MED437
KING SAUD UNIVERSITY

PATHOLOGY
TEAM 437

Pathology

teamwork 437

Lectures (5-8) : Inflammation.

Color Index :-

- VERY IMPORTANT
- Extra explanation
- Examples
- Diseases names: Underlined
- Definitions

تمت المراجعة
غيداء آل مصمع
&
عبدالرحمن الجيسوني

{قاتِل لحُلمك، فما قيمة الحُلم إن كان سهلاً مُيسراً...}

OBJECTIVES:

- DEFINITION OF INFLAMMATION
- THE PROCESSES OF INFLAMMATION IN GENERAL
- CARDINAL SIGNS AND CAUSES OF INFLAMMATION
- UNDERSTANDING ACUTE INFLAMMATION :
  1. ROLE OF ADHESION MOLECULES
  2. VASOACTIVE CHANGES
  3. INCREASED CAPILLARY PERMEABILITY
- OUTCOMES OF ACUTE INFLAMMATION.
- DIFFERENT PATTERNS OF INFLAMMATION.
- CHRONIC INFLAMMATION.
- DESCRIBE THE STEPS INVOLVED IN EXTRAVASATION OF LEUKOCYTES FROM THE BLOOD TO THE TISSUE.
- KNOW THE STEPS AT WHICH SELECTINS AND INTEGRINS ACT
- DESCRIBE THE MEANING AND UTILITY OF CHEMO TAXIS UNDERSTAND THE ROLE THAT CHEMOKINE PLAY IN INFLAMMATION
- DESCRIBE THE STEPS INVOLVED IN PHAGOCYTOSIS AND THE ROLE OF IGG AND C3B AS OPSONINS AND RECEPTORS
- THE MECHANISIM OF MICROBAL KILLING
- KNOW VARIOUS DEFECTS IN LEUKOCYTE FUNCTION

WHAT IS INFLAMMATION?

Inflammation is a local response of the vascularized living tissue to infection and damaged tissue that brings cells and molecules of the host defense from the circulation to the sites where they are needed.

Why does inflammation happen? To localize and eliminate the causative agent (stimulus), limit tissue injury and restore tissue to normality.

Therefore, Inflammation is a part of a broader protective response ***(innate immunity)***

The suffix "itis" is added to the base word to state the condition as in appendix/appendicitis

Infection: a term used to describe a biological agent inside tissue causing inflammation (e.g.: Bacteria , Fungi , Virus)

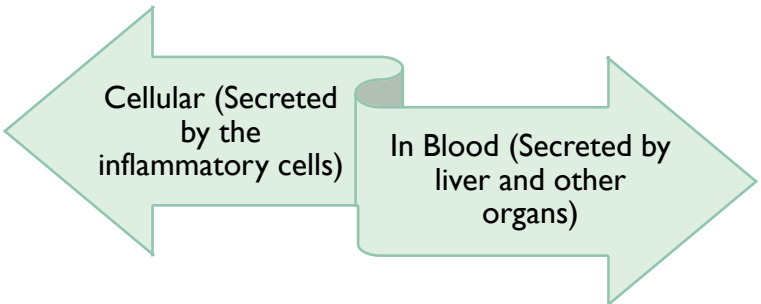
Inflammation can be acute or chronic (Acute and chronic inflammations can coexist) :-

Acute	Chronic
Fast onset	Slow onset
Mainly neutrophils	Mainly monocytes, macrophages. and lymphocytes
Usually mild and self limited tissue injury and fibrosis	Mostly severe, and can cause major problems
Prominent signs	Hidden signs

Inflammation stands on 3 pillars:

1. Cellular changes
2. Vascular changes
3. Chemical mediators (Chemicals that increase and act during chronic inflammation)

There are two types of chemical mediators :-



STEPS OF INFLAMMATION

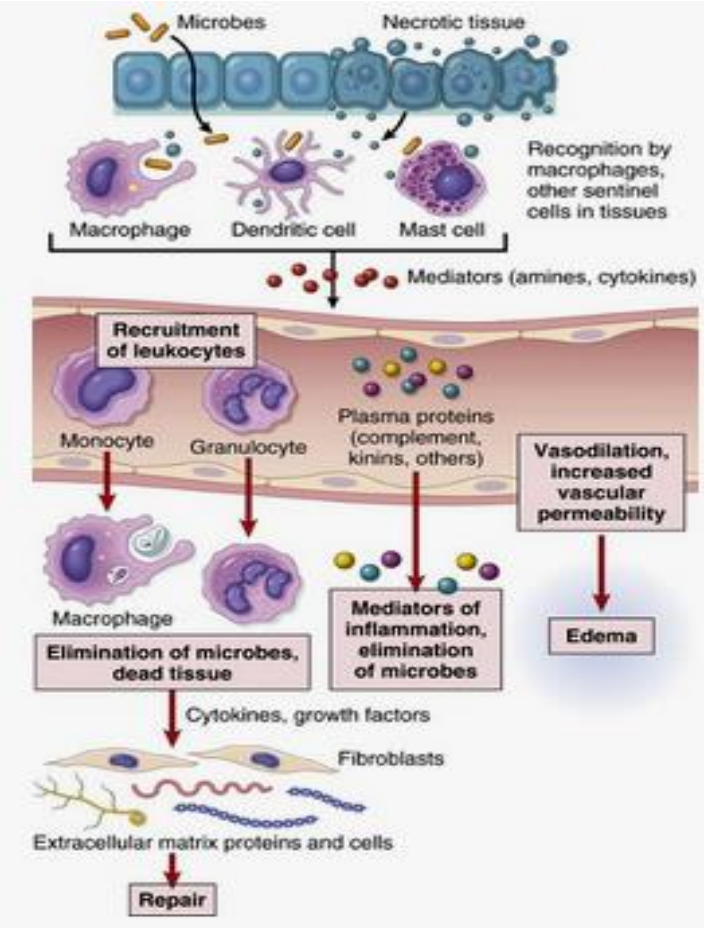
The offending agent is recognized by host cells and molecules.

Leukocytes and plasma proteins are recruited from the circulation to the site where the offending agent is located

The leukocytes and proteins are activated to destroy and eliminate the offending substance.

The reaction is controlled and terminated.

The damaged tissue is repaired.

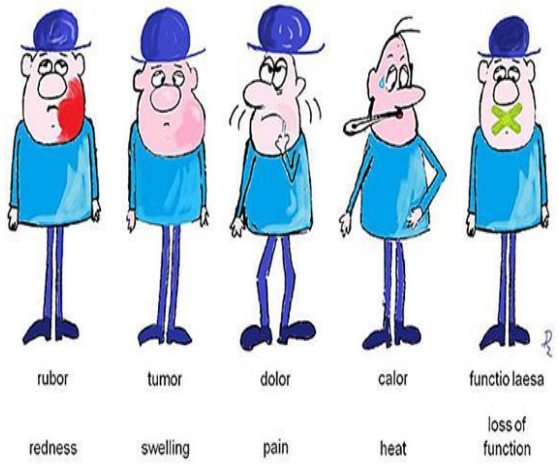


هذه واحدة من عدة احتمالات يلي ممكن تصير من الاحتمالات الممكنة يلي رح يتم نقاشتها لاحقا :..

1- Tissue might heal! ☺ but by replacing some parts with Connective tissue (fibrosis)
2- Tissue might develop to chronic inflammation!
3- Tissue might develop a Granuloma formation
(لكتشر كامل و منفصل)

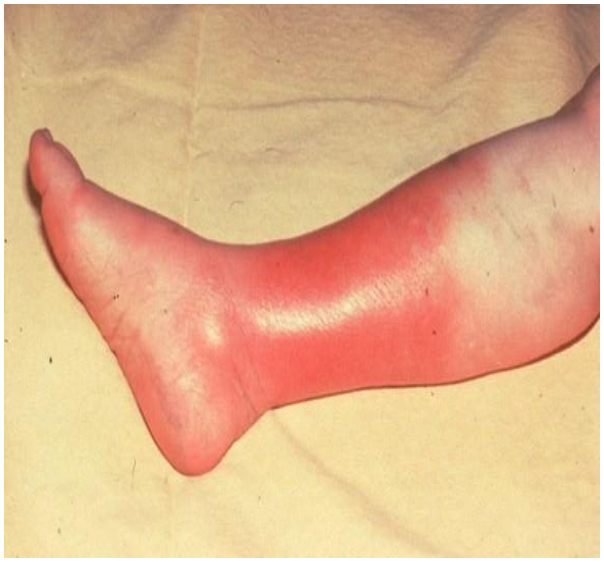
و احتمالات أخرى رح نناقشها في المحاضرات القادمة .

CARDINAL SIGNS AND CAUSES OF INFLAMMATION



- **Cardinal signs of inflammation:**

1. Swelling = tumor =تورم
2. Redness = rubor
3. Warmth = calor
4. Pain = dolor
5. Loss of function = functio laesa



- Causes of inflammation :

There are also ***Systemic signs*** that will be discussed later on , and they are :

1. Fever
2. Chills
3. Malaise (توعك) : Not feeling well overall
4. Vomiting : seen in children mostly
5. Increased Erythrocyte sedimentation rate : speed at which RBC fall to the bottom of tube (يترسب) / usually done for tests regarding inflammation
6. Increased C-Reactive protein

Bacteria	Physical injury	radiation	fungi	parasites
viruses	Thermal injury	Trauma	Burns	Immunological reaction
fractures	frostbite	Toxic substances	Infection after surgeries	

Frostbite(صقيع) happens with very low temperatures in exposed areas such as the ears, tip of the nose, etc.

VASOACTIVE CHANGES OF INFLAMMATION

- The main vasoactive changes that occur in response to acute inflammation are**, increased blood flow** (secondary to vasodilation) and **increase in vascular permeability.**

Vasodilation

- Increased blood flow to the site of injury
- Happens at the arteriole end of the vessels (due to presence of muscle lining allowing constriction/relaxation)
- Localized effect

Vasoactive changes:

1. Antigen first enters body

⟶short period of vasoconstriction.

2. After, vasodilation begins

⟶increased blood flow

⟶stasis (slowness of blood due to increased diameter)

3. Leukocytes begin to accumulate on the endothelial surface moving from center to peripheral, in a process known as marginization.

This process results in redness (erythema) and warmth, which are indicators of the inflammatory response.

Vascular permeability increase

- Caused by histamine
- Happens at the venule end (as it is much thinner in allowing the passage of blood components)
- Endothelial cells contract forming little pores allowing transport of neutrophils

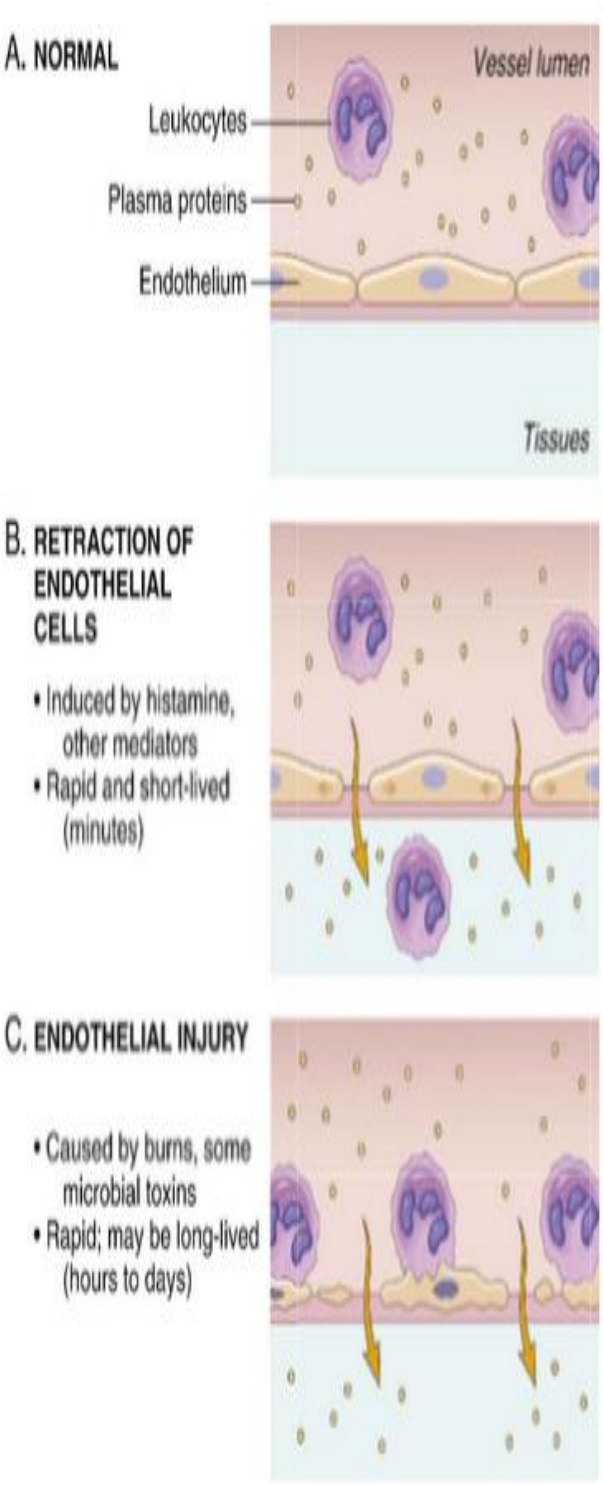
Increased permeability:

1. Release of histamine by mast cells
2. Causes contraction of endothelial cells and formation of intercellular gaps.
3. Neutrophils now pass through the newly formed pores into the extravascular tissue

A protein rich fluid called exudate also accompanies the blood cells

Increased Vascular Permeability

- A crucial identifier of acute inflammation:
  - The leakage of protein-rich fluid from blood vessels.
  - Induced by histamine, kinins, and other mediators.



Mechanisms leading to increased vascular permeability:

- Leakage from new blood vessels
- Endothelial cell contraction usually takes 15-30 min
- Endothelial injury:
  - Immediate sustained response 6-24 hours
  - Delayed prolonged leakage 12 hours - days
- Leukocyte-mediated endothelial injury
- Transcytosis (occurs via channels formed by fusion of intracellular vesicles) هي طريقة معينة لنقل المواد الكبيرة في الخلية عن طريق تدخيلها بوساطة حويصلة و تجري داخل الخلية .. ثم الخلية تطلعها من الطرف الثاني

This is explained later in the next slides ..

