بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Pathology | Lecture #1

Cellular Adaptations

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Cellular Adaptations

cell injury and adaptations

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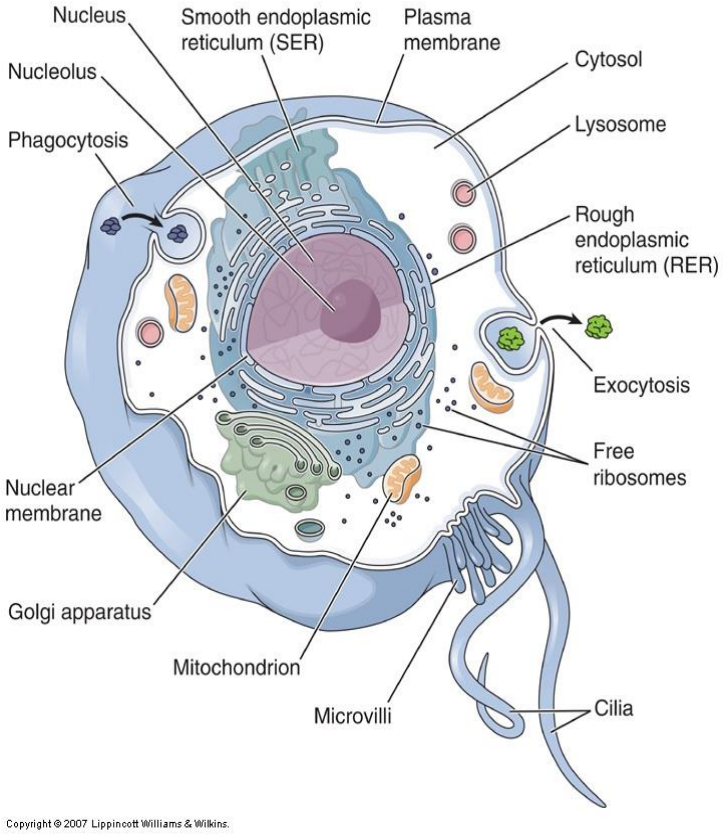
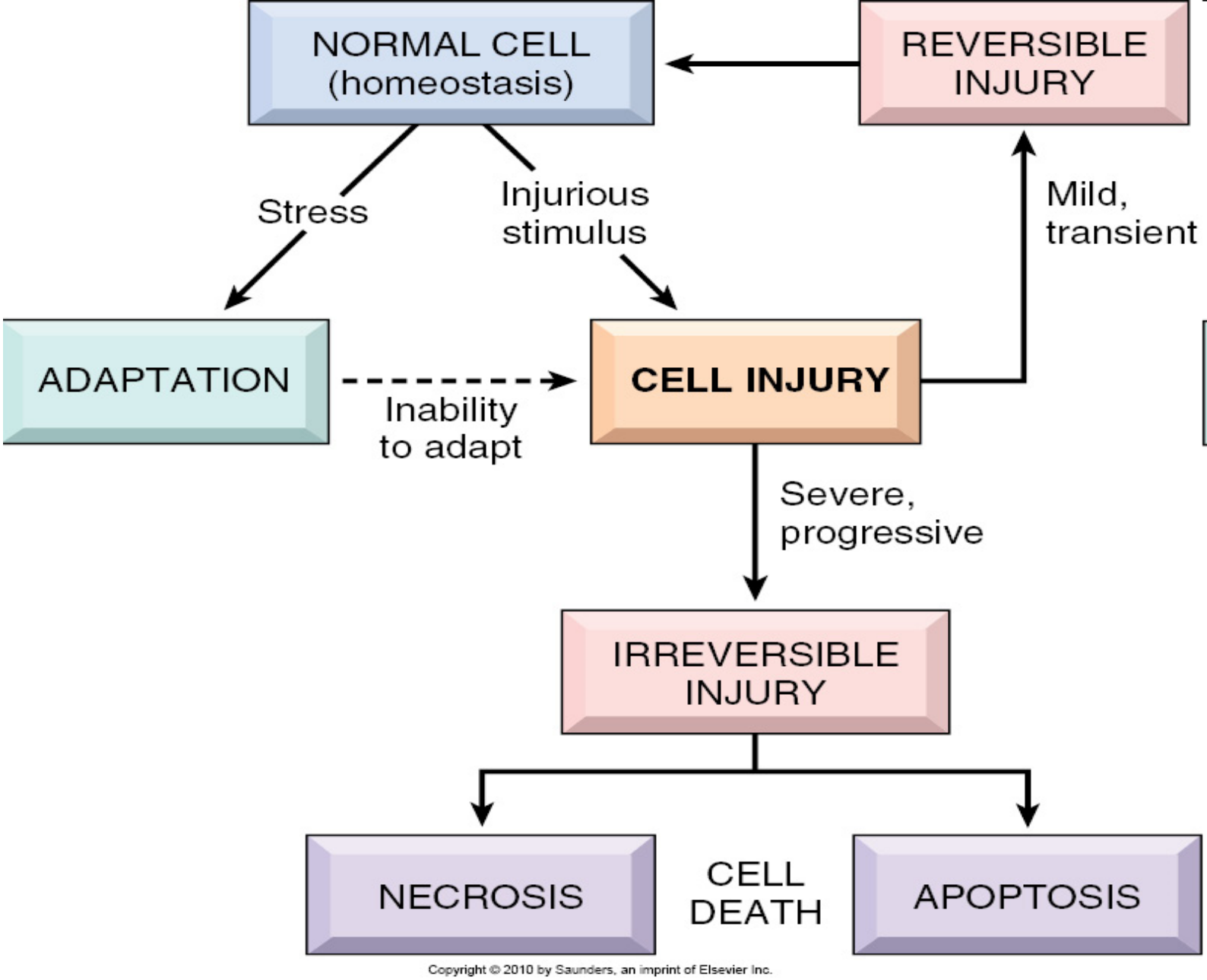
Outlines:

