



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
الَّذِي عَلَّمَ بِالْقَلَمِ ۖ عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ



PATHOLOGY

MID | Lecture 1

Cell Injury & Adaptations

Written by : NST

Reviewed by: Yamen Aljarrah



Color coding used in the modified:



Black: the original slides



Magenta: the doctor's explanation/words



Gray: additional information and explanation



Red: important information

Cellular Adaptations

It's important to study cellular adaptations because the cells are the building blocks for our bodies; they make up tissues which make up organs which make up the whole body. This helps in understanding the pathogenesis or the disease process of the cells.

cell injury and adaptations

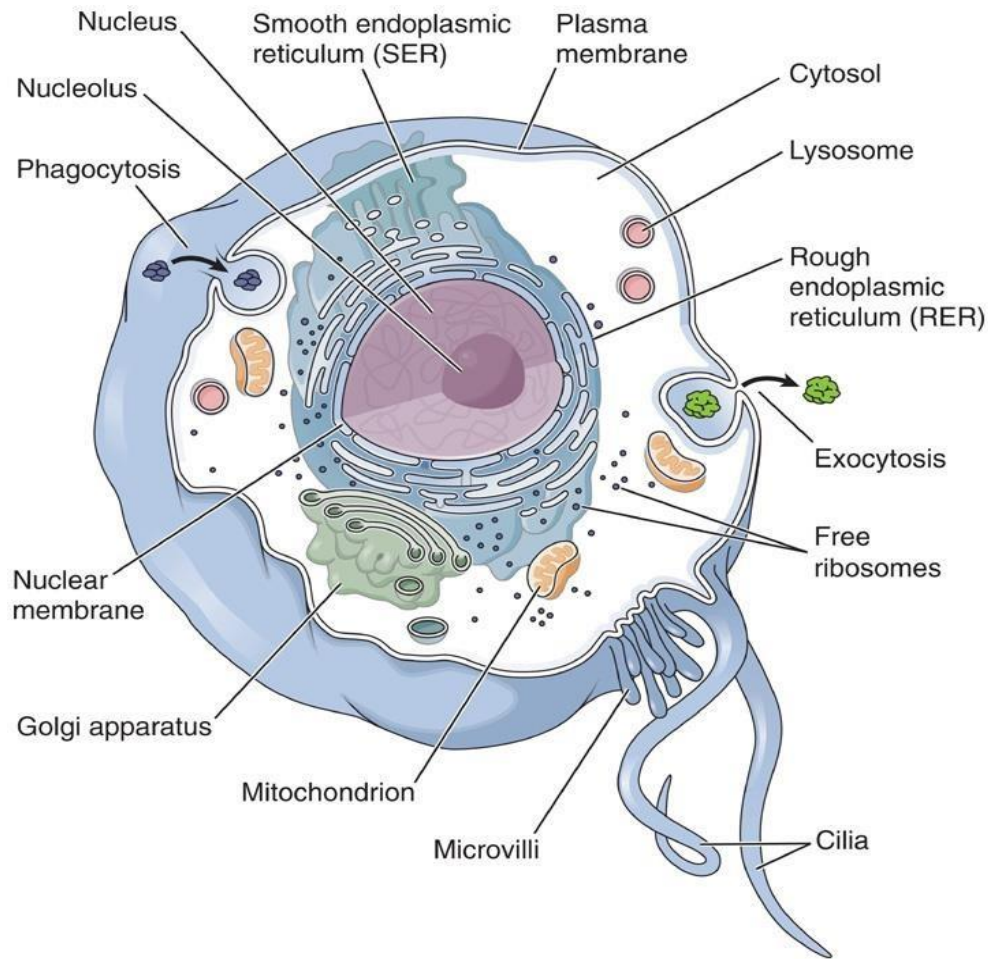
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Outlines:

Adaptive Mechanisms that cells do during cell stresses :

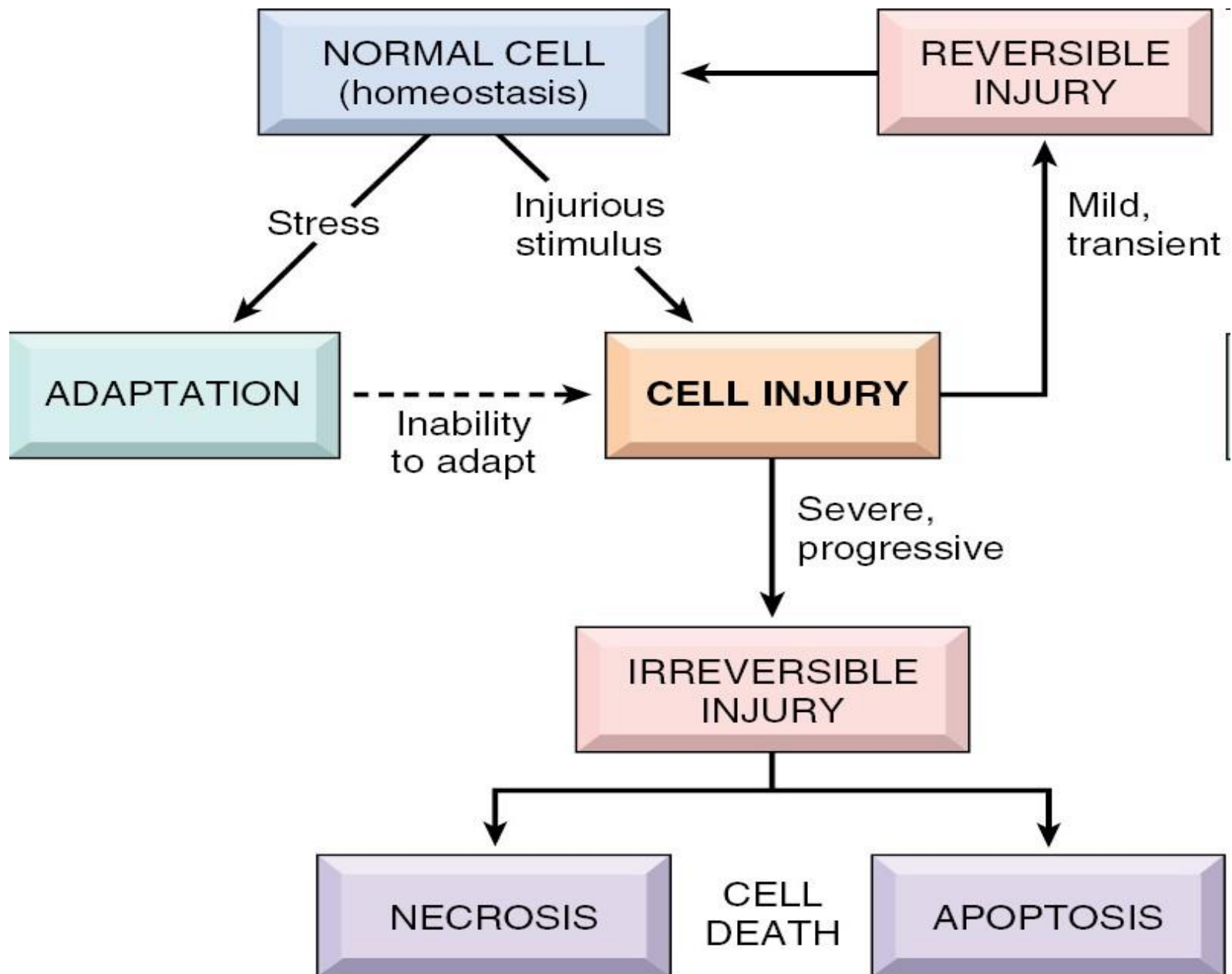
- Hypertrophy (increase in cell size – so increase in organ size – MORE function)
- Hyperplasia (increase in the number of cells – so increase in organ size)
- Atrophy (decrease in cell size – so decrease in organ size – LESS function)
- Metaplasia (change cell type to another type)
- Causes of cell injury.



