Biochemistry

Metabolism

Introduction

Metabolism

- It is the sum total of all integrated chemical activities occurring at cellular level which are concerned with anabolism or catabolism.

Anabolism

- It is the synthetic process concerned with synthesis of large, complex substances from small, simple molecules with utilization of energy, e.g. syntheses of protein.

Catabolism

- It is the break down process (mostly oxidative) concerned with breakdown of large complex substances into smaller and simpler forms with or without the release of energy e.g. oxidation of glycogen to glucose (here no energy is released)

Anabolic pathways in the metabolism:

1. Glycogenesis
2. Gluconeogenesis
3. Lipogenesis
4. Ketogenesis
5. Protein synthesis
6. Urea synthesis
7. Cholesterol synthesis
8. Fatty acid synthesis

Catabolic pathways in the metabolism:

1. Glycolysis
2. Glycogenolysis
3. Lipolysis
4. Beta oxidation of fatty acids
5. Respiratory chain oxidation
6. HMP shunt

Metabolic pathways in cytoplasm:

1. Glycolysis
2. HMP shunt
3. Glycogenesis and glycogenolysis
4. Lipogenesis (fatty acid synthesis)
5. Synthesis of TAG (fat)
6. Lipolysis (**hydrolysis of fat)**
7. Synthesis of cholesterol
8. Lipoprotein metabolism
9. Transamination

Metabolic pathways occurring in mitochondria are: Mnemonic: King COBRA

- **K**etogenesis
- **C**arboxylation of pyruvate to oxaloacetate
- **O**xidation of pyruvate to Acetyl co A
- Oxidative deamination
- **B**eta oxidation
- **R**espiratory chain (Electron transport chain)
- TC**A** cycle

Metabolic pathways in both mitochondria & cytoplasm: HUG

1. Urea cycle (mainly in cytoplasm)
2. Gluconeogenesis (mainly in cytoplasm)
3. Heme synthesis (mitochondria mainly)

Organ	Major pathways	Main substrates
Liver	Glycolysis, HMP shunt, Gluconeogenesis, lipogenesis, β-oxidation, citric acid cycle, ketogenesis, lipoprotein metabolism, transamination, drug metabolism, synthesis of bile salts, urea, uric acid, cholesterol, plasma proteins	No esterified fatty acids, glucose (in fed state), lactate, glycerol, fructose, amino acids, alcohol
Brain	Glycolysis, citric acid cycle, amino acid metabolism, neurotransmitter synthesis	Glucose, amino acids, ketone bodies in prolonged starvation
Heart	B-Oxidation, citric acid cycle, deamination and transamination	Ketone bodies nonsterile fatty acids, lactate, chylomicron and VLDL triacylglycerol, some glucoses
Adipose tissue	Lipogenesis, esterification of fatty acids, lipolysis (in fasting)1	Glucose, glycogen
Kidney	Gluconeogenesis	Nonsterile fatty acids, lactate, glycerol, glucose
Erythrocytes	Anerobic glycolysis, pentose phosphate pathway	Glucose
Muscle	Glycolysis, Beta oxidation, citric acid cycle, deamination and transamination	Lactate

Q. Metabolic pathways occurring in mitochondria *(Diploma July 2024)*

a) Glycogenesis
b) Glycolysis
c) HMP Shunt
d) Ketogenesis
e) TCA Cycle

Answer: F F F T T

Q. Metabolic pathways occurring in mitochondria are *(Residency March-2020)*

a) Ketogenesis
b) Cholesterol synthesis
c) TCA cycle
d) Fatty acid synthesis
e) β-oxidation of fatty acid

Answer: T F T F T

01. Bioenergetics

High energy phosphate compound

They have energy content more than 6.0 kcal/mol (usually 5-15 kcal/mol).

e.g. ADP, ATP, GDP, GTP, creatine phosphate, carbamoyl phosphate, phosphoenolpyruvate, cyclic AMP, pyrophosphate, 1,3 BPG etc.

* Standard free energy of the hydrolysis of ATP to ADP and ADP to AMP is – 7.3Kcal/mol in each case.

Low energy phosphate compound

They have energy content less than 5.0 kcal/mol (usually 1-3 kcal/mol).

e.g. AMP, glucose 1-P, glucose 6-P, fructose 6-P, glycerol 3-P etc.·

* Standard free energy of the hydrolysis of AMP to adenosine is - 3.4Kcal/mol

High energy phosphate	Low energy phosphate
ATP, ADP	AMP
GTP, GDP	Glucose 1 P
Cyclic AMP	Glucose 6 P
Carbamoyl Phosphate	Fructose 6 P
Creatine phosphate Pyrophosphate	Glycerol 3 P
Phosphoenol pyruvate	
1,3, BPG	

02. Phosphorylation

Phosphorylation is the addition of phosphate group ($P0_4^{3-}$) to an acceptor molecule by high or low energy phosphate bond.

It Occurs at **two levels**:

a. Oxidative phosphorylation at respiratory chain

- It is the oxidation of the components of respiratory chain with simultaneous ATP synthesis by phosphorylation of ADP to ATP.
- It is the major source of ATP in aerobic organism including human being.
- Mitochondria & oxygen must be needed
- About **90%** of the O_2 consumption in out body at basal state occur here in mitochondria.

Examples of oxidative phosphorylation at respiratory chain
α-ketoglutarate + NAD^+ → Succinyl-CoA + NAD2H + 3ATP
Succinate + FAD → Fumarate + FAD2H+ 2 ATP

b. Phosphorylation at substrate level

- It is the phosphorylation at the level of substrate transformation in metabolic pathway without involving respiratory chain.
- Mg, Zn needed (absence of oxygen, Mitochondria)
- It is the minor source of ATP in human body e.g.

Examples of oxidative phosphorylation at substrate level
Phosphoenol pyruvate + ADP → Pyruvate + ATP (in glycolysis)
Succinyl CoA → Succinate + ATP + CoA (In TCA cycle)
1, 3 bis phosphoglycerate + ADP → 3 phosphoglycerate + ATP (In glycolysis)

03. Respiratory Chain/Electron Transport Chain

Site: Inner mitochondrial membrane

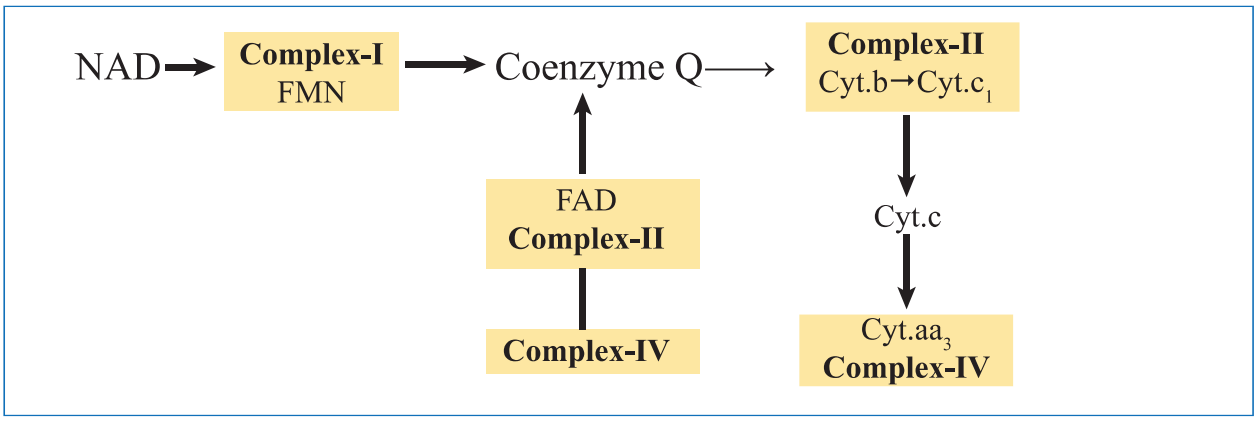
Component:

i) **Hydrogen carriers** e.g. NAD, FAD, FMN, Coenzyme Q

ii) **Electron carriers** e.g. cytochrome b, cytochrome c_1, cytochrome c, cytochrome aa3

NAD, Coenzyme Q & cyt. c are freely diffusible. Other components are grouped into four protein complexes e.g.

Complex-I	: FMN & its enzyme, NADH dehydrogenase (1 ATP produced)
Complex-II	: FAD & its enzyme, Succinate dehydrogenase,
Complex-III	: cyt. b & cyt.c1 (1 ATP)
Complex- IV	: cyt.aa_3 (cytochrome oxidase) (1 ATP)



Salient features of respiratory chain:

Substrate	: Reduced coenzyme (NAD2H, FAD2H)
Product	: ATP & water (metabolic water)
Site	: All mitochondria containing cells.
Compartment	: Inner surface of inner mitochondrial membrane
Nature	: Catabolic
Rate limiting enzyme	: Cytochrome oxidase & ATP synthase
ATP Production	: 03 per NAD2H & 02 per FAD2H
Purpose	: Oxidation of reduced coenzyme and production of ATP

Inhibitors of respiratory chain:

- Barbiturates
- Dimercaprol
- Antimycin A
- Malonate
- Oligomycin
- Inhibitors of cytochrome oxidase: Cyanide, H_2S & carbon monoxide.

Clinical disorders related to respiratory chain dysfunction:

- Hypoxic cell injury
- Mitochondrial myopathy
- Mitochondrial neuropathy
- Mitochondrial encephalopathy (MELAS –Mitochondrial encephalopathy lactic acidosis stroke)
- Stroke & Epilepsy
- Renal dysfunction
- Leber hereditary optic neuropathy

Q. Enzymes of respiratory chain are *(MPhil/Diploma July 2015)*

a) Glucose 6-phosphate dehydrogenase
b) Succinate dehydrogenase
c) NADH dehydrogenase
d) Lactate dehydrogenase
e) Cytochrome oxidase

Answer: F T T F T

Q. Electron transport chain *(Residency March 2014)*

a) Is present in inner mitochondrial membrane
b) Is present in nuclear membrane
c) Electron combine with oxygen and proton
d) Has three separate protein complexes
e) Flow of electron to oxygen directly synthesis ATP

Answer: T F T F F

04. Carbohydrate Metabolism

Intermediary Metabolism of Glucose (Carbohydrate)

Anabolic

- Glycogenesis: Synthesis of glycogen from glucose
- Gluconeogenesis: Synthesis of glucose from non-carbohydrate substance
- Lipogenesis (synthesis of fatty acid) and synthesis of TAG (fat)

Catabolic

- Glycolysis (Embden-Meyerhof pathway)

Oxidation of glucose to pyruvate or lactate

- Glycogenolysis: Breakdown of glycogen to glucose or glucose 1-P
- Hexose monophosphate shunt (HMP shunt)

Oxidation of glucose to ribose sugar, CO_2 & NADPH

- Oxidation of pyruvate to acetyl CoA
- Tricarboxylic acid cycle (TCA cycle or Citric acid cycle or Krebs cycle).
- It is the common metabolic pathway where acetyl CoA is oxidized to reduced coenzyme & CO_2

05. Glycolysis

Embden-Meyerhof pathway or EM pathway

Salient features:

Substrate	: Glucose
Product	: Pyruvate (in aerobic state) & Lactate (in anerobic state)
Site	: All cells and tissues
Compartment	: Cytoplasm
Nature	: Catabolic
Rate limiting enzyme	**: Phosphofructokinase**
Coenzyme needed	**: NAD**
ATP production	**: 08 ATP (in aerobic state) & 02 ATP (anerobic state)**
Unique specialty	: Can occur in both aerobic and anerobic condition
Regulation	**: Stimulated by insulin, ADH, AMP & inhibited by glucagon, ATP, citrate.**

Lactate is the end product of glycolysis in any cell without mitochondria (e.g. RBC) or few mitochondria (e.g. WBC, renal medulla etc) irrespective of their oxygen status. **In cells with adequate mitochondria, lactate will be formed if anerobic condition occurs**.

General Pharmacology

01. Introduction

- **Pharmacokinetics:** what the body do to drugs. Related to absorption, distribution, biotransformation and excretion of drugs
- **Pharmacodynamics:** what the drugs do to body. Related to action mechanism of action of drugs on different system of human body

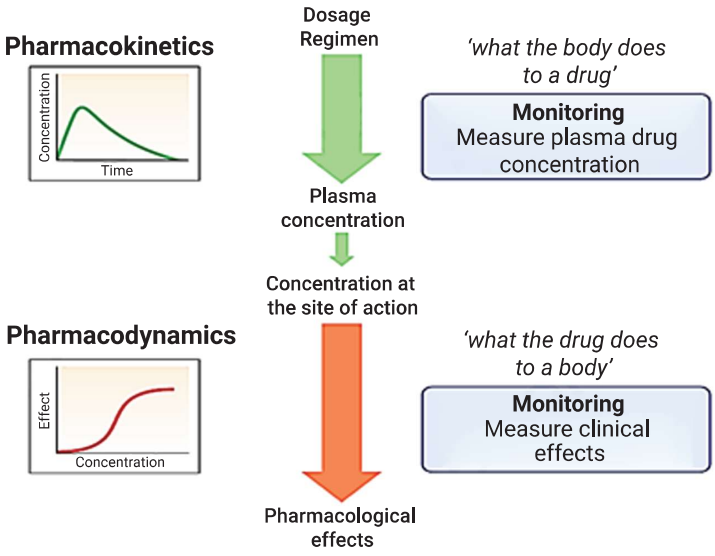


Fig. 2.1 **Pharmacokinetics and pharmacodynamics.**

Concept of essential medicines

➢ A limited range of carefully selected essential medicines leads to better health care, better drug management and lower costs.

Definition of essential medicines

➢ Essential medicines are those that satisfy the priority health care needs of the majority of population;they should be available at all times, in adequate amounts, in appropriate dosage forms and at affordable price.

Criteria to Guide selection of an Essential Drug

- Adequate data on its efficacy & safety.
- It should be available in form in which quality, including bioavailability & stability on storage can be assured.
- Selection of drug depend upon pattern of prevalent diseases, availability of facilities & trained personnel, financial resources, genetic, demographic & environmental factors.
- In case of two or more similar drugs, choice should be made on the basis of their relative efficacy, safety, quality, price & availability.
- Choices may be influenced by comparative pharmacokinetic properties and local facilities for manufacture and storage

- The most essential drugs are single compound. Thus combination medicines are avoided from prioritizing as essential medicines.
- Selection of the drug should be a continuous process which should take into account changing priorities for public health action, epidemiological condition as well as availability of better drugs formulation and progress in pharmacological knowledge

(Ref. Tripathi/8th/P-6-7)

Pro-drug:

❖ **Def:** That requires metabolic conversion for action

Application of Prodrugs

Pharmaceutical applications

- Improvement of taste
- Improvement of odour
- Reduction of irritation
- Reduction of pain on injection
- Enhancement of drug solubility and dissolution rate
- Enhancement of chemical stability of drug

Pharmacokinetic applications

- Enhancement of provability
- Prevention of pre-systemic metabolism
- Prolongation of duration of action
- Reduction of toxicity
- Site specific drug –delivery

Advantages

The use of a prodrug is to **optimize the absorption, distribution, metabolism, excretion and unwanted toxicity of the parent drug**.

- Improve absorption & bioavailability
- Avoid first pass Metabolism pre systemic Elimination
- Reduce Local adverse Drug Reactions
- Increase concentration at specific receptor site
- For pharmaceutical formulation to decrease offensive odour& taste

Prodrugs→ Active forms	Prodrugs → Active forms
Prontosil → Sulfonamide	Sulindac → sulindac sulphide
Levodapa → Dopamine	Cortisone → Hydrocortisone
Talamicillin / Bacampicillin → Ampicillin	Prednisone→ Prednisolone
Cyclophaosphamide → Phophormamide mustard	Enalapril → Enalaprilate
Dipivefrin → Adrenaline	Benorylate→ Aspirin and praracetamol
Diazepan → Oxazepam	Minoxide→ Minoxidil sulphate
Carbimazole → Methimazole	Valacyclovir→Acyclovir

Q. Prodrugs are *(Residency March 2020)*

a) Levodopa
b) Azathioprine
c) Paracetamol
d) Sulfasalazine
e) Frusemide

Answer: T F F T F

Q. Purpose of using prodrug is to modify *(Residency March 2017)*

a) Absorption of the drug
b) Biotransformation of the drug
c) Duration of action of the drug
d) Adverse effects of the drug
e) Distribution of the drug

Answer: T F T T T

Q. Following are inconsistent with the criteria of essential drugs *(Residency March 2017)*

a) Satisfy the health care need of majority people
b) Are available at low cost
c) May safely be prescribe in pregnancy
d) Are not expected to cause drug interaction
e) Should be included in rational prescription

Answer: F F T T F

Q. Which of the following drugs are made more active by metabolism *(Residency March 2011, Diploma 2011)*

a) Senna
b) Procaine
c) Levodopa
d) Cortisone
e) Thiopentone

Answer: T T T T F

Class Notes:

02. Routes of Administration

Different routes

i) Enteral routes

Oral	Sub lingual	Per-Rectal
Preferred in most **Variable absorption** **Extensive PSE** **Strict sterilization not needed** **• Cannot be used for uncooperative/unconscious/** vomiting patient [R-2012] **Certain drugs are not absorbed (streptomycin). [Diploma-20].** Destroyed by digestive juices (penicillin G, insulin) or in liver (GTN, testosterone, lidocaine)	Rapid absorption & Quick onset -Avoid FPM -Spitted after optimum action Nifedipine, GTN [Residency 2020] Others-buprenorphine, desamino-oxytocin,ergotamine,isoprenaline	-Avoid gastric irritation & FPM, 50% -Suitable for unconscious patient -Voltarine suppository, Analgesics-aspirin, Paracetamol, Purgatives.
Other enteral routes: Buccal, Nasogastric and rectal administration.		

ii) Parenteral

Intravenous	Intramuscular
• Rapid (most) effect, • Suitable for large volume watery solution • Sterile technique is needed • Can be stopped in ADRS	• Reasonably rapid onset, • Slow –sustained absorption Large volume cannot be given Require Sterile technique
Subcutaneous -Reasonably - Slow uniform sustained absorption large volume Irritant agent cannot be given, -Suitable for insoluble suspension **-**Insulin,Adrenaline.Vaccine	**Inhalation** **-Rapid onset,** need based Bypass FMP -Drug directly delivered to site of action -Avoid systemic toxicity, need special apparatus Ipratropium bromide, Salmeterol **R- 2016** -Local or Volatile anesthetics Examples: • NO • Salbutamol • GTN • Halothane • Sevoflurane • Isoflurane • Desflurane • Salbutamol • Cromoglycate • Volatile anesthetics

Previous Questions

Previous Residency & Diploma Questions

01. The pharmacokinetic half-life of the following drugs resemble their pharmacodynamic half- life is/are *(Residency March-24)*

a) Salbutamol
b) Phenelzine
c) Dobutamine
d) Omeprazole
e) Cyclophosphamide

Answer: F F T T F

02. Acidification of urine is useful in the treatment of poisoning with *(Residency March-2024)*

a) Aspirin
b) Morphine
c) Amphetamine
d) Phenobarbital
e) Cocaine

Answer: T T T F T

03. Receptors have been paired correctly with their agonists is/are- *(Residency March-2024)*

a) α_2 receptor - clonidine
b) $ß_1$ receptor - tarbutaline
c) $ß_2$ receptor - salbutamol"
d) D_2 receptor - chlorpromazine
e) 5HT3 receptor - ondansetrone

