

Doctor 2021 - رَوَّح - medicine - MU



pathology sheet

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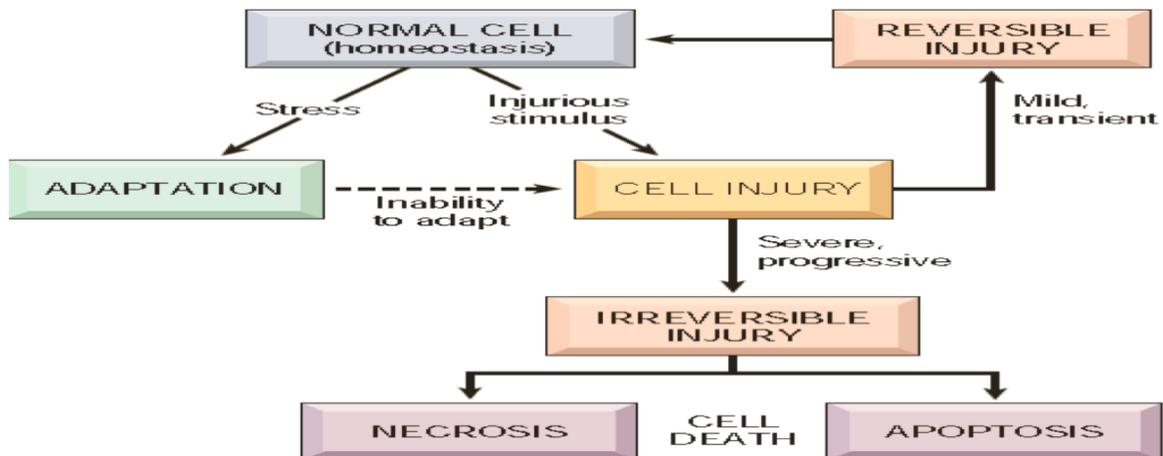
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Amatulshafi

Question) A 70 year old male patient who present with viral infections the (H&E) for his lung biopsy cellular fragmntion ,What is the action done by the cell will be ?Activation of BH3 only protein sensore(apoptosis)

Viral infection + cellular fragmentation = apoptosis (two key words for the question) but she could never mention (bacterial+cellular fragmentation)



المطب الجراحة Adaptations

- **Reversible** changes in the number, size, phenotype, metabolic activity, or functions of cells in response to changes in their environment.
 - Can be physiologic or pathologic.
 - **Physiologic**: responses of cells to normal (1) stimulation by hormones or endogenous chemical mediators. (Breast & uterus during pregnancy) or to the (2) demands of mechanical stress (bones and muscles).
 - **Pathologic**: responses to stress that allow cells to modulate their structure & function, thus escape injury, but at the expense of normal function. (squamous metaplasia of bronchial epithelium in smokers)

*Note :

some viral infections could be associated Apoptosis : Irreversible _____
(sever /progressive/abrupt) Reversible _____ (Mild/transient
/temporary)

*** Note:**

Smoking and chemical agents works in the field of cancer >>>>start from oral mucosa & end alveoli