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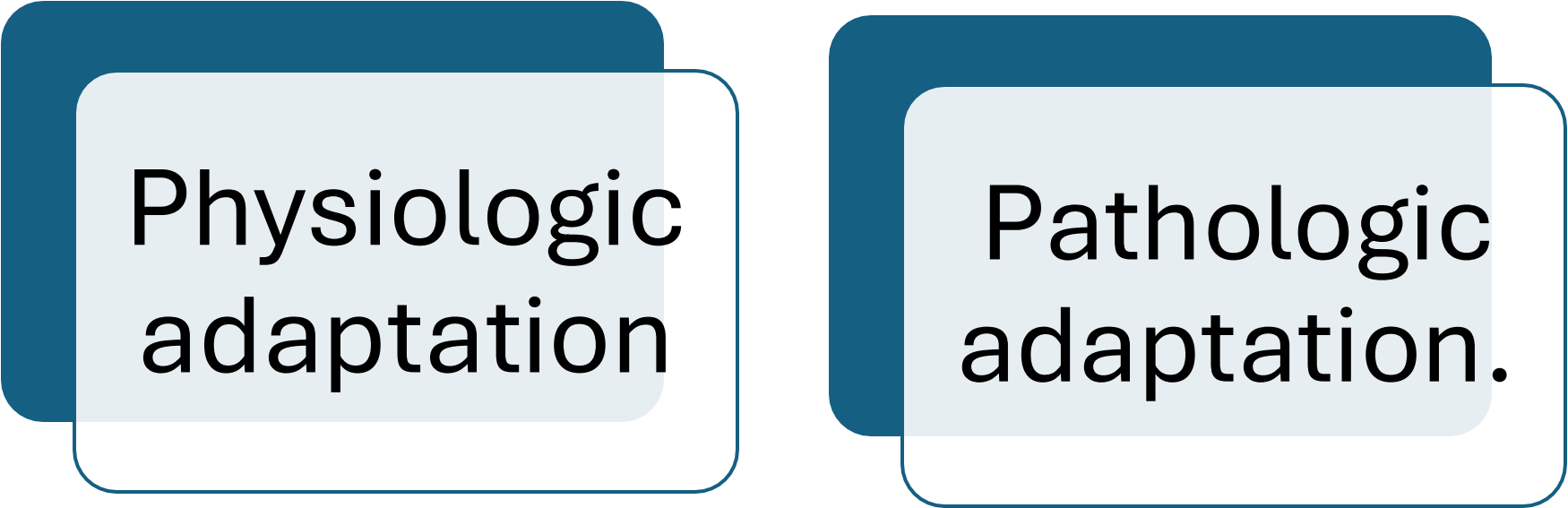
Cells in our body live in a normal state Called (**Homeostasis**) which is a healthy condition for the cell that describes the state of balance for everything in our cells such as **Temperature, pH, Concentrations, fluid contents** etc...

Revision: A cell has a cell membrane which is composed of a bilayer of phospholipids and associated proteins. Inside the cytoplasm there is the nucleus which has the genetic material and is surrounded by a nuclear membrane. The mitochondria are the energy apparatus. There are also the ribosomes which are attached to the rough endoplasmic reticulum and they are important in protein synthesis.



- Any normal cell lives in a state of homeostasis, but any cell can be exposed to stressful conditions (like an increase in temperature), so the cell tries to adapt to these conditions in order to stay alive and maintain its function. Once the stressful condition is removed the cell goes back to normal .and this is our lecture topic (Adaptation).
- There are other states when the adaption can't be maintained (if the stress continues at a higher magnitude or when the cell is under harmful (injurious) stimulus). In this case we are dealing with cell injury. There are two kind of cell injuries:
 - A. Reversible (when the stimulus disappears everything will return back to normal)
 - B. Irreversible(which equals cell death) .
- There are two mechanisms for cell death: -necrosis and -apoptosis. In the case of severe cell injury we are mainly talk about necrosis.

Adaptations



The diagram consists of two identical rectangular boxes with rounded corners, each with a dark blue header and a light blue body. The first box on the left contains the text 'Physiologic adaptation'. The second box on the right contains the text 'Pathologic adaptation.'.

Physiologic
adaptation

Pathologic
adaptation.

Adaptation has two main types with regard to the nature of its stimulus:

- **Physiologic** adaptation which occurs under normal physiological conditions like puberty and pregnancy.
- **Pathologic** adaptation which occurs under disease and pathological conditions.

