Unit – I

Basic Principles of injury and Adaptation

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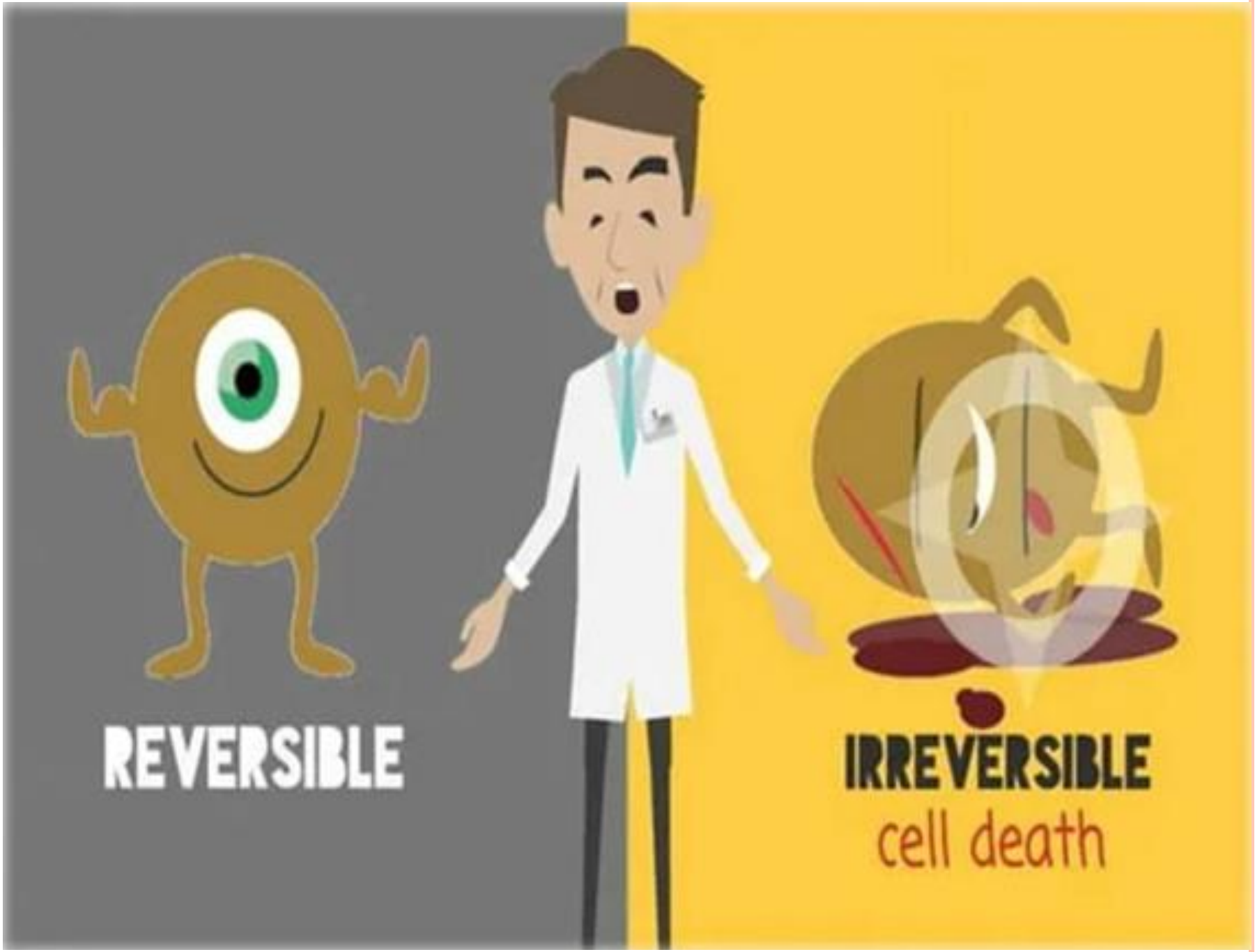
Definition

Cell injury is defined as a variety of stresses in cell that encounters as a result of changes in its internal and external environment.


REVERSIBLE
IRREVERSIBLE
cell death

Types of cell damage

The most notable components of the cell which are targets of cell damage are the DNA and the cell membrane.

There are two types of damages are as follows:

1. Sub-lethal (reversible) changes:

They are of two types: cellular swelling and fatty change.

a) Cellular swelling: two basic morphological changes manifested by sub- lethally injured cells are cell swelling and fatty change.

b) Fatty changes: sometimes the cells are damaged to such an extent that they are unable to metabolize fat adequately. In such cases small vacuoles of fat accumulate and become dispersed within cytoplasm.

2. Lethal (Irreversible) changes:

a) Necrosis:

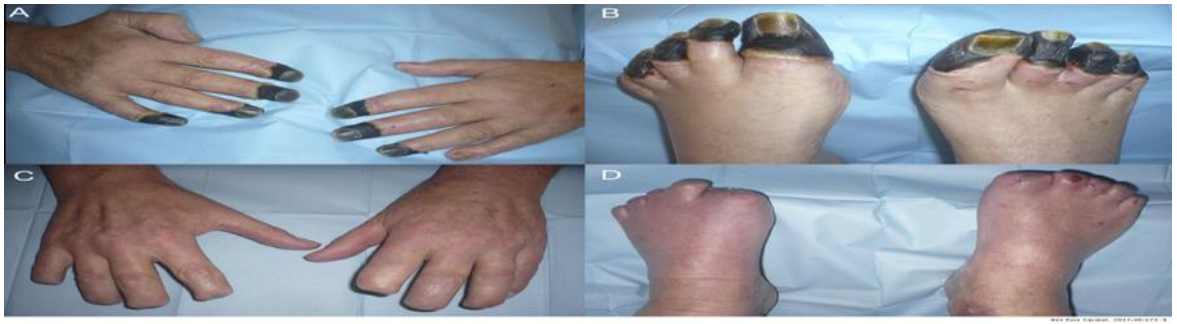
Definition: it is characterized by cytoplasmic swelling, irreversible damage to the plasma membrane, and organelle breakdown leading to cell death.

- The stages of cellular necrosis include following:

a) Pyknosis : clumping(bundle and grouping) of chromosomes and shrinking(Compress and Contract) to the nucleus of the cell.

b) Karyorrhexis: fragmentation of the nucleus and breakup of the chromatin into unstructural granules.

c) Karyolysis: dissolution of the cell nucleus.



b) Apoptosis:

Definition: it is form of coordinated and internally programmed cell death which is of significance in a variety of physiologic and pathologic conditions.

Biochemical changes: Proteolysis of cytoskeletal proteins Proteins-protein cross linking Fragmentation of nuclear chromatin by activation of nuclease. Appearance of phosphatidyl serine on the outer surface of cell membrane.

Homeostasis

- Homeostasis is the property of a system within the body of a living organism in which a variable, such as concentration of a substance in solution, is actively regulated to remain very nearly constant.

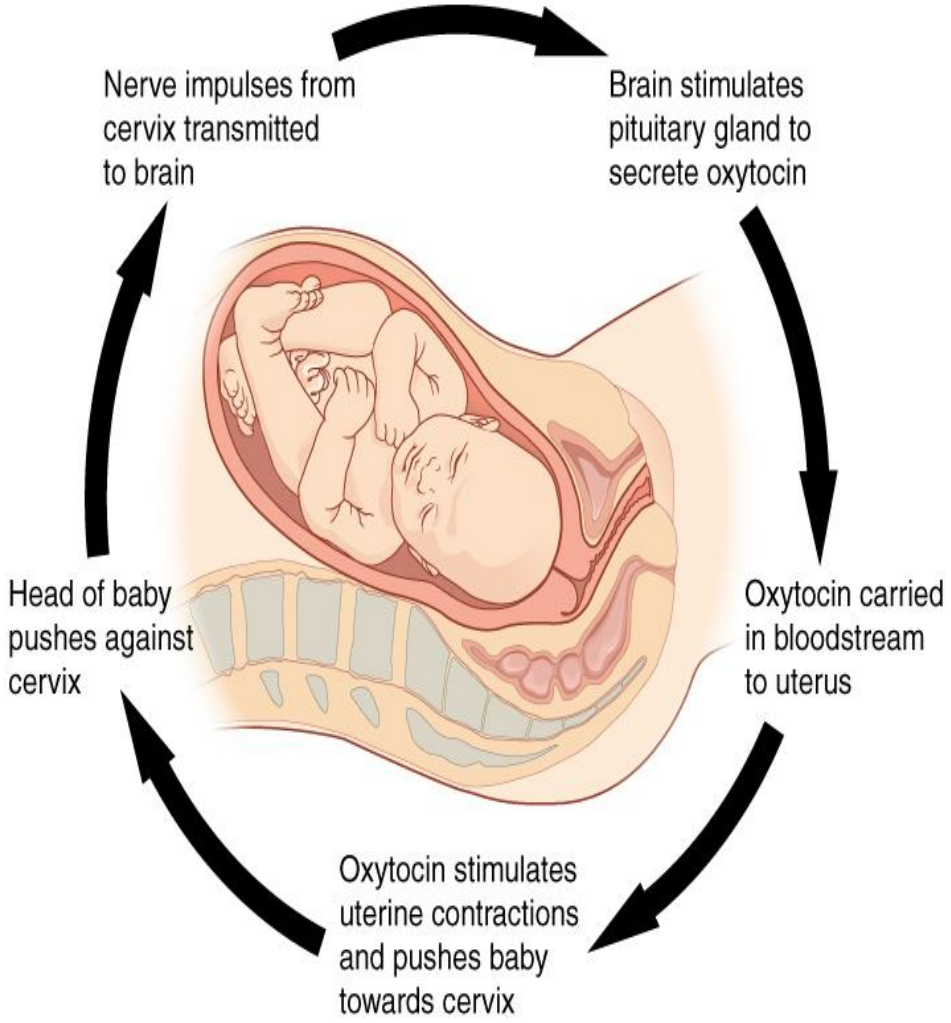
- The word originates from two words: homeo and stasis. In Greek language homoios means similar and stasis means standing still. Thus the word indicates “staying the same”.

- Operation of the feedback mechanisms involves 3 components:

