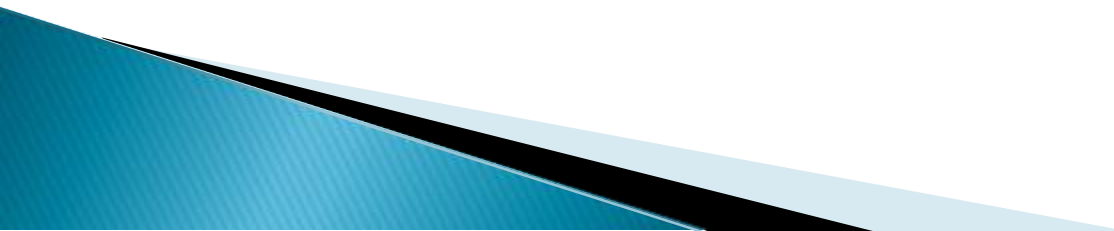


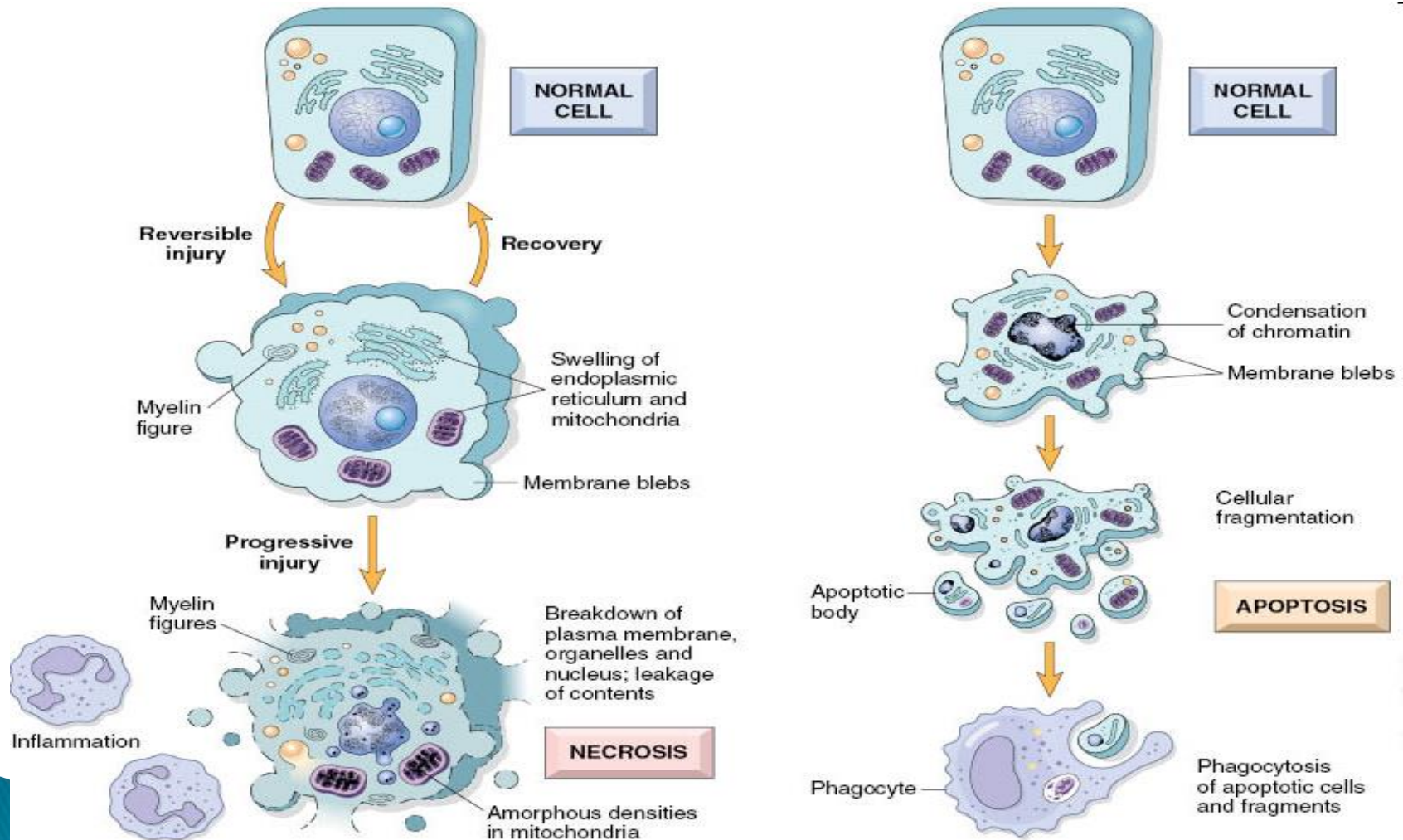
Reversible and irreversible cell injury

cell injury and adaptations
Manar Hajeer, MD, FRCPath
University of Jordan , school of medicine

Outlines:

- ▶ Reversible injury.
 - ▶ Irreversible injury (necrosis).
 - ▶ Clinical implications.
 - ▶ Patterns of necrosis.
- 

