

CELLS OF CENTRAL NERVOUS SYSTEM

- Two types of cells are seen in central nervous system: nerve cells or neurons and glial cells.
- Glial cells are 10 times more in number than neurons.

Types of glial cells are astrocytes, oligodendrocytes, Schwann cells and microglial cells.

- **Astrocytes:**
 - Seen as two groups—Fibrous astrocytes seen in white matter and Protoplasmic astrocytes seen in gray matter.
 - Astrocytes are involved in the formation of the blood-brain barrier.
 - Astrocytes also take up neurotransmitters and K^+ ions from synapses after release from neurons.
 - Astrocytes produce substances that are the major nourishment for neurons namely neurotrophins
- **Oligodendrocytes**—myelination neurons in the central nervous system.
- **Schwann cell** causes myelination of neurons in the peripheral nervous system.
- **Microglial cells** are phagocytic cells.

SENSORY PHYSIOLOGY

- Classified as somatic senses (touch, pain, temperature) and special senses (vision, hearing, smell, taste, balance).
- Somatic senses are conveyed by receptors in skin through first order neurons to spinal cord (second order neurons), to thalamus (ventroposterolateral nucleus third order neurons) and finally to Somatosensory cortex.

TOUCH RECEPTORS

Touch receptors along with their characteristics are as follows:

Touch receptors	Characteristics
Meissner corpuscles	<ul style="list-style-type: none"> • Mainly detect the initial contact of the hand with objects • Respond to changes in texture • Respond to low frequency slow vibrations
Merkel cells	<ul style="list-style-type: none"> • Sensitive to edges, corners and points • Distinguish textures— play key roles in the ability to read Braille for blind people
Pacinian corpuscles	<ul style="list-style-type: none"> • Detect deep pressure and high frequency fast vibration
Ruffini corpuscles	<ul style="list-style-type: none"> • Seen around joint capsules • They respond to sustained pressure • They are very sensitive to skin stretch

MUST KNOW

- Meissner corpuscles and Pacinian corpuscles are rapidly adapting receptors.
- Merkel cells and Ruffini corpuscles are slowly adapting receptors.

PAIN RECEPTORS

- Pain receptors are free nerve endings. They are slowly adapting receptors.
- Pain sensation is carried by $A\delta$ fibers and C fibers.

$A\delta$ fibers	C fibers
<ul style="list-style-type: none"> • Thinly myelinated • responsible for first pain • This type of pain is also called fast pain or epicritic pain • Mainly responsible for localizing the site and intensity of the noxious stimulus • Relatively new in evolution- carried by neospinothalamic tract • Release glutamate as neurotransmitter 	<ul style="list-style-type: none"> • Unmyelinated • responsible for second pain • This type of pain is also called slow pain, protopathic pain • Always dull, intense, diffuse, and gives unpleasant feeling • Very old in evolution- carried by paleospinothalamic tract • Release substance P as neurotransmitter

Gate Control Theory of Pain

- Proposed by Melzack and Wall.
- In Substantia Gelatinosa of spinal cord.
- Dorsal horn neuron receives collaterals from both the touch receptors and pain receptors. Simultaneous activation of innocuous touch receptors reduces the responsiveness of dorsal horn neurons to their input from pain receptor afferents.
- It is the basis behind transcutaneous electrical nerve stimulation (TENS) wherein electrodes are used to activate A α and A β fibers near the site of injury to relieve pain.
- Also, the reason for massaging and applying counterirritants over the injured area relieves pain.

SOMATOSENSORY PATHWAYS

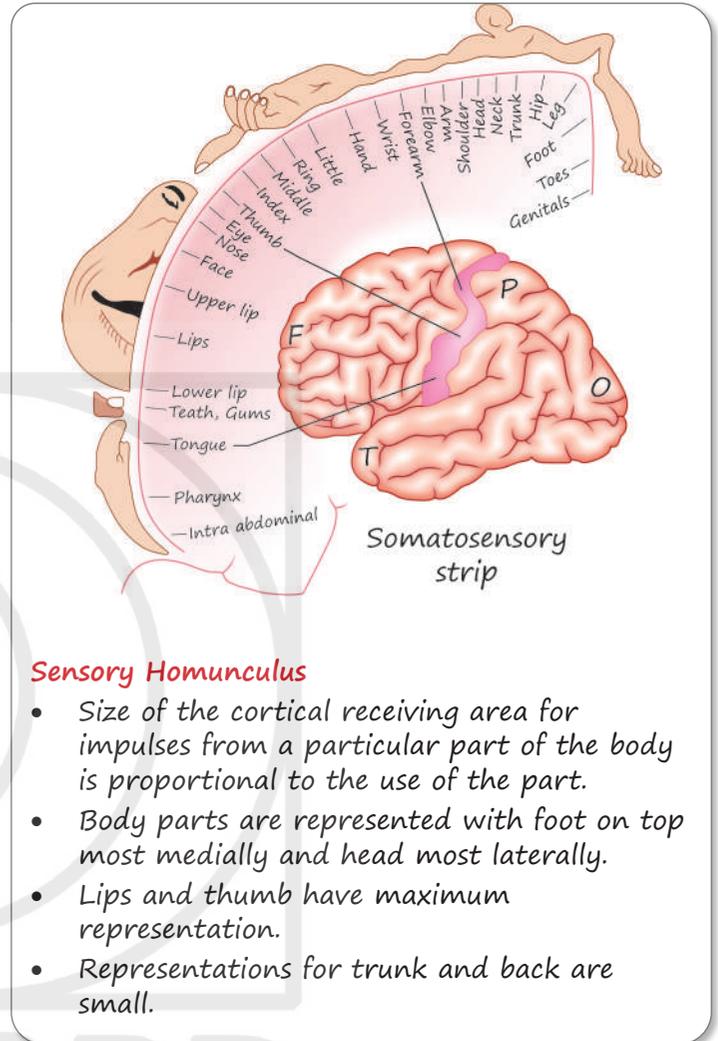
- Dorsal column pathway—Principal pathways for touch, vibration and proprioception. They primarily contain A α and A β afferents. They ascend ipsilaterally (same side) in dorsal column of spinal cord to medulla. In medulla, they synapse with two important nuclei, namely gracilis and cuneate nuclei.
- Anterolateral spinothalamic tract—Principal pathways for pain and temperature sensation. They cross the midline in spinal cord itself (contralateral tract).
- Brown-Sequard syndrome:
 - Ipsilateral loss of joint position and vibratory sense (dorsal column)
 - Contralateral loss of pain and temperature sense (anterolateral spinothalamic tract)
 - Ipsilateral weakness (corticospinal tract) below the lesion

