Cell Pathology
細胞病理學

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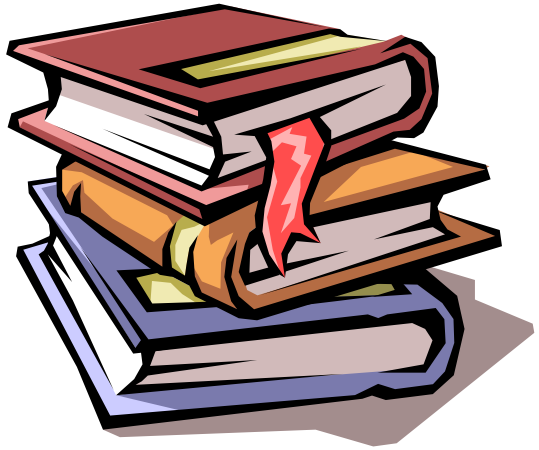
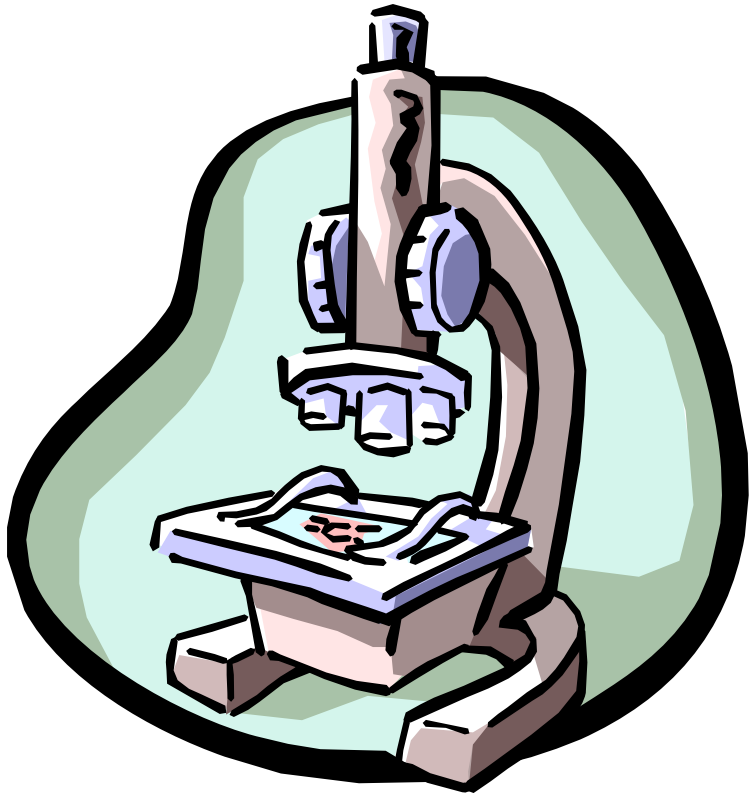


What Is Pathology (病理學)?

Pathology is the study (***logos***) of suffering (***pathos***), a bridging discipline involving both basic science and clinical practice.



Pathology

- General pathology (一般病理學)
- Systemic pathology (系統病理學)
- Disease:
  - Etiology 病因 (cause)
  - Pathogenesis 致病機轉 (mechanism)
  - Effect (morphologic change, clinical significance)
  - Prognosis 預後 (outcome)

學習目標

- 能說明細胞結構及其功能
- 能說明引起細胞傷害常見的原因及機制
- 能說明細胞的各種適應方式
- 能說明可逆及不可逆細胞傷害的原則及造成的基本形態變化

參考資料: Pathology for the Health-Related Professions, Ivan Damjanov, Saunders, Co. 3rd. ed. 2006, Chap 1

Outline of Cell Pathology

- The structure and function of the normal cell
- Integrated response of the cell to injury
  - Reversible and irreversible cell injury
- Cell adaptations
  - Atrophy, hypertrophy, metaplasia, intracellular accumulations, and aging
- Cell death
  - Necrosis and apoptosis

Structure of Normal Cells

Nucleus:chromatin,nucleolus

Cytoplasm:

Organelles

- **Mitochondria**
- **Ribosomes**
- **Endoplasmic Reticulum**
- **Golgi apparatus**
- **Lysosomes**

Hyaloplasm

Cytoskeleton

Plasma membrane

Components of the Nucleus

- Essential part of most living cells
- Contains DNA, RNA, and nuclear proteins
- Main components
  - Nuclear membrane
  - Chromatin
  - Nucleolus

Mitochondria

- Surrounded by double membrane
- Generate energy
- Are full of oxidative enzymes

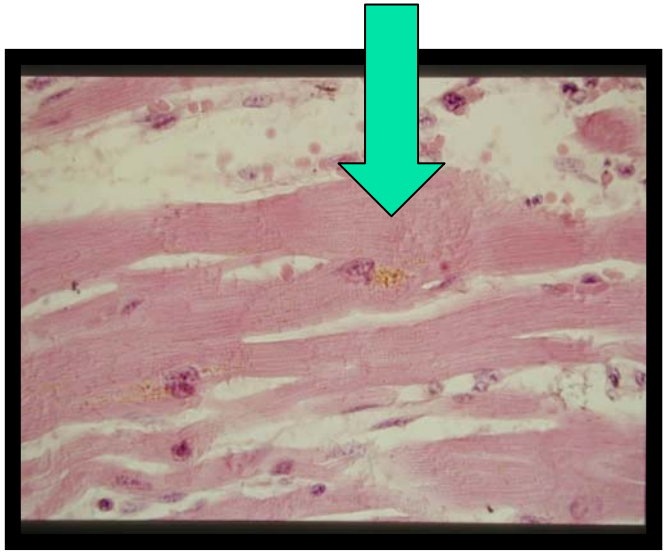
  (e.g., cytochrome oxidase)

Ribosomes and Rough Endoplasmic Reticulum (RER)

- Ribosomes ("polysomes")—synthesis of proteins for internal purposes
- RER—synthesis of proteins for export

Lysosomes

lipofuscin



- Primary lysosome
- Secondary lysosomes
- Heterophagosomes and autophagosomes
- Give rise to residual bodies ("lipofuscin"), accumulates in aging tissues

