PATHOPHYSIOLOGY

Cellular Response to Injury

A- Cellular adaptation
B- Mechanisms Of Cell Injury
C- Manifestations of cellular injury
D- Cell death
E- Tissue repair
F- Steps in tissue (wound) repair
G- Inflammation and Tissue repair
H-Edema

Course Name: Pathophysiology

Course Code: 0520300

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CELLULAR RESPONSES TO INJURY

Cellular responses to injury include:

1- Adaptation (hypertrophy or atrophy, hyperplasia , metaplasia or dysplasia)

2- Reversible injury

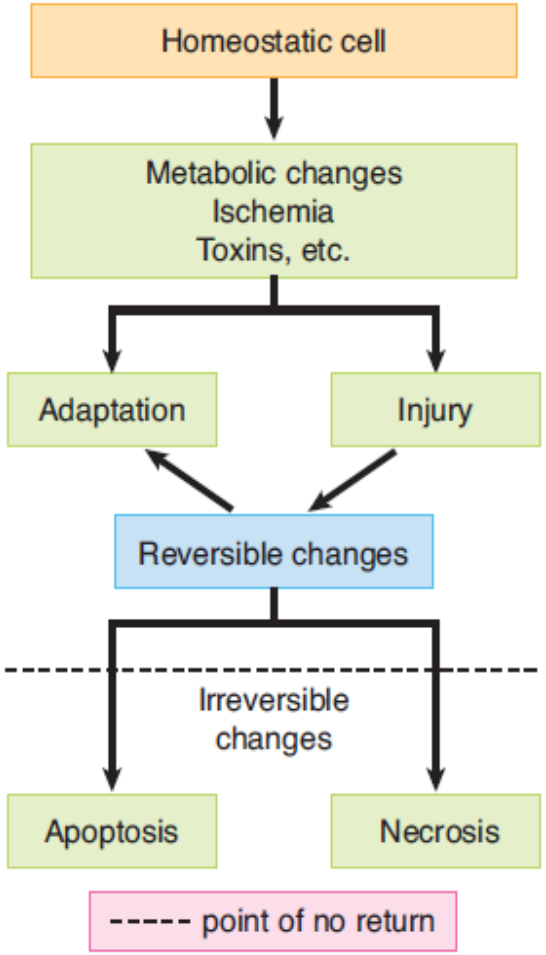
3- Irreversible injury

4- Cell death (necrosis, apoptosis, or necroptosis).

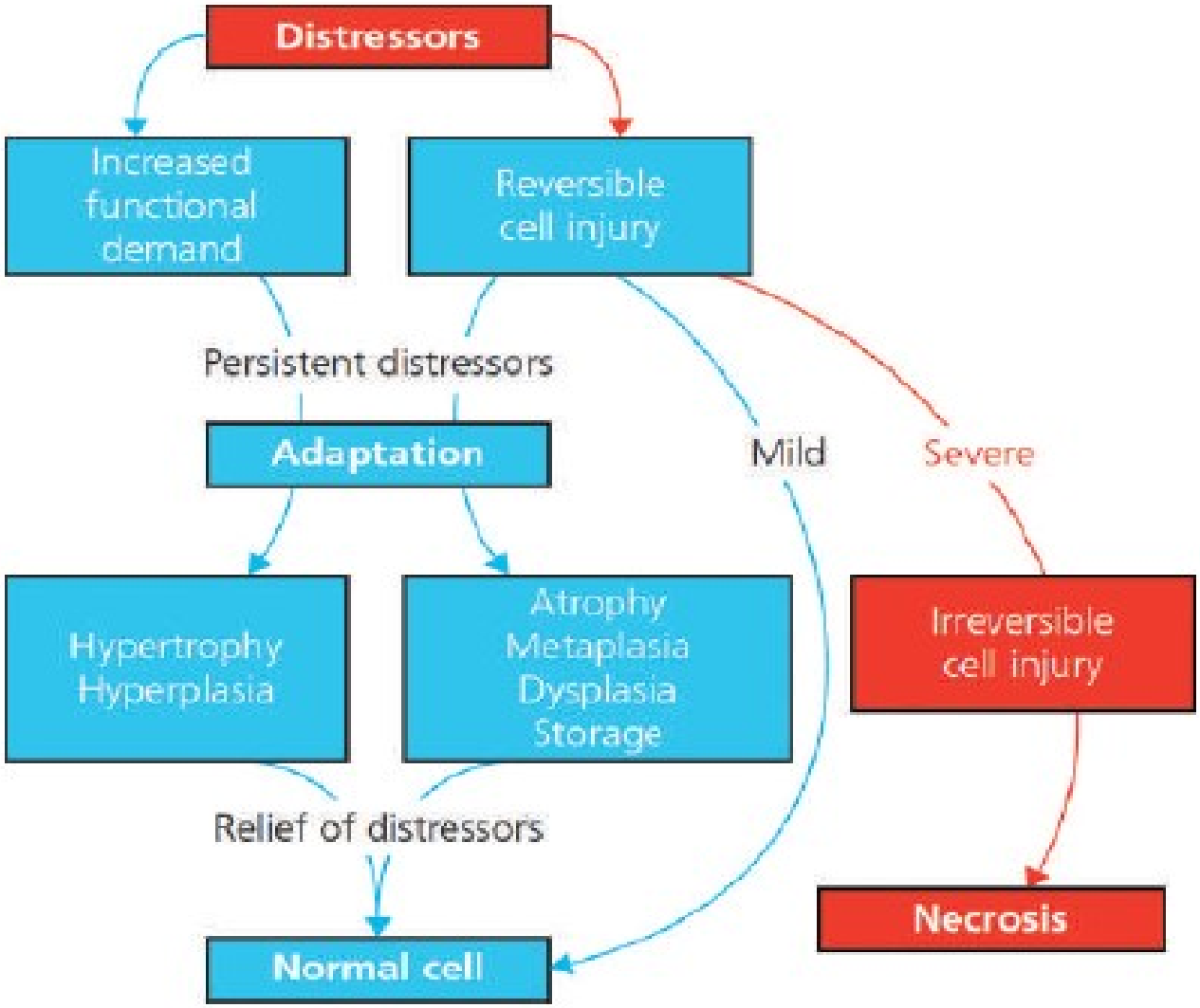
- **Cellular injury** can occur as a result of trauma, infection, ischemia, and exposure to toxins.
- Many disease processes begin with cellular injury.
- The environment around cells is dynamic and constantly changing. In this fluid environment, cells are exposed to numerous stimuli and stresses, some of which may be injurious.

Cellular responses to injury (continued)

- *In order for cells to survive, they must have the ability to **adapt** to variable conditions.*
- **This process of adaptation can involve changes in cellular size, cell number or cell type.**
- Adaptive changes may be physiologic and benefit the individual or be pathologic and detrimental to the individual.

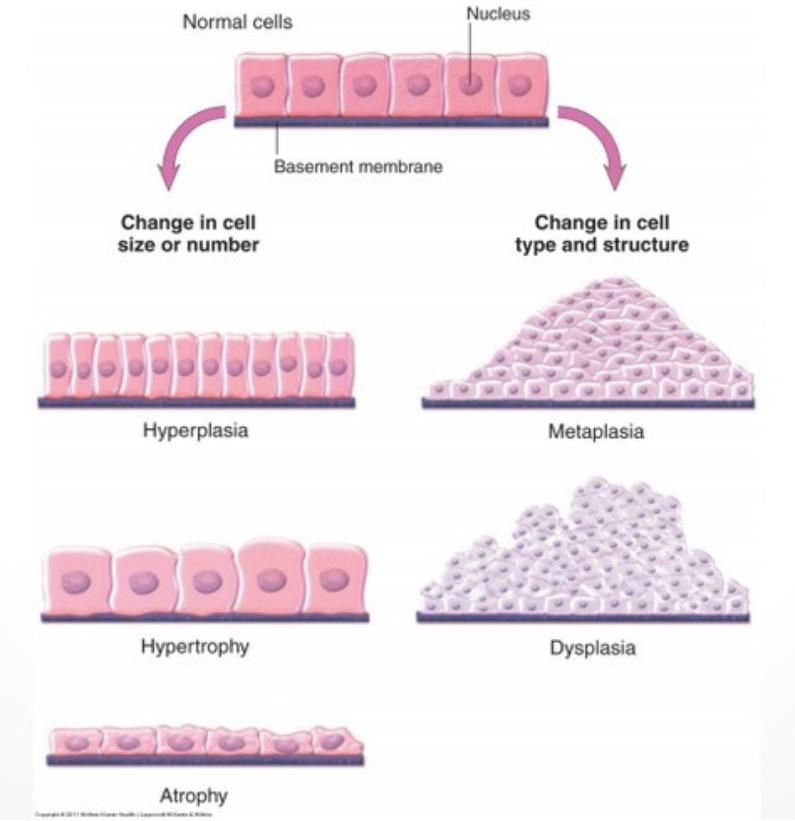


Cell injury (continued)



A- Cellular adaptation

- Cellular adaptation occurs when cells change in response to changes in their environment.
- Reference: https://quizlet.com/143680550/cellular-adaptations-flash-cards/

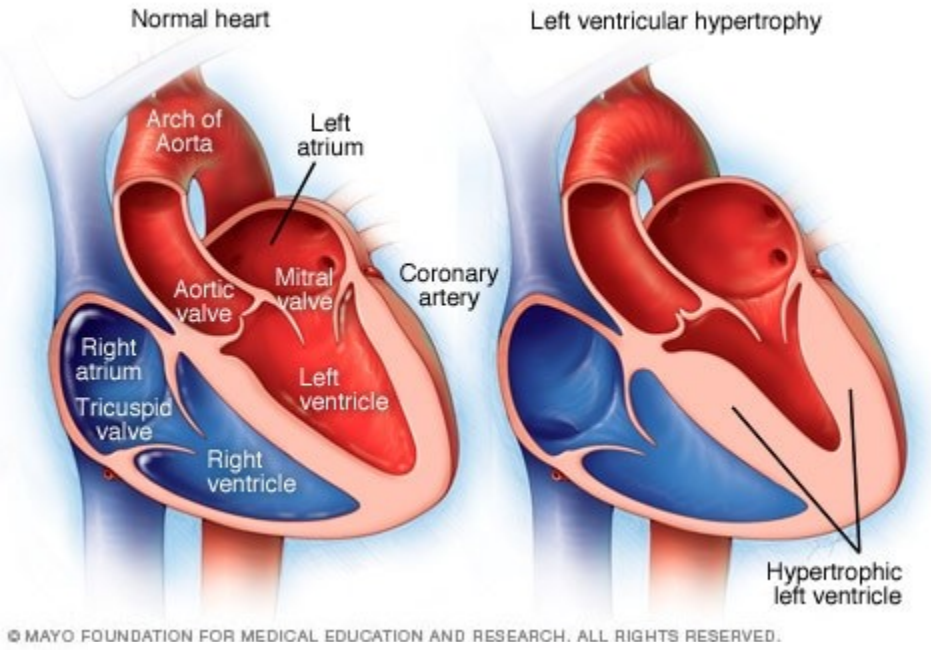


Cellular adaptation
1- Atrophy

- Atrophy is characterized by a decrease in size of a cell or tissue
- Causes of atrophy may include prolonged bed rest, disuse of limbs or tissue, poor tissue nutrition and ischemia
- Decreased size results in decreased oxygen consumption and metabolic needs of the cells and may increase the overall efficiency of cell function.
- Atrophy is generally a reversible process, except for atrophy caused by loss of nervous innervation to a tissue

