

DOCTOR 2020 | JU



# PATHOLOGY

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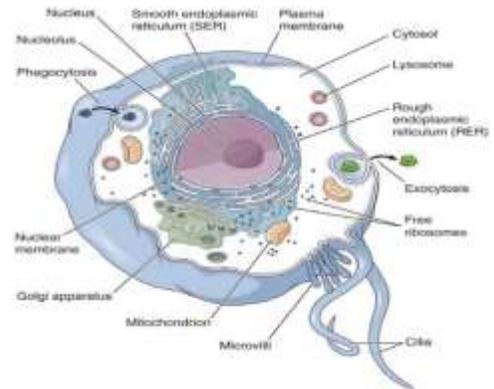
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## Cell injury, cell death and Adaptations.

- Our bodies consist of the basic unit of life, which is called the cell, which contains within it many organelles that mainly help to carry out various functions.

- a) Cell membrane surrounds all the cells which is mainly consists of phospholipids and a lot of proteins.
- b) Cytoplasm which has many organelles such as golgi apparatus , ER and **mitochondria (energy factory of cells)**.



- Cells interact with each other in their environment to adapt and maintain their function and structure in the event of stress and demands in their environment.
- We can say that a cell is in a “**homeostasis**” when the intracellular components are within a normal range (highly regulated).

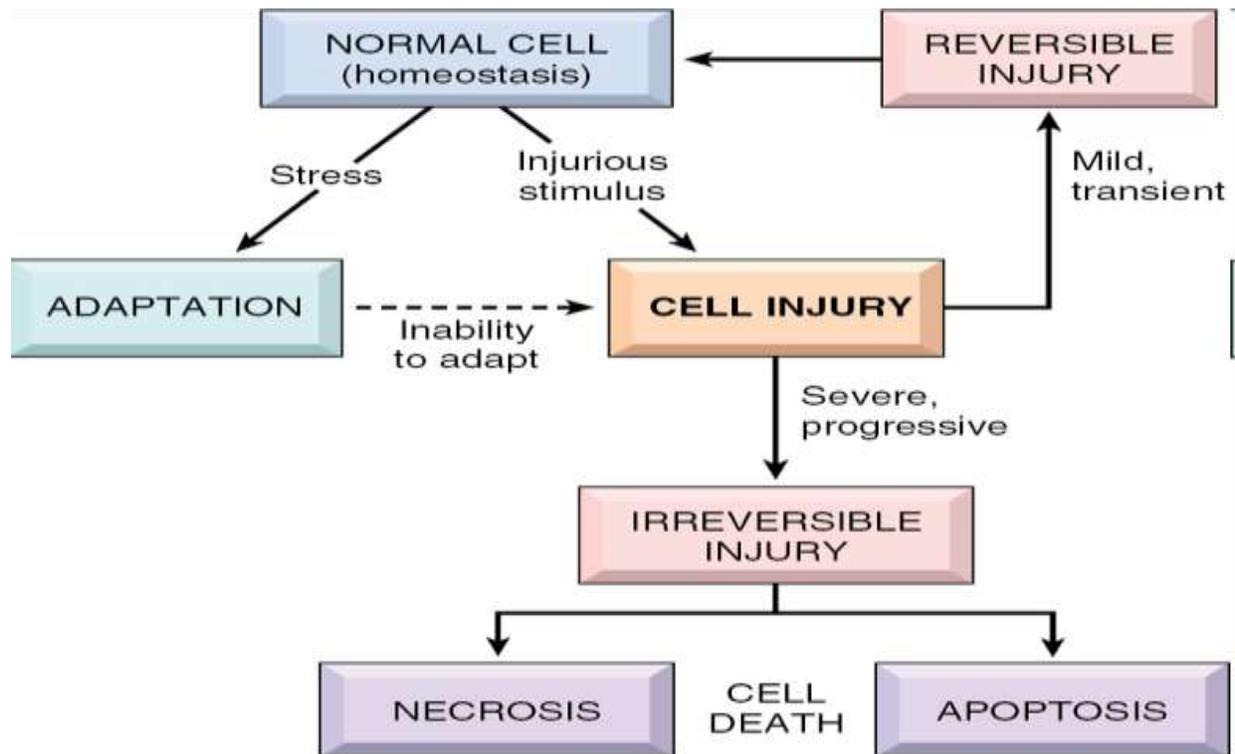
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- When a cell encounters in any increasing demand or increasing physiological stress or exposed to a highly injurious stimuli normally the cell will go under many changes.
  - As a result of exposure to these changes, the cell must behave in two pathways, the first of which is **adaptation**, which has a certain limit. If it is exceeded, the cell enters the other pathway, which is **cell injury**.
  - It can be first **reversible injury**. But if the stress or the injurious stimuli is very severe, constant progressive or very rapid, the cell will undergo **irreversible injury** or what we call **cell death**.