✓ The sensor

✓ The control center

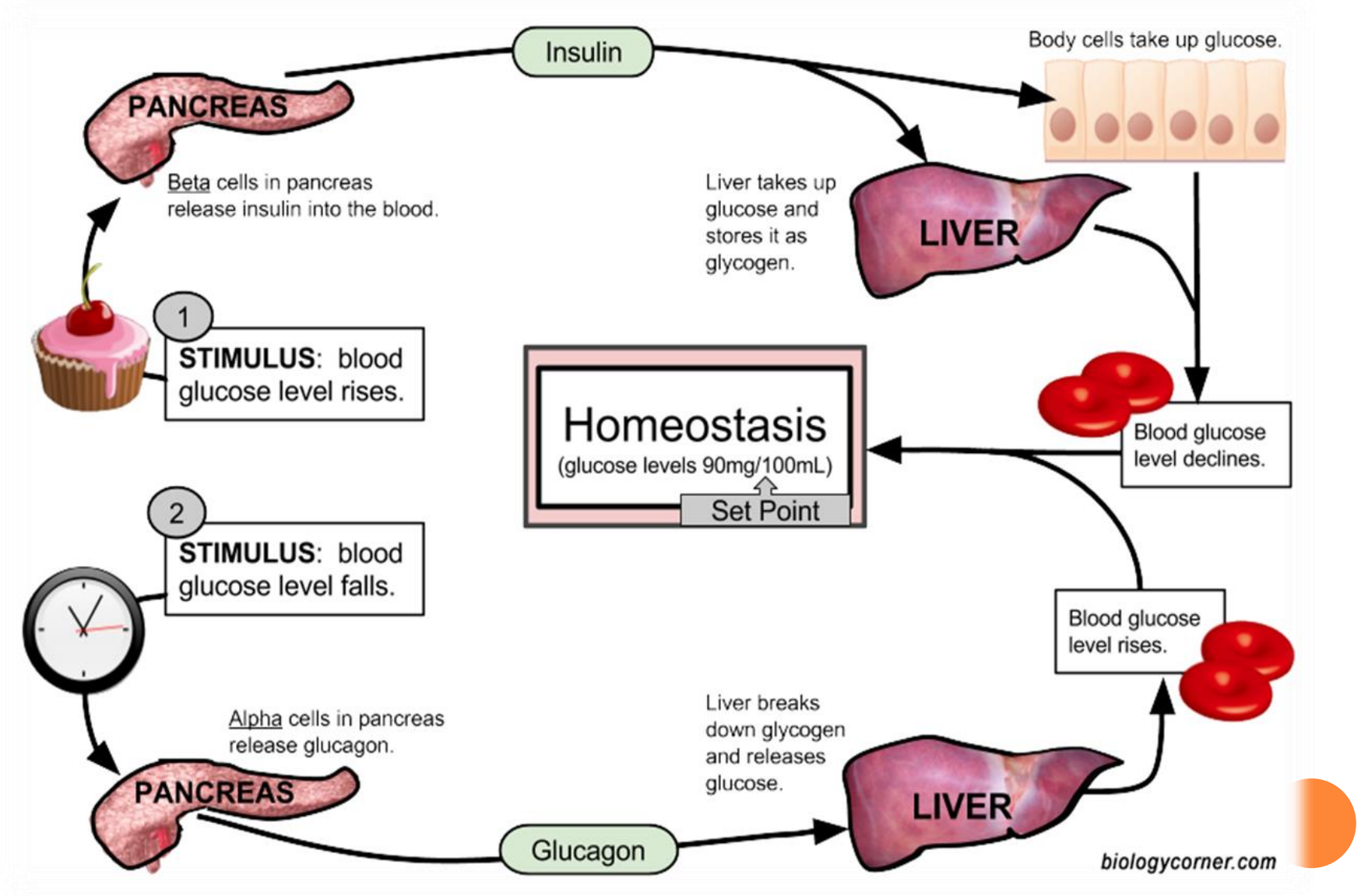
✓ The effector



Components and Types of Feedback Mechanisms Positive feedback

The onset of contractions in childbirth, known as Ferguson reflex.

When a contraction occurs, the hormone oxytocin, which increases uterine contractions. This results in contractions increasing in amplitude and frequency.


Insulin
PANCREAS
Beta cells in pancreas release insulin into the blood.
Body cells take up glucose.
Liver takes up glucose and stores it as glycogen.
LIVER
1
STIMULUS: blood glucose level rises.
Homeostasis
(glucose levels 90mg/100mL)
Set Point
Blood glucose level declines.
2
STIMULUS: blood glucose level falls.
Blood glucose level rises.
Alpha cells in pancreas release glucagon.
Liver breaks down glycogen and releases glucose.
PANCREAS
Glucagon
LIVER
biologycorner.com

CAUSES OF CELL INJURY

The causes of cell injury, reversible or irreversible may be broadly classified into two large groups:

a) Genetic causes

b) Acquired causes

1. Hypoxia and Ischemia
2. Physical Agents
3. Chemicals and drugs
4. Microbial Agents
5. Immunological agents
6. Nutritional derangements
7. Psychological factors
8. Iatrogenic factors
9. Idiopathic diseases

a) Genetic causes: Genetic defects may results in pathological changes as seen in Sickle cell anemia

b) Acquired causes: Based on the underlying agents the acquired causes of cell injury may be further classified as under:

1. Hypoxia and Ischemia:

- Cells require oxygen to generate energy and carry out metabolic functions.
- Deficiency of oxygen (hypoxia) results in failure to carry out these activities by the cells.
- Thus hypoxia is the most common cause of cell injury. The causes of hypoxia are as under: a) Reduced supply of blood to cells i.e Ischemia b) Other causes include: Anemia, carbon monoxide poisoning.

2. Physical Agents: These are

- Mechanical trauma (e.g: Road accidents)
- Thermal trauma (e.g: By heat and cold)
- Electricity
- Radiations (e.g: Ultraviolet and ionizing)
- Rapid changes in atmospheric pressure.

3. Microbial Agents:

Injuries by microbes includes infections caused by bacteria, viruses, fungi, rickettsia, protozoa, metazoan and other parasites.

4. Chemicals and drugs: These includes

- Chemical poisons (e.g: cyanide, arsenic, mercury)
- Strong acids and alkalis
- Environmental pollutants
- Insecticides and pesticides
- Hypertonic glucose and salts
- Oxygen at higher concentration
- Social agents (e.g: Alcohol, Narcotic drugs)

5. Immunological agents:

It protects the host against various injurious agents it may also turn lethal and cause cell injury. e.g: Hypersensitivity reaction, anaphylactic reaction, autoimmune reaction.

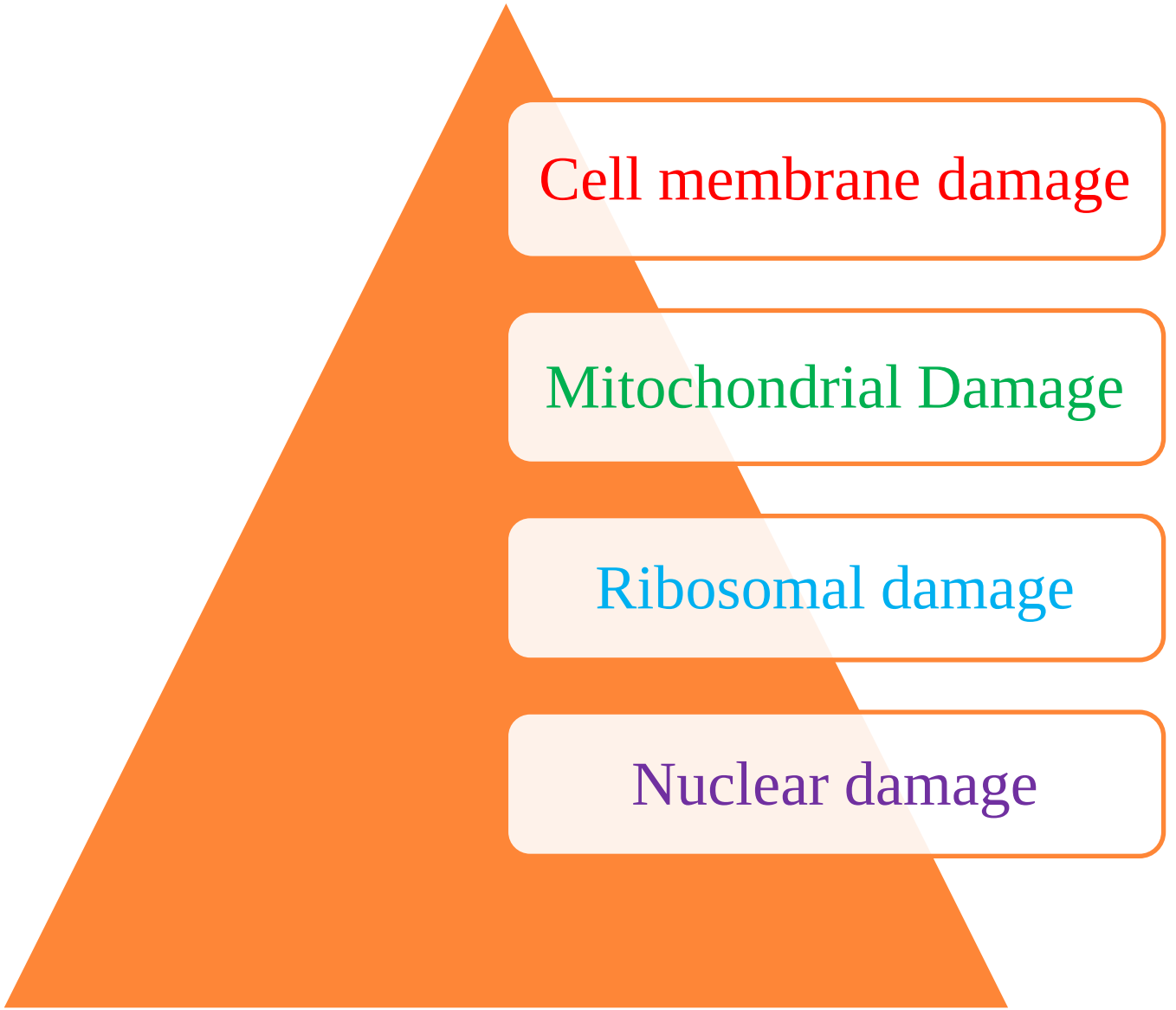
6. Nutritional imbalance:

Nutritional deficiency (protein deficiency Kwashiorkor, marasmus) or an excess of nutrients (e.g obesity, atherosclerosis, hypertension) may result in nutritional imbalance which causes cell injury.

7. Psychological factors:

There are no specific biochemical or morphological changes that occurs in common mental diseases. However, problem of drug addiction, alcoholism and smoking results in various organic diseases such as liver damage, chronic bronchitis, lung cancer, peptic ulcer, hypertension, Ischemic heart diseases etc.

Pathogenesis



Cell membrane damage

- Cell membrane diseases are life threatning disorders which are genetic in nature.
- They usually work against proteins in the body which are important for ion channels and receptors within the membrane.

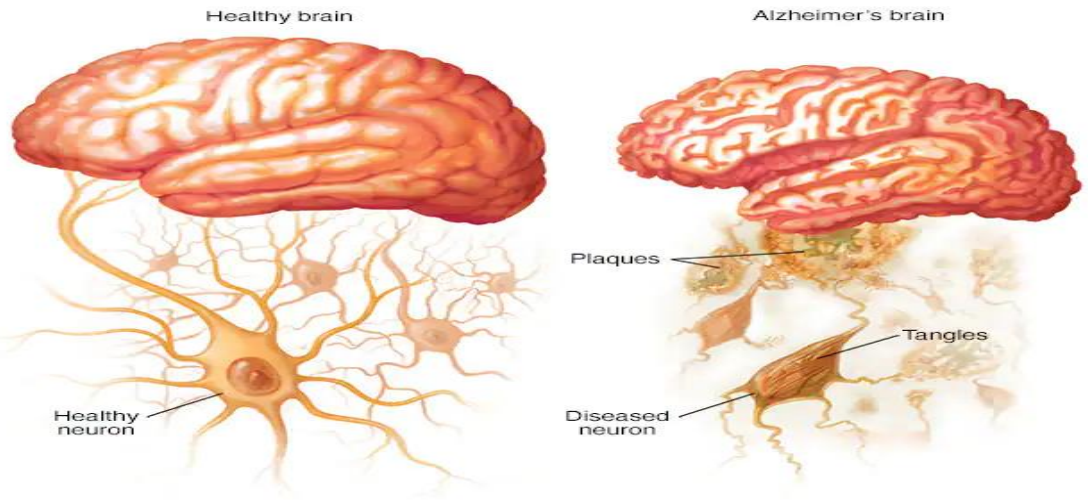
Following are some of the important disorders related to cell membrane:

a) Hyaline membrane disease

- It is commonly associated with pre-term infants. It affects the lungs at the time of birth causing respiratory distress. As a result, lungs require abnormal levels of oxygen and carbon dioxide exchange after birth.

b) Alzheimer's disease

- It is a progressive disease that destroys memory and other important mental functions. The oxidative stress caused by Alzheimer's disease in the brain results in phospholipid alterations. These alterations disrupt functions of the brain cells.



