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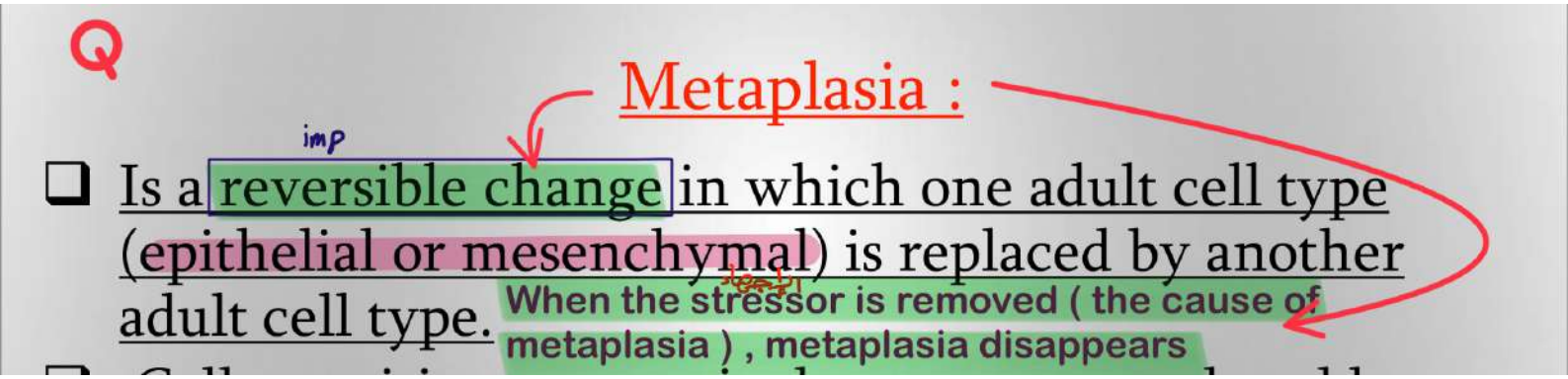
النادي الطبي MC راطيين

🤍لا تنسونا من دعائكم بالتوفيق🤍


Q
Metaplasia :
imp
Is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.
When the stressor is removed (the cause of metaplasia) , metaplasia disappears

Aging is caracterised by Senescence Q
but the term isn't interchangeably used
الدكتورة ركزت كثير عليه وعادته كثير.

Cardiac Myocyte ← مثال

Hypoxia / ischemia

① Loss of cellular function (1 - 2 minute)

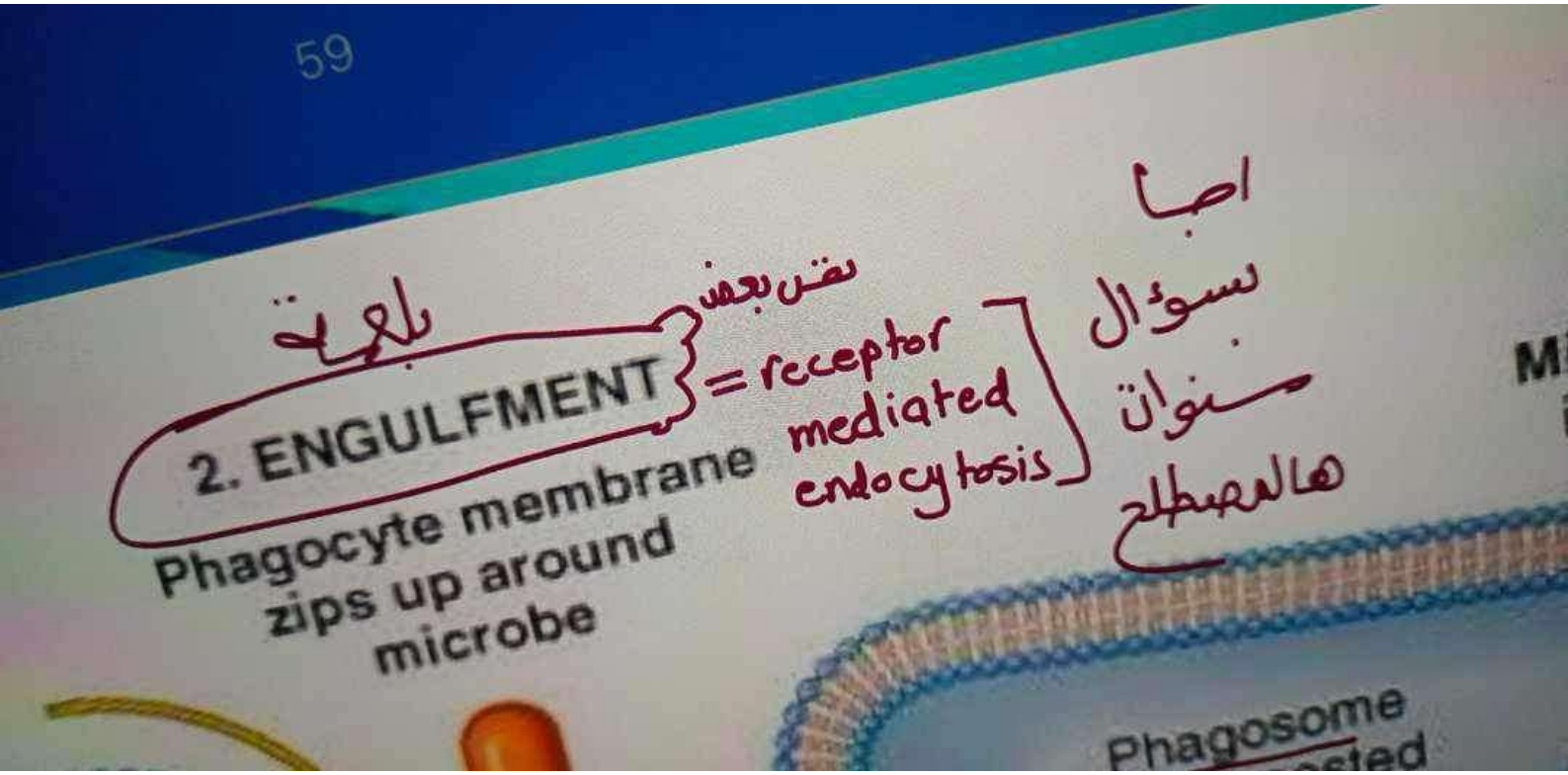
② Irreversible cell injury (20 - 30) minute

③ Ultrastructural changes (2-3 hours)

④ Light Microscopial changes (6 - 12 hours)