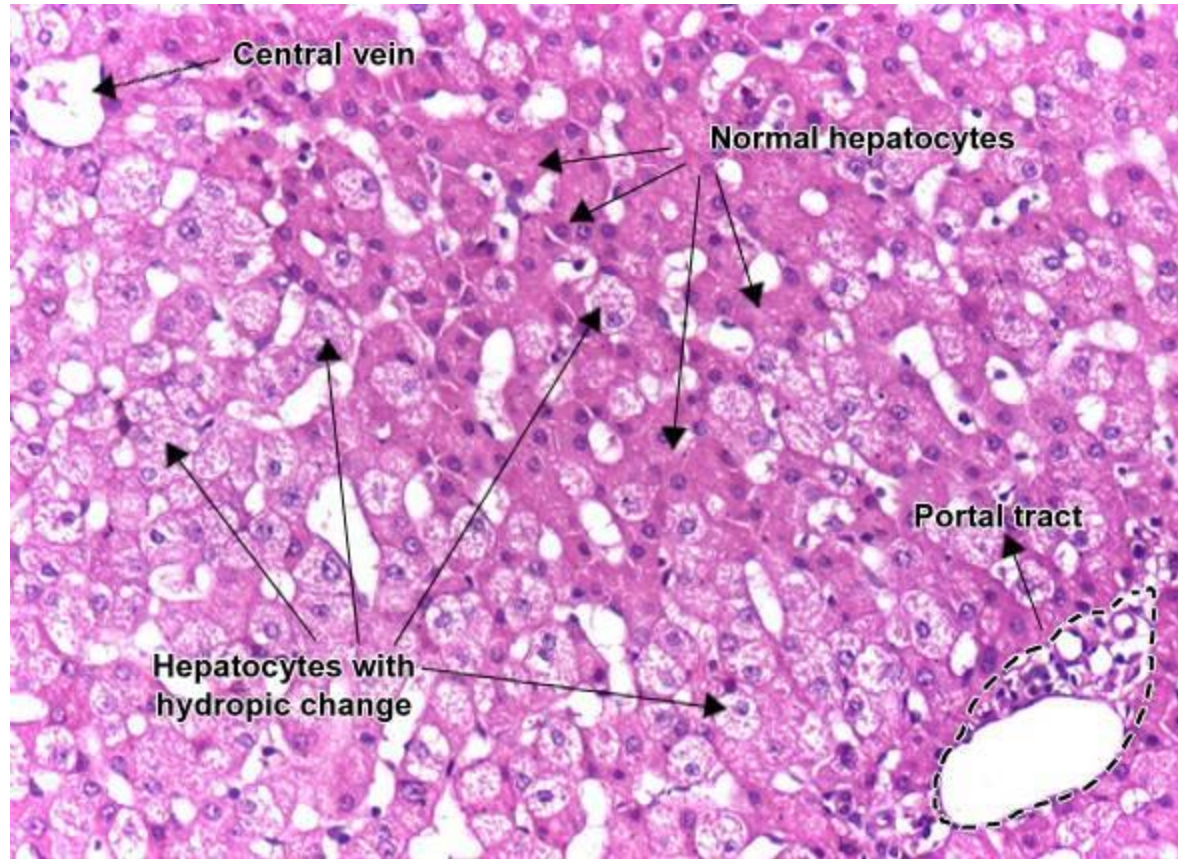
Cell injury:



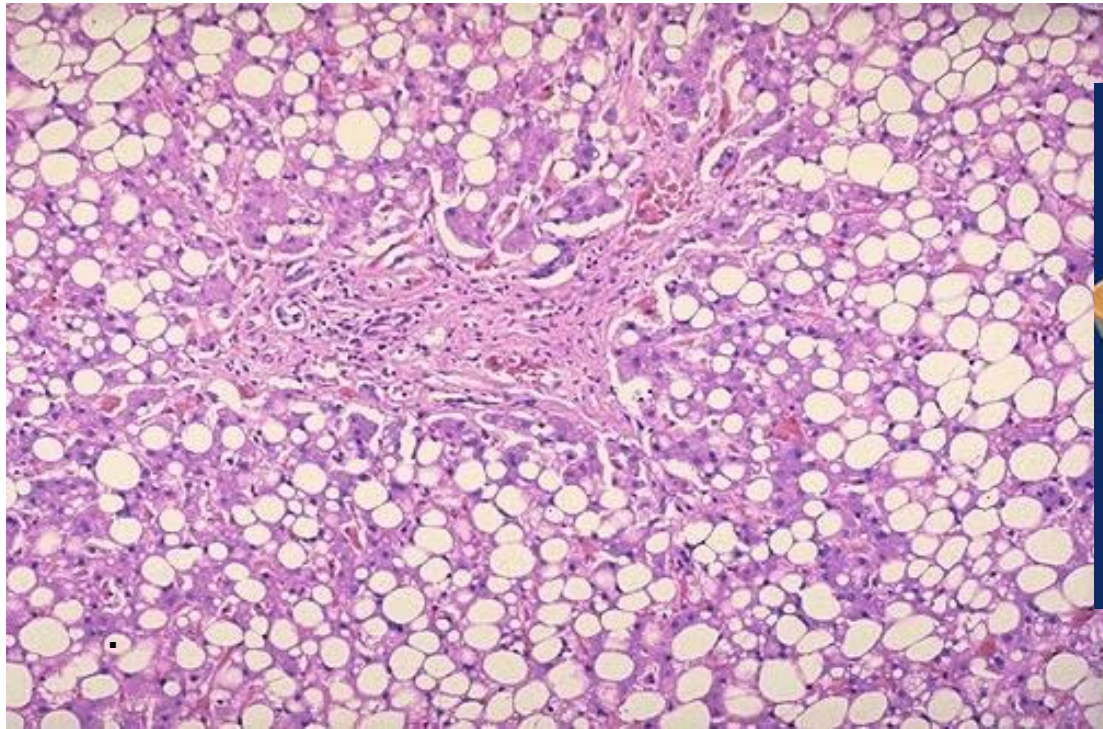
Reversible injury

- ▶ If the damaging stimulus is removed
>>>injured cells can return to normal
- ▶ **Morphology:**
- ▶ Cellular swelling/organ swelling
- ▶ Fatty change

