CELL INJURY-2

ILOs:

- **By the end of this lecture, students should be able to:**
- Define necrosis and apoptosis and its causes.
- Compare and differentiated the morphology of different type of necrosis in variant causes.
- Explain the mechanism of apoptosis and their clinical importance
- Define gangrene and explain its types.

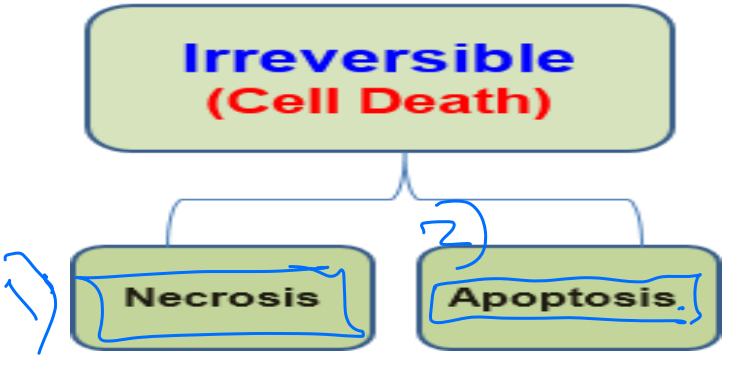
DR.SAJDA GAJDHAR
GENERAL PATHOLOGY

2

Irreversible cell injury (Cell Death)

Irreversible cell injury: Alterations in cell function and structure, which are uncorrectable if the damaging stimulus is removed. Occur in sever & progressive forms of injury.

Form: it has 2 form



1- Necrosis

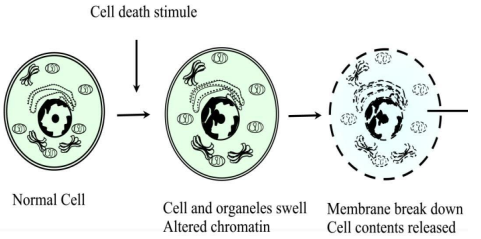
Definition: Local death of a large groups cells within the living body.

1- - Swelling of cell

2- - Rupture of cell membrane → leakage of cellular contents

3 - Induce inflammatory response

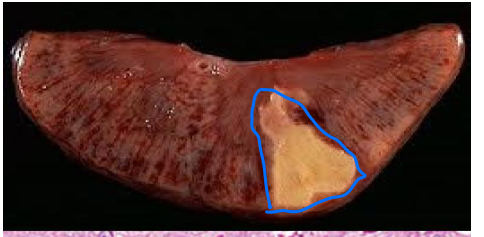
4- - Enzymatic digestion of cells



Pathological picture:

Gross picture:

-Opaque, white area



Microscopic picture:

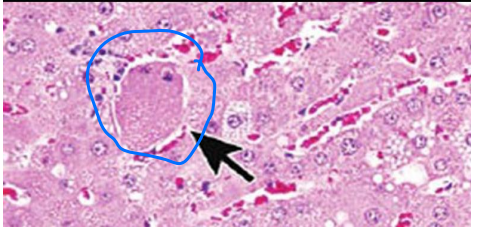
A- Cell: swelling

all Pink

B- Cytoplasmic change

1- Eosinophilic: stained red

2- Indistinct cell membrane.

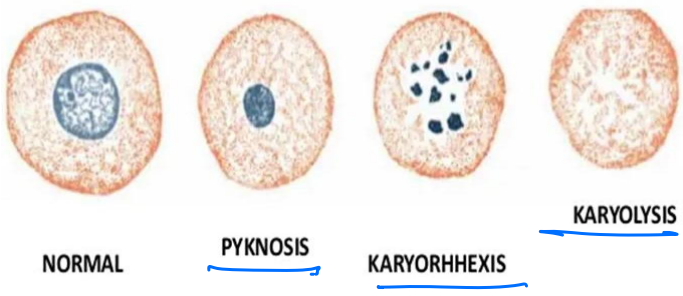


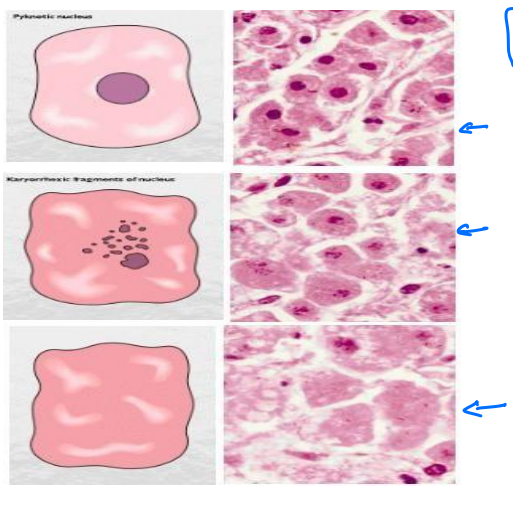
C- Nuclus:

