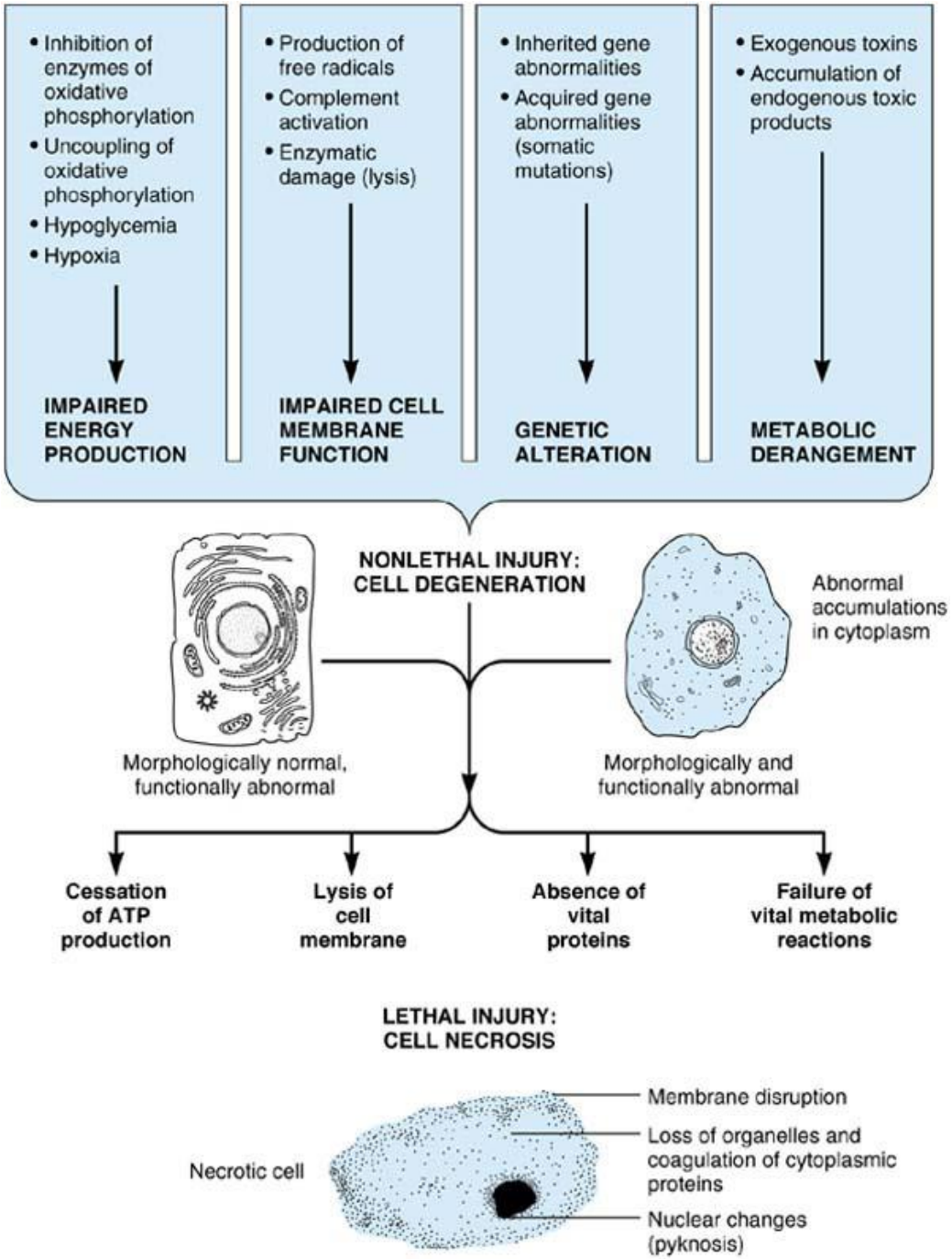
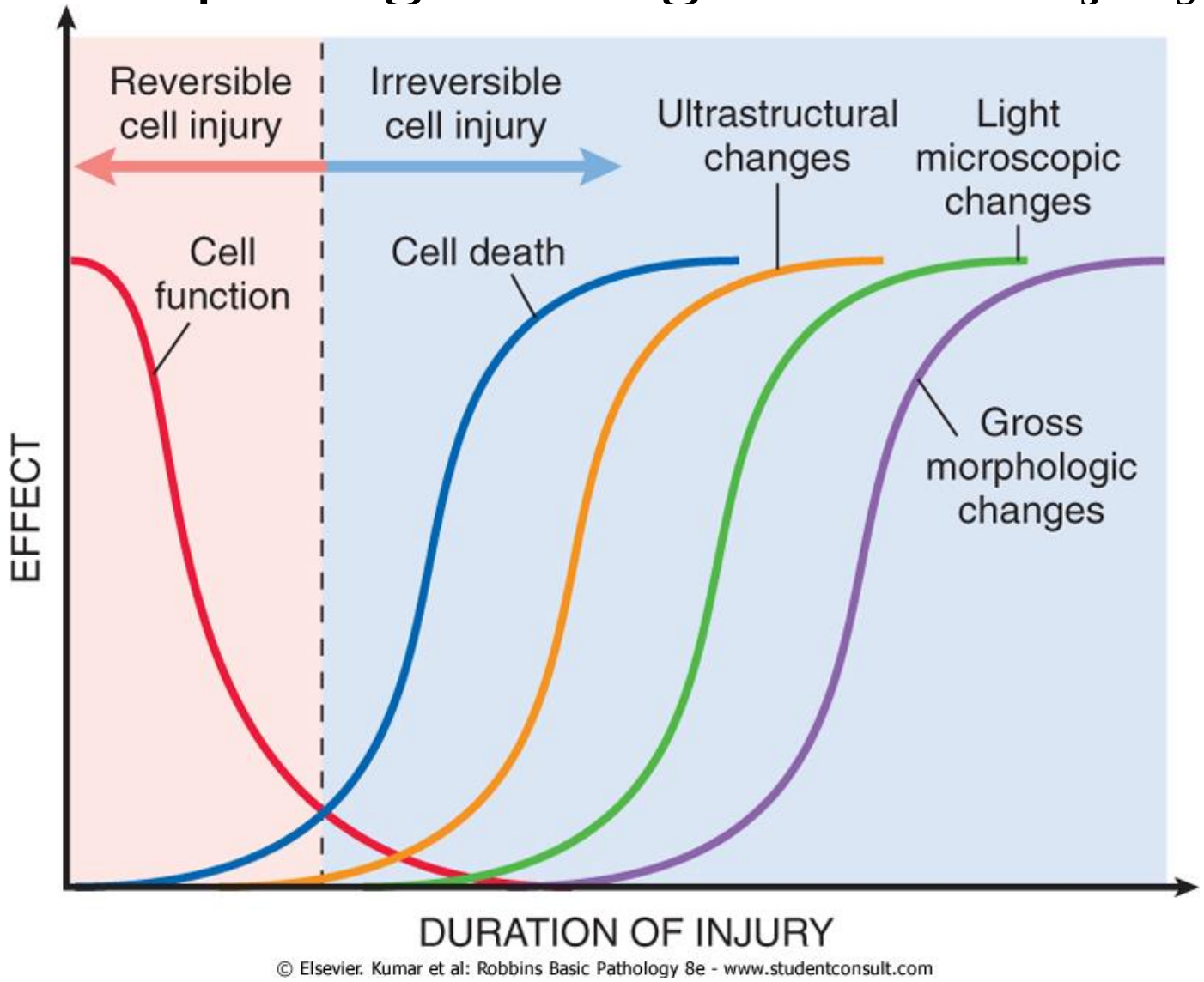
Cellular Injury
Morphological Aspects



Nonlethal Or Lethal

Relationship B/W cell function, cell death, &morphologic changes of cell injury.



Lethal Injury (Necrosis)

- Lethal injuries to the tissues of a living individual cause cell death **(necrosis)**
- Accompanied by biochemical and structural changes and is **irreversible.**
- The necrotic cells cease to function;
- Sufficiently extensive necrosis => clinical disease

Cell necrosis should be distinguished from the **death of the individual**

- Complete and irreversible cessation of brain function.

- Many individual cells and tissues in a legally dead individual remain viable for some time after death

Nonlethal Injury (Degeneration)

- Some abnormality of biochemical function, a recognizable structural change, or combined

- Reversible but may progress to necrosis if injury persists.

- Abnormal cell function + cell degeneration => clinical disease.

Morphologic Evidence of Necrosis
Early Changes

- In early necrosis, the cell is morphologically normal.

- Delay of 1-3 hours before changes of necrosis are recognizable on EM
- At least 6–8 hours before changes are apparent on light microscopy.