Cellular adaptation
2- Hypertrophy

- Hypertrophy is characterized by an increase in cell size and tissue mass but not cell number
- Hypertrophy may be a normal physiologic response to increased workload, such as the increase in muscle mass that is seen with exercise.
- It may, however, be pathologic as in the case of the cardiac hypertrophy that is seen with prolonged hypertension. Such pathologic hypertrophy is often irreversible.
- Hypertrophy may also be a compensatory process. When one kidney is removed, for example, the remaining kidney hypertrophies to increase its functional capacity
- ***Often occurs when a cell or tissue is exposed to an increased workload***
- ***Occurs in tissues that cannot increase cell number as an adaptive response***



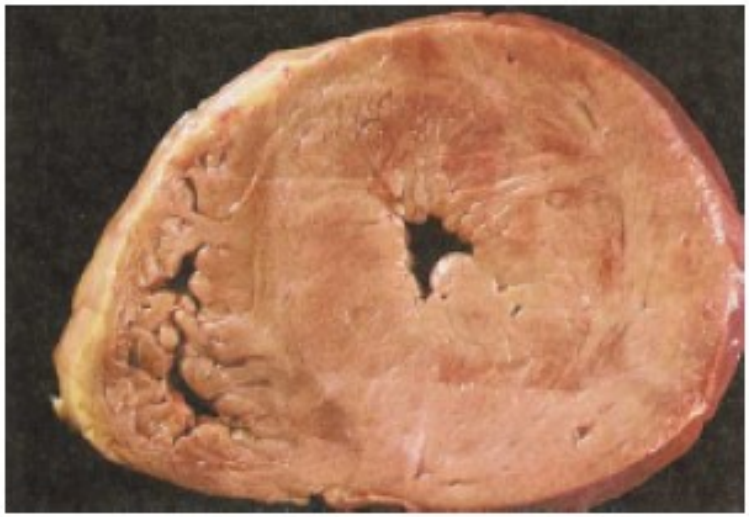
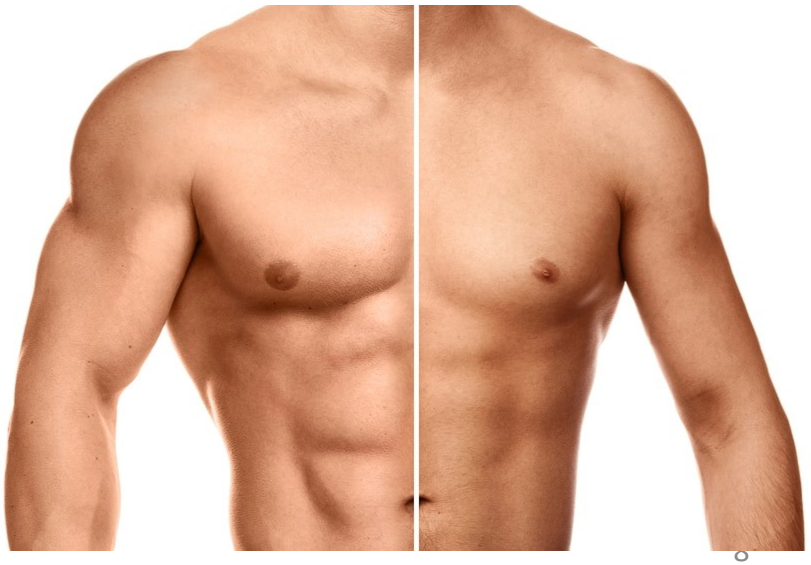


FIGURE 5-2 Myocardial hypertrophy. Cross-section of the heart in a patient with long-standing hypertension. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 9]. Philadelphia: Lippincott-Raven)

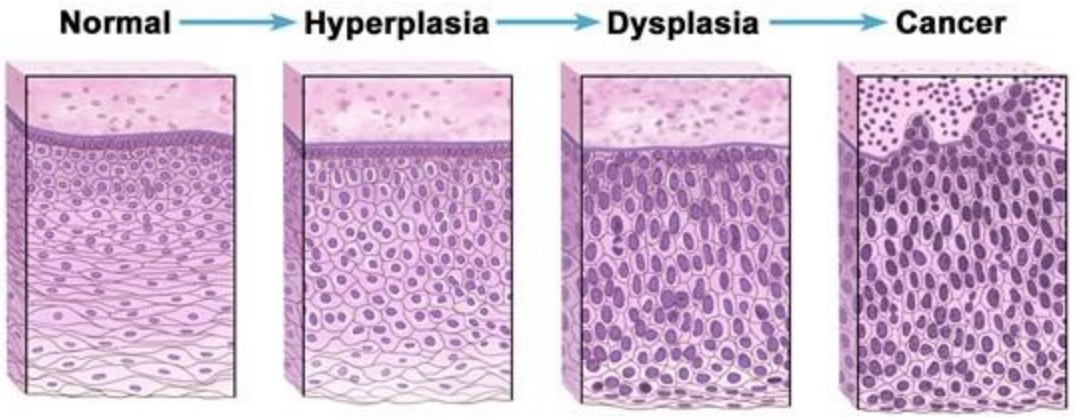


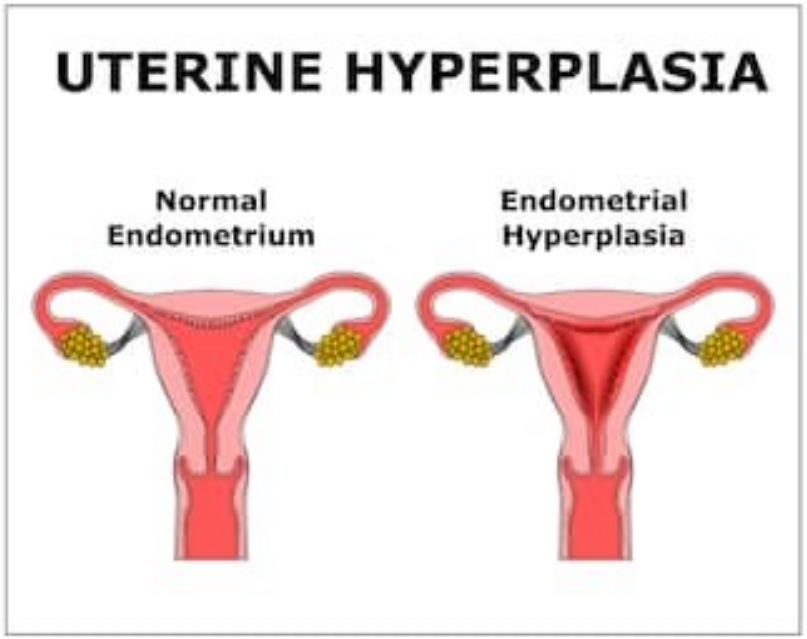
Cellular adaptation

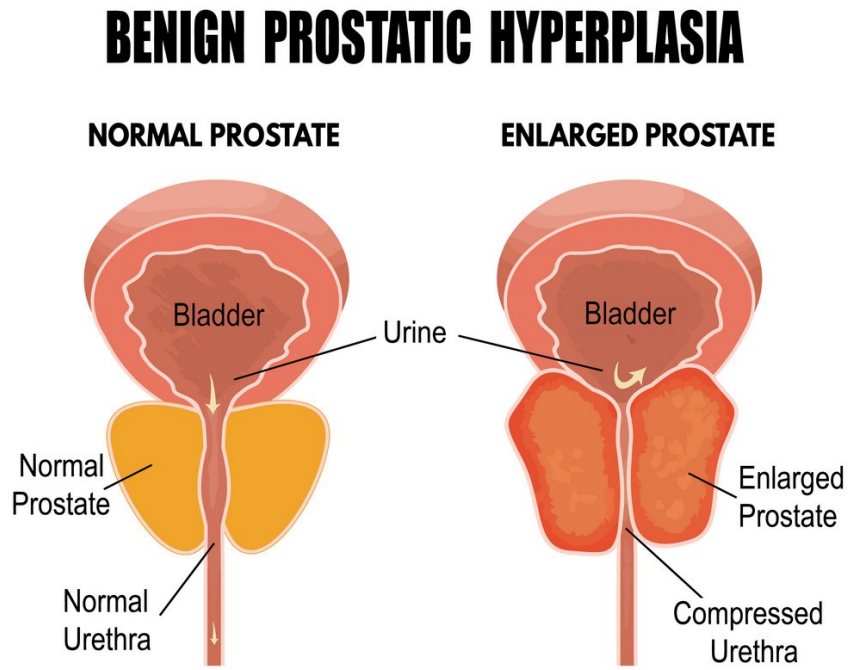
3- Hyperplasia

- Hyperplasia is characterized by an increase in the number of cells in an organ or tissue.
- Hyperplasia can only occur in cells capable of mitosis (therefore not in muscle or nerve cells).
- Hyperplasia may be a normal process, as in the breast and uterine hyperplasia that occurs during pregnancy,
- OR pathologic, such as gingival hyperplasia (overgrowth of gum tissues) that may be seen in certain patients receiving the drug phenytoin.
- As with hypertrophy, hyperplasia may also be a compensatory mechanism. For example, when a portion of the liver is surgically removed, the remaining hepatocytes (liver cells) increase in number to preserve functional capacity of the liver.

Normal Cells May Become Cancer Cells



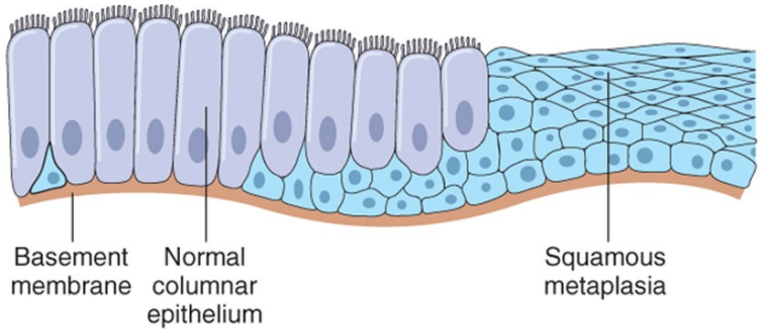




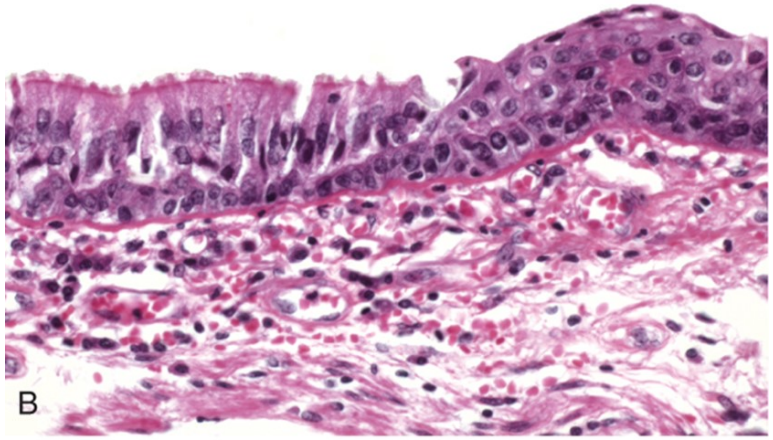
Cellular adaptation
4- Metaplasia

- Metaplasia is characterized by the conversion of one cell type to another that might have a better chance of survival under certain circumstances.
- Metaplasia often occurs in response to chronic irritation or inflammation.

