

Chemical mediator inflammation

Different patterns of inflammation

Outcomes of acute inflammation

Editing File

Objectives:

- ★ Chemical mediators of inflammation:
 - Definition
 - Know the general principles for chemical mediators.
 - Know the cellular sources and major effects of the mediators.
 - List the most likely mediators of each of the steps of inflammation.
- ★ Recognize the different patterns of inflammation.
- ★ List and describe the outcome of acute inflammation.

قال ابن القيم : لو أن
أحدكم همَّ بإزالة جبل
وهو واثق بالله لأزاله
قال تعالى: { وَمَنْ يَتَوَكَّلْ
عَلَى اللَّهِ فَهُوَ حَسْبُهُ }

Color Code:

Female's Notes

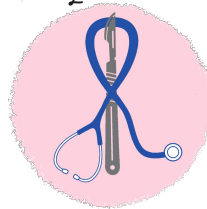
Male's Notes

Important

Extra

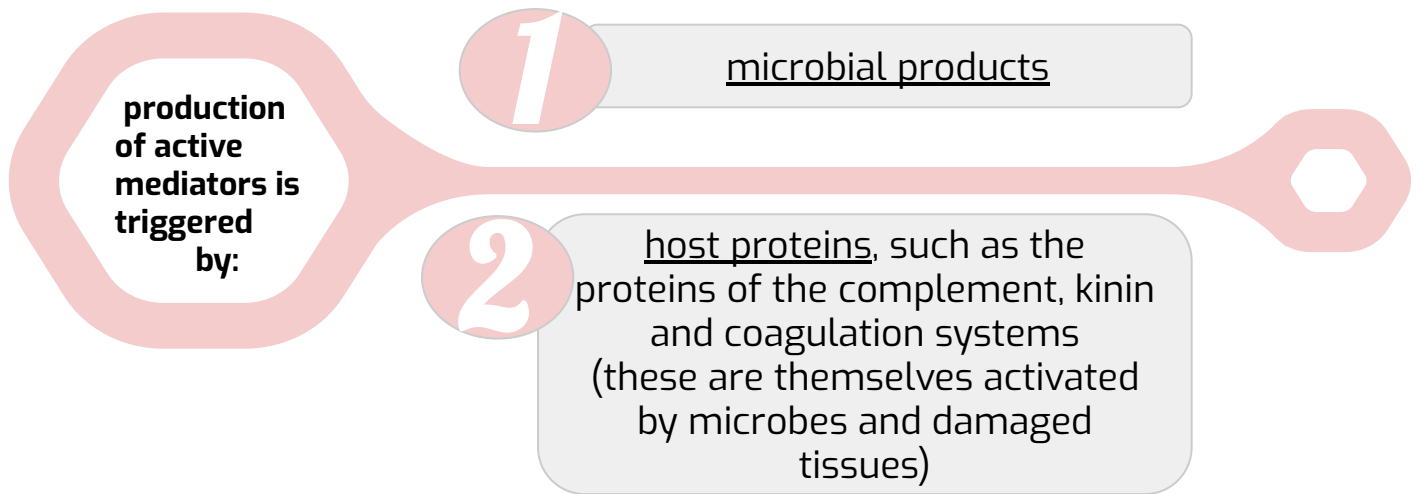


Revised & Reviewed
by:
Abdulaziz & Bahammam
Faye Wael Sondi



Mediators

- Chemical mediators of inflammation are substances produced during inflammation inducing a specific events in acute inflammation

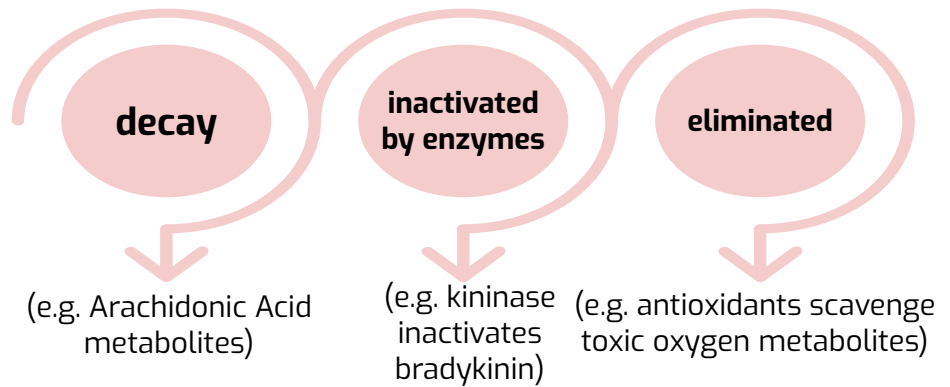


General principles for chemical mediators

Most mediators have the potential to cause harmful effects.

Therefore, there should be a mechanism to checks and balances their action.

Mediator function is tightly regulated by:



Source of Chemical mediators

cell-derived	plasma-derived <i>in blood</i>
1- Synthesized as needed (prostaglandin)	1- Complement 2- kinins 3-coagulation factors
2- Preformed, sequestered and released (mast cell histamine)	Many in "pro-form" <i>inactive</i> requiring activation (enzymatic cleavage)
against offending agents in <u>tissues</u>	against <u>circulating</u> microbes

Source of Chemical mediators cont..

