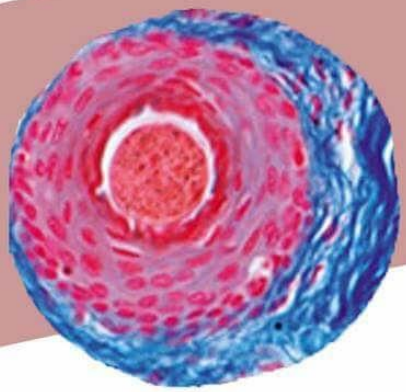
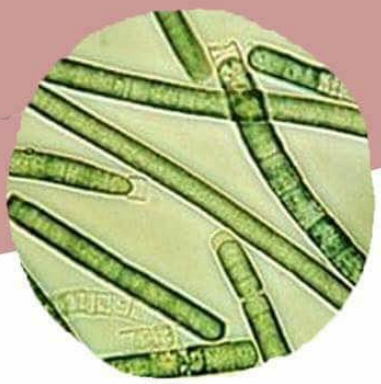
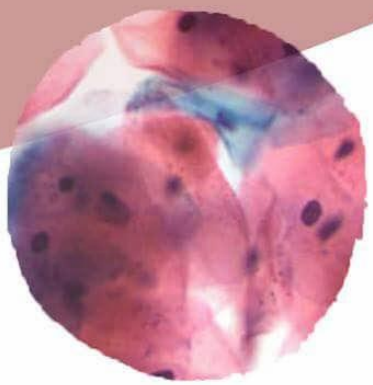
INTRODUCTION TO PATHOLOGY

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Sheet# 11

We talked about the mechanism of acute inflammation, and today we are going to talk about the outcome of acute inflammation.

- There are three possible outcomes for a patient that has got acute inflammation:
  1. Resolution, regeneration and repair
     There will be complete resolution, all excess inflammatory cells that came will die by apoptosis, the damage will be replaced by the sam cell type that is present in that area, like a patient who had tonsillitis (infection by bacteria)
  2. Chronic inflammation:
     The acute inflammation will turn into chronic inflammation
     For example: viral hepatitis (infection by virus) starts with small infection, it may undergo resolution, or it may turn into chronic and become lifelong problem to the patient.
  3. Scarring and fibrosis:
- Conditions that determine what will happen to the tissue:
  1. Resolution:
     A. If the injurious agent is **limited and short lived.**
     B. Minimal tissue damage.
     C. The injured tissue **can regenerate**: if there is minimal injury in the heart, neurons

(permanent tissues), it can't regenerate so we can't have resolution, fibrosis will happen.**(that was a question in the exam)**

2. Chronic inflammation:
   The acute will become chronic if the <u>offending agent can't be removed.</u>
   For example: if the patient inhale (anthrax الجمرة الخبيثة, TB bacilli, carbon particle) the phagocytes try to kill them but they can't, so they will stay in the body and they won't be removed, so the problem becomes chronic.
3. Scarring:
   A. If there is **extensive damage**: especially if we start losing stroma and stem cells (if we lose the architecture of the tissue).
   B. In tissues that <u>can't regenerate</u> (heart, skeletal muscles, neuron).

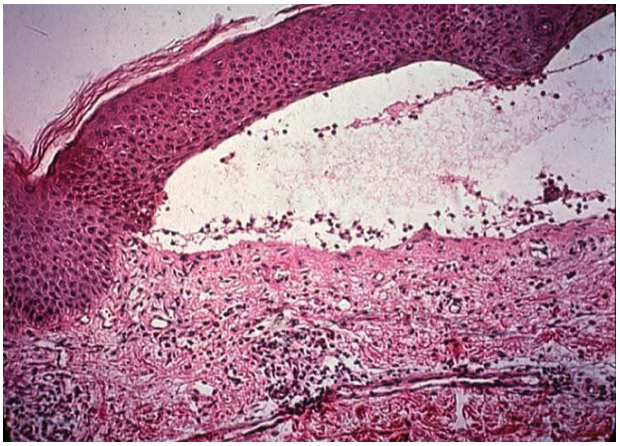
- What are the morphologic pattern for patient that has acute inflammation:

1. Serous inflammation:

A. It's the mildest.
B. Mechanism: vasodilation, few increase in the permeability (the water will go out) there is no need for other mechanisms (minimal number of cells and mediators) because there is no big damage.