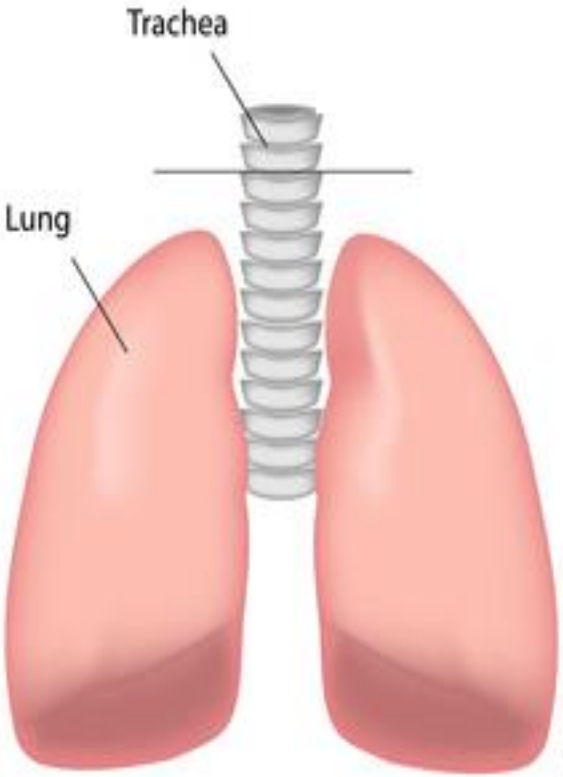
c) Cystic fibrosis:

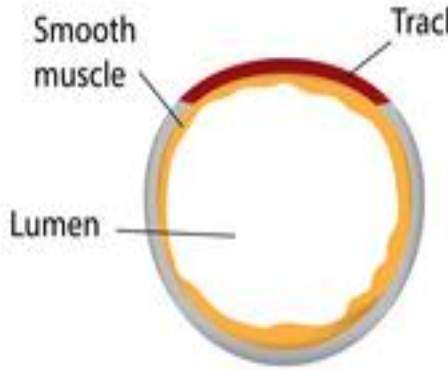
It is a disease which brings about an excessive production of fluid in the lungs due to a defective calcium ion channel. when the channel mutate leading to alteration in proteins, it causes the mucus to build up in the lungs, creating difficulty in breathing.

d) Duchene muscular dystrophy:

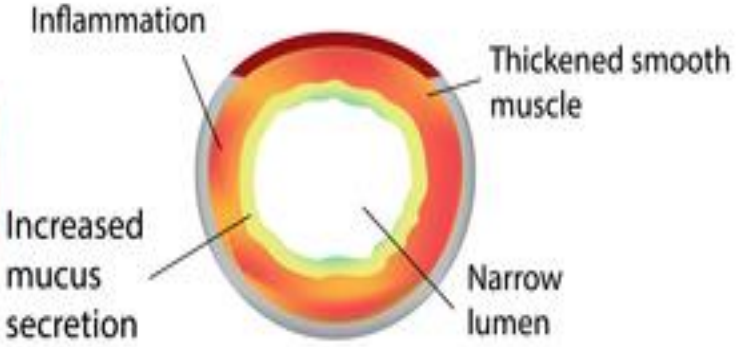
This disease affects dystrophin in the muscle cell. dystrophin allows the muscle cell wall to connect with the intracellular section. In absence of dystrophin, the cell membrane is incapable of repairing itself, destroying it and causing muscular dystrophy.

Cystic Fibrosis





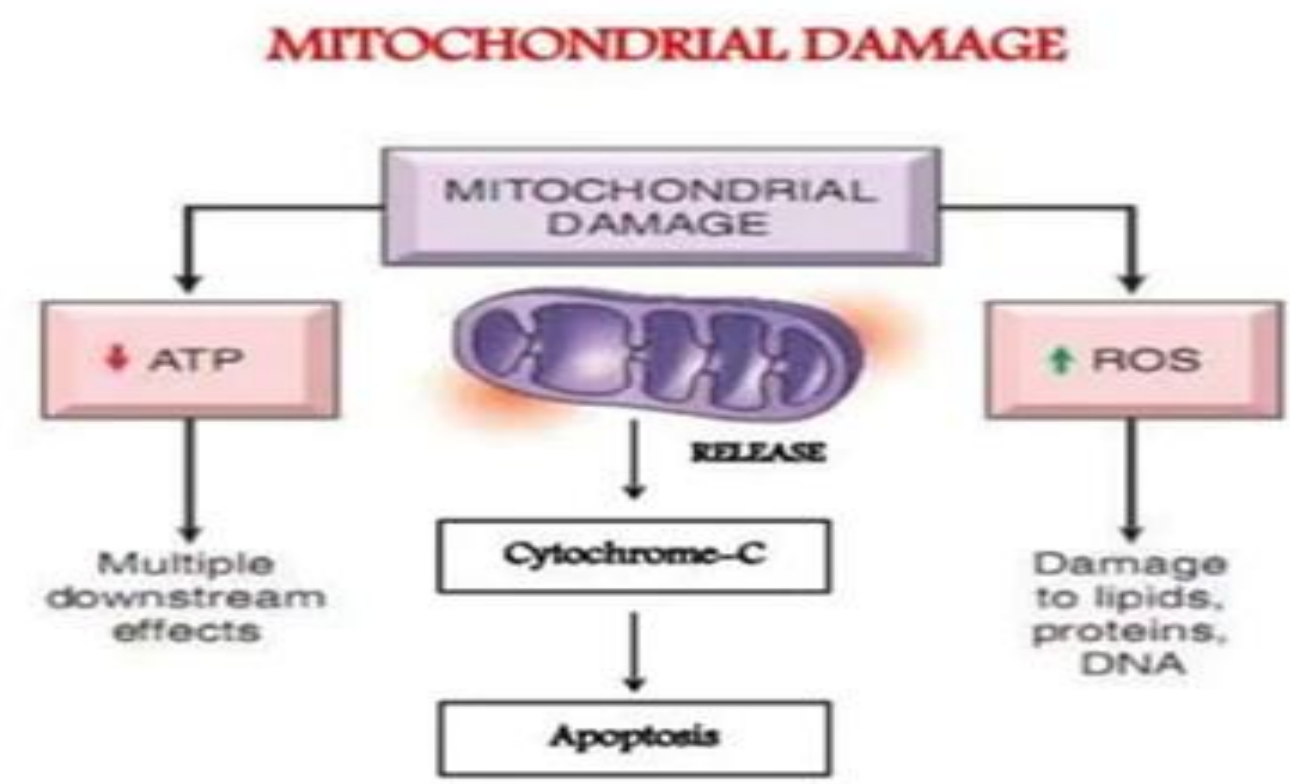
Healthy



Cystic Fibrosis

Mitochondrial damage

Mitochondrial damage can lead to diseases which are together termed as mitochondrial diseases.



Following are the examples of mitochondrial diseases:

a. Diabetes mellitus and deafness (DAD):

It is subtype of diabetes which is caused from a point mutation at position 3 to 2, 4 to 3 in human mitochondrial DNA and it is characterized by diabetes and sensorineural hearing loss.

b. Leber's hereditary optic neuropathy (LHON):

It is a mitochondrially inherited (transmitted from mother to child) dengeration of retinal ganglion cells (RGCs) and their axons that leads to an acute or sub acute loss of central vision; this affects predominantly young adult males.

c) Leigh syndrome: sub-acute sclerosing encephalopathy.

d) Neuropathy, ataxia, retinitis pigmentosa and ptosis (NARP): a type of dementia (can not control their emotion)

e) Myoneurogenic gastrointestinal encephalopathy (MNGIE): a type of neuropathy (damage to the nerves outside of the brain and spinal cord)

f) Mitochondrial myopathy encephalomyopathy

g) Mitochondiral neurogastrointestinal encephalomyopathy (MNE).

RIBOSOMAL DAMAGE

- Damage to ribosomes can lead to diseases which termed as Ribosomopathy.
- Ribosomopathies are caused by alterations in the structure or function of ribosomal.
- Name of some these disease are listed below.

a) Diamond - blackfan anemia:

- It is characterized normocytic or macrocytic anemia (low RBC counts) with decreased erythroid cells in the bone marrow.
- Affected individuals may also have an opening in the roof of the mouth (cleft palate) with or without a split in the upper lip (cleft lip).
- They may have a short webbed neck, shoulder blades that are smaller and higher than usual, and abnormalities of their hands, most commonly malformed or absent thumbs.

b) Dyskeratosis congenital (DKC): The entity was classically defined by the triad abnormal skin pigmentation, nail dystrophy and leukoplakia of the oral mucosa.

c) Shwachman-Diamond syndrome: It is characterized by bone marrow dysfunction, skeletal abnormalities and short height.

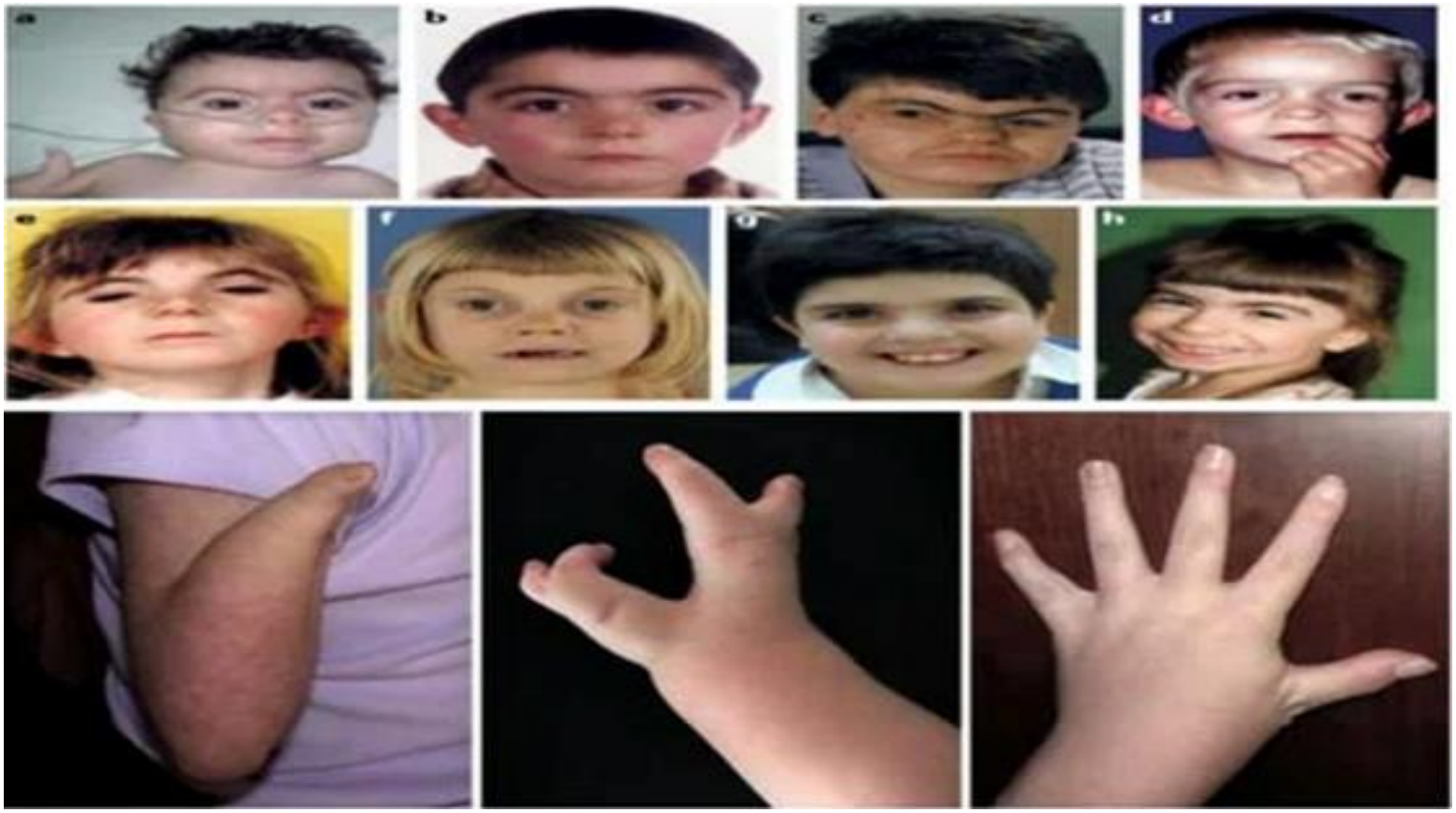
d) Myelodysplastic syndrome: It is type of bone marrow disorder.

e) Treacher Collins syndrome: A inherited condition in which bones and tissues in face aren’t developed.

Nuclear damage

Following diseases are caused by damage to the cell nucleus:

a) Cornella de lange syndrome



It is a rare genetic disorder present from birth.

