

**Tishk International University**  
**Science Faculty**  
**Medical Analysis Department**



## **Pathology**

### **Cell injury 2- Reversible & Irreversible cell injury**

**Fourth Grade- Spring Semester 2020-2021**

**Dr. Jalal A. Jalal**  
**Assistant Professor of Pathology**

# Objectives

1. Types of **reversible** cell injury
  - **Fatty change** and hydropic swelling.
2. Types of **irreversible** cell injury
  - **Necrosis** and apoptosis.
3. Patterns of tissue necrosis.

# OVERVIEW OF CELL INJURY AND CELL DEATH

- ***Reversible cell injury.***
- In early stages or mild forms of injury the functional and morphologic changes are reversible if the damaging stimulus is removed.
- At this stage, although there may be significant structural and functional abnormalities, the injury has typically not progressed to severe membrane damage and nuclear dissolution.

## ***Cell death***

- With continuing damage, the injury becomes irreversible, at which time the cell cannot recover and it dies.
- *There are two types of cell death-necrosis and apoptosis-which differ in their morphology, mechanisms, and roles in disease and physiology.*

# Necrosis

- When damage to membranes is severe, enzymes leak out of lysosomes, enter the cytoplasm, and digest the cell, resulting in *necrosis*.
- Cellular contents also leak out through the damaged plasma membrane and elicit a host reaction (inflammation).
- Necrosis is the major pathway of cell death in many commonly encountered injuries, such as those resulting from ischemia, exposure to toxins, various infections, and trauma.

## ***Apoptosis***

- When a cell is deprived of growth factors or the cell's DNA or proteins are damaged beyond repair, the cell kills itself by another type of death, called *apoptosis* which is characterized by nuclear dissolution without complete loss of membrane integrity.

- Apoptosis is an active, energy-dependent, tightly regulated type of cell death that is seen in some specific situations.
- *Whereas necrosis is always a pathologic process, apoptosis serves many normal functions and is not necessarily associated with pathologic cell injury.*

# Agents of cell injury

1. **Oxygen deprivation:** mainly due to lack of blood supply
2. **Physical agents** (trauma, temp, pressure, electric shock)
3. **Chemical agents** ( $\text{CN}^-$ , Hg, CO, drugs, ROS)
4. **Infectious agents** (viruses, bacteria, fungi)
5. **Immunologic reactions** (anaphylaxis, autoimmune diseases)
6. **Genetic defects** (Thalassemia, Down syndrome)
7. **Dietary** (vitamins def/x's, malnutrition, x's calories)

# THE MORPHOLOGY OF REVERSIBLE CELL INJURY

- **Reversible Injury**

- two main morphologic patterns of reversible cell injury are *cellular swelling* and *fatty change*.

- ***Fatty change (Steatosis)***

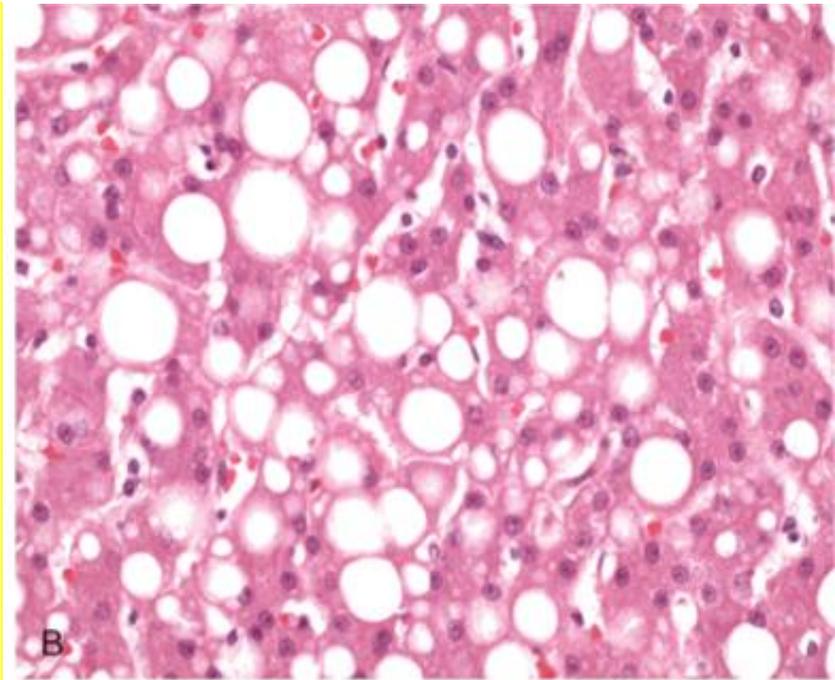
- Is abnormal accumulation of lipid in parenchymal cells of an organ.