- (Myocardial necrosis caused by anoxia due to occlusion of a coronary artery)

Nuclear Changes

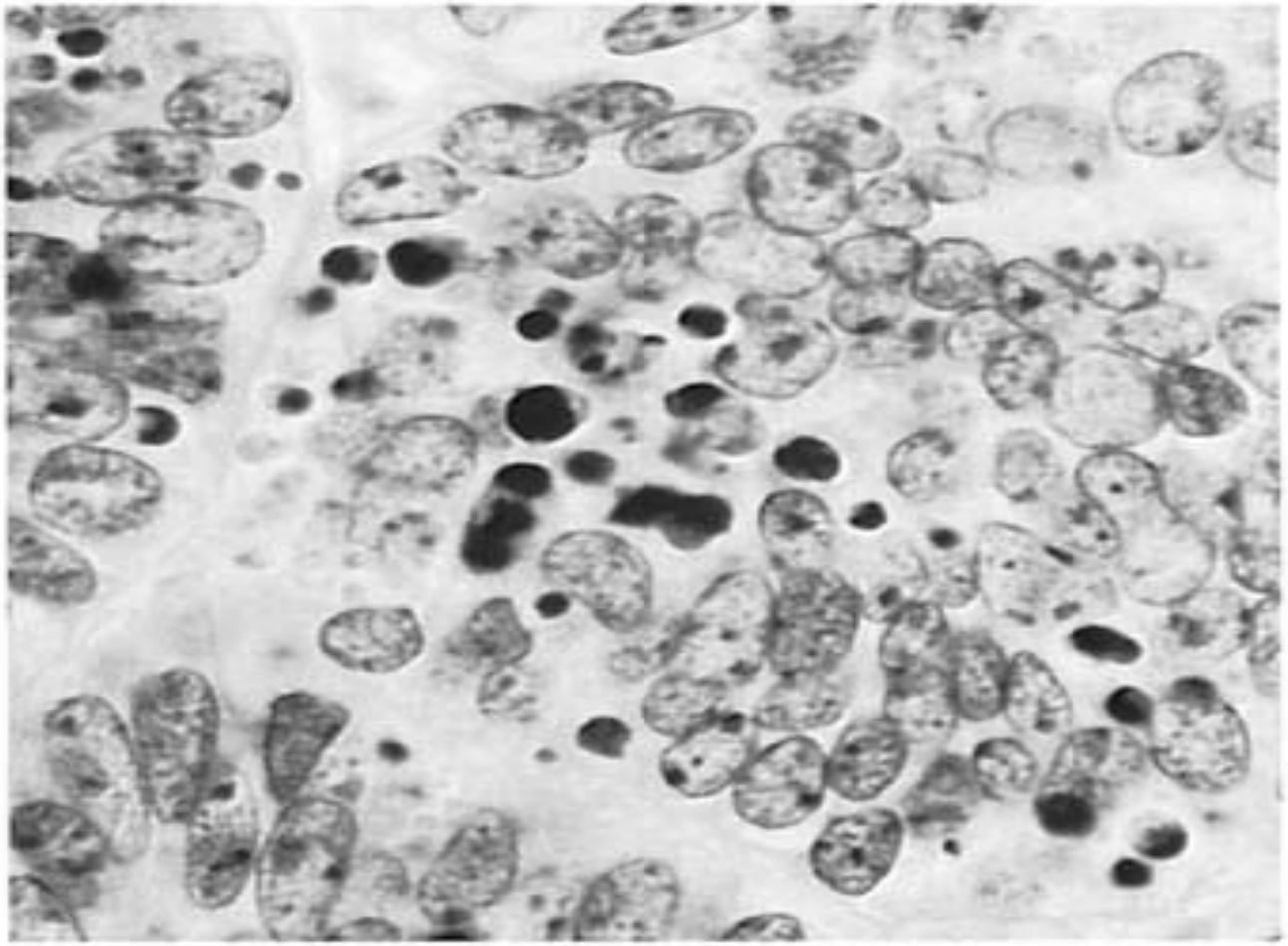
Best Evidence Of Cell Necrosis

- The chromatin clumps into coarse strands, and the nucleus becomes a shrunken, dense, and deeply basophilic mass **Pyknosis**

- **Karyorrhexis:** Break up into numerous small basophilic particles

- **Karyolysis:** (Lysosomal deoxyribonucleases) in rapidly occurring necrosis, the nucleus undergoes lysis without a pyknotic stage.

Cancer cells, showing nuclear pyknosis associated with cell necrosis. The pyknotic nuclei are dark and shrunken, in clear contrast with the nuclei of adjacent living cells, which have a well-defined nuclear membrane and dispersed chromatin.



Cytoplasmic Changes

- (RNA of the ribosomes is responsible for the basophilic tinge in normal cytoplasm.)

- About 6 hours, homogeneous deeply acidophilic (pink)First detectable change (LM)
- Denaturation of cytoplasmic proteins and loss of ribosomes.

- Myofibrils in myocardial cells, (lost early)

- Swelling of mitochondria and disruption of organelle membranes cause cytoplasmic vacuolation.
- Finally, **autolysis**

Biochemical Changes

- The influx of Ca^{2+} closely related to irreversible injury &appearance of morphologic changes of necrosis.
- Maintained by the cell membrane, which actively transports ca^{2+} out of the cell.

Calcium ions activate

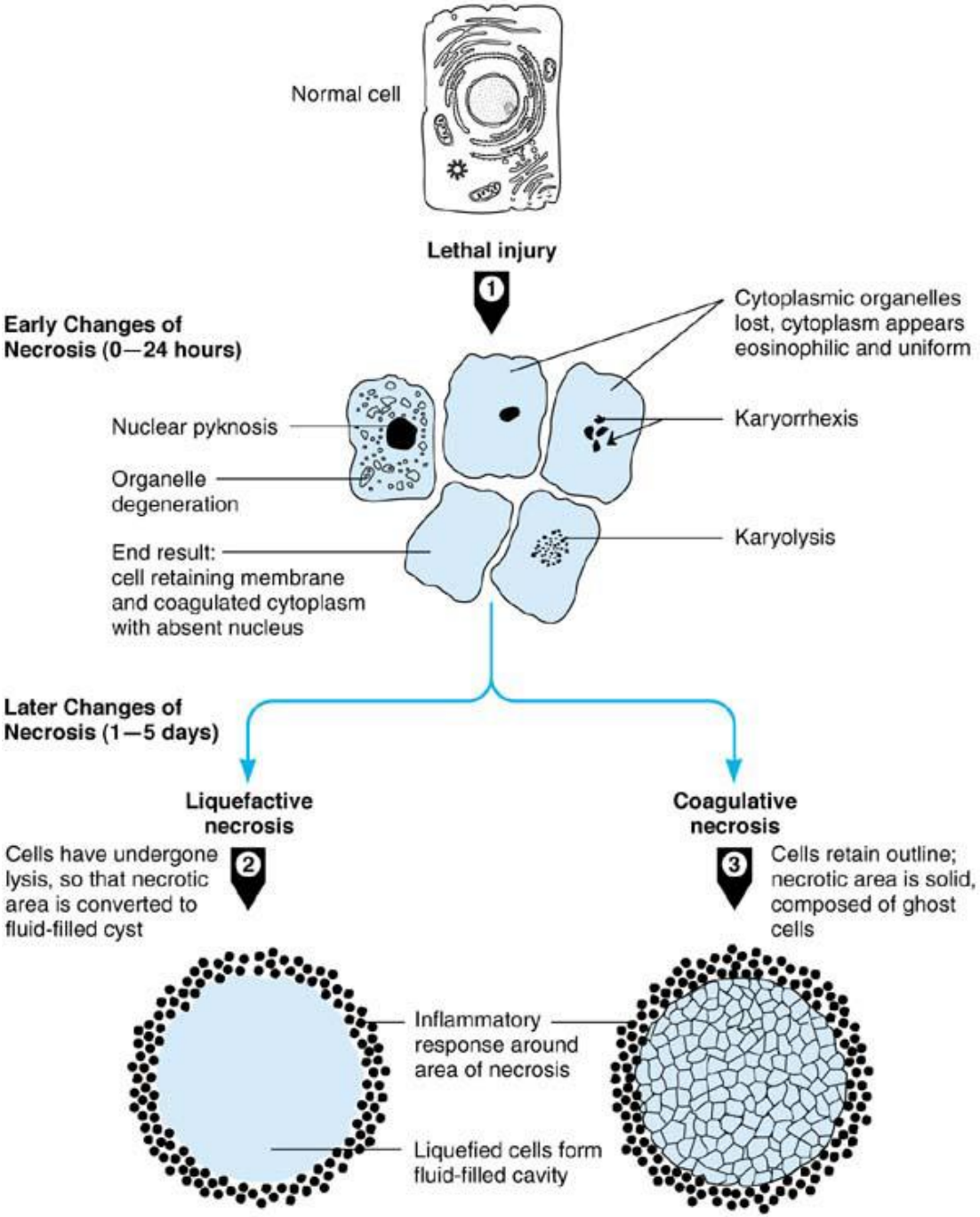
- Endonucleases (hydrolyze DNA),
- Phospholipases (disrupt membranes), and
- Proteases (digest the cytoskeleton)

