

B.PHARMACY2nd SEMESTER

SUBJECT: PATHOPHYSIOLOGY

UNIT-1

.Basic Principles of Cell Injury and Adaptation

Cell Injury: **Introduction**

- *Cell injury is defined as a variety of stresses a cell encounters as a result of changes in its internal and external environment.*
- The cellular response to stress may vary and depends upon the following:
 - The type of cell and tissue involved.
 - Extent and type of cell injury.

ETIOLOGY OF CELL INJURY:

1. Genetic causes

- *Developmental defects:*

Errors in morphogenesis

- *Cytogenetic (Karyotypic) defects:* chromosomal abnormalities
- *Single-gene defects:*

Mendelian disorders

- *Multifactorial inheritance disorders.*

2. Acquired causes

- Hypoxia and ischaemia
- Physical agents
- Chemical agents and drugs
- Microbial agents
- Immunologic agents
- Nutritional derangements
- Aging
- Psychogenic diseases
- Iatrogenic factors
- Idiopathic diseases.

2.1. Oxygen deprivation: HYPOXIA

- Ischemia (loss of blood supply).
- Inadequate oxygenation (cardio respiratory failure).
- Loss of oxygen carrying capacity of the blood (anemia or CO poisoning).

2.2. PHYSICAL AGENTS:

- Trauma
- Heat
- Cold
- Radiation

- Electric shock

2.3. CHEMICAL AGENTS AND DRUGS:

- Endogenous products: urea, glucose
- Exogenous agents
- Therapeutic drugs: hormones
- Nontherapeutic agents: lead or alcohol.

2.4. INFECTIOUS AGENTS:

- Viruses
- Rickettsiae
- Bacteria
- Fungi
- Parasites

2.5. Abnormal immunological reactions:

The immune process is normally protective but in certain circumstances the reaction may become deranged.

- Hypersensitivity to various substances can lead to anaphylaxis or to more localized lesions such as asthma.
- In other circumstances the immune process may act against the body cells – autoimmunity.

2.6. Nutritional imbalances:

- Protein-calorie deficiencies are the most examples of nutrition deficiencies.
- Vitamins deficiency.
- Excess in nutrition are important causes of morbidity and mortality.
- Excess calories and diet rich in animal fat are now strongly implicated in the development of atherosclerosis.
- Obesity alone leads to an increased vulnerability to certain disorders, such as atherosclerosis, coronary heart disease, diabetes mellitus.

2.7. Aging:

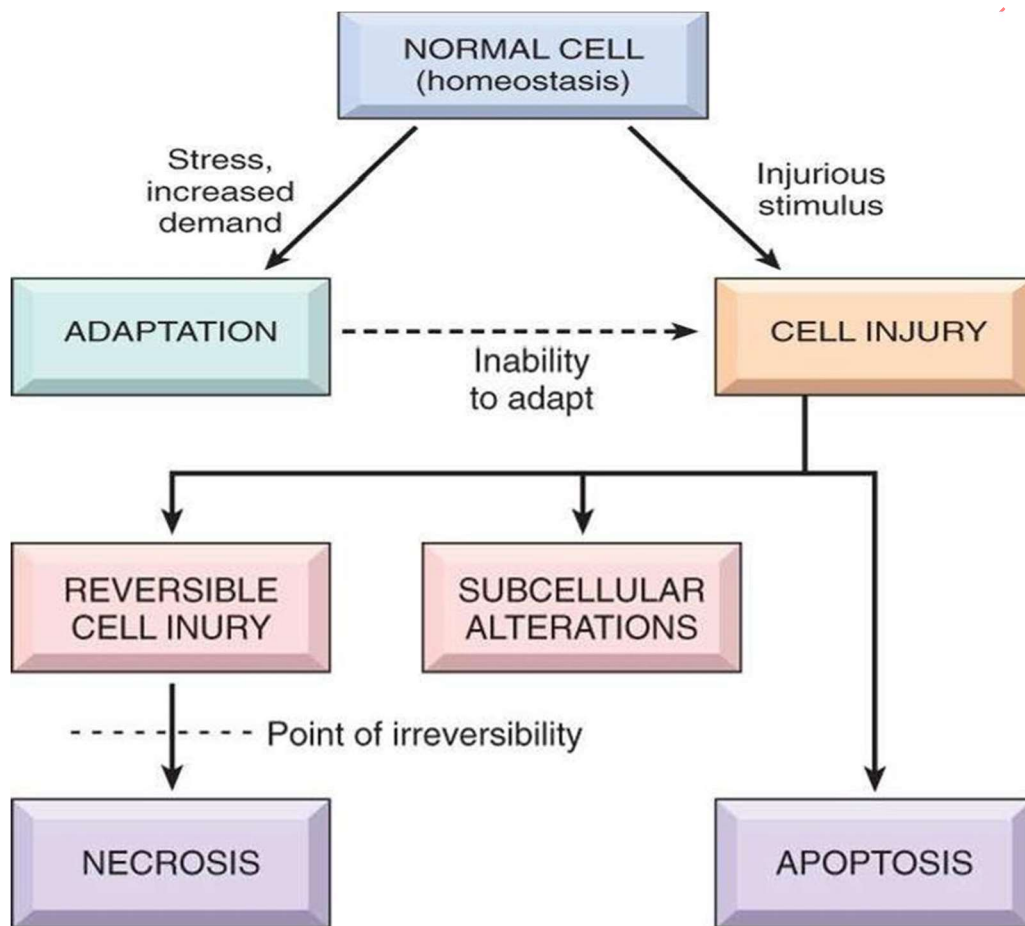
- Programmed aging whereby after a defined number of divisions the cell undergoes terminal differentiation.
- Development of an increasing population of cells irreversibly committed to senescence and death.