Adaptive Mechanisms

- 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.



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…



- 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 and becomes 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: -reversible (when the stimulus disappears everything will return back to normal) or -irreversible(which equal 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.

Everything will be discussed in details later this is just a our plan

Adaptations

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 in cell life.
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): causes increase in the size of organ

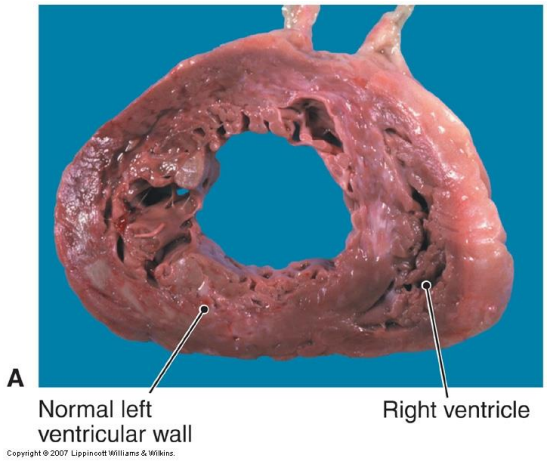
- Decrease in cell size(atrophy): causes decrease the size of organ
- Increase in number of cells. (hyperplasia): causes increase in the size of organ
- Change into another type of cell.(metaplasia)

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

Hypertrophy

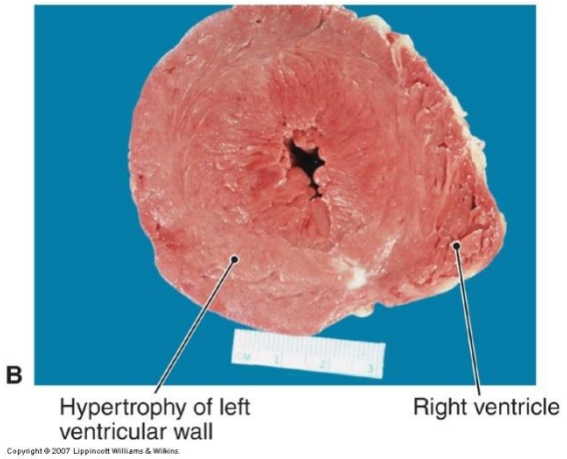
- **Increased size & functional capacity**
- **Pure or mixed**
- **Increased structural proteins and organelles.**
- **Pathologic vs physiologic**

Normal heart



- **Due to**
  - **hormonal stimulation**
  - **Growth factor stimulation**
  - **increased functional demand**