Integration and Coordination of Cell Function

- Autocrine
- Paracrine
- Endocrine

General Principles of Cell Injury

- Type, duration and severity of injury
- Type of cell is injured
- Intracellular systems particularly vulnerable
  - cell membrane, mitochondria, genetic apparatus
- Injury at one locus leads to wide-ranging secondary effects
- Morphologic changes takes time to develop

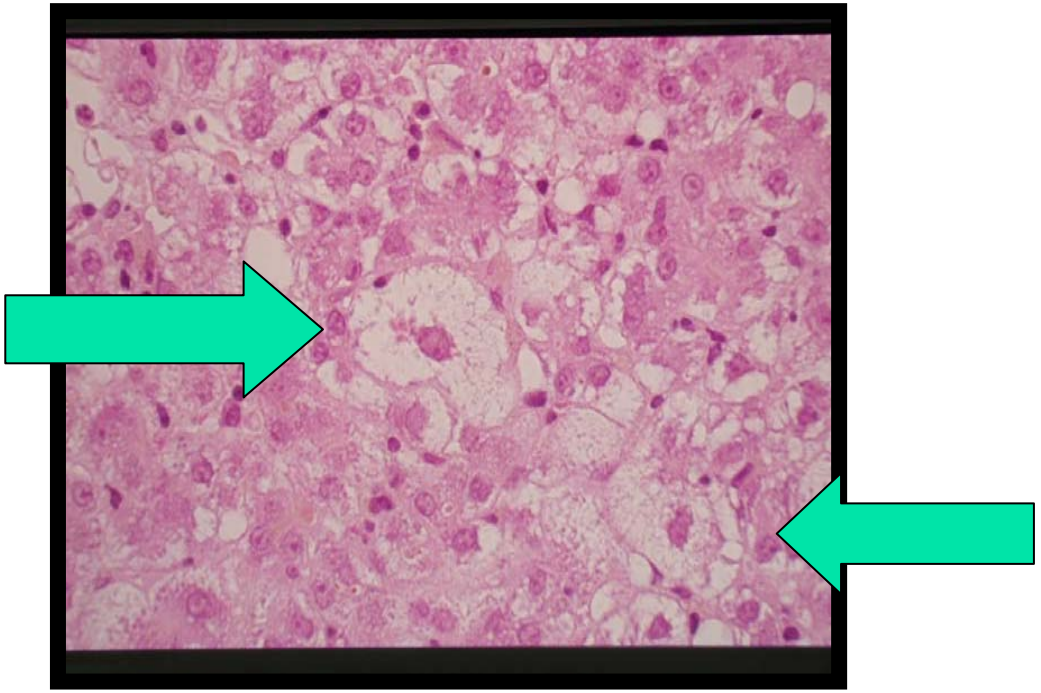
Causes of Cell Injury

- **Hypoxia低氧/anoxia缺氧: common cause**
  - **Ischemia缺血性傷害: most common cause of hypoxia**
- **Toxic injury:**
  - **Directly**
  - **Indirectly: converted to reactive toxic metabolites**
- **Microbial pathogens: bacteria, virus**
- **Mediators of inflammatory and immune reactions**
- **Genetic/metabolic disturbance**

Reversible Cell Injury

- **Cell's aerobic respiration↓ ATP ↓**
  →↓membrane sodium pump
  →↑Na^+ ↓K^+
  →cell swelling
- **↑Anaerobic glycolysis**
  →↑lactic acid, pH↓

Morphology of Reversible Cell Injury



- ***Cellular Swelling*: hydropic change or vacuolar degeneration**

Morphology of Dead Cells

Increased eosinophilia

Pyknosis (核皺縮) nuclear shrinkage and increased basophilia

Karyorrhexis (核崩解) pyknotic nucleus fragments

Karyolysis (核溶解) basophilia of the chromatin fade

Cell Adaptations

Cell adaptations occur after prolonged exposure to adverse or exaggerated normal stimuli

- **Atrophy (萎縮)**
- **Hypertrophy(肥大) & hyperplasia(增生)**
- **Metaplasia(化生)**
- **Intracellular accumulations**

Atrophy

- **Causes:**
  - **Decreased workload (e.g. immobilization of a limb)**
  - **Loss of innervation**
  - **Diminished blood supply**
  - **Inadequate nutrition**
  - **Loss of endocrine stimulation**
  - **Aging (senile atrophy)**
- **Results from**
  - **Decreased protein synthesis (Reduced metabolic activity)**
  - **Increased protein degradation in cells (Ubiquitin-proteasome pathway)**

