

Pathology

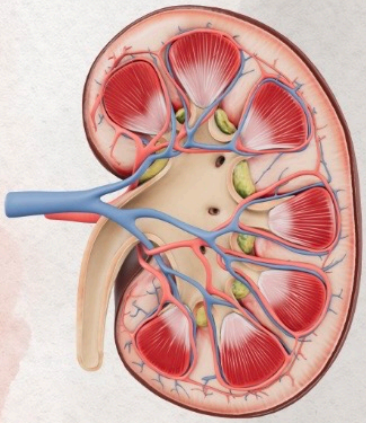
محاضرة 3 د.سامح

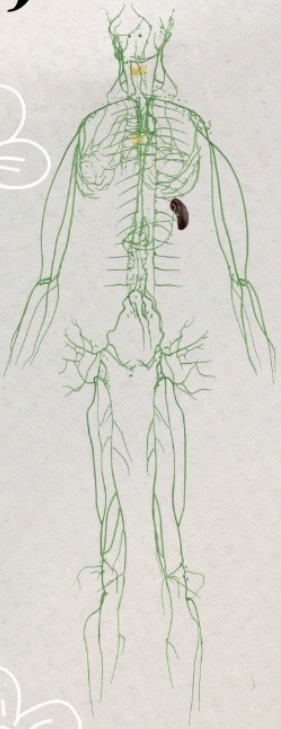
Inflammation

(Chemotaxis, phagocytosis, cells of inflammation)

Layan







Chemotaxis:

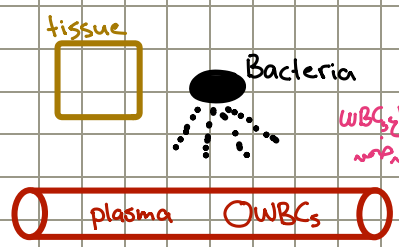
•It is the directed movement of emigrating leukocytes to the site of injury. The aim of this movement is **to reach the organisms or particles to be phagocytized by these leukocytes**

•Both of emigration & chemotaxis are controlled by **chemotactic factors:**

a) chemotactic factors **for neutrophils** include bacterial products (mainly derived from **cocci**), complement components particularly C5a &C3a, neutrophil components , lymphokines & others.

b) chemotactic factors **for monocytes** include bacterial products (mainly derived from **bacilli**), complement components particularly C5a &C3a, neutrophil components , lymphokines & others.

Chemotaxis : Chemical attraction of WBCs (inflammatory cells) towards the source of damage (microorganism).



البكتريا لما تدخل بتطلع toxins وفي بعض أنواع WBCs تنجذب لهذا toxin فمن ضمن الأشياء الي بتعمل Chemotaxis هي toxins

e.g
1. damaged tissue → lysosomal enzymes.
2. WBCs. — PMNL (WBCs لباقي attraction بتعمل Chemical substance تفرز WBCs الـ) — lymphocyts
3. Organism. → bacterial toxins.
4. plasm protien. → complement system.

كلهم عبارة عن Leukotaxins

عبارة عن مجموعة من plasma protiens inactive (under normal condition) وأول ما تدخل bacteria للجسم بصيرلهم activation (e.g C_{5a}) نوع من complement system. activated protiens of

• Chemotaxis is **selective process**: → يعني كل نوع من organism بيعمل attraction لنوع معين من WBCs

each irritant has specific chemical factor attract specific type of WBCs.

Cocci → PMNL. (mainly)

Bacilli → Monocytes. (mainly)

Virus → lymphocytes. (mainly)

parasites → eosinophils. (mainly)

Leukotaxins

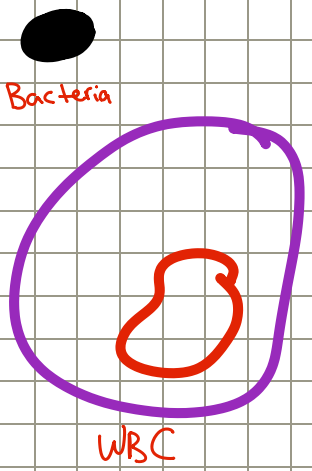
Chemical substance which attract leukocyts (WBCs).

•Mechanism of attraction & movement of leukocytes towards their target includes:

a) chemotactic agents bind to specific receptors on the cell membranes of the leukocytes → activation of the enzyme phospholipase C.

b) activation of phospholipase C → release of calcium from both the intracellular & extracellular stores. this calcium activates intracellular contractile proteins (tubulin and actin) leading to active cell movement as well as extracellular contractile proteins (laminin &fibronectin) leading to passive cell movement.

