SHEET NO. 10

PATHOLOGY

DOCTOR 2019 | MEDICINE | JU

DONE BY : Doctor 2019

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بسم الله الرحمن الرحيم

0:00

In the last lecture we talked about some of mediators of inflammation and the complement system and their regulatory protein inhibitors which control the inflammatory response so it will not go out of hand and be exaggerated to cause tissue injury.

Other mediators of inflammation:

1 – Platelet activating factor (PAF) : induce the platelet aggregation and other functions of platelet .
2 – Protease activating receptors (PARs) : also play a role in platelet aggregation .

- Both of them are incriminated of the pathogenesis of atherosclerosis and thromboembolic diseases in addition to the prostaglandin I2 and thromboxane .

3 – Kinins : is a specific group of vasoactive peptides , the prototype and the most important one is Bradykinin which causes vasodilation , increasing the permeability of blood vessels , smooth muscle contraction – so it plays a role in the active labor - and pain .
4 – Neuropeptides : Substance P and neurokinin A . → more important in CNS.

- THIS TABLE SUMMARIZE ALL THE MEDIATORS WHICH WE TALKED ABOUT AND THIER FUNCTIONS.

TABLE 3.8 Role of Mediators in Different Reactions of Inflammation

Reaction of Inflammation	Principal Mediators
Vasodilation	Histamine
	Prostaglandins
Increased vascular permeability	Histamine
	C3a and C5a (by liberating vasoactive amines from mast cells, other cells)
	Leukotrienes C_4, D_4, E_4
Chemotaxis, leukocyte recruitment and activation	TNF, IL-1
	Chemokines
	C3a, C5a
	Leukotriene B_4 → The most potent chemotactic agent
Fever	IL-1, TNF
	Prostaglandins
Pain	Prostaglandins
	Bradykinin
Tissue damage	Lysosomal enzymes of leukocytes → most of them can cause tissue damage if we fail to control the immune response throug Lysosymes degradation and activation of WBCs.
	Reactive oxygen species

Morphology of acute inflammation:

It's mean how the tissue looks like in the presence of acute inflammation. (appearance).

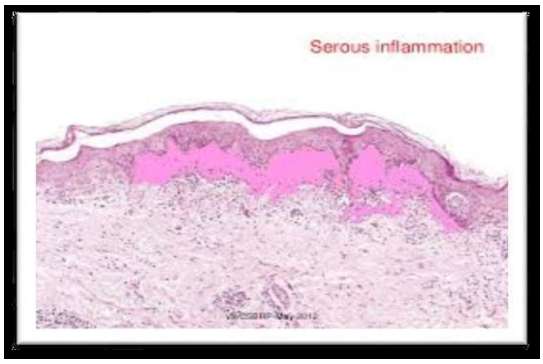
*as a pathogenist we will report a multiple parameters
1-gross pathogenic appearance of the organ (gross evaluation of the organ by my eye)
2-take sections and look through microscope regular microscope or electron microscope (morphologic microscopic appearance)
3-final diagnose

The critical issue here is the blood vessels dilatation (initial vascular phase) , accumulation of WBCs and fluid in the extravascular tissue .

Edema : too much fluids and protein in the interstitium after the vascular phase . Causing enlargement of the organ .	**Fluid and proteins in interstitium**
Redness : due to the presence of high amount of blood in the area (congestion and vasodilation).	***Rubor***
Warmth : caused by the vascular changes **.**	***calor***
Swelling : caused by edema .	***tumor***
Loss of function : because the presence of pain and edema .	***Functiolaesa***
Pain : caused by many mediators **.** (Prostaglandin and Bradykinin)	**dolor**

- ***<u>The microscopic features of some morphological patterns of inflammation:</u>***

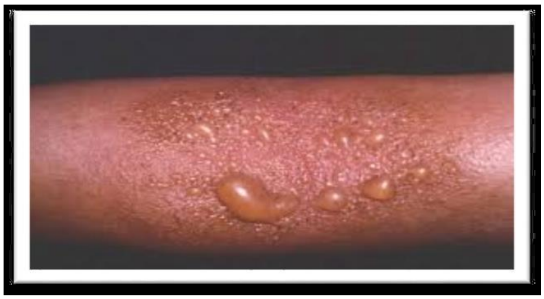
- *<u>1 – Serous inflammation</u>*: is an acute inflammation with accumulation of cell poor fluid (transudate) . When we examine it under microscope it looks clean, yellow and its solidarity is low.



