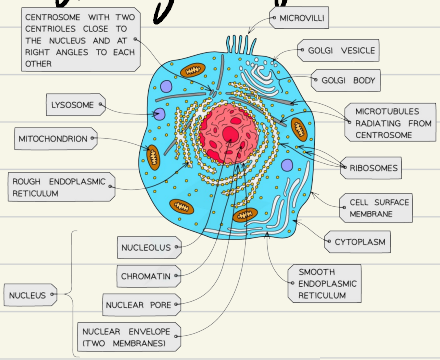
cellular adaptation

adaptive mechanisms ~ adaption of cells to stress

1- hypertrophy 2- hyperplasia 3- Atrophy 4- Metaplasia



↳ When changes occur they occur at the ultrastructural level of the cell ⇝ change in tissue ⇝ change in organs ⇝ chang of human body

* all normal cells lives in homeostasis → Proteins, PH, Temp, electrolytes

Reversible injury

any deviation of stress → reversible ☑ → adaptation

injurious stimulus → cell injury

inability to adapt
* prolonged * severe
* cell is diseased

cell injury → severe → irreversible injury ⇝ point of no return x cell death

irreversible injury → Necrosis
irreversible injury → adoptosis

Adaptations

Physiological

normal, healthy adjustments that cells or tissues make in response to changes in their environment or increased demands

Pathological

when cells or tissues adjust to abnormal or harmful conditions as a result of stress injury or disease

Forms of adaptation:

* hypertrophy : increase in cell size
* atrophy : decrease in cell size
* Hyperplasia : increase in number of cells
* Metaplasia : change into another type of cell

Reversible when stressful event is removed, cell will go back to normal

if stress is continued & cell is inable to adapt → cell injury

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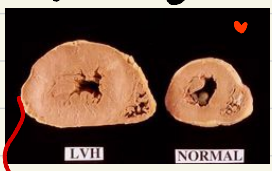
1 hypertrophy → increased size & functional capacity

↑ structural proteins ↑ organelles ↑ function



NOTE
* cells that cannot replicate & only undergo hypertrophy
* neurons *
* cardic & skeletal muscle *

* pure or mixed with hyperplasia → when they can replicate !!

cardic hypertrophy

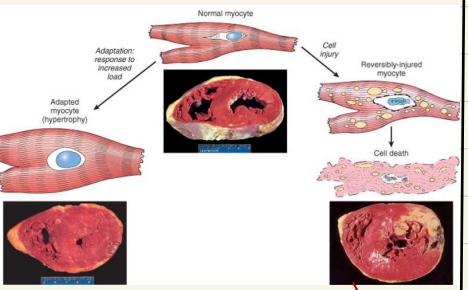
* in patients with hypertension & aortic valve stenosis heart has to pump blood against resistance → ↑ workload → ↑ hypertrophy

* can be pathological or physiological

* Due to →
  1. hormonal stimulation
  2. Growth factor stimulation
  3. increased functional demand

Pathological hypertrophy

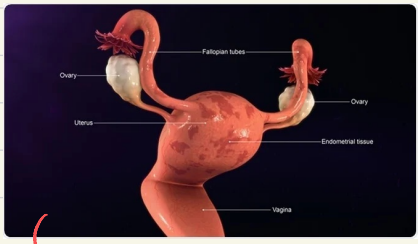
* Cardiac muscles in hypertension & aortic stenosis
  - in hypertension heart has to pump blood against increased resistance in arteries ; The left ventricle "the chamber of blood responsible for pumping oxygenated to body" thickens in response to increased workload
  - in aortic stenosis, aortic valve that allow blood to exit left ventricle becomes narrowed → forces heart to work much harder → left ventricle hypertrophy



incase of severe injury such as myocardial infraction "heart attack" → cell injury