MORPHOLOGY OF CELLULAR INJURY:

■ CELLS REACT TO ADVERSE INFLUENCES:

1. Cellular adaptation
 - Hyperplasia
 - Hypertrophy
 - Atrophy
 - Metaplasia

- Dysplasia
- 2. Reversible injury
 - intracellular edema,
 - fatty change,
 - hyaline change,
 - amyloidosis,
 - mucoid degeneration,
 - pathologic pigments
- 3. Irreversible injury and dying: Necrosis, Gangrene followed by pathological calcification.



© Elsevier. Kumar et al: Robbins Basic Pathology 8e - www.studentconsult.com

CELLULAR ADAPTATION:

- Adaptations are reversible changes in the size, number, phenotype, metabolic activity, or functions of cells in response to changes in their environment
- Cells must constantly adapt, even under normal conditions, to changes in their environment.
- These physiological adaptations usually represent responses of cells to normal stimulation by hormones or endogenous chemical substances.

– For example, as in the enlargement of the breast and induction of lactation by pregnancy.

Types of Adaptation:

- Pathologic adaptations may share the same underlying mechanisms, but they provide the cells with the ability to survive in their environment and perhaps escape injury.
- Cellular adaptation is a state that lies intermediate between the normal, unstressed cell and the injured, overstressed cell.
- **Cellular Adaptation:** Cell can adapt themselves by undergoing 5 different conditions
 1. Hyperplasia
 2. Hypertrophy
 3. Atrophy
 4. Metaplasia
 5. Dysplasia

1. **Hyperplasia:** An increase in the number of cells in an organ or tissue, which may then have increased volume.

Types of Hyperplasia- Physiological:

- a. Hormonal (influence of hormonal stimulation)
 - Hyperplasia of the female breast epithelium at puberty or in pregnancy.
 - pregnant uterus
 - Normal endometrium after a normal menstrual cycle.
 - Prostatic hyperplasia in old age.
- b. Compensatory- hyperplasia occurring following removal of part of an organ or a contralateral organ in paired organ.
 - Regeneration of the liver following partial hepatectomy
 - Regeneration of epidermis after skin abrasion
 - Following nephrectomy on one side, there is hyperplasia of nephrons of the other kidney.

Types of Hyperplasia- Pathological

- Excessive stimulation of hormones or growth factors
 - Endometrial hyperplasia
 - Wound healing - of granulation tissue due to proliferation of fibroblasts and endothelial cells.
 - Skin warts from hyperplasia of epidermis due to human papilloma virus.
 - Pseudocarcinomatous hyperplasia of the skin.

2 Hypertrophy:

An increase in the size of cells, and with such change, an increase in the size of the organ.

Types:

- **Physiologic:** physiologic growth of the uterus during pregnancy involves both hypertrophy and hyperplasia.

- **Pathologic causes:** increased workload, hormonal stimulation and growth factors stimulation.
 - Hypertrophy of heart the most common stimulus is chronic hemodynamic overload.

The relationship between hyperplasia and hypertrophy: Although hypertrophy and hyperplasia are two distinct processes, frequently both occur together, and they will be triggered by the same mechanism.

3. **Atrophy:** Acquired loss of size due to reduction of cell size or number of parenchymatous cells in an organ.

Types: Physiologic or Pathological

- Physiologic atrophy: A normal process of aging in some tissues, which could be due to loss of endocrine stimulation or arteriosclerosis.
 - Atrophy of lymphoid tissue in lymph nodes, appendix and thymus.
 - Atrophy of gonads after menopause.
 - Atrophy of brain with aging.

