PATHOLOGY

بسم الله الرحمن الرحيم

MID – Lecture 1

Cellular Adaptation

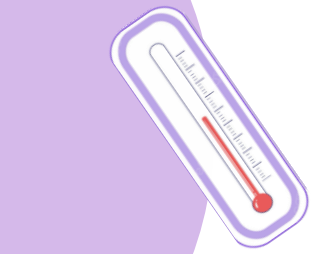
﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

Written by:

- **Sara Masadeh**
- **Fatma Attia**

Reviewed by:



Cellular Adaptations

cell injury and adaptations
Manar Hajeer, MD, FRCPath
University of Jordan , school of medicine

REFERENCE BOOK: Robbins basic pathology 10th edition

Cellular Adaptation: Coping with stress

Outlines:

- Adaptive mechanisms (4 mechanisms):

1-Hypertrophy
2-Hyperplasia
3-Atrophy
4-Metaplasia

All these adaptive mechanisms are reversible

Which means that once the stress is gone the cell can restore to its normal state (homeostasis)

- Causes of cell injury.

The cell

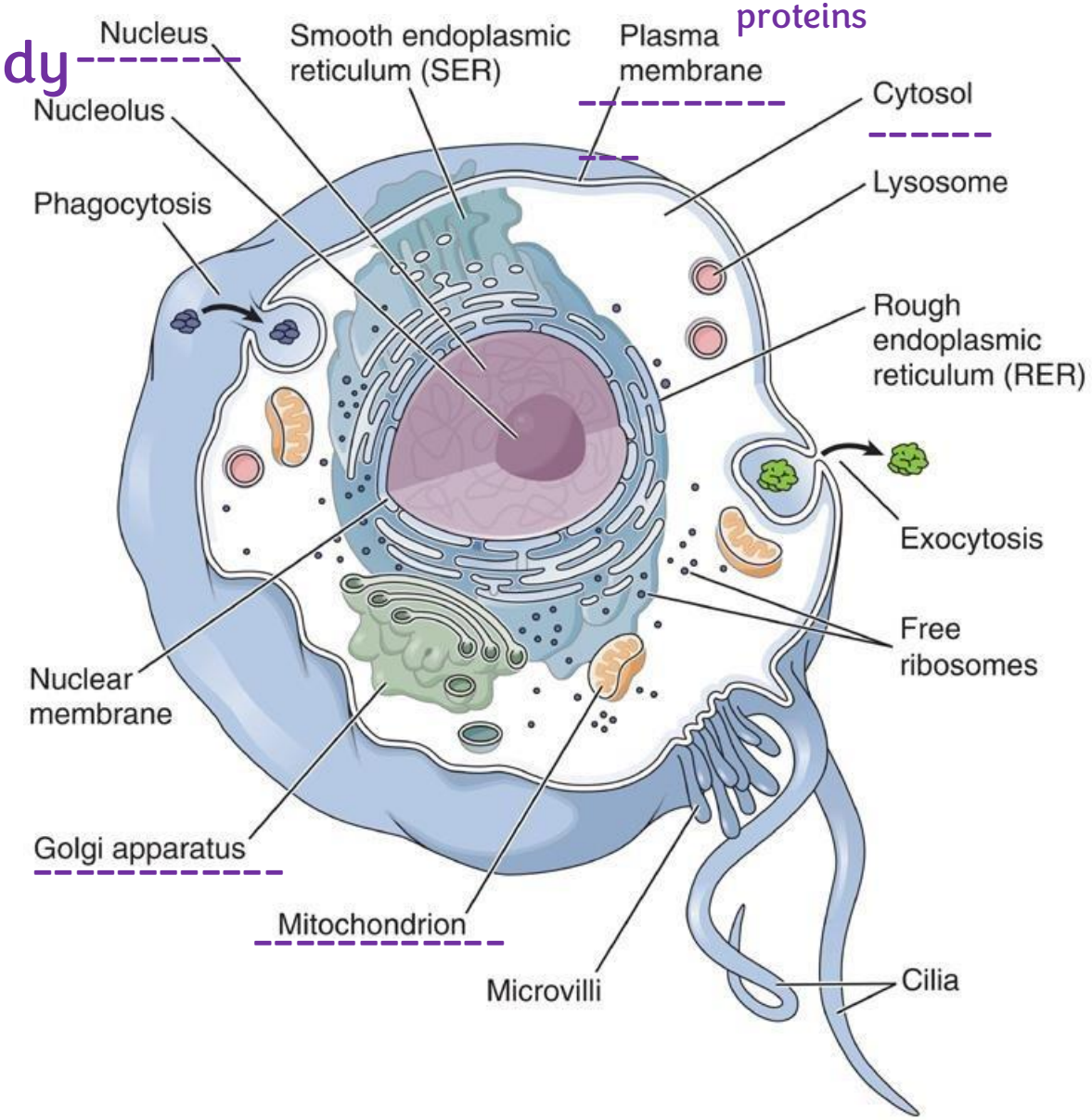
The building unit of the human body

When any disease starts ,it initially starts at the level of the cell → the level of the tissue → the level of the organ → the level of the human body

The cell lives in homeostasis (balanced environment) , so that every part of the cell is maintained within a narrow range of the PH , Temperature and concentration of different substances

