Apoptosis Necrosis

Apoptosis

- Cell death that is induced by a tightly regulated intracellular program

"**Programmed Cell Death**"

- Causes of Apoptosis
  - Physiologic situations
  - Pathologic conditions

Apoptosis in Physiologic Situations

- Programmed destruction of cell during *embryogenesis*
- Hormone-dependent involution
  - *endometrial cells* (menstrual cycle)
- Cell deletion in *proliferating cell* population
- Death of host cells - *neutrophils*
- Elimination of *self reactive lymphocyte*
- Cell death induced by cytotoxic T-cells
  - *viral infected* or *tumor* cells

Apoptosis in Pathologic Conditions

- Cell death produced by injurious stimuli – radiation, cytotoxic drug
- Cell injury in certain viral diseases – viral hepatitis
- Pathologic atrophy
- Cell death in tumors

Intracellular Accumulations

- Manifestation of "*metabolic derangements*"

  :*intracellular accumulation of abnormal amounts of various substances*

  Fat

  Protein

  Glycogen

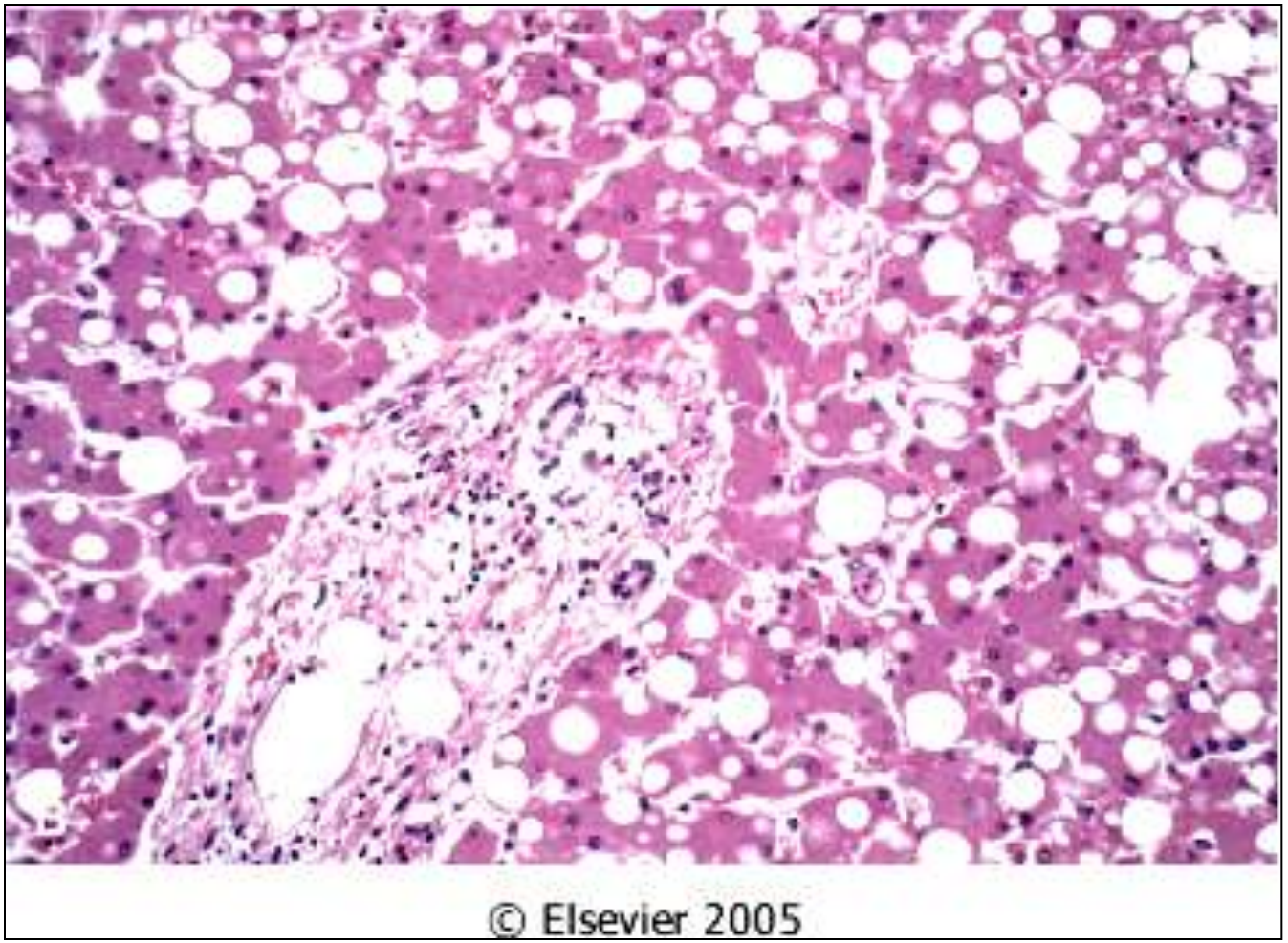
  Pigments

Intracellular Accumulations of Lipids

- Accumulation of Lipids
  - Triglycerides
  - Cholesterol

- Steatosis (fatty change)

  : abnormal accumulation of *triglycerides* within parenchymal cells
  - – fatty liver in chronic alcoholism