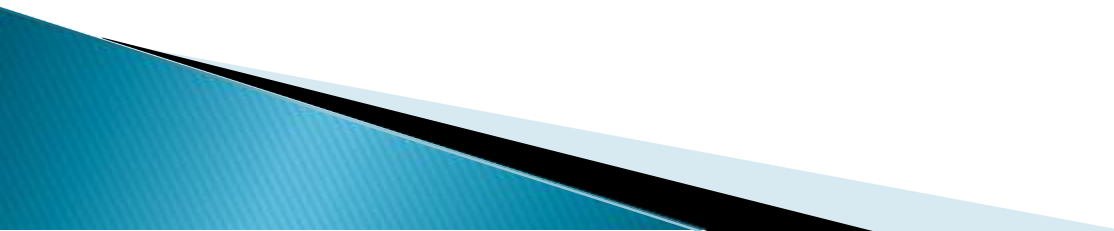
Reversible damage – cellular swelling



Reversible damage – fatty change



Other changes

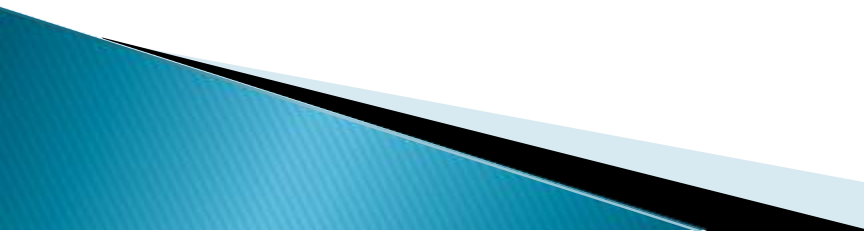
- ▶ (1) plasma membrane alterations (blebbing, blunting)
 - ▶ (2) mitochondrial change (swelling and densities);
 - ▶ (3) dilation of ER
 - ▶ (4) nuclear clumping of chromatin.
 - ▶ (5) Cytoplasmic myelin figures
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Irreversible injury (necrosis)

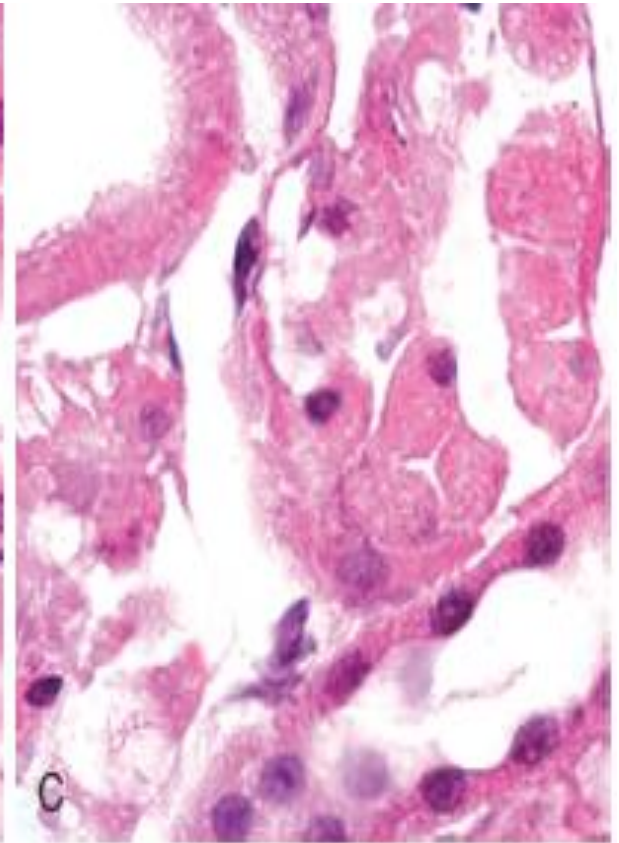
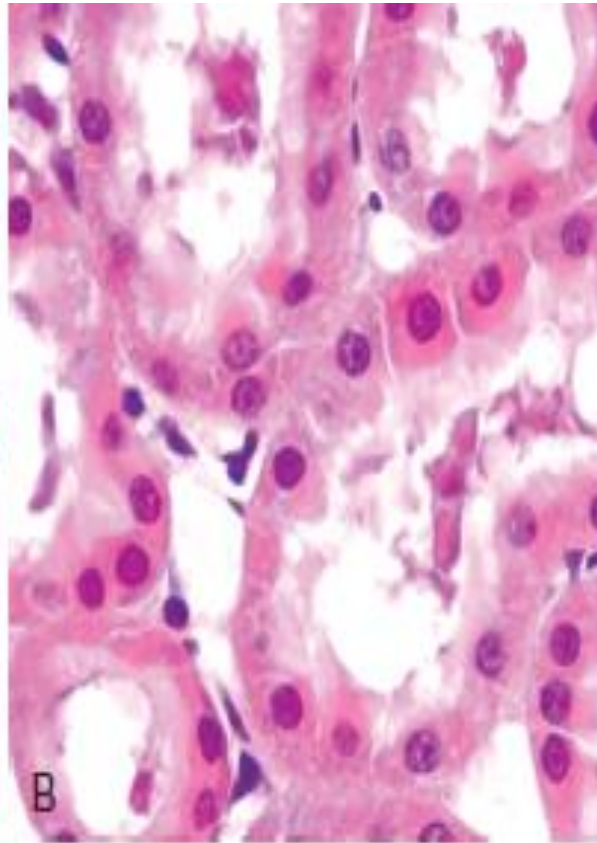
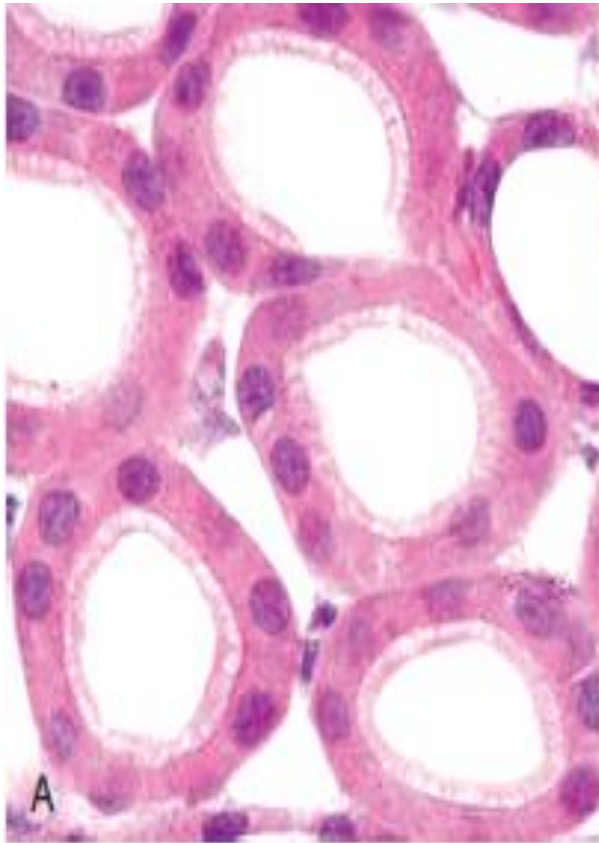
1. **Irrversible Mitochondrial dysfunction**
 2. Loss of **plasma membrane and intracellular membranes** >>> cellular enzymes leak out
 3. Loss of **DNA and chromatin structural integrity.**
- Local inflammation.