⑤ gross change بعد ١٢ ساعة

❖ طيب في معلومة مهمة الدكتورة ركزت عليها فركز وأفهم معي بتحكيلك غالباً غالباً وهذا اللي رح تسأل عليه في الإمتحان القلب في الغالب ال Hypertrophy اللي بتصييه في الغالب بكون السبب مرضي مش طبيعي يعني pathological يعني لما يحكيلك عن إنه القلب متضخم أعرف عطول إنه بسبب مرضي مش طبيعي ولا تكيفي وإنه تضخم في الخلايا نفسها يعني Hypertrohy مش زيادة في عددها يعني مش Hyperplasia لأنه زي ما حكينا القلب ما بتتجدد خلاياه ولا بتنقسم(مكررة لأهميتها)


59
2. ENGULFMENT
Phagocyte membrane zips up around microbe
Phagosome

Q. What is the first response in acute inflammation?
Ans: Homeostasis.

II- Metastatic calcification :

اللي قبله كانه العكس كانه الكالسيوم طبيعي والنسيج لا

It is characterized by deposition of **calcium salts in normal tissues** due to **increased calcium level** in blood :(hypercalcemia ↑Ca^{+2})

Causes of hypercalcemia are :

1- Increased secretion of parathyroid hormone

2- Destruction of bone : due to immobilization, or bone involvement by tumors as in in multiple myloma, leukemia (سرطان الدم), or diffuse skeletal metastases (أورام خبيثة). due to osteolytic activity (تكسير العظم للحصول على الكالسيوم)

(3) Vitamin D-related disorders. ⟶ increases the absorption of Ca^{+2} in intestine

(4) Renal failure in which phosphate retention leads to secondary hyperthyroidism . causes hypercalcemia

imp (III) In chronic gastric reflux : **During regurgitation of the acidic gastric contents to the esophagus the** normal stratified squamous epithelium of the lower esophagus may undergo metaplastic transformation to gastric or intestinal -type columnar epithelium , called mucous metaplasia , also refered to as "Barrett esophagus" which may predispose to peptic ulcer or even adenocarcinoma of the esophagus.

Vomiting

القرحة الهضمية

الدكتورة ذكرته بأكثر من محاضرة نفس المثال

Menorrhagia : excessive irregular bleeding because of ↑ Estrogen

Q : A 45 year old female suffers from excessive irregular bleeding.What's the cause of this condition?

Ans : Hyperplasia of endometrial tissue. Cells no. increases due to an increase of estrogen.
This condition can be treated by decreasing the estrogen level so the no. of cells can go back to normal ⟶ Reversible injury

- Normally, ROS which are produced in cells during mitochondrial respiration & energy generation, they are degraded & removed by **cellular defense systems**.

دفاع

بالوضع طبيعي رح تتشال مواد هاي عن طريق الطريقة هاي

- Telomerase activity is present at germ cells , less in stem cells & absent in most somatic cells .
  In cancer cells, telomerase is often reactivated.

4- Membranous or pseudomembranous inflammation :

Pseudomembrane → الغشاء الكاذب

This is a form of inflammatory reaction that is characterized by the formation of a membrane or more correctly a pseudo-membrane .

It is usually made up of precipitated fibrin , necrotic epithelium & inflammatory leukocytes.

When does? This occurs when the inflammation is so severe as to cause epithelial necrosis and sloughing . (انسلاخ)

imp.

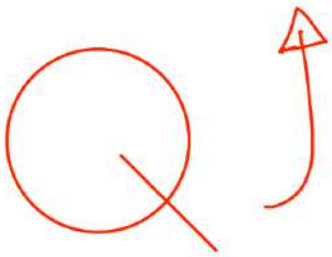
An example of this pattern is seen with Diphtheria affecting the larynx & pharynx.

Q

It may also affect the large bowel causing pseudomembranous colitis . The latter is caused by Clostridium difficile infection. (بالقولون) (مسبب الالتهاب)

In this type of inflammation there is an extensive confluent necrosis of the surface epithelium or mucosa & sever inflammation of the underlying tissue . (تجمع هائل)

بدك تعرف انه ال anaerobic glycolysis بنعتبرها compensatory mechanism .. والدكتورة حكت رح تجيب سؤال عنها بالامتحان



Q : True / False : Liver cells multiply even when the liver is healthy and not resected

Ans : FALSE !! They only multiply when a disease or resection occur.

Proteins

(1) In disorders with heavy protein leakage across the glomerular filter proteinuria, e.g., in **nephrotic syndrome**, there is marked increased pinocytic reabsorption of the protein, resulting in the appearance of pink, hyaline cytoplasmic droplets in the renal tubular epithelium.

The process is reversible ; if the proteinuria ends, the protein droplets disappear.

(2) Marked accumulations of synthesized immunoglobulines in the RER of some plasma cells, resulting Russell bodies. (this accumulation because of multiple myeloma in plasma cells (نوع من أنواع السرطان – malignant))

(3) Eosinophilic intracytoplasmic, protein inclusions in the liver cells that are highly characteristic of alcoholic liver disease are called "**alcoholic hyaline**" **or Mallory bodies**

These inclusions composed predominantly of aggregated intermediate filaments that resist degradation.

Hypertrophy:

مثل بعض الشباب الي عضلاتهم كبيره بسبب اللعب في الجيم

- Is an increase in the size of an organ due to increase in cell size caused by stress such as increased demand.
- Increased in functional capacity
- Hypertrophy is achieved via:

1. Gene activation
2. Increased protein synthesis
3. Increased organelles production within the cells.
4. Hormonal stimulation
5. Growth factor stimulation
6. Increased functional demand

(Hyperplasia) ×

زيادة عدد الميتوكندريا ← عشان تنتج طاقه تكفي لتغطيه الخليه

Q: The hallmark of the cellular response in acute inflamation is

الجواب: neutrophils

Q: The hallmark of acute inflamation

الجواب: neutrophils برمنز

The substances that cause chemotaxis are called **chemotactic agents** , these include substances such as