EDEMA

- Edema: Excessive accumulation of fluids within the body.
- Divided into:

Transudate

- Protein poor
- Due to excessive capillary filtration:

❖ **Congestive heart failure**

→ high hydrostatic pressure
→ transudate edema

- As well as low colloid osmotic pressure:

❖ **Renal disease**

→ low colloid osmotic pressure → transudate edema

❖ **Liver disease**

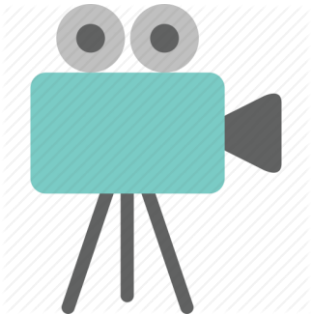
→ low colloid osmotic pressure → transudate edema

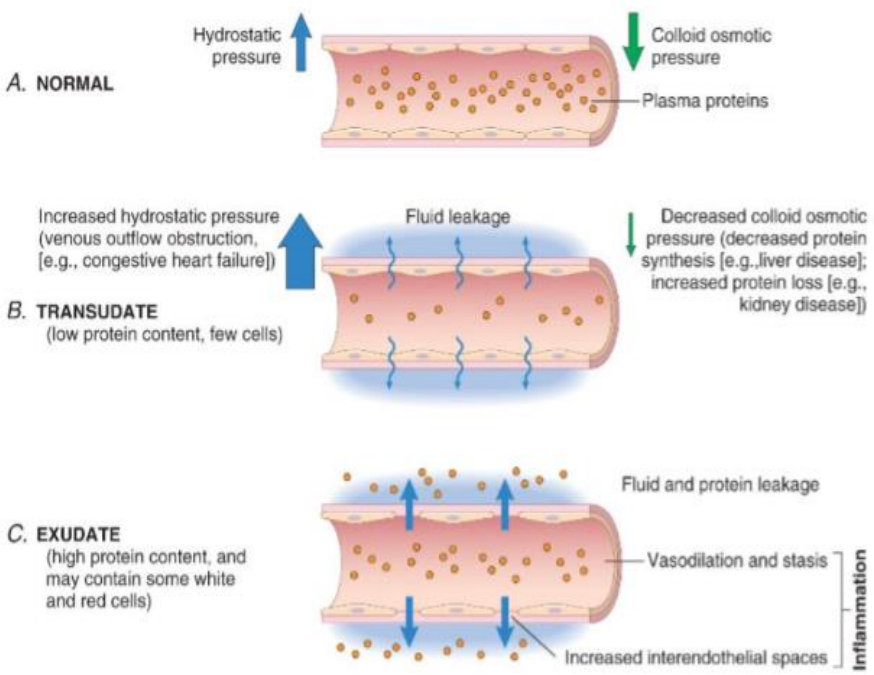
Exudate

- Protein rich
- Direct cause is inflammation

❖ **Increased permeability of vessels**

→Release of histamine by mast cells
→Contraction of epithelial cells forming gaps
→Outflow of neutrophils in addition to protein fluid
→ exudate edema





From Robbins →

IF YOU DIDN'T UNDERSTAND THE PREVIOUS SLIDE THEN THIS MIGHT ELABORATE MORE ☺

Increasing vascular permeability leads to the movement of **protein-rich** fluid and even blood cells into **extravascular** tissue.

This in turn increases the **osmotic** pressure of the interstitial fluid, leading to more outflow of water from the blood into the tissue. The resulting protein-rich accumulation from the blood is called ***exudate***.

● This exudate happens In **inflammation** conditions when the **Endothelial cell start to contract** –which is caused by (histamine, bradykinin, leukotrienes) - Leading to intercellular gaps in post capillary **venules**; causing the accumulation of a **exudate**. " لما تنقبض العضلات بتكون مساحات بالاندوثيليل يتسرب منها السائل مع البروتين"

- Exudate must be distinguished from **transudates**

-What is transudates? Its the are accumulations of interstitial fluid . (pure fluid without proteins).

- **How could it happen?**

1) increased **hydrostatic pressure** usually as a consequence of reduced venous return or heart failure or obstruction. عندما يرتفع ضغط القلب على الأوعية الدموية ، يطلع السائل عشان يخفف من الضغط

2) Decreased **colloid osmotic pressure.** Due to decreased protein synthesis. (liver disease) or increased protein loss (kidneys diseases) by homeostasis. It will force the water to go out , to the interstitial.

- Fluid accumulation in extravascular spaces, **whether** from an **exudate or a transudate**, produces tissue ***edema***.

Fluid type	Condition	Content	Specific Gravity
Transudate	Increased Hydrostatic pressure or decreased colloid osmotic pressure	Low protein	<1.020
Exudate	Acute inflammation	High protein	>1.020
Pus	Acute inflammation	High protein & neutrophils	>1.020

ROLE OF ADHESION MOLECULES

Selectins

1. E selectin: in endothelium, induced by TNF & IL-1
2. P selectin: in endothelium & platelets from Weasel-Palade bodies
3. L selectin: in leukocyte & endothelium

E selectin & P selectin bind to Sialyl-Lewis X glycoprotein & slow leukocytes

Integrins

- Transmembrane hetero dimeric proteins
- Composed of alpha and beta chains
- Expressed on leukocytes & bind to ligands on endothelial

Integrins are regulated on leukocytes by **C5a & LTB4** resulting in firm adhesion of vessel wall

Adhesion molecules

Immunoglobulin family molecules

1. ICAM-1
(intercellular adhesion molecule 1)

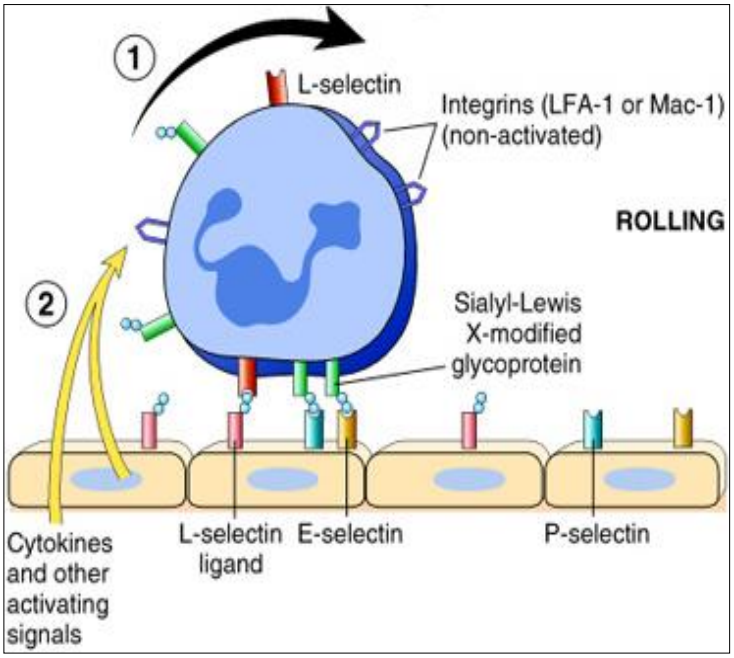
2.VCAM-1
(vascular adhesion molecule 1)

Activated by **IL-1** & **TNF** on venular endothelial cells

Mucin-like glycoproteins (PECAM-1)

- Form of glycoproteins
- Found in extracellular matrix & on cell surfaces

Selectins and Integrins are the most important ones here ☺

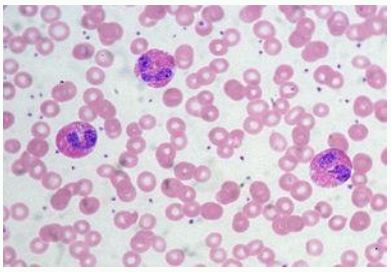
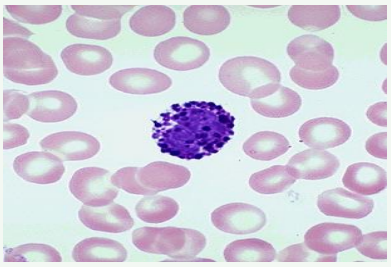
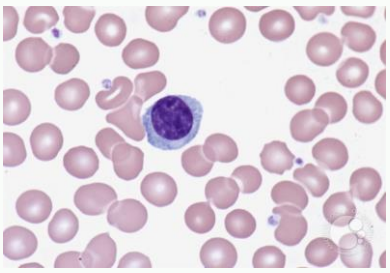
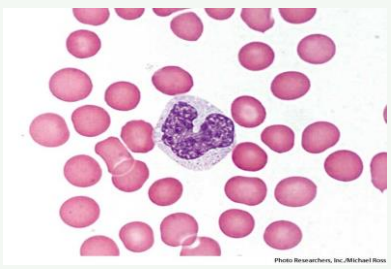


Weibel-Palade bodies: "glue factory" of the endothelial cells

- Produce P-selectin (adhesion molecule of leukocyte)
- Produce von Willebrand factor (adhesion molecule of platelet)

Salyl-Lewis X: glycoprotein that is very important in leukocyte "rolling"

TYPES OF INFLAMMATORY CELLS

Definition	Illustration
Neutrophils : Neutrophils are 3-5 lobed cells normally found in the bloodstream during the beginning phase of inflammation, **Elevated numbers of neutrophils are usually due to an acute infection** (e.g. appendicitis.)	
Eosinophils: Eosinophils are bi-lobed cells found in response to **parasitic infections** and allergic responses (e.g. bronchial asthma or hay fever.)	
Basophils: Basophils are bi-lobed cells that contain large basophilic granules that stain deep blue, and contain histamines that cause vasodilation and heparin that acts like an anticoagulant.	
Lymphocytes: Lymphocytes (T & B cells) have an agranular clear cytoplasm that stains pale blue, whereas the nucleus stains dark purple. A relative increase in the proportion of lymphocytes is typical in a **chronic infection. And viral infection.**	
Monocytes: Monocytes are agranular and have a kidney bean shaped nucleus. These phagocytic cells defend the body against viruses and bacteria. Usually seen in **chronic inflammation** , when monocytes are turned to Macrophages	

Just more details about them..we have already studied them in other subjects so if you're familiar with it you can just read it and focus in the red color.

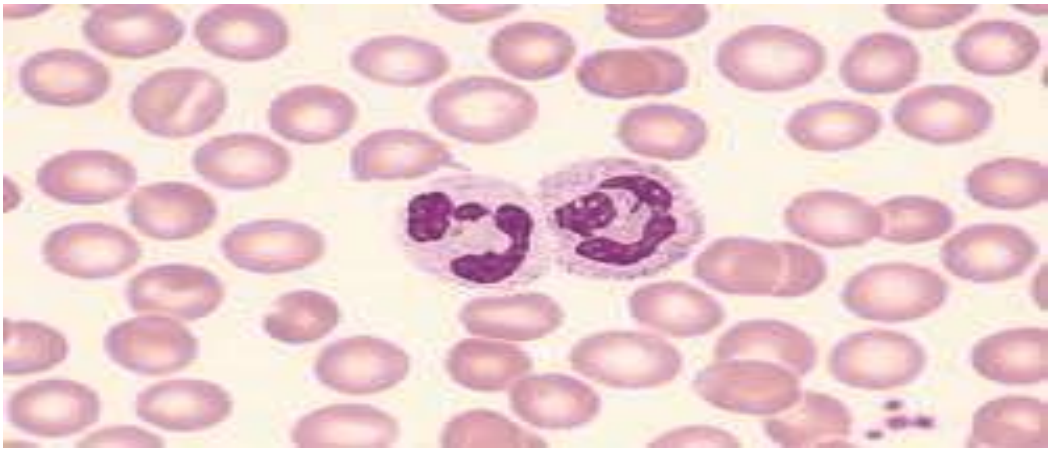
Neutrophils *(The superstar of Acute inflammation)*

- These cells are the most numerous leukocytes in the blood.
- They are also referred to as PMN's (Polymorphonucleated cells)

function	In bacterial inflammation
• Phagocyte foreign bodies • Secrete many enzymes most of them are oxidase & proteases (proteolytic enzymes) inside the lysosomes, they help in foreign body digestion	• The bone marrow in this station tries to synthesis more neutrophils via leukopoiesis in a short time • Some of the cells immature (due to rapid synthesizing), these immature cells (called band forms) means that the inflammation is fulminant "severe and sudden in onset" (there is left shift)

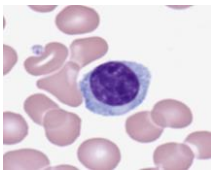
During ACUTE inflammation, neutrophils proliferate in huge amounts, and are the predominant leukocytes.

You can easily identify these cells because they contain multiple LOBES (فصوص) and are usually extensive in an inflammatory area



Lymphocytes

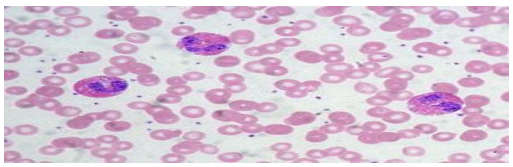
- Lymphocytes are mobilized in the onset of any specific immune stimulus (e.g. infections) as well as non–immune-mediated inflammation (e.g. due to ischemic necrosis or trauma).
- It is part of the adaptive immune system's response to infections and immunological diseases.
- B lymphocytes may develop into plasma cells, which secrete antibodies. (it is Humoral immunity)
- Lymphocytes migrate into inflammatory sites using similar adhesion molecule pairs and chemokines that recruit other leukocytes in the tissues.

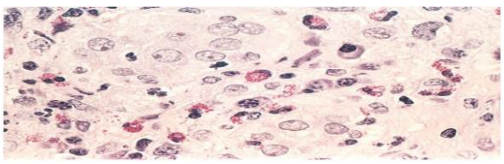


*Lymphocytes can be recognized easily, the nucleus is so huge that it covers more than 70% of the cell itself! اذا شفت خلية و النواة حقتها .. بسهولة **الليمفوسايت** تقدر تفرق مستولية على نصف المساحة فهي على طول **ليمفوسايت***

Eosinophils

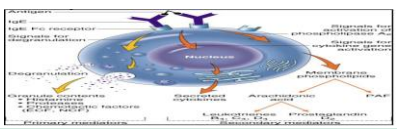
- Abundant in immune reactions mediated by igE in allergic reaction and in parasitic infections.
- Weak phagocytosis, it mostly has 2 lobes with acidophilic granules, they can release anti-histamine in the area of histamine release (increased in patients with: hypersensitivity infection and allergic reactions like bronchial asthma.)
- Can be seen in chronic and acute inflammation.
- Respond to chemotactic agents derived largely from mast cells.
- Granules contain major basic protein: toxic to parasites and lead to lysis of mammalian epithelial cells.
- Normal blood count: 1-2% , abnormal blood count: 20+% (tested from stool)





Mast cells

- Widely distributed in connective tissues and on their surface they express receptors that binds to the fc portion of igE antibody (plays an important role in type 1 allergic reactions), they are found in tissue and bone marrow.
- The cells degranulate and release mediators, such as histamine and serotonin and products of aa oxidation.