- An example of metaplasia can be observed in the respiratory passages of chronic cigarette smokers. Following years of exposure to irritating cigarette smoke, the ciliated columnar epithelium lining the respiratory passages gradually converts to stratified squamous epithelium. Although the stratified squamous cells may be better able to survive the constant irritation of cigarette smoke, they lack the cilia of the columnar epithelial cells that are necessary for clearing particulates from the surfaces of the respiratory passages.

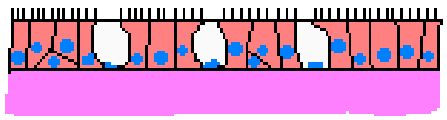


A

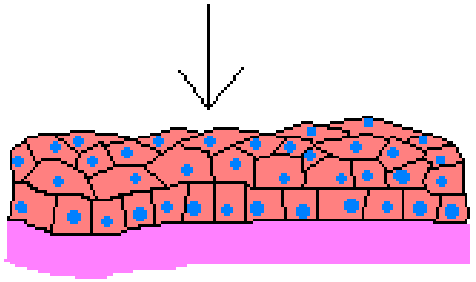


B

Metaplasia



Pseudostratified respiratory



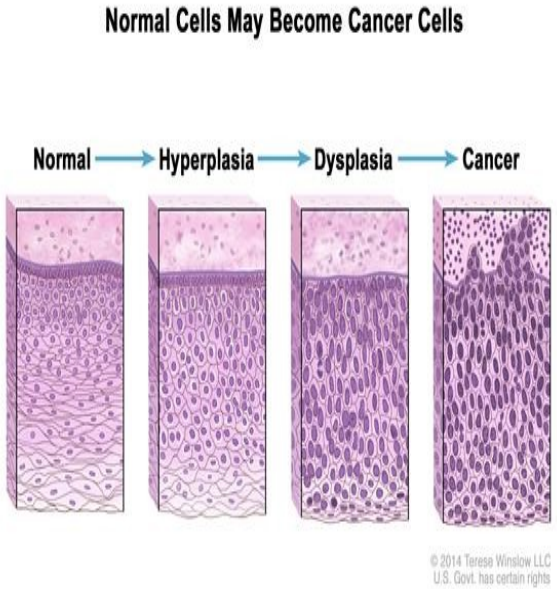
Stratified squamous

One mature tissue type replaces another mature tissue type.

Cellular adaptation

5- Dysplasia

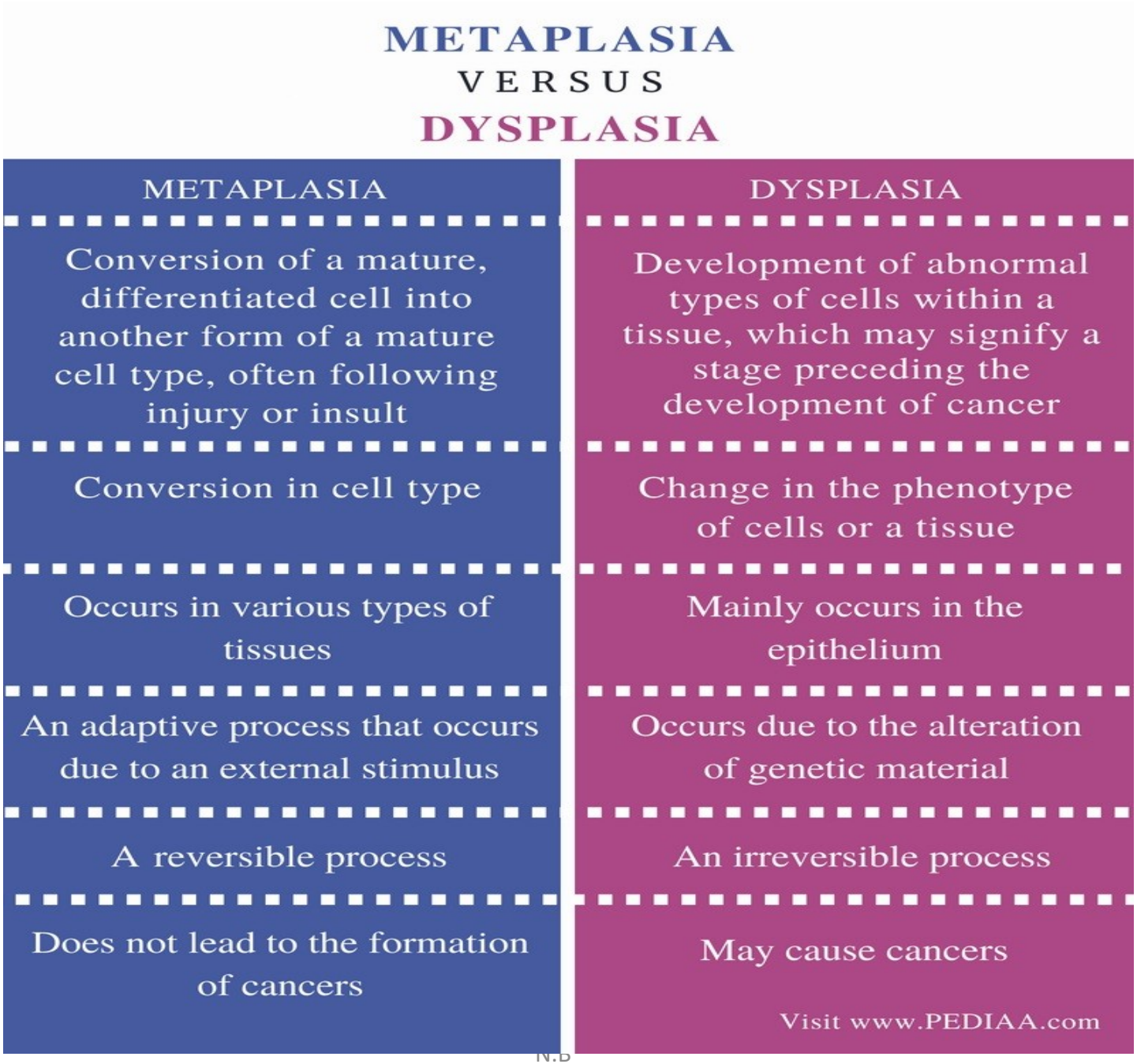
- Dysplasia is characterized by a derangement of cell growth that leads to tissues with cells of varying size, shape and appearance.
- It is not a true adaptive change but more so a pathologic change
- Dysplasia generally occurs in response to chronic irritation and inflammation.
- Dysplastic changes may be a precursor to cancer in certain instances such as in the cervix, GI or respiratory tract.



Reference: https://medicine.nus.edu.sg/pathweb/wp-content/uploads/2017/05/Table-1-Adaptive-Responses-14jblpm.jpg

Table 1: Types of Adaptive Responses

Adaptive response	Definition	Mechanism	Example (Physiologic)	Example (Pathologic)
Hypertrophy	Increase in size of cells, resulting in an increase in organ size. *Note: This can occur together with hyperplasia.*	Increased functional demand; simulation by hormones or growth factors → increased synthesis of structural components of cells	Eg. "Pumping iron" → increased work demand in skeletal muscle → muscle size increase due to hypertrophy Eg. Pregnancy – Hormone-induced uterine smooth muscle hypertrophy	Eg. Hypertension → increased workload in left ventricular myocardium → left ventricular hypertrophy
Hyperplasia	Increase in the number of cells in an organ/tissue, usually resulting in increased mass of the organ/tissue. *Note; This may occur together with hypertrophy.*	Only possible in cells capable of dividing. 1. Mature cells - Growth factor driven cell proliferation 2. Increased cell output from stem cells	Eg Compensatory hyperplasia – Liver cell proliferation after partial hepatectomy	Eg. Hormone-driven – Increased oestrogen levels gives rise to endometrial hyperplasia in the uterus
Atrophy	Reduced size of an organ or tissue resulting from a decrease in cell size and number.	Reduced metabolic activity → decreased protein synthesis. Nutrient deficiency, disuse → increased protein degradation in cells.	Normal embryonic development – thyroglossal duct atrophy during fetal development	Atrophy of disuse – Immobility (eg. limb in cast after fracture) leads to skeletal muscle atrophy due to decreased workload
Metaplasia	Reversible change from one mature (differentiated) cell type to another. This may be because certain cell types withstand adverse environment better than others.	Cytokines, growth factors, extracellular matrix components → reprogramme genetic expression in stem cells present in normal tissues → differentiate along a different pathway		Eg. Cigarette smoking → chronic irritation in respiratory tract → columnar epithelium changes to squamous epithelium (squamous metaplasia)


METAPLASIA
VERSUS
DYSPLASIA
METAPLASIA
Conversion of a mature, differentiated cell into another form of a mature cell type, often following injury or insult
Conversion in cell type
Occurs in various types of tissues
An adaptive process that occurs due to an external stimulus
A reversible process
Does not lead to the formation of cancers
DYSPLASIA
Development of abnormal types of cells within a tissue, which may signify a stage preceding the development of cancer
Change in the phenotype of cells or a tissue
Mainly occurs in the epithelium
Occurs due to the alteration of genetic material
An irreversible process
May cause cancers
Visit www.PEDIAA.com

B- Mechanisms Of Cell Injury

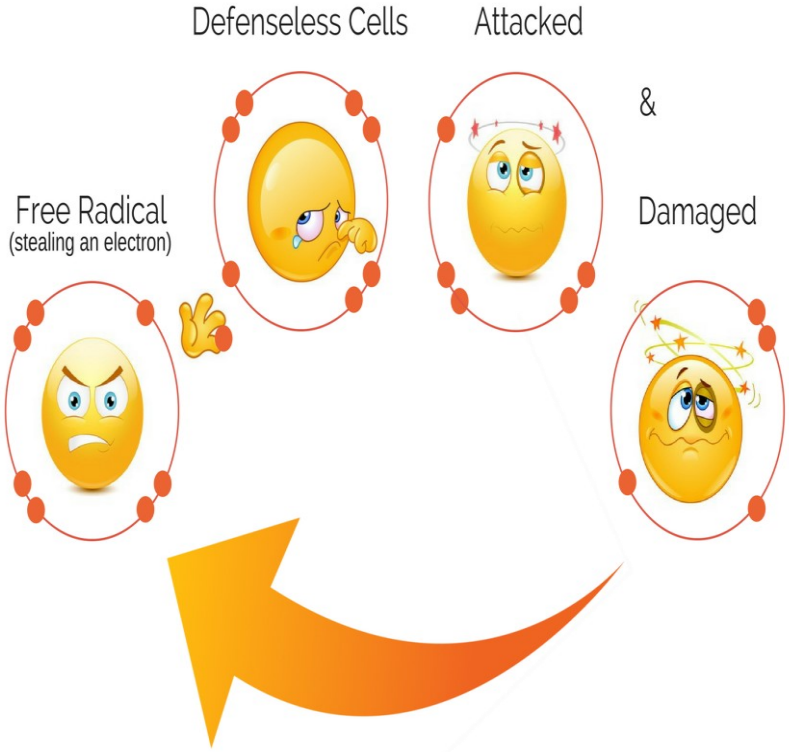
- Cell injury can occur in a number of different ways. The extent of injury that cells experience is often related to the ***intensity and duration*** of exposure to the injurious event or substance.
- Cellular injury may a **reversible** process, in which case the cells can recover their normal function, or **irreversible** and lead to cell death.
- Although the causes of cellular injury are many (see Table 1.1), the underlying mechanisms of cellular injury usually fall into one of two categories, ***free radical injury* or *hypoxic injury*.**

