# Pathology

Sheet ○Slide

## number

2

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**أخي الطالب أختي الطالبة تحية طيبة وبعد، تسهيلاً للعملية التعليمة والذي هو هدفنا الأسمى من هذا المشروع، أرفق لكم بعض المعلومات قد تودون معرفتها عند دراسة هذه المحاضرة**

## التفريغ الأول لكل من محاضرة دكتور غسان ومحاضرة دكتور محمد مختلفة المحتوى وبعيدة الترابط لذلك كان علينا أن نجمع التفريغين في ملف واحد كما لو كلٌ بمفرده.

***يحتوي هذا الملف على تفريغ محاضرة الدكتور غسان بعلوشة لمادة علم الأمراض**

***يشمل كافة الأمثلة، والمعلومات الخارجية، والشروح الإضافية، التي ذكرت من قبل مدرس المساق المذكور سابقاً بالإضافة الى شرائح "البوربوينت" المستخدمة**

***بعض الشرائح اكتُفي بعرضها لعدم وجود اي اضافة او تعليق من قبل مدرس المساق انما اكتفى بقراءة المعلومات الموجودة بداخلها.**

***تستخدم اللغة الانجليزية بشكل رئيسي في الملف مع الإشارة إلى بعض النقاط باللغة العربية لإيصال المعنى المراد من قبل مدرس المساق**

(أعانكم الله وسدد خطاكم)

When the cell is under stress it undergoes adaptation to remove the stress and return to its normal state.

So why does the cell in adaptation sometimes make Atrophy and other times make Hypertrophy or Hyperplasia? We're going to understand this selectivity.

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# Atrophy

- **Decrease cell size**, due to the loss of the cell substances, leading to diminished function of the cell and a new equilibrium is reached.
- Accompanied by **decrease in the organ size**, if sufficient number of cells is involved.
- The **cells are alive**

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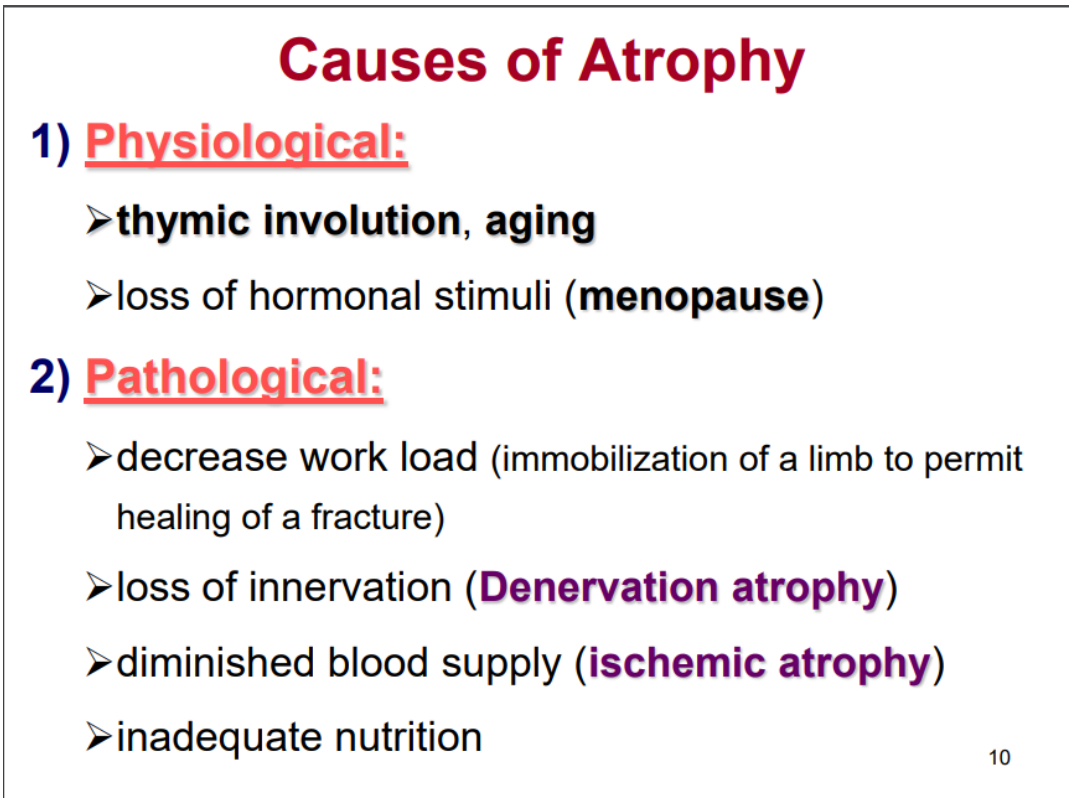
*في هذه الحالة يصغر حجم الخلية ولكن شكلها لا يتغير ولو كانت على مستوى اكبر سيصغر حجم العضو بالكامل ويرافق ضمور الحجم ضمور بالوظيفة (لكن ليس إلى درجة الانعدام وموت الخلية) سواء على مستوى الخلية أو العضو

وذلك للوصول إلى حالة الاستقرار "Equilibrium"




When is it Physiological and when is it Pathological?