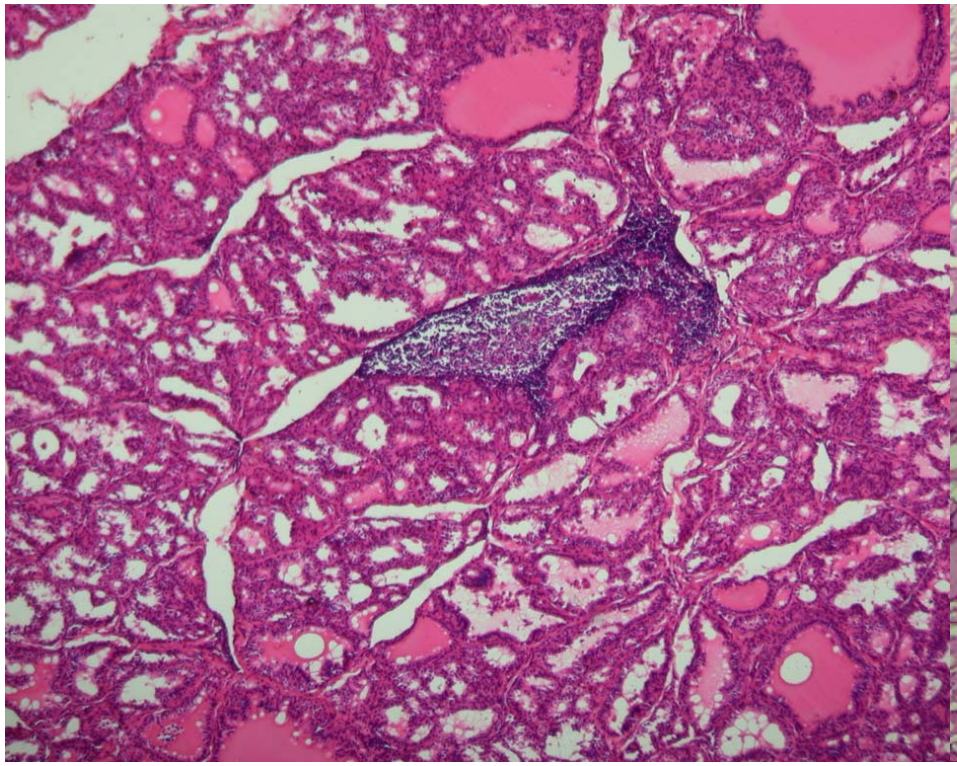
Hypertrophy and Hyperplasia

- **Hypertrophy: increase in the size of a cell**
- **Hyperplasia: increased number of cells**
- **Pure hypertrophy: cardiac muscle, skeletal muscle**
- **Hypertrophy with hyperplasia**
- **Hyperplasia: endometrial hyperplasia, benign prostate hyperplasia**

