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Ecological, Economic and Social Sustainbility

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İSTANBUL GELİŞİM ÜNİVERSİTESİ

Department PHYSICAL THERAPY AND REHABILITATION

Subject FTY145E-PATHOLOGY

Week of the Term: **3-4**

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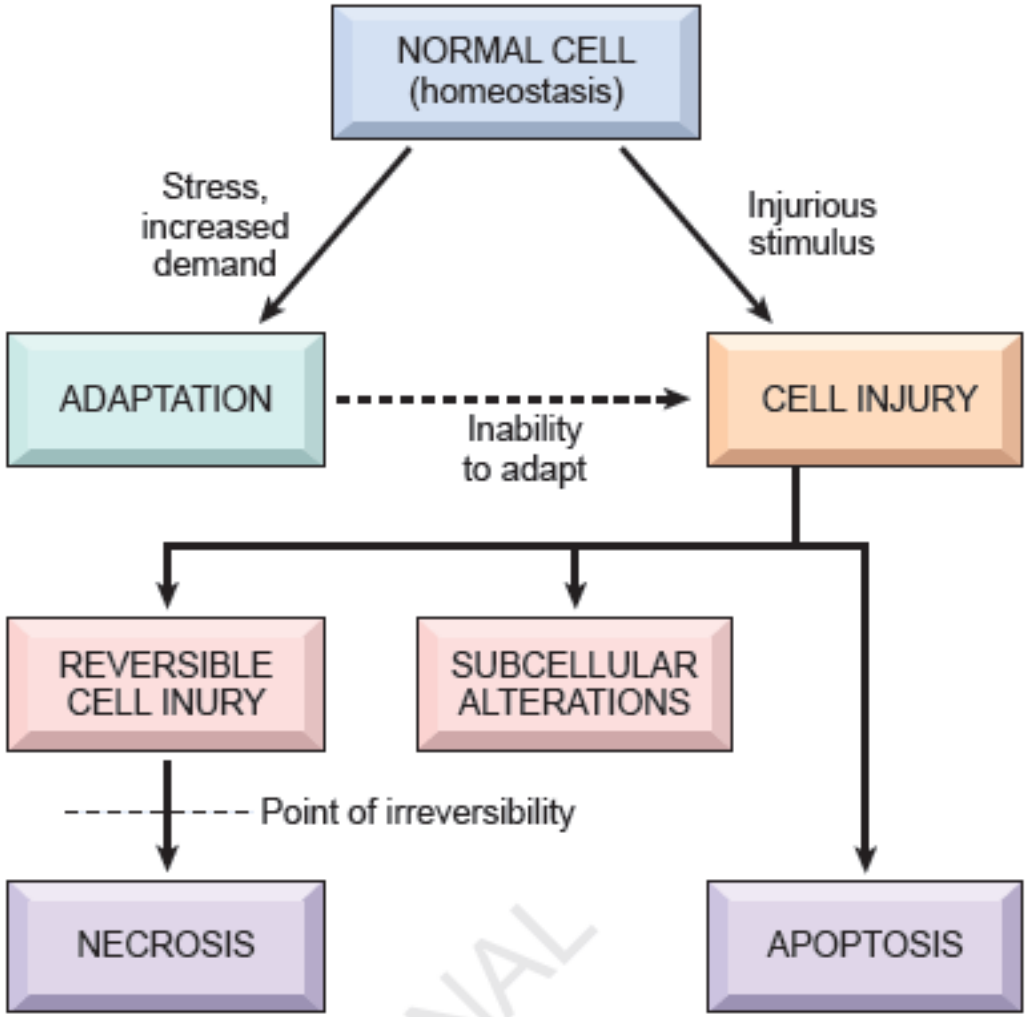
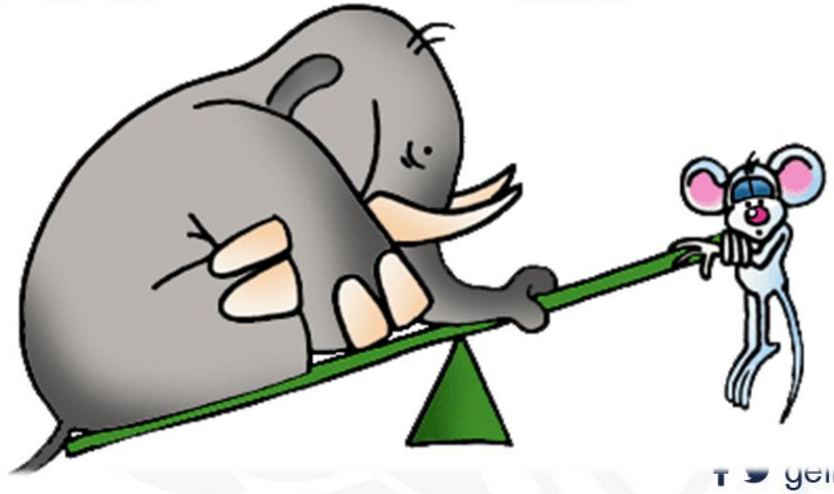
Consultation hours: Tuesday 10:00-12:00


NORMAL CELL
(homeostasis)
Stress,
increased
demand
Injurious
stimulus
ADAPTATION
Inability
to adapt
CELL INJURY
REVERSIBLE
CELL INURY
SUBCELLULAR
ALTERATIONS
Point of irreversibility
NECROSIS
APOPTOSIS

CELLULAR RESPONSE TO STRESS AND NOXİOUS STİMULİ

- When cells encounter physiological stress or pathological stimuli, they can achieve a new steady state while maintaining their function.
- Cell damage occurs if adaptability is exceeded or external stress is directly harmful.



Cell Response To The Damaging Agent;

Depends on the injurious agent:
1. Type
2. Exposure Time
3. Its Severity

- Therefore, low doses of toxins or short duration of ischemia cause reversible cell damage. Larger doses of toxins or longer-term ischemia result in irreversible injury and cell death.

- The type, condition, genetic structure and adaptation ability of the cell are also important in injury. For example, striated skeletal muscle in the leg can tolerate 2 to 3 hours of ischemia. On the other hand, the heart muscle cell can last 20-30 minutes and the neuron can last 2-3 minutes.

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CAUSES OF CELL DAMAGE

1- Oxygen Deficiency

Hypoxia and anoxia

Oxygen Losses: Hypoxia, is the most important and common cause of cell damage and death.

Ischemia the most important cause of hypoxia

- Ischemia is the loss of circulating blood that occurs when the arterial flow to tissues is blocked or venous return is reduced.

(Heart failure, vascular damage; viral, bacterial, parasitic diseases, immunological, atherosclerosis, arteriosclerosis and so on.)

- Asphyxia (difficulty breathing / respiratory failure), cell injuries may occur due to decreased oxygenation of the blood.
- Anemia (the decrease in the oxygen-carrying capacity of the blood) seen in anemia or carbon monoxide poisoning.

2- Chemical agents, poisons and drugs

Even when sugar and salt are concentrated sufficiently, they will alter the osmotic environment, leading to cell injury and death.

- Toxins, drugs by blocking or stimulating cell membrane receptors
- By affecting specific enzymes
- Forming toxic free radicals
- Distorting permeability

If we group the toxins;

A) Chemical toxins; acid, alkali, insecticides (pesticides) etc, directly or systemically effective

B) Animal and plant toxins; snake, bee, scorpion venom, hemlock, yew tree, maggot, white snake root, beautiful avladonna (atropa belladonna) etc,

C) Pathogen m.o. Toxins; anthrax bacilli, clostridium bacterial toxins etc, mycotoxins (aflatoxin, fusarium)

D) Endotoxins; autointoxication products, metabolites released in the body in common necrosis, free oxygen radicals and so on.

3- Physical and thermal factors

Trauma

Disintegration of tissues and cells, blood flow interruption

Extreme heat and cold

Pressure

Radiation

Formation of free radicals, ionization of intracellular water

Electricity

Denaturation of high heat formation tissues

4-Infectious agents

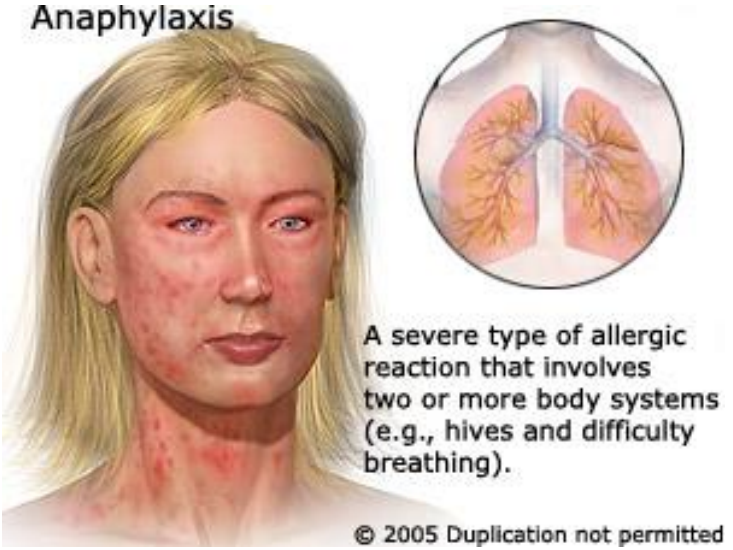
Viruses
Intracellularly damages the host's genetic material, the cells become the target of lymphocytes or drift into apoptosis (cell suicide).

Bacteria
Damages toxins, replicates in cells, initiates acute inflammation with chemotaxis

Parasites
Protozoa, intracellular
Metazoon, traumatic effect on tissues, inflammation

Fungus
It settles in tissues and causes chronic destruction.
They release toxins.

5-Immunological reactions



Autoimmune diseases

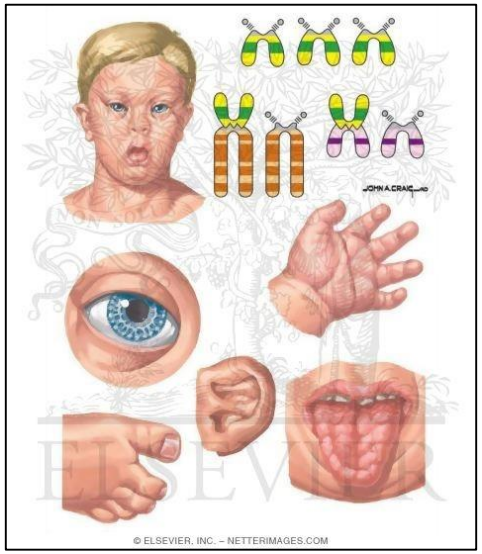
Detection of immune complexes in tissues by autoimmune reactions

Arthus reaction, Lupus disease, Hashimoto thyroiditis etc.

Hypersensitivity reactions to foreign proteins

Hay fever, Anaphylactic shock

6- Genetic disorders



- The mutation is not directly damaging

- The mutation-induced change in cell genetics, for example, the failure to synthesize a critically functional protein, is a damaging factor.