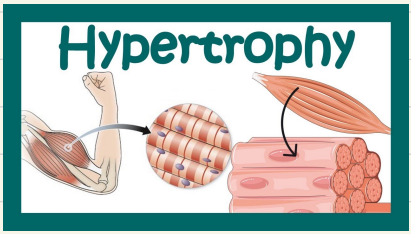
Physiological hypertrophy

* uterine smooth muscle in pregnancy ← can undergo both hypertrophy & hyperplasia
  - myometrial



reversible

* Skeletal muscle hypertrophy in athelets

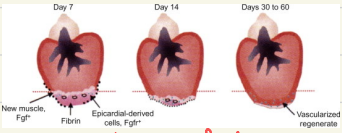


★ Pure hypertrophy

2 Hyperplasia → increase in the number of cells

* Tissues that have ability to proliferate
* pure or mixed

Physiological ⇝ reversible	Pathologic ⇝ Sometimes increase risk of cancer
* Hormonal Stimulation → Breast in Puberty & Pregnancy	* Excessive hormonal stimulation → Endometrial hyperplasia, estrogen induced → lining of uterus → risk of cancer !!
* Compensatory → liver after partial resection	* Benign Prostatic hyperplasia, androgen induced → does not increase risk of virus
	* Viral infections → warts (HPV) → human papillomavirus

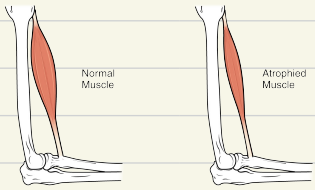


§ remaining hepatocyte proliferate

3 Atrophy → Decrease in cell size & function → ↓ protien synthesis, ↑ degredation, ↑ Autophagy

Note

° Atrophic cells can still function



Causes :
① decrease workload : immobilization of a limb after fracture
② loss of innervations → Ex. diabetes neuropathy, nerve injury → fracture, stab wounds
③ diminished blood supply
④ inadequate nutrition
⑤ loss of Endocrine stimulation → after menopause
⑥ Aging (Senile atrophy)

Physiological atrophy	Pathological atrophy
* loss of hormonal stimulation in menopause → endometrial atrophy	* Denervation injury * Chronic ischemia * Chronic malnutrition

4 **Metaplasia** → change from one cell type to another → stem cells → reversible

↳ functional cost

↳ presistent change → cancer !!

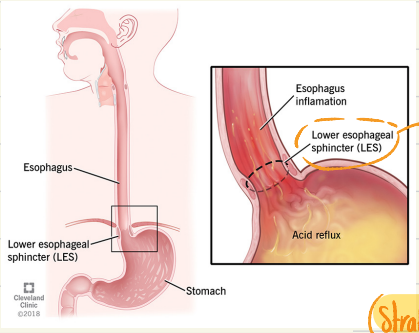
Causes: ① Smoking → affects bronchial lining (ciliated pseudostratified columnar epithilium) → cilia & mucus is lost

we lose protection of airways → stratified

↑↑ risk of lung cancer

② Vitamin A deficiency → which is needed to differentiate epithelium → leads to sqamous metaplasia of bronchi

③ GERD : Gastroesophageal reflux disease



→ this sphincter prevents reflux of acid which is harsh on the esophagus

loose sphincter → continuous exposure → lining of Esophagus (Stratified sqamous) changes into (glandular) with goblet cells