Chemical Mediators of Inflammation

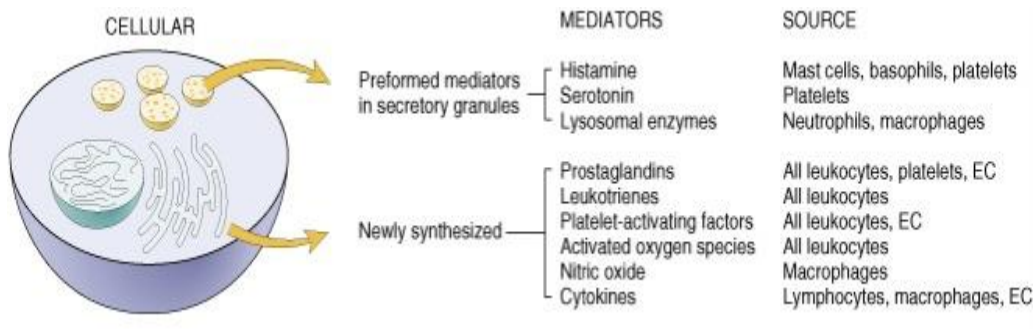


- Cell-Derived**
- Vasoactive Amines
 - Eicosanoids
 - PAF
 - Neuropeptides
 - Cytokines
 - Lysosomal Enzymes of Leukocytes
 - Chemokines
 - ROS
 - NO

- Plasma-Protein-Derived**
- Complement
 - Coagulation and Kinin Systems

Cell-Derived Mediators

Producing cells:

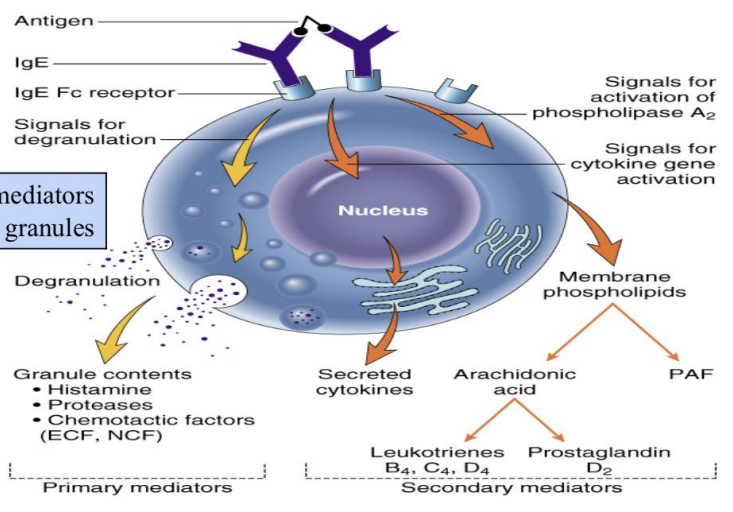


Vasoactive Amines

Histamine & Serotonin
Among first mediators in acute inflammatory reactions

Preformed mediators in secretory granules

Immune reaction involves linking of: Antigen IgE IgE Fc receptor 439



Chemical mediators of inflammation: cell derived- preformed

Histamine

plays a major role in the **early phase of acute inflammation** and **increases vascular permeability**

Source:

many cell types, esp. **mast cells**, circulating basophils, and platelets

Stimuli of Release:

- **Physical injury**
- **Immune reactions**
(cross-linking of cell-surface IgE by antigen)
- **C3a and C5a fragments**
- **Cytokines** (e.g. IL-1 and IL-8)
- **Neuropeptides**

Actions:

- 1-**ARTERIOLAR DILATION**
- 2-**INCREASED VASCULAR PERMEABILITY** (venular gaps)
- 3-**ENDOTHELIAL ACTIVATION**

Inactivated by:
Histaminase

Serotonin (its function not really known) (5-HT)

Source:

Platelets only

Action:

Neurotransmitter in the GIT gastrointestinal tract

A vasoconstrictor (the importance of this action in inflammation is unclear)

Stimulus:

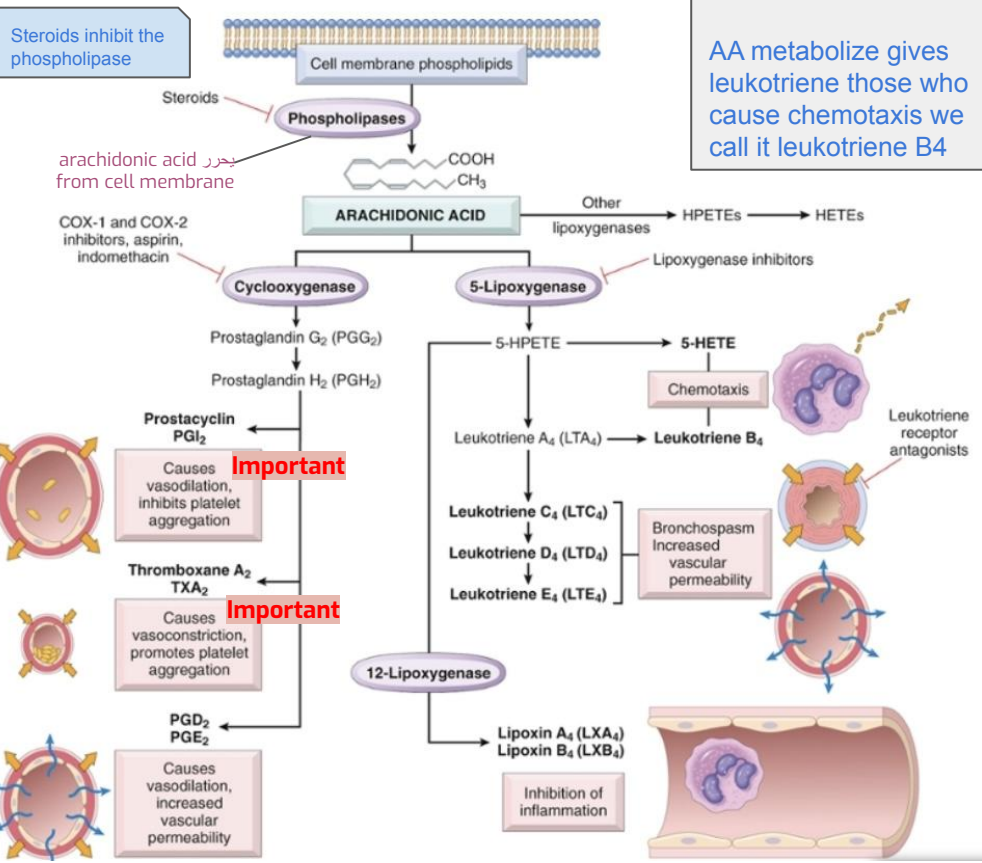
Platelet aggregation

5-HT receptors, 5-hydroxytryptamine receptors, or serotonin receptors, are a group of G protein-coupled receptor

Note 439:
It is important to know things that are only synthesized by one source

Chemical mediators of inflammation: cell derived- newly synthesized

Arachidonic Acid Metabolites (eicosanoids)

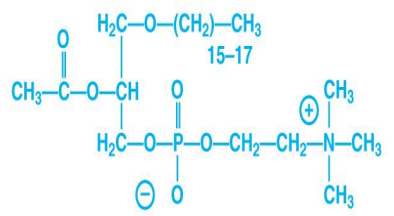


AA metabolize gives leukotriene those who cause chemotaxis we call it leukotriene B4

Source:
Leukocytes
Mast cells
Endothelial cells
Platelets

SOURCES
Mast cells/basophils
Neutrophils
Monocytes/macrophages
Endothelium
Platelets
Others

MAJOR INFLAMMATORY ACTIONS
Increased vascular permeability
Leukocyte aggregation
Leukocyte adhesion
Leukocyte priming/chemotaxis
Platelet activation
Stimulation of other mediators (LT, O₂⁻)



PLATELET-ACTIVATING FACTOR

Action	Eicosanoid
Vasodilation	Prostaglandins PGI ₂ (prostacyclin), PGE ₁ , PGE ₂ , PGD ₂
vasoconstriction	Thromboxane A ₂ , leukotrienes C ₄ , D ₄ , E ₄
Increased vascular permeability	leukotrienes C ₄ , D ₄ , E ₄
chemotaxis, leukocyte adhesion	Leukotriene B ₄
Smooth muscle contraction	Prostaglandins PGC ₄ , PGD ₄ , PGE ₄

Prostaglandins affect the thermoregulatory center of CNS in hypothalamus and cause fever

Chemical mediators of inflammation: cell derived- newly synthesized

Cytokines

Polypeptides

Actions:

- Involved in early immune and inflammatory reactions
- Some stimulate bone marrow precursors to produce more leukocytes
- Have roles in acute and chronic inflammation

Source:
Lymphocytes
Macrophages
Dendritic cells
Endothelial cells
Epithelial cells

Cytokine of **Acute inflammation:**
Interleukin (IL-1) & TNF

Action:

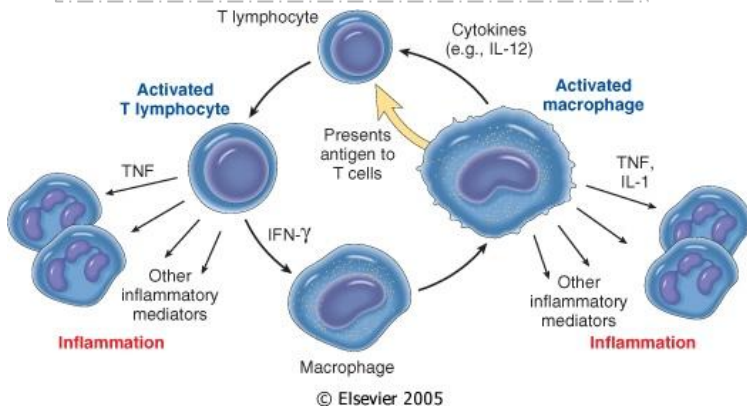
Stimulates expression of endothelial adhesion molecules and secretion of other cytokines; systemic effects