Fatty liver

Intracellular Accumulations of Lipids

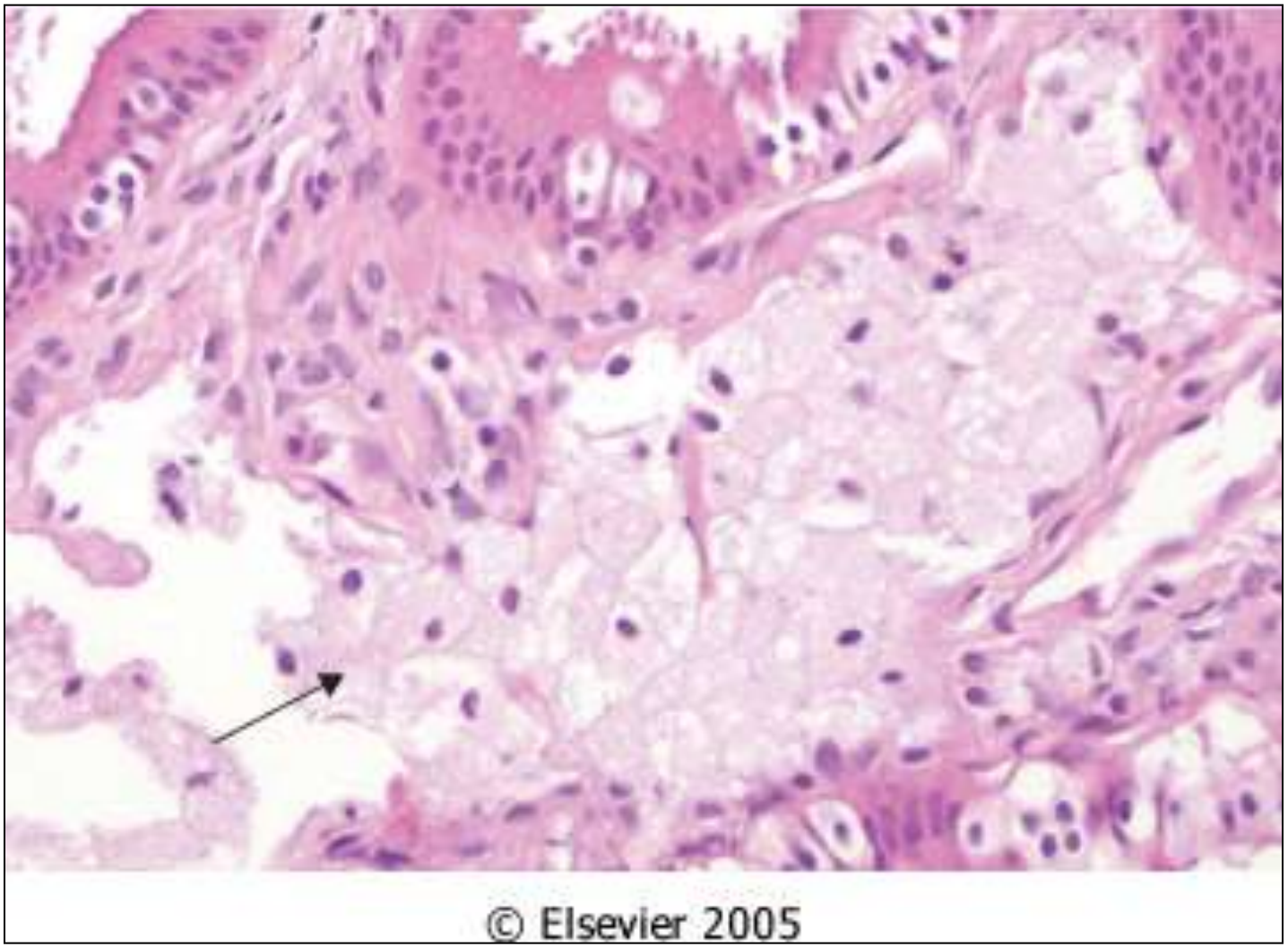
- Cholesterol and Cholesterol Esters

  :Atherosclerosis

  - accumulation of cholesterol-laden macrophage (*foam