***Note:**

Mouth

outside:- keratinized stratified squamous epithelial

Inside:- non keratinized stratified squamous epithelium

Trachea:-

From the top squamous epithelium

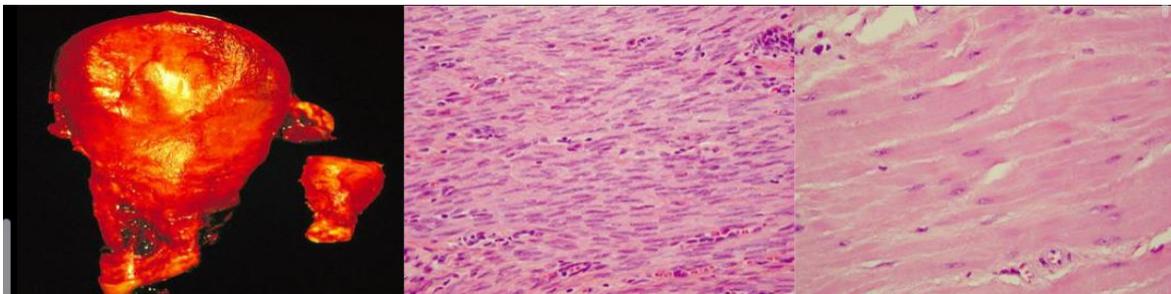
From the bottom Respiratory epithelium

***Note:**

In the case of smoking, trachea it will turn into squamous epithelium because of squamous more powerful(strong) (The tissue will try to change to another type to adapt)

1. Hypertrophy

- Hypertrophy is an increase in the size of cells resulting in an increase in the size of the organ.
- Hypertrophy & hyperplasia also can occur together.
- Hyperplasia happens in cells capable of replication, whereas hypertrophy occurs when cells have a limited capacity to divide.
- In pure hypertrophy there are no new cells, just bigger cells with increased amounts of structural proteins & organelles.
- Hypertrophy can be physiologic or pathologic



Question) What's the type of cell who can't divide AKA can only do hypertrophy ? Answer: heart cells (hypertrophy is the only way it responds to new stress)

Note:- only cells that can divide will do both mechanism: (1)Hypertrophy (2) Hyperplasia

Note:- In general adaptation could be both (1) physiology (2) pathology

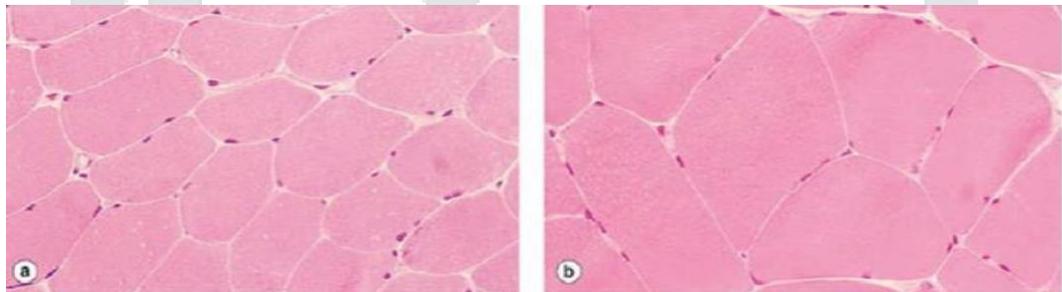
Hypertrophy – physiologic – stimulation

Notes for the first picture : the big uterus was taken after hysterectomy immediately after giving birth , while the tiny uterus was taken/excluded post-menopausal

The second pic : indicates cigaretted smooth muscle with no mitosis tap so it's a histological pic from the small uterus (no hypertrophy)

The third pic : indicates how the cells are so much wider and bigger now so it's taken from the big uterus (hypertrophy)

The massive enlargement of the uterus during pregnancy → a consequence of estrogen stimulated smooth muscle hypertrophy & smooth muscle hyperplasia.