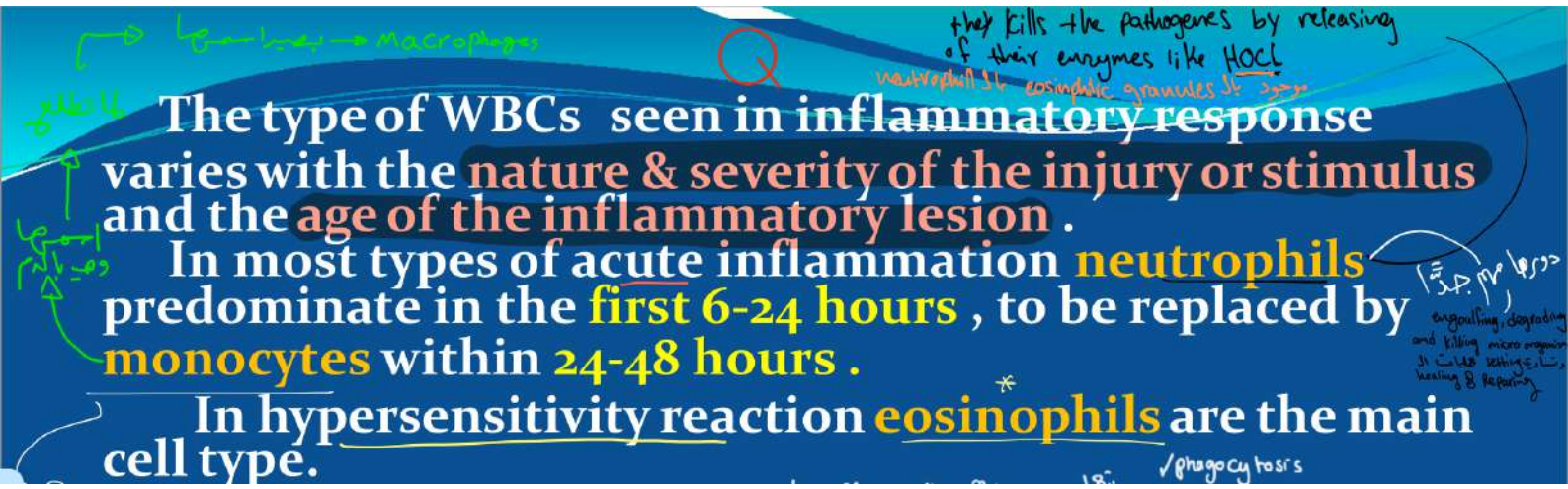
1. Soluble bacterial products.
2. Components of complement system such as, **C5a**.
3. Products of **lipoxygenase pathway** of arachidonic acid metabolism particularly **leukotrien B4 (LTB4)**.
4. Cytokines of the chemokine family .

The chemotactic agents **bind to specific receptors on leukocyte cell surface** & induce an **intra cellular cascade of phospholipids metabolites** associated with **increased intra cellular calcium** , which **triggers the assembly of cytoskeletal contractile elements necessary for cell movements.**

lost.

(This is a trichrome stain.)

The most common cause is disuse


Macrophages
they kills the pathogenes by releasing of their enzymes like HOCl
The type of WBCs seen in inflammatory response varies with the nature & severity of the injury or stimulus and the age of the inflammatory lesion .
In most types of acute inflammation neutrophils predominate in the first 6-24 hours , to be replaced by monocytes within 24-48 hours .
In hypersensitivity reaction eosinophils are the main cell type.
phagocytosis

- liquefactive necrosis occur due to fungal or bacterial infections
(جاي في الإمتحان)

2 kinds of adaptations happen in the uterus :