1 ***Pyknosis:*** Nuclear shrinkage with dense chromatin

2 ***Karyorrhexis:*** fragmentation to multiple small fragments

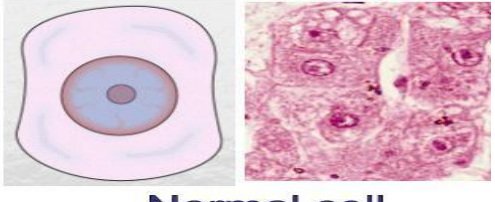
3 ***Karyolysis:*** The nucleus dissolve





1:4

ratio of nucleus to cytoplasm

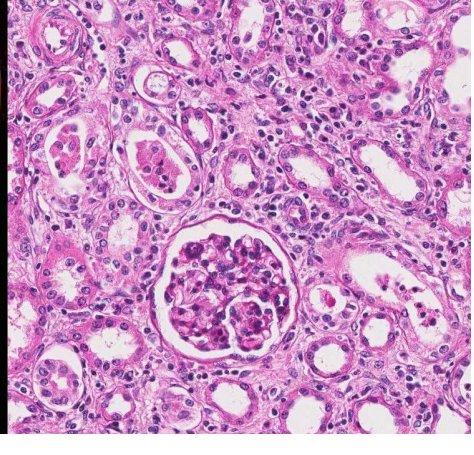


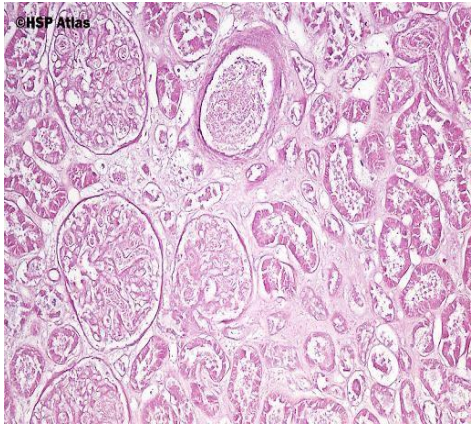
Normal cell

Types of necrosis:

1- Coagulative necrosis:

- **Most common type** of necrosis
- **Cause:** sudden cut of blood supply (ischemia)
- **Site:** in all organs except the brain.
- **Gross picture**: firm and opaque white.
- **Microscopic picture:** Dead tissues is preserved architecture for a span of at least some days with no cell details.





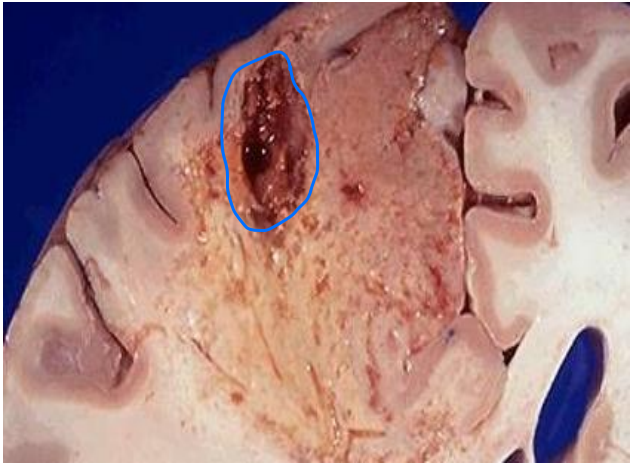
2- Liquefactive necrosis:

