Doctor 021

PATHOLOGY

Sheet no.5

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COMPLEMENT SYSTEM FUNCTIONS

There are many functions for complement system but these are the most important:

Inflammation: histamine like, anaphylatoxins (C5a).

CS is similar to histamine in it's function in the initial phase of inflammation, anaphylatoxin(C5a) which happen in the anaphylaxis reaction(allergy).

Opsonization & phagocytosis: enhance phagocytosis (C3b)

Opsonizing agent which help the phagocytes and macrophages to be more effective and stronger by C3b (strongest opsonizing in the CS)

Cell lysis: Membrane Attack Complex (MAC), C9 multiples. Makes small holes in thin membrane of microbial wall in order to kill them.

REGULATORY PROTEINSFOR CS

whenever we have a strong activated response we need to regulate, maintain, terminate, and decrease the impact of these processes.

There are four mechanisms to regulate the functions, the release, and the activation of the complement system:

C1 inhibitor: if deficient hereditary angioedema

Normally everyone have C1 inhibitor in a certain range, if there is deficiency in this inhibitor it will cause angioedema(severe swelling in all mucosal surfaces) because C1 is active and the inflammatory response increases with time due to C1 inhibitor deficiency.

Decay accelerating factor (DAF), which inhibit C3 convertases and CD59 inhibits MAC, Abnormalities cause PNH

Abnormalities in these factors cause a disease called paroxysmal nocturnal hemaglobinuria (PNH) (blood in urine).

Factor H: proteolysis of C3 convertase; mutations cause hemolytic uremic syndrome

HUS is a serious disease affects kidneys and blood clotting functions of infected people, it will cause renal failure followed by death.

*mortality rate of this disease is very high.

CS protein deficiencies can occur leading to infection susceptibility.

OTHER MEDIATORS:

1. Platelet activating factor (PAF): induce the platelet aggregation
2. Protease activating receptors (PARs):platelet aggregation

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

3. Kinins: a group of vasoactive peptide, the most important one is Bradykinin(active component of all kinins) it cause vasodilation, increasing the permeability of blood vessels, smooth muscle contraction and pain.
4. Neuropeptides: Substance P and neurokinin A(neurotransmitters)

***This table is very important (summary of all mediarors and it's function)**

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
Fever	IL-1, TNF
	Prostaglandins
Pain	Prostaglandins
	Bradykinin
Tissue damage	Lysosomal enzymes of leukocytes
	Reactive oxygen species

Most of them can cause tissue damage but those are the most important, we should control and neutralize them with specific proteases.

Summary

Actions of the Principal Mediators of Inflammation

- Vasoactive amines, mainly histamine: vasodilation and increased vascular permeability
- Arachidonic acid metabolites (prostaglandins and leukotrienes): several forms exist and are involved in vascular reactions, leukocyte chemotaxis, and other reactions of inflammation; antagonized by lipoxins
- Cytokines: proteins produced by many cell types; usually act at short range; mediate multiple effects, mainly in leukocyte recruitment and migration; principal ones in acute inflammation are TNF, IL-1, and chemokines
- Complement proteins: Activation of the complement system by microbes or antibodies leads to the generation of multiple breakdown products, which are responsible for leukocyte chemotaxis, opsonization and phagocytosis of microbes and other particles, and cell killing
- Kinins: produced by proteolytic cleavage of precursors; mediate vascular reaction, pain

MORPHOLOGY OF ACUTE INFLAMMATION

Appearance of the tissue in the presence of acute inflammation

• The critical issue is blood vessel dilatation (initial vascular phase) followed by accumulation of WBCs(R1&R2) and fluids in the extravascular tissue.

*Most of the time the morphological features that we can see grossly or in the microscope mainly caused by R1&R2(vascular phase, recruitment of WBCs and chemotaxis).