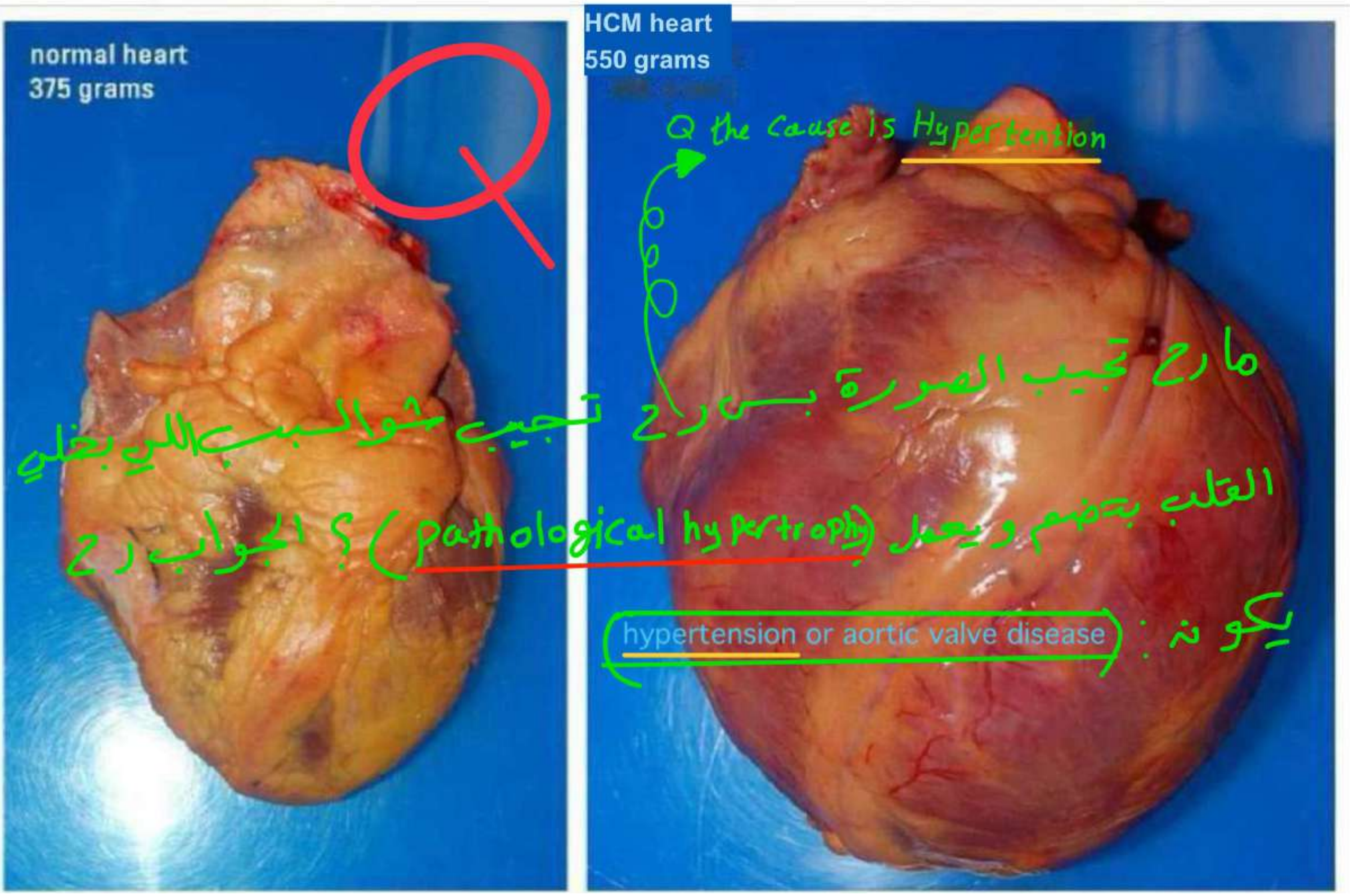
1. Hypertrophy
2. Hyperplasia

Hormonal

Physiological

QQ

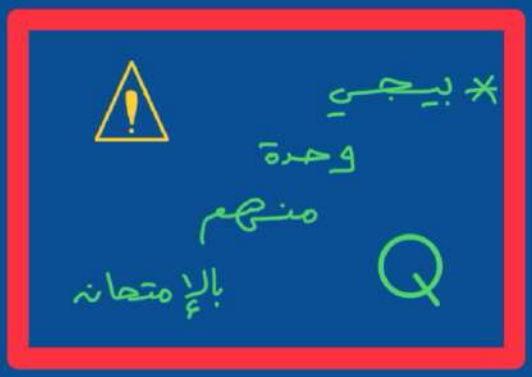
الدكتورة عادتها بتعاضيت وقالت أنها مهمة


normal heart
375 grams
HCM heart
550 grams
Q the cause is Hypertention
مارح تجيب الصورة بس رح تجيب شو السبب اللي بخلي
القلب بتضخم ويعمل (pathological hypertrophy) ؟ الجواب رح
يكون : hypertension or aortic valve disease

The cardinal signs of acute inflammation

(Celsus 30 B.C.) حفظ المصطلحات

* Heat (Calor) من كالوري
* Redness (Rubor)
* Swelling (Tumor) ورم
* Pain (Dolor)
* Loss of function (Functio laesa)



توضيح Hagman Factor :

___يصنع بال liver و بكون inactive و بمشي في الدم

____ تبقى في ال inactive forme حتى تصادف

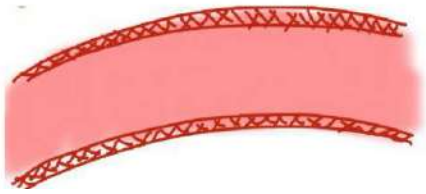
collagen /basement membrane /or activated platelets

هيك بتصير active

لي ؟؟؟

ال endothelial cells هي الوجه بالنسبة الهم من و جوا و تحتها مباشرة collagen و تحتهم Basment membrane

- فلو كان ماشي بالدم و صادف collagen بيعرف انه ال endothelial cells راحت
- ولو صادف Basment membrane رح يعرف انه ال endothelial cell & collagen راحوا



- Hyperplasia:

1- Simple : it is benign not malignant and no need to fear from it (such as endometrial and prosthetic)

2- Atypical : it can convert to malignant proliferation

لأنو السبب بال necrosis انزيمات

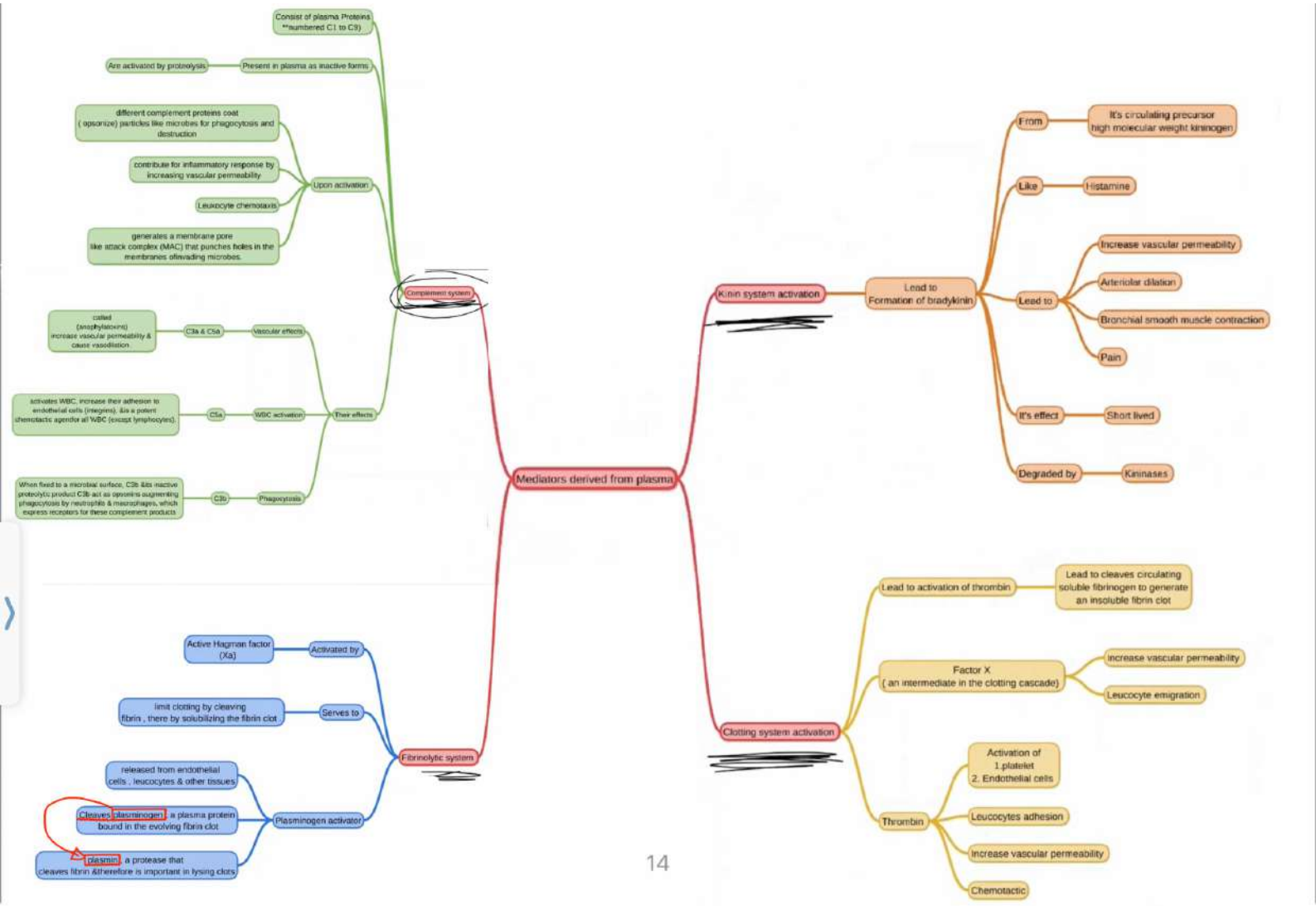
enzymatic necrosis

(4) Fat necrosis

تكسير
انه هاي
س.