Stevens et al: Core Pathology, 3rd Edition.
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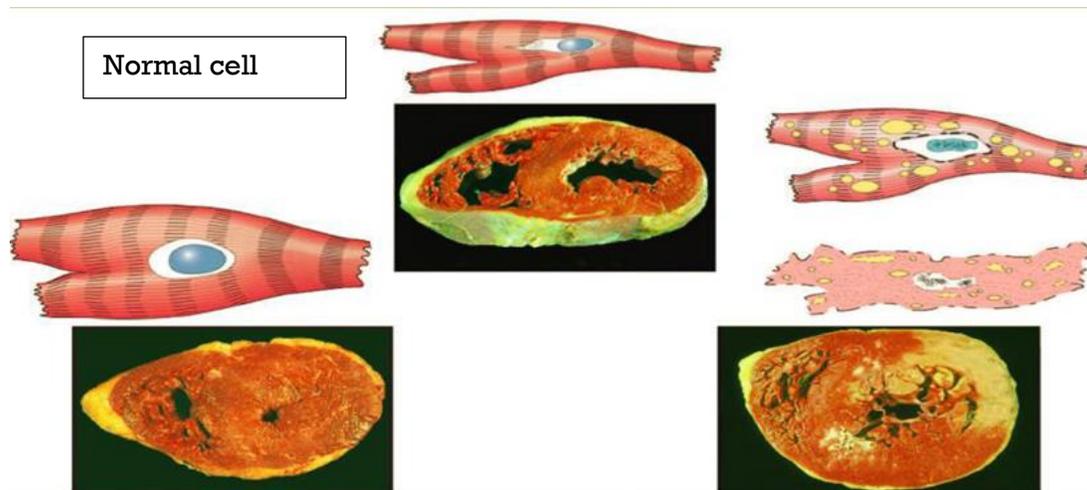
Hypertrophy – physiologic - ↑ demand

In response to increased workload the striated muscle cell undergo hypertrophy. **Adult muscle cells have a limited capacity to divide** → chiseled physique of weightlifter stems only from the hypertrophy.

Note:-The uterus is getting bigger because of the hormone estrogen (estrogen««««« « «uterine proliferation)

(progesterone««««« secretions)

Note: The uterus returns to its normal position due to (apoptosis)



Hypertrophy – pathologic - ↑ demand

Pic on the left? Increase thickness of the wall observation

Pic on the right ? Indication of emboli / fat (the yellow ones) that's also San observation of previous Myocardial infarction heart

In response to increased workload (hypertension or aortic valve disease) myocardial hypertrophy (lower left → to generate the required higher contractile force → heart undergo **only hypertrophy because cardiac muscles have a limited capacity to divide.**

The mechanisms driving cardiac hypertrophy involve two types of signals:

(1) mechanical triggers (e.g. stretch)

(2) soluble mediators that stimulate cell growth (growth factors & adrenergic hormones).

- stimuli → signal transduction pathways → the induction of a number of genes → stimulate synthesis of many cellular proteins (growth factors & structural proteins).

- The result is synthesis of more proteins & myofilaments per cell, which increases the force generated with each contraction, enabling the cell to meet increased work demands.

- Switch of contractile proteins from adult to fetal or neonatal forms. (α -myosin heavy chain is replaced by the fetal β -myosin heavy chain; which produces slower, more energetically economical contraction)

Note : either hypertrophy was pathological or physiological the reason is increase of the demand

Pathological case : if we found beta myosin heavy chain in adult (it's supposed to be in babies) and it was there for a long time in a massive amounts -> abnormal deposit / cells will die

What is the aim of hypertrophy? Compensate the demand but if it was prolonged it'll lead to irreversible injury

If the demand was prolonged – some cells die, some encounter dysplasia , some progress to cancer

An important point..

- An adaptation to stress such as hypertrophy can progress to functionally significant cell injury if the stress is not relieved:
- A limit is reached beyond which the enlargement of muscle mass can no longer compensate for the increased burden.
- In the heart, several degenerative changes occur in the myocardial fibers, the most important are fragmentation & loss of myofibrillar contractile elements, ultimately cardiac failure.

2. Hyperplasia

- **Hyperplasia is an increase in the number of cells in an organ that stems from increased proliferation, either of differentiated cells or, in some instances, less differentiated progenitor cells.**
- **Hyperplasia takes place if the tissue contains cell populations capable of replication.**
- **may occur concurrently with hypertrophy**
- **Hyperplasia can be physiologic or pathologic; in both situations, cellular proliferation is stimulated by growth factors that are produced by a variety of cell types.**

The two types of physiologic hyperplasia are

(1) **Hormonal** hyperplasia: the proliferation of the glandular epithelium of the female breast at puberty & during pregnancy.