We will see the start of **physiological**.

ex. thymic involution, aging

من الطبيعي ان ال "thymus gland" تبدأ بالضمور بعد سن25

فهي حالة فسيولوجية طبيعية وعدم حدوث ذلك يعتبر "مرض" .

## But in the pathological

The cause of the atrophy is a disease

Ex. -decrease work load

اي شخص يحدث لديه كسر في أطرافه نقوم بوضع الجبصين عليها للحد من حركتها

- Loss of innervations

كما في الحالات لدى الأشخاص الذين يحدث لديهم شلل في طرف واحد دون الطرف الاخر

It is called “Atrophic limb”

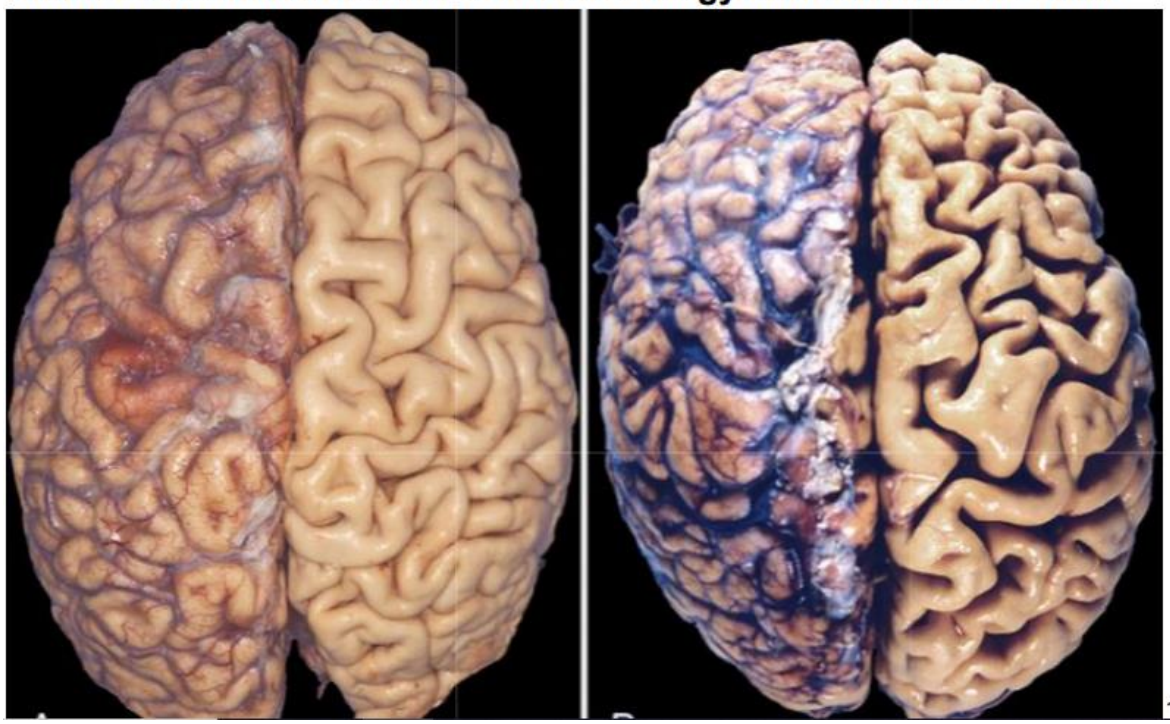
- Loss of blood supply

It is called ischemic atrophy

- Inadequate nutrition

Ex. بنية الأشخاص الذين يعيشون في المجاعات

**A, Normal brain of a 36-yr-old male. B, Atrophy of the brain in an 82-year-old male with atherosclerotic disease. Atrophy of the brain is due to aging and reduced blood supply. The meninges have been half stripped. Note that loss of brain substance narrows the gyri and widens the sulci**