• Pathologic atrophy:

- Starvation atrophy.
- Ischaemic atrophy
- Disuse atrophy.
- Neuropathic atrophy.
- Endocrine atrophy
- Pressure atrophy.
- Idiopathic atrophy

4. **Metaplasia:** Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type.

Causes:

- Changes in environment
- Irritation or inflammation
- Nutritional.

Types of Metaplasia: There are basically 2 types of metaplasia:

EPITHELIAL METAPLASIA

- Squamous metaplasia: changes in bronchus, uterine endocervix, gallbladder, prostate, renal pelvis and urinary bladder
- *vitamin A deficiency:* squamous metaplasia in the nose, bronchi, urinary tract, lacrimal and salivary glands
- Columnar metaplasia: Intestinal metaplasia in healed chronic gastric ulcer and Barrett's oesophagus

MESENCHYMAL METAPLASIA

- Osseous metaplasia.

- Cartilaginous metaplasia.
5. **DYSPLASIA:** disordered cellular development. It is also referred to as *atypical hyperplasia*. Epithelial dysplasia is characterised by cellular proliferation and cytologic changes
- a. Increased number of layers of epithelial cells
 - b. Disorderly arrangement of cells from basal layer to the surface layer
 - c. Loss of basal polarity i.e. nuclei lying away from basement membrane
 - d. Cellular and nuclear pleomorphism
 - e. Increased nucleocytoplasmic ratio
 - f. Nuclear hyperchromatism
 - g. Increased mitotic activity.

The two most common examples of dysplastic changes are the uterine cervix and respiratory tract.

Types of Cell Injury: Reversible and Irreversible:

1. **Reversible injury:** If the ischaemia or hypoxia is of short duration, the effects are reversible on rapid restoration of circulation. The sequential changes in reversible cell injury are as under:
 - Intracellular edema,
 - Fatty change,
 - Hyaline change,
 - Amyloidosis,
 - Mucoïd Degeneration,
 - Pathologic Pigments
2. **Irreversible Injury:-** Persistence of ischaemia or hypoxia results in irreversible changes in structure and function of the cell (cell death)
 - Increased cell volume.
 - Ruptured lysosome.
 - Damaged cell membrane.
 - Lysed ER
 - Aggregate cytoskeleton.
 - Mitochondrial Swelling and Calcification.

1. Reversible Injury-

- a) Intracellular Edema/ Intracellular Accumulation:
 - Also known as **cloudy swelling**.
 - Accumulation of watery fluid in cells.
 - Commonest and earliest form of cell injury
 - Caused by bacterial toxins, chemicals, poisons, burns, high fever, and intravenous administration of hypertonic glucose or saline.
 - Impaired regulation of sodium and potassium at the level of cell membrane.

- Morphologic change
 - Gross features: cloudy swelling
 - M/S Changes: Parenchymal cells swollen
- b) Fatty change: There is the accumulation of fat in non-fatty cells. Also known as **steatosis**.

Morphologic change:

Gross features: The organ enlarges and becomes yellow, soft, and greasy.

M/S: A Fatty change appears as clear vacuoles within parenchymal cells.

- **Fatty change (Liver):** Since this organ plays a central role in fat metabolism. The accumulation of fat in toxic conditions can be very dangerous. Depending upon the cause and amount of accumulation, fatty change may be mild and reversible, or severe producing irreversible cell injury and cell death.

Causes: Conditions with excess fat

- Obesity
- Diabetes mellitus
- Congenital hyperlipidaemia

Liver cell damage:

- Alcoholic liver disease (most common)
- Starvation
- Protein calorie malnutrition
- Chronic illnesses (e.g. tuberculosis)
- Acute fatty liver in late pregnancy
- Hypoxia (e.g. anaemia, cardiac failure)
- Hepatotoxins (e.g. carbon tetrachloride, chloroform, ether, aflatoxins and other poisons)
- Drug-induced liver cell injury (e.g. administration of methotrexate, steroids, CCl₄, halothane anaesthetic, tetracycline etc)
- Reye's syndrome

- **Fatty change (Heart):** It occurs in two patterns, Prolonged moderate hypoxia causes intracellular deposits of fat, grossly apparent bands of yellowed myocardium alterations with bands of darker, red-brown, uninvolved myocardium (tigered effect) and Profound hypoxia or diphtheritic myocarditis, the myocardial cells are uniformly affected.