Adaptations

The main common feature that all adaptation mechanisms have is that they are all reversible.

➤ Many forms:

Increase in cell size. (hypertrophy)

➤ Decrease in cell size (atrophy)

➤ Increase in number of cells. (hyperplasia)

➤ Change into another type of cell. (metaplasia)

- Adaptation to stress can progress to cell injury if the stress is not relieved.

Important: Cells that are not able to proliferate and divide can't undergo hyperplasia as a way of adaptation, such as neurons, cardiac and skeletal muscle cells.

Hypertrophy

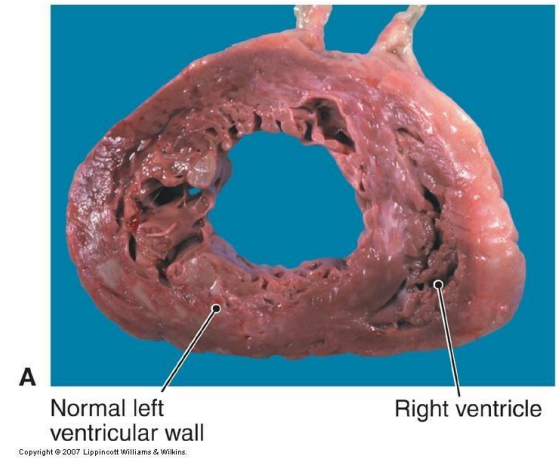
- Increased size & functional capacity
- Pure hypertrophy or mixed with hyperplasia in tissues that are capable of proliferation.
- Mechanism of hypertrophy: Increased structural proteins and organelles.
- Pathologic vs physiologic

Due to (Driving forces/ causes for hypertrophy):

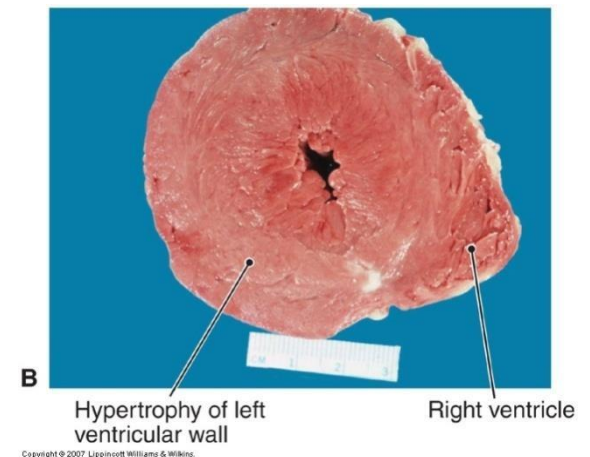
- hormonal stimulation (like the uterus during pregnancy).
- Growth factor stimulation
- increased functional demand (like the heart in hypertension or aortic stenosis)

In hypertrophy, the cell size increases due to the increased synthesis of structural proteins and organelles, whereas in swelling, the cell size increases because it contains more water.

Normal heart

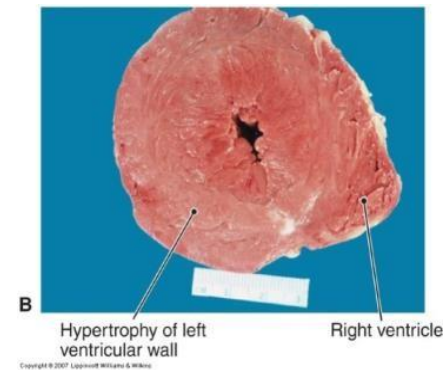
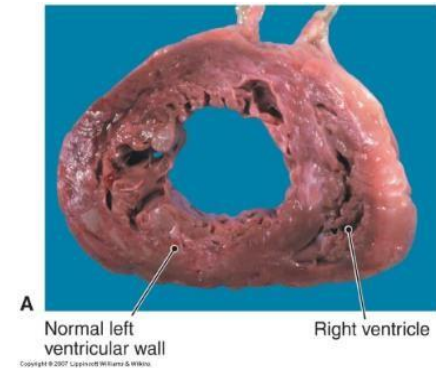


Heart with hypertrophy



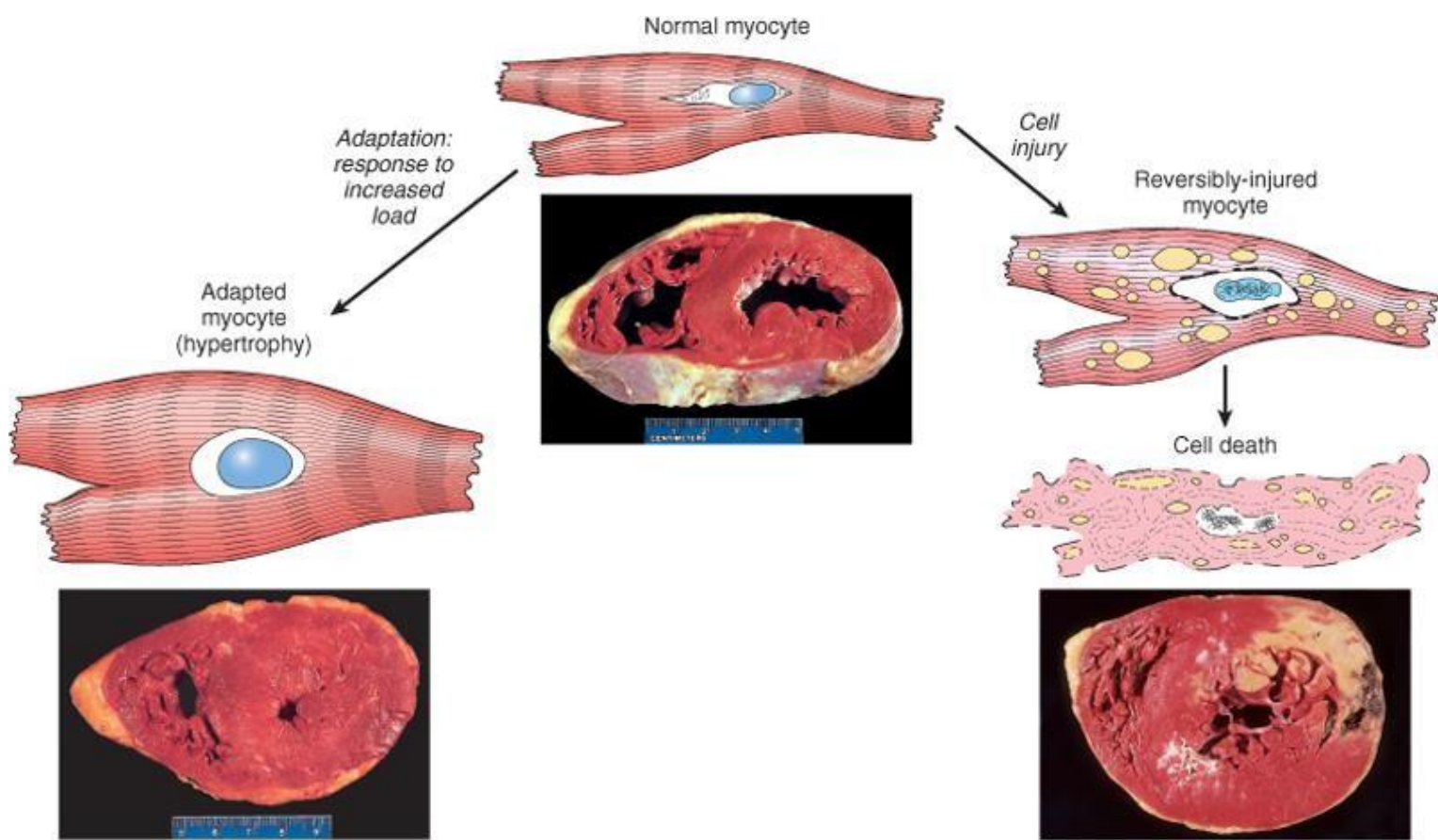
Pathologic(cardiac muscle in hypertension and aortic stenosis)