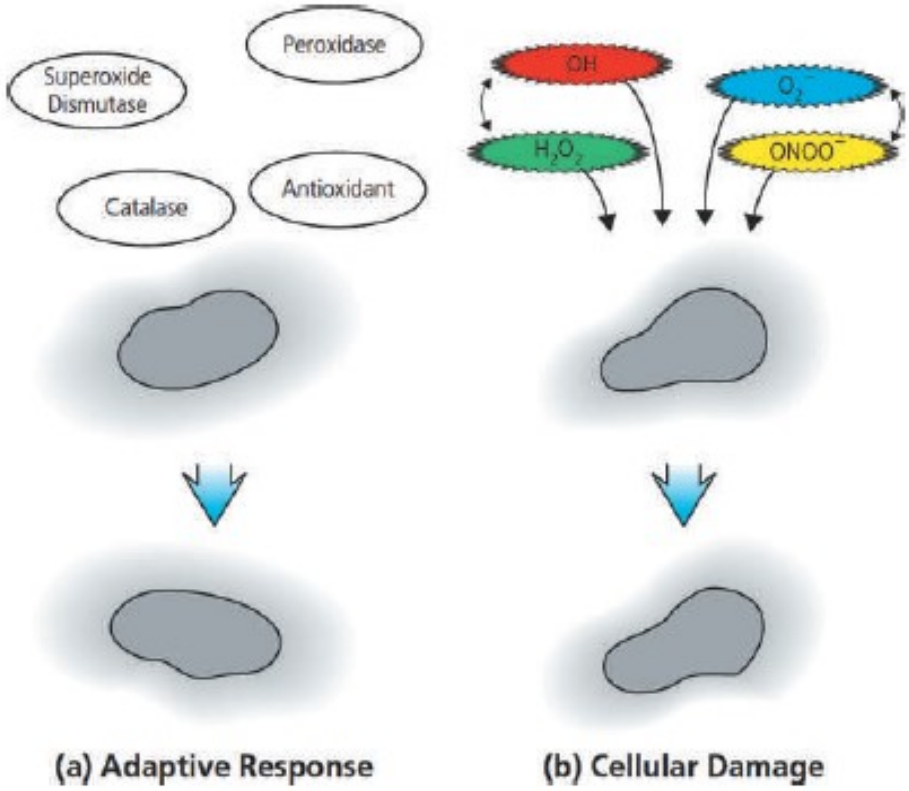
Table 1.1 Classification of Cellular Injury

Physical injury
Mechanical trauma
Temperature extremes (burn injury, frostbite)
Electrical current
Chemical injury
Chemicals, toxins, heavy metals, solvents, smoke, pollutants, drugs, gases
Radiation injury
Ionizing radiation — gamma rays, X rays
Non-ionizing radiation — microwaves, infrared, laser
Biologic agents
Bacteria, viruses, parasites
Nutritional injury
Malnutrition
Obesity

1. *Free Radical Injury*

- Free radicals are highly reactive chemical species that have one or more unpaired electrons in their outer shell.
- Examples of free radicals include *superoxide* (O2 –), *hydroxyl radicals* (OH), and *hydrogen peroxide* (H2O2).
- Free radicals are generated as **by-products** of normal cell metabolism and are **inactivated** by **free radical scavenging enzymes** within the body such as *catalase* and *glutathione peroxidase*.
- When excess free radicals are formed from exogenous sources or the free radical protective mechanisms fail, injury to cells can occur


Defenseless Cells
Attacked
&
Damaged
Free Radical
(stealing an electron)


Peroxidase
Superoxide Dismutase
Catalase
Antioxidant
OH
O_2^-
H_2O_2
$ONOO^-$
(a) Adaptive Response
(b) Cellular Damage

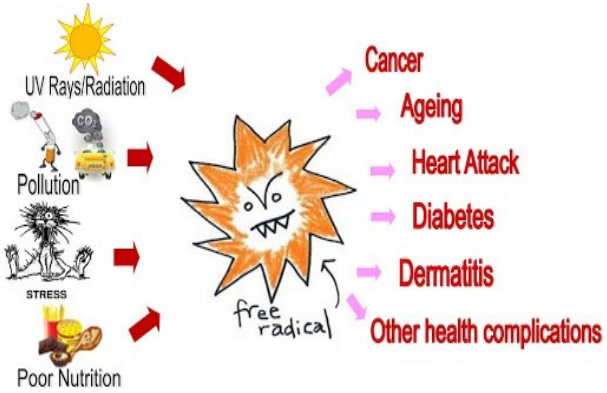
1. *Free Radical Injury (continued)*

Free radicals are highly reactive and can injure cells through:

– Peroxidation of membrane lipids

– Damage of cellular proteins

– Mutation of cellular DNA



- Exogenous sources of free radicals include tobacco smoke, organic solvents, pollutants, radiation, and pesticides

- Free radical injury has been implicated as playing a key role in the normal aging process as well as in a number of disease states such as diabetes mellitus, cancer, atherosclerosis, Alzheimer's disease, and rheumatoid arthritis

2. *Hypoxic Cell Injury*

Hypoxia is a lack of oxygen in cells and tissues that may result from *ischemia*, or *poor oxygenation of blood*

- During periods of hypoxia, aerobic metabolism of the cells begins to fail.

→ The cellular injury process may be **reversible**, **if** oxygen is quickly restored; or irreversible, and lead to cell death.

→ Certain tissues such as the brain are particularly sensitive to hypoxic injury. Death of brain tissues can occur only 4–6 minutes after hypoxia begins

2. *Hypoxic Cell Injury (continued)*

<u>This loss of aerobic metabolism leads to:</u>

1- Dramatic decreases in ATP production within the cells. Hypoxic cells begin to swell as energy-driven processes (such as ATP-driven ion pumps) begin to fail. → *Na/K pump → Na + H2O are trapped inside the cell*

2- The pH of the extracellular environment begins to **decrease** as waste products such as lactic acid, a product of anaerobic metabolism, begin to accumulate.

3- The loss of ionic balance in hypoxic cells can also lead to the accumulation of intracellular calcium, which is normally closely regulated within cells.

→ There are a number of ***calcium-dependent protease*** enzymes present within cells that become activated in the presence of excess calcium and begin to digest important cellular constituents

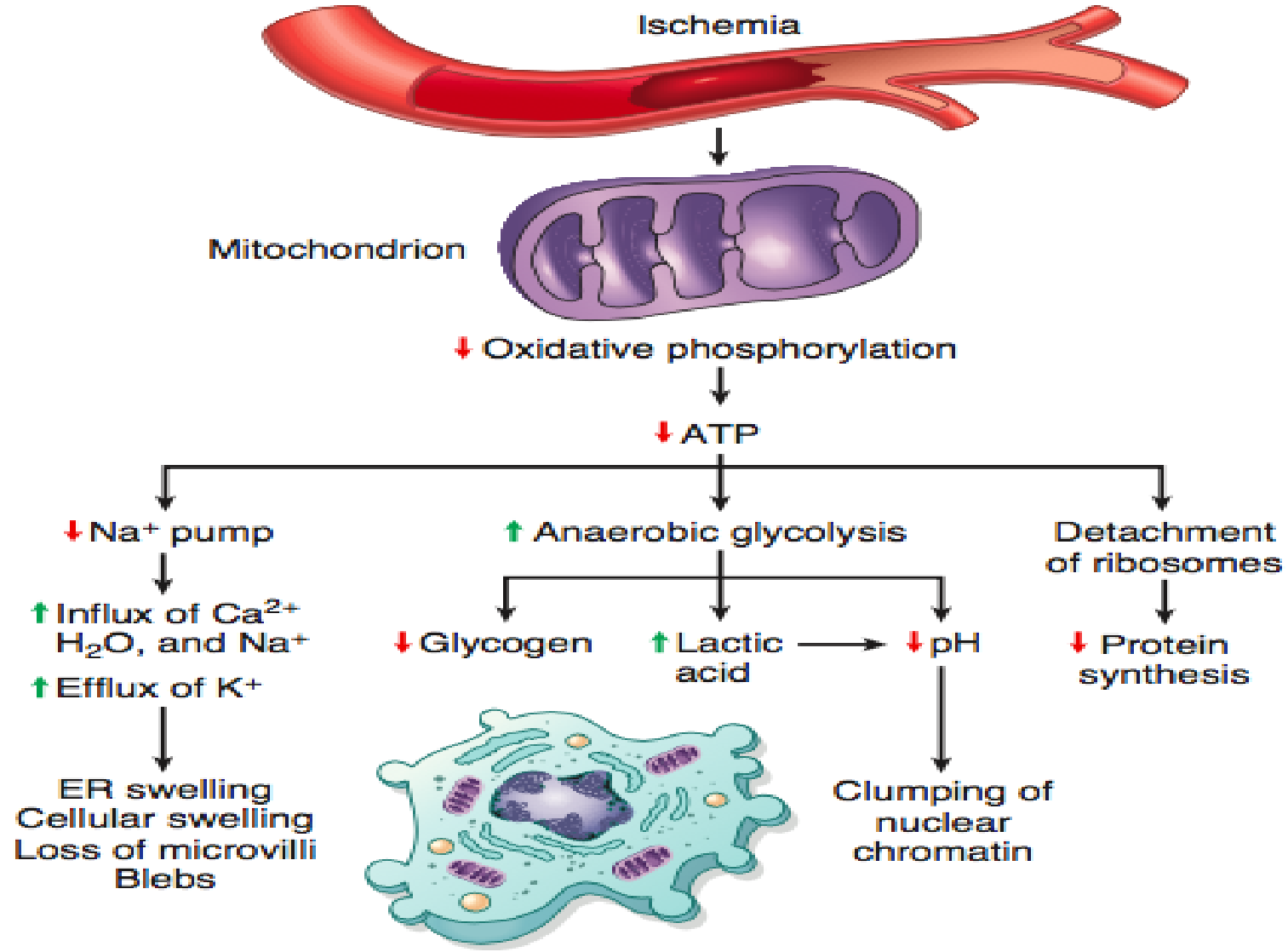


Figure 2-17 Functional and morphologic consequences of decreased intracellular adenosine triphosphate (ATP) during cell injury. The morphologic changes shown here are indicative of reversible cell injury. Further depletion of ATP results in cell death, typically by necrosis. ER, Endoplasmic reticulum.

C- Manifestations of cellular injury

1. *Cellular Swelling*:

- Caused by an accumulation of water due to the failure of ATP-driven ion pumps. Breakdown of cell membrane integrity and accumulation of cellular electrolytes may also occur
- Cellular **swelling** is considered to be a reversible change

2. *Cellular Accumulations*:

- In addition to water, injured cells can accumulate a number of different substances as metabolic and transport processes begin to fail.
- Substances that can be accumulated in injured cells may include fats, proteins, glycogen, calcium, uric acid and certain pigments such as melanin
- These accumulations are generally reversible but can indicate a greater degree of cellular injury. Accumulation of these substances can be so marked that enlargement of a tissue or organ may occur.

An example of this is the fatty accumulation (steatosis) that can develop in the liver of an alcoholic as the liver becomes injured and its function impaired

D- Cell death

- Cells death falls into two main categories, *apoptosis* and *necrotic cell death*.