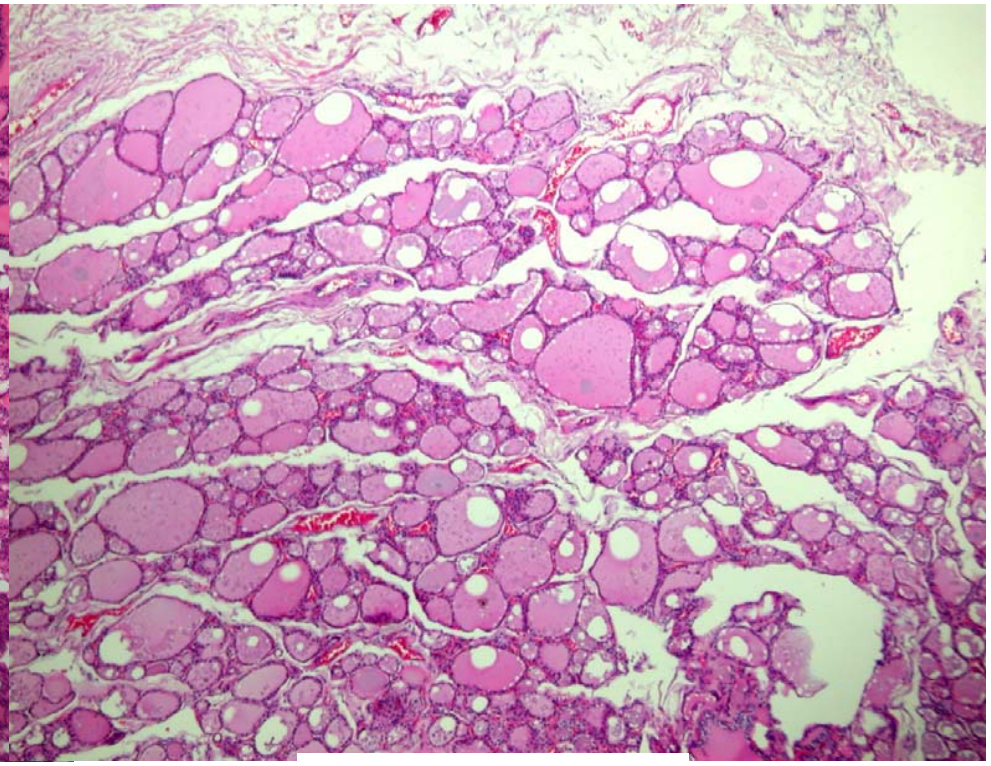
Hypertrophy With Hyperplasia

Uterine smooth muscles during pregnancy

Hyperplasia of Thyroid Gland



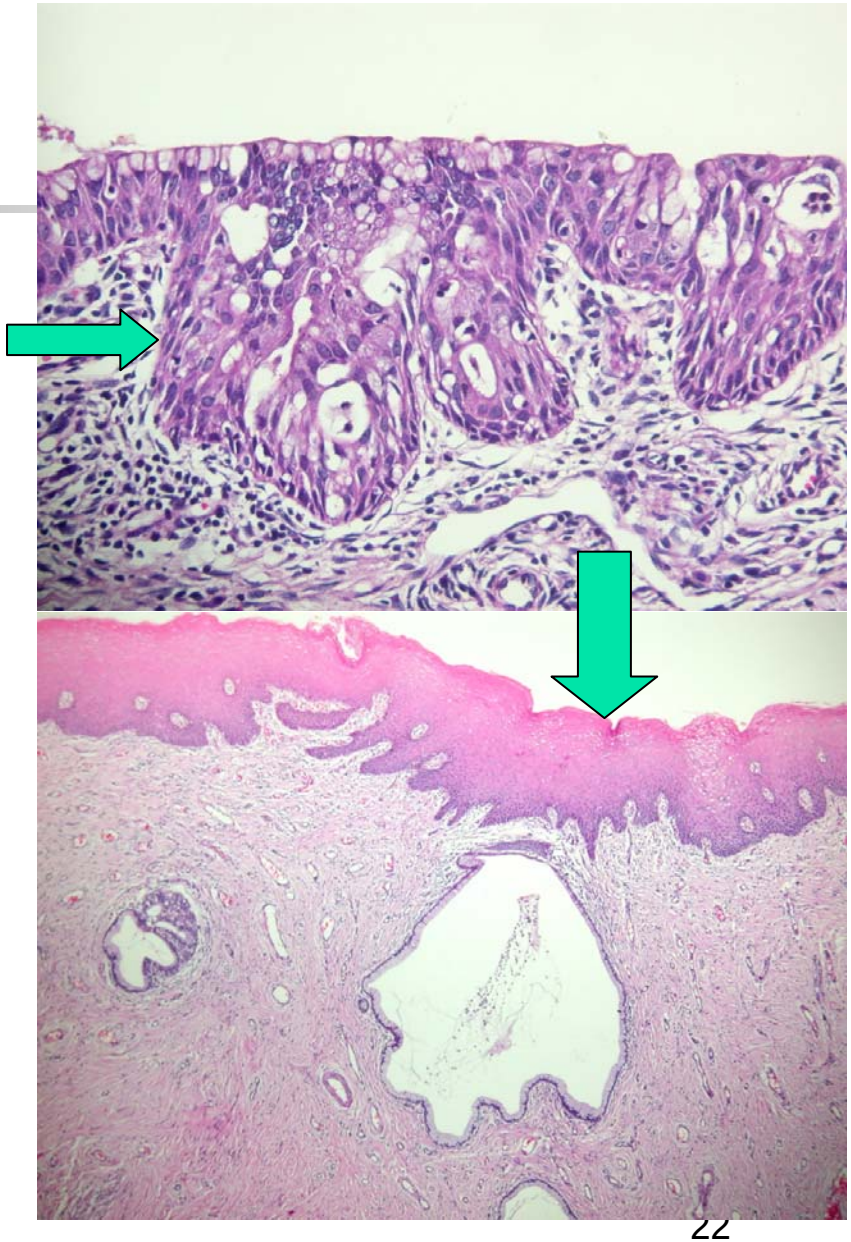
Hyperplasia



Normal

Metaplasia

- **Change of one cell type into another**
- **Squamous metaplasia of bronchial epithelium**
- **Reversible change**
- **May progress to dysplasia (異生)**



Intracellular Accumulations

May occur as a result of

- **an overload of various metabolites or exogenous material**
- **Metabolic disturbances**

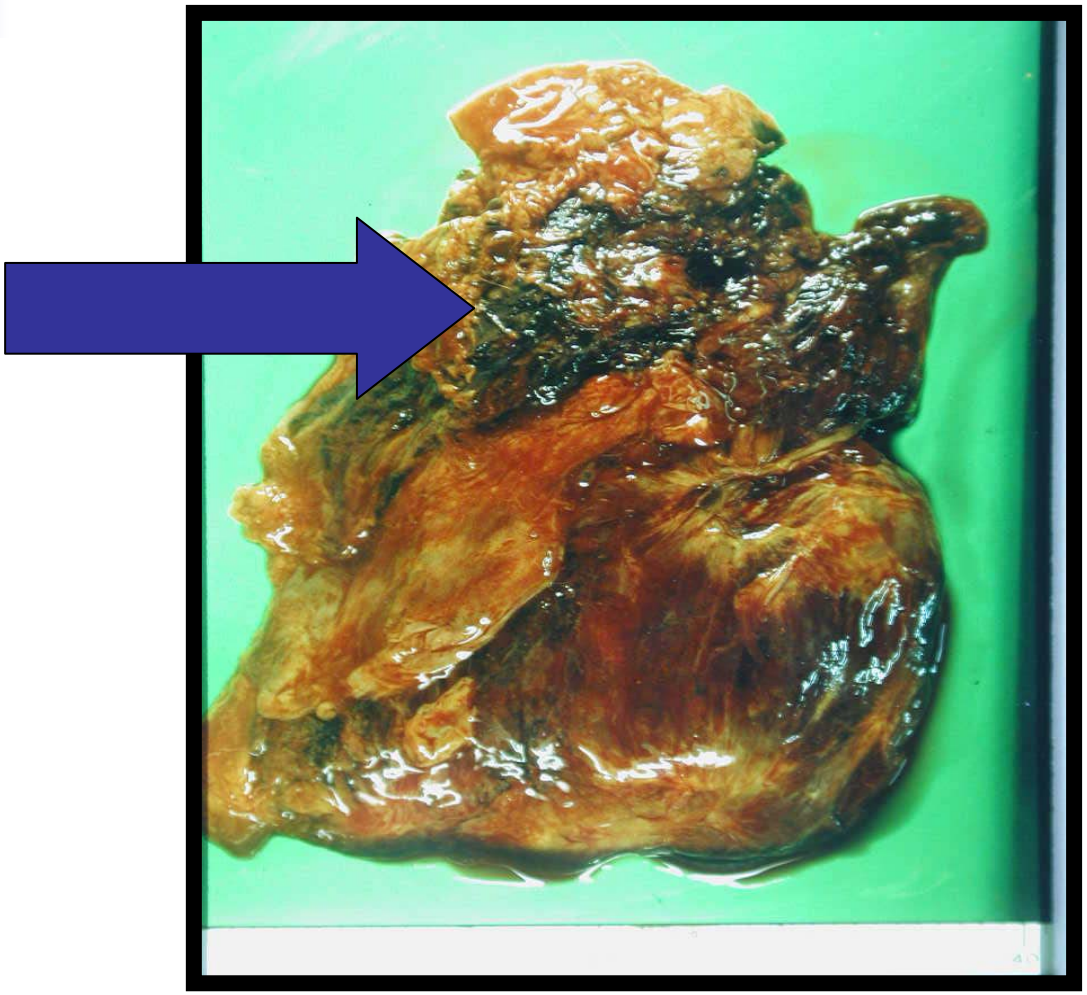
Pigments (色素)

Exogenous(外生性): anthracosis碳末沉積症

Endogenous(內生性): hemosiderin

Lipids (脂質)