Common examples:
A – <u>serous effusion</u>: the bilateral pleural effusion due to heart failure or hypoproteinemia from liver failure causes the osmotic pressure to decrease so more fluid will leak out into the interstitium.

→ when the intact epidermis repture there will be a clear slighty yellow seroum.
B – <u>serous blisters</u>: caused by the first degree burns of skin.
C – <u>seromas</u>: is a sac or collection of serum which is a transudate inflammatory fluid.They are common after certain surgeries like hernia repair and breast surgery

→ Collection of seroum around the surgical site.



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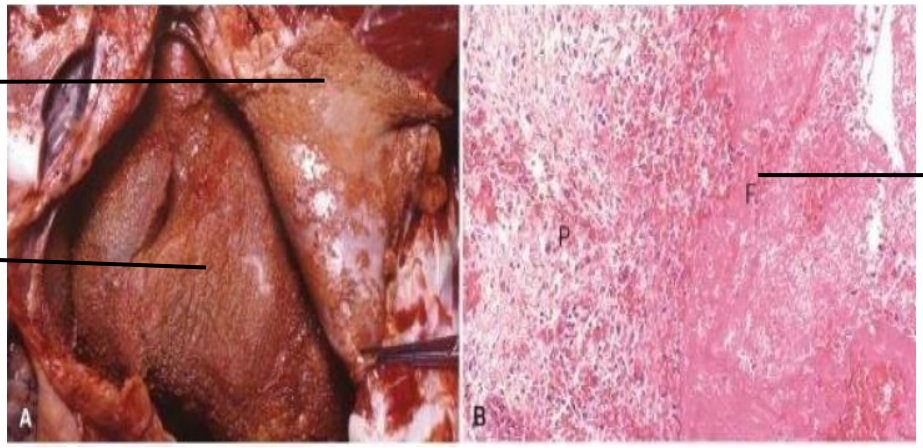
2 – fibrinous inflammation:

Is a little bit similar to serous inflammation, however, there is a large vascular leakage of fluids and fibers and a lot of coagulation. It characteristically seen in certain body cavities especially the pericardium. and Plural cavity

- Patient with fibrinous pericarditis has to be treated quickly because the thickened pericardium – which caused by the fibrinous pericarditis – will cause fatal consequences on the heart .
- it also happens in pleural cavity as a fibrinous pleuritis .



3 – Purulent (suppurative) inflammation ,Abscess:

It includes the formation of Pus which is an accumulation of fluids and PMNs, debris and edema (Exudate) . It may cause a sever acute inflammation when the body cannot cope with it which lead to death .

- It caused by some type of bacteria such as staphylococcus aureus.
- Abscess : is a localized collection of pus (exudate) .
- treatment of abscess is drainage or removal.

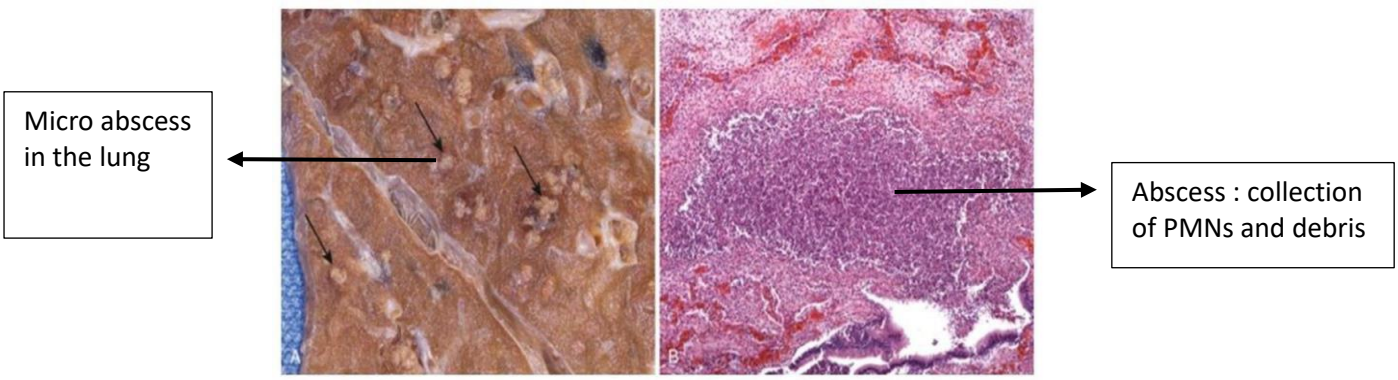
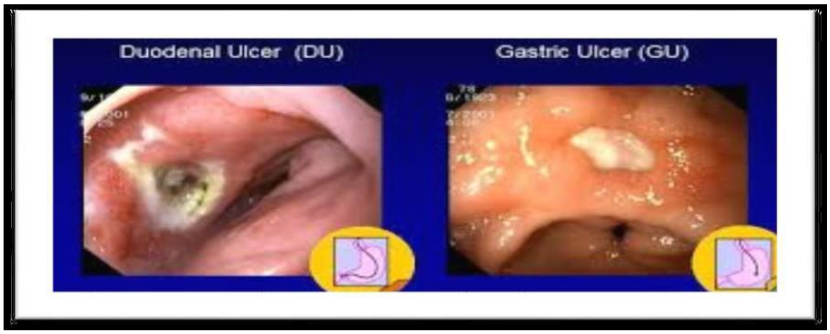