- At hypertension case, peripheral resistance in blood vessels is increased, so the heart has to pump against a higher resistance, so heart must pump stronger, so heart size will increase **only** by hypertrophy(pure) (No hyperplasia happens because cardiac muscles can't proliferate).
- hypertrophy is reversible, but it has limits so sometimes uncontrolled hypertension could lead to the cells reaching the point of cell injury. As you see, Myocardium thickness is increased so the lumen of the heart will decrease, and at the end this could lead to heart failure , ischemic heart disease or MI (Myocardial Infarction) in uncontrolled hypertension.
- Also, the increase in the myocardium size will lead to a higher blood demand, so ischemia (insufficient blood supply) in blood vessels that supply it could lead to myocardial infarction. If the hypertension was in systemic circulation, the hypertrophy will be in left ventricle and if it was pulmonary hypertension, it will be at right ventricle .



Pathologic

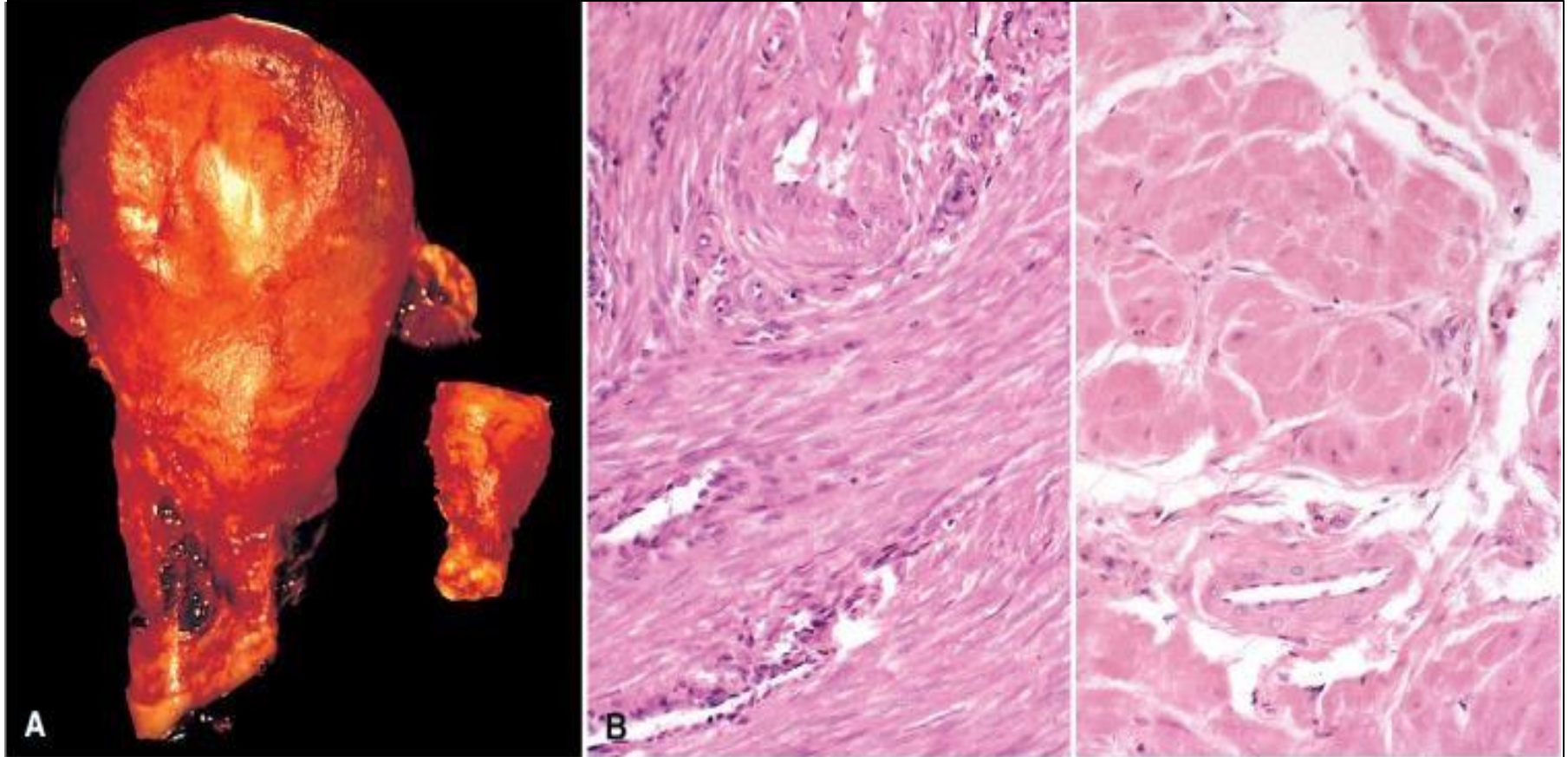
cardiac muscle in hypertension and aortic stenosis