Heart with hypertrophy



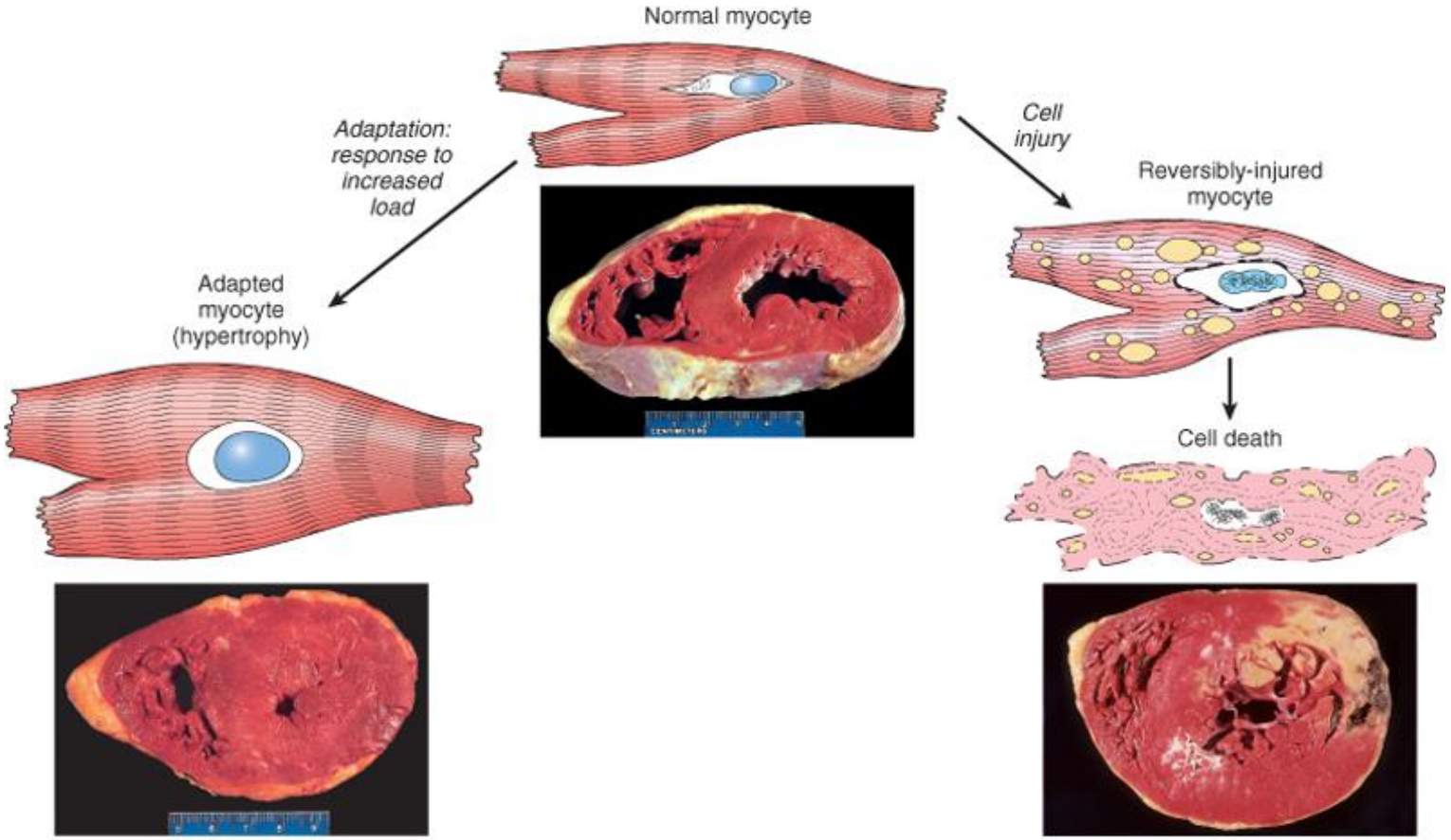
Hypertrophy increases the functional capacity of the cell. The heart, for example, will increase its pumping capacity and contraction force. Hypertrophy can be pure or mixed. The determining factor is proliferative capacity, so some tissues are terminally differentiated (can no longer proliferate) (like cardiac muscle, skeletal muscle, and neurons) so they can only undergo hypertrophy but can't undergo hyperplasia (pure). Whereas the cells that could undergo mitosis can get hypertrophy and hyperplasia at the same time (like epithelium cells) (mixed). The mechanism of hypertrophy is by increasing structural proteins and number of organelles. The cause could be pathologic and physiologic (like all adaptation mechanisms).

The causes of hypertrophy

1. hormonal stimulation(**leads to an increase in size and number of cells (hypertrophy and hyperplasia). For example during pregnancy due to estrogen)**
2. Growth factor stimulation
3. increased functional demand(**like heart in hypertension)**

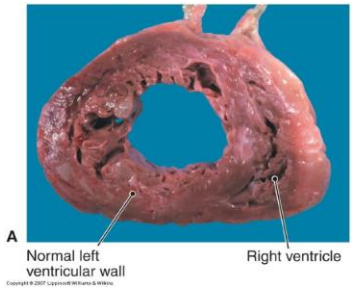
Pathologic

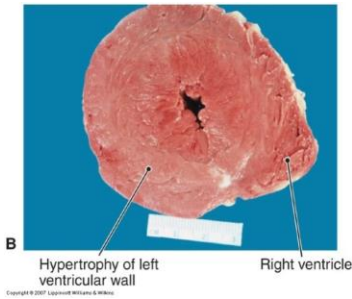
cardiac muscle in hypertension and aortic stenosis



Pathologic(cardiac muscle in hypertension and aortic stenosis)