- Gangrene is the clinical term used when a large area of tissue undergoes necrosis

D- Cell death

1. *APOPTOSIS:*

- **Apoptosis is a controlled, genetically "preprogrammed" cell death that occurs with aging and normal wear and tear of the cell.**
- Apoptosis may be a mechanism to eliminate worn out or genetically damaged cells. → Certain viral infections (e.g., the Epstein-Barr virus) may activate apoptosis within an infected cell, thus killing both the host cell and infecting virus
- Apoptosis may involve the activation of "suicide genes" that turn on in response to certain chemical signals and lead to cell lysis and destruction through the activation of cellular enzymes called *caspases*
- *It has been theorized that cancer may arise as a failure of normal apoptosis in damaged or mutated cells*
- A physiologic example of normal apoptosis would be the sloughing (shedding) of the endometrium during the menstrual cycle

D- Cell death

2. NECROTIC CELL DEATH:

- Involves the unregulated, enzymatic digestion ("autolysis") of a cell and its components
- Occurs as a result of irreversible cellular injury
- Different types of tissues tend to undergo different types of necrosis.

Types of cellular necrosis

Three main types of necrosis have been identified

1- Liquefaction Necrosis: → shape of the organ is not preserved→ cavity

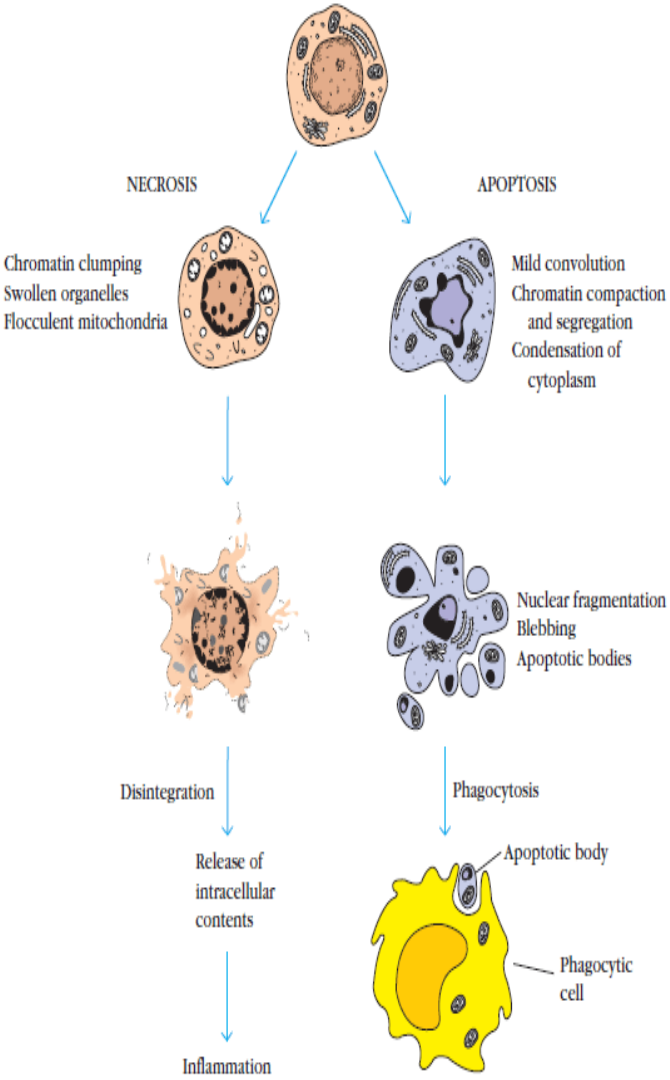
- Digestive enzymes released by necrotic cells soften and liquefy dead tissue
- Occurs in tissues, such as the brain, that are rich in hydrolytic enzymes

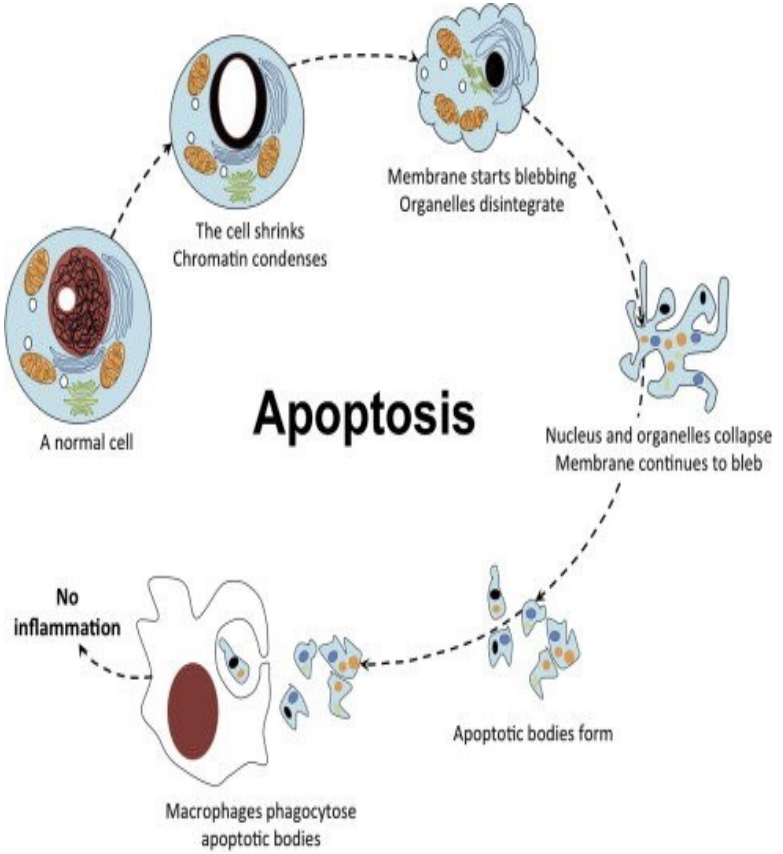
2- Coagulative Necrosis: → shape of the organ is preserved

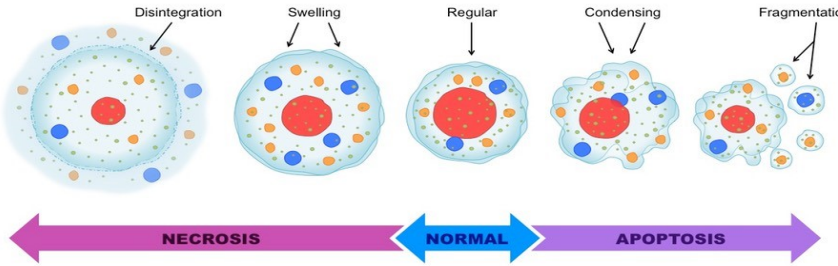
- Dead tissues appear firm, gray, and slightly swollen
- Often occurs when cell death results from ischemia and hypoxia; the acidosis that accompanies ischemia denatures cellular proteins and hydrolytic enzymes
- E.g., seen with myocardial infarction

3- Caseous Necrosis:

- Dead tissue takes on a crumbly, "cheese-like" appearance; dead cells disintegrate, but their debris is not fully digested by hydrolytic enzymes
- Occurs in conditions like tuberculosis where there is prolonged inflammation and immune activity


NECROSIS
APOPTOSIS
Chromatin clumping
Swollen organelles
Flocculent mitochondria
Mild convolution
Chromatin compaction and segregation
Condensation of cytoplasm
Nuclear fragmentation
Blebbing
Apoptotic bodies
Disintegration
Phagocytosis
Release of intracellular contents
Apoptotic body
Phagocytic cell
Inflammation


Apoptosis
A normal cell
The cell shrinks
Chromatin condenses
Membrane starts blebbing
Organelles disintegrate
Nucleus and organelles collapse
Membrane continues to bleb
Apoptotic bodies form
No inflammation
Macrophages phagocytose apoptotic bodies


Disintegration
Swelling
Regular
Condensing
Fragmentation
NECROSIS
NORMAL
APOPTOSIS

D- Cell death

3. GANGRENE:

- Gangrene is the clinical term used when **a large area of tissue undergoes necrosis**
- Gangrene may be classified as being "*dry gangrene*" or "*wet gangrene*."
- **Dry gangrene**, the skin surrounding the affected area shrinks, wrinkles and turns black. There is generally a clear line of demarcation between living and dead tissue.
- **Wet gangrene** presents with an area that is cold, wet from tissue exudates and swollen. Wet gangrene often occurs when venous return from the affected tissue is lacking and a clear line of demarcation is generally not evident between living and dead tissue.
- **A *gas gangrene*** may also occur if the area of necrosis becomes infected with bacteria (often *Clostridium*) that produce hydrogen sulfide gas as a by-product

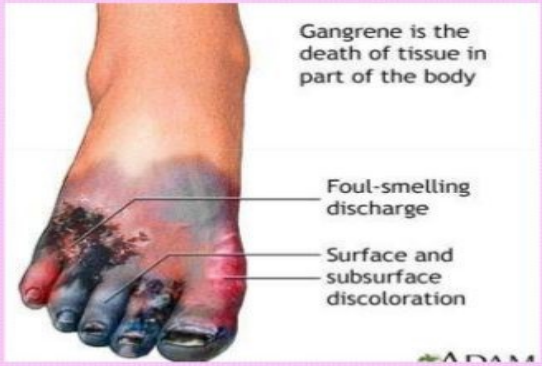
DOI: 10.2147/DMSO.S164199

Feature	Dry gangrene	Wet gangrene	Gas gangrene
Site	Commonly limbs	More common in bowel	Limbs
Mechanism	Arterial occlusion	More commonly venous obstruction	Gases produced by *Clostridium* bacteria
Macroscopy	Organ dry, shrunken, and black	Part moist, soft, swollen, rotten, and dark	Organ red, cold, pale, numb, shriveled up, and auto-amputation
Putrefaction	Limited due to very little blood supply	Marked due to congestion of organ with blood	Marked due to bacteria and infiltration of gases produced by them in tissues
Line of demarcation	Present at the junction between healthy and gangrenous parts	No clear-cut line of demarcation	No clear-cut line of demarcation
Bacteria	Bacteria fail to survive	Numerous present	Major cause
Prognosis	Generally better due to little septicemia	Generally poor due to profound toxemia	Generally poor due to quick spread to the surrounding tissues

Note: Data from NHP.gov.in.[11]

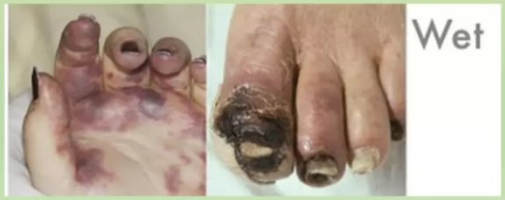
Types of Gangrene

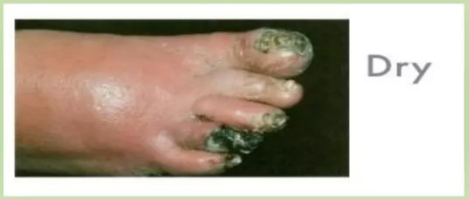
- 2 main forms of gangrene
- **Dry gangrene**
- **Wet Gangrene**
  - **Gas gangrene**: a kind of wet gangrene

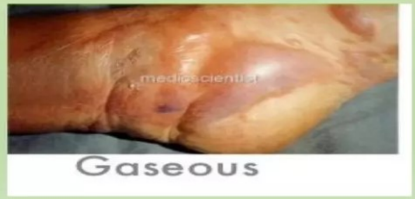


Types

- Wet gangrene ? =
  - Appears moist , results from severe bacterial infection superimposed on necrosis. Found on internal organs and exposed parts
- Dry gangrene ? =
  - Appears dry ,wrinkled and discolored , results from gradual obstruction of blood supply. Found on exposed parts.
- Gas gangrene ? =
  - Wet gangrene + gas formation , Found on exposed parts.