C. Serous fluid: It's a **transudate** (remember: inflammation makes exudate, changing in pressure make transudate, but if the inflammation is very mild it will make transudate)-so actually it can make both-. Transudate doesn't mean zero cells; there are minimal, occasional cells. Exudate needs more cells and more protein.

D. Examples: burn (the area→ blister, contains serous fluid), sun burn, viral infection, serous inflammation: if the pleura inflame minimally the fluid will go out(serous pleuritis in the lung, serous pericarditis in the heart)

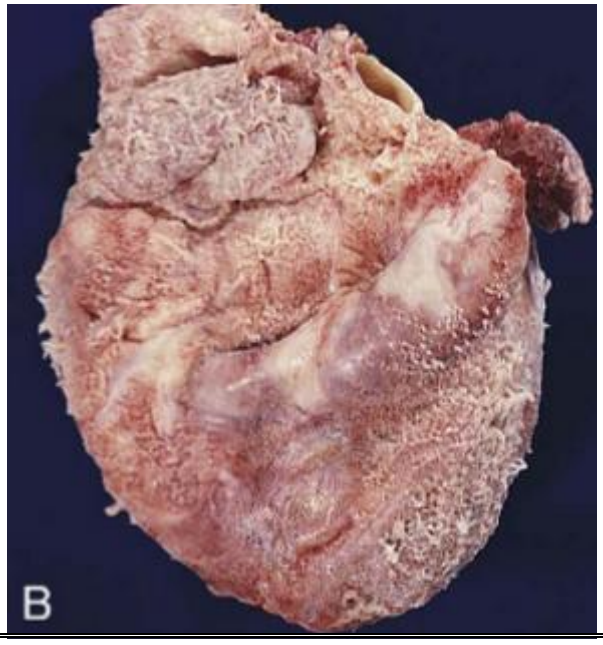


The dermis separates from the epidermis. Fluid comes between them. Notice clear fluid with minimal cells.

2. Fibrinous inflammation:

A. More severe than serous.
B. The permeability increases, more fluid and proteins will go out but without high numbers of cells. There are many proteins that come out but what I can see under the microscope is **fibrin** because it polymerizes to make fibrils
C. Under the microscope: mesh work of red colored area.
D. Example: Fibrinous pericarditis: the sac around the heart (pericardium) becomes inflamed; fibrin (and other proteins) and fluid will go out.

   Pay attention: <u>complete resolution or scarring may happen</u> depending on the severity because the damage will happen to the **pericardium not to the heart itself. (Which is lined by mesothelial cells which can regenerate).**



The white area is fibrin

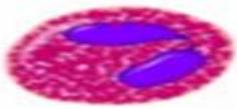
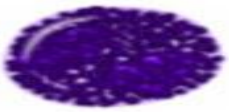
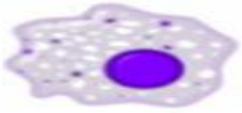
3. Suppurative:
    a. Severe damage (more than serous and Fibrinous), increasing in the permeability and we start seeing a lot of cells. We see abscess (accumulation of pus) indicating a lot of neutrophils.
    b. Cells (neutrophils mainly), fluid and proteins will go out, collection of neutrophils is called abscess.
    c. Usually (not always) the outcome is *scarring* because usually it's sever. But if the tissue can regenerate itself like lymphocytes in the case of tonsillitis, resolution may happen (or we could have minimal scarring).
    d. Example: patient have right abdominal pain, appendix is large→in other words "Appendicitis", and we found a lot of neutrophils under the microscope, the type of inflammation is: Suppurative.
4. Ulcer:
    a. **Losing tissue,** defect.
    b. Doesn't happen in solid organs (kidney, lung) it happens in the skin or tissues that have a surface-covering or lining- (intestine, stomach duodenum, esophagus).

Quick review:

1. Serous: transudate, mildest.
2. Fibrinous: severer, fibrin protein fibrils.
3. Suppurative: cells (mainly neutrophils).
4. Ulcer: losing tissue in organ that has surface.

Note: refer to slides for more images.