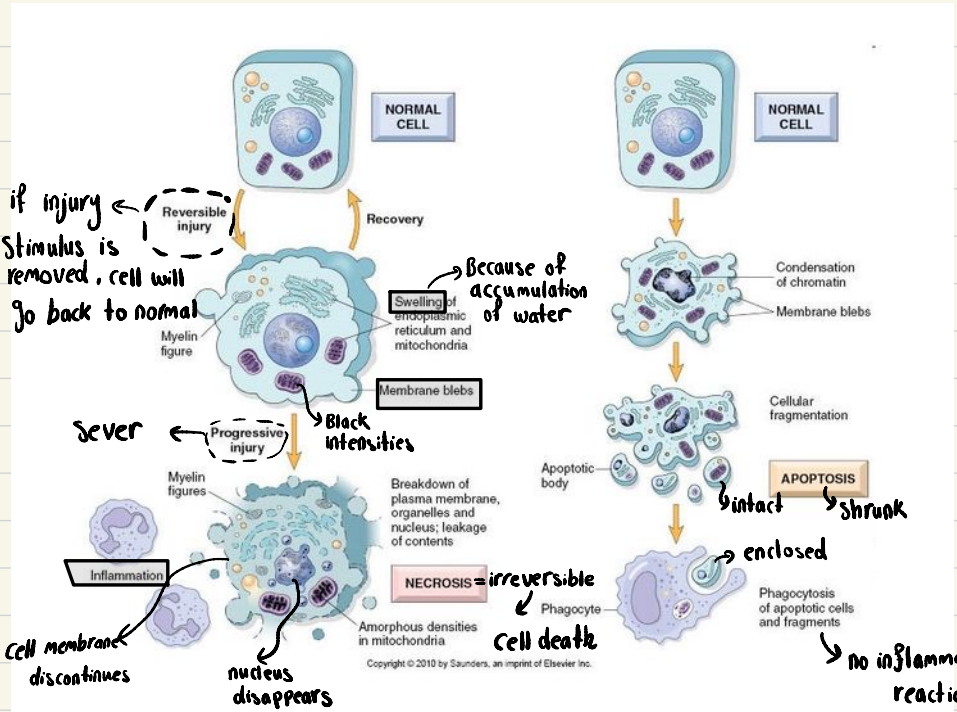
↑ risk of cancer

Causes of cell injury

1. Oxygen deprivation - hypoxia → ischemia, anemia, respiratory diseases
2. chemical agents → salt, sugar, pesticides, formaline
3. infectious agents → viruses & bacteria
4. immunologic reactions → allergy, auto immune disease, microbes
5. Genetic factors → chromosomal abnormalities → down syndrome
6. Nutritional imbalances → malnutrition / excessive nutrition
7. Physical agents → trauma / electrical injury / thermal injury

Reversible & irreversible cell injury

● Recorded lec



if injury ← Reversible injury

Stimulus is removed, cell will go back to normal

Because of accumulation of water

Black intensities

sever ← Progressive injury

irreversible

Cell death

Cell membrane discontinues

nucleus disappears

intact

shrunk

enclosed

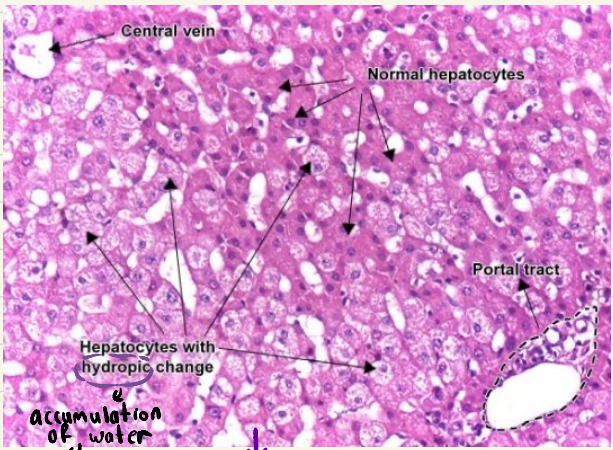
no inflammatory reaction

if damaging stimulus is removed in reversible injury → injured cells can return to normal

