Overview of Cell Injury and Cell Death

Cell Injury

if there is stress that is not enough to cause injury adaptation occurs(hyperplasia,atrophy,metaplasia,hypertrophy)

- Stress (if severe, prolonged or damaging) leads to Injury.
- Stress → Reversible Injury → Irreversible

- Irreversible Injury (cell death), Necrosis or Apoptosis

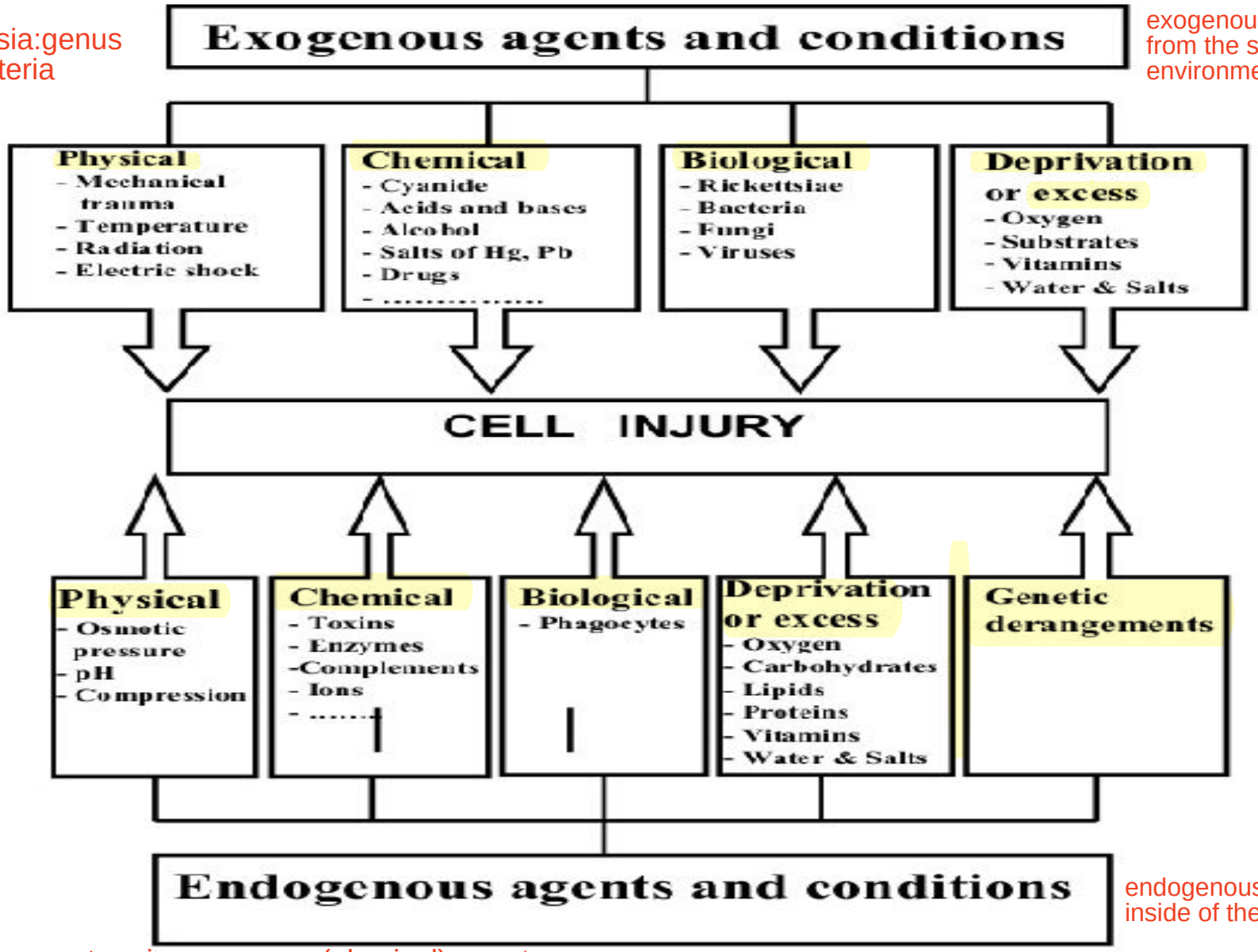
irreversible injury>eventually we will lose the whole cell either by necrosis or apoptosis

sometimes from the beginning in case the stress is very severe,irreversible injury occurs

exogenous agents:العواوملل الخارجية

Causes of cell injury

rickettsia:genus of bacteria



exogenous :external from the surrounding environment

endogenous from the inside of the body

temperature is exogenous(physical) agent
PH is endogenous physical agent

the main cause of cellular injury is ischemia (نقص التروية)

hypoxia,physical,infectious,immunologic, genetic derangements,aging

Causes of cell injury

- **Oxygen Deprivation**: hypoxia:ischemia,CR failure,decreased oxygen carrying capacity

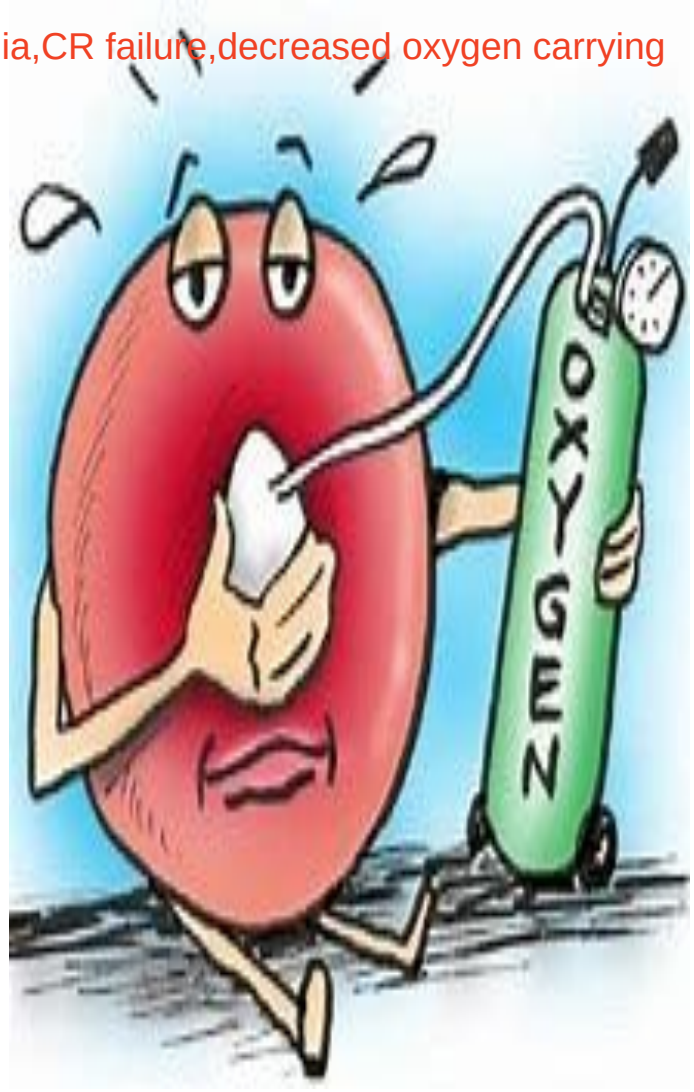
  Hypoxia: deficiency of O_2.