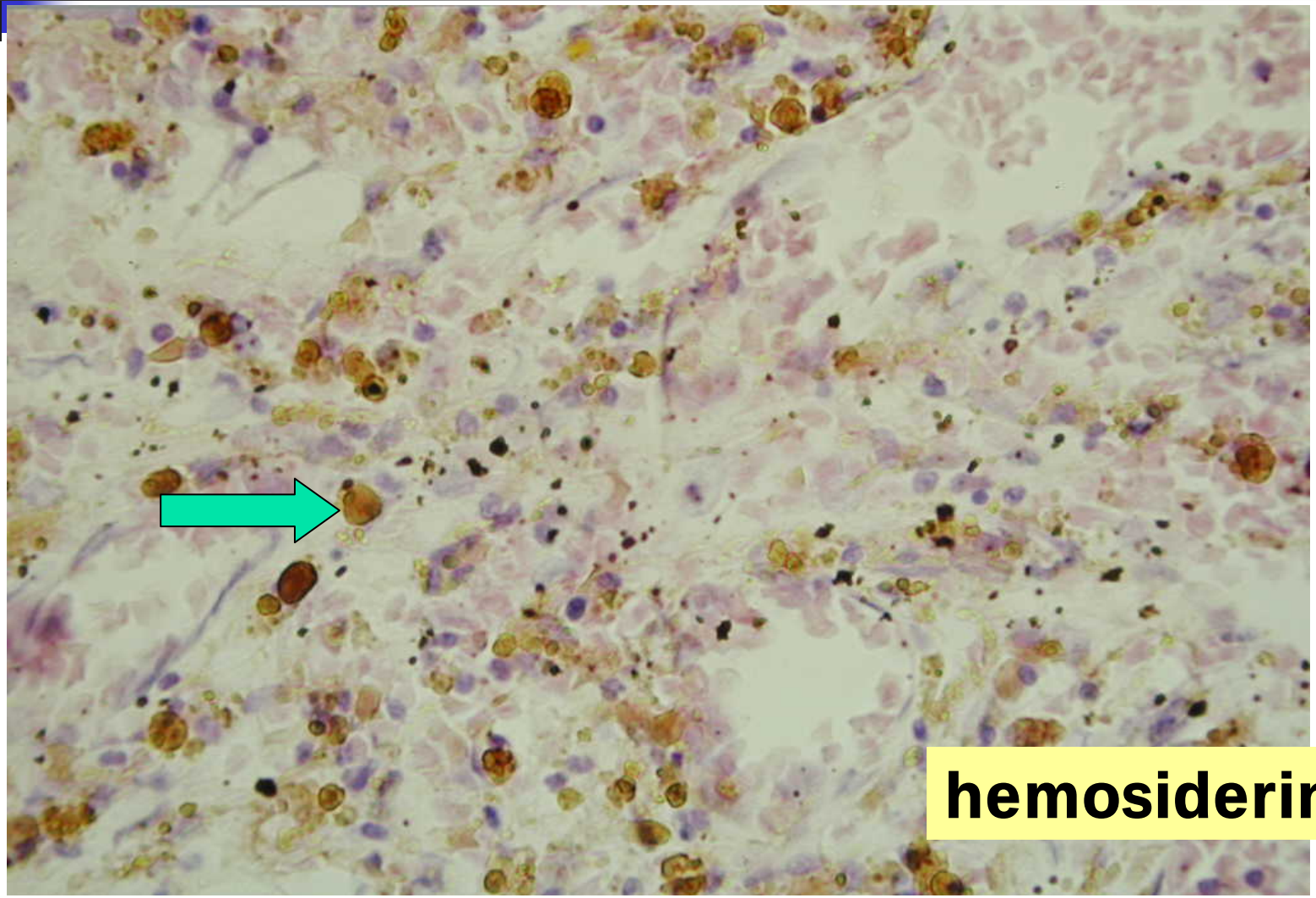
Pigments: Exogenous
Anthracosis碳末沉積症



Pigments: Endogenous

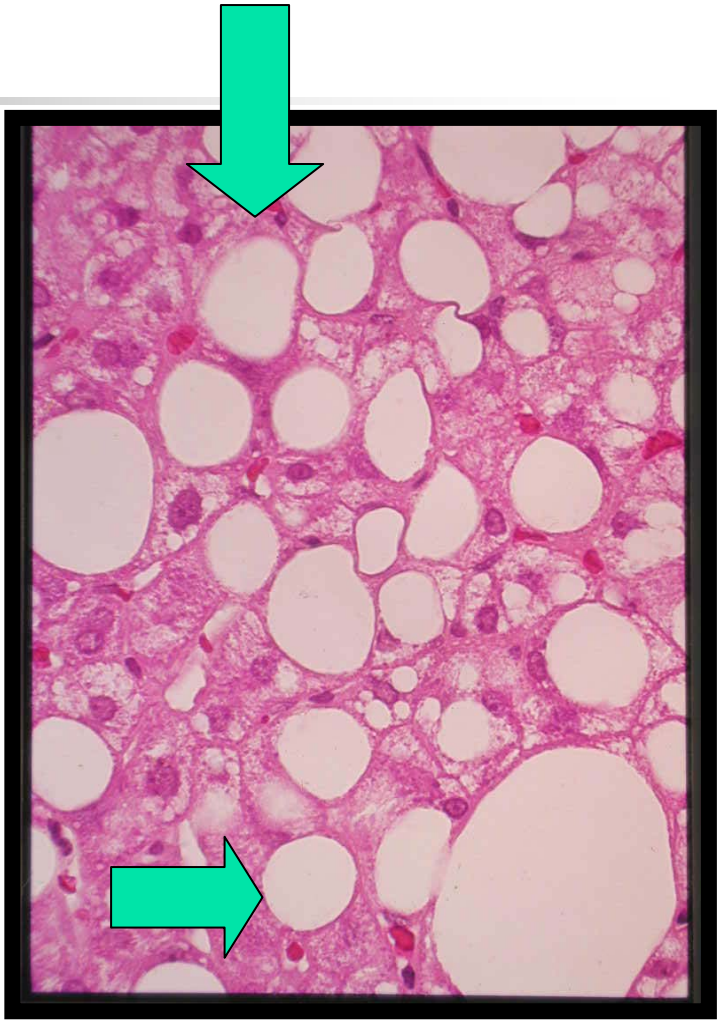
Hemosiderin (血鐵素):

blood-derived brown pigment



Lipids

- **Steatosis** (fatty change)
- Often seen in liver, heart, muscle, kidney
- Excess accumulation of triglyceride
- Alcoholic liver disease