(2) **Compensatory** hyperplasia: residual tissue grows after damage or resection of part of an organ. (part of a liver is resected → mitotic activity in the remaining cells begins as early as 12 hours later, eventually restoring the liver to its normal size.

• The stimuli here is polypeptide growth factors produced by uninjured hepatocyte and other nonparenchymal cells in the liver.

• After restoration of the liver mass, various growth inhibitors turn off cell proliferation.

Note:- 3 to 6 months it will have the normal size of the liver

Pathologic hyperplasia

- Caused by **excessive** hormonal or growth factor stimulation.
- E.g. **Normally**, after a normal menstrual period there is a burst of uterine epithelial proliferation (tightly regulated by the stimulatory effects of pituitary hormones and ovarian estrogen and the inhibitory effects of progesterone)

A **disturbance** in this balance → increased estrogenic stimulation → endometrial hyperplasia, (a common cause of abnormal menstrual bleeding).

- Benign prostatic hyperplasia is (hormonal stimulation by androgens)
- Certain viral infections (papillomaviruses cause skin warts & mucosal lesions - masses of hyperplastic epithelium)

An important point

The hyperplastic process remains controlled; if the signals that initiate it abate, the hyperplasia disappears.

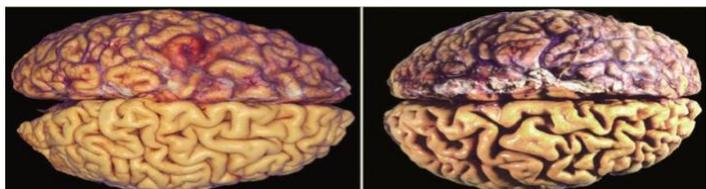


It is this responsiveness to normal regulatory control mechanisms that distinguishes pathologic hyperplasias from cancer (growth control mechanisms become permanently dysregulated or ineffective)

In many cases, pathologic hyperplasia constitutes a fertile soil in which cancers may eventually arise.**if the causative agent not removed**

3. Atrophy

- Atrophy is shrinkage in the size of cells by the loss of substance, at which survival is still possible.
- If a sufficient number of cells are involved, the entire tissue or organ is reduced in size (atrophic) .
- Atrophic cells may have diminished function, **they are not dead**.
- Causes of atrophy include a decreased workload (immobilization of a limb to permit healing of a fracture),loss of innervation, diminished blood supply, inadequate nutrition, loss of endocrine stimulation, & aging (senile atrophy). **Of aging she means that the 80 yrs old brain is so much smaller than a 20yrs old brain**
- Some of these stimuli are physiologic (the loss of hormone stimulation in menopause)& others are pathologic (denervation), but the fundamental cellular changes are similar.
- The process of cellular atrophy results from a combination of:
 - (1) **decreased protein synthesis**: reduced metabolic activity.
 - (2) **increased protein degradation**: occurs mainly by the ubiquitin proteasome pathway:
 - Nutrient deficiency and disuse may activate ubiquitin ligases, which attach multiple copies of the small peptide ubiquitin to cellular proteins and target them for degradation in proteasomes.
 - In many situations, atrophy also is associated with autophagy.



Atrophy – pathologic -↓ blood supply

82-year-old man with atherosclerotic disease. Atrophy of the brain is caused by aging & reduced blood supply. Note that loss of brain substance **narrows the gyri & widens the sulci**. The meninges have been stripped from the bottom half of each specimen to show the surface of the brain