Morphology

Cellular swelling ---→ organ swelling

Fatty change



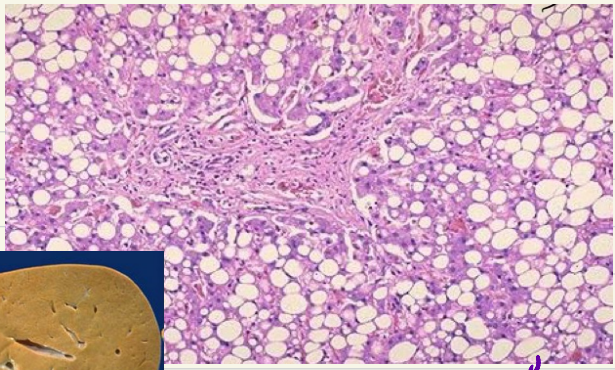
accumulation of water

whitish cytoplasm

Swollen cell ← Accumulation of Na^+ ← Failure of Na^+/K^+ pump

Reversible damage - fatty change

in organs involved in fat metabolism



reflected in macroscopic appearance

rich lipid droplets

Other changes ; note : these changes can be seen in irreversible injury but much more severe

1- plasma membrane alterations (blebbing, blunting) - remember it remains intact

2- mitochonderial change (swelling & densities)

3- dialation of ER - deattatchment of ribosomes

4- nuclear clumping of chromatin - nucleus still intact

5- cytoplasmic myelin figures - derived from phospholipid of altered plasma membrane & organelle membranes

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irreversible injury (necrosis)

1- irreversible Mitochondrial dysfunction → no ATP production - Mitochonderia won't go back to normal

2- loss of plasma membrane and intracellular membrane ⇝ cellular enzyme leak out → they can gain access to blood stream

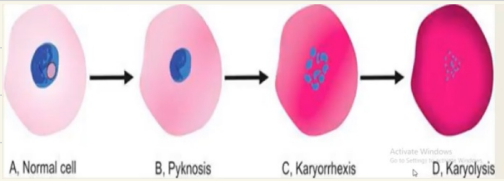
3- loss of DNA & chromatin structural integrity

4- local inflammation ★

irreversible injury Morphology

1. increased cytoplasmic eosinophilia - more pink color - Eosin stain → lot of denatured proteins
   → decreased transcription ↓ RNA
   ↓ Blue color
2. Marked dialation of ER , mitochonderia
3. Mitochondrial densities
4. More myelin figures

* Nuclear changes *



Pyknosis: shrinkage and increased basophilia

Karyorrhexis: fragmentation

Karyolysis: Basophilia fades & degeneration of nuclear material

Normal , reversible , irreversible cell injury

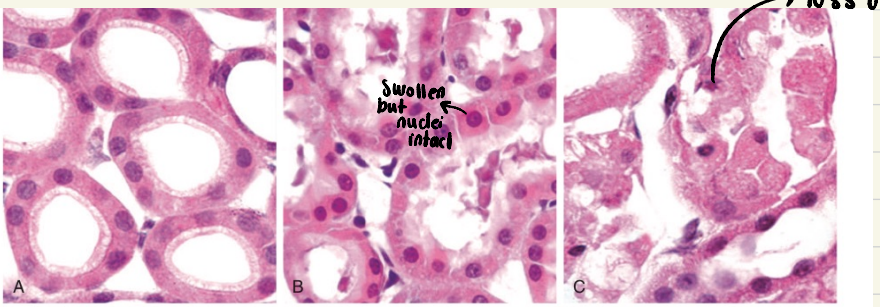


Fig. 2.4 Morphologic changes in reversible and irreversible cell injury (necrosis). (A) Normal kidney tubules with viable epithelial cells. (B) Early (reversible) ischemic injury showing surface blebs, increased eosinophilia of cytoplasm, and swelling of occasional cells. (C) Necrotic (irreversible) injury of epithelial cells, with loss of nuclei and fragmentation of cells and leakage of contents. *(Courtesy of Drs. Neal Pinckard and M.A. Venkatachalam, University of Texas Health Sciences Center, San Antonio, Texas.)*

Cell death - different mechanisms depending on nature and severity of injury

① Necrosis
* Rapid & uncontrollable
* Severe disturbances : ischemia , toxins , infections & trauma

② Apoptosis
* less severe injury → uv light , aging, loss of growth factors
* regulated by genes & signaling pathways
* precisely controlled
* can be manipulated → chemotherapy
* in healthy tissues → aged cells of skin
* clean cell suicide → no inflammation

