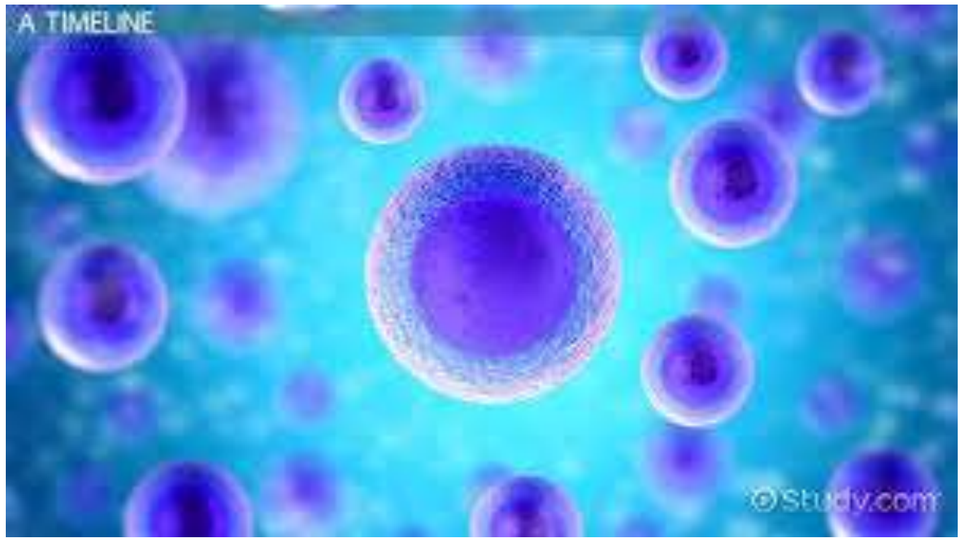
Cell --> Structural and Functional Unit of an organism.

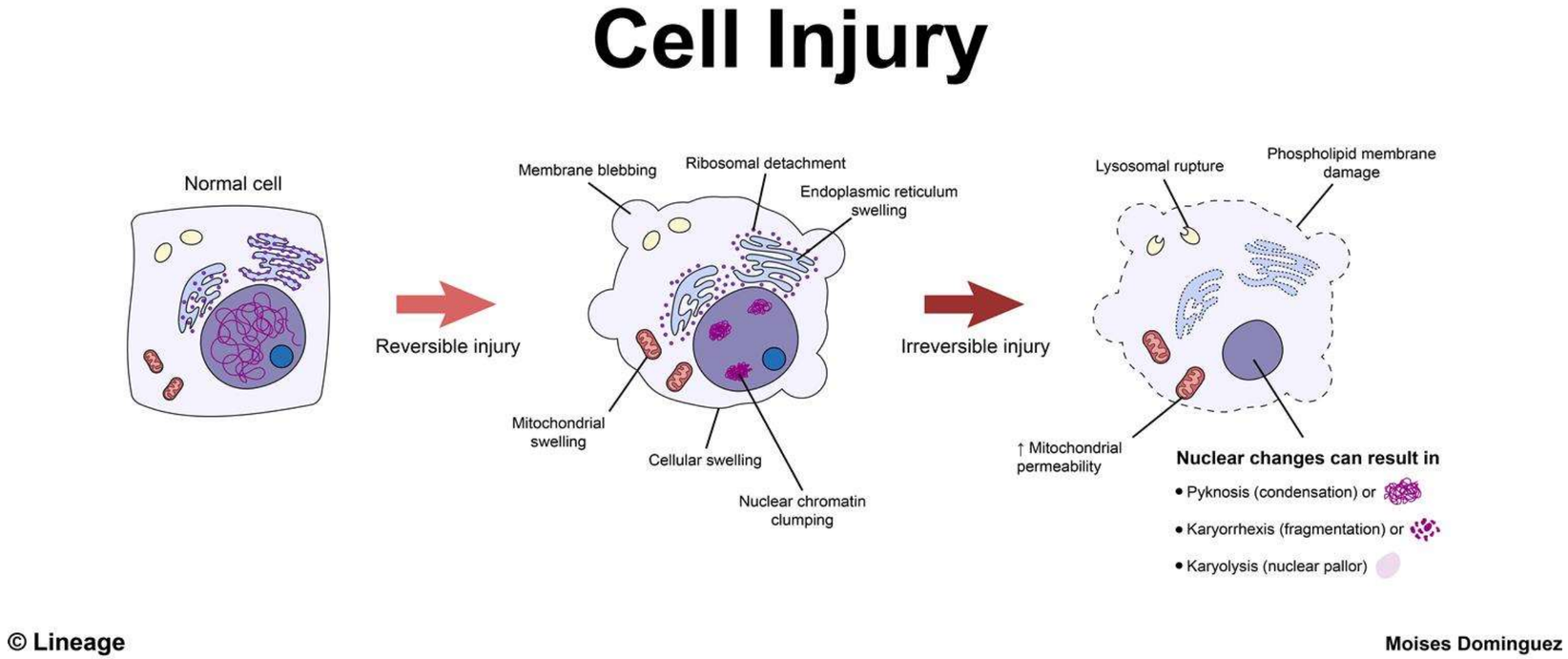
Cellular physiology characterized by
Closed interdependence of
various components & activities.