Cellular Aging

- **Two major hypothesis**
  - **Wear and tear hypothesis**
  - **Genetic hypothesis**
- **Pathologic change**

  atrophy, ↓functional reserve, ↑infection, ↑CV disease, ↑cancer

Cell Death

- **Necrosis, Apoptosis**

Death of single cells or groups of cells within a living organism

Forms of Necrosis

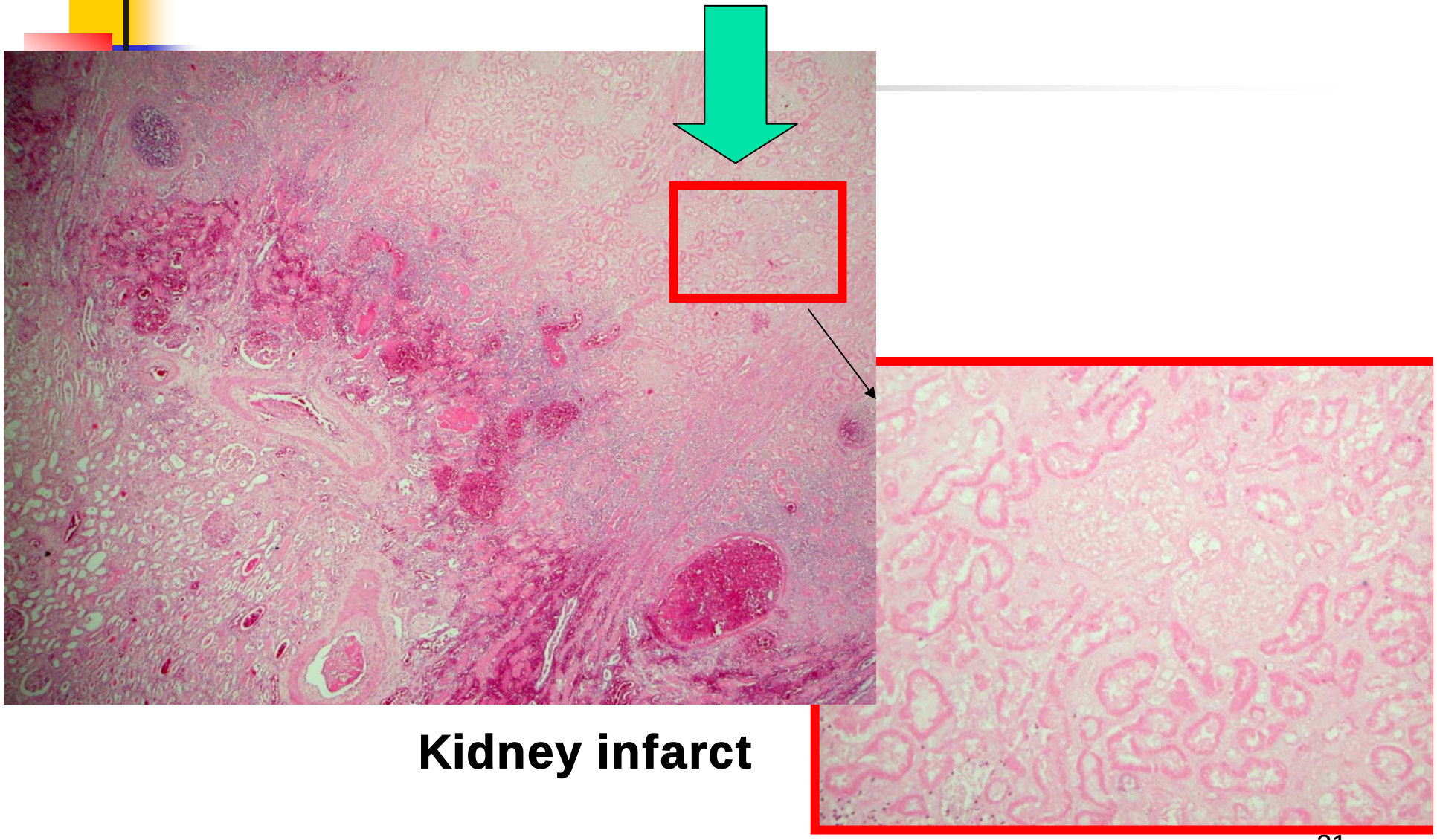
- **Coagulative necrosis** 凝固性壞死
- **Liquefactive necrosis** 液化性壞死
- **Caseous necrosis** 乾酪性壞死
- **Gangrenous necrosis** 壞疽性壞死
- **Fat necrosis** 脂肪壞死

Coagulative Necrosis

凝固性壞死

- **Most common form**
- **Preservation of basic structural outline of the coagulated cell or tissue**
- **Characteristic of hypoxic death of cells in all tissues except the brain**
- **Myocardial infarction (心肌梗塞), kidney infarction (腎臟梗塞)**