- occurs in hypoxic injury and various forms of toxic or metabolic injury.

- It occurs mainly in cells involved in and dependent on fat metabolism, such as hepatocytes and myocardial cells.

# Morphology OF Fatty change

- Grossly: *liver is enlarged and yellow in color and shiny or greasy in appearance because it contains excess fat.*
- Microscopically: is manifested by the appearance of small or large lipid vacuoles in the cytoplasm of hepatocytes.



# Irreversible cell injury-Necrosis

- Refers to a series of changes that accompany cell death, largely resulting from the degradative action of enzymes on lethally injured cells.
- Necrotic cells are unable to maintain membrane integrity, and their contents often leak out.

- The enzymes responsible for digestion of the cell are derived either from the lysosomes of the dying cells themselves or from the lysosomes of leukocytes that are recruited as part of the inflammatory reaction to the dead cells.

# Morphology

- The necrotic cells show **increased eosinophilia** (i.e., pink staining from the eosin dye, the "E" in "H&E").
- This is attributable in part to increased binding of eosin to denatured cytoplasmic proteins and in part to loss of the basophilia that is normally imparted by the ribonucleic acid (RNA) in the cytoplasm (basophilia is the blue staining from the hematoxylin dye, the "H" in "H&E").

- **Nuclear changes** assume one of three patterns, all due to breakdown of DNA and chromatin.
  1. **pyknosis**, characterized by nuclear shrinkage and increased basophilia; the DNA condenses into a solid shrunken mass.
  2. second pattern is, **karyorrhexis**, the pyknotic nucleus undergoes fragmentation.
  3. In the third pattern basophilia of the chromatin may fade (**karyolysis**), In 1 to 2 days, the nucleus in a dead cell completely disappears.