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### What do we mean by reversible and irreversible injuries ?

Reversible injury: cell can return back to its normal conditions after the harmful stimuli is gone.

Irreversible injury: cell cannot return to the homeostasis state again after the harmful stimuli is gone.



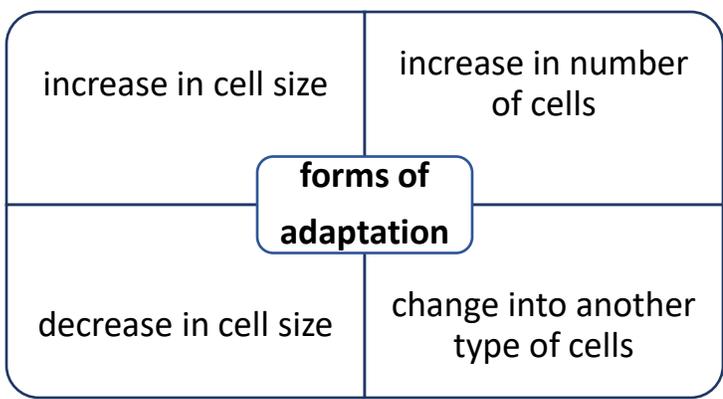
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**Why we study cell injury?**

Because cell injury is crucial and basic element in any disease process. All diseases in the body will start at first by cell injury. So, we have to study cell injury and the reaction of cells with its surrounding environment whether by first adaptation, second by reversible cell injury, third by irreversible cell injury or what we call it cell death.

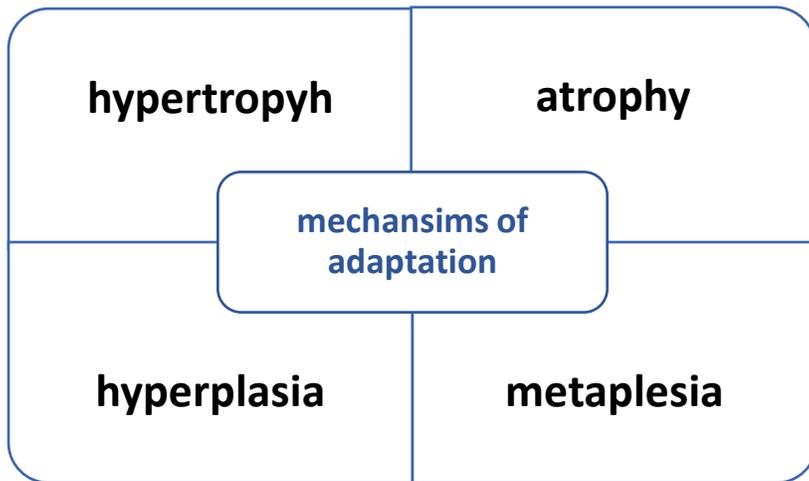
**Adaptation**

- Physiological adaptation:** phenomena which can be response for any physiologic stimulation.
- pathologic adaptation:** can be caused by a process of a disease.