Answer: T F T T T

04. Drug's metabolized by acetylation include/s *(Residency March 2024)*

a) Acetaminophen
b) Diazepam
c) Isoniazid
d) Morphine
e) Sulphonamide

Answer: F F T F T

05. Nicotinie feature/s of organophosphorus poisoning is/are *(Residency March-2024)*

a) Bradycardia
b) Bronchorrhea
c) Diarrhea
d) Hypertension
e) Mydriasis

Answer: F F F T T

06. Microsomal enzyme inducing drug(s) include(s) - *(Diploma July-2024)*

a) Carbamazepine
b) Erythromycin
c) Phenobarbitone
d) Penicillin
e) Rifampicin

Answer: T F T F T

07. A patient treated with warfarin shows skin necrosis, due to following causes- *(Diploma July-2024)*

a) Protein C deficiency
b) Protein S deficiency
c) Antitrhombin III deficiency
d) Factor VII deficiency
e) Factor X deficiency

Answer: T T T F F

08. Following drugs that causes bronchodilatation- *(Diploma July-2024)*

a) Ketamine
b) Atrocuronium
c) Halothane
d) Morphine
e) Salbutamol

Answer: T F T F T

09. Drug(s) that is (are) associated with a facial "butterfly rash" is/are- *(Diploma July-2024)*

a) Captopril
b) Isoniazid
c) Nifedipine
d) Phenytoin
e) Prednisolone

Answer: T T F F F

10. Factor(s) that may shorten the duration of action of drug is (are)- *(Diploma July-2023)*

a) Co-administration of vasoconstrictor agents
b) Extensive plasma protein binding
c) Rapid elimination through kidney
d) Rapid biotransformation
e) Redistribution of drug

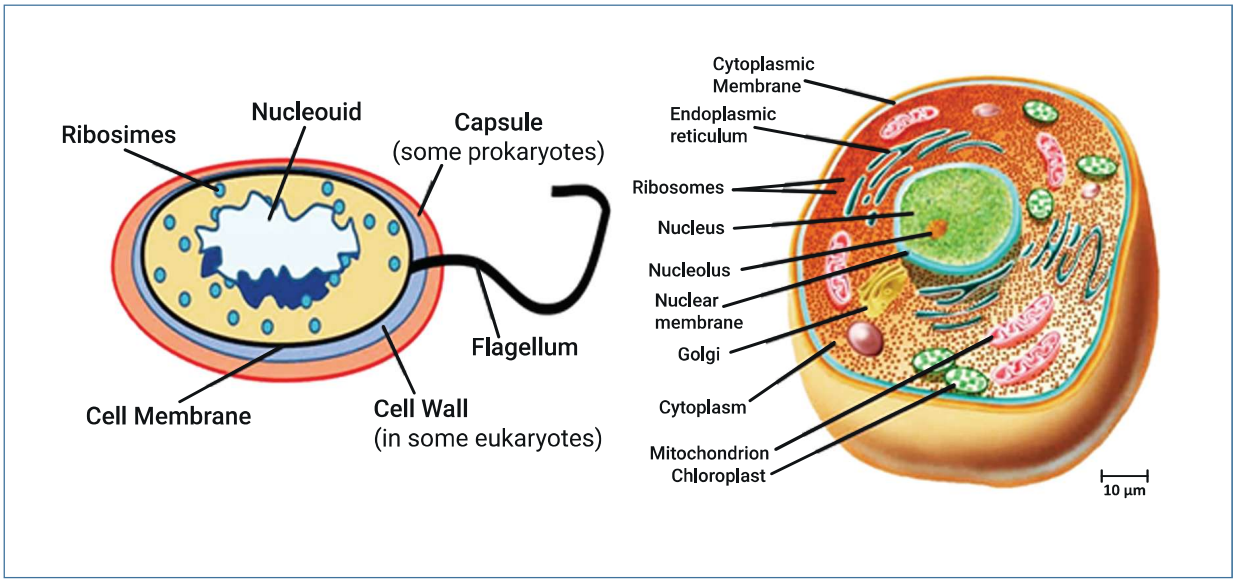
Answer: F F T T F

General Bacteriology

01. Comparison of Medically Important Organisms

Characteristic	Virus	Bacteria	Fungi	Protozoa and Helminthes
Cells	No	Yes	Yes	Yes
Approximate diameter (µm)	0.02-0.2	1-5	3-10 (years)	15-25 (years)
Nucleic acid	Either DNA or RNA	Bothe DNA and RNA	Both DNA and RNA	Both DNA and RNA
Type of nucleus	None	Prokaryotic	Eukaryotic	Eukaryotic
Ribosomes	Absent	70S	80S	80S
mitochondria	Absent	Absent	Present	present
***Nature of outer surface**	Protein capsid and **lipoprotein** envelope	Rigid wall containing **peptidoglycan**	Rigid wall containing **chitin**	Flexible membrane
Motility	None	Some	None	Most
***Method of replication**	Not binary fission	Binary fission	Budding or mitosis	Mitosis

Prokaryotes vs Eukaryotes



Non-Essential components (1) Non-Essential (2) Virulence (3) Adherent Factor		
Capsule (Antigenicity)	Polysaccharide	Protects against phagocytosis
Pilus or fimbria (Antigenicity)	Glycoprotein	Two types: (1) mediates attachment to cell surfaces; (2) sex pilus mediates attachment of two bacteria during conjugation
Flagellum (Antigenicity)	Protein	Motility
Spore	Keratin-like coat, dipicolinic acid	Provides resistance to dehydration, heat, and chemicals
Plasmid	DNA	Contains a variety of genes for antibiotic resistance and toxins
Granule	Glycogen, lipids, polyphosphates	Site of nutrients in cytoplasm
Glycocalyx	Polysaccharide	Mediates adherence to surfaces
[1]Except in Bacillus anthracis, in which it is a polypeptide of d-glutamic acid.		

Septic Shock Inducer:

1) Teichoic Acid
2) Lipopolysaccharide

Q. Bacterial component that Cause septic shock

a) Bacterial capsular protein
b) Lipopolysaccharide
c) Peptidoglycan
d) Phospholipid
e) Teichoic acid

Answer: F T F F T

Cell Wall

Peptidoglycan layer:

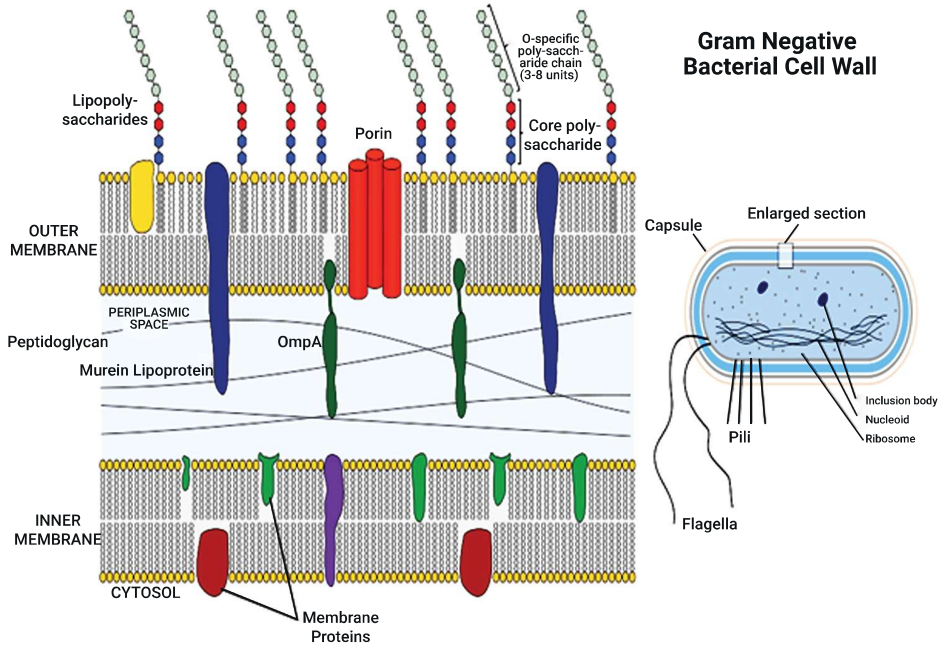
- Outer most component of all bacteria. Except mycoplasma (It has Trilaeyered cytoplasmic membrane & **sterol** coat)
- **Glycan back bone**: major subunits: **NAG(N-Acetyle glucosamine) and NAM(N-acetylemuramic acid)**
- **Peptide side chain**: cross linked by Tetra peptide chain attached to NAM.
- **Interpeptide** bridge in **gram positive** cell wall

Periplasm

It is space between cytoplasmic membrane & outer membrane of Gm (-) bacteria.

Importance

- Binding proteins for **transport of nutrients** (amino acids, sugars, vitamins & Ions)
- Hydrolytic enzymes–alkphsophatase & 5 nucleotides–breakdowns Non transportable to transportable ions
- Detoxifying enzymes-**Beta lactamases,** amino glycoside phosphorylase–drug resistance
- **Osmoregulation**–due to of D-glucos



Beta - lactamase producing bacteria:

❖ ***key to remember: Her Bf SPEaKs More Nicely***

- Haemophillus
- Bacteroids fragilis
- S.aurus
- Pseudomonas
- E.Coli
- Neisseria
- Klebsiella
- Moraxella

Anaerobic Bacteria of Medical Interest

Morphology	Gram Stain	Genus
Spore-forming Bacilli	+	Clostridium
Non spore forming Bacilli	+	• Non filamentous-Propionibacterium,Lactobacilus, listeria, Bifidobacterium, Eubacterium • Filamentous- Actinomyces
	-	Bacteroides, Fusobacteruim
Non spore forming Cocci	+	Peptococcus, Peptostreptococcus, Streptococcus
	-	Veillonella

Q. Anaerobic bacteria are

a) Pseudomonas
b) Propionibacterium
c) Acinetobacter
d) Clostridium
e) Bacteroids fragilis

Answer: F T F T T

15. Anti Phagocytic Factor

Anti Phagocytic Factor

- Capsule
- Protein A of Staph. Aureus
- M protein of group A streptococci (Strep. Pyogenes)
- Coagulase Enzyme

Immunoglobulin A proteas ★

- S. Pneumonae
- Haemophillus Influenzae
- Neisseria Meningitidis
- Neisseria Gonorrhoea

16. Virulence Factor

- Enzyme mediated tissue damage.eg-spreading factor /hyalurunidase
- **Adherence to cell surface involves-**
  - Pilli
  - Teichoic acid
  - Adhesins
  - IgA protease
  - Partial adhesion –biofilm
- **Toxin induced local and systemic effect**
- **Escape from immune response**
  - Invasion-through surface protein that allow an organism to bind to and invade non phagocytic cell thus escaping immune response.eg-yersinia

- Listeria monocytogen
- Group B streptococcus

Q. Organism causing Trans placental transmission are

a) Neisseria meningitides
b) Treponema pallidum
c) Polio virus
d) Listeria monocytogens
e) Toxoplasma Gondi

Answer: F (Respiratory) **T F** (Faeco oral) **T T**

Zoonotic Bacteria (Name only)

Zoonosis bacteria	Zoonosis: infections disease transmitted between animals and humans	
Species	Disease	Transmission and source
Anaplasma spp	Anaplasmosis	Ixodes ticks (live on deer and mice)
Bartonella spp	Cat scratch disease, bacillary angiomatosis	Cat scratch
Borrelia burgdorferi	Lyme disease	Ixodes ticks (live on deer and mice)
Borrelia recurrent is	Relapsing fever	Louse (recurrent due to variable surface antigens)
Brucella spp	Brucellosis / undulant fever	Unpasteurized dairy
Campylobacter	Bloody diarrhea	Feces from infected pets/ animals, contaminated meats/ foods/ bands
Chlamydophila psitteaci	Psittacosis	Parrots, other birds
Coxiella burnetiid	Q fever	Aersols of cattle/sleep amniotic fluid
Ehrlichia chaffeensis	Ehrlichiosis	Amblyomma (line star tick)
Francisella tularensis	Tularemia	Ticks, rabbits, deer flies
Leptospira spp	Leptospirosis	Animal urine in water recreational water use
Mycobacterium leprae	Leprosy	Humans with lepromatous leprosy armadillo (rate)
Pasteurella multocida	Cellulitis, osteomyelitis	Animal bite, cats, dogs
Rickettsio rickettsia	Epidemic typhus	Human to human via human body louse
Rickettsia rickettsia	Rocky mountain spotted fever	Dermacentor (dog tick)
Rickettsia typhi	Endemic typhus	Fleas
Salmonell spp (except S typhi)	Diarrhea (which may be bloody), vomiting, fever, abdominal cramps	Reptiles and poultry
Yersinia	Plague	Fleas (rats and prairie dogs are reservoirs)

3. Reduction of permeability of drug	Mutation in **porin proteins**	Penicillins, aminoglycosides
4. Pumping out of drug from bacterial cell/Efflux pump	Multidrug resistance pump	Tetracyclincs Sulfonamides

Organisms frequently develops resistance

1) Staphylococcus aureus (MRSA)
2) Enterococcus faecalis
3) Enterococcus faecium
4) Pseudomonas aeruginosa
5) Mycobacterium tuberculosis
6) Mycobacterium Leprae

Q. Antibiotic resistance

a) Results from irrational use of antibiotics
b) To vancomycin resistant enterococci can be treated with carbapenem
c) Is mostly plasmic mediated
d) To MRSA can be treated with aminoglycosides
e) Is associated with urease formation

Answer: F T F T T

Q. Methicillin resistant staphylococcus aureus-

a) Are sensitive to vencomycin
b) Causes deep seated infection
c) Is resistant to conventional anti-staphylococcal antibiotics
d) Is sensitive to linezolid
e) Phase typing is done for epidemiological purpose

Answer: T T T T T

25. Valuable Bacteriology

Hospital acquired infections: (EPS KES)

- S. Aureus, MRSA & coagulase neg staphylococcus
- Escherichia
- pseudomonas
- Klebsiella
- Enterobacter species
- Enterococci includin vancomycin resistant
- Serratia
- Acinetobacter
- H influenjae

Q. Common bacterial agents of hospital acquired infections are

a) Klebseillia
b) Streptococcus pneumoniae
c) Hemophilus influenzae
d) Pseudomonas aeruginosa
e) Enterococcus spp.

Answer: T F T T T

Transmittied by blood
Bacteria

- Treponema Pallidum(endo)
- Borrelia burgdorferi (endo)
- Brucella (endo)
- Yarsenia (endo)
- Salmonella (endo)
- Staphylococcus (Exogenous)
- Pseudomonas(exogenous)
- Serratia (Exogenous)
- Ricketsia ricketsi (rocky mountain spotted fever
- Coxiellia burneti (Q fever)

Transmittied by blood
Virus

- Hep B
- Hep C
- Hep D
- HIV
- HTLV
- CMV
- EBV
- HSV 8
- Parvo B19

Parasite by blood transfusion

- Malaria
- Kala azar
- Trypanosoma
- Babesia
- Wucheria (microfilariae)

Koch postulate

The postulate of Robert Koch that establishes the etiological relationship of microbe with disease.

1. The organism must be isolated from every patient with the disease
2. The Oranism must be isolated free from all other organisms and grown in pure culture in vitro
3. The pure organism must cause the disease in a healthy, susceptible animal.
4. The organism must be recovered from the inoculated animal.

Dont meet koch pustulate

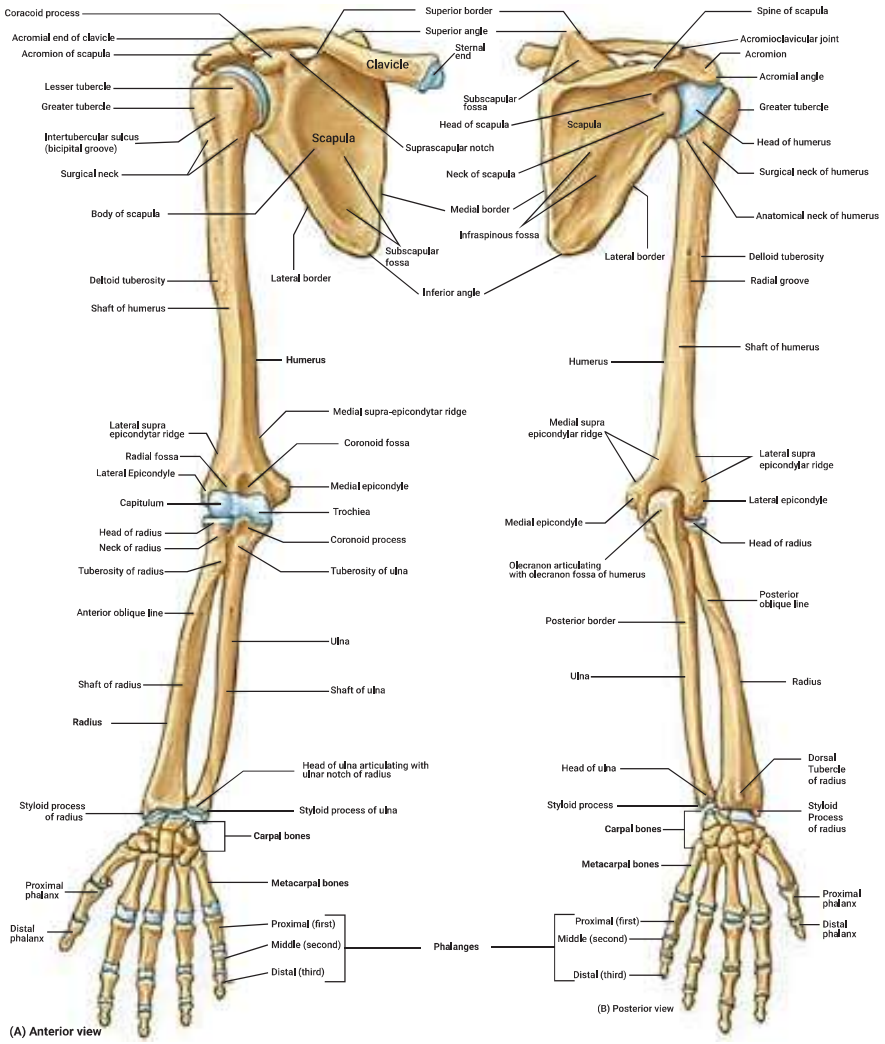
1. M.Tb (1)
2. M.Leprae (2)
3. T.Pallidum
4. Virus
5. Obligate intracellular bacteria(chlamydia+ricketsia)
6. Salmonella
7. N gonorrhoea

UTI organism

- E coli (gal gal pilli)
- Proteus
- Pseudomonas

Superior Extremity

01. Important Bones



A. Clavicle (Collar bone)

- Is a modified long bone transmit weight of the limb to sternum
- Forms the pectoral (shoulder)girdle with the scapula, which connects the upper limb to the sternum (axial skeleton).
- Is the first bone to begin ossification during fetal development, but it is the last one to complete ossification, at approximately
  21 years of age.
- Is the only long bone to be ossified intramembranously and forms
  from somatic lateral plate mesoderm.

– ***Loss of sensations***
along the medial border of the forearm and hand (T1).

– ***Horner's syndrome***,
(characterized by partial ptosis, miosis, anhydrosis, and enophthalmos) due to involvement of sympathetic fibres supplying head and neck, which leave the spinal cord through T1.

– ***Vasomotor changes***:
The skin area with sensory loss is warmer due to arteriolar dilation. It is also drier due to the absence of sweating as there is loss of sympathetic activity.

– ***Trophic changes***: Long-standing case of paralysis leads to dry and scaly skin. The nails crack easily with atrophy of the pulp of fingers

– ***Wasting*** of the small muscles of the hand supplied by segment T1.

Disability

- Biceps and supinator jerks are lost.
- Complete claw hand.
- Cutaneous anaesthesia and analgesia in a narrow zone along the ulnar border of the forearm and hand.