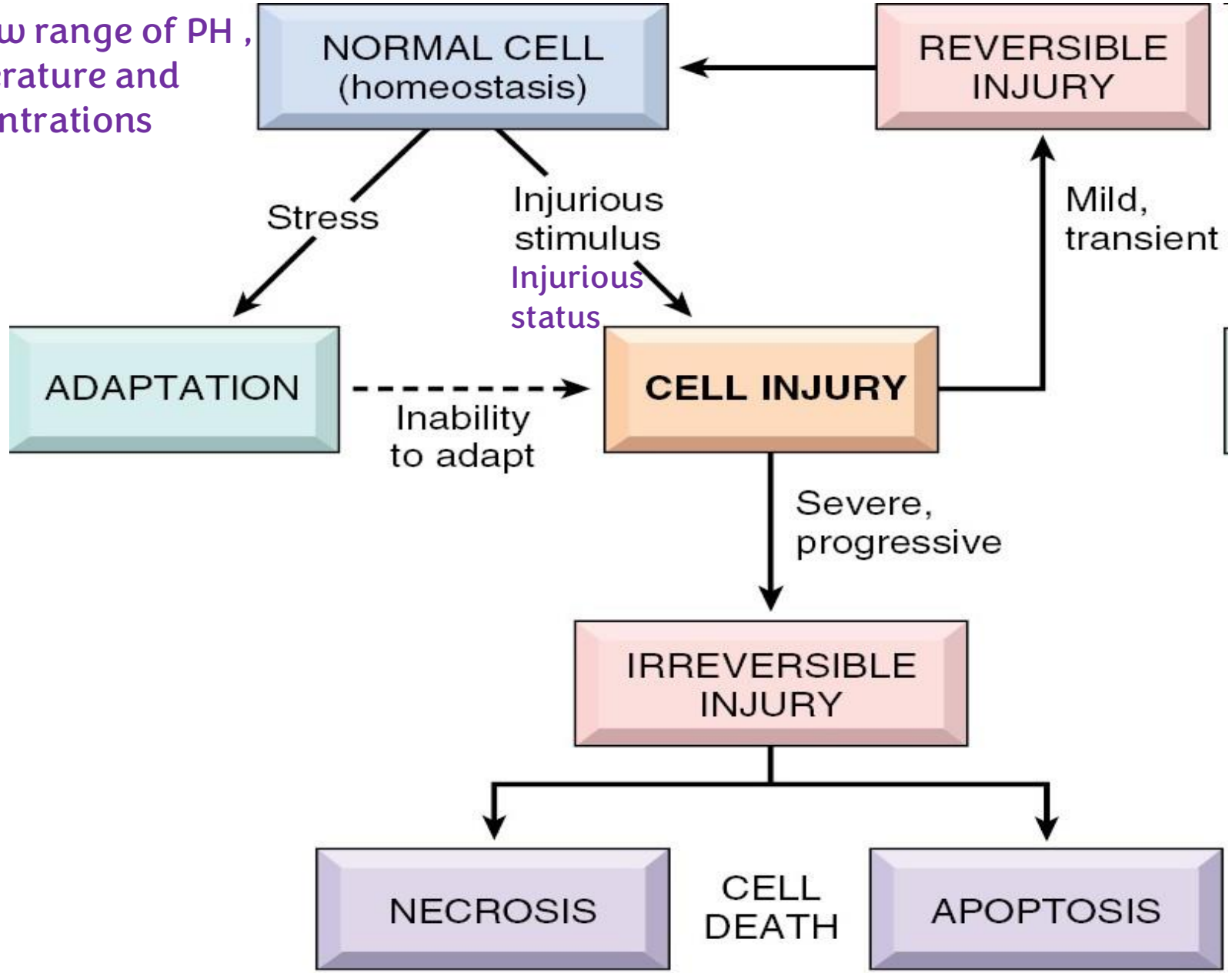
Contains the DNA material

Phospholipid bilayer + proteins



Narrow range of PH , temperature and concentrations

When the cell is under stress or cell injury (injurious status) . First it would try to adapt -by the 4 mechanisms-, if the adaptation failed (because of prolonged or very severe stress condition , or because the cell itself is diseased from the beginning - before the stress starts-) ,the cell will enter the cell injury which is also divided into 2 types;
1- Reversible injury: once the stressful condition is removed the cell will go back into its normal state (cell is alive but not functioning).
2- Irreversible injury : once the stressful condition is removed , the cell is already dead
Irreversible injury = cell death (by either necrosis or apoptosis).



In very severe injuries

When injurious stimulus is less severe or in certain conditions

Adaptations

Physiologic adaptation

There is no disease , happens for normal reasons (e.g.: pregnancy)

Pathologic adaptation.

Pathology : the study of diseases
So, in the pathologic adaptation the cause is usually a disease

Adaptations

- **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)

The cell should be able to replicate so that it can undergo hyperplasia

All these mechanisms are reversible ; once the stressful event is removed the cell can go back to the normal

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

Hypertrophy

- Increased size & functional capacity
- Pure or mixed

The function won't increase forever , it will reach a plateau and eventually the cell won't be able to function well

Pure hypertrophy :only hypertrophy ,no hyperplasia in the cells that has no differentiation ability (terminally differentiated cells) such as : cardiac cells , nerve cells and skeletal muscle cells.

Mixed hypertrophy : the cell is able to adapt both of hypertrophy and hyperplasia mechanisms at the same time , such as: epithelial cells, smooth muscle cells

- How the cell size increases (mechanism of hypertrophy)? By Increased structures' proteins and organelles.
- Pathologic vs physiologic

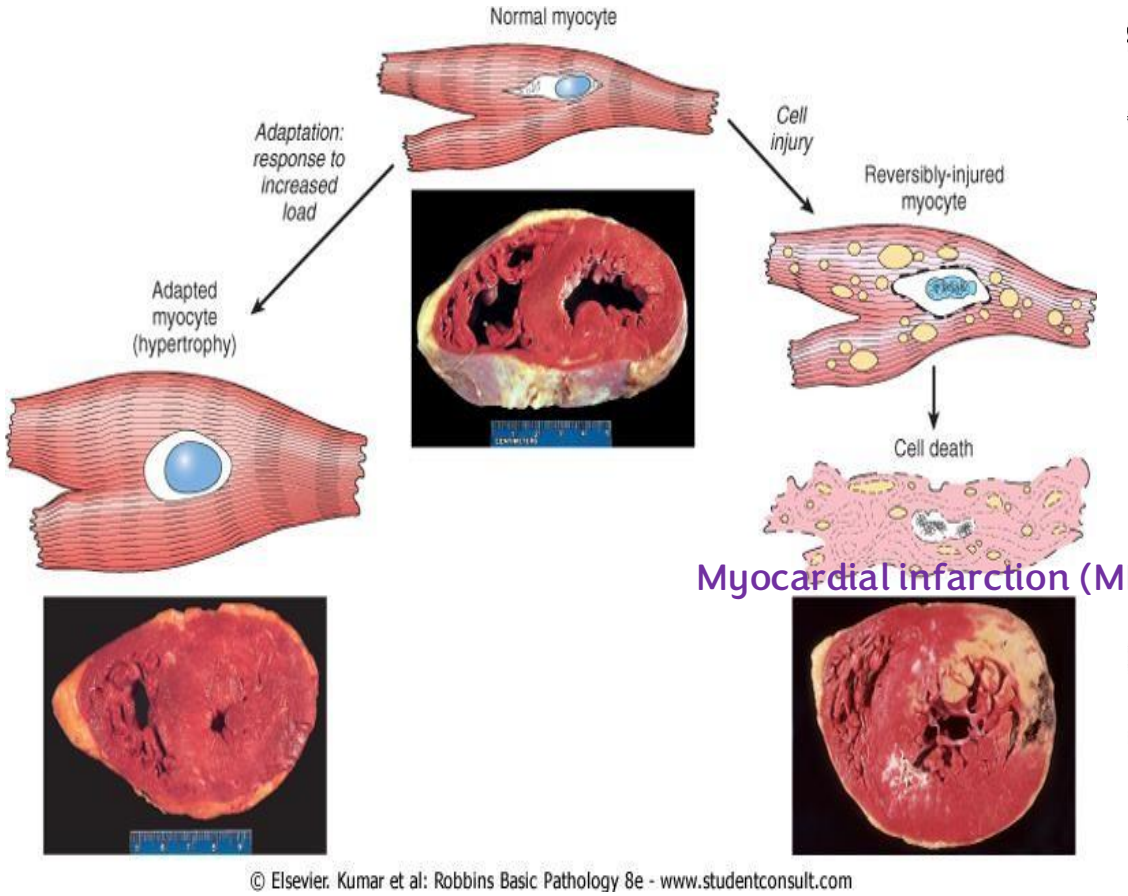
- Due to (the underlying causes of hypertrophy)
  - hormonal stimulation
  - Growth factor stimulation
  - increased functional demand (workload)