These forms of cells adaptations are presented in which the cells are still alive and functional. But it is possible for the functions of the cell to change according to the type of adaptation that it undergoes, but whether the functions of the cell changes or not, it stills alive and functional.

Note: in reversible injury the cell stops functioning until the stress is gone , while in adaptation the cell stills functional under stress.



Note: All of these adaptive mechanisms are considered **reversible** (when the stressful event is relieved, the cell will go back to normal).

## Hypertrophy

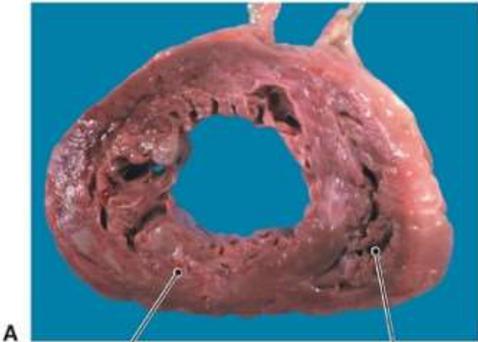
- **Increased in cell size and functional capacity,**  
because when you increase cell size, the function of the cell will increase so the net result is increase in the organ size.
- **Hypertrophy can be:**  
**Pure:** in organs or cells that have a limited capacity to divide, so they can't go hyperplasia. They only undergo hypertrophy. Eg: cardiac muscles & skeletal muscles.  
**Mixed:** in cells or tissues that can divide, so they can undergo hypertrophy and hyperplasia. Eg: smooth muscles of uterus.
- **The mechanism of hypertrophy** is by increase the production of structural proteins and organelles.
- **Physiologic vs pathologic**
- **The causes of hypertrophy:**  
Hormonal stimulation.  
Growth factor stimulation.  
Increased functional demand.

***The most common example on pathologic hypertrophy*** is the hypertrophy of the cardiac muscles as a response to hypertension or aortic valve stenosis.

After the patient go under hypertension or aortic valve stenosis the myocardial cells start to adapt with this condition by increasing the size of the cardiac cells in order to accumulate the high pressure forces. since the cardiac muscle cells cannot go under hyperplasia فبكون في تضخم في القلب يعني بكون حجمه كبير. The heart has limit for this adaptation after this limit the myocardial cells will go under cell injury.

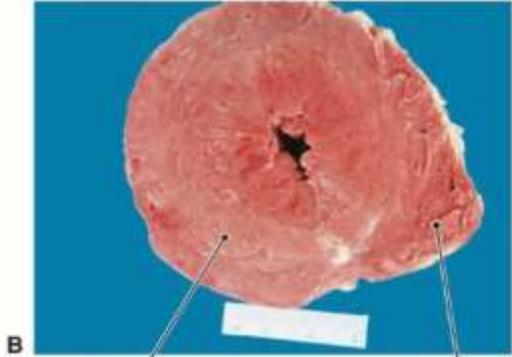
**Mechanism:** hypertrophied myocardial cells will need more blood supply which cannot not be sustained, so these cells start to degenerate and cell injury will take place. After a while patient with a such case will have a heart failure.

the normal state for ventricle. the thickness of the myocardial cells is normal.