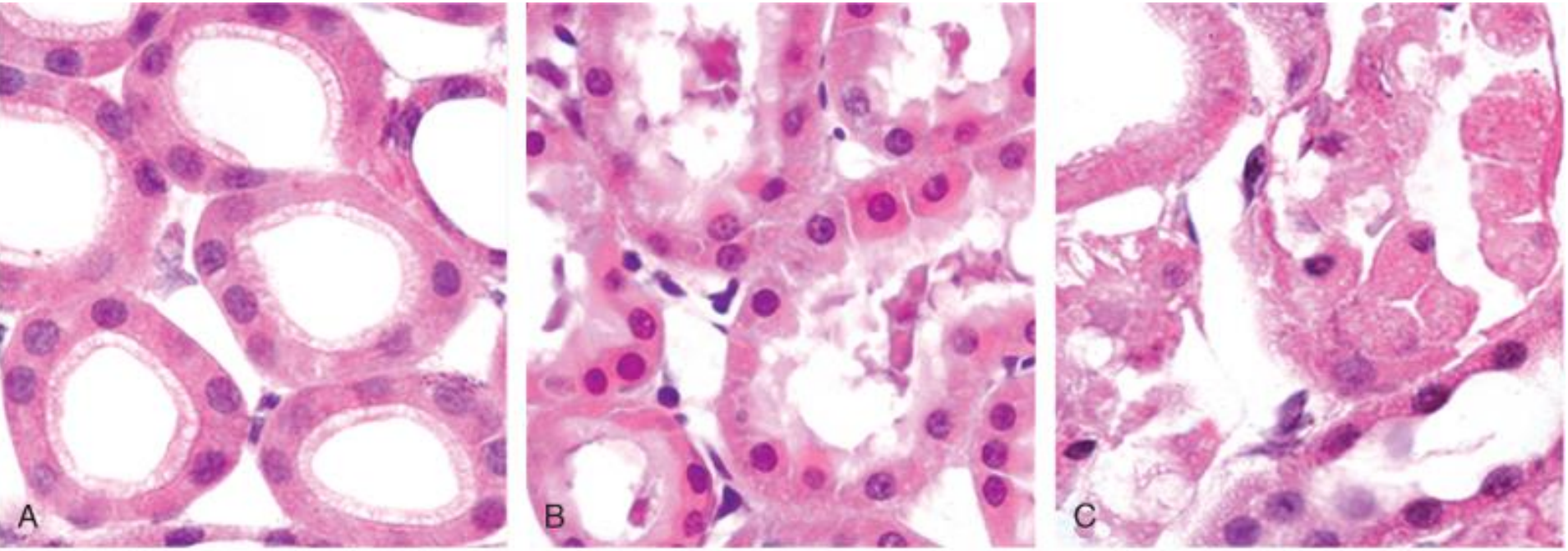
Types of Necrosis

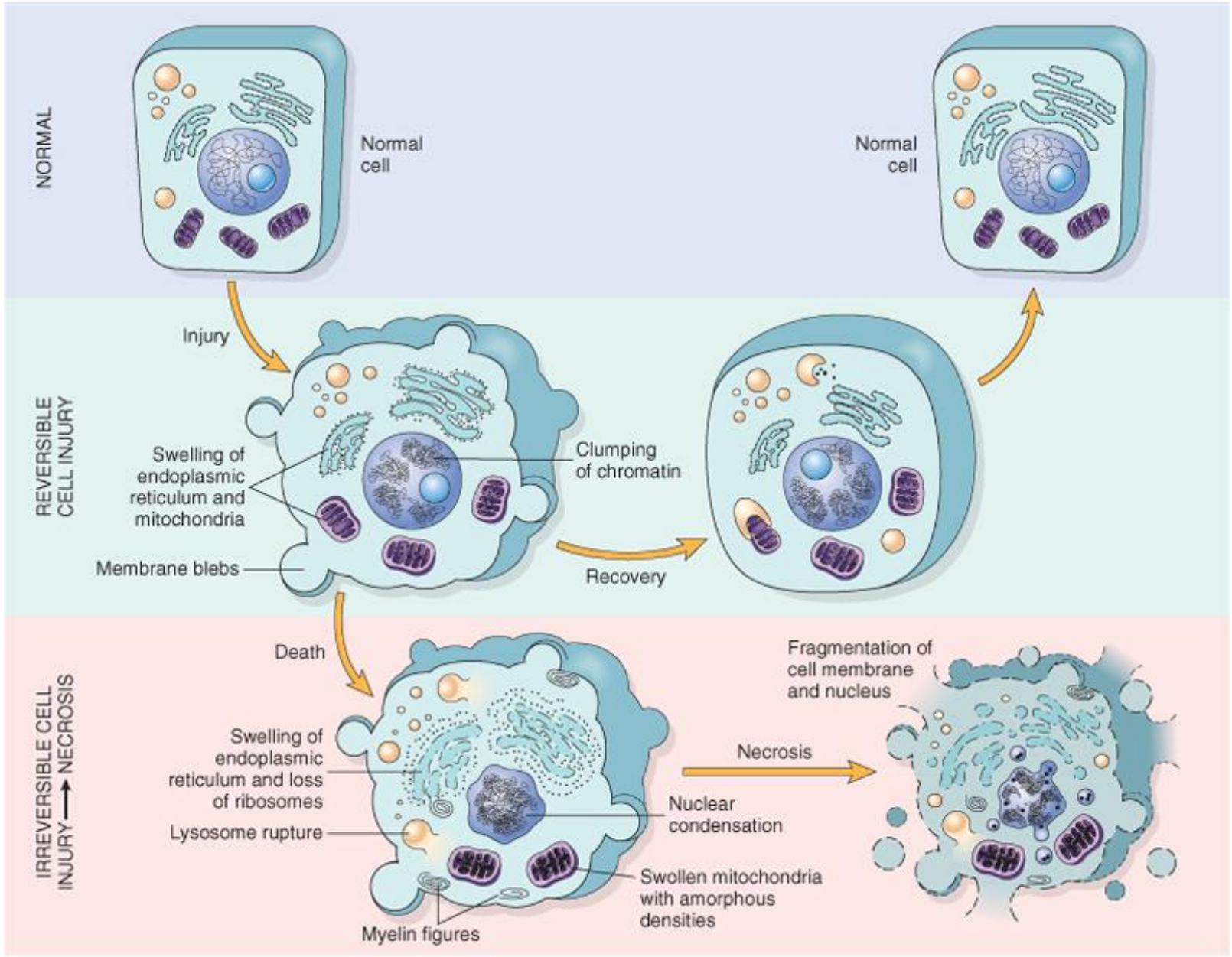
- Different cells show different morphologic changes

The differences reflect variations in

- Cell composition,
- Speed of necrosis, and
- Type of injury



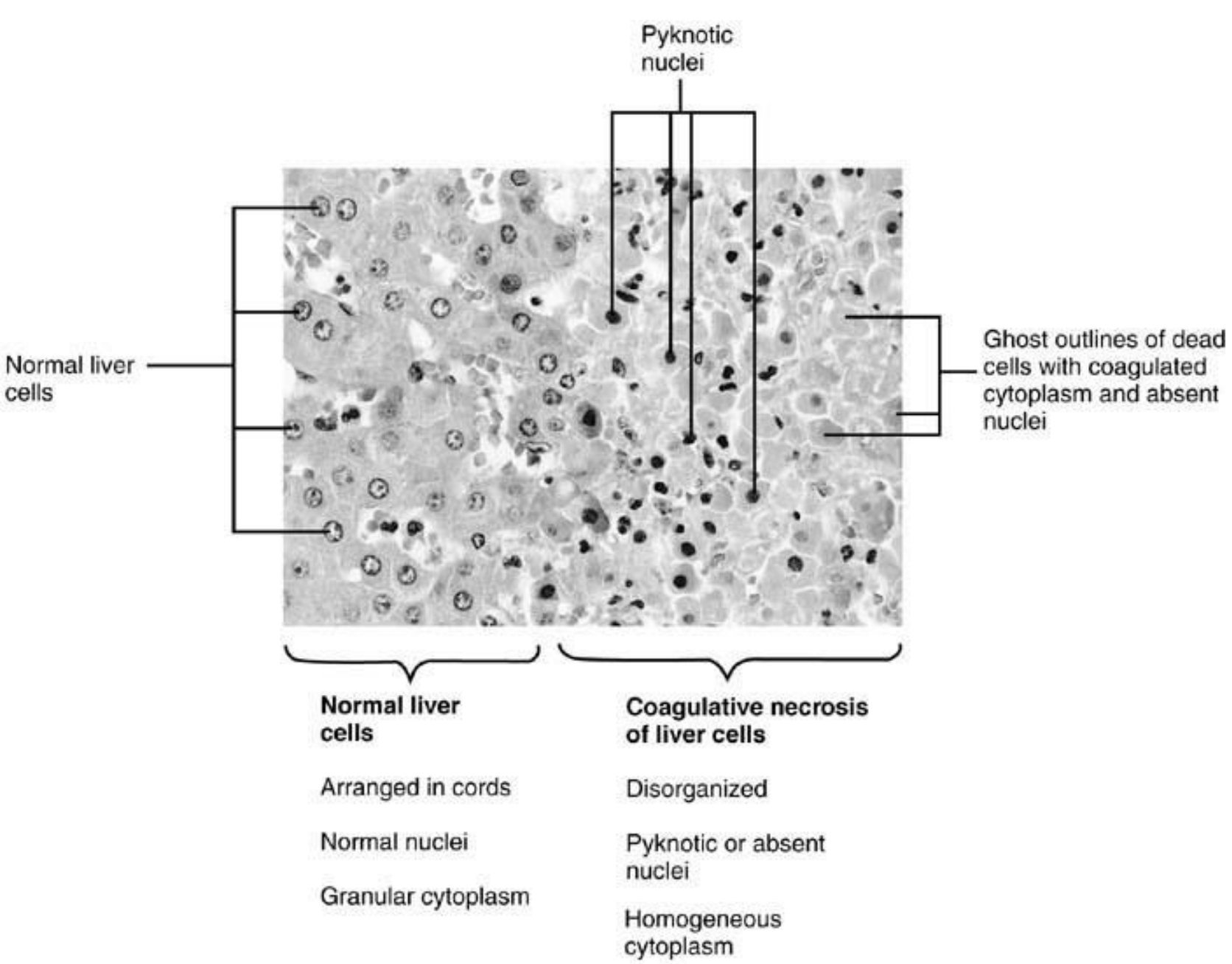




Coagulative Necrosis

- The necrotic cell retains its cellular outline, often for several days.