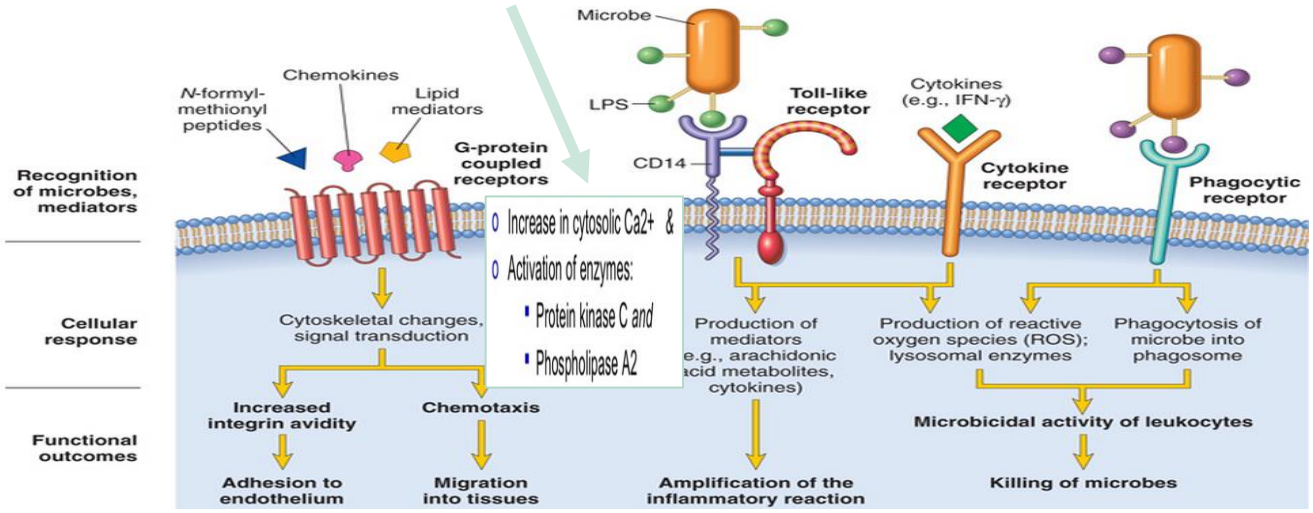


AA : Refers to Arachidonic acids .. Which are extremely important in inflammatory reactions. They are responsible for COX and Lipoxygenase reactions.

THE TYPE OF EMIGRATING LEUKOCYTE VARIES WITH THE TYPE OF STIMULUS:

The type of emigrating leukocyte varies	the type of stimulus
viral infections	lymphocytes may be the first cell to arrive
some hypersensitivity reactions and parasitic inflation	eosinophil may be the main cell type
Chronic inflammation	lymphocytes, plasma cell and macrophages are present

Lymphocyte transformation test



this is special for G protein - أهم شيء نعرفه receptor names

CELLULAR EVENTS

A critical function of inflammation is to deliver leukocytes to the site of injury

and to activate the leukocytes to perform their normal functions in host defense.*not enough to reach to the inflammation it must be activated form blood vessels to site of inflammation

WHAT ARE THESE FUNCTION?

Leukocytes ingest offending agents, kill bacteria and other microbes, and get rid of necrotic tissue and foreign substances.

But they **may induce tissue damage** and prolong inflammation, since the leukocyte products that destroy microbes and necrotic tissues can also injure normal host tissues. يعتبر سلاح ذو حدين، مجرد مايزيد اكثر من اللازم ممكن يأثر بشكل سلبي على الجسم.

Removal of the offending agent: we will explain each step during The lecture, so don't worry:)

Recognition of microbes by the receptors

Leukocyte Activation

- Increase in cytosolic Ca2+
- Activation of enzymes: -Protein kinase C - Phospholipase A2

Destruction of microbes

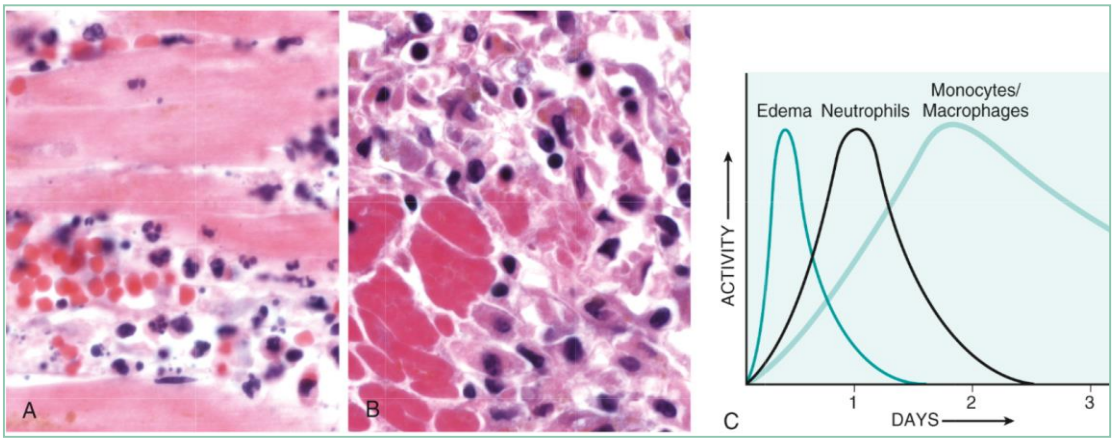
- Phagocytosis
- Intracellular killing

LEUKOCYTES ADHESION AND TRANSMIGRATION

The type of emigrating leukocyte varies with the age of the inflammatory response. In most forms of acute inflammation: neutrophils predominate in the inflammatory infiltrate during the first 6 to 24 hours, then are replaced by monocytes in 24 to 48 hours

Neutrophils = ready to defense (firs cell appear)- ماتعيش فترة طويلة

monocytes = their proteins not ready so it need more time to prepare the processing



WHY?

first day : edema

second day = neutrophils

monocytes = replace after the second day

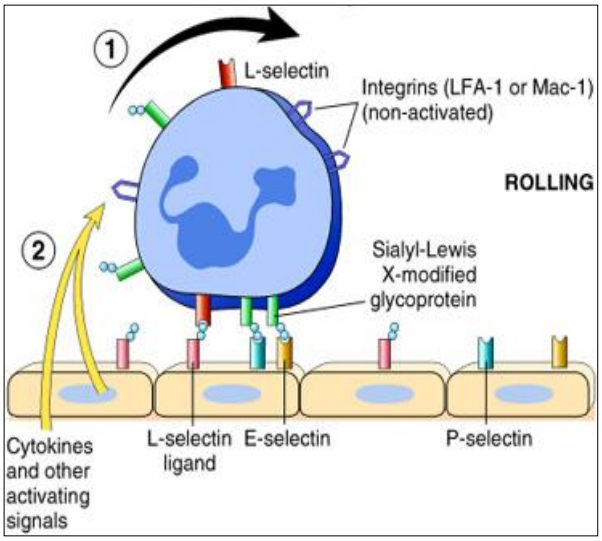
Leukocyte Adhesion Deficiency

LAD type 1	**deficiency** of β_2-integrin
LAD type 2	**mutations** in fucosyl transferase required for synthesis of sialylated oligosaccharide

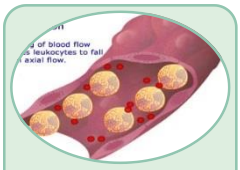
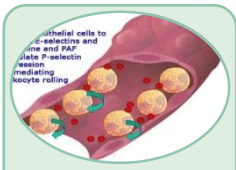
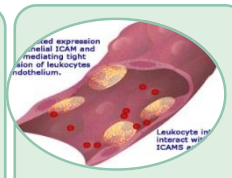
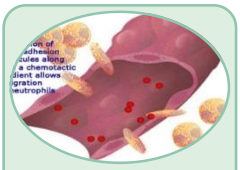
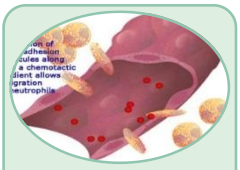
Clinical findings:

- Delayed separation of umbilical cord
- Increased circulating neutrophils (leukocytosis due to loss of the marginating pool)
- Recurrent bacterial infection that lack pus formation
- Poor wound healing

- E و p selictins الموجوده على الاندوثيليل راح تسوي رابطه ضعيفه مع silalyl-lewis x الموجود على سطح الليوكوسايت وبرضو inactive integrins راح تسوي روابط ضعيفه مع ICAM ولان الرابطه ضعيفه راح تنكسر بسرعه وهذا بيسوي لي (rolling) لليوكوسايت على سطح الاندوثيليل وبالتالي راح تقل سرعتها
- لما تتفعل inactive integins بسبب C5a & LTB4 راح تكون لي روابط قويه وبالتالي راح تلتصق الليكوسايت على الاندوثيليل



CELLULAR EVENTS "EXTRAVASATION"

Margination	rolling	Adhesion	Diapedesis (Transmigration)	Migrenation
				
WBC move from the center of the blood stream (as normal) to the side of the blood stream (peripheral) this makes them become closer to the vessel wall	WBC being rolling along the surface of the endothelium within the blood vessel *Leukocytes Rolling within a Venule	These cells will adhere to the endothelial cells because there are adhesion molecules called: *Integrin: they cover the outer surface of inflammatory cells. *Selectin: they cover the outer surface of endothelial cells.	When inflammatory cells through extension from their cytoplasm and go in between the gaps of endothelial cells to the outside of blood vessels (interstitial tissue) by incease vascular premaebility *it occurs predominantly in the postcapillary venules	- Cells move to the site of injury. - They are directed through chemotaxis - All types of WBC use the same pathway to migrate from blood to tissue **Chemotaxis:** is a guided margination of inflammatory cells from the blood vessels to the site of inflammation. **Phagocytosis:** When the inflammatory cell phagocytose (eat) the invader or the infected cell and digest it.

Margination, **rolling** & **Adhesion** in the lumin – **Transmigration** across the endothelium - **Migration** in interstitial tissues

Chemoattractant

Exogenous agents are bacterial products.

Endogenous chemoattractants include several chemical mediators:

components of the complement system, particularly C5a

products of the lipoxygenase pathway, mainly leukotriene B_4 (LTB_4)

cytokines, particularly those of the chemokine family (e.g., IL-8).

Phagocytosis

1. Recognition and attachment of the particle to be ingested by the leukocyte
2. Its engulfment, with subsequent formation of a phagocytic vacuole
3. Killing or Degradation of the ingested material.

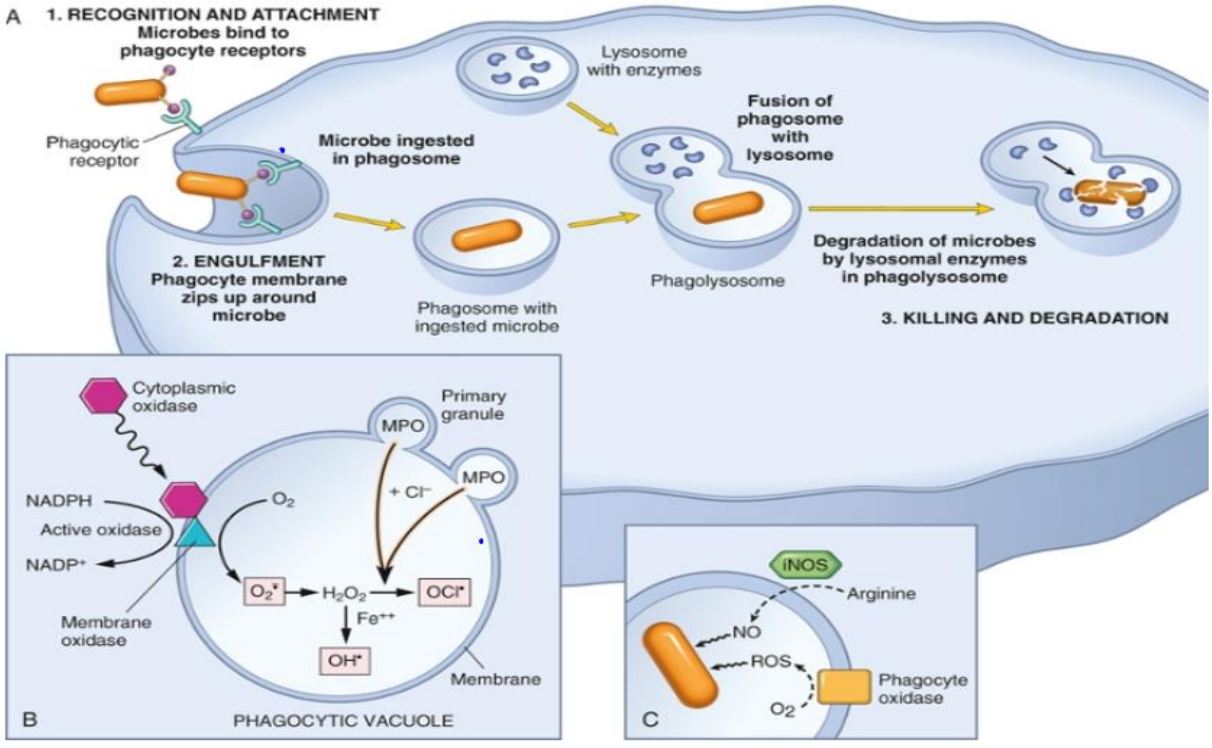
During engulfment, extensions of the cytoplasm (pseudopods) flow around the particle to be engulfed, eventually resulting in complete enclosure of the particle within a **phagosome**

The phagocytic vacuole then fuses with a lysosomal granule, resulting in **phagolysosome**

PHAGOCYTOSIS
KILLING AND DEGRADATION

2. Oxygen-independent mechanisms

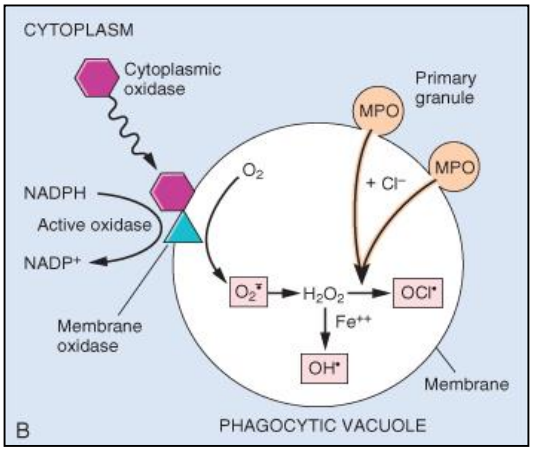
1. Oxygen-dependent mechanisms (more strong)



Oxidase enzyme cover oxygen to oxygen super radical by taking one electron which is very strong so will convert to h2o2 مادة معقمةbut not strong - after that the mpo which is inside the phagolysosomes will attach with h2o2 to give us ocl hypochlorite once it is form will destroy the bacterial membrane and kill it

1. Oxygen-Dependent Mechanisms

The H_2O_2-MPO-halide system is the most efficient bactericidal system in neutrophils



2. Oxygen-independent mechanisms

- through the action of substances in leukocyte granules. These include:
  - *Bactericidal permeability increasing protein* (BPI)
  - *Lysozyme*
  - *Lactoferrin*
  - *Major basic protein*
  - *Defensins*

- Neutrophil granules contain other *enzymes*, such as elastase, that also contribute to microbial killing

• Can potentiate further inflammation by damaging tissues
•These harmful proteases are controlled by a system of *anti-proteases* in the serum

	CHRONIC GRANULOMATOUS DISEASE	MYELOPEROXIDASE DEFICIENCY
Inheritance pattern	X-linked recessive	Autosomal recessive
NADPH oxidase	Absent	Present
Myeloperoxidase	Present	Absent
Respiratory burst	Absent	Present
Peroxide (H_2O_2)	Absent	Present
Bleach (HOCl)	Absent	Absent

Comparison of Chronic Granulomatous Disease and Myeloperoxidase Deficiency

Defects in Leukocyte Function

- Defects in leukocyte **function**, both **genetic and acquired**, lead to increased vulnerability to infections:

- **Defects in leukocyte adhesion.**
- **Defects in phagolysosome function.**
- **Defects in microbicidal activity.**

1) Genetic:

- **Defects in Adhesion**: Leukocyte adhesion deficiency type 1 and 2.
- **Defects in Phagocytosis**: Chédiak-Higashi syndrome. (Protein involved in organelle membrane fusion)
  - Protein trafficking defect (microtubule defect)
  - Autosomal recessive

Clinical feature:

- Increased risk of pyogenic infection
- Neutropenia (defect in generation from BM)
- Giant granule formation (granules formed cannot move in cytoplasm)
- Defective primary hemostasis (platelet granule are not secreted)
- Albinism
- Peripheral neuropathy

- Defects in Microbicidal Activity: Chronic granulomatous disease. (Decreased oxidative burst).