  Causes:

  – Ischemia: restriction in blood supply. low oxygen is delivered to cells

  – Inadequate oxygenation: cardiorespiratory failure.

  – Decreased oxygen carrying capacity: anemia, carbon monoxide poisoning or blood loss.



Causes of cell injury

- **Physical agents**: mechanical trauma, extremes of temperature, changes in atmospheric pressure, and radiation.

exogenous physical agents:Temperature,radiation,electric shock,trauma
endogenous physical agents:osmosis,pressure,compression,PH

- **Chemical agents and drugs**: Glucose or salt, arsenic compounds, cyanide, insecticides, herbicides, asbestos, alcohol, smoking and therapeutic drugs.

Causes of cell injury

- **Infectious agents**: viruses, bacteria, fungi and parasites.

- **Immunologic reactions**: to external stimuli and endogenous self antigens (allergy & Autoimmune).

specially for those with autoimmune diseases


Bacterium


Virus


Protozoan


Fungus


Helminth

Causes of cell injury

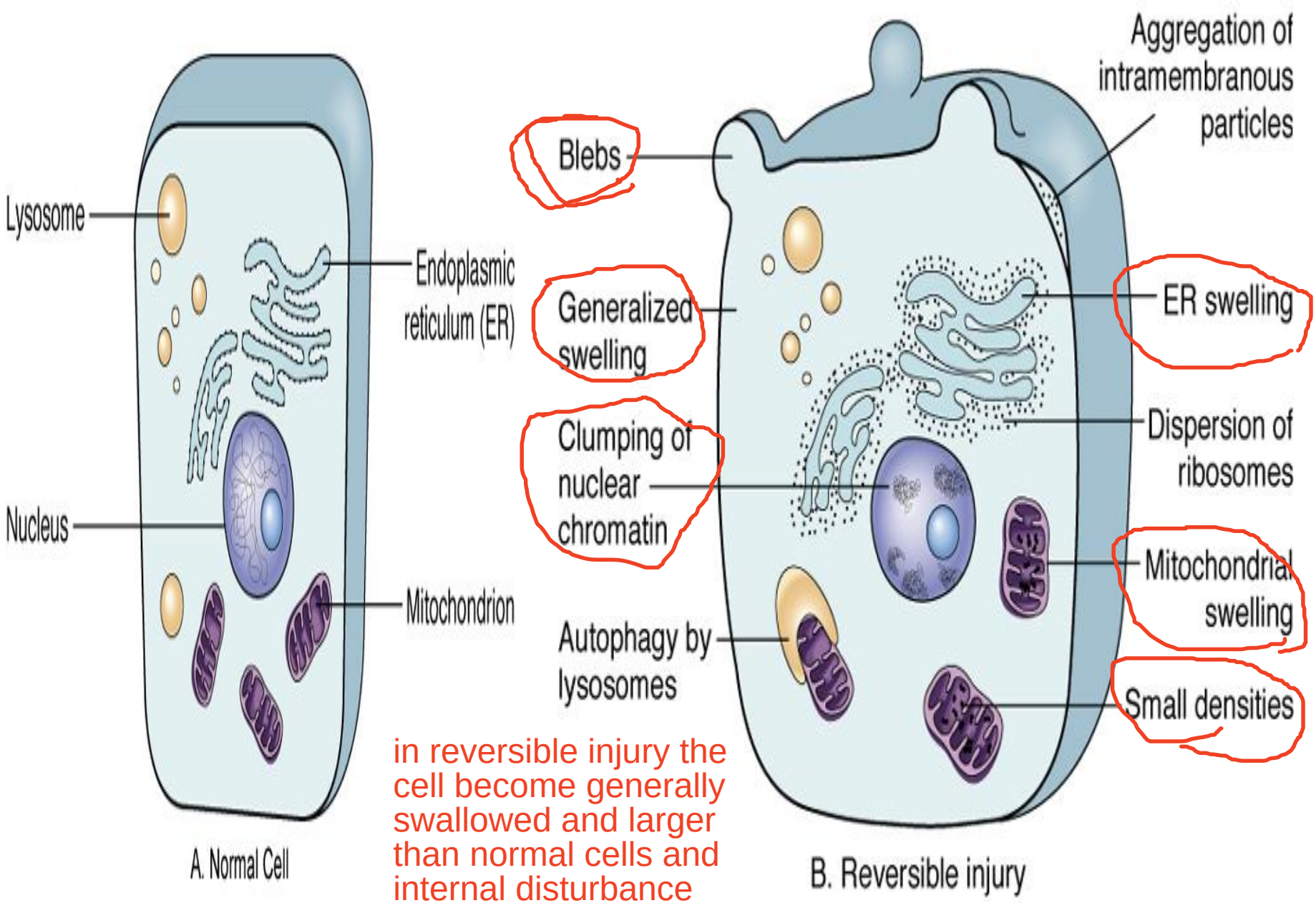
- **Genetic derangement**: Chromosomal anomalies, gene alteration or simple amino acid alteration.

inherited diseasesالاب ي ش ر ث ك

chrom anomalies:disorders in chrom(ش ذوذ)

- **Nutritional imbalance**: Protein calorie deficiencies, vitamin deficiencies.