The detailed account of clinical features of Erb's paralysis is as follows:

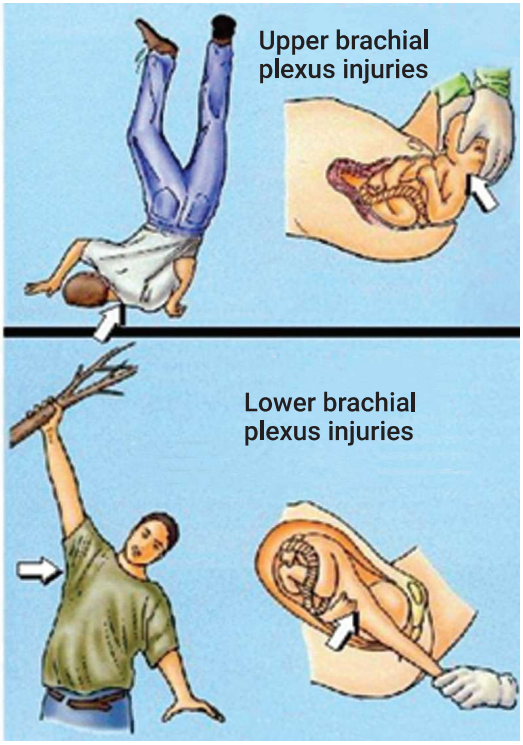
Rootlet Damage

Upper Brachial Plexus Inujuries
- Increase in angle between neck & shoulder
- Traction (stretching or avulsion) of upper rootlets (e.g, C5, C6)
- Produces Erb's Palsy

Lower Brachial Plexus Injuries
- Excessive upward pull of limb
- Traction (stretching or avulsion) of lower rootlets (e.g, C8, T1)
- Produces Klumpke's Palsy

Obstetrical or Birth Palsy
- Becoming increa singly rare
- Categorized on basis of damage
- Type I: Upper (C5, 6) Erb's
- Type II: All (C5-T1, T1), both palsies

Type III: Lower (C8, T1) Klmpke's Palsy



	supinator fossa and crest of ulna			
Abductor pollicis longus	Interosseous membrane, middle third of posterior surfaces of radius and ulna	Lateral surface of base of first metacarpal	Radial (PIN)	Abducts thumb and hand
Extensor pollicis longus	Interosseous membrane and middle third of posterior surface of ulna	Base of distal phalanx of thumb	Radial (PIN)	Extends distal phalanx of thumb and abducts hand
Extensor pollicis brevis	Interosseous membrane and posterior surface of middle third of radius	Base of proximal phalanx of thumb	Radial (PIN)	Extends proximal phalanx of thumb and abducts hand
Extensor indicis	Posterior surface of ulna and interosseous membrane	Extensor expansion of index finger	Radial (PIN)	Extends index finger

Golden Facts

- Tennis elbow (lateral epicondylitis) is caused by a chronic inflammation or irritation of the origin (tendon) of the extensor muscles of the forearm from the lateral epicondyle of the humerus as a result of repetitive strain. It is common in tennis players and violinists.
- Golfer's elbow (medial epicondylitis) :Inflammation or irritation in the origin of the flexor muscles of the forearm from the medial epicondyle.
- Nursemaid's elbow or pulled elbow is a radial head subluxation and occurs in toddlers when the child is lifted by the wrist. It is caused by a partial tear (or loose) of the annular ligament and thus the radial head to slip out of position
- Student's elbow: olecranon bursitis

Muscles of Hand (Intrinsic muscles)

- **Total 20 muscles**

I) Thenar muscles

1. Adductor pollicis
2. Flexor pollicis brevis
3. Abductor pollicis brevis
4. Opponens pollicis

II) Hypothenar muscles

1. Flexor digiti minimi
2. Abductor digiti minimi
3. Opponens digiti minimi
4. Plamaris brevis

III) Lumbricals -4 in number

IV) Palmar interossi-4

V) Dorsal interossi-4

Table Common nerve injuries

Injury	Nerve
Shoulder dislocation	Axillary
Humeral shaft fracture	Radial
Humeral supracondylar fracture	Radial or median
Elbow medial condyle	Ulnar
Monteggia fracture-dislocation	Posterior-interosseous
Hip dislocation	Sciatic
Knee dislocation	Peroneal

11. Volkmann's ischemic contracture

- Volkmann's ischemic contracture is a contracture of the muscles of the forearm that commonly follows fractures of the distal end of the humerus or fractures of the radius and ulna.
- The sudden complete occlusion (e.g.,due to tight plaster cast) or laceration (due to supracondylar fracture of the humerus) of the brachial artery can cause paralysis of muscles of the forearm due to ischemia within a few hours.
- In this syndrome, a localized segment of the brachial artery goes into spasm, reducing the arterial flow to the flexor and the extensor muscles so that they undergo ischemic necrosis.
- The flexor muscles are larger than the extensor muscles, and they are therefore the ones mainly affected.
- The muscles can tolerate ischemia up to 6 hours only therefore,
- The muscles are replaced by fibrous tissue, which contracts, producing the deformity.
- As a result, muscles shorten permanently producing a flexor deformity characterized by ---
- Flexion of the wrist,
- Extension of the MP joints, and flexion of the IP joints,
- which leads to loss of hand power.
- Contracture of the forearm muscles may follow circulatory insufficiency due to injuries at or below the elbow.
- Shortening of the long flexors causes the fingers to be held in flexion; they can be straightened only when the wrist is flexed so as to relax the long flexors.

Previous FCPS P-I Questions

MCQ

01. Anatomical snuff box- ***(FCPS P-1, January 2024)***

a) Contains radial artery
b) Superficial branch of median nerve
c) Scaphoid bone related under it
d) Cephalic vein
e) Insertion of abductor pollicis longus

Answer: T F T T F

SBA

05. Loss of Rounded shoulder contour, sensory loss lower part of deltoid, Shoulder dislocation which nerve injured? ***(FCPS, July 2024)***

a) Axillary Nerve
b) Musculocutaneous
c) Median nerve
d) Radial nerve
e) Ulnar nerve

Answer: A

06. Initiation of abduction ***(FCPS, July 2024)***

a) Supraspinatus
b) S. Anterior
c) Deltoid
d) Trapezius
e) Sternocleidomastoid

Answer: A

07. Most painful movement in Rotator cuff tear ***(FCPS, July 2024)***

a) Abduction
b) Circumduction
c) Extension
d) Flexion
e) Adduction

Answer: A

08. Muscle causing opposing thumb to little finger ***(FCPS, July 2024)***

a) Opponen pollicis
b) Adductor brevis
c) Abductor poficisbrems
d) Extensor policis brevis
e) Flexor policis brevis

Answer: A

09. Which one is more prone to be affected by ischemic injury following humerus factors? ***(FCPS, January 2024)***

a) Proximal
b) Medial epicondyle
c) Lateral epicondyle
d) Distal articular surface
e) Junction of upper / and lower 2/3 of shaft

Answer: E

10. Most dreadful complication of active limb ischemia- ***(FCPS, January 2023)***

a) Pulselessness
b) Paraesthesia
c) Pallor
d) Limb loss
e) Numbness

Answer: D

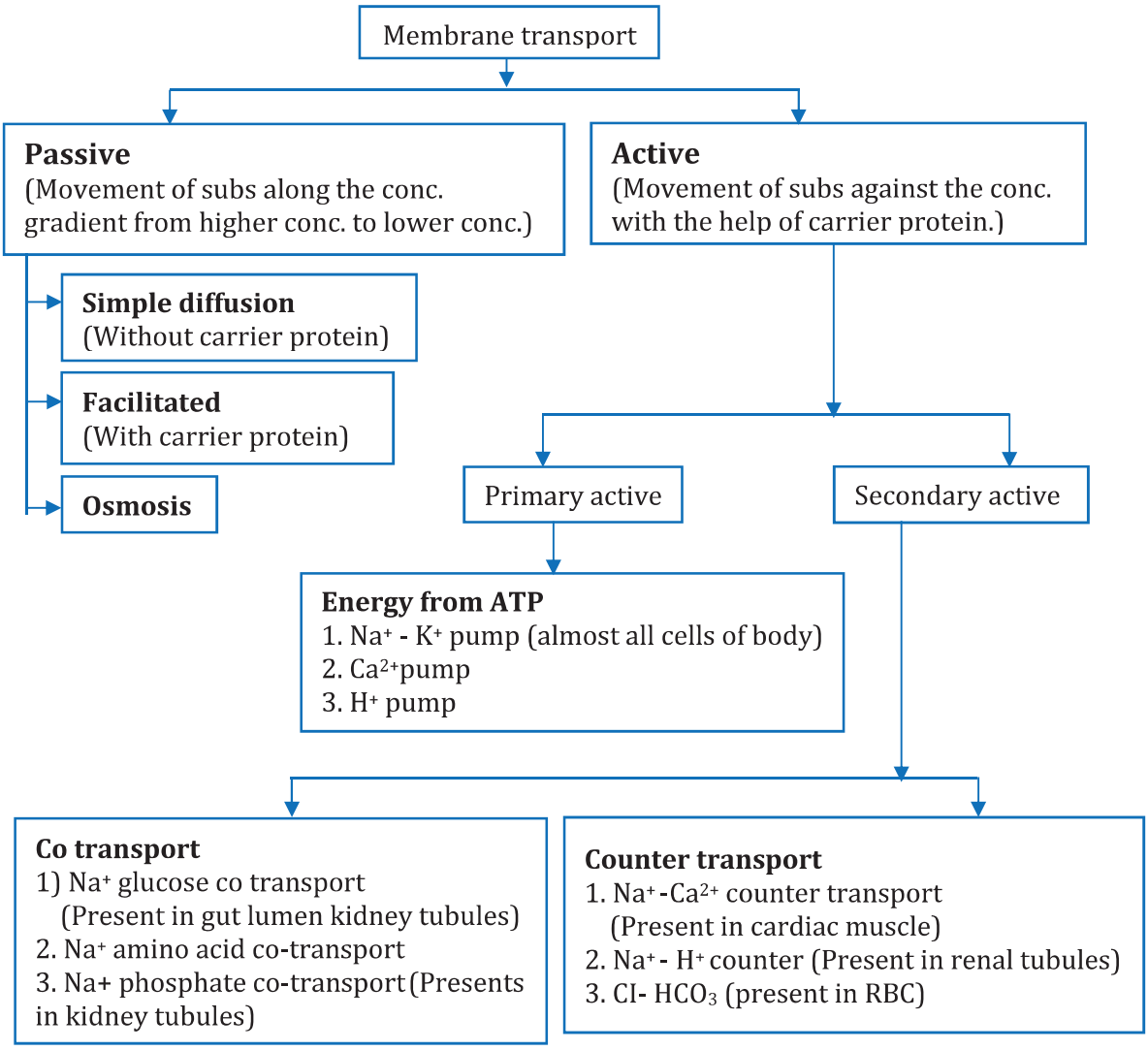
GP & Respiratory Physiology

01. General Physiology

❖ **Membrane transport:** It is bio-physio-chemical phenomenon by which different substance are transport through the cell membrane from inside to outside or voice versa in our body.

Classification:

A. Transport processes for macromolecules:



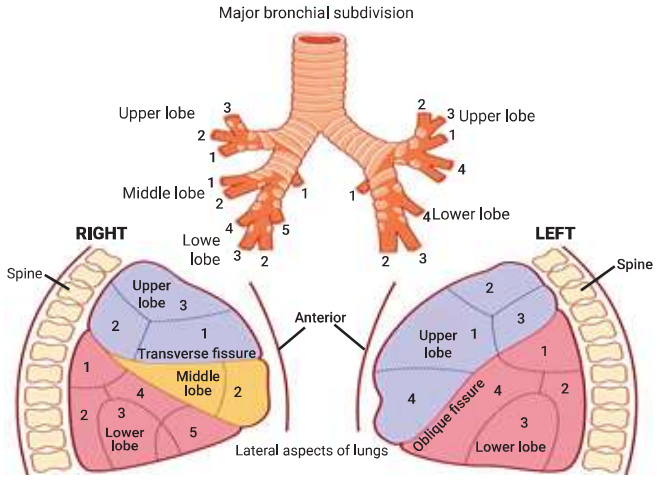


Fig. The major bronchial divisions and the fissures, lobes and segments of the lungs. The angle of the oblique fissure means that the left upper lobe is largely anterior to the lower lobe. On the right, the transverse fissure separates the upper from the anteriorly placed middle lobe, which is matched by the lingular segment on the left side. The site of a lobe determines whether physical signs are mainly anterior or posterior. Each lobe is composed of two or more bronchopulmonary segments that are supplied by the main branches of each lobar bronchus. *Bronchopulmonary segments*:

Right *Upper lobe*: (1) Anterior, (2) Posterior, (3) Apical. *Middle lobe*: (1) Lateral, (2) Medial. *Lower lobe*: (1) Apical, (2) Posterior basal, (3) Lateral basal, (4) Anterior basal, (5) Medial basal.

Left *Upper lobe*: (1) Anterior, (2) Apical, (3) Posterior, (4) Lingular. *Lower lobe*: (1) Apical, (2) Posterior basal, (3) Lateral basal, (4) Anterior basal.

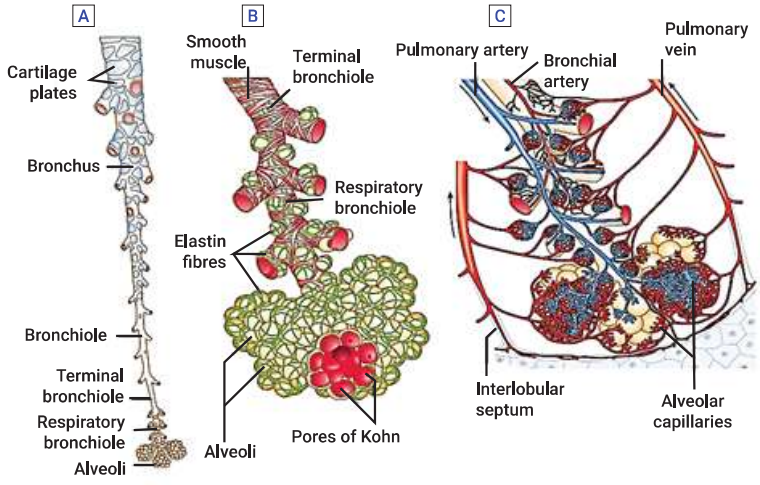
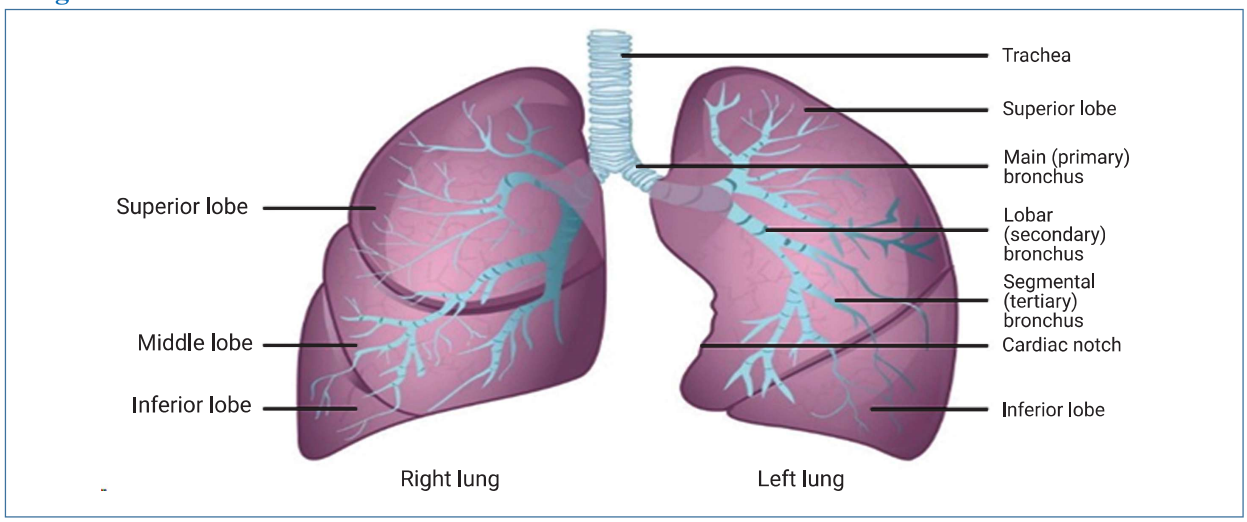


Fig. 17.2 Functional anatomy of the lung. The tapering, branching bronchus is armoured against compression by plates of cartilage. The more distal bronchioles are collapsible, but held patent by surrounding elastic tissue. The unit of lung supplied y a terminal bronchiole is called an aclnus. The bronchlolar wall contains smooth muscle and elastin fibres. The latter also run through the alveolar walls. Gas exchange occurs in the alveoll, which are connected to each other by the pores of Kohn. Vascular anatomy of an aclnus. Both the pulmonary artery (carrying desaturated blood) and the bronchial artery (systemic supply to airway tissue) run along the bronchus. The venous dralnage to the left atrium follows the Interlobular septa. From www. Netter.com: Illustrations 155 (bronchus, acinus) and 191 (circulation), Elsevier

Lung Lobes and Fissure:



- Right Lung- 2 Fissures & 3 Lobe
- Left Lung- 1 Fissure & 2 Lobe

Comparison between Bronchiole and Bronchus

Bronchiole	Bronchus
1. No Cartilage	1. Contains Cartilage
2. No gland present	2. Contains Gland
3. No Goblet cell	3. Contains Goblet cell
4. Thick smooth muscle layer	
5. Clara cell present	

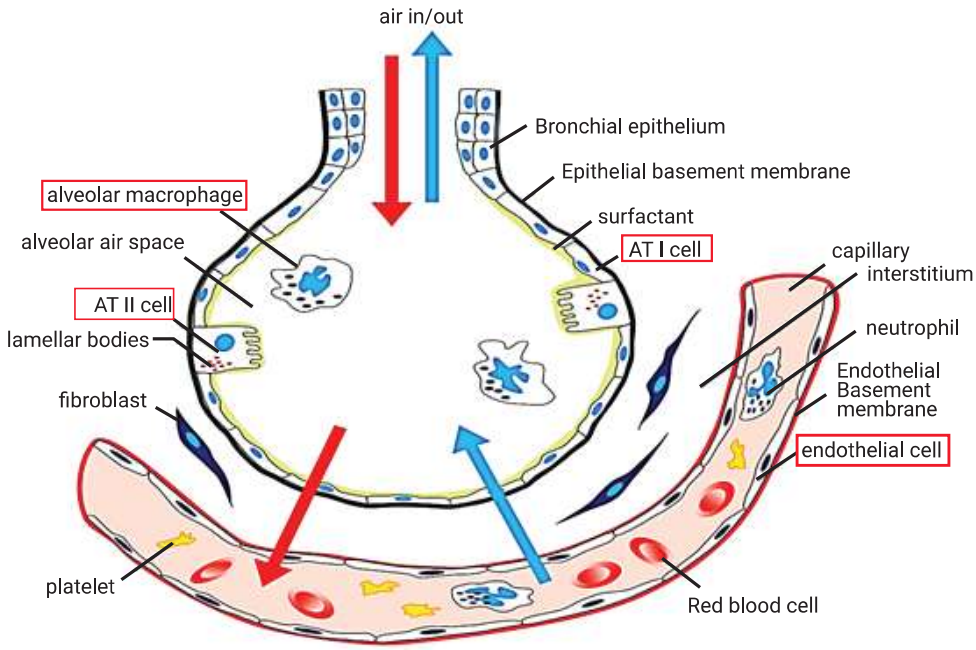
Humans have 300 million alveoli, and area of the alveolar walls in contact with capillaries in both lungs is about 70 m2.