Hemophilia disease, Combined immunodeficiency, lysosomal storage diseases

7-Nutritional deficiency or imbalance

- ✓Inadequate intake of vitamin mineral proteins
- ✓Presence of pathologies preventing the use of vitamin minerals by the organism
- ✓One-way nutrition

Vitamin E deficiency - Encephalopathy
Vitamin C deficiency - Scurvy
Excess carbohydrate and fat - diabetes, obesity

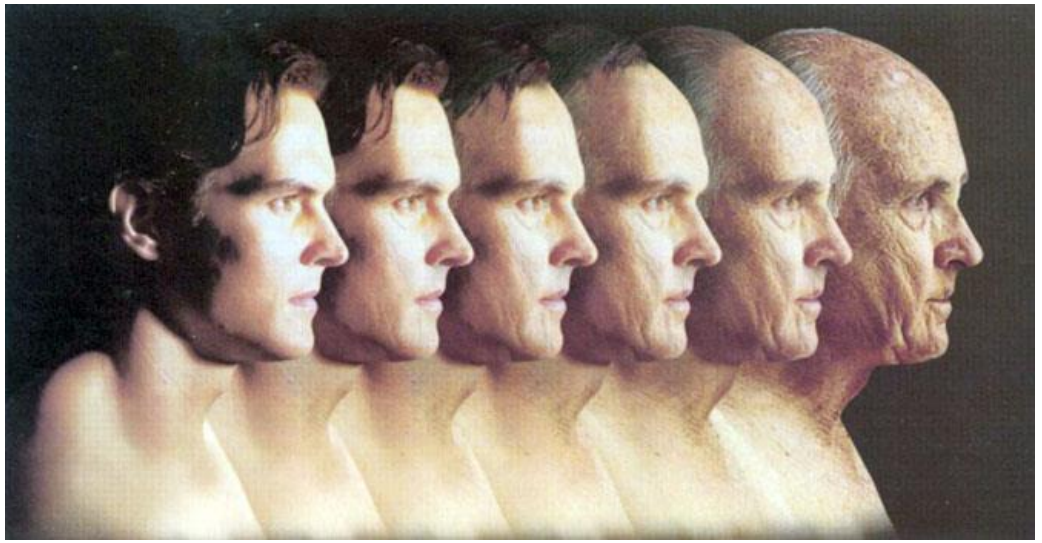
8-Lack of function or excess

Excessive work in muscles
(Myoglobinuria-nephrosis)

Loss of neural stimulation - atrophy and destruction of muscle cells

9-Aging

- Enzyme synthesis and progressive reduction of oxidative phosphorylation
- They are more easily affected by damaging factors than young cells

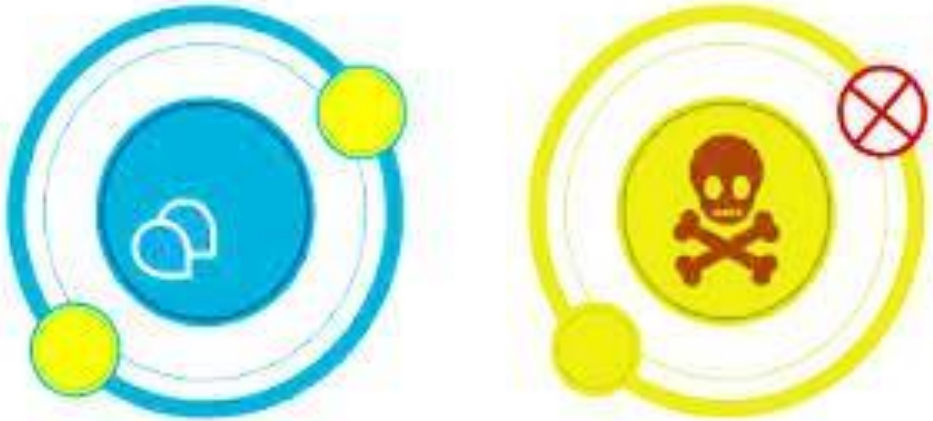


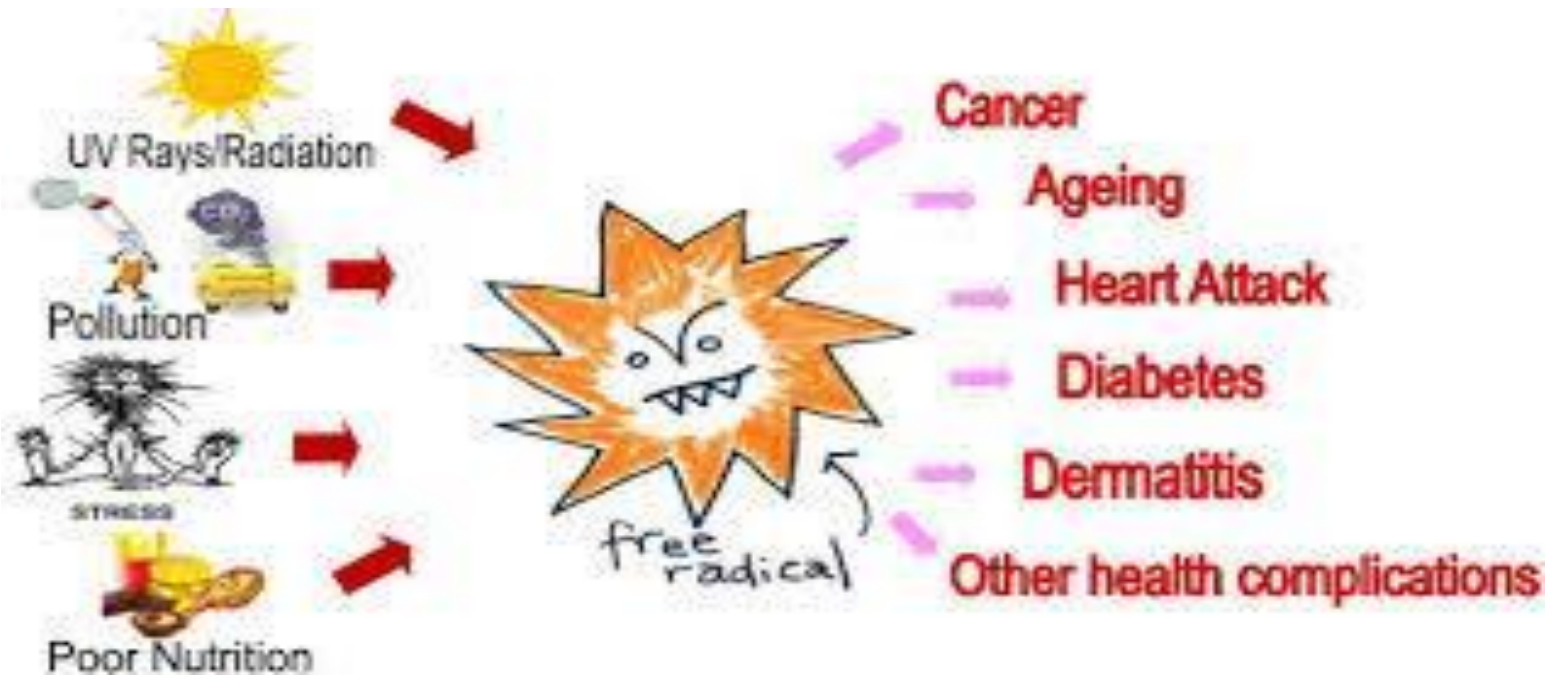
10-Free radicals

Oxygen-derived metabolites:

Superoxide anions,
Hydrogen peroxide,
Hydroxyl radical, Hypochloric acid, Chloramines, Nitrogen dioxide,
Ozone, lipid peroxides, etc.

-In the cell by mitochondrial respiratory chain
-It is formed by phagocytes outside the cell.


Healthy Atom
Free Radical


UV Rays/Radiation
Pollution
STRESS
Poor Nutrition
free radical
Cancer
Ageing
Heart Attack
Diabetes
Dermatitis
Other health complications

CELL ACCUMULATION

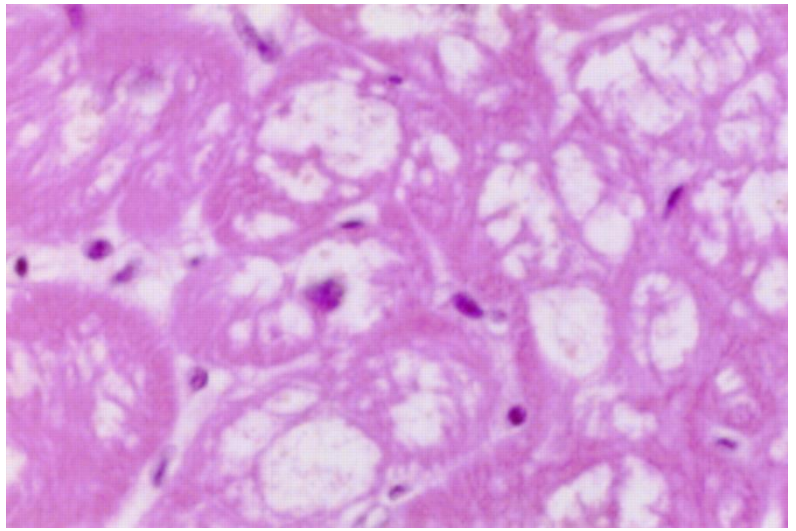
The first step of cell injury;

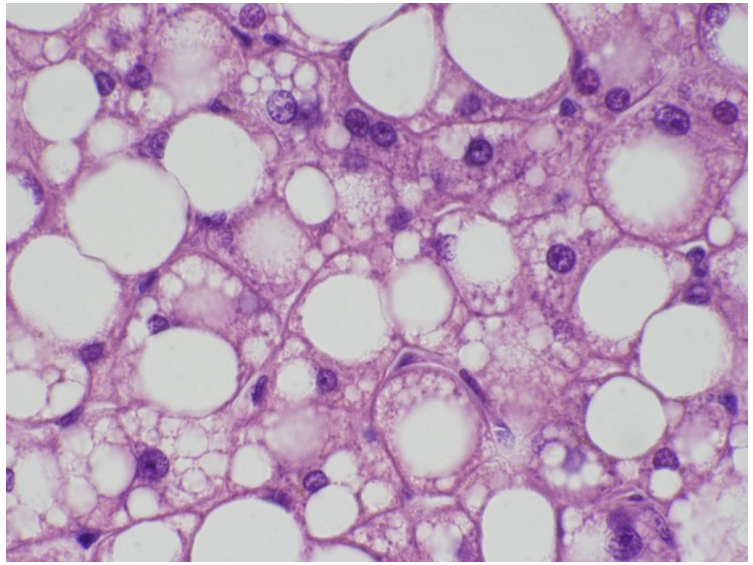
-Disruption of intracellular metabolism
-Swelling of the cell

-Accumulation of substances that are not present in the cell or that are very rare.
It can be reversible, when the causes disappear, the cells can return to their normal functions.
It takes different names according to the nature of the accumulated substance or morphological changes in the cell.

Cell Accumulation Types

1. Acute cell swelling- Parenchyma Degeneration
2. Hydropic Degeneration
3. Vacuolar Degeneration
4. Fat Degeneration,
5. Amyloid Degeneration
6. Hyaline Degeneration
7. Mucoid Degeneration
8. Fibrinoid Degeneration





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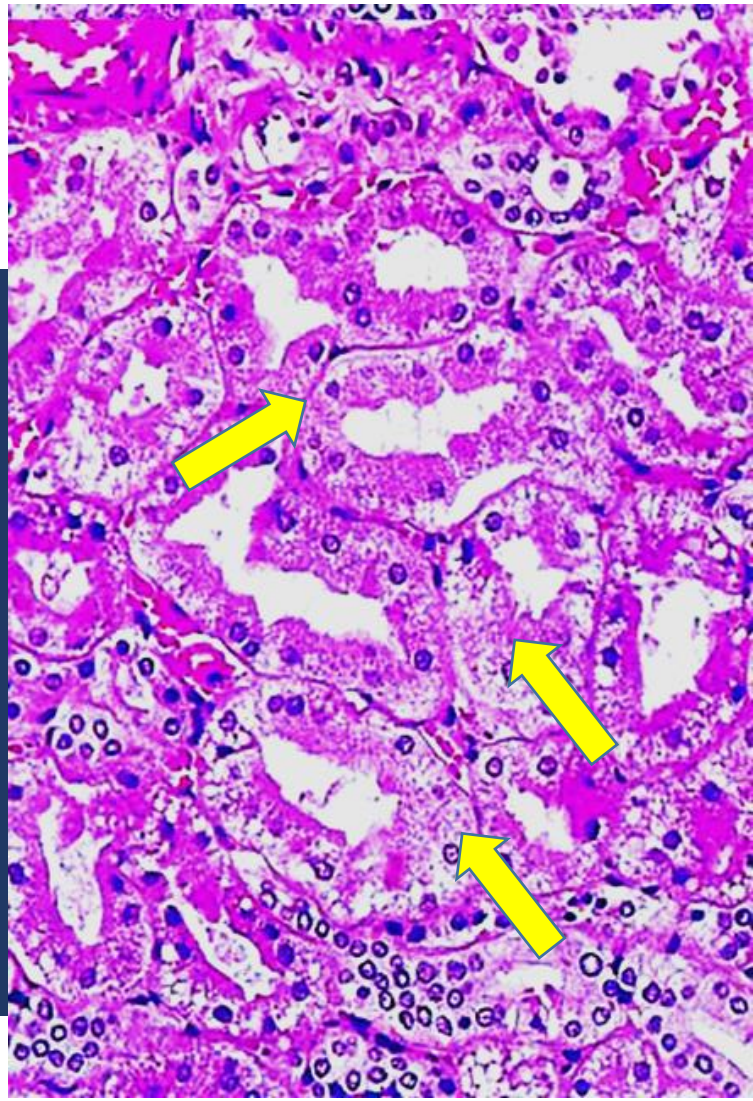
ACUTE CELL SWELLİNG