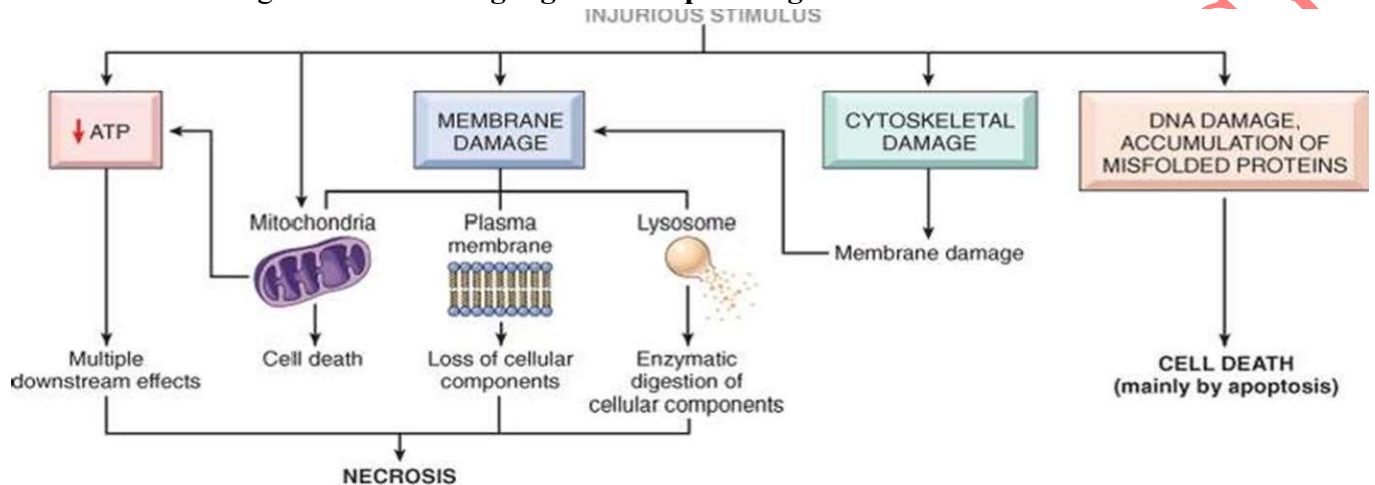
- **Fatty change (Kidney):** In most cases fatty change is confined to the epithelium of the convoluted tubules, but in severe poisoning it may affect all structures including the glomerule.

▪ *Causes:*

- Poisons. e. g. carbon tetrachloride, phosphorus (liver)
- Chronic alcoholism (liver)

- Infections
- Congestive cardiac failure
- Severe anaemia, Diabetes mellitus and Malnutrition and wasting disease.

2. Irreversible Injury: Cell death is a state of irreversible injury. It may occur in the living body as a local or focal change: **autolysis, necrosis and apoptosis**. The changes that follow it: **gangrene and pathologic calcification**.



- **NECROSIS:** Defined as a localised area of death of tissue followed by degradation of tissue by hydrolytic enzymes liberated from dead cells. It is invariably accompanied by inflammatory reaction. Various agents such as hypoxia, chemical and physical agents, microbial agents, immunological injury, etc. Two essential changes characterize irreversible cell injury in necrosis of all types
 - Cell digestion by lytic enzymes.
 - Denaturation of proteins.

Types of Necrosis: Morphologically, there are five types of necrosis:

- Coagulative
- Liquefaction
- Caseous
- Fat
- Fibrinoid

a) **COAGULATIVE NECROSIS:** It's a form of tissue necrosis in which the component cells are dead but the basic tissue architecture is preserved for at least several days. The affected tissues take on a firm texture. Presumably the injury denatures not only structural proteins but also enzymes and so blocks the proteolysis of the dead cells as a result, eosinophilic, anucleate cells may persist for days or weeks. Ultimately, the necrotic cells are removed by phagocytosis of the cellular debris.

Most common type of necrosis. Mostly from sudden cessation of blood flow (ischaemia). Less often from bacterial and chemical agents. It's characteristic of **infarcts**

(areas of ischemic necrosis) in all solid organs except the brain. The organs commonly affected are the heart, kidney, and spleen.