- The alveoli are lined by **two types** of epithelial cells.
- **Type I cells** are **flat cells**, covering approximately **95%** of the alveolar epithelial surface area. They represent 40% of epithelial cells in alveoli.
- **Type II** cells (granular pneumocytes) are **thicker** and contain numerous lamellar inclusion bodies. They secrete **surfactant; M**ake up approximately **5%** of the surface area, they represent approximately 60% of the epithelial cells in the alveoli.
- The alveoli also contain other specialized cells, including pulmonary **alveolar macrophages**, **lymphocytes**, **plasma cells**, **neuroendocrine cells,** and **mast cells.** The mast cells contain heparin, various lipids, histamine, and various proteases that participate in allergic reactions.

Q. Which is the most abundant cell in the surface epithelium?
Ans: Type-I pneumocyte

Q. Which is the most abundant cell in the alveoli?
Ans: Type-II Pneumocyte (60% of the total cell)

Ref: Ganong/26th /P-622



Regional distribution of the cell types in the respiratory tract epithelium:

Trachea to terminal bronchus	Ciliated columnar epithelial cells
	Goblet cells Basal cells Seromucous gland cells Neuroendocrine cells Brush cells
Lobular bronchiole	Ciliated cuboidal epithelial cells Basal cells Seromucous gland cells (upper part of region only) Brush cells
Terminal bronchiole	Ciliated and non-ciliated cuboidal epithelial cells Clara cells Brush cells
Respiratory bronchiole	Ciliated and non-ciliated cuboidal epithelial cells Clara cells Type I pneumocytes
Alveoli	Type I pneumocytes Type II pneumocytes

Q. Types of cell found in the alveoli are

a) Type I cells
b) Type II cells
c) Phagocytes
d) Brush Cells
e) Clara Cells

Answer: T T T F F

Tidal Volume (TV)

- Volume inspired or expired with each breath at rest
- 500ml in ♂s, 350ml in ♀s

Inspiratory Reserve Volume (IRV) = 2-3 L

- Maximum volume of air that can be inspired after normal tidal inspiration
- Inspiratory capacity = TV + IRV

Expiratory Reserve Volume (ERV) = 1100ml

- Maximum volume of air that can be expired after normal tidal expiration

Residual volume (RV) = 1.2L

- Volume of air remaining after maximal expiration
- increase with age
- Increased in obstructive lung disease due to air trapping
- RV = FRC – ERV (Functional Residual Capacity - Expiratory Reserve Volume)

The FEV1/FVC ratio:

- Is < 70% in obstructive lung disease
- And > 70% in restrictive lung disease.

Vital Capacity (VC) = 5L

- Maximum volume of air that can be expired after a maximal inspiration
- 4,500ml in ♂s, 3,500 mls in ♀s
- decrease with age
- VC = IC + ERV = TV + IRV + ERV
- In the absence of equipment, having the patient count at a steady rate for one breath gives a rough estimate of how much air they can expel. This is a common bedside or outpatient procedure that is done with myasthenic patients.

Forced vital capacity

- Is a measure of the force, volume, and speed with which air can be maximally expelled from the lungs
- The maneuver would be to take a deep breath, and then blow it out as hard as you can for as long as you can to maximally expel air from the lungs.
- This is commonly done to assess patients with asthma and chronic obstructive pulmonary disease.

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

- There are four pulmonary lung volumes that when added together, equal to the maximum volume to which the lungs can be expanded.
- These lung volumes vary considerably depending on physical fitness, age, height & other factors.
- The four Pulmonary volumes are –
  1. Tidal volume
  2. Inspiratory reserve volume (IRV)
  3. Expiratory reserve volume (ERV)
  4. Residual volume

Lung volumes

Types	Definition	Normal value
tidal volume (TV)	It is volume of air inspired or expired with each normal breath	500ml
Inspiratory reserve volume (IRV)	It is the maximum extra volume of air that can be inspired forcefully after completing a normal tidal inspiration	3000ml
Expiratory reserve volume (ERV)	It is the maximum extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration	1100ml
Residual volume (RV)	It is volume of air remaining in the lungs after the most forceful expiration	1200ml

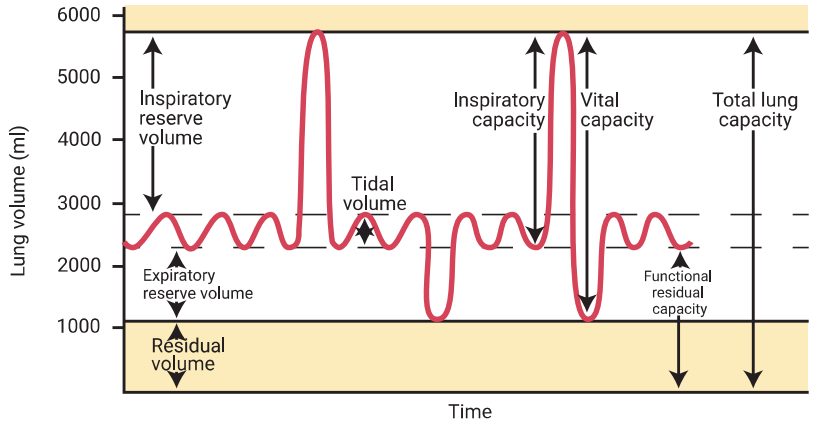


Figure 38-6. A diagram showing respiratory excursions during normal breathing and during maximal inspiration and maximal expiration.

Obstructive vs. Restrictive lung diseases

	Obstructive	Restrictive
Spirometry	FEV1/FVC < 80% **(FEV1/FVC <0.7)**	FEV1/FVC > 80% **(FEV1/FVC >0.7)**
	FEV1 - significantly reduced (<80% predicted normal)	**FEV1** - reduced (<80% predicted normal)
	FVC - reduced or normal FEV1% (FEV1/FVC) - reduced	**FVC** - significantly reduced (<80% predicted normal) FEV1% (FEV1/FVC) - normal (>0.7) or increased
Examples	Chronic obstructive pulmonary disease • chronic bronchitis • emphysema Asthma Bronchiectasis	**Intrapulmonary** • idiopathic pulmonary fibrosis • extrinsic allergic alveolitis • coal worker's • pneumoconiosis/progressive massive fibrosis • silicosis

		• sarcoidosis • histiocytosis • drug-induced fibrosis: amiodarone, bleomycin, methotrexate • asbestosis **Extrapulmonary** • neuromuscular disease: polio, myasthenia gravis • obesity • scoliosis

Spirometer Can't measure:

- Residual volume
- So, TLC= VC+RV, can't measure TLC
- So, FRC=ERV + RV, can't measure FRC
- Closed Volume

Q. Spirometer can be used to measure *(Residency March 2017)*

a) Functional residual capacity
b) Residual volume
c) Vital capacity
d) Inspiratory reserve volume
e) Closing volume

Answer: F F T T F

Pre-operative screen of pulmonary function
➢ What is the best pre-operative screen of pulmonary function for a smoker patient evaluated for a coronary artery bypass graft (CABG).? • **Ratio of the forced expiratory volume in 1 second to the forced vital capacity**

Transfer factor (**DLCO** or **TLCO** (diffusing capacity or transfer factor of the lung for carbon monoxide (CO))

- ➢ The transfer factor describes the rate at which a gas will diffuse from alveoli into blood.
- ➢ Carbon monoxide is used to test the rate of diffusion.

Causes of raised and lower TLCO:

Where alveolar haemorrhage occurs, the TLCO tends to increase due to the enhanced uptake of carbon monoxide by intra-alveolar haemoglobin

Causes of a Raised TLCO	Causes of a Lower TLCO
• Asthma • Pulmonary hemorrhage (Wegener's, Goodpasture's) • Left-to-right cardiac shunts • Polycythemia • Hyperkinetic states • Early left heart failure • Male gender, • Exercise • Obesity	• Pulmonary fibrosis • Pneumonia • Pulmonary emboli • Pulmonary oedema • Emphysema • Anemia • Low cardiac output

22. Factors Affecting vital capacity

1. Age: It is more in young due to increased muscular strength.
2. Sex: It is 10 % less in case of female due to
- Short thoracic cage
- Less surface area
- Less muscular activity.

3. Posture: It is more in erect posture than in lying posture due to
- Intra-abdominal pressure
- Pulmonary vascular blood volume.

4. Surface area: Vital capacity is proportional to surface area. It is usually 2.6L /m' surface area in male and | 2.1 L/m' in female.

5. Anatomical built of chest: Vital capacity decreases in some thoracic cage deformities such as
- Pigeon chest.
- Kyphosis: forward bending of vertebral column.

6. Disease of lungs & pleura: Diseased condition of lungs & pleura decreases the vital capacity (i.e. Emphysema, Poliomyelitis, Respiratory obstruction, oedema)

7. Paralysis of respiratory muscles: Vital capacity is decreased as low as 500-1000 ml in such condition.

8. Congestive left heart failure: It causes pulmonary vascular congestion & oedema which then decreases lung compliance and subsequently vital capacity.

9. It is reduced in pregnancy & ascites
10. It is increased in swimmers & divers.

23. O2-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

Inflammation

01. Inflammation

Definition:

Inflammation is a response of vascularized tissues to infections and damaged tissues that brings cells and molecules of host defense from the circulation to the sites where they are needed, in order to eliminate the offending agents.

Ref; Robbins/9th edition/P-69

Inflammation is protective response.

The purpose is:

1. To dilute, localize and destroy the injuries agent
2. To limit tissue injury
3. To restore the tissue towards normality

Inflammation may be harmful, e.g. inflammation due to hypersensitivity reactions.
Inflammations are mostly indicated by the suffix "itis" e.g. appendicitis, tonsillitis. There are exceptions, e.g. boil, abscess, pneumonia.

Causes of inflammation:

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

Types of inflammation:

1. Acute Inflammation:

- Acute inflammation is a rapid local response of living tissue to an injuries agent and lasts for minutes to a few days.
- There is extravascular accumulation of protein rich fluid and leucocytes predominantly neutrophils in many acute inflammations due to exudation.
- It is an exudative lesion

2. Chronic inflammation:

- Chronic inflammation is the inflammation that persists for weeks to months
- it is a proliferative lesion

Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophages & lymphocytes
Tissue injury, fibrosis	Usually mild and self-limited	May be severe and progressive
Local and systemic signs	Prominent	Less

Ref: Robbins/9th edition/P-71/Table-3-2

Key notes: Inflammation may be harmful in certain situations. Inflammatory reactions underlie common chronic diseases like: rheumatoid arthritis, atherosclerosis, lung fibrosis as well as life threatening hypersensitivity reactions to insect bites, drugs and toxins, type -2 DM, degenerative disorder like: Alzheimer disease

02. Acute Inflammation

Cells of acute inflammation:

- Neutrophil
- Basophil
- Eosinophil
- Macrophage
- Plasma cell

Cardinal signs of acute inflammation: Introduced by Celsus, a roman writer of first century

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

(Ref: Khaleque Pathology/P-16)

Events or Changes of acute inflammation:

Three major components of acute inflammation:

1) Dilation of small vessels
2) Increased permeability of the microvasculature and
3) Emigration of the leukocytes from the microcirculation.

Most of the changes happen in postcapillary venules

Reactions of blood vessels in acute inflammation:

Vascular Changes

A) Changes in vascular caliber and flow:

1) Vasodilatation:

- Vasodilation is induced by the action of several mediators, **notably histamine** & **NO** (Nitric Oxide) on vascular smooth muscle.
- It is one of the earliest manifestations of acute inflammation.

Role of Mediators in different reactions of inflammation

Reaction of Inflammation	Principal Mediators
Vasodilation	Histamine Prostaglandins
Increased vascular permeability	Histamine C3a and C5a (by liberating vasoactive amines from mast cells, other cells) Leukotrienes C_4, D_4, E_4
Chemotaxis, leukocyte recruitment and activation	IL-I, TNF Prostaglandins
Fever	IL-I, TNF Prostaglandins
Pain	Prostaglandins Bradykinin
Tissue damage	Lysosomal enzymes of leukocytes Reactive oxygen species

Ref; Robbin's/9th /p-90/Table-3-7

Key notes: chemokines have two main functions: they stimulate leukocyte recruitment in inflammation and control normal migration of cells through various tissues.

Q. The chemical mediator/s causing vasodilation is/are *(Residency March 2025)*

a) Bradykinin
b) Histamine
c) Leukotrienes
d) Platelet activating factors
e) Prostaglandins

Answer: T T F T T

Q. Chemical mediator(s) that cause(s) vasodilatation *(Diploma July 2024)*

a) Histamine
b) Platelet-activating factor
c) Leukotrienes
d) Bradykinin
e) Prostaglandin

Answer: T T F F T

Q. Chemical mediator(s) that cause(s) vasodilatation *(Diploma July 2024)*

a) Histamine
b) Platelet-activating factor
c) Leukotrienes
d) Bradykinin
e) Prostaglandin

Answer: T T F F T

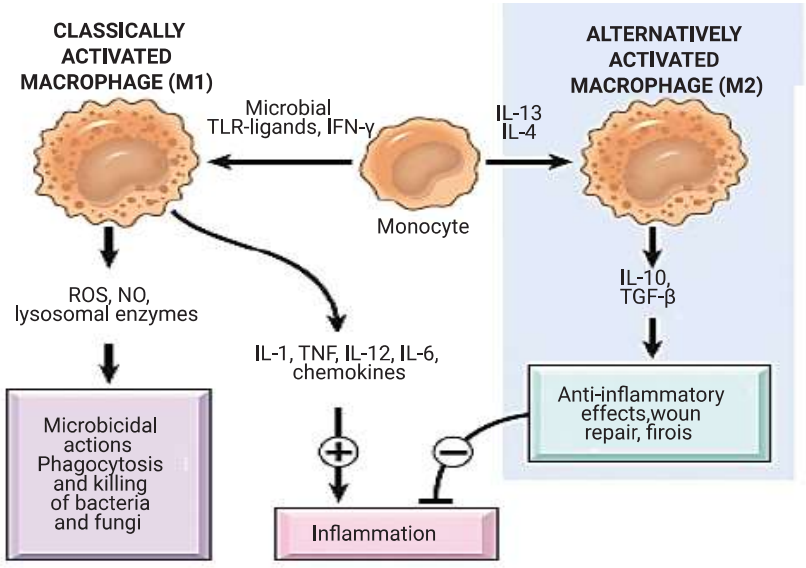


Fig. Classical and alternative macrophage activation. Different stimuli activatemonocytes/macrophages to develop into functionally distinct populations. Classically activated macrophages are induced by other cytokines and are important in tissue repair and the resolution of inflammation.

Function of macrophages:

1. Phagocytosis & digestion of invading organism
2. Release of chemotactic & permeability factor that may prolong inflammation.
3. Growth promoting factors for endothelial cells and fibroblasts
4. Antitumor activity by activated macrophages
5. Immune Response a) Antigen presenting cell (APC) b) delayed type hypersensitivity (DTH)
6. Control of erythropoiesis by supplying ferritin for synthesis of hemoglobin
7. Control of granulopoiesis by liberating colony stimulating factor (CSF)
8. Produce coagulation factors V. VII and tissue factor
9. Produce complement components-C1 to C5 and properdin.

(Ref: Robbin's/9th /P-94,95)

Key points: extravasation of monocytes are governed by the same factors that are involved in neutrophil emigration. The half-life of blood monocyte is 1 day while tissue macrophage is several months or years.

Examples of Diseases with Granulomatous Inflammation:

Tuberculosis	Mycobacterium tuberculosis	Tissue Reaction
Tuberculosis	Mycobacterium tuberculosis	Caseating granuloma (tubercle): Focus of activated macrophages (epithelioid cells), rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cells, central necrosis with amorphous granular debris; acid fast bacilli
Leprosy	Mycobacterium leprae	Acid fast bacilli in macrophages; noncaseating granulomas
Syphilis	Treponema pallidum	Gumma: Microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells are necrotic without loss of cellular outline
Cat-scratch disease	Gram-negative bacillus	Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon
Sarcoidosis	Unknown etiology	Noncaseating granulomas with abundant activated macrophages
Crohn disease (inflammatory bowel disease)	Immune reaction against intestinal bacteria, possibly self - antigens	Occasional noncaseating granulomas in the wall of the intestine, with dense chronic inflammatory infiltrate

(Ref: Robbin's/9th /P-98/Table-3-8)

Q. Epithelioid cell granuloma is found in

a) Syphilis
b) Rhinosporodiosis
c) Amyloidosis
d) Sarcoidosis
e) Toxoplasmosis

Answer: T T F T F

(Ref: Robbin's/9th Edition/P-98+ Khaleque/P-40-41)

Q. Granuloma are found in

a) Leprosy
b) Syphilis
c) Brucellosis
d) Rickettsia
e) Cryptococcus's

Answer: T T T F T

Q. Granulomas are composed of

a) Epithelioid cells
b) Lymphocytes
c) Newly formed blood vessels
d) Langhan's type of giant cells
e) Granulation tissue

Answer: T T F T F

Cell Injury Adaptation

01. Cellular Responses to Injury

Cellular responses to injury

Nature of injuries stimulus	Cellular Response
Altered physiologic stimuli, some nonlethal injurious stimuli	Cellular adaptations
Increased demand, increased stimulation (e.g., by growth factors, hormones)	Hyperplasia, hypertrophy
Decreased nutrients, decreased stimulation	Atrophy
Chronic irritation (physical or chemical)	Metaplasia
Reduced oxygen supply; chemical injury, microbial infections	Cell injury
Acute and transient	Acute reversible injury • Cellular swelling • Fatty change
Progressive and severe (including DNA damage)	Irreversible injury → cell death • Necrosis • Apoptosis
Metabolic alterations, genetic or acquired, chronic injury	Intracellular accumulation, calcification
Cumulative sublethal injury over long life span	Cellular aging

02. Cellular Adaptations

Definition: Cellular adaptation is physiological & morphological response of the cells towards physiological stress or pathological stimuli in which new but altered steady state is achieved, preserving the viability of the cell & modulating the function & thereby escaping injury.

Types of Adaptation:

1. **Atrophy:** Decrease in the cell size
2. **Hypertrophy:** Increase in the cell size
3. **Hyperplasia:** Increase in cell number
4. **Metaplasia:** Change in the type of the cell

Connective tissue metaplasia

Osteoblasts or chondroblasts produce **bone or cartilage** where it is normally not encountered. The metaplasia usually occurs in foci of injury.

A. Osseous Metaplasia. It is thought that 'fibroblasts' undergo metaplasia to 'osteoblasts'.

I. As an aging process in cartilage, e.g. Costal and thyroid cartilage.

II. In soft tissue, e.g. In scars, dystrophic calcifications, caseous foci. Long-standing goiters.

III. Myositis ossificans: In muscles due to trauma- commonest in the bend of the elbow after a supracondylar fracture of the humerus.