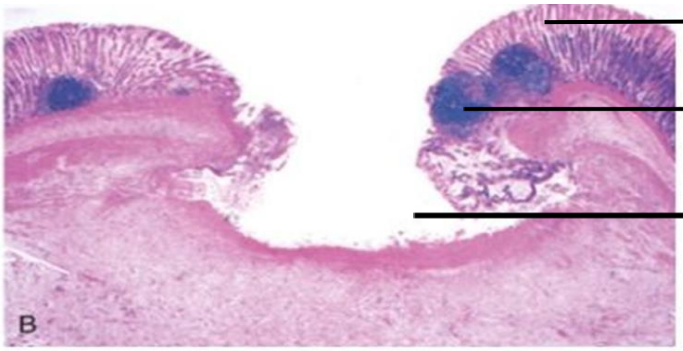
FIG. 3.14 Purulent inflammation. (A) Multiple bacterial abscesses *(arrows)* in the lung i...

4 – Ulcerative inflammation (ULCERS) :

Is a defect on the mucosal surface and skin . (discontinouity)

- It mostly acute and chronic Inflammation . sometimes it can be acute in top of chronic like sever bleeding .





Mucosal surface

Lymphoid follicles

Ulcer

Outcomes of acute inflammation

Chronic inflammation
When we cannot get rid of acute inflammation because a virulent injurious agent or bad immunity, it will become chronic inflammation which may be sever and cause a damage for that organ.

Complete resolution **:**
The 99% of the tissue is repaired and returns to the pre-inflammatory stage. It is the most preferred outcome. However, this does not happen in real time.

Healing by fibrosis:
Consist of scar formation which may have a negative impact on the cosmetic appearance or function of that organ

*Scar = fibrosis

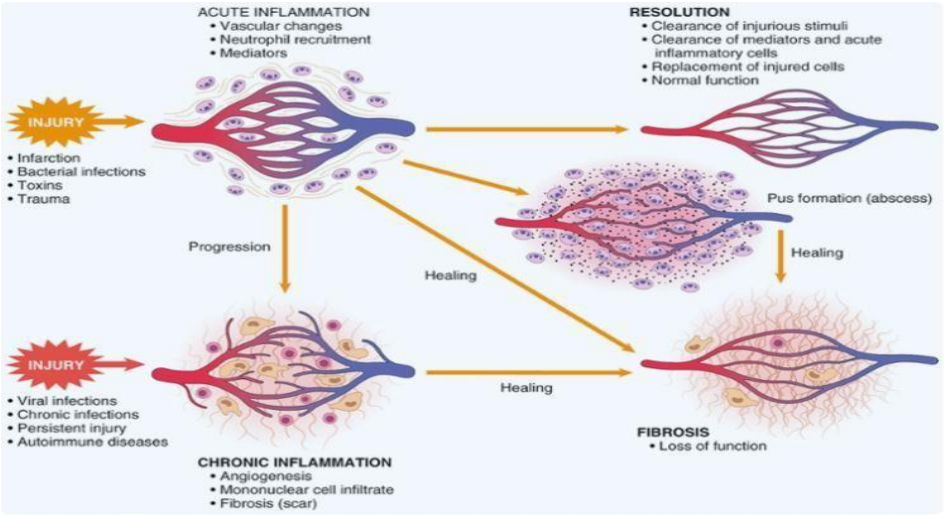


FIG. 3.16 Outcomes of acute inflammation: resolution, healing by fibrosis, or chronic i…

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Chronic inflammation:

It is prolonged inflammation (weeks- months -years). Associated with tissue injury and body attempts to repair it at the same time with varying degree.