cell*) and smooth muscle cells in the *intima* of aorta and arteries

  :Cholesterolosis

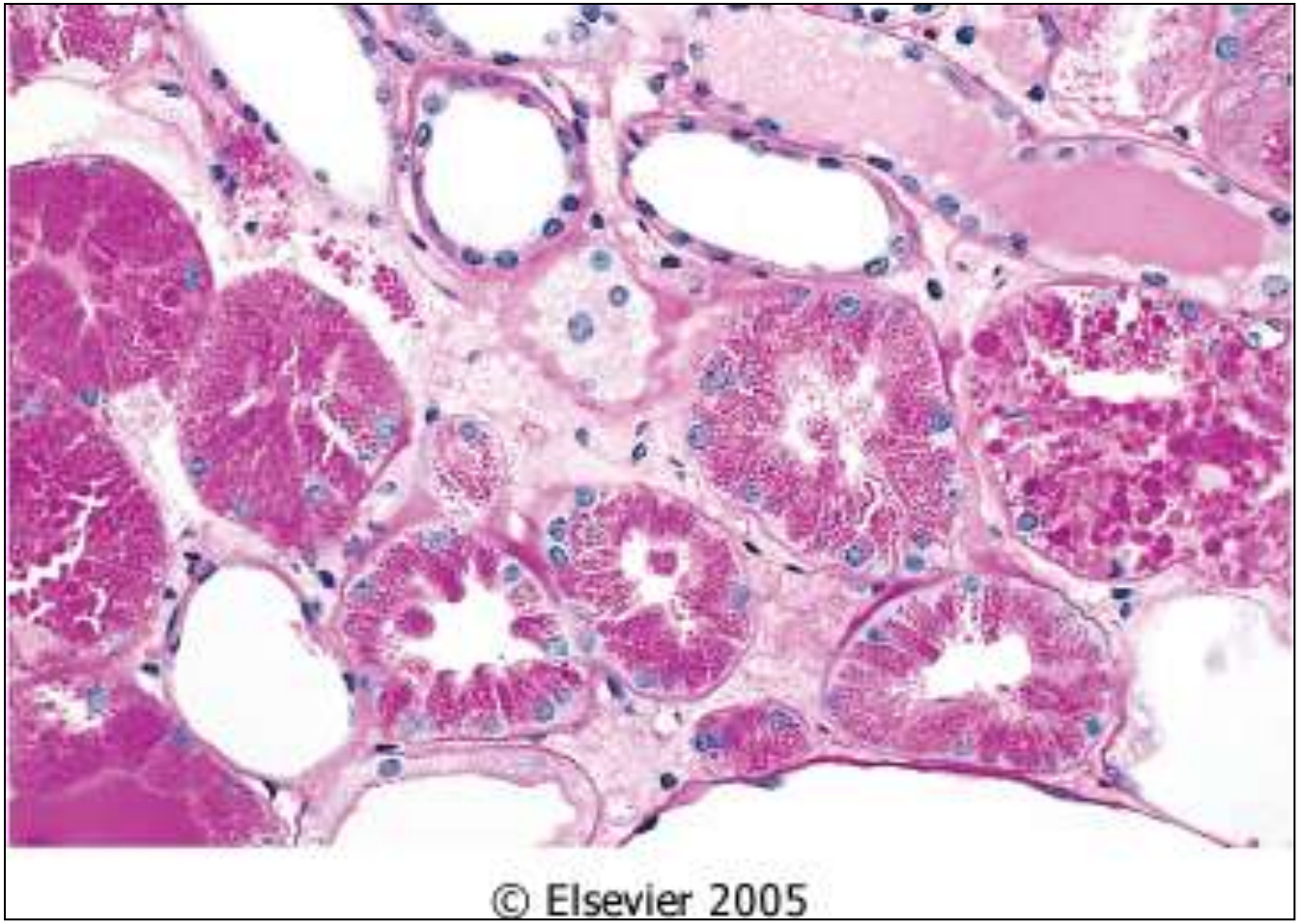
  - accumulation of *foam cells* in the lamina propria of gallbladder