- Morphology: Gross
 - foci of coagulative necrosis in the early stage are pale, firm, and slightly swollen. With progression, they become more yellowish, softer, and shrunken.
- b) **LIQUEFACTION (COLLIQUATIVE) NECROSIS:** Due to ischaemic injury and bacterial or fungal infections, degradation of tissue by the action of powerful hydrolytic enzyme. The common examples are infarct brain and abscess cavity. Whatever the pathogenesis, liquefaction completely digests the dead cells, resulting in transformation of the tissue into a liquid viscous mass. If the process was initiated by acute inflammation, the material is frequently creamy yellow and is called pus.
- Morphology: Gross
 - The affected area is soft with liquefied centre containing necrotic debris.
 - Later, a cyst wall is formed
- c) **CASEOUS NECROSIS:** It is found in the centre of foci of tuberculous infections. It combines features of both coagulative and liquefactive necrosis. Term "caseous" (cheese-like) is derived from the friable yellow-white appearance of the area of necrosis
- Morphology: Grossly
 - foci of caseous necrosis,
 - as the name implies, resemble dry cheese and are soft, granular and yellowish.
 - This appearance is partly attributed to the histotoxic effects of lipopolysaccharides present in the capsule of the tubercle bacilli, *Mycobacterium tuberculosis*
- d) **FAT NECROSIS:** Refers to focal areas of fat destruction. *Acute pancreatic necrosis, traumatic fat necrosis* commonly in breasts. Pancreatic enzymes that have leaked out of acinar cells and ducts liquefy the membranes of fat cells in the peritoneum. Lipases split the triglyceride esters contained within fat cells to fatty acid. These combines calcium to produce grossly visible chalky white areas (fat saponification)
- Morphology: Grossly
 - Fat necrosis appears as yellowish-white and firm deposits.
 - Formation of calcium soaps imparts the necrosed foci firmer and chalky white appearance.
- e) **FIBRINOID NECROSIS:** Characterised by deposition of fibrin-like material this has the staining properties of fibrin. It is encountered in various examples of immunologic tissue injury, immune complex vasculitis, autoimmune diseases, Arthus reaction, Arterioles in hypertension, peptic ulcer

CALCIFICATION: Abnormal deposits of calcium salts occur in any tissues except bones and teeth. Two distinct types of pathologic calcification:

- Dystrophic calcification: characterised by deposition of calcium salts in dead or degenerated tissues with normal calcium metabolism and normal serum calcium levels.
- Metastatic calcification: apparently normal tissues and is associated with deranged calcium metabolism and hypercalcaemia.

Dystrophic calcification: Encountered in areas of necrosis of any type. Although dystrophic calcification may be an incidental finding indicating insignificant past cell injury, it may also be a cause of organ dysfunction. May occur due to 2 types of causes:

- Dead tissue
- Degenerated tissue.
- Dead tissue: *Caseous necrosis* in tuberculosis is the most common site. *Liquefaction necrosis* in chronic abscesses may get calcified. *Fat necrosis* following acute pancreatitis or traumatic fat necrosis in the breast results in deposition of calcium soaps. *Gamna-Gandy bodies* in chronic venous congestion (CVC) of the spleen is characterised by calcific deposits admixed with haemosiderin on fibrous tissue. *Infarcts* may sometimes undergo dystrophic calcification. *Thrombi*, especially in the veins, may produce phleboliths. *Haematomas* in the vicinity of bones may undergo dystrophic calcification. *Dead parasites* like in hydatid cyst, *Schistosoma* eggs, and cysticercosis. Calcification in *breast cancer* detected by mammography. *Congenital toxoplasmosis* involving the central nervous system visualised by calcification in the infant brain.
- Degenerated tissue: *Dense old scars* may undergo hyaline degeneration and subsequent calcification. *Atheromas* in the aorta and coronaries frequently undergo calcification. *Mönckeberg's sclerosis* shows calcification in the tunica media of muscular arteries in elderly people. *Stroma of tumours* such as uterine fibroids, breast cancer, thyroid adenoma, goitre etc show calcification. *Psammoma bodies* or calcospherites: characteristic spherules of calcification such as in meningioma, papillary serous cystadenocarcinoma of the ovary and papillary carcinoma of the thyroid. *Cysts* which have been present for a long time e.g. epidermal and pilar cysts. *Calcinosis cutis* is a condition of unknown cause in which there are irregular nodular deposits of calcium salts in the skin and subcutaneous tissue. *Senile degenerative changes* may be accompanied by dystrophic calcification such as in costal cartilages, tracheal or bronchial cartilages, and pineal gland in the brain etc.
- **Dystrophic calcification: Pathogenesis-** Denatured proteins in necrotic or degenerated tissue bind phosphate ions, which react with calcium ions to form precipitates of calcium phosphate. It involves 2 steps: -
 - Initiation (or nucleation)
 - phase in which precipitates of calcium phosphate begin to accumulate intracellularly in the mitochondria,

- or extracellularly in membrane-bound vesicles: *matrix vesicles*
 - Propagation
- Phase in which minerals deposited in the initiation phase are propagated to form mineral crystals.