4. Metaplasia

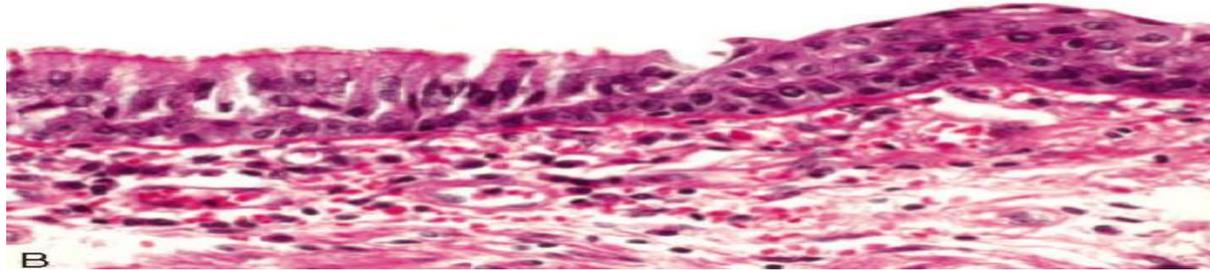
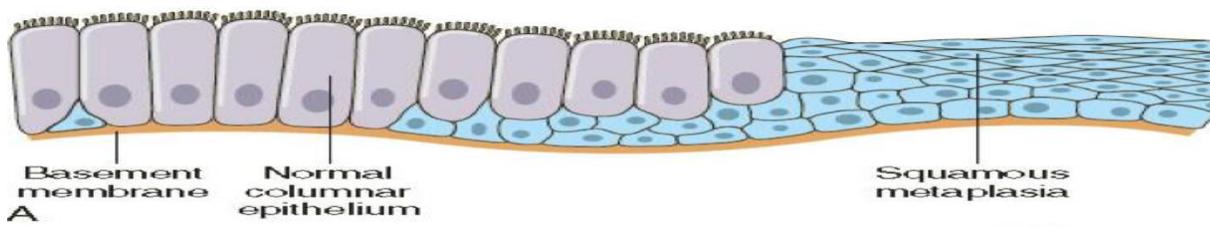
- In Metaplasia; one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.
- Here a cell type is sensitive to a particular stress is replaced by another cell type better able to withstand the adverse environment.
- It arise by the reprogramming of stem cells to differentiate along a new pathway & not by a phenotypic change (transdifferentiation) of already differentiated cells.



- In the respiratory epithelium of habitual cigarette smokers the normal ciliated columnar epithelial cells of the trachea and bronchi → metaplasia → stratified squamous epithelial cells.
- The rugged stratified squamous epithelium can survive the noxious chemicals in cigarette smoke that columnar epithelium would not tolerate.

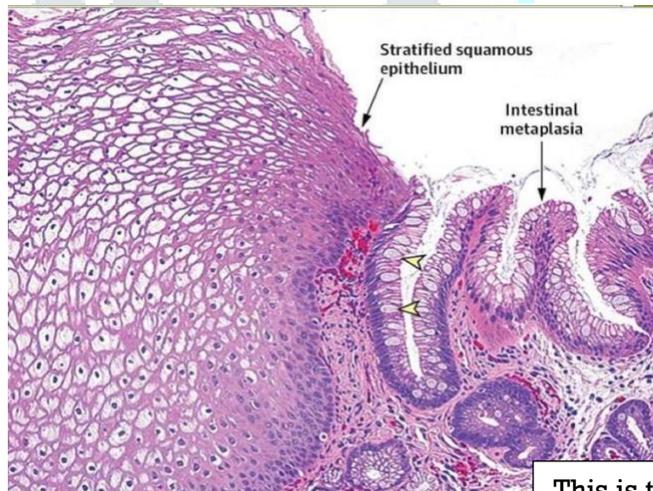
Most of the tissue will turn over to squamous epithelium In long inflammatory condition – bone metaplasia occurrence takes place Which means that bone will generate in unwanted places

- Metaplasia here has survival advantages, but important protective mechanisms are lost, such as mucus secretion and ciliary clearance.