E- Tissue repair

- Injured or damaged tissues can be repaired in one of two ways, by:

1- *regeneration* or through

2- *connective tissue replacement*.

- The mechanism used for repair will depend upon the type of cells that were injured.

→Certain cells in the body are fully or partially capable of regenerating after an injury,

→whereas other cells types are not and can only be replaced with connective (scar) tissue.

E- Tissue repair
1. Repair by Regeneration

- With regeneration, the injured tissue is repaired with the same tissue that was lost.
- A full return of function occurs and afterwards there is little or no evidence of the injury.
- Repair by regeneration can only occur in *labile cells* (cells that continue to divide throughout life) or *stable cells* (cells that have stopped dividing but can be induced to regenerate under appropriate conditions of injury).

- Examples of labile cells include those of the skin, oral cavity and bone marrow.
- Examples of stable cells include hepatocytes of the liver.
- Certain cell such as nerve cells and cardiac muscle cells are *fixed* cells and cannot undergo regeneration under any circumstances. These cell types are only capable of repairing injuries through connective tissue replacement.

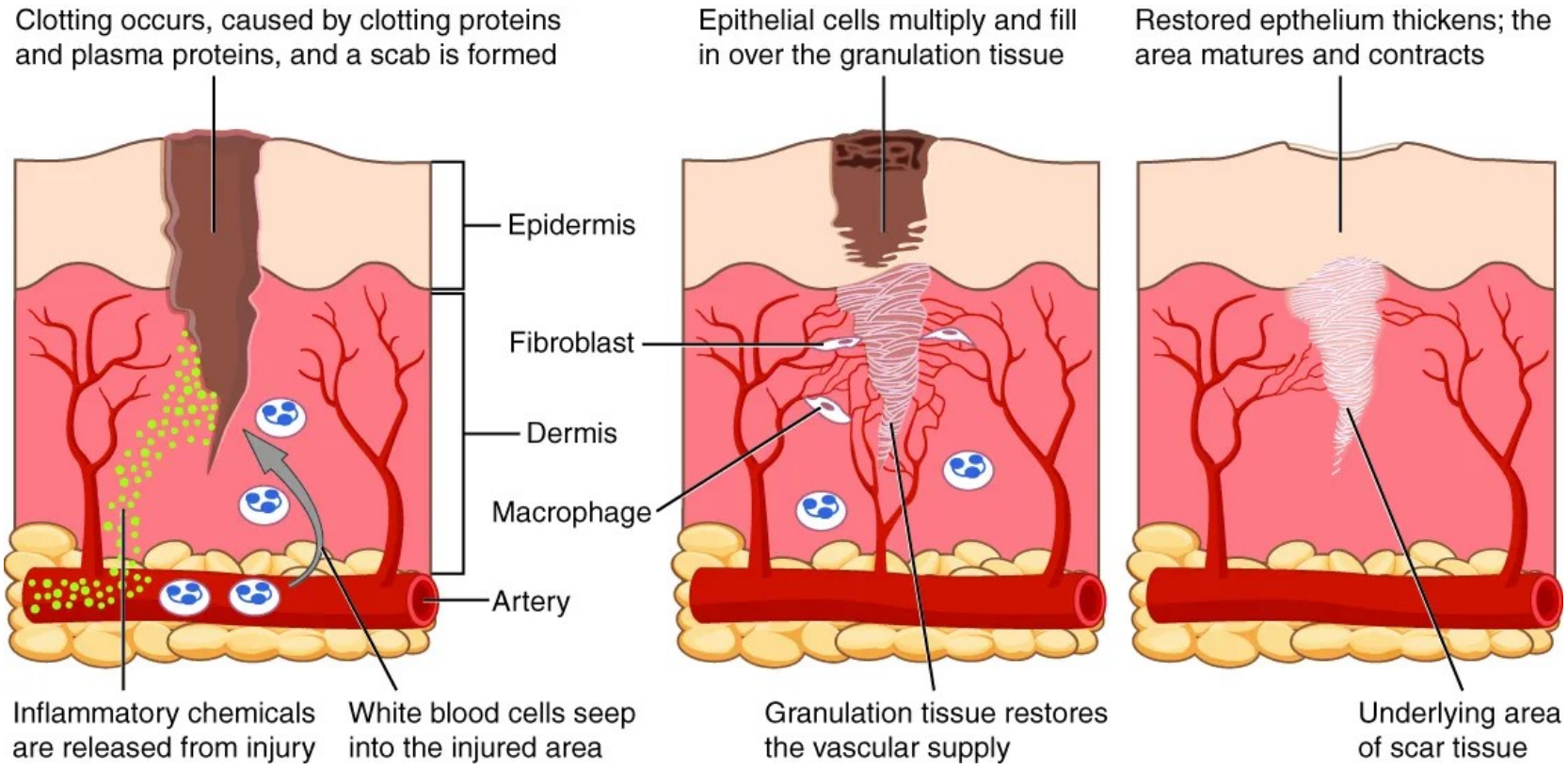
Regeneration	Replacement by connective tissue
•Injured tissue is repaired with the **same tissue** that was lost.	•Involves the **replacement of functional tissue with nonfunctional connective tissue (collagen)**.
•**Full return of function**	•**Full function does not return**
•Occur in **labile cells** (cells that continue to divide throughout life) or **stable cells** (cells that have stopped dividing but can be induced to regenerate under appropriate conditions of injury)	•**Scar tissue** remains as evidence of the injury.
	•Certain cells such as nerve cells and cardiac muscle cells are **fixed cells** and cannot undergo regeneration under any circumstances.
•**labile cells** include those of the skin, oral cavity and bone marrow •**stable cells** include hepatocytes of the liver.	

E- Tissue repair
2. Repair by Connective Tissue Replacement

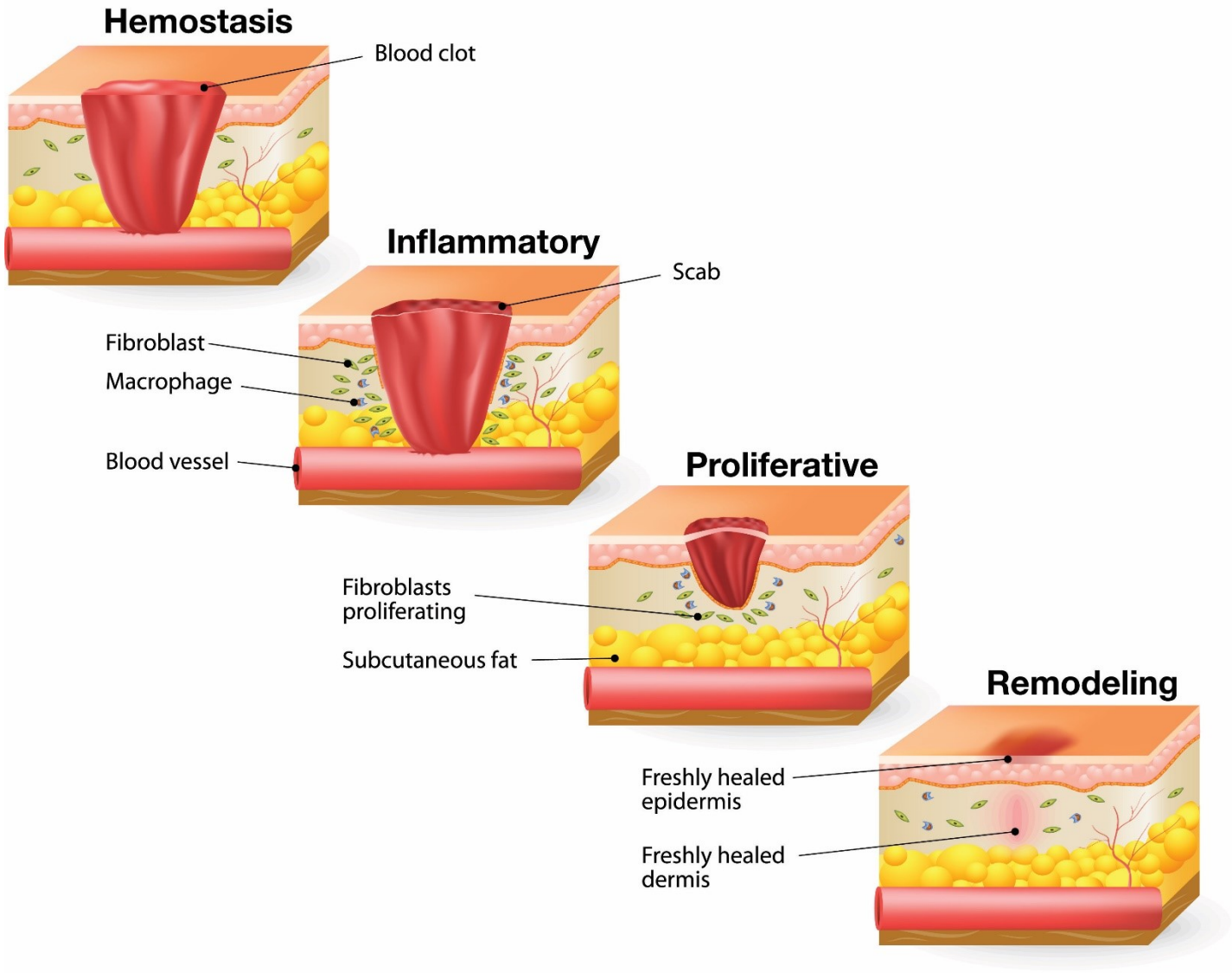
- Involves the replacement of functional tissue with nonfunctional connective tissue (collagen).
- Full function does not return to the injured tissue.
- Scar tissue remains as evidence of the injury.

F- Steps in tissue (wound) repair

- Clean, neat wounds such as surgical incisions are said to heal by *primary intention* because they tend to heal quickly and evenly with a minimum of tissue loss.
- *Sutures* are used to bring the edges of wounds together to facilitate the process of healing by primary intention.
- Larger, open types of wounds may take considerably longer to heal and are said to heal by *secondary intention*. In secondary intention, the edges of the wound are not able to come into contact with one another and, as a result, the gap must be filled by granulation tissue.
- These larger wounds often require a significant amount of tissue replacement, take longer to heal and tend to be associated with more obvious scar formation.
- In general, tissue repair involves three stages, the *inflammatory* stage, the *proliferative* stage, and the *maturational/remodeling* stage:


Clotting occurs, caused by clotting proteins and plasma proteins, and a scab is formed
Epithelial cells multiply and fill in over the granulation tissue
Restored epthelium thickens; the area matures and contracts
Epidermis
Fibroblast
Dermis
Macrophage
Artery
Inflammatory chemicals are released from injury
White blood cells seep into the injured area
Granulation tissue restores the vascular supply
Underlying area of scar tissue

WOUND HEALING



F- Steps in tissue (wound) repair
1. Inflammatory Stage

- Starts with the formation of a fibrin blood clot to stem bleeding from the injury.
- Infiltration of phagocytic white blood cells occurs.
- Neutrophils tend to arrive first followed by larger macrophages.
- The arriving macrophages produce *growth factors* that stimulate growth of epithelial cells around the wound as well as *angiogenesis* (the formation of new blood vessels).