Intracellular Accumulations of Proteins

- Accumulation of protein droplets in proximal renal tubule

  - renal disease with *heavy protein leakage* across the glomerular filter



Protein reabsorption droplets in the renal tubular epithelium.

Intracellular Accumulations of Proteins

- *Defects in protein folding*

  :Defective intracellular transport and secretion

  :ER stress induced by unfolded and misfolded protein – cell death

  :Aggregation of abnormal folded protein - amyloidosis

Intracellular Accumulations of Glycogen

"Patients with abnormal metabolism of glucose or glycogen"

- Diabetes mellitus

  :disorder of glucose metabolism

  - glycogen accumulate in epithelial cells of renal tubules, liver cells, beta-cells of the islets of Langerhans and heart muscle cells

Intracellular Accumulations of Glycogen

- Glycogen storage disease (Glycogenosis)

  - genetic diseases

  - defect of enzymes in the synthesis or breakdown of glycogen

accumulation → cell injury → death

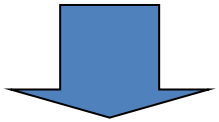
Accumulation of Pigments

- Exogenous pigments

  Carbon (anthracosis) →

  Coal dust (pneumoconiosis) →

Lung: pick up by alveolar macrophages
regional lymph nods →



blackening the tissues of the lungs
(anthracosis)

Accumulation of Pigments

- Endogenous pigment

  :*Lipofuscin* – aging pigment

  lipid, phospholipid-protein complex (lipid peroxidation)

  :*Melanin* – in melanocyte

  :*Hemosiderin* – aggregates of ferritin micelles (iron + apoferritin = ferritin)

Pathologic Calcification

- Abnormal tissue deposition of *Calcium Salts*
- Two forms
  1. *Dystrophic calcification*
  2. *Metastatic calcification*

Pathologic Calcification

- Dystrophic Calcification

  - Area of tissue necrosis

  - Aging or damage heart valve

  - Atherosclerosis

  - Single necrotic cell

    “psammoma body”

Pathologic Calcification

- **Metastatic Calcification**

- Occur in normal tissue in "hypercalcemia"

Hypercalcemia

- Hyperparathyroidism
- Destruction of bone tissue
- Renal failure

Morphology of Cell Injury and Necrosis

- Cell Injury – Reversible
  – Irreversible

- Cell Death – Necrosis
  – Apoptosis

Morphology of Cell Injury

Reversible Injury

Cellular swelling

Fatty change

- Plasma membrane alteration
- Mitochondrial Changes
- Dilation of Endoplasmic reticulum
- Nuclear Alteration