Interferons have many uses in medicine especially in hepatitis

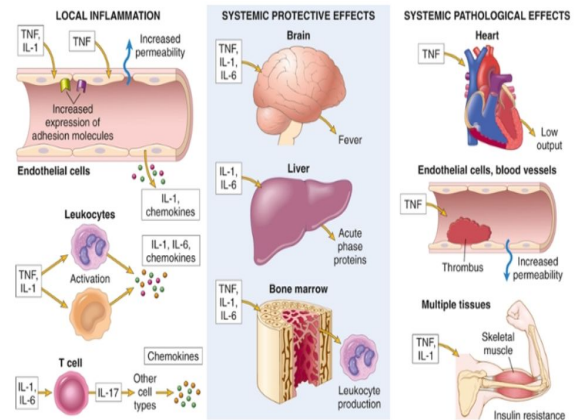
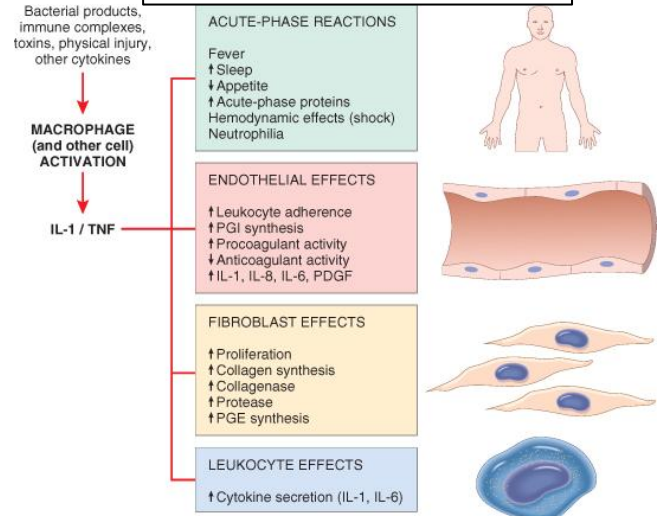
Cytokines of

Chronic Inflammation:

Interferon- γ (INF- γ) & Interleukin (IL-12)



Activated lymphocytes and macrophages influence each other and also release inflammatory mediators that affect other cells.



TNF antagonists is effective in the treatment of rheumatoid arthritis

Chemokines

Small proteins
They are chemoattractants for leukocytes

Main functions:

- Leukocyte recruitment & activation in inflammation
- Normal anatomic organization of cells in lymphoid and other tissues

Chemokines play major role in chemotaxis and leukocyte activation.

No chemotaxis no defense against inflammation no migration of leukocyte from blood vessels to the tissue.

Reactive Oxygen Species (ROS)

Synthesized via
NADPH oxidase pathway

Source:

Neutrophils and Macrophages

Stimuli of release:

- Microbes
- Immune complexes
- Cytokines

Action:

Microbicidal (cytotoxic) agent

Oxidative action make tissue injury but kill the bacteria

Chemical mediators of inflammation: cell derived- newly synthesized

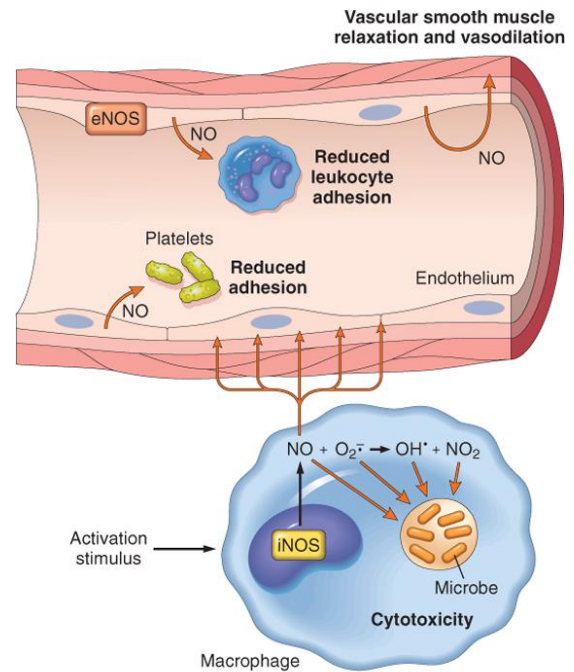
Nitric Oxide (NO)

Short-lived

Soluble free-radical gas

Functions:

- Vasodilation
- Antagonism of platelet activation (adhesion, aggregation, & degranulation)
- Reduction of leukocyte recruitment
- Microbicidal (**cytotoxic**) agent (with or without ROS) in activated macrophages



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Neuropeptides

Small proteins
 Secreted by nerve fibers mainly in lung & GIT
 Initiate inflammatory response
 e.g. Substance P :
 Transmits pain signals
 Regulates vessel tone
 Modulates vascular permeability

Lysosomal Enzymes of Leukocytes

Neutrophils & Monocytes

Enzymes:

Acid proteases
 Neutral proteases (e.g. elastase, collagenase, & cathepsin)

Their action is checked by:

Serum antiproteases (e.g. α 1-antitrypsin)