- Describes focal areas of e
resulting from release of activat
substance of the pancreas & th

❑ The hyperplasia in this setting is due to stimulation by polypeptide growth factors (GF) produced by remnant hepatocytes as well as non-parenchymal cells found in the liver.


Mediators derived from plasma
Complement system
Consist of plasma Proteins **numbered C1 to C9)
Present in plasma as inactive forms
Are activated by proteolysis
Upon activation
different complement proteins coat (opsonize) particles like microbes for phagocytosis and destruction
contribute for inflammatory response by increasing vascular permeability
Leukocyte chemotaxis
generates a membrane pore like attack complex (MAC) that punches holes in the membranes ofinvading microbes.
Their effects
C3a & C5a
Vascular effects
called (anaphylatoxins) increase vascular permeability & cause vasodilation.
C5a
WBC activation
activates WBC, increase their adhesion to endothelial cells (integrins), &is a potent chemotactic agentfor all WBC (except lymphocytes).
C3b
Phagocytosis
When fixed to a microbial surface, C3b &its inactive proteolytic product iC3b act as opsonins augmenting phagocytosis by neutrophils & macrophages, which express receptors for these complement products
Fibrinolytic system
Activated by
Active Hagman factor (Xa)
Serves to
limit clotting by cleaving fibrin , there by solubilizing the fibrin clot
Plasminogen activator
released from endothelial cells , leucocytes & other tissues
Cleaves plasminogen , a plasma protein bound in the evolving fibrin clot
plasmin , a protease that cleaves fibrin &therefore is important in lysing clots
Kinin system activation
Lead to Formation of bradykinin
From
It's circulating precursor high molecular weight kininogen
Like
Histamine
Lead to
Increase vascular permeability
Arteriolar dilation
Bronchial smooth muscle contraction
Pain
It's effect
Short lived
Degraded by
Kininases
Clotting system activation
Lead to activation of thrombin
Lead to cleaves circulating soluble fibrinogen to generate an insoluble fibrin clot
Factor X (an intermediate in the clotting cascade)
increase vascular permeability
Leucocyte emigration
Thrombin
Activation of 1.platelet 2. Endothelial cells
Leucocytes adhesion
Increase vascular permeability
Chemotactic

With some exceptions as

- pneumonia for inflammation of the lung,
- pleurisy for inflammation of the pleura.
- Bladder-cystitis,
- Liver-Hepatitis,,
- Skin-Dermatitis,
- Ovary –Oopheritis .
- Testis-Orchitis etc.

❑ Fat necrosis is also seen following trauma to fat as in breast or subcutaneous tissue .

gigantism or acromegally.

عملقه

ضخامة اطراف

قبل البلوغ

بعد

تسبب

Very important

Hormonal stimulation is irreversible and it's a pathological adaptation

- As in conditions of starvation & also seen in alcoholic or viral hepatitis ,or other diseases .

Causes of fatty change in cell injury Q

ربي إني أحاول فأعني.

In the heart , prolonged moderate hypoxia (as in severe anemia) result in focal intracellular fat deposits, with a characteristic ('tiger-like, tabby-cat' pattern)

سؤال العام الماضي Q

Q Types of mediators

They are divided into two major categories :

I-Mediators that are derived from the plasma :

4 System ------ synthesised in liver (inactive form

including :

- The kinin system.
- The complement system.
- The coagulation & fibrinolytic system.

II. Mediators released from cells :

من قبل حدوث ال inflammation
مخزنات في الخلية

Either :

A- Preformed mediators in secretory granules of cells.like :

- Histamine secreted by mast cells , basophils & plateletes.

Tissues ← → blood

- Serotonin secreted by platelets.
- Lysosomal enzymes secreted by neutrophils & macrophages.

B- Newly synthesized mediators :

يتم تصنيعها لحظيًا عند الحاجة

Prostaglandins Leukotriens

Platelets activating factors → activate platelets → Plug

Reactive oxygen species Nitric oxide

Cytokines Neuropeptides

Produce histamin ...etc

تحفز انتاجهم

- لون الصبغات المستخدمة في صبغ العينات في المختبر (مهم)
  1- Hemotoxinin = لون النواة =بنفسجي غامق
  2- Eurosin = لون النسيج = برتقالي أو زهري

Metaplasia

الخلايا تتحول من شكل لآخر.

بنفس المعنى

- Is a reversible change in which one adult cell type (epithelial or mesenchymal) is replaced by another adult cell type.

(mature)

بتروح تحول شكلها لشكل — بتبطل الخلايا قادرة تتعامل مع هالضغط — Stress او محفز — الخلايا بيجي عليها