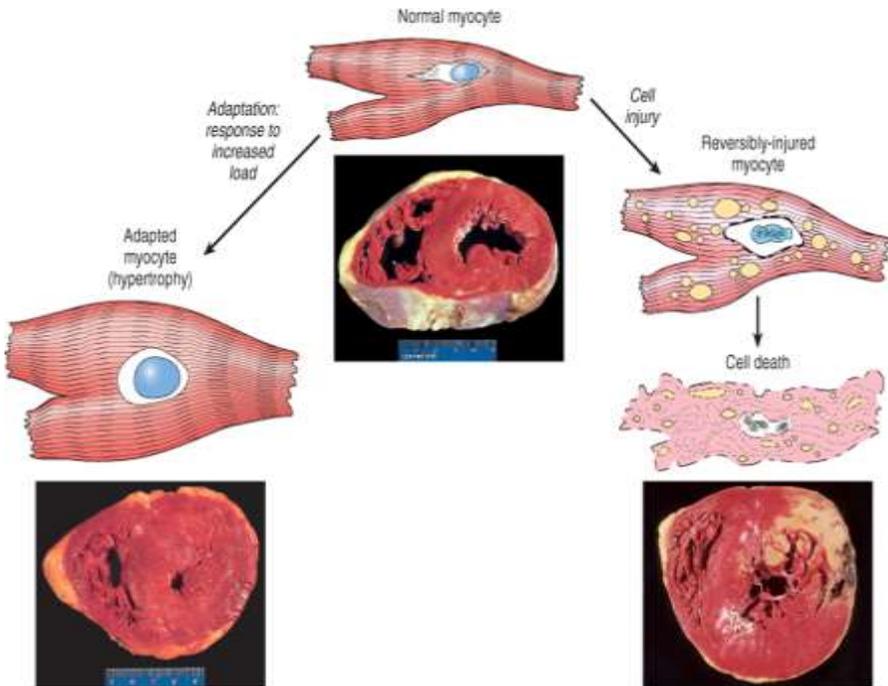


A Normal left ventricular wall Right ventricle

Ventricle after hypertension. myocardial cells undergo hypertrophy so the thickness of the ventricle increases.



B Hypertrophy of left ventricular wall Right ventricle



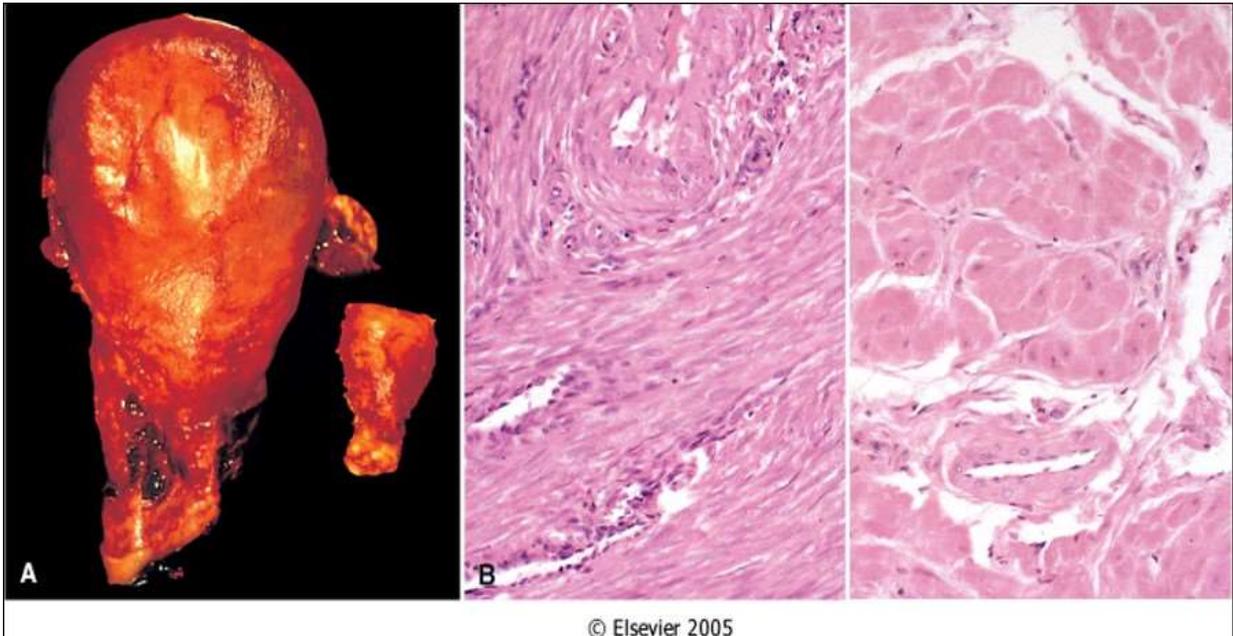
After skipping the adaptation stage, the cell enters to cell injury stage, and then this may lead to cell death, and thus the occurrence of **ischemia** and **heart infarction**.