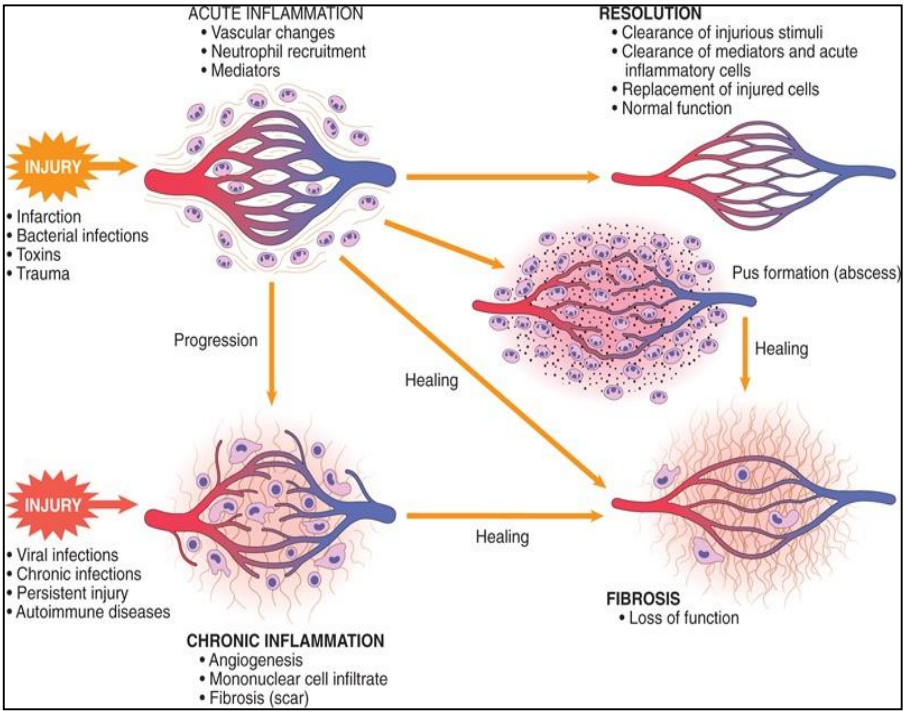
2) Acquired:

- **Chemotaxis**: Thermal injury, diabetes, malignancy, sepsis, immunodeficiencies.
- **Adhesion**: Hemodialysis, diabetes mellitus.
- **Phagocytosis and microbicidal activity:** Leukemia, anemia, sepsis, diabetes, neonates, malnutrition.

hemodialysis:
تنقية الدم لدى الأشخاص المصابين بالفشل الكلوي عن طريق الأجهزة

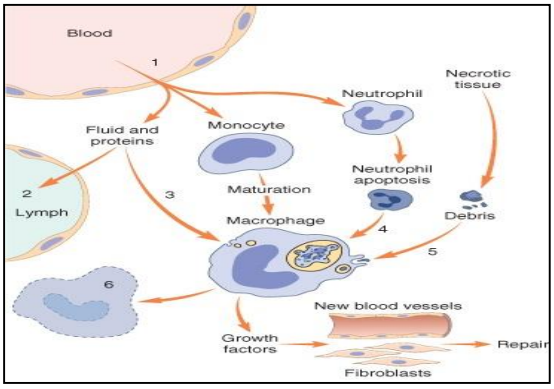
OUTCOMES OF ACUTE INFLAMMATION.

- Complete resolution
- Healing by connective tissue replacement (fibrosis)
- Progression of the tissue response to chronic inflammation
- Abscess formation



Events in the resolution of inflammation : how resolution happens? Basically every thing goes back to its normal state.

1. This involves **neutralization**, decay, or enzymatic degradation of the various chemical mediators
2. Normalization of vascular permeability
3. Cessation of leukocyte emigration and apoptosis
4. The necrotic debris, edema fluid, and inflammatory cells are cleared by phagocytes and lymphatic drainage



- The types of inflammation vary in their morphology and clinical correlates, **why**? **(depending on:)**
- **The severity of the reaction**
- **specific cause**
- **the particular tissue**
- **site involved**

MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION :

Serious Inflammation

Fibrinous Inflammation

Suppurative/ Purulent Inflammation

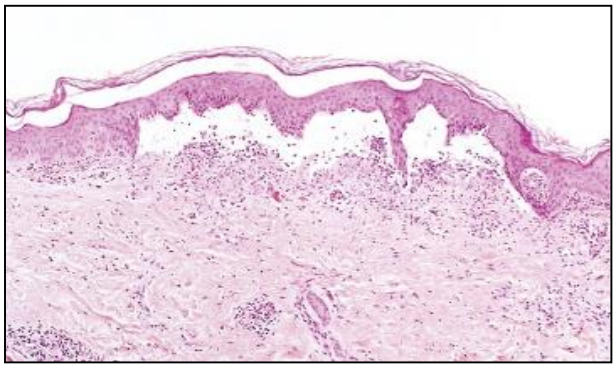
Ulcers

PATTERNS OF ACUTE INFLAMMATION

1) <u>Serous Inflammation:</u> characterized by the outpouring of a **watery,** relatively **protein-poor fluid**. derived either from the **plasma**, or from the secretions of **mesothelial cells** lining the **p**eritoneal, **p**leural, and **p**ericardial cavities. Fluid in a serous cavity is called an **effusion**.

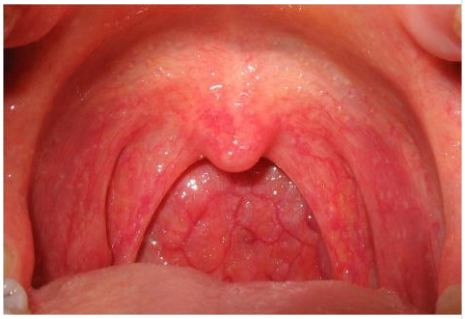
Example: The skin blister (resulting from a burn), or viral infection (having cold)

- Burn makes injury in the endothelium of the vessels so we lose a lot of fluid
- It is marked by a large amount of fluid under the epidermis and lack of cells especially neutrophils because of the burn



2) <u>Catarrhal inflammation</u>: Inflammation affects **mucosa-lined** surfaces with the outpouring of **watery mucus**

Example: Common cold.



PATTERNS OF ACUTE INFLAMMATION

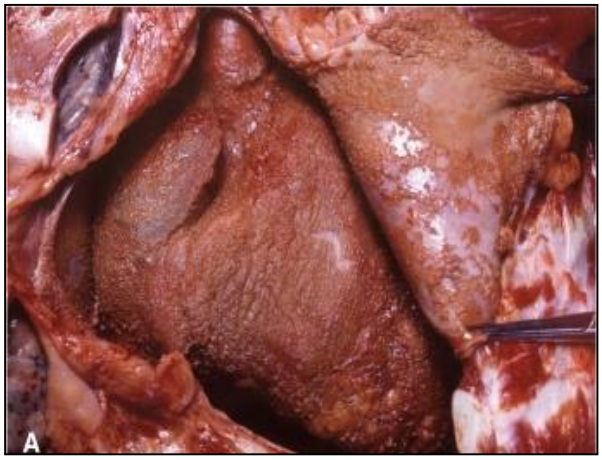
3) Fibrinous Inflammation: A fibrinous exudate is characteristic of inflammation in the lining of body cavities, such as the **meninges**, **pericardium** and **pleura** (larger molecules such as fibrinogen pass the vascular barrier).

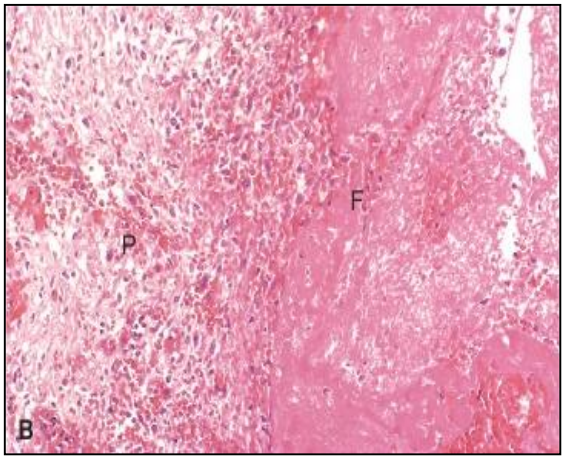
- Fibrinous exudates may be removed by fibrinolysis, **if not:** it may stimulate the ingrowth of granulation tissue *(organization)*

- It is a consequence of more **(repeated) severe injuries**, this result in an **increase vascular permeability** that allows large molecules (i.e. Fibrinogen) to pass the endothelial barrier.

Note: greater vascular permeability → Exudate feature → indicates inflammation.

Note: come back to this after reading the vascular events..





PATTERNS OF ACUTE INFLAMMATION

4) 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 bacteria**.

Dr alrekabi's note : What does pus contain?

1. **Bacteria**.
2. **Fibrin** (end result of the coagulation cascade).
3. **Inflammatory cells** (neutrophils).

Pyogenic bacteria: Bacteria that produces lots of pus.

Examples: (Staphylococcus aureus and streptococci)

5) Suppurative abscess:

Abscess: are focal **collections of bus** that may be caused by seeding of pyogenic organism into a tissue or by a secondary infections of necrotic Foci. It's typically a bus within a cavity.

So abscess is **a cavity lined by granulation tissue** and containing neutrophils, necrotic cells, bacteria and fibrinous material. It is an **enclosed collection of pus** consists of a mixture of neutrophils and necrotic debris.

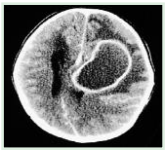
*When we have **only neutrophils without cavity** we call it suppurative inflammation or purulent inflammation.

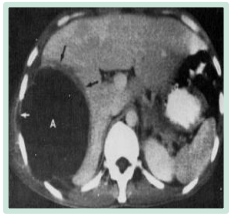
but when we have a cavity filled with necrotic material and pus and neutrophils or bacteria or amoeba this called abscesses.

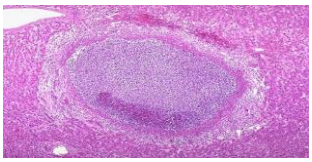
MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION
SUPPURATIVE OR PURULENT INFLAMMATION

Abscesses:

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

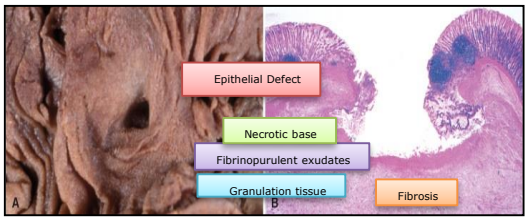






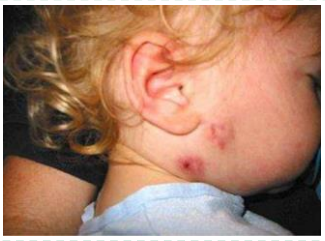
Ulcer:

A local defect of the surface of an organ or tissue that is produced by the sloughing (shedding) of inflammatory necrotic tissue . Note: ulcers have acute and chronic inflammation at the same time; they coexist. An ulcer is a focal loss of the mucosal layer in a part of the GIT (Gastrointestinal Tract), usually in the duodenum or stomach.

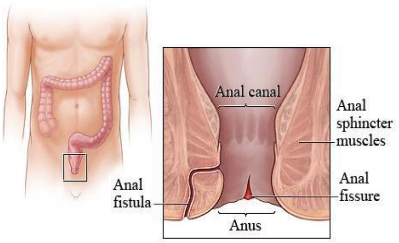


Sinus:

inflammatory tract with **one opening** (pilonidal sinus in the lower back). It contains pus + ingrown hairs (foreign body) chronic inflammatory reaction (very common)

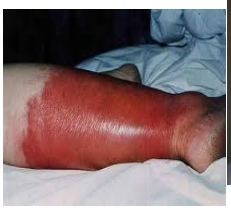


Fistula: ناسور شرجي chronic inflammatory tract that has **two openings** between two various epithelia (usually starts from the colon and open in the skin (حكة وافرازات تلوث الم بس) (common but nonspecific)



Cellulitis:

Denotes a spreading acute inflammation through interstitial tissues.



Pseudomembranous colitis: an inflammation that doesn't produce pus or abscess. occurs in some people who have taken antibiotics. It is most often seen in people who are in the hospital.

CHRONIC INFLAMMATION :

- It is **slow** evolving (weeks to months) resulting into **fibrosis**
- The **essential changes are (features of chronic inflammation):**

1. Absence of polymorphs (natural life span of 1–3 days); replaced by **macrophages, lymphocytes and often plasma cells**
2. Continuous tissue injury and necrosis
3. Proliferation of vascular endothelium by 'budding' – formation of new capillaries **(angiogenesis)**
4. Proliferation of **fibroblasts** with collagen production leading to **Fibrosis**.

Important notes:

- Some diseases, such as hepatitis B&C, & tuberculosis (TB), start as chronic. There is no acute
- Staphylococcus aureus bacteria is always associated with acute inflammation.
- Viral hepatitis B & mycobacterium TB are always-chronic.
- Etiological factors determine whether it is **acute or chronic.**

Angiogenesis: formation of new vessels caused by sprouting, old blood vessels **produce new ones.** This can be seen in connective tissue to increase the blood supply and help in the healing process and they are mediated by some chemical mediators (vascular proliferation factor / vascular derived proliferation factor) (VPF/VDPF).