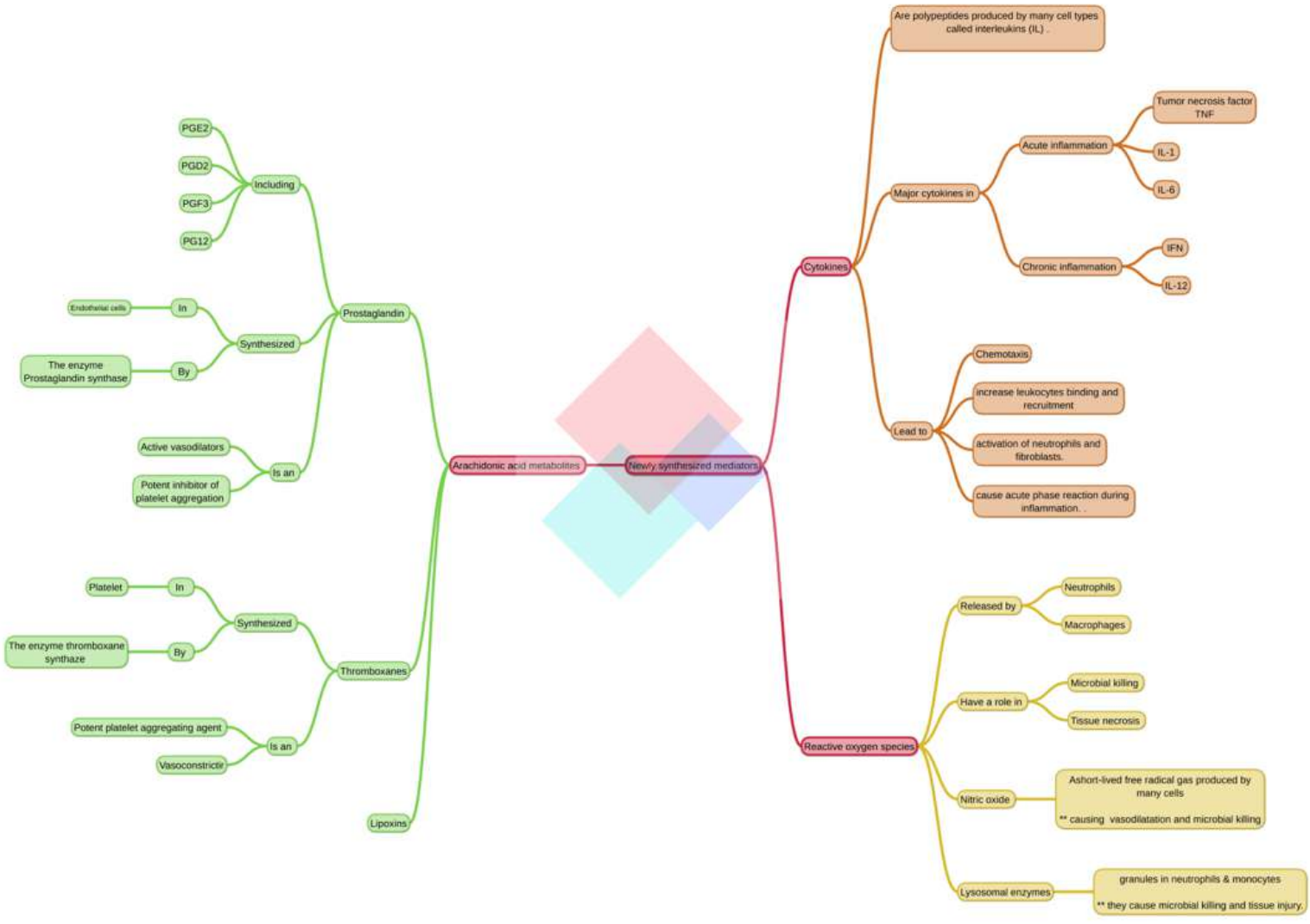
ال macrophages بتطلع cytokines يلي رح تعمل activation لـ B,T cells

وكمانه بتكبر البكتيريا عشانه الـ (T-cells) تقتلها

Q

Macrophages, scattered diffusely in most connective tissues normally, but found in increased numbers in certain organs: Liver (Kupffer cells), CNS (microglial cells), Lungs (alveolar macrophages), Spleen & lymph nodes (sinus histiocytes) , or called dendritic cells ..

مهم جدا


Arachidonic acid metabolites
Prostaglandin
Including
PGE2
PGD2
PGF3
PG12
Synthesized
In
Endothelial cells
By
The enzyme Prostaglandin synthase
Is an
Active vasodilators
Potent inhibitor of platelet aggregation
Thromboxanes
Synthesized
In
Platelet
By
The enzyme thromboxane synthaze
Is an
Potent platelet aggregating agent
Vasoconstrictir
Lipoxins
Newly synthesized mediators
Cytokines
Are polypeptides produced by many cell types called interleukins (IL) .
Major cytokines in
Acute inflammation
Tumor necrosis factor TNF
IL-1
IL-6
Chronic inflammation
IFN
IL-12
Lead to
Chemotaxis
increase leukocytes binding and recruitment
activation of neutrophils and fibroblasts.
cause acute phase reaction during inflammation. .
Reactive oxygen species
Released by
Neutrophils
Macrophages
Have a role in
Microbial killing
Tissue necrosis
Nitric oxide
Ashort-lived free radical gas produced by many cells
** causing vasodilatation and microbial killing
Lysosomal enzymes
granules in neutrophils & monocytes
** they cause microbial killing and tissue injury.

Sundus Nser

- the different between hyperplastic and neoplastic is the hyperplastic can controlled it when we remove the tumor or control the cause of hormone imbalance the hyperplasia will treated but the neoplastic we can`t controlled it

❖ طيب نشرح شوي الكلام بحكيلك في نوعين من الزيادة في أعداد الخلايا واحد اسمه Hyperplasia والثاني اسمه neoplastic شو الفرق بينهم بحكيلك ال hyperplasia عبارة عن ورم حميد بنقدر نسيطر عليه ونتخلص منه بمجرد السيطرة على سببه الرئيسي وتنظيم الهرمونات وبعدها بروح لحاله ما في داعي للخوف منه بس ال neoplastic ورم خبيث ما بنقدر نسيطر عليه بالسيطرة على أسبابه بشكل كامل

❑ Cellular swelling & Fatty change

سبب cellular swelling هو defect in plasma membrane

1. Cellular swelling:

Is the first manifestation of almost all forms of injury to cells ; **it is the result of failure of energy-dependent ion pumps in the plasma membrane** , leading to inability to maintain ionic & fluid homeostasis , resulting in the accumulation of Na & water within the cytoplasm .

Q

غير مميتة / قاتلة

- ❑ This pattern of **non-lethal** , such reversible injury is sometimes called **Hydropic change** , **Vacuolar degeneration** , or **Cloudy swelling** .

كل هالثلاث سميناهم أنه الـ (NA+) والماء داخل الخلية كثير بس هاي بالذات معناها أنه الـ (NA+) أكثر من الماء

Q

Apoptosis

physiologic

2 .**Hormone deprivation** : resulting in involution of hormone-dependent tissue such as

(a) **endometrial cell breakdown during the menstrual cycle.** حيض المرأه — بسبب نقصان الاستروجين

(b) **regression of the lactating breast after weaning.** فطام — رجوع الصدر الى حجمه الطبيعي

hyperplasia لانو صارله

3. **Cell loss in proliferating cell populations, as in intestinal crypt epithelia, so as to maintain a constant number.** انتشار

4. **Death of cells** that have served their useful purpose such as neutrophils in an **acute inflammation**, & lymphocytes at the end of an immune response.

Body response to the cell injury

Apoptosis occurs in these cells because they are deprived of necessary survival signals, such as growth factors. نقص

It will be eliminated by apoptosis

What is the first be lost when the cell expose to the injury?

It is the cellular function

MECHANISMS OF CELL INJURY:

(1) **The cellular response to injurious stimuli depends on:**

A.- Type of injury,

B. - Duration of injury,

C. Severity of Injury

D. Type of injuerd cell

Serous inflammation

- Effusion
- from blood
- mesothelial cells of pleura, pericardium or synovial cells in joints.
- like in TB infection.
- And skin blisters in burns or viral infection.

Suppurative inflammation

- Production of pus.
- infection with staphylococci.
- like skin pustule.
- massive infilteration of neutrophiles.
- may form abscess.