Cardiac Muscle Hypertrophy

Pathologic | Happens because of increased workload

cardiac muscle in hypertension and aortic stenosis تضيق

- Because of hypertension and aortic stenosis, workload increases because heart is bumping blood against high resistance. How? By increasing pumping capacity by hypertrophy
- Since pathological causes (hypertension / aortic stenosis) caused the adaptation → it's a pathological adaptation.
- Although the muscle's capacity increases initially ,but a certain point the muscle will become weak which can lead to heart failure.



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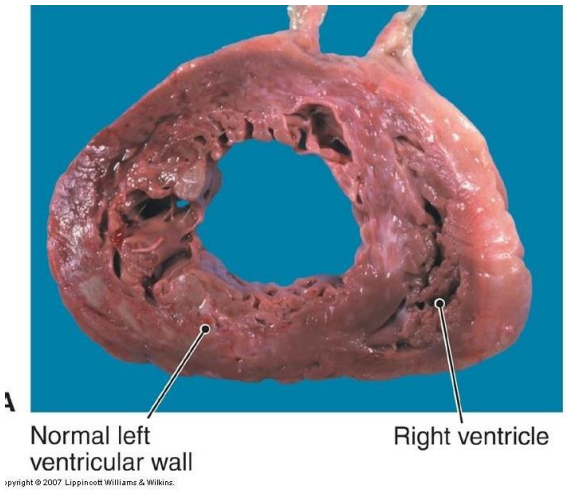
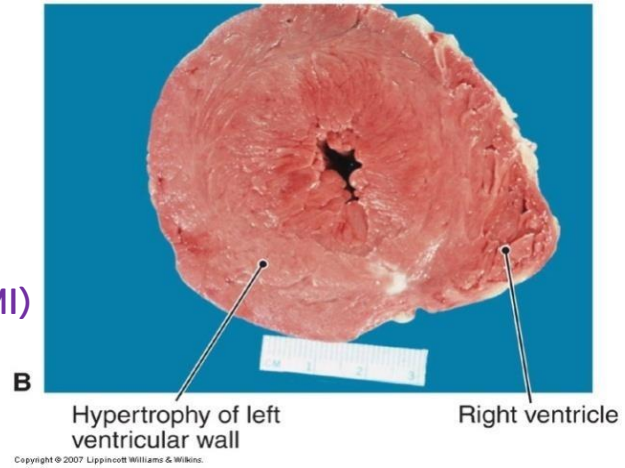
Myocardial infarction (MI)



Normal heart wall thickness (no hypertrophy)



Hypertrophy of the left ventricle of the heart

Notice the lumen of the left ventricle decreased a lot , so even though the pumping capacity increased it won't be able to compensate and supply all the heart muscles

Uterine Smooth Muscles Hypertrophy

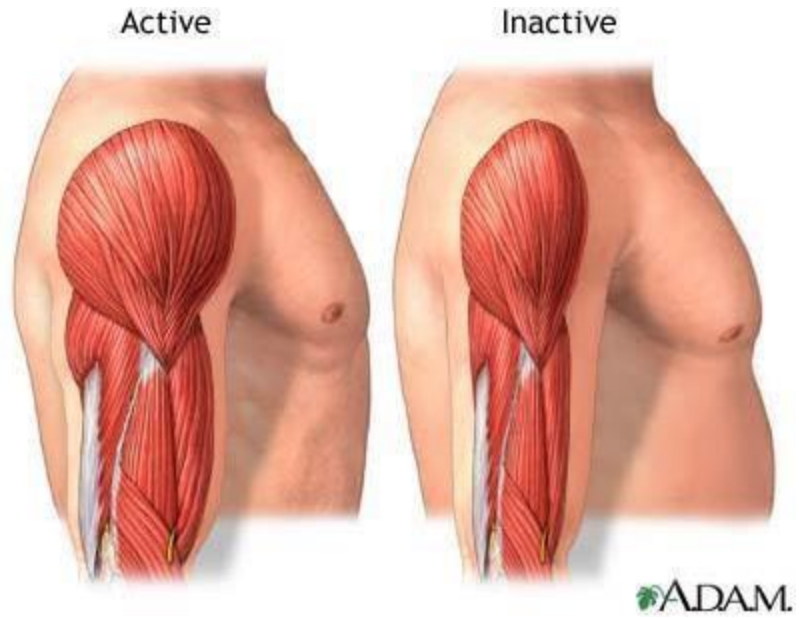
Physiologic

Mixed Hypertrophy ,since uterine smooth muscle can undergo both Hypertrophy and Hyperplasia

uterine smooth muscle in pregnancy

Skeletal Muscle Hypertrophy

Physiologic
skeletal muscle in athletes



- It's pure hypertrophy
- Caused by increasing demand on muscles

Hyperplasia

Recall: all cells have proliferative ability except:
Nerve cells
Skeletal muscle cells
Cardiac muscle cells

- Increase in number of cells
- Tissues that have proliferative ability
- Pure vs Mixed
- Physiologic vs Pathologic vs cancer (Depending on the driving force)