Some of the important symptoms of the disease are as follows:

- Low birth weight
- Delayed growth and small height
- Development delay
- Missing limbs or portions of limbs
- Microcephaly: small head size
- Excessive body hair
- Hearing impairment and vision abnormalities
- Partial joining of second and third toes

b) Revesz syndrome:

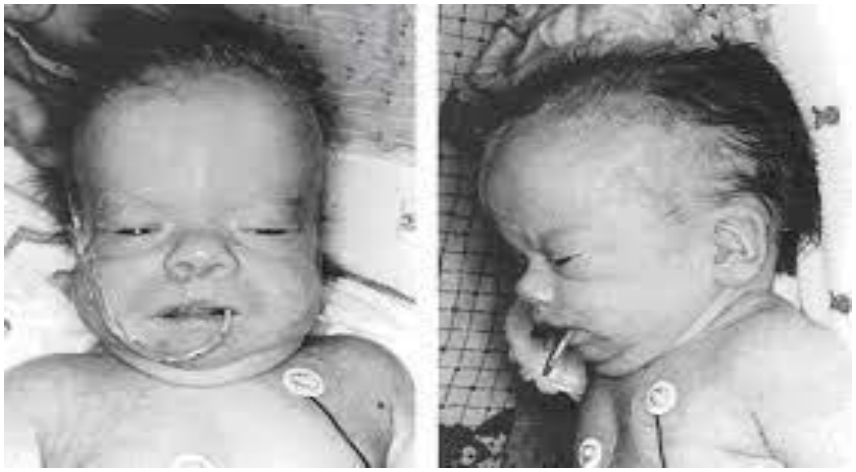
It is a dengerous disease which causes exudative retinopathy and bone marrow failure.

Other symptoms include:

- severe aplastic anemia
- intrauterine growth retardation
- fine sparse hair
- fine reticulate skin pigmentation
- It is genetic disease thought to be caused by short telomeres

c) Schinzel giedon

- It is congenital, neurogenerative terminal syndrome.
- It exhibits severe midface retraction, skull abnormalities.
- Babies with the syndrome have severe mental retardation, growth retardation and global development delay.



d) Spinal muscular atrophy

- It is characterized by loss of motor neurons and progressively muscle wasting, often leading to early death.
- It is caused by a genetic defect in the SMN1 gene, which encodes SMN, a protein which is needed for survival of motor neurons.
- It causes loss of function of neuronal cells in the anterior horn of spinal cord leading to atrophy of skeletal muscles. Muscular atrophy first affects proximal muscles and lung muscles.

MORPHOLOGY OF CELL INJURY

1. Morphology of reversible cell injury
- Cellular swelling
- fatty changes

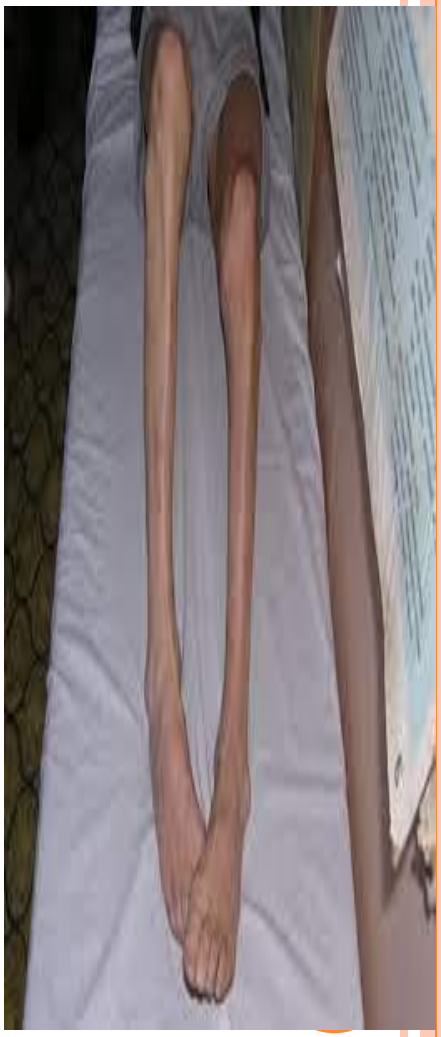
2. Morphology of irreversible cell injury
- Necrosis
- Apoptosis

3. Intracellular accumulations
- Accumulations of lipids, proteins, carbohydrates.
- Abnormal substances e.g: as in storage disease
- Accumulations of pigments e.g: endogenous pigment, exogenous pigment.

4. Subcellular alterations in cell injury

ATROPHY

- Definition: It is the complete or partial wasting of any part of cell.
- It includes mutations, which can destroy the gene to build up the organ, poor nourishment, poor circulation, loss of hormonal support and loss of nerve supply to the target organ.
- e.g. Atrophy as a part of normal development include shrinkage and involution of the thymus in early childhood and the tonsils in adolescence.
- In old age it may include loss teeth and hair, weakening of muscles or loss of weight in organ.

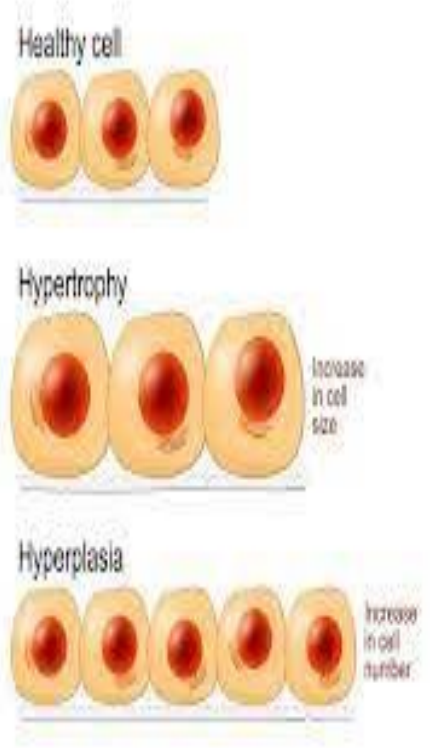


Pathologic atrophy

- Muscle atrophies:
  - Disuse atrophy of muscle and bones, with loss of mass and strength, can occur after prolonged immobility, such as extended bed rest.
- Ischemic atrophy
- Neuropathic atrophy

HYPERTROPHY

- Definition: It is the increase in the size of cell.
- Physiologic hypertrophy:
- e.g: enlarged size of the uterus in pregnancy.
- Pathologic hypertrophy:
- e.g i) hypertrophy of cardiac muscles in systemic hypertension
- ii) hypertrophy of smooth muscle e.g: pyloric stenosis (in stomach)
- iii) hypertrophy of skeletal muscles e.g. hypertrophied muscles in athletes



HYPERPLASIA

- Definition: It is an increase in number of cell.

- Physiologic hyperplasia:
- e.g: 1) hormonal hyperplasia i.e hyperplasia due to hormonal stimulation. during pregnancy.
- 2) compensatory hyperplasia i.e. hyperplasia occurs due to removal of organ.

- Pathologic hyperplasia:
- e.g: 1) Endometrial hyperplasia following oestrogen excess.
- 2) In wound healing there is formation of granulation tissue due to proliferation of fibroblast and endothelial cells.

METAPLASIA

- Definition: It is defined as reversible change in type of cell.
- Metaplasia is broadly divided into two types:

1. Epithelial Metaplasia:

a) Squamous metaplasia

e.g: In bronchous of chronic smokers

b) Columnar metaplasia

e.g. In vitamin A deficiency

2. Mesenchymal metaplasia:

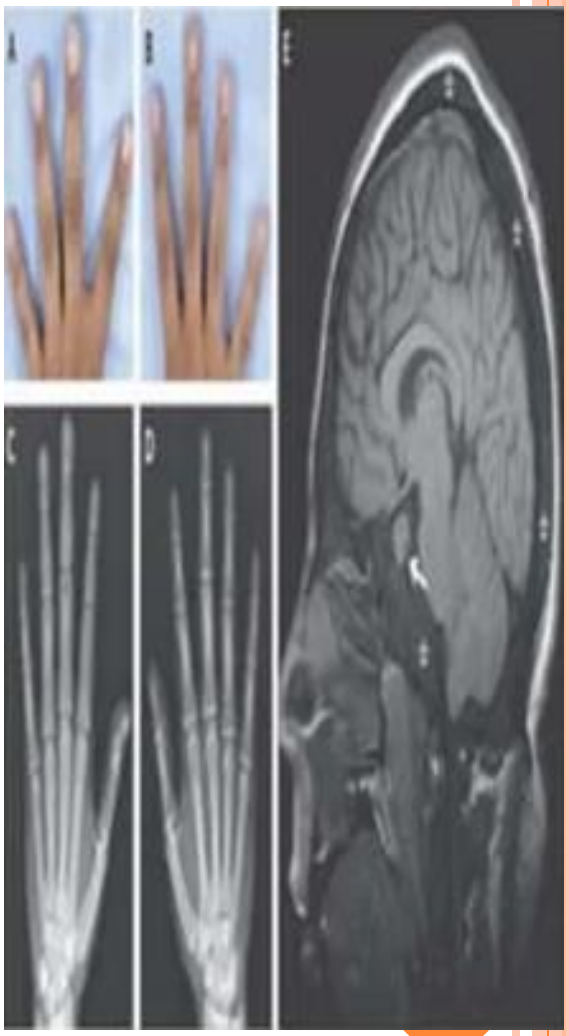
In this case transformation of mesenchymal tissue to another.

DYSPLASIA

- Definition: It is a abnormality of cell development, growth and differentiation.

- Dysplasia is characterized by 4 major pathological microscopical changes:

1. Anisocytosis: cells of unequal size.
2. Poikilocytosis: abnormally shaped cells.
3. Hyperchromatism: excessive pigmentation.
4. Presence of mitotic figures: An unusual number of cells which are currently dividing.



Intracellular Accumulation

- Intracellular accumulation is the metabolic dearrangements in cells is the intracellular accumulations of abnormal amounts of various substances.

- It falls into two main categories:
- A Normal cellular constituent like water, lipids, proteins and carbohydrates, which accumulate in excess (accumulate in maximum amount)

- An abnormal substance, either exogenous like products of infectious agents of endogenous such as product of abnormal synthesis or metabolism.

LIPIDS

All major classes of lipids can accumulate in cells: triglycerides, cholesterol and phospholipids.

Some of the diseases related to lipids are mentioned below:

a) Steatosis (fatty changes): It is an abnormal accumulation of triglycerides within parenchymal cells.

b) Atherosclerosis: In atherosclerotic plaques, smooth muscle cells and macrophages within the intimal layer of the aorta and large arteries are filled with lipid vacuoles, most of which are made up of cholesterol and cholesterol esters.

c) Xanthomas: Intracellular accumulation of cholesterol within macrophages is a characteristic of hereditary hyperlipidemic states.

d) Cholesterolosis: it refers to the focal accumulation of cholesterol-laden macrophages in the lamina propria of the gall bladder.

Proteins

Intracellular accumulation of proteins appears as rounded, eosinophilic droplets, vacuoles or aggregates in the cytoplasm. Excess of proteins within the cells sufficient to cause morphologically visible accumulation have different causes as follows:

a) proteinuria : Droplets in proximal renal tubules are seen in renal diseases.

b) Accumulation of cytoskeletal proteins: There are several types of cytoskeletal proteins. e.g: Microtubules (20-25 nm in diameter)

c) Aggregation of abnormal proteins: Abnormal or misfolded proteins may deposit in tissues and can interfere with normal functions.

Glycogen: Glycogen accumulates within cells which are collectively referred to as the glycogen storage disease or glycogenesis.

Calcification

- It is accumulation of calcium salts in a body tissue. It normally occurs in formation of bone, but calcium can be deposited abnormally in soft tissue, causing it to harden.
- e.g: Calcification of soft tissues like arteries, cartilage and heart valves can be caused by vitamin K deficiency. Some of them may be caused by poor calcium absorption.
- The symptoms are as follows:
- Kidney stones
- Gall stones
- Tartar on teeth

Enzyme leakage and death

- The major cellular organelle containing digestive enzymes are lysosomes.
- Following enzymes are present in lysosomes:
- ✓ Acid phosphatases for phosphate esters.
- ✓ Nucleases: DNAase, RNAase for breakdown of nucleic acids.
- ✓ Protein digesting enzymes: collagenase, cathepsins etc.
- ✓ Carbohydrate digesting enzymes: beta - glycosidases, hexosaminidase A etc.
- ✓ Lipid digesting enzymes: sphignomyelinase, esterases.
- ○ Silicosis: It may lead to tuberculosis.
- Pompe disease (alpha-glucosidase).
- Gaucher disease.
- Sandhoff disease.