Morphology of Necrotic Cells

- Increased Eosinophilia
  - loss of RNA (basophilia)
  - denatured cytoplasmic protein
- Nuclear Changes
  - Pyknosis
  - Karyorrhexis
  - Karyolysis
- Myelin figure
  – large, whorled phospholipid mass (phospholipid precipitate)

Morphologic pattern of Necrotic Cell mass

- Coagulative necrosis
- Liquefactive necrosis
- Caseous necrosis
- Fat necrosis

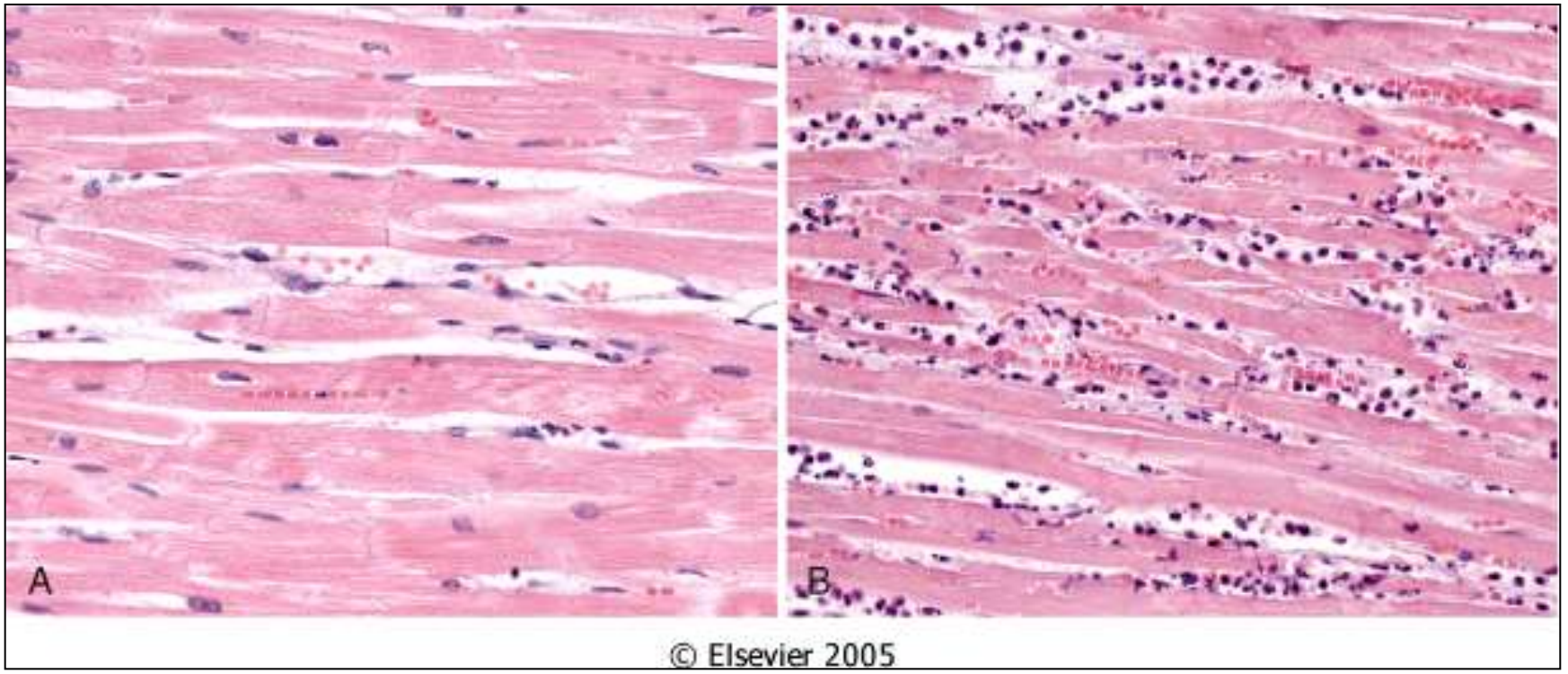
Morphologic pattern of Necrotic Cell mass