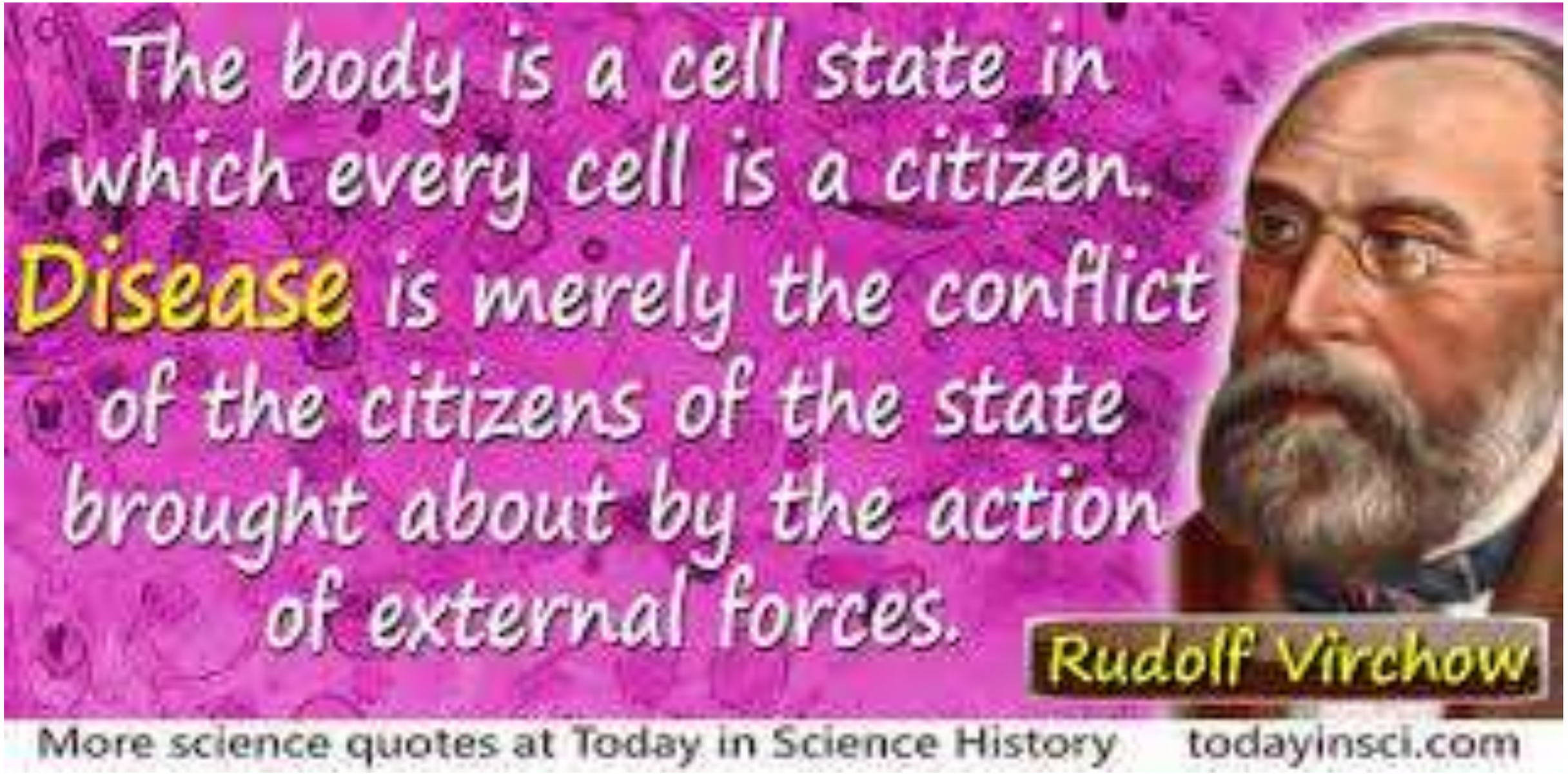
Cell being a basic unit of life, any alteration in its function affects the entire system (structurally followed by functionally)



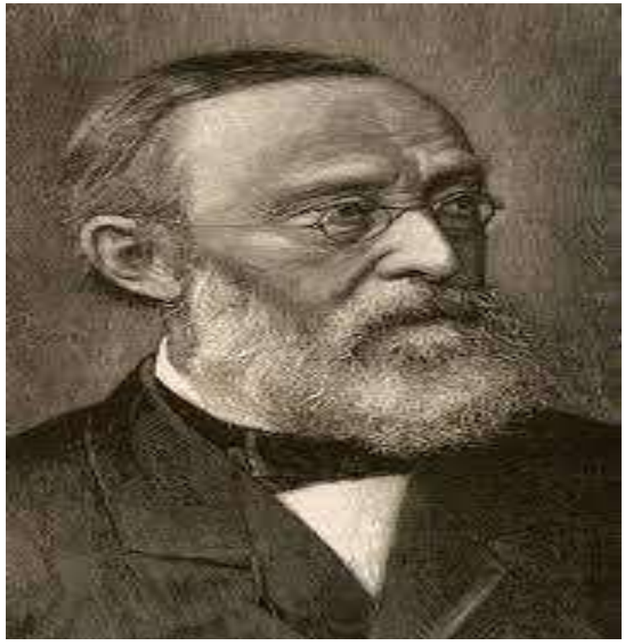
Definition

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




The body is a cell state in which every cell is a citizen.
Disease is merely the conflict of the citizens of the state brought about by the action of external forces.
Rudolf Virchow
More science quotes at Today in Science History
todayinsci.com

Virchow's Cellular Theory of Disease (1859)

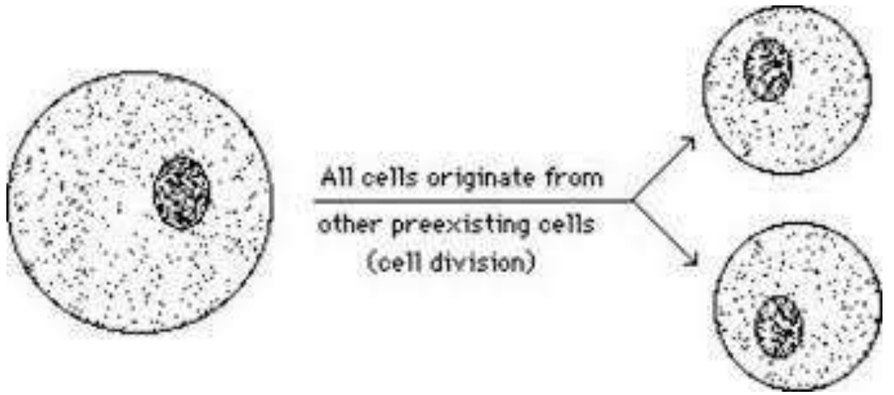


Diseases occur due to abnormalities at the level of cells

"OMNIS CELLULA E CELLULA"

With this approach Virchow launched the field of cellular pathology.

He stated that all diseases involve changes in normal cells, that is, all pathology ultimately is cellular pathology.



Inbuilt mechanism to deal with the CELL INJURY (altered state) with changes in environment (to an extent)

variables for cellular response to stress:

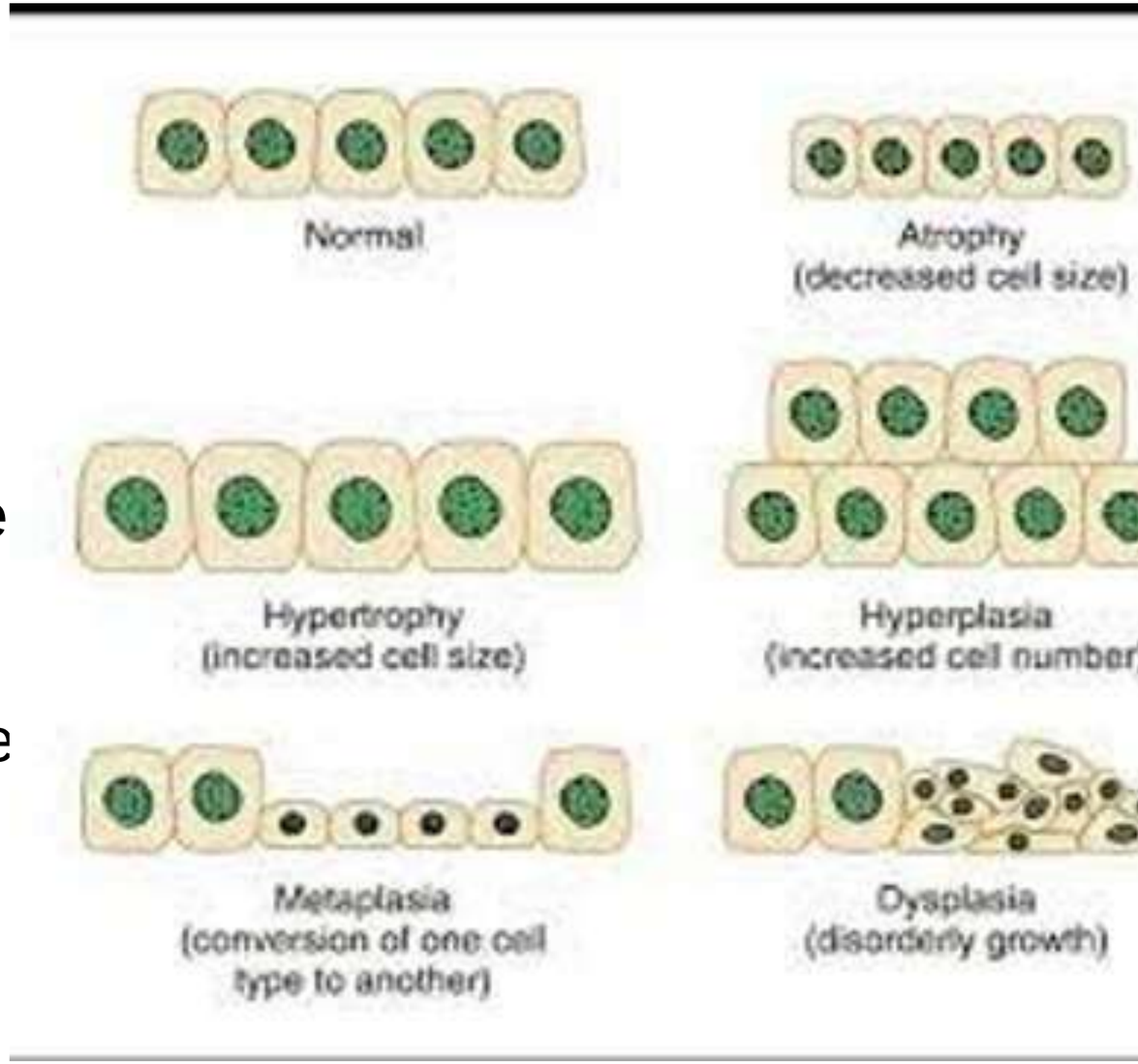
i) The type of cell and tissue involved.

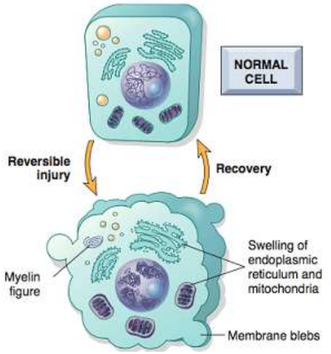
ii) Extent and type of cell injury.

Cellular responses to injury

Cellular adaptations

Due to Increased functional demand,
Cell adapts to change (expressed morphologically).
Adaptation is reversible changes in size, numbe phenotype, metabolic activity or functions in response to changes in environment.
Revert back to normal after the stress is remove cellular adaptations