Edema: too much fluids and protein in the interstitium after the vascular phase . Causing enlargement of the organ .	**Fluid and proteins in interstitium** Most of the time it's transudate but sometimes it can be exudate.
Redness: vascular phase due to high amount of blood (congestion and vasodilation)	***Rubor***
Warmth: caused by vascular changes	***Calor***
Swelling: caused by edema	***Tumor***
Loss of function: due to presence of pain and edema	***Functio laesa***
Pain: caused by mediators (prostaglandin and bradykinin)	***Dolor***

***the microscopic features of some morphological patterns of inflammation:**

SEROUS INFLAMMATION:

-Cell poor fluid(transudate)

*it looks clean, yellow and it's solidarity is low.

Common examples:

A – serous effusion: 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.

B – serous blisters: caused by the first degree burns of skin.

C – seromas: 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

FIBRINOUS INFLAMMATION:

Full of fibrin and protein products.

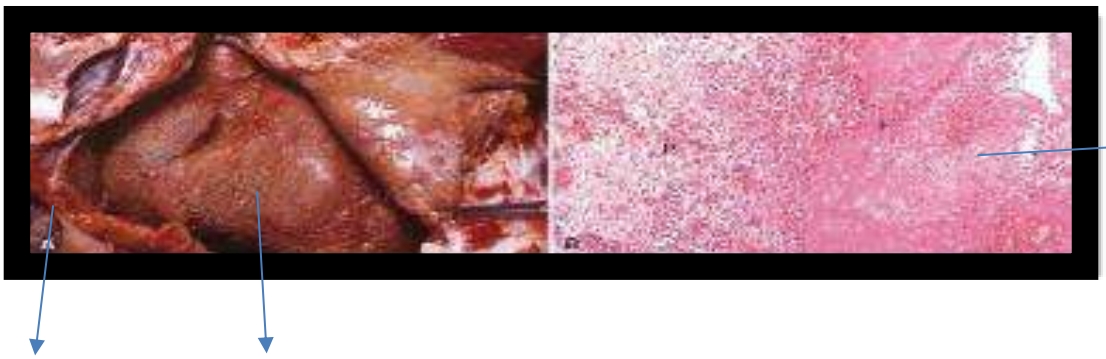
it happens in case of severe trauma or severe injuries in body cavities especially the pericardium and plural cavity there will be big holes in blood vessels in which large amounts of proteins get out of it.

large vascular leakage+ coagulation

Body cavities: pericardium

• 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-pureulent (suppurative) inflammation, abscess:

Severe acute suppurative inflammation (full of pus, bacteria and proteins)

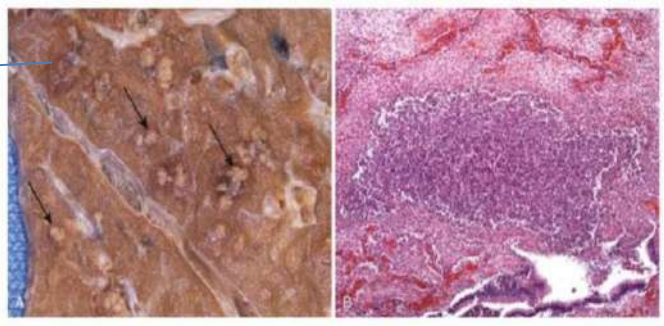
It caused by some type of bacteria such as staphylococci (from the book) .

Abscess : localized collection of pus (exudate) (pus formation) .

Treatment of an abscess is incision and drainage.