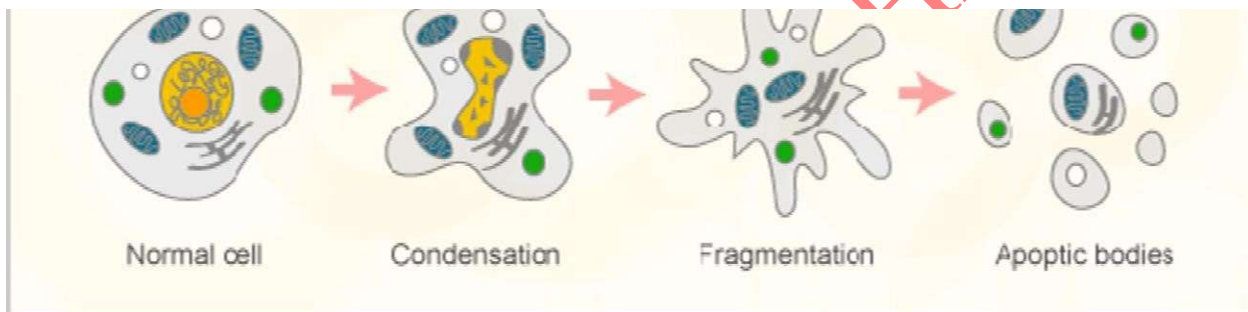
Metastatic calcification: Calcification in normal tissue whenever there is hypercalcemia.

These may be due to

- Excessive mobilisation of calcium from the bone
- Excessive absorption of calcium from the gut .

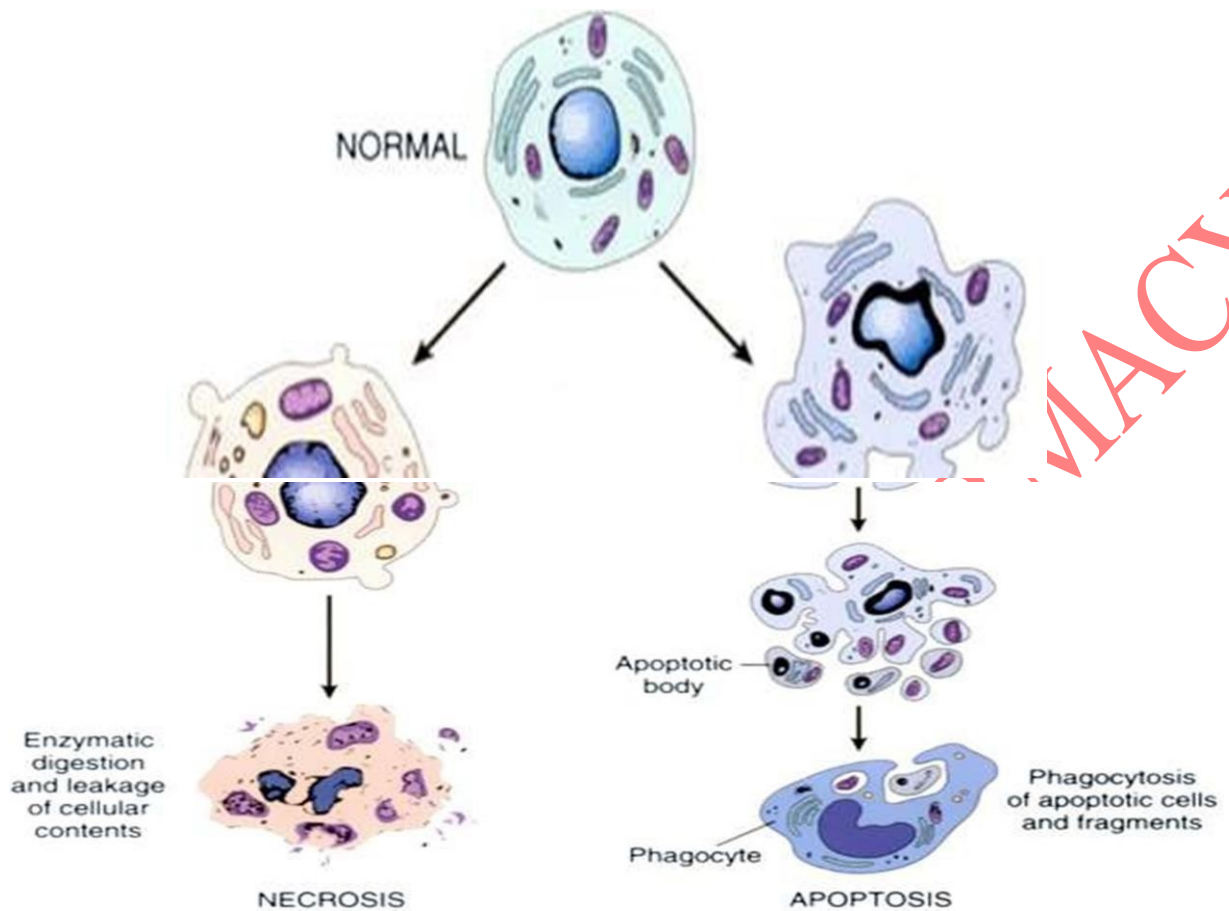
CELL DEATH: APOPTOSIS-

- a form of ‘coordinated and internally programmed cell death’
- pathway of cell death that is induced by a tightly regulated suicide program in which cells destined to die activate enzymes capable of degrading the cells' own nuclear DNA and nuclear and cytoplasmic proteins
- Apoptosis is responsible for mediating cell death in a wide variety of physiologic and pathologic processes.