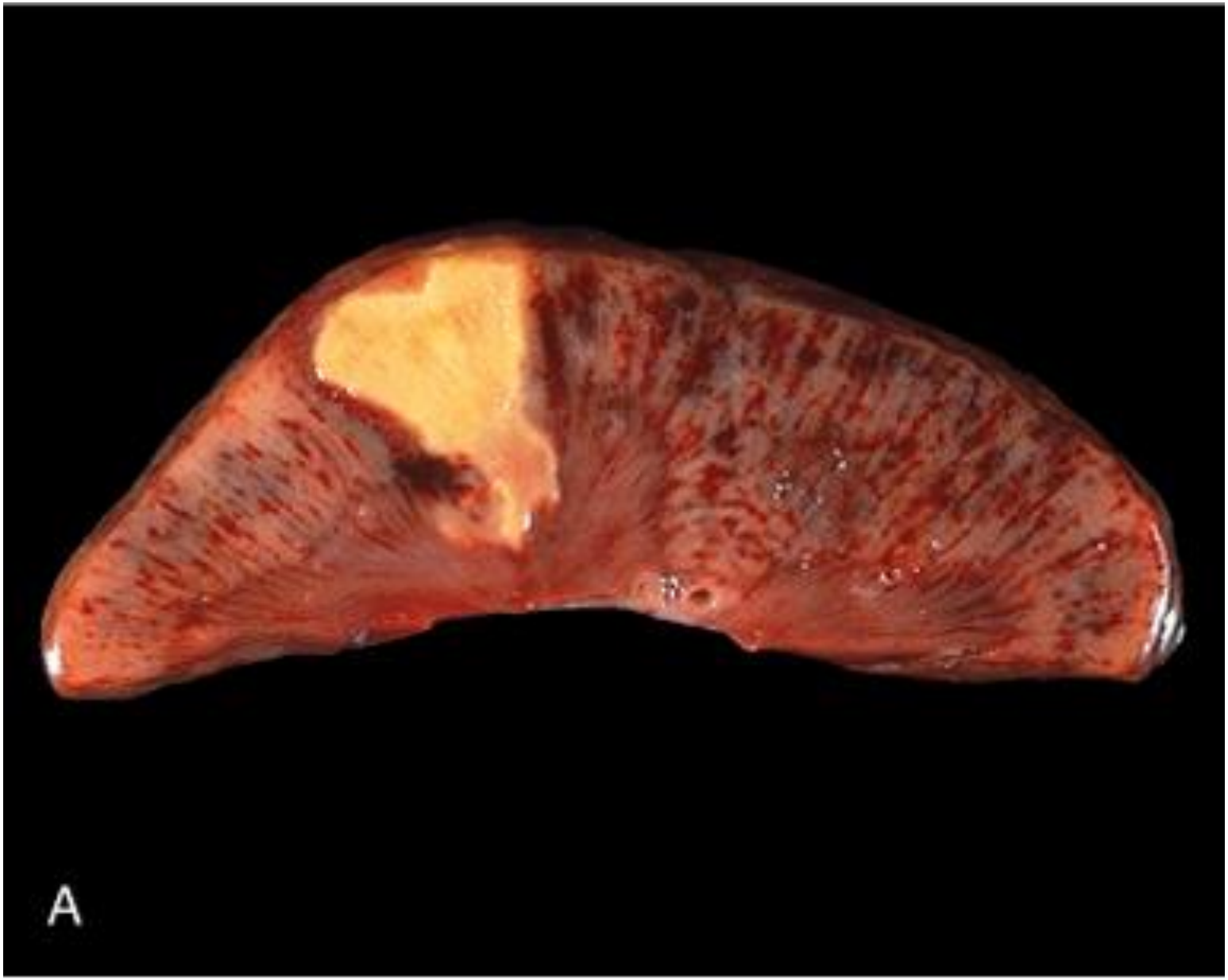
- The cell, devoid of its nucleus, appears as a mass of coagulated, pink-staining, homogeneous cytoplasm

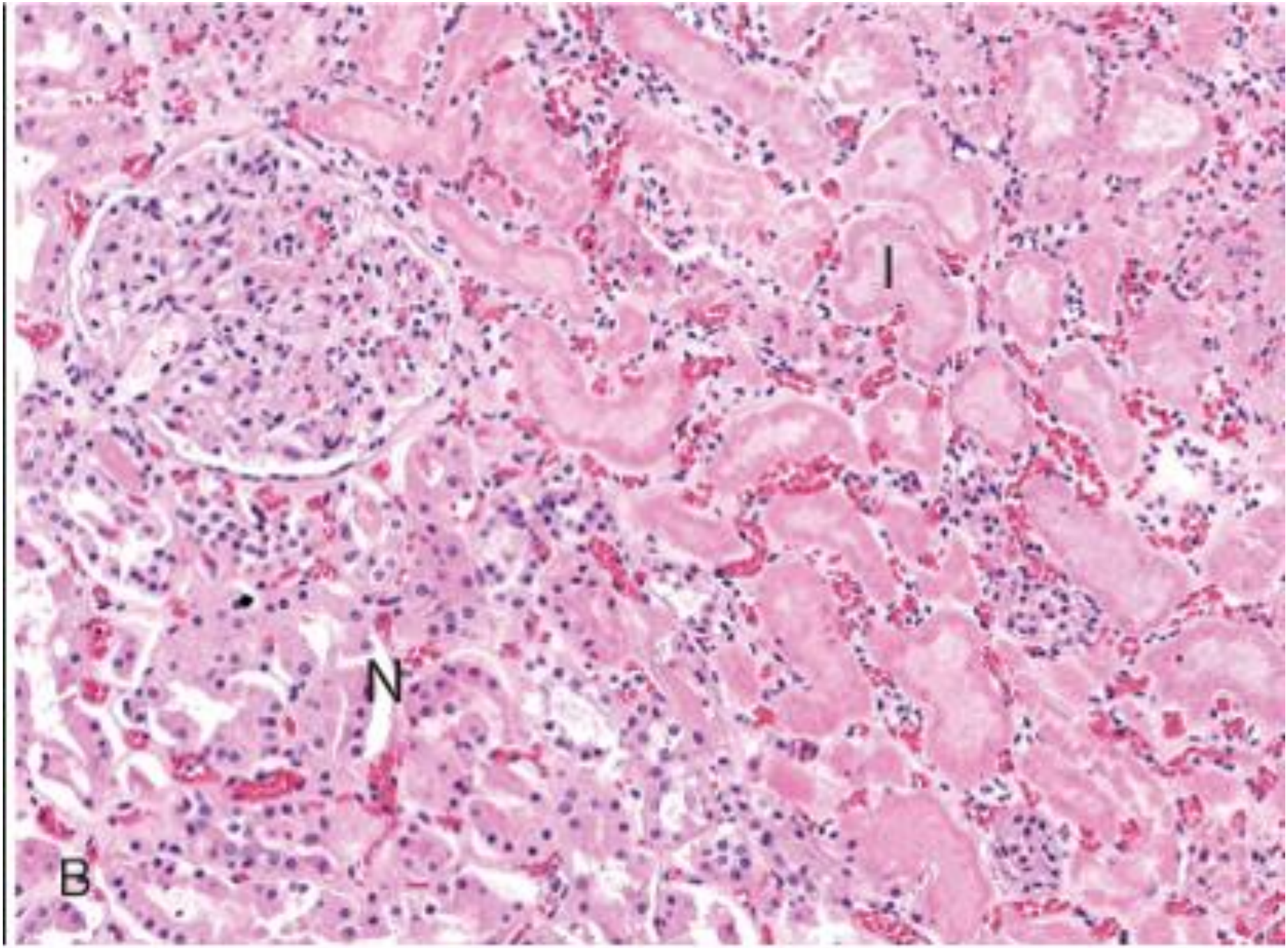


- Solid organs, (kidney, heart and adrenal gland)
- usually deficient blood supply and anoxia

- With other types of injury, eg, coagulative necrosis of liver cells due to viruses or toxic chemicals

- Skin in burns.