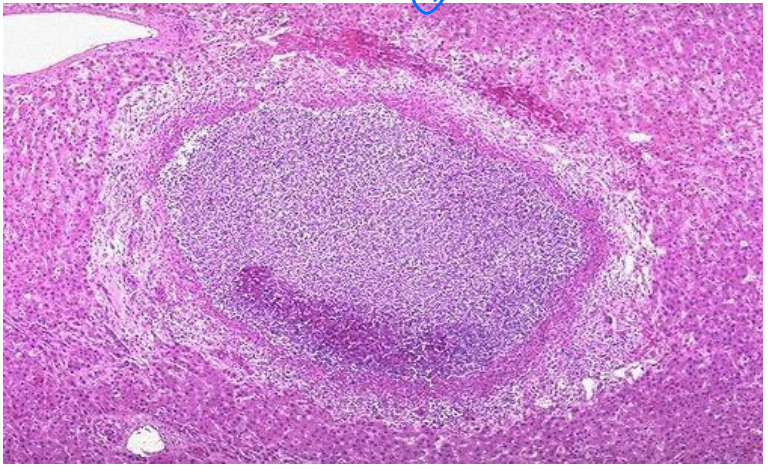
Characterized by: digestion of the dead cells → transformation of the tissue into a liquid viscous mass.

Cause & site:

- CNS (brain and spinal cord)
- Bacterial or fungal infections (Abscess)

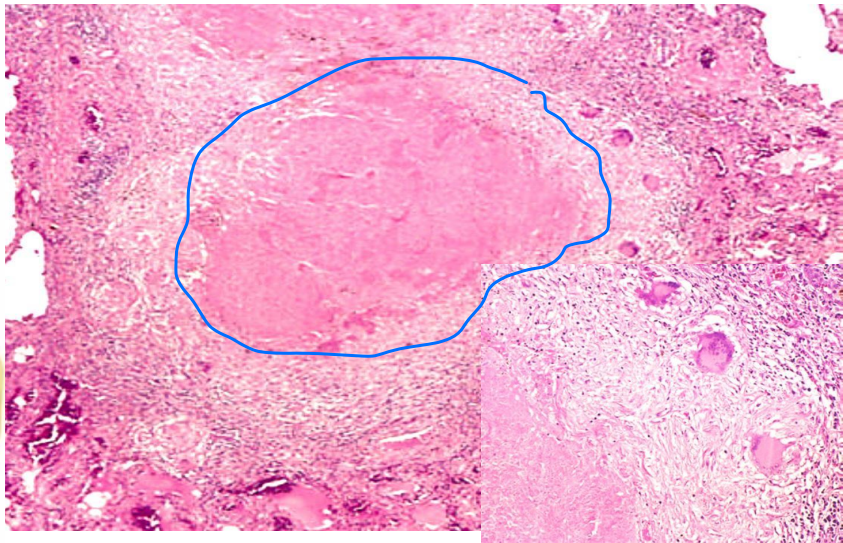
Gross picture: creamy yellow area (pus).





3- Caseation necrosis: " (cheese like)

- **Cause:** tuberculous (TB) infection
- **Gross picture:** friable white " (cheese like)
- **Microscopic picture**: loss of tissue architecture and cell details (tissue appear pink, structureless & homogenous)

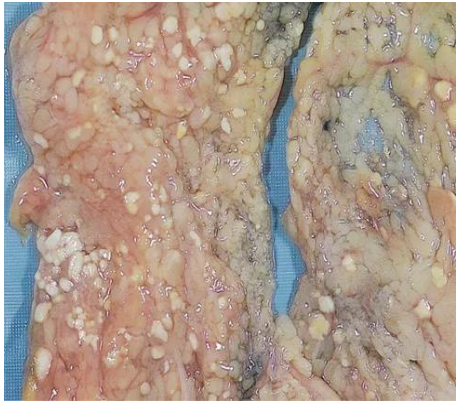


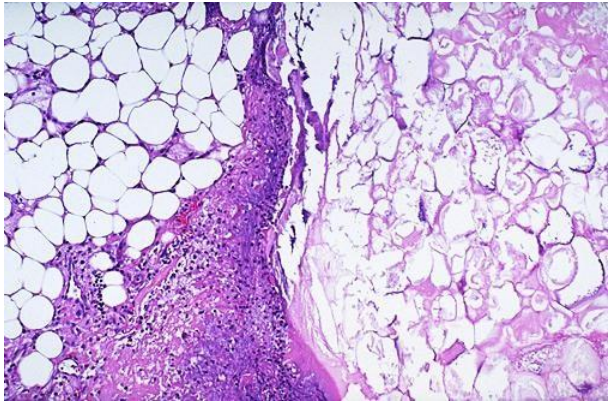
4- Fat necrosis: local area of fat destruction. It is of two types:

A) Traumatic fat necrosis: trauma to adipose tissue (e.g. breast) → rupture of fat cells

B) Enzymatic fat necrosis:

- It occurs in acute pancreatitis → released pancreatic enzymes liquefy fat cell in peritoneal cavity



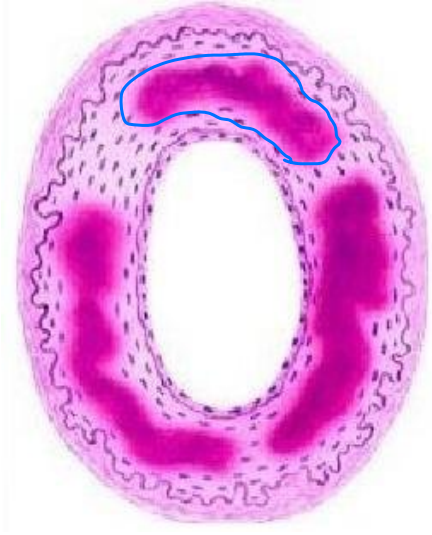


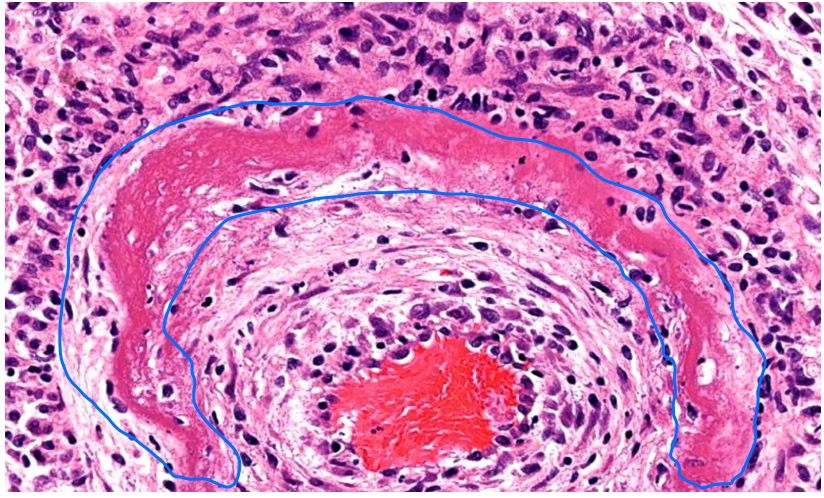
5- Fibrinoid necrosis:

Site: in blood vessels (vasculitis)

Cause: in autoimmune disease

Microscopic picture: pink fibrin like material in the walls of arteries



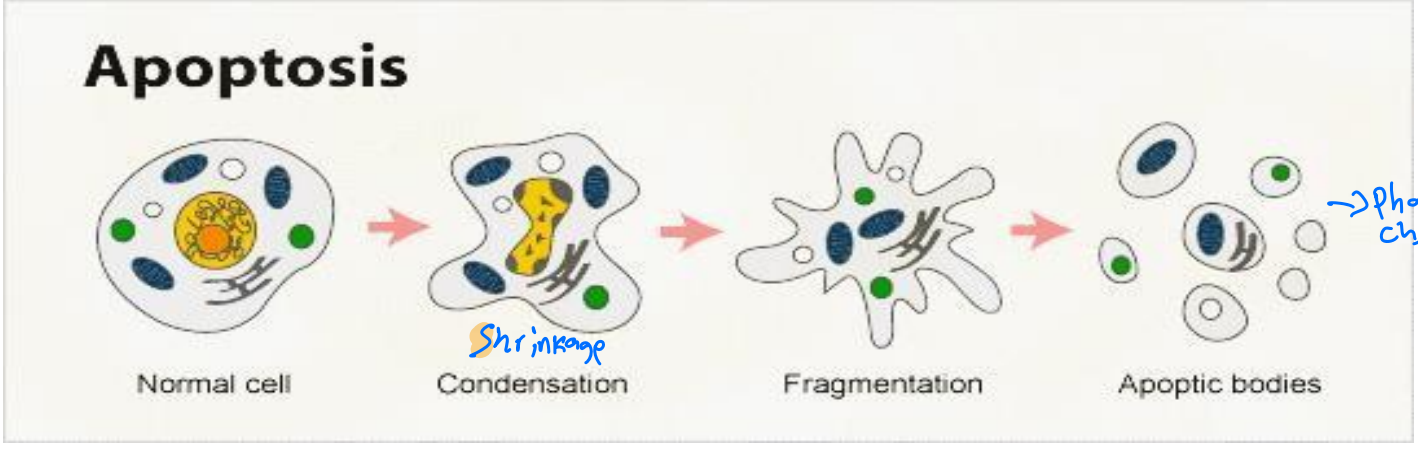


2- Apoptosis

Definition: Programmed cell death to remove unwanted cells (single cell or small groups of cells).