Fibrosis: increase in extracellular **matrix** (ECM) → formed of **collagen** and may have proteoglycan but the most important is the collagen (**Connective Tissue).**

Amyloid: It is a protein secreted by the **liver**. It is secreted in large amounts when there is **chronic inflammation**. It accumulates in the blood vessels, and kidneys causing problems it's not seen in acute Inflammation. Note that this process requires long periods of time.

	Acute Inflammation	Chronic Inflammation
Duration	Days to weeks	Months to years
Inflammatory Cells	Neutrophils	Lymphocytes & plasma cells.

Note: Eosinophils are found with allergies or parasitic infections, and macrophages are found in both acute and chronic, but are increased at the end of acute inflammation.

An important point: Although the presence of neutrophils is the hallmark of acute inflammation, many forms of chronic inflammation may continue to show extensive neutrophilic infiltrates, as a result of either persistent microbes or necrotic cells, or mediators elaborated by macrophages.

Causes of chronic inflammation:

Persistent infections by microbes that are difficult to eradicate.

- e.g.
  - Mycobacterium tuberculosis
  - Treponema pallidum (the causative organism of syphilis)
  - certain viruses and fungi (ex: hepatitis C\B)
- Persistent infections elicit a T lymphocyte-mediated immune response called delayed-type hypersensitivity.

. Immune-mediated inflammatory diseases (hypersensitivity diseases- Autoimmune diseases)

- e.g.
  - Rheumatoid arthritis
  - inflammatory bowel disease *جميع الالتهابات التي تصيب الجهاز الهضمي منها القولون
  - psoriasis * الصدفية
- Or Immune responses against common environmental substances that cause allergic diseases, such as bronchial asthma. *example ; have allergy against certain food,cat,dog

Prolonged exposure to potentially toxic agents.

- Examples are nondegradable exogenous materials such as inhaled particulate silica, which can induce a chronic inflammatory response in the lungs (silicosis)
- Endogenous agents such as cholesterol crystals, which may contribute to atherosclerosis

4. Mild forms of chronic inflammation may be important in the pathogenetsis of many diseases

e.g.:

- neurodegenerative disorders such as Alzheimer disease
- atherosclerosis
- metabolic syndrome and the associated type 2 diabetes,
- and some forms of cancer in which inflammatory reactions promote tumor development

Chronic inflammation is characterized by 3 different set of reactions:

1. **Infiltration with mononuclear cells**, including:
   - Macrophages
   - Lymvphocytes
   - Plasma cells
2. **Tissue destruction**, largely induced by the products of the inflammatory cells
3. **Repair**, involving new vessel proliferation (angiogenesis) and fibrosis

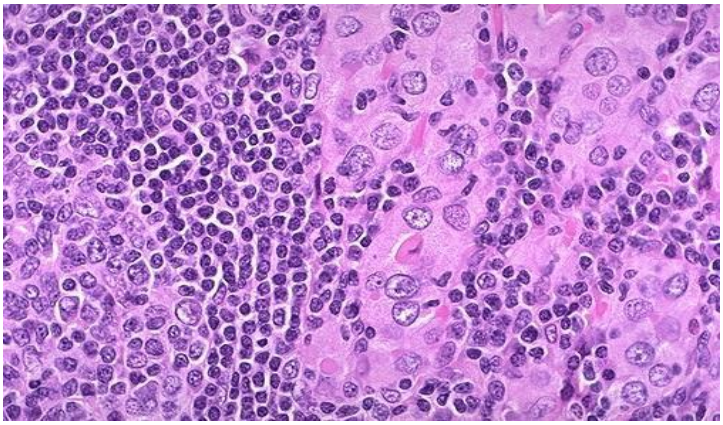
Chronic inflammation patterns

- **Chronic non specific inflammation**

Features chronic inflammation, e.g:

-Foreign material, e.g. silicates, including asbestos.

-Auto-immune diseases, e.g. auto-immune thyroiditis.

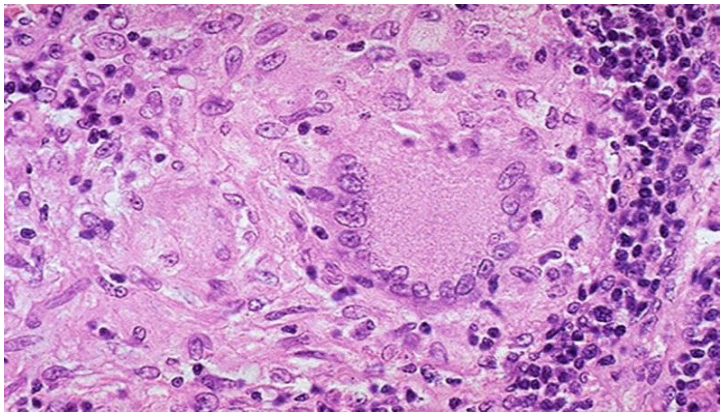


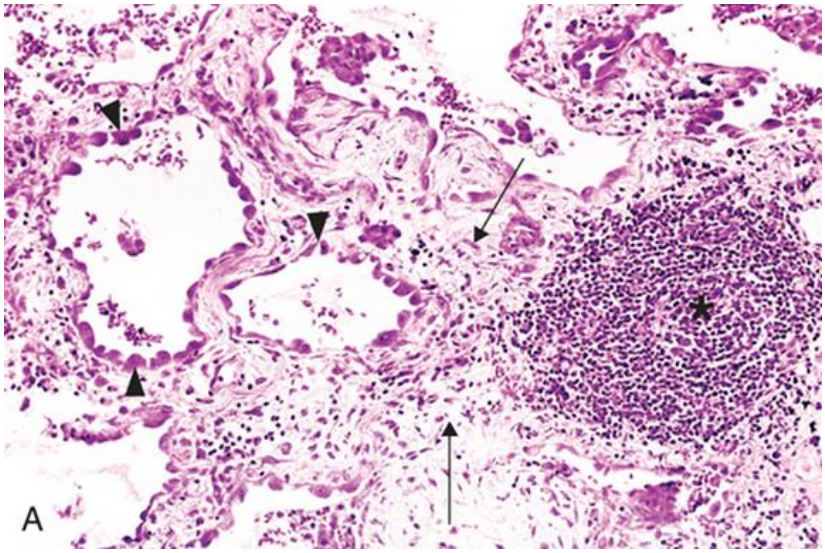
- **Chronic granulomatous Inflammation**

Chronic inflammation in which modified macrophages (epithelioid cells) accumulate in small clusters surrounded by lymphocytes.

The small clusters are called: Granulomas

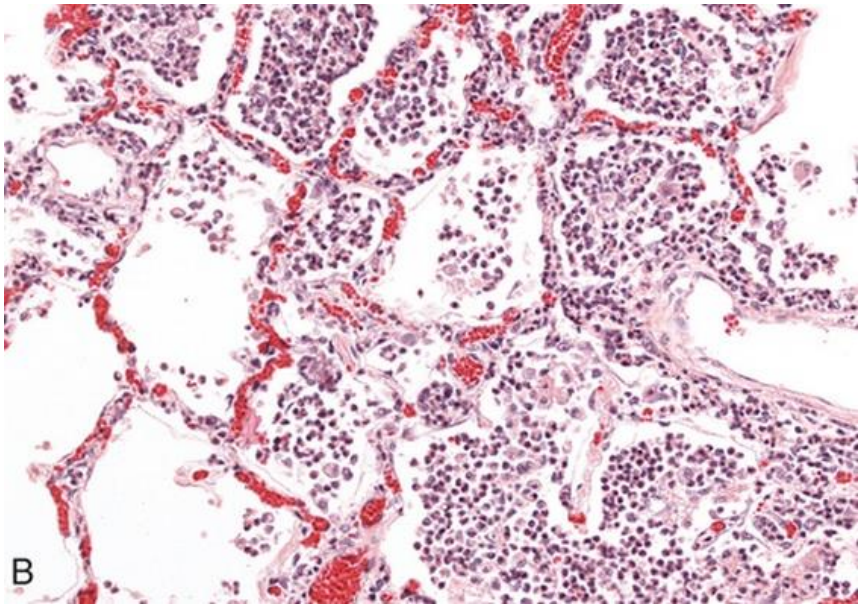
e.g. **Tuberculosis**





Lung chronic inflammation

Lung acute inflammation



CHEMICAL MEDIATORS OF INFLAMMATION

- **Chemical meditators are:**

A- responsible for the vascular and cellular events in acute inflammation.
B- substances produced during inflammation inducing a specific events in acute inflammation

طريقة عمل الأدوية المضادة للالتهاب تعمل أساساً على تثبيط
chemical mediator

- Meditators may be produced locally by cells at the site of inflammation, or maybe derived from inactive circulating precursors.

So these chemicals were circulating in the blood plasma (produced by the liver) and when they reach the site of inflammation, they become active.

- e.g.: complement system & kinin system.

- **General principles for chemical mediators**

➢ Production of active mediators is triggered by:
1. Microbial products
2. Host proteins **e.g proteins of complement, kinin and coagulation systems** (these are themselves activated by microbes and damaged tissues)

➢ Mediator function is tightly regulated by:
1. decay **(e.g. AA metabolites)**
2. inactivated by enzymes **(kininase inactivates bradykinin)**
3. eliminated antioxidants scavenge toxic oxygen metabolites

Most mediators have the potential to cause harmful effects.
Therefore, there should be a mechanism to checks and balances their action. (regulator)

Source of chemical mediators

Cell-derived:

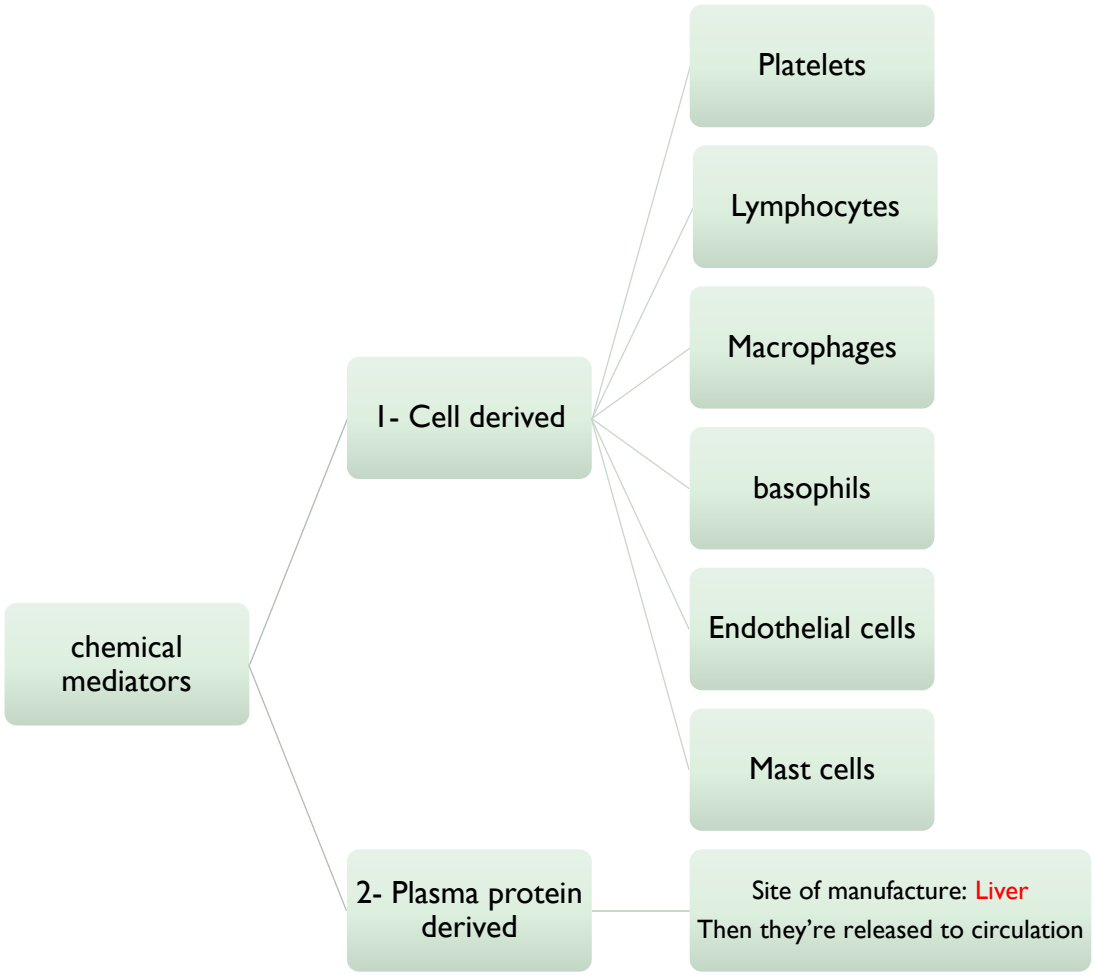
1. Synthesized as needed (prostaglandin)

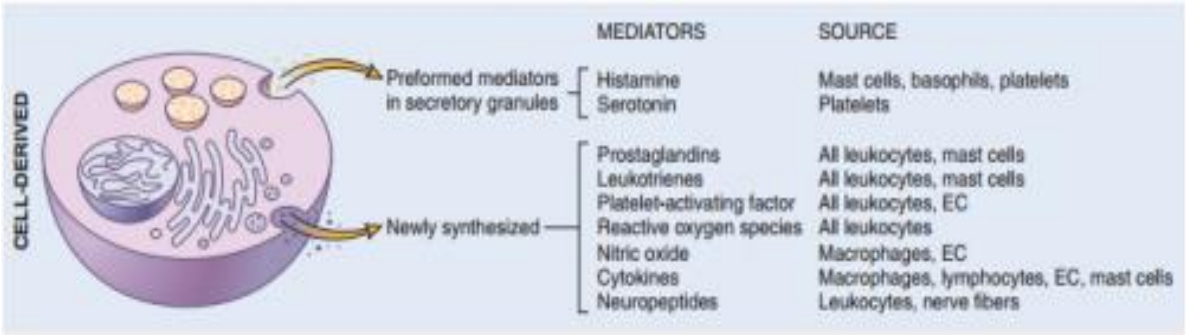
2. Preformed, sequestered and released (mast cell histamine)

Plasma-derived:

1. Complement
2. kinins
3. coagulation factors

Many in "pro-form" requiring activation (enzymatic cleavage)





1- Cell derived:

Histamine

Secreted by many cell types esp:

1. *Mast cells:* (It's a type of inflammatory cells that is found only in the tissue and it has granules which contain histamine and serotonin).
2. *Circulating Basophils*: (Basophils are found in peripheral blood. They usually have multiple granules. And its nuclei has more than one lobe).
3. *Platelets.*

Histamine causes:

- Arteriolar Dilation. (vasodilation)
- Increase vascular permeability (venular gaps).
- Endothelial activation.