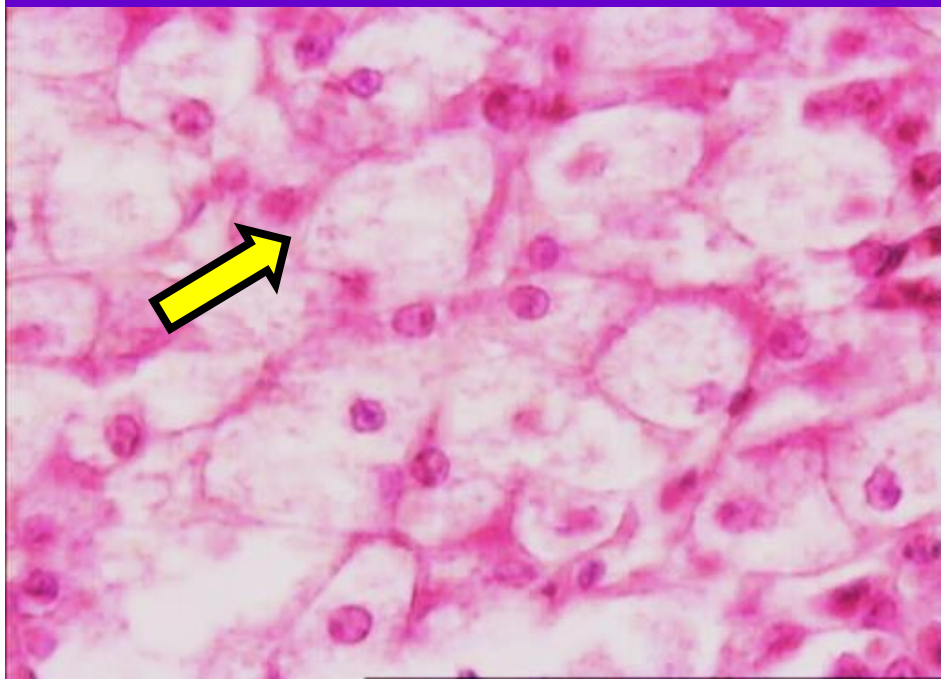
- It is the swelling of the cell by taking in water.
- It can occur due to toxic, metabolic, hypoxia, mechanical and infectious reasons.
- It is usually seen in parenchymal cells of organs with high metabolism such as liver, kidney and brain.
- Return back when the cause is removed



Hydropic and Vacuolar Degeneration

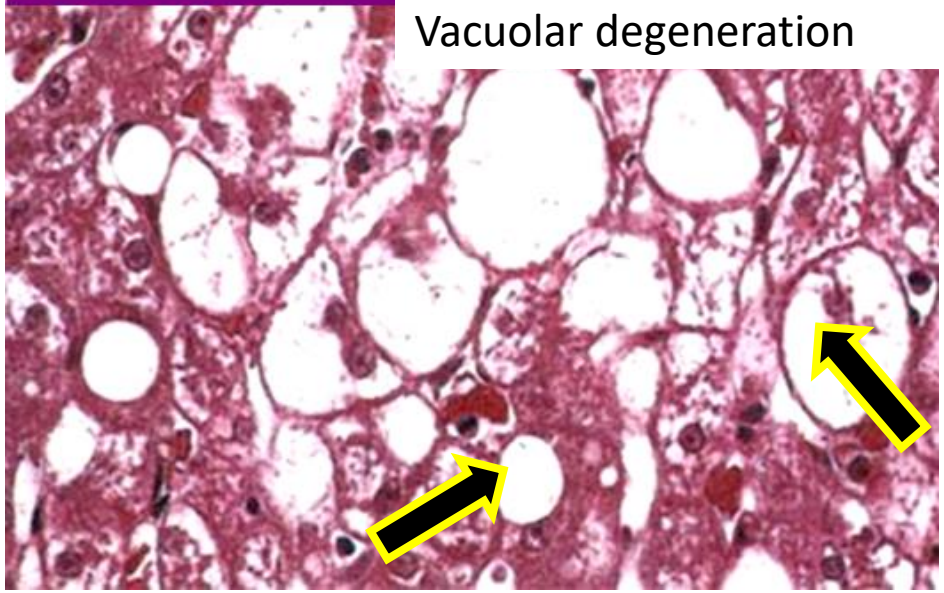
- They are more severe forms of acute cell swelling.
- In hydropic degeneration, there is an excess of fluid in the cytoplasm of the cell and diffuses throughout the cytoplasm.
- In vacuolar degeneration, it is in the form of vacuoles.

Hydropic degeneration.



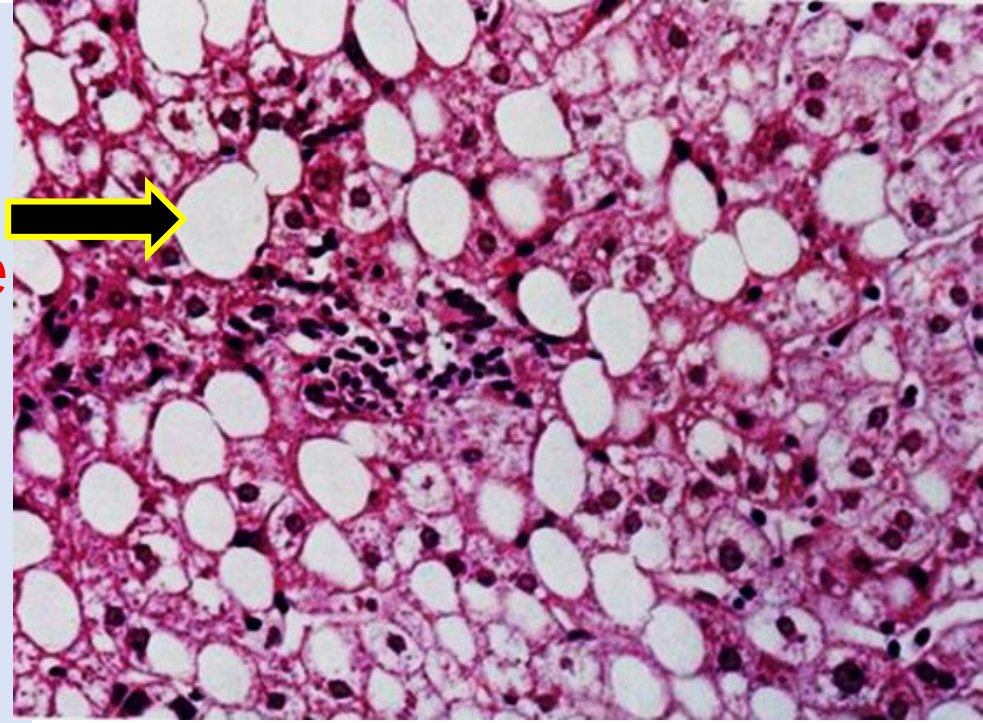
Vakuoler dejenerasyon

Vacuolar degeneration



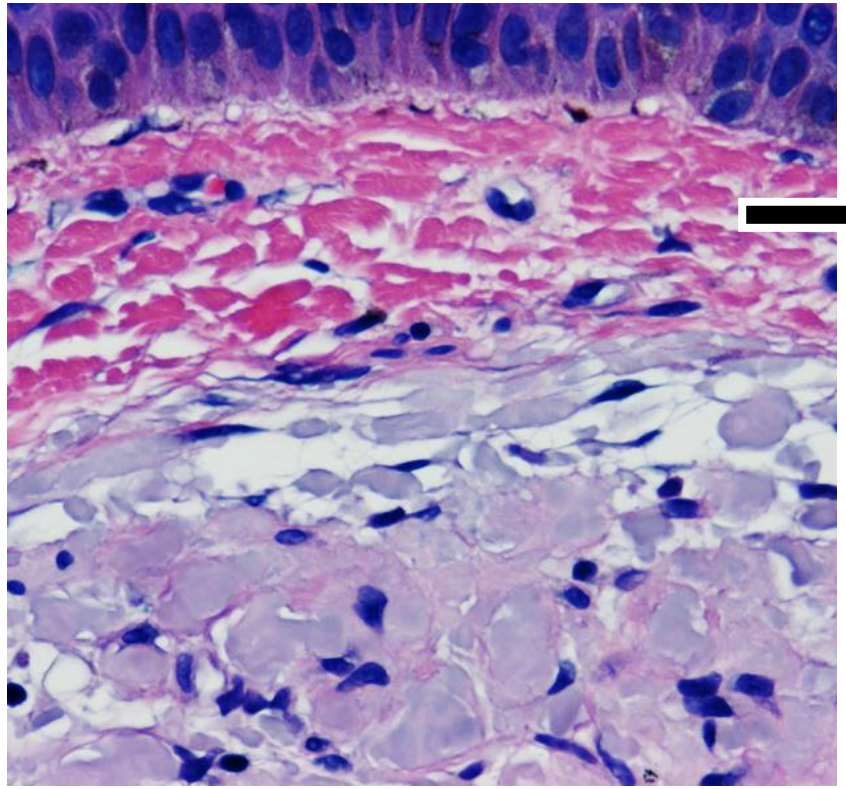
FAT DEGENERATION

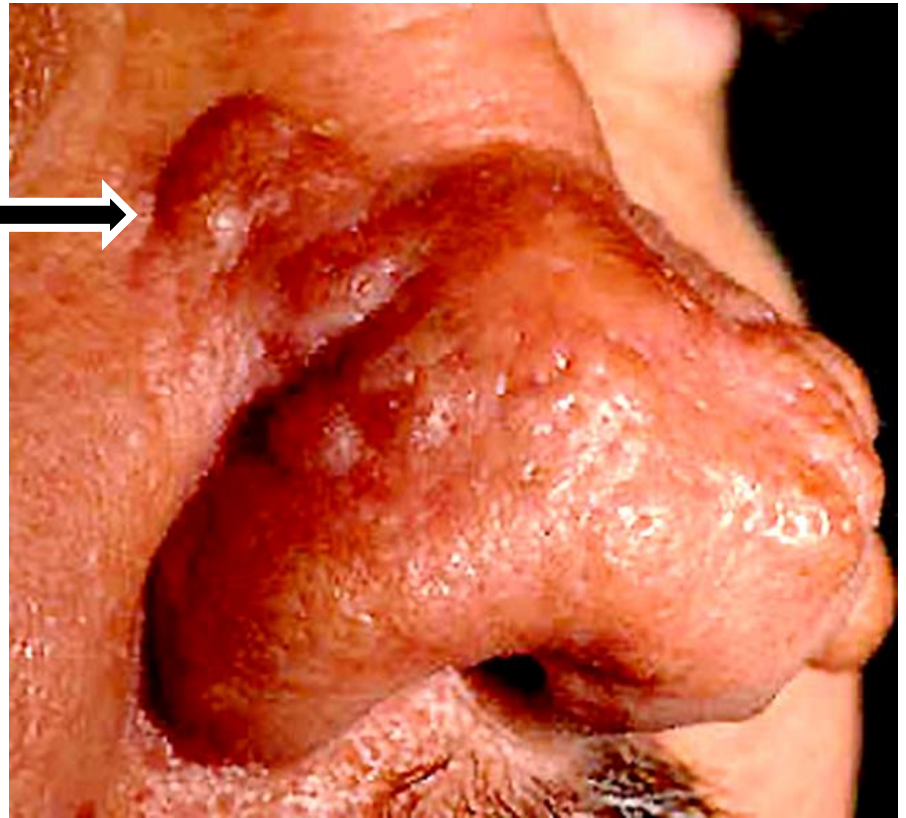
- It is the accumulation of neutral fats (triglycerides) in limited droplets in the cytoplasm of parenchymal cells.
- It is the infiltration of lipocytes (fat cells) into the interstitial tissue of organs that do not normally contain adipose tissue.
- It is shaped as a result of excessive intake of fatty and carbohydrate foods and insufficiency in body movements.
- This condition, which is usually associated with obesity, is encountered in organs such as the heart and pancreas.



