month in response to a surge in the luteinizing hormone (LH)
- One oocyte continues meiosis I, producing two haploid cells, a secondary oocyte and the first polar body
- The first polar body receives no cytoplasm or organelles, but the secondary oocyte retains material enlarging it
- First polar body is released during ovulation and may undergo meiosis II resulting in two tiny polar bodies
- The secondary oocyte arrests during metaphase II and it is this cell that is ovulated and later fertilized
- When a spermatozoon penetrates the secondary oocyte, it quickly completes meiosis II, forming an ovum and a second polar body
- Therefore, one oogonium undergoes oogenesis to form one functional ovum and three polar bodies

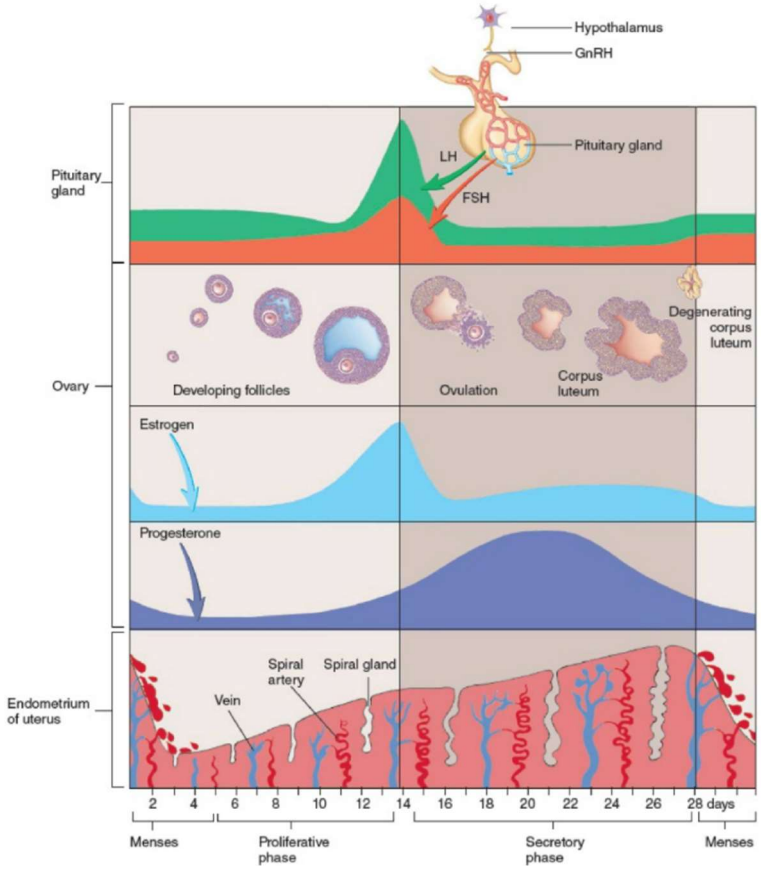
Follicular development

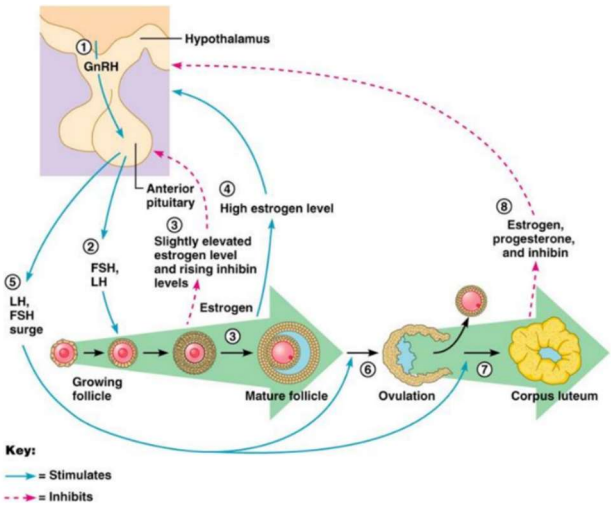
1. The primordial follicle consists of a primary oocyte surrounded by a single layer of squamous granulosa cells
2. A primordial follicle becomes a primary follicle as the granulosa cells become enlarged and cuboidal
3. The primary follicle enlarges are granulosa cells form more than one layer. Zona pellucida surrounds the primary oocyte
4. A secondary follicle forms when fluid-filled vesicles develop among the granulosa cells and a theca becomes apparent around the granulosa cells
5. A mature follicle is formed when the fluid-filled vesicles form a single atrium, and the follicle reaches its maximum size. The primary oocyte undergoes meiosis II to form a secondary oocyte
6. During ovulation, the follicle ruptures to release the secondary oocyte. Cumulus cells surrounding the secondary oocyte form the corona radiata
7. After ovulation, the granulosa cells divide to form the corpus luteum
8. The corpus luteum degenerates to form the corpus albicans

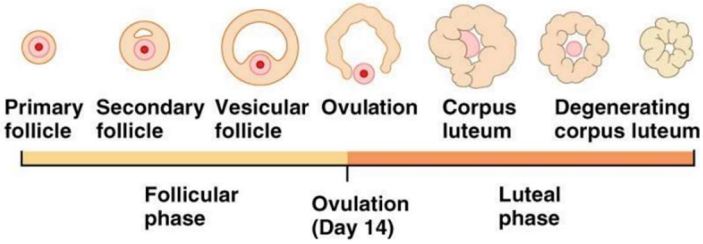
Ovarian Cycle

Average cycle lasts 28 days, although it can vary between 21 and 40 days

Phase	Day	Events
Menstruation	1-5	Uterine bleeding and endometrium shedding
Proliferation	6-14	Phase of follicular development and endometrium build up
Ovulation	14	Rupture of the mature follicle to release the secondary oocyte
Luteal	15-28	Period of corpus luteum activity. Maturation and secretion of uterine glands.







Fertilization and Pregnancy

- Approximately 300 million spermatozoa are ejaculated into the vagina during copulation and are transported through the cervical canal and uterus to the ampulla of the fallopian tubes
- Out of the few dozen sperm that reach the ovum, one spermatozoon must get through the zona pellucida to fertilize the egg
    - Oocyte can be fertilized up to 24 hours after ovulation
    - Sperm are viable in the female reproductive system for 6 days
- One spermatozoon unites with the secondary oocyte to form a diploid cell called the zygote
- The diploid cell multiplies to form an embryo
- The embryo implants in the uterine wall up to 6 days after fertilization
    - Ectopic pregnancy: embryo implants anywhere other than the uterine wall such as the fallopian tube

By Joseph B.