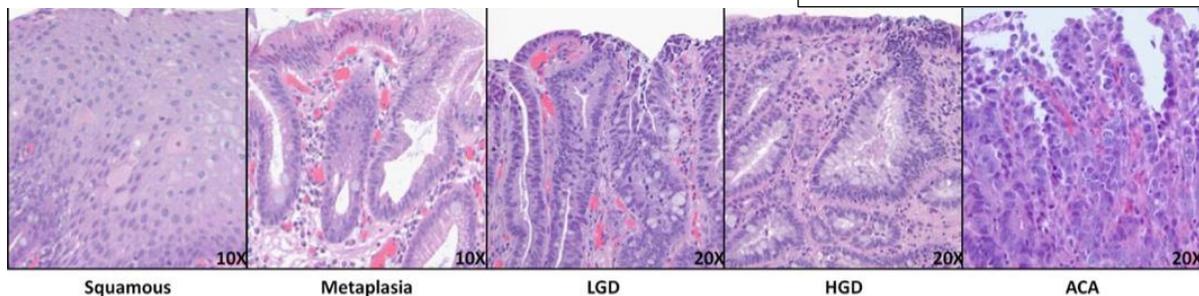


• In chronic gastric reflux; the normal stratified squamous epithelium of the lower esophagus → metaplasia → gastric or intestinal-type columnar epithelium.

• Metaplasia also occur in mesenchymal cells, where it is generally a reaction to some pathologic alteration (bone is occasionally formed in soft tissues, particularly in foci of injury).



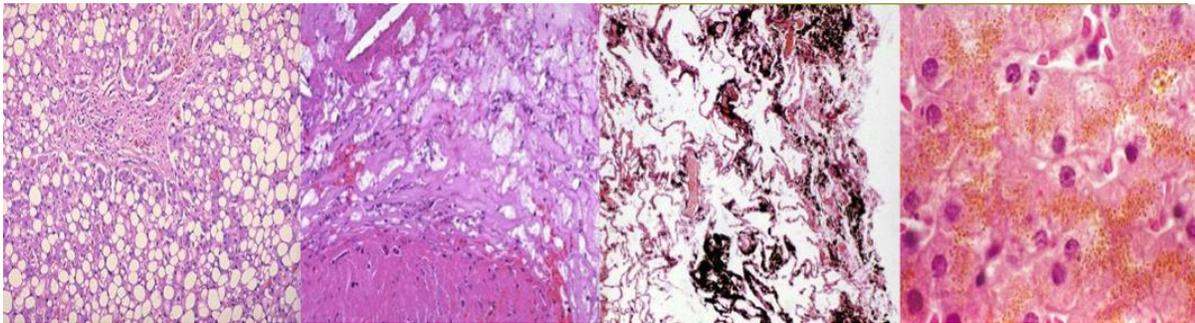
This is the barret disease



ACA: adenocarcinoma

LGD: dysplasia

- The influences that induce metaplastic change in an epithelium, if persistent, may predispose to malignant transformation.
- Squamous cell metaplasia of the respiratory epithelium often coexists with lung cancers composed of malignant squamous cells.
- And columnar epithelium in the esophagus can coexist also with esophageal cancer of adenocarcinoma type.

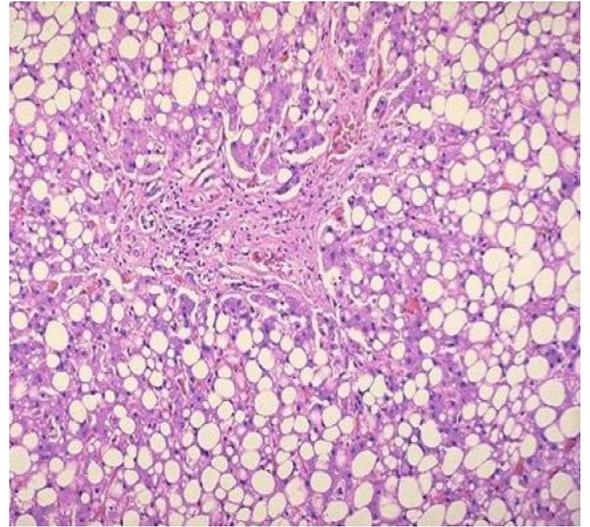


Intracellular Accumulations

- Cells may accumulate abnormal amounts of various substances under some circumstances, can be harmless or cause varying degrees of injury.
- The substance may be located in the cytoplasm, within organelles (lysosomes), or in the nucleus.
- Synthesized by the affected cells or it may be produced elsewhere.
- The main pathways of abnormal intracellular accumulations are
 - (1) inadequate removal and degradation.
 - (2) excessive production of an endogenous substance.
 - (3) deposition of an abnormal exogenous material.