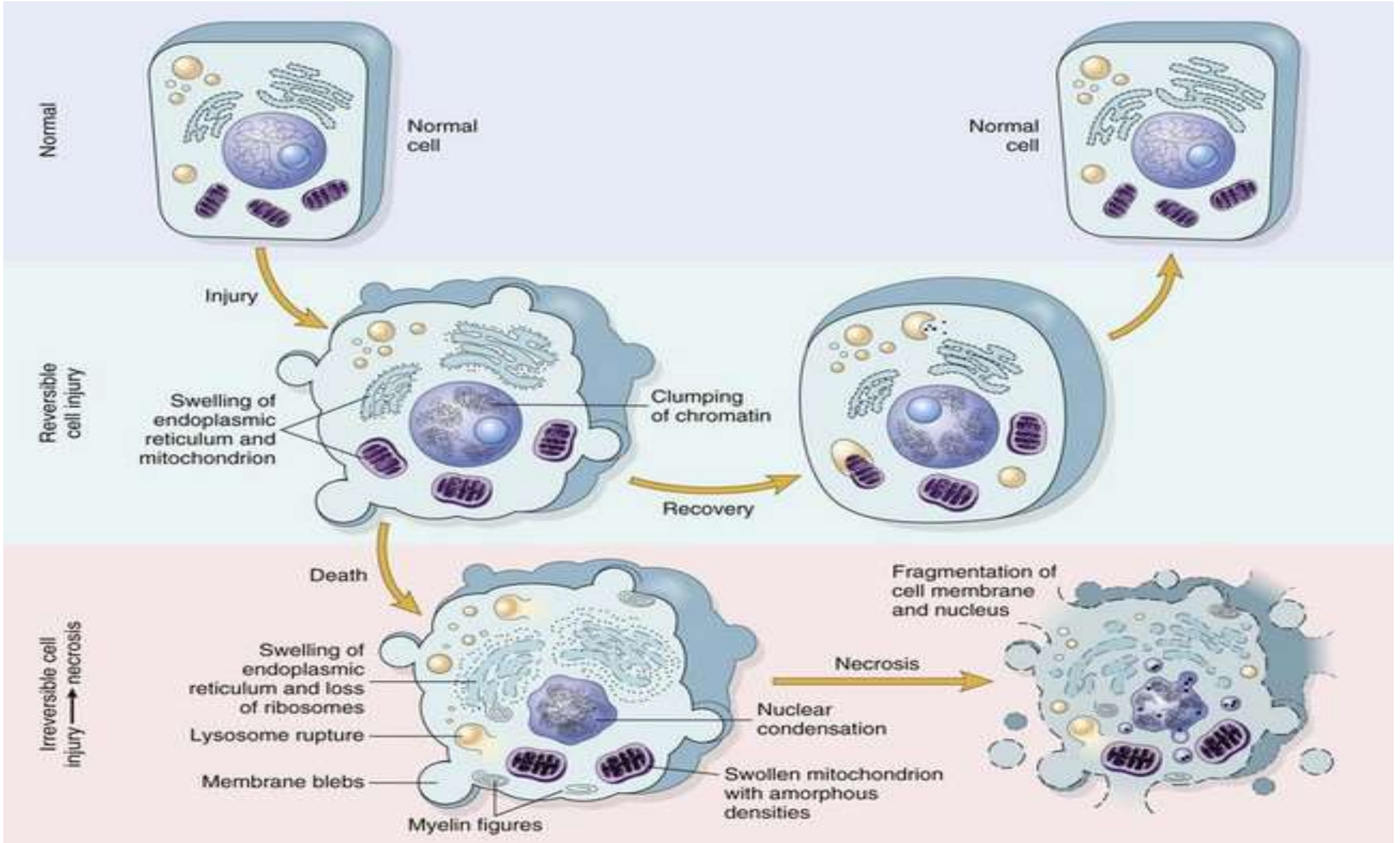


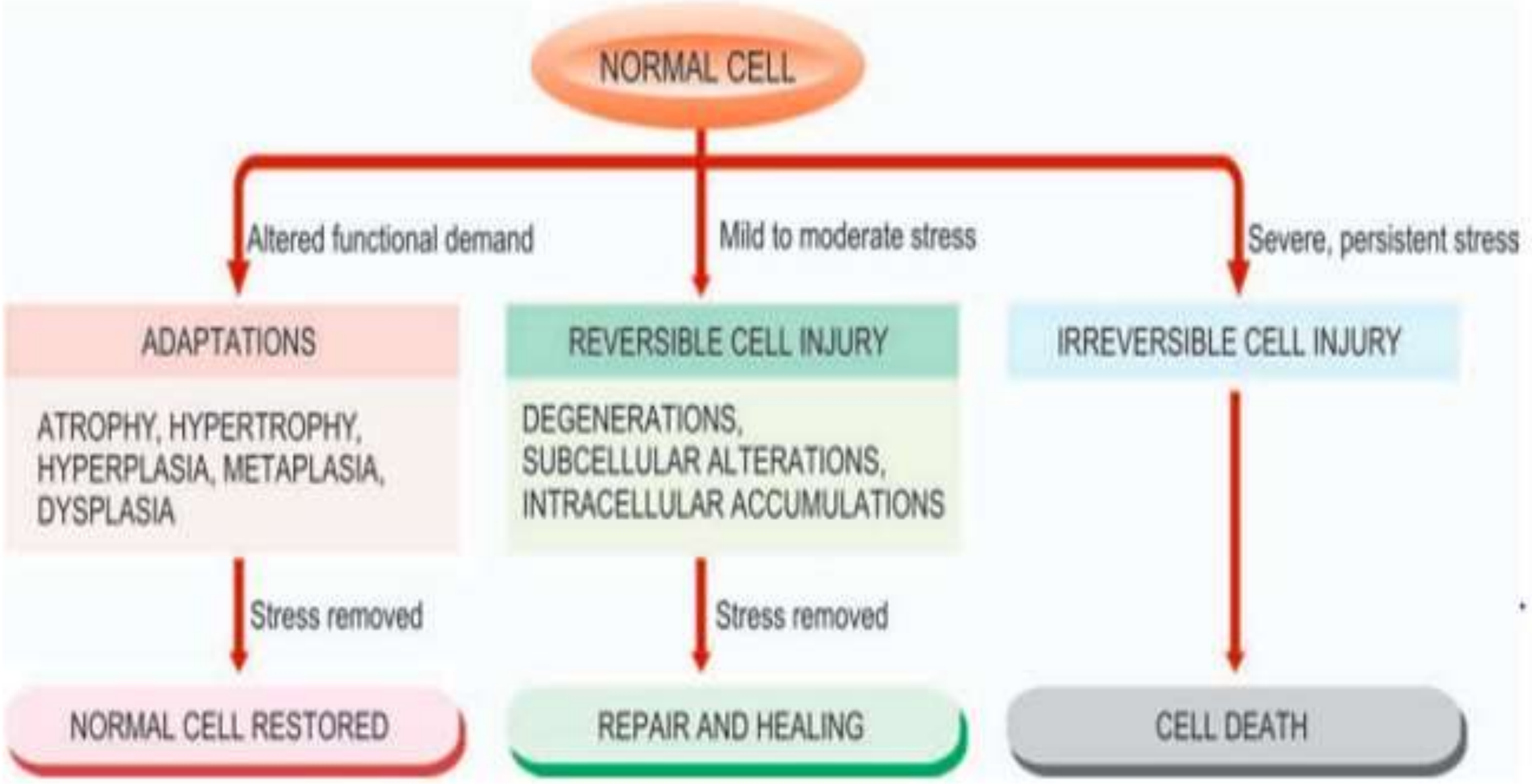
Mild to moderate Stress

Injury happens -->
(a) when injured cell recover (reversible cell injury),
(b) when the injury is persistent cell death may occur (irreversible cell injury).

After effect of Injury -

Residual effects of reversible cell injury may persist in the cell as evidence --> subcellular changes
Metabolites may accumulate within the cell --> intracellular accumulations.


Normal
Normal cell
Normal cell
Injury
Reversible cell injury
Swelling of endoplasmic reticulum and mitochondrion
Clumping of chromatin
Recovery
Death
Irreversible cell injury → necrosis
Swelling of endoplasmic reticulum and loss of ribosomes
Lysosome rupture
Membrane blebs
Myelin figures
Nuclear condensation
Swollen mitochondrion with amorphous densities
Necrosis
Fragmentation of cell membrane and nucleus


NORMAL CELL
Altered functional demand
Mild to moderate stress
Severe, persistent stress
ADAPTATIONS
ATROPHY, HYPERTROPHY, HYPERPLASIA, METAPLASIA, DYSPLASIA
REVERSIBLE CELL INJURY
DEGENERATIONS, SUBCELLULAR ALTERATIONS, INTRACELLULAR ACCUMULATIONS
IRREVERSIBLE CELL INJURY
Stress removed
Stress removed
NORMAL CELL RESTORED
REPAIR AND HEALING
CELL DEATH

Intercellular Communination

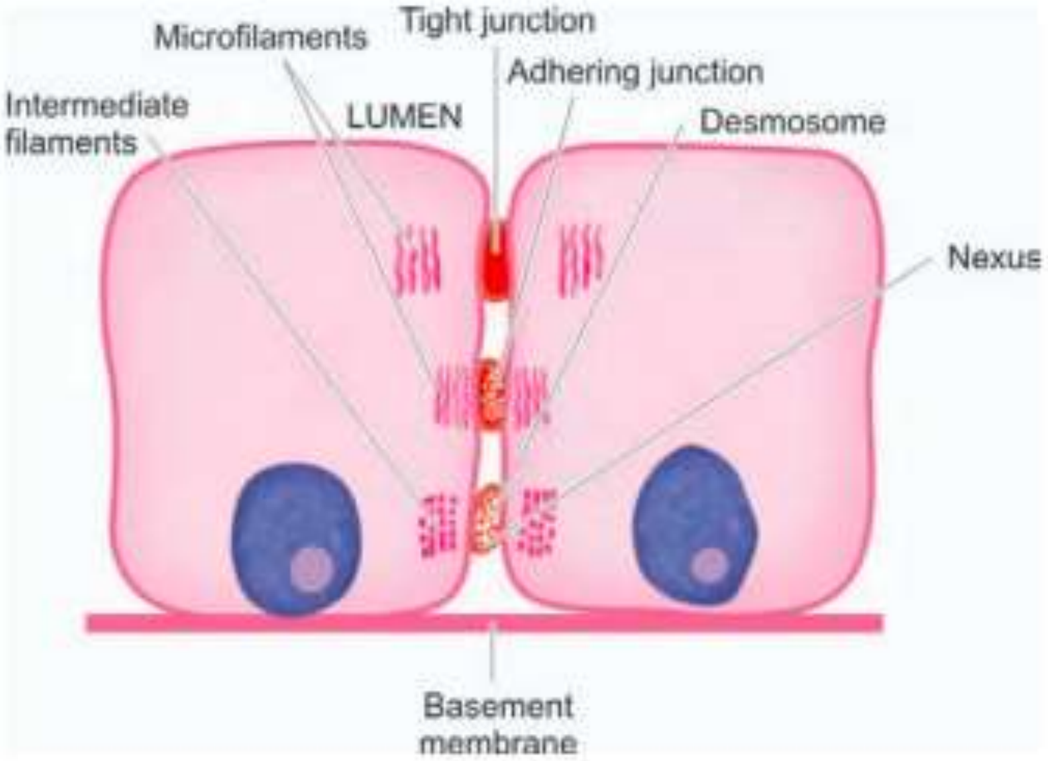
I. Intercellular junctions:-

Occluding junctions (Zonula occludens)

Adhering junctions (Zonula adherens)

Desmosomes (Macula densa)

Gap junctions (Nexus)



II. Molecular interactions between cells

1. Cell adhesion molecules (CAMs)

2. Cytokines

3. Membrane receptors

CELL Adehsion Molecule

Chemicals which mediate the interaction between cells (cellcell interaction) as well as between cells and extracellular matrix (cell-ECM interaction).
Contribution :- participate in fertilisation, embryogenesis, tissue repair, haemostasis, cell death by apoptosis and in inflammation.

