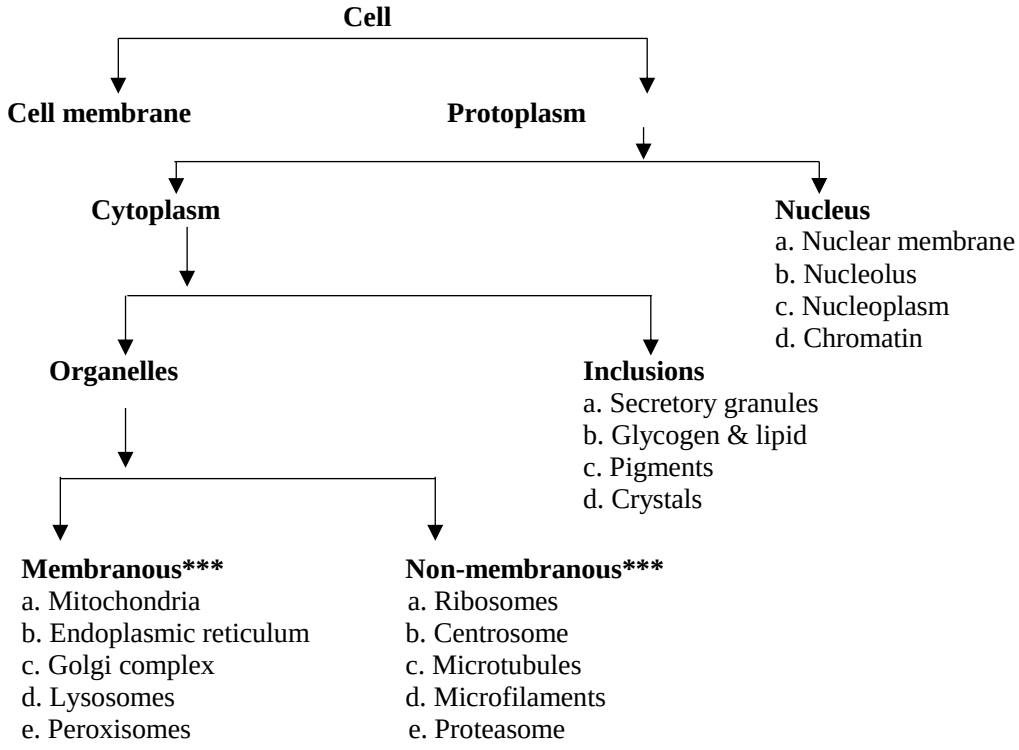
Anatomy

01. Anatomy of Cell

1.1 Parts of Cell*****

Introduction to the Cell

- The cell is the functional unit of all living organisms.
- The simplest organisms, such as bacteria and algae consist of a single cell.
- More complex organisms consist of many cells as well as extracellular matrix (e.g. the matrix of bone).
- **Eukaryote:** Organisms whose cells consist of cytoplasm and a defined nucleus & bounded by a nuclear membrane
- **Eukaryote includes:** Plants, fungi and animals (both unicellular and multicellular.)
- **Prokaryote:** Refers to bacteria and archaea, whose cells do not have a membrane-bound nucleus; they also have other major structural differences.



1. 2 Cell Membrane***

Thickness: 7.5 to 10 nm
Composition: It is composed of -

- Proteins: 55% (Transmembrane & peripheral protein)
- Lipids: 42% (Phospholipids, Cholesterol, other lipid)
- Chains of oligosaccharides: 3% (that are covalently linked to phospholipid and protein molecules)

Functions of cell membrane:

1. The plasma membrane gives boundary of the cell
2. Maintains the shape of the cell, Regulates cell-cell interactions
3. Acts as a interface between the cytoplasm and the external milieu.
4. Facilitates the transport of specific molecules
5. Performs a number of specific recognition and regulatory functions via receptors, antigens etc.
6. Maintains the structural integrity of the cell by membrane proteins
7. **CHO Present in the RBC membrane acts as Blood group antigens.**

Q. Blood group antigens are: *(39th BCS Question)*

a) Present in the RBC membrane b) Present in the plasma
c) Present in the molecules d) Present in the dense granules of platelets

Answer: A

Functions/significance of membrane proteins

A. Integral protein:

1. Acts as adhesion molecules that anchors cells to their neighbors or to basal lamina
2. **Act as pumps: Transport ions across the membrane**
3. **Act as carriers: Transport substances by facilitated diffusion**
4. **Act as ion channels: When activated, permit the passage of ions into or out of the cells**
5. Act as receptors: Bind with neurotransmitters & hormones
6. Act as enzymes: Catalyzes reactions at the surface of the membrane.
7. Act as glycoprotein: Function in antibody processing & distinguishing self from nonself.

B. **Peripheral proteins:** The act almost entirely as enzymes or as other types of controllers of intracellular function.

(Ref: Janqueira's Basic Histology/13th /Page 19-22)

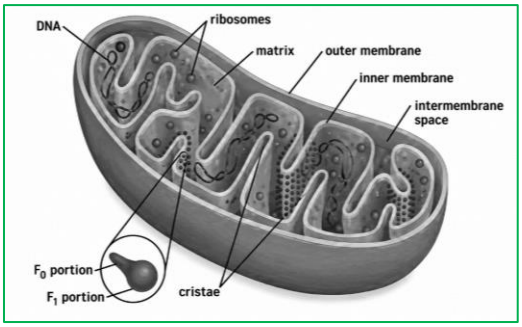
1.3 Mitochondria***

Mitochondria

- Mitochondria are one of the membranous organelles
- Abundant in cells that generate and expend large amount of energy e.g. striated muscle cells, cardiac muscle, liver, renal tubule, spermatozoa, ion and electron transporting cells.
- They are called **Power house of the cells**.
- They are **absent in RBC and terminal keratinocytes**. Mitochondria are self-duplicating organelle.
- **Size:** It is 0.5-1µm wide & up to 10 µm long.
- **Shape**: spherical or filamentous organelle
- **Number:** its number depends on the cell's energy needs. Thus, cells with a high energy metabolism (e.g. cardiac muscle, cells of some kidney tubules) have abundant mitochondria.
- **Location:** it accumulates in cytoplasmic regions where energy utilization is more intense.

Structure:

- Mitochondria are composed of an outer and an inner mitochondrial membrane.
- The inner membrane is highly folded into the matrix to form incomplete partitions called cristae.
- These membranes enclose compartments
- Intermembrane space: The space in between the two membranes
- Matrix space: it is enclosed by the inner membrane & filled with granular matrix, rich in protein & containing some DNA & RNA



Enzymes found in mitochondria: Three important enzymes are found in the mitochondria

1. **Kreb's cycle enzymes, Beta oxidation of fatty acid.**
2. **Flavo- protein, dehydrogenase and cytochrome- which are involved in respiratory chain.**
3. **Oxidative phosphorylase.**

(Ref: Junqueira's/14th/P-38)

Functions

- Generation of ATP through electron transport mechanism (respiratory chain)
- **Power house of cell thus provides energy in different energy dependent process e.g., Proton pump mechanism.**
- **Oxidative phosphorylation, beta oxidation and TCA cycle occur in mitochondria**
- It is the capacity of accumulating Ca-ions in their matrix, there by maintaining a low level of calcium ion in cytosol
- **Helps in Programmed cell death regulation**
- Synthesis of nucleic acid, RNA and protein

Absent in:	Abundant in:
• **RBC** • **Terminal Keratinocytes**	• Striated muscle cells, Cardiac muscle • Hepatocytes Liver, renal tubule, spermatozoa • Ion and electron transporting cells, Steroid secreting cells

Q. The function of mitochondria includes: *(39th BCS Question)*

a) Vesicle transport b) Proton pump operation
c) Anaerobic glycolysis d) Activation of intrinsic pathway of apoptosis

Answer: B

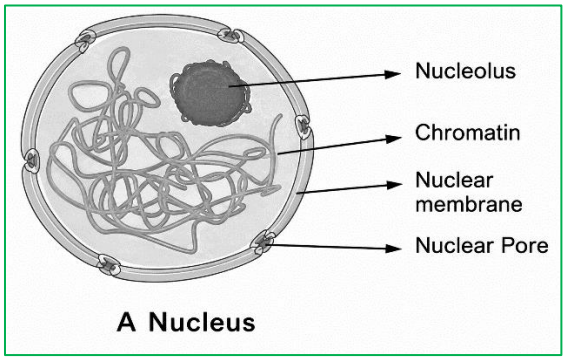
Q. Programmed cell death is regulated by *(48th BCS Question)*

a) Endoplasmic reticulum b) Golgi apparatus
c) Lysosome d) Mitochondria

Answer: D

1.4 Nucleus

- **Number:** Most cells have a single nucleus: other cells may exhibit multiple nuclei. Skeletal muscle cells have numerous nuclei, whereas mature red blood cells in mammals are not nucleated.
- **Staining:** the nucleus is stained with basic dyes since it contains abundant DNA and a small amount of RNA.
- **Structures found in the nucleus:**
  1. Nuclear envelope
  2. **Chromatin:** Two types
     - **Heterochromatin:** Condensed, approximately 90% of total chromatin.
     - **Euchromatin:** transcriptionally active, approximately 10% of total chromatin.



A Nucleus

3. Nucleolus

- The nucleolus is a generally spherical, highly basophilic structure present in the nuclei of cells active in protein synthesis
- It is a compressed mass of a mixture of RNA (ribosome) granules and proteins
- It disappears during prophase and reappears during telophase of cell division

Function:

- The molecules of RNA synthesized and modified in the nucleus
- Involved in cell division.
- Stores hereditary information and transforms it.

1.5 Endoplasmic Reticulum

Functions:

Smooth endoplasmic reticulum:

- Synthesis of lipids and steroids.
- It also participates in cholesterol metabolism.
- Detoxification of certain lipid soluble drugs by means of hydroxylating enzymes.
- Participates in the contraction processes of striated muscle cells as **sarcoplasmic reticulum.**
- Participates in the secretion of CI^- in the oxyntic cells.
- Helps in glycogenolysis.
- Helps in Oxidation, Conjugation & Methylation in Liver.

Rough (granular) endoplasmic reticulum:

- Synthesis and segregation of proteins not destined for the cytosol,
- Initial (core) glycosylation of newly formed polypeptides
- Synthesis of phospholipids
- Assembly of multichain proteins
- Post translational modification of newly formed polypeptides.

➢ **During Expiration:**

1) fall in venous return to the Rt heart
2) reduction in output from Rt heart
3) Blood is squeezed out of the lungs
4) rise in the venous return to the left heart
5) rise in the output of left heart.

➢ **During normal quiet breathing:**

- ✓ **At the end of inspiration:** Both Intrapleural& intra esophageal pressure lowest
- ✓ **At the end of expiration:** Both Intrapleural& intra esophageal pressure highest
- ✓ **At mid inspiration:** Interalveolar pressure lowest rate of airflow greatest
- ✓ **At mid expiration:** intra alveolar pressure highest.

Nice to know:

Respiratory rate at different age groups:

Age in year	Respiration rate per minute
At birth	14-60
First year	**25-35**
2—4 years	20-30
Adult (male)	14-18
Adult (female)	14-18

6.3 Transport of O_2 and CO_2 ****

Transport of O_2 in the blood:

O_2 is transported in the blood in two forms-

1. In the form of Hb-O_2: About 97 % of O2 is carried in the form of Hb-O_2. 4 O2 molecules bind reversibly with 4 iron atoms of a Hb molecule by the process of oxygenation and form oxy-hemoglobin (O-Hb) which is transported in the blood.
2. In dissolved state: Remaining 3% of O2, is transported in the dissolved state in the water of plasma and cells.