Thalamus

- Thalamus is the general “sensory relay station”:
- Somatic senses reach ventroposterolateral (VPL) nuclei of thalamus.

Somatosensory Cortex

- Primary somatosensory cortex is located in post central gyrus of the parietal lobe, Brodmann area—Areas 3, 1, 2
- Major function of somatosensory cortex is localization of the stimulus.
- Exact localization is possible because all our body regions are represented in the cortex. This representation is called Homunculus.



Sensory Homunculus

- Size of the cortical receiving area for impulses from a particular part of the body is proportional to the use of the part.
- Body parts are represented with foot on top most medially and head most laterally.
- Lips and thumb have maximum representation.
- Representations for trunk and back are small.

Cortical Plasticity and Phantom Limb

- After limb amputation: corresponding area of the somatosensory cortex will not receive input from the limbs.
- Nearby areas encroach upon the somatosensory cortical area previously dedicated for limb by the phenomenon of cortical plasticity or Neuroplasticity.
- Brain interprets the signals from these areas and think as if the information is coming from the missed limb creating phantom sensations and phantom pain.

SPECIAL SENSES

Vision

- Visual information is processed at three important regions, which are retina, lateral geniculate body (thalamus) and visual cortex.
- Retina has seven types of cells.

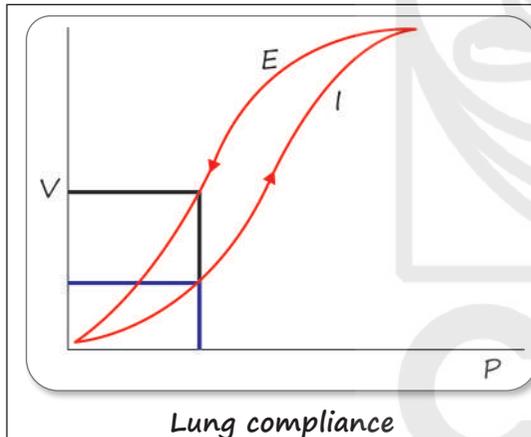
MUSCLES OF INSPIRATION AND EXPIRATION

Pressure changes are aided by contraction of certain muscles to aid the movement of air inside and out of the lung.

- **Muscles of inspiration:** Diaphragm—major muscle for inspiration, external intercostal muscle, Scalene, Sternocleidomastoid.
- **Muscles of expiration:** Expiration is largely a passive process at rest. Because of the elastic nature of lung, it recoils itself during expiration. Active expiration occurs during exercise. Muscles of active expiration are rectus abdominis, external and internal oblique muscles, transversus abdominis, internal intercostal muscles.

PRESSURE VOLUME RELATIONSHIP IN LUNG—THE CONCEPT OF “COMPLIANCE”

- During inspiration, alveoli distend. This distension force is Compliance.

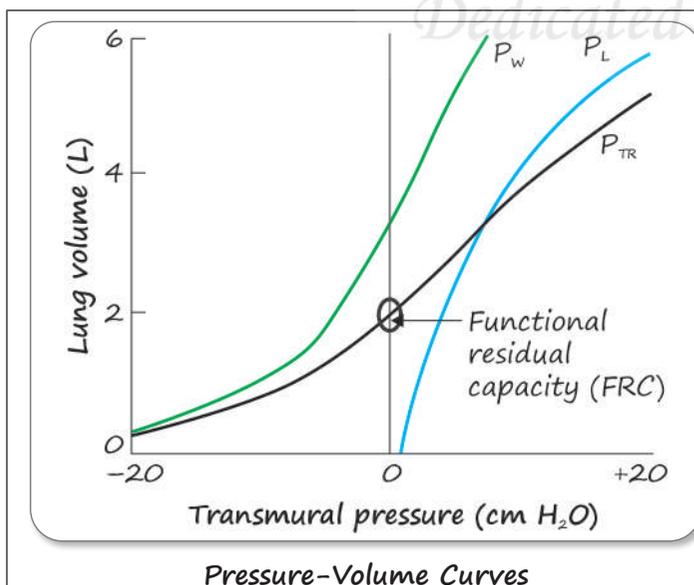


MUST KNOW

Important points to be noted in compliance curve are:

- The curve has inspiratory (I) and expiratory (E) components
- Note that the inspiratory and expiratory compliance curves do not coincide. This difference is called hysteresis
- Compliance is the slope $\Delta V/\Delta P$
- The lung volume at any given pressure is greater during expiration than during inspiration
- Compliance is greatest at mid pressure range
- At high pressures, compliance is lowest (curve flattens)

PRESSURE VOLUME CURVES OF LUNG (P_L), CHEST WALL (P_w), LUNG AND CHEST WALL COMBINED (P_{TR})

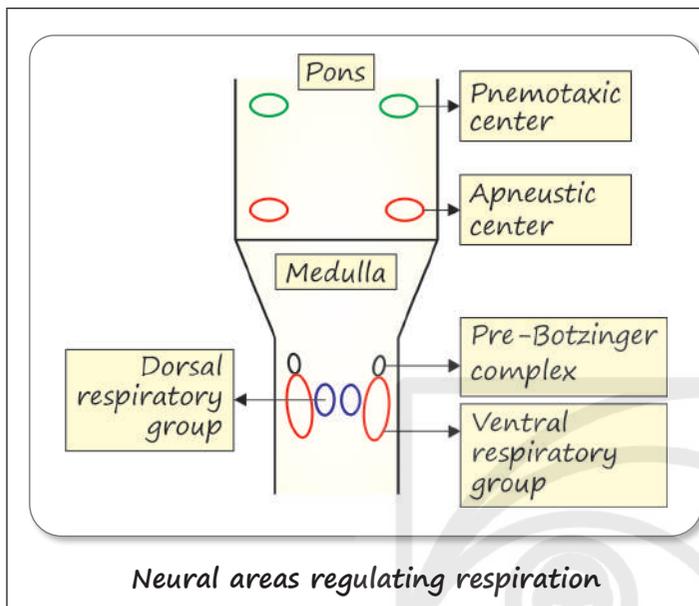


- This distension will be opposed by two opposing forces namely elastic recoil forces and surface tension forces. This surface tension force is held in check by surfactant.
- Compliance is defined as “the change in volume per unit change in the pressure”.
- Compliance = $\Delta V/\Delta P$
- Compliance of lung is 0.2 L/cm water

There are three types of compliance namely Static compliance, Dynamic compliance and Specific compliance.

1. Static compliance is the compliance measured when breathing does not take place.
2. Dynamic compliance is the compliance measured when the subject is breathing. Airway resistance (Impedance to airflow) is considered here.
3. Specific compliance = Compliance/Functional residual capacity (FRC).

- At rest, lung volume is at functional residual capacity (FRC)—the circled point in graph
- The system is relaxed at rest meaning that the inward recoil of lung is balanced by the outward expansion of chest wall (equilibrium point)
- FRC is also called “relaxation volume” or “equilibrium volume”
- If lung was allowed to recoil without the chest wall in expiration at zero pressure the lung is at its MINIMAL VOLUME, which is below residual volume



Brain area	Function
Pre-Botzinger complex	Pacemaker: initiates respiration
Pneumotaxic center	<ul style="list-style-type: none"> Limits inspiration by inhibiting apneustic center. Controls respiratory rate
Apneustic center	Prolong inspiration
Dorsal respiratory group	Generates RAMP signal for smooth increase in tidal volume during inspiration
Ventral respiratory group	Controls forceful expiration during exercise

- If vagus is cut, then respiration becomes slow and deep.
- Lesion below medulla—respiration stops.
- Pontomedullary junction lesion—pons and medulla are separated: Irregular respiration
- Mid pons lesion with vagus cut—pneumotaxic center separated from apneustic center: Inspiration is markedly prolonged. This breathing pattern is called **apneusis or inspiratory spasm**.

Respiratory Reflexes

Hering-Breuer Inflation Reflex

- Hering-Breuer Inflation reflex is atypical negative feedback reflex where “overinflation of lung inhibits further lung inflation”.
- Receptors for this reflex are “slowly adapting receptors.” Afferent information is carried by large myelinated fibers in the vagus.
- Protective reflex prevents overdistension of lung alveoli at larger tidal volumes (1500 mL).

Hering-Breuer Deflation Reflex

- Hering-Breuer deflation reflex is also a preventive reflex where “deflation of the lungs increases the ventilatory rate”.
- Afferent information is carried by large myelinated fibers in the vagus.
- It is a protective reflex which helps prevent atelectasis (collapse) in conditions like pneumothorax.

The Paradoxical Reflex of Head

- The paradoxical reflex of head is paradoxical to **Hering-Breuer inflation reflex** where inflation of lungs causes further inflation.
- This reflex is the cause for lung inflation in newborn immediately after birth when the newborn takes the first breath.

J Receptor Reflex

- J receptors were discovered by an Indian physiologist A S Paintal.
- These receptors are located very close to the pulmonary capillaries (juxtapulmonary receptors).
- These receptors are the endings of slowly conducting unmyelinated vagal C fibers.
- J receptors are activated by increase in the interstitial fluid volume—pulmonary edema
- J receptor reflex is also called “Pulmonary chemoreflex”.
- J receptor reflex response consists of rapid breathing, bradycardia and hypotension.