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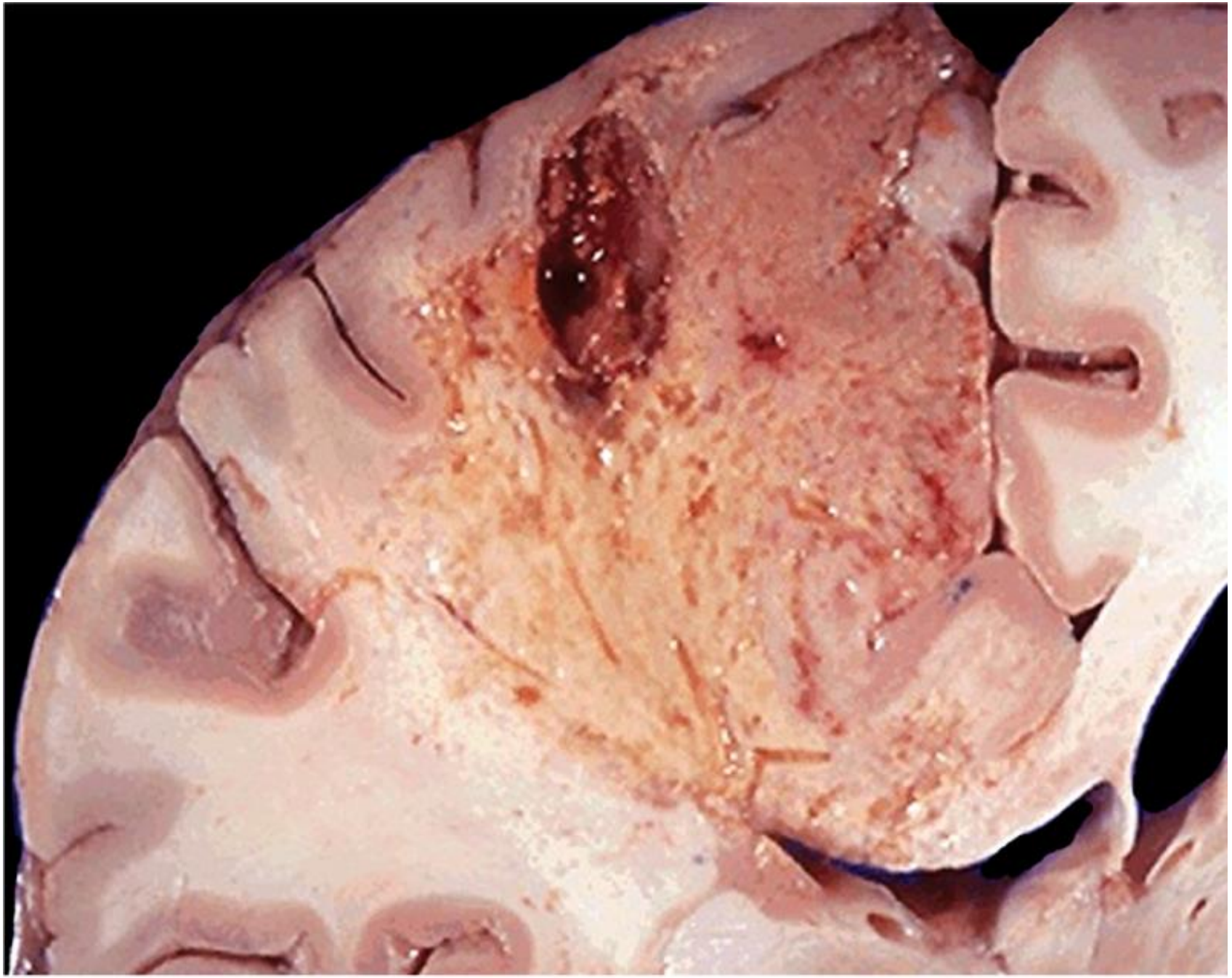
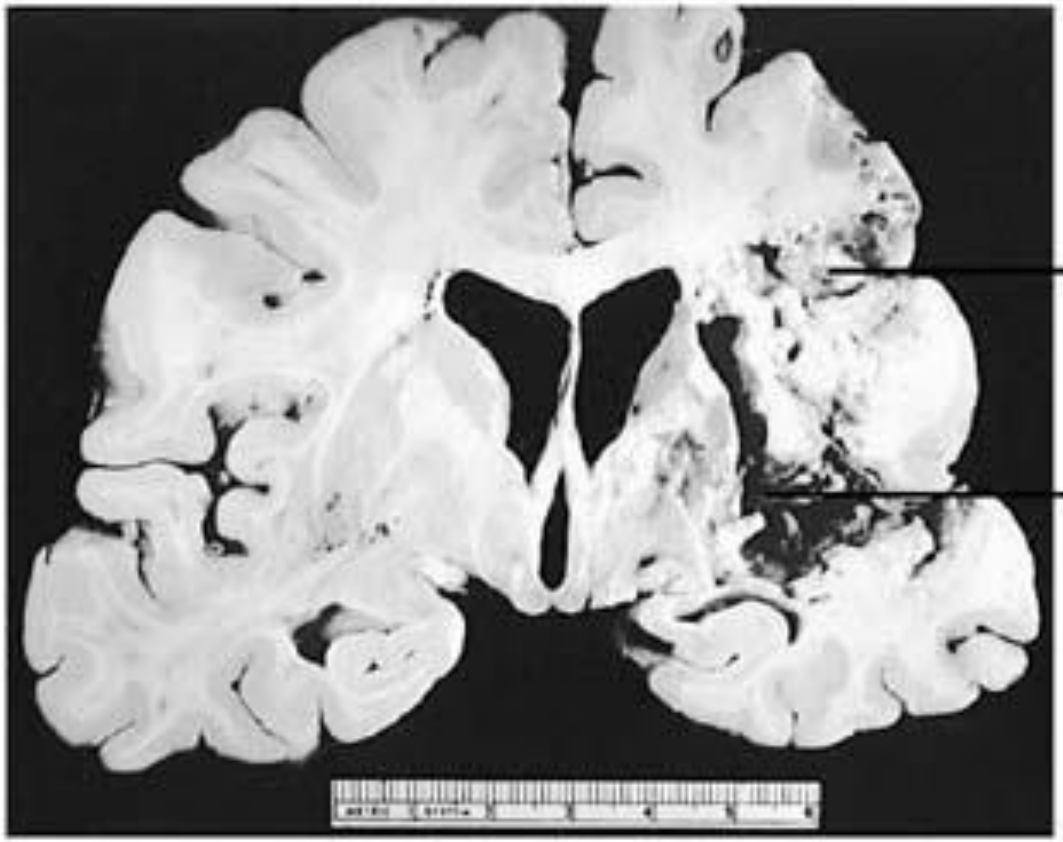
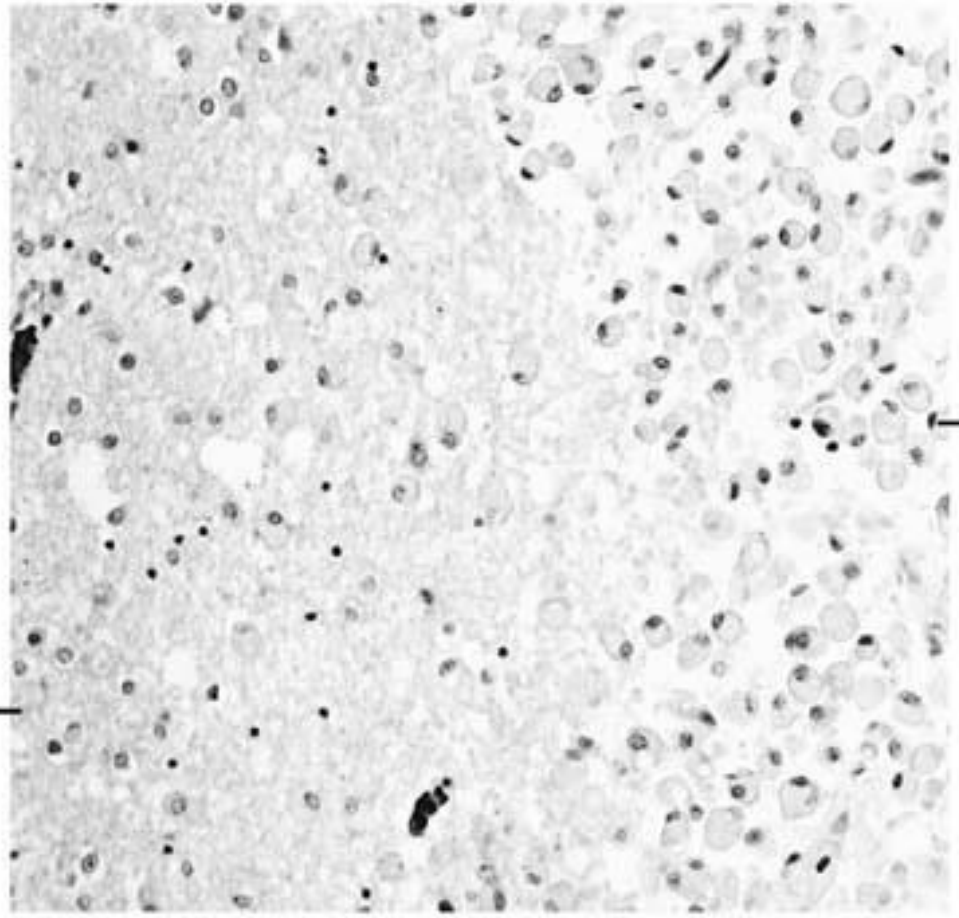
Liquefactive Necrosis

- Results when lysosomal enzymes released by the necrotic cells cause rapid liquefaction.
- **Autolysis.**
- Typically in the brain following ischemia







Fat Necrosis

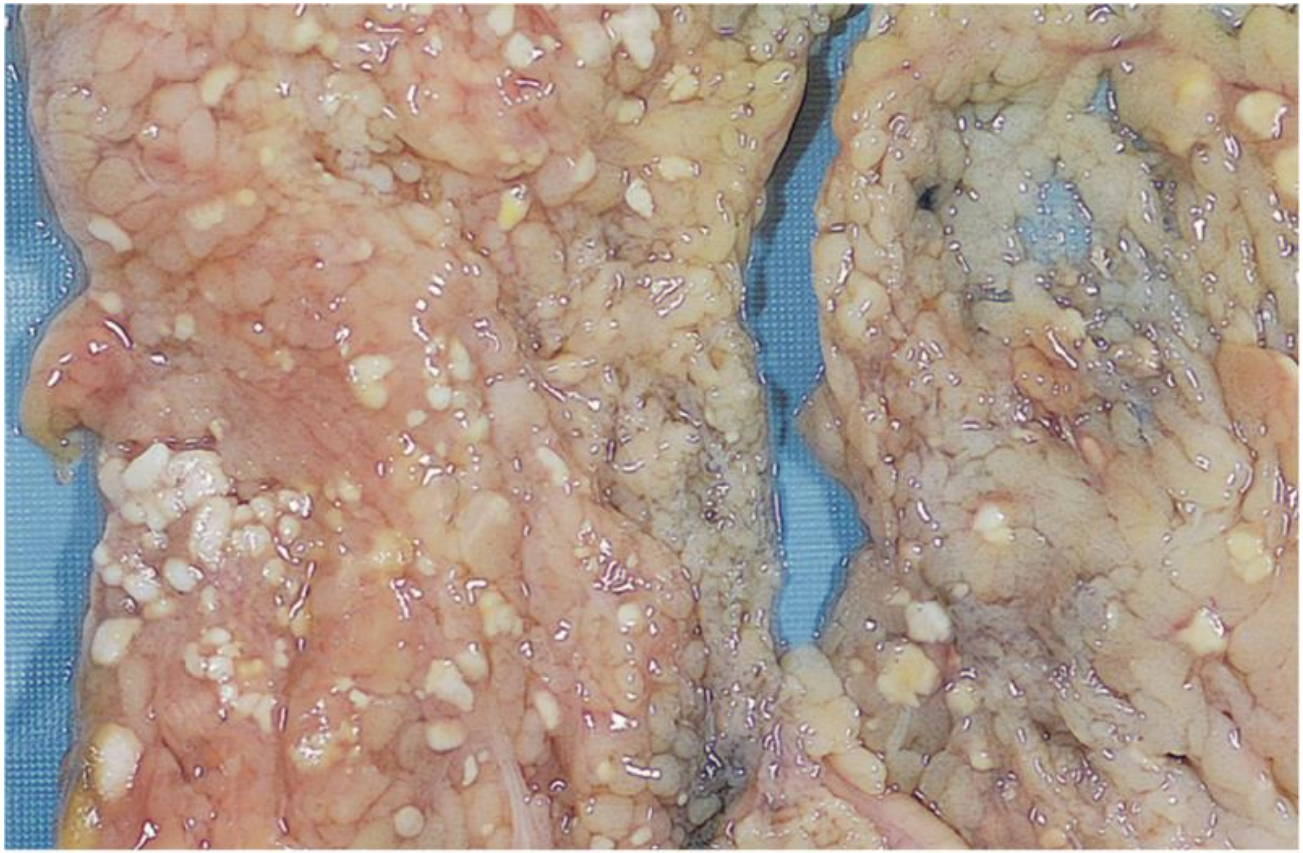
Enzymatic Fat Necrosis

- Acute pancreatitis when pancreatic enzymes are liberated

- Pancreatic lipase acts on the triglycerides in fat cells,
- Breaking these down into glycerol and fatty acids,
- Which complex with plasma calcium ions
- To form calcium soaps.

The gross appearance

- Opaque chalky white plaques and nodules in the adipose tissue surrounding the pancreas.