- **Aging**



in reversible injury the cell become generally swallowed and larger than normal cells and internal disturbance occurs

Morphologic alterations in cell injury

Reversible injury

- **Generalized swelling of the cell (Hydropic change or vacuolar degeneration)**: failure of energy-dependent “ion pumps” in the plasma membrane result in disturbances in ionic and fluid homeostasis.
- It is usually the **first** manifestation.

the most important difference between reversible and irreversible injury is the integrity of the membranes(cell membrane and nuclear membrane)

if these membranes start to be fragmented the injury is irreversible

in reversible injury you may see swallowing of the mitochondria,ER,also blebs in the membrane appearsbut the nuclear membrane and cell membrane must be compact (also chromatin clumping occurs and autophagy by lysosomes)

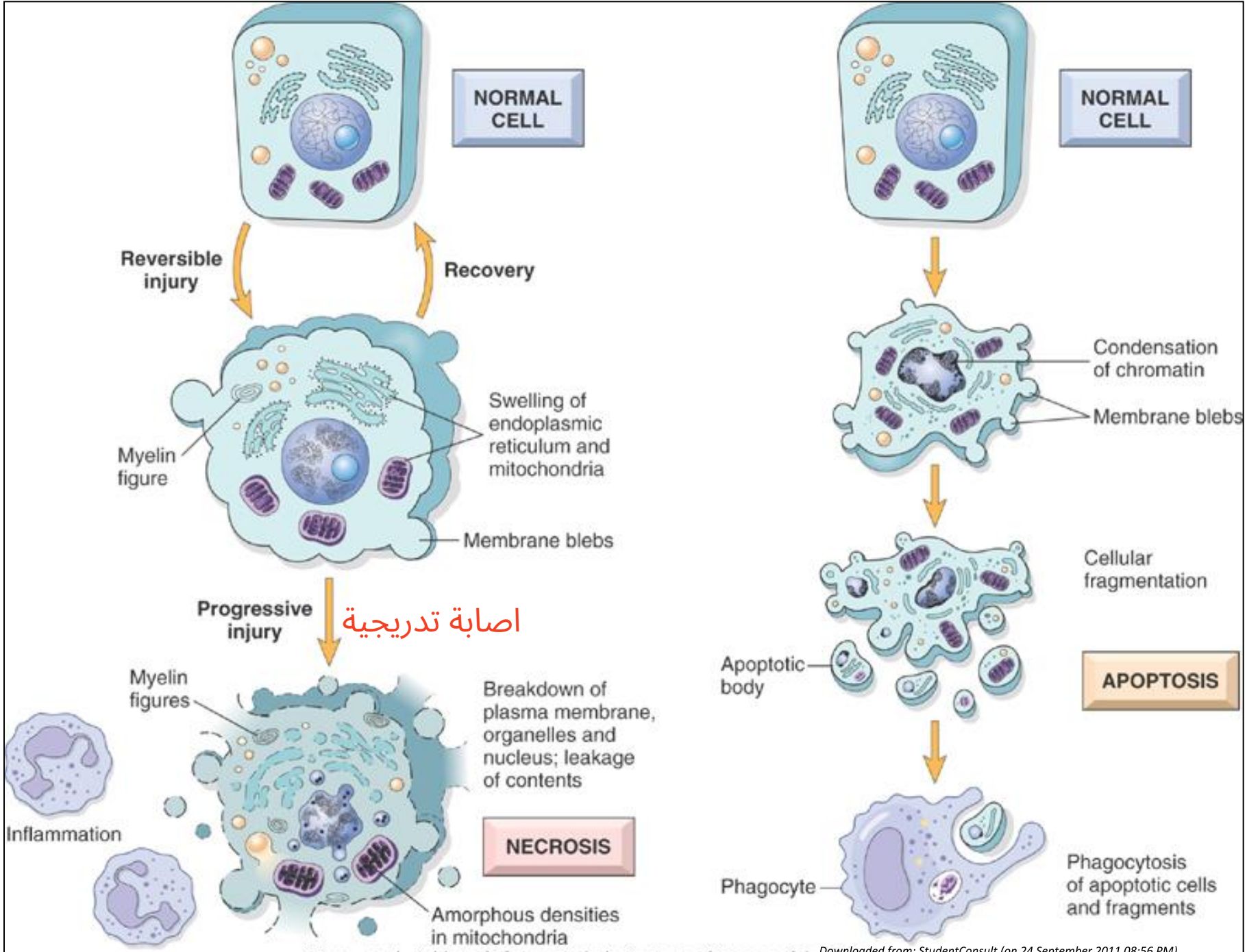
blebs:فقاعات