pus: exudate rich in PMNs +debris + edema

micro abscess in the lung



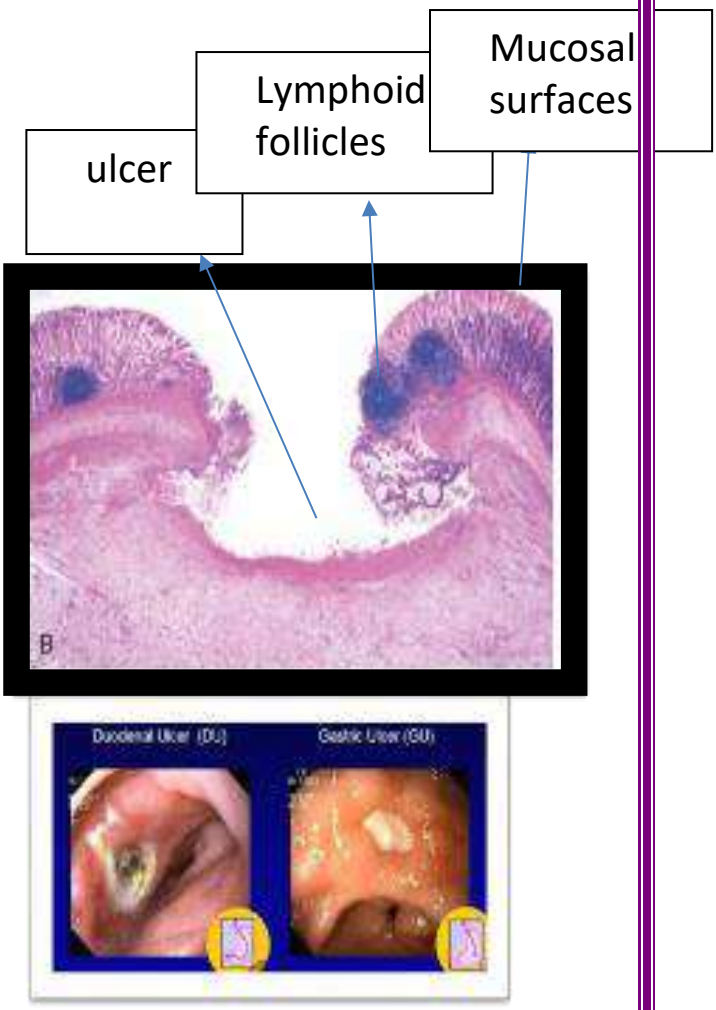
ULCERS:

*(morphological form of inflammation)

***Defect on a surface** (loss of continuation)

* Common in mucosal surfaces and skin

*Mostly acute and chronic inflammation



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 severe and cause damage for that organ.

Complete resolution :

99% of the tissue is repaired and returns to the pre-inflammatory stage. It is the most preferred outcome.

85% of time complete resolution happens.