Coagulative Necrosis



Kidney infarct

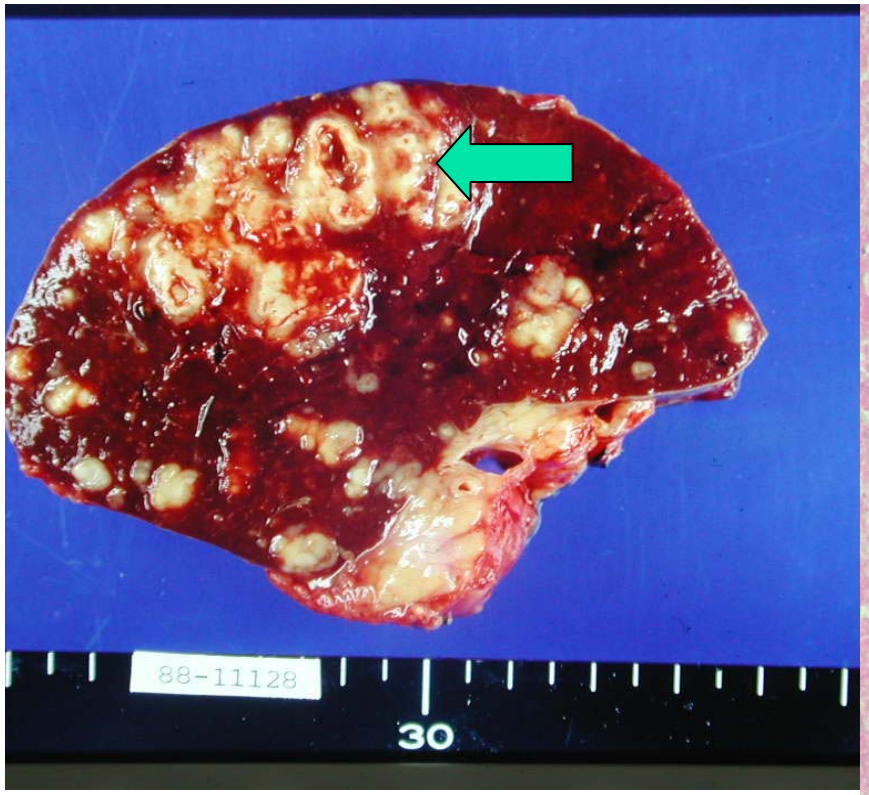
Liquefactive Necrosis

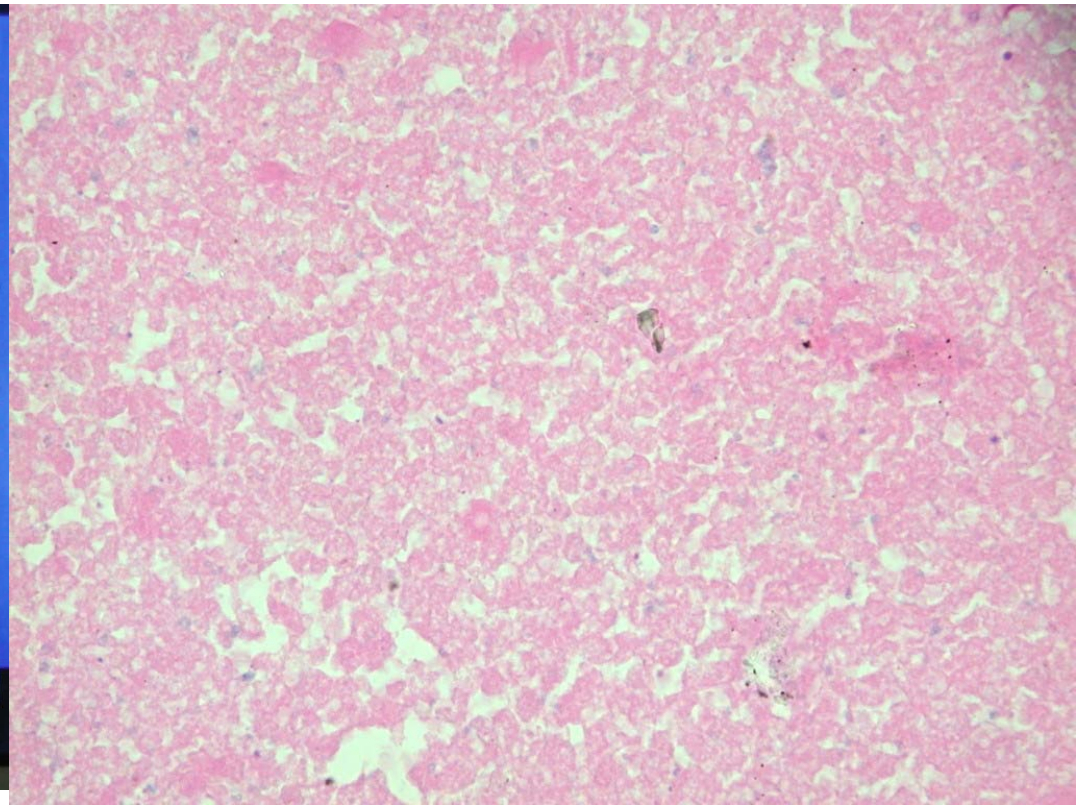
- Characteristic of bacterial or sometimes fungal infections
- Hypoxic death in the brain

Caseous Necrosis

- **Most often in foci of tuberculous (結核菌) infection**
- **Cheesy, white gross appearance, structureless amorphous granular debris**
- **Completely obliterated tissue architecture**