B. Mesothelium: Squamous metaplasia in the pleura and peritoneum has been recorded.

Key Concepts

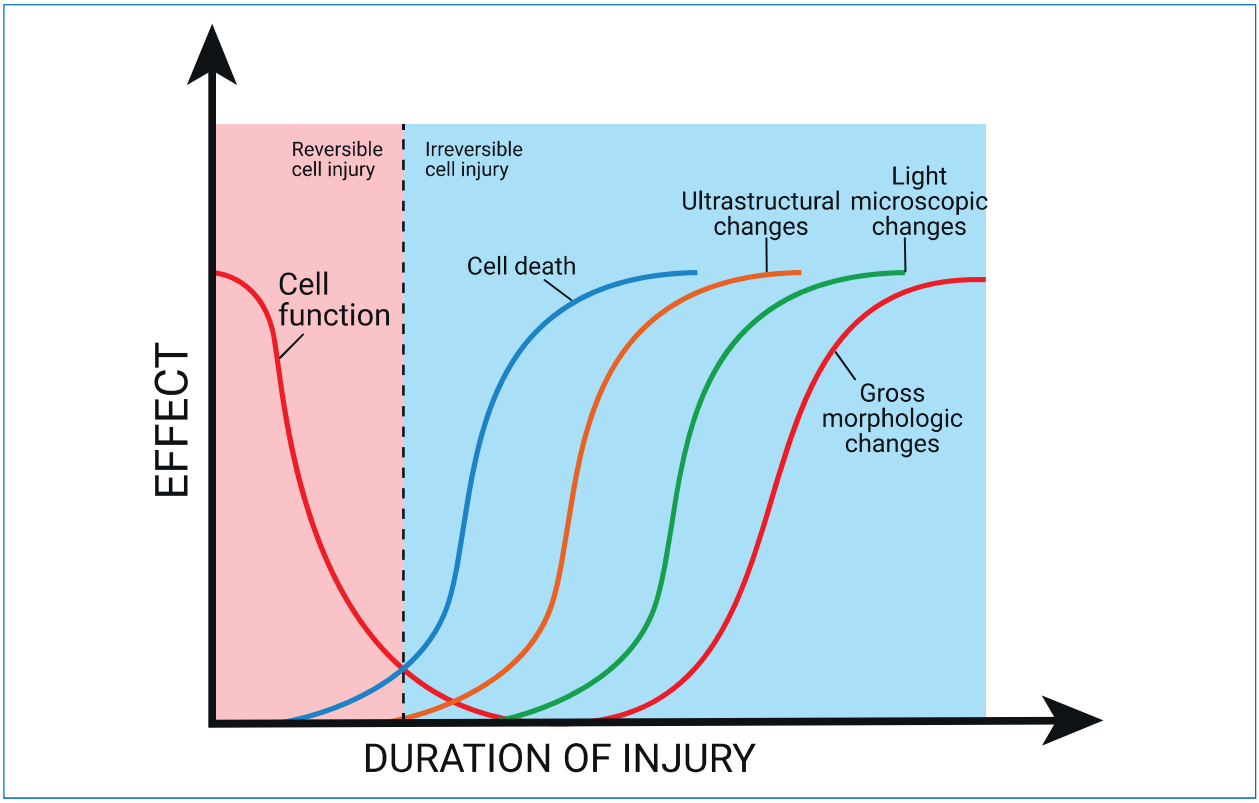
Cellular Adaptations to Stress

- **Hypertrophy**: Increased cell and organ size, often in response to increased workload; induced by growth factors produced in response to mechanical stress or other stimuli; occurs in tissues incapable of cell division. It may be physiologic (e.g., enlargement of the uterus in pregnancy) or pathologic (e.g., enlargement of the uterus in pregnancy) or pathologic (e.g., enlargement of the heart in hypertension of valvular disease).
- **Hyperplasia**: increased cell numbers in response to hormones and other growth factors; occurs in tissues whose cells are able to divide or contain abundant tissue stem cells. It may be physiologic in response to increased need (e.g., breast acini during lactation) or pathologic in response to inappropriate secretion of hormones (e.g., endometrial hyperplasia due to excessive estrogenic stimulation).
- **Atrophy**: decreased cell and organ size, as a result of decreased nutrient supply or disuse; associated with decreased synthesis of cellular building blocks and increased breakdown of cellular organelles by increased autophagy
- **Metaplasia**: Change in phenotype of differentiated cells, often in response to chronic irritation, that makes cells better able to withstand the stress; usually induced by altered differentiation pathway of tissue stem cells; may result in reduced functions or increased propensity for malignant transformation.

Q. Disuse atrophy follows *(Residency March 2025)*

a) Blockage of the duct of an exocrine gland
b) Diminished secretion of trophic hormones
c) Immobilization of a joint
d) Interference with the blood supply
e) Interference with the nerve supply to the muscles controlling joint movement

Answer: F F T T T



Biochemical mechanism of cell injury:

- **Depletion of ATP:**
  - Failure of Na^+-K^+ pump → Na^+ and H_2O enters and K^+ goes out of cell → cellular swelling and dilatation of endoplasmic reticulum
  - Anerobic glycolysis →↑lactate → ↓pH → clumping of nuclear chromatin and ↓activity of many cellular enzyme
- **Mitochondrial damage:**
  - Leakage of cytochrome C → trigger apoptotic death
- **Influx of intracellular Ca^{2+} and loss of Ca^{2+} homeostasis:**
  - ↑Ca^{2+} activates a number of enzymes- **phospholipase**, **proteases**, **ATPases**, **endonucleases** →fragmentation of DNA and chromatin
- **Accumulation of oxygen derived free radicals**
- **Defects in membrane permeability**

04. Reversible Cell Injury

Reversible cell injury:

i) Cellular swelling
ii) Fatty change

Cellular swelling is the first manifestation of almost all forms of injury to cells.

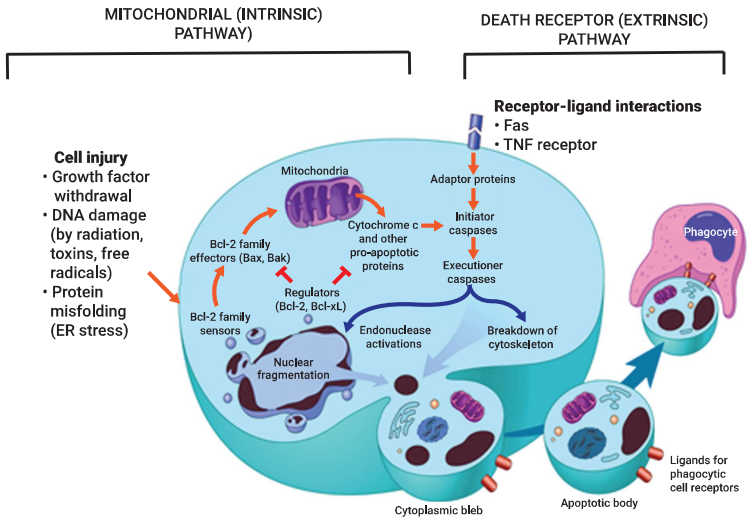


Fig. Mechanisms of apoptosis. The two pathways of apoptosis differ in their induction and regulation, and both culminate in the activation of caspases. In the mitochondrial pathway, proteins of the Bcl-2 family, which regulate mitochondrial permeability, become imbalanced and leakage of various substances from mitochondria leads to caspase activation. In the death receptor pathway, signals from plasma membrane receptors lead to the assembly of adaptor proteins into a "death –inducing signaling complex," which activates caspases, and the end result is the same.

Sensor: BIM, BID, BAD, PUMA, NOXA.

Anti-apoptotic proteins: BCL 2, BCL-XL, MCL1

Pro-apoptotic proteins: BAX, BAK

Disorder associated with dysregulated apoptosis:

1) **Disorder associated with defective apoptosis and increased cell survival:**
   - Cancer
   - Autoimmune disorders
2) **Disorder associated with increase apoptosis and excessive cell death:**
   - Neurodegenerative diseases, e.g. Alzheimer's, Huntington disease
   - Ischemic injury as in MI, Stroke
   - Death of virus infected cells in many viral infections

Apoptosis is triggered by:

Intrinsic Pathway	Extrinsic Pathway
• Loss of survival signal • DNA damage • Accumulation of misfolded proteins (ER stress) • Pro-apoptotic protein BAX & BAK • P53 gene.	Receptor-ligand interaction • Fas • TNF receptor

(Ref: Robin's 9th /P-54,55,58)

Effects: Free radicals play role in-

- Microbial killing by phagocytic cells,
- Inflammatory damages,
- Chemical injury to cells,
- Radiation injury,
- Cellular aging.
- Destruction of tumor cells by macrophages.

Removal of free radicals may occur by

1. **Spontaneous decay**
2. **Antioxidants**, e.g. vitamins E. A and C, serum albumin, glutathione, transferrin, ceruloplasmin and cysteine.
3. Enzymes act as a free radical scavenging system. These enzymes include **superoxide dismutase**, **catalase**, and **glutathione peroxidase**.

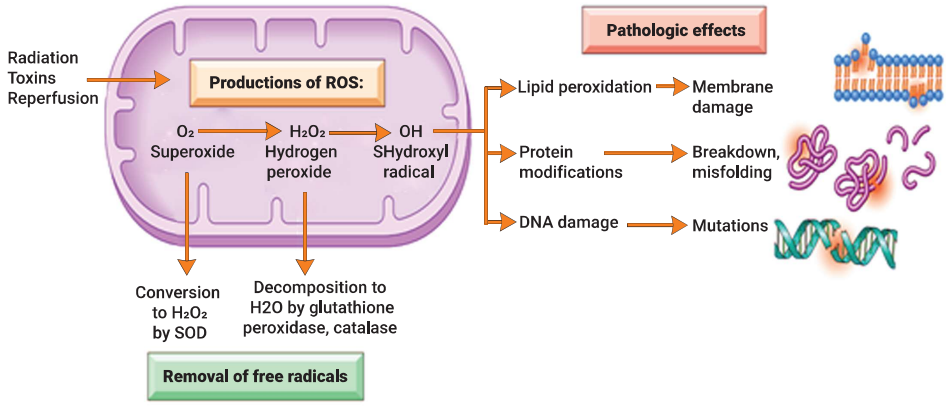


Fig. The generation, removal, and role of reactive oxygen species (ROS) in cell injury. The production of ROS is increased by many injurious stimuli. These free radicals are removed by spontaneous decay and by specialized enzymatic systems. Excessive production or inadequate removal leads to accumulation of free radicals in cells, which may damage lipids (by peroxidation), proteins, and deoxyribonucleic acid (DNA), resulting in cell injury.

Q. Free radicals cause cell injury by *(Residency March 2024)*

a) apoptosis
b) oxidative modification of protein
c) cellular swelling
d) lipid peroxidation of membrane
e) DNA change

Answer: F T F T T

Ref. Robbin's 9th p-47-48

Q. Hydrogen peroxide can be neutralized in our body by *(Residency March 2021)*

a) Superoxide dismutase
b) Glutathione peroxidase
c) Myeloperoxidase
d) Catalase
e) Glucose 6-phosphate dehydrogenase (G6PD)

Answer: F T F T F

Superior Extremity

01. Important bones of lower limb

Hip Bone

- Is formed by the fusion of the **ilium, pubis**, and **ischium** in the acetabulum.
- Articulates with the sacrum at the sacroiliac joint.

Ilium

- Forms the lateral part of the hip bone and consists of the **body**, which joins the pubis and ischium to form the acetabulum, and the **ala** or wing, which forms the iliac crest.

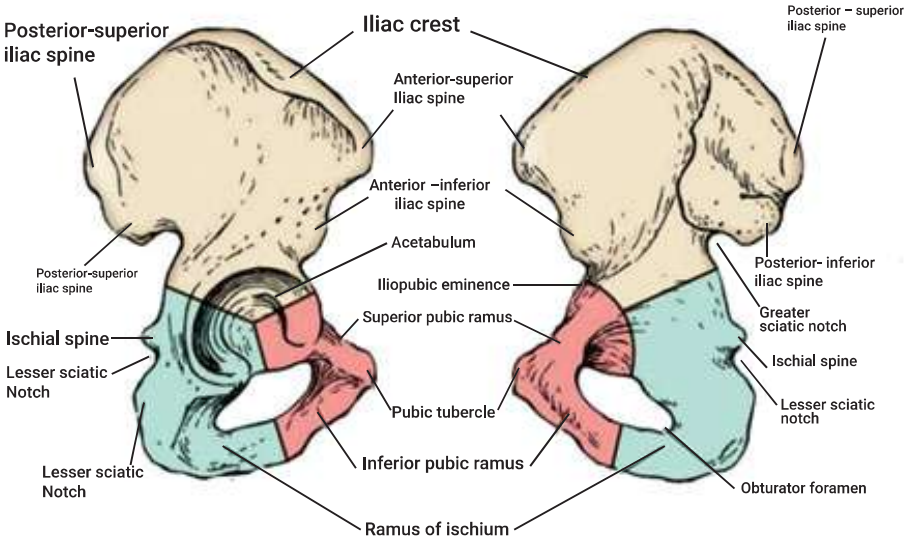
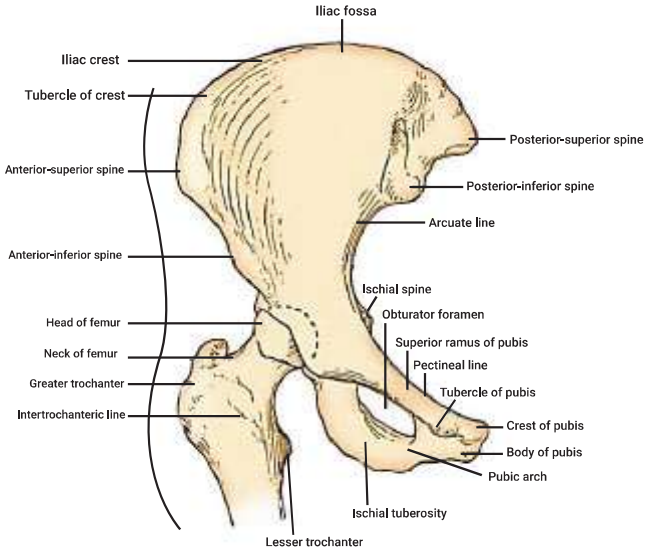


Figure 6.1. Coxal (hip) bone (lateral view)



4. **The *intertrochanteric line*** provides:
   - Capsular ligament of the hip joint.
   - Upper band of the iliofemoral ligament
   - Lower band of iliofemoral ligament
   - Origin to the highest fibres of the vastus lateralis
   - Origin to the highest fibres of the vastus medialis

5. **The *quadrate tubercle*** receives the insertion of the quadratus femoris

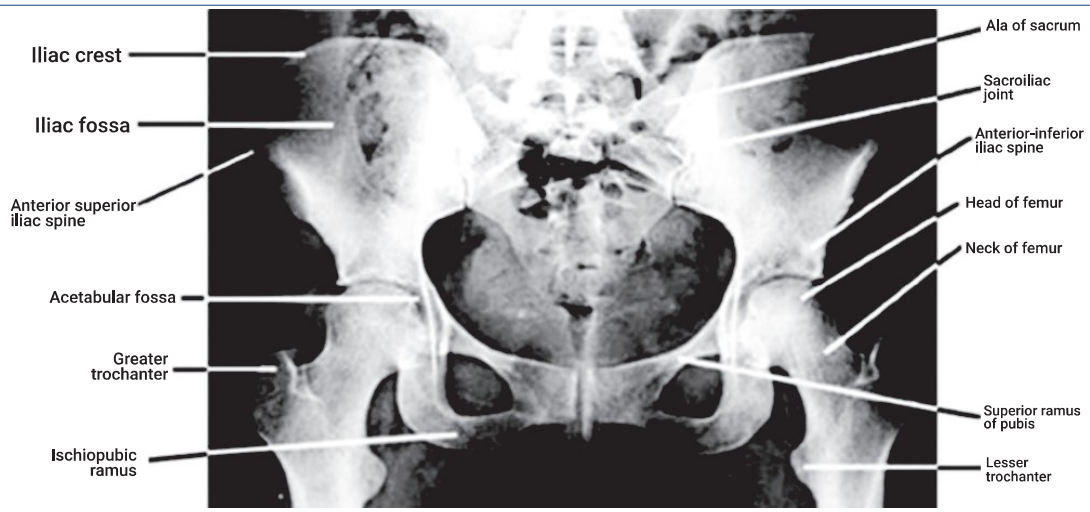


Figure 6.3. Radiograph of the hip, thigh and pelvis

Shenton line is an imaginary curved line drawn along the inferior border of the superior pubic ramus (superior border of the obturator foramen) and along the inferomedial border of the neck of femur. This line should be continuous and smooth.

Interruption of the Shenton line can indicate (in the correct clinical scenario):
- Developmental dysplasia of the hi (DDH)
- Fractured neck of femur

Patella

- Is the ***largest sesamoid bone*** and is located within the tendon of the quadriceps femoris, which articulates with ***the femur but not with the tibia.***
- Attaches to the tibial tuberosity by a continuation of the quadriceps tendon called the patellar ligament.

Tibia

- Is the weight-bearing medial bone of the leg.
- Has the tibial tuberosity into which the patellar ligament inserts.
- Has medial and lateral condyles that articulate with the condyles of the femur.
- Has a projection called the medial malleolus with a malleolar groove for the tendons of the tibialis posterior and flexor digitorum longus muscles and another groove (posterolateral to the malleolus groove) for the tendon of the flexor hallucis longus muscle. It also provides attachment for the deltoid ligament.
- The tibia ossifies from one primary and two secondary centres.
- The primary centre appears in the shaft during the seventh week of intrauterine life.

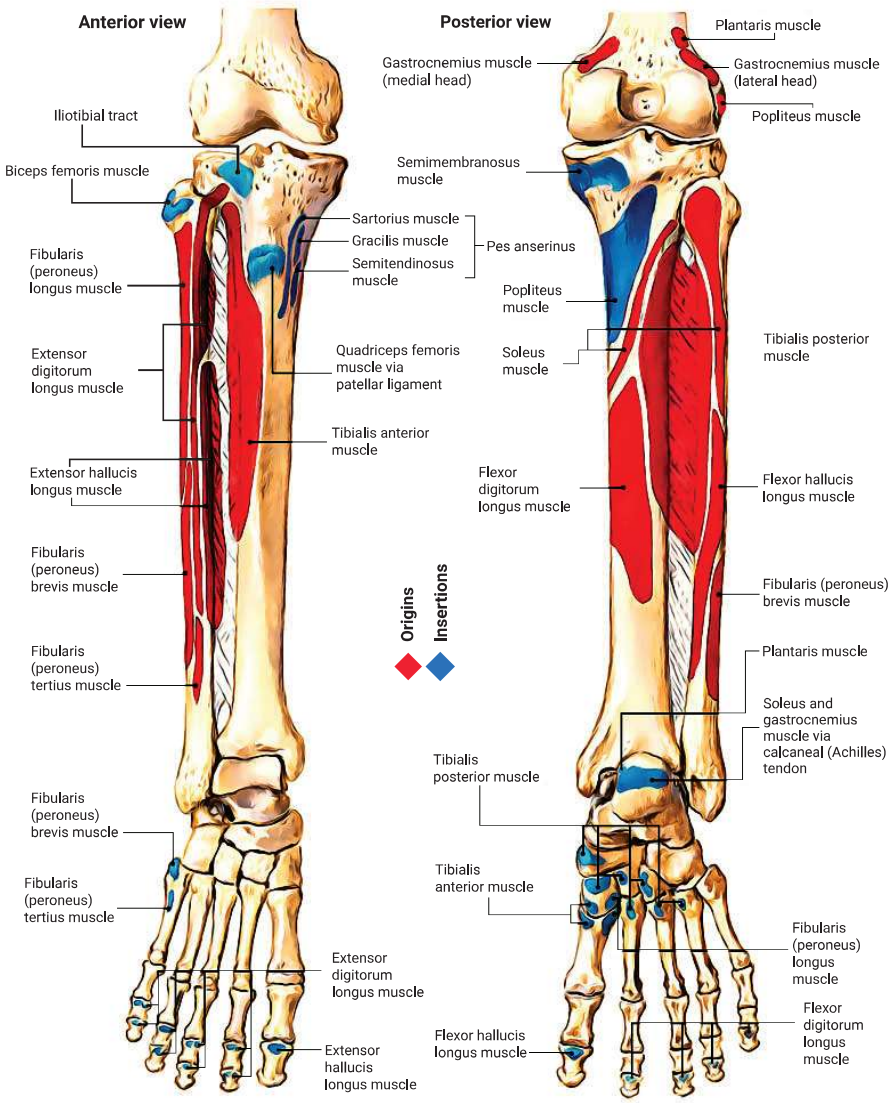
- ❖ The nutrient foramen of the tibia is located at the upper end transmits the nutrient artery which is a branch of the *posterior tibial artery* and the largest nutrient artery of the body.