- But it also may continues and form a sever scar and fibrosis that negatively impact the function of that organ. like the active hepatitis for 10 – 15 years leads to liver failure.

• usually it follows acute inflammation but may be insidious or smoldering when the acute inflammatory phase is subclinical and does not bother.

Causes of chronic inflammation:

Persistent infections	Mycobacteria (TB), viruses, fungi, parasites. Delayed hypersensitivity reaction. Granulomatous inflammation.
Hypersensitivity diseases (auto immune disease)	RA, asthma, MS. May end in fibrosis of end organs
Prolonged exposure to toxic agents (exogenous or endogenous)	Silica (silicosis) → exogenous Atherosclerosis(cholesterol) endogenous
Other associated diseases	Alzheimer's, Metabolic syndrome of DM → Diabetes mellitus

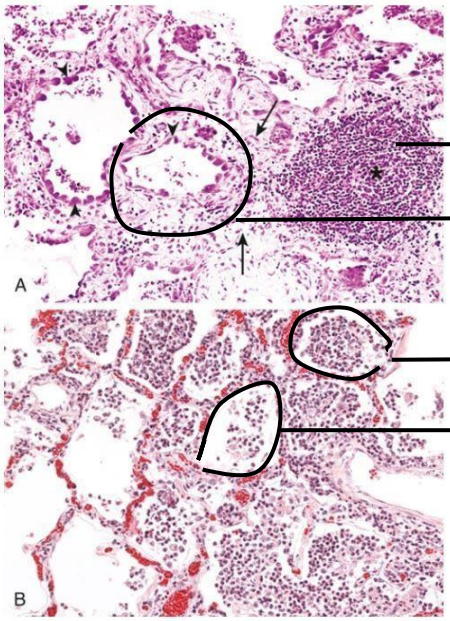
Morphological features of chronic inflammation:

1 – The first critical feature is the infiltration of the chronic inflammatory cells (macrophages, lymphocytes and plasm cells).

2 - Tissue destruction (damage) at varying levels .

- The sever tissue destruction leads to sever changes like the replacement of the normal liver parenchyma by thick bands of fibrosis.

3 - Attempts at healing and repair by angiogenesis (producing new blood vessels) and fibrosis.



This is a chronic inflammatory follicle contains chronic inflammatory cells (macrophage, lymphocytes , plasma cells)

This is a damaged alveoli replaced by fibrous tissue

These are alveolus filled with acute inflammatory cells (neutrophils)

FIG. 3.17 (A) Chronic inflammation in the lung, showing all three characteristic histolo…

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Cells and mediators of chronic inflammation:

- The chronic inflammation also requires mediators produced by:

1 - **Macrophages**
2 - **Lymphocytes**
3 - **Eosinophils**
4 - **Mast cells**

Macrophages

The monocyte circulates in the blood but when it resides in the tissue it is called a Macrophage.

1- They secret some mediators such as TNF, IL1 and Chemokines.
2- They have a strong connection with T lymphocyte. It gives the macrophage a feedback about the increasing or decreasing inflammatory response.
3- Phagocytosis is the peculiar function of the macrophage.

- It produced in the bone marrow and mature in the right side . in the fetal life it produced in the yolk sac and mature in the tissue.
- The half-life of the circulating monocyte is approximately 1 day . but when it gets into the tissue the half-life is extended for weeks or months.
- Tissue Macrophages: (mononuclear phagocytic system)
  Kupfer cells (liver), sinus histiocytes (lymph nodes) , alveolar macrophages (lung) , microglia (brain).
- The monocyte is less granule and has a kidney shaped nucleus.