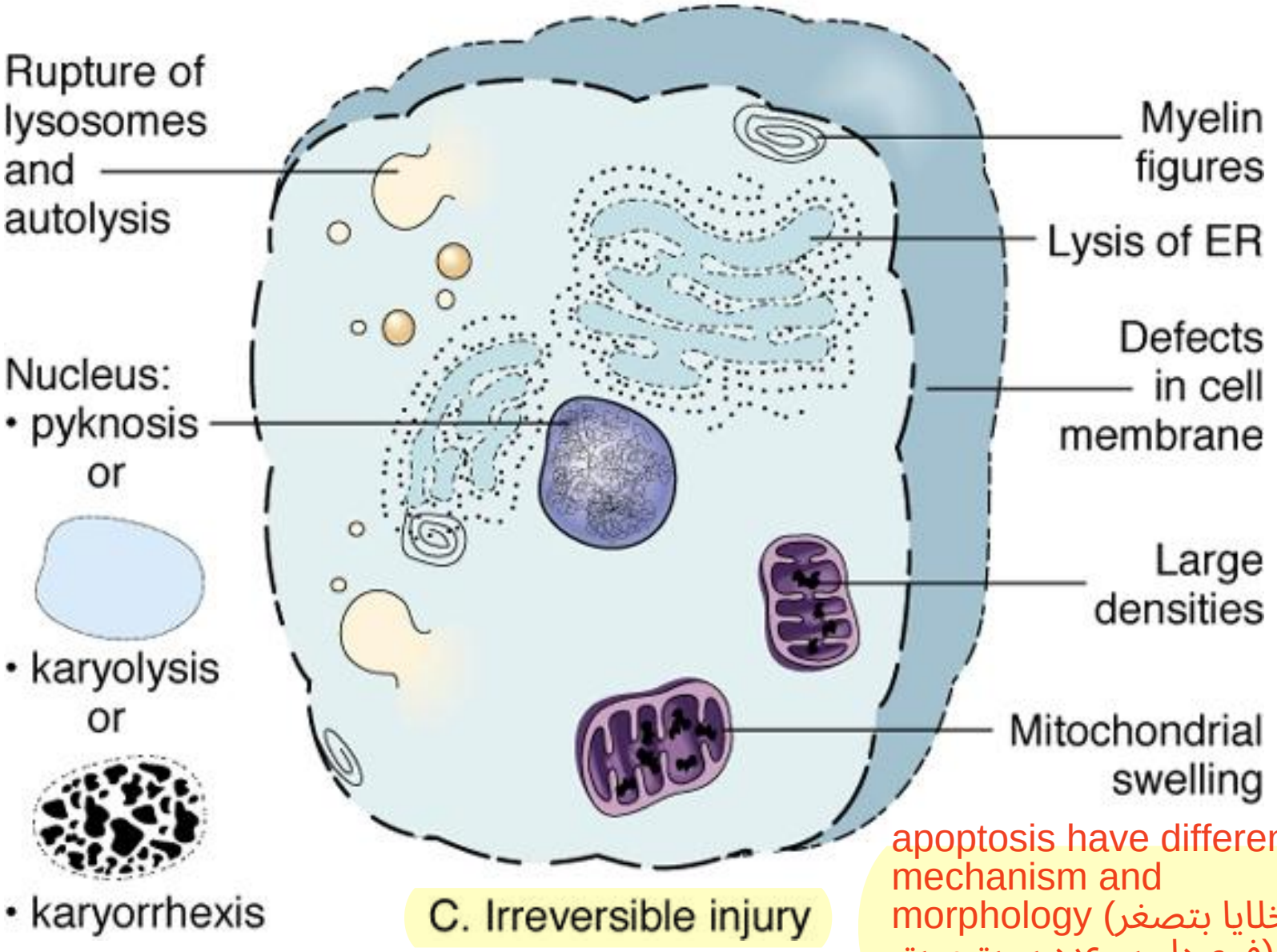
Reversible injuriy:alternations in plasma membrane,mt changes,nuclear alternations

- **Plasma membrane alterations**: blebs, blunting or loss of villi and loosening of intercellular attachments.
- **Mitochondrial changes**: swelling and appearance of small amorphous densities.
- **Nuclear alterations**: nuclear chromatin clumping.

amorphous:غير منظم

clumping:تتجمع





C. Irreversible injury

apoptosis have different mechanism and morphology (الخلايا بتصغر وبعده تموت)also the no inflammatory cells attracted

Morphologic alterations in cell injury **irreversible** injury (**Necrosis**)

- **Loss of membrane integrity.** it ruptures then inflammation occurs

- Denaturation of intracellular proteins and enzymatic digestion of cells.

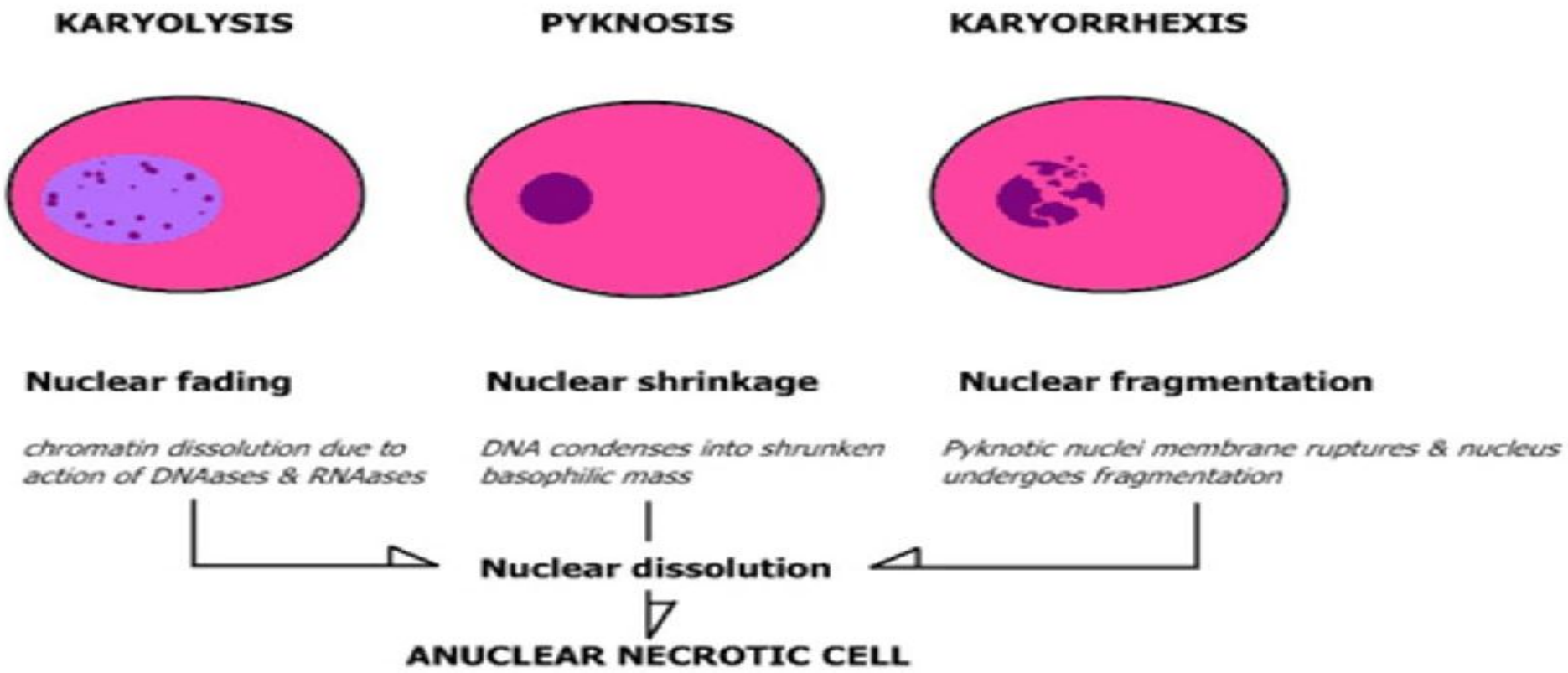
- Digestion enzymes: from lysosomes of dying cells and from leukocytes (inflammatory response).