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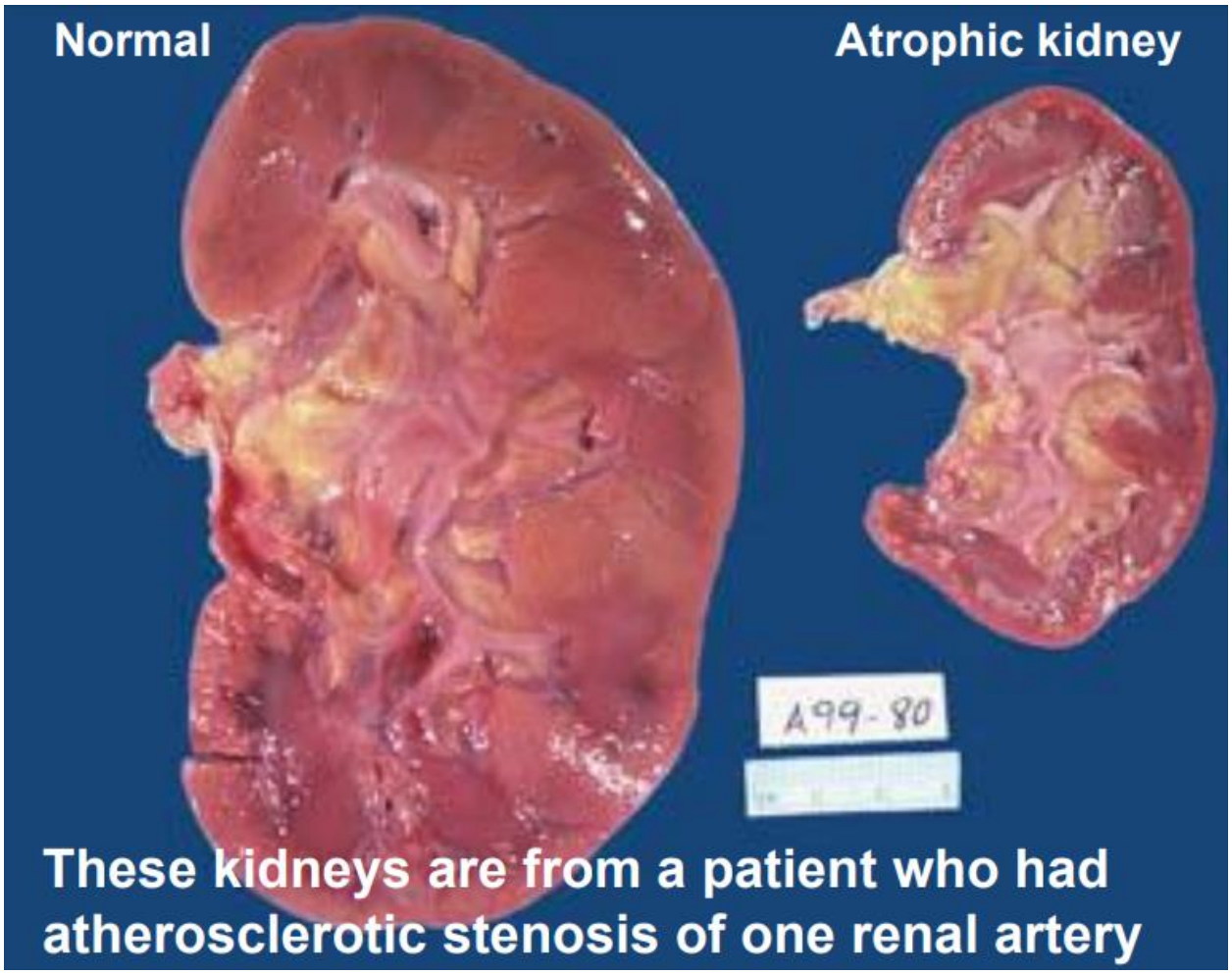
مثال على ال "Atrophy" التي تحدث على مستوى عضو كامل

نلاحظ في الدماغ في الحالة الطبيعية تكون المسافات بين"folds"

صغيرة على عكس الدماغ الذي تعرض لل Atrophy تكون

واسعة كما يحدث في مرض الزهايمر.




Another example of atrophy that is caused by atherosclerotic stenosis of one renal artery so the size and function of the injured kidney will decrease.

# Mechanisms of Atrophy

- **Imbalance between protein synthesis and degradation** is the fundamental step, leading to reduction in structural components.
- **Decreased synthesis, increased catabolism**, or both
- the fundamental cellular changes are identical in physiological and pathological causes.
- Sometimes the number of cells can be reduced by the process **apoptosis**

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عادة ما يكون لدينا توازن بين ال anabolism & catabolism

وتوازن بين انتاج البروتين وهدم البروتين

ولنحصل على خلية أصغر نزيد من مستوى ال catabolism ونقلل مستوى ال anabolism والعكس صحيح

Sometimes the number of cells can be reduced by the process apoptosis.

Example: Uterus during pregnancy

It makes 2 adaptations

1- Smooth muscle hypertrophy 2- Hyperplasia

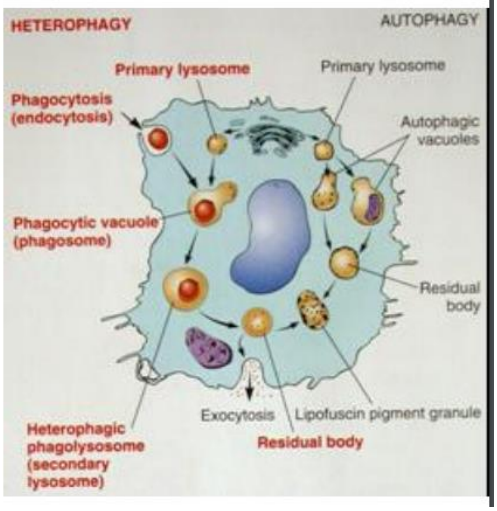
بعد الحمل لازم يرجع لحجمه الطبيعي ف نقلل عدد الخلايا عبر apoptosis ولنقلل من حجم الخلية نزيد عمليات الهدم ونقلل عمليات البناء كما ذكر سابقاً