- Rarely, pancreatic disease may be associated with entry of lipase into the bloodstream and
- Subsequent widespread fat necrosis throughout the body;
- The subcutaneous fat and bone marrow are most affected

Nonenzymatic Fat Necrosis
TRAUMATIC FAT NECROSIS

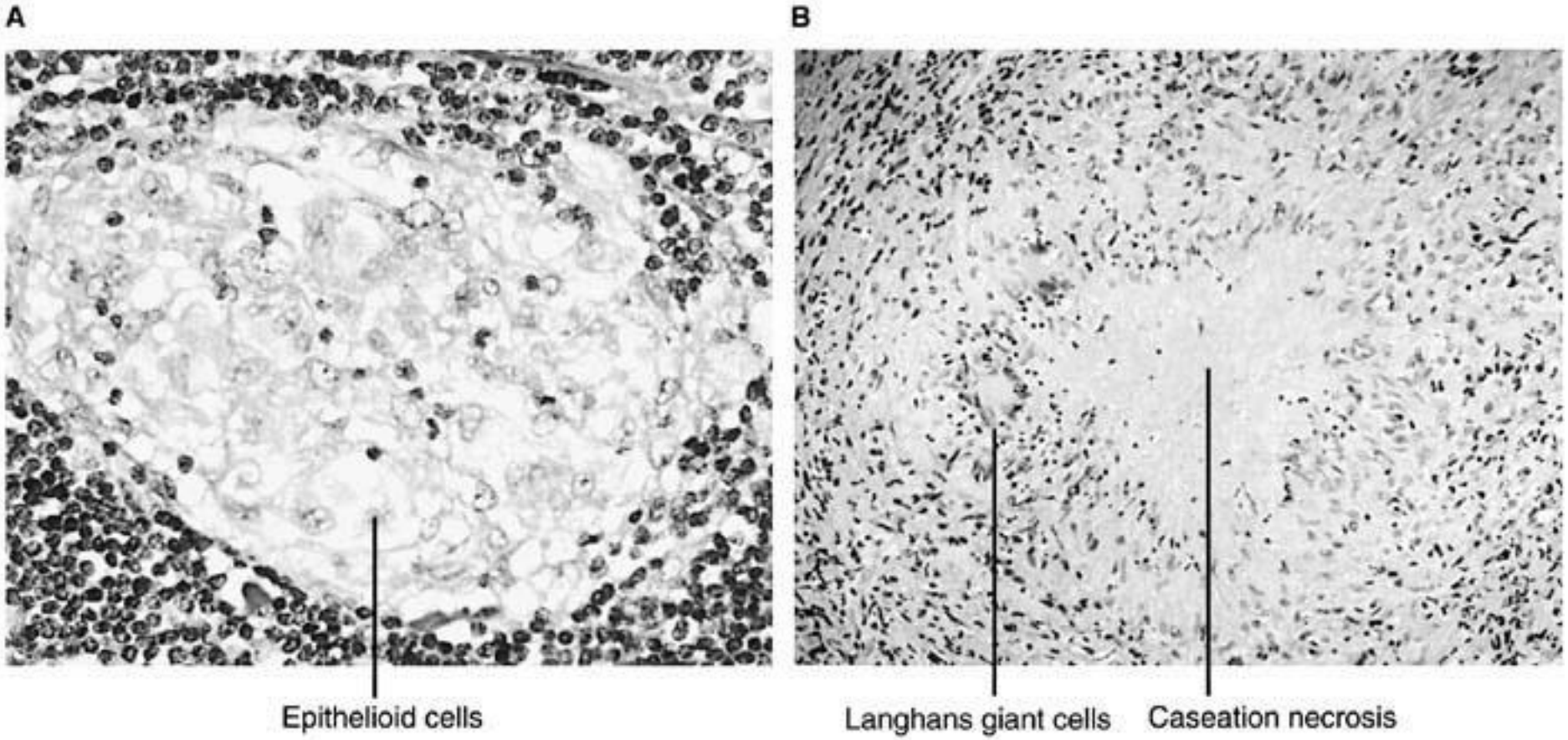
- Breast, subcutaneous tissue, and abdomen.
- History of trauma.
- Evokes an inflammatory response characterized by numerous foamy macrophages, neutrophils, and lymphocytes.

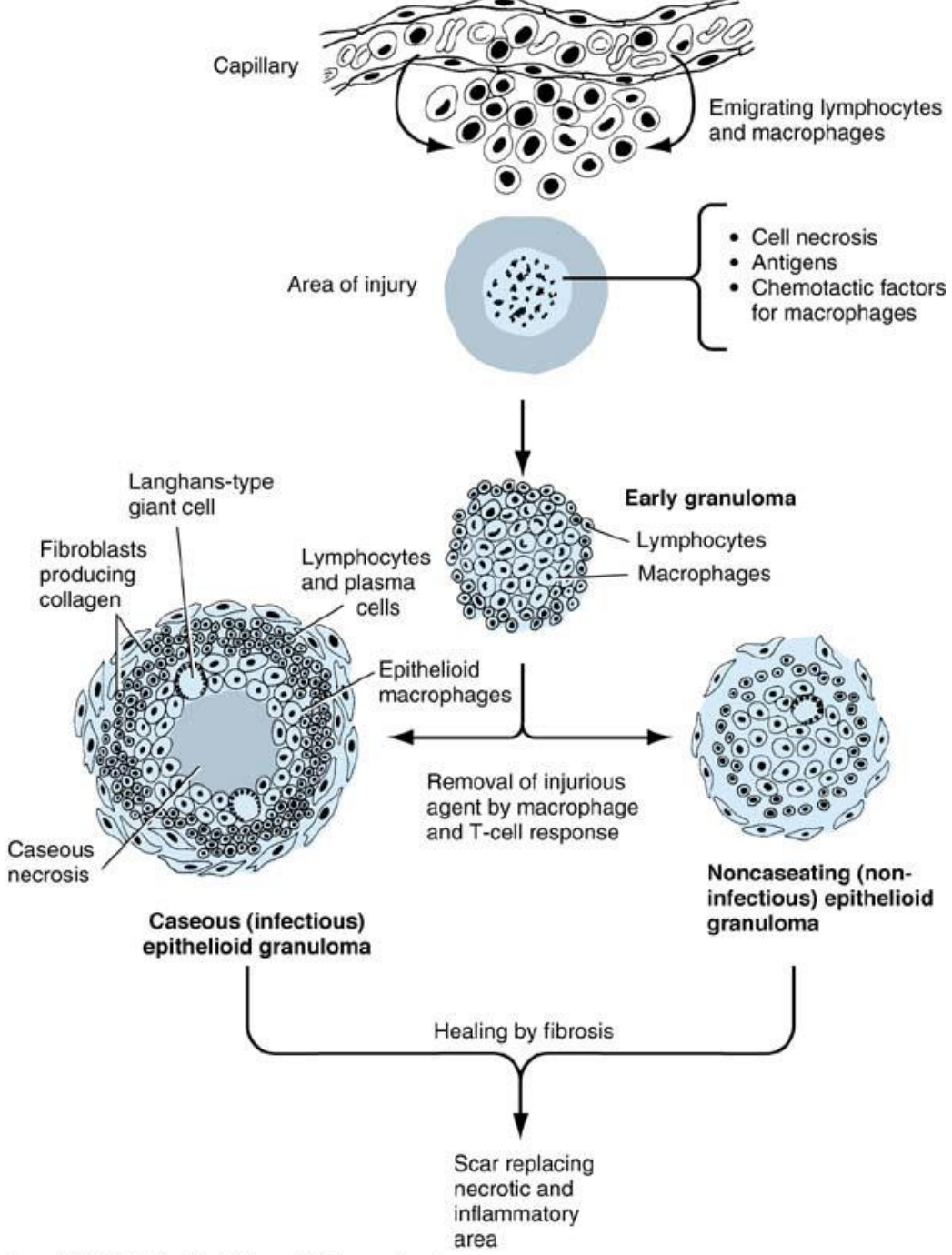
- Fibrosis follows, producing a mass that may be difficult to distinguish from a cancer

Caseous and Gummatous Necrosis

- Caseous (cheese-like) and
- Gummatous (gum- or rubber-like) necrosis
- Occur in infectious granulomas (localized chronic inflammatory lesions)