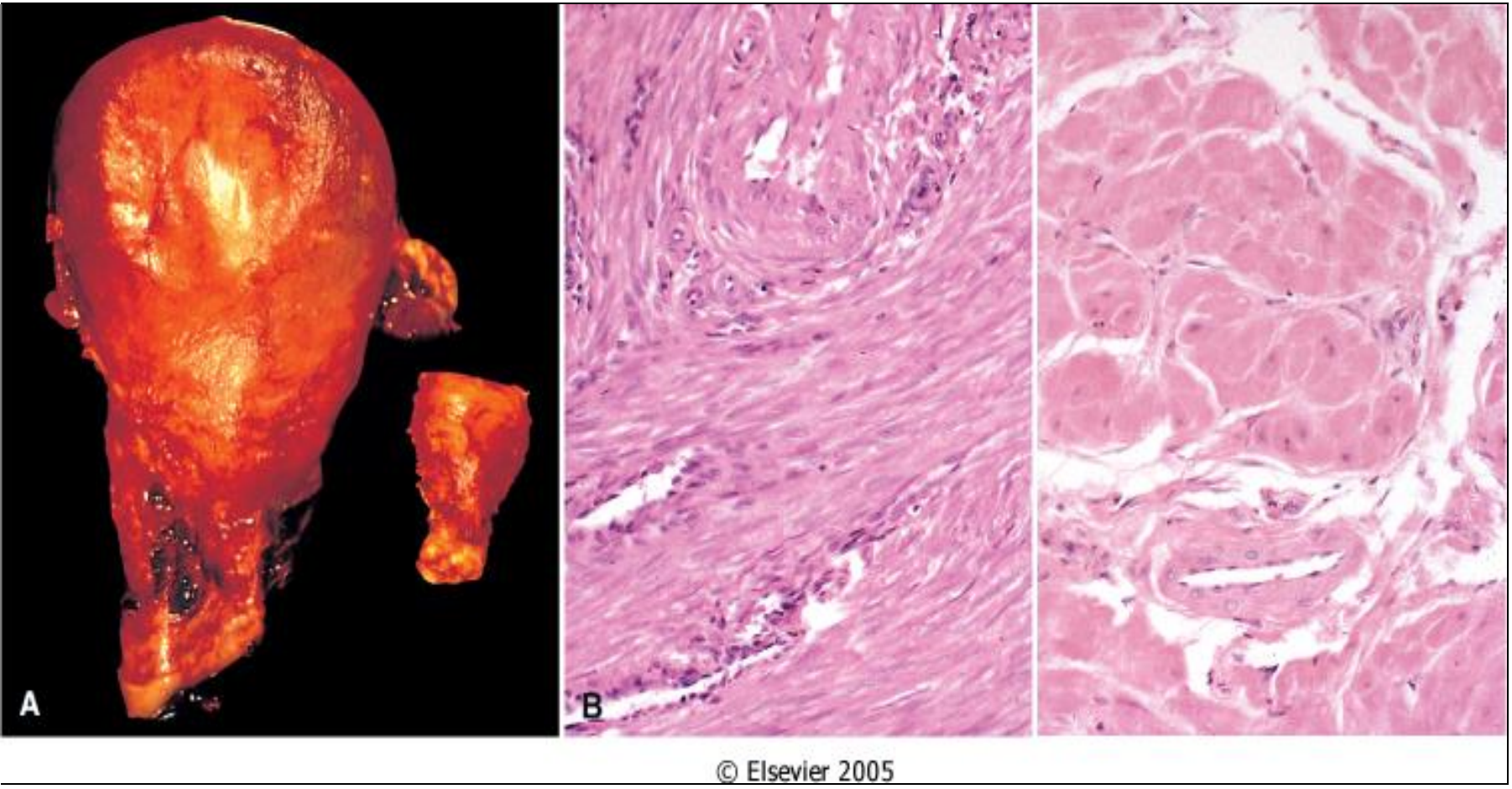
At hypertension case, peripheral resistance in blood vessels is increased, so the heart has to pump against a higher resistance, so heart must pump stronger, so heart size will increase **only** by hypertrophy(pure). As we said, hypertrophy is reversible, but it has limits so sometimes uncontrolled hypertension 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 could lead to heart failure in uncontrolled hypertension. In few words (hypertension .....hypertrophy (we get a benefit initially).....heart failure). Also, the increase in the myocardium size will lead to a higher 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 .