**Example2:** The smooth muscles of uterus can undergo hypertrophy and hyperplasia in response to **estrogenic stimulation** during pregnancy (physiologic adaptive mechanism).

It is reversible, why? after pregnancy when estrogen goes back to its normal range, these enlarged muscles will go back to normal size and the newly formed muscles due to hyperplasia will disappear.

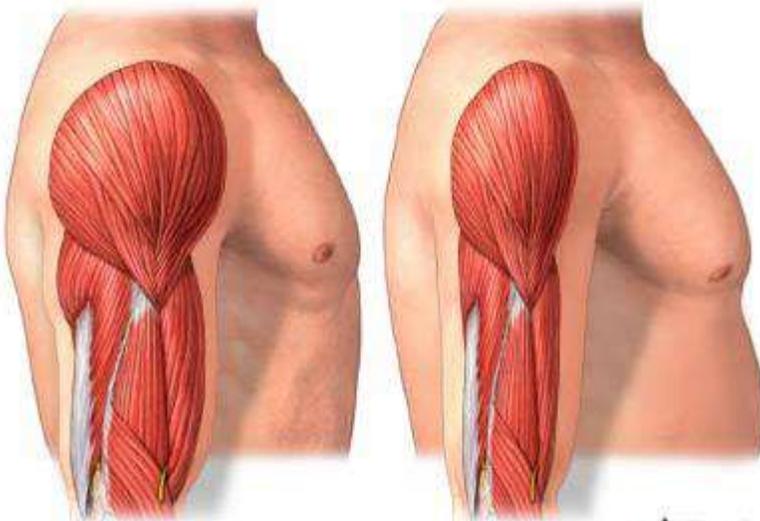
The normal appearance for the smooth muscle of the uterus in the absence of pregnancy

Hypertrophied uterine cells during pregnancy. (physiological adaptation)



Active

Inactive



**Example3:** Skeletal muscles of athlete(physiologic): the skeletal muscle will adapt due to this increased demand by hypertrophy. That's why you will find the muscles of the bodybuilders and the athletes are enlarged.

# Hyperplasia

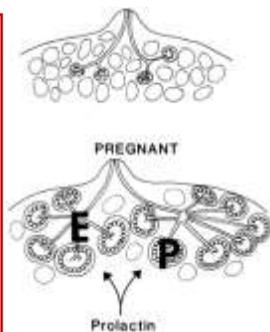
- **Increase in the number of cells** with a correspondent increase in the size of the organ.  
Tissues that have proliferative ability to divide can go under hyperplasia.
- **Hyperplasia can be pure** (without hypertrophy occurrence) **or mixed** (both hypertrophy and hyperplasia occur).  
Notice that skeletal muscles, neurons and cardiac muscle cells cannot go under hyperplasia **only hypertrophy**.
- **Hyperplasia can be physiologic or pathologic.**

- Hormonal stimulation
- Compensatory (تعويض)

- Excessive hormonal stimulation.
- Viral infections.

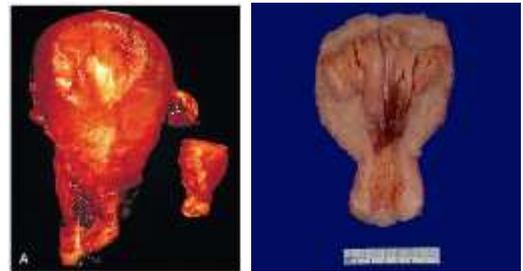
## 1. Breast in puberty and pregnancy (during the preparation for lactation).

No. of mammary glands increased as result of hyperplasia. this case is physiologic so after the pregnancy and lactation are gone everything back to normal.