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

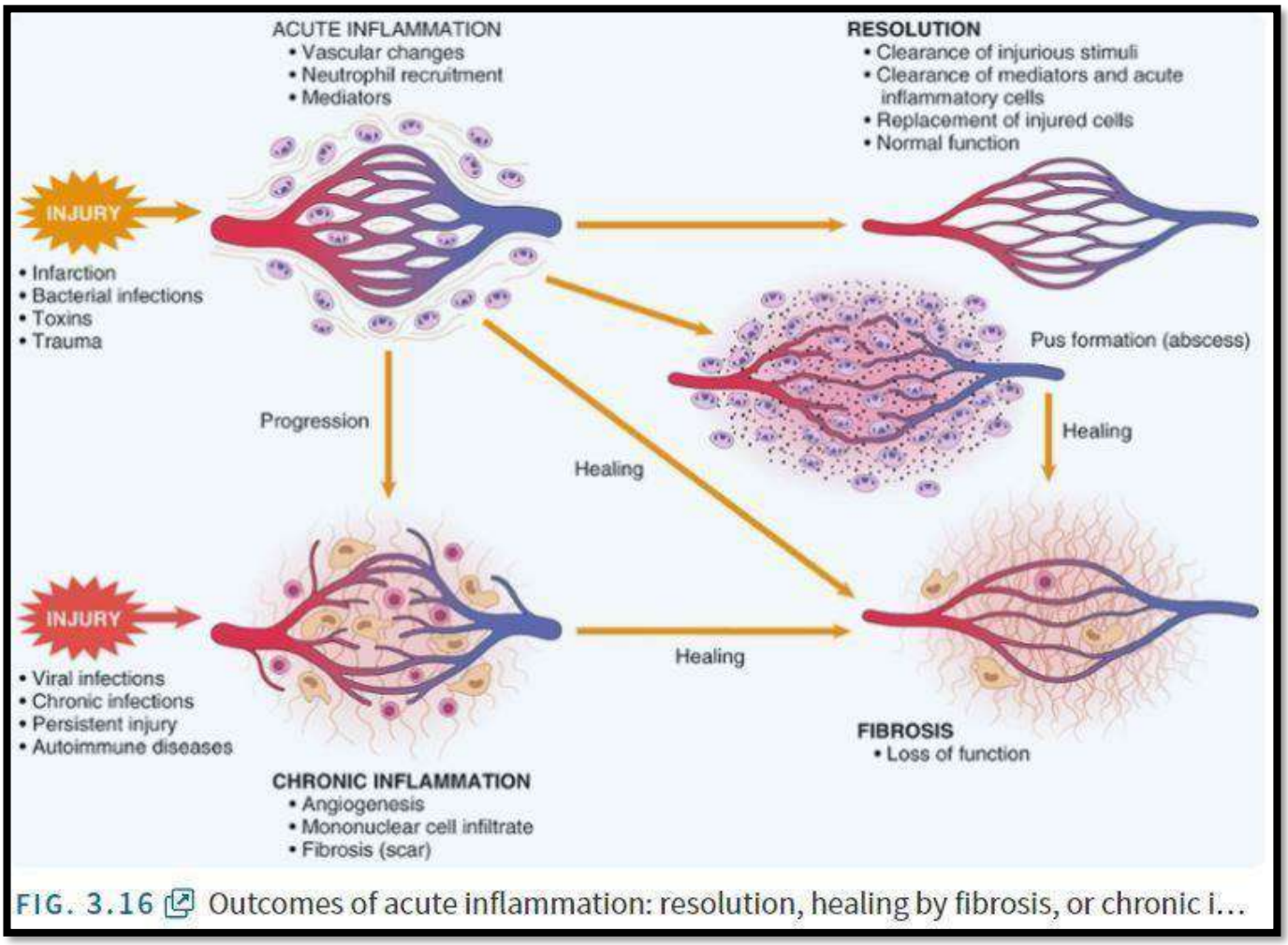


FIG. 3.16 Outcomes of acute inflammation: resolution, healing by fibrosis, or chronic i…

CHRONIC INFLAMMATION:

(characterized by continued accumulation of mononuclear leykocytes (lymphocytes, macrophages and plasma cells)

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.

*tissue damage is more common in chronic inflammation.

*chronic inflammation does not always follow acute inflammation.

• usually it follows acute inflammation but may be insidious or smoldering when the acute inflammatory phase is subclinical and does not bother (without any signs).

CAUSES OF CHRONIC INFLAMMATION:

Persistent infections	**Mycobacteria (TB), viruses,fungi, parasites. Delayed hypersensitivity reaction. Granulomatous inflammation.**
Hypersensitivity diseases	**RA, asthma, autoimmune diseases , 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,** **Metabolicsyndrome of DM** (diabetes mellitus)

MORPHOLOGIC 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 severe tissue destruction leads to severe 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.

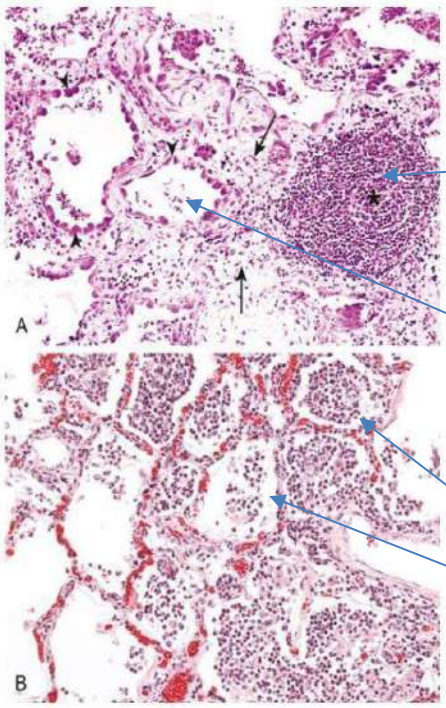


FIG. 3.17 (A) Chronic inflammation in the lung, showing all three characteristic histolo...

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)

Chronic pneumonia

((أنا التاريخ و الأمجاد
و الحاضر أنا القدس))