Acidosis and alkalosis

- Acidosis:

It is an increased acidity in the blood and other body tissue. Usually it refers to acidity of blood plasma. Acidosis is said to occur when arterial pH below 7.35, except in the foetus. There is another term called acidemia, which describes the state of low blood pH.

Acidosis is used to describe the processes leading to these states.

- ✓ Metabolic acidosis: It may results from either increased production of metabolic acids, like lactic acid.
- Severe hypoxemia
- Hypoperfusion

- Respiratory acidosis: in respiratory acidosis, carbon dioxide is increased while the bicarbonate is normal or increased. It results from a build up of carbon dioxide in blood, termed as hypercapnia.

- Sign and symptoms of acidosis:
  - Headaches
  - confusion
  - feeling tired
  - sleepiness

Alkalosis

- Alkalosis is a process by which the pH is increased. Alkalemia refers to pH which is higher than normal in the blood. (normal range of 7.35 to 7.55)
- It is a result of decreased hydrogen ion concentration, increased bicarbonate concentration.
- The causes of metabolic alkalosis can divided into 2 categories, depending on urine chloride levels.

Causes of alkalosis

a) Chloride responsive alkalosis: It caused by following reasons:

- Loss of hydrogens ions: caused by vomiting or kidney failure.
- Congenital chloride diarrhoea-a rare condition
- Contraction alkalosis: caused by dehydration/use of diuretics.

b) Chloride resistant alkalosis: It caused by following reasons:

- Retention(existence) of bicarbonate
- Shift of hydrogen ions into intracellular space: seen in hypokalemia.

Electrolyte Imbalance

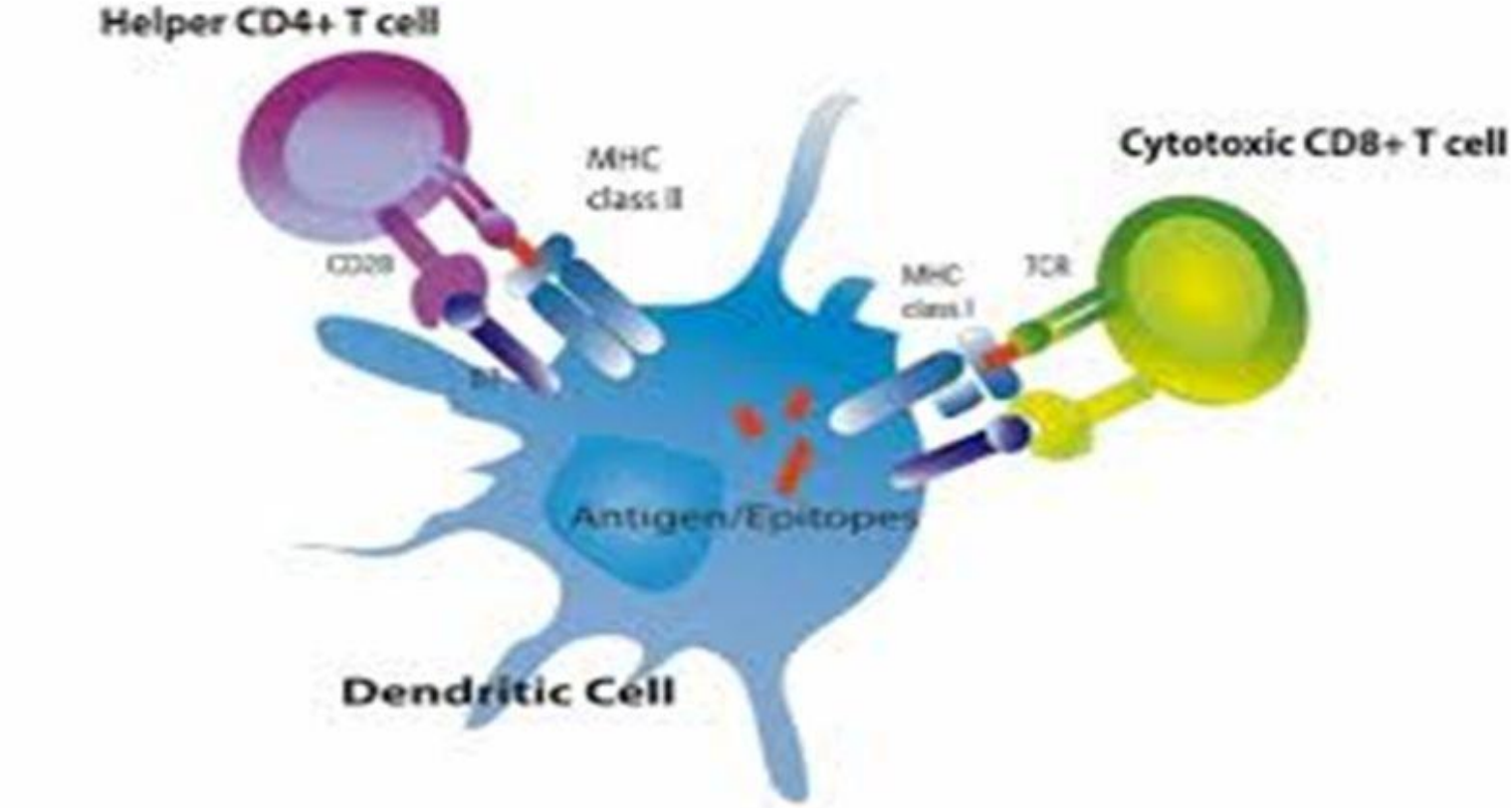
- Electrolytes play a vital role in maintain homeostasis within the body.
- They help to regulate heart and neurological function, fluid balance, oxygen delivery, acid-base balance etc.
- Electrolyte imbalances can develop by one the following mechanisms:
- Excessive ingestion
- Diminished elimination
- Diminished ingestion
- Excessive elimination
- The most serious electrolyte disturbances involve abnormalities in the level of sodium, potassium, or calcium.

- Severe diarrhea or vomiting can cause electrolyte disturbances along with dehydration.

- Electrolytes are important because cells like nerve, heart and muscle use them to maintain voltages across their cell membranes.

- Electrolytes are loss through sweat particulary in the form of sodium and potassium. Excessive sweating in summer causes weakness due to loss of electroytes. Electrolytes must be replaces to keep their concentration in body fluids constant.

Thank you


Helper CD4+ T cell
MHC
class II
CD28
Cytotoxic CD8+ T cell
MHC
class I
TCR
Antigen/Epitopes
Dendritic Cell

UNIT – I
BASIC MECHANISM INVOLVED IN THE PROCESS OF INFLAMMATION AND REPAIR

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INFLAMMATION

- Inflammation is derived from latin word Inflammare (to set on fire)
- Inflammation is defined as the local response of living mammalian tissues to injury due to any agent.

CAUSES OF INFLAMMATION

- Infective agents like bacteria, viruses and their toxins.
- Physical agents like heat, cold, radiation(x-ray).
- Chemical agents like organic and inorganic poisons.

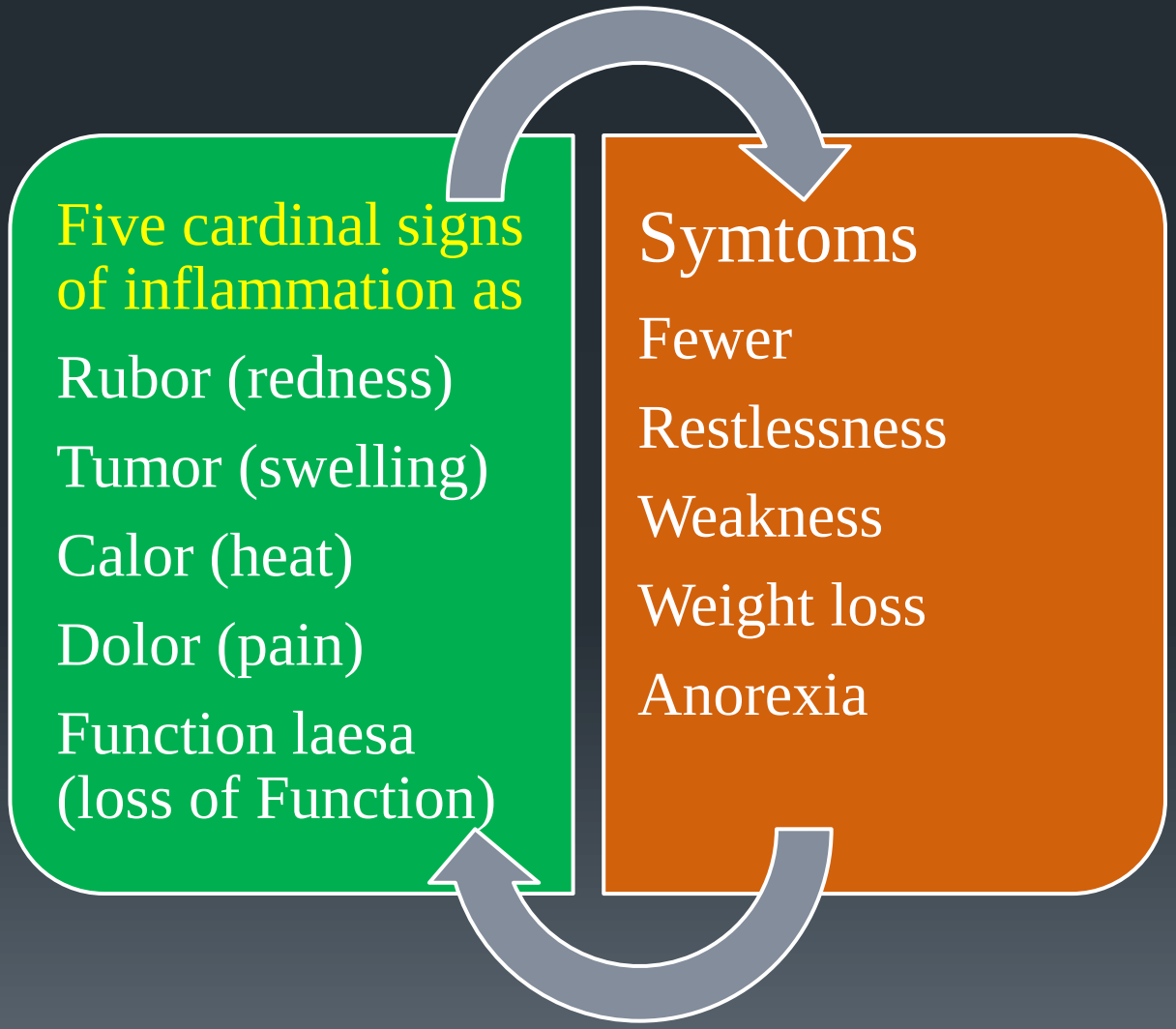
CLINICAL SIGN OF INFLAMMATION

- It is a damage locally lead to release of inflammatory mediators into blood called systemic inflammatory. Acute phase response sometime called systemic inflammatory response syndrome.

- Inflammation is a body defense reaction in order to eliminate or limit the spread of injurious agent as well as to remove the necrosed tissue or cell.

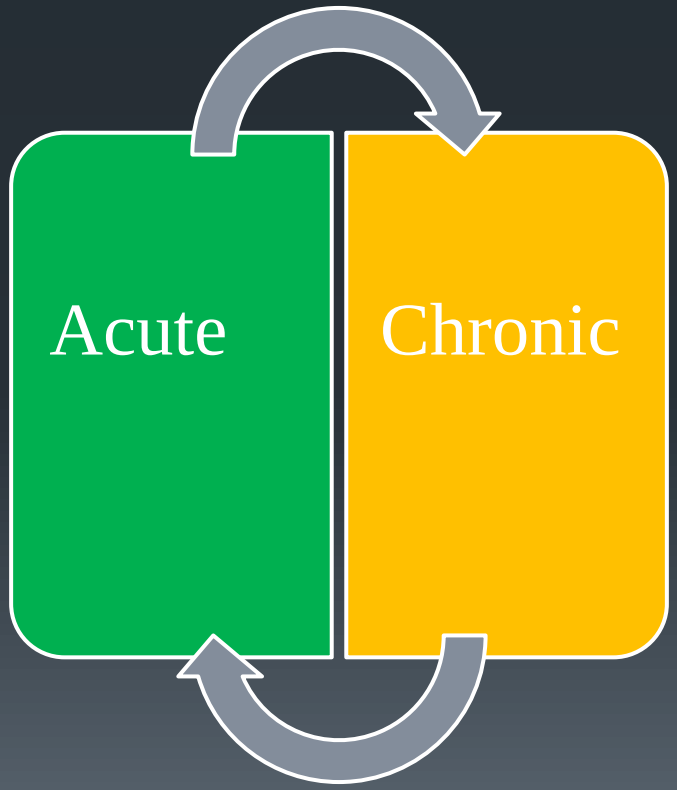
- It involve host cell blood vessel and protein of our own body in order to eliminate the initial case of cell injury.