- Physiologic hyperplasia:
- hormonal stimulation (examples: uterus during pregnancy / breast during puberty and lactation)
  - Compensatory (in liver)

تعويضي

  - Pathologic hyperplasia constitutes a fertile soil in which cancers may eventually arise. (endometrial)

- Pathologic hyperplasia
  - excessive hormonal stimulation
  - Viral Infections

Hypertrophy and Hyperplasia will both lead to enlargement of the organ eventually

- **Physiologic**
- Breast in puberty and pregnancy
- Liver after partial resection (compensatory hyperplasia)

*Removed because of a tumor or a trauma accident

If a part of the liver is removed (even if its ¾ is removed) ,the liver can restore its original volume in 3 months سبحان الله

- **Pathologic**
- Endometrial hyperplasia, estrogen induced. (prolonged excessive estrogenic stimulation)

The problem with pathologic hyperplasia that it can develop to malignancy if left untreated (fertile soil For cancer development) ,For example : endometrial hyperplasia can develop into endometrial cancer

- Benign حميد prostatic hyperplasia, androgen induced. Aka Nodular prostatic hyperplasia

Hormonal stimulus

Since its benign it won't develop into cancer

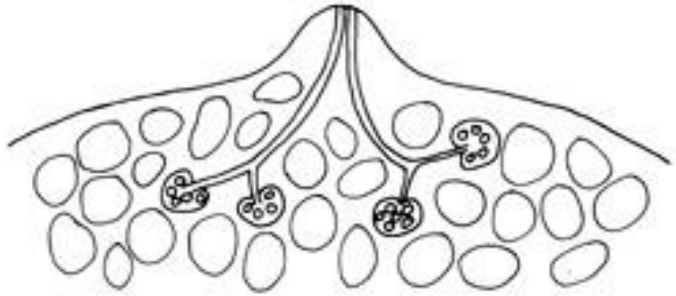
Although aging is normal and physiological, but its prostatic hyperplasia causes pathological symptoms (urinary symptoms)

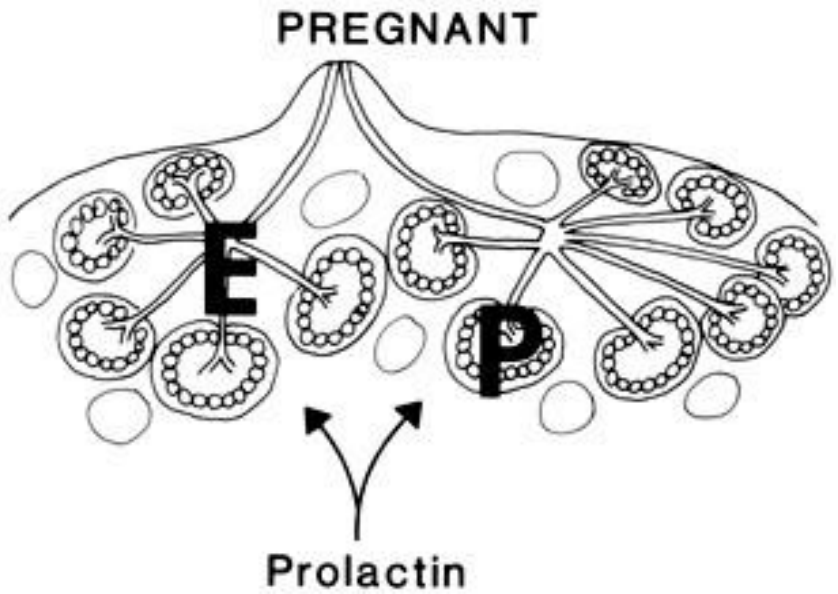
- Warts (HPV). Viral infection which caused by HPV (Human papillomavirus) which affect squamous epithelial cells and its contagious معدي

Breast Hyperplasia

Physiologic
breast in pregnancy and lactation

Hormonal stimulation → increase the number of glands→ enlargement in the size of the breast