Chemical mediators of inflammation: Plasma protein derived

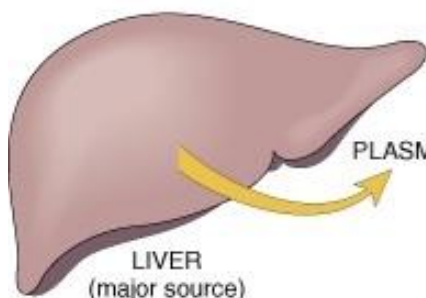
1

Kinin & clotting systems

2

Complement system

the 3 systems produced by the liver

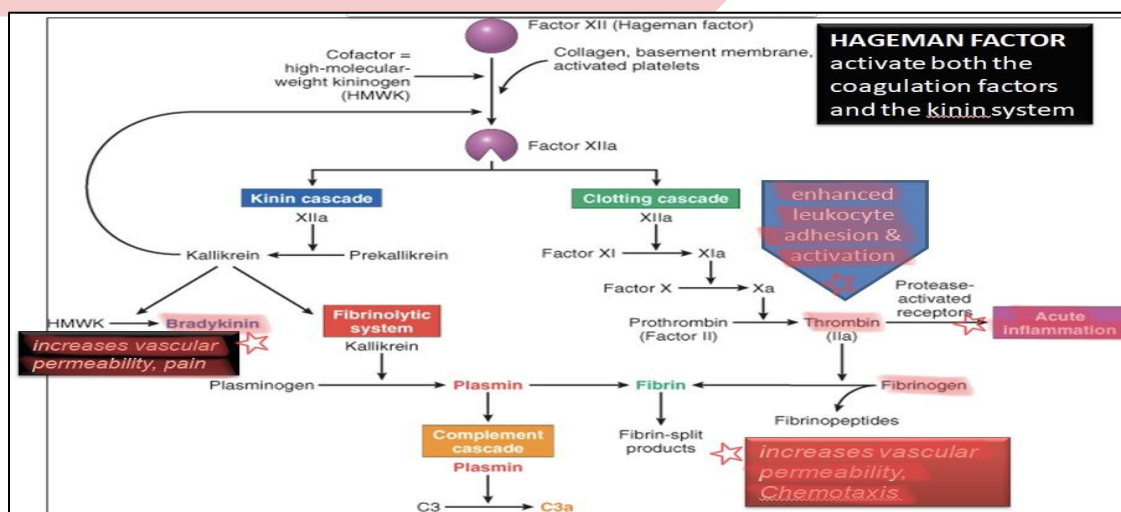


Factor XII (Hageman factor) activation — Kinin system (bradykinin)
 Coagulation / fibrinolysis system

Complement activation — C_{3a} , C_{5a}] anaphylatoxins
 C_{3b} , C_{5b-9} (membrane attack complex)

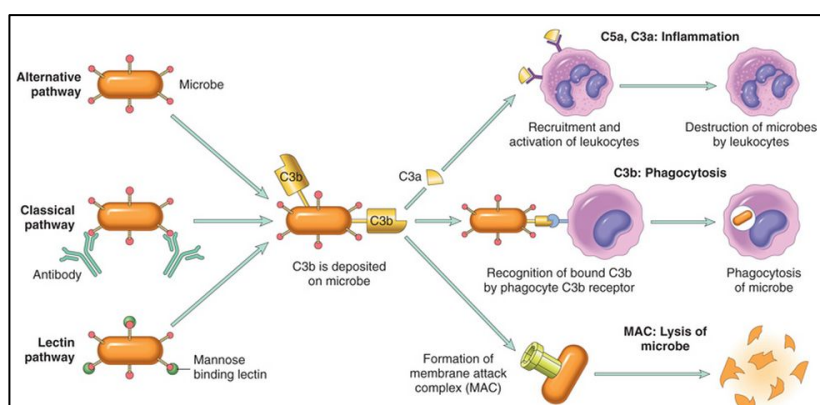
Chemical mediators of inflammation: Plasma protein derived

1- Kinin & Clotting systems



2- Complement System

- C3a & C5a** → Increase vascular permeability (anaphylatoxins)
- C5a** → Chemotaxis
- C3b** → Opsonization
- C5-9** → membrane attack complex, lead to bacterial lysis