after loss of membrsne integrity cell organelles are faced to the external medium where inflammatory cells and lysosomes digest them

- Increased eosinophilia in H&E stain.
- Vacuolation due to digestion of cytoplasmic organells.
- Plasma and organelle membrane discontinuities.
- **Myelin figures**: aggregates of damaged cell membranes (phospholipids).
- Marked dilatation of mitochondria and appearance of large densities.

dilatation:اتساع

- **Nuclear changes: breakdown of DNA** three steps
  - Pyknosis: nuclear shrinkage and increased basophilia.
  - Karyolysis: loss of DNA, fade of basophilia.
  - Karyorhexis: fragmentation of the pyknotic nucleus.
  - Disappearance of the nucleus.



أي شي بنشوفه بالعين

Patterns of tissue necrosis

how does the necrotic tissue appears under microscope and under naked eye

- Coagulative necrosis:

- Preservation of the architecture of dead tissue for at least some days.

- Eosinophilic anucleated cells.

- **Ischemia in any organ except the brain may lead to coagulative necrosis.**

it is necrosis that occurs initially (no inflammation action yet occurs)

occurs in all body tissues except the CNS

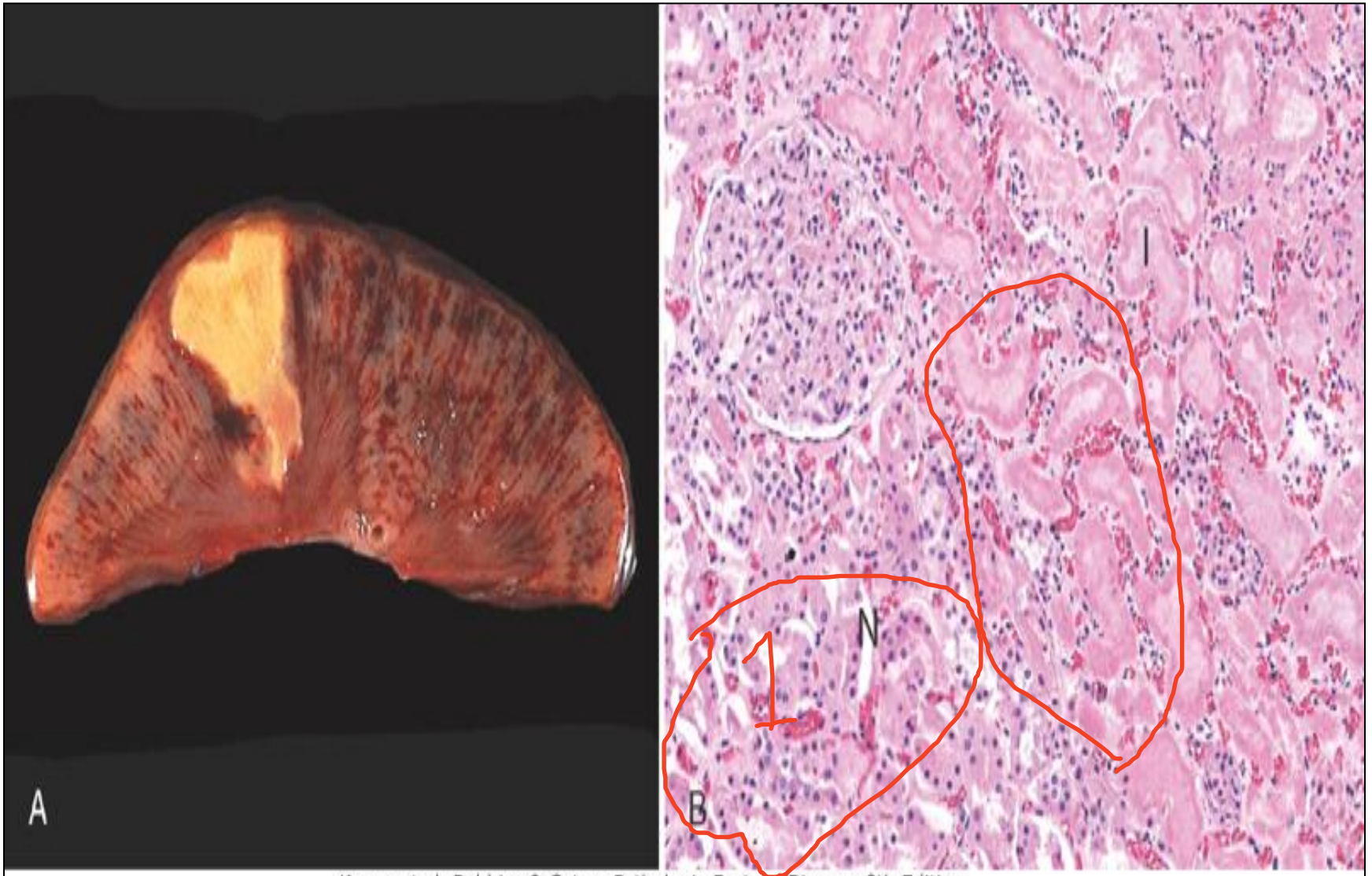
وصف للصورة الموجودة على اليمين
viable cells عشان الانوية دائرية,ومنتظمة داخل الخلايا