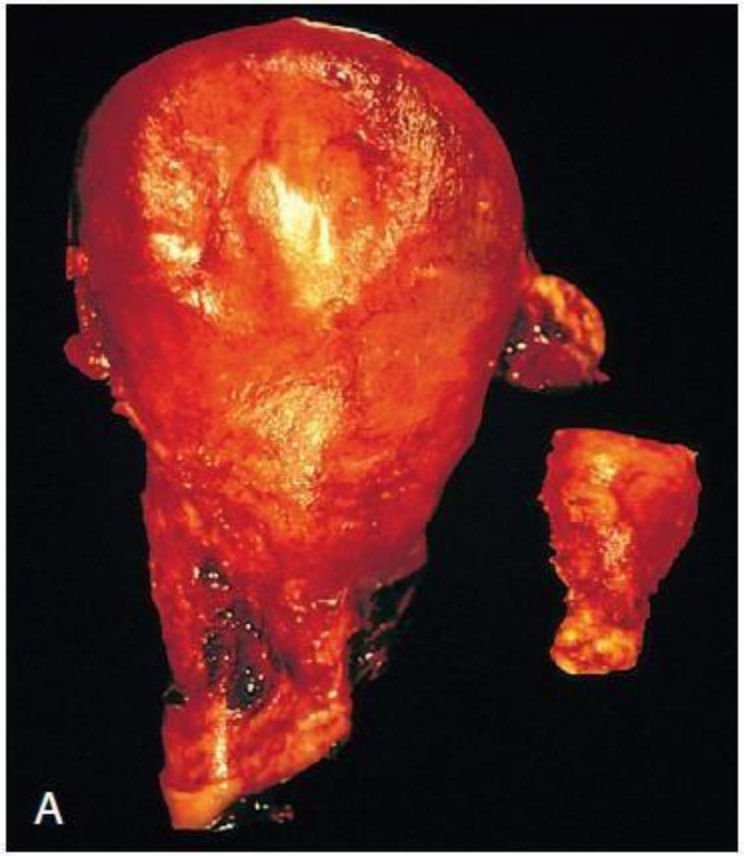
Endometrial Hyperplasia

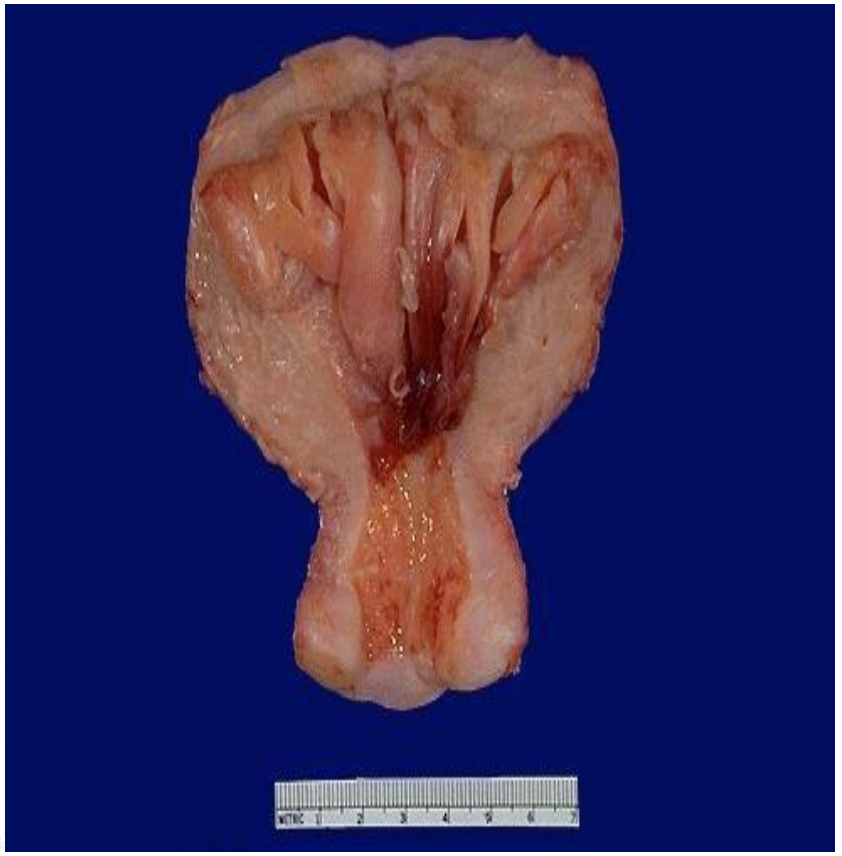
Pathologic

endometrial hyperplasia, estrogen induced

Doesn't cause uterus enlargement

Thick folds of the endometrium



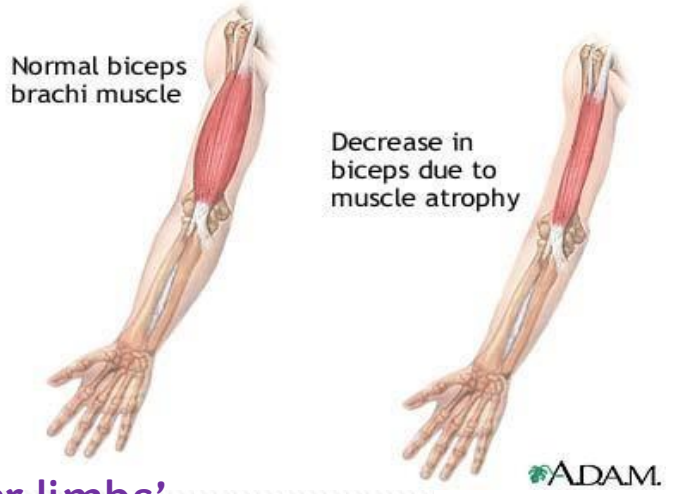


Note: Dr Manar mentioned that there is no images in the exam , however , they are important to understand the concepts

Atrophy

- Decreased cell size & function Cell becomes weaker
- Mechanism:↓ Protein synthesis
  ↑protein Degradation
  ↑ Autophagy (self-eating) The cell is in starvation status
- Atrophic cells can still function (although it's shrunk it's still alive and functioning but with decreased capacity)

Causes:



- Decreased workload (immobilization of a limb after fracture)

  That's why patients usually need physiotherapy after cast removal

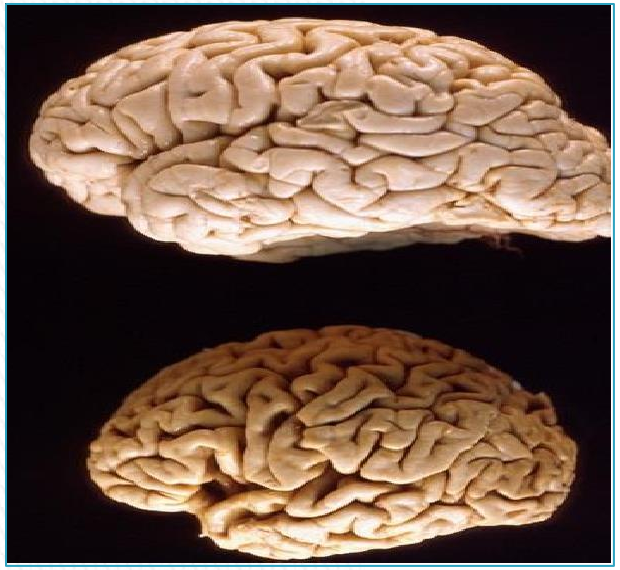
- Loss of innervations
  - like what happens after huge accidents of spinal cord injury ,since these nerves supply skeletal muscles , they will atrophy .
  - Wasted muscles are also noticeable in diabetic neuropathy patients' lower limbs' .
  - MS (multiple sclerosis) can cause muscle atrophy as well.
- Diminished blood supply. (Ischemia)
- Inadequate nutrition

People with protein allergy malnutrition are susceptible to muscle atrophy

- Loss of endocrine stimulation

One the opposite side of endometrial hyperplasia which are caused by induced estrogen , estrogen stimulation in women after menopause stops ,so the decreased estrogen levels will cause endometrial atrophy

→since it's a physiological cause it won't turn into cancer

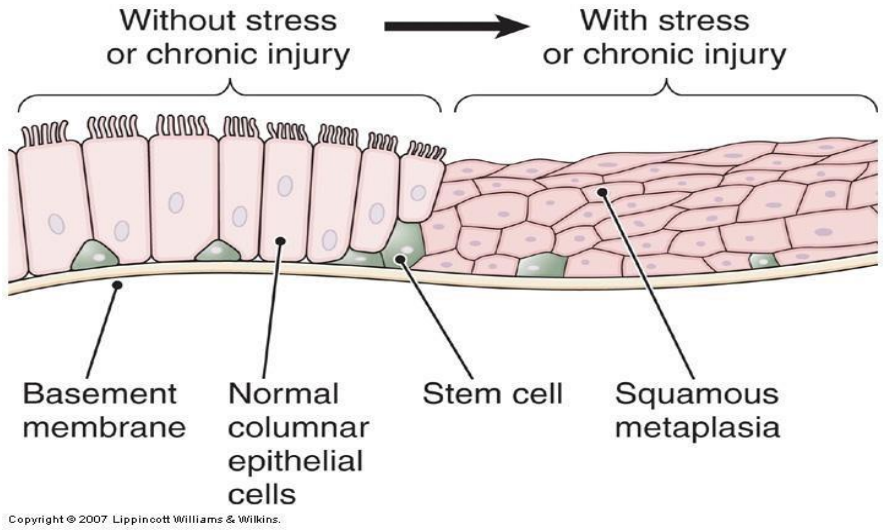


- Aging (senile atrophy)

- **Physiologic**
- Loss of hormone stimulation in menopause (endometrial atrophy)

- **Pathologic**
- Denervation injury.
- Chronic ischemia.