## Atrophy: increase catabolism

### Proteolytic systems for degradation:

1) Lysosomes contain proteases and other enzymes

- **degrade exogenous proteins** engulfed by endocytosis
- **degrade subcellular components** (e.g. organelles) leading to the formation of **autophagic vacuoles**




**1- Lysosomes**

Materials that enter the cell from the outside to the inside, will pass the plasma membrane; the membrane will surround it to form a vacuole so the lysosome can bind and secrete its enzymes to digest it and get it out by exocytosis. This process is called **heterophagy**.

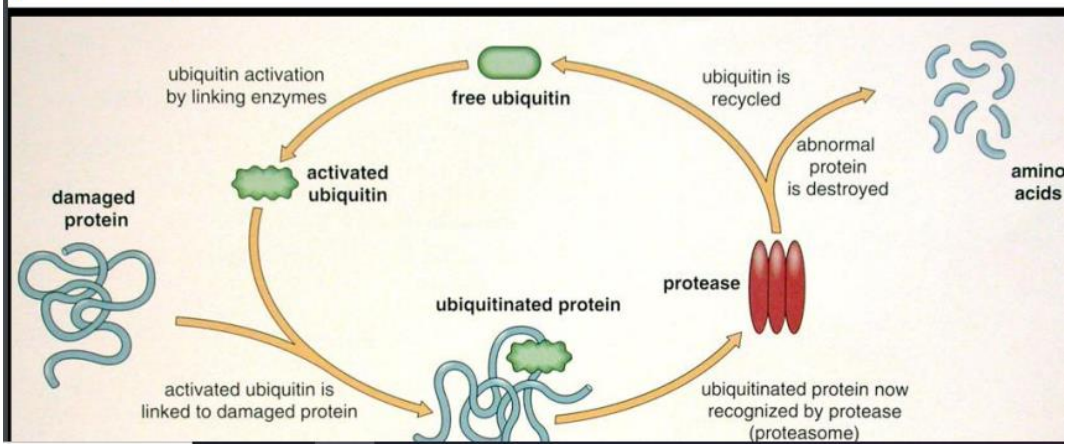
In **autophagy** we want to digest material inside the cell. The ER will surround this material (ex. old organelle) and make an autophagic vacuole then complete the same mechanism as heterophagy.

**2) The ubiquitin-proteasome pathway:**

•Degradation of cytosolic and nuclear proteins

•Responsible for the accelerated proteolysis in hypercatabolic states (e.g. cancer)

•The protein/ubiquitin complex are engulfed by the cytoplasmic proteasome




## 2- Ubiquitin

It is found in all normal cells but in an inactive state.

This protein removes damaged proteins that act as cofactors for proteolysis.

Proteasomes are not lysosomal proteolysis.

- Mechanism:

  If any of our cells want to atrophy it will increase the catabolism by activating the Ubiquitin.

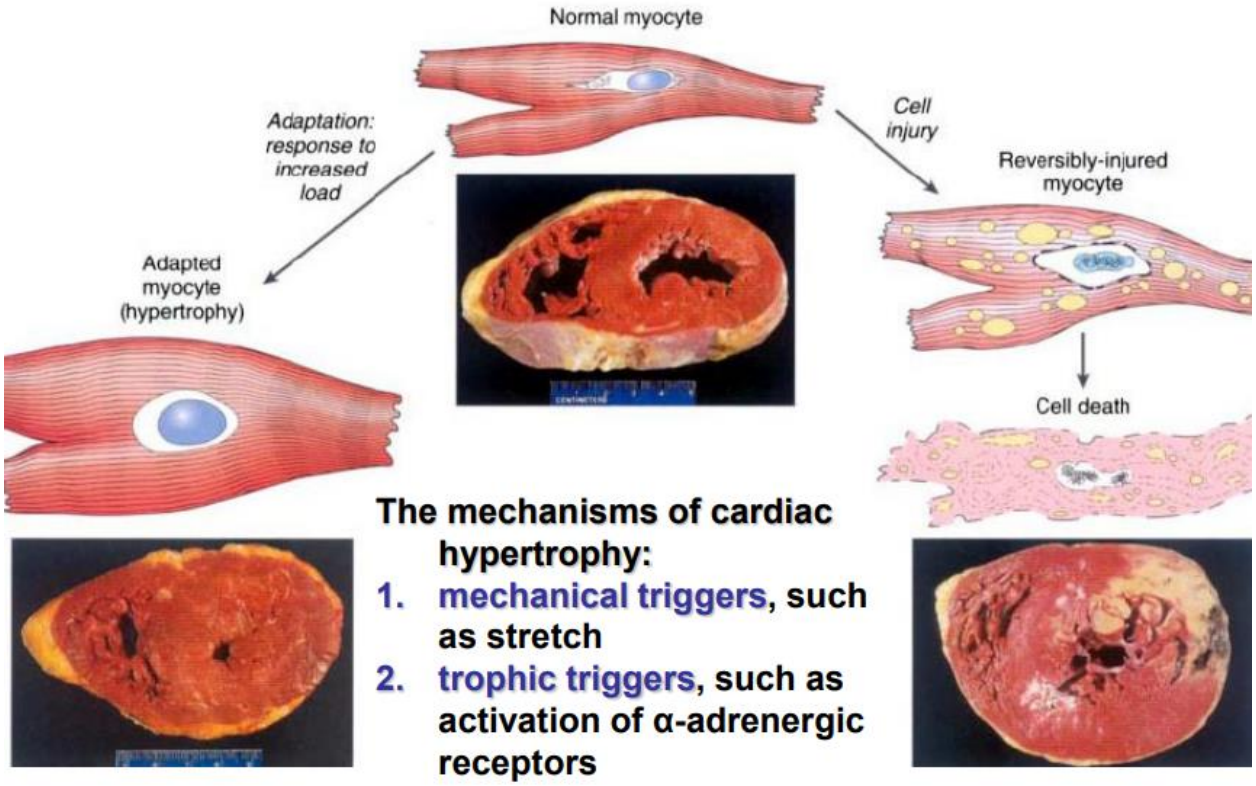
  Usually its function is the removal of damaged proteins by binding the damaged protein to the Ubiquitin (it's called Ubiquitinated protein) and this will act as a cofactor for proteolysis that breaks down the protein into amino acids.