Transport of CO_2 in the blood:

In the blood CO_2 is carried in the following forms-

1. In the dissolved state- 7 %
2. In the form of HCO_3^--70 %
   a) KHCO3 in RBC
   b) NaHCO3 in plasma
3. In combination with Hb & plasma proteins forming carbamino compounds- 23%
   a) Carbamino-Hb in RBC
   b) Carbamino-Protein in RBC & plasma

Q. Primary blood buffer system is *(48th BCS Question)*

a) Ammonia buffer b) Bicarbonate buffer c) Phosphate buffer d) Protein buffer

Answer B

3.4 Regulation of Respiration ***

Respiratory Centers

Control of respiration central regulatory centres

➢ **Inspiratory centre (Dorsal respiratory group):** Dorsal portion of Medulla

- **Expiratory centre (Ventral respiratory group):** Anterolateral part of Medulla
- Apneustic centre (lower pons)
- Pneumotaxic centre (upper pons)

Central and peripheral chemoreceptors

- Central: raised [H^+] in ECF stimulates respiration
- Peripheral: carotid + aortic bodies, respond to raised PCO2 & [H^+], lesser extent low PO2

Q. Respiratory Center is located in *(48th Special BCS)*
a) Medulla b) Spinal Cord c) Brain Cortex d) Cerebellum
Answer: A

Pulmonary receptors

- Stretch receptors (Hering breur reflex)
- Irritant receptor, leading to bronchoconstriction
- Juxta capillary receptors, stimulated by stretching of microvasculature

Stimuli Affecting the Respiratory Center

Control Type	Stimuli
Chemical Control	• CO_2 (via CSF and brain interstitial fluid H^+ concentration) • O_2 (via carotid and aortic bodies) • H^+ (via carotid and aortic bodies)
Nonchemical Control	• Vagal afferents from receptors in the airways and lungs • Afferents from the pons, hypothalamus, and limbic system • Afferents from proprioceptors • Afferents from baroreceptors: arterial, atrial, ventricular, pulmonary

Groups	Location	Name of nucleus	Function
1. Inspiratory center (Dorsal respiratory group	Dorsal portion of medulla oblongata	Nucleus of Tractus solitarius	It causes inspiration while stimulated
2. Expiratory centre (ventral respiratory group)	Antero lateral part of medulla oblongata.	Nucleus ambiguous and nucleus retro ambiguous	1. It causes either expiration or inspiration depending upon which neurons in the group are stimulated. But generally, causes expiration. 2. It sends inhibitory impulse to the apneustic center.
3. Pneumotaxic center	Upper part of pons	Nucleus parabrachialis	1. It controls both rate & pattern of breathing. 2. It sends impulse to limit inspiration.
There may be 4th center			
4. Apneustic	Lower part of pons		1. It sends stimulatory impulse to the inspiratory centre causing inspiration. 2.It receives inhibitory impulse from pneumotaxic centre and from stretch receptor of lung. 3. It sends inhibitory impulse to expiratory centre.

6.4 Hypoxia ***

Definition:
Hypoxia means decrease O2 in the tissue level.

Classification:

Types	Definition	Causes
A. Hypoxic hypoxia (It occurs mainly in High altitude)	When hypoxia occurs due to decreased O_2 availability in the atmosphere or in the source, this is called hypoxic hypoxia	1. Lung failure (gas exchane failure) 2. Pulmonary fibrosis 3. ventilation perfusion imbalance 4. Shunt 5. pump failure (ventilatory failure) 6. Fatigue 7. Mechanical defects 8. Depression of respiratory controller in the brain.

B. Anaemic hypoxia	When O_2 tension in air is normal but hypoxia develops due to less O_2 carriage is called anaemic hypoxia.	1. Lack of Hb 2. CO poisoning 3. Altered Hb
C. Stagnant hypoxia	When O_2 tension is normal but the amount of O_2 reaching the tissue is inadequate, this hypoxia is called stagnant hypoxia.	1. ↓Cardiac output 2. Impaired venous return 3. ↓Blood flow to the orgen 4. Hemorrhage, shock ctc.
D. Histotoxic hypoxia	when hypoxia occurs due to failure of cell to utilize O_2 is called histotoxic hypoxia	1. Poisoning with KCN 2. Narcotics
Role of O_2 therapy in different types of Hypoxia		
A. Hypoxic hypoxia	O_2 therapy is 100% effective	
B. Anemic hypoxia	O2 therapy is less effective	
C. Stagnant hypoxia	It is less value due to decreased O_2 carriage by blood.	
D. Histotoxic hypoxia	It is of no value because cell cannot utilize O_2	

6.5 Cyanosis**

Definition; Cyanosis is a clinical condition characterized by bluish discoloration of skin & mucous membrane due to **Excessive amount of deoxygenated Hb in the peripheral tissue Capillaries.**
Site of observation: Nose, tongue, ear lobe, lips, mucous membrane of oral cavity, nail bed, sole.

Causes of central cyanosis: Seen in the tip of the tongue
A. Lung disease:
1. Massive pulmonary embolism
2. Acute exacerbation of COPD
3. Acute severe asthma
4. Severe pneumonia
5. Interstitial pneumonia
6. infection (Acute laryngo-tracheal bronchitis)

B. Heart diseases:
1. Congenital cyanotic heart disease: **Tetralogy of Fallot,** transposition of great vessels, tricuspid atresia.
2. LVF
3. Eisenmenger's syndrome (Rt to Lt shunt) in VSD, PDA.

C. Inadequate O2 uptake:
1. Methemoglobinemia
2. Sulphaemoglobinaemia

6.6 Surfactant***

- **Surfactant** is a lipoprotein, fully saturated with phospholipid, dipalmitoyl & **lecithin.**
- **Site of secretion:** Surface is composed of phospholipids, cholesterol and a specific protein, all of these substances are formed by **type II alveolar epithelial cells**. Surfactant begins to secrete at the beginning of **28th weeks** of intrauterine life.

Approximate composition of surfactant:

Component	Percentage
Dipalmitoilphosphatidyl choline	62
Phosphatidyl glycine	5
other phospholipids	10
Neutral lipids	13
proteins	8
Carbohydrate	2

Functions of Surfactant****

1. Dipalmitoyl lecithin of surfactant decreases the surface tension of the fluid lining the alveoli, thus prevents the collapsing of the lungs during expiration.
2. It helps in the expansion of lungs of new born babies.
3. It increases compliance & stability of the lung.
4. It stabilizes the size of alveoli.
5. It prevents the pulmonary edema by reducing pulmonary capillary filtration.
6. It has some bactericidal effects.

6.7 O_2- Hb Dissociation Curve****

Oxygen Dissociation Curve describes the relationship between the percentage of saturated hemoglobin and partial pressure of oxygen in the blood.

- **It is not affected by hemoglobin concentration**, but affected by its quality (HbF, methemoglobin).
- Each hemoglobin molecule has the capacity to carry four oxygen molecules.

Basics

- Shifts to right = for given oxygen tension there is decrease saturation of Hb with oxygen i.e.Enhanced oxygen delivery to tissues
- Shifts to left = for given oxygen tension there is increase saturation of Hb with oxygen i.e. decrease oxygen delivery to tissues

Shifts to Right = Raised oxygen delivery	Shifts to Left = Lower oxygen delivery
• Raised [H+] (acidity) • Raised PCO2 • Raised 2,3-DPG • Raised temperature	• **L**ow [H+] (alkali) • **L**ow PCO2 • **L**ow 2,3-DPG • **L**ow temperature • HbF, methemoglobin, carboxyhaemoglobin

Q. The major function of surfactant is to increase *(42nd Special BCS)*

a) Alveolar surface tension b) Pulmonary compliance
c) Work of breathing d) The tendency of lungs collapsed

Answer: B

Bronchopulmonary Segment Importance:

1. Infection is restricted to one or more Bronchopulmonary segment Except Malignancy and Tb
2. Infection is more common in apical segment of lower lobe
3. Knowledge of Bronchial branching is essential for Bronchoscopy & Bronchograms
4. Knowledge of segment helps in surgery
5. Helps in Postural Drainage of Infected pulmonary segment.

07. Layers of Respiratory Membrane

1. Surfactant layer: (A layer of fluid the alveolus and containing surfactant.)
2. Alveolar epithelium layer
3. Epithelial basement membrane
4. A very thin interstitial space between the alveolar epithelium and the capillary membrane.
5. Capillary basement membrane (in many places it fuses with the epithelial basement membrane)
6. Capillary endothelial membrane.

Functions of plasma proteins: *

Plasma Proteins	Functions / Importance
1) Albumin	**• Maintains 80% colloidal osmotic pressure of blood.** • Maintains viscosity of blood. • Acts as buffer & maintains acid-base balance. • Acts as a carrier for hormones, bilirubin, fatty acids, bile salts, amino acids, heavy metals & some drugs.
2) Globulin	1. Maintains 20% colloidal osmotic pressure of blood. 2. Maintains viscosity of blood. **3. α1-globulin transports lipid & steroids.** **4. α2-globulin transports Cu as ceruloplasmin.** **5. β-globulin transports Fe as transferrin.** **6. γ-globulin acts as antibody for defensive action.**
3) Fibrinogen	• Essential for blood coagulation. • Maintains the viscosity of blood. • Increases ESR.
4) Prothrombin	• Helps in blood coagulation.

Q. Plasma albumin helps in *(48th Special BCS)*

a) Colloidal osmotic pressure maintenance
b) Blood clotting
c) Iron transport
d) Copper transport

Answer: A

Haem containing substances / proteins: *

1) Haemoglobin.
2) Myoglobin.
3) Cytochrome oxidase.
4) Catalase.

Blood sample collection

Biechemical changes occur in collected blood when estimation is delayed:

1. Diffusion of K^+ from cell → **↑ K^+ ion.**
2. Conversion of pyruvate & glucose into lactic acid → ↑ Lactic acid.
3. Loss of CO_2.
4. ↑ Cl^- in the cell due to shift of Cl^- in the cell.
5. ↑ Plasma inorganic phosphate.
6. ↑ Ammonia concentration.
7. **↓ RBC,** pH, protein factor, Na^+, DPG.
8. **↓ Clotting factor.**
9. Inactivation of Na^+-K^+ pump.

Differences between plasma and serum:

Traits	Plasma	Serum
1) Definition	Non-cellular fluid portion of the blood.	If the blood is allowed to clot and the clot is removed, the remaining fluid is called serum.
2) Clotting factors	Contains all the blood clotting factors.	It does not contain fibrinogen, clotting factors II, V & VIII.
3) Serotonin content	Serotonin content is low.	Serotonin content is high due to breakdown of platelets during clotting.
4) Clot	Plasma can clot because it has all the blood clotting factors.	Serum cannot clot due to lack of some of the clotting factors.
5) Colour	It is yellowish in colour.	It is straw in colour.

Anti-coagulants

Classification:

1) Acting in vitro (outside the body): Citrate, oxalate, EDTA, heparin, dextran sulphate etc.
2) Acting in vivo (within the body): Warfarin, heparin, rivaroxaban, dabigatran.
3) Both in vitro and in vivo: Heparin, dextran sulphate.

Some anticoagulants that are used clinically / therapeutic purpose: **

- **Injectable anticoagulants** : Heparin, ancrod.
- **Oral anticoagulants** : Warfarin, dicoumarol.

37. Heparin is *(39th Special BCS)*

a) Secreted by goblet cell b) Found in the bone marrow c) A natural anticoagulant d) An enzyme

Answer: C

Liver and liver Function tests (LFT) **

Liver function tests:

Liver function tests (LFTs or LFs) are groups of laboratory assays designed to give information about the state of a patient's liver. The liver function tests are as follows:

1) Test for excretory & conjugation function:

Done by the measurement of **serum bilirubin** concentration (total, direct & indirect).
Normal level: 0.2 – 1.2 mg/dl (3 – 17 µmol/L).

2) Enzyme concentration:

► **Evidence of hepatocellular damage (as in hepatitis):**

- Serum ALT / SGPT [10–40 U/L]
- Serum AST / SGOT [10–35 U/L]

► **Evidence of cholestasis (as in obstructive jaundice):**

- Alkaline phosphatase (ALP) [40–125 U/L]
- Gamma-glutamyl transferase [Male: 10–55 U/L, Female: 5–35 U/L]

3) Tests for synthetic functions:

Test	Normal value
Serum total protein	6 – 8 gm/dl
Serum albumin	3 – 4 gm/dl
Serum albumin to globulin ratio	2:1
Prothrombin time	12 – 14 sec

4) Test for metabolic function of liver:

- Done by **galactose tolerance test**.

5) Test for detoxification function

- **NH_3 concentration in blood.**

6) Other biochemical tests:

- Serum electrolytes (**Hyponatraemia** may occur in severe liver disease).
  Blood urea level.
- Serum ferritin level (**Haemochromatosis**).
- Serum & urinary copper (**Wilson's disease**).
- Serum ceruloplasmin (**Wilson's disease**).

7) Tumour marker (for hepatocellular carcinoma):

- **α-fetoprotein (AFP).**

8) Viral markers:

- Different viral markers for different types of viral hepatitis.

9) Immunological tests (for autoimmune liver disease):

- Anti-mitochondrial antibody.
- Anti-smooth muscle antibody.
- Antinuclear antibody (ANA).

Bilirubin and Jaundice

Jaundice: *(French: jaune – yellow)*
Jaundice may be defined as yellow discoloration of the skin, sclera and mucous membranes due to an elevated bilirubin concentration in the body fluid above normal.