الدائرة رقم 2 :
cells are having their compact architecture but with fragmented nucleus(their architecture is similar to normal cells but they have no nucleus)

maintained outer architecture=coagulative necrosis

the picture of the kidney identifies an viable part and a necrotic part

the tissue is still preserved

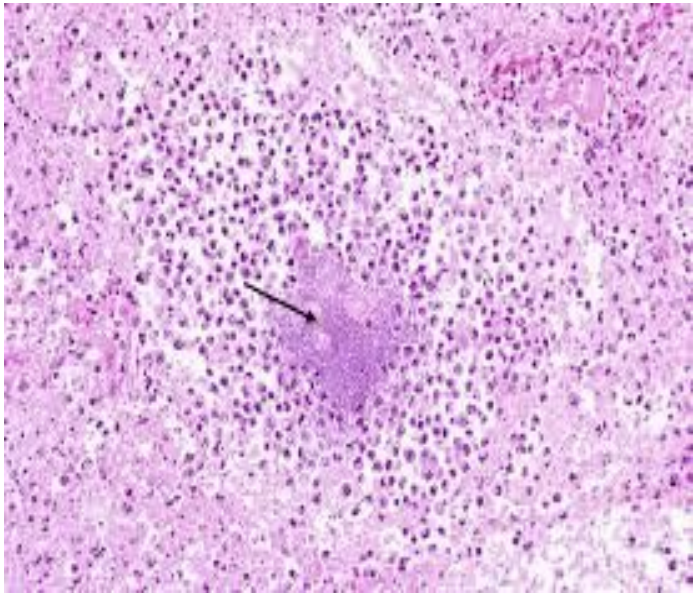


Patterns of tissue necrosis

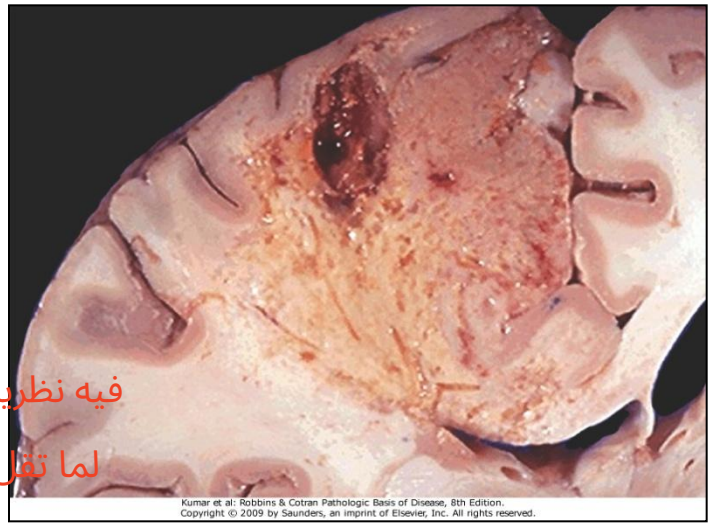
- Liquefactive necrosis:

- Digestion of dead cells resulting into a liquid viscous mass.

there is no preservation for architecture and there is abscess rich in inflammatory cells



- In focal bacterial or fungal infections and **in hypoxic death in central nervous system.** CNS undergoes liquifactive necrosis not coagulative necrosis

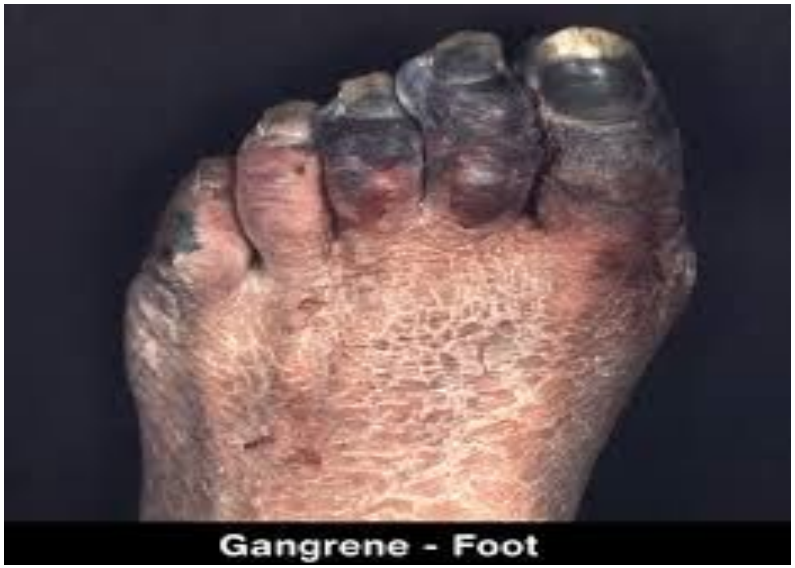


فيه نظرية بتحكي انه الدماغ لانه عننده اعداد هائلة من الانزيمات الهاضمة فحتى
لما تقل تروية الدماغ بالاكسجين ما بتوقف عمل كل هالانزيمات فبضل منهم
عدد ما اتوقف حتى يحلل الخلايا الدماغية

Patterns of tissue necrosis

- Gangrenous necrosis:

- Not a distinctive pattern. Used clinically in describing lower limb coagulative necrosis secondary to ischemia.