  These two activate lysosomal and Ubiquitin pathways which decrease the cell size and function (Atrophy).

## Mechanisms of Hypertrophy

- **an increased synthesis of structural proteins** and organelles leading to an overall increase in the workload of the organ.

# hypertrophy after myocardial infarction




These two photos are **pre-cancerous.**

This cell became this abnormal form because of stress when it is removed the cell will return to its normal state.

**Hypertrophy**: increase in the cell size and function but in the same shape by increasing the number and density of the cellular substances.

How do we increase them?

- By increasing the synthesis and decreasing the catabolism.

Hypertrophy mainly occurs in cells which are hard to divide like cardiac and skeletal muscles.

Is the state of hypertrophy good?

The answer: it's not good.

A person who has hypertrophy in their cardiac muscles is sick. If this stress continues it may cause a failure.

In skeletal muscle hypertrophy the muscle fibers get thicker so there's no sickness.

**Notice that:**

* Skeletal muscle hypertrophy (body building) is– physiological

* Cardiac muscle hypertrophy (hypertension) is– pathological

# Hyperplasia

- an **increase in the size of the organ** due to **increase in the number of the cells** in the organ, leading to increase in the function.
- **SEEN IN CELLS THAT CAN DIVIDE**

Ex. Uterus

## Hyperplasia

In many instances, hyperplasia and hypertrophy occur at the same time. **Uterus during pregnancy** is a good example.

# Causes of Hyperplasia:

- **Physiological**:

  **1. hormonal hyperplasia**

  (e.g. female **breast** at puberty and during pregnancy)

  **2. compensatory hyperplasia**: occurs when a portion of the tissue is removed or diseased which is under the influence of growth factors

  (e.g. **partial liver resection**, **wound healing**)

- **Pathological**:

  – Under the effect of hormones or growth factors.

  (e.g. **Endometrial hyperplasia**, **skin wart**)

2. Compensatory hyperplasia

كما في عمليات زراعة الكبد لا يتم زراعته كاملا بل جزء صغير منه ويقوم هذا الجزء بزيادة خلاياه إلى أن يصل إلى الوضع والحجم الطبيعي

Both physiological and pathological causes contain hormones, but the difference between them is that the pathological hormones are secreted by a tumor.

# Hyperplasia

- Both hypertrophy and hyperplasia are **reversible**, if the stimulus is removed.
- This **differentiates these processes from cancer**, in which cells continue to grow despite the absence of hormonal stimuli.
- pathologic hyperplasia constitutes a fertile soil in which cancerous proliferation may eventually arise.

e.g. patients with hyperplasia of the endometrium are at increased risk of developing **endometrial cancer**