AMILOIDOSIS

- The accumulation of amyloid material in tissues is called **amyloidosis.**
- Amyloid is an abnormal protein that accumulates extracellularly.

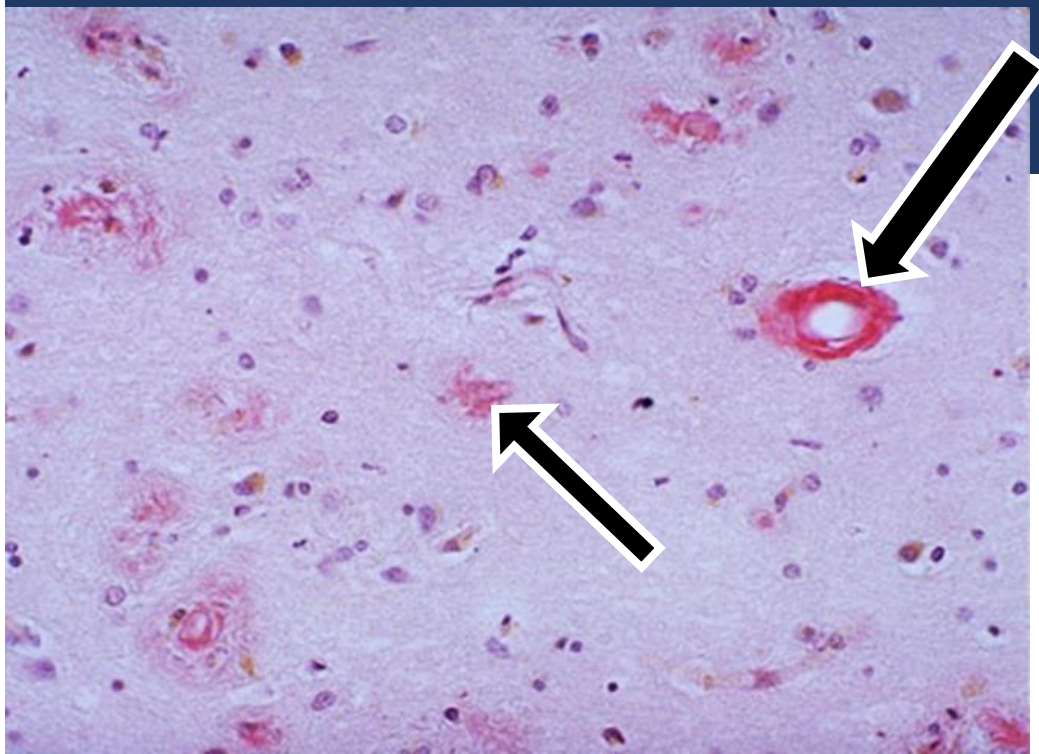




- Amyloid substance can accumulate in various organs.
- Amyloid accumulates mostly in the kidney, spleen, liver and adren.

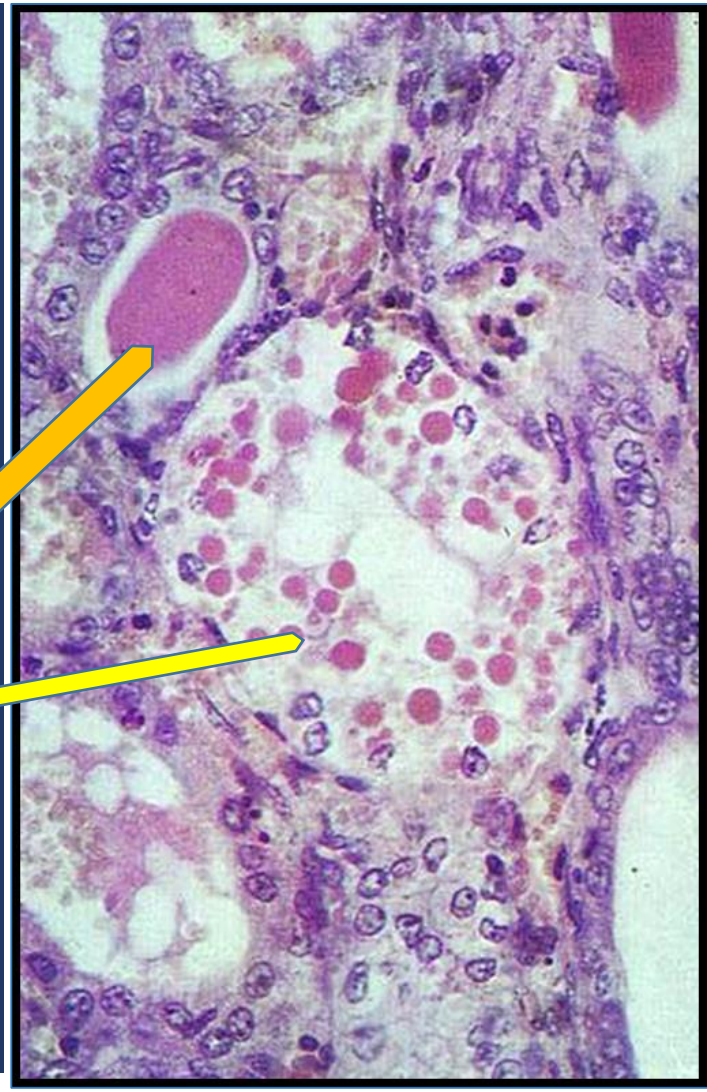
Senile amyloid

It is the name given to amyloid deposits around degenerated neurons and vessels in the cerebral cortex of older people.These deposits, called senile (neuritic) plaques, are the first sign of Alzheimer's disease in humans.



Hyaline Degeneration

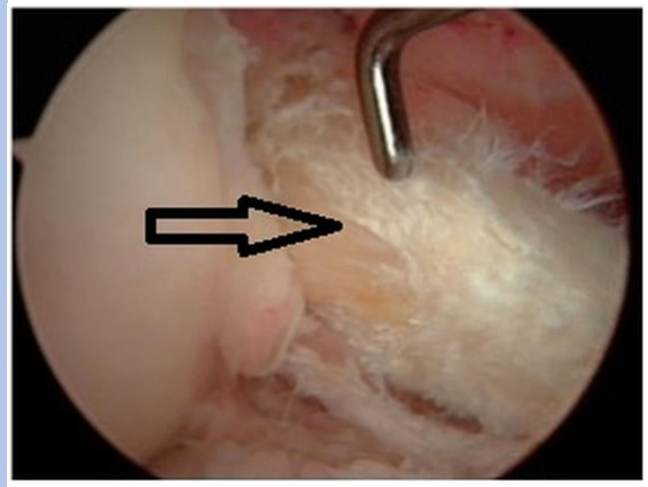
- **Hyaline** means glassy and is used to describe homogeneous, pink-colored material under the microscope.
- Hyaline is not a substance, it is the name given to the image.
- In kidney diseases, proteins that pass the glomerular filter (albuminuria) are seen in the renal tubulus lumens and epithelial cytoplasm homogeneously, pink in color.
- The striated muscles undergoing hyaline degeneration are pale in color and have the appearance of fish flesh.



MUCOID DEGENERATION

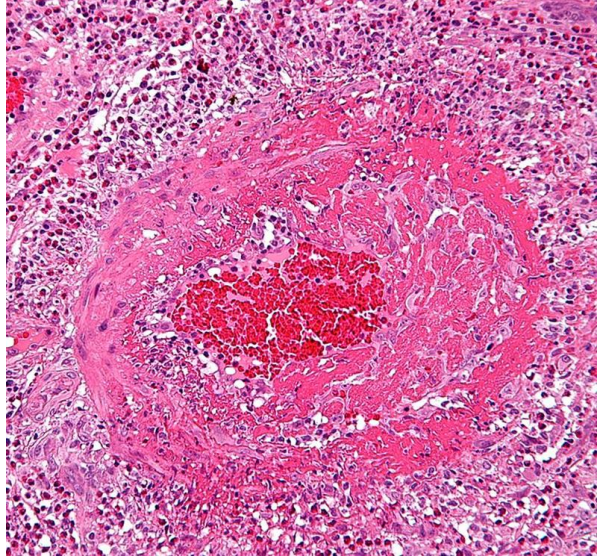
It consists of a mixture of mucin, glycoprotein and mucoprotein. It is of two types, epithelial and connective tissue origin.

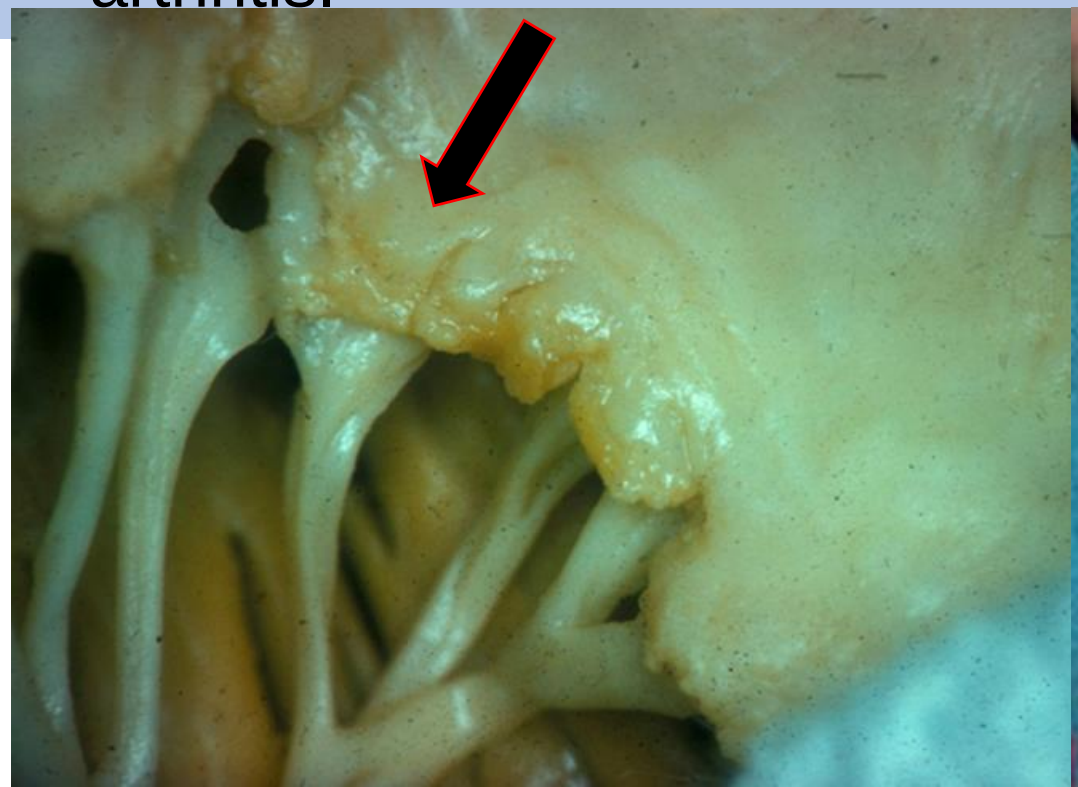
- **Epithelial mucin** is produced in the mucous membranes. It increases in rhinitis, enteritis.
- **Mucin** increase in connective tissue is seen in starvation, inflammation and connective tissue tumors (myxoma).
- **Mucoid degeneration** is the accumulation of mucin between cells, especially in connective and muscle tissue, and occurs in the absence of proteins.
- It is an important disorder following starvation events and is seen following starvation events in nutritional deficiency.
- The tissues are translucent, gelatinous and mushy.