Physiologic

uterine smooth muscle in pregnancy

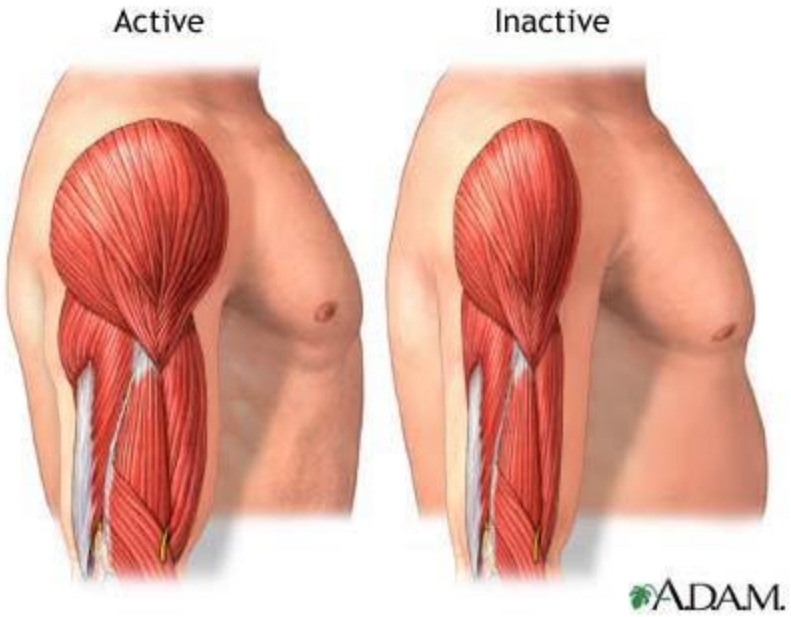


Physiologic(uterine smooth muscle in pregnancy)

- 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, the uterus enlarges to accommodate the baby. It is reversible so after pregnancy, uterine shrinks when hormone levels are back to normal.

Physiologic skeletal muscle in athletes

Increasing the load on the skeletal muscles will increase the muscle size(hypertrophy)



Hyperplasia

- Increase in number of cells(**definition)**

- 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)

Physiologic

- hormonal stimulation e.g uterus in pregnancy

  e.g Breast in puberty and pregnancy(increase in the number of glandular cell in the breast)

- Compensatory

  e.g liver after partial resection due to cancer (benign or malignant) or accidents, it will proliferate and return back to its normal size.

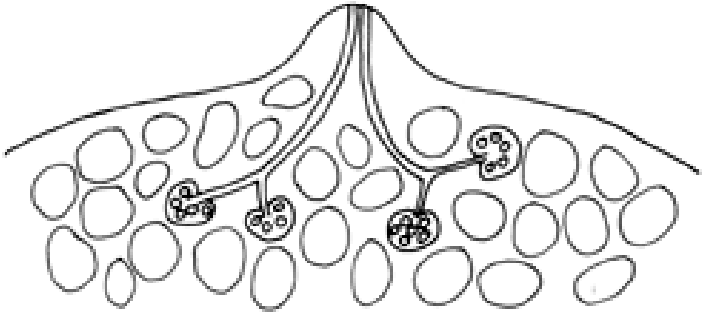
• Pathologic

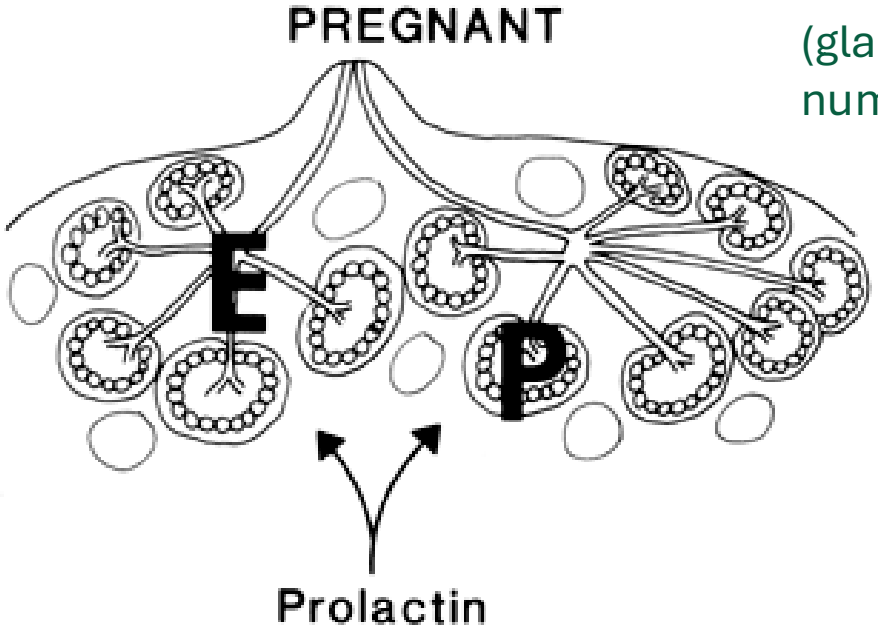
- excessive hormonal stimulation
  - Endometrial hyperplasia(serous disease and could cause cancer) and it is estrogen induced.
  - Benign prostatic hyperplasia(prostate of elderly men and cause enlargement of prostate under hormonal effect) and it is androgen induced.
- Viral Infections Warts (HPV) (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