## 2. Compensatory hyperplasia of the liver after partial resection (استئصال) of the liver.

Sometimes a part of the liver is removed in cases of trauma and hepatic tumor. The remaining cells of the liver will produce some growth factors that will stimulate the proliferation of hepatocytes to retain the normal pre resection size of the liver. This is a peculiar ability of the liver cells to restore the normal size of the liver.



**1. hyperplasia, estrogen induced  $\uparrow$ :** endometrial hyperplasia is driven by continuous **estrogenic stimulation**. Continuous estrogenic stimulation in these females can lead to endometrial hyperplasia. If this endometrial hyperplasia persists or not treated, it can transform at some point into the endometrial carcinoma. It can also happen even in premenopausal women.

## 2. Benign prostatic hyperplasia. Androgen induced $\uparrow$ .

In males, the prostate glands undergo hyperplasia. caused by hyper androgenic stimulation enlargement of the prostate gland.

## 3. Warts (ثوالميل)

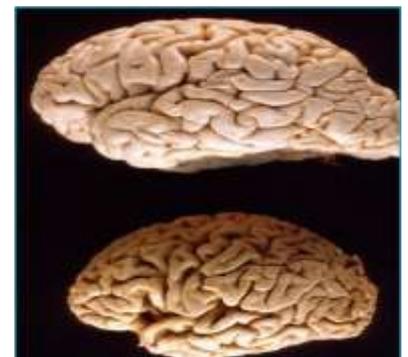
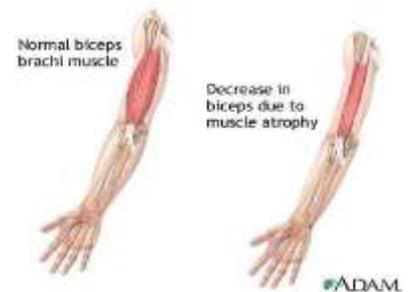
Caused by a virus called Human papilloma virus (HPV)

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## Atrophy

- **Decreased cell size & function** since the cell is still functioning that's means that the cell is still viable.
- **Mechanisms of cell atrophy:**
  - 1- Decrease protein synthesis
  - 2- Increase protein degradation.
  - 3- Increase in cell autophagy (in which the newly adaptive cell will eat it own organelles to generate energy زي كانها بتاكل نفسها عن طريق انها بتعمل autophagic vacuoles).
- **Atrophic cells can still function but in less activity.**
- **Causes:**
  - 1) **Decreased workload** (immobilization of a limb after fracture like when you put a splint جبيرة).
  - 2) **Loss of innervations** (if you cut a nerve after Trauma this will lead to decrease in your innervation for corresponding muscles or tissue which leads to atrophy).
  - 3) **Diminished blood supply** (patients that have ischemic issues in their limbs or the have arteriosclerosis of the skin in their lower limbs will be atrophied).
  - 4) **Inadequate nutrition.** (you are not supplying your body with what it needs)
  - 5) **Loss of endocrine stimulation.**

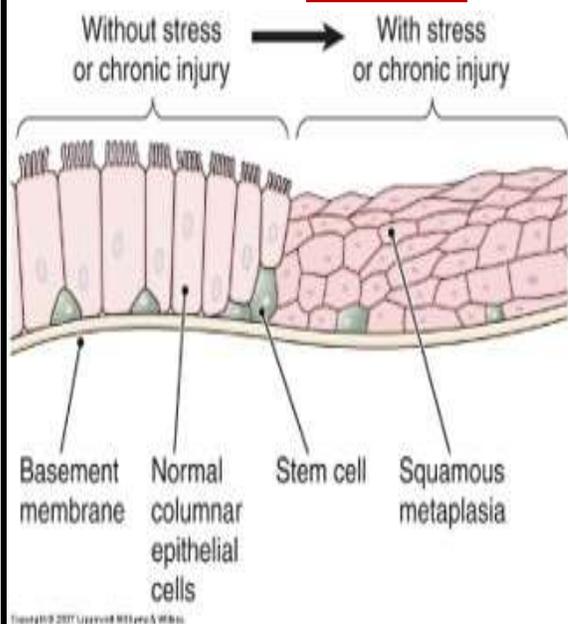
It can be **physiologic** (patients after menopause have normally decreased levels of estrogen in the blood, so they will develop endometrial atrophy) or **pathologic**.
  - 6) **Aging (senile atrophy)** of the brain the gyri shrunken, and the sulci increased in size.
- **Physiologic** Loss of hormone stimulation in menopause (endometrial atrophy) **or pathologic** Denervation injury. 1) Chronic ischemia (like the skin of lower limb in patients who have arteriosclerosis or diabetes).