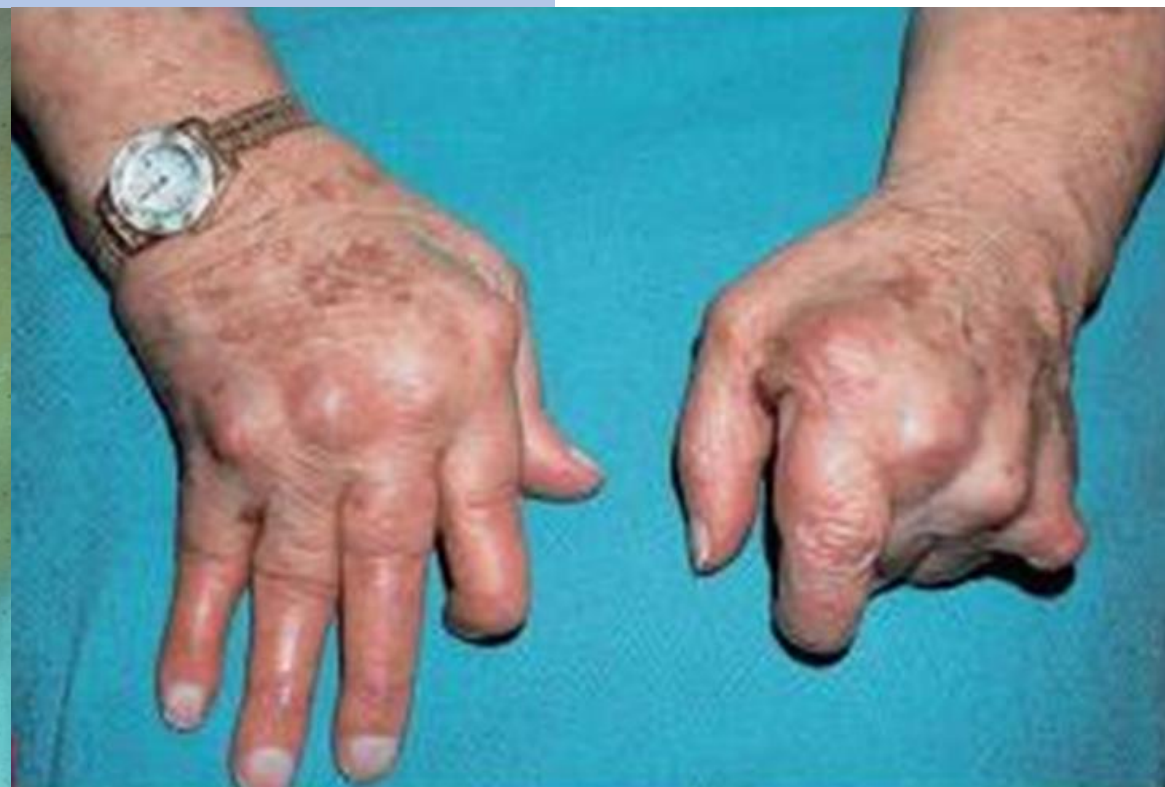


FIBRINOID DEGENERATION

- It is a degeneration characterized by the formation of fibrin in the walls of the vessels and in the connective tissue.
- Necrosis may occur in severe cases (fibrinoid necrosis) It is seen in humans around Aschoff nodules in cardiac rheumatism and rheumatoid arthritis.







Pigments

- They are colored substances with different chemical structures in the form of granules or crystals, dissolved in the tissues.
- They are either intracellular or intercellular (between cells) according to their location.
- Pigments are divided into two groups according to their origin: endogenous and exogenous.

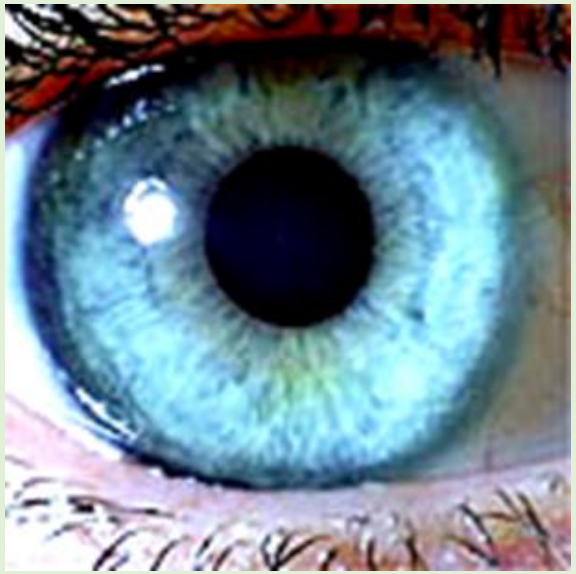
Endogenous pigments.

a. Hemoglobinogen pigments

Hemosiderin
Hematoidin
Formalin pigment
Pseudomelanin
Bile pigments
Hematoporphyrin
Malaria pigment

a. Anhemoglobinogen pigments

Melanin
Lipofuscin
Ceroid
Kloisonne kidney
Dubin-Johnson pigment

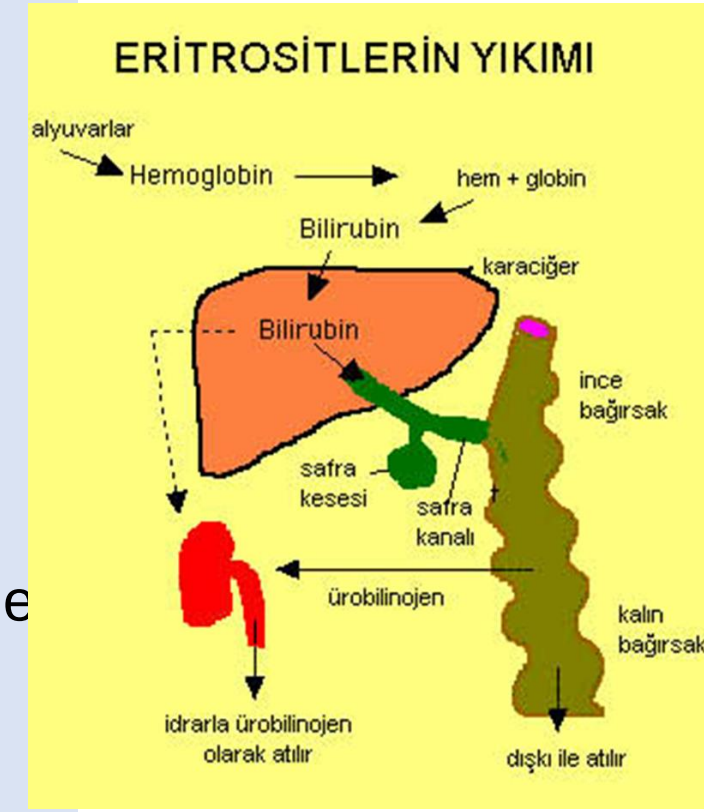


Exogenous pigments

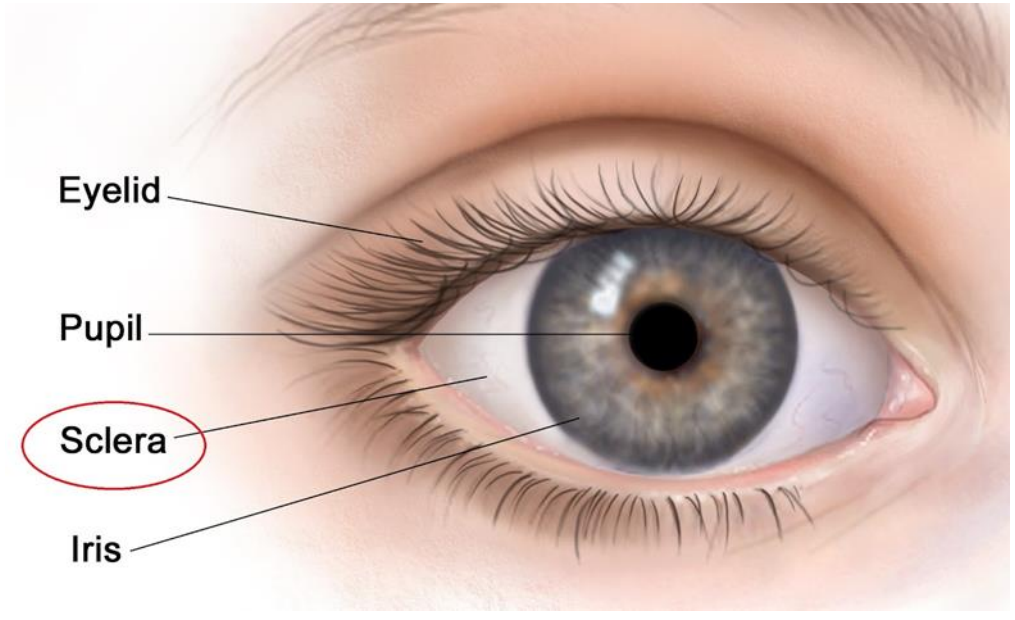
Anthracose
Siderosis
Silicosis
Asbestosis
Calomel
Argyrostattoos
Kaolin
Carotenoid pigments