Endometrial Hyperplasia which is physiologic. (glandular epithelium number is increased)

Pathologic
endometrial hyperplasia, estrogen induced

In this case uterus could 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)**

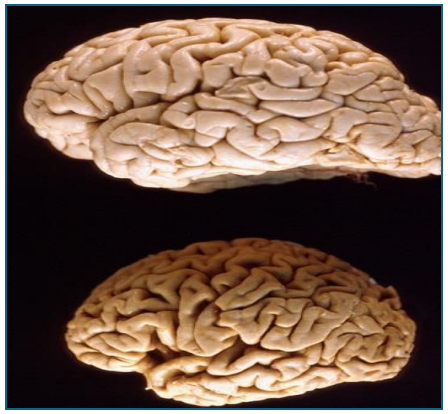
↑ Autophagy **(cell will start eating itself to produce energy)**

- 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 factor 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,
- Inadequate nutrition
- Loss of endocrine stimulation **NEXT SLIDE**
- Aging (senile atrophy)



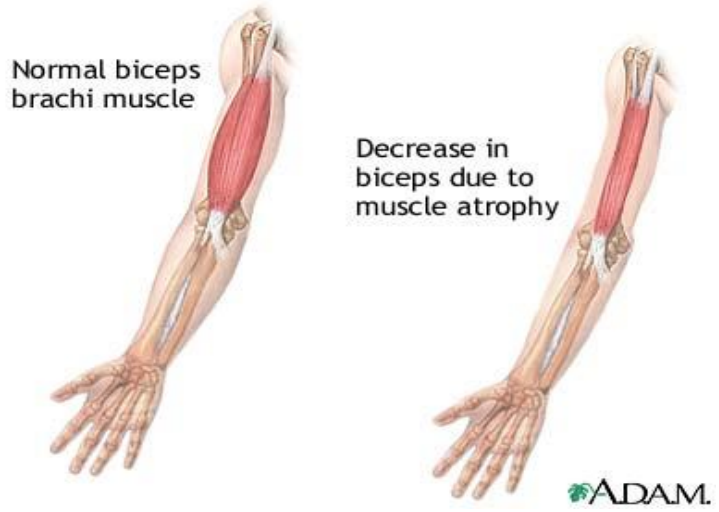
Loss of innervations and blood supply is an important cause, all muscles need oxygen, blood and nerves to contract and do its function, so if we have a problem in the blood supply, nutrients, oxygen or nerve supply because of ischemia, nutritional deficiency, or any other reason, muscles will start to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

Brain can suffer atrophy because of : aging – chronic ischemia – Alzheimer and this will lead to a shrink in the brain tissue.

Causes of Atrophy

- **1- <u>Decreased workload demand</u>**, 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 if we a lower levels in hormones the cells will start to shrink and become thinner.

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



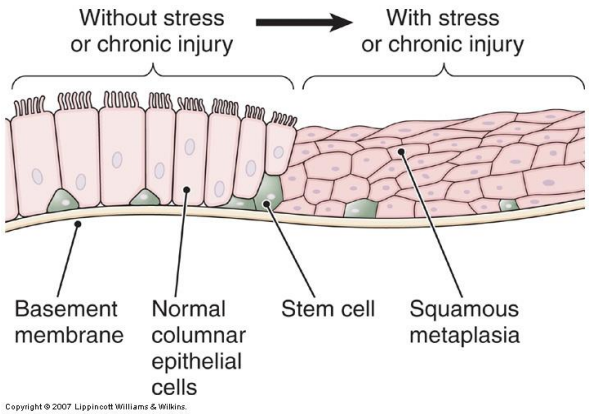
As a conclusion of reasons

- **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
- Diabetes mellitus

Metaplasia

- 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)



What is Metaplasia ? **Important**

- We mean that the cells are now of 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 if the cell didn'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, these pseudostratified columnar epithelial cells are replaced with squamous cells as a protective mechanism to deal with stress, but this comes at the cost of normal function(dust and microorganisms could enter lungs).
- Vitamin A is needed for the terminal differentiation of cells, so its deficiency could cause metaplasia mainly in bronchi.
- 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.
- 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.