- **Normal serum bilirubin:** 0.2 – 1 mg/dl (5.1 – 17 µmol/L).
- **Clinical jaundice:** When bilirubin in plasma exceeds **2 – 2.5 mg/dl (50 µmol/L)**.
- **Latent jaundice:** Clinically there is no jaundice but serum bilirubin is more than normal & < 3 mg/dl.

Kernicterus / neonatal-physiological jaundice / jaundice due to genetic defects:
When serum conjugated bilirubin level rises >25 mg/dl, it can cause toxic encephalopathy & mental retardation, is called kernicterus.

Treatment:

- **Phototherapy.**
- **Drug:** The drug **phenobarbital** is used in the treatment, which **induces bilirubin metabolizing enzymes in liver**.
- In some neonates, **blood transfusion** may be necessary to prevent brain damage.

Laboratory findings / tests of jaundice: **

Investigations	Haemolytic jaundice	Hepatocellular jaundice	Obstructive jaundice
A) Blood Biochemistry			
1) Serum bilirubin	Raised, mostly unconjugated	Raises; both conjugated & unconjugated	Raises; conjugated
2) Alkaline phosphatase	Normal	Small rise	Raised
3) AST (SGOT)	Normal	High rise	Small
4) ALT (SGPT)	Normal	High rise	Small rise
5) Prothrombin time	Normal	Prolonged	Prolonged
6) Serum albumin	Normal	low	normal
B) Haematological test	Findings of haemolytic anaemia	Low. Leucopenia in viral hepatitis	
C) Urine			
1) Bilirubin	Absent	Variable	Present
2) Urobilinogen	Increased	Normal or increased	Decreased
3) Bile salts	Absent	Absent	Present
D) Stool			
1) Naked eye	Dark	Normal colour or pale	Pale or normal colour, bulky, frothy due to high fat content
2) Stercobilinogen	Increased	Decreased	Decreased
E) Special blood test			
1) Viral markers (HBsAg, HBeAg etc.)	Not found	Found in viral hepatitis	Not found
2) α-fetoprotein	Not found	Found in hepatocellular carcinoma	Not found

Thyroid Function Tests **

Interpretations of thyroid function tests:

Most likely interpretation(s)	T_4	T_3	TSH
Thyrotoxicosis / hyperthyroidism			
Primary thyrotoxicosis	Raised	Raised	Undetectable
Subclinical thyrotoxicosis	Normal	Normal	Undetectable
Secondary thyrotoxicosis (e.g. TSH-secreting pituitary tumour) Thyroid hormone resistance	High	High	Elevated
Hypothyroidism			
Primary hypothyroidism	Low	Low	Elevated > 20 mU/l
Subclinical hypothyroidism	Normal	Normal	Mildly elevated 5–20 mU/l
Secondary hypothyroidism (i.e. pituitary or hypothalamic disease)	Low	Low	Undetectable

Renal Function Tests (RFT)

Creatinine clearance rate (CCR) test:
Creatinine clearance may be defined as the volume (ml) of plasma that would be completely cleared of creatinine per minute.

Clinical importance of creatinine clearance rate (CCR):

1. **The value of creatinine clearance is close to GFR**; hence its measurement is a **sensitive and good approach to assess the renal glomerular function**.
2. **A decrease in creatinine clearance value**
   → decreased GFR, due to renal damage value (<75% normal) serves as **sensitive indicator of a kidney function**, often before the damage. This test is useful for an early detection of impairment in kidney function, often before the clinical manifestations are seen.
3. The excretion of creatinine is rather constant and is not influenced by body metabolism or dietary factors.
4. Since the production is continuous, the **blood level will not fluctuate** much, making creatinine an **ideal substance for clearance test**.
5. Since creatinine excretion is a **constant** in a particular person, the urine creatinine is sometimes used to check whether the 24 hours urine sample does actually contain total urine volume or not.
   - This is important when urine is collected from children and mentally retarded persons.
6. In order to circumvent the difficulty of urine collection, nowadays it is customary to express urinary concentration of other substances per gram of creatinine rather than per 24 hours urine.

Criteria of creatinine

$$\text{Creatinine clearance rate (CCR), } C_a = \frac{\text{Urine creatinine (UC)} \times \text{Urine flow rate (V)}}{\text{Plasma creatinine (PC)}}$$

Biochemical tests to assess kidney function

A) Blood analysis:

1. **Blood urea level** (15 – 40 mg/dl)
2. **BUN** (Blood urea nitrogen) level
3. **Plasma uric acid level** (2 – 7 mg/dl)
4. **Plasma creatinine level** (0.7 – 1.4 mg/dl)
5. **Plasma electrolytes**

B) Clearance tests:

1. **Creatinine clearance test** (Usually used: 70 – 140 ml/min)
2. **Urea clearance test** (60 – 70 ml/min)
3. **Inulin clearance test**

C) Chemical tests in urine:

1. **Reaction (pH)**: Litmus paper test
2. **Albumin**: Heat coagulation test
3. **Sugar**: Benedict test
4. **Blood**: Orthotolidin test.
5. **Ketone bodies**: Rothera's test
6. **Bile salts:** Hay's surface tension test.
7. **Bile pigment:** Foucher's test.
8. Phosphate.
9. Urobilinogen

Clinical classification of proteinuria: *3 types*

1. **Asymptomatic proteinuria:** When protein excretion rate (PER) < **1 gm/day**.
2. **Moderate proteinuria:** When PER **1–3 gm/day**.
3. **Massive proteinuria:** When PER > **3 gm/day**.

28. Abnormal constituent of urine is *(39th Special BCS)*
a) Disodium mono hydrogen phosphate b) Albumin c) Creatinine d) Urea
Answer: A

Blood glucose level and Diabetes Mellitus (DM)

Biochemical approach / diagnostic criteria of DM:

1) Blood glucose level:

Blood glucose level	Normal	Impaired	Diabetes mellitus
Random blood glucose (RBS)	< 7.8 mmol/L (< 140 mg/dl)	7.8 – 11.0 mmol/L (140 – 198 mg/dl)	≥ 11.1 mmol/L (≥ 200 mg/dl)
Fasting blood glucose (FBS)	3.6 – 6 mmol/L (65 – 108 mg/dl)	6.1 – 6.9 mmol/L (110 – 124 mg/dl)	≥ 7.0 mmol/L (≥ 126 mg/dl)
2 hours after 75g glucose load / 2 hr post-prandial	< 7.8 mmol/L (< 140 mg/dl)	7.8 – 11.0 mmol/L (140 – 198 mg/dl)	≥ 11.1 mmol/L (≥ 200 mg/dl)

2. HbA_1c:

Normal: <6%

Diabetes mellitus: > 6%

Gestational diabetes mellitus (GDM)

Gestational diabetes mellitus (GDM):

It is the clinical condition characterized by **hyperglycaemia for the first time during pregnancy** in a woman who was previously non-diabetic.

Cause of hyperglycaemia in pregnancy:

Due to **insulin antagonistic activity** of **progesterone** and **human placental lactogen** hormones that are produced by the placenta during pregnancy.

Diagnostic criteria of diabetes mellitus in non-pregnant woman:

- **Fasting blood glucose**: ≥ 7 mmol/L (≥ 126 mg/dl)
- **Blood glucose 2 hours after meal**: ≥ 11.1 mmol/L (≥ 200 mg/dl)

Diagnosis of GDM:

A) Screening by 1 hour 50 gm OGTT:

- Irrespective of food intake, 50 gm glucose is given orally & at the end of 1 hour, blood glucose is measured.
- **If blood glucose is ≥ 7.8 mmol/L (140 mg/dl):**
  → Patient is suspected for GDM & subjected to **100 gm OGTT**.

B) Diagnosis of GDM by 100 gm OGTT:

- After 12 hours overnight fasting, patient FBS is measured and then 100 gm glucose with 300 ml of water is given orally.
- Then blood glucose is measured at **1, 2 & 3 hours** after glucose load.

Interpretation:

GDM is diagnosed if 2 or more positive findings are observed from the following:

Test	Threshold
FBS	≥ 5.8 mmol/L (105 mg/dl)
1 hour after glucose load	≥ 10.5 mmol/L (190 mg/dl)
2 hour after glucose load	≥ 9.1 mmol/L (165 mg/dl)
3 hour after glucose load	≥ 8.0 mmol/L (145 mg/dl)

Complications of GDM: **

1. **Macrosomia** (large baby)
2. **Polyhydramnios** (excessive amniotic fluid)
3. **Increased risk of still birth**, **birth trauma**, etc.
4. **Development of maternal DM** later on.

Cerebrospinal fluid (CSF) Examination **

CSF changes in different types of meningitis

Traits	Bacterial meningitis	Tubercular meningitis	Viral meningitis
1) Physical			
• Pressure	Normal / increased	Normal / increased	Normal / elevated
• Colour	Cloudy	Clear / cloudy	Clear
• Clot	Formation of clot	Formation of spider web clot	No clot
2) Cytological			
• WBC Count	> 200 × 10^6 /L (Predominantly neutrophils)	> 10 × 10^6 /L (Predominantly lymphocytes)	> 10 × 10^6 /L (Predominantly lymphocytes)
3) Biochemical			
• Protein	Increased	Increased	Increased
• Glucose	Decreased	Decreased	Normal / slightly decreased
• Chloride	Normal / slightly decreased	Decreased / normal	Normal / slightly decreased
4) Staining	Causative organism found on Gram stain	Acid fast bacilli on Ziehl-Neelsen stain	Not done
5) Culture	Organism on blood agar and Mac. Conkey's media	Organism on Lowenstein Jensen Media	Not cultured usually.

43. Which component is not present in CSF *(39th Special BCS)*

a) Erythrocyte b) Leucocyte c) Glucose d) Protein

Answer: A

Tumor marker ***

Tumor Markers and Associated Tumors

Tumor Marker	Associated Tumor
Carcinoembryonic antigen (CEA)	Colorectal cancer, breast cancer, bronchial carcinoma.
Human chorionic gonadotropin (β-HCG)	Choriocarcinoma, germ cell tumor of testis & ovary.
α-fetoprotein (AFP)	Hepatocellular carcinoma, germ cell tumor of testis & ovary.
CA-15-3	Breast cancer.
CA-19-9	Colon cancer, pancreatic cancer.
CA-125	Ovarian cancer.
Prostatic acid phosphatase	Prostate cancer.
Immunoglobulins	Multiple myeloma.

Q. CA-125 is the tumor marker for *(48th Special BCS)*

a) Breast cancer b) Colon cancer c) Ovarian cancer d) Pancreatic cancer

Answer: C

4. Food & Nutrition

Food, Diet, Nutrition, Nutrients and Dietary Fiber Food

Classification of food:

According to chemical composition:

1. Proteins
2. Fats
3. Carbohydrate
4. Vitamins
5. Minerals
6. Water

Nutrition & Nutrient

Nutrition

Nutrition is a dynamic process concerned with ingestion, digestion, absorption and assimilation (metabolism) of food substances by which growth, repair and maintenance of activities in the body as well as a whole or in any of its parts are accomplished.

Nutrient

Nutrients are those chemical substances that are essential for growth & maintenance of normal cells.

Classification / Types: *

Nutrients can be subdivided into **2 groups**:

1. **Macronutrients:** These are carbohydrate, protein, and fat.
2. **Micronutrients:** These are vitamins and minerals. They are called micronutrients because they are required in small amounts. (**< 100 mg/day**)

Dietary fiber

Importance of dietary fiber:

- Prevents constipation
- **Eliminates bacterial toxins**
- Decreases GIT cancers
- **Reduces plasma cholesterol level**
- Satiety value
- **Improves glucose tolerance**

Disadvantages of Dietary Fiber: **

1. **Bind with trace elements (e.g., Zn^{++}) and decrease their absorption.**
2. Decrease the absorption of **fat soluble vitamins**.
3. **Colonic fermentation** of fiber may produce gases such as **CO_2, H_2 & CH_4**, producing **abdominal cramps**.

Basal Metabolic Rate (BMR) / Resting Metabolic Rate (RMR)

Basal metabolic rate (BMR) / resting metabolic rate (RMR) / basal energy expenditure (BEE):

Basal metabolic rate (BMR) is the energy expenditure by the body when at rest, but not asleep, under controlled conditions of thermal neutrality, measured about 12 hours after the last meal.

Pathological Factors Affecting BMR

Increased (↑) BMR under the following conditions:	**Decreased (↓) BMR under the following conditions:**
1. Hyperthyroidism 2. Fever 3. Leukemia 4. Polycythemia 5. Congestive cardiac failure 6. Renal failure 7. Diabetes insipidus 8. Pregnancy 9. Emotional state 10. Caffeine	1. Hypothyroidism: Myxoedema & cretinism 2. Addison's disease 3. Nephrotic syndrome 4. Malnutrition 5. Anaesthetic use

Specific Dynamic Action (SDA)

Specific dynamic action (SDA): The SDA of a food is the obligatory energy expenditure that occurs during its assimilation into the body.