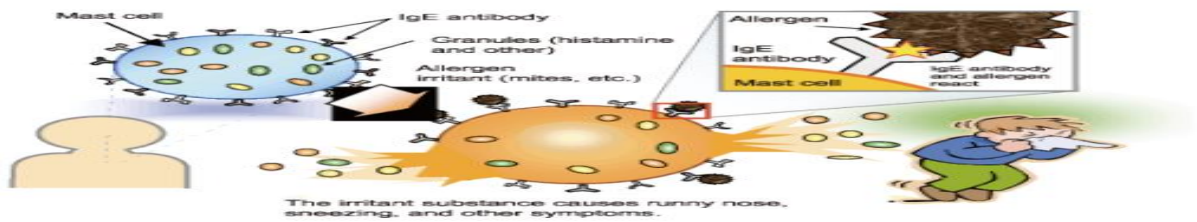
Stimuli of Release:

- Physical injury (trauma or heat)
- Immune reactions
- C3a and C5a fragments
- Cytokines (e.g. IL-1 and IL-8)
- Neuropeptides

Release of Histamine:

- Location: locally
- Duration: few seconds
- **When**? the antigen bind to Fc receptor which is on the surface of mast cell
- **How**? When there is a **physical injury**, such as trauma or heat, immune reactions involving binding of **IgE antibodies** to their receptors on **mast cells**. After this binding, mast cells will release histamine from its granules.

When a bee stings you, its antigen will cause a *hypersensitivity reaction* in the body.
This will lead to increased production of IgE, which will bind to mast cells to produce *histamine*.
This explains how the bee sting leads to the production of all these effects on the body.



Serotonin (5 hydroxytryptamine) (5HT)

- Secreted by **platelets**.
- Serotonin causes: **vasoconstriction**. (Similar to Histamine)
- Stimulus: Platelet aggregation

-serotonin comes from metabolized amino acid called tryptophan.
-Platelets play a major role in blood Coagulation.
So serotonin is secreted by the platelets to cause vasoconstriction.

Histamine and Serotonin

- Among first mediators in acute inflammatory reactions
- Preformed mediators in secretory granules

Platelet activating factor (PAF)

- **Secreted by:**

1 - mast cell
2-basophils
3-neutrophils
4-monocytes/macrophages
5-platelets **(leukocytes)**
6- endothelial cells

- **PAF causes:**

1 - in crease vascular permeability
2 - leukocyte adhesion
3 – chemotaxis/leukocyte priming
4 - degranulation and oxidative burst
5-Leukocyte aggregation
6-Platelet activation
7-Stimtulation of other mediators (LT,O2)
8-vasodilation

Reactive oxygen species (free radical) – ROS

- **Secreted** by: Neutrophils and Macrophages (leukocytekocytes).
- **Synthesized** via: NADPH oxidase pathway
- **Stimuli** of release:

-Microbes

-Immune complexes

-Cytokines

- **Action**:

Microbicidial (cytotoxic) agent (cauuses damage of tissue and killing of microbes).

Note: in leukocytes there are different oxidative enzymes lead to formation of ROS.
ROS are not stable and have to go into reactions and these reactions damage the cell.

Recall :ROS types:
1 - Hydroxyl group (OH).
2 - Superoxide (O_2-).
3 - Hydrogen peroxide (H_2O_2)

NITRIC OXIDE (NO)

- Short-lived
- Soluble free-radical gas

Nitric oxide causes:

1 - **vasodilation**: it relaxes the smooth muscles of the blood vessels.

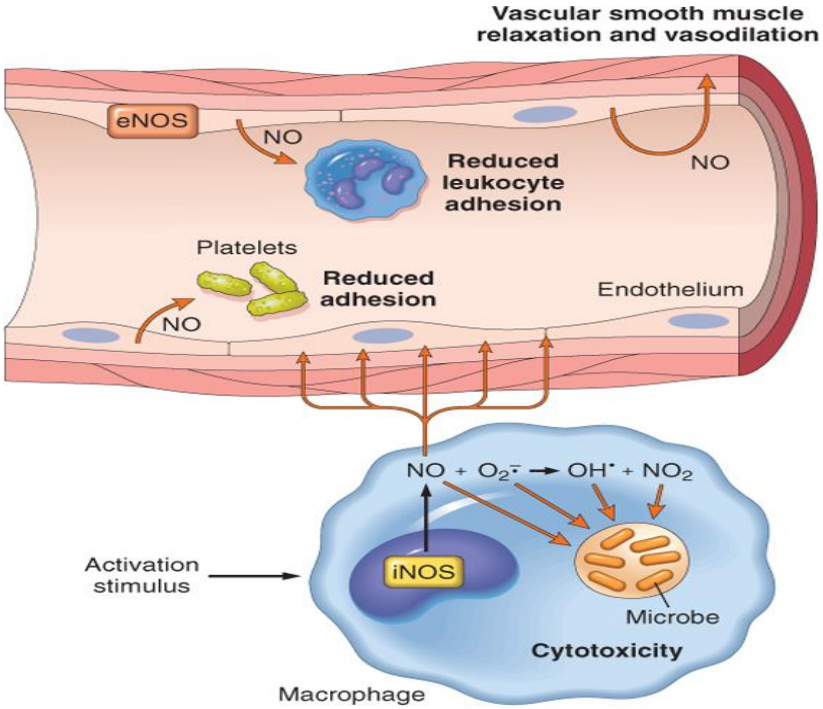
2 - **killing of microbes** (Reduction of leukocyte recruitment Microbicidial (cytotoxic) agent (with or without ROS) in activated macrophages)

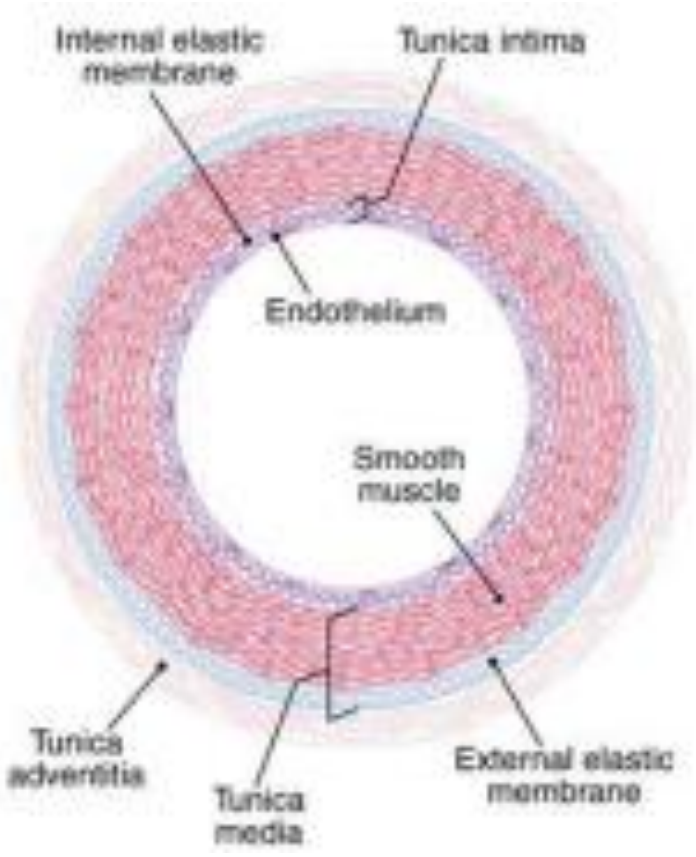
3- **Antagonism** of platelet activation (adhesion, aggregation, & degranulation)

Secreted by:

1 - endothelial cells (also called endothelium)
2 - macrophages

Note: The structure of blood vessels:
"Inside the vessel" Endothelial cells → basement membrane → smooth muscles → serosa (adventitia) **"Outside"**





Numbers show function of nitric oxide

CYTOKINES

• **Cytokines**: Polypeptide products of many cell types that function as mediators of inflammation and immune responses and they carry signals to neighboring cells. They have roles in **acute and chronic inflammation**, and some stimulate bone marrow precursors to produce more leukocytes.

•Cytokines has different elements such as : **Tumor Necrosis Factor (TNF)** and **Interleukin**.

•Secreted by:

1. Macrophages
2. Endothelial cells
3. Mast cell
4. Lymphocyte

•Cytokines in **acute** inflammation: TNF, IL-1, and IL-6.

•Cytokines in **chronic** inflammation: IL-12 and Interferon-γ (INF- γ)

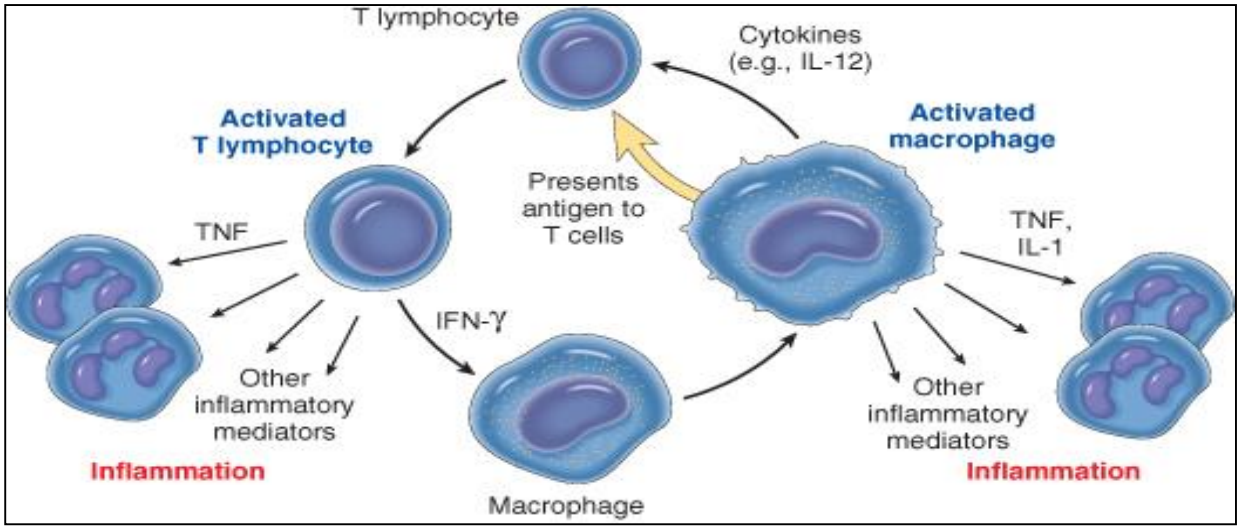
•**TNF and IL-1** cause:

1 - local: stimulate the expression of adhesion molecules on endothelial cells (endothelial activation).

2 - Systemic: fever, metabolic abnormalities and shock (hypothesen).

•Most of modern anti inflammation and immunity diseases drugs are anti TNF.

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



CHEMOKINES

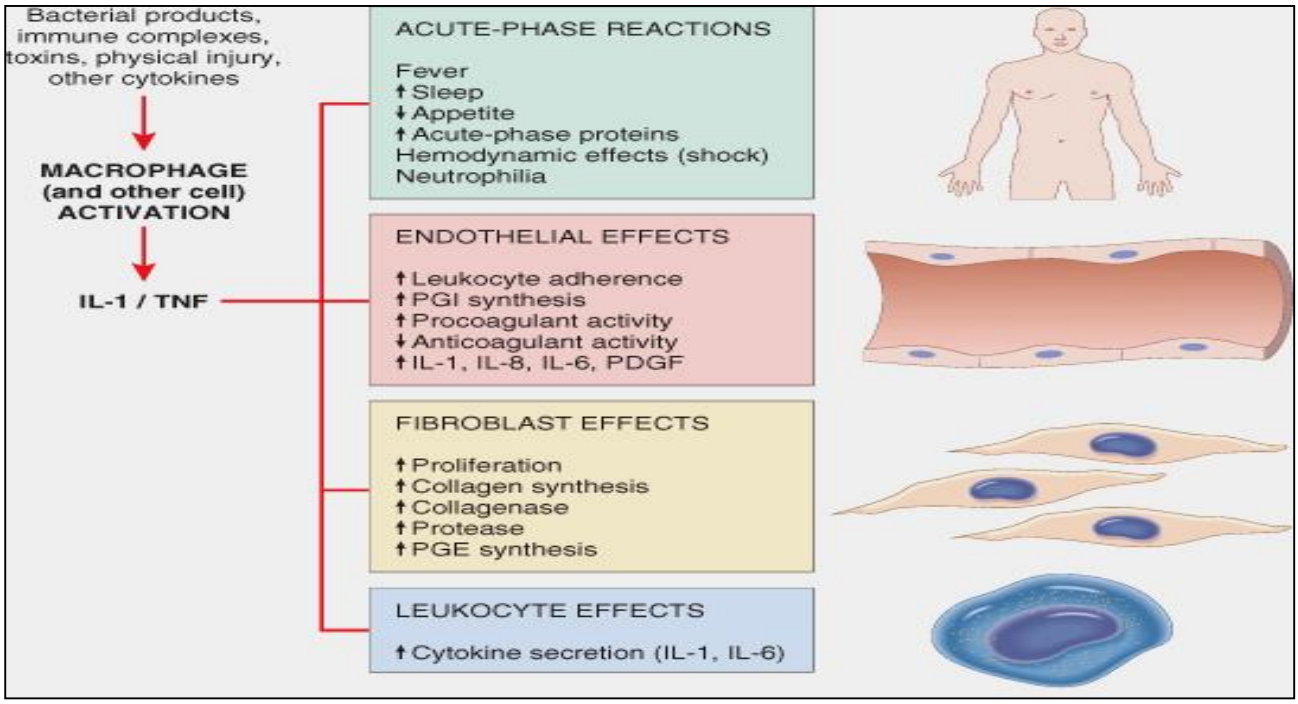
- **Chemokines**: Small proteins of any of a class of cytokines with functions that include attracting leukocytes to sites of infection (chemotaxis). They are chemoattractant for leukocytes.

