HM/CH-1/L-9

MORPHOLOGY OF CELL INJURY

MORPHOLOGIC FORMS OF CELL INJURY

MECHANISMS

1. Reversible cell injury
2. Deranged cell metabolism
3. Irreversible cell injury
4. Programmed cell death
5. Residual effects
6. After-effects

NOMENCLATURE

1. Retrogressive changes(degenerations)
2. Intracellular accumulations
3. Cell death-necrosis
4. Apoptosis
5. Subcellular alterations
6. Gangrene, pathologic calcification

Definition

- Described in 1972
- Apo+ptosis
- “Coordinated and internally programmed cell death”
- Rate of cell division *versus* activation of pathways of cell death (cell suicide)
- No inflammation, no collateral damage

Apoptosis in biologic processes

PHYSIOLOGIC

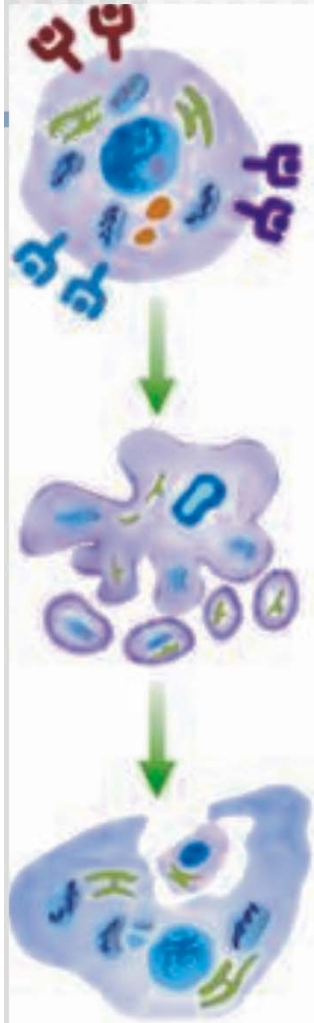
- Developing embryo
- Involution of hormone-dependent tissues
- Replacement proliferation
- Involution of thymus

PATHOLOGIC

- Chemotherapy for tumours
- Cell death by CTL
- Depletion of CD4+ cells in HIV
- Certain viral infections
- Pathologic atrophy
- Some agents causing necrosis
- Degenerative diseases
- Heart diseases

Molecular mechanisms

- Initiators of apoptosis
- Process of programmed cell death
- Phagocytosis



INITIATORS OF APOPTOSIS

- Transmembranous (e.g. absence of hormones, growth factors, cytokines)
- Intracellular (e.g. heat, radiation, hypoxia)
- Extracellular (e.g. FAS receptor activation)

PROCESS OF PROGRAMMED CELL DEATH

- Activation of caspases
- Activation of death receptors (*CD95*)
- Activation of growth controlling genes (*BCL-2, p53*)
- Cell death

PHAGOCYTOSIS

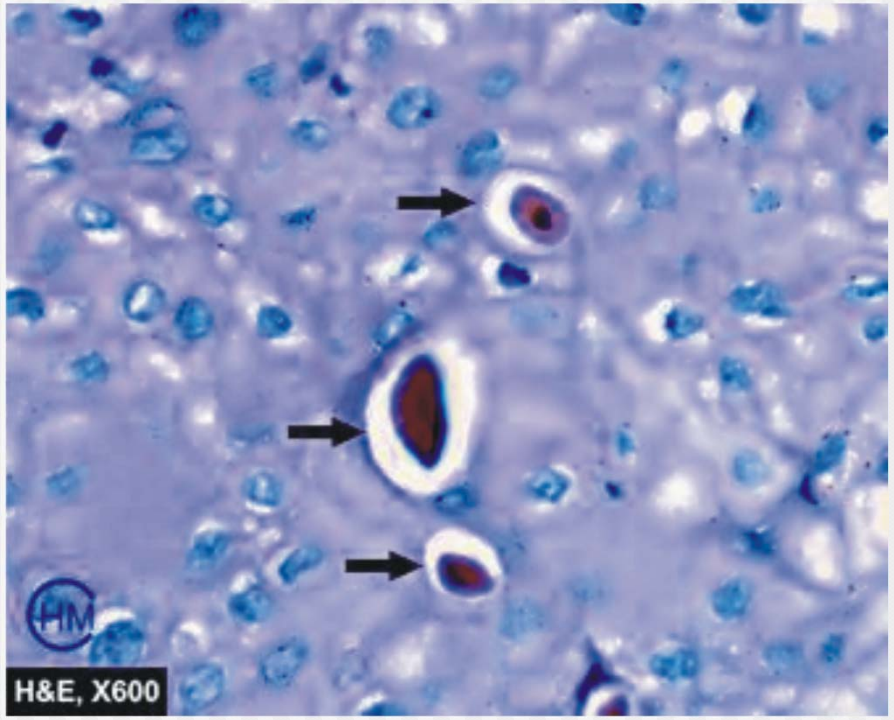
- Membrane changes (e.g. expression of phosphatidylserine, thrombospondin)
- No inflammatory cells

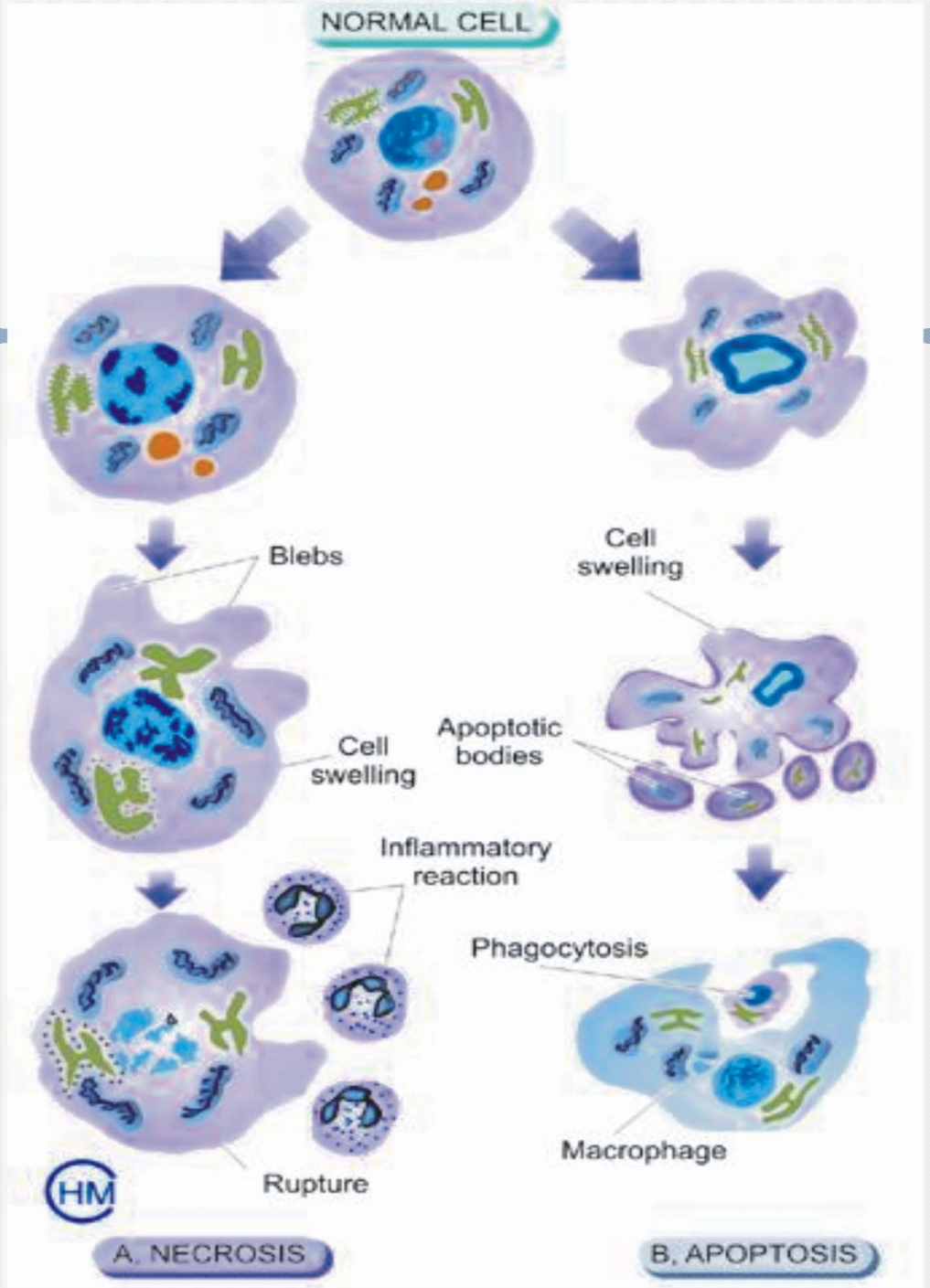
Biochemical changes

- Proteolysis of cytoskeleton
- Protein-protein cross linking
- Nuclear chromatin fragmentation
- Phosphatidylserine
- Thrombospondin
- Cell recognition by macrophages

Morphologic features

- Single cells/ small clusters
- Cell shrinkage (mummified cells)
- Nuclear chromatin pyknosis/karyrrehexis
- Projections
- Apoptotic bodies
- Phagocytosis
- No inflammatory cells




NORMAL CELL
Blebs
Cell swelling
Cell swelling
Apoptotic bodies
Inflammatory reaction
Phagocytosis
Rupture
Macrophage
HM
A. NECROSIS
B. APOPTOSIS

Techniques to identify & count apoptotic cells

- Chromatin stains (haematoxylin, Feulgen, acridine orange)
- Flow cytometry
- In situ hybridisation
- Annexin V

Web Table 3.4: Contrasting Features of Apoptosis and Necrosis

	Feature	Apoptosis	Necrosis
1.	*Definition*	Programmed and coordinated cell death	Cell death along with degradation of tissue by hydrolytic enzymes
2.	*Causative agents*	Physiologic and pathologic processes	Hypoxia, toxins
3.	*Morphology*	i) No Inflammatory reaction ii) Death of single cells iii) Cell shrinkage iv) Cytoplasmic blebs on membrane v) Apoptotic bodies vi) Chromatin condensation vii) Phagocytosis of apoptotic bodies by macrophages	i) Inflammatory reaction always present ii) Death of many adjacent cells iii) Cell swelling initially iv) Membrane disruption v) Damaged organelles vi) Nuclear disruption vii) Phagocytosis of cell debris by macrophages
4.	*Molecular changes*	i) Lysosomes and other organelles intact ii) Genetic activation by proto-oncogenes and oncosuppressor genes, and cytotoxic T cell-mediated target cell killing iii) Initiation of apoptosis by intra- and extracellular stimuli, followed by activation of caspase pathway (FAS-R, BCL-2, p53)	i) Lysosomal breakdown with liberation of hydrolytic enzymes ii) Cell death by ATP depletion, membrane damage, free radical injury