Altered Breathing Patterns (Periodic Breathing)

- **Cheyne-stokes respiration**
 - Characterized by periods of hyperpnea, hypopnea and apnea—waxing and waning

There are four important types of hypoxia: hypoxic hypoxia, anemic hypoxia, stagnant hypoxia and histotoxic hypoxia

1. Hypoxic hypoxia

- Characterized by low tissue and arterial PO_2
- **Causes:** High altitude, COPD
- Since arterial PO_2 is less, peripheral chemoreceptors are stimulated in hypoxic hypoxia
- **Cyanosis:** Bluish discoloration of skin, when the concentration of reduced hemoglobin in capillary blood exceeds 40 g/L (4 g/dL), is seen in hypoxic hypoxia
- Oxygen therapy with 100% pure oxygen is very helpful in this type of hypoxia

2. Anemic hypoxia

- Characterized by reduction in hemoglobin concentration and reduced oxygen content in blood
- Arterial PO_2 is normal—peripheral chemoreceptors are NOT stimulated
- Anemic hypoxia is seen in carbon monoxide poisoning. Hyperbaric oxygen therapy is helpful in treatment

3. Stagnant hypoxia

- Also called ischemic hypoxia or circulatory hypoxia or hypoperfusion hypoxia
- Arteriovenous O_2 difference (a-v- O_2 difference) is increased in stagnant hypoxia
- Commonly seen in congestive cardiac failure
- Cyanosis is present

4. Histotoxic hypoxia

- Occurs due to blockage of cellular enzymes that utilize oxygen
- Commonly seen in cyanide poisoning
- Cyanide inhibits cytochrome oxidase enzyme in mitochondria leading to blockage of oxidative phosphorylation
- Arteriovenous O_2 difference (a-v- O_2 difference) is decreased in histotoxic hypoxia

ENVIRONMENTAL PHYSIOLOGY

High Altitude Physiology and Pathophysiology

- The most important problem associated with high altitude is “hypoxia”. All the compensatory mechanisms develop to tackle this hypoxia effectively.
- Acclimatization refers to the changes in body tissues in response to long-term exposure to low PO_2 .
- Physiological compensatory responses to high altitude hypoxia are:
 - **Increase in pulmonary ventilation:** Earliest response, Oxygen dissociation curve shifts to RIGHT.
 - **Increased numbers of red blood cells:** Erythropoietin increases RBC count and hemoglobin concentration.
 - **Increased vascularity of the peripheral tissues:** Vascular endothelial growth factor (VEGF)—promotes angiogenesis.
 - Increased diffusing capacity of the lungs.
 - Increased ability of the tissue cells to use O_2 despite low PO_2 .
- **Acute mountain sickness (AMS)**
 - Develops 6–12 hours after ascent to a high altitude.
 - Characterized by nonspecific symptoms like headache and nausea.
 - Symptoms resolve spontaneously if the subject descends to lower altitude.
- **Chronic mountain sickness**
 - Also called **Monge’s disease**.
 - Characterized by excessive erythrocytosis, pulmonary hypertension (moderate to severe), Cor pulmonale.
 - This condition is usually treated with venesection and acetazolamide.
- **High altitude pulmonary edema (HAPE)**
 - Lung responds to hypoxia by vasoconstriction. HAPE develops within 2–4 days after arrival at high altitude.
 - Treatment involves Immediate descent to lower altitude, administration of oxygen (4–6 L/min) and calcium channel blocker nifedipine.

CONDUCTION SYSTEM OF HEART

SA node: “The Pacemaker”—Impulse originates here. Generates impulse at fastest rate (100 impulses/min)

AV node

- AV node conduction is slow. There is a delay of about 0.1 second in spread of impulse.
- This delay is mainly responsible for the sequential contraction of atrium followed by ventricles. It is for this reason AV node is also called “Gatekeeper” to the ventricles.
- Has the slowest impulse conduction velocity (0.04 m/s) due to less number of gap junctions.

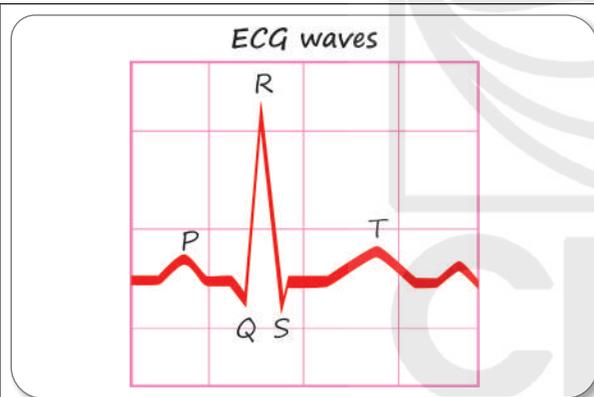
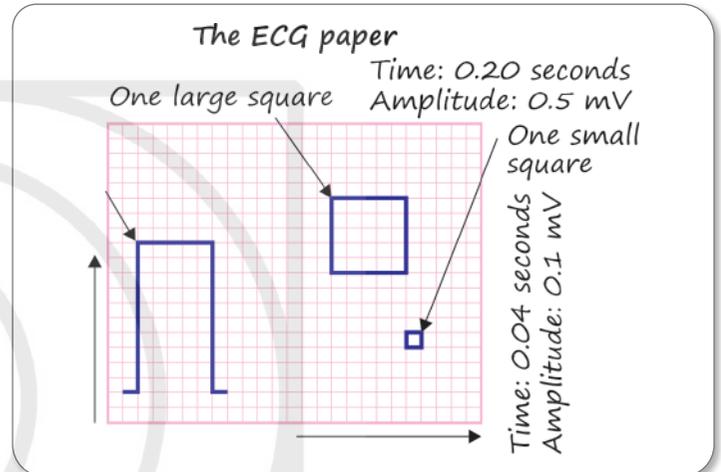
Bundle of His: Receives the impulse from AV node