- Secreted by:

1. Leukocytes
2. Activated macrophages

- Chemokines main functions:

1. Chemotaxis
2. Recruitment and activation of leukocytes
3. Normal anatomic organization of cells in lymphoid and other tissues



ARACHIDONIC ACID METABOLITES (EICOSANOIDS)

- Product derived from **arachidonic acid (AA)** effect a variety of biological processes, including **Inflammation and hemostasis**.
- It's also called **eicosanoids**. Because they're derived from 20 carbon fatty acids. The Greek word eicosanoids means twenty. بإختصار الاراكودونيك عباره عن مكونات مشتقة من البلازما ممبرين من ٢٠ فآتي أسد، تستخدم هذه المكونات لوظائف مختلفة
  - Arachidonic acid derived from the cell membrane phospholipids by the enzyme **phospholipase**.
  - Leukocytes, endothelial cells, platelets, and mast cell are the major sources of AA. يعني هذه يا الخلا

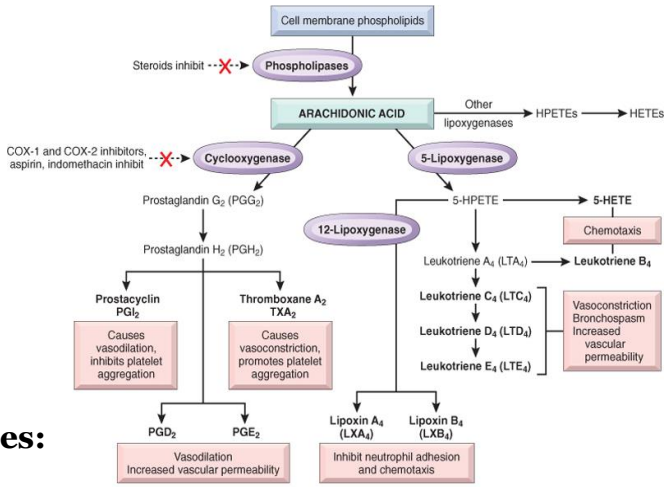
تصنع الاراكادونك من السيل ممبرين حقها عند حاجتها له.

We have two pathways of arachidonic acid:

1) **Cyclooxygenase enzyme,** pathway: which produces ***prostaglandins***.

2) **Lipoxygenase enzyme**, pathway: which produces ***lukotrience, chemokines, lipoxin*.**

*everything in this picture is very important! **Especially the products and their functions.**



Improrant notes:

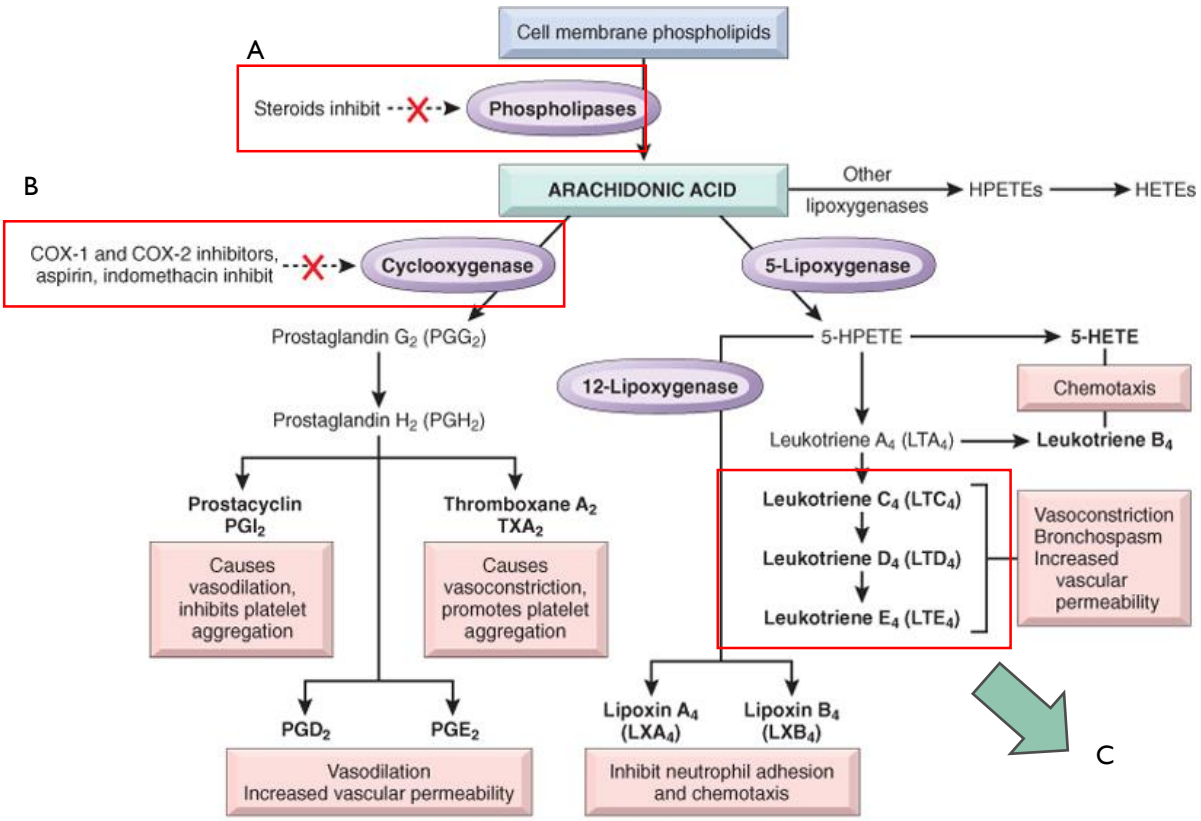
Some of these enzymes have a **restricted tissue distribution**. For example:

1)platelets contains the enzyme thromboxane synthase, because it needs it for platelets aggregation and vasoconstriction for the blood vessels during injuries.

2) Endothelial cells in the other hand lack thromboxane synthase. But has prostacyclin synthase. So it could prevent clotting during normal state without injuries.

Lipoxins: once leukocytes enter tissues, the gradually change their major lipoxygenase derived AA products, to **Anti-inflammatory** mediators called **lipoxins**. Which inhabit neutrophils chemotaxis and adhesion.

From Robbins ☺



A. When we have severe **anaphylactic shock,** we give **steroids** to inhibit the phospholipase pathway to reduce vascular permeability & edema.

B. Here we use **NSAIDs** (Non-steroidal anti-inflammatory drugs) to inhibit **Cyclooxygenase**

C. These factors are affected in bronchial asthma so when the doctor gives medication for patients who suffer from asthma, it will inhibit these factors.

So if I want to stop the inflammation in the patient, I can inhibit the **phospholipase** and make it stop producing arachidonic acid by using **steroids**.

ARACHIDONIC ACID METABOLITES (EICOSANOIDS)

Prostaglandins

- Secreted by:

1 – Mast cells
2 – Leukocytes
3- Endothelial cells
4- Platelets

- Prostaglandins causes:

1 - Pain
2 - Vasodilation
3 – Fever

Prostaglandins are very important because a lot of anti inflammatory drugs, such as antipyretics and analgesics work on blocking prostaglandins (anti-prostaglandins).

Phospholipid →**(via phospholipases)** arachidonic acid → **(via cyclooxygenases) prostaglandins.**

Leukotrienes

- **Secreted by**:

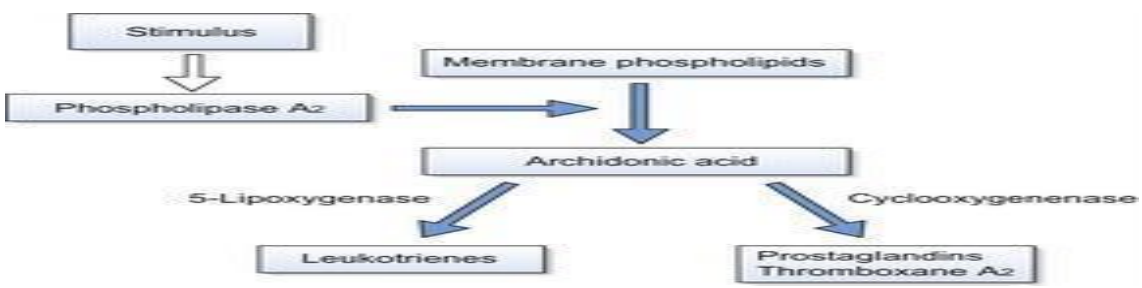
1 – Mast cells
2 – Leukocytes

- **Leukotriene causes:**

1 - increase vascular permeability
2 - chemotaxis
3 - leukocyte adhesion and activation

- Leukotriene **B4** induced chemotaxis.
- Leukotriene C4 , D4 and E4 increase vascular permeability and active leukocytes.

phospholipid → (via phospholipase) arachidonic acid → (via 5-lipoxygenase) leukotriene



ARACHIDONIC ACID METABOLITES (EICOSANOIDS)

Action	Eicosanoid
Vasodilation	Prostaglandins PGI_2 (prostacyclin) PGE_1 PGE_2 PGD_2
Vasoconstriction	Thromboxane A_2 (TXA2) Leukotrienes C_4, D_4, E_4
Increased vascular permeability	Leukotrienes C_4, D_4, E_4 PGD_2, PGE_2
Chemotaxis, leukocyte adhesion	Leukotriene B_4
Inhibit chemotaxis and leukocyte adhesion	Lipoxin A_4 and B_4
Smooth muscle contraction	Prostaglandins PGC_4, PGD_4, PGE_4
Promote platelet aggregation	Thromboxane A_2 (TXA_2)
Inhibit platelet aggregation	Prostacyclin (PGI_2)
Bronchospasm	Leukotrienes C_4, D_4, E_4

*To help you memorize: TXA_2 and PGI_2 have opposite functions.

PLASMA PROTEIN DERIVED MEDIATORS:

- **Complement system**:
- The complement system ,which is consisted of a group of plasma proteins, is synthesized by the liver and is found in the plasma.
- **The complement system is made from 20 proteins.**

- **- The complement system can be activated by :**

Classical pathway	Alternative pathway	Mannose-binding lectin (MBL) pathway
• Activated by Immune Complexes that contain antibodies bound to an antigen.	• Microbial products directly activate complement system.	• MBL binds to mannose on microorganisms and activates the complement system.

- ● be careful, the classical pathway requires antibody to activate the pathway, but the alternative pathway does not require antibodies for its activation.

- **What is the difference between plasma and serum?**
- They are the same; but plasma has coagulation factors and serum has no coagulation factors (they were used).

- - Immunology talks about the complement system in detail, but **what is important in pathology and inflammation?**
-

1. C3a and C5a (anaphylatoxins) —Stimulate mast cell release of histamine → inflammation.
2. C5a —Leukocyte chemotactic factor.
3. C3b —It is an opsonin, it prepares the microorganism for phagocytosis. It will coat the antigen and prepare it for phagocytosis.
4. C5b-C9 (Membrane Attack Complex [MAC]) —Cell lysis.

PLASMA PROTEIN DERIVED MEDIATORS:

- **MAC ((C5b-9)):**

is a part of the complement system. It will work on the cell membrane of the microorganism and cause their lysis. It can kill the bacteria. It may also cause cell injury.

- **Opsonins**

enhance recognition, attachment and phagocytosis of bacteria. • Important opsonins include immunoglobulins (Fc portion of IgG), complement system product (C3b), and plasma proteins such as **collectins** (which bind to bacterial cell walls).

• When immunoglobulins coat the bacteria or antigen they make them amenable

- **What area phagocytic cells?**

1. Macrophages (**histiocytes**). Histiocytes is less active in phagocytosis, but other than that they are the same.
2. Neutrophils.
3. Eosinophil (weakly phagocytic).

In some diseases we check the blood for complement system protein. If they were **low**, this means that they have been used, and this means that I am dealing with an inflammatory process or **inflammation**.

If it was **normal** it means that immunological system is not active and I am not dealing with an inflammatory process.

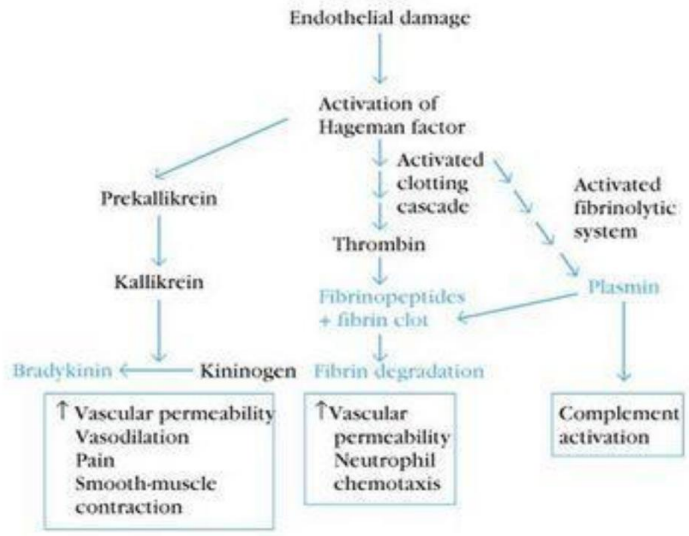
- **cascade**: It is a process where one thing leads to another. We should know tvwo cascades : The complement system cascade and coagulation cascade.

KININ SYSTEM

The kinin–kallikrein system, or simply the kinin system, consists of blood proteins that play a role in inflammation, blood pressure control, coagulation and pain. Its important mediators bradykinin and kallidin are vasodilators and act on many cell types.

- The Kinin System does not get activated unless the **coagulation cascade** is activated.
- If the **coagulation cascade** was activated (especially factor 12 which is called the Hageman factor) it stimulates the cascade of the kinin system.
- What is important from the kinin system? **Bradykinin**

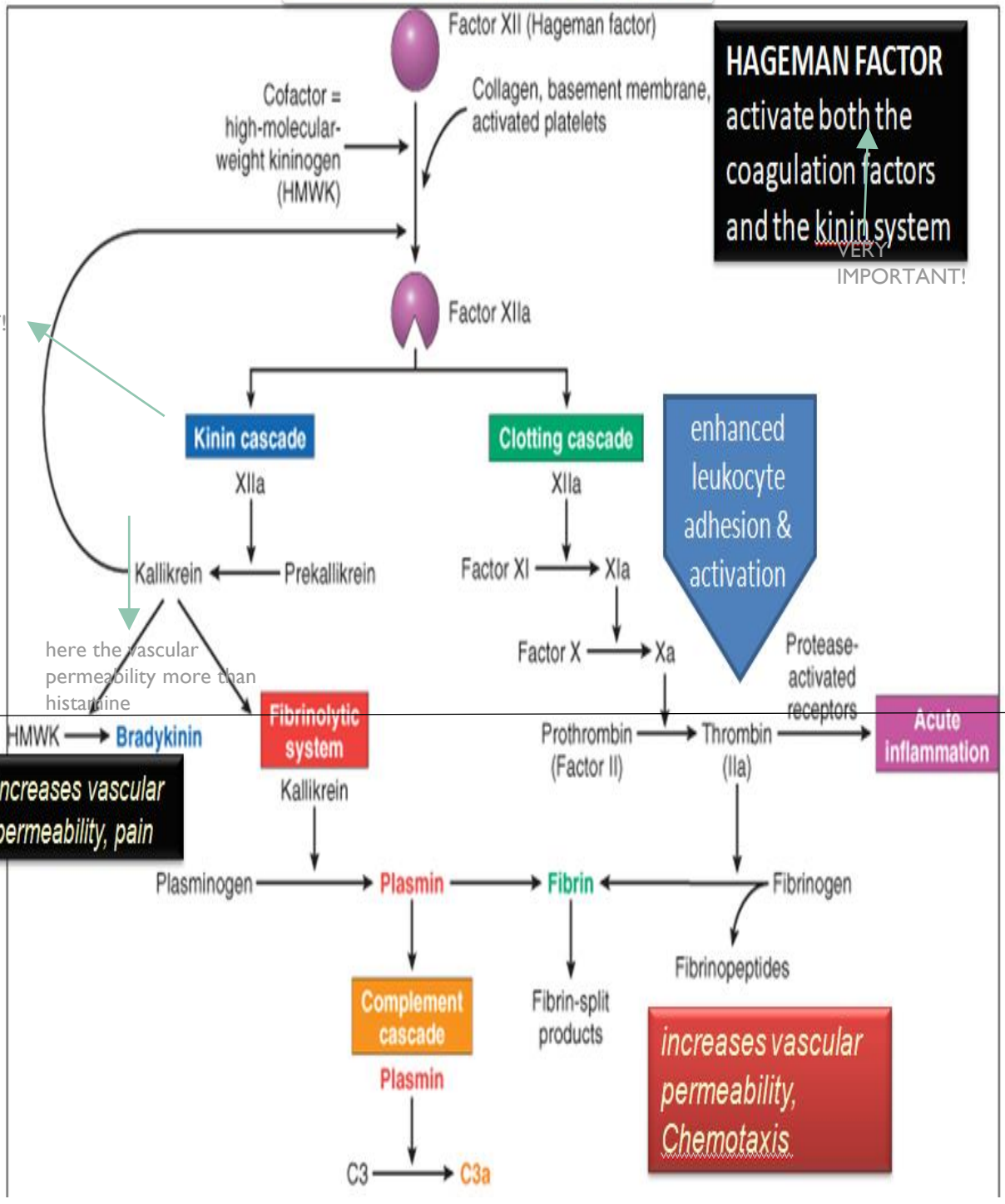
- **Bradykinin** is a **pain stimulator** and increases the **vascular permeability**.
- The actions of Bradykinin are short-lived. **WHY?** Because it is rapidly degraded by **kininases** present in plasma and tissues.
- So when there is **inflammation**, the coagulation system is **activated**.
- Protease