Consists of the following :

i) fibrillar structural proteins (collagen, elastin);

ii) adhesion proteins (fibronectin, laminin, fibrillin, osteonectin, tenacin); and

iii) molecules of proteoglycans and glycosaminoglycans (heparan sulphate, chondroitin sulphate, dermatan sulphate, keratan sulphate, hyaluronic acid)

i) Integrins. cell-ECM interactions and in leucocyte-endothelial cell interaction.

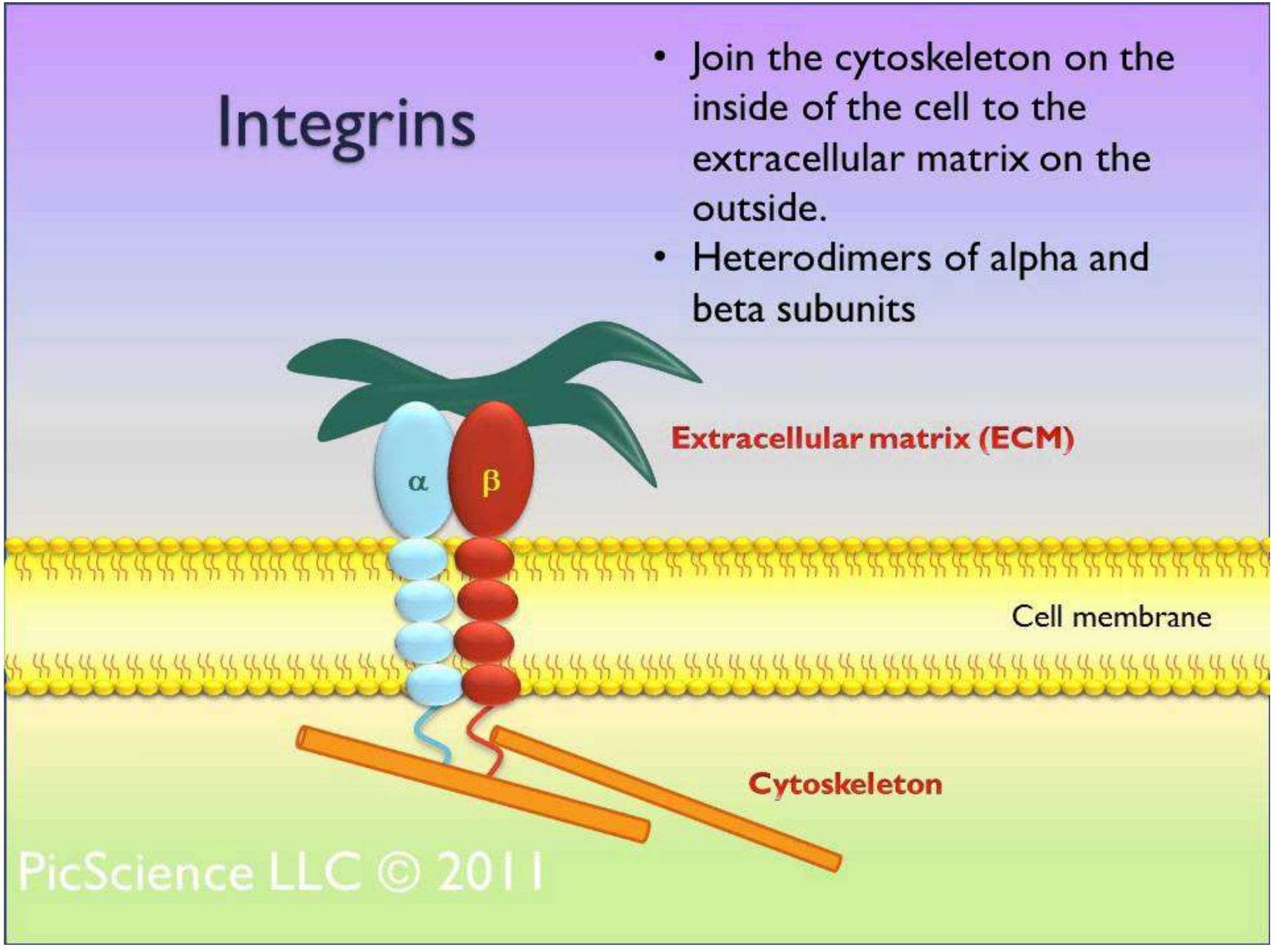
ii) Cadherins. These are calcium-dependent adhesion molecules which bind adjacent cells together and prevent invasion of ECM by cancer cells. Types: E-cadherin (epithelial cell), N-cadherin (nerve cell), M-cadherin (muscle cell), and P-cadherin (placenta).

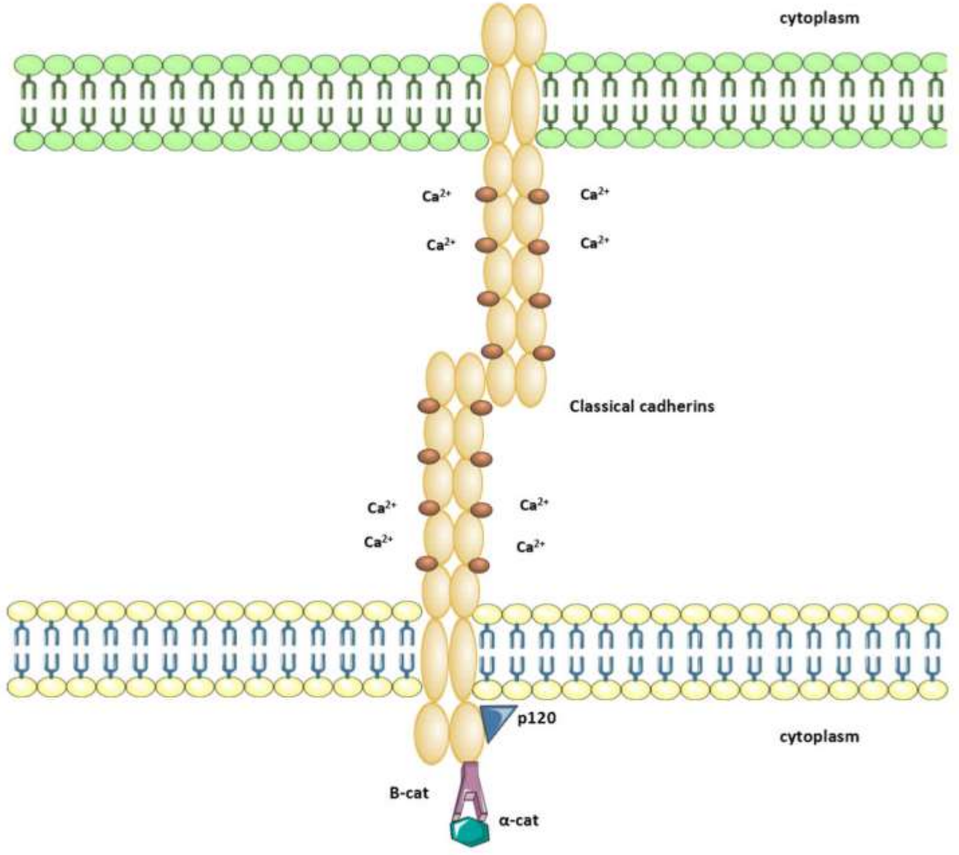
iii) Selectins/ lectins
Binds to glycoproteins and glycolipids on the cell surface. Their major role is in **movement of leucocytes and platelets and develop contact with endothelial cells.**