- We talked about acute inflammation and now we are going to talk about chronic inflammation.
- Chronic inflammation: infiltration with **mononuclear cells** (macrophage, lymphocyte).
  Here we change the cell; in acute inflammation we had polynuclear cells (neutrophils because their nuclei are lobed so they look as many nuclei).
  That neither means that we will not find neutrophils in chronic inflammation, nor means we can't find macrophage in acute inflammation, but we are talking about the most common cells (predominant) that appear in each kind of inflammation.
- Mononuclear vs. polynuclear
  Mononuclear: the nucleus doesn't have lobes (monocyte: kidney shape, lymphocyte: one nucleus in the middle, plasma cell: the nucleus in the periphery)
  Polynuclear: the nucleus has lobes (neutrophils, eosinophils).

Neutrophil	Eosinophil	Basophil
		
Lymphocyte	**Monocyte**	**Macrophage**
		

Student question: It's not necessary to have neutrophils as the main cell even in acute inflammation, for example: viral infection we will have lymphocytes, while allergy ,fungal infection, parasitic infection we will have eosinophils.

- The characteristics of chronic infection:
    1. There are mononuclear cells like macrophage.
    2. There is tissue destruction (continuously).
    3. I can see evidence of repair (Angiogenesis, fibrosis).

       2+3 can appear in acute inflammation but in lesser extent and not all of the time; just in severe acute inflammation.
- The cause of chronic inflammation：
    1. Acute inflammation becomes chronic.
    2. the infection stays persistent (TB, fungi, virus)
    3. Prolonged exposure to toxic substance (Silica, atherosclerosis caused by plasma lipid, Uric acid crystal), toxic material in body and the body can't get rid of it .

4. Auto-immune disease, because the immune reaction is against something in the body and the body can't get rid of it.

- Cells of chronic inflammation：
  1. the most predominant cell is (macrophage)

     A- When these cells are in the blood we call them (monocytes), when they go to the tissue they change a lot of their properties for example they can live longer in the tissue and they are called (macrophages). Monocytes can live for 48 hours, macrophages can live for weeks or months (that's happen if the cell goes out normally not during inflammation because if it goes out during inflammation, it has to die by apoptosis when it finishes its job .

     ***macrophages names:

  1. according to place they are present in:There are macrophages that live inside tissues that need continuous protection, and these macrophages have names according to the place that they live in:

     A- in the liver: kupffer cells

     B- Spleen, lymph node: sinus histiocytes.

     C- CNS: microglial cells

     D- lung: alveolar macrophages.

2. According to the pathway they are stimulated by: The macrophages cause inflammatory response by making phagocytosis and also by releasing mediators, but also it can make anti inflammatory response .

    A- M1 macrophages: they are stimulated by classical pathway and they act as inflammatory cells and phagocyte.

    B- M2 macrophages: they are stimulated by alternative pathway and they act as anti inflammatory response (function associated with fibrosis and scarring).

2. Lymphocyte: macrophages and lymphocytes love each other; a macrophage releases mediators to stimulate a lymphocyte, once it's stimulated it will release mediators to stimulate macrophages again that's called (**bidirectional stimulation**) and causes very severe inflammation.

3. Plasma cells: activated B lymphocyte that release immunoglobulins against persistent antigen or against altered tissue component.

4. Eosinophils: important in two condition

    A- Parasitic infection.

    B- Immunologic reaction and allergy

Remember that the nucleus in eosinophils have lobes

- Granuloma/Granulomatous inflammation：

There is no relation between granulation or granules granulomatous (granuloma). (The doctor said that according to student answers for the definition)

Granuloma is a specific type of chronic inflammation seen mainly in TB but also in other conditions. It's an aggregate of macrophages around something (bacteria or a substance (like glass)) that's not properly digested.

It's composed of: aggregate of epitheloid histiocytes (the shape of macrophages change from kidney shape into epithelial like cells because they are activated too much) (we say epitheloid histiocytes, epitheloid macrophages, epitheloid monocytes…)

Why does the aggregation happen? If I have *Mycobacterium tuberculosis* inside the body, the macrophage tries to phagocyte it and it can't so other macrophages will surround the bacteria developing granuloma .