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# Metaplasia

- Change from one cell type to another
- Reprogramming of stem cells NOT differentiated cells  
(the stem cells will change to another type of cells not the already differentiated cells)
- Persistent change increases risk of cancer
- New cell type copes better with stress but function less.
- Reversible



Metaplasia is not a transformation for differentiated cells, but it is a transformation at the level of stem cells. Eg: the epithelium that covers the bronchi is called **ciliated pseudostratified respiratory epithelium** which is generated from stem cells >>when this epithelium faces stress like smoking immediately will transform the stem cells into **squamous epithelium**. This epithelial tissue can withstand to these stresses more, but its function in purifying the air is reduced due to its inability to produce mucus and the disappearance of the cilia. When smoking continues, the risk of developing cancer increases, and therefore smokers are more vulnerable to lung cancer.

- Causes: (pathological)
  - 1- **Smoking**
  - 2- **Vitamin A deficiency** ---> Vitamin A is needed for normal epithelial differentiation; deficiency leads to squamous metaplasia of the bronchi.
  - 3- **GERD (Gastroesophageal reflux disease)** -----> in these patients, the normal lining of the esophagus is squamous epithelium, but when the patient has continuous reflux of gastric acidic content to the lower part of the esophagus, the squamous epithelium will change into glandular epithelium that can withstand to acidity, but its protection to the esophagus is less. The patient might have esophageal carcinoma if metaplasia persisted.

**Most of the time metaplasia is because of pathological causes .(the doctor didn't mentioned a physiological cause).**

## Causes of cell injury

### ❖ Oxygen Deprivation (Hypoxia )

there is a difference between hypoxia and ischemia, hypoxia means decrease in oxygen supply, while ischemia means decrease in blood supply which can lead to hypoxia .

- ischemia mostly is the result of occlusion of an artery by a thrombus or a blood clot, if it happened in the cerebral vessels, it could lead to O<sub>2</sub> deprivation in the brain, or in the heart and causes myocardial infraction.
- The main mechanism of ischemia in causing cell injury is the lack of blood supply which leads to lack of oxygen supply (oxygen is needed by all cells in their metabolism and their energy production).
- All cells needs O<sub>2</sub> to work ,so hypoxia leads to cell injury.
- Hypoxia has other reasons than ischemia such as pulmonary hypertension, emphysema, and obstructive pulmonary diseases.(Doctor said don't worry about the other causes)

### ❖ Chemical Agents.

Like sugar, drugs, Pesticides and insecticides.

### ❖ Infectious Agents.

Such as viruses, bacteria, protozoa, parasites and worms.

### ❖ Immunologic Reactions.

Autoimmune, allergic, microbes. allergic conditions such as: rhinitis, conjunctivitis and eczema.

### ❖ Genetic Factors.

Starting from chromosomal abnormalities such as: down Syndrome ending with single gene defects that lead to abnormal enzymatic activity.

It also could lead to some diseases such as certain types of anemia.

### ❖ Nutritional Imbalances.

Whether from **under nutrition or malnutrition**(سوء التغذية) by not getting enough of certain types of food, **or from excess nutrition** by getting excess food, which leads to obesity and it is associated with diseases.

### ❖ Physical Agents.

Such as: Trauma, extremes of temperature and Electric shock.

### ❖ Aging.

# THE END