Physiologic hypertrophy (uterine **smooth muscle** in pregnancy)

- Smooth muscles of uterus during pregnancy are an example of hormonal stimulation, so they undergo both hypertrophy and hyperplasia(mixed)
- Under the effect of **estrogen** (hormonal stimulation), the uterus enlarges to accommodate the fetus. It is reversible so after pregnancy, uterine shrinks when hormone levels are back to normal.

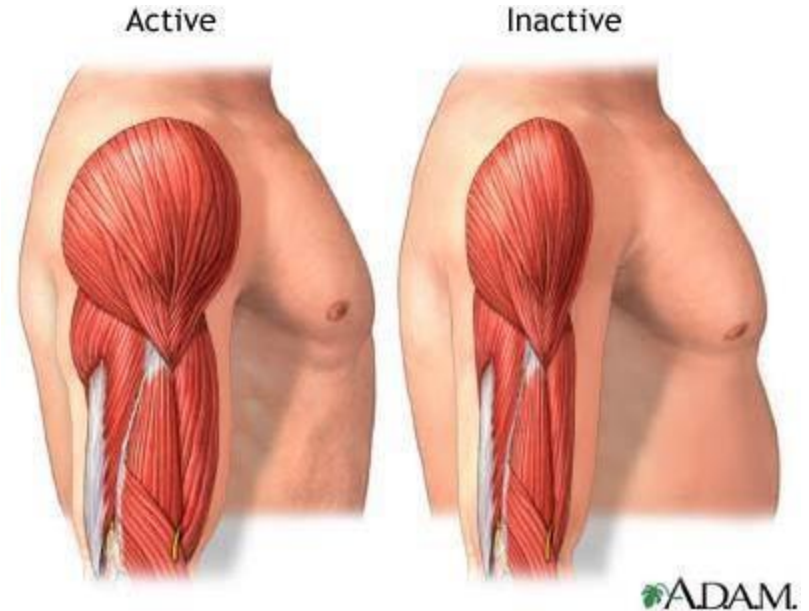
Physiologic uterine smooth muscle in pregnancy



Physiologic skeletal muscle in athletes

Cause of hypertrophy: increased functional demand.

- Increasing the load on the skeletal muscles will increase the muscle size(**PURE** hypertrophy because skeletal muscles are not capable of proliferation).



Hyperplasia

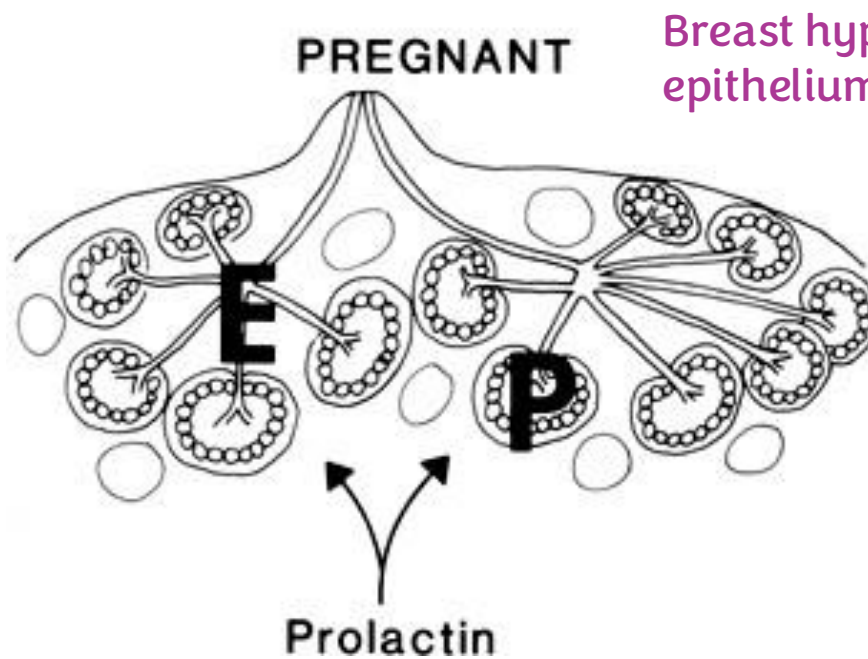
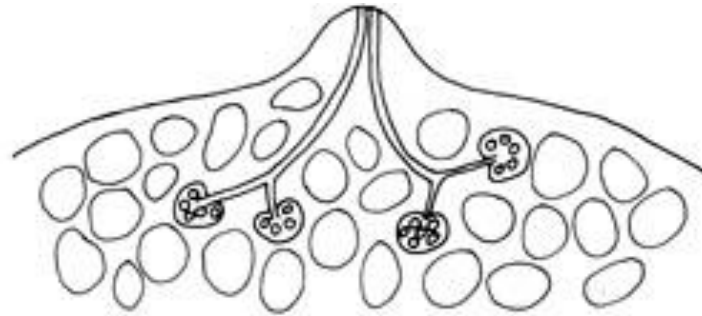
- **Definition:** Increase in number of cells in tissues that have proliferative ability(e.g epithelium tissue)
- Pure (only hyperplasia) vs Mixed (hyperplasia with hypertrophy)
- Physiologic vs Pathologic vs cancer (pathological hyperplasia could lead to cancer)

Hyperplasia is reversible, but once it starts the processes of mutations that develops to cancer it becomes irreversible.