- Coagulative Necrosis

  :intracellular acidosis

  – protein denatured

  – proteolysis inhibited



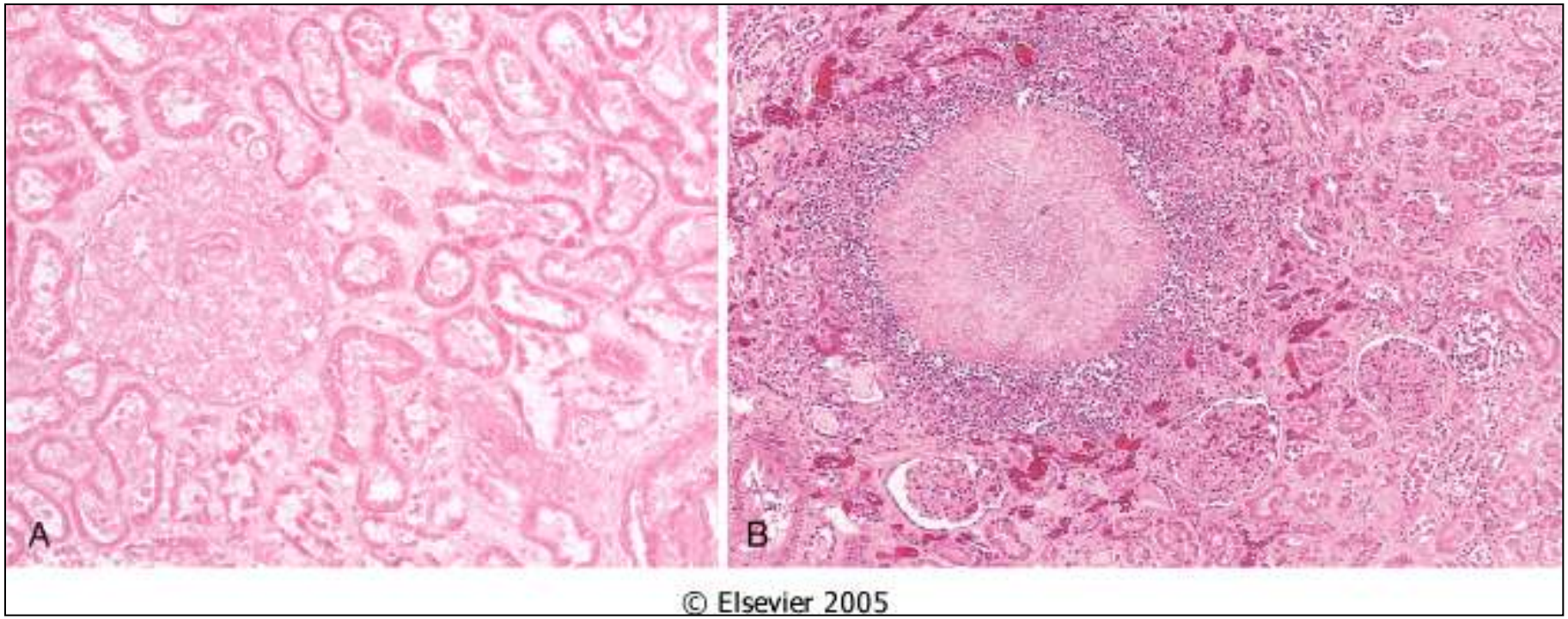
Ischemic necrosis of the myocardium

A, Normal myocardium.