Morphology irreversible injury (Necrosis)

- ▶ Increased cytoplasmic eosinophilia.
 - ▶ Marked dilatation of ER , mitochondria.
 - ▶ Mitochondrial densities.
 - ▶ More myelin figures.

 - ▶ **Nuclear changes:**
 - ▶ **Pyknosis:** shrinkage and increased basophilia;
 - ▶ **Karyorrhexis** :fragmentation;
 - ▶ **Karyolysis:** basophilia fades
- 

Normal, reversible and irreversible cell injury



Cell death

- ▶ Different mechanisms, depending on nature and severity of injury.
- ▶ **Necrosis:**
 - ▶ Rapid and uncontrollable.
 - ▶ Severe disturbances
 - ▶ Ischemia, toxins, infections, and trauma
- ▶ **Apoptosis:**
 - ▶ Less severe injury.
 - ▶ Regulated by genes and signaling pathways
 - ▶ Precisely Controlled.
 - ▶ Can be manipulated.
 - ▶ In healthy tissues.
 - ▶ Clean cell suicide.
- ▶ **Necroptosis.**

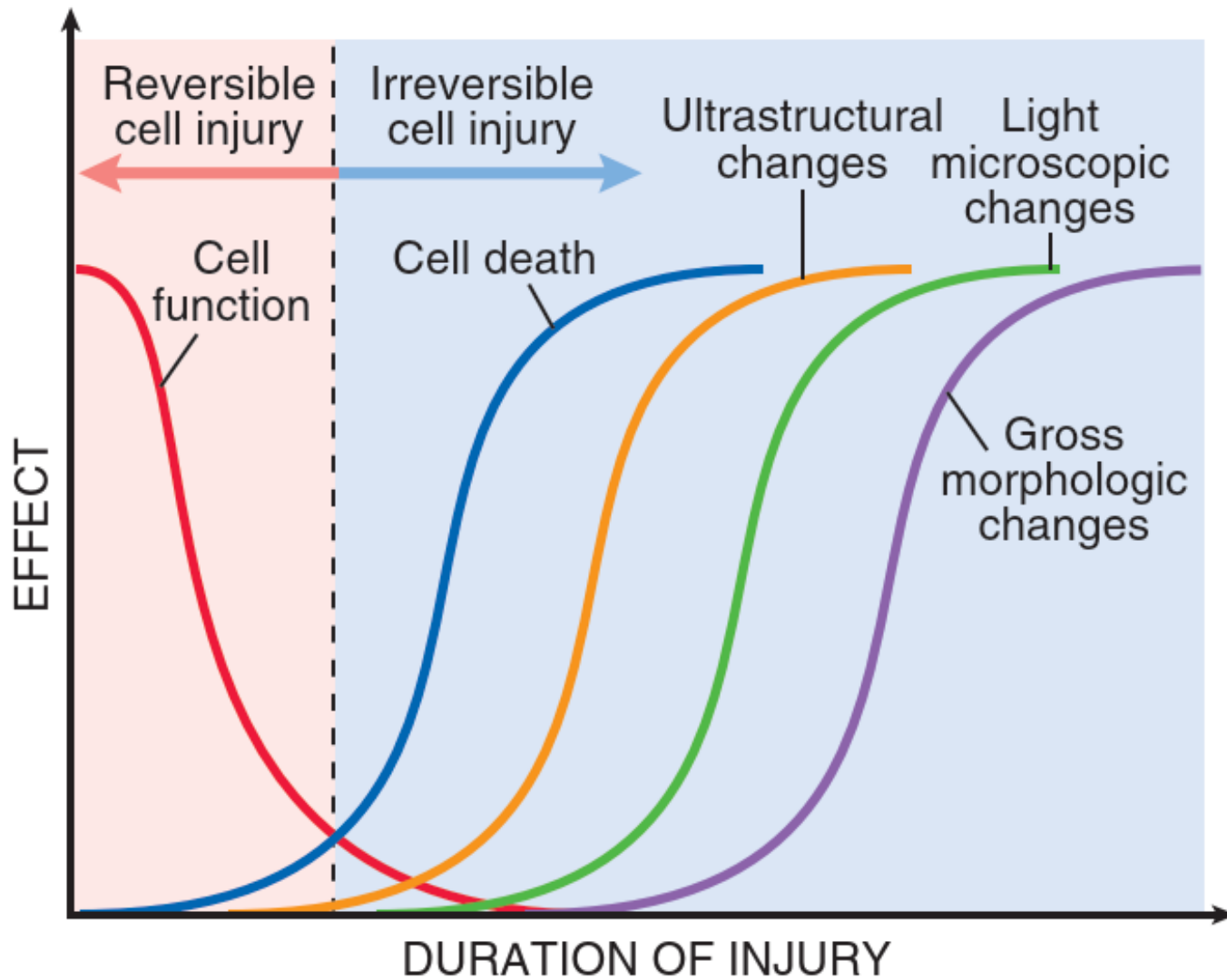
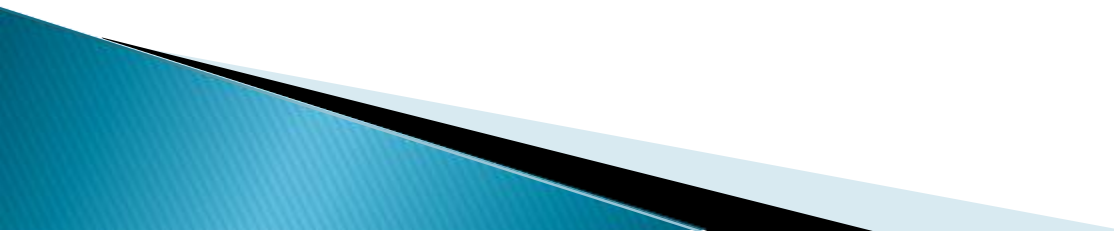