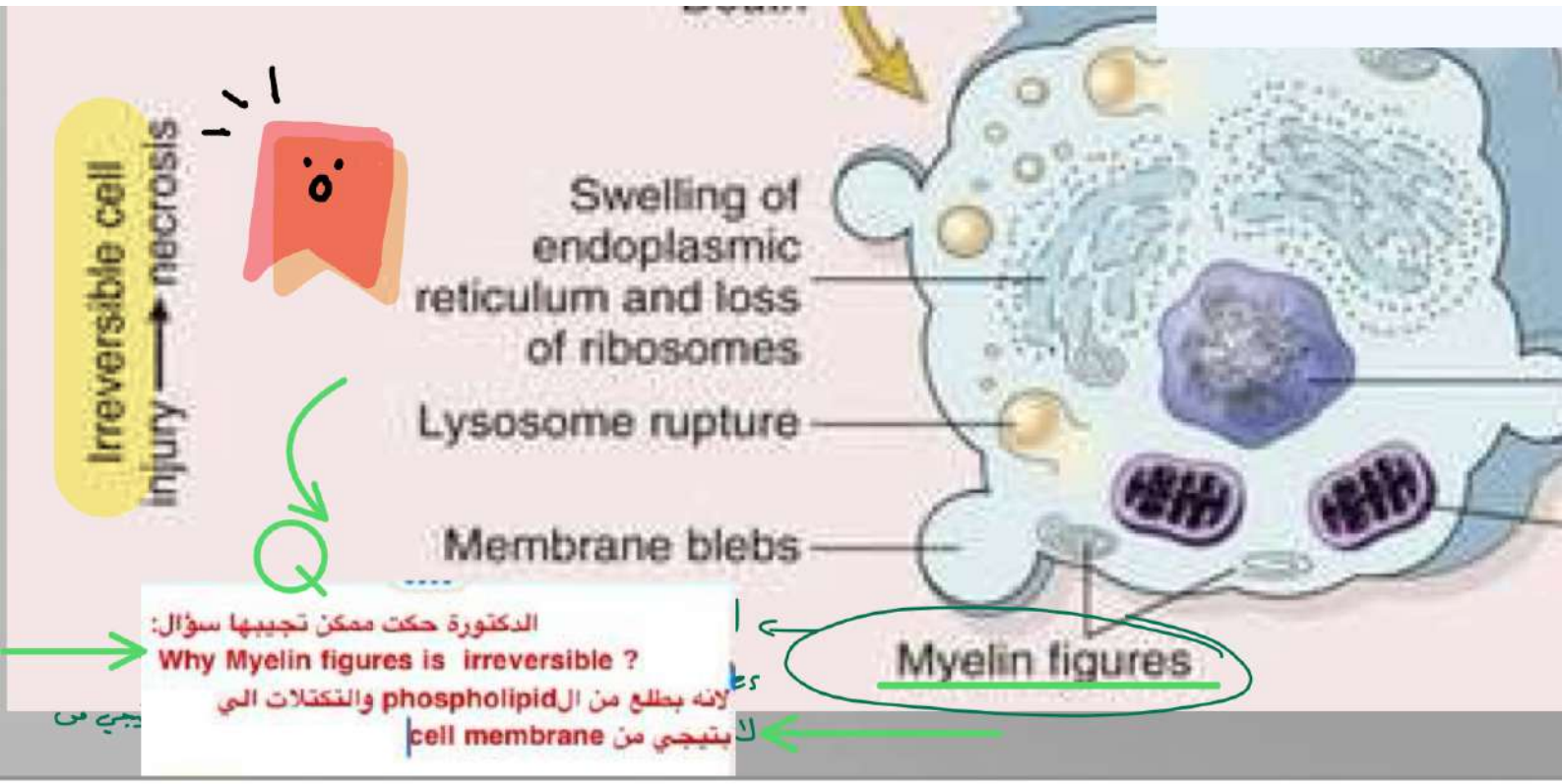
Fibrinous inflammation

تلخيص بطيئة

- Extensive fibrin exudate.
- in severe response.
- Bread and butter
- Eosinophilic mesh work in body cavities & meninges.
- Resolution by fibrinolysis.
- organization

Pseudomembraneous inflammation.

- Formation of a structure that resembles a membrane.
- from fibrin, necrotic tissue & leukocytes.
- When the inflammation is too severe.
- Diphtheria affecting larynx & pharynx.
- Clostridium difficile affecting large bowel.


Irreversible cell injury → necrosis
Swelling of endoplasmic reticulum and loss of ribosomes
Lysosome rupture
Membrane blebs
Myelin figures
الدكتورة حكت ممكن تجيبها سؤال:
Why Myelin figures is irreversible ?
لانه بطلع من الphospholipid والتكتلات الي
cell membrane بتيجي من

Apoptosis in pathologic situation

2. Accumulation of misfolded proteins → case ممكن يجيبي سؤال

Improperly folded proteins may arise because of mutations in the genes encoding these proteins, or damage caused by FR. **Free radicals, inflammation and radiation**

3. Cell injury in certain viral infections, in which loss of infected cells is largely due to apoptotic death that may be induced either by

(1) by the virus itself (as in adenovirus & HIV infections), or

(2) by the host immune response (as in viral hepatitis) .

عدوى فايروسيه للكبد بعدين بصيرة apoptosis

4. Pathologic atrophy in parenchymal organs after duct obstruction , such as occurs in the pancreas, parotid gland, and kidney .

duct أي عضو فيه

(5) Genetic Defects

Any abnormal defect in gene

Causes of cell injury

May result in pathologic changes as clear as the congenital malformation associated with Down syndrome (Trisomy of chromosome 21) & sickle cell anemia .

تشوه

مثال اخر : Thalassemia

فقر الدم المنجلي (التوجيهي)

(6) Nutritional Imbalances

Nutritional deficiencies are major cause of cell injury

* Protein —calorie insufficiency among poor populations is the most obvious example .

C and D

* specific vitamin deficiencies (scurvy, rickets) .

كاج

* Excesses of nutrition are also important causes of morbidity & mortality; e.g. obesity markedly increase the risk for type 2 diabetes mellitus, endometrial & breast cancers,& hypertension.

الاعتدال

بطانة الرحم

Diets rich in animal fat is strongly implicated in the development of atherosclerosis .