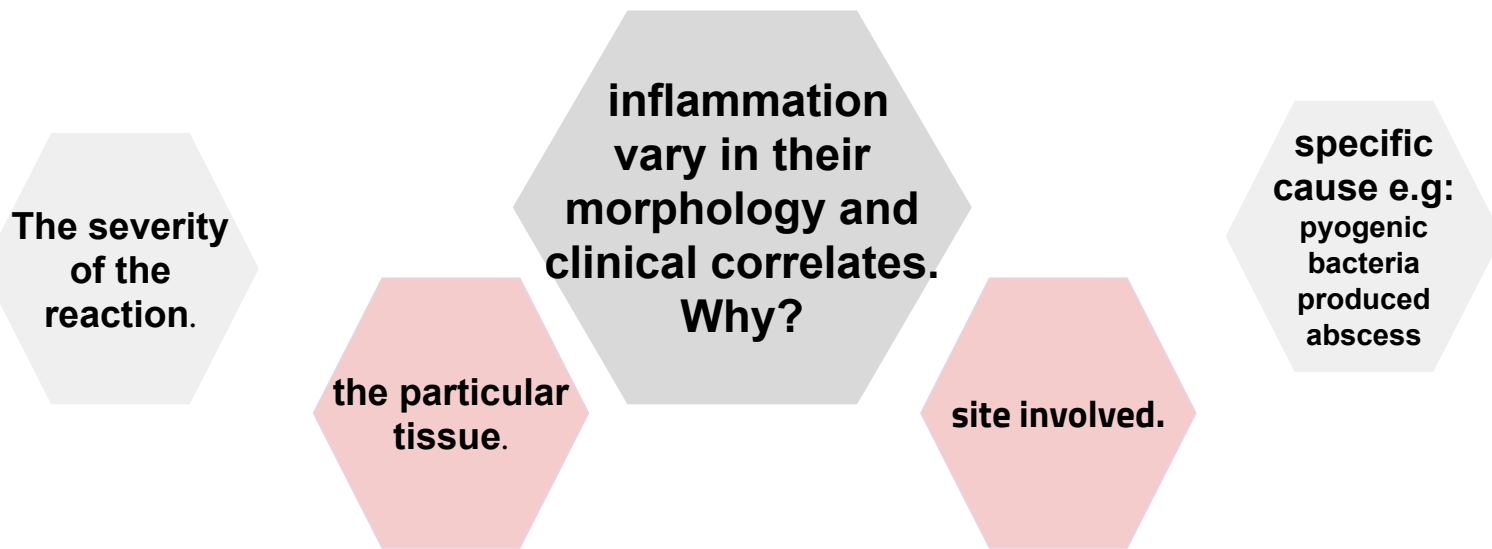


Role of Mediators in Different Reactions of Inflammation ★

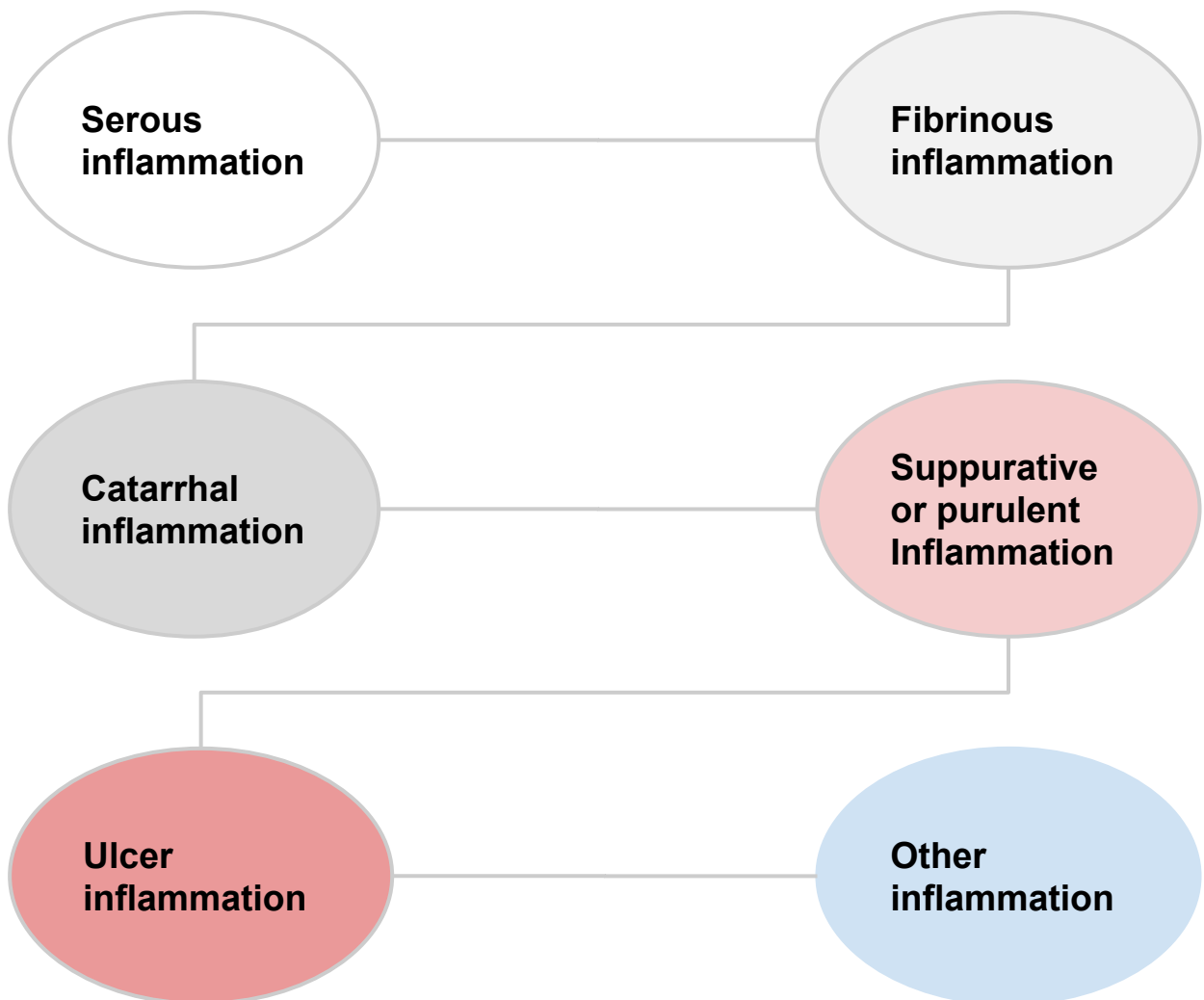
C reactive protein يطلب غالباً في
التشخيص و يعطينا فكرة اذا المريض عنده
tissue damage
و في الغالب inflammatory condition يس ما
يعلمك نوع الحالة