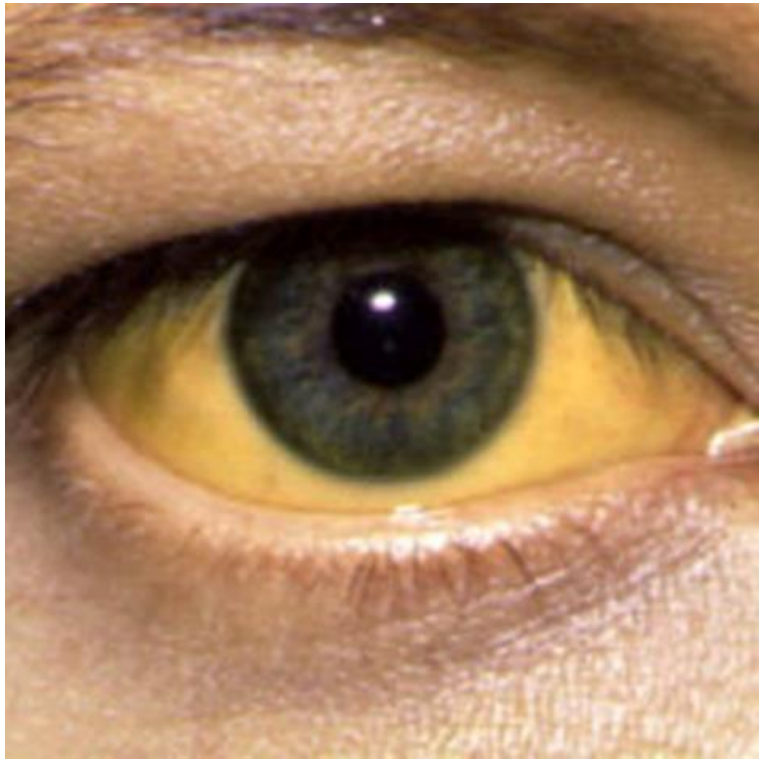
Bile pigments

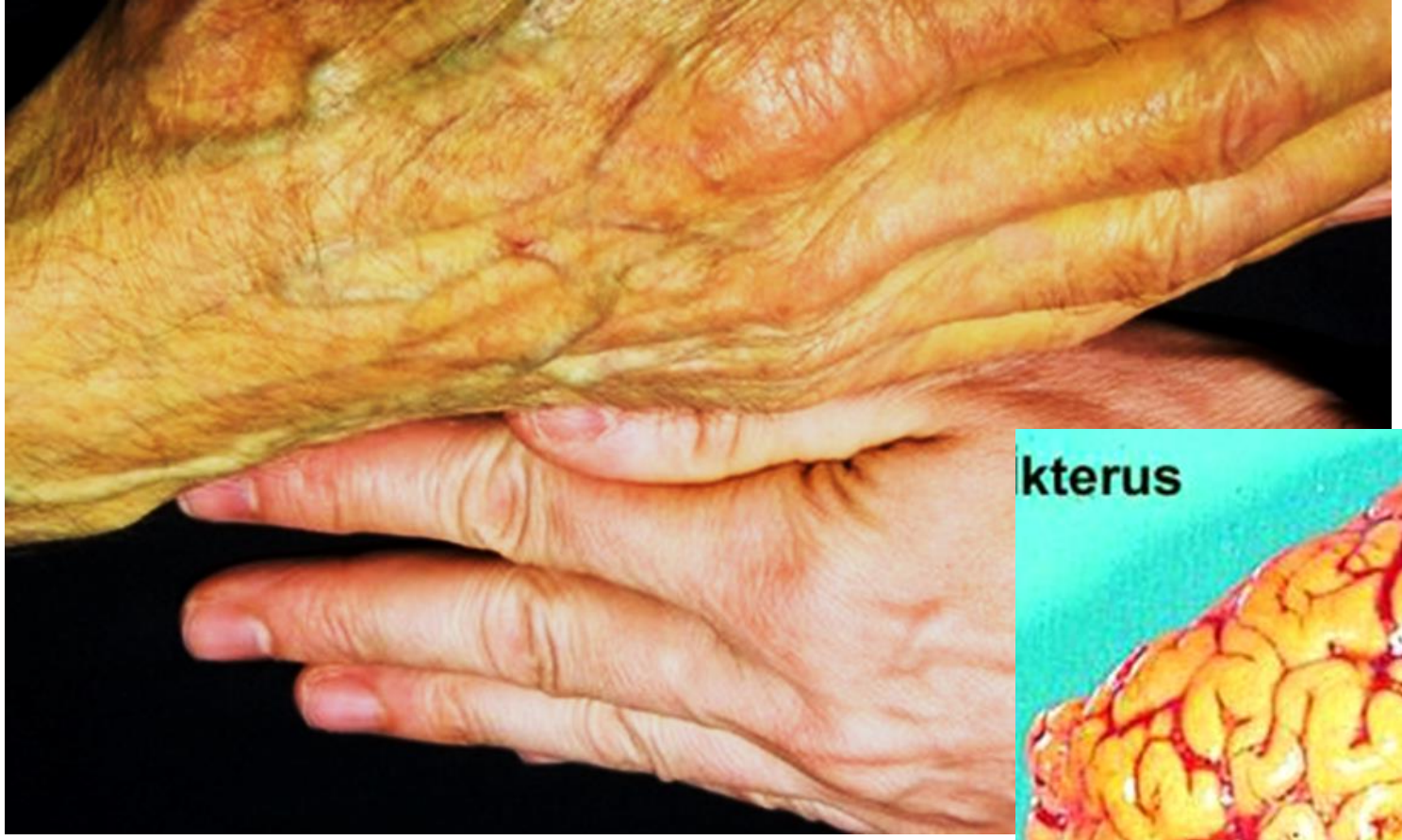
- Normally, erythrocytes are phagocytosed and hemolyzed by macrophages in the spleen, partly liver, lymph node and bone marrow.
- Hemoglobin is also degraded, forming hemosiderin and bilirubin I (not excreted in the urine).
- Bilirubin I is water soluble, so it goes out of the cell, while hemosiderin stays inside the cell.
- The bilirubin I, which comes to the liver through the blood, turns into bilirubin II (bile) by hepatocytes and flows into the gallbladder.
- Bile (bilirubin II), which is poured into the small intestine through the bile duct, is converted to urobilinogen by the bacteria there.
- Some of the urobilinogen is excreted in the feces, some of it is reabsorbed, passes to the liver, blood and kidney and is excreted in the urine.

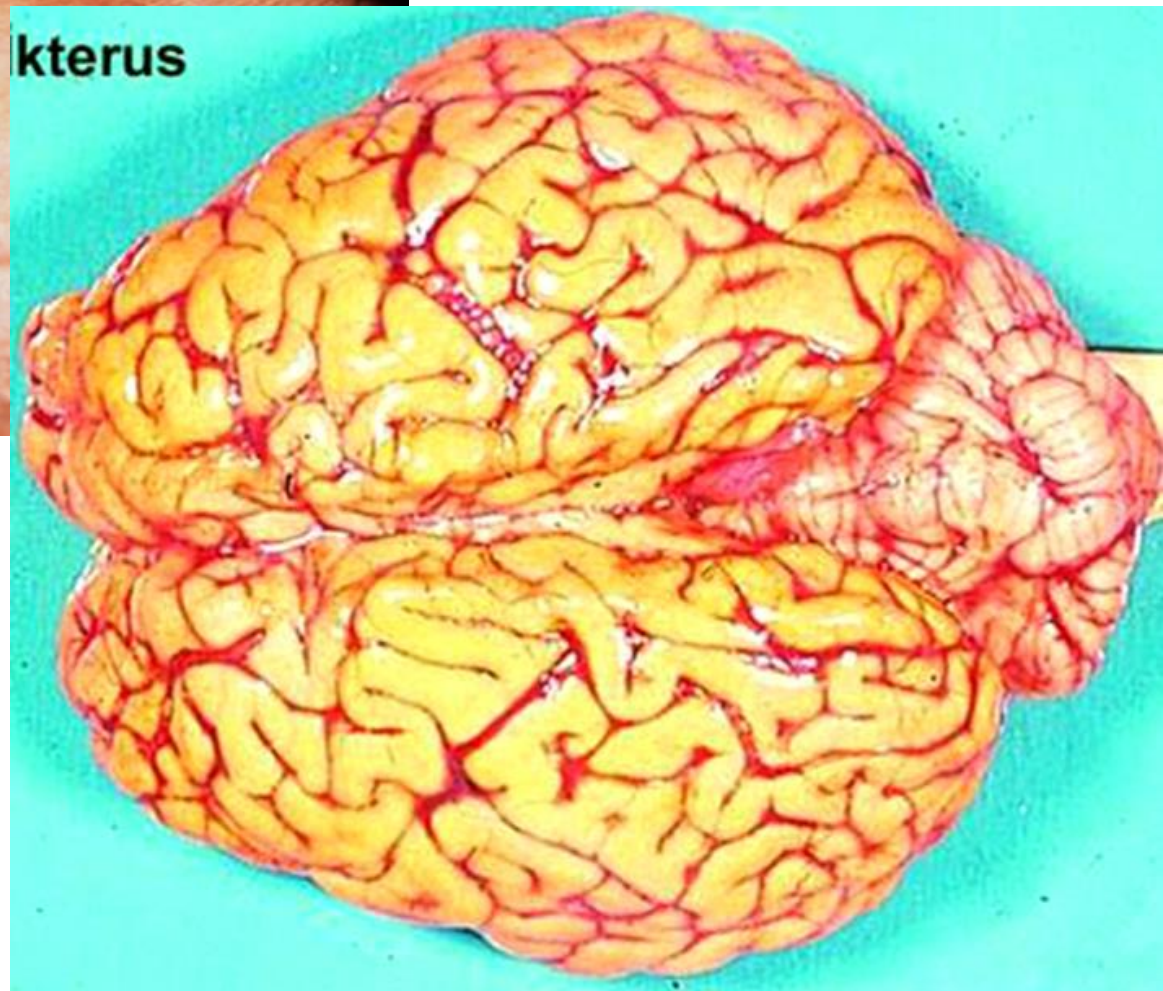


- A number of disorders occur in the organism in relation to the production and discharge of bile pigments.
- Cholemia to the mixing of the bile with the blood,
- The staining of tissues as a result of accumulation of bile pigments in the blood is called icterus (jaundice).
- It is most prominent in the sclera and conjunctiva of the eye, vaginal mucosa, omentum, intima of the aorta and adipose tissue.








kterus

Icterus (Jaundice) is examined in three groups;

a. Hemolytic (prehepatic, superfunction) icterus

As a result of excessive hemolysis and the liver cannot convert all of the released bilirubin I to bilibrubin II, bilirubin I accumulates in the blood and jaundice occurs.

b. Hepatotoxic (intrahepatic, retention) icterus

It is the icterus formed as a result of the destruction of hepatocytes. In this case, the liver cannot adequately convert bilirubin I and bilirubin I accumulates in the blood causes jaundice.

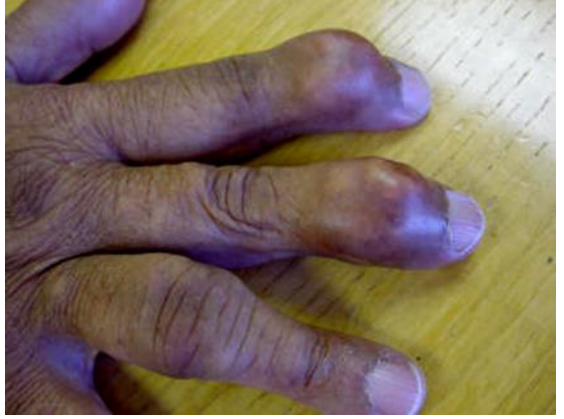
c. Obstruction (posthepatic, resorption) icterus

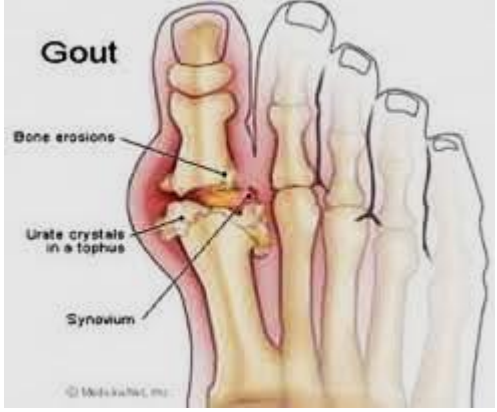
It is related to bile duct obstructions (gallstones, tumors), and it occurs when bilirubin II cannot be discharged to the gallbladder or intestines, as a result of which it accumulates in the liver or gallbladder and mixes with the blood.

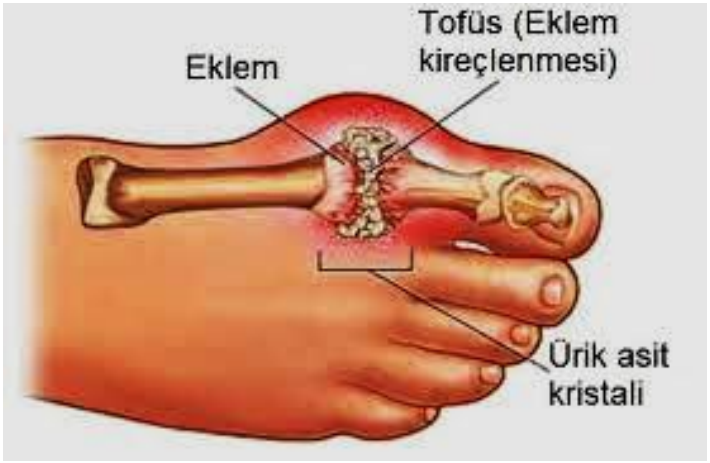
CRYSTALS

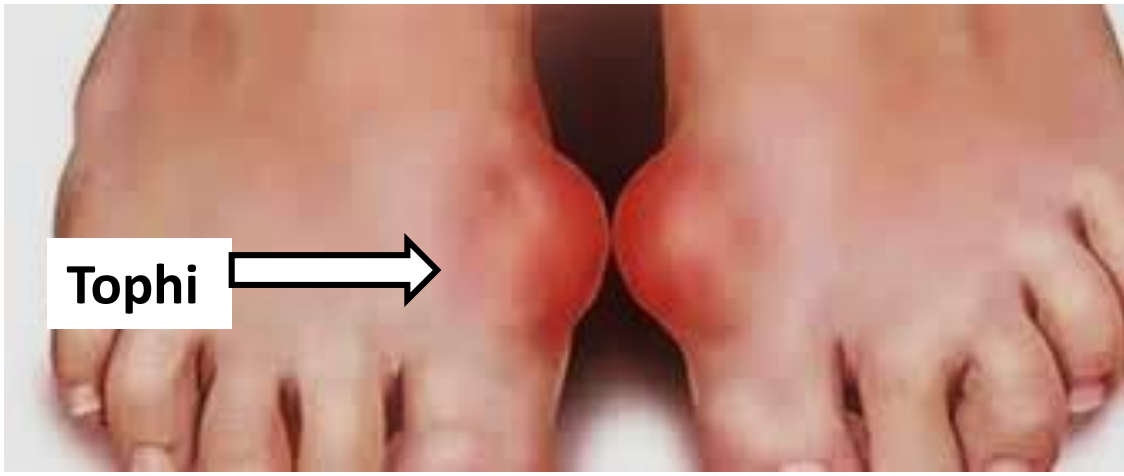
Uricosis (Gout-Drop Disease)

- It is the accumulation of uric acid or urate crystals in tissues.
- The reason is the inability to solubilize the uric acid related to the protein metabolism disorder.
- Diet rich in protein (meat, offal) and calcium) and Vit. In cases of A deficiency, it mostly occurs in the joints.
- Swellings/nodules formed by the accumulation of uric acid in gout are called tophi.