Osteomyelitis of the upper end of tibia:

- The upper end of tibia is the commonest site of **acute osteomyelitis**
- but knee joint remain unaffected because the capsule of knee joint is attached near to the margins of articular surfaces proximal to the epiphyseal line.

Fracture of tibia:

- (The tibial shaft is narrowest at the junction of upper 2/3rd and lower 1/3rd, hence the commonest site of fracture.)
- The lower one-third of the tibial shaft is bare area (hence devoid of any muscular attachment) and have low blood supply; for this reason, the fractures in the lower 1/3rd of the shaft of tibia show delayed union or non-union



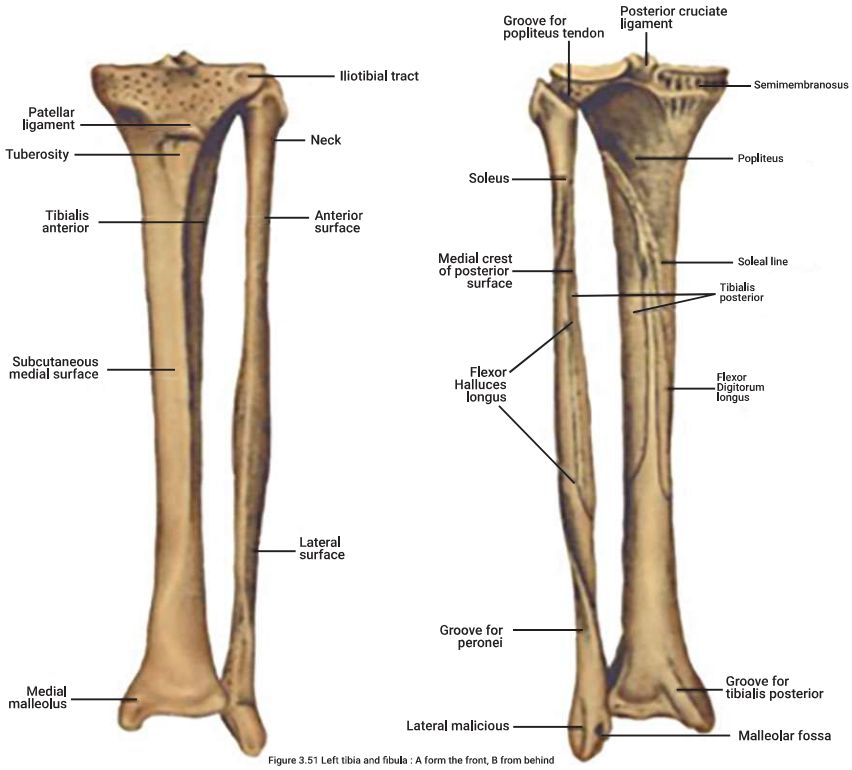


Figure 3.51 Left tibia and fibula : A form the front, B from behind

Fibula

- ***Has little or no function in weight-bearing but provides attachment for muscles.***
- Has a **head** (apex) that provides attachment for the fibular collateral ligament of the knee join
- Has a projection called the **lateral malleolus** that articulates with the trochlea of the talus; lies more inferior and posterior than the medial malleolus; and provides attachment for the anterior talofibular, posterior talofibular, and calcaneofibular ligaments. It also has the **sulcus** for the peroneus longus and brevis muscle tendons.

- Potts fracture (Dupuytren fracture) is a fracture of the lower end of the fibula, often accompanied by a fracture of the medial malleolus or rupture of the deltoid ligament. It is caused by forced eversion of the foot.
- Pillion fracture is a T-shaped fracture of the distal femur with displacement of the condyles.

It may be caused by a blow to the flexed knee of a person riding pillion on a motorcycle.

- *Fracture of the fibular neck may cause an injury to the common peroneal nerve, which winds laterally around the neck of the fibula.*

CNS Pharmacology

01. Anti-Psycotic Drugs

Dopamine hypothesis: Excessive dopaminergic activity in brain is responsible for Psychosis or schizophrenia.

Others:
The serotonin hypothesis
The glutamate hypothesis

Anti- psychotic includes:
Anti-psychotic drugs/ drugs for schizophrenia/ D2 receptor antagonist in CNS:

A. Traditional or typical neuroleptic drugs (also called conventional or first -generation antipsychotics) are competitive inhibitors at a variety of receptors, but their antipsychotic effects reflect competitive blocking of dopamine receptors.

According to chemical nature

1. Phenothiazine derivatives	• **Chlorpromazine** • **Prochlorperazine** • Thioridazine • Perphenazine • **Trifluoperazine** • Fluphenazine • Promethazine
2.Thioxanthene derivatives	• Thiothixene • Flupentixol
3.Butyrophenone derivatives	• **Haloperidol**
4.Miscellaneous structure	• Pimozide • Molindone • Sulpiride

B. Atypical (or second-generation antipsychotics):

Atypical (or second-generation antipsychotics): The newer antipsychotic drugs are referred to as atypical (or second-generation antipsychotics), because they have fewer extrapyramidal adverse effects than the older traditional agents. These drugs appear to owe their unique activity to blockade of both serotonin and dopamine (and perhaps, other) receptors. The atypical antipsychotic drugs are now the most widely used type of antipsychotic drug	1.Loxapine 2**.Clozapine** 3.Asenapine 4**. Olanzapine** 5**. Quetiapine** 6. Paliperidone 7**. Risperidone** 8.Sertindole 9. Ziprasidone 10. Zotepine 11.Aripiprazole

Q. The adverse effects of typical antipsychotic drugs due to "dopaminergic receptor blockade" are ***(Residency March 2013)***

a) Galactorrhea
b) Orthostatic hypotension
c) Urinary retention
d) Neuroleptic Malignant syndrome
e) Sedation

Answer: T F F T F

Q. Adverse effects of chlorpromazine include ***(Residency March 2011)***

a) Hair loss
b) Galactorrhea
c) Sedation
d) Emesis
e) Akathisia

Answer: F T T F F

Q. About chlorpromazine ***(Residency March2014)***

a) Is a selective Dopaminergic receptor blocker
b) Is an anti depressant
c) Produce severe vomiting at high dose
d) Should be used in jaundice patient
e) Can be used in drug induced parkinsonism

Q. Anticholinergic side effects of chlorpromazine include ***(Diploma July 2010)***

a) Mydriasis
b) Cholestatic jaundice
c) Urinary retention
d) Photosensitivity
e) Constipation

Answer: T F T F T

02. Drugs used as Mood Stabilizers

Drugs used as mood stabilizers:

- Carbamazepine
- Divalproex
- Lamotrigine
- Lithium carbonate
- Topiramate
- Valproic acid

Adverse effect of spinal anesthesia:

- Bradycardia
- Hypotension
- Respiratory depression
- Post operative urinary retention

Drugs Avoid before OT

- ACEI, ARB – Stop 24 hours before
- MAOI-2-3 Weeks before
- Metformin – 24 hours before
- Short acting insulin – avoid OT morning dose
- Levodopa – avoid on that day
- OCP -4 weeks before OT
- Antiplatelet – stop 7 days before OT
- LMWH-stop 24 hours before OT
- UFH – 2-6 hours before OT
- Any vitamin - 48 hours before OT

Q. Pre-anesthetic medications include *(Residency March 2021)*

a) Metoclopramide
b) Atropine
c) Lignocaine
d) Tranexamic acid
e) Propranolol

Answer: T T F F F

Q. Ketamine *(Residency March 2021)*

a) Causes profound analgesia
b) Usually produces bradycardia and fall of BP
c) Produces muscle relaxation
d) Decreases intracranial and intraocular pressure
e) Causes hallucination

Answer:

a) **T**
b) **F** (It produces tachycardia, hypertension and increased cardiac output)
c) **F** (no muscle relaxation)
d) **F** (increases intracranial and intraocular pressure),
e) **T**

Q. Inhalational anesthetic drugs are *(Residency March 2020)*

a) Propofol
b) Halothane
c) Ketamine
d) Nitrous oxide
e) Savoflurane

Answer: F T F T T

Explanation:

Others- Isoflurane, desflurane, chloroform

Virology

01. Basic Virology

Characteristics of viruses

- **Acellular**
- Contain **either DNA or RNA**
- **Obligate intracellular** organism
- One virus **replicate** to produce hundreds of progeny viruses (not by binary fission)
- **Capsid** protein
- Outside capsid protein **lipoprotein** envelope present in some viruses
- Enzyme **polymerase**
- Do **not** have nucleus, cytoplasm, mitochondria or ribosome
- **No** organalle, **no** nucleous, **no** nuclear membrane
- **Envelope** virus –Sensitive to heat **lipid solvent** than non envelope & transmit usually through **sexual blood or respiratory droplet**
- **Non envelope** virus transmit through **faeco oral** route
- Reproduction by **replication**
- **Highly antigenic**
- **Death occurs at 50-60°C**
- **Antiviral** not kill the virus only delays the replication
- **DNA > RNA** = Transcription
- **RNA > DNA** =Reverse transcription
- **Reverse transcriptase** enzyme – Hep B, HIV, HTLV

Basic structure of virus

- An internal core of DNA or RNA (but not both)
- Surrounded by a protective protein coat called **capsid**
- Some viruses may have an outer **lipoprotein** membrane **envelop**

Atypical virus-like Agents

- **Defective viruses** e.g. hepatitis D virus
- **Pseudovirions** (contain host cell DNA instead of viral DNA)
- **Viroids**consist solely of a single molecule of circular RNA without capsid or envelop
- **Prions** are **infections** particles that are composed **solely** of **protein**

Steps of viral replication

Attachment
↓
Penetration
↓
Uncoating
↓
Synthesis of nucleic acid & protein
↓
Progeny virion assembly
↓
Virion release from cell (either by budding or by cell lysis)

	Hepatitis Disease in immunocompromised patients: retinitis, encephalitis, pneumonitis, hepatitis, enteritis Fever with abnormalities in haematological parameters
Epstein–Barr virus (EBV)	Infectious mononucleosis Burkitt's and other lymphomas Nasopharyngeal carcinoma Oral hairy leucoplakia (AIDS patients) Other lymphomas, post-transplant lymphoproliferative disorder
Human herpesvirus 6 and 7 (HHV-6, HHV-7)	Exanthem subitum Disease in immunocompromised patients
Human herpesvirus 8 (HHV-8)	Kaposi's sarcoma, primary effusion lymphoma, multicentric Castleman's disease

Characteristics of herpes viruses 3*

- They replicate in the nucleus Form intranuclear inclusions
- HSV-1, HSV-2, VZV and CMV causes formation of multinucleated giant cell cause latent infection in sensory ganglia
- Associated with certain cancer
- Primary infections are usually more severe than recurrence

Herpes Simplex Virus

- HSV-1 mainly causes infection ***above the waist*** (characteristically the face, lips and **eyes** and is spread by saliva
- HSV-2 generally gives rise to ***sexually transmitted infection*** (genital herpes) and is spread by direct genital contact via infected secretions

Usually site of latency of HSV-1

- **Cranial sensory ganglia (trigeminal)**

How HSV is transmitted?

- Transmitted by **saliva**

Disease caused by HSV-1

- Gingivostomatitis
- Herpes labialis
- Keratoconjunctivitis
- **Encephalitis** (**temporal lobe**)
- Herpetic whitlow (**paronychia**)
- Disseminated infections e.g. Pneumonia esophagitis in immunocompromised

The lesions of condyloma acuminatum appear as tiny finger-like projections on the perianal or genital skin, often with a cauliflower-like appearance, in clusters or as single entities.

Types of HPV

- HPV 1 to 4 – skin wart (**Rx** – N2 liquid) & plantar warts (**Rx-** Surgically or treated with salicylic acid)
- HPV 6 & 11--- anogenital wart (most common STD), Respiratory tract papilloma, (lanyngeal oedema)
- HPV 16 & 18 --- Dysplasia and Carcinoma of cervix, Penis, Uterus, Anus & Vulva
- HPV 16 Oral cancer
- **Condylomata acuminata (**6 & 11) **Rx-** phylopoin
- **Vaccine** available – 6,11,16,18

Q. HPV vaccine available against by

a) HPV-1
b) HPV-4
c) HPV-6
d) HPV-11
e) HPV-16

Answer: F F T T T

Parvovirus B19

Important Properties

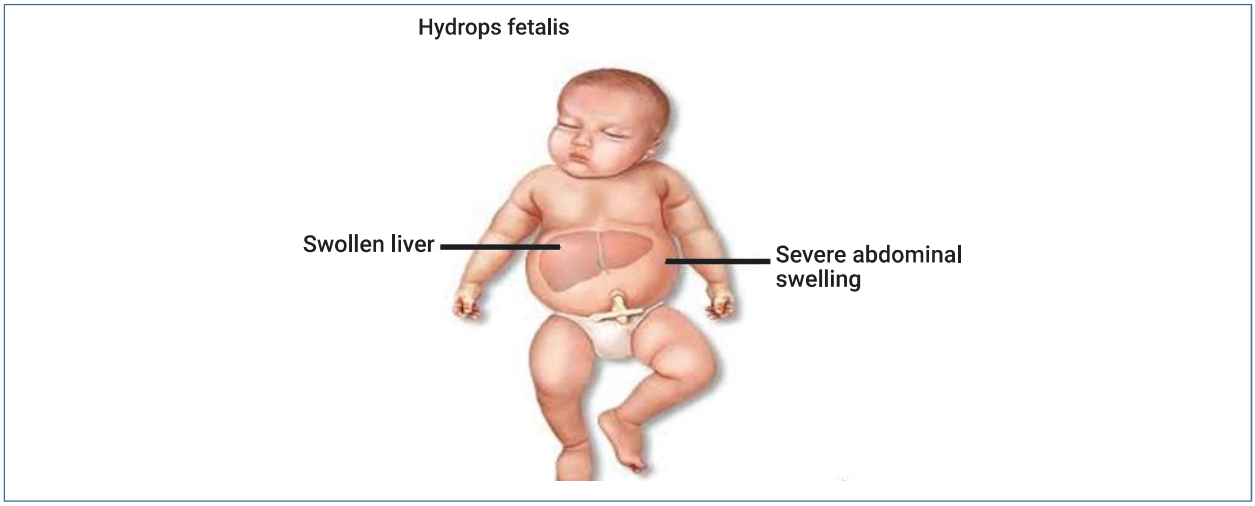
- **Single-stranded** DNA. Has particular tropism for red cell precursors/erythroblasts. Infection provides **lifelong** immunity against reinfection
- **Transmission -** Respiratory, Transplacental, Blood transmission
- Dx - IgM, PCR
- **No vaccine**
- A '**slapped cheek'** rash is characteristic but the rash is very variable
- **Affect 2 types of cells: RBC precursors (erythroblasts) in bone marrow - aplastic anemia & endothelial cells in blood vessels - rash**

Mode of transmission of parvovirus B 19

- Respiratory droplets
- Transplacental
- Blood transfusion

Diseases caused by parvovirus B19

- **Erythema infectiosum** (slapped cheek syndrome, fifth disease)(four other macular or maculopapular rash diseases - measles,rubella,scarlet fever, & roseola)
- **Aplastic anemia** - especially with sickle cell anemia,thalassemia,spherocytosis
- **Fetal infections** - during first two trimesters of pregnancy can result in intrauterine infection & impact on fetal bone marrow
- **Hydrops fetalis** - 10–15% of non-immune (non-Rh-related) hydrops fetalis, a rare complication of pregnancy
- **Immune complex Arthritis** - Small joints of hand & feet bilaterally resembling RA, Women
- **Chronic B19 Infection**



11. Maculopapular Rash Diseases of Children

Maculopapular Rash –

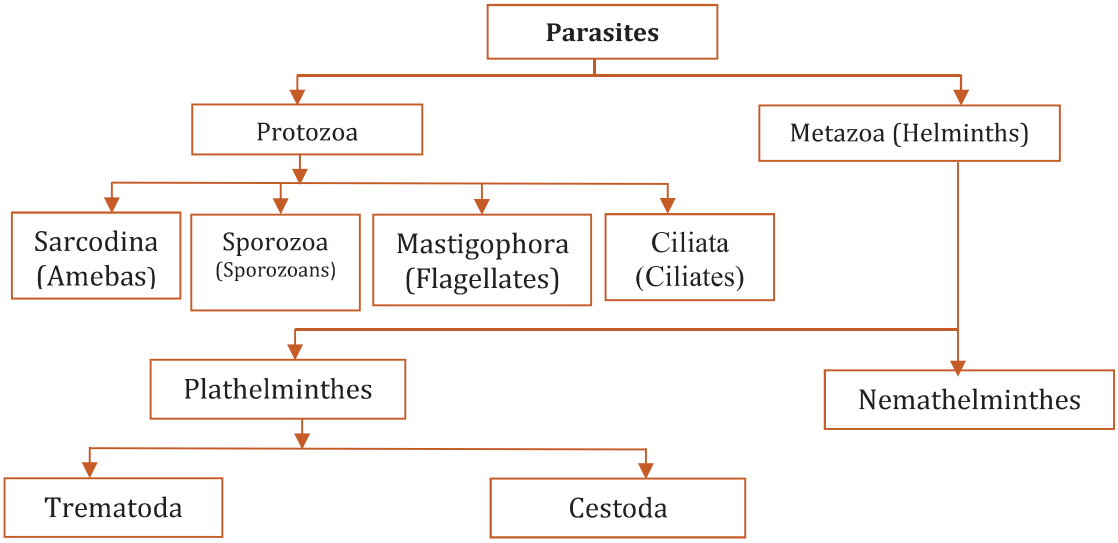
- Measels (**koplik's spot** on buccal mucosa)
- Scarlet fever
- Roseola (Caused by HHV 6 and HHV 7)
- Erythrema infectosum (Parvo B19) (Fifth disease)
- Dengue
- Typhoid
- IM
- Zika
- Secondary syphillis