SDA of Different Foods

Types of Food	SDA
Carbohydrate	6%
Protein	30%
Fat	4%
Mixed Diet	6–10%

Site: Liver is the main site for production of **SDA of protein (only)**.

Nutritional Disorders

Malnutrition: Malnutrition has been defined as a pathological state resulting from a relative or absolute deficiency or excess of one or more essential nutrients.

Common Malnutrition / Nutritional Diseases / Nutritional Problems in Bangladesh:

1) Nutritional Anaemia:

According to cell size (based on MCV, MCH, MCHC), it is of two types:

a) Microcytic hypochromic anaemia: (↓ MCV, MCH & MCHC)

- Iron deficiency anaemia.

b) Macrocytic / megaloblastic anaemia: (↑ MCV, MCHC normal)

- Vitamin-B_{12} deficiency anaemia
- Folic acid deficiency anaemia

2) Protein Energy Malnutrition (PEM):

- Kwashiorkor
- Marasmus
- Marasmic kwashiorkor

3) Obesity **

4) Iodine Deficiency Disorders:

- Goiter

5) Low-Birth Weight (LBW) Baby

6) Avitaminosis:

a) Deficiency of fat-soluble vitamins:

- e.g., Vitamin-A & D deficiency

b) Deficiency of water-soluble vitamins:

- e.g., Vitamin-B complex, Vitamin-C deficiency

7) Hypervitaminosis:

- Hypervitaminosis-A
- Hypervitaminosis-D

Protein energy malnutrition (PEM): Protein energy malnutrition refers to a range of disorders of starvation and malnutrition that involve deficiencies of other nutrients such as vitamins and minerals in addition to protein & energy-providing carbohydrates & fats. This condition is common in children but uncommon in adults.

FAO/WHO Classification

Types	Body weight % of international standard	Oedema	Deficit in weight for height
Kwashiorkor	80 – 60	Present	+
Marasmic kwashiorkor	< 60	Present	++
Marasmus	< 60	Absent	++
Nutritional dwarfing	< 60	Absent	+
Underweight child	80 – 60	Absent	Minimal.

Difference between Marasmus & Kwashiorkor **

Traits	Marasmus	Kwashiorkor
1) Main nutritional cause	Due to calorie deficiency.	Due to protein deficiency.
2) Age	Weaned infant (<1 year).	Pre-school children (1–5 years).
3) Body weight	Less than 60% of normal.	60–80% of normal.
4) Growth retardation	Severe.	Mild
5) Edema	Absent.	present in lower legs or generalized.
6) Facial appearance	Like old man's face.	Moon face.
7) Abdomen	Shrunken.	Protruding & hepatic enlargement.
8) Skin changes	Dermatitis.	Dry & atrophic
9) Muscle	Weak & atrophic.	Undergo wasting.

Pathology & Microbiology

1. Cell Biology: General Concept

Cell: Structural and functional unit of human body.

Composition of cell:

a. Cell membrane
b. Protoplasm:
   I. Cytoplasm
   II. Nucleus

Cell Cycle:

Cell cycle is the sequence of events by which a cell grows, replicates its DNA, and divides into two daughter cells.

Phases of Cell Cycle

Phase	Key Event
Interphase	90% of cell cycle
G1	Cell growth, RNA and protein synthesis
S	DNA replication (chromosome duplication)
G2	Preparation for mitosis (DNA repair)
M (Mitosis)	
	Prophase
	Metaphase
	Anaphase
	Telophase

Types of cells:

- **Labile (continuously dividing) tissues:**
  - ✓ They are **continuously being lost** and **replaced** by maturation from tissue stem cells
  - ✓ **Example**:
    - **Hematopoietic stem cells** in the bone marrow.
    - **Surface epithelia**, such as **stratified squamous epithelia** of the skin, oral cavity, vagina, and cervix.
    - The **cuboidal epithelia** of the ducts draining exocrine organs (e.g., salivary glands, pancreas, biliary tract).
    - C**olumnar epithelium** of the GIT, genital tract.
    - The **transitional epithelium** of the urinary tract
- **Quiescent (or stable) tissues**:
  - ✓ Cells of these tissues are quiescent **(G_0 stage of cell cycle**) and
  - ✓ **Minimal (low) proliferative activity** in normal state.
  - ✓ **Capable of dividing in response to injury or loss of tissue mass.**
  - ✓ **Examples:**
    - The parenchyma of **liver, kidney, and pancreas**.
    - **Endothelial cells, fibroblasts, and smooth muscle cells**. The proliferation of these cells is particularly important in wound healing.
    - **Limited capacity to regenerate** after injury (except hepatocytes)
- **Non dividing (Permanent) tissue:**
  - ✓ **Terminally differentiated**
  - ✓ Examples: **Neurons, skeletal muscle and cardiac muscle cells**

Stem cell:

- **Very high level of replication**
- **Has important role in tissue homeostasis**
- **Two important properties:**
  - ✓ **Self renewal**- maintain their numbers
  - ✓ **Asymmetric division**- gives rise to mature cells

- **Two types-**
  - ✓ **Embryonic stem cell:**
    - Most undifferentiated
    - Virtually limitless renewal capacity
    - **Can give rise to any cell (Totipotent)**
  - ✓ **Adult stem/ tissue stem cell**:
    - Differentiated cells of a particular tissue (**multipotent**)
    - Protected within stem cell niches

2. Inflammation

2.1 Acute Inflammation

Causes/etiology of acute inflammation**

1) Infectious Agents-Bacteria, virus, fungi, protozoa, helminths and microbial toxins.
2) Immunologic injury: Hypersensitivity reaction e.g.-allergic rhinitis, acute rheumatic fever etc.
3) Physical agents-e.g. burn, ionizing radiation.
4) Chemical Agents, e.g. corrosives, acids, alkalis.
5) Foreign bodies like sutures, dirt, splinters.
6) Tissue necrosis: e.g.-Infarct.

Cells of acute inflammation: ***	Cells of chronic inflammation
• Neutrophil • Eosinophil • Basophil • Macrophage	• Macrophage • Lymphocytes • Mast cells • Plasma

Q. Following cells are involved in Acute inflammation *(42nd Special BCS)*

a) B cells b) Lymphocytes c) Epitheloid cells d) Neutrophil

Answer: D

Cardinal signs of inflammation (Introduced by Celsius, a roman writer of first century)

Cardinal signs	Physiological rationale
Rubor (Redness)	Increased blood flow
Calor (Heat)	Exudation of Fluid
Tumor (Swelling)	Increased blood flow, exudation of fluid, release of inflammatory mediators
Dolor (Pain)	Stretching of pain receptors by inflammatory exudates and chemical mediators
Function lease (loss of function)	Pain, disruption of tissue structure, fibroplasia and metaplasia

(Ref: Khaleque Pathology/P-16)

Effects of inflammation:

- ✓ Local: Rubor, tumor, calor, dolor, function laesa
- ✓ **Systemic:**
  - **Brain:** Fever **(IL-1**, IL-6, PGE_2)
  - **Liver:** Increased production of **acute phase reactants**:
    - **Fibrinogen: ↑ESR**
    - **CRP**
    - **Serum amyloid A**
    - **Haptoglobin**
    - **Hepcidin**
  - **Bone marrow:** Increased **Leukocyte production**

Q. Fever is mediated by- ***(48th Special BCS)***
a) Bradykinin b) Complements c) Hagemen factor d) Interleukin- 1
Answer: D

Leukocyte mediated acute tissue damage occurs in the acute inflammatory reactions.

Q. Leukocyte induced acute tissue injury- ***(48th Special BCS)***
a) Arthritis b) Asthma c) Atherosclerosis d) Pulmonary fibrosis
Answer: A

Events or Changes of acute inflammation:

Three major components of acute inflammation:

1) Alterations in vascular caliber that lead to an increase in blood flow. (**Vascular changes**)
2) Structural changes in the microvasculature that permits the plasma proteins and leukocytes to leave the circulation
3) Emigration of the leukocytes from the microcirculation and their accumulation in the focus of injury.

2.1.1 Chemotaxis

Migration of leukocytes toward the site of injury along a chemoattractant gradient

Chemoattractant:

1. Exogenous - Bacterial products
2. **Endogenous**:
   - Cytokines **(IL-8)**
   - Components of the complement (**C5a)**, and
   - Arachidonic acid (AA) metabolites **(LTB_4)**

Box: ***

In acute inflammation neutrophil predominate in first 6-24 hours, and replaced by monocytes in 24-48 hours.
In Pseudomonas infection neutrophil predominates for several days, in viral infection lymphocytes predominates.

For Neutrophils	For Monocyte macrophages	For eosinophils
• Bacterial peptides and lipids • Complement component C5a • LTB4, IL-8	• Complement component C5a • Bacterial peptides and lipids • LTB4, MCP-1, MIP-1, • 1β, IL-1, TNF, Kallikrein, PDGF	C5a, LTB4, ECF, PGD2, and exotoxin

2.1.3 Phagocytosis

Major opsonins are: Helps in phagocytosis

1. **C3b, and ic3b**
2. IgG antibodies
3. Plasma proteins mannose-binding lectin (MBL) C-reactive proteins, Fibrinogen, Fibronectin.

Q. Phagocytosis is promoted by ***(42nd Special BCS)***
a) Hyaluronidase c) Neuraminidase b) Complement d) The Hexose monophosphate shunt
Answer: **B**

Killing and Degradation

Killing of microbes by reactive oxygen species and reactive nitrogen species and lysosomal enzymes destroy phagocytosed debris.

a. Oxygen-dependent mechanism: Most cases.

i) **H_2O_2 MPO-Halide system: most efficient bactericidal** system in neutrophils.

ii) Reactive oxygen intermediates (ROIs): O_2^- (superoxide), H_2O_2, $0H^-$

iii) Microbicidal reactive nitrogen intermediate particularly NO.

b. Oxygen-independent mechanisms:

i) Lysozyme hydrolyses muramic acid substance

ii) Lactoferrin

iii) BPI (Bactericidal permeability increasing protein).

iv) Defensins.

Lysosomal Enzymes and Other Lysosomal Proteins:

Neutrophils and monocytes contain lysosomal granules that contribute to microbial killing and, when released, may contribute to tissue damage.

Eosinophil release major basic protein which is cytotoxic to many parasites.

2.1.2 Exudate vs Transudate

Difference between Exudate and Transudate: ***

Features	Exudate	Transudate
Total protein count	High protein concentration (30g/L to as in plasma)	Less than 10g/L
Distribution of protein	As in plasma	Mostly albumin
Fibrinogen	**Present,** clots spontaneously	Absent. No tendency to clot
Specific gravity	High (> 1.020)	Low (< 1.012)
Cells	Inflammatory cells and much cell debris	Few present, nearly all are mesothelial
Cause	Increased vascular permeability	Imbalance of hydrostatic pressure along the vascular endothelium
Occurrence	Inflammatory condition	Non-inflammatory conditions e.g NS

(Ref: Khaleque Pathology/P-43/Table-4.1)

