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Tissue changes in reversible and irreversible injury
Necrosis and apoptosis
Postmortem changes
Cellular swelling

- Cells are incapable of maintaining ionic and fluid balance
- Acute infections
- Toxic conditions
- Physical injury
- Anoxia
- Malnutrition
- Circulatory disturbances
Hydropic/Vacuolar degeneration

- More severe than cellular swelling
- Causes and gross pathology similar
- Swollen, opaque organs (cloudy)
- Capsule is tense
- Cut surface bulges
Hydropic/Vacuolar degeneration

- Clear vacules in the cytoplasm
- Reversible
- Water accumulation within cells
- Cells are swollen, cytoplasm pale, reticulated
- Nuclei are unaffected
- Increased water content of the cytoplasm
- Distertion of the endoplasmic reticulum
Irreversible cell injury

- Cell membrane damage—central factor
- Severe vacuolization of mitochondria
- Swelling of lysosomes
- Massive influx of calcium in cells
- Loss of proteins, enzymes, RNAs
- Injury to lysosomal membranes—enzyme leakage—digestion of cell
Necrosis

- Sequence of changes
- In a living tissue or organism
- Most serious result of injury
- Cell death
- As a whole body—somatic death
- Irreversible cell injury
- Earliest change in nucleus
- Progressive degradative activity of enzymes
• Autolysis---Catalytic enzymes are derived from the lysosomes of dead cells
• Heterolysis---Catalytic enzymes are derived from the lysosomes of immigrant leukocytes
Macroscopy of dead tissue

- Opaque
- The normal translucency is lost
- Whitish or yellowish color
Microscopy of dead tissue

• The dead cells shows increased eosinophilia
• Glossy, homogenous appearance
• Cytoplasm becomes vacuolated
• Calcification of dead cells
Nuclear changes

- Pyknosis---Nucleus shrinks, stains more intensely basophilic
- Karyorrhexis---Fragmentation of nucleus
- Karyolysis---Nucleus loses its ability to stain differentially with basic dyes (Hematoxylen)
Types of necrosis

- Coagulation necrosis
- Liquefactive necrosis
- Fat necrosis
- Caseous necrosis
- Gangrenous necrosis
Coagulation necrosis

- Cutting of blood supply (INFARCTION)
- Certain poisons (Phenol, formaldehyde)
- Most common form of necrosis
- Loss of nuclei (tombstone)
- Preservation of basic outlines of cells
- Recognition of tissue architecture
- Sudden severe ischemia
Myocardial infarct due to coronary occlusion
Coagulation necrosis
Demarcation line
Fresh infarct in kidney
Acute tubular necrosis
Splenic infarct
Liquefaction necrosis

- Ischemic destruction of brain tissue
- The dead area softens, liquefies
- Bacterial lesions (enzymes of bacteria and leucocytes)
- Action of powerful hydrolytic enzymes
- Cystic structure filled with debris and fluid
Liquefaction necrosis
Fat necrosis

- Acute pancreatic necrosis
- Pancreatic enzymes (Lipases)
- Abdomen
- Hydrolysis of the neutral fat
- Shadowy outlines of necrotic fat cells
- Inflammatory reaction
- Released free fatty acids and calcium—SOAPS—CHULKY/WHITE OPAQUE AREAS
Fat necrosis 2

- Breast, subcutaneous tissue
- Trauma
- Traumatic fat necrosis
- Inflammatory reaction
- FOREIGN BODY TYPE
- Resembling TUMOR
Caseous necrosis

- Soft, friable, whitish/gray debris
- Clumped cheesy material
- The cells are not totally liquefied nor are their outlines preserved (Coagulation and liquefaction)
- Amorphous, granular debris
- Granuloma (central necrosis, epithelioid histiocytes, Langhans giant cells, fibroblasts, lymphocytes)
Caseous necrosis
Gangrenous necrosis

- Not a distinctive pattern of necrosis
- Surgical clinical term
- Limb (lower leg)
- Lost its blood supply—-ischemic cell death,
- Bacterial agents---modifies by liquefaction
- Coagulative pattern—dry gangrene
- Liquefactive pattern—wet gangrene
- Atherosclerosis / Diabetes mellitus
Postmortem changes

- Rigor mortis
- Livor mortis
- Algor mortis
- Postmortem clots
- Autolysis
- Putrification
Rigor mortis

- Stiffening of the muscles
- Precipitation of proteins
- Chemical change
- Involuntary muscle
- 2-4 hours after death voluntary muscles,
- Completes in 12 hours
- Gradually disappears in 24-48 hours
Livor mortis