Purkinje fibers

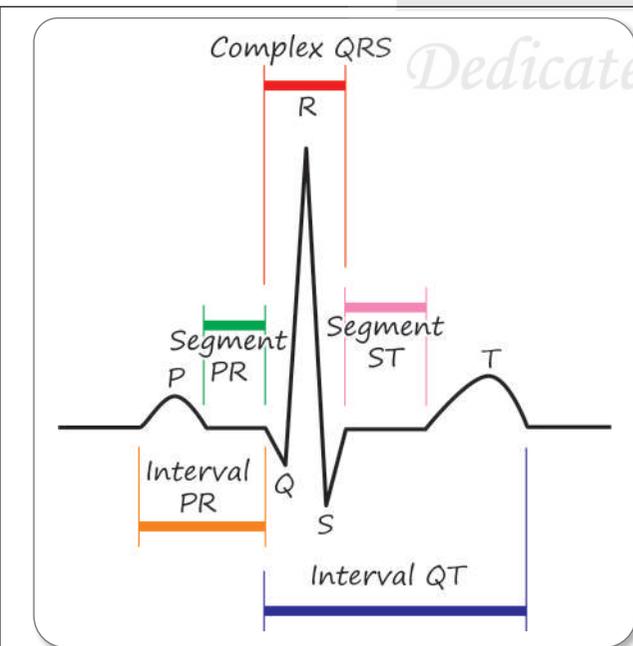
- These are interconnected by numerous gap junctions.
- Have the fastest impulse conduction velocity (4 m/s).

Last parts of the heart to be depolarized are posterobasal portion of the left ventricle, the pulmonary conus, and the uppermost portion of the septum. These are the areas which repolarize first.

ELECTROCARDIOGRAM (ECG)