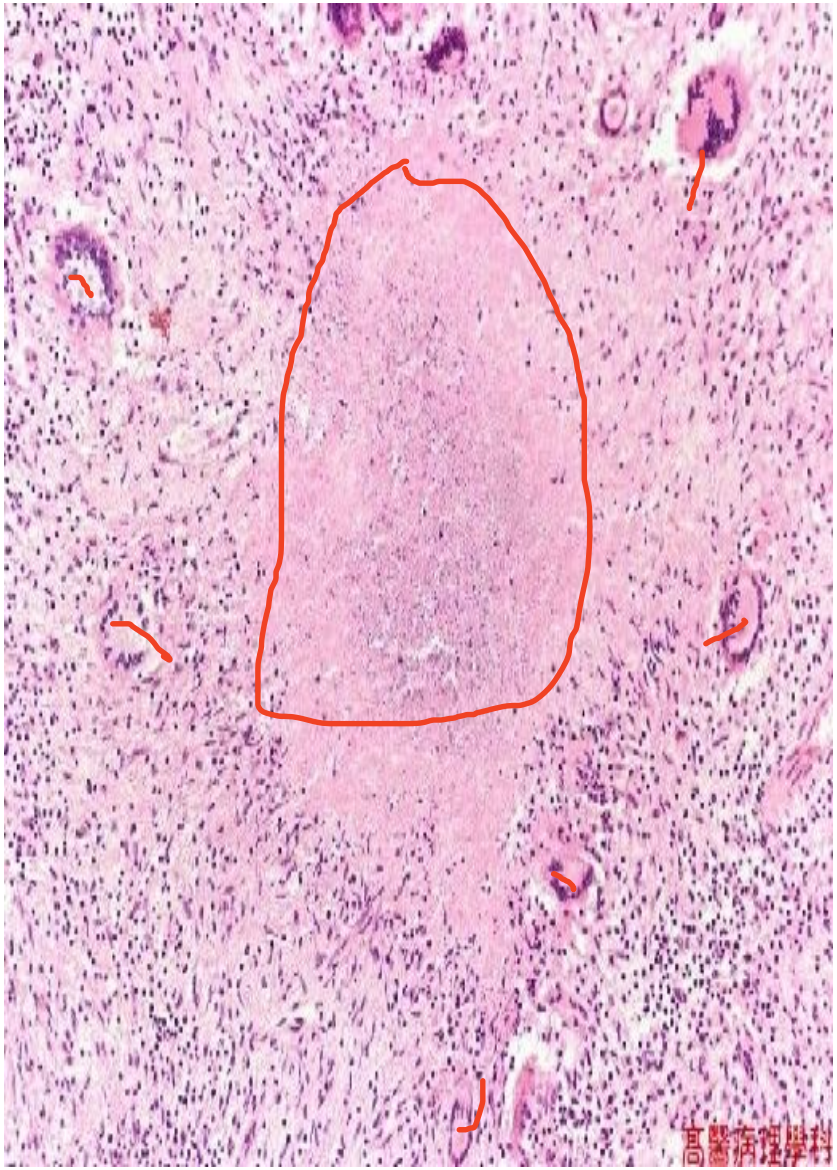
it could be dry or wet
it is a coagulative necrosis that is specual for lower peripheral organs

- Once infected by bacteria it becomes wet gangrene (liquefaction).

Patterns of tissue necrosis

- Caseous necrosis: relatively specific to TB infections

- White cheeselike friable necrosis.
- Ex: Tuberculosis
- Collection of fragmented or lysed cells surrounded by histiocytes (macrophages), known as granuloma.



caseous necrosis is a liquifactive necrosis made by TB
cells in the circle has no compact architecture and surrounded by inflammatory cells (histocytes)

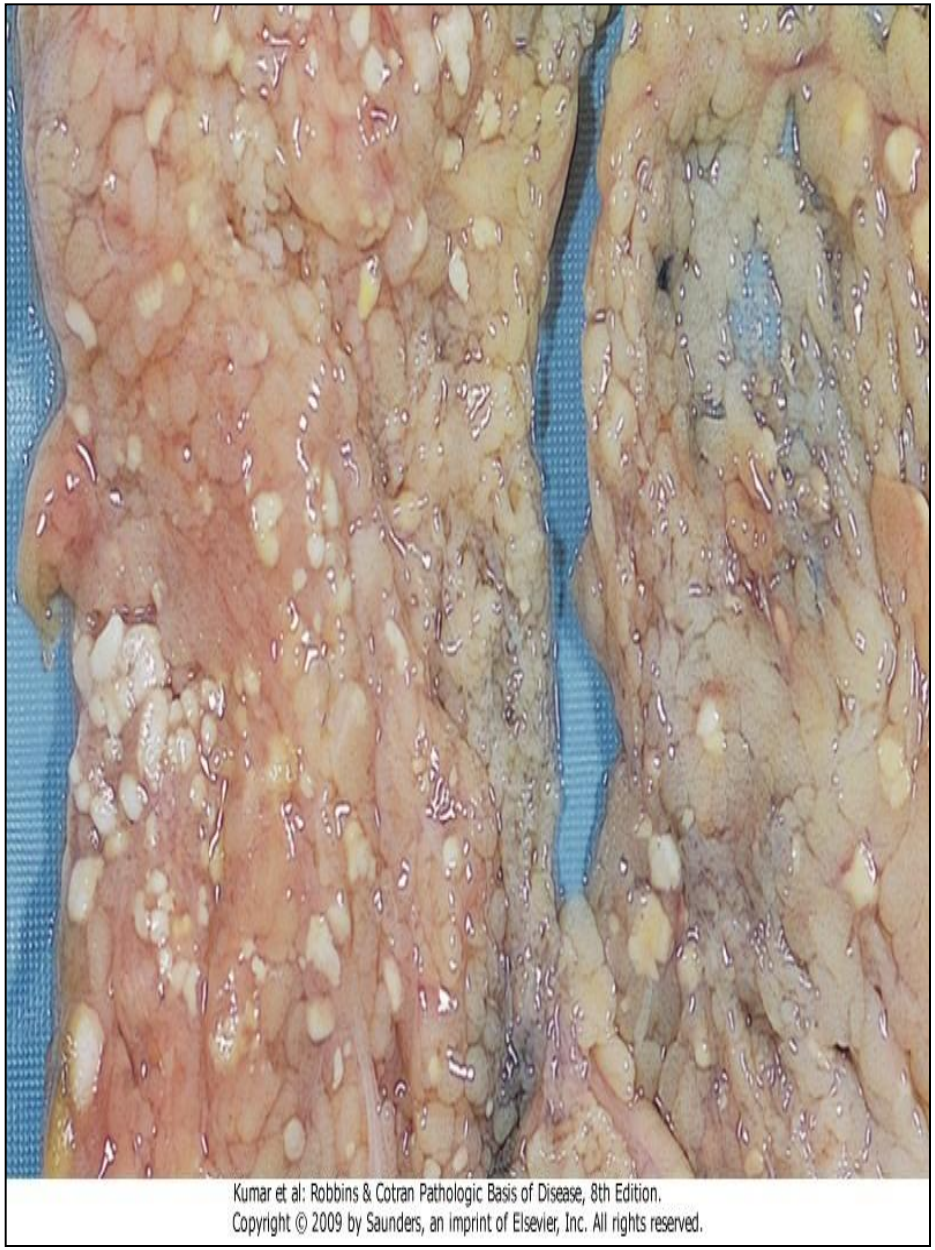
gross anatomy of caseous necrosis appear like cheese