Vasodilation	Prostaglandins Histamine Nitric oxide
Increased vascular permeability	Vasoactive amines (Histamine+serotonin) Bradykinin Leukotrienes C4, D4, E4 PAF ,Substance P
Chemotaxis, leukocyte recruitment and activation	C3a, C5a Leukotriene B4 Chemokines ,IL-1, TNF
Opsonization	IgG, C3b
Fever	IL-1, TNF ,Prostaglandins
Pain	Prostaglandins Bradykinin
Tissue damage	Neutrophil and macrophage lysosomal enzymes ,Oxygen metabolites Nitric oxide

Morphologic of Acute Inflammation



Morphologic patterns of acute inflammation :



Morphologic of Acute Inflammation

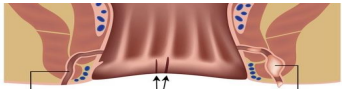
Other inflammation

1. sinus



-A tract between the abscess and a surface (skin).
-has one channel, and drains outside.(team 439)

2. fistula



-A tract between two surfaces.
- has two channels (to the skin & to the closest mucosa)(team439)

3. cellulitis



-a spreading of acute inflammation through interstitial tissues.
 - extends into large surface area(not localized).

Ulcer inflammation

-An ulcer is a local defect of the surface of an organ or tissue that is **produced by the sloughing** (shedding) of inflammatory necrotic tissue.



suppurative or purulent inflammation

-Characterized by **the production of large amounts of pus or purulent exudate** consisting of neutrophils, necrotic cells, and edema fluid caused by pyogenic (pus-producing) bacteria.

-An abscess is a cavity lined by granulation tissue and containing:

1- inflammatory cells

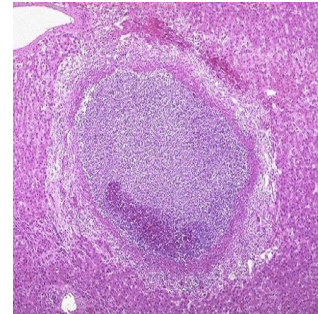
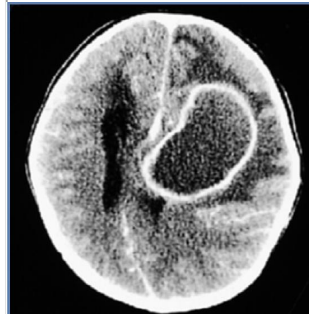
2- necrotic cells

3- bacteria

4- fibrinous material.

-Abscesses:

A localized collections of purulent inflammatory tissue caused by suppuration buried in a tissue, an organ, or a confined space.



Morphologic of Acute Inflammation

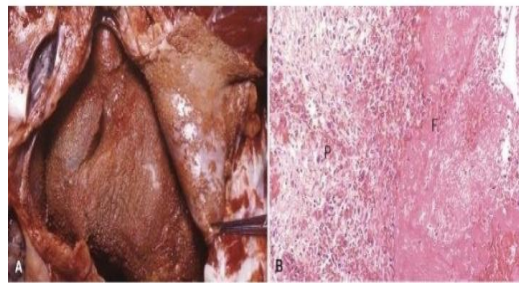
catarrhal inflammation

-Inflammation affects mucosa-lined surfaces with the **outpouring of watery mucus.**



fibrinous inflammation

-A **fibrinous exudate (fluid accumulation)** is a characteristic of inflammation in the lining of body cavities, such as the meninges, pericardium and pleura (larger molecules such as fibrinogen pass the vascular barrier).
 – Fibrinous exudates may be removed by **fibrinolysis**.
 – If not: it may stimulate the ingrowth of granulation tissue (**organization**).



Serous inflammation

-Marked by the **outpouring of a thin fluid** this fluid occurs immediately and has less amount of inflammatory cell.
 -Bubble formation after **burns**.



Outcomes of Acute Inflammation

1

Complete resolution

Events in **the resolution** of inflammation:

1- Neutralization, decay, or enzymatic degradation of the various chemical mediators; normalization of vascular permeability; and cessation of leukocyte emigration and apoptosis.

2- The necrotic debris, edema fluid, and inflammatory cells are cleared by phagocytes and lymphatic drainage.

3- Lymph node become enlarged and inflamed.

2

Progression of the tissue response to chronic inflammation.