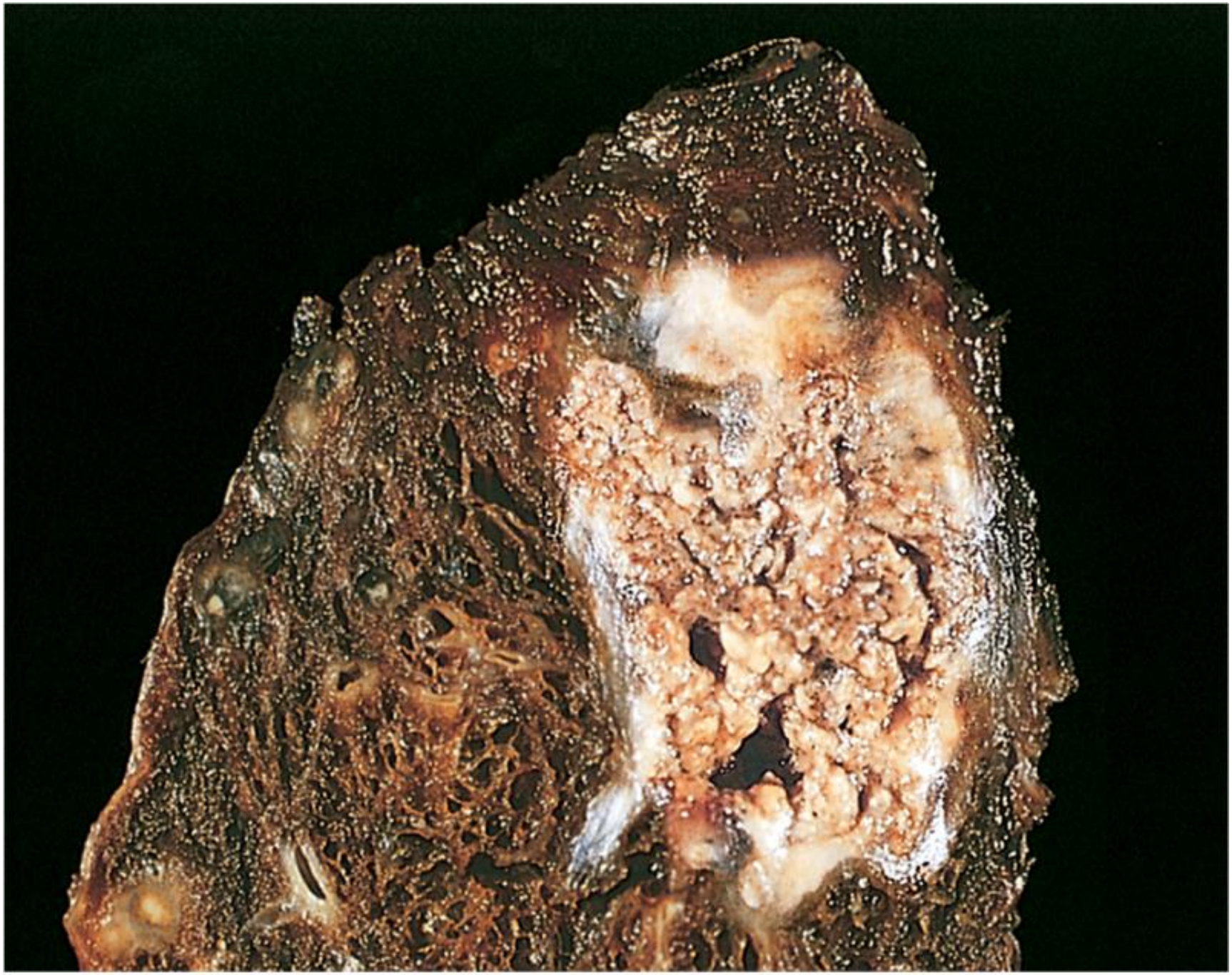
A: Early granuloma composed of an aggregate of epithelioid cells with vesicular nuclei, abundant cytoplasm, and indistinct borders. This is surrounded by lymphocytes. **B:** with central caseation.





Phases in formation of epithelioid granulomas during chronic inflammation. Caseous necrosis occurs especially in those cases in which an infectious agent is responsible for the injury (eg, tuberculosis).

Disease	Antigen	Caseous Necrosis
Immunologic response		
Tuberculosis	*Mycobacterium tuberculosis*	++
Leprosy (tuberculoid type)	*Mycobacterium leprae*	–
Histoplasmosis	*Histoplasma capsulatum*	++
Coccidioidomycosis	*Coccidioides immitis*	++
Q fever	*Coxiella burnetii* (rickettsial organism)	–
Brucellosis	*Brucella* species	–
Syphilis	*Treponema pallidum*	++
Sarcoidosis	Unknown	–
Crohn's disease	Unknown	–
Berylliosis	Beryllium (? +protein)	–
Nonimmunologic response		
Foreign body (eg, in intravenous drug abuse)	Talc, fibers (? +protein)	



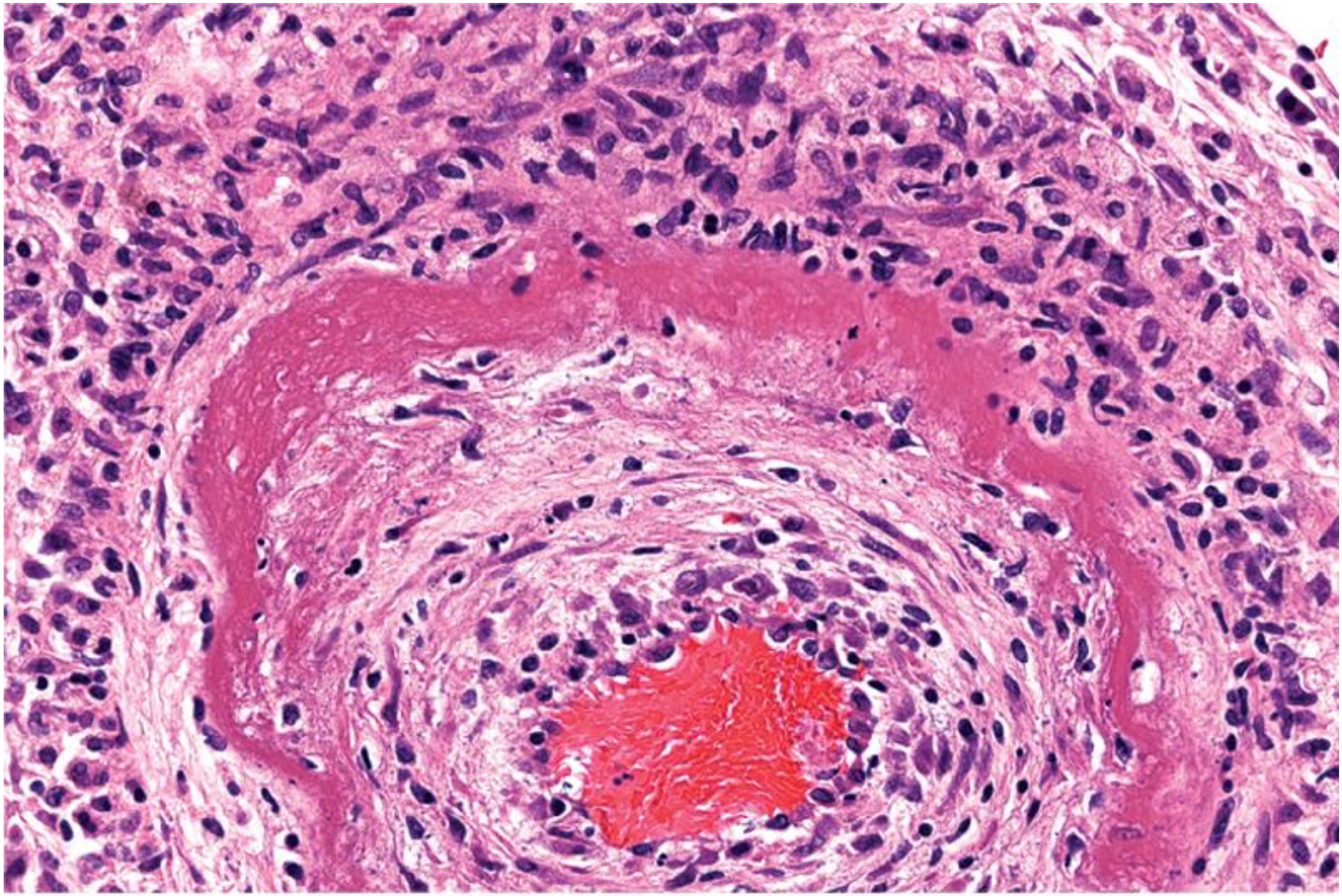
Fibrinoid Necrosis

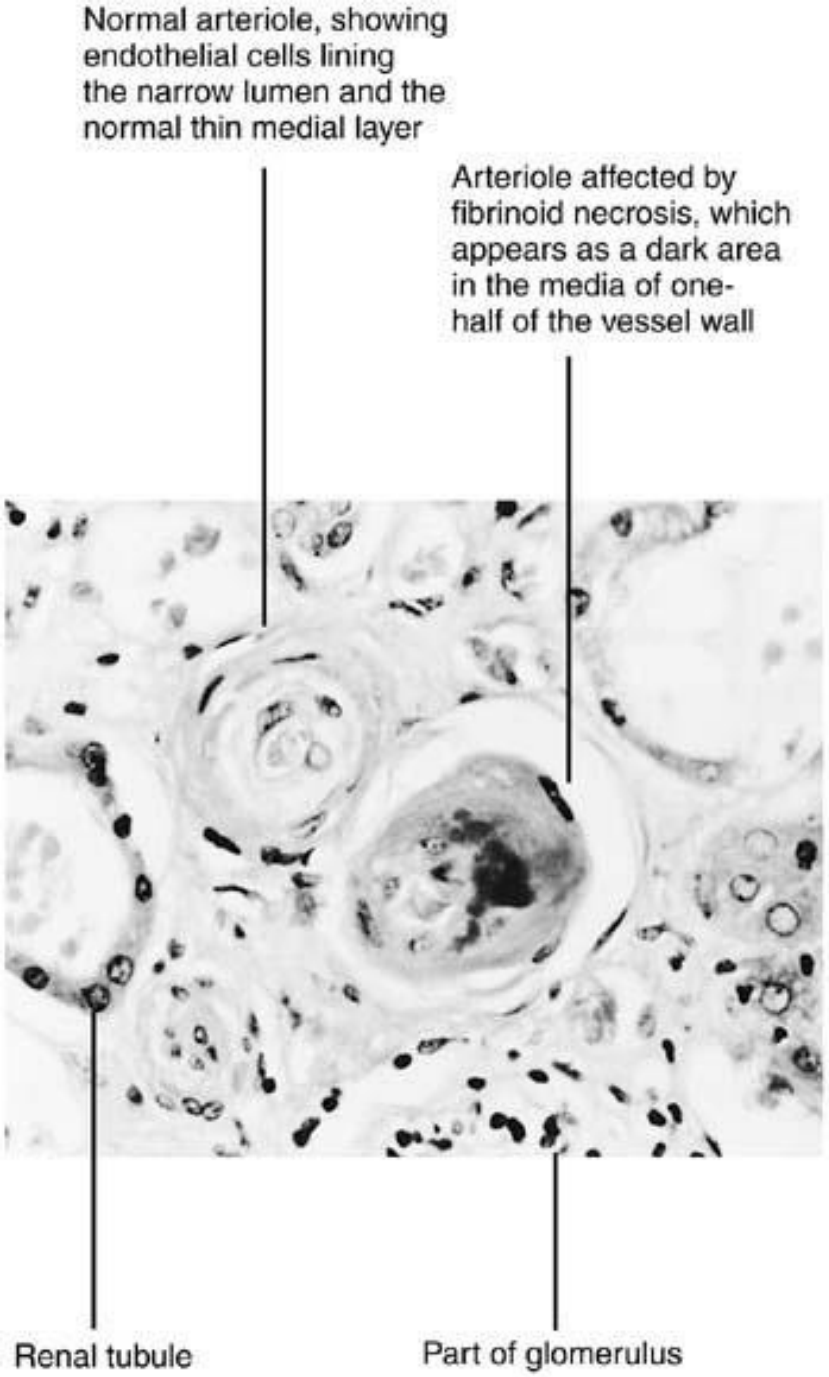
- Connective tissue necrosis seen particularly in autoimmune diseases (eg, Rheumatic fever, polyarteritis nodosa, and SLE)
- Collagen and smooth muscle in the media of blood vessels are especially involved.