NOTE: That looks like homework3: it talks about CGD (chronic granulomatous disease) and the question ask us why can't monocytes get rid of the infection even in numerous numbers?

The answer: CGD is a disease caused by monocytes impairment to kill, due to the lack of NADPH oxidase, so they can't kill the bacteria and other macrophages will come to the site of infection but they can't succeed because they have a defect and the collection of them causes the disease.

Mechanism/causes of Granuloma:

A. Granuloma inflammation occurs if there is persistent T cell response to certain microbes like TB. This causes aggregation of macrophages because the T cells and the macrophages have bidirectional stimulation (when T cells fail, they're going to call and stimulate macrophages) so there will be aggregation of macrophages.
B. Foreign bodies: like sutures or glass, because it can't be eaten by microphages so they will aggregate, we call that foreign body granuloma.

Diseases that cause granuloma：

A. tuberculosis (TB)
B. leprosy
C. Sarcoidosis: it's a disease like (TB) found in the lung but makes non-caseous granuloma.

More detail about these disease in respiratory system.

- **<u>Caseous necrosis: in TB only</u>**

A- Sometimes in some granuloma there is necrosis in the centre; the cells completely die and are converted to pink material-under the microscope- (cheese-like material macroscopically). Cells die completely and no cell boundaries remain (not like Coagulative necrosis).

B- Occurs only in tuberculosis so if the patient has caseous granuloma he's got TB in majority of cases

Question in the exam: TB can make caseous and non caseous granuloma (caseous is only in TB, but TB can make caseous and non-caseous granuloma).

C- Under the microscope it's pink because there is increase in eosinophilia .

D- Why does that central necrosis happen:1- free radical damage, 2-ischemia at the central of granuloma.

*********That is the end of material

31:12 exam question (clinical cases)

In the exam there will be direct and indirect questions, so how to answer indirect questions

1. These questions are easy if you know the trick try to solve as much as you can of examples.
2. Don't be afraid of long questions.
3. Read the question carefully.
4. if you don't know the answer leave it and go to the direct questions

Q1: 60 years old male (irrelevant) that has tachycardia, laboratory show elevated cardiac enzyme (that's mean cell injury) coronary angiography shows more than 90% occlusion of left anterior ascending artery (that's mean ischemia) irreversible injury to his myocardial fiber will happen when which of the following occur:

The last sentence tills us what the question want so if you don't understand the question from the beginning don't worry…

When the question is about the occlusion, the question asks us about ischemia (reversible, irreversible, reperfusion(

A- Glycogen stored depletion (in an anaerobic glycolysis there is glycogen depletion)
B- Cytoplasmic sodium increase (that happens in reversible and irreversible injury because there is depletion in ATP)
C- Nucleus undergoes karyorrhexis (this means that the nucleus is destroyed so it's irreversible injury)
D- Intracellular PH diminished (that happens because of accumulation of lactate)

E- Blebs form on cell membrane (this means edema so it's reversible but the destruction of cell membrane is irreversible)

The answer is C

Q2: 34 years old male present with mild burning substernal pain following the meal for the past three years (irrelevant). upper GI endoscopy performed and biopsy taken for the area of lower esophagus mucosa .....(irrelevant) the biopsy show the appearance of columnar epithelium with goblet cells

Answer: it's metaplasia because in normal cases the esophagus has squamous epithelium.

Q3: 22 years old recently Wed female missed her last two menstrual cycle and she's happy about that if we have to look at her uterus we would found following adaptive cellular response

Answer: hypertrophy and hyperplasia

Q4: 57 years old female is becoming increasingly forgetful, radiologic examination show narrow gyri and wide sulci. All of the following cellular processes are likely to be encountered except

Answer: it is atrophy→ there is no way to increase in protein synthesis.

Q5: at the end of menstrual cycle examination of the endometrium sloughed microscopy shows fragmentation. which of the following state is true

Answer: (apoptosis because it's shedding normally) there will be decrease in PCl2 because it's anti apoptotic you need to decrease it.

Q6: you examined a biopsy of bronchus of 50 years old man and found squamous epithelium lining which of the following is correct

This question talks about metaplasia because the bronchus is columnar

Answer: associated vitamin A deficiency because vitamin A makes differentiation to columnar.

The metaplasia isn't neoplastic it's adaptive