الدهون بتزيد بالجسم ← لزيادة الكوليسترول بالدم

ترسبات الهون بالاوعية الدموية ← والنهاية death

Ricktes	يصيب بالكساح بسبب نقص vitamin D
Scurvy	يسبب السقربوط بسبب نقص vitamin C

كل انواع cell injury برافقهم membrane damage الا apoptosis

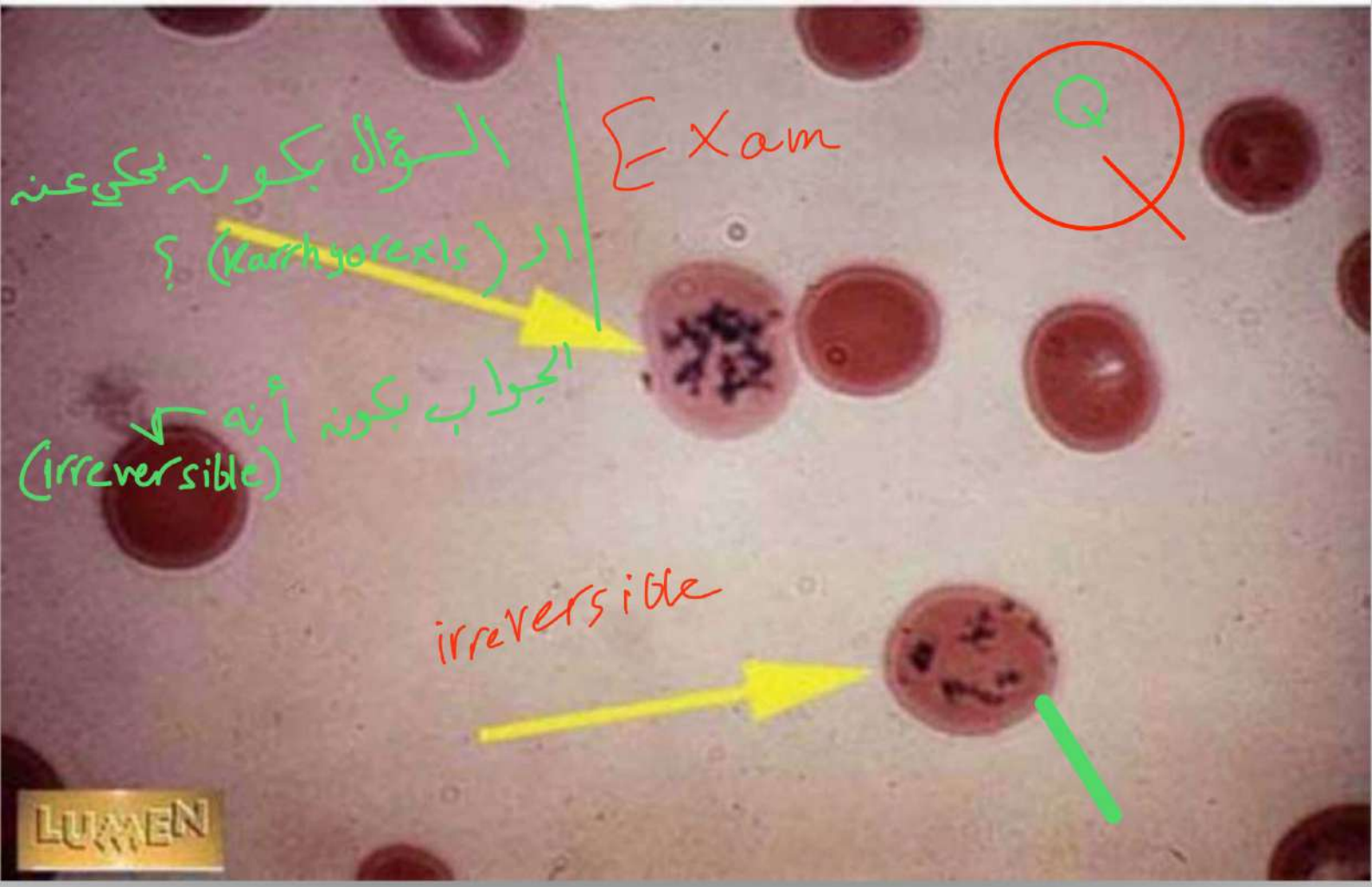


Fig 50 - Karrhyorexis i.e. nuclear chromatin fragmentation

* الدهون التي تترسب في ال (liver) هي Triglycerides.

Patterns of Tissue Necrosis

Grossly, necrotic tissue may show either:

(1) Coagulative necrosis. (solid tissue) → the most common
أحمر → like (MI)
Architecture

(2) Liquefactive necrosis. (Brain) → Brain infarction → Hydrolytic Enzymes
→ Abscess → lysosomes
No-Architecture

(3) Caseous necrosis. (Tuberculosis) → yellowish white
No-A

(4) fat necrosis . (Pancreas) oil red o on fresh frozen tissues / يتفاعل الدهون مع الكاسيوم

(5) fibrinoid necrosis. (Autoimmune diseases) limited to small blood vessels

(6) Gangrenous necrosis. (Gangilial) Saprophytic bacteria

resultant coagulative necrosis which later on becomes liquified by the action of saprophytic bacteria.

→ hormone can Caused phathological and Physiological Adaptation (correct)

→ (significant) increase Functional capicity (incorrect)
لأنو الزيادة ما بتكون كبيرة

❑ Here the mechanism of hypertrophy occurs due to

(5) Endoplasmic Reticulum swelling with loss of ribosomes

(6) Mitochondrial dilatation with the appearance of large amorphous densities

Mitochondrial dilatation اما اذا reversible

هذا السلايد جاي عليه سؤال بالامتحان

(III) Mitochondrial Alterations :

- Mitochondrial dysfunction plays an important role in acute cell injury & death.
- In some nonlethal pathologic conditions, however, there may be alterations in the number, size, shape, & presumably function of mitochondria.
- **In cellular hypertrophy, there is an increase in the number of mitochondria in cells** ; conversely, **mitochondria decreased in number during cellular atrophy(probably via autophagy).**
- Mitochondria may assume extremely large & abnormal shapes (megamitochondria), as seen in hepatocytes **in alcoholic liver disease & in nutritional deficiencies.**
- **In NASH, megamitochondria (giant mitochondria) are most frequently observed within hepatocytes with microvesicular steatosis as round or needle-shaped eosinophilic intracytoplasmic inclusions.**
- **NASH(Non-Alcoholic steatohepatitis)**

هون بنحكي عن التغيرات يلي بتصير بالميتوكوندريا ، يلي رح يزيد عددها بحالة ال hypertrophy ورح يقل عددها بحالة ال atrophy عن طريق ال autophagy

Gangrenous Necrosis

Gangrene can be :

Dry gangrene (Diabetes mallitus)

Wet gangrene (Intestine)

Gas gangrene (Caused by Clostridia Welchii infection of ischemic tissue .)