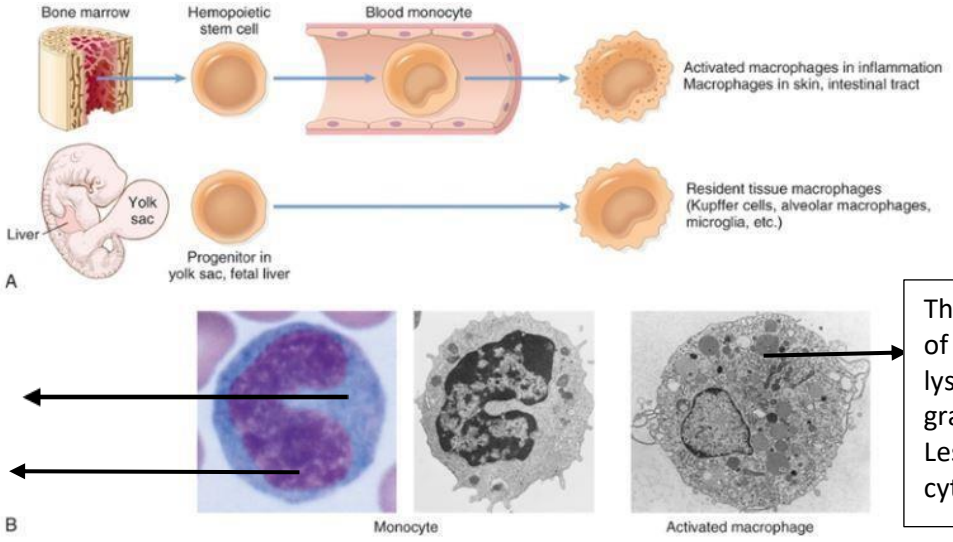
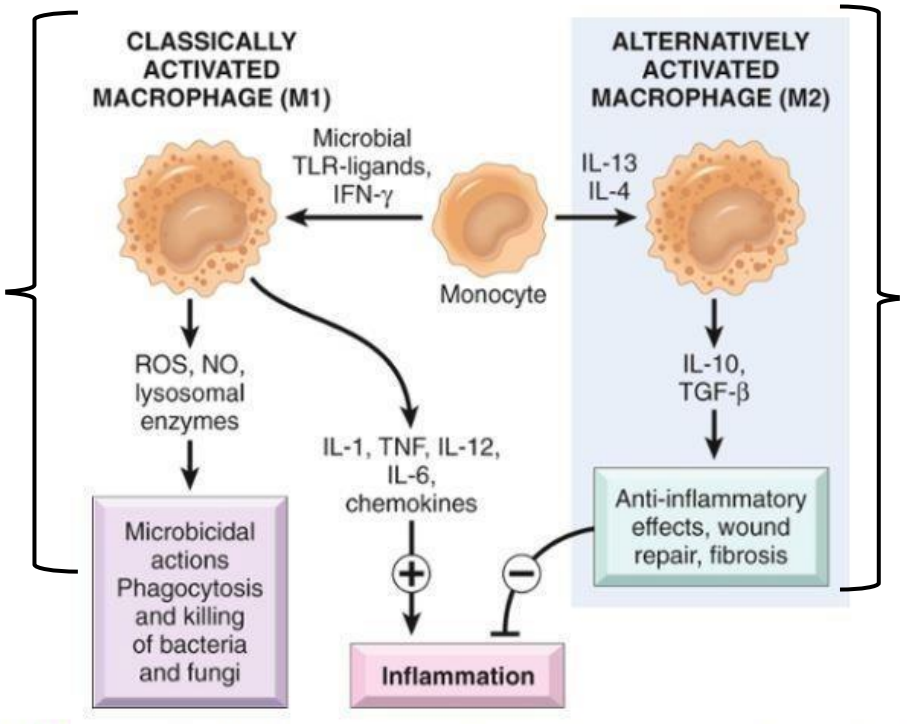


FIG. 3.18 Maturation of mononuclear phagocytes. (A) During inflammatory reactions, t…

•The activation of Macrophages by : M1 classic pathway or M2 alternative pathway.

It is activated by IFN-gamma and the microbial TLR-ligands.

It is the pro-inflammatory pathway which augment the inflammatory response to kill the microbes and produce other cytokines such as IL-1 , TNF, IL-12, IL-6 and chemokines.



Activated by IL-13 and IL-4

Induce the production of IL-10 and TGF-beta which induce the scar formation and repair process.

FIG. 3.19 Classical and alternative macrophage activation. Different stimuli activate m…

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