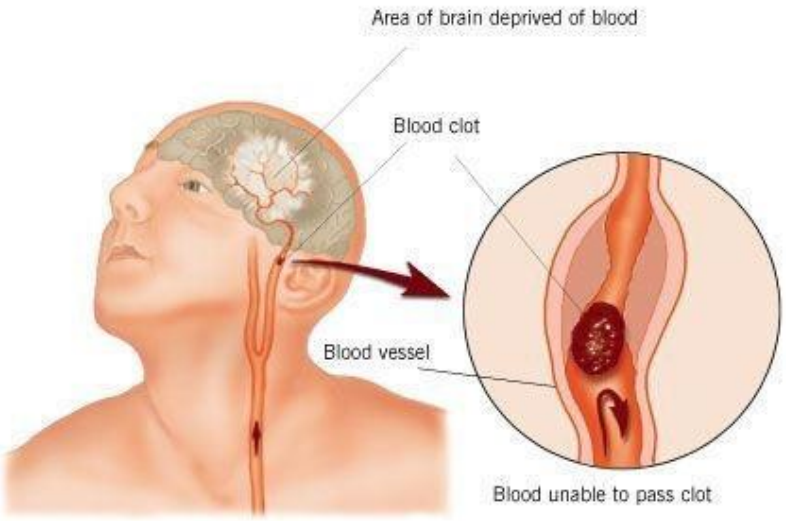
CAUSES OF CELL INJURY

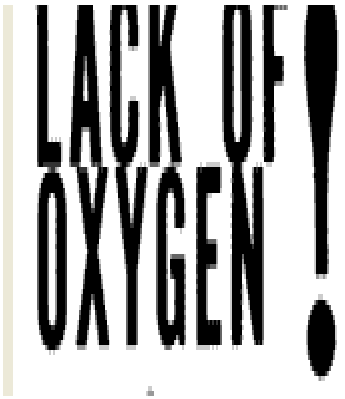
- Oxygen Deprivation (Hypoxia Vs ischemia)
- Chemical Agents
- Infectious Agents
- Immunologic Reactions
- Genetic Factors
- Nutritional Imbalances
- Physical Agents
- Aging

(Each will be explained in a slide)

Oxygen Deprivation

The most common Cause of cell injury





The most common reason of hypoxia is ischemia(ischemia to the heart causes angina or myocardial infarction, ischemia to the kidney causes infarction, etc.), but there are other reasons that can lead to hypoxia such as respiratory diseases for example (asthma-anemia), carbon monoxide poisoning, and high altitudes.

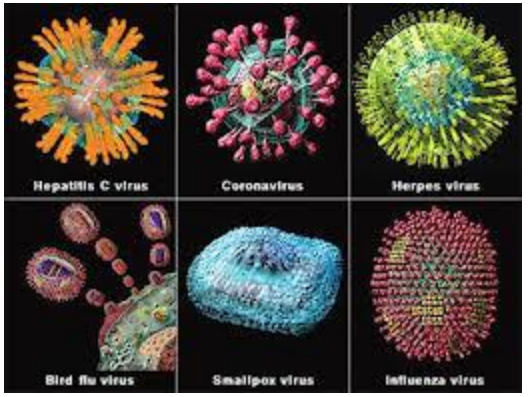
Chemical Agents

The strong chemicals such as pesticides, insecticides, or glucose

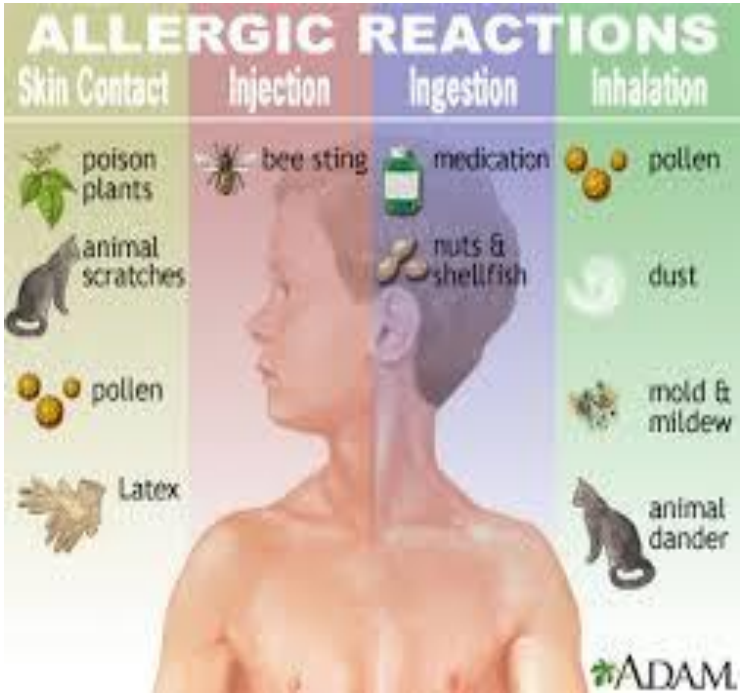
Cell injuries that are happened by diabetes are mainly caused by glucose so if our body has a high levels of glucose this can lead to the death of cells if it is not controlled.