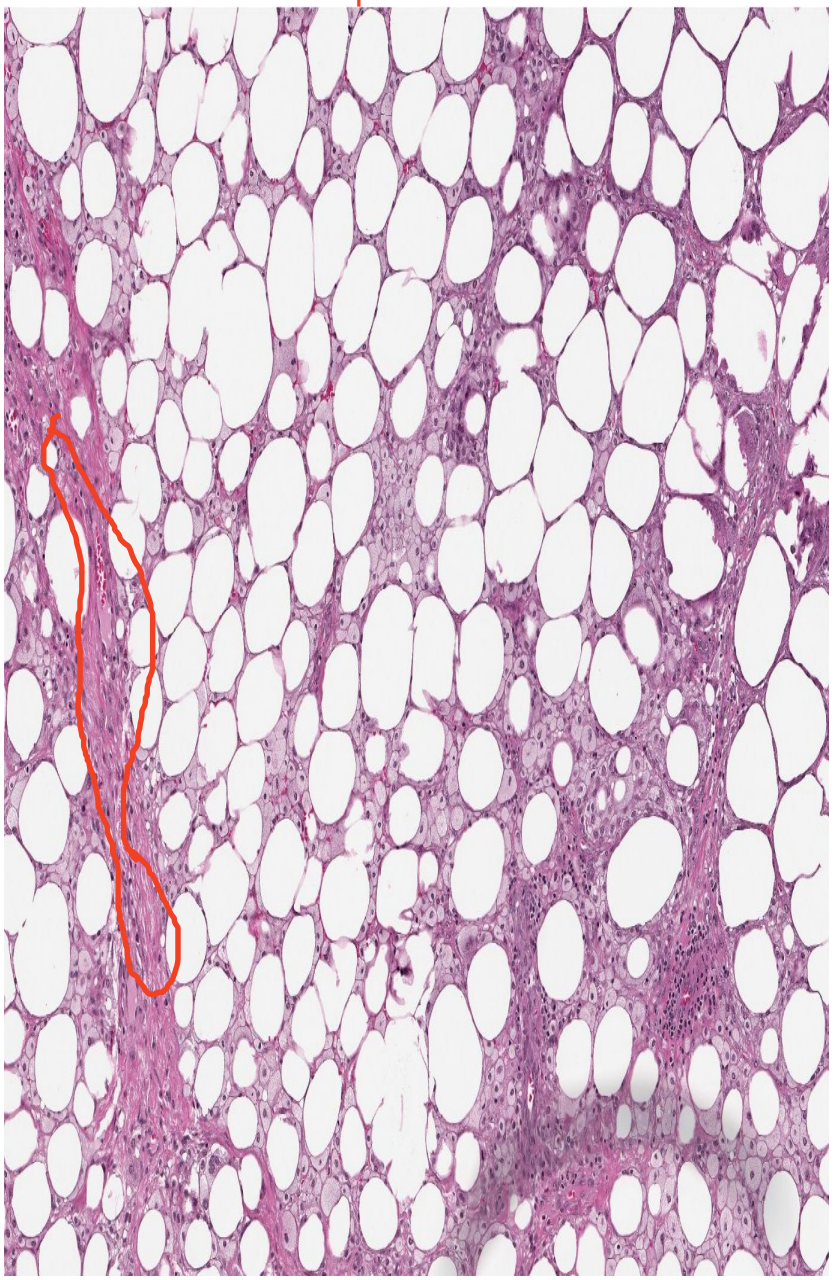
Patterns of necrosis

- Fat necrosis: occurs in fats due to reactions of lipases
  has unique appearance and is specific for adipose tissue

- usually used in clinical terms and it is not a specific type.
- Necrosis (destruction) of fat.
- Typical example: pancreatic enzymes (lipases) release in acute pancreatitis.
- The fatty acids result from the breakdown of fat combine with calcium leading to the formation of white chalky areas (Saponification).

macrophages becomes in between adipose tissue

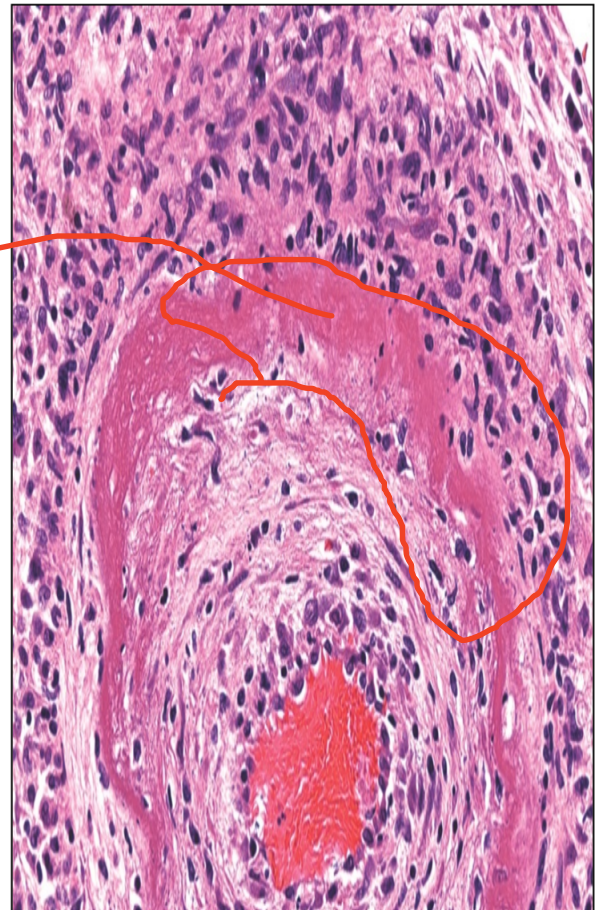




Patterns of necrosis

- Fibrinoid necrosis:

- Immune reactions involving blood vessels.
- Complexes of antigens and antibodies deposited in the walls of arteries.
- Immune complexes deposits along with fibrin result in a bright pink material on H&E.



Fate of necrotic tissue

- Phagocytosis.
- Replacement by scar.
- Regeneration.
- Calcification.

MEDICINE IS ONLY FOR THOSE WHO CANNOT IMAGINE DOING ANYTHING ELSE.

DR. LUANDA GRAZETTE, MD