- The plasma membrane of the apoptotic cell remains intact, but the membrane is altered in such a way that the cell and its fragments become avid targets for phagocytes.
- The dead cell is rapidly cleared before its contents have leaked out, and therefore cell death by this pathway does not elicit an inflammatory reaction in the host
- Thus, apoptosis differs from necrosis
- However, apoptosis and necrosis sometimes coexist, and apoptosis induced by some pathologic stimuli may progress to necrosis.

APOPTOSIS Vs NECROSIS :



- **Pathologic Processes:** Cell death in tumours exposed to *chemotherapeutic agents*. Cell death by *cytotoxic T cells* in immune mechanisms such as in graft-versus-host disease and rejection reactions. Progressive *depletion of CD4+T cells* in the pathogenesis of AIDS. Cell death in *viral infections* e.g. viral hepatitis. *Pathologic atrophy* of organs and tissues on withdrawal of stimuli e.g. prostatic atrophy after orchiectomy, atrophy of kidney or salivary gland on obstruction of ureter or ducts, respectively. Cell death in response to *injurious agents* involved in causation of necrosis e.g. radiation, hypoxia and mild thermal injury. In *degenerative diseases of CNS* e.g. in Alzheimer's disease, Parkinson's disease, and chronic infective dementias.

- **Recognition of Cell death:**

Ultrastructural changes- Margination or progressive loss of nuclear chromatin. Focal rupture of the nuclear membrane. Breakdown of the plasmalemma. Development of flocculent densities in mitochondria.

Changes in the nucleus-

Pyknosis: condensation of chromatin of chromatin and shrinkage of the nucleus.

Karyorrhexis: fragmentation of the nucleus.

Karyolysis: dissolution of the nucleus.

- **Metabolic Acidosis:** A fall in the blood pH due to metabolic components is brought about by fall bicarbonate level and excess of H^+ ions in the blood. This occurs in the following situation-

1. Production of large amounts of lactic acid. (Example-vigorous exercise shock.)
2. Uncontrolled diabetes mellitus.
3. Chronic renal failure.

- **SYMPTOMS OF METABOLIC ACIDOSIS:**

- Breath fast.
- Have a fast heart beat
- Have a headache
- Feel weak
- Feel tired.

- **Treatment of metabolic acidosis:**

- Ketoacidosis-when you have diabetes and don't get enough insulin and get dehydrated your body burns fat instead of carbs as fuel, and makes ketones.
- Lactic acidosis-the cells in your body make lactic acid when they don't have a lot of oxygen to use. This acid builds up too.
- Renal tubular acidosis-healthy kidney takes acids out of your blood and gets rid of them in your pee.
- Hyperchloremic acidosis-severe diarrhea and kidney problems can cause lower levels of bicarbonate, the base that helps neutralize acids in blood

- **METABOLIC ALKALOSIS:** A rise in the blood pH due to rise in the bicarbonate levels of plasma and loss of H^+ is called as metabolic alkalosis. In the following conditions:

- Severe and prolonged vomiting.
- Hypokalemia of alkaline salts like sodium bicarbonate.
- Clinically metabolic alkalosis is characterized by depression of respiration.
- Depressed renal function with Hypokalemia and increased bicarbonate excretion in the urine.

- **SYMPTOMS:**

- Muscle twitching
- Nausea
- Vomiting
- confusion

- **TREATMENT:**

- Treatment the underlying cause.

- Treatment of metabolic alkalosis with acute or chronic kidney disease.
- Summary of causes of metabolic or alkalosis
- Loss of gastric secretion- vomiting
- Cystic fibrosis
- Loss of colonic secretion-villous adenoma.

- **Basics mechanism involved in the process of inflammation and repair:**

What is Inflammation?

➤ Inflammation is defined as the local response of living mammalian tissues to injury due to any agent. It is a body defense reaction in order to eliminate or limit the spread of injurious agent as well as to remove the consequent necrosed cells and tissue.

➤ Types of Inflammation:

i) Acute inflammation

- Short duration

- Edema

- Mainly neutrophils

Granulomatous inflammation

- Distinctive pattern of chronic inflammation

- Activated macrophages (epithelioid cells) predominate

- +/- multinucleated giant cells

ii) Chronic inflammation

- longer duration

- Lymphocytes & macrophages predominate

- Fibrosis and New blood vessels (angiogenesis)

i) **Acute Inflammation:** Two major events:

1. Vascular events

Transient Vasoconstriction

- Edema results from increased hydrostatic pressure (vasodilation) and lowered intravascular osmotic pressure (protein leakage)

- Increase in blood flow (redness & warmth)

2. Cellular events

- Leukocytes extravasation from microcirculation and accumulate in the focus of injury

Stimuli: infections, trauma, physical or chemical agents, foreign bodies, immune reactions.