Signs and symtoms



TYPES OF INFLAMMATION

- Depending upon the defense capacity of the host and duration of response, inflammation can be classified as



ACUTE INFLAMMATION

- ✓Acute inflammation – Of short duration (lasting less than 2 weeks) and
- Represents the early body reaction,
- Resolves quickly and is usually followed by healing.

- ✓The main features of acute inflammation are:
- 1. Accumulation of fluid and plasma at the affected site
- 2. Intravascular activation of platelets and
- 3. Neutrophils as inflammatory cells.

CHRONIC INFLAMMATION

- ✓ Chronic Inflammation • Of longer duration
- The characteristic feature of chronic inflammation is – Presence of chronic inflammatory cells such as Lymphocytes, plasma cells and macrophages, granulation tissue formation, and in specific situations as granulomatous inflammation.

CAUSES CHRONIC INFLAMMATION

- Chronic inflammation following acute inflammation
- Recurrent attacks of acute inflammation

TYPES OF CHRONIC INFLAMMATION

1) Chronic non-specific inflammation:

- It is characterised by non-specific inflammatory cell infiltration e.g. chronic osteomyelitis, lung abscess.

2) Chronic granulomatous inflammation:

- It is characterised by formation of granulomas e.g. tuberculosis, leprosy, syphilis, actinomycosis etc.

ACUTE (LEAD TO FEVER)	CHROMIC (LEAD TO WEIGHT LOSS)
✓ Onset action (Rapid, In min/hrs)	✓ Onset action Slow (Days)
✓ Cell involved are Neutrophils and Mast cells.	✓ Cell involved are Lymphocyte, Monocyte, and Macrophages
✓ Here tissue injury is mild	✓ Severe and Progressive
✓ Local and systemic sign in case of acute inflammation is very prominent.	✓ Local and systemic sign in case of acute inflammation is less prominent.
✓ Most time is beneficial (increase body temperature) Ex. Common cold, headache.	✓ Can develop several ways – auto immune disorder.

Inflammatory (Due to any cause)

↓

Mast cell activated

↓

Release neurotransmitter

(Histamine, Serotonin, Leukotriene, Prostaglandin)

↓

Lead to increase capillary permeability

↓

Oedema

MEDIATORS OF INFLAMMATION

- Mediators may be produce locally by cells at the site of inflammation or that are activated at the site of inflammation.

- Chemical mediator of inflammation is defined as a substance which may be release from the cells, plasma or damage tissue itself.

- The chemical mediator are broadly classified into following types :-

CELL DERIVED MEDIATORS	PLASMA DERIVED MEDIATORS
a) Vasoactive amine (Histamine and Serotonin)	Complement activation
b) Lysosomal Components	Kinin system
c) Platelet activating factor	Fibrinolytic system
d) Cytokines	Clotting system
e) Free radicals: Nitric oxide and oxygen metabolites	
f) Arachidonic acid metabolites Prostacyclin, Prostaglandins, Thromboxane, Leukotriene.	

Vasoactive amine

Histamine

- G-protein couple receptor(GPCR) (H1R,H2R,H3R,H4R and H1 receptor)
- Store in the form of granule in mast cell, basophils and platelets
- Function – Vasodilation. Increase vascular permeability.

Serotonin

- It is Present in tissue like chromaffin cell of Gastrointestinal tract (GIT), Spleen, Nervous tissue, Mast cell and Platelets.
- It is less potent mediator of inflammation as compared to histamine.

LYSOSOMAL COMPONENT

- The inflammatory cell neutrophil and monocyte contain lysosomal granule.
- When the lysosomal granule are released then it elaborate a variety of mediator of inflammation.

✓Granule of Neutrophil –

- Primary – lactoferrin, lysozyme, alkaline phosphate
- Secondary – Acid hydrolase, Neutral protease.

✓Granule of Monocytes –

- Acid proteases, Collagenases, elastases, Plasminogen activator.

PLATELET ACTIVATING FACTOR

- It is released from antibody – senitised basophils, mast cell, endothelium and platelets.
- Function – increased vascular permeability, Bronchoconstriction vasodilation (in low concentration)

CYTOKINES

- They are polypeptide substance that is produced by activated lymphocytes and activated monocytes.

✓Types of cytokines

- gamma-interferon
- Interleukin-1
- Alpha and beta tumour recrosis factor(TNF)

FREE RADICALS
NITRIC OXIDE AND OXYGEN METABOLITES

- Free radicals act as potent mediator of inflammation:
- Oxygen-derived metabolites are released from activated neutrophils and macrophages and include superoxide oxygen(O2).

- Endothelial cell damage

- Activation of protease and inactivation of anti protease causing tissue matrix damage.
- Function - Increased vascular permeability.

Arachidonic acid metabolites

Activated arachidonic acid

↓

PGG2

↓

PGH2 + free oxygen radical

↓

PGD2 Vasodilator Bronchodilator Increase permeability	TXA2 Vasoconstrictor Bronchoconstrictor

PLASMA-DERIVED MEDIATORS

THE KININ SYSTEM

- This system on activation by factor XIIa generates bradykinin,
- Smooth muscle contraction
- Vasodilation
- Increased vascular permeability

THE CLOTTING SYSTEM

- Increased vascular permeability
- Anticoagulant activity

Alteration in Vascular Permeability & Blood Flow

- When inflammation occur
- In this case (increased blood flow, increased permeability)
- Pore size increased - increased permeability
- Pore size decreased - decreased permeability

Types

- Retraction of endothelial cell and leakage
- Direct endothelial injury
- Leukocyte dependent cell injury
- Increased transcytosis
- Leakage from new capillary

Retraction of Endothelial Cell and Leakage

Inflammatory mediators
Histamine, Prostaglandin

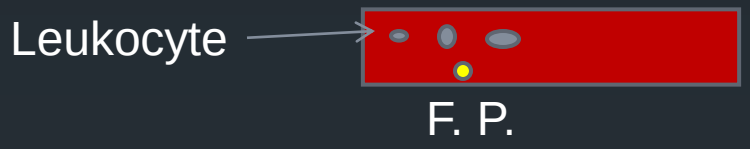
Pore extend here

- When inflammation occur, this mediator are come in contact and stick with endothelial cells
- And this inflammation mediator cause constriction in endothelial wall
- And stretch in endothelial wall due to this stretch the size of pore become extend
- Now transfusion, permeability and blood flow, all are increase

DIRECT ENDOTHELIAL INJURY

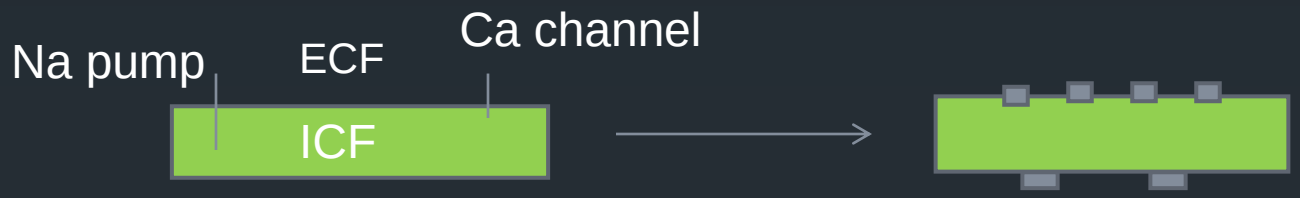
- Here endothelial damage
- Due to this size of pore (increase)
- And vascular permeability and transfusion increase.

LEUKOCYTE DEPENDENT CELL INJURY



- Here leucocytes surrounded the foreign particle
- This leucocyte release inflammation mediators
- Due to this constriction take place in endothelial wall
- And retraction takes place in endothelial
- Due to retraction, the pore size become extended
- Leads to increase in vascular permeability and transfusion

INCREASED TRANSCYTOSIS

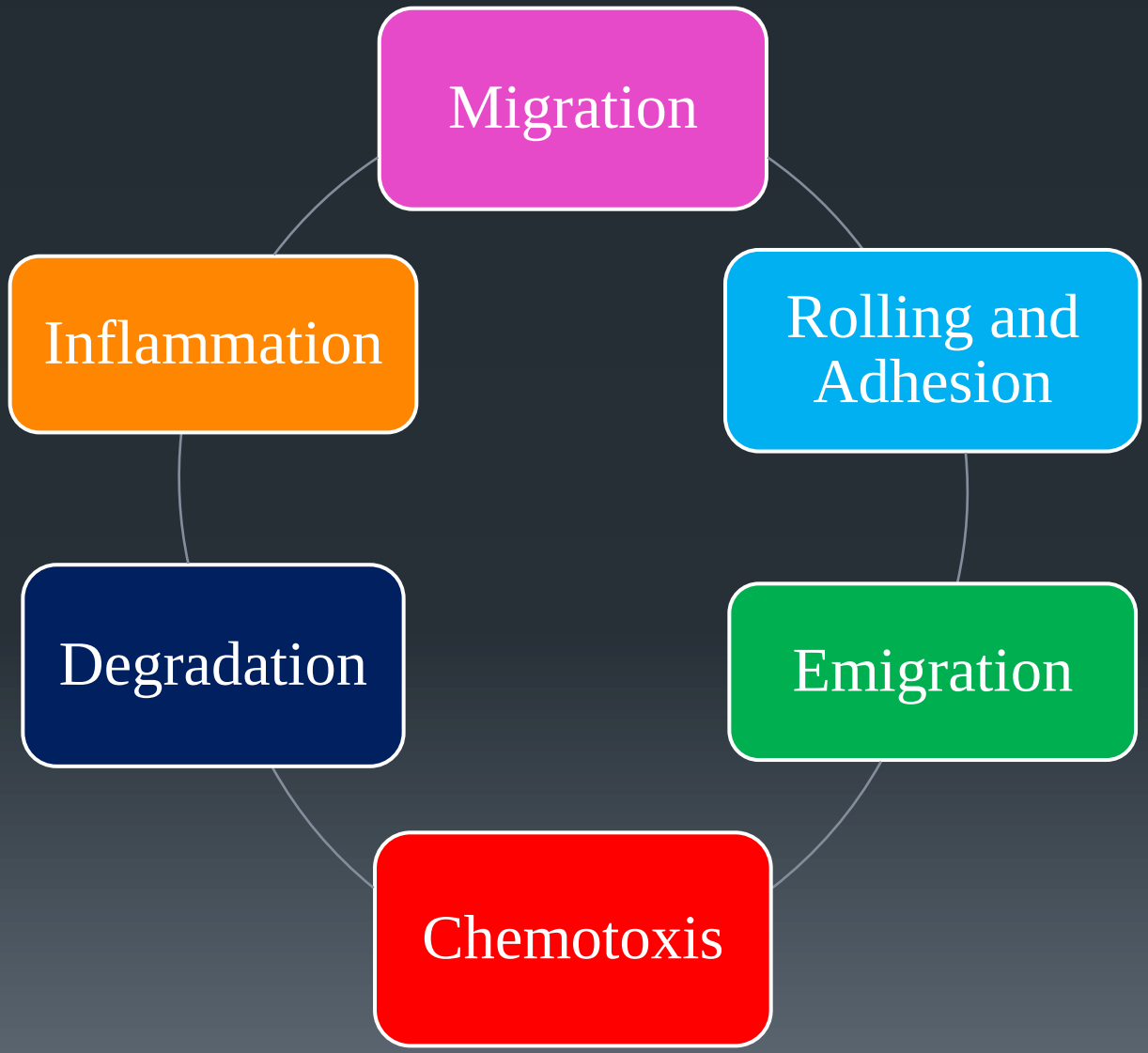


- Pump no. increase or pump size increase
- Movement of ion from ICF to ECF or ECF to ICF
- Called transcytosis
- Due to this, here also transfusion and blood flow(increase)