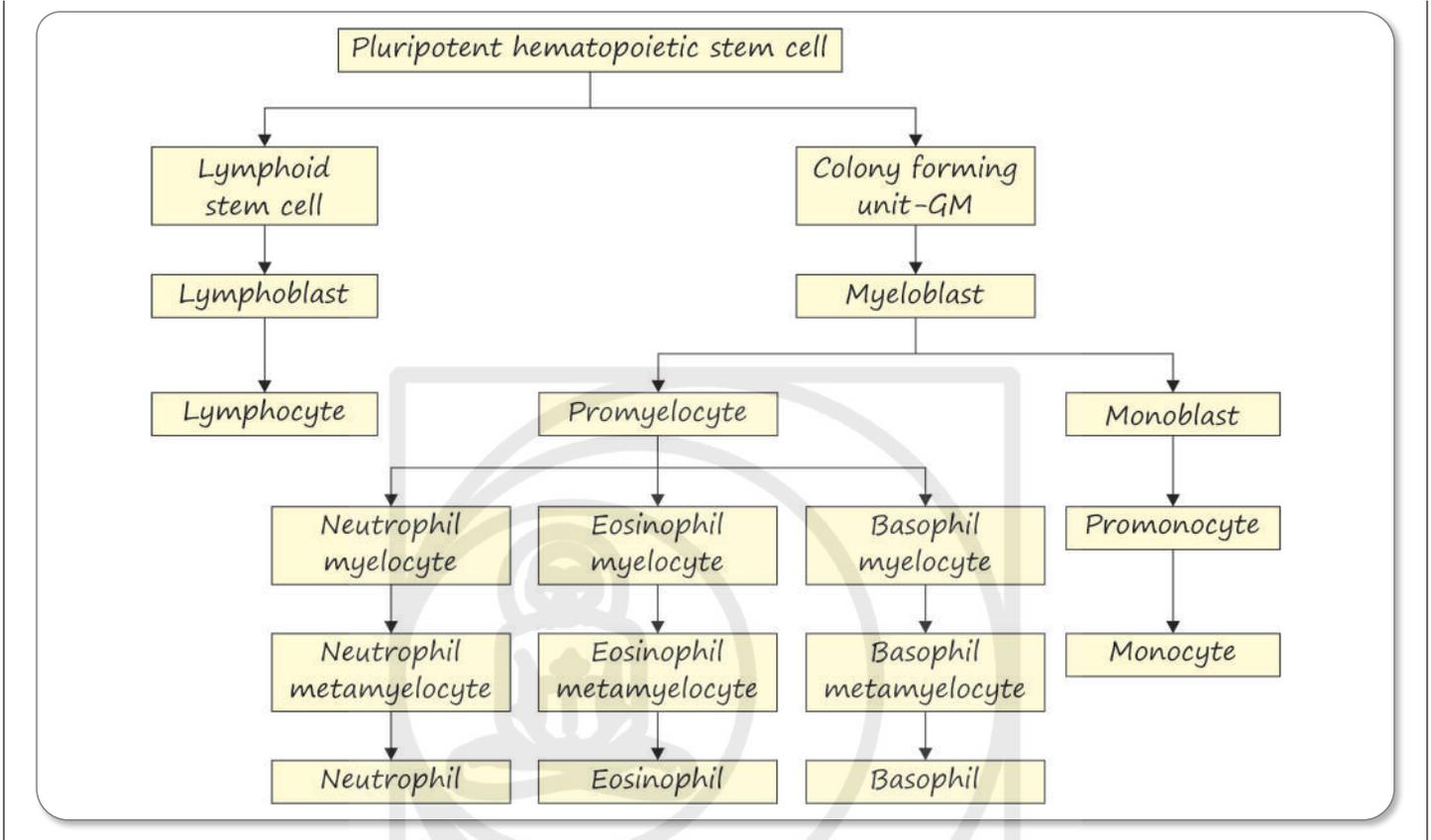


Wave	Cause
P wave	Atrial depolarization
QRS complex	Ventricular depolarization
T wave	Ventricular repolarization
U wave	Papillary muscle repolarization, Purkinje fiber repolarization



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Segments	From to	Denotes
PR	From the end of P wave to the beginning of QRS complex	An isoelectric line that denotes the normal AV nodal delay
ST segment	From the end of S wave (J point) to the beginning of T wave	An isoelectric line that denotes the plateau phase of ventricular action potential



Thrombopoiesis—Formation of Platelets

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            graph TD
              A[Pluripotent hematopoietic stem cell] --> B[GM-CSF thrombo]
              B --> C[Megakaryocyte]
              C --> D[Platelets]
          
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- Important factors that regulate thrombopoiesis are called as megakaryocyte growth factors. They are Thrombopoietin (TPO), IL-11
- **Oprelvekin—recombinant form of IL-11:** Commonly used in cancer chemotherapy induced thrombocytopenia
- **Romiplostim—Thrombopoietin agonist:** Useful in treatment of chronic immune thrombocytopenia
- **Eltrombopag—Thrombopoietin agonist:** Useful in treatment of chronic immune thrombocytopenia, thrombocytopenia in hepatitis C

BLOOD GROUPS AND THEIR CHARACTERISTICS

Blood group	Characteristics
ABO blood group system	<ul style="list-style-type: none"> • Inheritance of ABO blood groups—“Autosomal codominant” • ABO blood group antigens are present in blood, saliva, semen, amniotic fluid • O group—Universal donors • AB group—Universal recipients
The Rh system	<ul style="list-style-type: none"> • Second most important blood group system • D antigen is most important • Rh incompatibility—“Hemolytic disease of the fetus and newborn” or Erythroblastosis fetalis: damage basal ganglia leading to kernicterus

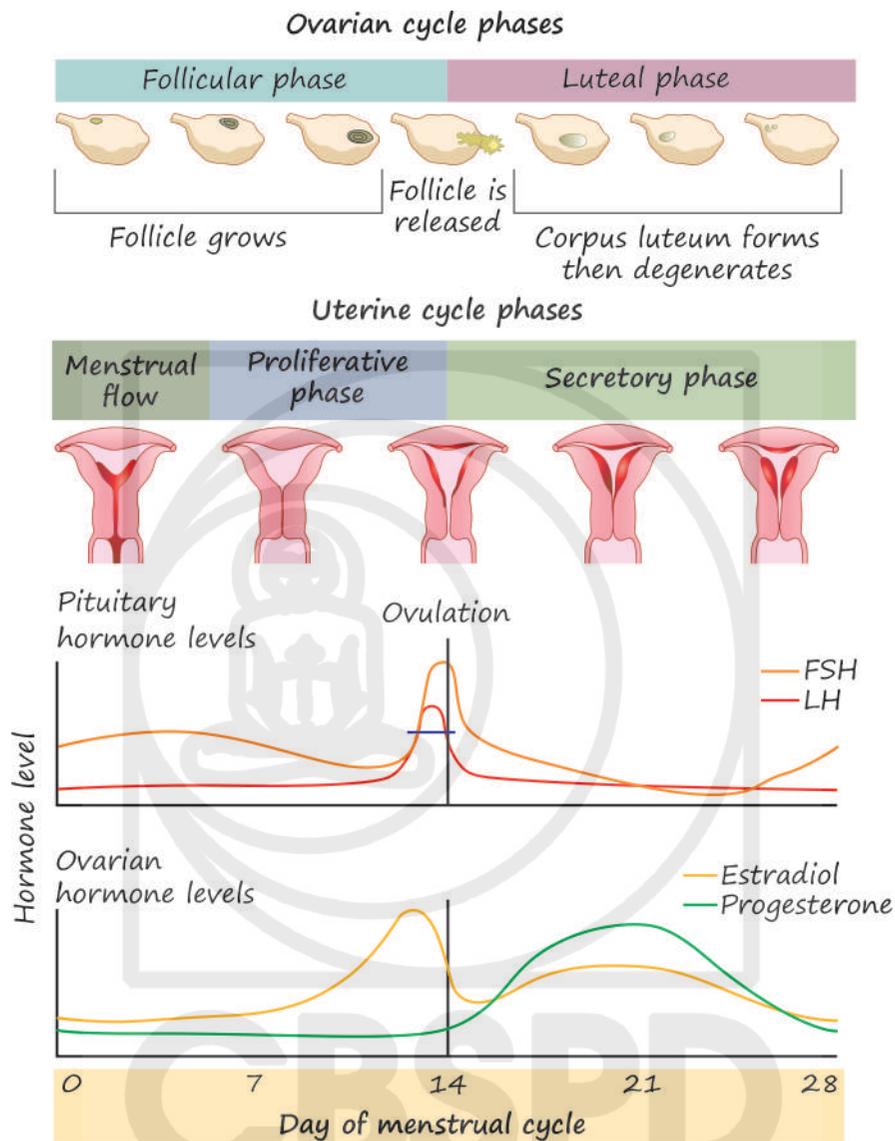
Contd...