# Patterns of Tissue Necrosis

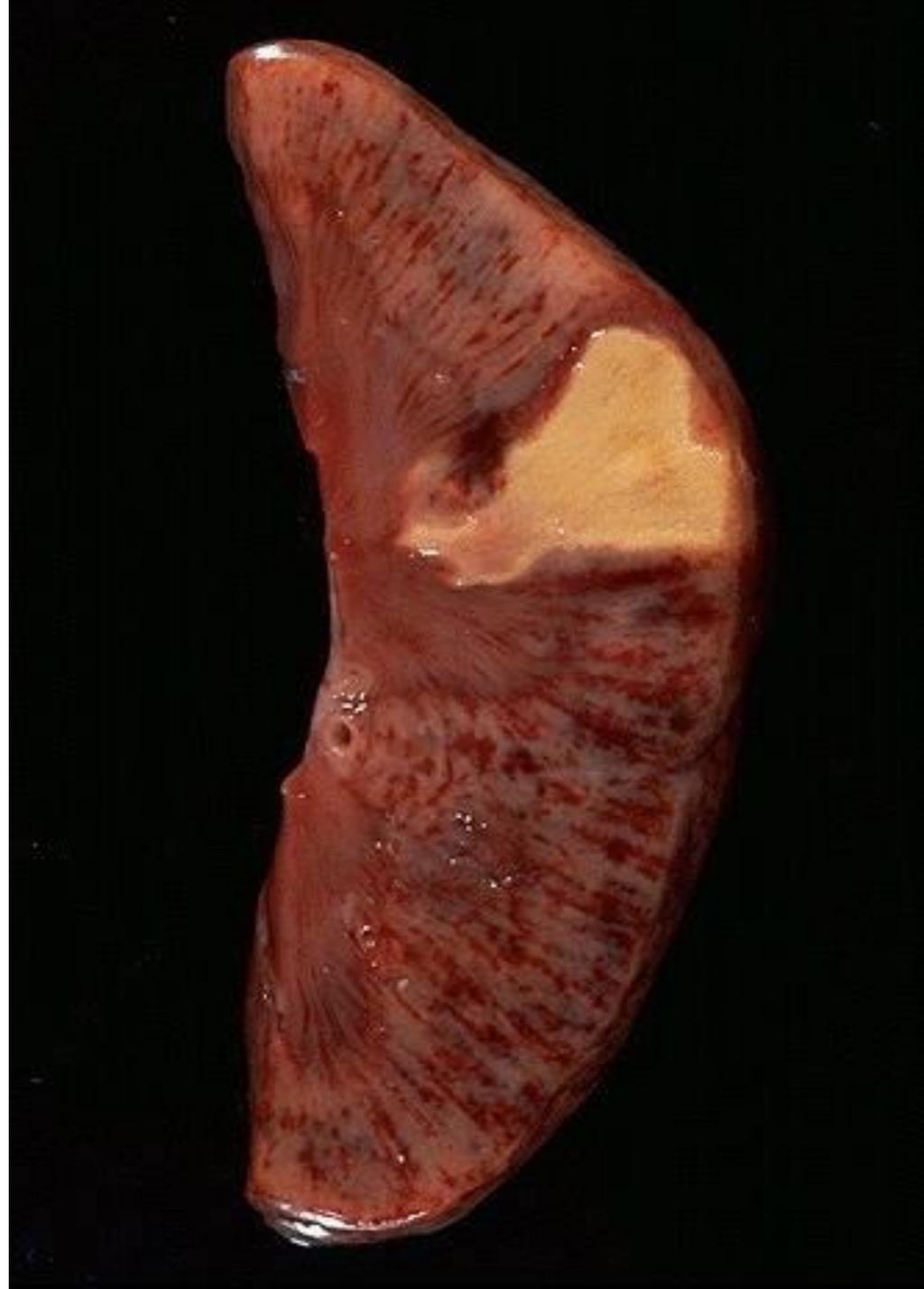
## 1. Coagulative necrosis

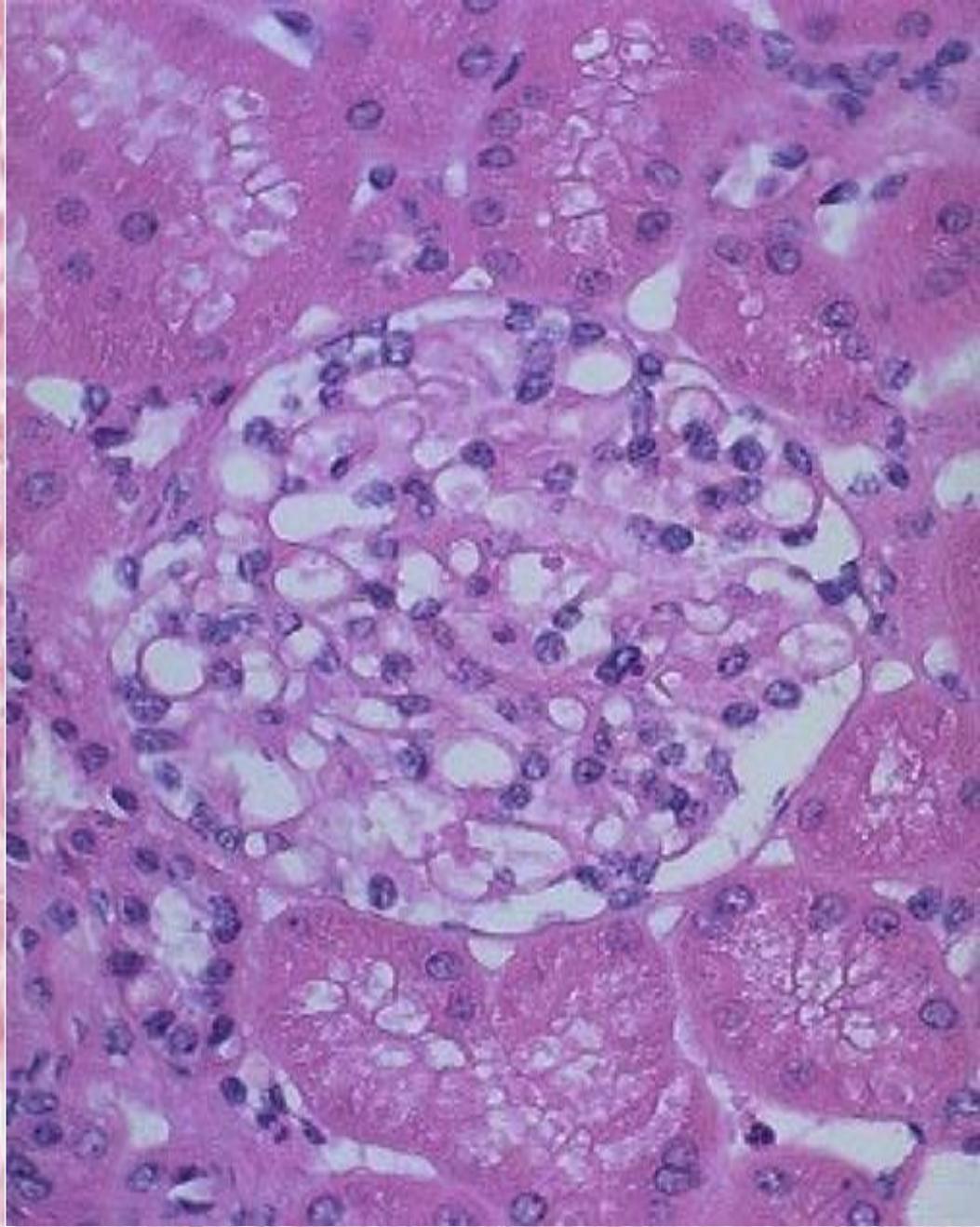
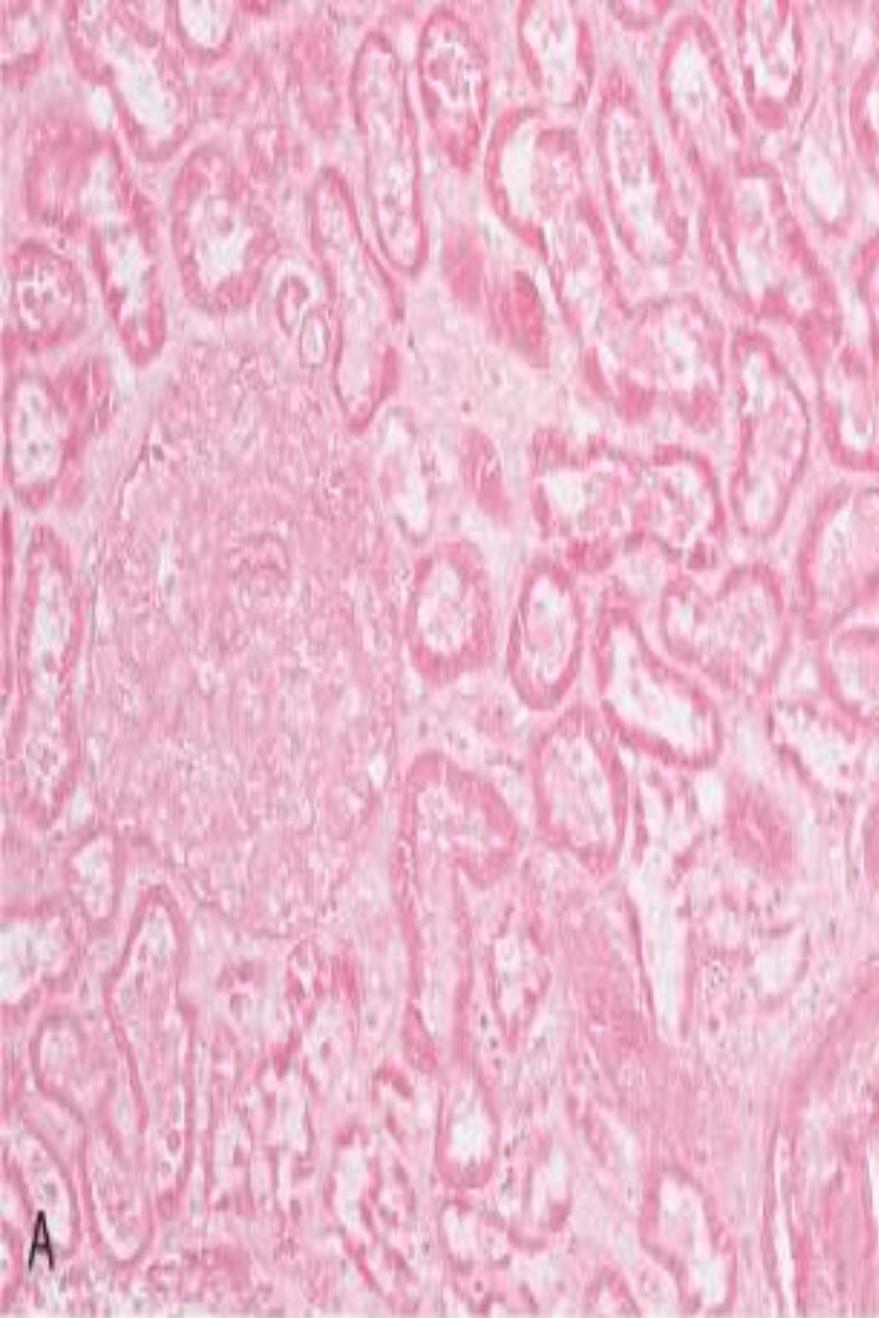
- is a form of tissue necrosis in which the component cells are dead but the basic tissue architecture is preserved for at least several days.
- The affected tissues take on a firm texture. Presumably the injury denatures not only structural proteins but also enzymes and so blocks the proteolysis of the dead cells; as a result, eosinophilic, ***anucleate*** cells may persist for days or weeks.