Table 1-1 Features of Necrosis and Apoptosis

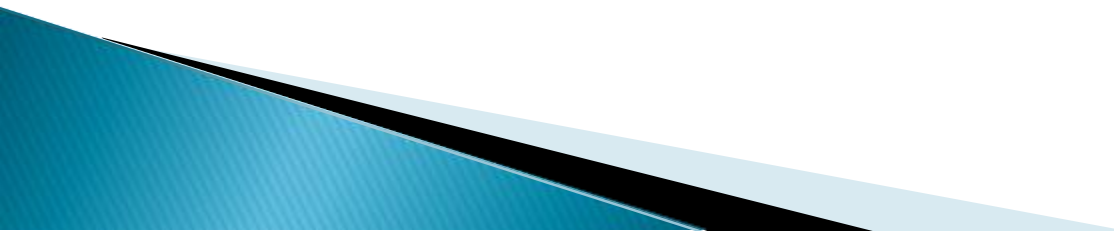
Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic; means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA and protein damage

DNA, deoxyribonucleic acid.

Clinical implications

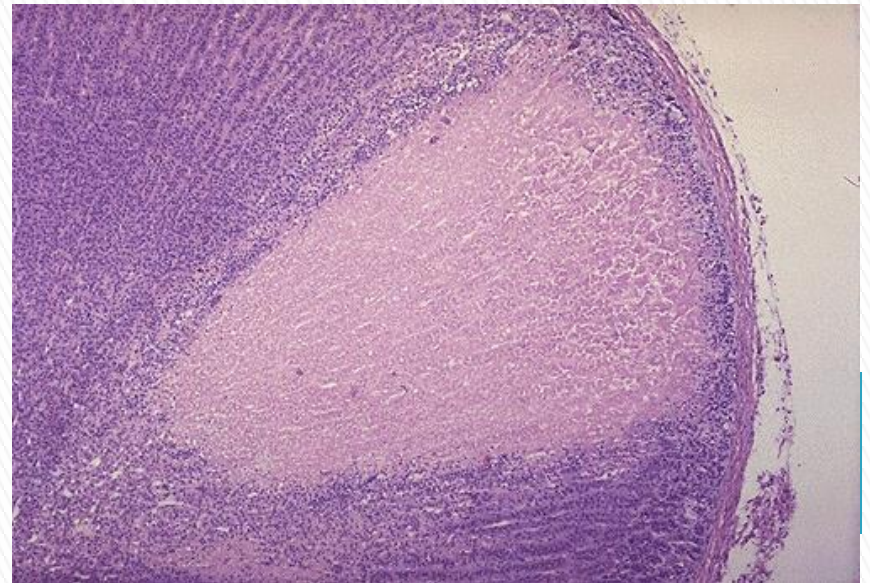
- ▶ Leakage of intracellular proteins through the damaged cell membrane and ultimately into the circulation provides a means of detecting tissue-specific necrosis using blood or serum samples.
 - ▶ Cardiac enzymes, liver enzymes.
- 

Morphologic Patterns of tissue necrosis (Etiologic clues)