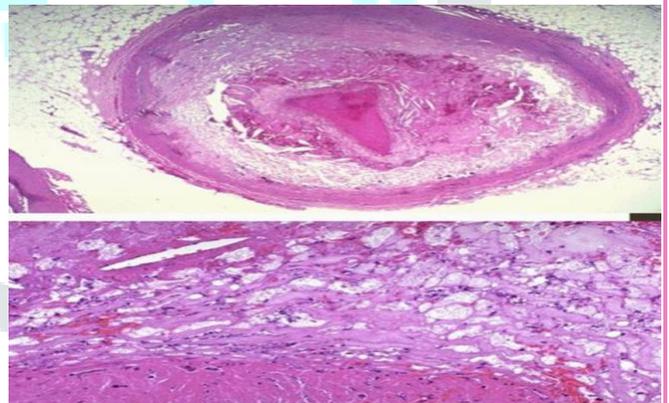
Fatty Change

- ❑ Fatty change, called steatosis.
- ❑ Any accumulation of triglycerides within parenchymal cells.
- ❑ Mostly seen in the liver, (the major organ involved in fat metabolism) , also occur in heart, skeletal muscle, kidney, and other organs.
- ❑ Caused by toxins, protein malnutrition, diabetes mellitus, obesity, or anoxia.
- ❑ Alcohol abuse and diabetes associated with obesity are the most common causes of fatty change in the liver.



Cholesterol and Cholesteryl Esters

- ❑ Cellular cholesterol metabolism is tightly regulated to ensure normal generation of cell membranes (in which cholesterol is a key component) without accumulation.
- ❑ Phagocytic cells may become overloaded in different pathologic processes, mostly increased intake or decreased catabolism of lipids.
- ❑ Atherosclerosis is the most important.

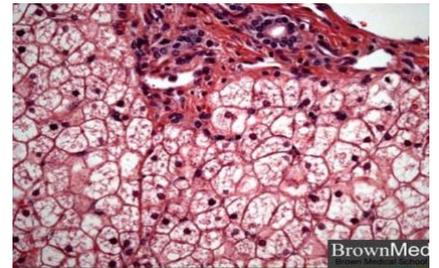


Glycogen

- ❑ Excessive intracellular accumulation of glycogen are associated with abnormalities in the metabolism of glucose or glycogen.
- ❑ In poorly controlled diabetes mellitus, the prime example of abnormal glucose metabolism, glycogen accumulates in renal tubular epithelium, cardiac myocytes, and β cells of the islets of Langerhans.

The needles-lookalike bodies indicates cholesterol deposits

❑ Glycogen also accumulates within cells in a group of related genetic disorders collectively referred to as glycogen storage diseases.



Pigments – Carbon

- Pigments are colored substances :
- + exogenous (from outside the body) such as carbon,
- + endogenous (synthesized within the body) itself, such as lipofuscin, melanin, and certain derivatives of hemoglobin.
- The most common exogenous pigment is carbon, a ubiquitous air pollutant of urban life.
- When inhaled → phagocytosed by alveolar macrophages → transported by lymphatic channels to regional lymph nodes.
- Aggregates of the pigment blacken the draining lymph nodes and pulmonary parenchyma (called anthracosis)