- Fibrinoid necrosis of arterioles also occurs in accelerated (malignant) hypertension.

- Loss of normal structure and replacement by a homogeneous, bright pink-staining necrotic material that resembles fibrin microscopically

- Areas of fibrinoid necrosis contain various amounts of immunoglobulins and complement, albumin, breakdown products of collagen, and fibrin





Gangrene

- Necrosis of the tissue with superadded putrefaction
- Clinical condition in which **extensive tissue necrosis** is complicated to a variable degree by secondary bacterial infection.

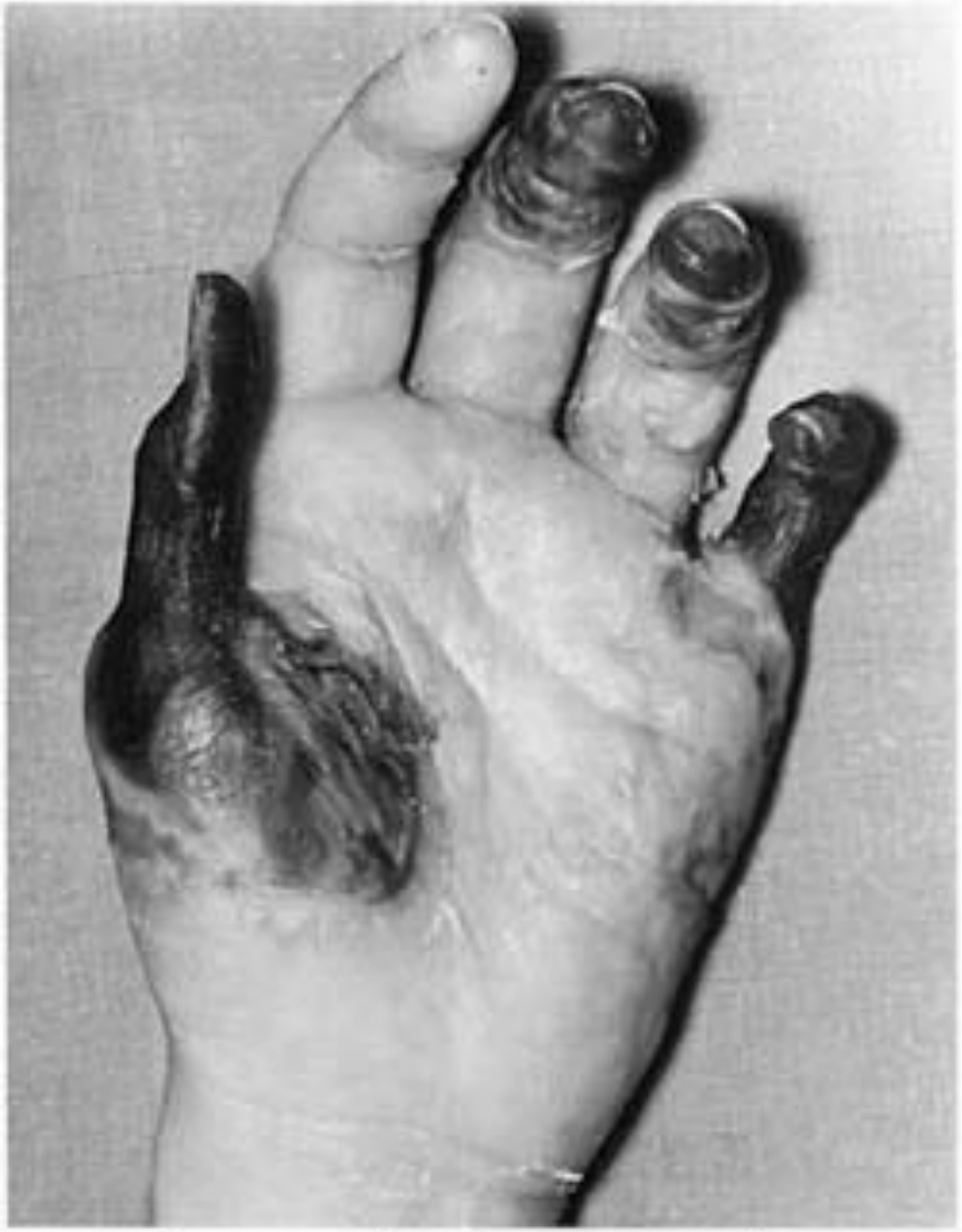
- Black, foul smelling area that is in continuity with living tissue

Putrefaction in a dead tissue

- Invasion by protien splitting,anaerobic
- Saprophytic organisms => gas formation & foul smelling substances
- Black or dark green
- Broken down Hb is converted to Iron sulphide by these organisms

Dry Gangrene

- Extremities as a result of ischemic coagulative necrosis of tissues due to arterial obstruction.
- The necrotic area appears black, dry, and shriveled and is sharply demarcated from adjacent viable tissue.
- Secondary bacterial infection is usually insignificant.
- Debridement

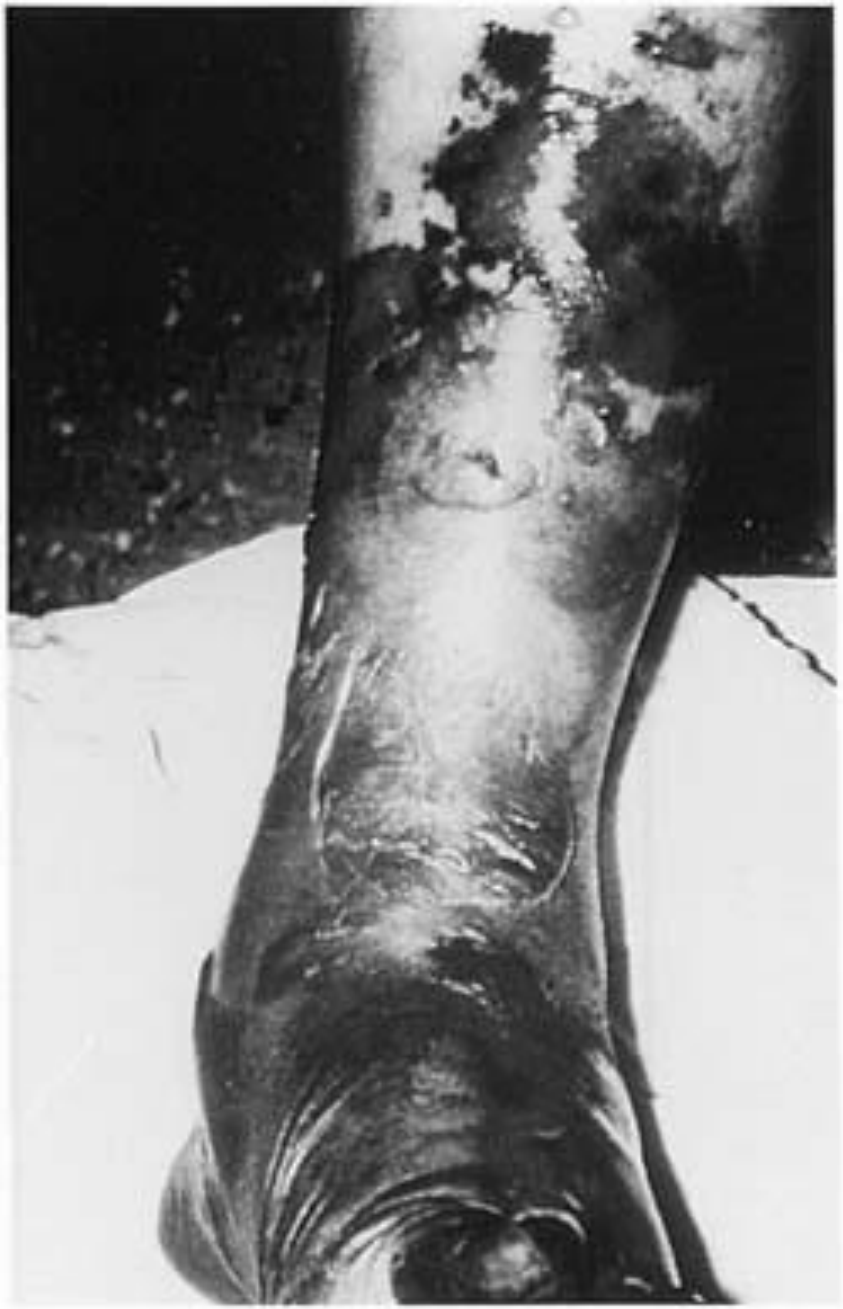


Wet Gangrene

- Severe bacterial infection superimposed on necrosis.
- Extremities & internal organs (intestine).

- Acute inflammation and growth of invading bacteria cause the necrotic area to become swollen and reddish-black, with extensive liquefaction of dead tissue

- Spreading necrotizing inflammation that is not clearly demarcated (difficult to treat surgically)
- Bacterial fermentation => typical foul odor.
- The type of bacteria involved varies with the site.
- The mortality rate is high.



Gas Gangrene

- Wound infection caused by *clostridium perfringens* and other clostridial species.
- Extensive necrosis of tissue and production of gas by the fermentative action of the bacteria.
- The gross appearance is similar to that of wet gangrene, with the additional presence of gas in the tissues.

- **Crepitus** (a crackling sensation on palpation over the site) can often be detected clinically, and gas may be seen on soft tissue x-rays.
- The mortality rate is high.

Have a nice day