B, Myocardium with coagulation necrosis

Morphologic pattern of Necrotic Cell mass

- Liquefactive Necrosis
  :focal bacterial (or fungal) infections
  – accumulation of inflammatory cells
  :hypoxic death of cells within CNS



Coagulative and liquefactive necrosis

A, Kidney infarct exhibiting coagulative necrosis

B, A focus of liquefactive necrosis in the kidney

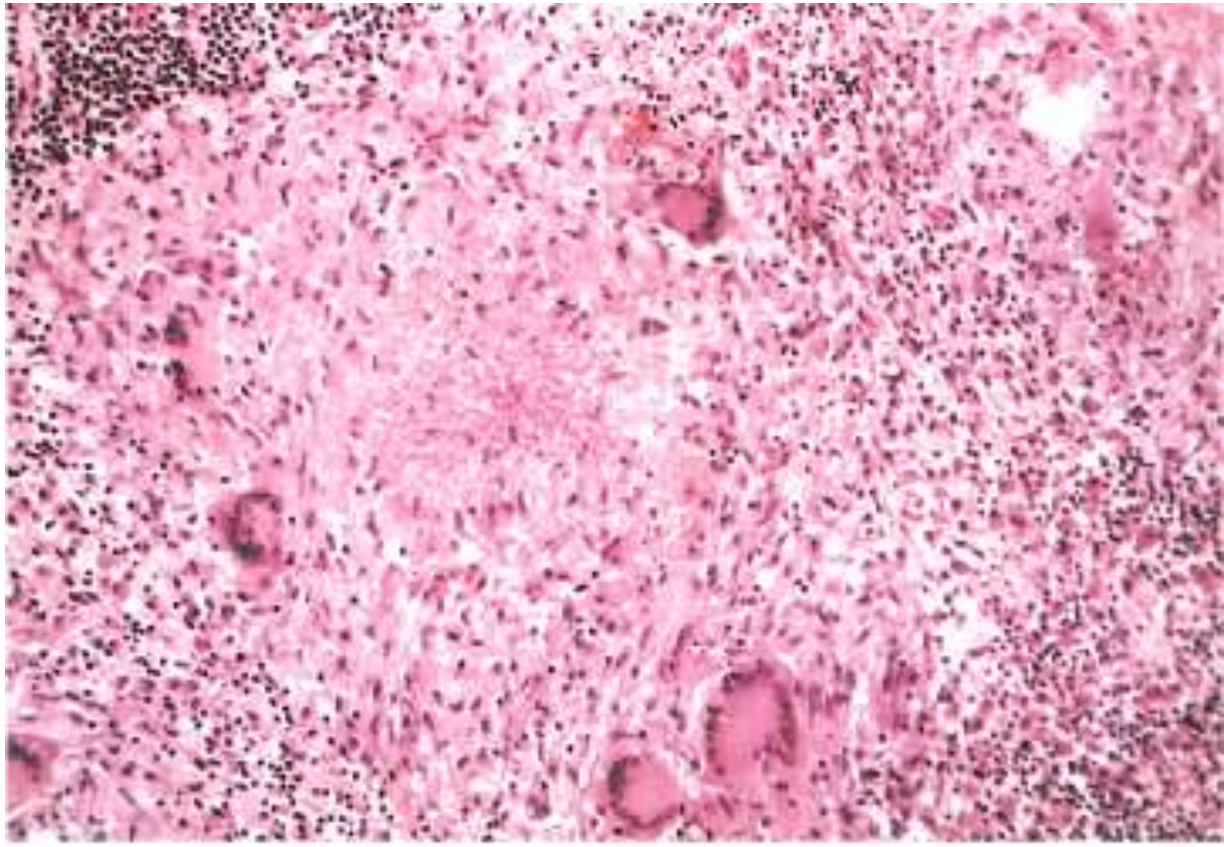
Morphologic Pattern of Necrotic Cell Mass

- Caseous necrosis

  :gross appearance

  :microscopic – granulomatous inflammation

A tuberculous lung with a large area of caseous necrosis



Tuberculous granuloma showing an area of central necrosis, epithelioid cells, multiple Langhans-type giant cells, and lymphocytes.

Foci of fat necrosis with saponification in the mesentery