Metaplasia



- Change from one cell type to another
- Reprogramming of stem cells NOT differentiated cells
  Since its reversible, when the cause ends , the stem cells reprogram to its original system
- Persistent change increases risk of cancer
- New cell type copes better with stress but function less.
- Reversible
- Causes:

Smoking : turns the bronchial tree epithelium which has cilia and mucus production to stratified squamous epithelium which is devoid of protective mechanisms and increases the risk of lung cancer.

Vitamin A deficiency : Vitamin A is needed for normal epithelial differentiation; deficiency leads to squamous metaplasia of the bronchi (instead of respiratory type epithelium –pseudostratified ciliated columnar epithelium with goblet cells–)

GERD (Gastroesophageal reflux disease):reflux of acidic juices of the stomach to the esophagus cause the lining of the esophagus which is originally stratified squamous epithelium to switch off to another type which is intestinal type epithelium with goblet cells (intestinal metaplasia aka Barrett's esophagus) , it will also increase the risk of esophageal carcinoma.

Cell injury and death

CAUSES OF CELL INJURY

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

Lack of oxygen

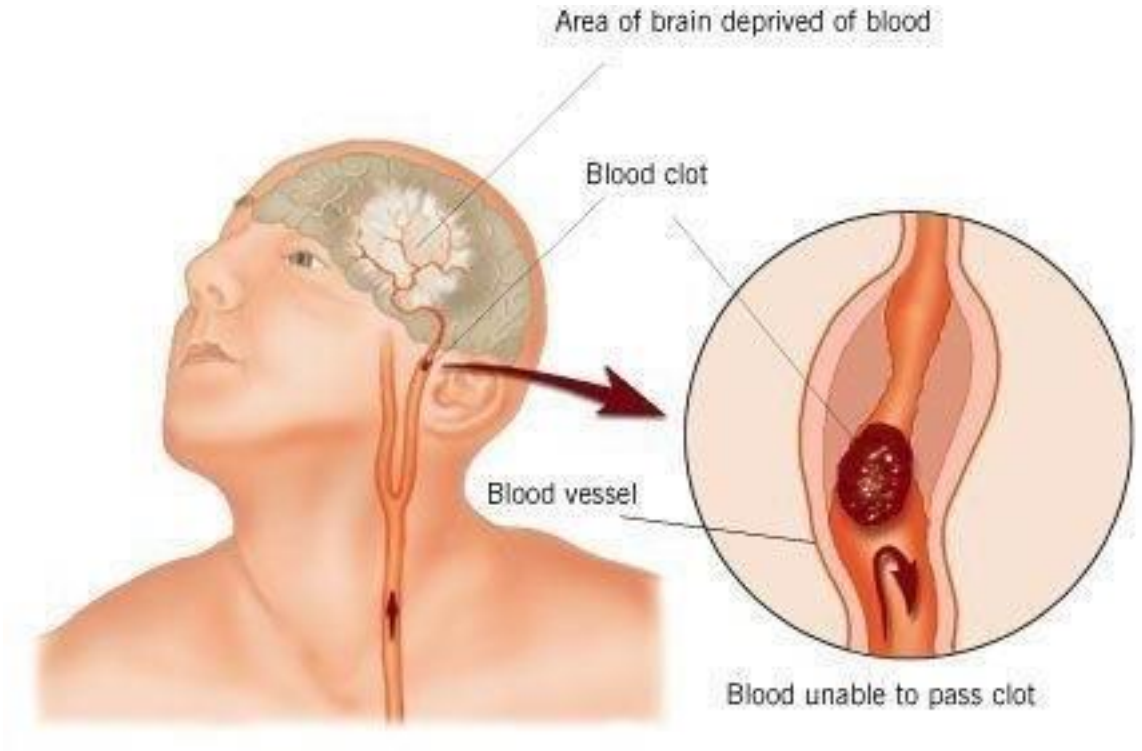
decrease in blood supply

Some cells do NOT resist long term hypoxia which could lead to its death (myocardium, neurons..)

Hypoxia can be caused mainly by ischemia ,but it also can be caused by different factors (e.g anemia, carbon monoxide, longstanding asthma, higher altitudes, chronic obstructive pulmonary diseases, chronic bronchitis..)

Oxygen Deprivation

It is the main cause of cell injuries because all cells need oxygen they differ their level of endurance of oxygen deprivation (e.g cardiac & nerve cells are not as tolerant to oxygen deprivation as other cells)

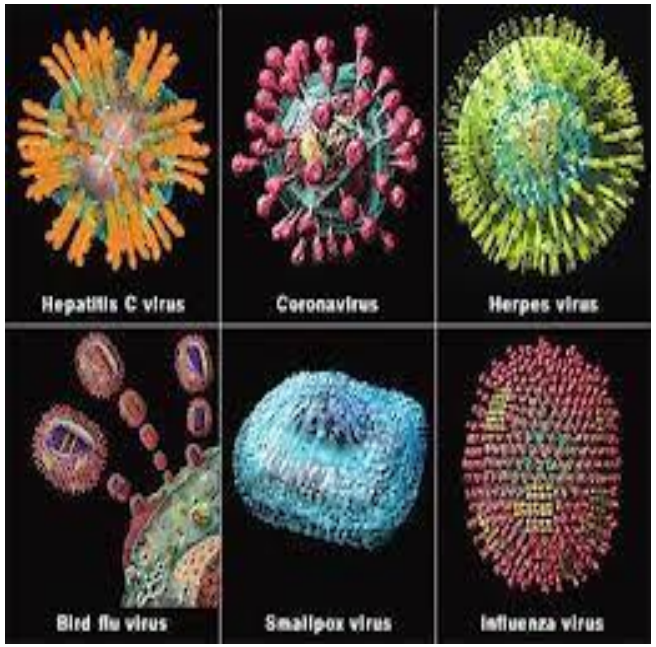


Chemical Agents

Caused by either consumption (even innocent ones :salt or sugar) or exposure to certain pesticides and chemicals..