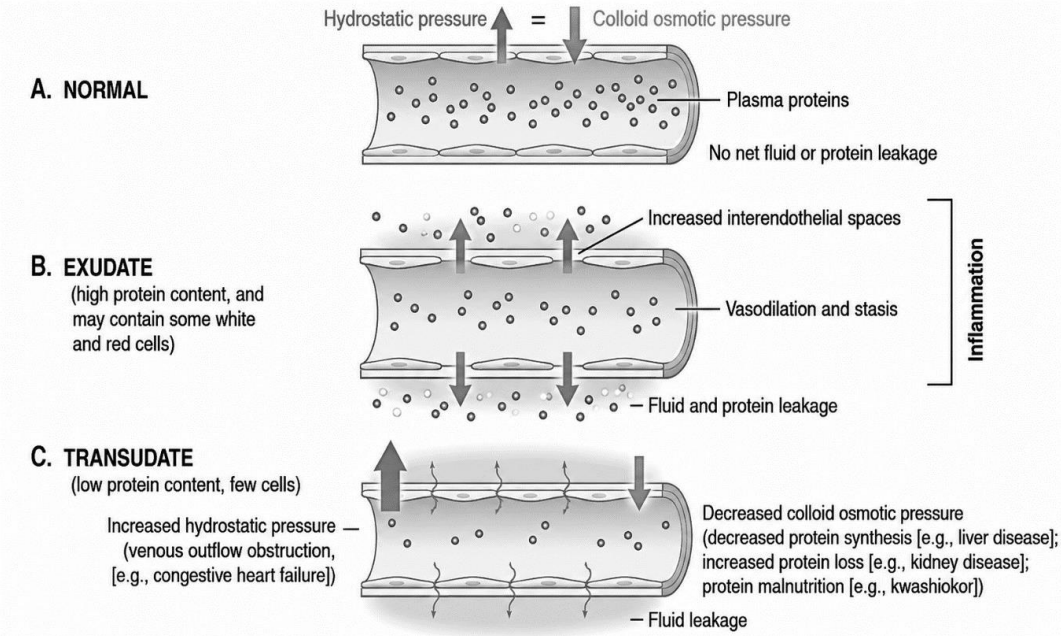


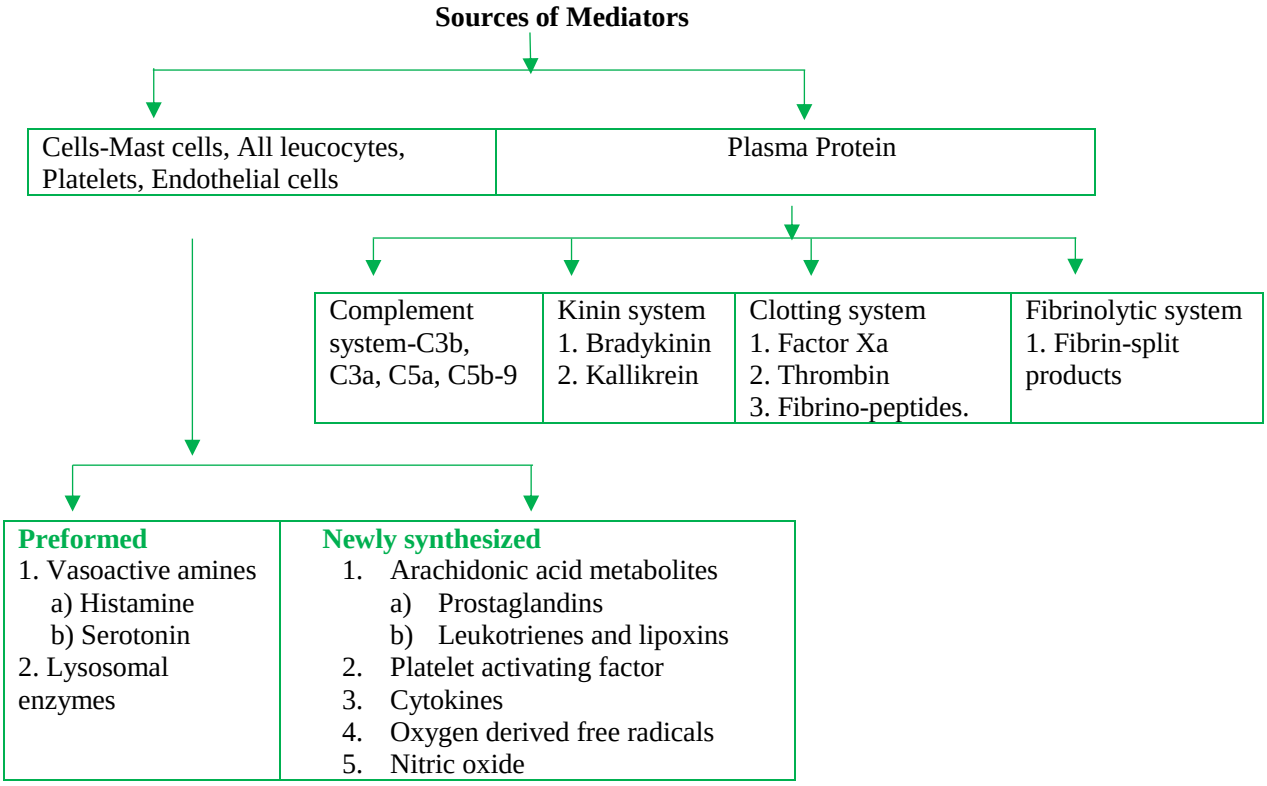
Fig. Formation of exudates and transudates. **(A)** Normal hydrostatic pressure (**blue arrow**) is about **32 mm Hg** at the arterial end of a capillary bed and **12 mm Hg** at the venous end; the mean colloid osmotic pressure of tissues is approximately **25 mm Hg** (**green arrow**), which is equal to the mean capillary pressure. Therefore, the net flow of fluid across the vascular bed is almost nil. **(B)** An exudate is formed in inflammation because vascular permeability increases as a result of retraction of endothelial cells, creating spaces through which fluid and proteins can pass. **(C)** A transudate is formed when fluid leaks out because of increased hydrostatic pressure or decreased osmotic pressure.

(Ref: Robbin's/9th edition/P-73)

Key point: Pus is inflammatory exudate rich in leukocytes (mainly neutrophil), debris of dead cells, and in many case microbes and edema fluid.

2.1.3 Mediators of Inflammation*****

- Histamine (most important mediator)
- Mediators are either *secreted by cells* or generated from *plasma proteins*.



(Ref: Khaleque Pathology/P-21)

Plasma derived mediators are produced mainly from liver, one mediator can stimulate the release of another mediator, are short lived.

The action of the principal mediators of inflammation

Mediator	Principal sources	Actions
Cell derived		
Histamine	Mast cell, basophils, platelets	Vasodilation, increased vascular permeability, endothelial activation
Serotonin	Platelets	Increased vascular permeability
Prostaglandins	Mast cell, leukocytes	Vasodilation, pain, fever
Leukotrienes	Mast cell, leukocytes	Increased vascular permeability, chemotaxis, leukocyte adhesion and activation
Platelet activating factor	Leukocytes, mast cell	Vasodilation, increased vascular permeability, leukocyte adhesion, chemotaxis, degranulation, oxidative burst
Reactive oxygen species	Leukocytes	Killing of microbes, tissue damage
Nitric oxide	Endothelium, Macrophages	Vascular smooth muscle relaxation, killing of microbes

05. Diseases of the Cardiovascular System

5.1 Ischaemic heart disease

Coronary artery disease: clinical manifestations and pathology***

Clinical problem	Pathology
Stable angina	Ischaemia due to fixed atheromatous stenosis of one or more coronary arteries
Unstable angina	Ischaemia caused by dynamic obstruction of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Myocardial infarction	Myocardial necrosis caused by acute occlusion of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Heart failure	Myocardial dysfunction due to infarction or ischaemia
Arrhythmia	Altered conduction due to ischaemia or infarction
Sudden death	Ventricular arrhythmia, asystole or massive myocardial infarction

Management of acute ST elevated MI/acute coronary syndrome;
Clinical features:
Symptoms:

- Prolonged cardiac pain: Chest, throat, arms, epigastrium or back
- Anxiety and fear of impending death
- Nausea and vomiting
- Breathlessness
- Collapse/synocope

Signs:

a) Signs of sympathetic activation: Pallor, sweating, tachycardia
b) Signs of vagal activation: Vomiting, bradycardia
c) Signs of impaird myocardial function
   - Hypotension, oliguria, cold peripheries
   - Narrow pulse pressure
   - Raised jugular venous pressure
   - Third heart sound
   - Quiet first heart sound
   - Diffuse apical impulse
   - Lung crepitations

Investigations:

1) **ECG: ST elevation, followed by T-wave inversion, then pathological Q-wave development.**

2) Plasma biochemical markers:

- **Troponin-I:** Released within 3-6 hours, peak at about 36 hours and remain elevated up to 2 weeks.
- **CK-MB:** Starts to rise at **4-6 hours, peaks at about 12 hours, and falls to normal within 48- 72** hours.

3) Other blood tests: Leucocytosis, raised ESR and C-reactive protein.
4) Chest X-ray: Features of pulmonary oedema if LVF develops.
5) Echocardiography: Detects infarct associated regional wall motion abnormalities.
6) Coronary angiography.

Treatment of acute MI:***

1) Immediate hospitalization where defibrillation facility is available.
2) High-flow oxygen.
3) Intravenous access.
4) ECG monitoring.
5) Aspirin 300 mg chewed and clopidogrel 300 mg oral.
6) Sublingual glyceryl trinitrate: Tablet or spray (if systolic BP > 110 mmHg).

7) Intravenous analgesia: Opiates (Morphine or Pethidine) and antiemetic.
8) Beta blockers (if no contraindication): For ongoing chest pain, hypertension, tachycardia.
9) Thrombolytic or anticoagulant:
    - If ST-elevated MI: Thrombolysis with streptokinase 1.5 million U in 100 ml of saline given as an intravenous infusion over 1 hour. Alteplase and retiplase are the other options
    - If non-ST-elevated MI: Low molecular weight heparin (e.g. enoxaparin).
10) If percutaneous intervention (PCI) is available, patient should be prepared for that.
11) Detection and management of acute complications e.g. arrhythmias, cardiogenic shock, heart failure.
12) Coronary bypass surgery when indicated.

Population-based strategies to prevent coronary disease

- Do not smoke
- Take regular exercise (minimum of 20 mins, three times per week)
- Maintain an 'ideal' body weight
- Eat a mixed diet rich in fresh fruit and vegetables
- Aim to get no more than 10% of energy intake from saturated fat

Advice to patients with stable angina

- Do not smoke
- Aim for an ideal body weight
- Take regular exercise (exercise up to, but not beyond, the point of chest discomfort is beneficial and may promote collateral vessels)
- Avoid severe unaccustomed exertion, and vigorous exercise after a heavy meal or in very cold weather
- Take sublingual nitrate before undertaking exertion that may induce angina

Risk factor of Ischamic heart disease****	
• Age and sex- Pre-menopausal women have lower rates of disease than men, although the gender difference disappears after the menopause. • Genetics • Smoking-There is a strong relationship between cigarette smoking and CAD, especially in younger (<70 years) individuals, and this is probably the most important modifiable risk factor. • Hypertension • Hypercholesterolaemia • Diabetes mellitus. • Haemostatic factors: Platelet activation and high plasma fibrinogen concentrations are associated with an increased risk	• Physical activity- Regular exercise (brisk walking, cycling or 20 minutes two or three times a week) has a protective effect, whereas inactivity roughly doubles the risk of CAD and is a major risk factor for stroke. • Obesity. • Alcohol. • Diet. The introduction of a Mediterranean-style diet reduces cardiovascular events. • Personality • Social deprivation

Factors influencing myocardial oxygen supply and demand***

Oxygen demand: Cardiac work

- Heart rate
- Blood pressure
- Myocardial contractility
- Left ventricular hypertrophy
- Valve disease

Oxygen supply: Coronary blood flow*

- Duration of diastole
- Coronary perfusion pressure

(aortic diastolic minus coronary sinus or right atrial diastolic pressure)

Activities precipitating angina***

Common	
• Physical exertion • Cold exposure	• Heavy meals • Intense emotion
Uncommon	
Vivid dreams (nocturnal angina)	• Lying flat (decubitus angina)

Acute coronary syndrome
Acute coronary syndrome is a term that encompasses both unstable angina and myocardial infarction.