- Ultimately, the necrotic cells are removed by phagocytosis of the cellular debris by infiltrating leukocytes and by digestion of the dead cells by the action of lysosomal enzymes of the leukocytes.
- Coagulative necrosis is characteristic of **infarcts** (areas of ischemic necrosis) in all solid organs except the brain.

# Coagulative necrosis Kidney

- **Preservation of structure**
- **Firm**
- **Protein denaturation**
- **Hypoxic tissue death (except brain)**





A

## 2. Liquefactive necrosis

- Is seen in focal bacterial or, occasionally, fungal infections, because microbes stimulate the accumulation of inflammatory cells and the enzymes of leukocytes digest ("liquefy") the tissue.
- For obscure reasons, hypoxic death of cells within the central nervous system often evokes liquefactive necrosis.

- Whatever the pathogenesis, liquefaction completely digests the dead cells, resulting in transformation of the tissue into a liquid viscous mass.



# 3. Gangrenous necrosis

- It is usually applied to a limb, generally the lower leg, that has lost its blood supply and has undergone coagulative necrosis involving multiple tissue layers.
- When bacterial infection is superimposed, coagulative necrosis is modified by the liquefactive action of the bacteria and the attracted leukocytes (so-called **wet gangrene**).

## 4. Caseous necrosis

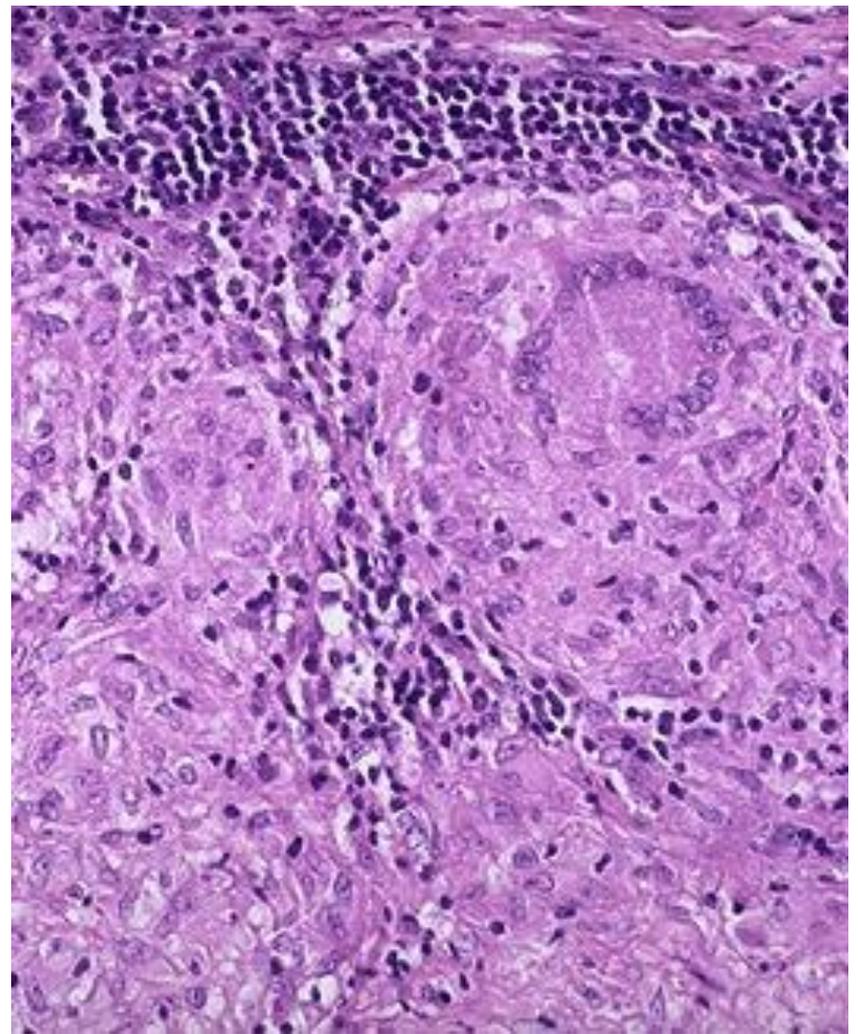
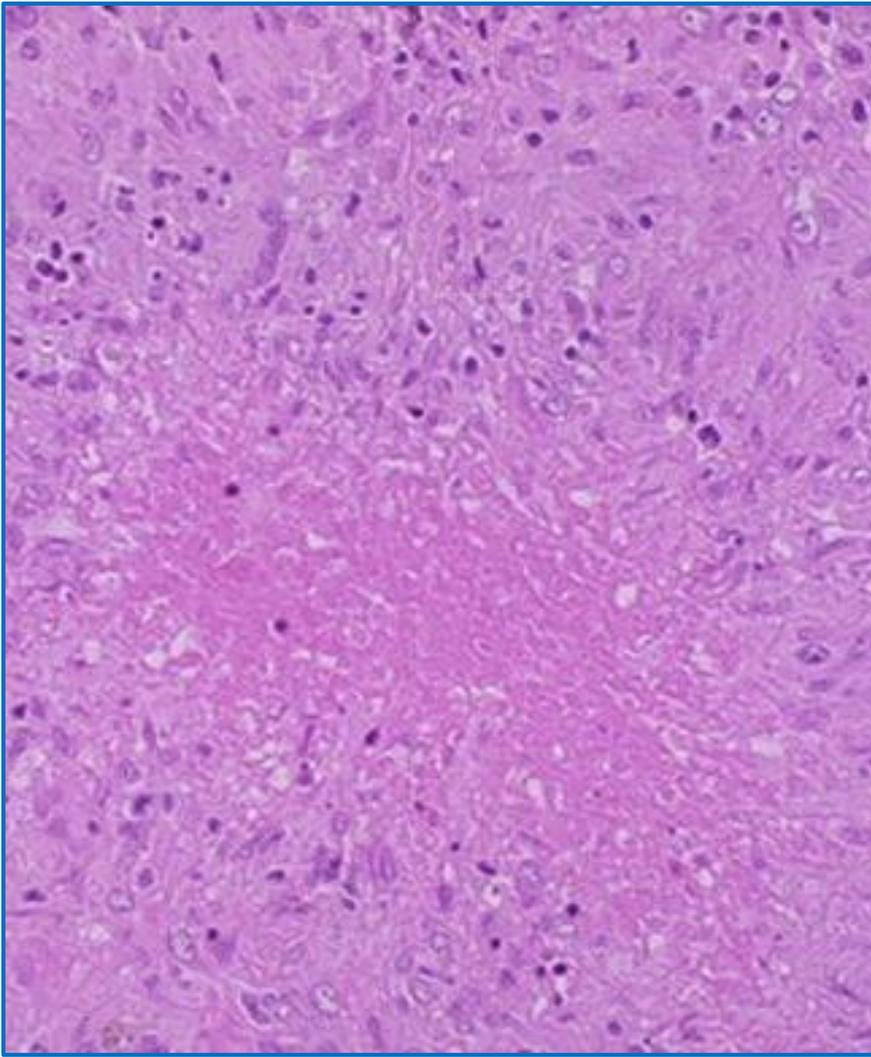
- Is encountered most often in foci of tuberculous infection.
- The term "caseous" (cheese-like) is derived from the friable yellow-white appearance of the area of necrosis.
- On microscopic examination, the necrotic focus appears as a collection of fragmented or lysed cells with an amorphous granular appearance.