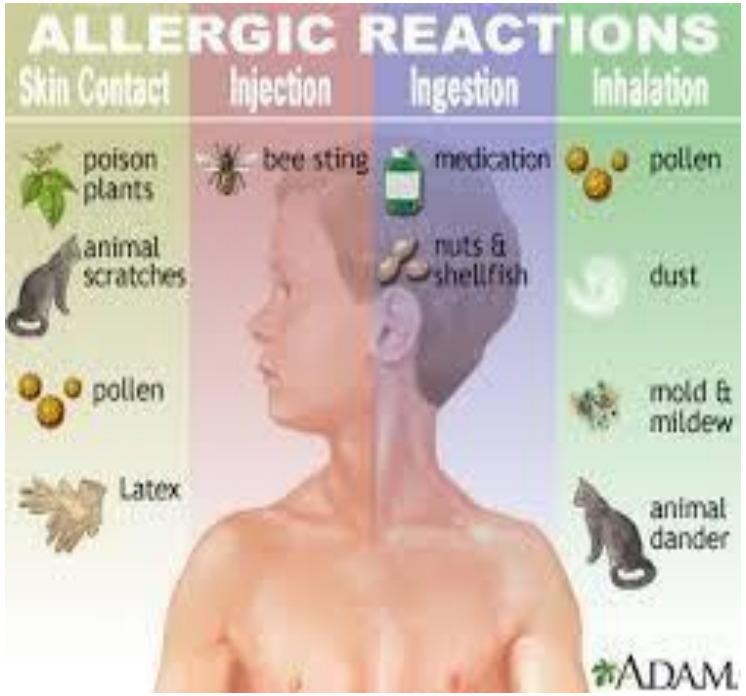
Infectious Agents

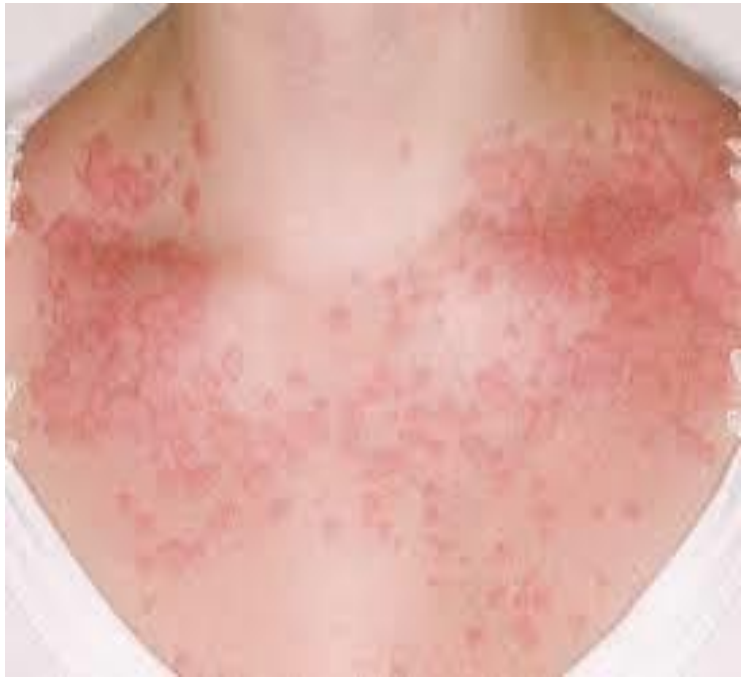
e.g viruses,
bacteria, worms..



Immunologic Reactions
autoimmune, allergic, microbes

Allergic reactions, autoimmune diseases..





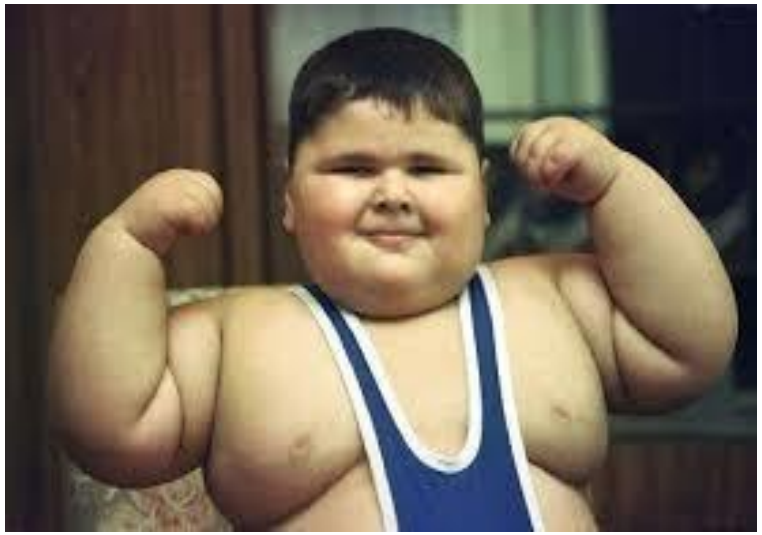
Genetic Factors

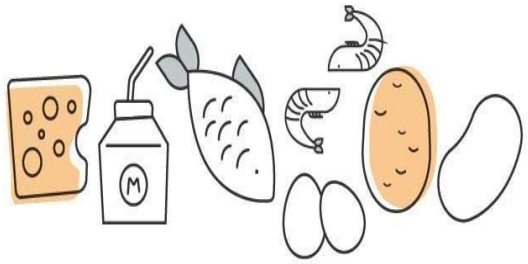
Any change in the chromosomal number (mainly caused by mutations) (supposedly 46) can cause cell injury such as Down Syndrome (extra copy of chromosome 21)

+ single cell mutations (cystic fibrosis)