Criteria for diagnosis of a prior myocardial infarction

- Pathological Q waves with or without symptoms in the absence of non-ischaemic causes
- Imaging evidence of a region of loss of viable myocardium that is thinned and fails to contract, in the absence of a non-ischaemic cause
- Pathological findings of a prior myocardial infarction

Common arrhythmias in acute coronary syndrome**	
• Ventricular fibrillation • Ventricular tachycardia • Accelerated idioventricular rhythm • Ventricular ectopics • Atrial fibrillation	• Atrial tachycardia • Sinus bradycardia (particularly after inferior myocardial infarction) • Atrioventricular block

Late management of myocardial infarction**

Risk stratification and further investigation Lifestyle modification	
• Diet (weight control, lipid-lowering, 'Mediterranean diet')	• Cessation of smoking • Regular exercise
Secondary prevention drug therapy	
• Antiplatelet therapy (aspirin and/or clopidogrel) • β-blocker • ACE inhibitor/ARB • Statin	• Additional therapy for control of diabetes and hypertension • Mineralocorticoid receptor antagonist
Rehabilitation Devices	
• Implantable cardiac defibrillator (high-risk patients	
(ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker)	

Relative contraindications to thrombolytic therapy **

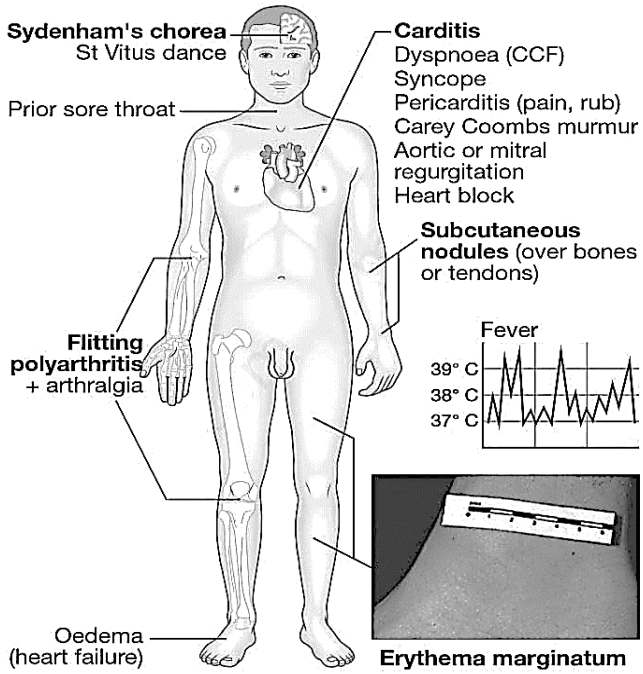
- Active internal bleeding
- Previous subarachnoid or intracerebral haemorrhage
- Uncontrolled hypertension
- Recent surgery (within 1 month)
- Recent trauma (including traumatic resuscitation)
- High probability of active peptic ulcer
- Pregnancy

Q. Which of the following type of necrosis is seen in acute myocardial infarction? *(39th Special BCS)*
a) Coagulative necrosis b) Fat necrosis c) Caseous necrosis d) Gangrenous necrosis
Answer: A

5.2 Rheumatic Fever and Rheumatic Heart Disease**

- Acute rheumatic fever is a multisystem disorder that usually presents with fever, anorexia, lethargy and joint pain, **2–3 weeks** after an episode of streptococcal pharyngitis. The main pathological process in chronic rheumatic heart disease is **progressive fibrosis.**
- The heart valves are predominantly affected but involvement of the pericardium and myocardium also occurs and may contribute to heart failure and conduction disorders. The mitral valve is affected in more than 90% of cases; the aortic valve is the next most frequently involved, followed by the tricuspid and then the pulmonary valve.(MATP)

Clinical features of rheumatic fever.



Jones Criteria for the Diagnosis of Rheumatic Fever***

Major manifestations	
• Carditis (Pancarditis) • Polyarthritis (commonest major manifestation) • Chorea(Sydenham's Chorea)	• Erythema marginatum • Subcutaneous nodules
Minor manifestations	
• Fever • Arthralgia • Raised erythrocyte sedimentation rate or • C-reactive protein	• Previous rheumatic fever • Leucocytosis • First-degree atrioventricular block
Plus	
• Supporting evidence of preceding streptococcal infection: recent scarlet fever, raised antistreptolysin O or other streptococcal antibody titre, positive throat culture*	
*Evidence of recent streptococcal infection is particularly important if there is only one major manifestation.	

Investigations in acute rheumatic fever

Evidence of a systemic illness

- Leucocytosis, raised erythrocyte sedimentation rate and C-reactive protein

Evidence of preceding streptococcal infection

- Throat swab culture: group A β-haemolytic streptococci (also from family members and contacts)
- Antistreptolysin O antibodies (ASO titres): rising titres, or levels of > 200 U (adults) or > 300 U (children)

Evidence of carditis

- Chest X-ray: Cardiomegaly; pulmonary congestion
- ECG: first- and, rarely, second-degree atrioventricular block; features of pericarditis; T-wave inversion; reduction in QRS voltages
- Echocardiography: Cardiac dilatation and valve abnormalities

Management:

- Bed rest
- Treatment of cardiac failure
- Antibiotic therapy- A single dose of benzathine benzyl penicillin or oral phenoxymethyl penicillin (250 mg 4 times daily for 10 days)
- Aspirin- Response within 24 hours helps diagnosis.
- Glucocorticoid- indicated in carditis or severe arthritis.

5.3 Valvular Diseases of Heart

Collapsing pulse: AR
Pulsus alternans: LVF
Slow rising pulse: AS
Dancing carotid sign/ Corrigan's sign (forceful rise & quick fall of JVP)
Narrow pulse pressure: AS
Wide pulse pressure: AR
p2 is palpable in pulmonary HTN.
A thrill, a palpable vibration, is the tactile equivalent of a murmur.
The most common thrill is that of AS- palpable at the upper right sternal border.
Thrill of VSD is best felt at the left & right sternal edge.
Systolic thrills coincide with carotid pulse.
2nd heart sound-S2, caused by closure of aortic & pulmonary valves, there is physiological splitting of S2 (A2.....P2)

- Wide & fixed splitting in ASD.
- Reverse splitting in left bundle branch block (LBBB), AS.

In heart failure, S3 with tachycardia is referred to as a gallop rhythm.

JVP:

- Raised pulsatile: Cor pulmonale
- Raised non pulsatile: SVC obstruction

Causes of acute valve failure:

Aortic regurgitation
• Aortic dissection • Infective endocarditis
Mitral regurgitation
• Papillary muscle rupture due to acute myocardial infarction • Infective endocarditis • Rupture of chordae due to myxomatous degeneration
Prosthetic valve failure
• Mechanical valves: fracture, jamming, thrombosis, dehiscence • Biological valves: degeneration with cusp tear

Clinical features of mitral stenosis**

Clinical feature	Cause
Symptoms Breathlessness	 Pulmonary congestion, low cardiac output
Fatigue	Low cardiac output
Oedema, ascites	Right heart failure
Palpitation	Atrial fibrillation
Haemoptysis	Pulmonary congestion, pulmonary embolism
Cough	Pulmonary congestion
Chest pain	Pulmonary hypertension
Thromboembolism	Atrial stasis and atrial fibrillation
Signs	
Atrial fibrillation	Atrial dilatation
Mitral facies	Low cardiac output
Auscultation: Loud first heart sound, opening snap, Mid-diastolic murmur	Pressure gradient across the valve
Crepitations, Pulmonary oedema, Pleural effusions	Left heart failure
Right ventricular heave, loud P2	Pulmonary hypertension

Causes of Mitral Regurgitation**
• Mitral valve prolapse • Dilatation of the left ventricle and mitral valve ring (e.g. coronary artery disease, cardiomyopathy) • Damage to valve cusps and chordae (e.g. rheumatic heart disease, endocarditis) • Ischaemia or infarction of the papillary muscle • Myocardial infarction

Causes of aortic regurgitation**

Congenital
• Bicuspid valve or disproportionate cusps
Acquired
• Rheumatic disease • Infective endocarditis • Trauma • **Causes of aortic dilatation:** Marfan's syndrome, Aneurysm, Aortic dissection, Syphilis, Ankylosing spondylitis

Q.A regurgitating aortic valve in a non-functioning heart causes *(42nd Special BCS)*	**Q. Features of aortic stenosis includes *(42nd Special BCS)***
a) Decrease in diastolic pressure b) Decrease in heart rate c) Systolic murmur d) Decrease in systolic blood pressure	a) Irregular pulse b) Heaving apex beat c) Left parasternal heave d) Mid-diastolic murmur
Answer: A	**Answer: B**

Timing and pattern of murmur:

- **Pansystolic murmur (throughout systole):** MR, TR, VSD
- **Ejection systolic murmur:** AS, PS
- **Early diastolic murmur:** AR
- **Mid-diastolic murmur:** MS

Heart murmurs are graded 1 to 6.

- **Grade 4:** Loud with associated thrill
- **Grade 6:** Heard without stethoscope.

Surgery

01. History, Evolution and Scope of Surgery

History & Evolution of Surgery

- History of surgery is as old as humanity
- It is said that where medicine ends, surgery begins.
- Surgery derived from Latin word – **Chirurgia**
  - ✓ Cheir- Hand
  - ✓ Ergon- work

Ancient Period:

- Surgical practices date back to ancient civilizations like Egypt, India, and Greece.
- Procedures such as **trepanation (drilling into the skull)** and cataract surgery were performed.
- **Sushruta (India, ~600 BCE) is considered one of the earliest surgeons;** his texts describe over 300 surgical procedures.

Medieval Period:

- Surgery was often performed by **barber-surgeons,** and pain management was minimal.
- Knowledge stagnated due to religious and cultural restrictions on dissection.

Renaissance to 18th Century:

- Surgeons like **Ambroise Paré** advanced battlefield surgery and introduced more humane methods.
- **John Hunter** emphasized anatomical studies and experimentation.

19th Century:

- Anesthesia (ether, chloroform) made pain-free surgery possible.
- **Antisepsis (Joseph Lister's work) reduced infections.**
- Surgery became a respected medical discipline.

20th Century Onward:

- Advances in surgical precision
- Minimally invasive techniques
- Organ transplants

21st Century (Modern Era):

- **Robotic surgery**
- **AI- assisted procedures**

- ❖ Founding father of surgery – **Sushruta Samhita**
- ❖ Father of modern surgery – **Joseph Lister**
- ❖ Father of modern scientific surgery – **John Hunter**

Scope of Surgery:

General Surgery:	Abdominal surgeries, Soft Tissue, Hernia operations etc.
Orthopedic Surgery:	Musculoskeletal issues, fractures, joint replacement etc.
Neurosurgery:	Brain, spinal cord and peripheral nerve surgeries
Cardiothoracic surgery:	Heart, Lungs and major blood vessel surgeries
Surgical Oncology:	Tumor removal, Cancer related surgery
Endoscopic & Laparoscopic surgery:	Small-incision procedures for diagnostics and therapeutics
Plastic & Reconstructive surgery:	Burn, Cosmetic and functional restoration, Congenital defect repairs
Gynecological Surgery :	Focuses on the female reproductive system, Includes hysterectomy, fibroid removal etc.
Others:	Includes paediatrics, urologic and other specialized surgeries

02. Assess and Prepare Patient for Surgery

Patient Assessment

1. History taking
2. Examination
3. Investigations—
   - ✓ Full blood count
   - ✓ HbA1c
   - ✓ Sickle cell test
   - ✓ Urea and electrolytes
   - ✓ Liver function test
   - ✓ Clotting/coagulation screen
   - ✓ ECG
   - ✓ Chest radiographs
   - ✓ Echo
   - ✓ Urine test
   - ✓ Beta HCG (pregnancy test)
   - ✓ Others-Venous bicarbonate
   - ✓ ABG
   - ✓ Blood group and cross match
   - ✓ MRSA swabs
   - ✓ Covid-19--- PCR swabs
   - ✓ Spirometry

Preoperative preparation

Cardiovascular disease:

*****Ischemic heart disease:**

- Beta blockers and statins should have their medication continued preoperatively.
- Most long term cardiac medications should be continued over the perioperative period.
- Angiotensin converting enzyme **(ACE) inhibitors** and receptor blockers **(ARB)** are often **omitted 24 hours** prior to surgery to prevent intraoperative hypotension and restarted the next day for most surgery.
- After a proven myocardial infraction elective surgery should be postponed for **3-6 months** to reduce the risk of perioperative reinfarction

*****Hypertension:**

- Prior to elective surgery blood pressure should be controlled to **< 160/100 mmHg.**
- If a new antihypertensive agent is introduced a stabilisation period of at least **two weeks** should be allowed.

*****Heart failure:**

- **Beta blockers** and probably **ACE inhibitors** should be continued.
- A left ventricular ejection fraction of less than 35% should be discussed with the cardiologist and optimised.

*****Dysrhythmias:**

- In patients with atrial fibrillation (AF), B-blockers, digoxin or calcium channel blockers should be continued in order to control rate.
- Warfarin in patients with AF should be stopped 5 days preoperatively to achieve an international normalised ratio (INR) of 1.5 or less, which is safe for most surgery.
- The newer articoagulants such as dabigatran (direct thrombin inhibitor) or rivaroxaban, apixaban and edoxaban (direct factor Xa mhibitors) do not have antagonists and must be stopped preoperatively, generally 2-3 days in patient with normal renal function and longer when renal function is impaired.

**** Diabetes mellitus:**

- For elective surgery an **HbA_1C of less than 69 mmol/mol is recommended.**

- Lipid lowering medication should be started in patients who are in a high risk group for cardiovascular complications of Diabetes.
- Patients with diabetes should be first on the operating list.

**** Thrombophilia:**

The progesterone only contraceptive pill should be continued.
Consider stopping oestrogen containing oral contraceptives or hormone replacement therapy **4 weeks** before surgery.

*** Neurological and psychiatric disorders:**

- Anticonvulsants and anti Parkinson's medication must be continued perioperatively to help early mobilisation of the patient.
- **Lithium should be stopped 24 hours prior to major surgery.**

Starvation before surgery: Pre-operative starvation / fasting times are as follows:

Preoperative fasting time	
Adult	**Avoid solid diet for 6 hours & clear fluids for 4 hours**
Babies under 1 year	No breast milk for 2-3 hours before anaesthesia. No formula feed for 6 hours before anaesthesia. Clear fluids may be given upto 3 hours before anaesthesia.
Children over 1 year	No feed/milk for 6 hours before anaesthesia. Clear fluids up to 3 hours before anaesthesia.