Parasitology

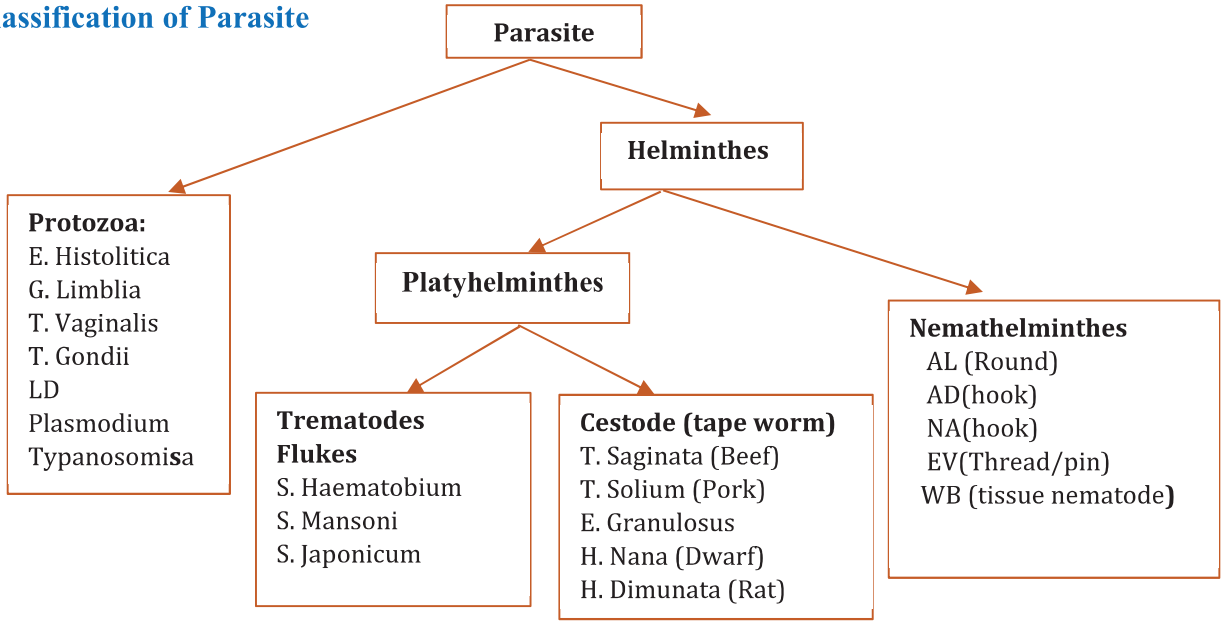
01. Parasites

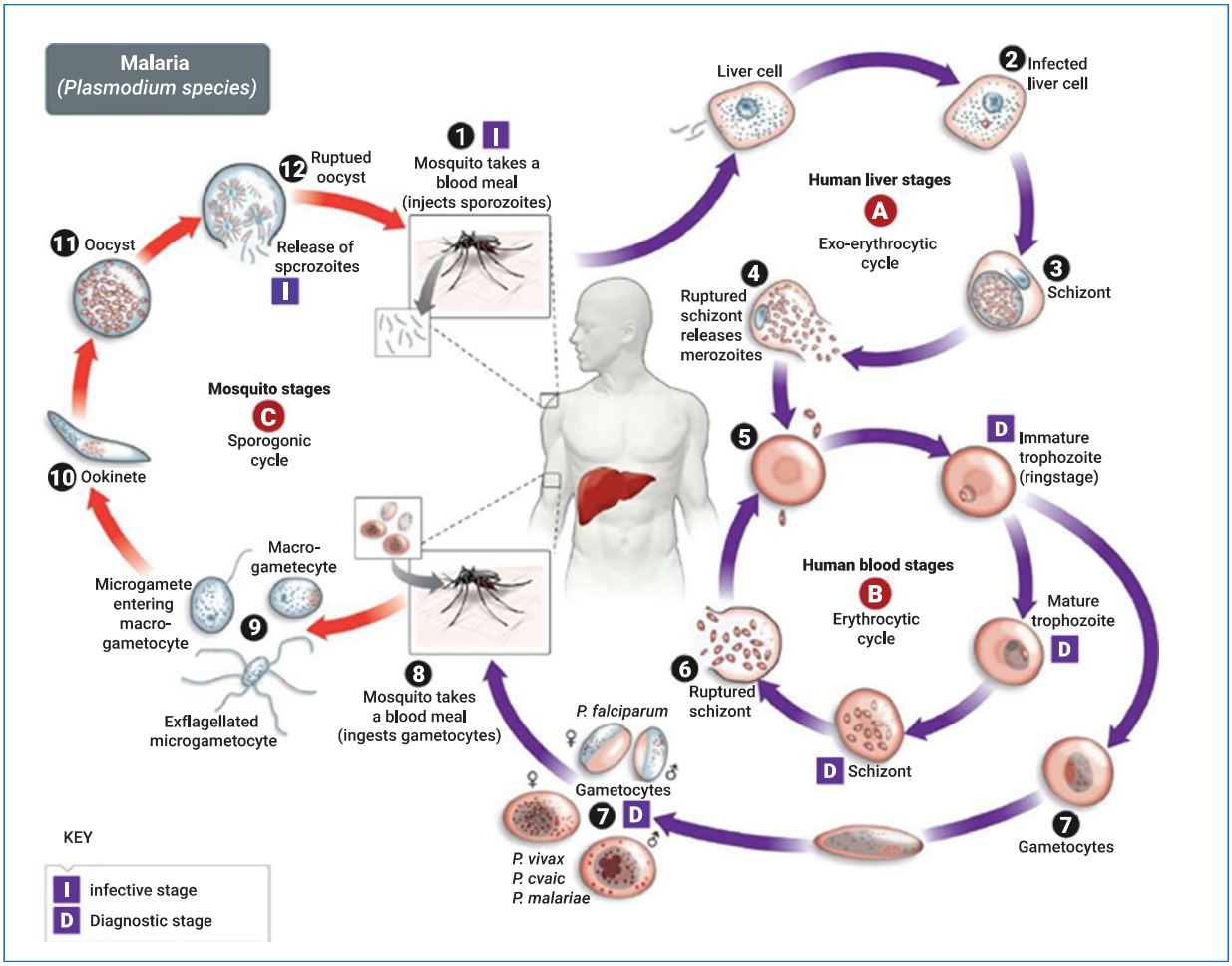
❑ Parasite:

- A living organism which receives nourishment and shelter from another organism where it lives.
- Parasites occur in two distinct forms:
  - ✓ Single celled protozoa and
  - ✓ Multicellular metazoan called helminths or worms.



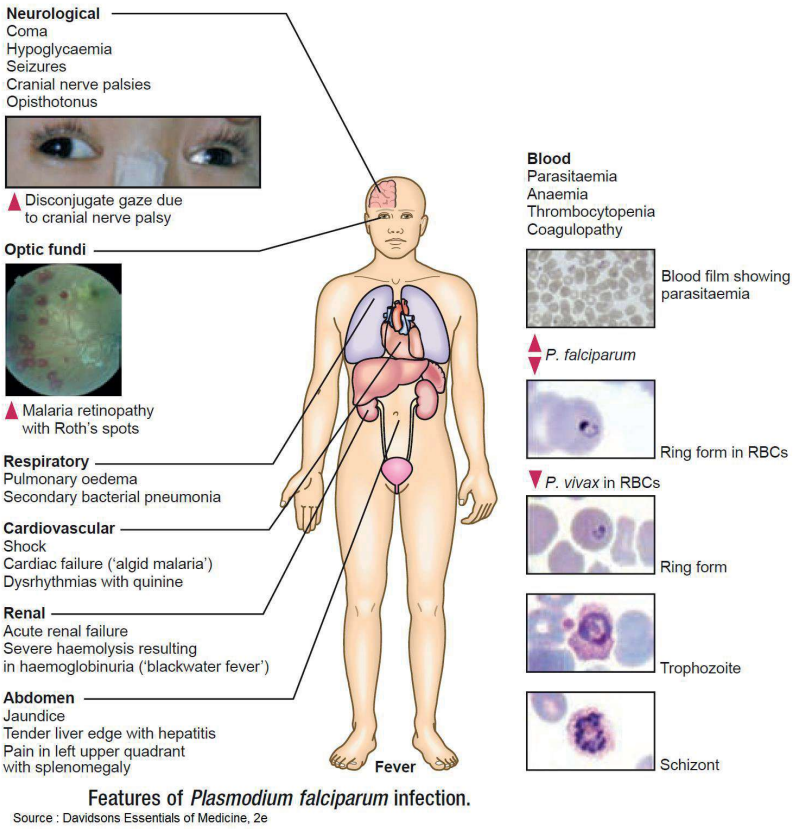
❖ Easy to Learn Classification of Parasite





❑ Difference between Species

Cycle/feature	Plasmodium vivax, P.ovale	P. malariae	P.falciparum
Pre-patent period (minimum incubation)	8-25 days	15-30 days	8-25 days
Exo erythrocytic cycle	Persistent as hypnozoites	Pre-erythrocytic only	Pre-erythrocytic only
Asexual cycle	48 hrs synchronous	72 hrs synchronous	<48 hrs asynchronous
Fever periodicity	Altenate days	Every third day	None
Delayed onset	Common	Rare	Rare
Relapses	Common upo to 2 years	Recrudescence many years later	Recrudescence up to 1 year



Features of *Plasmodium falciparum* infection.

Source : Davidsons Essentials of Medicine, 2e

Q. Complications of falciparum malaria are-

a) Hyperglycaemia
b) Pulmonary edema
c) Hypoglycemia (<40mg/dL)
d) Metabolic alkalosis
e) Acute renal failure

Answer: F T T F T

06. Leishmaniasis (Kala-azar or black sickness)

❑ Important Properties

- *Kala-azar* causative agent -L. Donovani, (Affects macrophage)
- L. Donovani has 2 form
  - ✓ Promastigote
  - ✓ Amastigote
- **Promastigote is infective form & found in parasite and culture media (NNN)**
- **Amastigote form found in**
  - ✓ Monocyte
  - ✓ Macrophage
  - ✓ Bone marrow
  - ✓ Splenic aspirate
  - ✓ Lymph node

Previous Questions

Previous Residency & Diploma Questions

MCQ

01. Dermatophytes *(Residency March-2024)*
a) Are dimorphic fungus
b) Cause ring worm in skin
c) Infect keratinized tissue
d) Infections result from inhalation of spores
e) Produce morphologically identical microconidia in all genera
Answer: F T T F F

02. Subcutaneous mycoses are *(Residency March-2021)*
a) Sporotrichosis
b) Cryptococcosis
c) Mycetoma
d) Histoplasmosis
e) Chromoblastomycosis
Answer: T F T F T

03. Systemic deep fungal infection(s) is/are caused by-*(Diploma July-2024)*
a) Blastomyces dermatitidis
b) Malassezia furfur
c) Histoplasma capsulatum
d) Coccidioides immitis
e) Microsporum spp
Answer: T F T T F

04. In Pneumocystis jirovecii pneumonia *(Diploma July-2024)*
a) Diagnosis is made by silver staining of sputum
b) Pleural effusion is common
c) Shortness of breath is a prominent feature
d) WBC count is high
e) Mediastinal lymphadenopathy is a characteristic feature
Answer: T F T T F

05. Cryptococcus neoformans *(Diploma July 2022)*
a) Reproduces by the process of budding
b) Causes disease in immunocompromised host
c) Forms germ tube in human serum
d) Possesses a polysaccharide capsule
e) Causes human to human transmission
Answer: T T F T F

06. Condition/s lead/s to lymphocytosis in CSF is/are *(Diploma July 2022)*
a) Meningococcal meningitis
b) Tubercular meningitis
c) Viral meningitis
d) Gullian Barrie syndrome
e) Subarachnoid haemorrhage
Answer: F T T F F

07. Agents of invasive fungal infections is/are: *(Residency March 2022)*
a) Candida spp
b) Aspergillus spp.
c) Rhizopus spp
d) Malassezia furfur
e) Madurella mycetomatis
Answer: T T T F T

SBA

08. Stem: A 65-year-old woman complains of pain on swallowing. She is diabetic for the last 10 years. On examination, whitish lesions are seen on the tongue, palate and pharynx. Gram stain of material from the lesions reveals budding yeast and pseudohyphae. Lead in: Which is the most likely causative agent? *(Diploma July-2023)*
a) Blastomyces dermatitidis
b) Coccidioides immitis
c) Candida albicans
d) Histoplasma capsulatum
e) Paracoccidioides brasiliensis
Answer: C

Neoplasm

01. Neoplasm

- Neoplasia means new growth. And collection of cells and stroma composing new growth are referred to as neoplasm.
- Tumor usually denotes swelling caused by inflammation. But now equated with neoplasm.
- Oncology (greek oncos = tumor) study of tumor or neoplasm.

Neoplasm is defined as
"A **neoplasia is a new growth, comprising an abnormal collection of cells the growth of which exceeds and is uncoordinated with that of the normal tissue**."

General phenomena associated with neoplasia:

- Fever
- Cachexia
- Thrombotic episode
- Polycythaemia
- Dermatomyositis

Cancer cachexia

- Equal loss of both fat & lean muscle mass
- Calorie expenditure remains high, increased BMR, despite reduced food intake
- Evidence of systemic inflammation (eg. acute phase reactant)
- Mediator – TNF alpha, IL 1, PIF, IFN gamma

Local Features of Malignant Disease

Symptom	Typical site or possible tumor
Hemorrhage	Stomach, colon, bronchus, endometrium, bladder, kidney
Lump	Breast, lymph node (any site), testicle
Bone pain or fracture	Bone (primary sarcoma, secondary metastasis from breast, prostate, bronchus, thyroid, kidney)
Skin abnormality	Melanoma, basal cell carcinoma (rodent ulcer)
Ulcer	Esophagus, stomach, anus, skin
Dysphagia	Esophagus, bronchus, gastric
Increasing constipation, abdominal discomfort or pain	Colon, rectum, ovary
Airway obstruction, stridor, cough, recurrent infection	Bronchus, thyroid
Odynophagia, early satiety, vomiting	Bronchus, stomach, esophagus, colon, rectum
Abdominal swelling (ascites)	Ovary, stomach, pancreas

02. Cells According to Proliferative Capacity

Types of cell according to proliferative capacity:

- The ability of tissue to repair themselves is determined by their intrinsic proliferative capacity and presence of tissue stem cells. Divided into 3 types.

1. **Labile tissue:**
   - Cells of this type continuously being lost and replaced by maturation from tissue stem cell and proliferation of mature cells.
   - Regenerate as long as pool of stem cell preserved.

   Example:
   - Haematopoietic stem cell of bone marrow
   - Surface epithelial cells e.g. stratified squamous cells of skin, oral cavity, vagina and cervix.
   - Cuboidal epithelial of ducts of draining exocrine organs: salivary gland, pancreas, biliary tract.
   - The columnar epithelia of GI tract, uterus, fallopian tube.
   - Transitional epithelium of urinary tract.

2. **Stable Tissue: Cells of these tissues are in quiescent stage** (Go stage of cell cycle) and have minimal proliferative activity in normal state.
   - They have limited regenerative capacity in response to injury except liver.
   - Proliferation of these cells particularly important in wound healing.

   Example:
   - Parenchyma of most solid tissues e.g. Liver, kidney and pancreas.
   - Endothelial cell
   - Fibroblast
   - Smooth muscle cell

3. **Permanent tissue: cells of these tissues** considered to be terminally differentiated and non-proliferative in post natal life.
   - Injury to **brain and cardiac muscle** is irreversible and results in scar. (Scar formation)
   - Limited cell replication and differentiation occurs in some areas of adult brain.

Example:
- Majority of neurons. (Neuron)
- Cardiac muscle
- Skeletal muscle (Satellite cell attached to endomyseal sheath may show some regenerative capacity)

Q. Example of stables tissue includes -

a) Liver
b) Heart
c) Epithelia of oral cavity
d) Pancreas
e) Transitional epithelium of urinary tract

Answer: T F F T F

03. Stem Cell

- Stem cells: have dual property of being able to self-renew and give rise to differentiated cells and tissues.
- Stem cells have two types of self-division –

Asymmetric division:

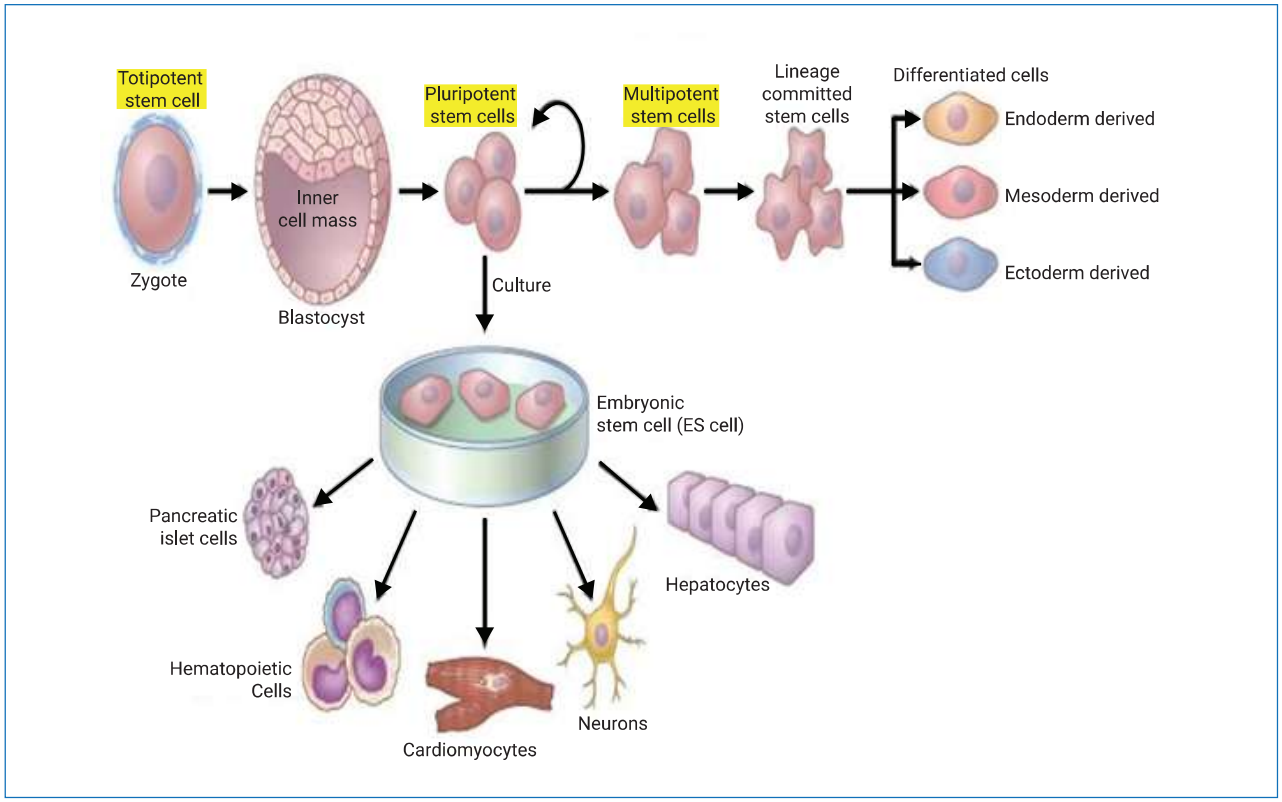
One daughter cell enters a differentiation pathway and give rise matures cell, while other remains undifferentiated and remains its self-renewal capacity.

Symmetric division:

Both daughter cells retain self-renewal capacity. Such replication occurs early in embryogenesis and stressed condition like bone marrow repopulation after ablative chemotherapy

Fundamentally two variety

- **Embryonic stem cell:** Most undifferentiated. They present in inner cell mass of **blastocyst**. Have virtually limitless self-renewal capacity and can give rise to every cell of the body. So they are said **totipotent**.
- **Tissue stem cell**: (also called adult stem cell): They are protected within tissue microenvironment called *stem cell niches,* located in **Bone marrow** (Haematopoietic stem cell), intestine (Crypts), Bulge region of hair follicle, limbus of cornea and sub ventricular zone in brain.