Vasoconstriction
↓
vasodilitation
↓
margination of WBCs.
↓
emigration of WBCs.
↓
Chemotaxis



ال WBC راحت لل Bacteria فتبتلعها phagocytosis (هتبلعها)

•**Definition & mechanism of phagocytosis:** phagocytosis is the process by which the phagocytic cells recognize then engulf abnormal particles such as bacteria, dead cells, fibrin and foreign bodies, followed by their degradation:

باختصار phagocytosis ⇒ White blood cells engulf :
1. microorganism.
2. damaged tissue.
3. foriegn substance.

ال phagocytosis بتحدث عشان تشيل أي صديد وتُؤهِّل المنطقة لعملية repair لأنها في أنسجة تدمرت (لأنها فايبتخ ليصير repair على أنسجة ممزقة أو مدمرة).

a) recognition & attachment of bacteria (opsonisation): bacteria are coated by an opsonin which is an immunoglobulin or complement factor

b) Engulfment: phagocytic leukocytes surround the opsonised bacteria & send engulfed . fusion of pseudopodia phagocytic vacuole (phagosome).

Phagosome fusion with the limiting membrane of the lysosomal granules

Discharge of granule content phagolysosome bacterial degradation.

C) degradation : killing bacteria may be done through :

I) oxygen dependent mechanism: formation of hydrogen peroxide or superoxide which bactericidal.

II) oxygen independent mechanism: lysosome hydrolyzes bacterial wall glycoprotein a powerful bactericidal activity.

Steps of phagocytosis:-

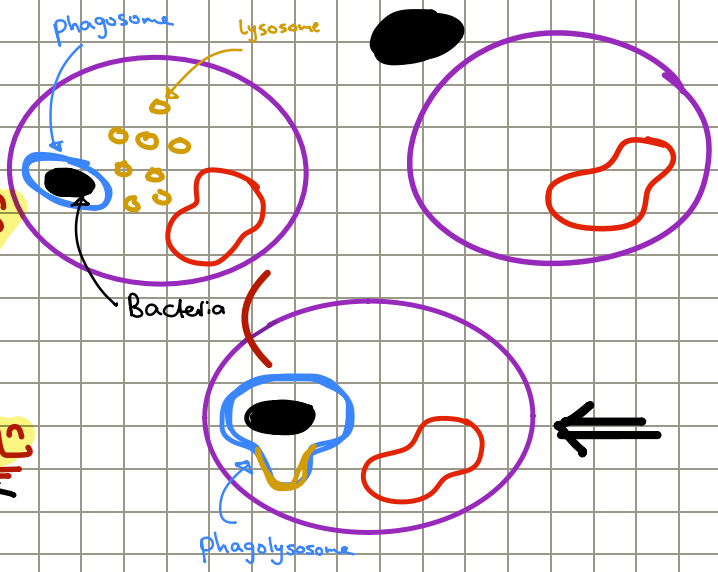
1. recognition and attachment
2. engulfing and formation of phagosomes.
3. degradation of microorganism.

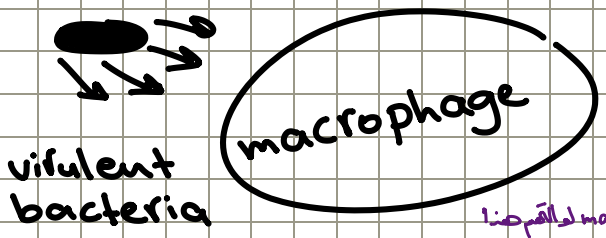
باختصار

أولاً: هتبدأ الـ WBC تتحرك خلال الأنسجة وتبدأ تتعرف عليهم وهتتعرف على الـ Bacteria وهتلزم فيها.
(recognition and attachment)

ثانياً: هيحدث الـ WBC (engulfing) بلعة للـ Bacteria داخل الـ phagosome (اللي هي عبارة عن visscle) وبتبدأ الـ lysosomes تلزم مع الـ phagosomes وبيكبر أكتر وبيلزم مع lysosome وبيعمل (phagolysosome).