03. Trauma

Definition:

Trauma can be defined as an injury to any part of the human body as a result of energy transfer from an inflicting source. The forces that can lead to injury include chemical,thermal,ionising radiation and mechanical.
Major trauma is defined as as ISS (Injury severity score) **> 15.**

*****ATLS:**

Advanced trauma life support.
Components /Steps:

1. **Primary survey with simultaneous resuscitation:** Identify and manage the most immediately life threatening injuries
2. **Secondary survey:** A detailed head to toe examination to identify all other injuries
3. **Definitive care:** Specialist treatment of identified injuries

Primary survey & resuscitation: The standard sequence of the initial primary survey is –cABCDE
c- Control of massive external hemorrhage

A-Airway maintenance and cervical spine protection

- Immediate assessment of the patient airway
- Immediate stabilization of the cervical spine(e.g.cervical collar,neck brace)
- Supporting the airway by **chin -lift & jaw thrust**
- Maintenance patency of airway by Oropharyngeal tube,supraglottic device or ET tube

B- Breathing and ventilation

- The chest must be exposed & examined by looking, listening and feeling
- **High flow oxyge**n in a patient with inadequate breathing
- Tension pneumothorax must be decompressed immediately by rapid insertion of a large bore cannula into the **second intercostal space** in the mid clavicular line of the affected side, followed by insertion of a chest drain tube through the **fifth intercostal space in the anterior axillary line(Triangle of safety)**

C- Circulation and hemorrhage control

- Identify the site of bleeding
- External bleeding is controlled by direct pressure & tourniquets.
- **Two 14-G (gauge)** cannula for iv fluid and blood administration.
- Send blood for screening & cross matching

D- Disability (Neurological status)

- Assessing patients neurological status by **GCS score**.
- Examination of pupils for signs of raised ICP or brain damage

E- Exposure & environment

- All clothing should be removed
- Require log rolling to examine the posterior aspects
- Patient should be kept warm with a blanket to prevent hypothermia

Adjunts to primary survery:

- ECG monitoring
- Pulse oximetry
- End-tidal carbon dioxide monitoring (EtCO2;capnography)
- ABG
- Urethral catheter
- NG tube
- Chest x -ray
- Pelvic x -ray

Increasingly Ultrasonogrphy & CT scan are used as adjuncts during or immediately after the primary survey.

Secondary survey:

Components of secondary survey-

1. The history: a detailed history about – (AMPLE)

- A-Allergy
- M-Medication
- P-Past medical history
- L-Last meal
- E-Event of incidence

2. Physical examination: detailed **head to toe examination** to identify all other injuries

3. Tubes and fingers in every orifice

4. Neurological examination:

• Rapid neurological assessment to detect lateralizing signs,loss of sensation and motor power and abnormality of reflexes.

5. Further diagnostic test:

- X ray
- MRI
- CT scan
- Ultasound

6. Re-evaluation

Definite care: Definitive care describes the specialist care required to manage the injuries identified during the initial assessment and subsequent investigations.

*****Triage:**

Definition: Triage means to sort and is the cornerstone of the management of mass casualties

Or

Triage is a system to attend trauma patient, formulated by Committee of Trauma of the American College of Surgeons.

*** Origin of triage:**

- The word '**Triage**' derived from the French verb '**Trier**')
- Baron Dominique Jean Larre (1766-1842). Surgeon in Napoleon's Army.

Types of triage / Application of Triage / Phases of triage:

1) Field triage:

- ✓ Used at the scene of the event
- ✓ Identify patients who need critical attention and immediate transport

Obstetrics

01. Conception and development of Fetoplacental unit

Fundamental of Reproduction

Gametogenesis
The process involved in the maturation of the two highly specialized cells, spermatozoon in male and ovum in female before they unite to form zygote, is called gametogenesis.

Oogenesis
The process involved in the development of a mature ovum is called oogenesis. The primitive germ cells take their origin from the **yolk sac** at about the end of 3rd week and their migration to the developing gonadal ridge is completed round about the end of 4th week.

Maturation of the oocytes
The first stage of maturation occurs with full maturation of the ovarian follicle just prior to ovulation but the final maturation occurs only after fertilization.

Ovulation occurs soon after the formation of the secondary oocyte.
The secondary oocyte completes the second meiotic division (homotypical) only after fertilization by the sperm in the Fallopian tube.

Structure of a mature ovum: A fully mature ovum is the largest cell in the body and is about 130 microns in diameter. It consists of cytoplasm and a nucleus with its nucleolus which is eccentric in position and contains 23 chromosomes (23, X).

- Stem cell to develop mature sperm (spermatogenesis)-74 days
- Spermatogonium to develop into mature spermatozoon is 61 days

Ovulation
Ovulation is a process whereby a secondary oocyte is released from the ovary following rupture of a mature Graafian follicle and becomes available for conception.

Spermatogenesis
The process involved in the development of spermatids from the primordial male germ cells and their differentiation into spermatozoa is called spermatogenesis.

Shortly before puberty, the primordial germ cells develop into spermatogonia and remain in the wall of seminiferous

Fertilization, Implantation

Ovulation
Ovulation is a process whereby a secondary oocyte is released from the ovary following rupture of a mature Graafian follicle and becomes available for conception. It occurs about 14 days prior to the next Menstruation.

Fertilization
Fertilization is the process of fusion of the spermatozoon with the mature ovum.

Site: Ampullary part of the uterine tube
Timing of fertilization:

Fertilization begins with sperm egg collision and ends with production of a mononucleated single cell called the zygote. It usually occurs on Day-15 from the last menstrual period (LMP).

Fertilizable life span:

- **Oocyte:** 12 to 24 hours
- **Sperm:** 48 to 72 hours

Results of fertilization

1. Restoration of the diploid number of chromosomes
2. Determination of the sex of the new individual
3. Initiation of cleavage

Cleavage

Two cell stage is reached approximately 30 hours after fertilization

Morula	**Blastocyst**
-16 to 64 cell stage - no increase of volume - Zona pellucida remains intact - Enters the uterine cavity on D4 - Divides into inner cell mass and outer cell mass	-Within the uterine cavity - Blastocele (cavity) formation - Zona pellucida disappears - Inner cell mass develops into embryoblast - Outer cell mass develops into trophoblast

Implantation

Implantation is the process which involves the attachment, penetration and embedding of the **blastocyst** in the lining of the uterine wall.

Site: Endometrium of the posterior wall of the body near the fundus

Timing: On the 6th day which corresponds to the 20th day of a regular menstrual cycle

This process is completed by 10th or 11th day which corresponds to D 24-25 from LMP

Important events following fertilization

- 'O' hour : Fertilization (D-15 from LMP)
- 30 hours : 2 cell stage (Blastomeres)
- 40-50 hours : 4 cell stage
- 72 hours : 12 cell stage
- 96 hours : 16 cell stage. Morula enters the uterine cavity
- 5th day : Blastocyst
- 4-5th day : Zona pellucida disappears
- 5-6th day : Blastocyst attachment to endometrial surface
- 6-7th day : Differentiation of cyto and syncytiotrophoblastic layers
- • 10th day : Synthesis of hCG by syncytiotrophoblast
- 9-10th day : Lacunar network forms
- 10-11th day : *Trophoblasts invade endometrial sinusoids establishing utero-placental
- Circulation

*Interstitial implantation completed with entire decidual coverage

- 13th day : Primary villi
- 16th day : Secondary villi
- 21st day : Tertiary villi
- 21st -22nd day : Fetal heart, feto-placental circulation
- 5 weeks : EEC (gestational sac on USG)
- 5.5 weeks : Yolk sac
- 12 week : Obliteration of EEC.

Nice to know**

- Embryonic stem cell comes from inner cell mass of Blastocyst
- Outer cell mass of blastocyst consists of trophoblasts or trophectoderm
- Syncytiotrophoblast derived from cytotrophoblasts
- Placenta & fetal membrane derived from trophoblasts
- Chorionic villi derived from extra embryonic mesoderm

Oogenesis:
Primitive germ cells arises from the yolk sac > at 4 week migrates by ameboid movement to the developing gonads, arrive by the end of the 5th week.

Maturation of ovum begins in intrauterine life.

- At 5 month or 20th week 7 million oogonia
- At birth 2 million oogonia remains undergo 1" meiotic division >Arrest at diplotene stage of prophase 1 >known as primary oocytes.
- Total number of 1° oocyte is 4,00,000 at puberty
- About 5 to 15 primordial follicles begin to mature with each ovarian cycle.
- Total number of primary oocytes to ovulate throughout female reproductive life is 400
- Zona pellucida layer of glycoprotein secreted by granulosa cells and the oocytes
- First meiotic division resumes shortly before ovulation
- Meiosis-II is completed only if the oocyte is fertilized.
- fibroblast like cells Theca interna and secretory type of cells Theca externa
- A fully mature ovum(23,X) largest cell in the body about 130 microns in diameter.
- The ovum is surrounded by a cell membrane called vitelline membrane

Spermatogenesis:

- Maturation of sperm begins at puberty
- Takes place in seminiferous tubules of testis.
- Epididymis maturation occurs and sperm become motile.

Store house of sperm

1. Efferent ductules
2. Epididymis
3. Ductus different

Morphological changes of Spermatid to Spermatozoa:**

1. Formation of acrosome
2. Condensation of nucleus
3. Formation of tail, middle piece and neck
4. Shedding out most of the cytoplasm

Capacitation

- Physiochemical change in the sperm becomes hypermotile and able to bind & fertilize a secondary oocytes
- Takes place in the female genital tract

Acrosome reaction

- Induced by zona pellucid Release of hydrolytic enzymes, hyaluronidase, proacrosin acrosin etc.
- Occurs when sperms are just touching zona pellucida

Zona reaction

- Refers to an alteration in the structure of the zona pellucida catalyzed by proteases from cortical granules.
- The importance of the zona reaction is that it represents the major block to polyspermy.

The Placenta & Fetal Membranes, Placental Barrier

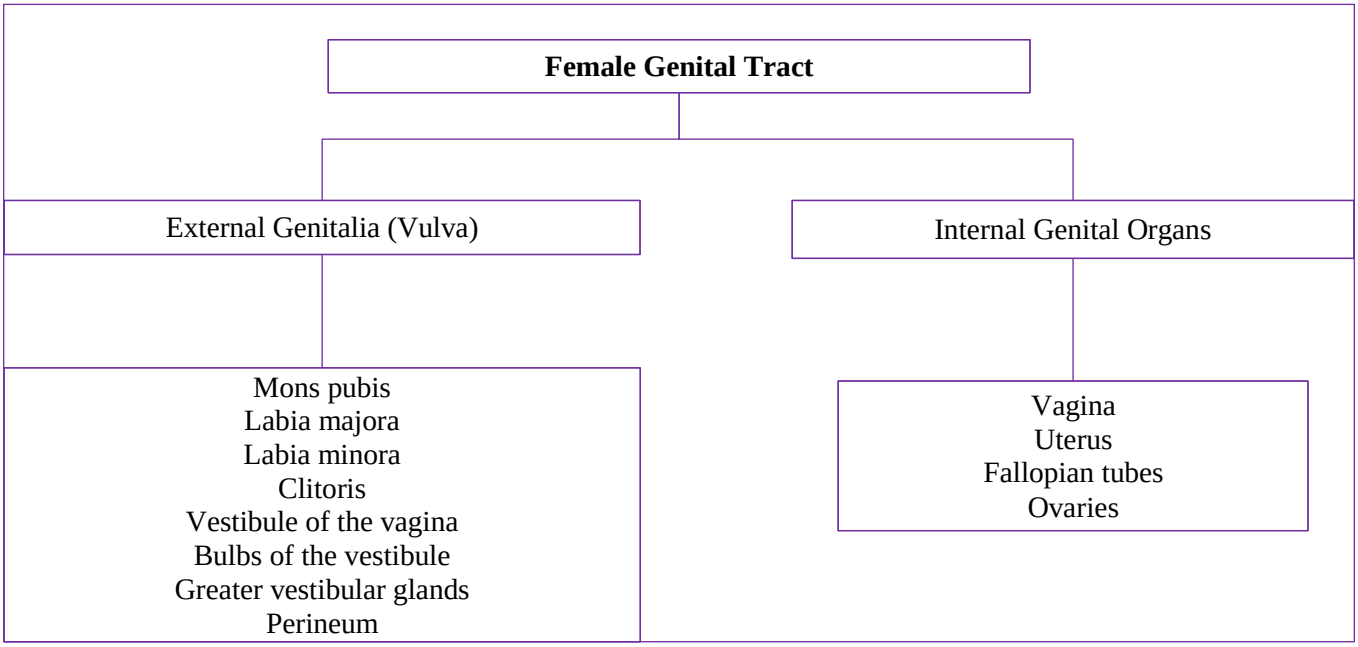
Placenta
The placenta is a discoid, haemochorial and deciduate organ in gravid uterus which is attached to the uterine wall and establishes connection between the mother and fetus through the umbilical cord.