Apoptotic cells shrinkage then break up into plasma membrane–bound fragments,

called *apoptotic bodies* → *phagocytosis*



Causes:

A- Physiological

OR

B- Pathological

A.Physiological: a normal phenomenon that serves to eliminate cells that are no longer needed.

- *Example:*
- **During embryogenesis**
- **Death of cells that have served their useful purpose**: neutrophils in an acute inflammatory response
- **Elimination of harmful self- destructive cells:** e.g. self reactive lymphocyte auto immune cells

B.Pathological: eliminates injured cells

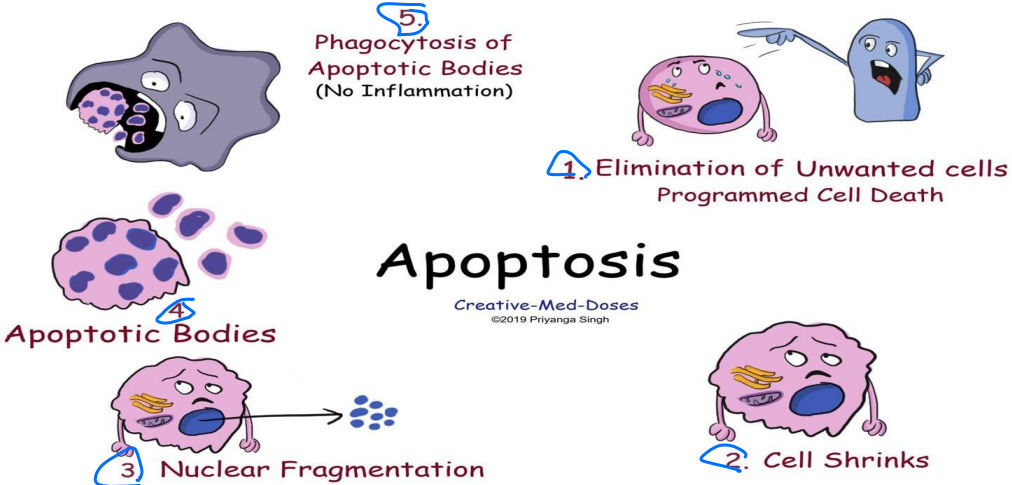
- *Example:*

A. **DNA damage**: Radiation and cytotoxic anticancer drugs

B. **Odd Cells**: in certain viral infections (HIV infections), transplanted cells.

Pathological picture:

1. **Shrinkage of cells**
2. **Nuclear fragmentation**
3. **Formation of apoptotic bodies**. The apoptotic cell fragmented into membrane-bound apoptotic bodies composed of cytoplasm and organelles, with or without nuclear fragments.
4. **Phagocytosis** of apoptotic cells, usually by macrophages.



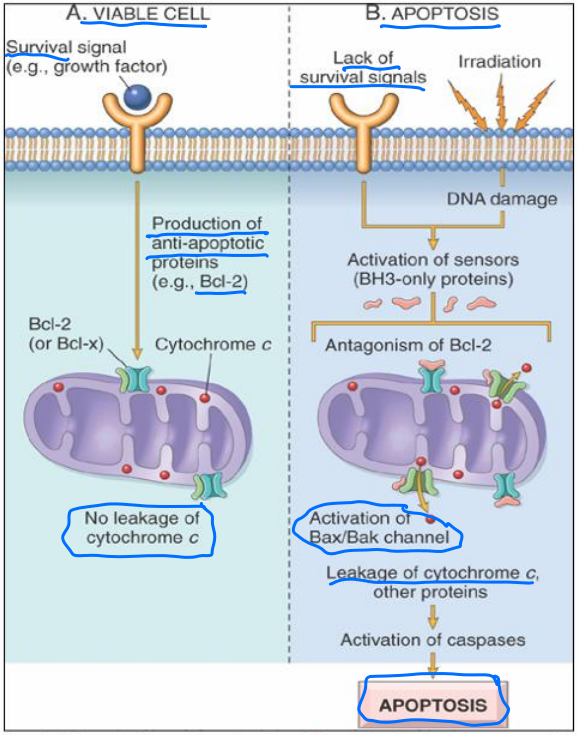
MOLECULAR MECHANISM OF APOPTOSIS

- Apoptosis is regulated by pathways that control the balance of **death and survival inducing signals**.