- Unlike coagulative necrosis, the tissue architecture is completely obliterated and cellular outlines cannot be discerned.
- Caseous necrosis is often enclosed within a distinctive inflammatory border; this appearance is characteristic of a focus of inflammation known as a **granuloma**



© Elsevier 2005

**A tuberculous lung with a large area of caseous necrosis**

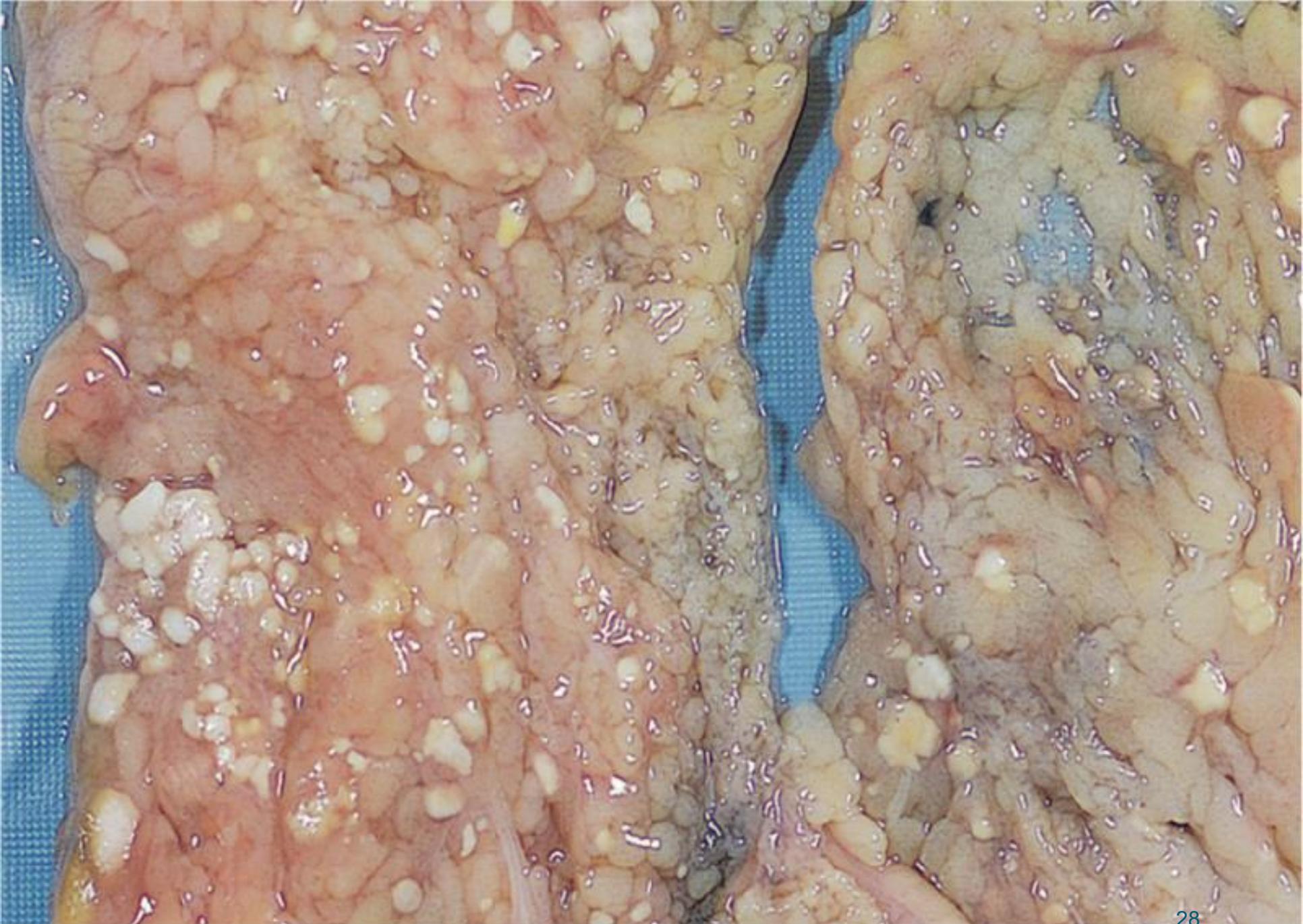


**Tuberculosis : caseous necrosis at the right and granuloma at left.**

# 5. Fat necrosis

- Refers to focal areas of fat destruction, typically resulting from release of activated pancreatic lipases into the substance of the pancreas and the peritoneal cavity.
- This occurs in acute pancreatitis.
- In this disorder, pancreatic enzymes that have leaked out of acinar cells and ducts liquefy the membranes of fat cells in the peritoneum, and lipases split the triglyceride esters contained within fat cells.

- The released fatty acids combine with calcium to produce grossly visible chalky white areas (fat saponification).
- On histologic examination, the foci of necrosis contain shadowy outlines of necrotic fat cells with basophilic calcium deposits, surrounded by an inflammatory reaction.



# Summary

- Examples of Reversible Cellular changes are
  - Fatty change and hydropic swelling
- Cellular changes which are irreversible include
  - Necrosis and apoptosis
  - Types of necrosis include:
    - Coagulative, liquefactive, gangrenous, caseous, and fat necrosis.
- Necrosis is always a pathologic process.

**Look for good in others...  
no one is without faults and  
everyone has some good  
qualities!**

**Thank you so much**