- Vasopressin and its analog **Terlipressin** are useful in treatment of variceal bleeding.
 - **Angiotensin II:** Constricts arteriolar smooth muscle leading to vasoconstriction and increase in BP.
 - Norepinephrine
- Vasodilators (Decrease BP)**
- **Calcitonin gene-related peptide (CGRP):** Most potent vasodilator
 - Nitric oxide
 - Also called **endothelium-derived relaxing factor (EDRF)**.
 - Prostacyclins (PGI₂)
 - Kinins
 - Histamine
 - Nitric oxide is synthesized from arginine. The enzyme responsible for its synthesis is nitric oxide synthase (NOS).
 - Nitric oxide acts by increasing the levels of second messenger cGMP.
 - Drugs like sildenafil that potentiate the actions of NO by inhibiting the phosphodiesterase enzymes that degrade cGMP—useful in treatment of erectile dysfunction

MUST KNOW

Important cardiac reflexes

- **Bainbridge reflex or atrial reflex**
 - This reflex is activated whenever there is increase in venous return to the heart.
 - Stimulation of SA node—**increase heart rate (Tachycardia)**.
- **Bezold-Jarisch reflex**
 - Intracardiac injections of chemicals like serotonin, veratridine, capsaicin, phenylbiguanide activate this reflex.
 - The reflex responses are:
 - Apnea followed by rapid breathing
 - Hypotension
 - Bradycardia
 - This reflex is responsible for sinus bradycardia seen during myocardial infarction.
- **Cushing reflex**
 - Cushing reflex is characterized by increase in BP and reflex decrease in heart rate (bradycardia).
 - It is mainly seen in conditions causing increase in intracranial pressure.
- **The Oculocardiac reflex**
 - Also called **Aschner phenomenon or Aschner-Dagnini reflex**.
 - This reflex is activated during traction applied to extraocular muscles and/or compression of the eyeball.
 - Afferents for this reflex travel through long and short ciliary nerves to the trigeminal nucleus.
 - Efferent travel through vagus nerve to the heart.
 - Oculocardiac reflex is characterized by **profound bradycardia**.
- **Marey's Law**
 - This law states that heart rate and BP are inversely related.
 - This law explains reflex bradycardia associated with increase in BP.



Ovarian Cycle

Consists of the following phases: pre-ovulatory phase or follicular phase, ovulation and post-ovulatory phase or luteal phase.

1. Follicular Phase

- Starts from the fifth day of the cycle till the time of ovulation (usually happens at 14th day of the cycle).
- 15–20 follicles are selected and they mature under the influence of Follicle Stimulating Hormone (FSH).
- Dominant follicle: It is the largest follicle characterized by maximum FSH receptors, highest antral concentration of estrogen and Inhibin A and high aromatase activity.

2. Ovulation

- Process of release of ovum that happens around 14th day of the cycle.
- A surge of Luteinizing Hormone (LH) is necessary for ovulation: Exactly around 24–36 hours before ovulation, estrogen increases the levels of LH. This is an example of positive feedback.
- LH reaches its peak value around 8–12 hours before ovulation, termed **LH peak**.
- There is also a rise in FSH (FSH surge) around the time of ovulation. This rise in FSH is responsible for increase in plasmin that helps in lysis of wall of the follicle.

3. Luteal Phase

- Constant period of about 14 days.

MUST KNOW**Two Cell – Two Gonadotropin Model**

- Two cells: Theca cells and Granulosa cells.
- Two Gonadotropins: Luteinizing hormone (LH) and Follicle Stimulating Hormone (FSH).
- LH acts on theca cells to increase the production of androstenedione.
- Granulosa cells convert this androstenedione to estradiol with the help of an enzyme “aromatase”.
- Estradiol and progesterone always inhibit LH (negative feedback).
- Inhibin inhibits FSH secretion.