Nutritional Imbalances

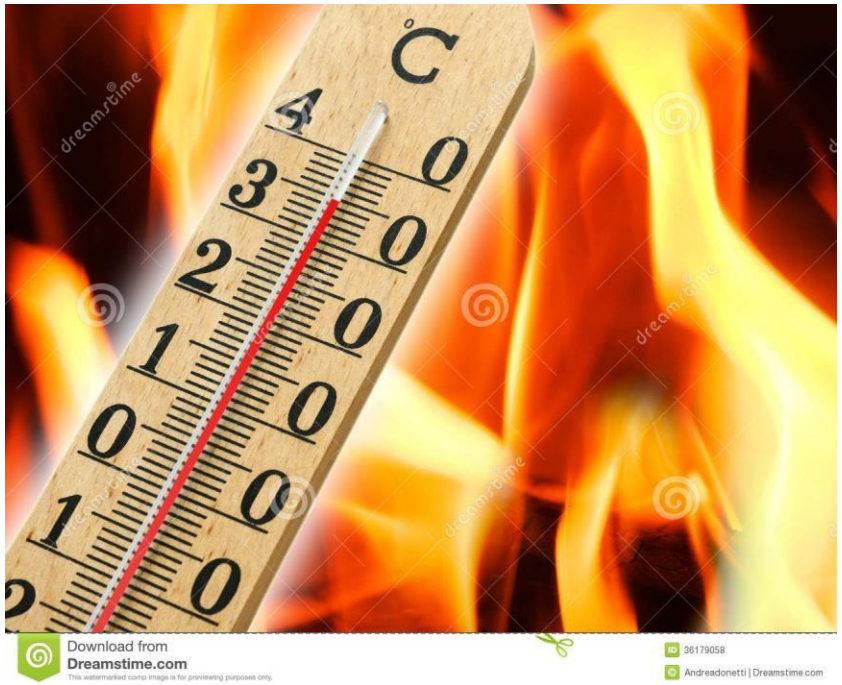
Lack of nutrition and excessive nutrition both have consequences as injuries

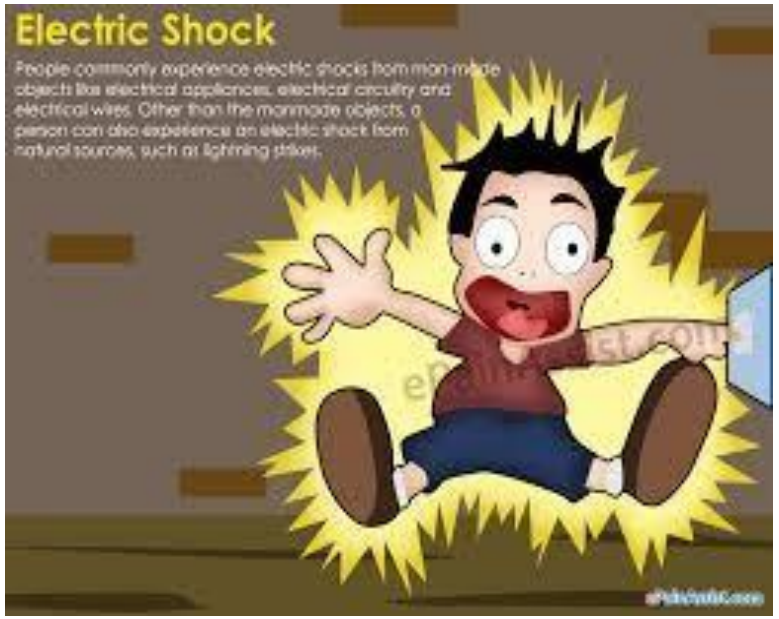




Physical Agents

Such as electrical injury, trauma, falling down and extremes of temperature..





- A 43 year old male presents with mild burning substernal pain following meals for the past 3 years. Upper GI endoscopy is performed and biopsies are taken of an erythematous area of the lower esophageal mucosa 3 cm above the gastroesophageal junction. There is no mass lesion, no ulceration, and no hemorrhage noted. The biopsies show the presence of columnar epithelium with goblet cells. Which of the following mucosal alterations is most likely represented by these findings?

- A Dysplasia
- B Hyperplasia
- C Carcinoma
- D Ischemia
- E Metaplasia

Answer: E

Explanation: This patient suffers from GERD , which caused the type of esophageal lining epithelium to change to intestinal epithelium so its Metaplasia

- A 22 year old recently wed female has missed her last two menstrual cycles . Her OB/GYN confirms her pregnancy. If we were to have a look at her uterus we would find which of the following adaptive cellular responses?

- A Hyperplasia
- B Dysplasia
- C Atrophy
- D Hypertrophy
- E More than one of the above

The answer is: E.
This patient is pregnant and as we mentioned before the smooth muscles in the uterus are mixed hypertrophy (both A and D are correct)

- A 56 year old female heavy smoker presents with chronic cough, but recently has noted increased sputum production. After a thorough history & physical examination bronchoscopy with biopsy is performed. The biopsy reveals bronchial epithelium with squamous metaplasia. Which of the following statements is applicable to these findings?

- A Physiologic process of aging
- B Irreversible, even if she stops smoking
- C Metastases to the lung
- D Risk for infection
- E Thromboembolism with infarction

Note: "Metastasis" is the spread of cancer cells from the place they first formed.

The answer is: D

This patient is a smoker therefore the cells undergo Metaplasia , which changes the original pseudostratified columnar ciliated epithelium with goblet cells to lining squamous epithelium , this change deprive the cell of its defensive mechanisms (cilia and mucus from goblet cells) which increases the risk of infections

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	Slide 22 “ than other cell” Slide 13 “HPV” Slide 9 (bellow the image of “cell death “) Slide 9 Slide 19 (GERD) paragraph Slide 5 “Injourious state “	“ than other cells” No abbreviation mentioned Myocardial Infraction There is overlapping between 2 lines Wrong color code (black) Position indicates both adaptation and cell injury	“As other cells” HPV (Human papillomavirus) Myocardial Infarction No overlapping Correct color code (purple) Position indicates only cell injury
V1 → V2	Slide 5	cell is alive and still functioning	cell is alive but not functioning

Additional Resources:

Reference Used:

1. ROBBINS and CORTAN Pathologic Basis of Disease pages (34-35)

Extra References for the Reader to Use:

1. https://youtu.be/BJ2kEpjrgII?si=opgJPIB3BbM6j90F
2. First Aid book page 202 (good summary)

رسالة من الفريق العلمي:

اللهم ارزقني فهم النبيين وحفظ المرسلين والهام الملائكة المقربين
اللهم ارفع الضرر عن أهلنا في غزة ولبنان والسودان وأرنا عجائب قدرتك في نصرهم