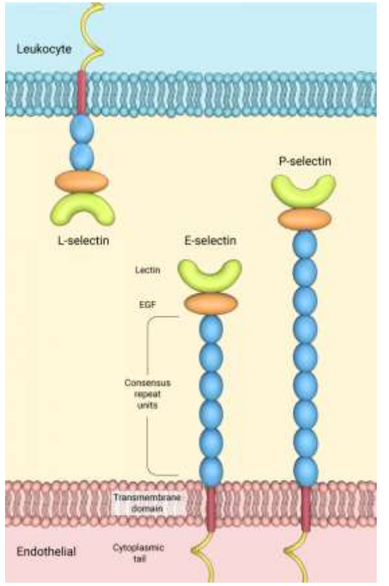
Types: P-selectin (from platelets, also called CD62), E-selectin (from endothelial cells, also named ECAM), and L-selectin (from leucocytes, also called LCAM).

Integrins

- Join the cytoskeleton on the inside of the cell to the extracellular matrix on the outside.
- Heterodimers of alpha and beta subunits




cytoplasm
Ca2+
Ca2+
Ca2+
Ca2+
Classical cadherins
Ca2+
Ca2+
Ca2+
Ca2+
p120
cytoplasm
B-cat
α-cat


Leukocyte
P-selectin
L-selectin
E-selectin
Lectin
EGF
Consensus repeat units
Transmembrane domain
Endothelial
Cytoplasmic tail

iv) Immunoglobulin superfamily.

They have a major role in recognition and binding of immunocompetent cells.

This group includes

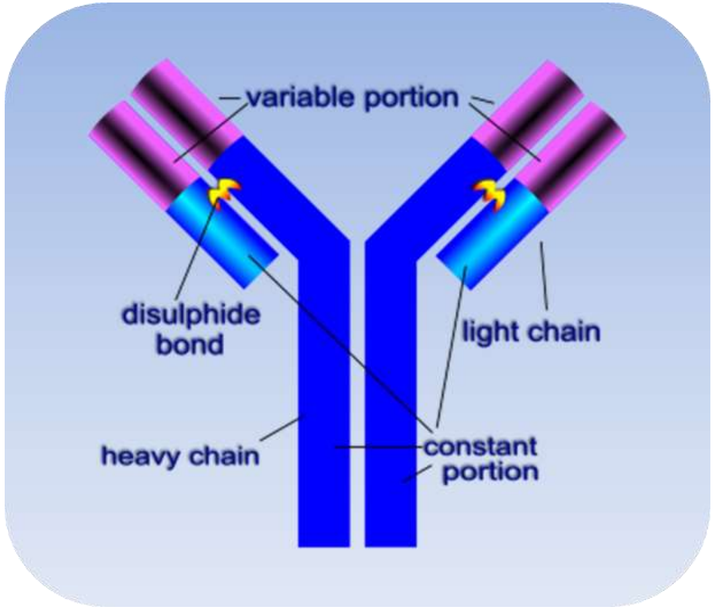
ICAM-1,2 (intercellular adhesion molecule, also called CD54), VCAM (vascular cell adhesion molecule, also named CD106), NCAM (neural cell adhesion molecule).

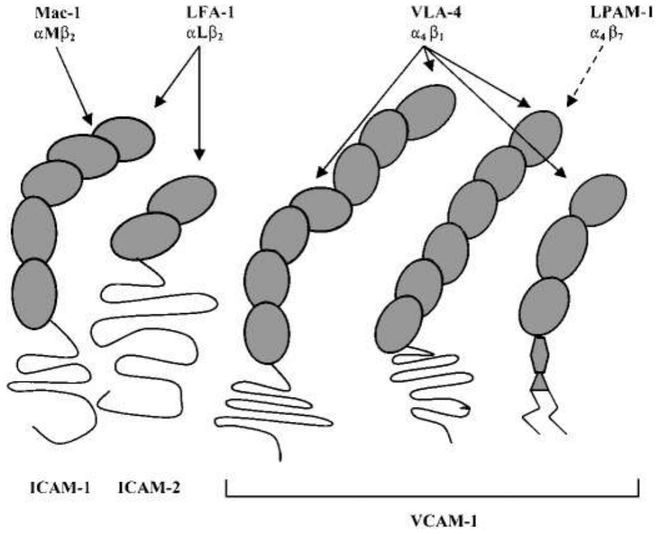
v)CD44.

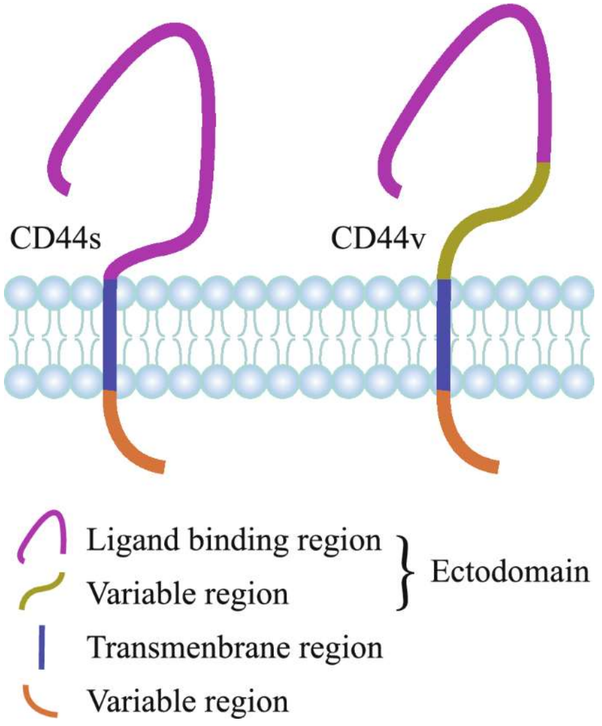
The last group of adhesion molecules is a break away from immunoglobulin superfamily.

CD44 molecule binds to hyaluronic acid and is expressed on leucocytes.