- Reddish discoloration
- Resulting from the gravitational sinking of blood
- Lungs, skin
- Hemolysis of red cells
- Hemolytic organisms
- Hb stains the intimal lining and serous surfaces
Algor mortis

- Cooling of the body
- Until the temperature of the environment
- Environmental temperature affects
- Clothing
- State of nutrition
Postmortem clots

- Moist
- Elastic, homogenous
- Not adherent to the lining endothelium
- Forms a cast of the vessel and its branches
Autolysis

- Self-digestion/breakdown of tissues
- Caused by ferments released after death
- Stomach, gall bladder rapidly
- Highly differentiated tissues (ganglion cells, glandular epithelium more rapid than connective tissue)
- NO INFLAMMATORY REACTION
- NECROSIS WITH INFLAMMATORY RX
autolysis
Putrification

- Entrance of saprophytes from intestinal tract
- Production of gases
- Greenish discoloration of tissues
- Gas producing bacteria
- Foamy or spongy appearance of tissues (LIVER)
APOPTOSIS

- Genetically determined
- Internal
- Self destruct mechanism of cell death
Apoptosis

- Physiologic/pathologic events
- Programmed destruction of cells
- During embryogenesis
- Hormone dependent involution in the adults
- Cell deletion in proliferating cell population intestinal epithelium
- Cell death in tumors (during regression)
Apoptosis 2

- Death of immune cells
- Pathologic atrophy in parenchymal organs after duct obstruction (pancreas, parotis)
- Atrophy of hormone dependent tissues
- Cell death induced by cytotoxic T cells
- Cell injury in certain viral disease
- Mild thermal injury, radiation, cytotoxic cancer drugs
Apoptosis viral hepatitis
Apoptosis/ morphology

- Cell shrinkage (small size, dense cytoplasm)
- **Chromatin condensation** (most characteristic)
- Formation of cytoplasmic blebs—apoptotic bodies------fragmentation
- Phagocytosis of apoptotic cells or bodies
- Single cell or cluster of cells
- Does not elicit inflammation
- DISTINCT FORM OF CELL DEATH
Mechanism of apoptosis

- Cell death by stimuli---necrosis
- Low doses---apoptosis
- Apoptosis may occur before apparent
- Plasma membranes intact until last stage
Biochemical features

• Protein cleavage (activation of cysteine protease) Caspase—triggers endonuclease activity
• Protein-cross linking (transglutaminase activation)—covalently linked shrunken shells
• DNA breakdown—(not specific, endonuclease activity—late autolytic phenomenon
• Phagocytic recognition—early reco. of dead cell
• Macrophage/adjacent cells
Mechanisms

- Signaling pathways--- Initiate apoptosis—transmembrane signals---negatif/positive determinants (certain hormones, growth factors, cytokins)

- Intracellular signaling (glukocorticoids, physicochemical agents, hypoxia, viral infections)
Control and integrating stage

- Specific proteins
- Connect death signals to execution program
- Commitment or abortion of potentially lethal signals
- Bcl-2 family of proteins—apoptotic regulations ANTIAPOPTOTIC—regulating mitochondrial function
Apoptotic signals

- Mitochondrial permeability formation of pores mitochondrial swelling
- Increased permeability of outer membrane
- Releasing cytochrome C (apoptotic trigger)
- Cytochrome C release—preceeds the morphologic changes of apoptosis
Execution Phase

- Final pathways of apoptosis
- Proteolytic cascade
- Caspase—disrupts cytoskeleton, nuclear matrix proteins
- Proteins involved in transcription, DNA replication, DNA repair
Removal of dead cell

- Apoptotic cells—marker molecules on their surfaces
- Early recognition by adjacent cells and phagocytes
- Phagocytic uptake
- Dead cells disappear without leaving a trace
- NO INFLAMMATION
Features of necrosis vs apoptosis

• Hypoxia, toxins
• Cellular swelling, coagulation necrosis, disruption of organelles
• Random, diffuse DNA damage, ATP depletion, membrane injury, free radical damage
• Inflammation

• Physiologic/pathologic
• Single cell, chromatin condensation, apoptotic bodies
• Internucleosomal, gene activation, endonuclease
• No inflammation, phagocytosis of apoptotic bodies
References and further reading

- Robbins Pathologic Basis of Disease, Cotran, Kumar 2004
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- Basic Pathology, 6th ed, Kumar, Kotran, Robbins
- Pathology Rubin, Farber, 1999
- Mohan Harsh Textbook of Pathology, 2005
- Cerrahpaşa Pathology archives
- Internet (various medical web sites)