Female Reproductive Hormones

- Steroid hormones: Estrogen, Progesterone
- Protein/Peptide Hormones: Activin, Inhibin, Relaxin

1. Steroid Hormones**Estrogen**

- C₁₈ steroids
- Naturally occurring estrogens are:

- Estradiol (E₂)—predominant estrogen during reproductive years.
- Estrone (E₁)—predominant estrogen in menopausal women.
- Estriol (E₃)—predominant estrogen in pregnant women.
- Major binding proteins for estradiol are Albumin—60% and Gonadal steroid-binding globulin (GBG) or Sex Hormone-binding globulin (SHBG)—38%

Actions of estrogen:

Effects on	Effects of estrogen
Uterus	“Estrogen-dominated” uterus has: <ul style="list-style-type: none"> • Increased uterine blood flow • Increased content of contractile proteins in uterine smooth muscle • Uterine muscle more active and excitable
Secondary sexual characteristics	<ul style="list-style-type: none"> • Promotes female body contour • Female distribution of fat in the breasts and buttocks
Breasts	<ul style="list-style-type: none"> • Promotes mainly ductal growth in breast • “Growth hormone of breast”
Bone	<ul style="list-style-type: none"> • Promotes survival of osteoblasts • Induces apoptosis of osteoclasts • Inhibits activity of osteoclasts by inhibiting RANKL and increasing the production of osteoprotegerin • Loss of estrogen at menopause—leads to osteoporosis
Liver	<ul style="list-style-type: none"> • “Plasma cholesterol lowering action”
CVS	<ul style="list-style-type: none"> • Estrogen promotes vasodilation by increasing nitric oxide • inhibits platelet activation
CNS	<ul style="list-style-type: none"> • Estrogen is “neuroprotective”
Kidney	<ul style="list-style-type: none"> • Promotes salt and water retention

Progesterone

- C₂₁ steroid
- Major sources of progesterone are corpus luteum and placenta.



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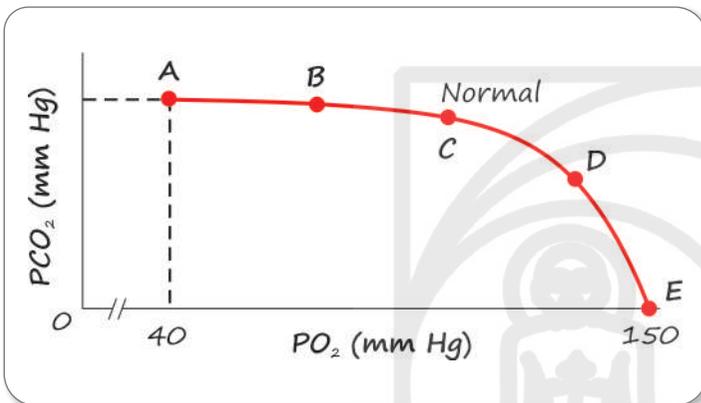
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1. The given graph shows pCO_2 and pO_2 of the right lung along with ventilation and perfusion ratio. Which point on the graph represents V/Q ratio if there is a complete block of the blood supply at alveolar level of right lung due to pulmonary embolism?

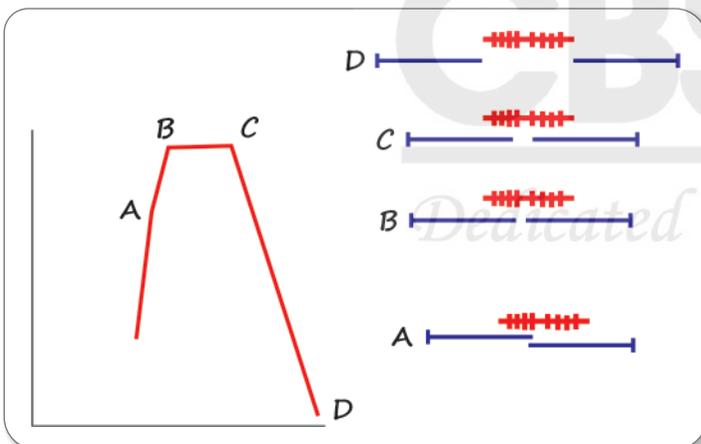


- a. Point A
b. Point E
c. Point B
d. Point D

Ans. b. Point E

Ref: Guyton 13th ed p. 525

2. The point B in the length tension graph of the sarcomere depicts which of the following illustrations?



- a. Point A
b. Point B
c. Point C
d. Point D

Ans. b. Point B

Ref: Guyton 13th ed p. 81

3. A young man was flying from Delhi to Leh at 3700 m above the sea level and started to experience dizziness, nausea, discomfort and headache. Which of the following mechanisms is responsible for these symptoms?

- a. Increased HCO_3^- leading to cerebral vasodilation and fluid leakage from the intravascular space
b. Decreased pO_2 leading to cerebral vasodilation and fluid leakage from the intravascular space
c. Increased H^+ leading to cerebral vasodilation and fluid leakage from the intravascular space
d. Decreased pO_2 leading to cerebral vasoconstriction and fluid leakage from the intravascular space

Ans. b. Decreased pO_2 leading to cerebral vasodilation and fluid leakage from the intravascular space

Ref: Ganong 25th ed p. 649

4. If the net filtration across the capillaries is zero, what is the interstitial hydrostatic pressure (P_i), given that: Capillary hydrostatic pressure- 18 mm Hg Capillary oncotic pressure- 27 mm Hg Interstitial oncotic pressure- 7 mm Hg

- a. 0 mm Hg
b. 1 mm Hg
c. +2 mm Hg
d. -2 mm Hg

Ans. d. -2 mm Hg

Ref: Ganong 25th ed p. 579

5. An experimental study of insulin after glucose administration. Blood glucose was brought to 300 mg/dL and maintained at this level. What will happen with insulin in this condition?

- a. Steady increase in insulin concentration
b. Rapid increase in insulin initially and gradual decrease
c. Increase followed by below baseline
d. Insulin increased initially and maintained at that level

Ans. d. Insulin increased initially and maintained at that level

Ref: Guyton 13th ed p. 990