It is involved in leucocyte-endothelial interactions as well as in cell-ECM interactions


variable portion
disulphide bond
light chain
heavy chain
constant portion


Mac-1
αMβ2
LFA-1
αLβ2
VLA-4
α4 β1
LPAM-1
α4 β7
ICAM-1
ICAM-2
VCAM-1


CD44s
CD44v
Ligand binding region
Variable region
Ectodomain
Transmenbrane region
Variable region

CYTOKINES

Release of peptides and other molecules acting as paracrine function.

Soluble proteins secreted by haemopoietic and non-haemopoietic cells in response to various stimuli.

Their main role is in activation of immune system.
200 cytokines have been identified

6 categories:
i) Interferons (IFN)
ii) Interleukins (IL)
iii) Tumour necrosis factor group (TNF, cachectin)
iv) Transforming growth factor (TGF)
v) Colony stimulating factor (CSF)
vi) Growth factors (e.g. platelet-derived growth factor PDGF, epidermal growth factor EGF, fibroblast growth factor FGF,endothelial-derived growth factor EDGF, transforming growth factor TGF).

CELL MEMBRANE RECEPTORS

Found on the outer cell membrane, inside the cell, or may be trans-membranous.

There are 3 main types of receptors:

i)Enzyme-linked receptors. These receptors are involved in control of cell growth e.g. tyrosine kinase associated receptors take part in activation of synthesis and secretion of various hormones.

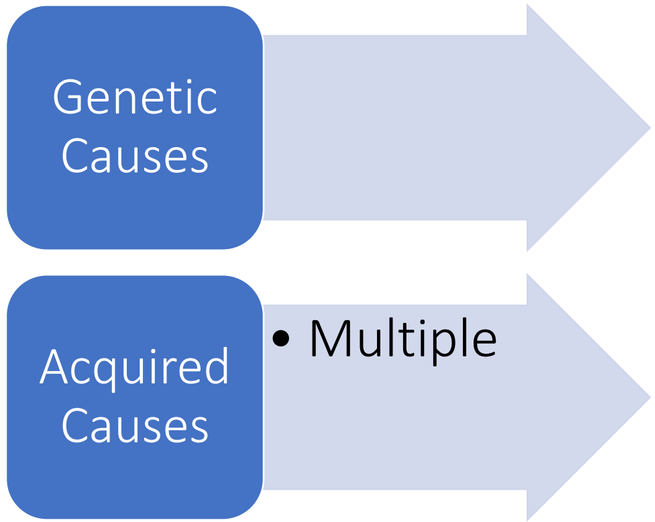
ii)Ion channels. The activated receptor for ion exchange such as for sodium, potassium and calcium and certain peptide hormones, determines inward or outward movement of these molecules.

iii)G-protein receptors.

These are trans-membranous receptors and activate phosphorylating enzymes for metabolic and synthetic functions of cells.

activation of adenosine monophosphate-phosphatase cycle (c-AMP) by the G-proteins (guanosine nucleotide binding regulatory proteins) is the most important signal system, also known as ‘second messenger’ activation. The activated second messenger (cyclic-AMP) then regulates other intracellular activities.

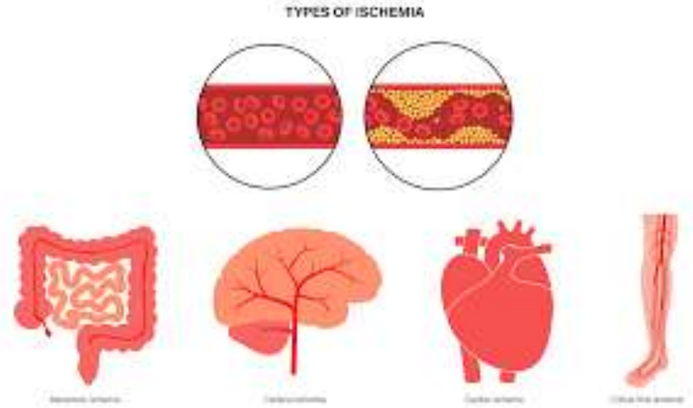
ETIOLOGY OF CELL INJURY



1. HYPOXIA AND ISCHAEMIA - Hypoxia is the most common cause of cell injury.

Oxygen is to generate energy and perform metabolic functions.

Deficiency of oxygen or hypoxia results in failure to carry out these activities by the cells.

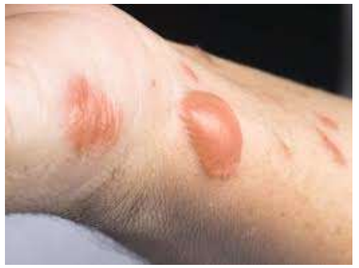


Hypoxia may result from the following:
1. reduced supply of blood to cells due to interruption i.e. ischaemia

2. hypoxia may result from other causes as well e.g. disorders of oxygen-carrying RBCs (e.g. anaemia, carbon monoxide poisoning), heart diseases, lung diseases and increased demand of tissues

PHYSICAL AGENTS.

-> mechanical trauma (e.g. road accidents);

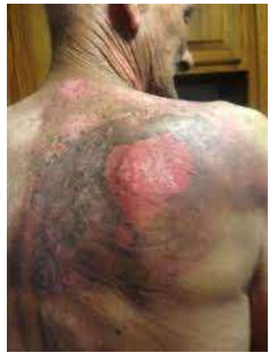


-> thermal trauma (e.g. by heat and cold);

->electricity;

-> radiation (e.g. ultraviolet and ionising);

->rapid changes in atmospheric pressure



CHEMICALS AND DRUGS.

chemical poisons such as
cyanide, arsenic, mercury; strong acids and alkalis;

environmental pollutants;

insecticides and pesticides;

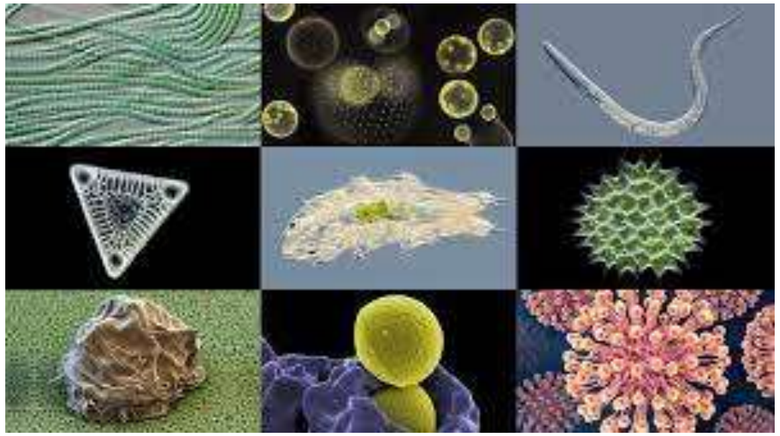
oxygen at high concentrations;

hypertonic glucose and salt;

social agents such as alcohol and narcotic drugs;

therapeutic administration of drugs.

MICROBIAL AGENTS.



Injuries by microbes include infections caused by

bacteria, rickettsiae, viruses, fungi, protozoa, metazoa, and other parasites

IMMUNOLOGIC AGENTS.