Physiologic hyperplasia

- Hormonal stimulation e.g: 1. Smooth muscles of the uterus during pregnancy
2. Breast development during puberty, pregnancy and lactation (increase in the number of glandular cell in the breast which leads to the increase of the size of breast).
- Compensatory تعويض
e.g liver after partial resection due to cancer (benign or malignant) or traumas and accidents, it will proliferate and return back to its normal size. The liver could get back to its normal size even if more than $\frac{3}{4}$ of it is removed.
- Pathologic
 - **excessive** hormonal stimulation:
 - I. Endometrial hyperplasia (serous disease and could progress to cancer if not treated) it is **estrogen** induced.
 - II. Benign prostatic hyperplasia (prostate of elderly men and cause enlargement of prostate under hormonal effect) it is **androgen** induced.
 - Viral Infections Warts (HPV) (Human Papilloma Virus)
HPV virus make warts on skin and the mechanism is hyperplasia of squamous epithelium cells .
 - ▶ Pathologic hyperplasia constitutes a fertile soil in which cancers may eventually arise. (endometrial)

Physiologic breast in pregnancy and lactation

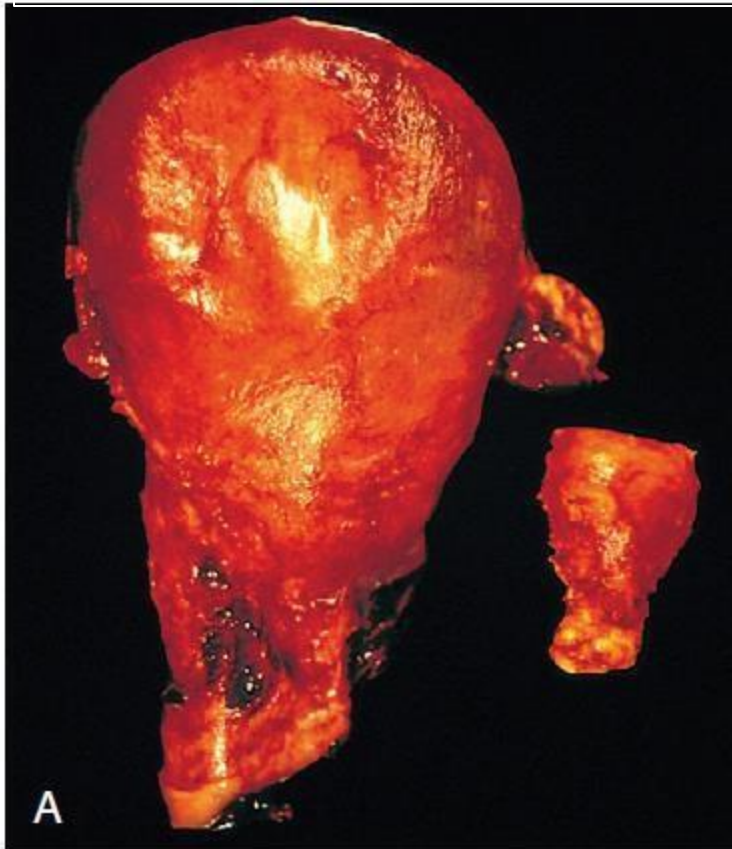


Breast hyperplasia (glandular epithelium cells are increased).

Pathologic

endometrial hyperplasia, estrogen induced

In this case the uterus is not enlarged but only the thickness of the endometrium is increased. (From the cross sectional picture, you can see it looks folded due to the increase of the epithelium thickness)



Atrophy

It is the opposite of hypertrophy, we will have a smaller cell with less function, but it is still alive.

➤ Decreased cell size & function

➤ Mechanism:

↓ Protein synth (less production of new proteins)

↑ Degradation (More breakdown of proteins to amino acids)

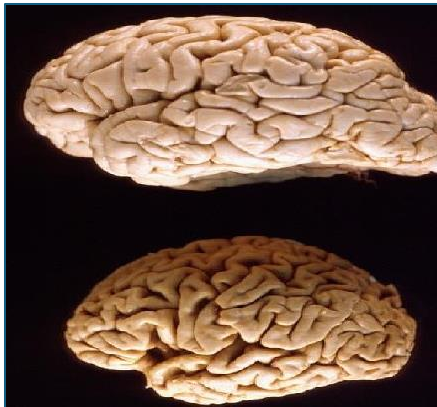
↑ Autophagy (cell will start eating itself to produce energy)

▶ Atrophic cells can still function

As we mentioned before, atrophy is a type of adaptive mechanisms and that means that the cell can go back to the normal state when the stress ends (physiological or pathological) so it is not dead for now and still it can give its functions but to lesser rates.

Causes:

- Decreased workload (immobilization of a limb after fracture) **NEXT SLIDE**
- Loss of innervations
- Diminished blood supply (**Ischemia**)
- Inadequate nutrition
- Loss of endocrine stimulation **NEXT SLIDE**
- Aging (senile atrophy)



Loss of innervations and blood supply is an important cause, all muscles need oxygen, blood and nerves to contract and do its function, so if we have a problem in the blood supply, nutrients, oxygen or nerve supply because of ischemia, nutritional deficiency, or any other reason, muscles will start to shrink and lose their size with time.

Diabetes patients have a chronic ischemia in their lower limb and a decrease in innervations in their lower limbs, if we don't control these cases they will suffer from muscle weakness, and their skin will be thinner by the time.

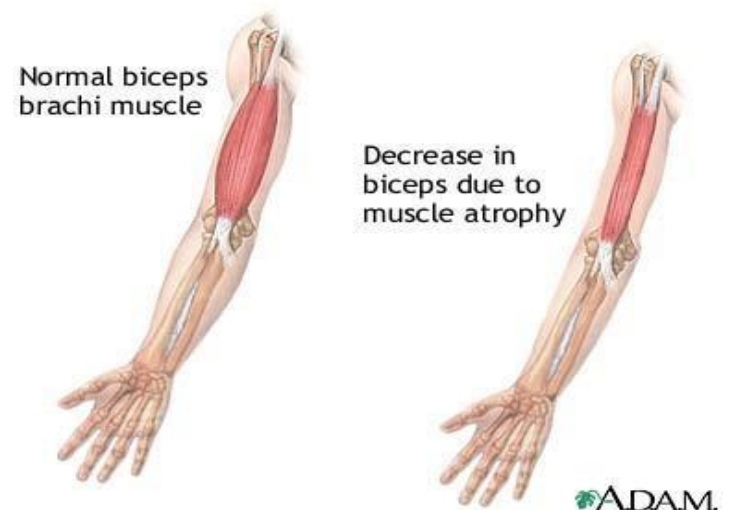
The Brain can suffer atrophy because of aging and Alzheimer's disease and this will lead to a shrink in the brain tissue and neurons to atrophy.