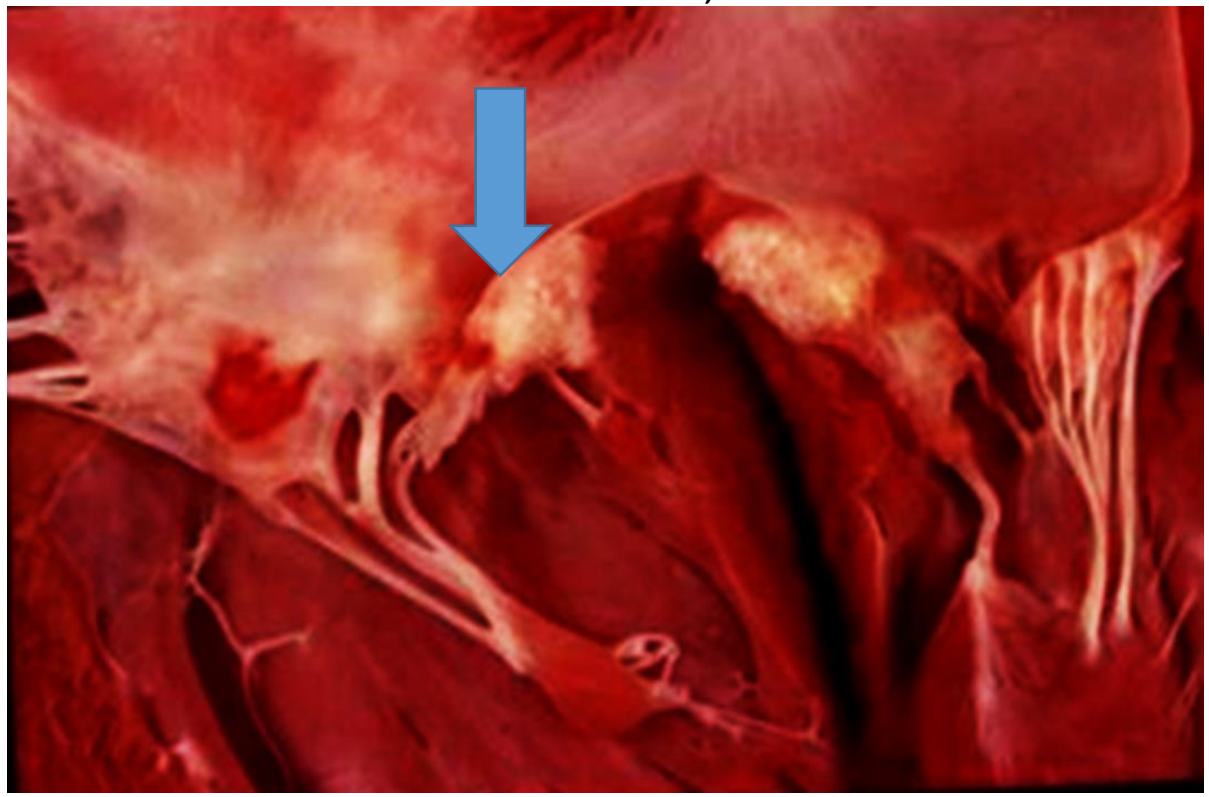




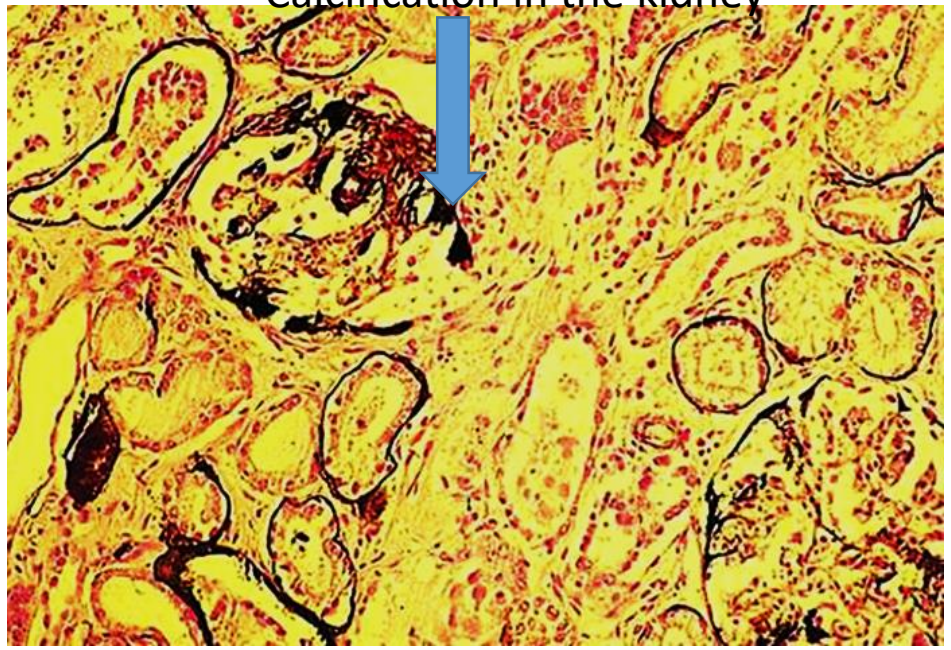


- Pathological Calcification
- It is the deposition of calcium salts in soft tissues.
- Calcium accumulates in tissues, usually in the form of calcium carbonate and calcium phosphate.

Endocardial calcification, Tuberculosis



Calcification in the kidney



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CELL DEATH

Two kinds of cell death:

-Necrosis

-Programmed cell death (apoptosis, cell suicide)

Necrosis (Irreversible Cell Damage)

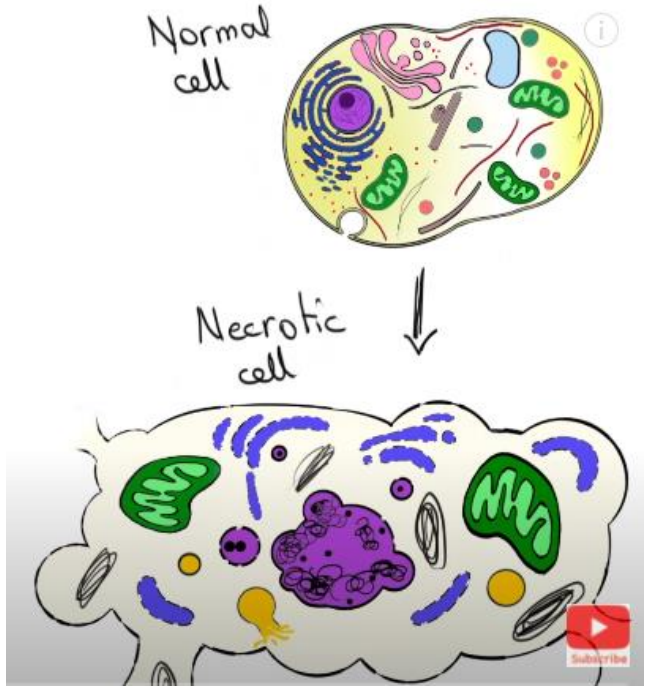
Teretorial death of cells in living organism = necrosis

Necrosis; follows cell death and changes caused by enzymes (Irreversible)

Loss of function in the necrosis region

Two main events in necrosis;

- ✓ enzymatic digestion of cells
- ✓ protein denaturation



Enzymatic digestion

- Enzymatic digestion of a cell is defined as "autolysis" if it is caused by its own lysosomal enzymes. The cell digests itself.
- Digestion with hydrolytic enzymes derived from bacteria and leukocyte lysosomes that come to the environment is called "heterolysis". The cell becomes necrotic with the external enzymatic effect.

Microscopic Properties of Necrotic Cells

First, the cytoplasm then changes in the nucleus.

Cytoplasmic changes:

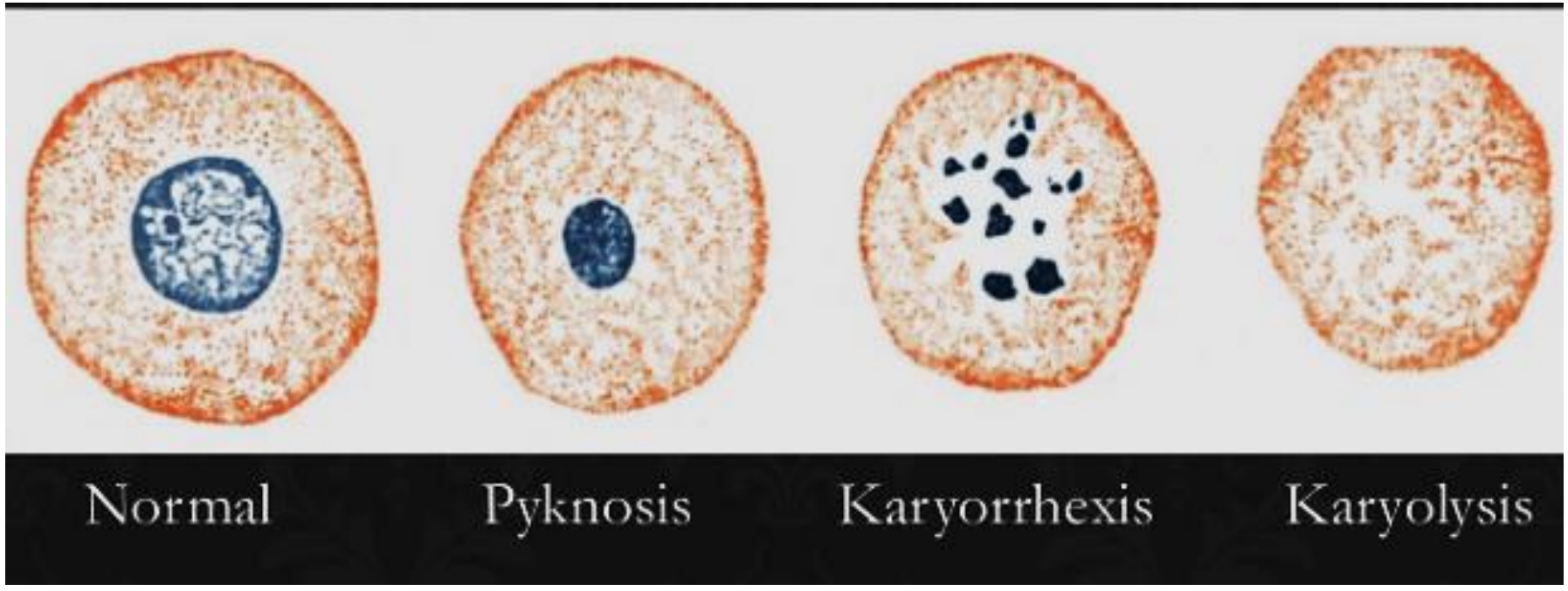
a. Depletion of glycogen in the cytoplasm
b. Eosinophilic staining of cytoplasm
c. Sitoplazmoliis
d. Advanced changes