F- Steps in tissue (wound) repair
2. Proliferative Stage

- Over the first 1–3 days after the initial injury, *fibroblasts* in and around the injured tissue proliferate in response to growth factors such as *fibroblast-activating factor* produced by infiltrating macrophages.
- These activated fibroblasts produce the collagen that will repair the bulk of the wound.
- Epithelial cells at the margins of the wound also proliferate in response to macrophage-produced growth factors.
- Angiogenesis is likewise occurring at this point.
- The soft, pink tissue that forms during this phase of wound healing is referred to as *granulation tissue*.
- Over time, the collagen that is laid down adds mechanical strength to the repaired area. *Contraction* of the wound occurs over the course of 1–2 weeks as the edges of the wound grow closer to one another.
- *Suturing* a wound can facilitate healing by primary intention and minimize scar tissue formation by bringing the margins of the wound into close contact with one another.

F- Steps in tissue (wound) repair
3. Maturation and Remodeling

- Over the course of one to several months following the injury, there is continued synthesis of collagen in conjunction with removal of old collagen by *collagenase* enzymes.
- This *remodeling* of the collagen is designed to maximize strength of the repair.
- Capillaries that were present in the repaired area begin to disappear, leaving an avascular scar.
- The maturation and remodeling phase of the healed wound may continue for a number of years; however, for larger wounds, the final healed scar will never have the full tensile strength that the original tissue had prior to the injury.
- A number of factor can impair the wound healing process (see Table 1.7)

Table 1.7 *Factors that impair wound healing*

- Malnutrition
- Poor blood flow and hypoxia (*hyperbaric oxygen* may be used to facilitate wound healing)
- Impaired immune response (immunosuppressive drugs, diseases affecting immune function such as HIV and diabetes)
- Infection of wound
- Foreign particles in the wound
- Old age (decreased immune activity, poor circulation, poor nutrition)

G- Inflammation and Tissue repair

- ✓Inflammation is a defensive host response to foreign invaders and necrotic tissue, but it is itself capable of causing tissue damage.

- ✓The main components of inflammation are:

1. Vascular reaction
2. Cellular response

- ✓Both are activated by mediators derived from plasma proteins and various cells.
- ✓Although inflammation helps clear infections and noxious stimuli and initiates repair, the inflammatory reaction and the subsequent repair process can cause considerable harm. It is itself capable of causing tissue damage.

Steps of the inflammatory response

The steps of the inflammatory response can be remembered as the five rules:

(1) Recognition of the injurious agent,
(2) Recruitment of leukocytes
(3) Removal of the agent
(4) Regulation (control) of the response
(5) Resolution (repair).

Sequence of Events in (Acute) Inflammation
A- Vascular changes

- The vascular changes in acute inflammation are characterized by **increased blood flow** secondary to arteriolar and capillary bed dilation (erythema and warmth).
- Increased vascular permeability, as a consequence of either widening of interendothelial cell junctions of the venules or direct endothelial cell injury, results in an exudate of protein-rich extravascular fluid (tissue edema).

Sequence of Events in (Acute) Inflammation
<u>B-Cellular events:</u>

- Emigration of the leukocytes from the microcirculation and accumulation in the focus of injury (cellular recruitment and activation).
- The principal leukocytes in acute inflammation are **neutrophils**.

→ Neutrophils:

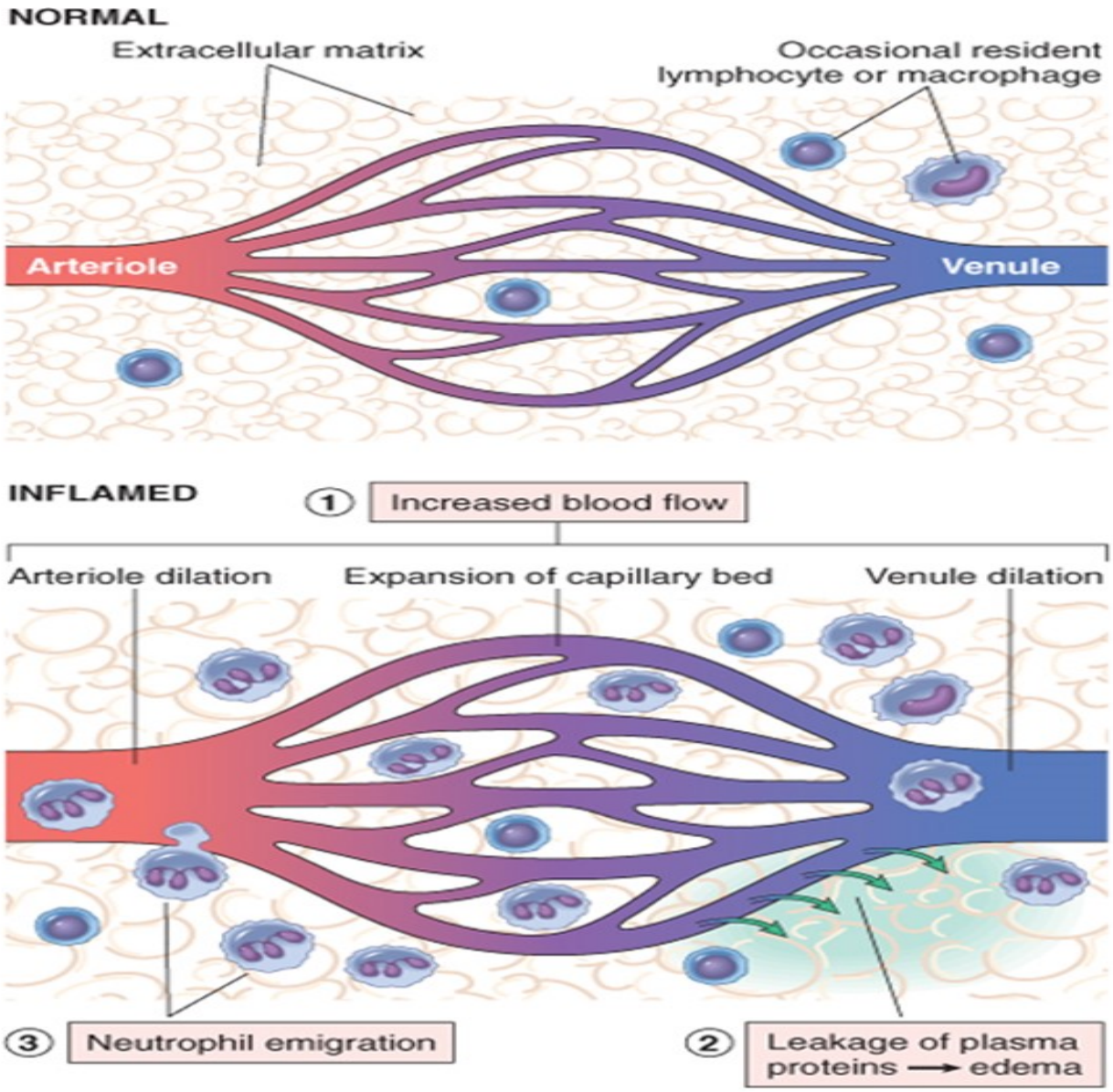
✓ *Adhere to the endothelium via adhesion molecules and then leave the microvasculature and migrate to the site of injury under the influence of chemotactic agents.*

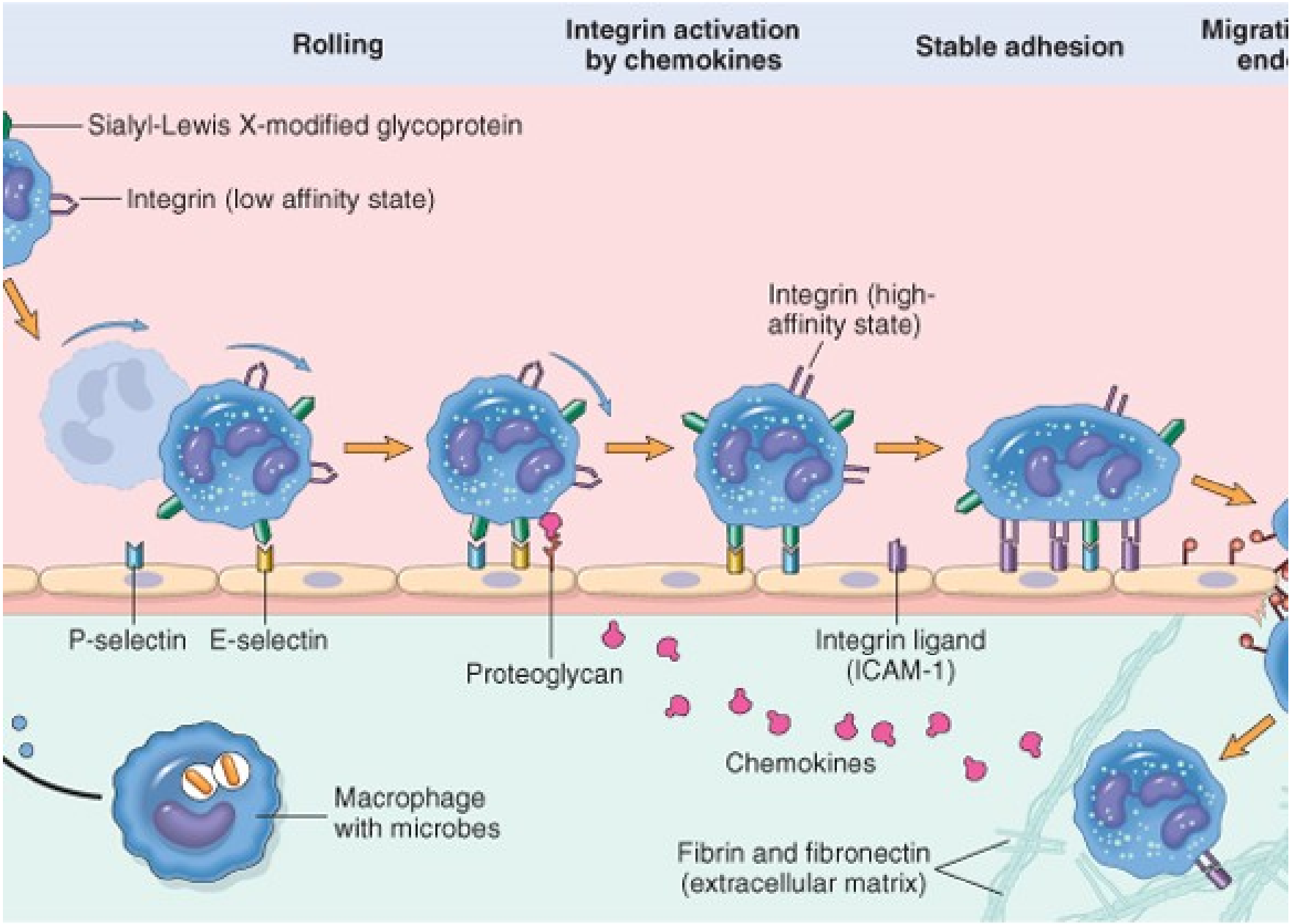
→ Phagocytosis:

✓ *Killing, and degradation of the offending agent follow.*

✓ *Leukocyte products (microbicidal substances) include: lysosomal enzymes and reactive oxygen species(ROS) and nitrogen species (NO).*

- **Genetic or acquired defects in leukocyte functions give rise to recurrent infections.**





The outcome of acute inflammation

1. Removal of the exudate with restoration of normal tissue architecture (resolution).

2. Transition to chronic inflammation.

3. Extensive destruction of the tissue resulting in scarring.

Chronic inflammation

- Chronic inflammation is inflammation of prolonged duration (weeks to months to years) in which active inflammation, tissue injury, and healing proceed simultaneously.