Carbon

Note : this is a pic from the lung

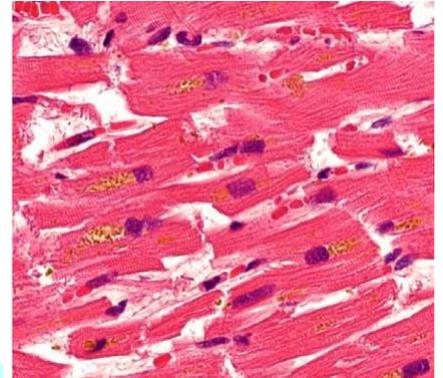
Pigments-Lipofuscin “wear-and-tear pigment”

- An insoluble brownish-yellow granular intracellular material that accumulates in a variety of tissues (heart, liver, and brain) with aging or atrophy.
- Lipofuscin represents complexes of lipid & protein that are produced by the free radical– catalyzed peroxidation of polyunsaturated lipids of subcellular membranes.
- It is not injurious to the cell but is a marker of past free radical injury.

Note: happens in chronic conditions -irreversible injury- chronic inflammation

Also associated with previous injury

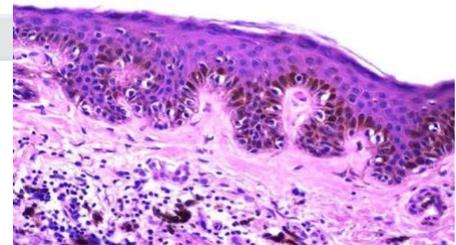
- When present in large amounts, imparts an appearance to the tissue that is called brown atrophy.



Pigments – Melanin

Note: the normal place of melanin is the basal cell layer so if we found it below that layer it's abnormal and pathological condition

- An endogenous, brown-black pigment that is synthesized by melanocytes located in the epidermis.
- Acts as a screen against harmful UV radiation.
- Although melanocytes are the only source of melanin, adjacent basal keratinocytes in the skin can accumulate the pigment (e.g., in freckles), as can dermal macrophages.



Pigments - Hemosiderin.

A hemoglobin-derived granular pigment that is golden yellow to brown.

Accumulates in tissues when there is a local or systemic excess of iron.

Iron is normally stored within cells in association with the protein apoferritin, forming ferritin micelles.

Hemosiderin pigment represents large aggregates of these ferritin micelles, readily visualized by light and electron microscopy.

Hemochromatosis : is iron accumulation within the tissue / is iron metabolism dysfunction

Pigments - Hemosiderin.

the iron can be unambiguously identified by the Prussian blue histochemical reaction

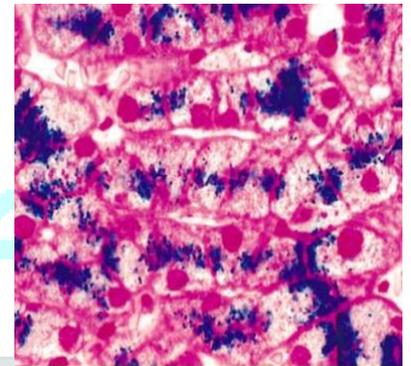
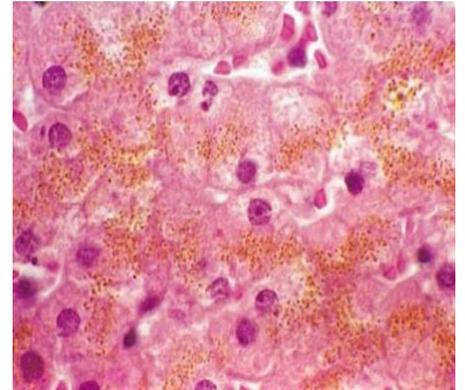
Small amounts of this pigment are normal in the mononuclear phagocytes of the bone marrow, spleen, and liver, where aging red cells are normally degraded.

Excessive deposition of hemosiderin, called hemosiderosis.

Note: lipofusion and hemosidern have the same color indication (yellow brownish so we can differentiate by the two of them by immunological pigment called the Prussian blue as it appears in the below pic that iron deposit now observed bluish

more extensive accumulations of iron seen in hereditary hemochromatosis.

Note : the blue dots is iron



الحمد لله على السلامة