③ Necroptosis → mixture

Table 2.1 Features of Necrosis and Apoptosis

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis	Fragmentation into nucleosome-sized fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell	Intact; may be released in apoptotic bodies
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA and protein damage

loss of function ← is a feature of both reversible & irreversible injury

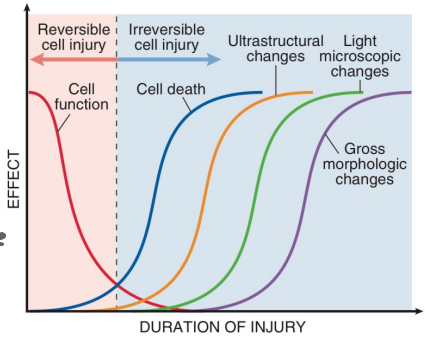


Fig. 2.5 The relationship among cellular function, cell death, and the morphologic changes of cell injury. Note that cells may rapidly become nonfunctional after the onset of injury, although they are still viable, with potentially reversible damage; with a longer duration of injury, irreversible injury and cell death may result. Note also that cell death typically precedes ultrastructural, light microscopic, and grossly visible morphologic changes.

Clinical implications

leakage of intracellular protiens through damaged cell membrane & ultimately into circulation

provides a means of detecting specific tissues necrosis using blood serum or samples

Cardic enzymes , liver enzymes → hepatic toxicity , viral infections , hepatits

after myocardial ischemia
we can detect cardic enzymes

Morphologic patterns of tissue necrosis (Etiologic clues)

the way tissues look when they are necrotic can provide insights into what caused the tissue damage or death.

1 Coagulative necrosis

Conserved tissue architechture initialy - damages protiens & Enzymes → Block autolytic processes
↳ Just for a few days

↳ Enzyme dysfunction

* leukocyte lysosomal enzymes & phagocytosis required for clearance

* Anuclear eosinophilic on LM

* wedge shaped

* ischemia to all solid organ (infraction)
((cause))
except the brain

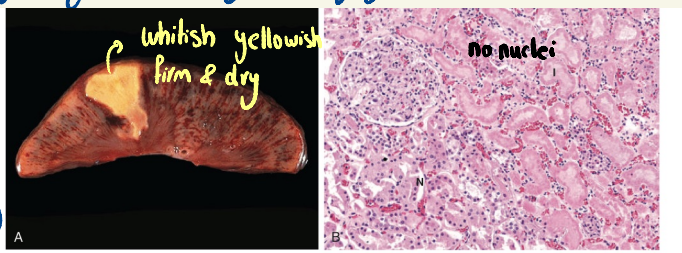


Fig. 2.6 Coagulative necrosis. (A) A wedge-shaped kidney infarct *(yellow)* with preservation of the outlines. (B) Microscopic view of the edge of the infarct, with normal kidney *(N)* and necrotic cells in the infarct *(I)*. The necrotic cells show preserved outlines with loss of nuclei, and an inflammatory infiltrate is present (difficult to discern at this magnification).

2 liquefactive Necrosis

* focal infections by bacterial & fungal organisms

*Pus

* CNS infract - Ischemia of brain

*center liquefies and digested tissue is removed by phagocytosis

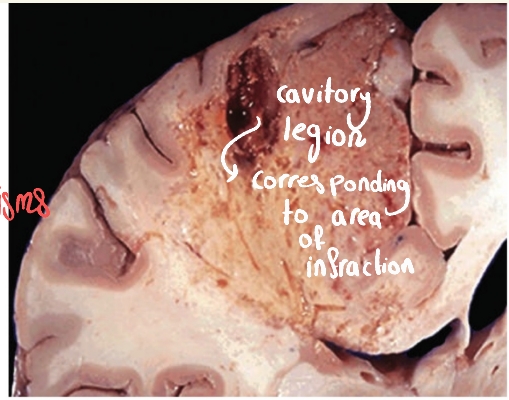
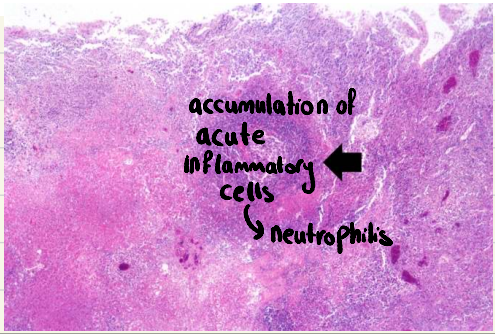