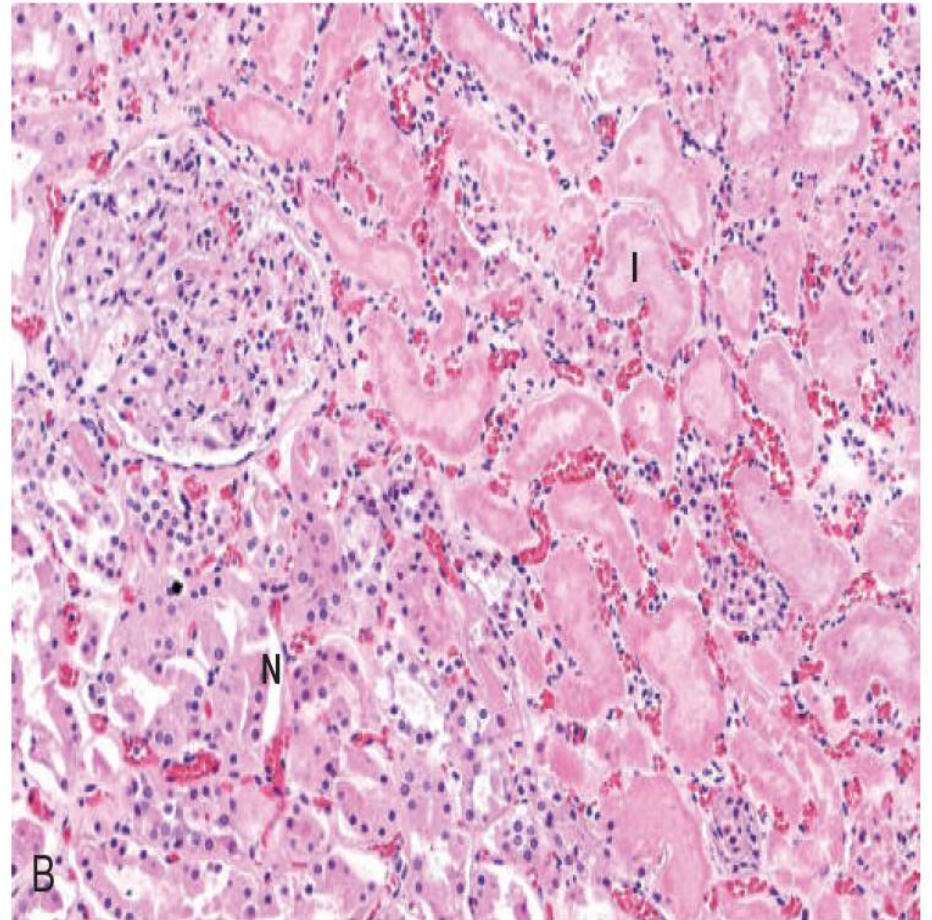


Coagulative necrosis

- ▶ Conserved tissue architecture initially.
- ▶ Enzyme dysfunction.
- ▶ Anuclear eosinophilic on LM
- ▶ Wedge shaped (following blood supply)
- ▶ Leukocyte lysosomal enzymes and phagocytosis required for clearance.
- ▶ Ischemia to all solid organ (infarcts) except the brain

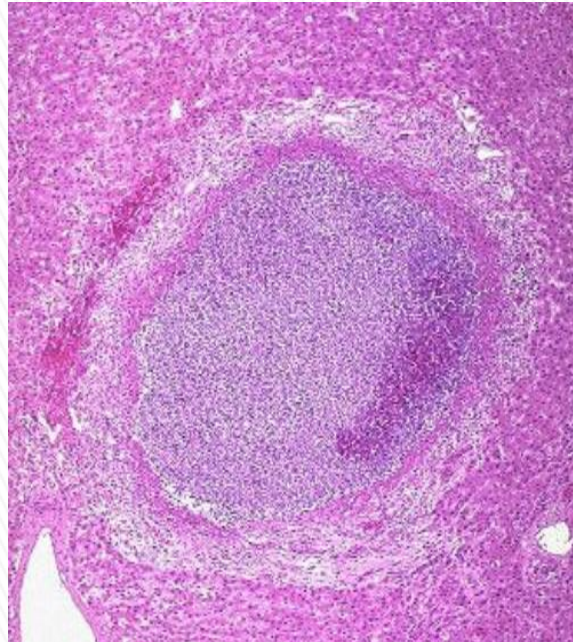


Coagulative necrosis



Liquefactive necrosis

- ▶ Focal infections by Bacterial and fungal organisms.
- ▶ Pus.
- ▶ CNS infarcts
- ▶ Center liquefies and digested tissue is removed by phagocytosis