‘doubleedged sword’—

it protects the host against various injurious agents

turn lethal and cause cell injury

e.g. hypersensitivity reactions; anaphylactic reactions; and autoimmune diseases

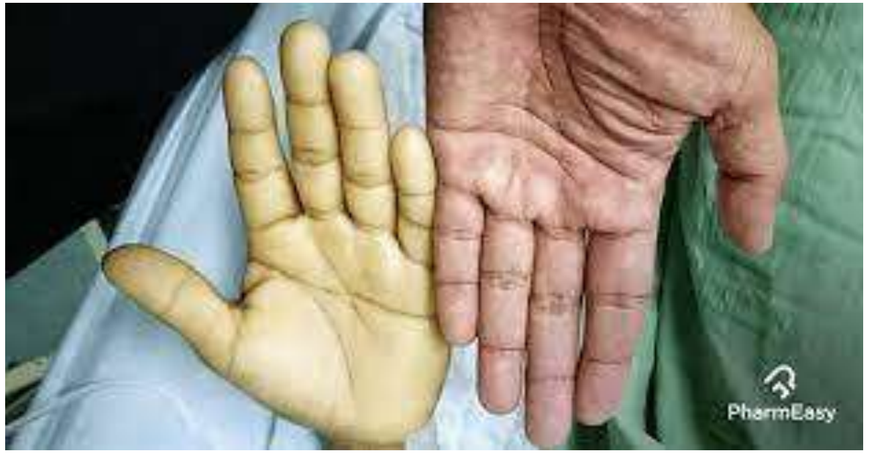
NUTRITIONAL DERANGEMENTS.

A **deficiency** or an **excess** of nutrients may result in nutritional imbalances.

--> Overall deficiency of nutrients (e.g. starvation)
--> Deficiency of protein calorie (e.g. marasmus, kwashiorkor),
--> Deficiency of minerals (e.g. anaemia), or of trace elements.

Nutritional excess --> obesity, atherosclerosis, heart disease and hypertension.


Vs
Marasmus
Kwashiorkor


PharmEasy


TYPE 2 DIABETES
HYPERLIPIDEMIA
HYPERTENSION
OBSTRUCTIVE SLEEP APNEA
OBESITY
OSTEOARTHRITIS

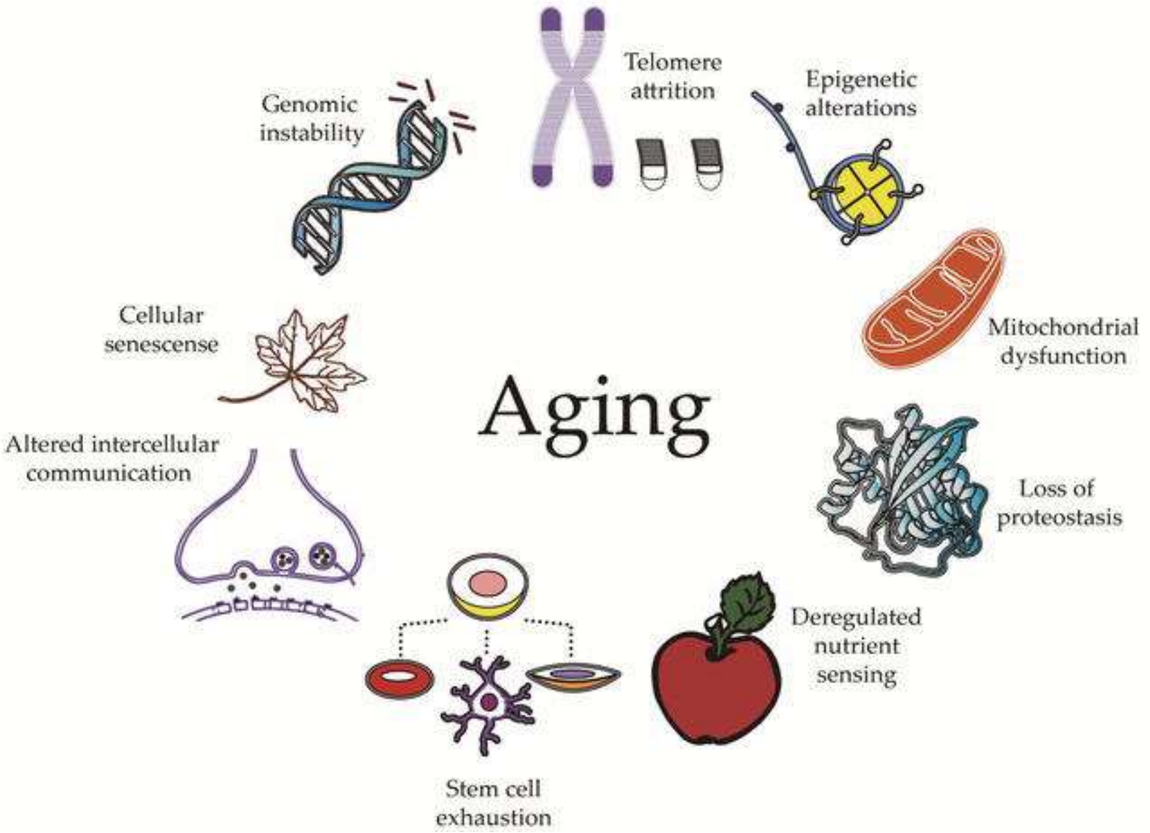

DNA
High
Low
HYPERTENSION

AGING.

Cellular aging / enescence

impaired ability of the cells to undergo replication and repair

ultimately lead to cell death culminating in death of the individual.



PSYCHOGENIC DISEASES.

Psychological impairment

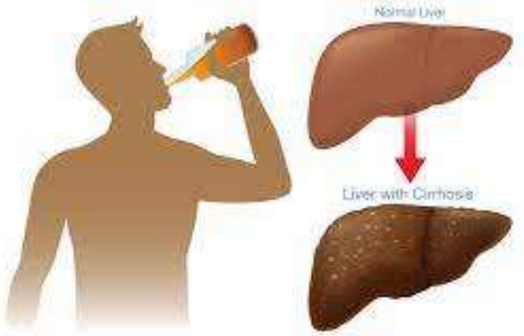
Disease occur due to mental stress, strain, anxiety, overwork and frustration

e.g. depression, schizophrenia.

Organic impairment

problems of drug addiction, alcoholism, and smoking

Leads to liver damage, chronic bronchitis, lung cancer, peptic ulcer, hypertension, ischaemic heart disease etc.



IATROGENIC CAUSES --> owing to physician

Hippocratic oath, every physician is bound not to do or administer anything that causes harm to the patient, there are some diseases as well as deaths attributed to iatrogenic causes .

Examples include occurrence of disease or death due to
-->error in judgment by the physician and untoward effects of administered therapy (drugs, radiation)

IDIOPATHIC DISEASES.

“of unknown cause”.

There still remain many diseases for which exact cause is undetermined.

For example, most common form of hypertension (90%) is idiopathic (or essential) hypertension.

Similarly, exact etiology of many cancers is still incompletely known.