- **<u>Caused by:</u>**

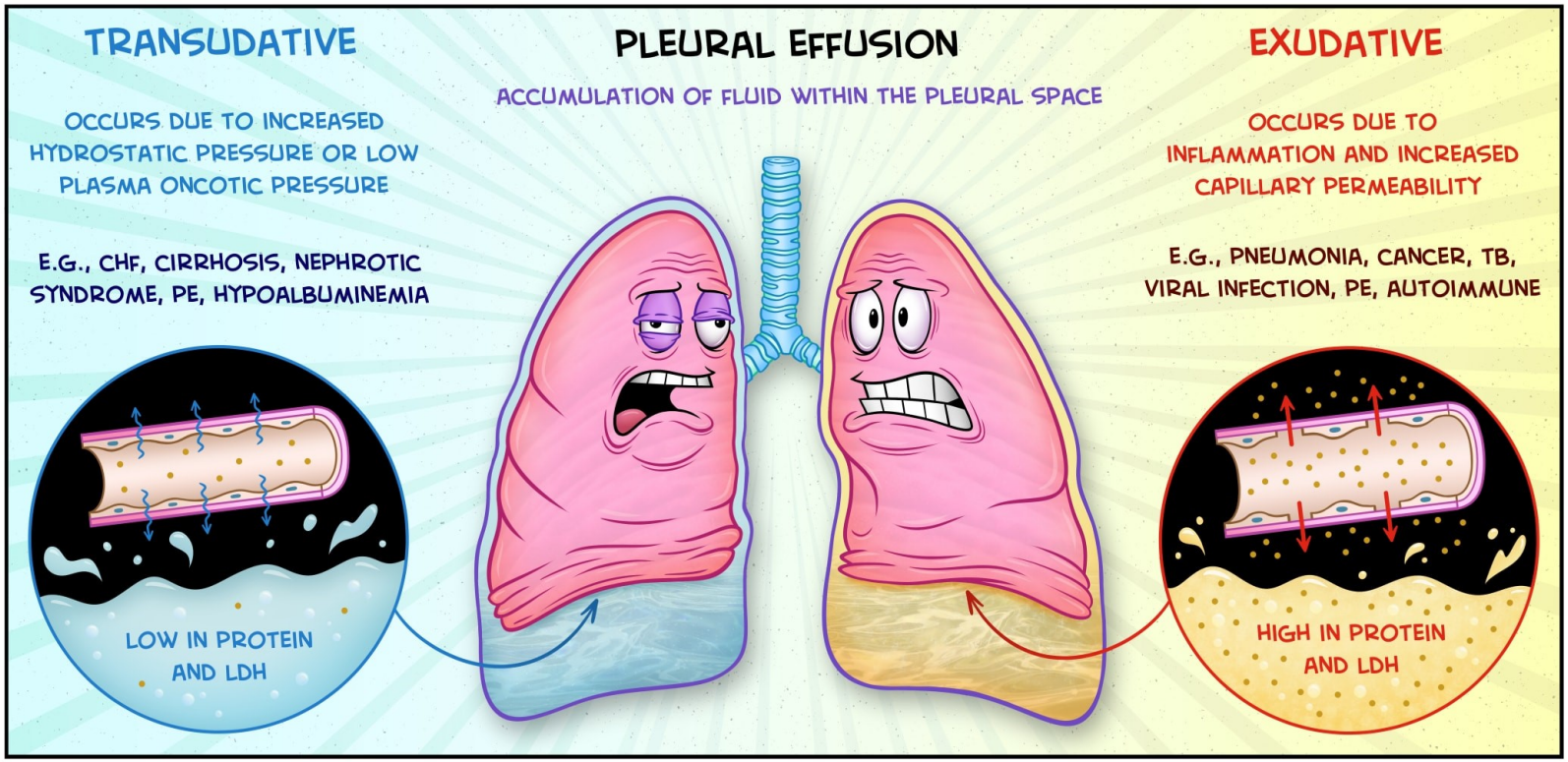
- ✓ Persistent infections: microbes that resist elimination,
- ✓ Autoimmune diseases: immune responses against self ,
- ✓ Allergic diseases Immune responses against common environmental antigens,
- ✓ Prolonged exposure to potentially toxic agents (e.g., silica).

H- EDEMA

Edema is the result of the movement of fluid from the vasculature into the interstitial spaces; the fluid may be:

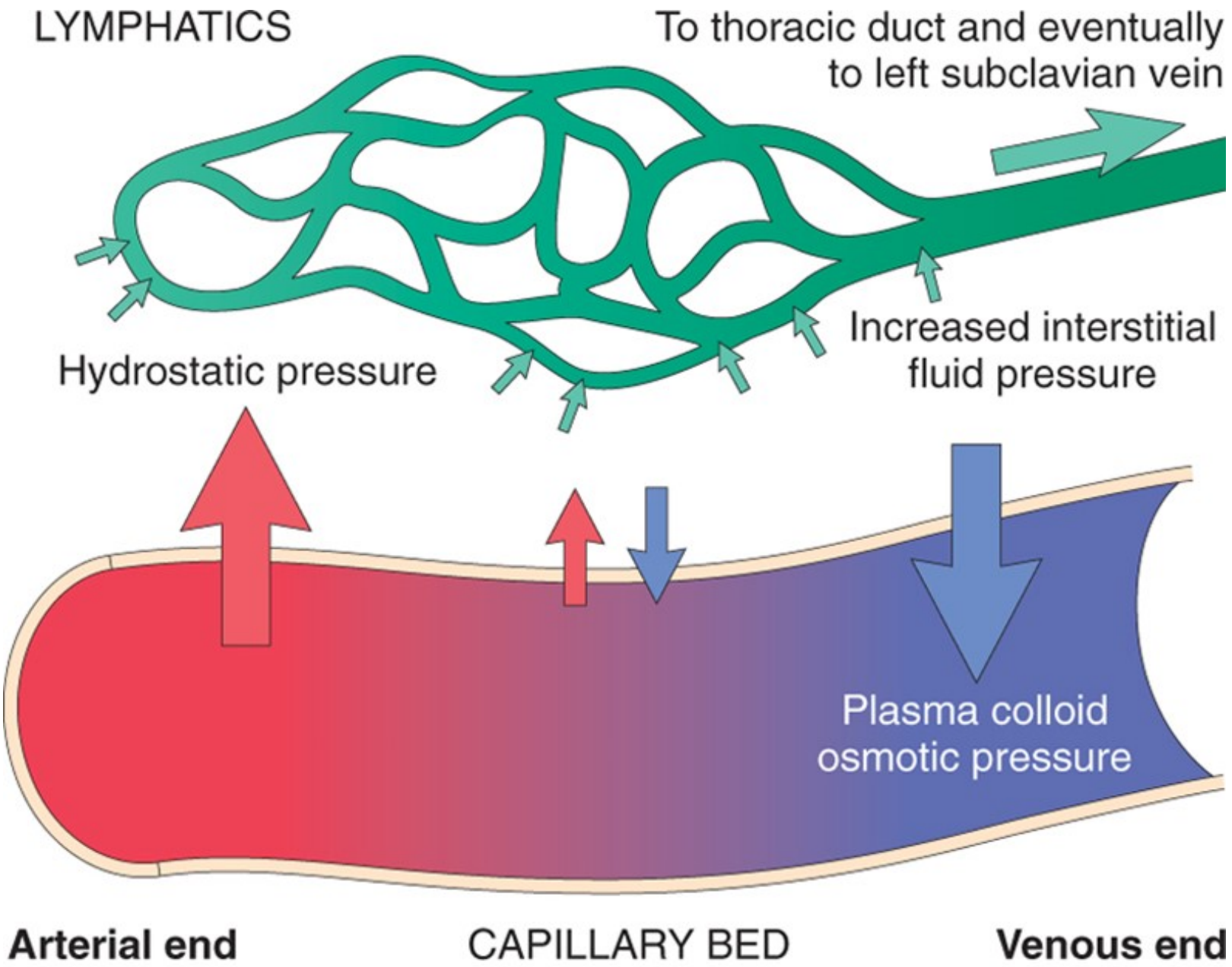
a. Protein-poor (transudate)

b. Protein-rich (exudate).



EDEMA MAY BE CAUSED BY:

1. Increased **hydrostatic pressure** (e.g., heart failure)
2. Increased **vascular permeability** (e.g., inflammation)
3. Decreased **colloid osmotic pressure**, due to reduced plasma albumin:
    A. Decreased synthesis (e.g., liver disease, protein Malnutrition)
    B. Increased loss (e.g., nephrotic syndrome)
4. **Lymphatic obstruction** (e.g., inflammation or neoplasia).
5. **Sodium retention** (e.g., renal failure)



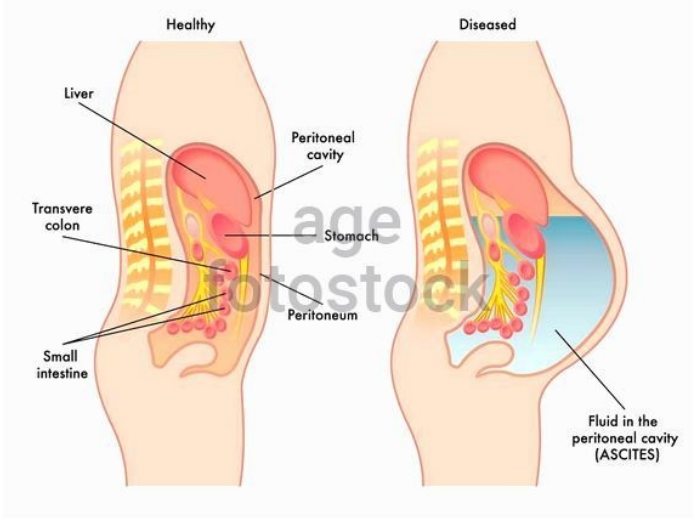
EDEMA (continued)

- Although any organ or tissue in the body may be involved, **edema** is most commonly encountered in subcutaneous tissues, lungs, and brain.

- Fluid collections in different body cavities are variously designated **hydrothorax (**is a type of pleural effusion in which transudate accumulates in the pleural cavity), **hydropericardium**, or **hydroperitoneum** (ascites).

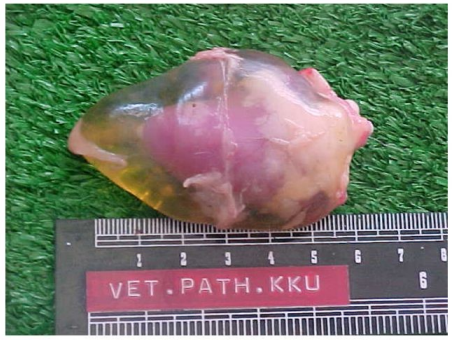
- **Anasarca** is a severe and generalized edema with profound subcutaneous tissue swelling.

ANASARCA



ASCITES

Hydropericardium



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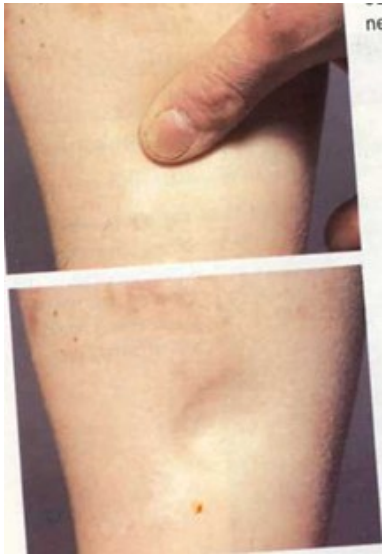

PITTING EDEMA