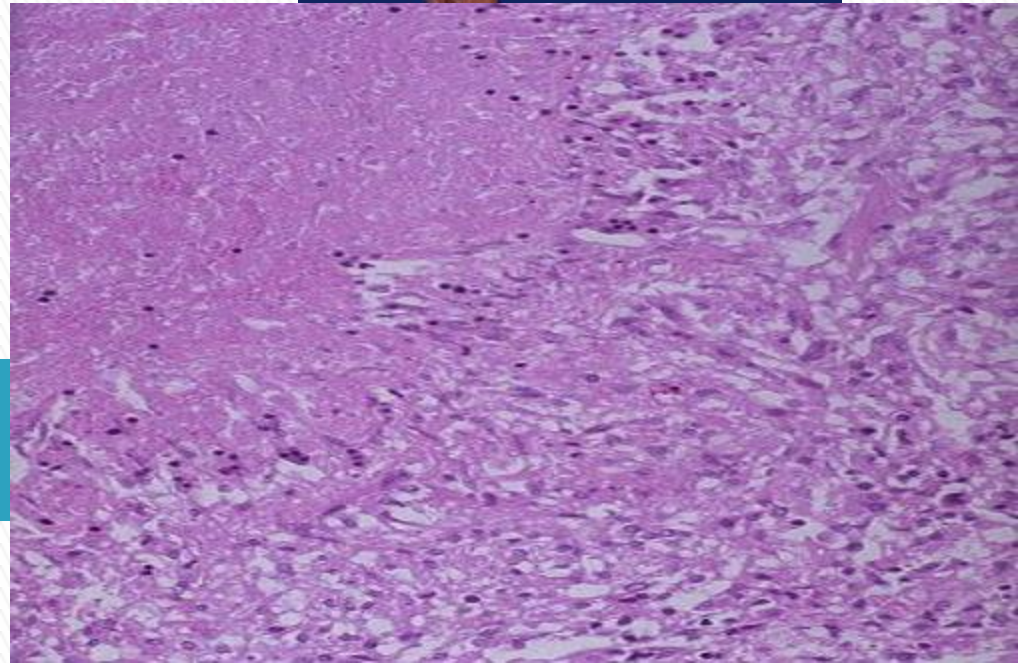
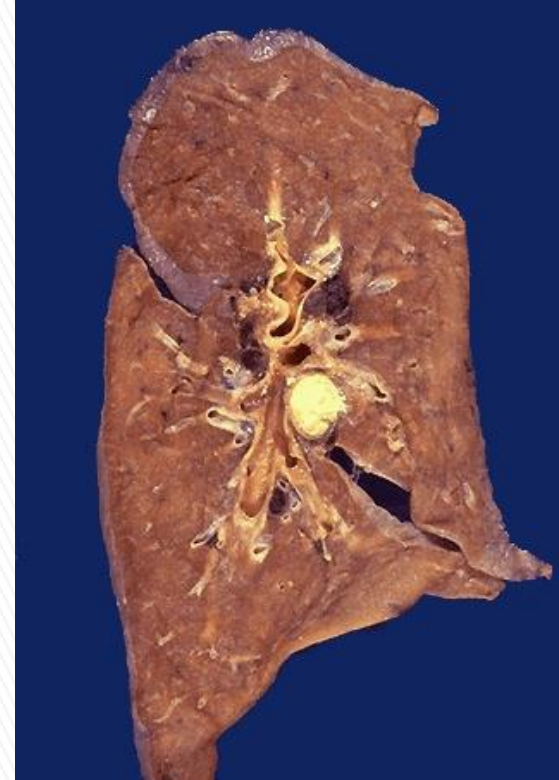
Gangrenous necrosis