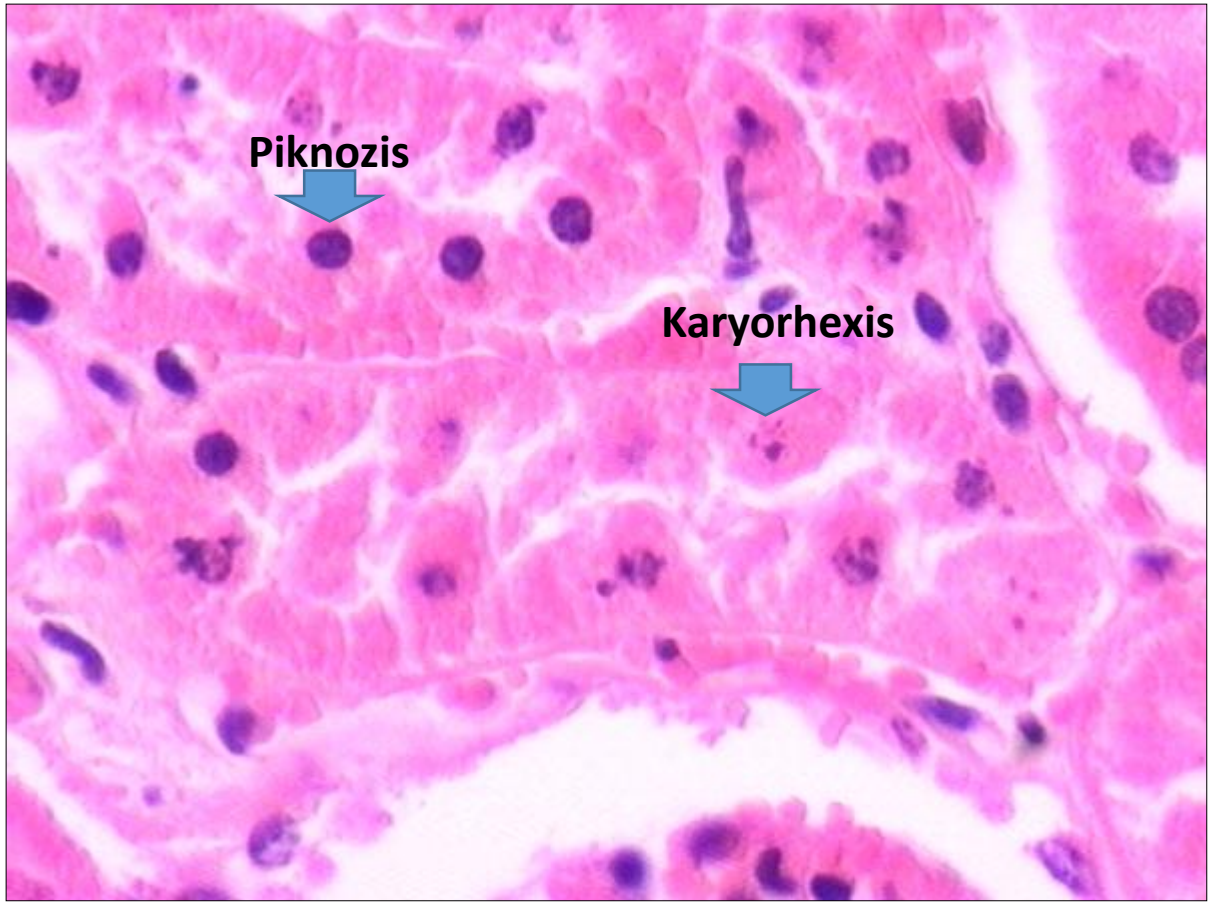
Changes in the nucleus

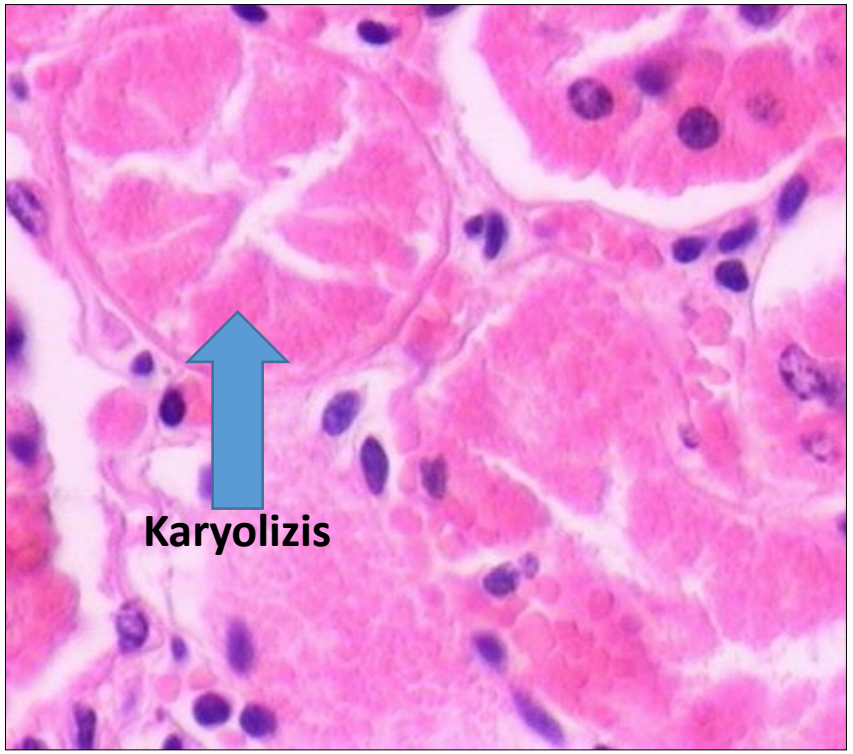
a. Piknozis: Shrinkage, size decreases, hyperchromatic, dark purple-black, breakdown of nucleic acids.

b. Karyorhexis: Tearing of the nuclear membrane, dispersing chromatin into granules to the cytoplasm.

c. Karyolizis: The melting of chormatine by nuclease, nucleus membrane completely disappears




Piknozis
Karyorhexis


Karyolizis

Apoptosis Programmed Cell Death

Elimination of unwanted cells that occur by activating a series of events in which the gene products are regulated internally under coordination

This event is programmed cell death or physiological cell death

The cells that make up the organism are born, live for a certain time and then die. The life span of these cells varies according to the type of cell.

For example, intestinal cells die after 3-5 days of life, whereas epidermal cells of the skin die after 20-25 days.

Myocardial cells or neurons live for life.
We lose 10-15% of them with aging.

For any other reason (viral effect, environmental effect, etc.), in the cells whose DNA is damaged, they kill themselves to prevent damage to the organism and do this for the benefit of the organism.

Apoptosis occurs continuously in some tissues and cells of the organism and continues for life.

Thus, death (apoptosis) and reconstruction (mitosis) continue in equilibrium to provide homeostasis in these tissues.

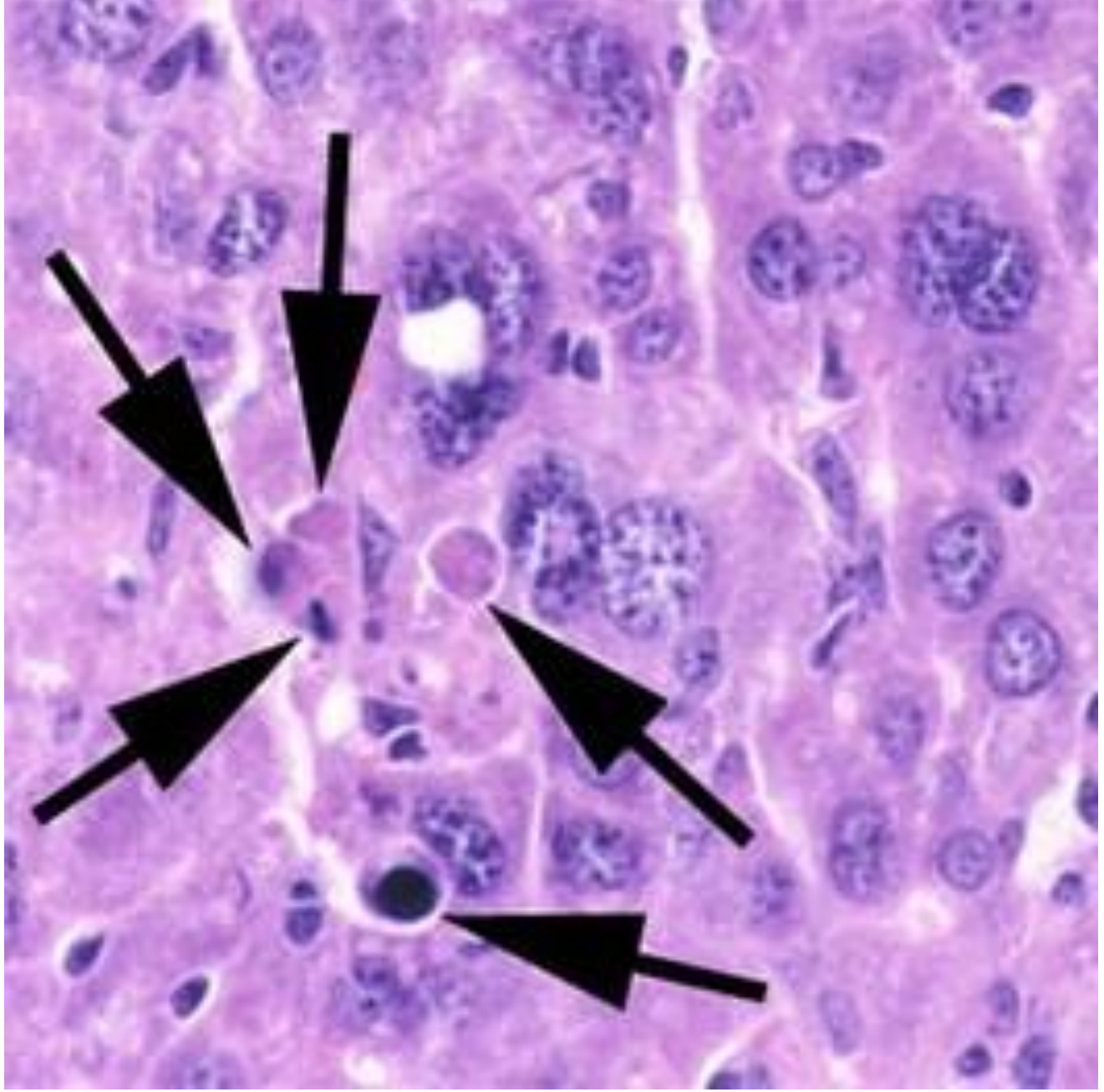
Apoptosis differs from necrosis, the classic form of cell death, in many aspects:

- 1-Reasons are different.
- 2-Cell membrane integrity is impaired in necrosis. In apoptosis, membrane integrity is not impaired, but there are blebs on the membrane
- 3-There is chromatin condensation in necrosis. In apoptosis, chromatin accumulates around the nucleolus membrane and condenses

4-In the necrosis organelles are completely disrupted. No disruption of organelles in apoptosis

5- There are large vacuoles in necrosis. Apoptosis has apoptotic bodies covered with membrane containing intact organelles and core fragments.

6-In necrosis, the cell bound to lysosomal enzymes lyses. In apoptosis, the cell does not dissolve, apoptotic bodies are formed and are phagosized by the surrounding cells.



7-In necrosis cells die in groups, in apoptosis cells die individually or in small groups.

8-Necrosis occurs as a result of pathological effects, Apoptosis also occurs due to physiological reasons.

9-Necrosis cells are inflamed around. No inflammatory changes occur around the apoptotic cells.

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