Infectious Agents

Viruses, bacteria and fungi are examples of pathogens that cause cell injury. Any disease starts with cell injury, the cell injury start at the level of cells->tissues->organs->whole body.



Immunologic Reactions
autoimmune, allergic, microbes

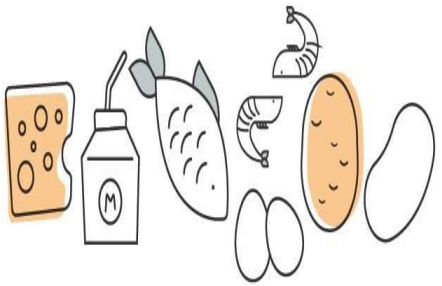


Genetic Factors

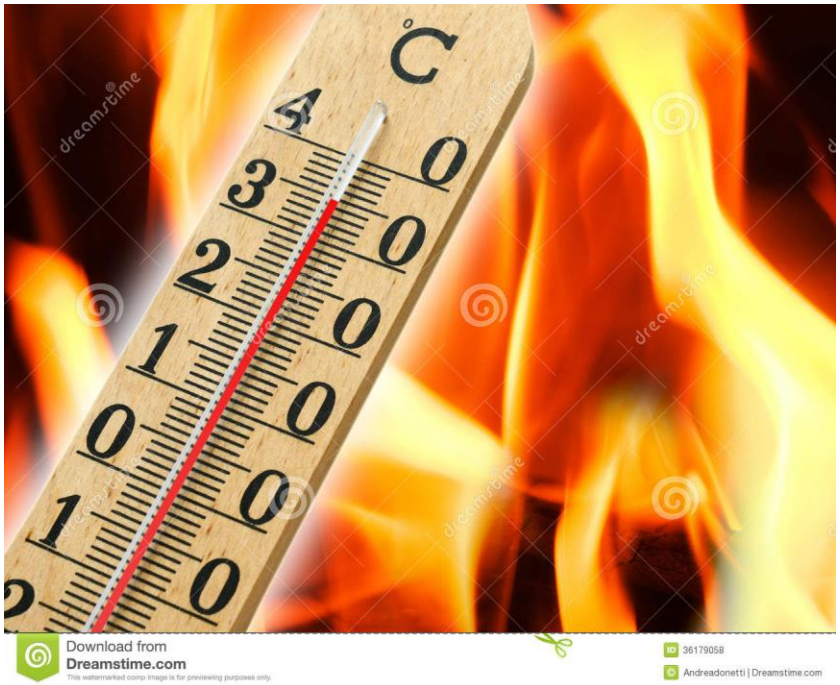
Down syndrome or cystic fibrosis are examples of genetic cell injuries; it mainly happens when there is a change in the DNA and it will lead to different cell injuries in different systems of the body.

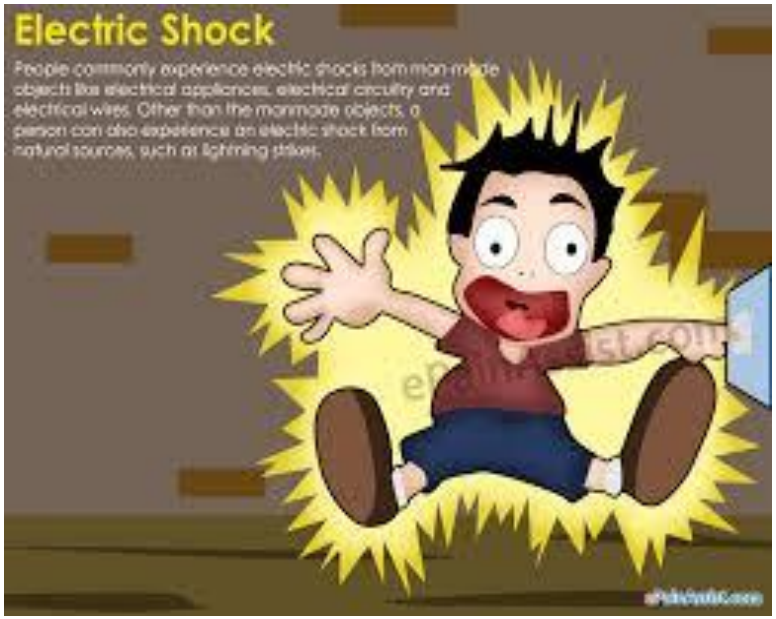
Nutritional Imbalances

Over-nutrition or under-nutrition can lead to cell injuries.



Physical Agents





Additional Resources:

رسالة من الفريق العلمي:

Extra References for the Reader to Use:

1. MED Today (cell injury) - youtube

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

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			