ثالثاً: (degradation) الـ enzymes الموجودة داخل الـ phagolysosome هتبدأ تذوب الـ Bacteria أو الـ deep tissue





phagocytosis نقطة مهمة في الـ

هذه نوع من أنواع الـ bacteria عندها powerful toxins

وهنا الـ macrophage لما لقم هنا الـ bacteria هتعرف وبيموت وبعيك النوع من الجهاز المناعي متى هيأدي وظيفته، فبيعمل إنه plasma موجودة opsonins هتجي لـ proteins وهتحاوطها الـ virulent bacteria وهتحرج على

masking to the surface of this bacteria وبعيك هذه الـ opsonins على

opsonization بالتالي هتقلل شيء من افراز هذه الـ toxins وهنا إجرائية اسمها
(covering the surface of virulent bacteria by opsonins)
(engulfing the bacteria) macrophage والهدف من الـ opsonization إنه تسهّل وظيفة

Types of phagocytic cell in acute inflammation:

a) Neutrophils (polymorphnuclear neutrophils ,PMNS or microphages) these are mainly attracted to & engulf cocci.

Some neutrophils may die due to bacterial toxins (leukocidins). Dead neutrophils may be called pus cells. These dead cells release their proteolytic enzymes digestion (liquefaction) of necrotic tissue and fibrin facilitation of both of their phagocytosis by macrophages and their drainage by lymphatics

b)Macrophages:

-they include emigrating monocytes, as well as tissue histiocytes

-mainly attracted to & engulf bacilli, necrotic cells, fibrin, pigment & foreign bodies.

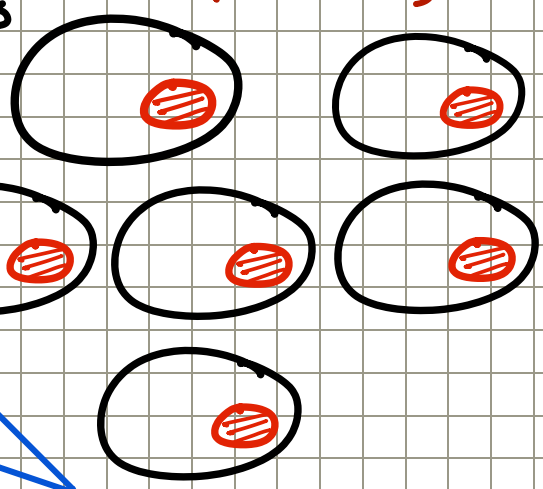
c)other cells of the mononuclear phagocyte system such as Kupffer cells of liver, littoral cells of spleen and lymph nodes, microglia cells of CNS...etc

Types of phagocytic cells

- microphage (PMNL) سريعة جداً (الأصغر)
- macrophage بطيئة (كبيرة جداً)
  - in blood (monocyte)
  - in tissues (histiocyte)
    - in CNS (microglial cells)
    - in lung (alveolar macrophage)
    - in liver (kupffer cells).
    - in bone (osteoblast)

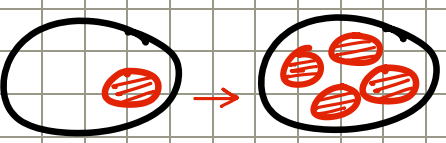
* في الأول بتدخل bacteria معينة ← أول حاجة هتطلعلها ال microphage (إمكانياته قليلة جداً بالنسبة للbacteria) بعدها هيطلع histiocyte الموجودة في ال tissue لكن الأعداد كبيرة جداً فهيطلع Chemical factors عشان يعملوا attraction لـ other macrophage فطلع كمية كبيرة جداً من الـ macrophage وعملوا إحاطة لهذه الأنسجة واستمروا في ال phagocytosis وضلوا داخل هذه الأنسجة (يعني صار الأشي Chronic) شو اللي بيحصل؟!

macrophages



- أنه في بعض أنواع inflammation وبالتحديد ال Chronic

division of nucleus without division of cytoplasm

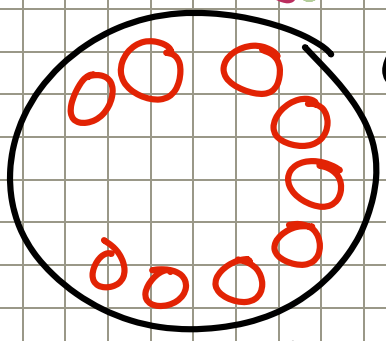


or

① ②

mechanism of formation of Griant cells

Fusion of many macrophages.



Giant Cells:
(large cells with multiple nuclei)

* في عملية ال inflammation كلها موجود Chemical factors هي اللي عملت الـ:
phagocytosis & Chemotaxis & vasodilation & vasoconstriction
وأيضاً موجود خلايا مناعية خرجت.

Chemicals

↓

Chemical mediators of acute inflammation.

هي عبارة عن

(Chemical substance released during the course of acute inflammation and responsible for all process of inflammation).

Cells

↓

Cells of inflammation
(عبارة عن WBCs)

examples: 1- Bacterial toxins
2- Chemicals from damaged tissue $\xrightarrow{e.g}$ lysosomal enzymes.