- ▶ Clinical term
- ▶ It is coagulative necrosis
- ▶ Dry vs wet

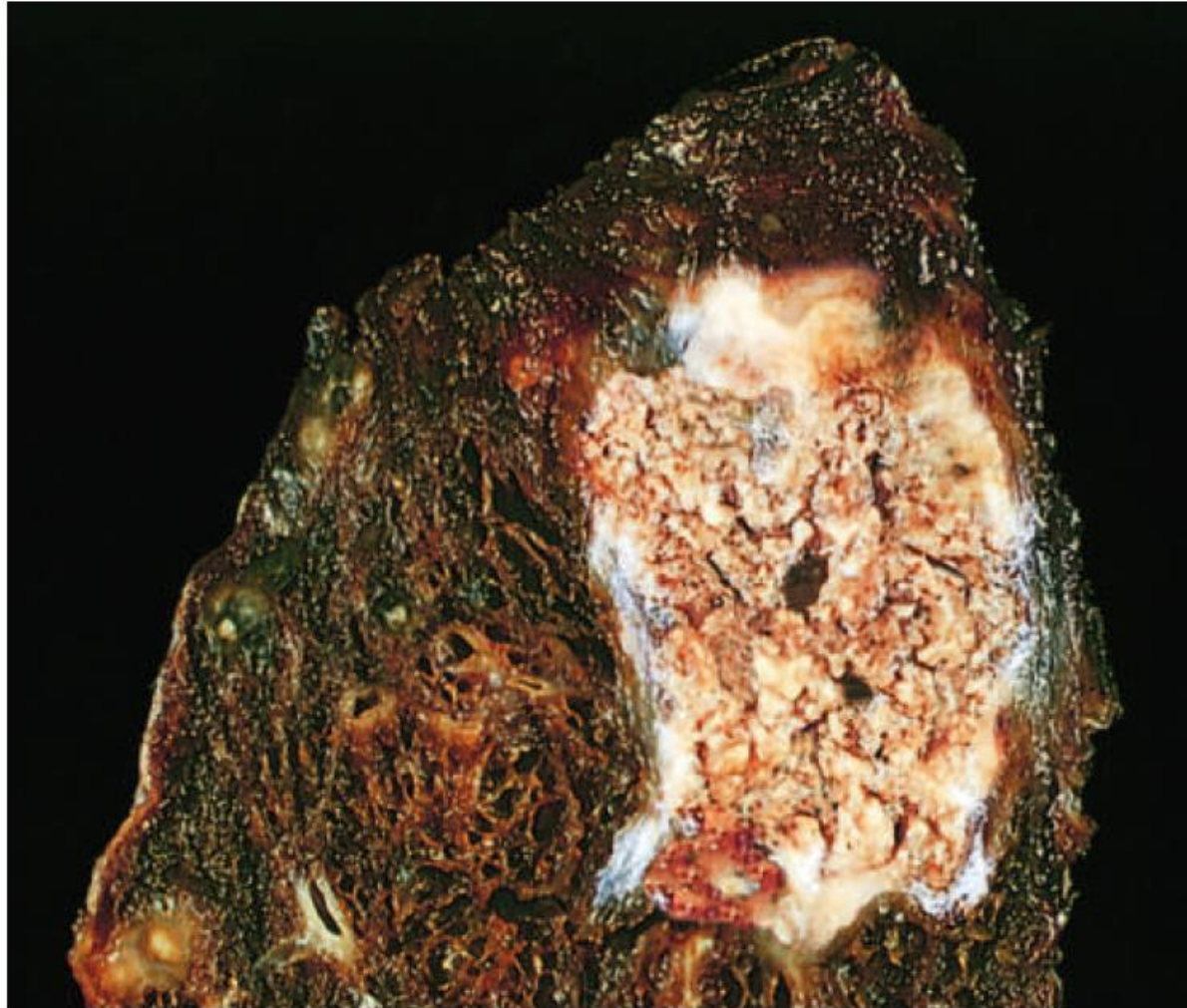


Caseous necrosis

- ▶ “Cheese like”
- ▶ Tissue architecture is not preserved
- ▶ Acellular center
- ▶ Usually enclosed by collection of macrophages. (granuloma)
- ▶ Most often seen in TB

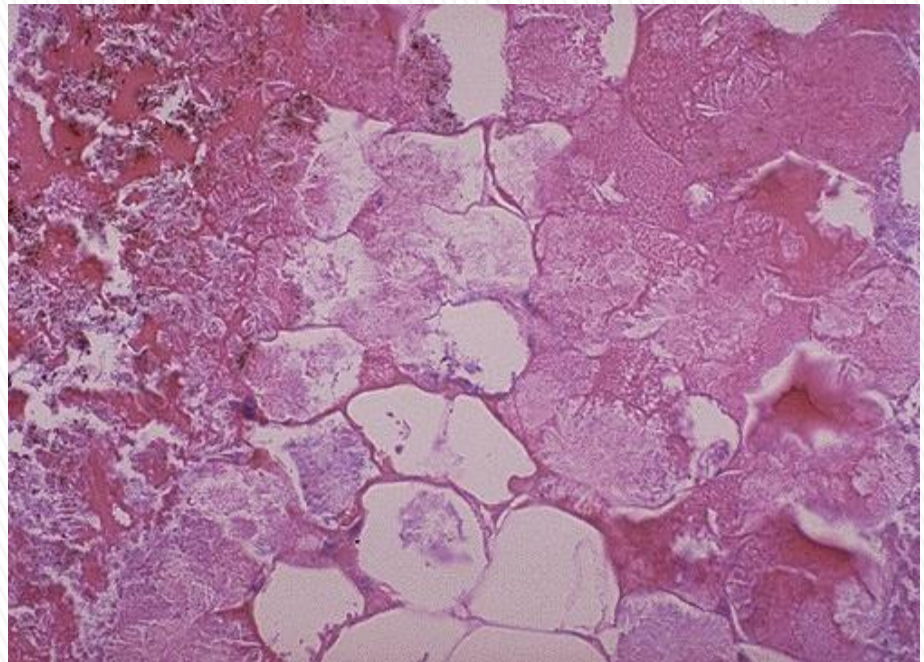
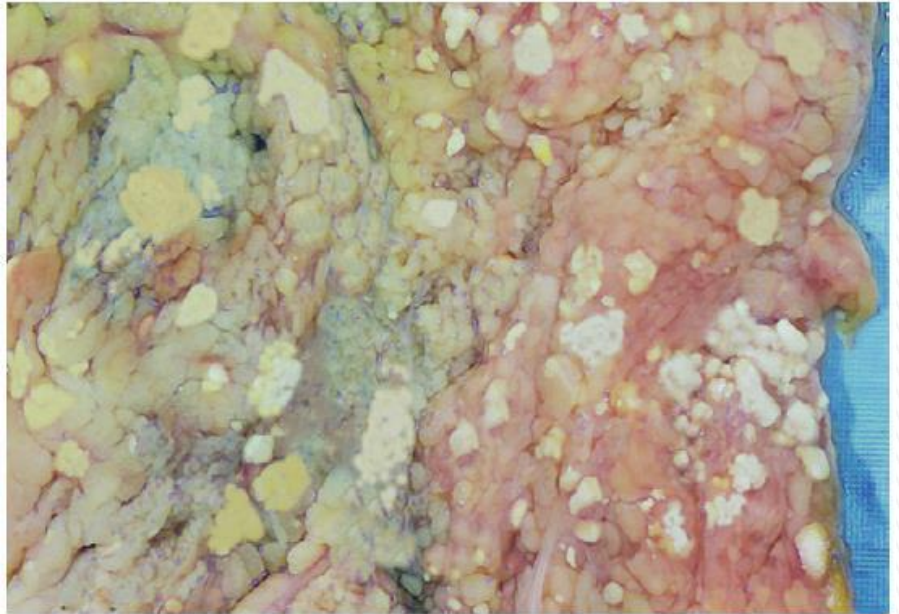


Caseous necrosis



Fat necrosis

- ▶ Occurs in acute pancreatitis
- ▶ Due to release of pancreatic lipases
- ▶ Focal fat destruction
- ▶ Released FA's combine with Ca^{2+} (saponification) to produce the whitish chalky appearance
- ▶ Shadows of necrotic fat cells



Fibrinoid necrosis

- ▶ Visible only microscopically.
- ▶ Deposits of antigen – antibody and fibrin complexes in arterial walls
- ▶ Seen in vasculitis (PAN)
- ▶ Severe hypertension.