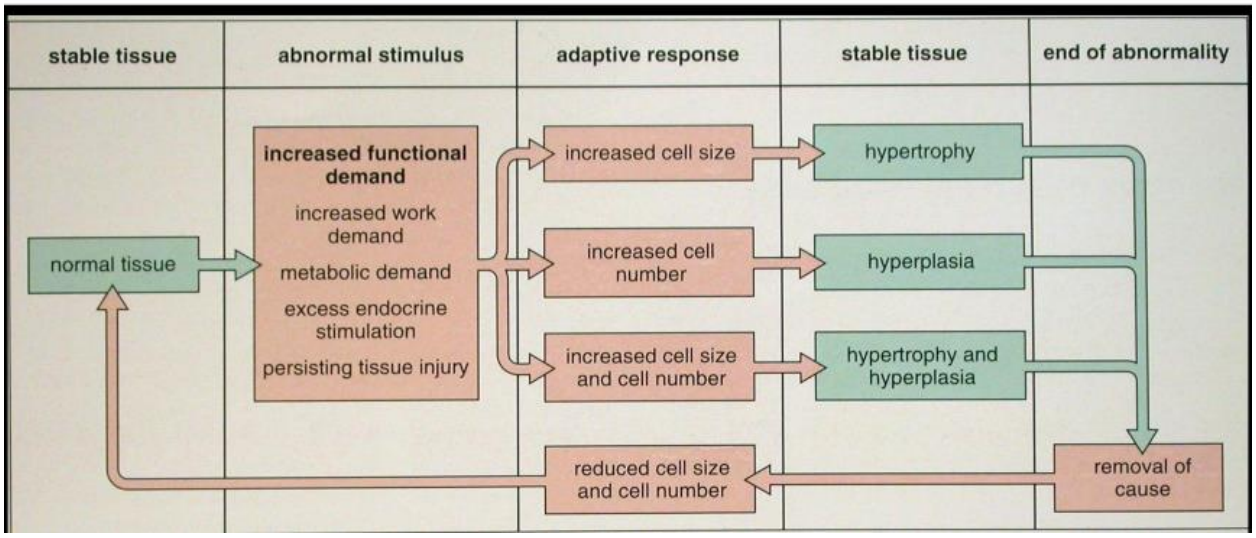
e.g. papillomavirus infections predispose to **cervical cancers**

e.g. patients with hyperplasia of the endometrium are at increased risk of developing endometrial cancer.

* لذلك يتم إزالة الرحم لدى هؤلاء النساء خوفا من خطر الإصابة بالسرطان.

Notice that adaptation is not always good.

# Hypertrophy & hyperplasia Summary




Summary:

If a normal tissue is injured it makes an adaptation by:

Increasing the cell size and/or cell number so if we had a removal of the cause (stress) the cell will return to its normal state (both size and number).

# Metaplasia

- **Replacement of one type of adult cell**, whether epithelial or mesenchymal, **by another type** of cell
- aiming at **replacing cells that are sensitive to certain stimuli by a more resistant cell type**.
- This happens through reprogramming of stem cells or undifferentiated mesenchymal cells.
- the influences that induce metaplastic transformation, if persistent, **may induce cancer transformation** in the metaplastic epithelium

- Usually metaplasia is named by relying on the new name.

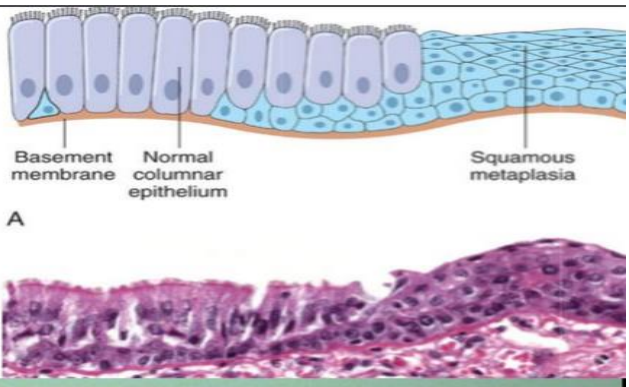
Ex. Squamous metaplasia means that the new cells are squamous.

Ex. Intestinal metaplasia means that the new cells are similar to the intestine's cells.

Supposing that we know the old cells ☺

- Hyperplasia and metaplasia are more dangerous than the others because they can make cancer.

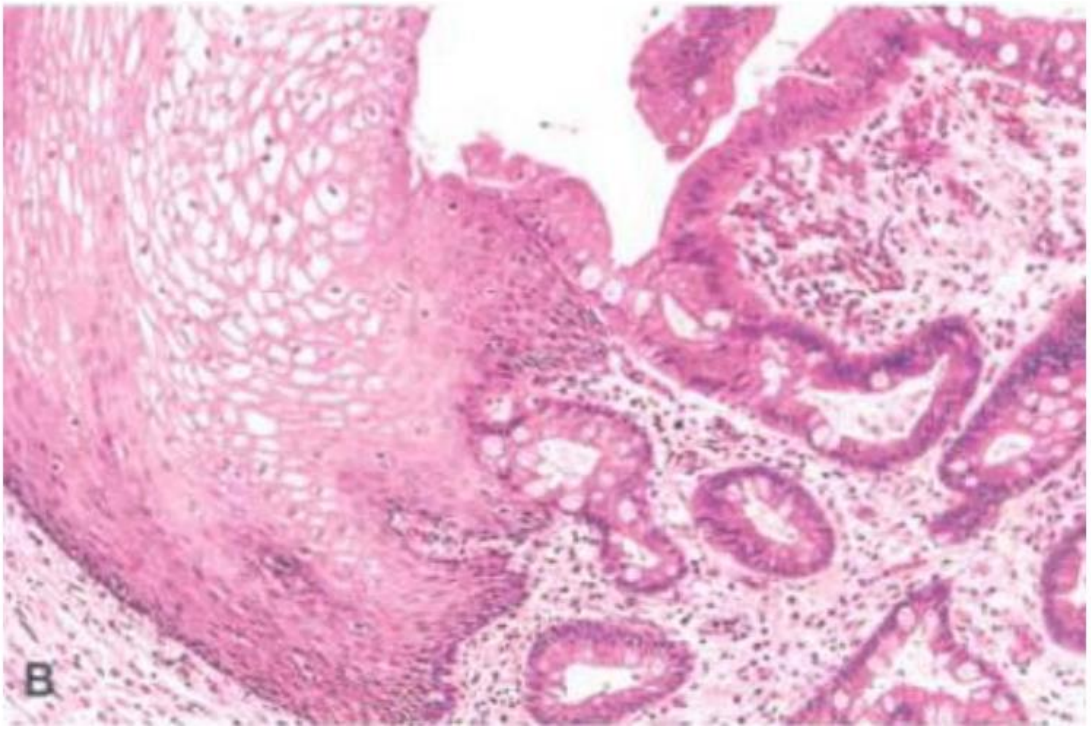
# Examples of Metaplasia




Examples of metaplasia

| Original tissue | Stimulus | Metaplastic tissue |
|---|---|---|
| Ciliated columnar epithelium of bronchial tree | Cigarette smoke ★ | Squamous epithelium |
| Transitional epithelium of bladder | Trauma of bladder calculus | Squamous epithelium |
| Columnar epithelium in gland ducts | Trauma of calculus | Squamous epithelium |
| Fibrocollagenous tissue | Chronic trauma | Bone (osseous) tissue |
| Esophageal squamous epithelium | Gastric acid ★ | Columnar epithelium |
| Columnar glandular epithelium (respiratory epithelium) | Vitamin A deficiency | Squamous epithelium |

## Metaplastic transformation of esophageal stratified squamous epithelium *(left)* to mature columnar epithelium (so-called Barrett metaplasia)




*Because the columnar cells are more resistance to gastric juice acidity

# Subcellular responses to injury:

1. **Lysosomal catabolism**:
   - **Primary lysosomes**: membrane bound intracellular organelles containing a variety of hydrolytic enzymes
   - **Secondary lysosomes**, "**phagolysosome**" : when the primary lysosomes fuse with vacuoles containing material for digestion.

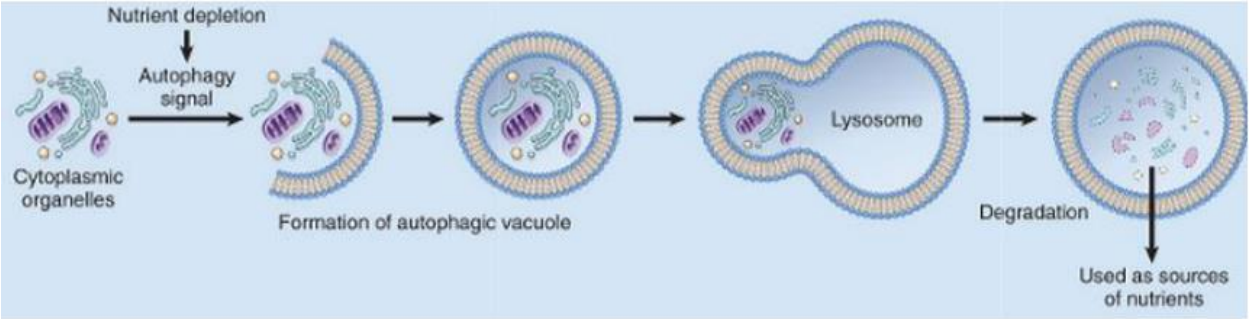
## Subcellular responses to injury

1. **Lysosomal Catabolism**
   - ***Heterophagy***
   - **Autophagy**
2. **Induction (Hypertrophy) of Smooth Endoplasmic Reticulum**
3. **Mitochondrial Alterations**
4. **Cytoskeletal Abnormalities**
5. **Heat Shock Proteins**

# Type of phagocytosis:

## 1. Autophagy:

- When intracellular organelles are sequestered from the cytoplasm in an autophagic vacuole. This combines with primary lysosome to form autophagolysosome.
- **seen especially with atrophy and aging.**




# Type of phagocytosis:

## 2. Heterophagy:

- **Inflammatory cells engulf and destroy foreign bodies**
- e.g. bacteria are ingested and degraded by neutrophils
- e.g. macrophages engulf and catabolize necrotic cells.

**Pinocytosis**: is engulfment of soluble small material

**Phagocytosis**: engulfment of large material

# Type of phagocytosis:

- **Lysosomes** can **completely catabolize most proteins and carbohydrates**
- **Lysosomes with undigested debris may persist within cells as *residual bodies*** or may be extruded
- **Lipofuscin pigment** granules represent **indigestible material** resulting from intracellular lipid peroxidation, and certain indigestible pigments, such as **carbon particles** inhaled from the atmosphere or inoculated pigment in tattoos, can persist in phagolysosomes of macrophages for decades

Lysosomes digest most proteins and carbohydrates.

The undigested materials inside the lysosome are called **residual bodies**.

Ex. Lipofuscin pigment: its color is golden brown; this can be seen in long life cells such as cardiac muscles & nerve cells.

* Cells that contain more lipofuscin can live longer.

## 2. Hypertrophy of the smooth endoplasmic reticulum:

- **Stimulation and activation of SER and its enzymes** (P-450 oxidase) to increase the solubility and excretion of various compounds, like drugs.
- **Increase solubility of drugs** (e.g., steroids, alcohol, aryl hydrocarbons, insecticides) and thereby facilitate their excretion.
- E.g. patients who increase their alcohol intake while taking phenobarbital for epilepsy may end up with subtherapeutic levels.

**Increased solubility of drugs caused by ER stimulation:**

اي دواء يعطى للمريض يؤخذ بجرعات محددة ف مثلا يصف الطبيب لمريضه 10ملغم بحيث ان جسم المريض يأخذ 5مل من ال 10 ويصرّف الباقي ولكن في حال زيادة الذائبية للدواء فان الجسم ياخذ ال 5ملغم وبسبب ذائبية ال 5 ملغم الاخرى لا يستطيع التخلص منها فكأنما تناول المريض جرعة مضاعفة من الدواء قد تسبب الموت في بعض الحالات

# 3. Mitochondrial alternations:

- **Increase number in hypertrophy**
- **Decrease number in atrophy**

- **Example**: **alcoholic liver disease**
  - large and abnormal shapes (megamitochondria)

When the cell is in hypertrophy, the mitochondria makes hypertrophy, and when the cell is in atrophy the mitochondria does the same as well.

So the mitochondria can increase or decrease it's number and can change its shape.

End of the lecture

**Dr mohammad barakat**
**Pathology**

Gross pathology: فحص المريض

Gross description: إعطاء العينة وصف عند وصولها الى الطبيب

* Gross description is important for physicians and pathologists, gross description includes giving the sample its characteristics like (size, hard or soft, encapsulated or capsulated, …etc.)

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Divisions of pathology:

-General pathology: is about tumors, inflammation, degenerative changes, and genetic changes.

-Systemic pathology: describes specific diseases in individual organs or system like: GI tract, respiratory tract, skin, …etc.

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**Subdivisions of Pathology:**

- Histopathology: study in the tissues.
- Cytopathology: in the cells and its very important.

Example: شخص معه ماء حول صدره، يتم سحب منها وفحصها اذا كانت تحتوي على خلايا سرطانية او لا تحتوي... الخ

- Hematology: study the disorders of blood components. Ex: leukocytosis

مثال عليها ارتفاع عدد كريات الدم البيضاء وتشير الى وجود اللوكيميا

- Forensic pathology: في الطب الجنائي
- Chemical pathology: biochemical disorders (glucose, blood urine, …)

Microbiology: study of diseases caused by bacteria, malaria, …

Immunology: امراض زي الروماتيزم

**- Nomenclature**

| Prefix | Meaning | Example |
|---|---|---|
| Ana- | Absence | Anaphylaxis |
| Dys- | Disordered | Dysplasia |
| Hyper- | Excess over normal | Hyperthyroidism |
| Hypo- | Deficiency below normal | Hypothyroidism |
| Meta- | Change from one state to another | Metaplasia |

Dysplasia: might have cancer (malignant)

Metaplasia: might not be malignant

| Suffix | Meaning | Example |
|---|---|---|
| -itis | Inflammatory process | Appendicitis |
| -emia | Vascular | Ischemia |
| -oma | Tumour | Carcinoma |
| -osis | State or condition | Osteoarthrosis |
| -oid | Bearing a resemblance to | Rheumatoid disease |
| -penia | Lack of | Thrombocytopenia |
| -cytosis | Increased number of cells | Leukocytosis |
| -ectasis | Dilation | Bronchiectasis |
| -plasia | Disorder of growth | Hyperplasia |

Itis: التهاب, emia: related to blood or blood vessels, oma: there is a tumor but it could be malignant or not, osis: أشياء تزيد عن كميتها ,

******

*Tumors cannot happen in two parts of the body:

1- Hair

2- Nails

**Notes:**

* Hyperplasia: increase of the amount of tissue. In the endometrium it may become cancer.

* Hypoplasia: normal tissue

نسيج عادي لكن لم يعد يعمل

Ex: In parathyroid gland (parathyroid hypoplasia)

* Metaplasia: change from one state to another.

مثال في عنق الرحم يتحول

Mucus secretion epithelium to squamous epithelium by irritation.