Fig. 2.7 Liquefactive necrosis. An infarct in the brain shows dissolution of the tissue.

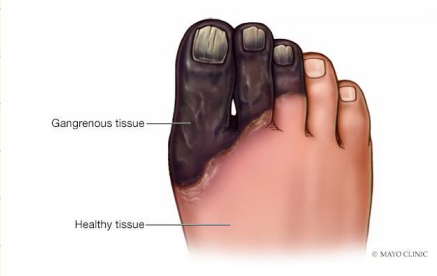


3 Gangrenous necrosis

*clinical term

*coagulative necrosis to multiple Tissues

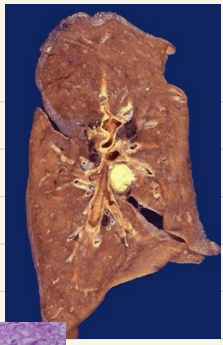
* Dry / wet
  - Dry → without infection
  - wet → with infection



- Although **gangrenous necrosis** is not a distinctive pattern of cell death, the term is still commonly used in clinical practice. It usually refers to the condition of a limb (generally the lower leg) that has lost its blood supply and has undergone coagulative necrosis involving multiple tissue layers. When bacterial infection is superimposed, the morphologic appearance changes to liquefactive necrosis because of the destructive contents of the bacteria and the attracted leukocytes (resulting in so-called "wet gangrene").

4 Caseous necrosis ⇝ cheese like

ok it can be cheese aka cascoh 😂

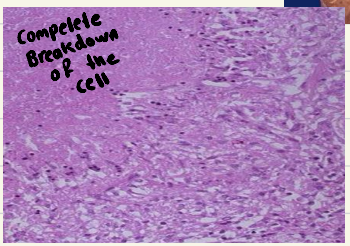


↳ Tissue architecture is not preserved

Acellular center

Usually enclosed by collection of macrophages (granuloma)

* TB *



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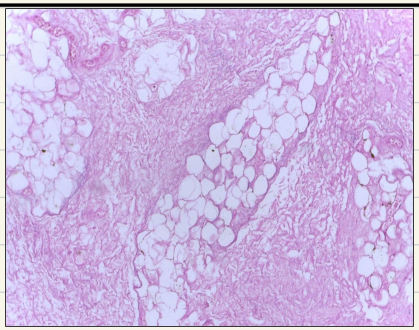
5 Fat necrosis



↳ Occurs in acute pancreatitis

↳ Pancreatic lipases

↳ Focal fat destruction

↳ released fatty acids combine with (Ca^{+2}) → saponification to produce whitish chalky apperance

* shadows of necrotic fat cells

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6 Fibrinoid necrosis

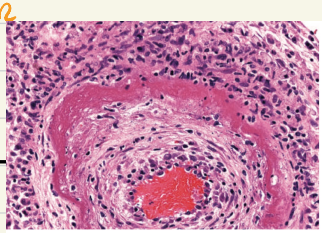

Fig. 2.10 Fibrinoid necrosis in an artery in a patient with polyarteritis nodosa. The wall of the artery shows a circumferential bright pink area of necrosis with protein deposition and inflammation.

* Visible only microscopically

* Deposit of antigen-antibodies and fibrin complexes in arterial walls

* seen in vasculitis (PAN) - autoimmune disease

* severe hypertension