LEAKAGE FROM NEW CAPILLARY

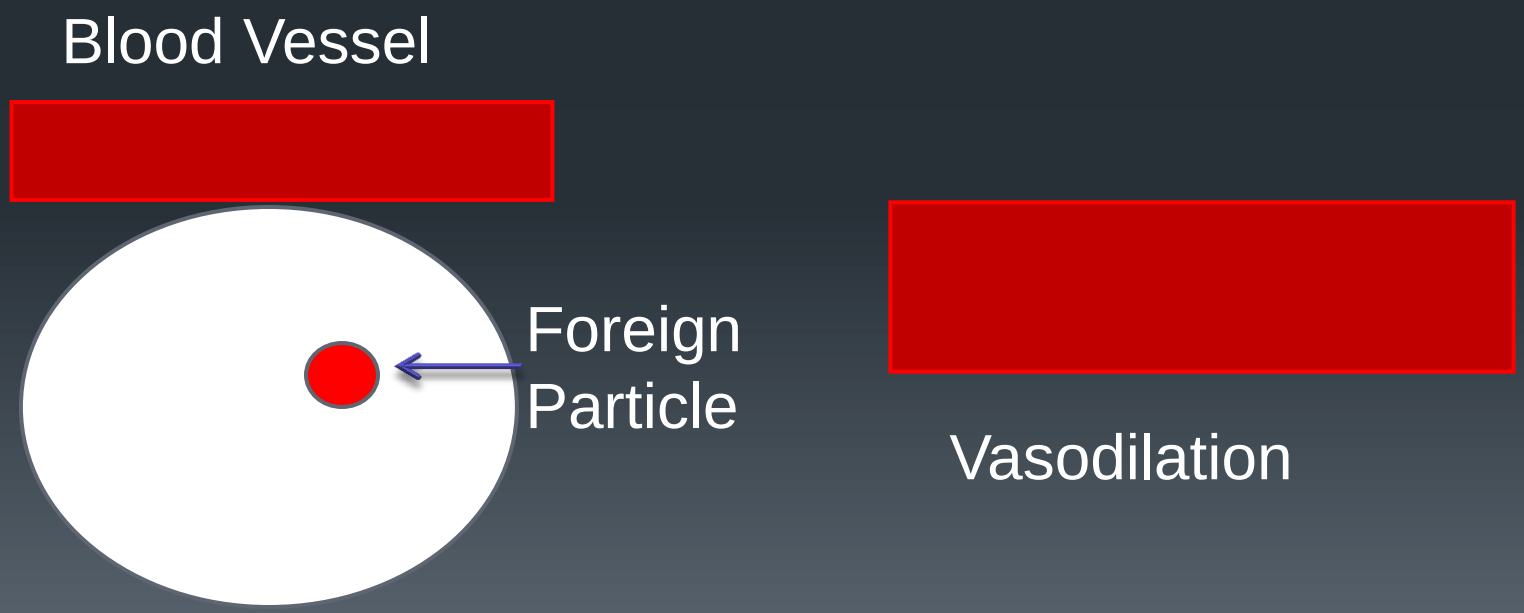
- If blood vessel is damage or rupture
- Our immune system makes
- May small blood or capillaries to fill his gap
- And this newly formed blood vessel secretes a chemical VEGF (vascular endothelial growth factor)
- Due to release of this chemical the newly formed blood vessel lead vascular permeability increase, blood flow also increase.

Migration of WBC's



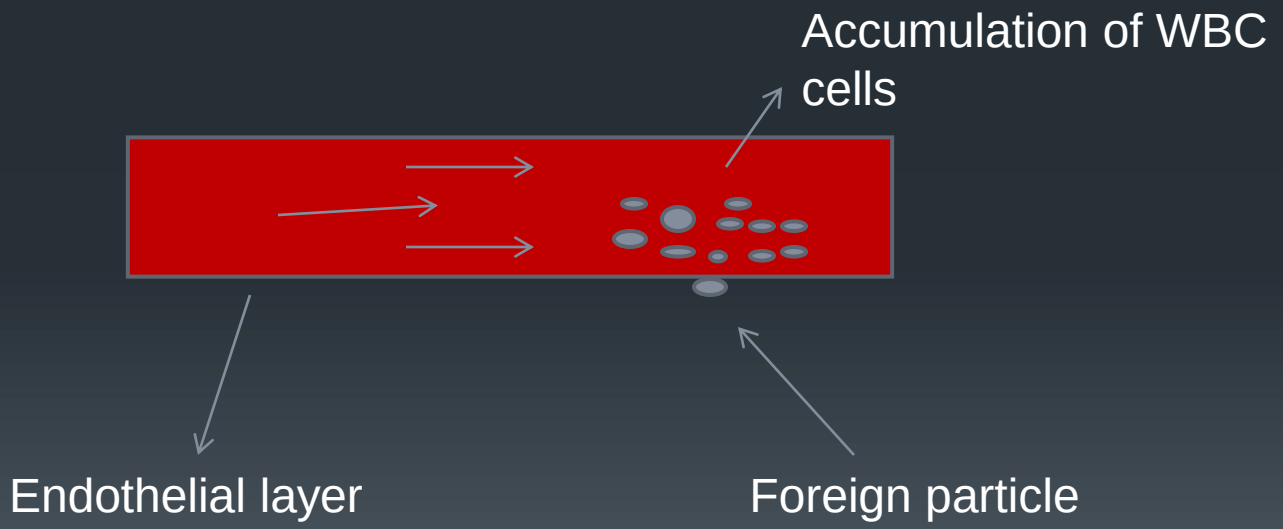
MIGRATION

- In migration step, the side of body where foreign particle attack.
- At this side of infection blood vessel become dilate.
- Now blood flow increase.



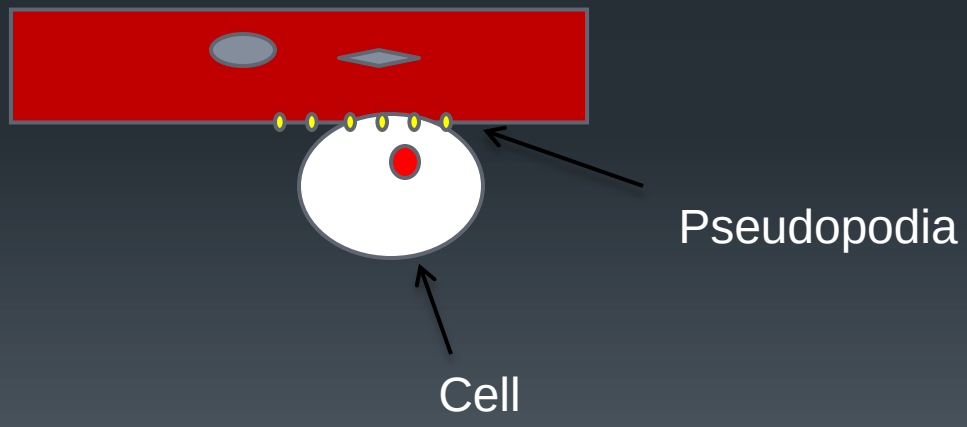
Rolling and Adhesion

- Since in previous step blood flow increase lots of WBC cell become flow by rolled and adhesion of WBC on the upper site of blood where the foreign particle attack.



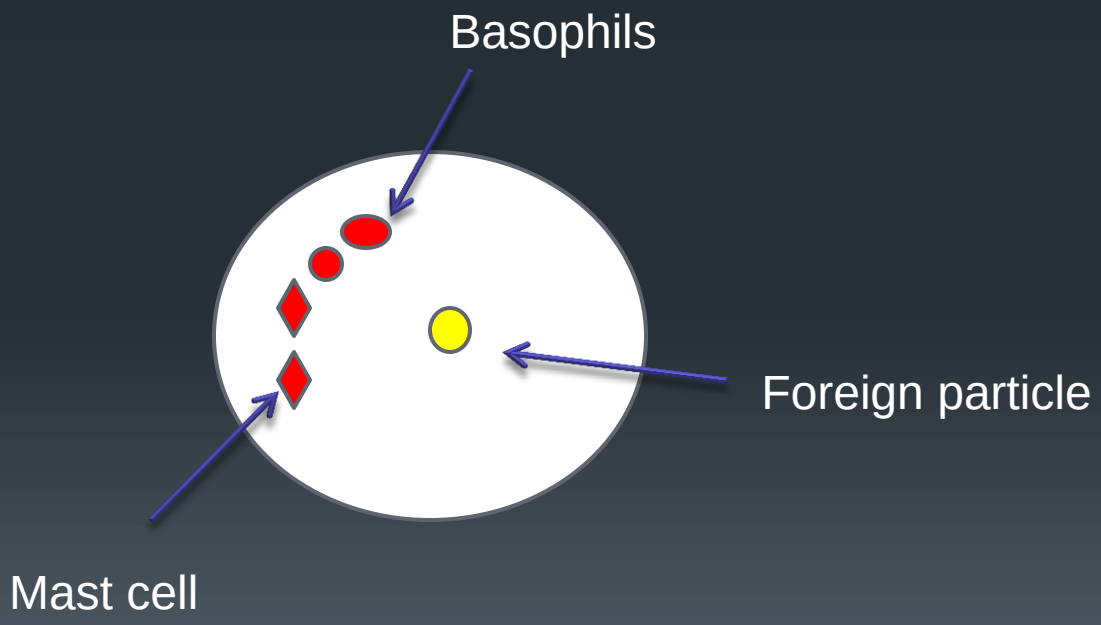
EMIGRATION

- Our mast cell and basophil cell are come and stick on upper side of endothelial. both mast cell and basophil cell are come at a site of infection through pores present in endothelial known as pseudopodia and enter in cell where foreign particle attack



CHEMOTOXIS

- Now here mast cell and basophil cell attack on foreign particle by release chemicals – Histamine, leucotrine to kill the foreign particle.



DEGRADATION

- When they release chemical cell degradation take place.

INFLAMMATION

- When our own cell damage then inflammation occur in our body.
- (Swelling, Heat, Pain, Redness, loss of function)

HEALING OF TISSUES

- Healing is the body response to injury in an attempt to restore normal structure and function. Healing involves 2 distinct processes:

- Regeneration: healing takes place by proliferation of parenchymal cells and usually results in complete restoration of the original tissues

- Repair: healing takes place by proliferation of connective tissue elements resulting in fibrosis and scarring. Both the processes take place simultaneously

REGENERATION

- Some parenchymal cells are short-lived while others have a longer lifespan.

- In order to maintain proper structure of tissues, these cells are under the constant regulatory control of their cell cycle. These include growth factors such as -
- Epidermal growth factor (EGF),
- Vascular endothelial growth factor (VEGF),
- Platelet-derived growth factor (PDGF),
- Fibroblast growth factor (FGF),
- Transforming growth factor-β (TGF-β).