Q. Example of tissue stem cell

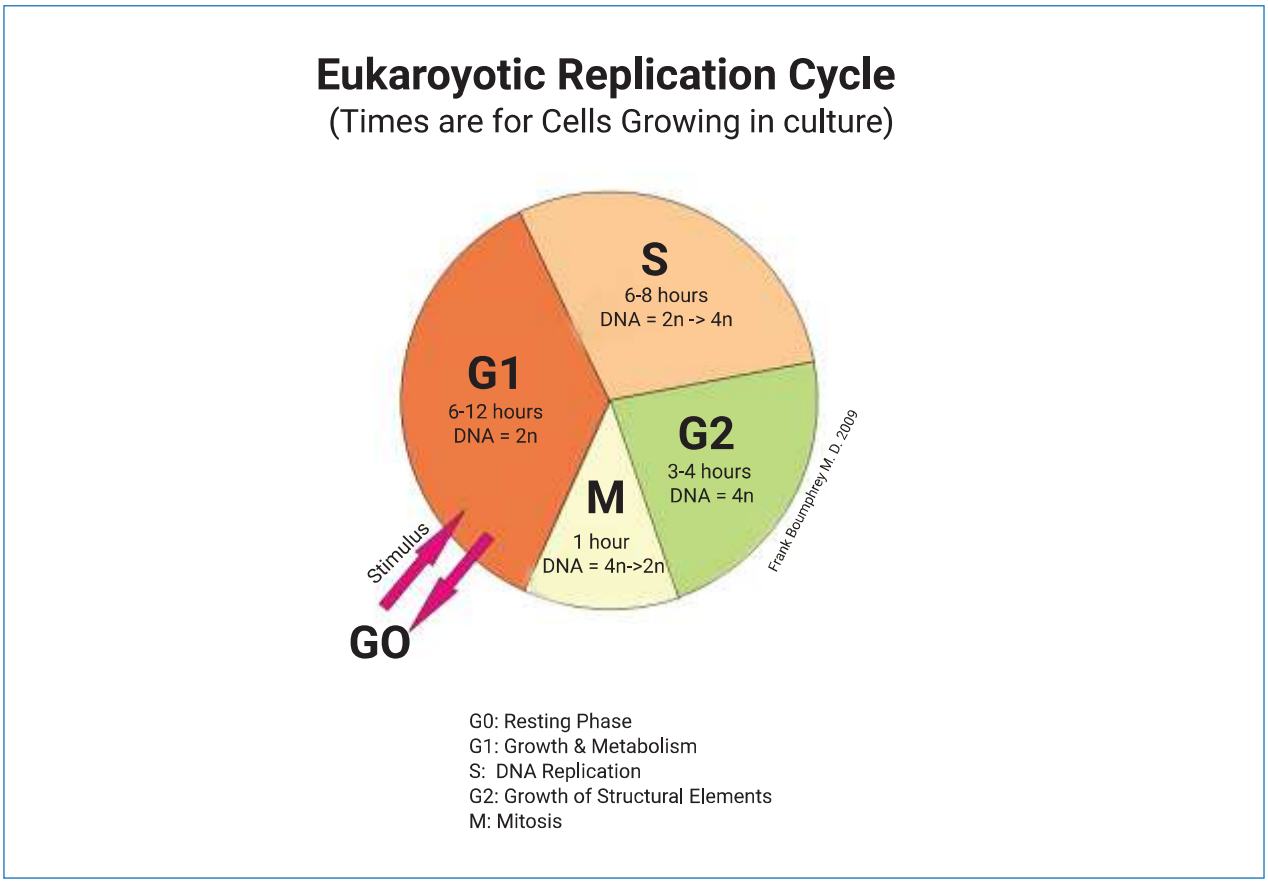
a) Embryo
b) Placenta
c) Hematopoietic stem cell
d) Crypts of intestine
e) Bulge region of hair follicle

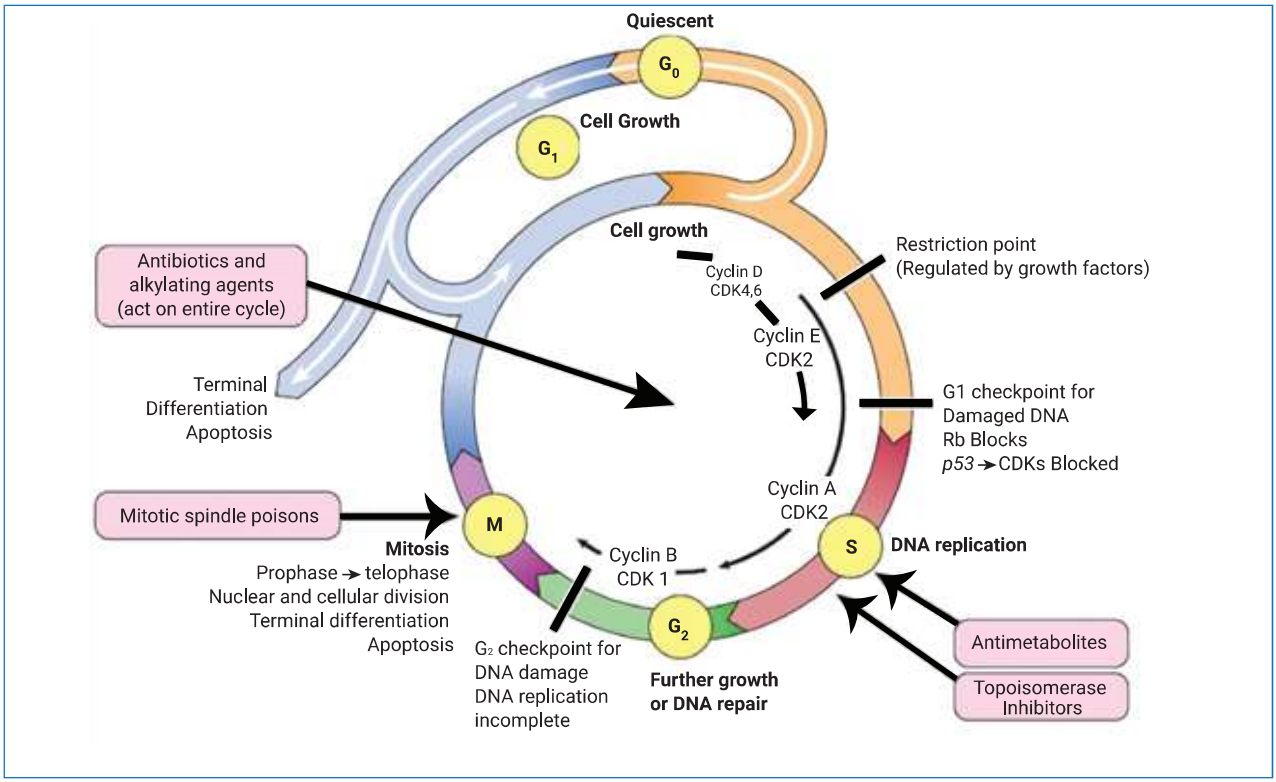
Answer: F F T T T

04. Cell Cycle

Cell cycle

- Cell Cycle is **a series of events that takes place in a cell as it grows and divides**.
- **Phase:**
  1. Interphase: cell spends most of its time in what is called interphase, and during this time it grows, replicates its chromosomes, and prepares for cell division.
  2. Cell division
- **Checkpoint:**
  1. Cell growth checkpoint
  2. DNA synthesis checkpoint
  3. Mitosis Checkpoint
- **Significance:** Cancers occurs when cell cycle regulation is lost.





The cell cycle and sites of action of chemotherapeutic agents. (CDK = cyclin-dependent kinase; RB= retinoblastoma gene)

05. Benign & Malignant Tumors

Classification of tumors on histological basis

Tissue	Benign	Malignant
Composed of One Parenchymal Cell Type		
Connective tissue and Derivatives	Fibroma Lipoma Chordoma Osteoma	Fibrosarcoma Liposarcoma Chondrosarcoma Osteogenic sarcoma
Endothelial and related tissues, Blood vessels Lymph vessels Mesothelium Brain coverings	 Hemangioma Lymphangioma Meningioma	 Angiosarcoma Lymphangiosarcoma **Mesothelioma** Invasive meningioma
Blood cells and related cells Hematopoietic cells Lymphoid tissue		**Leukemia** **Lymphomas**
Smooth Muscle Striated muscle	Leiomyoma Rhabdomyoma	Leiomyosarcoma Rhabdomyosarcoma
Tumors of epithelial origin Stratified squamous	Squamous cell papilloma	Squamous cell or epidermoid carcinoma

Basal cells of skin or adnexa Epithelial lining of glands or ducts Respiratory passages Renal epithelium Lover cells Urinary tract epithelium (transitional)	 Adenoma Papilloma Cystadenoma Bronchial adenoma Renal tubular adenoma Liver cell adenoma Urothelial papilloma Hydatidiform mole	**Basal cell carcinoma** Adenocarcinoma Papillary carcinomas Cystadenocarcinoma Bronchogenic carcinoma Renal cell carcinoma Hepatocellular carcinoma Urothelial carcinoma Choriocarcinoma Seminoma Embryonal carcinoma
Tumors of melanocytes	Nevus	Malignant melanoma
More than one neoplastic cell Type -Mixed tumors, Usually derived from one germ cell layer		
Salivary glands Renal angle	Pleomorphic adenoma (mixed tumor of salivary gland	Malignant mixed tumor of salivary gland Wilms tumor
More than one neoplastic cell type derived from more than one germ cell layer – teratogens		
Totipotential cells in gonads or in embryonic rests	mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma

Heard Benign but malignant:

- Melanoma
- Synovioma
- Mesothelioma
- Medulloblastoma
- Lymphoma
- Glioma
- Seminoma
- Hepatoma
- Dysgerminoma
- Chordoma

Q. Following tumors are histologically benign -

a) Astrocytoma
b) Meningeoma
c) Schwannoma
d) Medulloblastoma
e) Craniopharyngioma

Answer: F T T F T

Classification of bone tumor:

Category and fraction (%)	Behavior	Tumor Type	Common Locations
Cartilage forming (30)	Benign	• Osteochondroma • Chondroma • Chondroblastoma • Chondromyxoid Fibroma	Metaphysis of long bones small bones of hands and feet Epiphysis of long bones Tibia, pelvis
	Malignant	Chondrosarcoma (Conventional)	Pelvis, Shoulder

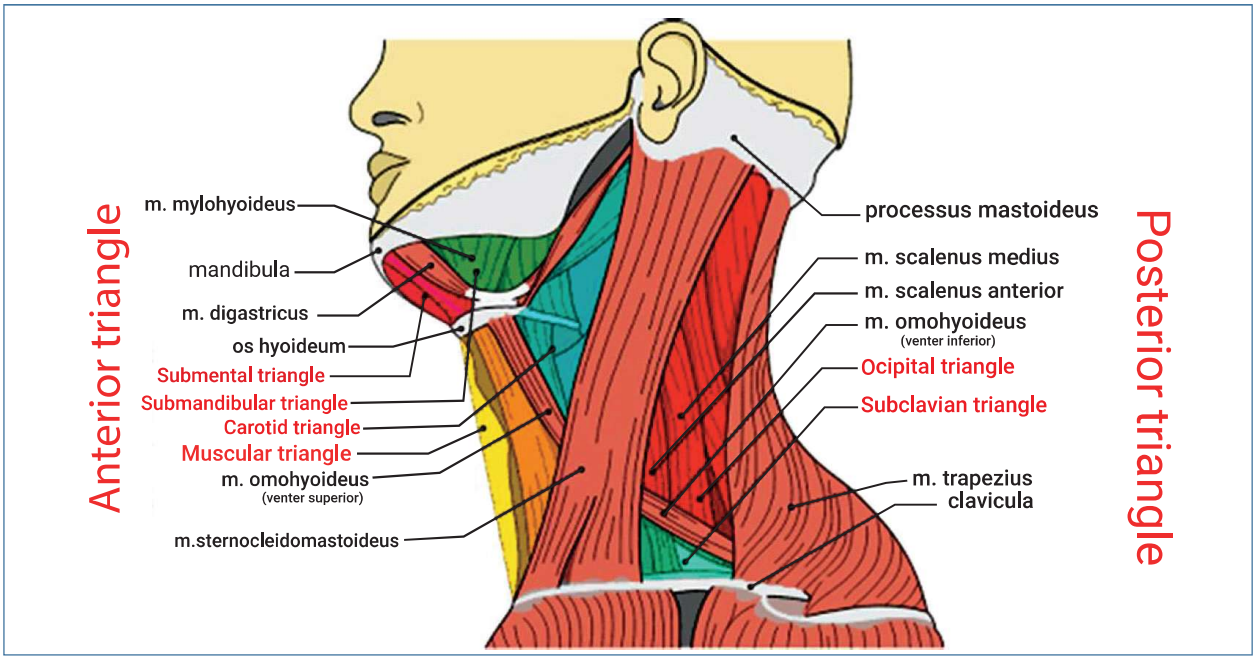
Head & Neck

01. Triangles of Neck

Anterior Triangle

Boundaries:

Is bounded by the anterior border of the sternocleidomastoid, the anterior midline of the neck, and the inferior border of the mandible. Has a roof formed by the platysma and the investing layer of the deep cervical fascia.



Subdivision: Is further divided by the omohyoid anterior belly and the digastric anterior and posterior bellies into the digastric (submandibular), submental (suprahyoid), carotid, and muscular (inferior carotid) triangles.

Sternocleidomastoid muscle divides each side of neck into anterior & posterior triangle.
Anterior triangle is again subdivided into 4 sub-triangles by omohyoid & digastric muscles.
Posterior triangle is subdividede by inferior belly of omohyoid into 2 sub-triangles.

Contents:

- ✓ **Submental triangle:** Submental lymph node, commencement of anterior jugular vein
- ✓ **Submandibular / Digastric triangle:** Submandibular gland, submandibular LN, facial vein & artery, Mylohoid vessels & nerve, part of hypoglossal nerve
- ✓ **Carotid triangle:** Carotid sheath contents
- ✓ **Muscular triangle:** Muscles; beneath its floor lies thyroid, larynx, trachea & esophagus

Posterior Triangle

Boundaries: Bounded by the posterior border of the sternocleidomastoid muscle, the anterior border of the trapezius muscle, and the superior border of the clavicle.

- Has a roof formed by the platysma and the investing (superficial) layer of the deep cervical fascia.
- Has a floor formed by the splenius capitis, semispinalis capitis, levator scapulae and the scalenus medius muscle.

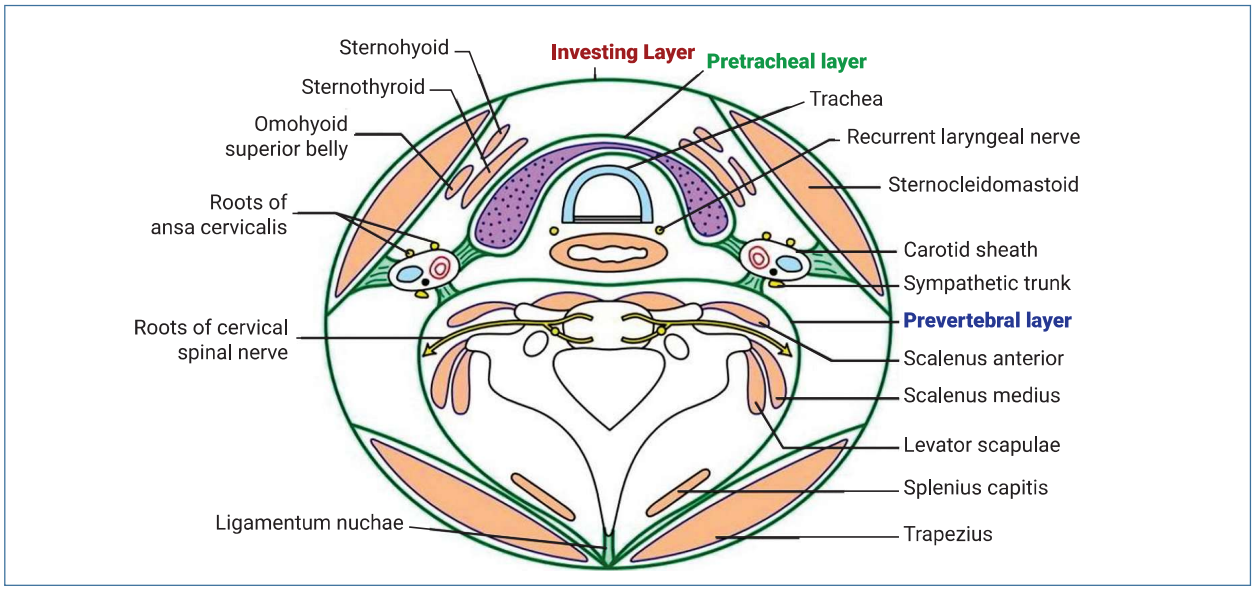
Contents:

- **Nerves**: Accessory nerve, cutaneous branches of the cervical plexus, roots and trunks of the brachial plexus, Long thoracic nerve, Nerve to subclavius
- **Vessels:** lower end of external jugular vein, transverse cervical and suprascapular vessels, subclavian vein (occasionally) and subclavian artery (3rd Part)
- **Others:** Supraclavicular Lymph node, occipital node, posterior (inferior) belly of the omohyoid.

02. Deep Cervical Fascia

Superficial (Investing) Layer of Deep Cervical Fascia

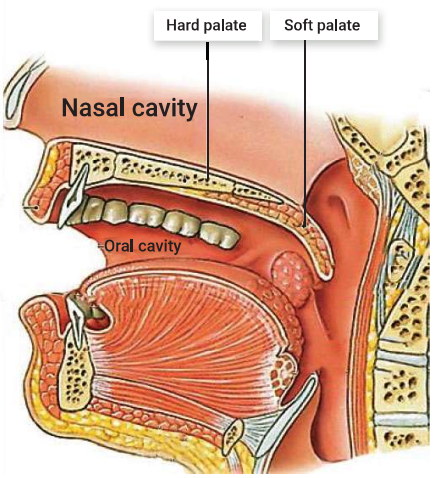
- It lies deep to the platysma, and surrounds the neck
- like a collar. Splits to enclose the sternocleidomastoid and trapezius muscles.
- Is attached superiorly along the mandible, mastoid process, external occipital protuberance, and superior nuchal line of the occipital bone.
- Inferiorly it is attached to the spine of scapula, acromion process, upper aspect of clavicle, and jugular notch of manubrium sterni from behind forwards.

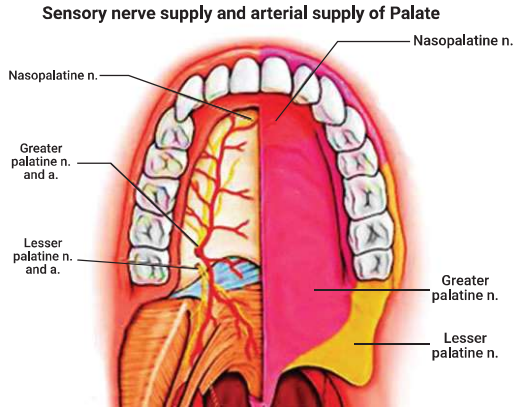


Prevertebral Layer of Deep Cervical Fascia

- Is cylindrical and encloses the vertebral column and its associated muscles.
- Covers the scalene muscles and the deep muscles of the back.

- **Epithelium:** Above-Respiratory pseudo stratified columnar epithelium, Below- Stratified squamous epithelium
- **Palatine Aponeurosis**: The palatine aponeurosis is a fibrous sheet attached to the posterior border of the hard palate. It is the expanded tendon of the **tensor veli palatini muscle.**
- Muscles of the Soft Palate The muscles of the soft palate are the tensor veli palatini, the levator veli palatini, the palatoglossus, the palatopharyngeus, and the musculus uvulae





Muscle	Nerve supply
Tensor veli palatini	Mandibular branch of trigeminal
Levator veli palatini	Pharyngeal plexus(Cranial part of accessory nerve via Vagus nerve) Arising from Nucleus ambiguus
Palatoglossus	
Palatopharyngeus	
Musculus uvulae	

All muscles of palate are supplied by vagus nerve except tensor vali palatini.

Q. Which is not a muscle of soft palate? ***(FCPS July 2019)***

a) Tensor veli palatine
b) Levator veli palatine
c) Palatoglossus
d) Palatopharyngeus
e) Muscular palatal

Answer: E

21. Tongue

Muscles of the Tongue: The muscles of the tongue are divided into two types: *intrinsic and extrinsic.*

- ***Intrinsic Muscles*** These muscles are confined to the tongue and are not attached to bone. They consist of
  1. Superior longitudinal.
  2. Inferior longitudinal.
  3. Transverse.
  4. Vertical

  Nerve supply: Hypoglossal nerve
  Action: Alter the shape of the tongue

- ***Extrinsic Muscles*** These muscles are attached to bones and the soft palate. They are.
  1. Genioglossus.
  2. Hyoglossus.
  3. Styloglossus.
  4. Palatoglossus.

  Nerve supply: Hypoglossal nerve, except palatoglossus
  Action: Change the position of tongue (Movement of tongue)