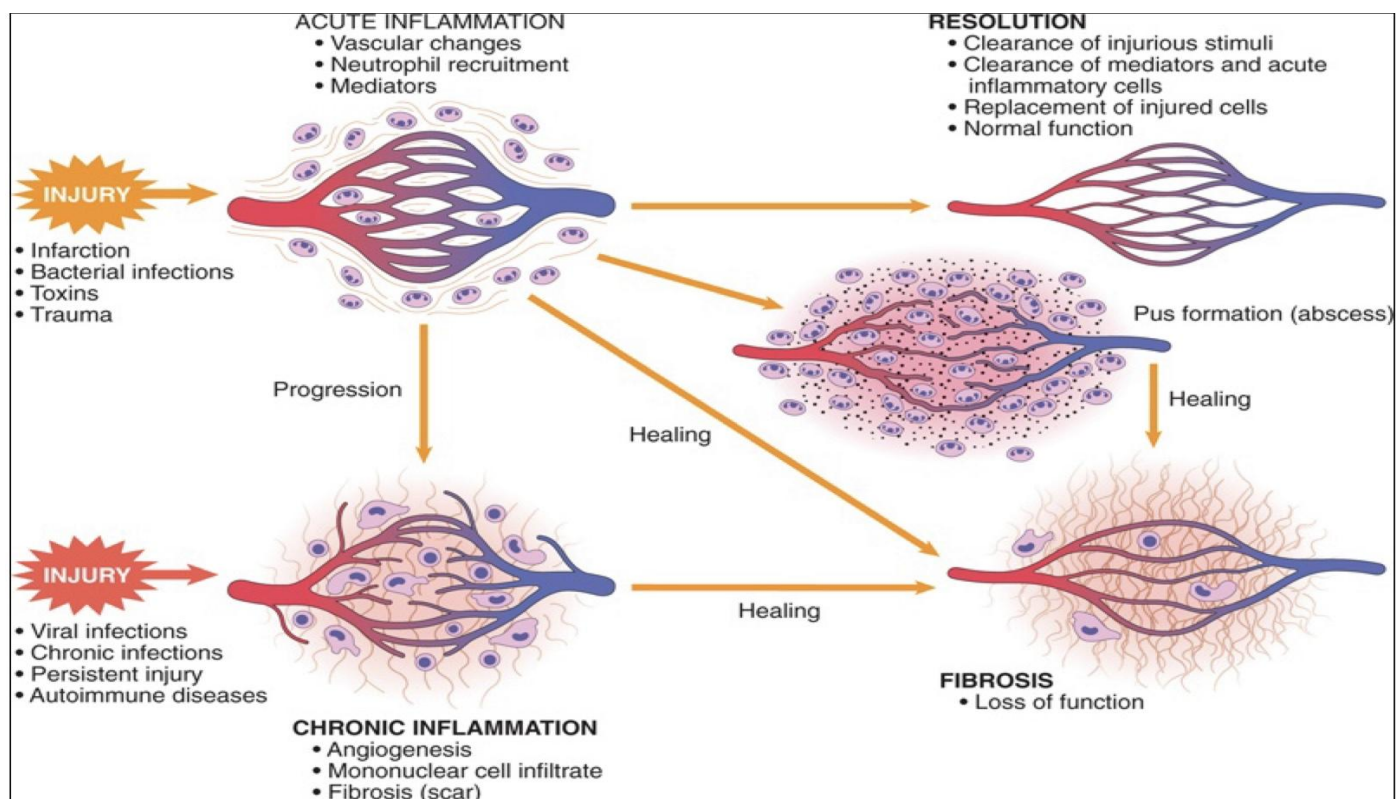
3

Fibrosis: Healing by connective tissue replacement.

4

Abscess formation.

واحد صار عنده inflammation و انتهى الامر فيه بتكون abscess (liquefactive necrosis) سببه staphylococcus aureus or streptococcus و سببت له infection بس الانفلاميشن منع الانتشار لكن سبب له sub tissue damage and formation of abscess



1-What is the source of serotonin ?			
A-Mast cells	B-Platelets	C-Lymphocytes	D-Epithelial cells
2-Which of the following is cytokines of chronic inflammation ?			
A-IL-1	B- IL-6	C-TNF	D-IL-12
3-Which of these following can cause fever Which of these following can cause fever ?			
A-C3a	B-PAF	C-prostaglandins E	D-bradykinin
4-which of the following Inflammation affects mucosa-lined surfaces with the outpouring of watery mucus?			
A- serous inflammation	B- ulcer inflammation	C- catarrhal inflammation	D- cellulitis inflammation
5-which of the following cells Containing abscess cavity lined by granulation tissue ?			
A- necrotic cells	B- endothelial cells	C-inflammatory cells	D- both A , C

★ SAQ

Q1:Write the mediators that is responsible for increased vascular permeability ?
Slide 8

Q2: enumerate 3 Morphologic patterns of acute inflammation?
Slide 9

Q3: enumerate the outcomes of acute inflammation?
Slide 12

The secret of getting ahead is getting started .



Leaders:

Lama Al-Jamili
Salem Abokhanjar

Sub-Leader:

Manar Al-Abdullah

Members:

Lama Bin Salamh
Rahmah Alzahrani
Noyer Awad
Rahaf alamri
Layan Alhelal
Taif alshehri
Renad Aldawayan
laila almeshariy
Alanoud Albawardi
Reema Alrashedi

Shouq Alhathal
Tarfa albaz
Jumana AL-qahtani
Lama Alrumaih
Ayah Sayed
Shahad Helmi
Norah Alsewailem
Leen Alhadlaq
Arwa Alenzi
Reem Al Kulaibi

Mohammed Alwahibi
Sultan Alosaimi
Rakan alobaid
Abdullah Abdulrazaq
Ibrahim Al Hazza
Nawaf Alzaben
Abdelaziz Alabdulraman

Organizer:

Aya Alhossain
Abdulmajeed Namshah

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