- **Outcomes of Acute Inflammation:**

- Complete resolution.

- Abscess formation

- Fibrosis

- After substantial tissue destruction

- In tissues that do not regenerate
 - After abundant fibrin exudation, especially in serous cavities (pleura, peritoneum)
- Progression to chronic inflammation

- **Morphologic Patterns of Acute Inflammation:**

- Serous inflammation: Outpouring of thin fluid (serous effusion, blisters)
- Fibrinous inflammation: Body cavities; leakage of fibrin; may lead to scar tissue (adhesions).
- Suppurative (purulent) inflammation: Pus or purulent exudate (neutrophils, debris, edema fluid); abscess: localized collections of pus.
- Ulcers: Local defect of the surface of an organ or tissue produced by the sloughing (shedding) of inflammatory necrotic tissue.

- ii) **Chronic Inflammation:** Inflammation of prolonged duration (weeks or months)

- Active inflammation, tissue destruction, and attempts at repair are proceeding simultaneously

May follow acute inflammation or begin insidiously and often asymptotically

- Persistent infections, exposure to toxic agents such as silica (silicosis), or by autoimmunity.

- Persistent infections

- *Tuberculosis*, syphilis, viruses, fungi, parasites

- Exposure to toxic agents

- exogenous: silica (silicosis)

- Endogenous: toxic plasma lipid components (atherosclerosis)

- Autoimmunity

- Rheumatoid arthritis, systemic lupus erythematosus.

- Histological features

- Infiltration with mononuclear cells (macrophages, lymphocytes, and plasma cells)

- Tissue destruction (induced by the inflammatory cells)

- Healing by replacement of damaged tissue by connective tissue (fibrosis) and new blood vessels (angiogenesis).

- **Chemical Mediators of Inflammation:**

- i) **Vasoactive mediators**

- Histamine
- Bradykinin
- Complement (C3a, C5a)
- Prostaglandins/leukotrienes
- Platelet activating factor
- Nitric oxide

- ii) **Chemotactic factors**

- Complement (C5a)
- Leukotriene (B4)

- Platelet activating factor
- Cytokines (IL-1, TNF)
- Chemokines
- Nitric oxide

- **Summary of Inflammatory Mediators:**

- Vasodilation : Prostaglandins, Nitric oxide, Histamine
- Pain: Prostaglandins, Bradykinin
- Increased vascular permeability: Histamine, serotonin, Complement (C3a, C5a), Bradykinin, Leukotrienes (C₄, D₄, E₄) , Platelet Activating Factor, Substance P.
- Tissue Damage: Neutrophil and macrophage lysosomal enzymes, Oxygen metabolites, Nitric oxide

- ❑ **Wound Healing:** Healing is the body response to injury in an attempt to restore normal structure and function. Two Distinct processes: -- Regeneration and Repair.
- ❑ Regeneration:- Complete restoration of the original tissues.
- ❑ Repair: - When the healing takes place by proliferation of connective tissue element resulting in fibrosis and scarring.

It occurs in the following steps:

- i) Injury induces acute inflammation
- ii) Parenchymal cells regenerate
- iii) Both parenchymal and connective tissue cells migrate and proliferate
- iv) Extracellular matrix is produced
- v) Parenchyma and connective tissue matrix remodel
- vi) Increase in wound strength due to collagen deposition

Variables affecting repair:

- i) **Infection** –prolongs inflammation, increases degree of tissue injury
- ii) **Nutrition** –protein or vitamin deficiency can impair synthesis of new proteins
- iii) **Anti-inflammatory drugs** –can impede fibrosis necessary for repair
- iv) **Mechanical variables** –tension, pressure, or the presence of foreign bodies can affect repair.
- v) **Vascular disease** –limits nutrient and oxygen supply required for repairing tissues.
- vi) **Tissue type** –only tissues capable of renewing will regenerate, otherwise healing is by fibrosis.
- vii) **Degree of exudates removal** –adequate removal of exudates allows Resolution of the injury (general restoration of the normal tissue architecture); inadequate removal results in Organization (abnormal, dysfunctional tissue architecture).
- viii) **Regulation of cell proliferation** –abnormal proliferation of connective tissue may inhibit re-epithelialization and/or raised scars (keloids)

DDR COLLEGE OF PHARMACY

DDR COLLEGE OF PHARMACY