REPAIR

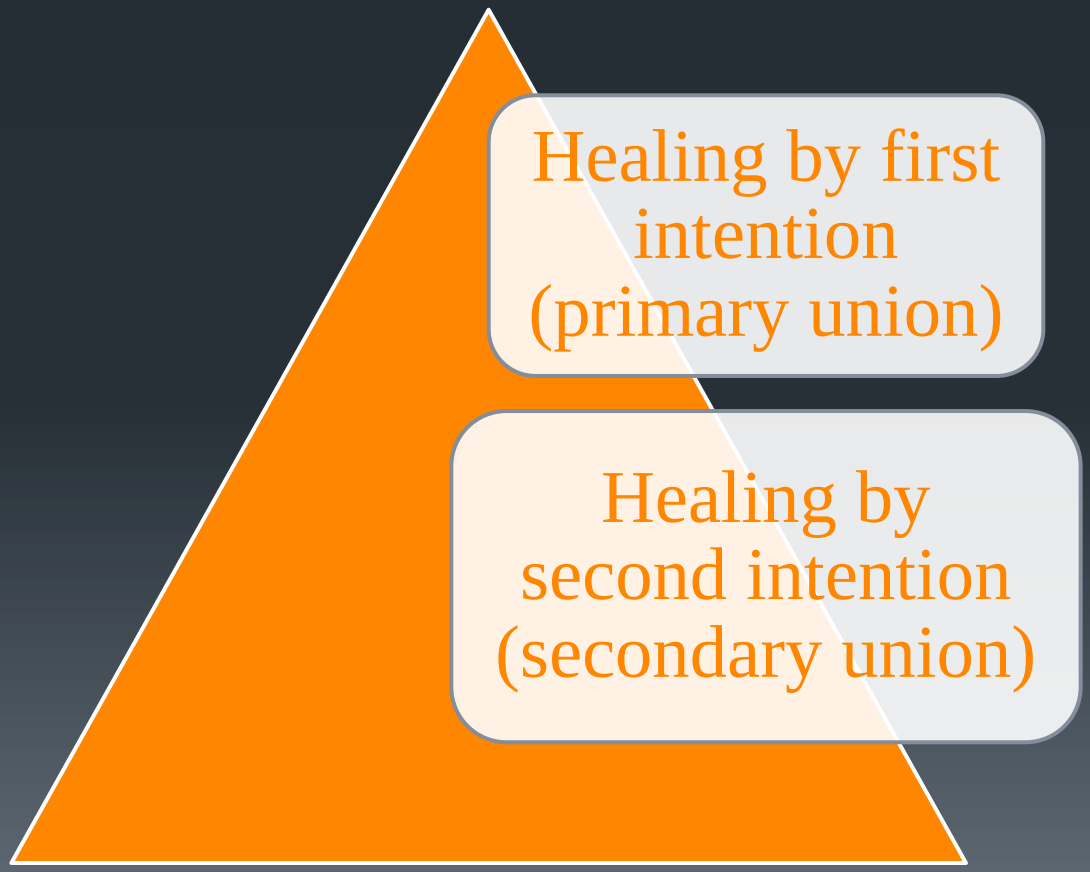
- Repair is the replacement of injured tissue by fibrous tissue.

- Two processes are involved in repair:
- Granulation tissue formation
- Contraction of wounds.

- Repair response takes place by participation of mesenchymal cells, endothelial cells, macrophages, platelets, and the parenchymal cells of the injured organ.

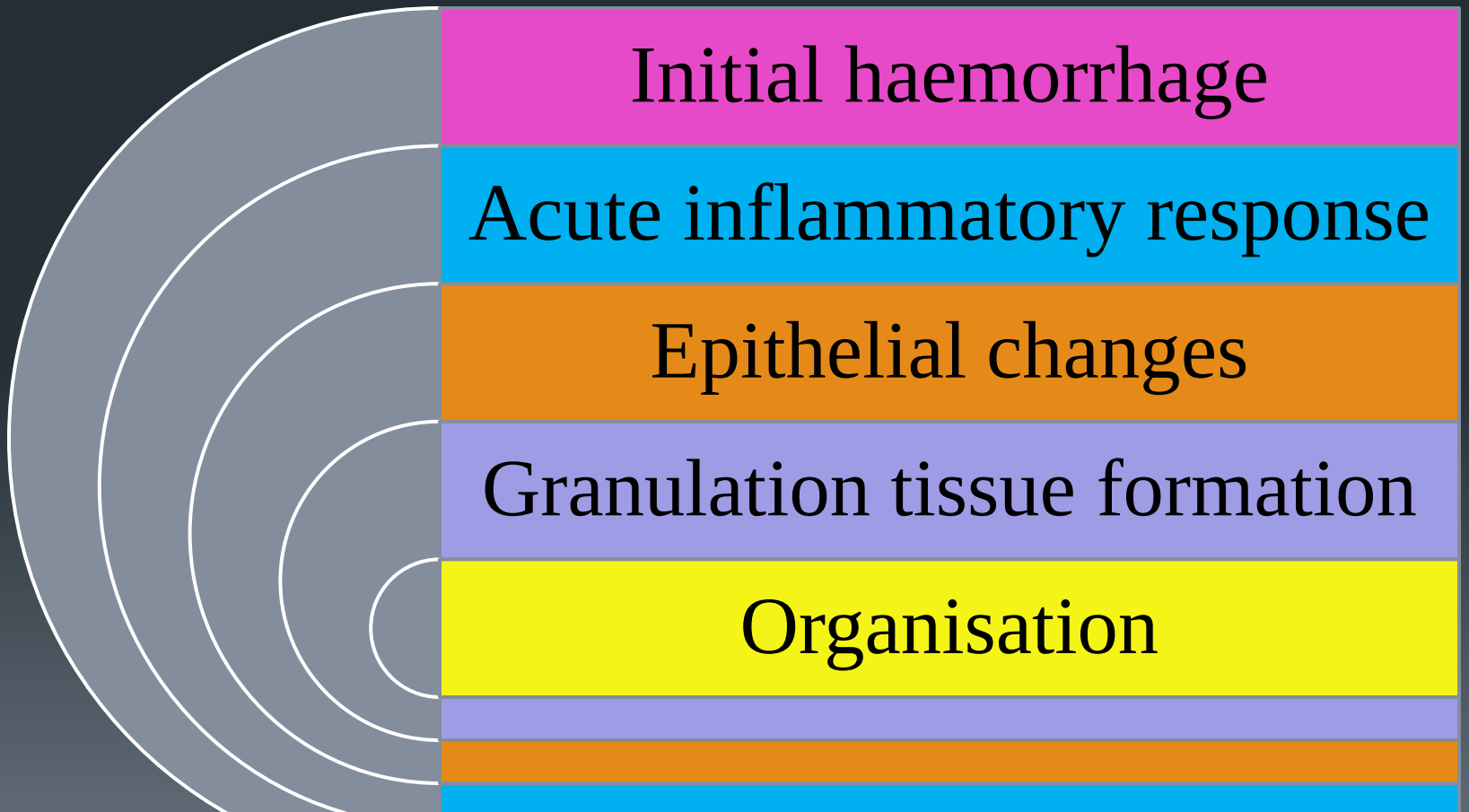
Wound healing

- Healing of skin wounds provides a classical example of combination of regeneration and repair. Wound healing can be accomplished in one of the following two ways:



Wound healing

- Healing by first intention (primary union)
- Sequence of events in primary union:



INITIAL HAEMORRHAGE

The incised wound is filled with blood, which then clots the wound.

ACUTE INFLAMMATORY RESPONSE

Occurs within 24 hours of the injury and is characterized by the appearance of neutrophils at the margins of the clot.

EPITHELIAL CHANGES

Within 24 hours of the injury, mitosis begins to appear in the base of the injured epithelial.

Wound is covered by epithelium within 24-48 hrs.

GRANULATION TISSUE FORMATION

- By the 3rd day, granulation tissue begins to form within wound and fills the entire wound cavity by the 5th day.

ORGANISATION

- There occur marked fibroblastic proliferation by the 2nd week leads to continuous collagen deposition.
- This is followed by a complete resolution of inflammation and the wound is completed covered by intact epithelium by the 8-10 weeks.

WOUND HEALING

- Healing by second intention (secondary union)
- Sequence of events in secondary union:

- Initial haemorrhage
- Inflammatory phase

- Epithelial changes
- Granulation tissue

- Wound contraction and
- Presence of infection

INITIAL HAEMORRHAGE

The incised wound is filled with blood, which then clots the wound.

ACUTE INFLAMMATORY RESPONSE

Occurs within 24 hours of the injury and is characterized by the appearance of neutrophils at the margins of the clot.

EPITHELIAL CHANGES

Within 24 hours of the injury, mitosis begins to appear in the base of the injured epithelial.

Wound is covered by epithelium within 24-48 hrs.

GRANULATION TISSUE FORMATION

- By the 3rd day, granulation tissue begins to form within wound and fills the entire wound cavity by the 5th day.

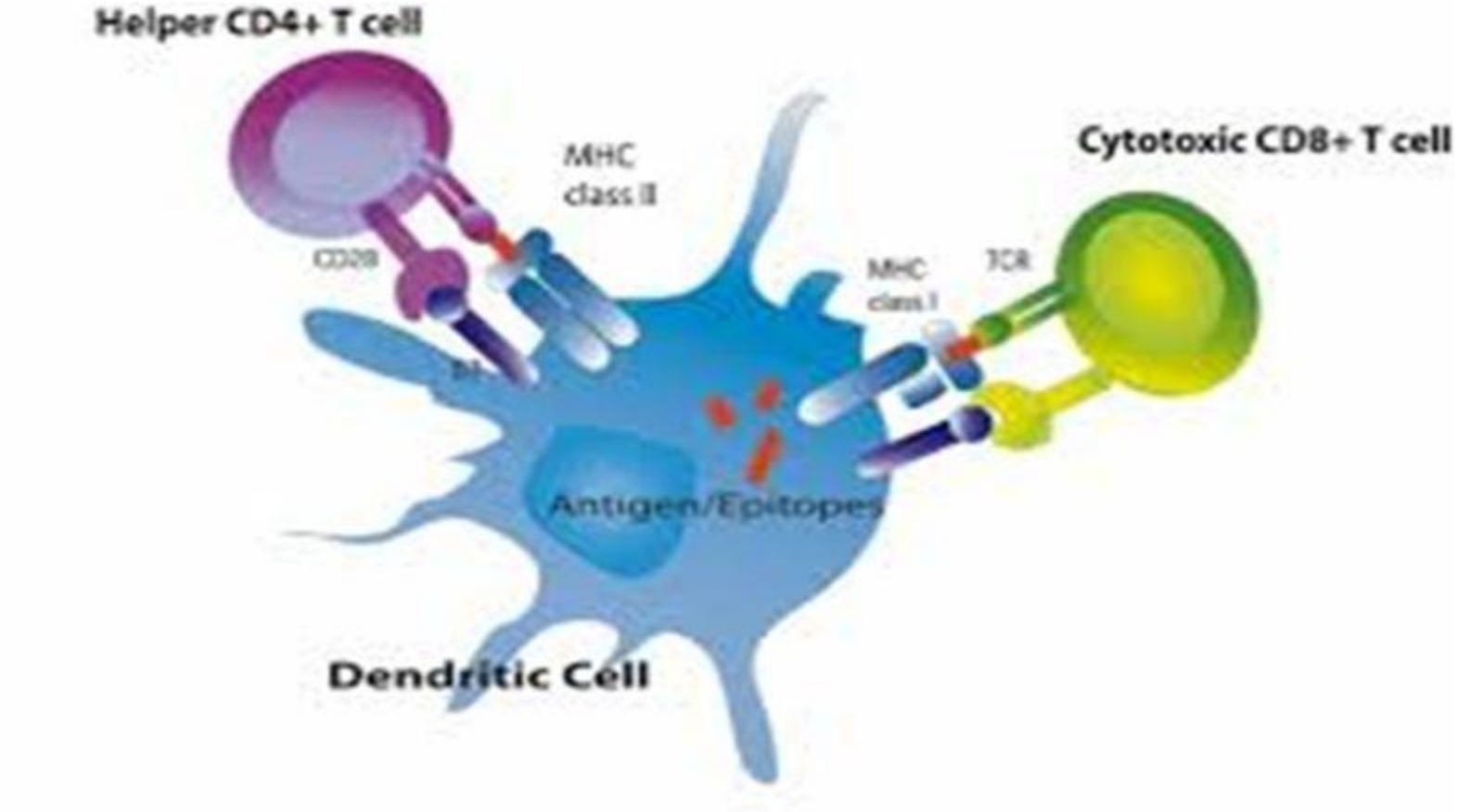
WOUND CONTRACTION

- This is the main differentiating feature between healing by primary intention and secondary intention.
- In large gaping wounds, which heal by secondary intention there is marked wound contraction due to the action of myofibroblasts.

INFECTION

- Open wounds are more chances to get infected
- This delays the process of healing due to
- Release of bacterial toxins that provoke necrosis, and inflammation.

Thank you


Helper CD4+ T cell
MHC
class II
Cytotoxic CD8+ T cell
MHC
class I
TCR
Antigen/Epitopes
Dendritic Cell