Causes of Atrophy

1- **Decreased workload demand**, if the organ has a higher functional demand its size will increase, example muscles when you go to gym their size will become bigger, but if the organ has a lower functional demand its size will decrease with time. For example, when you have a fracture in your hand you must put a splint to treat it. During this period, if you don't move your hand continuously, the muscles will become thin and weak because they didn't perform their function as required – lower functional demand will cause decrease in the size.

2- **lose of endocrine stimulation**,(physiological) after menopause, the endometrium becomes thinner and smaller due to decrease in the levels of hormones (estrogen and progesterone) as mentioned before hormones can stimulate the cell to the hypertrophy state so lower levels of hormones in cells will cause them to atrophy.

Note : increase or decrease of hormones in our body is a normal physiological state in general.



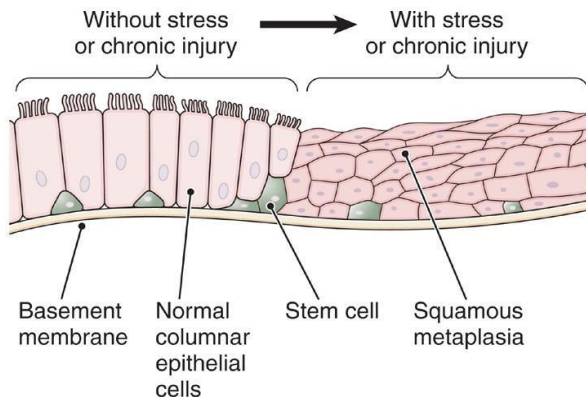
As a conclusion of reasons

- **Physiologic** - Normal
- Loss of hormone stimulation in menopause (endometrial atrophy)
- **Pathologic** - Not Normal and must be treated
- Denervation injury. (Lose of nerves)
- Chronic ischemia. (Lose of blood supply)
- Chronic nutrition deprivation

Metaplasia

Most of metaplasia occurs in epithelial tissues.

- Change from one cell type to another
- Reprogramming of **stem cells** NOT differentiated cells
- Persistent change increases risk of cancer
- New cell type copes better with stress but function less.
- Reversible (**can go back to the normal cell**)
- Causes: Smoking , Vitamin A deficiency, GERD.
- Vitamin A is needed for normal epithelial differentiation; deficiency leads to squamous metaplasia of the bronchi)



Metaplasia

- the cells transform to a new type but to explain deeply: we can say that the stem cells (parent cells) are now producing new types of cells by reprogramming themselves. This can be good for a short time by helping the tissues cope with stress but it does its functions less efficiently. if the cell don't go back to the normal state this can lead to high risk of cancer.
- For example, bronchial cells are normally lined with ciliated pseudostratified columnar epithelial cells along with goblet cells (to produce mucus to trap dusts and microorganisms which will be propelled outside by cilia). In squamous metaplasia (happens to smokers), these pseudostratified columnar epithelial cells are replaced with squamous cells as a protective mechanism to deal with stress which is smoking, but this comes at the cost of normal function(dust and microorganisms could enter lungs because no mucus will be produced).
- Vitamin A is needed for the epithelial differentiation of cells, so its deficiency could cause metaplasia mainly in bronchi, urinary bladder or any site that's lined with differentiated epithelium.
- Gastroesophageal Reflux Disease(GERD) means the reflux of gastric contents back to the lower part of the esophagus. Lower part of the esophagus is normally lined by stratified squamous epithelium which doesn't tolerate the acidity coming from the constant reflux from the stomach, so it changes into the intestinal epithelium containing goblet cells, this type of tissue tolerance higher acidity but it comes with a higher risk of cancer.
- Stress factors that could lead to metaplasia could lead to cancer (smoking and Vitamin A deficiency lead to lung cancer(squamous cell carcinoma) – Gastroesophageal Reflux Disease(GERD) leads to Esophageal adenocarcinoma). So we need to get rid of these factors because our cells will become normal again and this will decrease the risk of cancer.

Cell injury and death

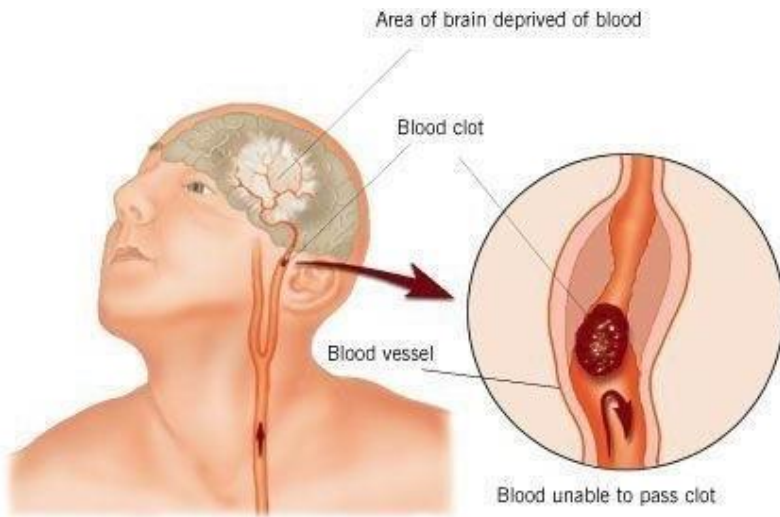
A note from the Dr :
Study and understand the diseases that are
mentioned in the slides only.

CAUSES OF CELL INJURY

- Oxygen Deprivation (Hypoxia Vs ischemia)
- Chemical Agents
- Infectious Agents
- Immunologic Reactions
- Genetic Factors
- Nutritional Imbalances
- Physical Agents
- Aging

(Each will be explained in a slide)

Oxygen Deprivation



The most common reason of hypoxia is ischemia which is caused mostly by atherosclerosis.

