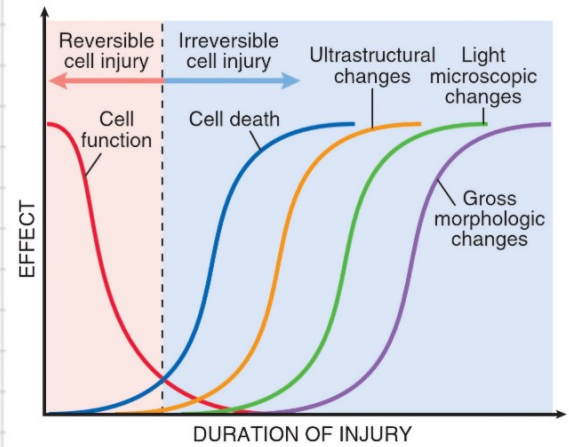
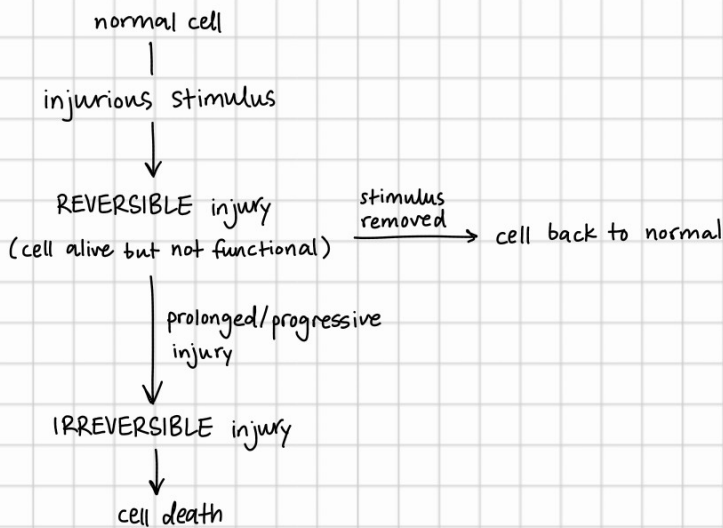


REVERSIBLE & IRREVERSIBLE CELL INJURY

lec no. 2



- * cell function starts declining once REVERSIBLE injury starts (1st response)
(cell not functional in both REVERSIBLE & IRREVERSIBLE injury)
- * IRREVERSIBLE injury changes:
Ultrastructural → LM changes → Gross (naked eye observation, organ level)

Reversible

- removing damaging stimulus = return to normal
- cell alive but not functional
- cellular swelling due to mitochondrial failure (no ATP → Na^+/K^+ ATP dependent pump failure → accumulation of Na^+ inside & K^+ outside → water moving into cell due to high Na^+ concentration)
- membrane & nucleus change but still intact
- Morphology :
 - macroscopic → organ swelling (hydropic change) ex. hepatitis, liver enlargement
→ fatty change (damage in lipid bilayer, accumulation of fat droplets in cytoplasm)
 - microscopic → cellular swelling (hydropic change) ex. enlarged, yellow, greasy liver (organs involved in fat metabolism)
→ fatty change (clear cytoplasmic vacuoles due to lipid accumulation)
 - ultrastructural → plasma membrane alterations (blebbing/blunting)
→ nuclear chromatin clumping (very dark blue under microscope)
→ mitochondrial change (swelling & black densities)
→ ER dilation → ribosomes detach → decreased protein synthesis
→ cytoplasmic myelin figures (from phospholipids of damaged plasma membrane)

Irreversible

- no way back
- local inflammation (helps immune cells find & deal with cellular damage)
- irreversible mitochondrial dysfunction (No ATP)
- loss of plasma & intracellular membranes (organelle & cell content leakage, detectable in blood/serum)
- Nuclear Changes (3 stages)
 - 1) Pyknosis : shrinkage, increased basophilia (blue staining)
 - 2) Karyorrhexis: fragmentation of nuclear material
 - 3) Karyolysis : basophilia fades (degradation of nuclear material)
- Morphology :
 - macroscopic → depends on type of necrosis
 - microscopic → increased cytoplasmic eosinophilia (due to • accumulation of degraded proteins
• ↓ protein transcription & translation = ↓ RNA content)
→ loss of DNA & chromatin structural integrity
 - ultrastructural → mitochondrial change (swelling & black densities)
→ severe ER dilatation (=dilation)
→ more cytoplasmic myelin figures (↑ membrane damage)

Cell Death depending on nature & severity of injury

Apoptosis

- less severe injury (UV light, sun damage, aging, loss of growth factors, ...)
- in healthy tissues, no inflammation
- controlled, regulated by genes & signaling pathways
- clean cell suicide

Necrosis

- rapid & uncontrollable
- severe disturbances
- ischemia, toxins, infections (viral/bacterial), severe trauma

Necroptosis

- Necrosis & Apoptosis at the same time

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling, increased water content)	Reduced (shrinkage)
Nucleus	Pyknosis → Karyorrhexis → Karyolysis	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact, altered structure (lipid orientation)
Cellular contents	Enzymatic digestion, may leak out of cell	Intact, may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic/Pathologic role	Invariably pathologic (culmination of irreversible injury)	Often physiologic, eliminating unwanted cells, example of pathologic: after DNA and protein damage cell injury

Morphologic Patterns of Tissue Necrosis

Coagulative Necrosis

- conserved tissue architecture initially
- enzyme disfunction
- anuclear eosinophilic on LM
- wedge shaped (following blood supply)
- leukocyte lysosomal enzymes & phagocytosis required for clearance
- ischemia to all solid organ (infarcts) except brain & spinal cord (liquefactive necrosis)

- pallor → macroscopic (blood deprivation / ischemia)
→ microscopic (devoid of nuclei)

Liquefactive Necrosis

- focal (localized) infections by bacterial & fungal organisms
- pus (or abscess) → filled with inflammatory cells, mainly neutrophils
- CNS infarcts
- center liquefies (cavitary lesion) & digested tissue is removed by phagocytosis

Gangrenous Necrosis (= coagulative necrosis affecting multiple tissues at the same time)

- dry (without infection) vs wet (with superimposed infection)

Caseous Necrosis

- "cheese like", yellowish/whitish
- tissue architecture NOT preserved
- caseating granuloma → acellular center (area of debris) enclosed by macrophages
- most often seen in tuberculosis (TB)

Fat Necrosis

- in acute pancreatitis
- due to release of pancreatic lipases
- focal fat destruction
- fat digestion ⇒ released FA's + Ca^{+2} (saponification)
↓
white chalky appearance
- shadows of necrotic fat cells with lost nuclei

Fibrinoid Necrosis

- visible only microscopically
- caused by deposits of antigen-antibody & fibrin complexes in arterial wall
- seen in vasculitis (Polyarteritis Nodosa, PAN) & severe hypertension