3- plasma
- kallikrein.
- bradykinin.
- complement component.

4- WBCs
- PMNL. $\xrightarrow{\text{تعزز}}$ PGE4 + leukotriens.
- lymphocytes. $\xrightarrow{\text{تعزز}}$ lymphokines.
- mast cells. $\xrightarrow{\text{تعزز}}$ heparin, histamin.

الكفاءة • The efficiency of phagocytosis

مدى ضراوة البكتيريا

a) it depends on many factors as patients immunity, dose & virulence of bacteria and nature of tissue (e.g phagocytosis is less efficient in serous sacs).

b) in adverse conditions, bacteria may resist phagocytosis. Examples:

- phagocytic cells may be killed by bacterial toxins (leukocidins).
- some bacteria may remain alive inside macrophages (as tubercle bacilli).

مظاهر/أعراض manifestation of acute inflammation

local

- redness
- hotness } بسبب vasodilation
- ورم Swelling ← inflammatory exudate بسبب
- pain ← brady kinin بسبب وجود ال
- loss of function ← due to the pain.

Cardinal signs of acute inflammation

general

• FAHM

- Fever
- Anorexia. فقدان الشهية
- Headache.
- Malaise = general weekness

• Leukocytosis ↓

in acute inflammation

هيطلع ↳ LPF (leukocytosis promoting factor).

هيروح ↳ Bone marrow $\xrightarrow{\text{هيعمل}}$ increase formation of leukocytes

وهذه اسمها (Leukocytosis)

SYSTEMIC (GENERAL) CHANGES IN ACUTE INFLAMMATION

1- Leukocytosis:

Increased blood leukocytes above normal (> 10,000 per mm3) is due to bone marrow stimulation by leukocytosis promoting factors (cytokines), mainly IL-1 &TNF.

REMARK: some infections as typhoid may cause leucopoenia instead of leukocytosis.

2- fever (pyrexia):

Pyrogenic factors, principally IL-1 & TNF disturbance of the thermoregulatory center in the hypothalamus vasoconstriction of skin vessels fever (reduced heat loss).

LOCAL SIGNS & SYMPTIOMS OF ACUTE INFAMMATION

1- Redness due to vasodilatation & opening of capillary bed increased blood flow.

2- Hotness due to increased blood flow. Redness & hotness are celled flare swelling (the wheal) due to accumulation of exudate (inflammatory edema).

3- Pain: due to:

- Nerve compression by exudate
- Irritation by mediators as bradykinin and prostaglandin E2

4- Loss of function: due to pain and tissue damage.

Cells of inflammation

① Phagocytic cells
- → PMNL (microphage)
- → macrophage
  - → blood (monocyte)
  - → tissue (histiocyte).
  - ← Giant cells بتطلع منه فئة

② Lymphocyts
- → B-lymphocytes. —بيحدث لها→ activation —تتحول إلى→ plasma cells —بتطلع→ immunoglobulins
- → T-lymphocytes. → release lymphokiens.

NOTE

مهم جداً

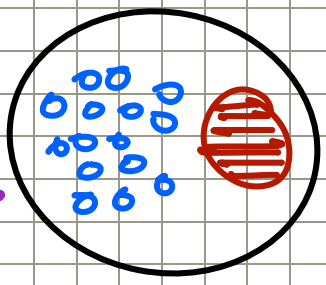
PMNL → acute inflammation.

B-lymphocyte
T-lymphocyte
plasma cell
} ⇒ Chronic inflammation

③ mast cells + basophils

↳ tissues موجودة في

↳ blood موجودة في

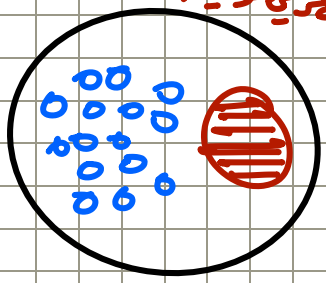


بتطلع ⇒ heparin + histamin

Allergic inflammation بكونوا موجودين في

④ eosinophils

تظهر في نوعين



→ Allergic inflammation

→ release chemicals antagonise histamine
↳ reduce signs of allergy.

→ may exaggerate some allergic conditions as bronchial asthma.

→ parasitic infection

release chemicals kill parasites.

* ال mast cell & basopil هما اللي بيعملوا أعراض ال Allergy عن طريق ⇐ release histamine

* ال eosinophils تعمل as anti allergic بتطلع ⇐ anti-histamine

لكن في بعض أنواع Allergy ممكن eosinophil تطلع Chemicals تزوّد ال Allergy

(حالات نادرة)