Human placenta is

- **Discoid** : Because of its shape
- **Haemochorial** : Because of direct contact of the chorion with the maternal blood
- **Deciduate** : Because some maternal tissue is shed at parturition

Gynaecology

01. Anatomy of the Female Pelvic



Summary:**

- Accessory Reproductive organ: The Breasts
- Main Reproductive organ: uterus
- Organ of copulation: Vagina
- Sex glands or gonads in female: Ovaries

1. No glands : BTV • B- urinary bladder • T- uterine tube • V- vagina	**2. No submucosa :** • Uterus • Fallopian tube • Ureter • Urinary bladder • Gall bladder • Bile duct	**3. Racemose type gland : BBC** • B- Bartholin • B-Brunner's • C- Cervical glands

Q. Which one of the following is reproductive organ? *(48th Special BCS)*

a) Uterus b) Urinary bladder c) Urethra d) Bone

Answer: A

External genitalia

Summary:

Mons Veneris - Coitus buffer

Labia majora - Produce hematoma during childbirth

Labia minora - Thick folds of skin, resemble ventral aspect of penile urethra, fourchette most commonly injured during child birth

-Clitoris - most sensitive part
-Vestibule - triangular area contain 4 openings

- Vagina
- Urethra
- Ducts of Bartholin's glands

-Hymen - elastic, relatively avascular, tear most commonly posteriorly or posterolaterally

Vagina

The vagina is an elastic, fibromuscular canal which lies in between the urinary bladder and the rectum. It is the organ of copulation and forms the birth canal of parturition.

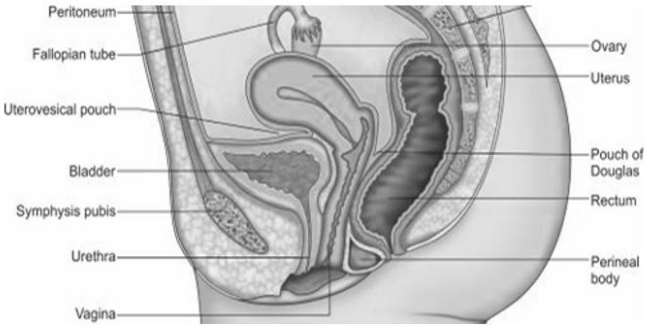


Figure: Mid sagittal section of the female pelvis showing relative position of the pelvic organs

Direction:
The canal runs upwards and backwards from the vulva to the uterus and forms an angle of about 45° with the horizontal plane in erect posture.

Walls:

- Anterior wall: 8 cm long
- Posterior wall: 10 cm long
- Two lateral walls

Fornices:
The fornices are the clefts formed at the vault of the vagina as the uterine cervix projects through the anterior wall. There are **four fornices** in relation to the cervix:

- One anterior (shallow)
- One posterior (deep and capacious)
- Two lateral

➤ **Relations:**

Anterior:

- Upper one-third → Base of the bladder
- Lower two-thirds → Urethra

Posterior:

- Upper one-third → Pouch of Douglas
- Middle one-third → Anterior rectal wall (separated by rectovaginal septum)
- Lower one-third → Separated from anal canal by perineal body

Lateral walls:

- Upper one-third → Pelvic cellular tissue
- Middle one-third → Blended with levator ani muscles
- Lower one-third → Bulbocavernosus muscles, vestibular bulbs and Bartholin's glands

➢ **Structures: (Layers from within outwards):**

1. Mucous coat (lined by stratified squamous epithelium without any secreting glands)
2. Submucous layer
3. Muscular layer
4. Fibrous coat

A. Arterial Supply

1. Cervicovaginal branch of the uterine artery
2. Vaginal artery
3. Middle rectal artery
4. Internal pudendal artery

B. Venous Drainage

- Drains into internal iliac and internal pudendal veins.

C. Lymphatic Drainage

On each side, the lymphatics drain into:

Region	Drainage Group
Upper one-third	Internal iliac group
Middle one-third up to hymen	Internal iliac group
Below the hymen	Superficial inguinal group

Nerve Supply

- **Sympathetic and parasympathetic:** Pelvic plexus
- **Lower part:** Pudendal nerve

Secretion:*

In reproductive age, pH becomes acidic due to presence of dorderlein bacilli in increasing estrogen.

Supports of vagina:

1. Upper part:
- Lower components of transverse cervical ligaments

2. Lower part:
- Levator ani muscle fibres
- Urogenital diaphragm
- Perineal muscles

3. Anterior vaginal wall:
- By pubocervical fascia

4. Posterior vaginal wall:
- Rectovaginal fascia
- Perineal body

Uterus

Uterus is a thick-walled, hollow muscular organ situated in the pelvis in between the urinary bladder and the rectum.

● **Normal position:****
- Anteversion (between cervix & vagina - 90°, V90)
- anteflexion(between uterus & cervix - 120°)

● **Measurements:**
- 8 cm long
- 5 cm wide (at the fundus)
- 1.25 cm thick wall

● **Parts: ****
1. **Body or corpus**
   a. *Fundus* – Lies above the openings of the uterine tubes
   b. *Body proper* – Lies between the openings of the tubes and the isthmus
2. **Isthmus**
3. **Cervix**

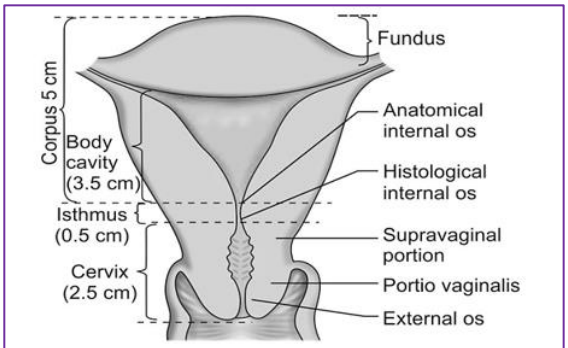


Fig: Coronal section showing different parts of uterus

● **Relations:**
1. **Anterior**
   - *Upper part:* Uterovesical pouch and either intestines or bladder in front
   - *Lower part:* Base of the bladder
2. **Posterior**
   - Pouch of Douglas with coils of intestine
3. **Lateral**
   - Broad ligament and its contents, especially the uterine artery

Anatomy

01. Cell Biology & Histology

1. Which organelle is responsible for intracellular digestion of damaged organelles?
a) Peroxisome
b) Lysosome
c) Golgi apparatus
d) Ribosome

2. Marker enzyme of lysosome is:
a) Catalase
b) Acid phosphatase
c) Succinate dehydrogenase
d) Cytochrome oxidase

3. Tight junction is also called:
a) Macula adherens
b) Zonula occludens
c) Zonula adherens
d) Hemidesmosome

4. Which collagen type is most abundant in hyaline cartilage?
a) Type I
b) Type II
c) Type III
d) Type IV

5. Basement membrane is best demonstrated by:
a) H&E stain
b) Silver stain
c) PAS stain
d) Masson trichrome

6. Which cell junction prevents passage of materials between adjacent cells?
a) Gap junction
b) Desmosome
c) Tight junction
d) Hemidesmosome

7. Main function of peroxisome:
a) Protein synthesis
b) β-oxidation and detoxification
c) ATP production
d) Glycogen storage

8. Which cells produce myelin in CNS?
a) Schwann cells
b) Astrocytes
c) Oligodendrocytes
d) Microglia

9. Which collagen type is present in basement membrane?
a) Type I
b) Type II
c) Type III
d) Type IV

10. Features of nucleus except
a) RNA synthesis
b) A single layered membrane
c) Most of the chromosomal material remains in condensed form
d) Binucleated cells present in liver

11. False statement about Barr body
a) Found during interphase of cell cycle
b) Located below the nuclear membrane
c) Diagnostic of genetic female
d) Absent in normal male

12. Function of rough endoplasmic reticulum
a) Synthesis of lipid
b) Synthesis of Protein
c) Synthesis of steroid hormone
d) Synthesis of cholesterol

13. Golgi apparatus is concerned with
a) Energy production
b) Synthesis of protein
c) Breaking down of secretory vesicle
d) Post translational modification of protein

14. Function of Golgi apparatus except
a) Formation of acrosome in spermatozoa
b) Storing of protein
c) Packaging of enzymes
d) Modification of protein

15. Which organelle does not help in post translational modification
a) Golgi apparatus
b) RER
c) Mitochondria
d) Ribosomes

16. Mitochondria is absent in
a) Kidney tubule
b) Terminal keratinocyte
c) Pancreas
d) Secretory cell

17. Structure does not synthesize protein
a) Mitochondria
b) Ribosome
c) Endoplasmic reticulum
d) Golgi apparatus

18. Function of centriole
a) Assists in cell division
b) Synthesis of lipid
c) Formation of ATP
d) Supports Intermediate filaments

19. Cell membrane is not associated with
a) Formation of ATP
b) Facilitates transport of specific molecules
c) Serves as a site of receptor
d) Acts as a selective barrier

20. Which one is not true about ribosome
a) Present in ER
b) Contains rRNA
c) Contains 3 subunits
d) Synthesize protein

21. Microtubules are found in
a) Microvilli
b) Collagen fibre
c) Centriole
d) ER

22. Contractile cells
a) Fibroblast
b) Myoepithelial cell
c) Fat cell
d) Chondrocyte

23. Main function of lysosome
a) Storage
b) Secretion
c) Transport
d) Digestion

24. Vimentin found in
a) Astrocyte
b) Squamous epithelium
c) Fibroblast
d) Muscle cell

25. Which Intermediate filaments present in muscular tissue
a) Desmin
b) Cytokeratin
c) Vimentin
d) Above all

26. Cells are attached to ECM by
a) Desmosome
b) Zona adherens
c) Hemidesmosome
d) Zona occludens

27. Meiosis -2
a) Reductional division
b) Disjunction occurs with centromere splitting
c) Chiasma occurs
d) Pairing of homologous chromosome

28. Mitotic cell division occurs in
a) Primordial germ cell
b) Spermatid
c) Mature neuron
d) Skeletal muscle

29. Stratified columnar epithelium is not found in
a) Trachea
b) Conjunctiva
c) Ducts of exocrine gland
d) Male urethra

30. Transitional epithelium is absent in
a) Urinary bladder
b) Major calyx
c) Ureter
d) Membranous part of urethra

31. Organ having lymphatic nodules & lined by stratified squamous epithelium
a) Tongue
b) Palatine tonsil
c) Lymph node
d) Male urethra

32. Sweat gland present in
a) Glans penis
b) Tympanic membrane
c) Nipple
d) Sole

33. Sebaceous gland absent in
a) Face
b) Forehead
c) Palm
d) Scalp

86. Which biochemical component of the erythrocyte cell surface is primarily responsible for determining blood type (e.g., the A-B-O system)
a) Fatty acid
b) Carbohydrate
c) Nucleic acid
d) Protein

87. Flagella is present on:
a) Lining of small intestine
b) Uterine tube
c) Spermatozoa
d) Inner ear

88. Which gland produce serous secretion?
a) Pancreas
b) Goblet cells
c) Sublingual gland
d) Mammary gland

89. Which one is fixed connective tissue cell?
a) Adipocytes
b) Mast cells
c) Macrophages
d) Plasma cells

Answer Sheet

No.	Ans.
1	B
2	B
3	B
4	B
5	C
6	C
7	B
8	C
9	D
10	B
11	C
12	B
13	D
14	B
15	C
16	B
17	D
18	A
19	A
20	C
21	C
22	B
23	D

No.	Ans.
24	C
25	A
26	C
27	B
28	A
29	A
30	D
31	B
32	D
33	C
34	B
35	A
36	D
37	C
38	D
39	C
40	A
41	A
42	C
43	D
44	C
45	B
46	A

No.	Ans.
47	D
48	C
49	A
50	D
51	C
52	C
53	B
54	A
55	C
56	A
57	C
58	C
59	A
60	C
61	B
62	D
63	C
64	C
65	B
66	B
67	B
68	A
69	B

No.	Ans.
70	B
71	B
72	D
73	A
74	B
75	B
76	B
77	A
78	A
79	A
80	B
81	D
82	A
83	A
84	C
85	A
86	B
87	C
88	A
89	A