Caseous Necrosis in Tuberculosis

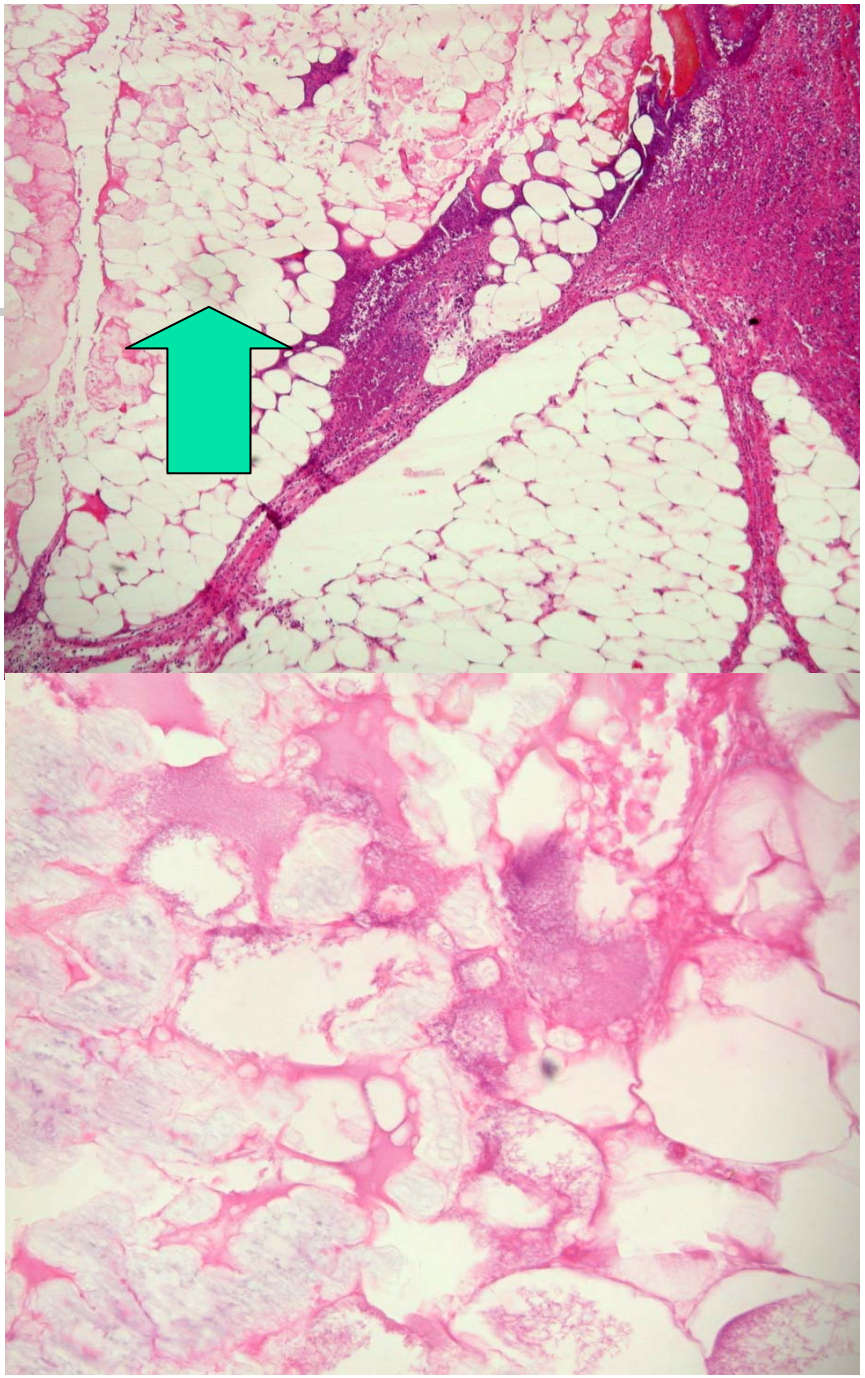




Spleen TB

Fat Necrosis

- Caused by action of lipolytic enzyme
- Limited to fat tissue
- Typically occurring pancreatic injury



Gangrenous Necrosis

- Not a distinctive pattern, ischemic coagulative necrosis, frequently of a limb, especially common in diabetes
- Gangrenous Necrosis of the Small Intestine

Apoptosis

- An “active” form of cell death
- Programmed cell death
- Energy dependent
- Typically affects single cell

- **Physiologic apoptosis**: during embryogenesis
- **Pathologic apoptosis:** a consequence of endogenous intracellular events or caused by adverse exogenous stimuli

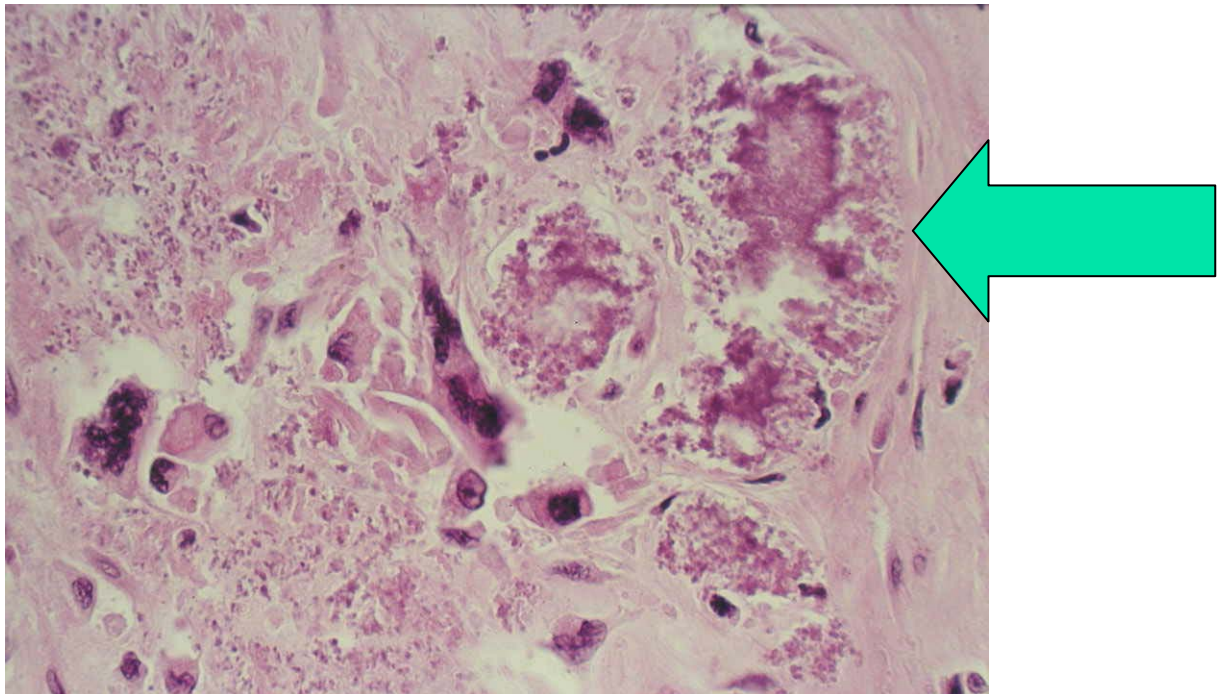
Features of Necrosis & Apoptosis

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis, karyorrhexis, karyolysis	Fragmentation
Plasma membrane	Disrupted	Intact
Cellular contents	Enzymatic digestion	Intact
Inflammation	Frequent	No
Role	Pathologic	Physiologic or pathologic

Dystrophic Calcification

失養性鈣化

- **Area of necrosis**
- **Atherosclerotic arteries, damaged heart valves, necrotic tumor, etc**



Metastatic Calcification
轉移性鈣化

- **Hypercalcemia (高血鈣), widely throughout the body**
- **principally affects the interstitial tissues of kidneys, lungs, and blood vessels, etc.**

Summary

- **Cell injury** (reversible or irreversible) develops when cells are stressed beyond that they can tolerate.
- **Adaptations** (hyperplasia, hypertrophy, atrophy, and metaplasia) are reversible changes in the number, size, phenotype, or functions of cell in response to changes in their environment.
- **Necrosis** is death of tissue following irreversible injury; often involves areas of tissue.
- **Apoptosis** is individual cell death; may be physiological or pathological cell turnover.