- **Complement system**: Leukocyte chemotaxis (**C3a** and **C5a**), opsonization (**C3b**) and cell killing (by **C5b-9** Membrane attack complex).
- Hageman factor activation leads to **kinin activation**.
- **Bradykinin** is created after the kinin activation and it causes pain.

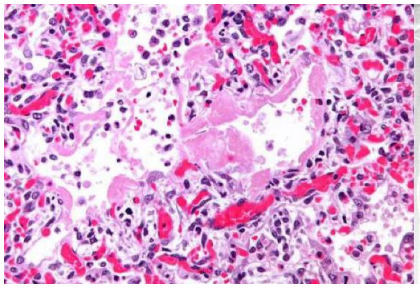
- [31] a compound released in the blood in some circumstances that causes contraction of smooth muscle and dilation of blood vessels.
- [32] an enzyme that catalyzes the transfer of a phosphate group from ATP to a specified molecule.

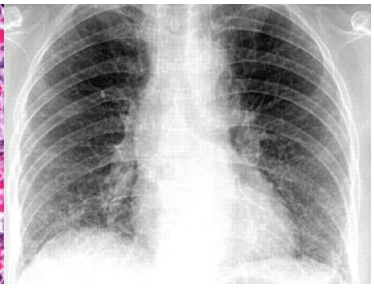
Kinin & clotting systems



CLINICAL CASES :

Acute Interstitial Pneumonia:





It is an inflammatory condition affecting the alveoli.
You can see that there's a lot of neutrophils.
Symptoms: cough, fever, high ESR, malaise, vomiting, high neutrophil count in the blood.

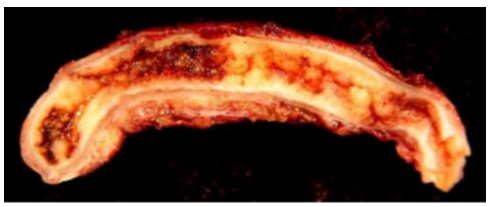
Diagnoses: bacterial inflammation in the lung. (acute pneumonia).
Acute interstitial pneumonitis occurs most frequently among people older than forty years old.

Viral Infection

Symptoms: fever, malaise53 and weakness.
What is happening? Viral infection are usually associated with leukocytosis (increased number of leukocytes). They could go up to 60%. Neutrophils are usually elevated in bacterial
infection, but not viral.

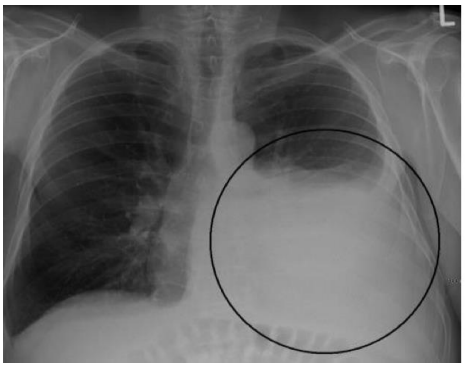
Diagnose: viral infection.

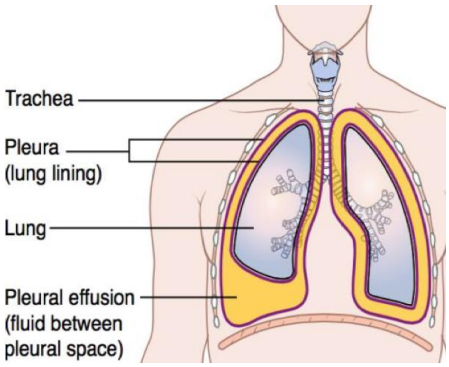
Acute Appendicitis



A 12 years old boy came to the emergency room.
Symptoms: he has a lower abdominal pain in the right side 20 - 30 times a day.
Examination: The surgeon found the his appendix was swollen, with vascular conjunction (cause of redness), and inflammatory exudate.
Diagnose: acute appendicitis

Tuberculosis





A large left sided pleural effusion as seen on an upright chest X-ray

A 20 year old patient, with exudate in his pleural cavity.
His CBC (Complete blood count) showed increased neutrophils.
Diagnose: We should think of an inflammatory condition, and namely, a bacterial infection. TB could be a cause.
)تدبه(.If you see an x-ray of a TB patient you will find a chronic abscess that has fibrosis

In acute inflammation of the lung, the alveoli are intact, and the normal architecture of the lung is preserved. There is exudate but the architecture is preserved.
On the other hand, in chronic inflammation of the lungs, we see lots of fibrosis and lymphoid follicles and proliferation of type 3 monocytes to compensate the cells that have been destroyed.

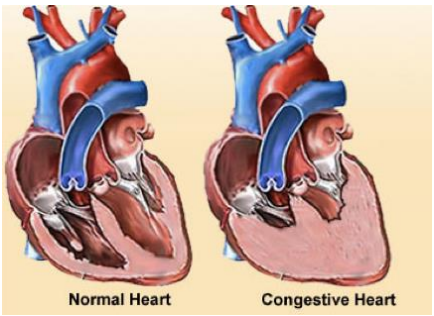
Why are some cells destroyed?
Because fibrosis obstructs the gas exchange and some cells die.

Pathogenesis:
Alveolar fibrosis→ hypoxia→ pulmonary failure → death

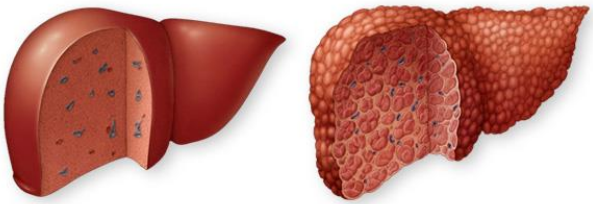
Congestive Heart Failure

A 90 year old patient came to the clinic with swollen feet.
Lab results: The fluid had very low protein content (transudate), The CBC showed no elevated leukocytes.

Diagnose: you should think of congestive heart failure.



Alcoholic Hepatitis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A 35 year old man يحب السياحه. He had a swelling somewhere in his body and it was transudate. You take a biopsy from his liver (because you suspected liver steatosis) and you find fatty change. تقول له خفف من الرح ت السياحيه يابو شربل فقد أثر فيك الكحول وعمل لك مشاكل في الكبد

Diagnose: Alcoholic hepatitis. In conclusion, the liver protein synthesis is reduced.
Pathogenesis:
The chronic inflammation leaves fibrosis, and in some cases it causes a disease; eg: alcohol induced liver damage.

(alcohol metabolites → cell injury → formation of free radicals → fibrosis)
At the beginning, there will be fatty change, but after some time, there will be chronic alcoholic hepatitis. As a result, there will be fibrosis, which leads to hepatic cirrhosis. The liver cells will be in nodules and it will be surrounded by fibrosis and this leads to death

Renal Problem

A 52 year old patient came to the clinic with edema in a part of his body.
The patient shows no inflammatory signs and his liver is OK and the edema is transudate. Because you are smart you should think of a renal problem.

"فتقوله:"أكرمنا بقطرات من بولك الثمين..
"فيقول: "أبشر يا دكتور... نحن في الخدمة دائماً"

The patient's urine has lots of protein, his kidneys are abnormally removing the proteins from the blood, causing the edema.
Note: plasma proteins are albumins and globulins.

MCQS (TEST YOURSELF !)

- **1)** A seven-year-old patient complains of abdominal pain, he is weak and thin. you took a stool sample and found parasites in the stool what type inflammatory cell will increase in his blood?
- a) neutrophils
- b) macrophages
- c) eosinophils
- d) lymphocytes

- **2)** A patient with acute bacterial infection will have an increased number of?
- a) neutrophils
- b) macrophages
- c) eosinophils
- d) lymphocytes

- **3)** Which one of these cells produce immunoglobulins?
- a) neutrophils
- b) macrophages
- c) eosinophils
- d) plasma cells

- **4)** A patient with chronic viral infection will have an increased number of?
- a) neutrophils
- b) macrophages
- c) eosinophils
- d) lymphocytes

- **5)** A patient who has recurring runny nose and secretion from his nose was diagnosed with acute allergic rhinitis. The patient will have an increased number of?
- a) neutrophils
- b) macrophages
- c) eosinophils
- d) lymphocytes

- **6)** All of the following are cardinal signs of inflammation except?
- a) swelling
- b) warmth
- c) pain
- d) chills

- **7)** What is cause of the redness (erythema), warmth, and stasis of blood flow ?
- a) vasodilation
- b) vasoconstriction
- c) margination.
- d) pavementing

- **8)** Which of the following is an adhesion molecule found on the surface of inflammatory cells (leukocytes)?
- a) selectins
- b) integrins
- c) IL-1
- d) TNF

- **9)** Receptors on mast cells bind to which antibodies to release histamine from its granules?
- a) IgM
- b) IgG
- c) IgE
- d) IgD

- **10)** Which of the following stimulates the expression of adhesion molecules?
- a) IL-1 and TNF
- b) selectins
- b) integrins
- d) mast cell

- **11)** Which one of the following is the first vascular response to tissue injury (during inflammation):
- a) vasodilation
- b) vasoconstriction
- c) margination
- d) pavementing

1-c
2-a
3-d
4-d
5-c
6-d
7-a
8-b
9-c
10-a
11-b

Helpful Videos:

Vasodilation and Increased Permeability:
https://www.youtube.com/watch?v=vZ9ykvRhWK0

Crash Course (The Immune System):
https://www.youtube.com/watch?v=GIJK3dwCWCw
https://www.youtube.com/watch?v=2DFN4IBZ3rI
https://www.youtube.com/watch?v=rd2cf5hValM

A lot of the subjects are also discussed in other Materials such as : Immunology .. So try to combine them together and it will make things easier to understand ☺

Questions (Advanced ☺)

One best answer question:

1. Which one of the following substances in the inflammatory exudate[55] is a substrate for thrombin?

a. arachidonic acid

b. fibrinogen

c. kallikrein

d. PGE2

e. serotonin

Answer: B

Substrate: target for the enzyme (we need substance so that this enzyme can act upon).

Example: What's the substrate of amylase? Carbohydrates.

Thrombin: One of the products which occurs as a result of **activation of the coenzyme factor (cascade)**, we know that **coagulation cascade** is activated during the inflammation and it ends with factor 12. The end product will be **clutor thrombus** and **thrombin** is one of these products.

---

2. Which of the following is *not* a "cardinal sign" of inflammation?

a. atrophy

b. heat

c. pain

d. redness

---

3. A 46-year-old man presents with a painful nodule on the skin of his neck. The nodule is inflamed and tender. When incised, it drains sticky yellow fluid that contains large numbers of neutrophils. Which organism is most likely to be responsible?

a. *Clostridium perfringens*

b. Guinea worm (*Dracunculus medinensis)*

c. Louse (*Pediculus* sp.)

d. *Mycobacterium tuberculosis*

e. *Staphylococcus aureus*

Answer: E

Fluids that come with inflammation: exudate, transudate & pus.

Which type of inflammation that gives you transudate? serous inflammation.

a. Clostridium perfringens → Cause of Gangrene.

b. Guinea worm (Dracunculus medinensis) → Parasite → Eosinophil.

c. Louse (Pediculus sp.) → in hair & skin (قمل)

d. Mycobacterium tuberculosis → Causes TB which is a chronic inflammation. Chronic inflammation contains granulomas but not neutrophils (neutrophils are in acute inflammation only).

e. Staphylococcus aureus → Most common pus producing organism.

MEMBERS :

Females:

-Leader : بثينة آل ماجد

-روان الحربي
-وفاء العتيبي
-الجوهرة الشنيفي
-رزان الزهراني
-رهف الشمري
-روان مشعل
-منيرة المسعد
-لميس السويلم
-نوف العتيبي
-رزان الزهراني
-هديل عورتاني
-فاطمة بالشرف
-ابتسام المطيري
-رناد الفرم
-غرام جليدان
-بلقيس الراجحي
-نورة القاضي
-آلاء الصويغ
-ريم القحطاني
-نورة بن حسن

Males:

-Leader : فيصل الطحان

عبدالجبار اليماني
محمد باحاذق
أحمد الراشد
عبدالله بالعبيد
عبدالله السرجاني
أحمد الحربي
أنس السيف
داود إسماعيل
خالد الدوسري
فهد الفايز
محمد بن معيوف
فهد النحابي
معاذ العبد الغني
سعد الفوزان
سيف المشاري
تميم الوهيبي
أحمد الرخيمي
رشيد البلاع
محمد النجيم
عبدالاله الدوسري
خالد العقيلي
محمد الصويغ
محمد العمر
ماجد الجهني
محمد الأصقه
فايز الدرسوني
يزيد الدوسري
نواف السبيعي
عبدالعزيز المحنا

Kindly contact us if you have any questions/comments and suggestions:

* EMAIL: pathology437@gmail.com
* TWITTER : @pathology437

GOOD LUCK! ☺

Resources:-

1- Females slides
2- Robbin's Basic Pathology

Pathology

teamwork 437