- Apoptosis progresses through one of the 2 pathways:

1. Intrinsic (mitochondrial) pathway: Major pathway

2. Extrinsic (Death Receptor) pathway:



In a healthy cell (through survival signals), Bcl-2 (Antiapoptotic) maintain the integrity of mitochondrial membranes, by holding back proapoptotic proteins Bax & Bak

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation
Plasma membrane	Disrupted	Intact
Cellular contents and inflammation	leak out of cell Enzymatic digestion Inflammatory response	Intact; released in apoptotic bodies No Inflammatory response
Physiologic or pathologic role	Pathologic	Physiologic or pathologic

Gangrene

Definition: is massive tissue necrosis followed by putrefaction.

Pathogenesis:

Putrefaction is caused by saprophytic bacteria which break down the protein of the necrotic tissue liberating hydrogen sulphide that gives the tissue a foul odour. Hydrogen sulphide unites the iron of haemoglobin forming iron sulphide that stains the gangrenous tissue black.

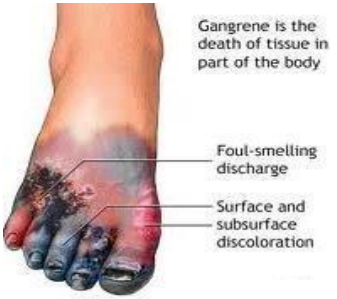
Types:

Dry gangrene : occurs in parts poor in blood supply and tissue fluids

Moist gangrene : in parts rich in tissue fluids

Infective gangrene

Gas gangrene



Dry gangrene

Etiology: Arterial occlusion by thrombus, embolus, ligation

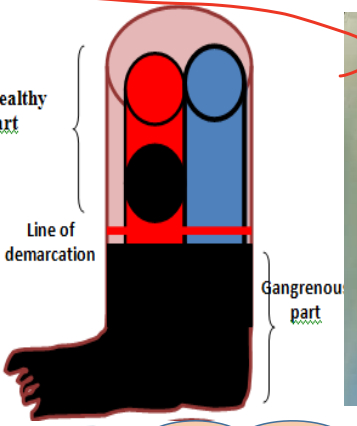
Site:exposed organs such as limbs

Gross picture:

-limb is Black in color, Offensive, dry and mummified

-A red line separating healthy from dead area (line of demarcation)

-self separation may occur.



Moist (Wet) gangrene

Etiology: Sudden arterial and venous occlusion

Site :

-Internal organs (**intestine** i.e strangulated hernia)

Gross picture:

-Intestine is Black in color ,Offensive, swollen and congested.

-No line of demarcation (masked by congestion)

Why it is wet or moist :
Tissue is congested and edematous due to occlusion of venous drainage.

Dry gangrene

1 Gradual arterial occlusion

2 Exposed parts (limbs)

3 Tissue mummification

4 Marked line of demarcation

5 Self separation my occur

Moist gangrene

1 Sudden arterial and venous occlusion

2 Internal organs (intestine)

3 Tissue oedema

4 poor line of demarcation

5 Self separation absent

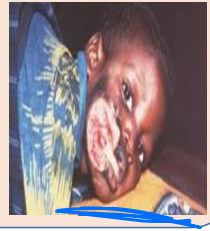
Infective gangrene

It is a gangrene in which bacteria cause both tissue necrosis (by its toxins) and putrefaction e.g. Bed sores, cancrum oris

cancrum oris

Infective gangrene of the cheeks of debilitated children recovering from fevers, Pain caused by Treponema vincenti and Bacillus fusiformis. bacteria

Toxaemia is sever and bronchopneumonia may results from aspiration of the septic necrotic tissue.



Gas gangrene: most dangerous

is a bacterial infection that produces gas within tissues.

It is a deadly form of gangrene usually caused by **Clostridium perfringens (**bacteria produces gases inside tissues) common after crush accidents.


THANK
YOU