**LACK OF
OXYGEN !**

Chemical Agents



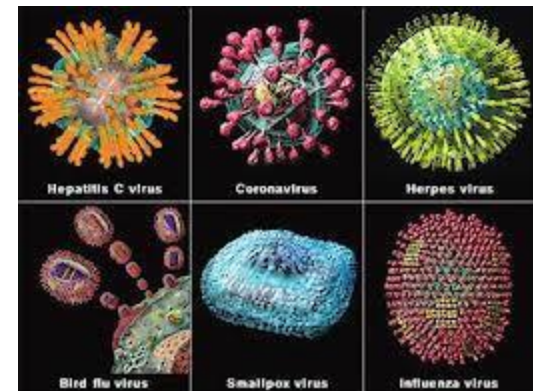
The strong chemicals such as pesticides, insecticides, or glucose

Cell injuries that are happened by diabetes are mainly caused by glucose so if our body has a high levels of glucose this can lead to the death of cells if it is not controlled.



Infectious Agents

Viruses, bacteria, fungi and Protozoa are examples of pathogens that cause cell injury. Any disease starts with cell injury.



Immunologic Reactions

autoimmune, allergic, microbes



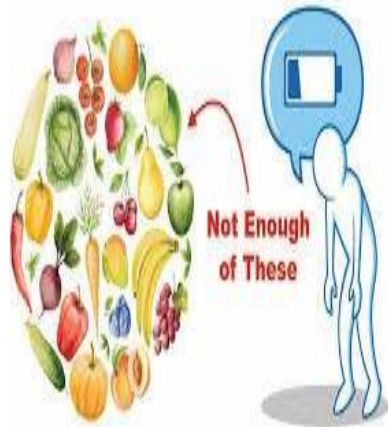
Genetic Factors



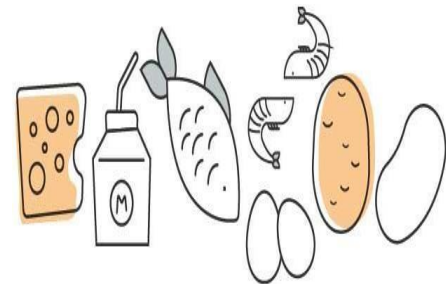
Down syndrome or cystic fibrosis are examples of genetic cell injuries; it mainly happens when there is chromosomal abnormalities (like Down syndrome).



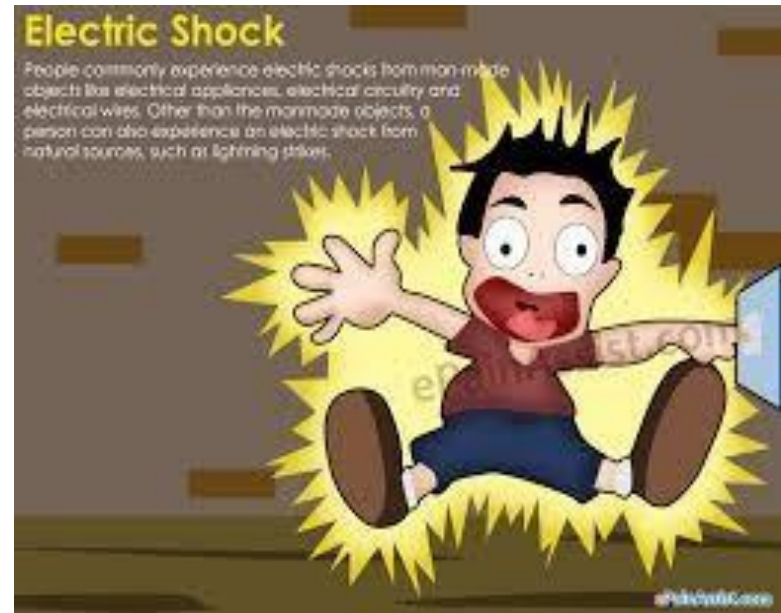
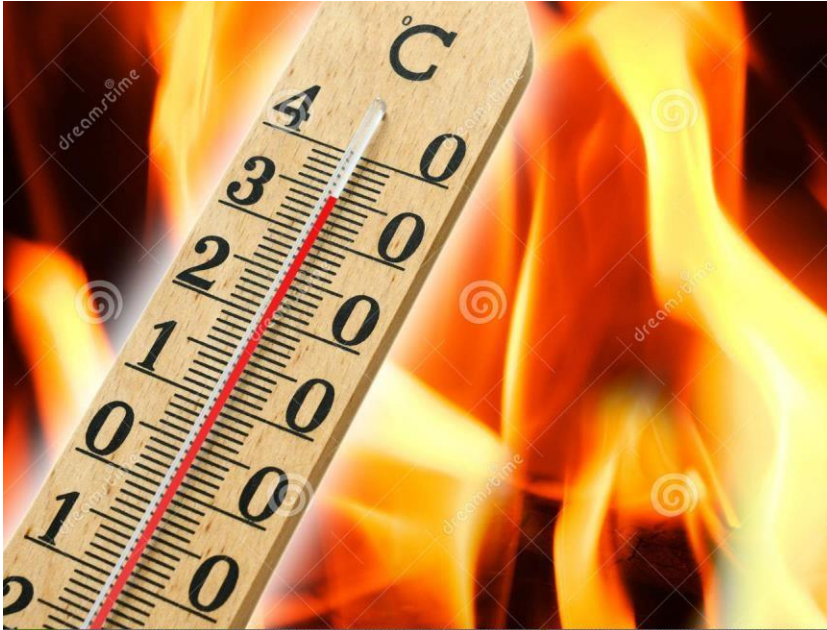
Nutritional Imbalances



Over-nutrition (which causes obesity) or under-nutrition (causes atrophy) both could lead to cell injuries.



Physical Agents



Increase of temperature, electric Injuries
or any physical trauma like falling down.

For any feedback, scan the code or click on it.



Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide 10	-	Fixed text overlap
	Slide 18	Endometrial hyperplasia is physiologic	Breast hyperplasia is physiologic
V1 → V2			

Additional resources:

References Used:

Prof. Manar Hajeer recorded lecture.

Extra References for The Reader to Use:

Robbin's Basic Pathology (10th Edition).



رسالة من الفريق العلمي: