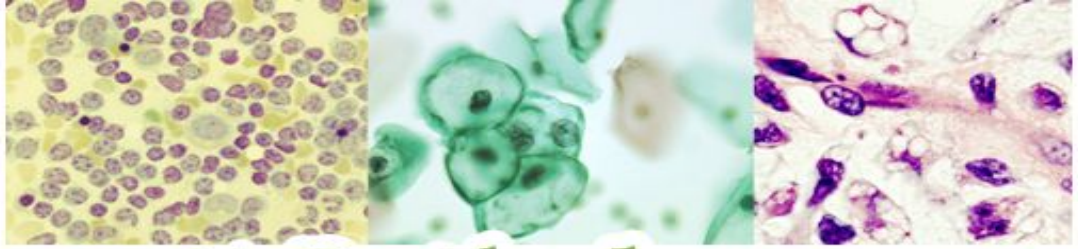


Pathology

LECTURE (2,3,4)

CELL INJURY

As a doctor you should know what can threaten your patient's life
you should know what makes your patient suffers from pain
THAT'S WHY YOU LEARN PATHOLOGY

" هذا العمل لا يغني عن المصادر الأساسية للمذاكرة"

Definition: BLUE Examples:GREEN Important: RED Extra explanation:GRAY Disease names: **UNDERLINED**.

OBJECTIVES

- Understand the concept of cells and tissue **adaptation** to environmental stress including the meaning of **hypertrophy**, **hyperplasia**, **aplasia**, **atrophy**, **hypoplasia** and **metaplasia** with their clinical manifestations.
- Is aware of the concept of **hypoxic(نقص الأوكسجين)** cell injury and its major causes.
- Understand the definitions and **mechanisms of free radical injury.**
- Knows the definition of **apoptosis(موت الخلايا المبرمج)**, tissue **necrosis** and its various types with clinical examples.
- **Able to differentiate between necrosis and apoptosis.**
- Understand the **causes of and pathologic** changes occurring in **fatty change (steatosis)**, accumulations of **exogenous** and **endogenous pigments** (**carbon, silica, iron, melanin, bilirubin and lipofuscin**).
- .Understand the causes of and differences between **dystrophic** and **metastatic** calcifications.

LECTURE 1

LECTURE 2

LECTURE 3

Lecture 1 outline

Adaptation to environmental stress:

hypertrophy, hyperplasia, aplasia, hypoplasia, atrophy, squamous metaplasia, osseous metaplasia and myeloid metaplasia.

Hypoxic cell injury and its causes (ischaemia, anaemia, carbon monoxide poisoning, decreased perfusion of tissues by oxygen, carrying blood and poor oxygenation of blood).

Free radical injury:

definition of free radicals, mechanisms that generate free radicals, mechanisms that degrade free radicals.

Reversible and irreversible cell injury

Adaptation (التكيّف) to environmental stress

Cells are constantly adjusting their structure and function to accommodate changing demands i.e. **they adapt within physiological limits**.
Adaptations are **REVERSIBLE** changes.

If the adaptive capability is exceeded or if the external stress is harmful, **cell injury develops.**

- Within certain limits injury is **reversible** → return to normal
- severe or persistent stress results in **irreversible** → **Cell death**

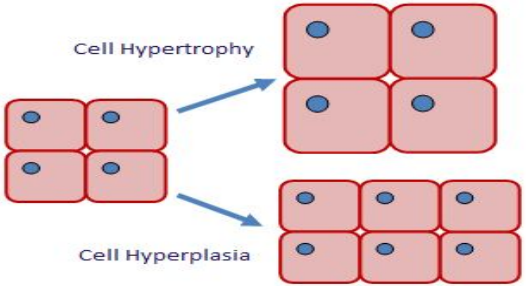
As cells encounter(تواجه التكيّف) physiologic stresses or pathologic stimuli(المؤثرات المرضية), they can undergo adaptation. **The principal adaptive responses are:**

- **Hypertrophy(تضخّم)**
- **Hyperplasia(تضخّم)**
- **Atrophy(ضمور)**
- **Metaplasia(تحوّل)**

Hypertrophy

Is an increase in the size of the tissue/organ due to the **increase in the size of the cells**.

- Increased demands lead to hypertrophy.
- Hypertrophy takes place in cells that are <u>not capable of dividing</u> e.g. striated muscles.



Hypertrophy can be physiologic or pathologic

physiologic

happen to normal people

- Breast during lactation(الرضاعة)
- Pregnant uterus
- the skeletal muscles undergo only hypertrophy in response to increased demand by <u>exercise</u>.

pathologic

The cardiomyocytes of the myocardium in heart failure (e.g. hypertrophy in hypertension(ارتفاع ضغط الدم) or aortic valve (صمام) disease).

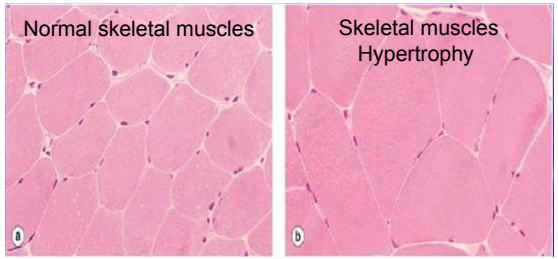
it shows in the x-ray as Large Heart

Examples of hypertrophy

Physiologic Muscular hypertrophy due to anabolic steroid misuse.

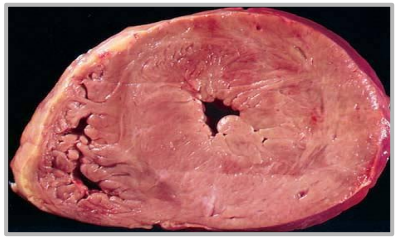
تضخم العضلات بسبب سوء استخدام المنشطات

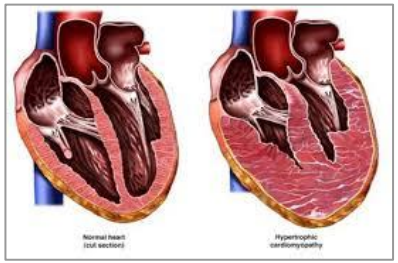
Exercise itself is normal and harmless but with talking anabolic steroid this gives pathologic hypertrophy to the muscle.



Pathologic Myocardial hypertrophy:

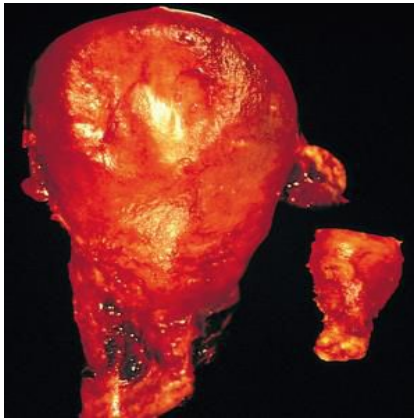
When there is increase work in the left ventricle over a long period of time it became hypertrophied(متضخما), this patient have left ventricle hypertrophy as a result of chronic hypertension. (ارتفاع ضغط الدم المزمن)

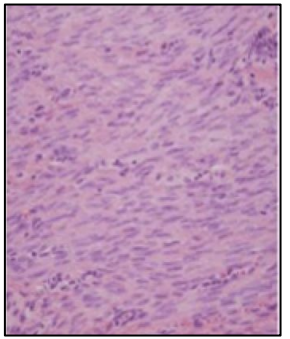




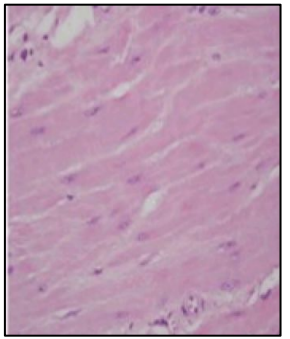
Physiologic hypertrophy of the uterus during pregnancy.

Gross appearance of a **normal uterus** (right) and a **gravid uterus**(رحم الحامل) (left) that was removed for postpartum bleeding(نزيف مابعد الولادة)



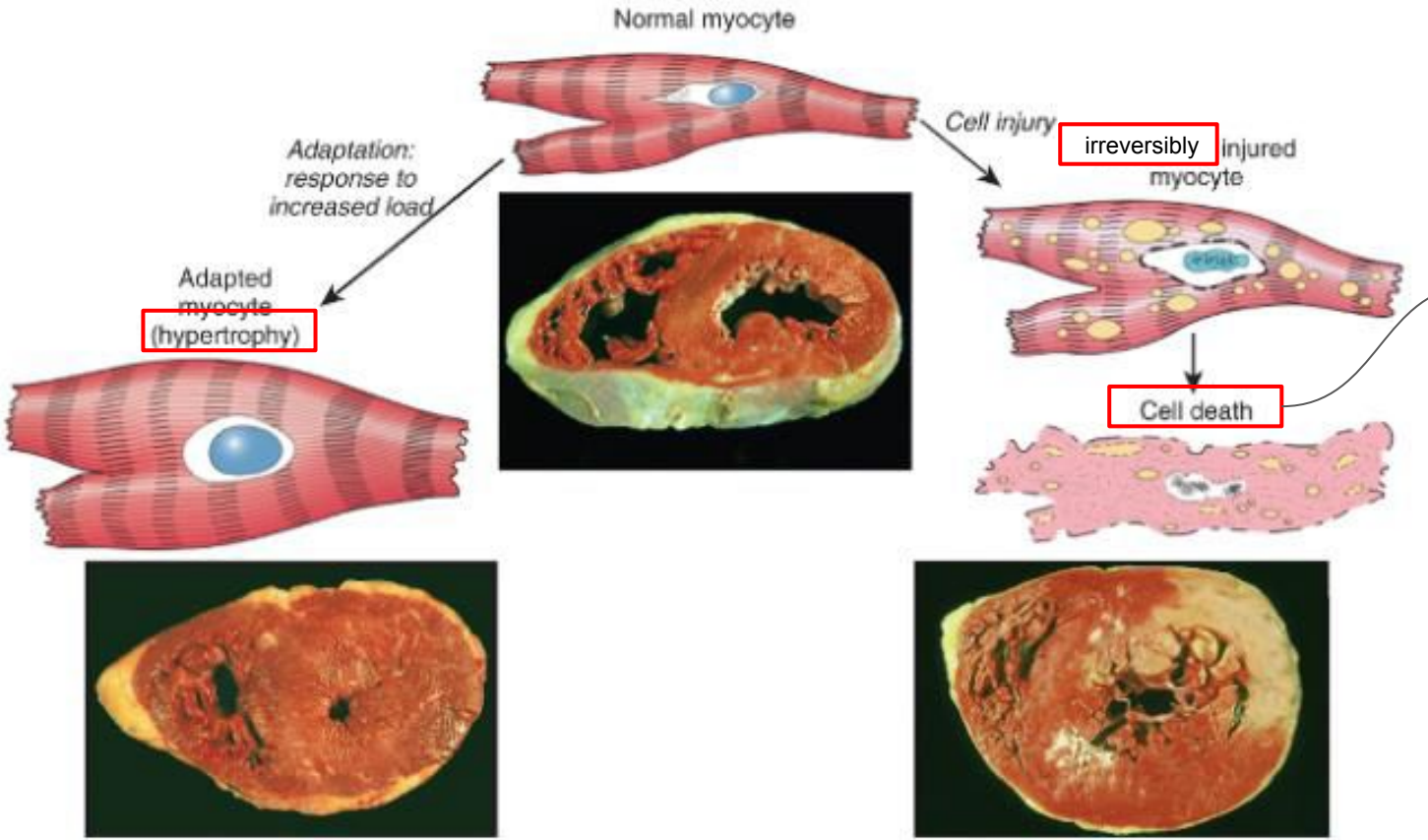


Smooth muscle cells of normal uterus



Smooth muscle cells of gravid uterus

Adaptative response



There are two principal patterns of cell death, **necrosis** and **apoptosis.**

We will talk about them next lecture.

Adaptative response

Hyperplasia

Is the increase in the size of an organ or tissue caused by an **increase in the number of cells.**

- Increased demands lead to hyperplasia.
- Hyperplasia occurs in tissues that are <u>able to divide or capable replication</u>(قادرة على التكرار), so some types of cells cannot undergo hyperplasia e.g.(nerve, cardiac, skeletal muscle cells).
- hyperplasia can be induced by hormones e.g. (endometrial hyperplasia induced by estrogen)

Hyperplasia can be physiologic or pathologic

physiologic

1.Hormonal hyperplasia e.g. the proliferation (زيادة في عدد خلايا) of the glands of the female breast at puberty(البلوغ) and during pregnancy.

2.Compensatory hyperplasia (التضخم التعويضي) e.g. when a portion of liver is partially resected (استؤصل جزئيا), the remaining cells multiply and restore the liver to its original weight.

Extra: e.g. People who remove one kidney usually experience hypertrophy in the other one, because it compensates(تعويض النقص) the other (removed) one.

pathologic

Caused by **abnormal excessive hormonal** or **growth factor stimulation.** e.g. excess estrogen leads to endometrial hyperplasia which causes abnormal menstrual bleeding(نزف).

Sometimes pathologic hyperplasia acts as the base for cancer to develop from.

Thus, patients with hyperplasia of the endometrium are at increased risk of developing endometrial cancer.

Involution

A decrease in number of cells.

(It is the opposite of Hyperplasia)

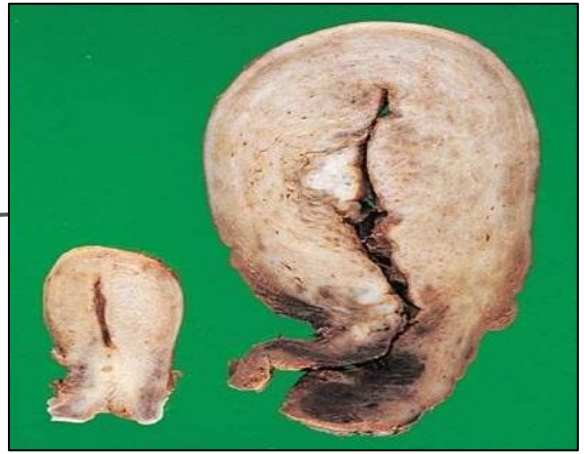
e.g. : When the uterus is transformed from pregnant to non-pregnant state.

Hypertrophy and hyperplasia

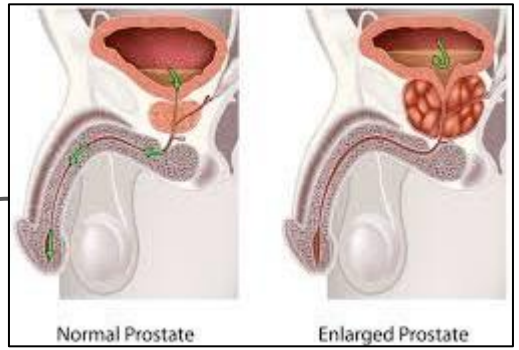
Hypertrophy and hyperplasia can occur together.

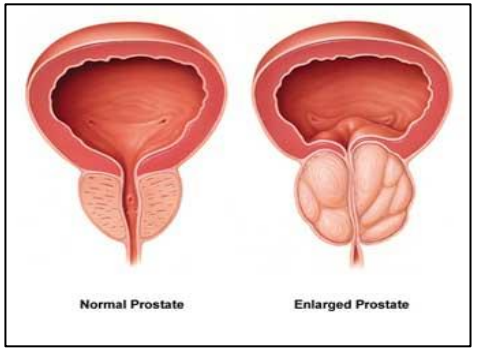
- e.g.the uterus during pregnancy in which there is smooth muscle hypertrophy and hyperplasia.(يعني خلال الحمل يزيد عدد الخلايا ويزيد حجمها بنفس الوقت)

- e.g. Benign (حميد) prostatic hyperplasia.



on the left :
is a normal uterus showing the normal mass of smooth muscle in its wall.
on the right :
is a uterus from a recently pregnant women.





Atrophy

A decrease in size (Shrinkage) of a body part, cell, organ, or tissue by the loss of cell substance.

- Atrophic cells are not dead but have diminished (تضاءلت) function. In atrophy there is decreased protein synthesis and increased protein degradation(تدهور) in cells.
- In the human embryo, for example, a number of structures are transient (مؤقت) and at birth have already undergone atrophy, e.g. The adrenal glands become smaller shortly after birth because an inner layer of the cortex has shrunk.

Opposite of Hypertrophy

Causes of atrophy include :

- **Poor nourishment** (نقص التغذية)
- **Poor circulation** (الدورة الدموية ضعيفة).
- **Loss of hormonal support.**
- **Loss of nerve supply to the target organ.**(بسبب اصابة تسببت بقطع العصب مثلاً)
- **Disuse or lack of exercise** (الإهمال وعدم ممارسة الرياضة) **or disease intrinsic to the tissue itself**(مرض متأصل في النسيج نفسه).
- **Aging(الشيخوخة)** e.g. senile atrophy (ضمور الشيخوخة أو الخرف) and it can lead to **Dementia (الجنون)**

Examples of Atrophy

PATHOLOGY TEAM

Poor nourishment

(نقص التغذية)

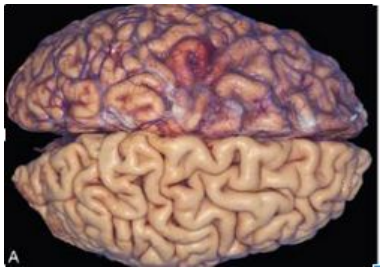
كما هو الحال في الدول الأفريقية الفقيرة التغذية يؤدي بهم الحال إلى تقلص ونقصان بعض الأنسجة والأعضاء لديهم

Poor circulation

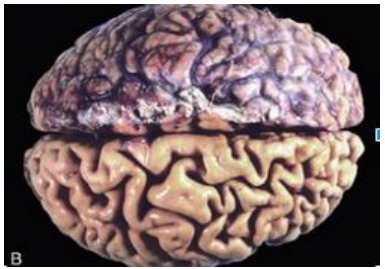
(ضعف الدورة الدموية)

عدم وصول الدم لبعض المناطق في الجسم تؤدي إلى تدهور وظيفتها وتقلصها مثل : عدم وصل الدم لبعض الأصابع

Aging(الشيخوخة) as seen in the brain



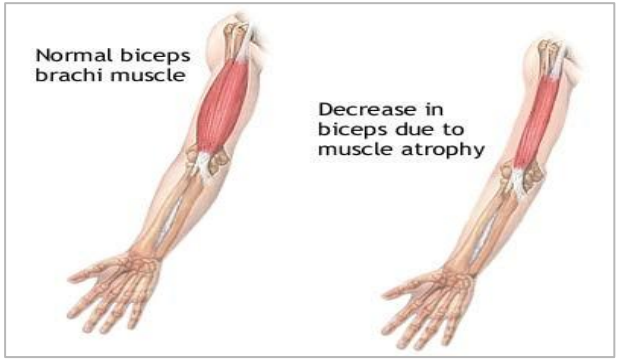
A. Normal brain of a young adult

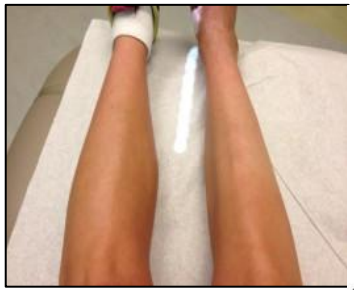


B. Atrophy of the brain in an 82-year-old man with atherosclerotic(تصلب الشرايين)

Disuse or lack of exercise

(الإهمال وعدم ممارسة الرياضة)





Developmental disorders

P A T H O L O G Y T E A M

Hypoplasia and Aplasia are not the opposite of Hyperplasia !

They are **Developmental disorders**(اضطراب النمو) and not an **adaptive response**. (استجابة تكيفية)

Hypoplasia

Incomplete development of a tissue or organ.

e.g.Testes in Klinefelter's syndrome(متلازمة)

Hypoplasia is a congenital(خلقي) condition, while hyperplasia generally refers to excessive cell growth later in life.

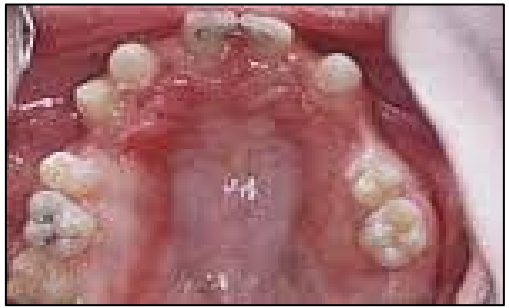
R.Abnormal testis N.Normal testis

Aplasia

A developmental failure resulting in the absence of an organ or tissue.

e.g. pure red cell aplasia and congenital absence of teeth (عدم إكتمال نمو الأسنان)

it is an uncommon disorder in which maturation arrest (توقف نمو أو نضوج الأسنان) occurs in the formation of erythrocytes(الكريات الحمراء). Erythroblasts are virtually absent in bone marrow; however, WBC and platelet production is normal.



Metaplasia

It is the an adapt change (Transformation) in the type of cell to another type.

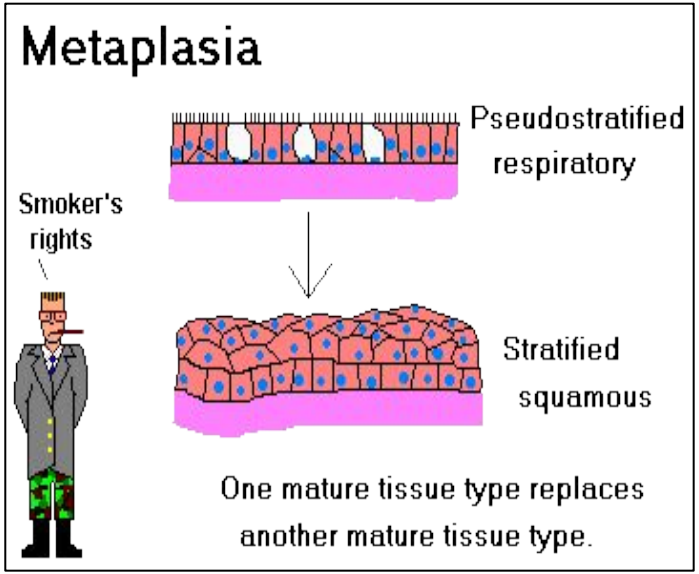
- It is always occur in response to a particular agent.
- Metaplasia is usually reversible. when the agent is removed it will go back to normal.

Examples include:

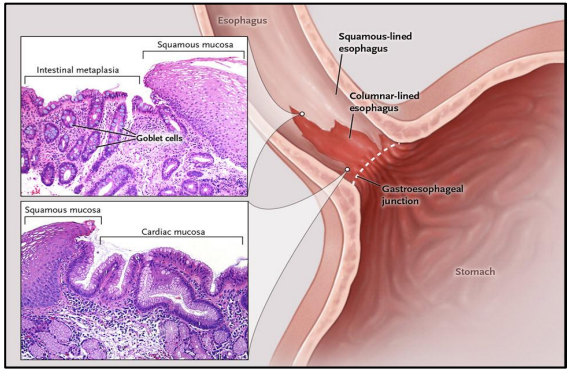
- Squamous metaplasia.
- Columnar cell metaplasia.
- Osseous metaplasia.
- Myeloid metaplasia.

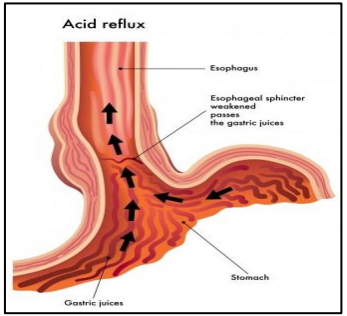
METAPLASIA EXAMPLES

Squamous metaplasia



Columnar cell metaplasia





Examples of Metaplasia

P A T H O L O G Y T E A M

Squamous metaplasia

Transformation of columnar cells to squamous cell.

e.g.

1- In cervix : Replacement at the squamocolumnar junction.

2-In respiratory tract: people who smoke a lot their columnar epithelium of the bronchies will transfer to squamous.

- it can reverse and back to normal (Columnar) but it will lose its function. e.g no more mucus secretion and ciliary action.
- It provide the base of cancer for malignant transformation (carcinoma سرطان)

(Look the figure in previous slide)

Columnar cell metaplasia

Replacement of squamous by a columnar cell.

e.g.

Chronic gastro-esophagal reflux disease.

(لما شخص دائماً يحس بحموضة يكون بسبب إن سائل المعدة الحمضي ارتفع للمريء وبكثرتها يحول الخلايا إلى خلايا أكبر ممكن تتحمل أكثر)

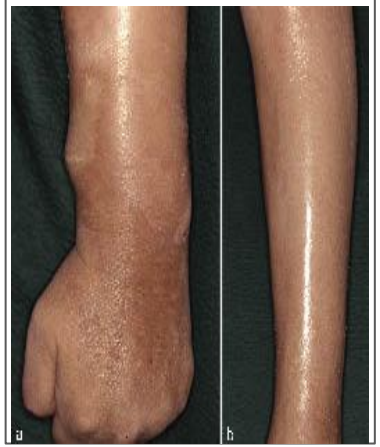
so the normal stratified squamous epithelium of the lower esophagus will turn to a columnar and that called (Barrett's esophagus)

- It can lead to development of adenocarcinoma of esophagus.

(Look the figure in previous slide)

Osseous metaplasia

Formation of new bones at sites of tissue injury or a cartilage (Cartilaginous metaplasia).



Myeloid metaplasia

Proliferation of hematopoietic tissue in sites other than bone marrow.

e.g.

liver and spleen

- It called Extramedullary hematopoiesis

which means blood formation occurs in another part than bone marrow.

some metaplasia diseases

Original tissue	Stimulus	Metaplasia tissue
ciliated columnar epithelium of bronchial tree (القصبات الهوائية)	cigarette smoke(السجائر)	**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 (الصدمات النفسية المزمنة)	**Bone (Osseous) tissue**
Esophageal squamous epithelium	Gastric Acid (حمض المعدة)	**Columnar epithelium**
Columnar glandular epithelium	Vitamin A deficiency (نقص فيتامين أ)	**Squamous epithelium**

Summary

Change in size of cells	
Atrophy	Reduction in the size of cells
Hypertrophy	Increase in the size of cells
Change in number of cells	
Involution	Decrease in the number of cells
Hyperplasia	Increase in the number of cells
Change in differentiation of cells	
Metaplasia	Stable change to another cell type

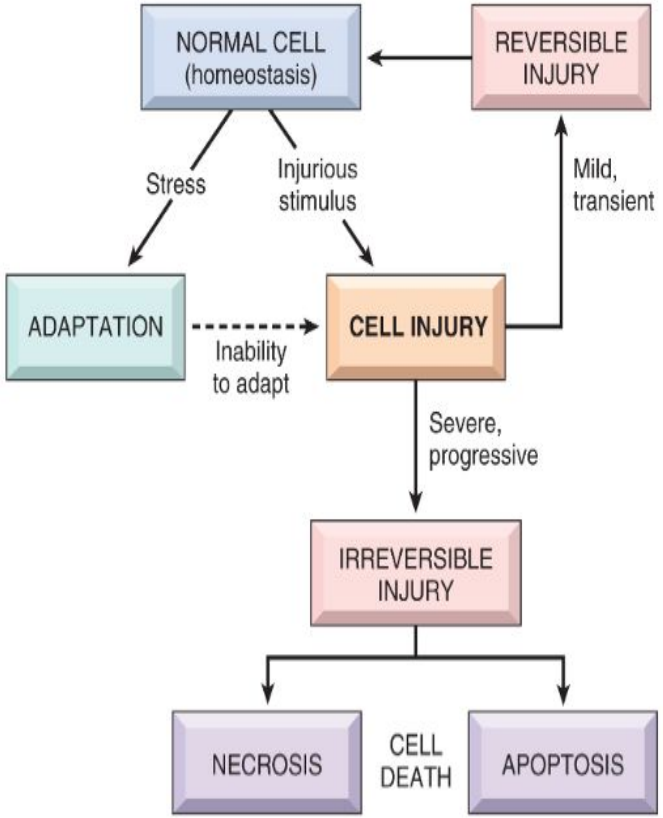
CELL INJURY

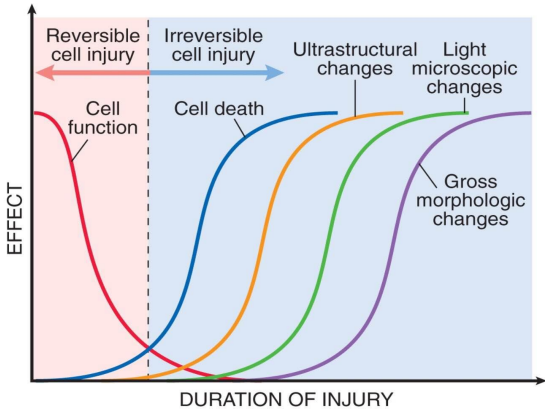
P A T H O L O G Y T E A M

Definitions:

- When cells are stressed so severely that they are no longer able to adapt.
- When cells are exposed to inherently damaging agents.
- When cells are suffer from intrinsic abnormalities. (e.g. DNA or proteins)

الصور هنا جيدة جداً للفهم





NOTE: The mitochondria contain several proteins that, when released into the cytoplasm, tell the cell there is internal injury and activate a pathway of apoptosis.

CELL INJURY

جميع الصور من روبنز للفهم أكثر
لكل صورة الشرح موجود بالكتاب

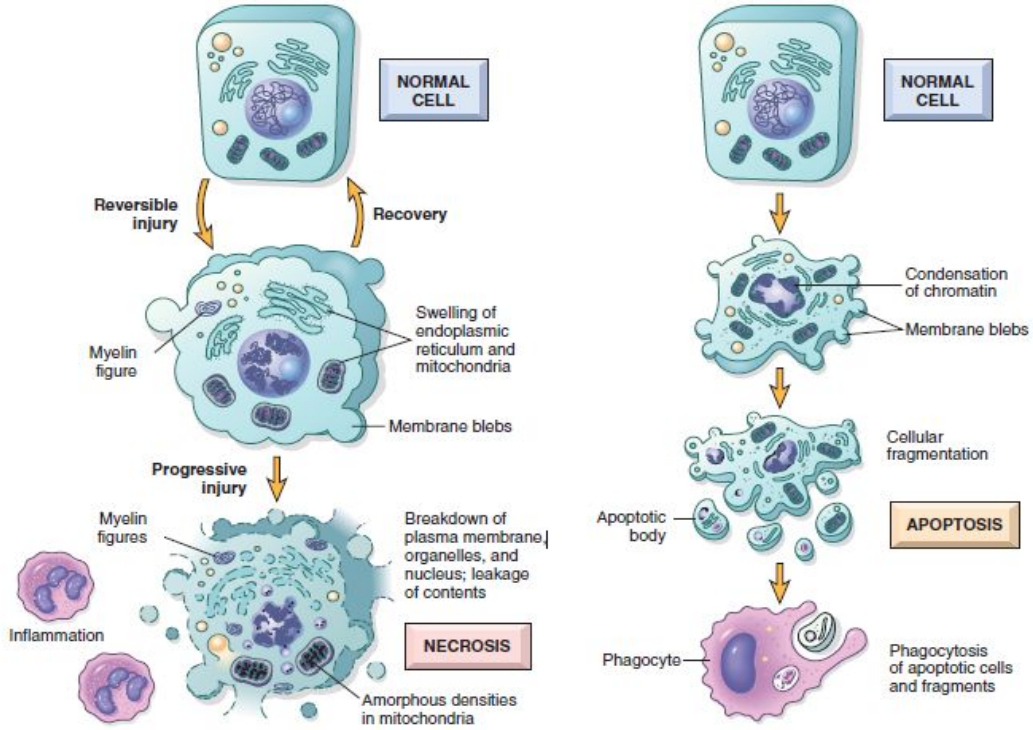


Figure 1–6 Cellular features of necrosis (*left*) and apoptosis (*right*).

CAUSES OF CELL INJURY

"Causes of both reversible and irreversible injury are the same"

Oxygen Deprivation

(Hypoxic cell injury) Means, Oxygen deficiency.
It common cause of cell injury and cell death.

Causes of Hypoxia:

- **Ischemia**: loss of blood supply in the tissue due to impeded arterial flow or reduce venous drainage.
  E.g. in myocardial infarction and atherosclerosis.
- **Inadequate**(غير كافٍ)**oxygenation of the blood**
  e.g. lung disease and carbon monoxide poisoning.
- **Decreased oxygen-carrying capacity of the blood**
  e.g. anemia.
- **Inadequate tissue perfusion**(تروية/نضج) **due to**:
  cardiorespiratory failure, hypotension(انخفاض ضغط الدم), shock.

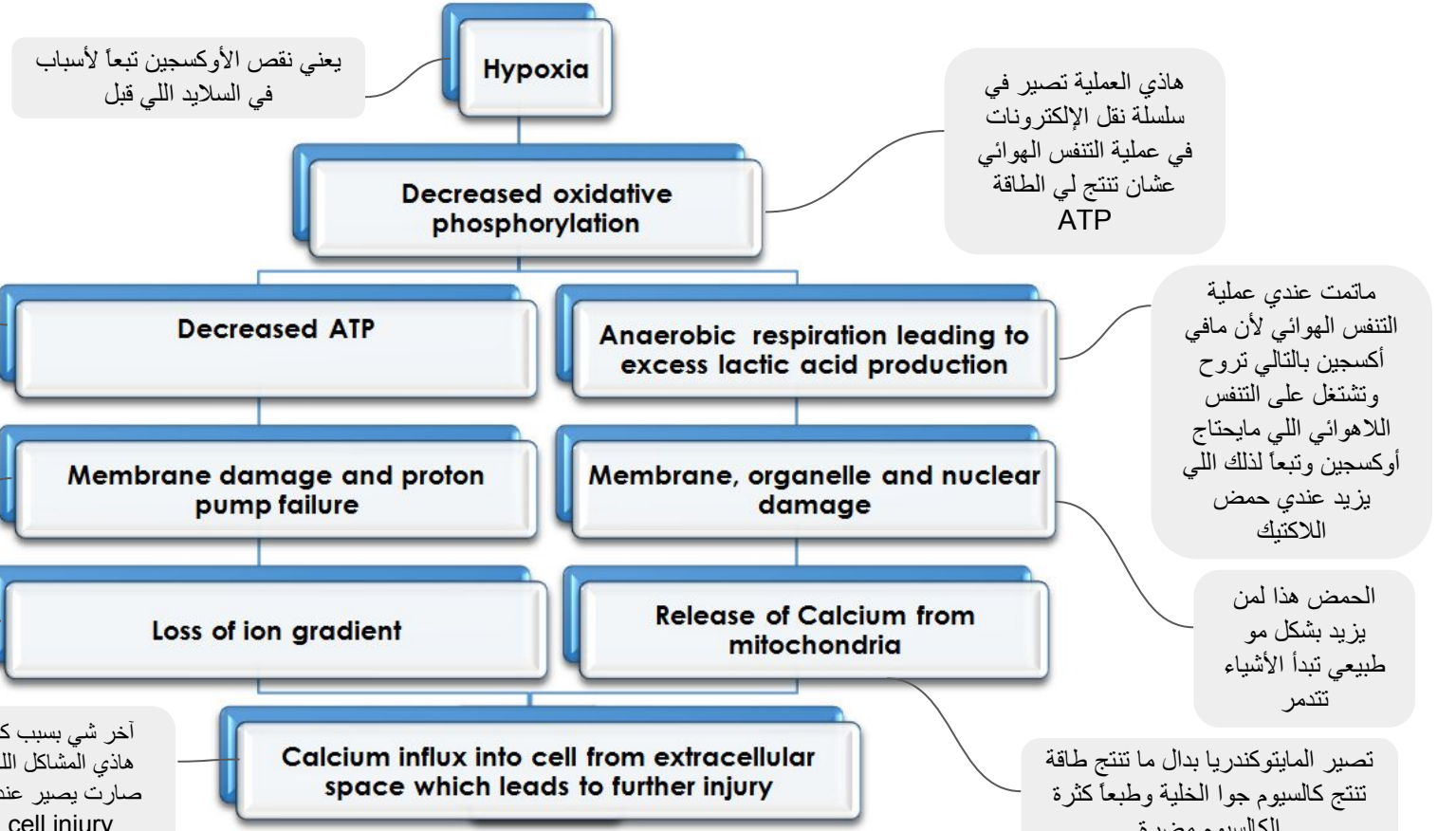
*some cell types are more vulnerable(أكثر عرضة) to hypoxic injury than others.
e.g. **neurons(the more sensitive) > cardiac muscle > hepatocytes > skeletal muscles (the less sensitive)**

Is the most common cause of hypoxia.

Depending on the severity(خطورة) of the hypoxic state, cells may :

- **Adapt.**
- **undergo injury.**
- **or die.**

Oxygen Deprivation Cont...



CAUSES OF CELL INJURY

"Causes of both reversible and irreversible injury are the same"

Physical Agents

- Any mechanical trauma.(إصابة)
- Extreme heat : e.g. Burns
- Extreme cold : e.g. Deep cold
- Sudden changes in atmospheric pressure.
- Radiation.

Either sun radiation which is ultraviolet light or the radiation used in cancer treatment.

- Electric shock

Chemical Agents

Any chemical substance in abnormal amount can cause cell injury.

For Example:

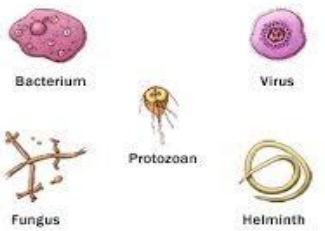
- ➔ Oxygen in high concentrations.
- ➔ poisons.(السموم)
- ➔ pollutants.(الملوثات)
- ➔ insecticides.(المبيدات الحشرية)
- ➔ industrial and occupational hazards.(المخاطر الصناعية والمهنية)
- ➔ Alcohol and narcotic(تخديري) drugs and therapeutic(علاجي) drugs.

Infectious Agents

(العوامل المُعدية)

It caused by :

- ➔ Bacteria.
- ➔ Viruses.
- ➔ Fungi.
- ➔ protozoans



CAUSES OF CELL INJURY

"Causes of both reversible and irreversible injury are the same"

Immunologic agents

When the immune system start produce immune response **AGAINST** our cells or tissue. Then cause Cell injury.

It's called: autoimmune reactions(ردود الفعل المناعية الذاتية)

(يعني بدال ما تحارب الجسيمات الضارة تروح وتحارب خلايانا السليمة)

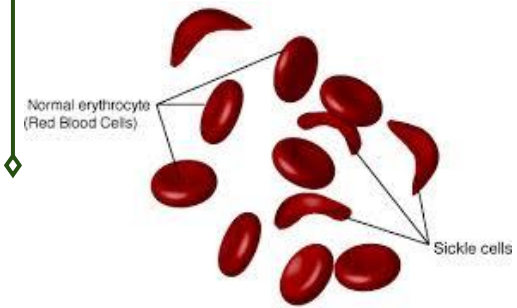
E.g. Thyroid damage caused by autoantibodies (HIV)

Genetic Derangements

(خلل وراثي)

For example:

- **Down syndrome.**
  (خلل وراثي في الكروموسوم رقم21)
- **Sickle cell Anemia.**
  (فقر الدم المنجلي)



Nutritional Imbalances

Nutritional **"Imbalance"** **NOT "Malnutrition".**
Because malnutrition means only less nutrition, BUT here also over nutrition can cause cell injury.

- **Less nutrition:**
  In underdevelopment countries.
  (النحف الحاد)
- **Over nutrition:**
  In development countries.
  (السمنة المفرطة)

MECHANISM OF CELL INJURY..What happens when have cell injury?

P A T H O L O G Y T E A M

Depletion* of ATP

Any cell needs **ATP** for its normal function. but when ATP is decreased due to **(hypoxia, toxins, malnutrition (سوء تغذية) and Mitochondrial damage)**

It will cause cell injury → irreversible → necrosis

Mitochondrial damage

Mitochondria is necessary for the aerobic respiration(التنفس الهوائي)of the cell. This means that any damage will cause cell damage especially in hypoxic injury and Cyanide* poisoning. And it will absolutely cause ATP depletion and it will produce Oxygen free radicals instead.

Influx* of calcium activation of enzymes

Ischemia cause→ Too much calcium in the cell Due to failure of ATP-dependent Ca2+ pumps. and this leads to cell imbalance!!

Increased Ca2+ in cell will activates a number of enzymes that damage cellular components and may also trigger* **apoptosis.**

Ribosomal damage

Ribosomes are essential for protein synthesis and protein is a very important element for the cell so when it gets damaged??? than the cell will be injured .. SO!!

1- People who are addicted to alcohol their liver cells will get → Ribosomal damage → Cell injury

2- People taking antibiotic are using bacterial infection and too much of antibiotic will cause → Ribosomal damage → Cell injury

Nuclear and DNA damage

The cell has its own mechanism to repair DNA but, when the damage is too severe … than the DNA will undergo apoptosis (Suicide) (انتحار الخلية)

Cell membrane damage/ defects

Any damage in the cell membrane will cause a defect* in membrane permeability

note: main cause is the function of the free radical or the Reactive Oxygen Species (R.O.S)

Depletion = Decreased
Cyanide = poisonous gas
Influx =تدفق
trigger (V.) = cause (an event or situation) to happen or exist
defect = خلل

لا ترتاعون من كمية الكلام !! ترا كله مب مطالبين فيه وحطيناه لمجرد التوضيح ,اخذوا الدعوة سالفة واقروها بس عشان توصل المعلومة صح

MECHANISM OF CELL INJURY. CONT...

Accumulation of oxygen derived free radicals (oxidative stress)

What are free radicals?
They're harmful chemical atoms that have single unpaired electron in an outer orbit.
They are unstable and highly reactive(you can stabilize them by a biochemical reaction).

What is Reactive oxygen species (ROS)?
It is a type of oxygen derived free radical that has a role in cell injury.

Why do you think free radicals cause injury?
Because it might enter a dangerous and toxic reaction that damages the cell.

What are the factors that increase the production of free radical ?
1- Normal metabolism / respiration → free radicals produced as a bi-product.
2- Ionizing Radiation injury.
3- Immune(WBC) response to inflammation.
4- Chemical toxins.
5-Oxygen therapy and reperfusion injury.
6- Transition metals such as iron and copper can trigger production.

What are the main damaging effects of these reactive species ?
They attack **(Nucleic acid / proteins / lipids)**.
The moment they're reacting with molecules (ما يبون يخلصون) So they initiate another reaction to transform the other molecule into free radicals.

How does our body fight the free radicals ? (Tha scaverning system)
1- Antioxidants : Vit E,A and C (Ascrobic acid)
2-Enzymes :
- $O_2 \rightarrow H_2O_2$ BY: **Superoxide dismutase (SOD)**
- $H_2O_2 \rightarrow H_2O$ BY: **a) Glutathione Peroxidase (Found in cytoplasm)**

b) Caspase (Found in peroxmosis)
- **Catalase and mannitol.**

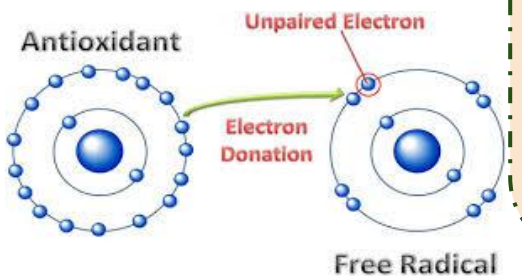
The important chemical mediator generated by various cells .

Most common free radicals: (cause cell injury)
superoxide anion radical **(O_2-)**
hydrogen peroxide **(H_2O_2)**
and hydroxyl ions **(OH).**
Nitrogen oxide (NO)

أي عدم توازن بين الفري راديكال والعوامل اللي تقضي عليها يسبب
Cell injury

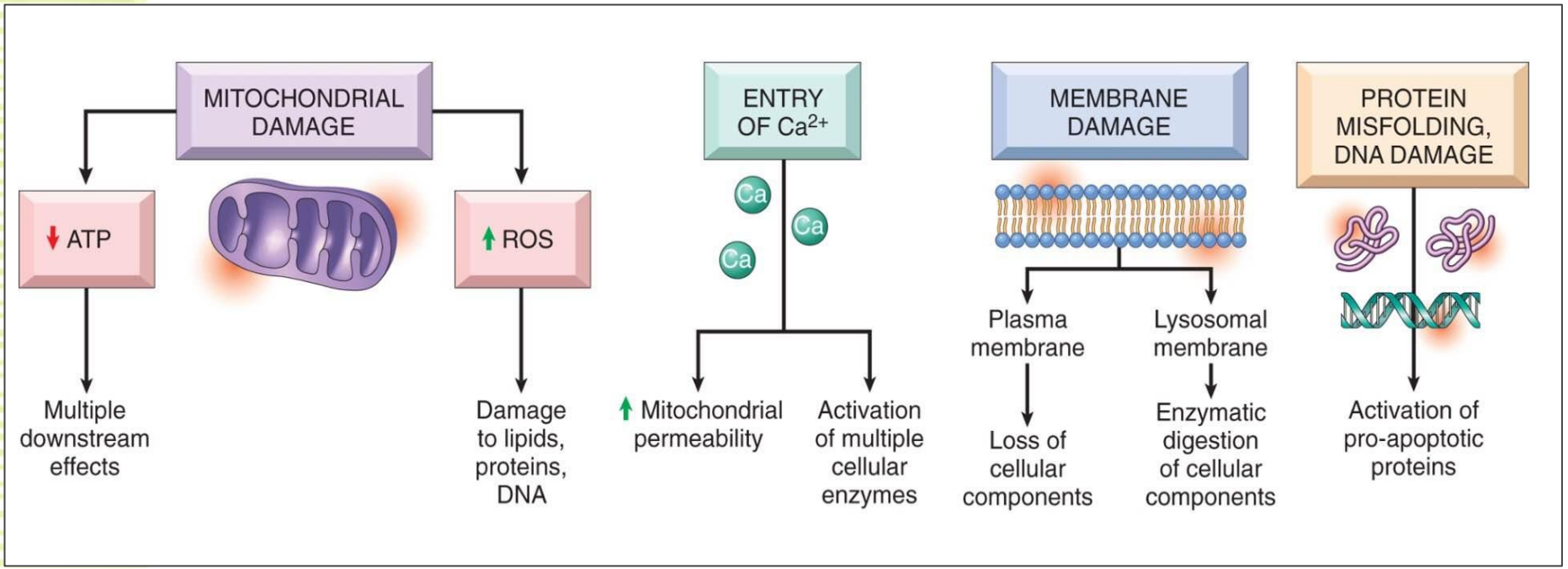
FREE RADICALS IN THE CELL ARE USUALLY FROM OXYGEN

NOTE: increased intracellular Ca2+ activates a number of enzymes:
Phosolipase: (membrane damage)
proteoses: (break membrane and cytoskeletal proteins)
endonuclease: (DNA and chromatin fragmentation).
Adenosine: triphospase (ATPases).



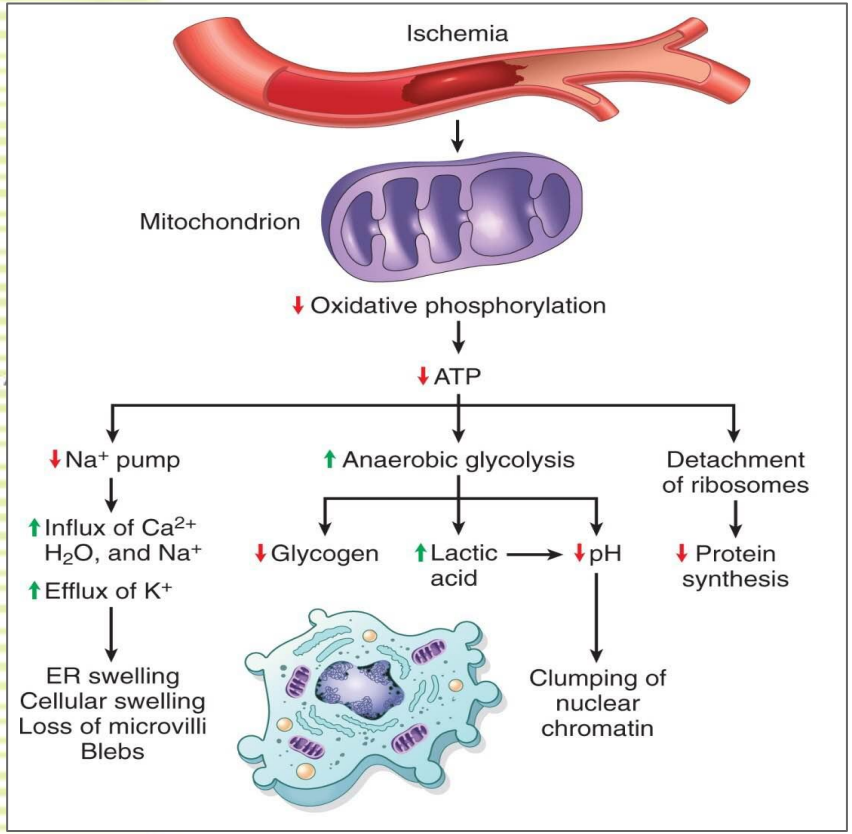
جميع الصور من روبنز للفهم أكثر
لكل صورة الشرح موجود بالكتاب

Summary

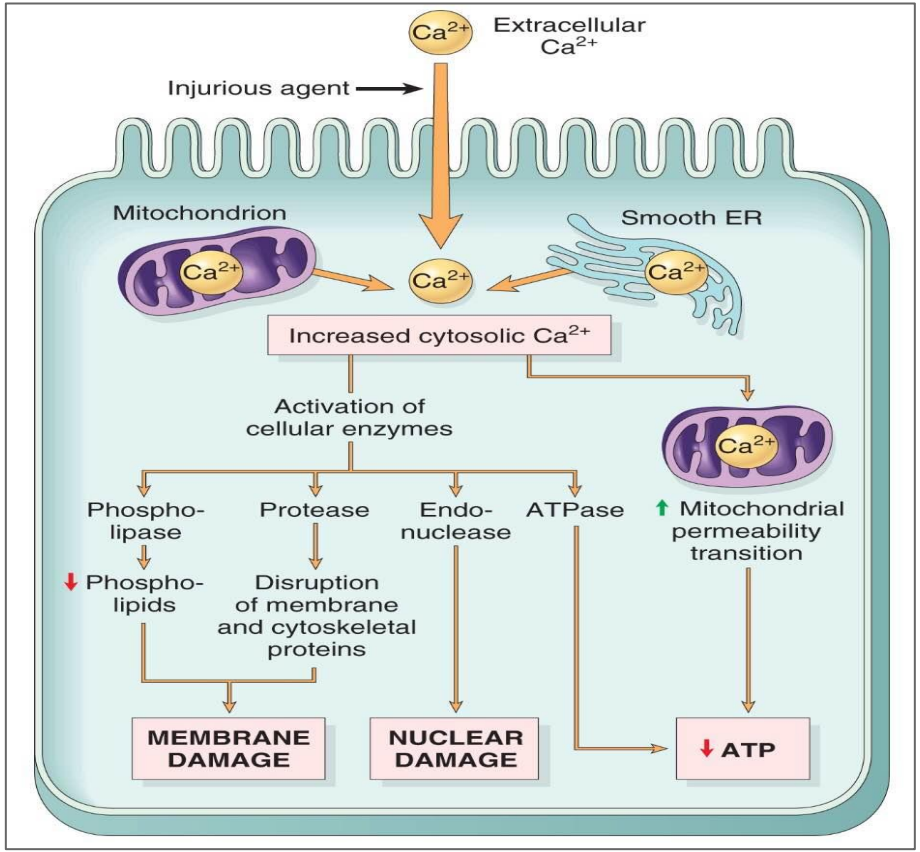


جميع الصور من روبنز للفهم أكثر
لكل صورة الشرح موجود بالكتاب

Depletion* of ATP

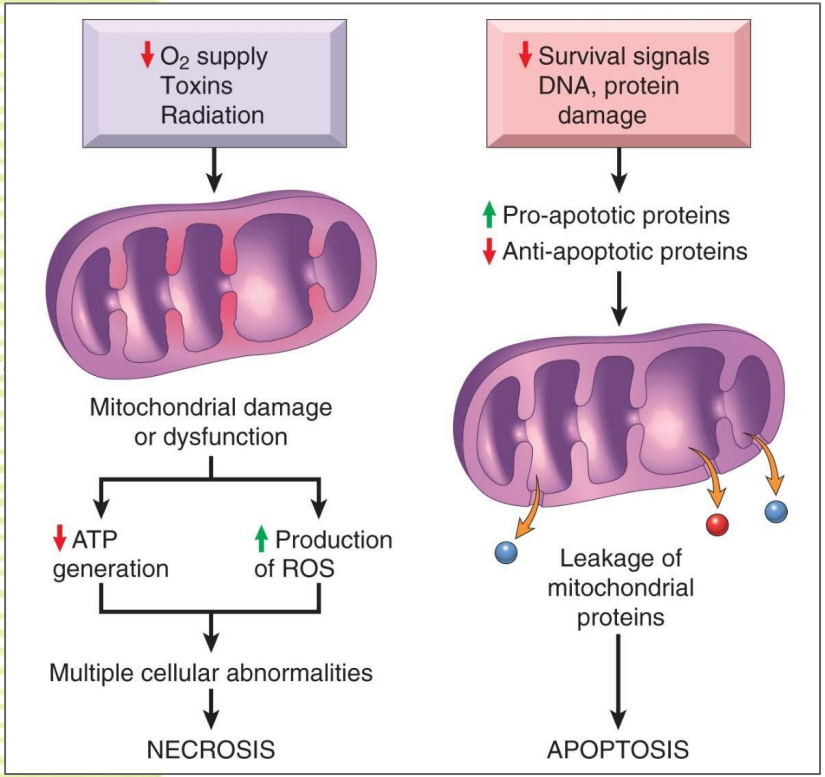


Influx of calcium activation of enzymes

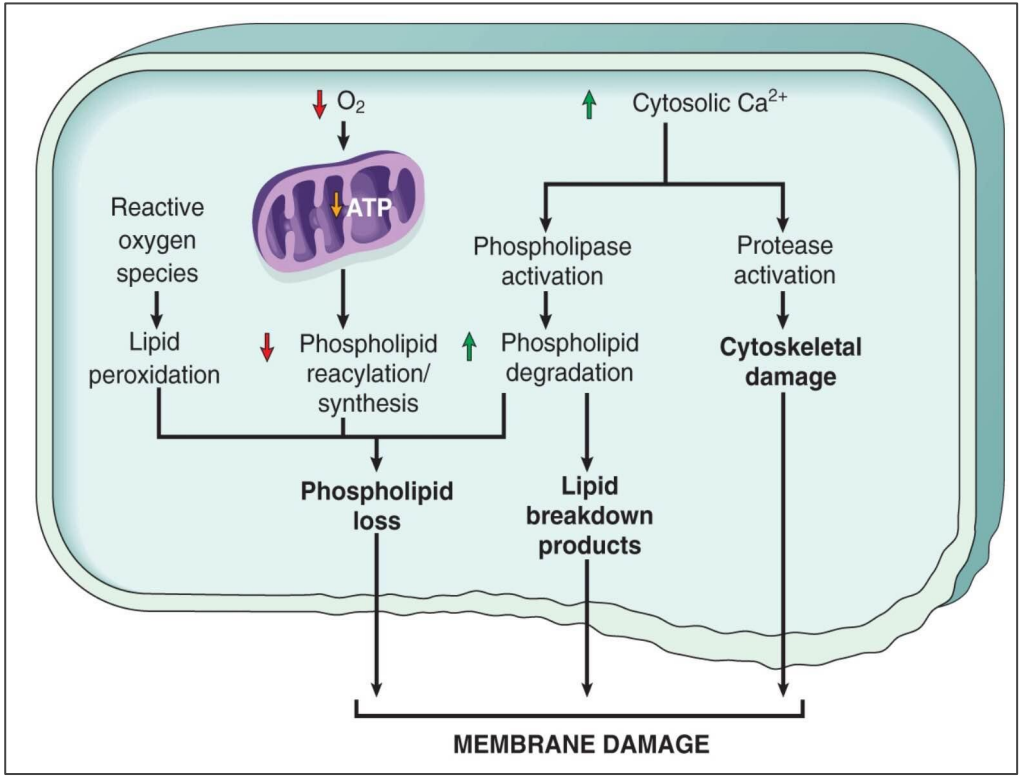


جميع الصور من روبنز للفهم أكثر
لكل صورة الشرح موجود بالكتاب

Mitochondrial damage



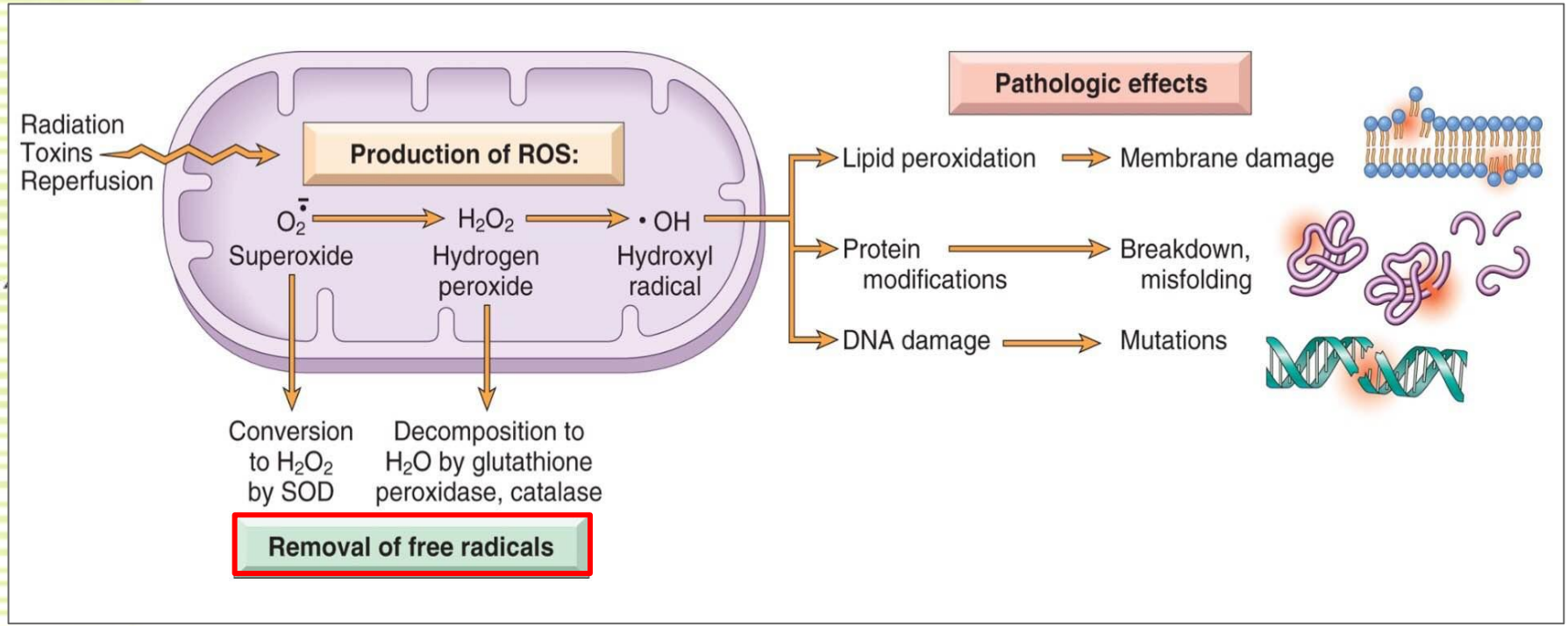
Cell membrane damage/ defects



جميع الصور من روبنز للفهم أكثر
لكل صورة الشرح موجود بالكتاب

Accumulation of oxygen derived free radicals (oxidative stress)

Removal of free radicals



reversible cell injury VIDEO

when the cell can compensate(تعوض) the derangements (خلل) and the injurious stimulus is removed and the cell is reversed At this stage, the injury has typically not progressed to severe membrane damage and nuclear dissolution.

The changes that occur in reversible cell injury:

- Swelling of cell cytoplasm with vacuolization of cytoplasm called hydropic or vacuolar degeneration
- Mitochondrial swelling
- Fatty change.
- Plasma membrane blebbing.
- Damage to the rough endoplasmic reticulum leading to loss of protein synthesis
- Eosinophilia (due to decreased cytoplasmic RNA)(تظهر تحت المايكروسكوب)

Why is there **increased eosinophilia**?

reason: the DNA is damaged → cannot form RNA → decrease RNA in cytoplasm.

صح عندنا صبغتين تظهر تحت المايكروسكوب؟ صبغة الهيموتوكسلين تظهر النواة باللون الأزرق ومن مكونات النواة ال RNA فلمن ما يكون عندي RNA هذا يعني ماعندي صبغة هيموتوكسلين ماعندي لون أزرق وبالتالي يزيد صبغة اليوزين فتلقونها تحت المايكروسكوب لونها غالباً يكون وردي

irreversible cell injury VIDEO

when there is Persistent(مستمر) or excessive (مفرط) injury that causes cells to pass the threshold (بداية) into irreversible injury. Marked by:

- severe (وخيم) mitochondrial damage with the appearance large, amorphous densities (كثافة غير منتظمة) in mitochondria.
- extensive damage of cell membrane.
- increased eosinophilia.
- Numerous myelin figures
- swelling and rupture (تمزق) of lysosomes leakage (رشح) and enzymatic digestion of cellular contents

- **Nuclear damage:**

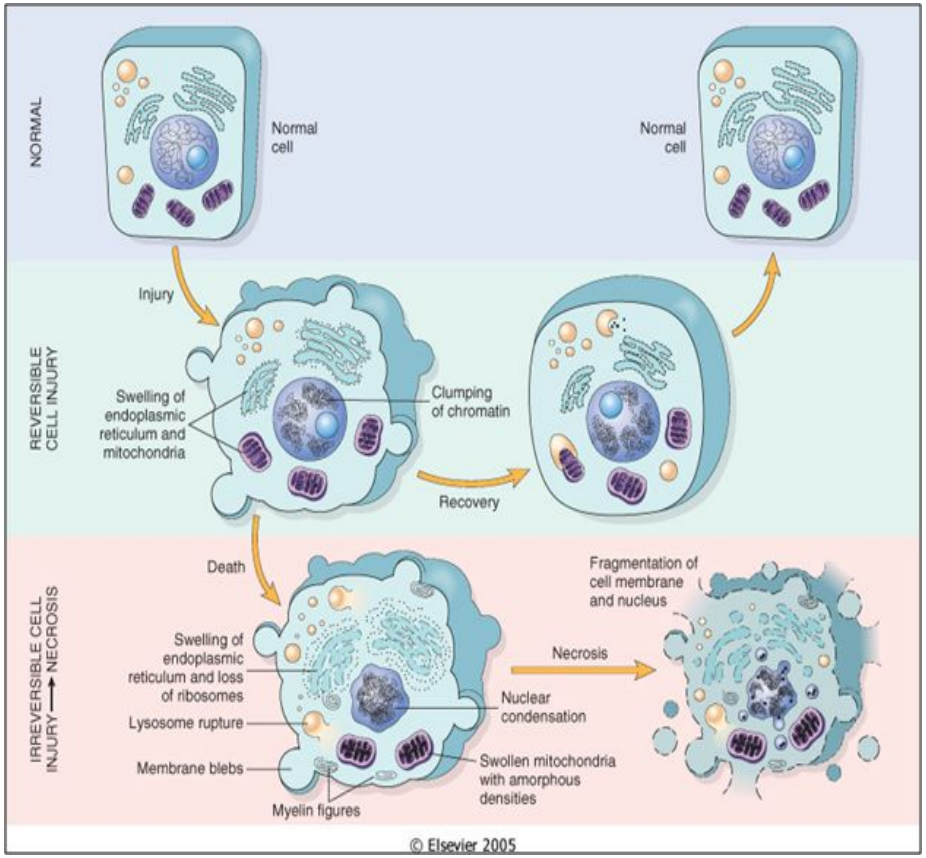
➔ pyknosis (shrinkage) انكماش النواة

➔ karyorrhexis (break down) تمزق النواة

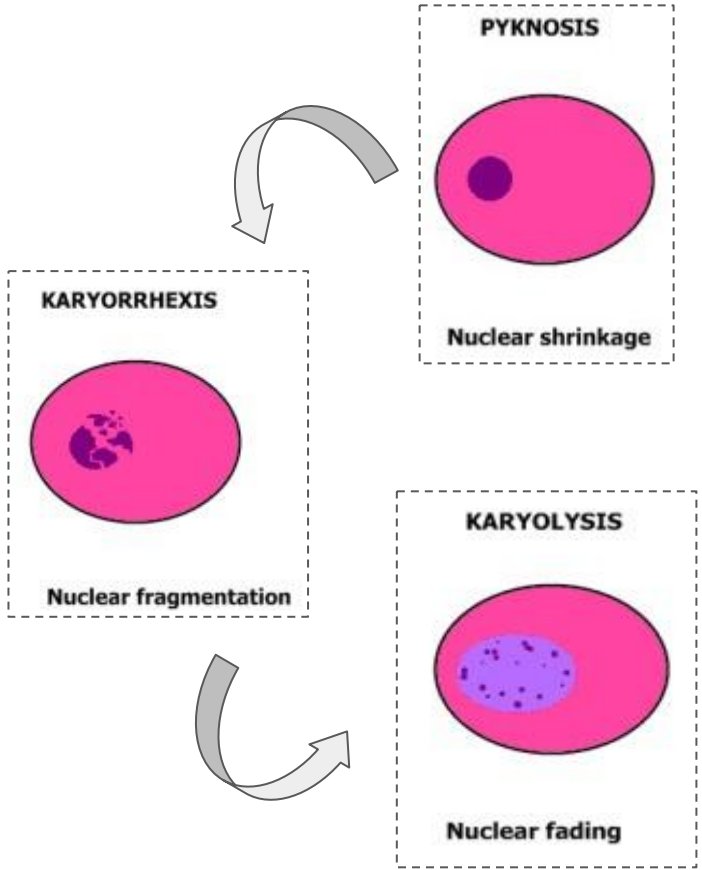
➔ karyolysis (dissolution) انحلال النواة

(See the figure next slid please)

Summary



Nuclear damage



Lecture 2 outline

- **Types of necrosis** : Coagulative, Liquefactive, Caseous, gangrenous, fibrinoid and fat necrosis.
- **Apoptosis** : definition, morphologic features, regulation of apoptosis
- A.**Comparison** between necrosis and apoptosis.

Necrosis

Necrosis is changes that follow cell death in living tissue, due to enzymatic digestion(الهضم الأنزيمي) and denaturation (تدمير) of intracellular protein in the injured cell.

It occurs in irreversible injury.

It is usually associated with inflammation in the surrounding tissue.

It involves the death of a group of cells in one area. (النيكروسيس ما يصيب خلية واحدة لازم مجموعة)

لو ترجمنا كلمة
نيكروسيس بيطلع لنا
معناها نخر
طيب .. خلونا نشبهه
بتسوس الأسنان لمن
السوس يجلس ينخر
الضرس نخر لين
يتآكل كله ويترك وراه
فجوة متضررة بالضبط
نفس النيكروسيس لمن
تنخر الأنسجة

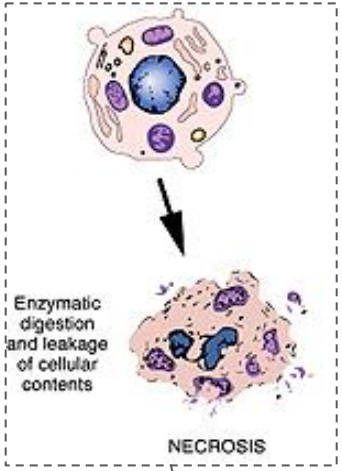
Necrosis can result in :

- Cessation (توقف) of function of the involved tissue or organ.
- Release of certain cellular enzymes that can be detected in blood. e.g. Cardiac enzymes in myocardial infarction (heart attack).
- An inflammatory response.(يصير فيه التهابات في المنطقة اللي صار فيها نيكروسيس)

مستوى هذه الأنزيمات استخدمها كإشارة لوجود نيكروسيس في التشخيص و تساعد في تحديد وقت النيكروسيس ومدى الإصابة
يعني كل ما زاد مستوى هالأنزيمات دليل على إن مدى الإصابة عالي ووصل مراحل خطرة

Types of lysis(تحلل)

HETEROLYSIS
(تحلل بسبب غير ذاتي)
The enzymes from lysosomes of neighboring leukocytes. (WBC)



AUTOLYSIS
(تحلل بسبب ذاتي)
The enzymes used in this degradation of a cell come from either the lysosomes of the dying cell itself.

- Autolysis is the death/disintegration of cells or tissues by it's own enzymes.
- Autolysis is also seen in cells after death/ post mortem (بعد الوفاة)

  is also seen in some pathologic conditions in living organisms.

Types of Necrosis

Coagulative.

Liquefactive.

Caseous necrosis.

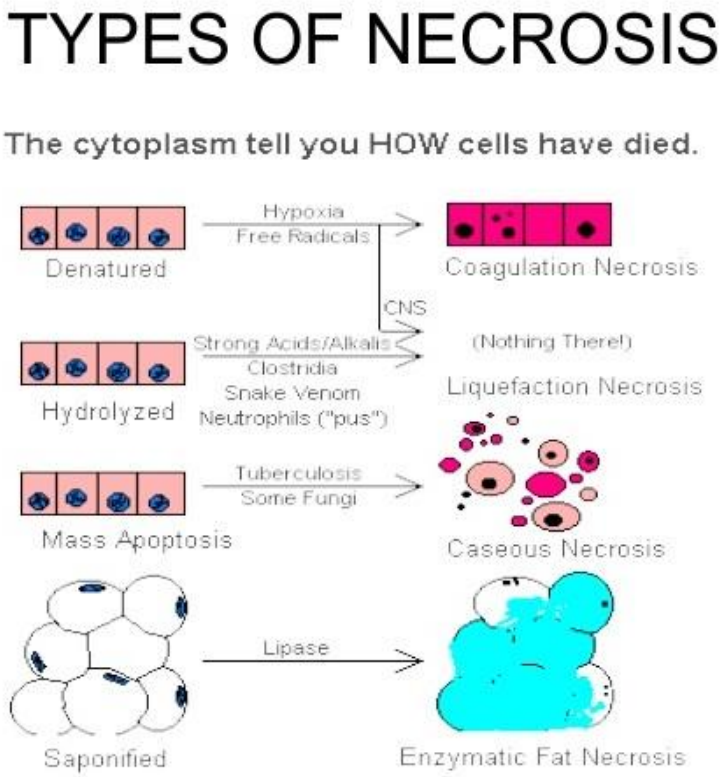
Fat necrosis.

Fibrinoid necrosis.

Gangrenous necrosis.

Wet gangrene: Coagulative > Liquefactive

Dry gangrene: It is a form of Coagulative.



Coagulative necrosis (متخثر):

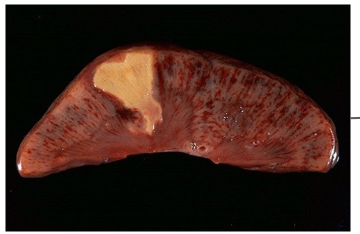
Seen when blood flow to an organ is affected leading to ischemic/hypoxic (نقص الأوكسجين) death of cells in that organ.

It is seen in all organs except the brain

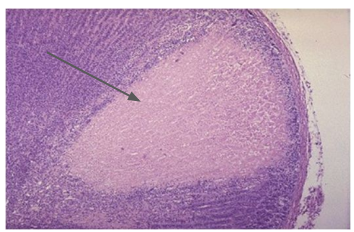
It causes infarct and is seen in:

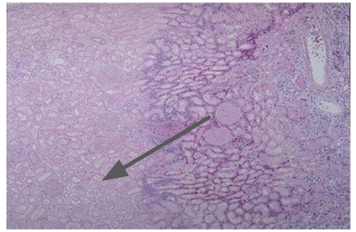
- heart (myocardial infraction الذبحة القلبية)
- kidney (renal cortical necrosis/ infarct)
- spleen.
- liver (infarct)

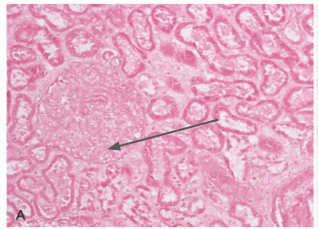
Kidney



Gross: The affected organ looks pale(شاحب) and firm/solid. It looks likes cooked meat or boiled egg.

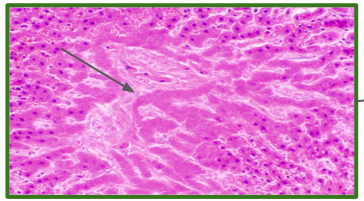






Microscope: The nucleus is lost. The cell cytoplasm is eosinophilic.Cell outlines are preserved (cells look ghostly), and everything looks red.

Liver



some of the cells don't have nuclei at all **WHY?** Because there's lysis of nuclei (karyolysis).

Liquefactive necrosis (مُميّع):

Is a type of necrosis which results in transformation of the tissue into a liquid viscous mass.(كتلة لزجة سائلة)

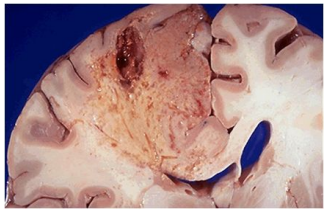
Is characteristically seen in :

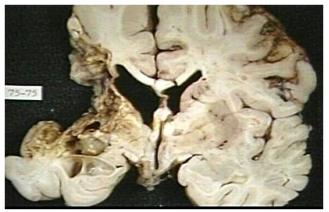
- Hypoxic cell death in **the central nervous system/brain.**
- And in suppurative infections(التهابات قيحيّة) **(pus or abscesses)** especially bacterial. (القيح والصديد أو الخرّاج التي تسببها البكتيريا)

Ultimately, most necrotic cells are phagacytosed.

The affected tissue is softened/liquefied by the action of :

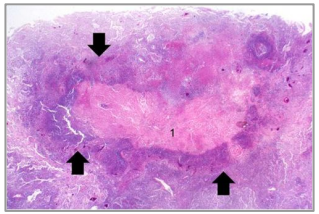
In the brain : hydrolytic enzymes released from the lysosomes **in the brain cells.**

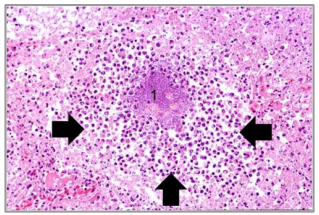




The center is soft liquefied creamy yellow.

In the pus/abscess: The enzymes released **from the neutrophils.**

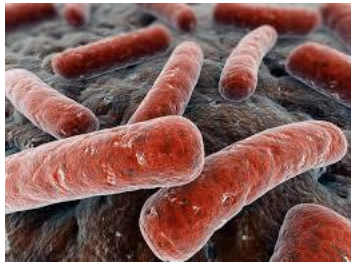




The center labeled surrounding is neutrophils.

Caseous(التجبن) necrosis:

is a type of coagulative necrosis classically seen in: e.g. tuberculosis(مرض السل) (infection by mycobacterium tuberculi).

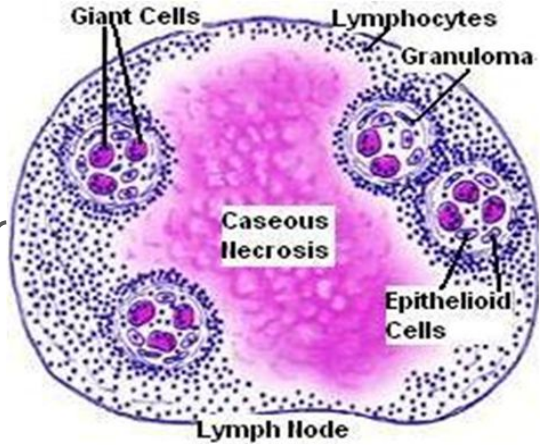


*A **granuloma** is a small area of inflammation in tissue. **Granulomas** are most often the result of an infection and most frequently occur in the lungs.

Lungs with Tuberculosis

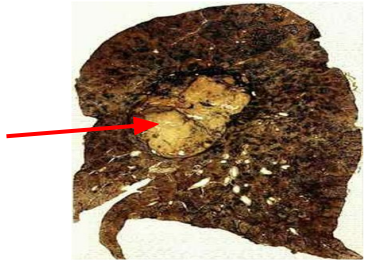
Microscopic

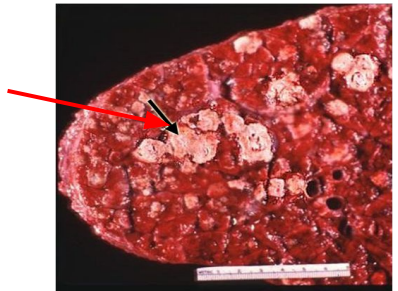
Appears as **amorphous pink granular** debris(حطام) surrounded by a collar(طوق) of **epithelioid cells (modified macrophages)**, and **lymphocytes** and **giant cells. This is known as granuloma.**



Gross

White, soft, curd like, cheesy-looking(جبني) "caseous" material.





Fat necrosis(دهني):

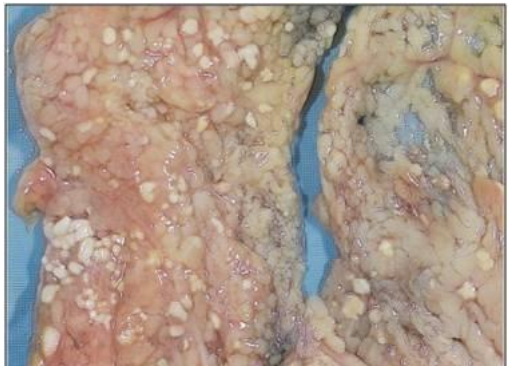
Is focal areas of **fat destruction/ necrosis** due to enzymatic action of lipase (which is released from injured **pancreatic tissue**) into the surrounding fat in the abdominal cavity. Seen in:acute pancreatitis. (التهاب البنكرياس الحاد) and in breast fat and other fatty areas due to traumatic injury.

HOW?

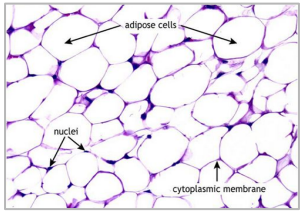
الخلايا المصابة تبدأ تفرز أنزيم اللايبيز وتفصل مكونات الدهون إلى ثلاثة فاتي أسيد + جليسرول. الثلاث فاتي أسيد المفصولة تبدأ تتحد مع الكالسيوم في الدم وتكون شي اسمه صابون الكالسيوم يكون شكله كبقع بيضاء بالخلايا الدهنية المصابة بالنيكروسيس.

calcium soaps (called as fat saponification) (التصبّن)

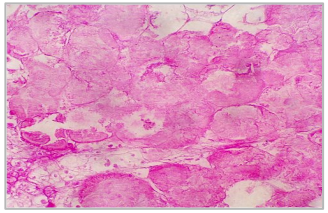
Example:



fat necrosis with saponification in the mesentery(المساريقا بالأمعاء). The areas of white chalky deposits represent calcium soap.



Normal adipose tissue



fat necrosis

Fibrinoid necrosis(شبه ليفي):

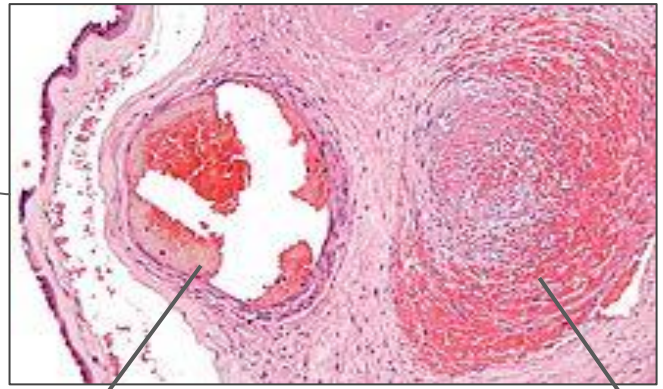
Is necrosis in the blood vessels (arteries, arterioles and capillaries)

There is deposition of **fibrin material** in the arterial walls, which appears smudgy (blurred ضبابية) and acidophilic/eosinophilic.

It is seen in immune mediated diseases (autoimmune diseases : develops when your immune system attacks our healthy cells) and also seen in malignant hypertension. (ارتفاع ضغط الدم الخبيث)

Fibrin material : (dark pink amorphous material)

Example:



An artery with some fibrin material make it narrow.

Blocked vein surrounded by extravasated red blood cells.

Gangrenous necrosis: A term commonly used in clinical practice by surgeons.

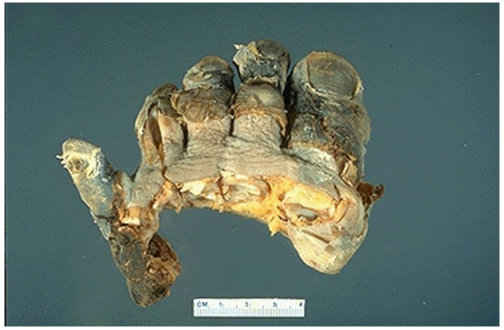
Dry Gangrene (mummification) / Non-infected

- It is a form of **coagulative necrosis** that develops in ischemic tissue,where the blood supply is inadequate.(غير كافٍ)
- **It is without infection.**
- Dry gangrene is often due to peripheral artery disease is usually seen **in limbs, especially the leg**, that has lost its blood supply and has undergone coagulative necrosis.
- Dry gangrene is dry non-infected ischemic necrosis of tissue.
- It is seen as a complication in atherosclerosis and diabetes mellitus.
- The affected part is dry, shrunken and dark reddish-black.

تعتبر الغرغرينا مثال على ال Coagulative
تصيب الخلايا اللي ما يوصلها دم كاف بالتالي ما يوصلها أوكسجين كافي ويؤدي إلى **Ischemic**

WHY LEGS?
لأنها هي الجزء الأبعد عن القلب بالتالي احتمال يكون وصول الدم لها قليل يؤدي إلى كوأقيوليتف وبعدين يصيبها غرغرينا جافة

الغرغرينا الجافة تصيب الخلايا الغير مصابة بالأسكيميك نيكروسيس وتقوم تجففها مع الوقت



Gangrenous necrosis:

Wet Gangrene / infected

- When there is superadded bacterial (putrefactiveمعفن) infection the coagulative necrosis is modified **by the action of the bacteria** into liquefactive necrosis, and it is called **wet gangrene**.
- So, initially there is coagulative necrosis and then there is **superaddedinfection** leading to liquefactive necrosis.
- The bacteria is usually **saprogenic** (نوع للبكتيريا) it lives in the **gut** (الجهاز الهضمي) or the **soil**(تربة) and it can thrive in low oxygen states.
- **(gram-positive Clostridia or *Bacillus fusiformis*)**. It has a poor prognosis compared to dry gangrene because the infection can spread to the rest of the body (septicemia) and be life threatening (death), so the limb has to be amputated(بتر العضو). The limb becomes foul smelling and black and starts decomposing.(تحلل)

يعني: الكوأقيوليتيف نيكروسيس متى يتحول ويصير لكويفاكتيف ؟
لمن تجيه بكتيريا وتبدأ تاكل فيه

NOTE: Diabetes mellitus is a risk-factor for peripheral vascular disease and thus for dry gangrene, but also a risk factor for wet gangrene.

الغرغينا بسبب نشاط البكتيريا ممكن تكبر الإصابة وينتشر في الجسم ويسبب septicemia (تسمم الدم)
وتصير حياة الشخص معرضة للخطر
إذا لازم نبتر هالرجل أو اليد
وتكون رائحة الغرغرينا سيئة جداً
وبعدين تبدأ الخلايا بالتحلل

Apoptosis

Apoptosis is programmed cell death.(موت الخلاي المبرمج)
Apoptosis means “falling off”. It is a type of cell suicide.(انتحار الخلية)

Is results from activation of ‘death pathway genes’.

Regulation of apoptosis It is mediated by a number of genes and their products e.g: **bcl-2 gene** inhibits apoptosis **bax genes** facilitates apoptosis , **p53 gene** facilitates apoptosis by inhibiting **bcl2 and promoting bax genes.**

It is a pathway of cell death in which cells destined to die (تتحضر للموت) activate their own enzymes to degrade their own nuclear DNA and proteins.**Important enzymes of apoptosis:**

- Cysteine proteases named caspases
- Ca2+- and mg2+-dependent endonucleases

NOTE: Apoptosis and necrosis sometimes coexist.(يتواجدون مع بعض)

EXTRA

Like the BC12 oncogene(جين ورمي) which switch off apoptosis and allows the neoplastic cells (الخلايا الورمية) to live.
(The BC12 is an antiapoptotic (مضاد لموت الخلاي) (الخلاي المبرمج) oncogene located in chromosome 18

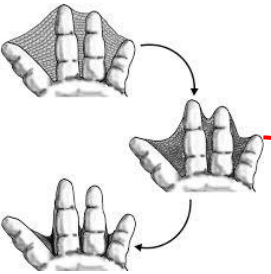
سبب السرطان هو نمو الغير طبيعي للخايا وعدم وجود موت مبرمج لها بسبب إن هذا الجين يوقف عملية موت الخلايا المبرمج وبالتالي يتكون عندي ورم خبيث

neoplastic cells

لمن تتحضر الخلية للموت تبدأ تفرز أنزيمات داخلها عشان تحلل العضيات فيها وبالتالي تموت

EXTRA

Clearance(تخلص) of apoptotic cells: they entice(جذب) phagocyte by producing **“eat-me”** signals, where it lead tissue macrophages to phagocytosis of the apoptotic cells.



Apoptosis it can be :

Physiological or adaptive

- **The programmed destruction of cells during embryogenesis.**
- **Hormone-dependent:** e.g. endometrial cell breakdown during the menstrual cycle, the regression of the lactating breast after weaning, and prostatic atrophy after castration (adaptive atrophy).
- **Apoptosis in proliferating cells** e.g. intestinal epithelial lining is always being replaced.
- **Cells that after performing their function undergo apoptosis** e.g neutrophils and lymphocytes in inflammation.
- Sometimes body produced harmful lymphocytes and they are also destroyed **by apoptosis.**

Pathologic

- **Cell death produced by injury** e.g. radiation.
- **In certain diseases e.g. viral hepatitis(التهاب الكبد) the infected hepatocytes undergo apoptosis (acidophilic bodies)** or **injury of skin cells (keratinocytes) leads to apoptosis of keratinocytes (Civatte bodies).**
- **Pathologic atrophy in organs** e.g. pancreas, parotid gland, and kidney
- **Corticosteroid induced atrophy of the neonatal thymus.**
- **Cell death in tumors** (usually accompanied (مصحوبة) by necrosis).

EXTRA

Apoptosis of the thymus gland is physiological in adolescence..
يعني البالغ خلاص معد يحتاج ثايمس فيصير لها ضمور ويبدا عدد الخلايا يقل بشكل كبير .. لكنه طبيعي
لكن الـ neonate أو اللي توه مولود غير طبيعي يجي للغدة ضمور لانه محتاجها.. متى يصير لحديث الولادة أبوبتوزيز بالثايمس ؟ لما نعطيه corticosteroids (توقف الالتهابات + الجهاز المناعي)

ليش يصير أبوبتوزيس للـ ثايمس لما يبلغ الانسان؟؟
بسبب زيادة بهرمونات البلوغ اللي هي بالاصل Steroid

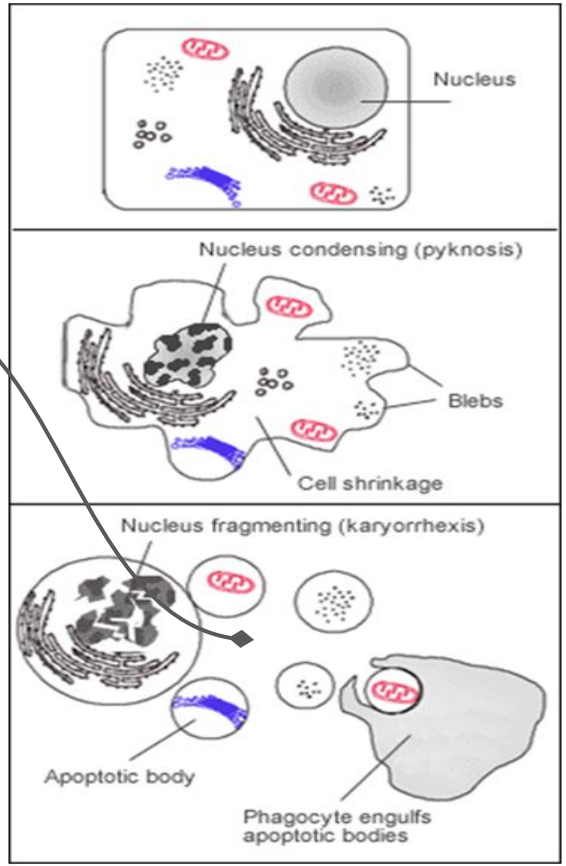
Mechanism of apoptosis

1. **Activation by death pathway genes**
2. **Cell shrinkage.**
3. **Chromatin condensation in the nucleus:** This is the most characteristic feature of apoptosis. The nucleus may break up into fragments.
4. **Formation of cytoplasmic blebs and apoptotic bodies:** (يبدأ الغشاء ينكمش ويحيط بكل عضية بالسيتوبلازم ويحوصلها وبالتالي يتكون عندي الأبوبتوتيك بديز)

The apoptotic bodies contain cytoplasm and organelles, with or without nuclear material.

5. **The cell's plasma membrane remains intact.**(سليم و غير مصاب بأذى) The plasma membrane of the apoptotic cell sends signal to macrophages to phagocytose it.
6. **Phagocytosis of apoptotic bodies, mainly by macrophages.**

VIDEO

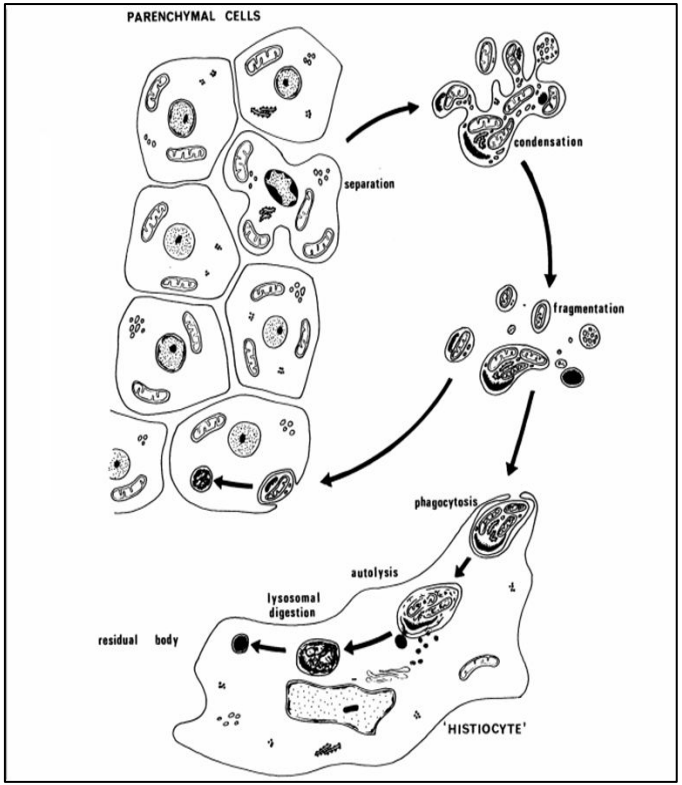


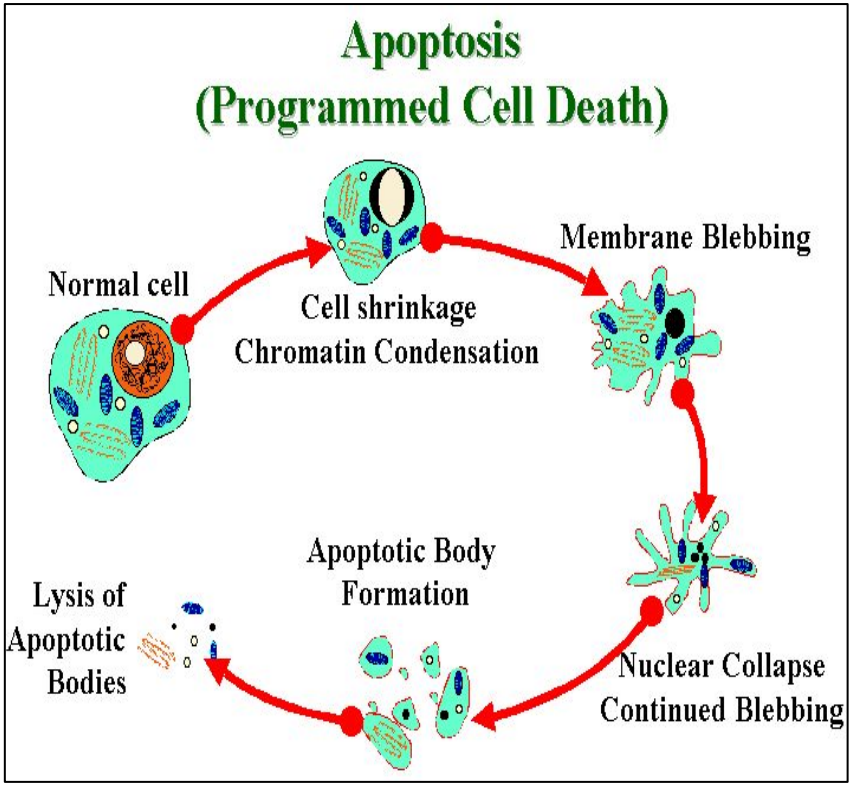
EXTRA

* The mitochondrial pathway seems to be the pathway that is responsible for apoptosis in most situations.

Mitochondreal damage → ATP depletion → Failure → Necrosis → Leakage of proteins that cause apoptosis

Mechanism of apoptosis





EXTRA

NOTE

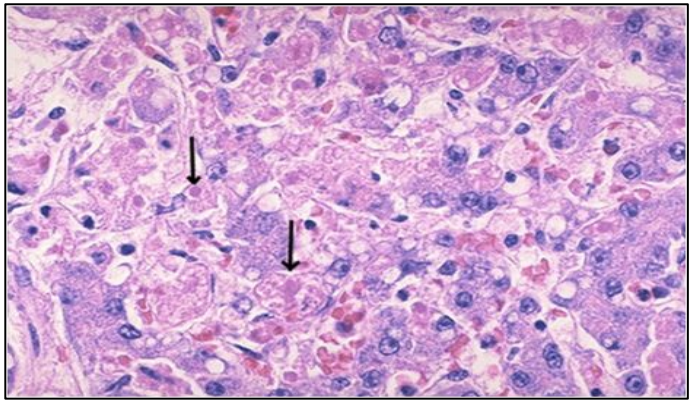
*Apoptosis can be also used in medical uses, as it kills bacteria by stopping it from producing proteins by targeting Rough ER inside bacteria cell .

Morphology of apoptosis

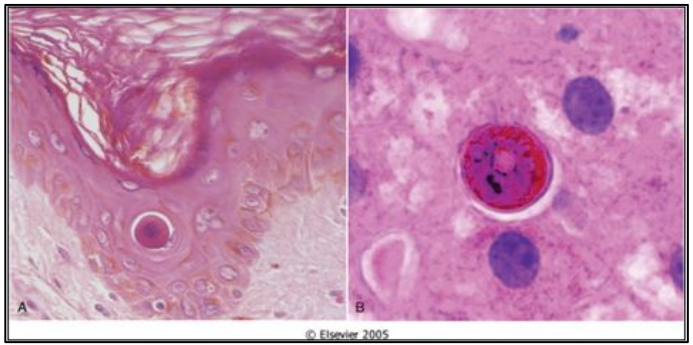
On histology apoptosis involves **single cells** or **small clusters/group of cells.**

The apoptotic cell appears as a **round** or **oval mass** of intensely **eosinophilic cytoplasm** with **dense nucleus**.

There is no inflammation.



apoptosis in liver cell

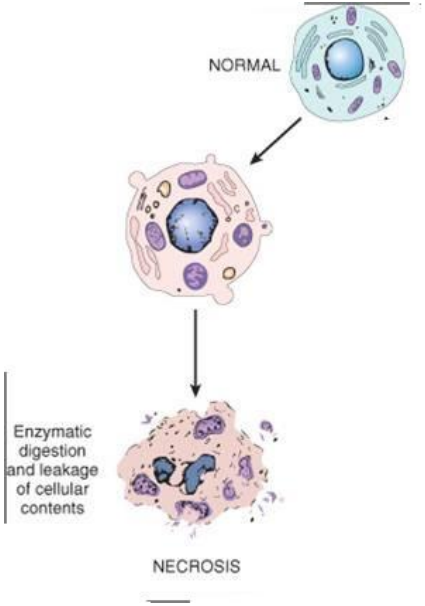


apoptosis in epidermis

The mean differences between NECROSIS and APOPTOSIS

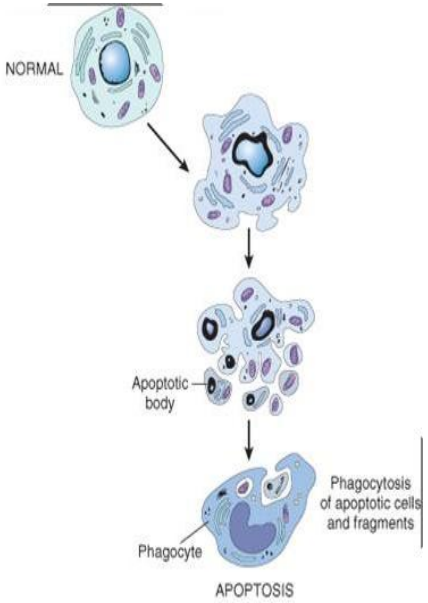
NECROSIS

- Necrosis can is associated with inflammatory reaction.
- Necrosis is almost always pathologic.
- Necrosis is almost always occur in groups of cells.



APOPTOSIS

- Apoptosis is <u>NOT</u> associated with inflammatory reaction.<u>WHY?</u>
  Because there is no release of the cytoplasmic content in apoptosis!
- Apoptosis can be physiologic or pathologic.
- Apoptosis may occur as a single cell or in group.

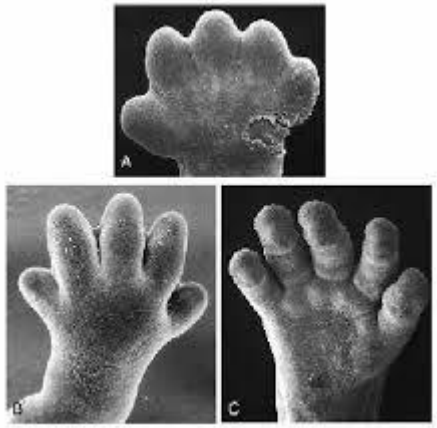


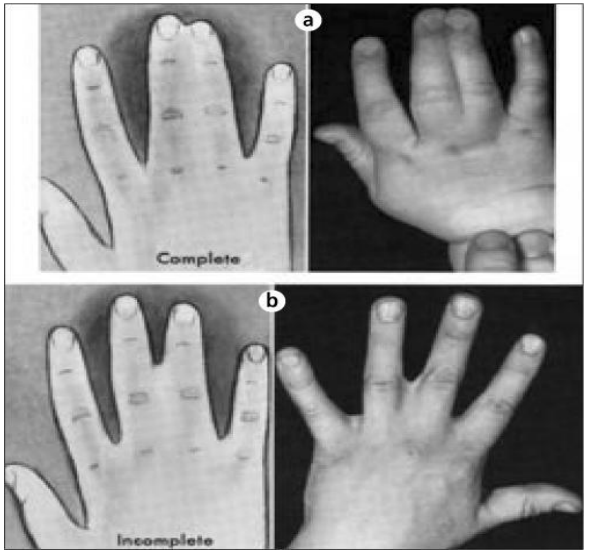
(Comparison between necrosis and apoptosis)

Feature	Necrosis	Apoptosis
Cell size	Enlarged (swelling)	Reduced (shrinkage)
Nucleus	Pyknosis → karyorrhexis → karyolysis.	Fragmentation into nucleosome size fragments
Plasma membrane	Disrupted	Intact; altered structure, especially orientation of lipids
Cellular contents	Enzymatic digestion; may leak out of cell (تتسرب خارج الخلية)	Intact; may be released in apoptotic bodies.
Adjacent inflammation	Frequent	No
Physiologic or pathologic role	Invariably pathologic (culmination of irreversible cell injury)	Often physiologic, means of eliminating unwanted cells; may be pathologic after some forms of cell injury, especially DNA and protein damage

EXTRA INFORMATION

During embryological life when developing fingers it'll first develop as buds(براعم) and between the fingers there will be excessive skin, in one of the stages; **apoptosis will happen and the development of the five fingers will be complete**. If apoptosis doesn't happen, then he has a congenital(خلقي) malformation and some of his fingers are stuck together (the treatment is to undergo surgery to remove the excessive skin).





Lecture 3 outline

INTRACELLULAR ACCUMULATION Reversible cellular changes and accumulations**:**

- fatty change, hyaline change, accumulations of exogenous pigments (carbon, silica, iron dust, lead and argyria)
- Accumulations of endogenous pigments: melanin, bilirubin, haemosiderin (haemosiderosis and haemochromatosis), lipofuscin.

PATHOLOGIC CALCIFICATION: metastatic calcification and dystrophic calcification

Intracellular Accumulations(تراكمات)

Accumulation of abnormal amounts of various substances as a result of a variety of different pathological and physiological processes, and this is usually an early indicator of cell stress or reversible injury, may or may not cause diseases.

The accumulating substance can be:

- Substance that is present in the cell normally but has accumulated in excess, such as water, lipids, glycogen, proteins, and carbohydrates.
- An abnormal substance that is **not** present in the cell normally.
  - Exogenous (from outside the body) e.g. a mineral or component of bacteria etc.
  - Endogenous (from inside the body) e.g. a product of abnormal synthesis or metabolism
- **Pigments:** pigments can also be **endogenous or exogenous.**

Some of the substances accumulate in excess in the cell:

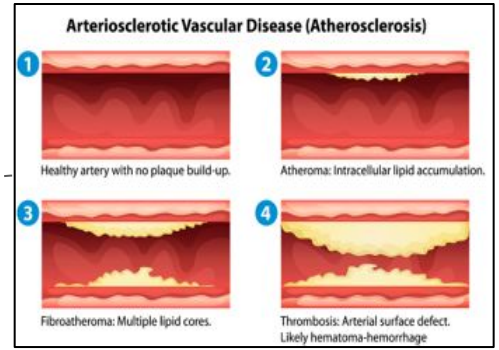
Lipids

All major classes of lipids can accumulate in cells:

- **Triglycerides** e.g. steatosis (fatty change)
- **cholesterol/cholesterol esters** (accumulation of cholesterol in the form of intracellular vacuoles can be seen in atherosclerosis in which there is accumulation of cholesterol in the smooth muscle cells and macrophages in the wall of arteries).
- **phospholipids.**

Steatosis (Fatty Change)

Accumulation of triglycerides of parenchymal cells (the function part of an organ) in the cytoplasm.It is mainly seen in liver, but it is also seen in heart, muscle, and kidney.



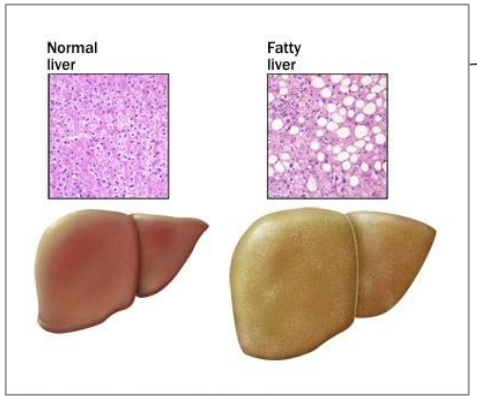
The causes of steatosis include:

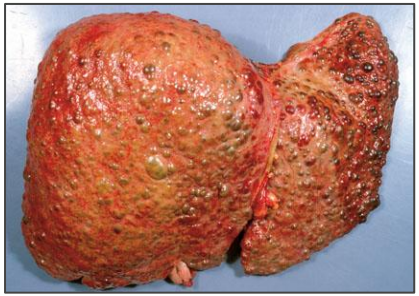
- Toxins e.g. alcohol abuse
- protein malnutrition,
- diabetes mellitus.
- obesity.
- Anoxia/starvation
- Pregnancy
- Severe anemia

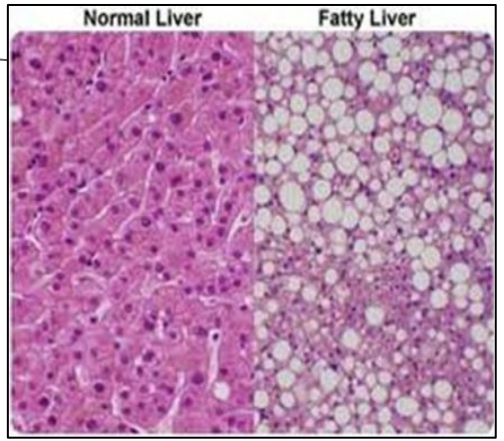
Some of the substances accumulate in excess in the cell:

Lipids

Morphology of Steatosis in liver:







Gross: In mild cases liver looks normal. In severe cases liver is enlarged, yellow and greasy.

Light microscopy: clear vacuoles in the cytoplasm displacing the **nucleus to the periphery of the cell Occasionally**, cells rupture, and the fat globules merge, producing a so-called **fatty cyst.**

Some of the substances accumulate in excess in the cell:

GLYCOGEN

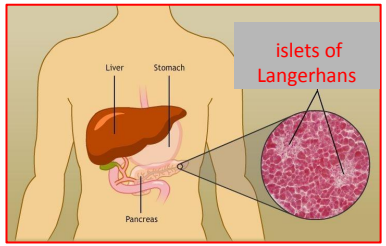
Glycogen is a readily available energy store that is **present in the cytoplasm.**

Excessive intracellular deposits of glycogen are seen in patients with an abnormality in either glucose or glycogen metabolism.

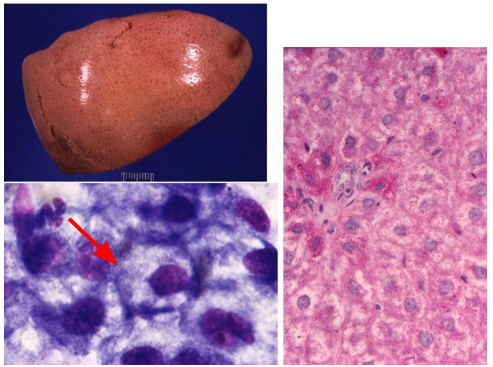
Glycogen accumulation is seen in:

Diabetes mellitus: is a disorder of glucose metabolism. **In this disease,** glycogen is found in the proximal convoluted tubules of kidney, in liver, the β cells of **the islets of Langerhans,** heart muscle cells etc.

Glycogen storage diseases: it is a group of genetic diseases in which there is abnormal glycogen metabolism.



accumulation of glycogen in liver



They appear as clear vacuoles within the cytoplasm. **Glycogen stains pinkish/violet with mucicarmine stain or the periodic acid schiff (PAS) stain.**

Some of the substances accumulate in excess in the cell:

PIGMENTS

PIGMENTS are colored substances.

Endogenous pigments

Synthesized within the body itself.

Some endogenous pigments are normal constituents of cells (e.g. melanin)

others are not normal constituents of cells. Examples include:

- Lipofuscin
- Melanin
- Bilirubin
- Hemosiderin

Exogenous pigments

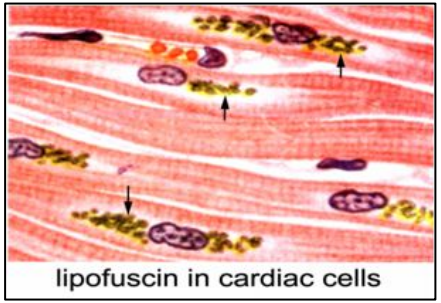
They are not synthesized within the body itself and are coming from outside the body.

Extra : Such as carbon most common, silica, iron, tattoo. Can find their way into the body in a variety of ways.

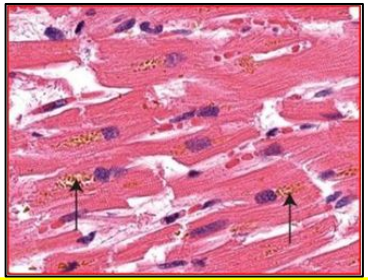
Endogenous Pigments

(1) Lipofuscin

Heart



lipofuscin in cardiac cells

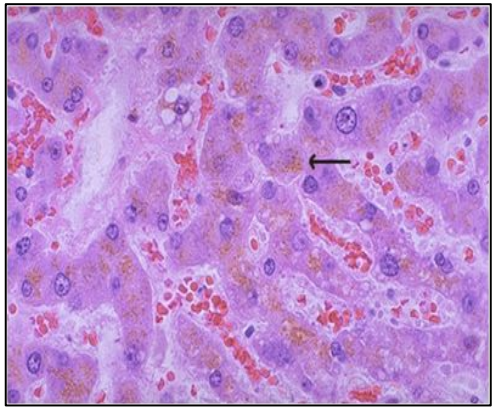


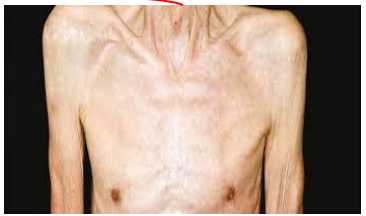
- It is yellow-brown, granular intra-cytoplasmic pigment .

Is also Called : (the aging pigment) (the tear-and-wear pigment)

- is endogenous and causes **NO damage** to cells , **it is NOT pathologic.**
- It indicates history of free radical injury and lipid peroxidation.
- It is prominent in the liver and heart of **aging** patients (مرضى الخرف), in atrophic tissue, patients with **severe malnutrition** and **cancer cachexia.**
- Found in The lysosomes of older people. It is a sign of aging.

Bottom from the liver

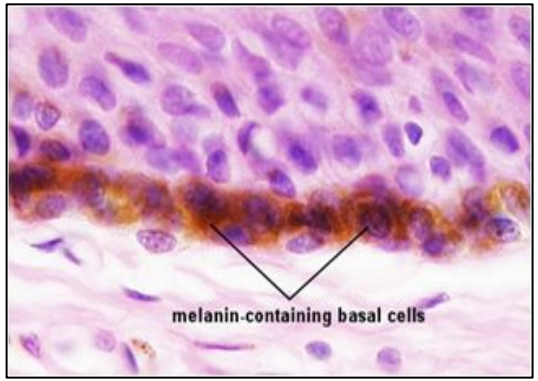


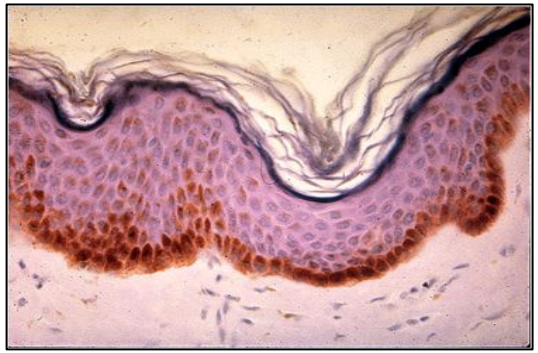


Endogenous Pigments

(2) Melanin

normal skin with basal melanin.

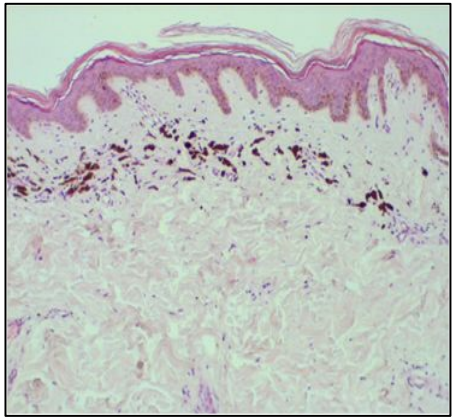




FEATURES :

- An endogenous.
- Non-hemoglobin.
- Brown-black pigment normally present in the cytoplasm of melanocytes in the skin's epidermis.
- **It is responsible for the color of our skin.**
- It is derived from tyrosine and stored in melanosomes of the melanocytes.
- It accumulates in large amounts in benign and malignant melanocytic tumors.
- In inflammatory conditions of the skin it spreads from epidermis into the underlying dermis.This is called as post inflammatory hyperpigmentation of the skin.

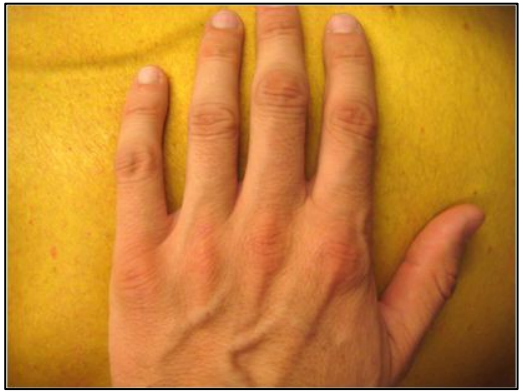
post inflammatory hyperpigmentation

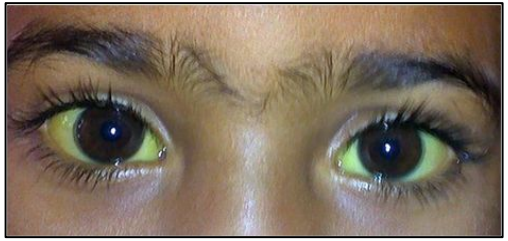


Masson-Fontana stain is used to identify melanin.

Endogenous Pigments

(3) Bilirubin



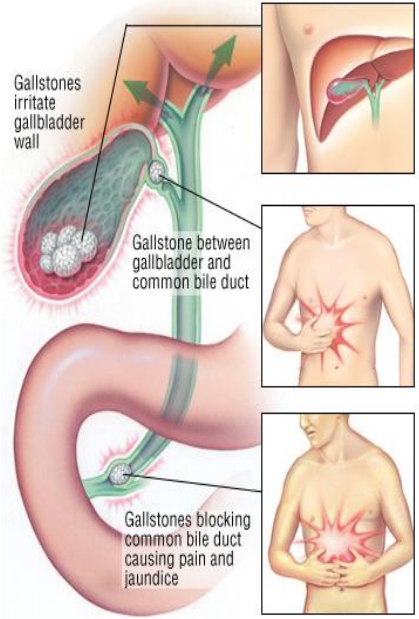


FEATURES :

- **is a yellowish pigment found in bile, a fluid made by the liver.**
- Bilirubin is a breakdown product of **heme catabolism.**
- Most of the bilirubin is derived **from the breakdown of hemoglobin.**
- High levels of serum bilirubin leads to a condition called as **jaundice**.
- **Jaundice** (also known as **icterus**) **is a yellowish pigmentation of the skin, the conjunctiva, the sclerae (whites of the eyes), and other mucous membranes and it is caused by high blood bilirubin levels. Urine is also dark in color. It can also cause itching.**
- **Jaundice is often seen in liver disease such as hepatitis or liver cancer or obstruction of the biliary tract by gallstones or tumors.**

The biliary tract by gallstones or tumors.

(حصى المرارة)

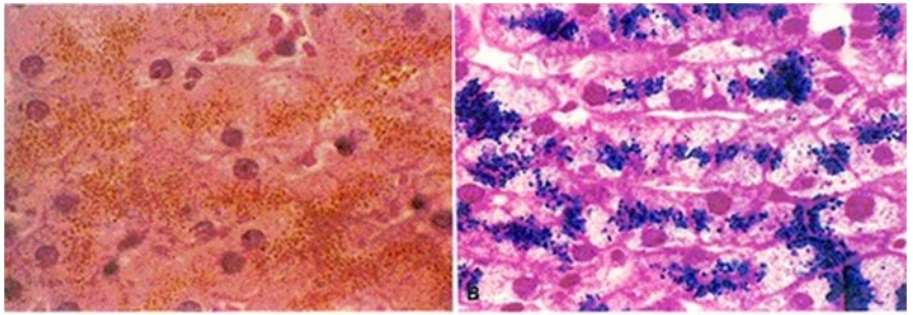


Endogenous Pigments

(4) Hemosiderin (IRON)

FEATURES :

- **Is a hemoglobin-derived golden brown iron containing pigment in cells.**
- Hemosiderin exists normally in small amounts in tissue macrophages of the bone marrow, liver, & spleen.



hemosiderin granules in liver cells

Left: HE stain, Right: Prussian blue stain

Morphology:

- Iron pigment is golden and granular in cytoplasm of macrophages or in cells of the liver, pancreas, heart etc.
- It appears **blue-black** with Pearl Prussian blue stain.

Endogenous Pigments

(4) Hemosiderin (IRON)

Hemosiderin accumulates in excess after RBC's breakdown (hemolysis) or hemorrhage and leads to **2 main types of conditions:**

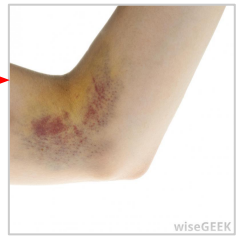
Hemosiderosis:

accumulation of hemosiderin mainly in macrophages. The pigment does not cause tissue damage. It can be:

- **localized hemosiderosis:**

(e.g. common bruise كدمة)

there is lysis of RBC's, release of hemoglobin and the iron is converted to hemosiderin)



- **Systemic hemosiderosis:** **The causes of excess systemic iron are:**
  - increased absorption of dietary iron.
  - impaired use of iron.
  - hemolytic anemias.
  - Exogenous iron from blood transfusions.

Hemochromatosis(داء ترسب الأصبغة الدموية) :

A more extensive accumulation of hemosiderin, often in parenchymal cells with tissue damage, scarring & organ dysfunction. Results in:

- liver fibrosis.
- heart failure
- diabetes mellitus.
- skin discoloration(bronzed diabetes).

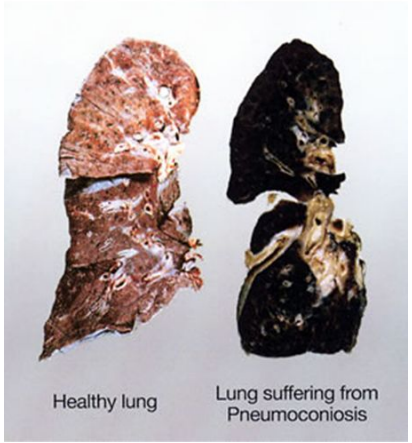
Exogenous Pigments

(1) Anthracosis

- **Is the most common exogenous pigment is carbon pigment or coal dust, which is an air pollutant.**
- Accumulation of this pigment blackens the lungs (anthracosis) and the involved lymph nodes.
- Smokers have the most pronounced anthracosis.
- The anthracotic pigment looks bad, but it **<u>causes no major organ dysfunction.</u>**

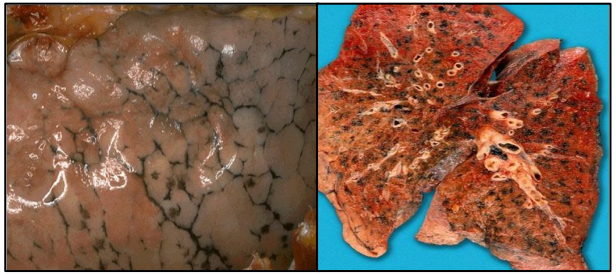
Other exogenous pigments that can be harmful when they accumulate in large amounts are silica, lead, iron dust and silver.

In the coal mining industry there is too much carbon dust in the lung of coal miners, which leads to lung disease known as **coal worker's pneumoconiosis.**

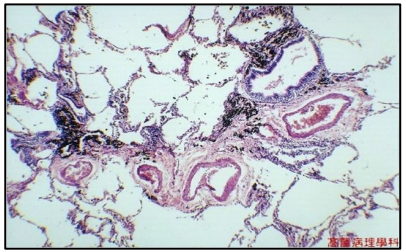


When breathing dirty polluted air, it is picked up by macrophages in the lung alveoli and also transported to the neighboring lymph nodes.

Anthracosis lung (Gross appearance)

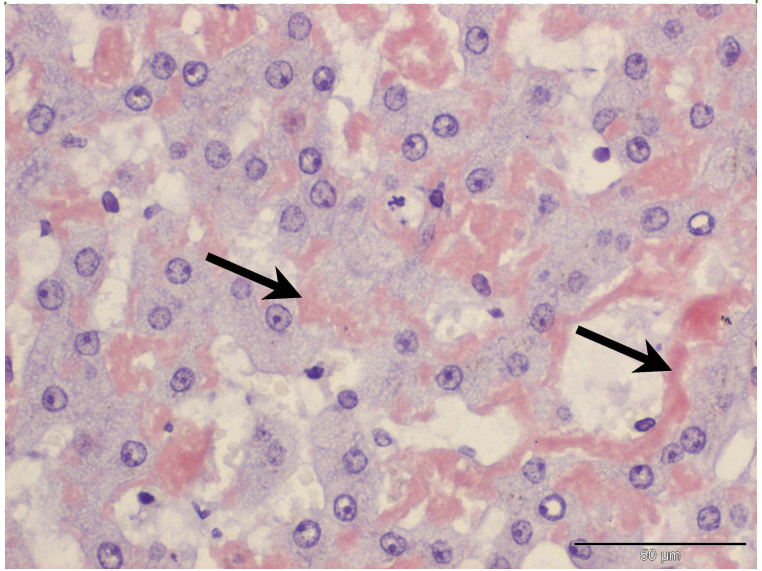


Anthracosis lung (LM appearance)



Amyloidosis

It is a rare disease and occur from deposition of amyloid proteins (misfolded proteins have beta pleated sheet structure) between the cells and the body cannot break it down.



light microscopy : amyloid appears like hyaline (homogenous eosinophilic material)

There is two types of amyloidosis:

Primary :
Deposits of AL amyloid derived from the immunoglobulin light chain, found in the kidneys, blood vessels and heart.

Secondary :
Deposits of AA amyloid derived from serum amyloid-associated protein, found in the kidneys, liver and spleen

Serum amyloid-associated protein is produced by the liver in chronic inflammatory or autoimmune diseases like :

- Chronic osteomyelitis (التهاب العظم ونقي العظم المزمن)
- Tuberculosis (السل)
- Rheumatoid arthritis التهاب المفاصل الروماتويدي)

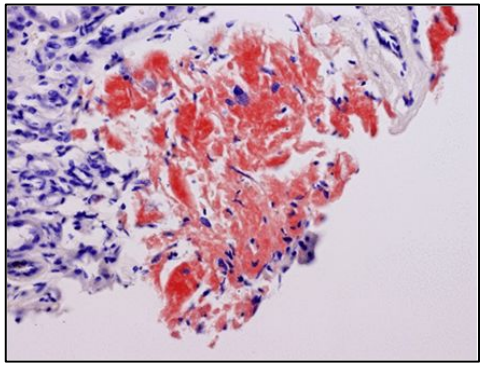
The diagnosis of amyloidosis can made ONLY by biopsy.

Amyloidosis

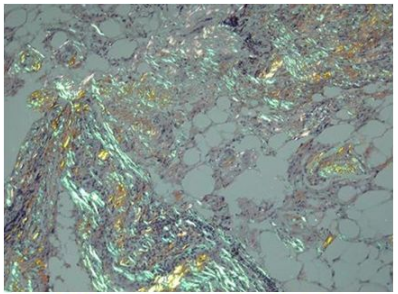
Morphology of amyloid

- **Light microscopy:** it is pink eosinophilic material. It appears bright orange with Congo red stain. And when the congo red stained tissue is exposed to polarized light it produces an apple-green birefringence.
- **Electron microscopy:** amyloid deposits are composed of nonbranching fibrils, 7.5 to 10 nanomicron in diameter.
- **Diagnosis:** can be made with biopsy of organs like the kidney, rectum, gingiva and skin.

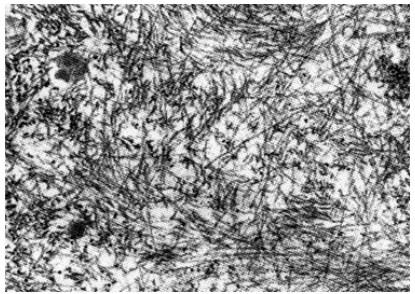
STAINS



CONGO RED STAIN



POLARIZED LIGHT



EM.

Pathologic Calcification

Deposition of calcium salts in tissues

Dystrophic Calcification

- In dead or degenerated tissue (injured tissues).
- May happen in normal calcium in the blood.

Pathogenesis:

1)Initiation:

- ❖ Intracellular : Calcification occurs in the mitochondria of dead or dying cells that accumulate(تكدس/ تجمع) calcium.
- ❖ Extracellular: Dystrophic calcification in membrane-bound vesicles forming calcium phosphate.

2)Propagation(الانتشار):

Depend on the concentration of Ca2+ and PO4 and the presence of inhibitors and other proteins.

Dystrophic calcification disorder: atherosclerotic plaques(لويحات تصلب الشرايين) , aging (هرم)or damaged heart valves, and tuberculous lymph node

Metastatic Calcification

- In normal tissue and may occur widely throughout the body.
- Caused by hypercalcemia(فرط كالسيوم الدم) (an increase of calcium in the blood) or altered Ca2+ metabolism.

There are four principal causes of hypercalcemia

- ❑ Increased secretion of parathyroid hormone (PTH)
- ❑ Destruction of bone tissue.
- ❑ Vitamin D-related disorders.
- ❑ Renal failure.

The process seems to affect mostly interstitial tissues(نسيج واقع بين فرج نسيج حي) of the gastric mucosa, kidney, lungs, systemic arteries and pulmonary(رئوي) veins.

Both types of calcifications consist of calcium phosphate crystals.

جميع الحالات لإثراء معلوماتكم عنها

CLINICAL CASES

The cases which we will mention it :

- Glomerulonephritis
- Hepatitis
- Left Ventricular hypertrophy
- Benign Prostatic Hyperplasia
- Pancreatitis
- Tuberculosis or TB

جميع الحالات لإثراء معلوماتكم عنها

CLINICAL CASES

GLOMERULONEPHRITIS

What is Glomerulonephritis ?

Inflammation of the glomerulus of the kidney, characterized by proteinuria, hematuria , decreased urine production and edema.

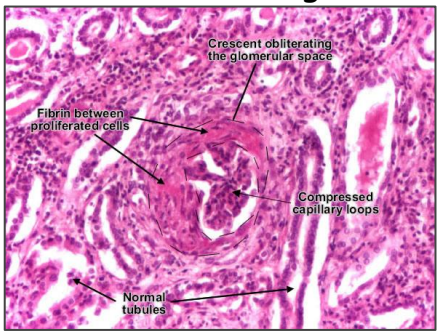
Kinds of glomerulonephritis are :

- Acute glomerulonephritis
- Chronic glomerulonephritis
- Subacute glomerulonephritis

Also called **Membranous Nephropathy**

Extra Information

This's a blood vessel taking from the **kidney**, this person has got an **autoimmune disease** so this patient has and immune complex inside his blood (a large molecule consisting of antigens and antibodies bound together) this molecule goes into the circulation, but because it has got a very large molecular weight, it gets entrapped in the walls of the blood



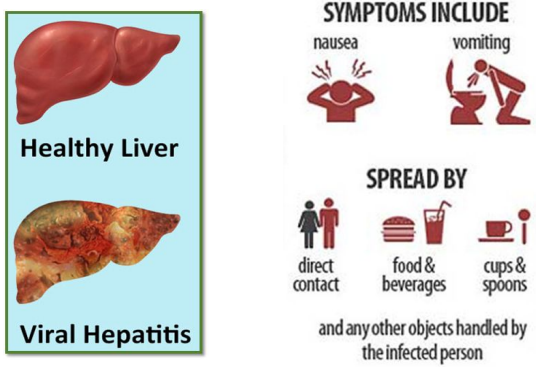
vessels, then it creates an inflammatory reaction and this reaction will lead to cell injury and the injury will lead to **Fibrinoid necrosis**.

جميع الحالات لإثراء معلوماتكم عنها

CLINICAL CASES

HEPATITIS

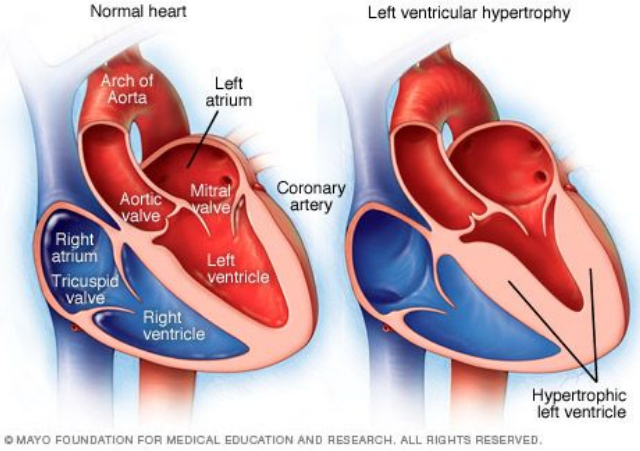
a male has **hepatitis B&C** (كبد التهاب) common in Saudi Arabia Cause: pathological apoptosis in hepatocytes (liver cells)induced by a virus.



BCL2 gene which is on the chromosome number 18 acts as an anti-apoptotic gene. In some diseases, there is a malfunction in this gene and tumors form **Follicular Lymphoma**. Patients always have a lot of BCL2 because it's anti-apoptosis so the cells in the lymph nodes will proliferate above each other's and apoptosis won't happen, resulting **cancer** .

LEFT VENTRICULAR HYPERTROPHY

A man has hypertension for 20 years, after his death we took a perpendicular section of his heart and found that his left ventricle is very thick (3-4 times). Left ventricular myocardial hypertrophy causes this enlargement of the left ventricular wall.



جميع الحالات لإثراء معلوماتكم عنها

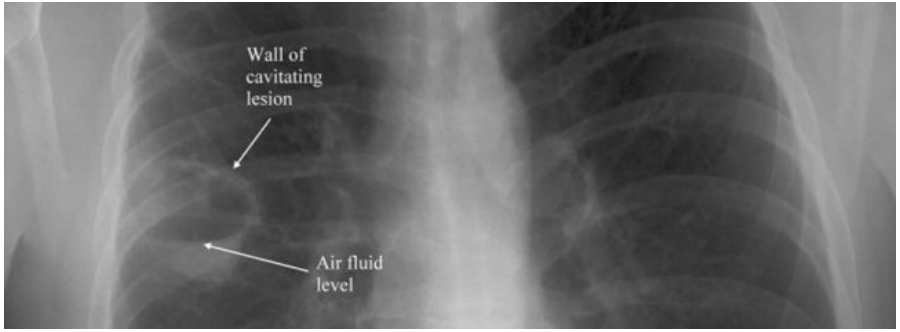
CLINICAL CASES

Left ventricular hypertrophy con,

What is the reason of this left ventricular myocardial hypertrophy?

The hypertension is characterized by the increased of the pressure exercised by the blood on the vessels' walls. The vessel walls would be solid because this disease is usually accompanied with atherosclerosis. This makes the heart work more to pump the blood because there is some resistance from the atherosclerotic blood vessels. When taking an X Ray, we find the heart enlarged and the left ventricle thickened. The next stage (if no medication is taken), the heart can't hypertrophy anymore and there will be heart failure, and can lead to death.

Tuberculosis (TB)



Saud is a 19 years old male from Jizan suffering from Fever, Excessive sweating, weight loss and hemoptysis (coughing blood). So what's wrong with him?

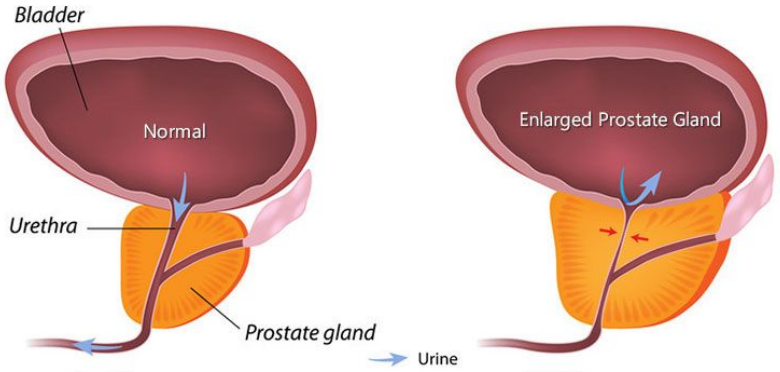
Diagnoses: the symptoms shows that he has an **inflammatory condition**, specially that he comes from jizan so the disease is prevalent in that area. The percentage that the patient has TB (**Tuberculosis**) is **85%** however, we still have to make sure by taking a chest X-ray, **cavitating lesion** in his lung should be present on the picture. A sample of the patient's sputum will show that he has a **mycobacterium** (Tuberculosis bacteria).

VEDIO

جميع الحالات لإثراء معلوماتكم عنها

CLINICAL CASES

Benign Prostatic Hyperplasia (BPH)



Benign Prostatic Hyperplasia is :

Extra Info.

a histological diagnosis associated with noninmalignant, noninflammatory enlargement of the prostate,most common among men over 50 years of age .

A normal man goes to the toilet to urinate three to four times a day. This patient goes about 20 times a day. He wakes up at night to urinate. He can't empty his bladder. The prostate of our patient is full of nodules, there is a **benign prostatic hypertrophy** & it is usually associated with hyperplasia, which is called **nodular prostatic hyperplasia**. The urethra becomes smaller and the patient has difficulties in micturition (urination). It is very common in men after the age of 50. In this case, the **prolonged effect of testosterone** causes this problem in different levels and different intensities. In very intense cases, the patient can't urinate and we put a catheter (tube) inside his urethra to his urinary bladder and urine passes. The prostate contains glandular epithelium which is surrounded by smooth muscles, drugs may be used to relax the muscles at early stages where there isn't a big problem. At severe stages nothing works and a surgery (TURP) must be done to remove some of the area that is blocking the urethra. (something I forgot to write: a symptom of this problem is that the patient has dribbling when urinating (البول ينقط) this is because his bladder isn't empty yet.

VEDIO

جميع الحالات لإثراء معلوماتكم عنها

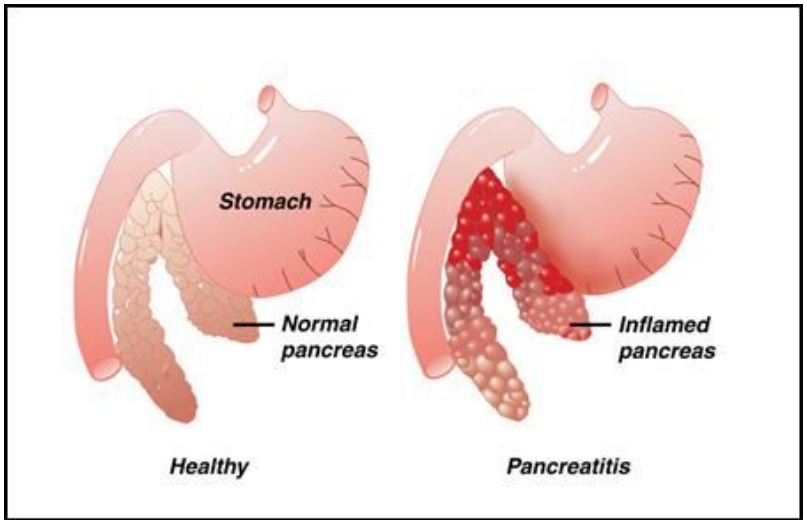
CLINICAL CASES

pancreatitis

Patient came to the ER suffering from **abdominal pain**, one of the causes of abdominal pain is **pancreatitis** (inflammation in the pancreas) could be acute or chronic. There are 2 enzymes, which are secreted by the pancreas *lipase* and *amylase* and those are **lipolytic** enzymes (their function is to help in digestion of lipids)

Inflammation → irreversible cell injury → distraction of the cells of the pancreas → the enzymes (amylase + lipase) are released to the blood vessels and to the abdomen (the abdominal cavity always contain fats (adipocyte: is the name of the cells that form fat tissues)→ the enzymes (lipolytic enzymes) lyse and digest the fat → saponification of fats (تصبن) → Calcium deposits on this fat (X-Ray shows this) → **fat necrosis**.

- The enzymes in the blood helps us in diagnosis.



How can the doctor make sure that this patient has a pancreatitis?
You should take a blood sample and look for the amount of lipase and amylase if it's raised and he has abdominal pain then he has acute or chronic pancreatitis.

HOPEFULLY WE DID
A GREAT JOB

ONLINE TEST

FOR ANY QUESTIONS AND SUGGESTIONS CONTACT US ...

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To make sure that all students are aware of any changes, please check out this link to know if there are any additions or changes.
The same link will be used for all of our work:
(Pathology Edit)

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DIFFICULTIES IN YOUR LIFE DON'T COME TO DESTROY YOU.. BEST OF LUCK