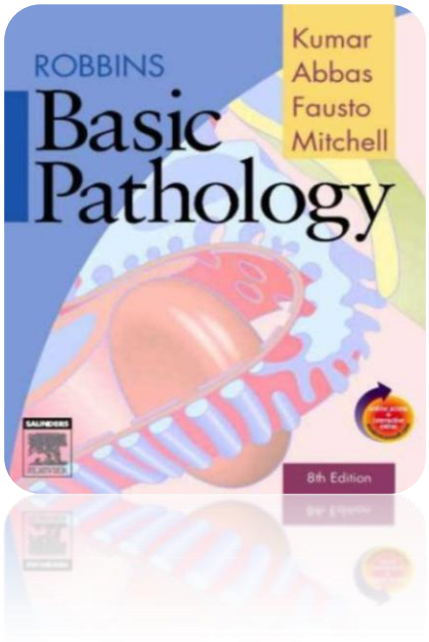
NFLAMMATION

Lecture 2

Cellular Events in Inflammation

Notes on Dr. Ammar C. Al-Rikabi's handout,
Dr. Maha Arafah



First year Medicine-Foundation Block

Pathology Team

September 2012

Please note: This paper does not replace the main sources, it's only a facilitator

Acknowledgement

Dear colleague, this paper was a result of hours and days of hard work from both female & male pathology teams...
All what they want from you is "Dua'a"

*Objectives:

1. **Describe the steps involved in extravasation of leukocytes from the blood to the tissues. Know the steps at which selectins and integrins act.**
2. **Describe the meaning and utility of chemotaxis. UNDERSTAND the role that chemokines play in inflammation.**
3. **Describe the steps involved in phagocytosis and the role of IgG and C3b as opsonins and receptors.**

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some Key words:

***EXTRAVASATION** = attachment of circulating leukocytes to endothelial cells and their migration through the endothelium (in 3 steps).*

***PHAGOCYTOSIS** = the process of eating microorganisms (foreign particles) by Phagocytes.*

***STASIS** (means stands by) = blood flow slows in inflammation, it happens during Margination.*

Date of lecture:

30 September, 09:00 a.m. to 10:00 a.m.

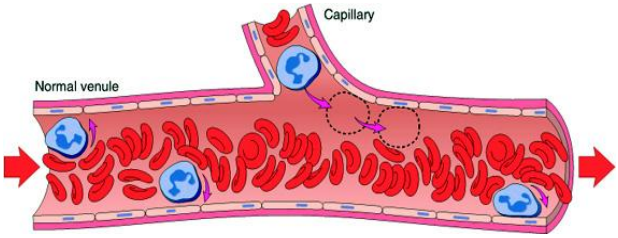
What is the critical function of Inflammation?

1- Deliver leukocytes to the site of injury
2- Activate the leukocytes to perform their normal functions in host defense.

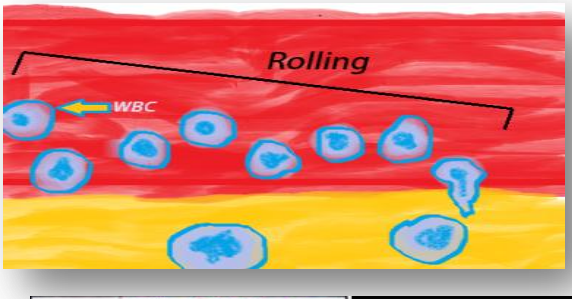
Note; Vascular endothelium normally does not bind circulating cells

the 3 steps of ***extravasation*** ***(***means outside of *blood vessels****)***:

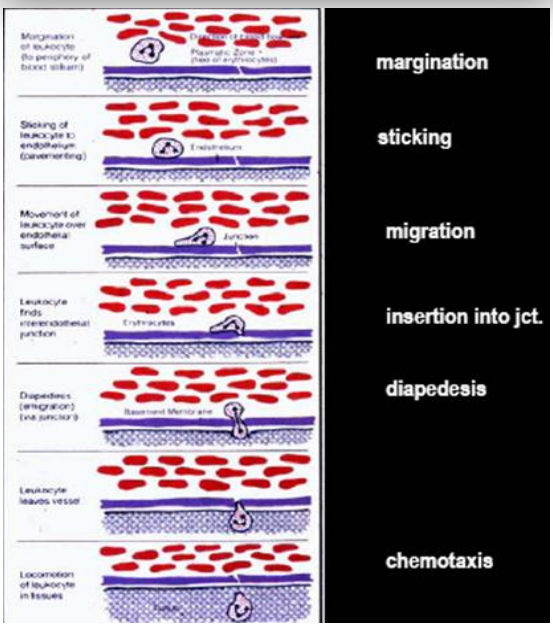
1) In the lumen by:



i) Margination (WBC moves from the center of blood vessel to margins)



ii) Rolling (while the WBC tries to goes through the vessel its rolls)



iii) Adhesion to endothelium

2) Transmigration (also called diapedesis) WBC cross from vessels to the endothelium.

Where does it occur? Mainly in Venules.

3) Migration in interstitial tissues toward a chemotactic stimulus

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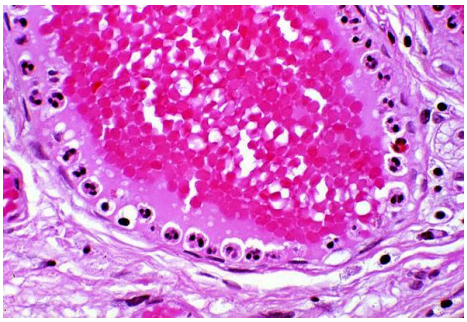
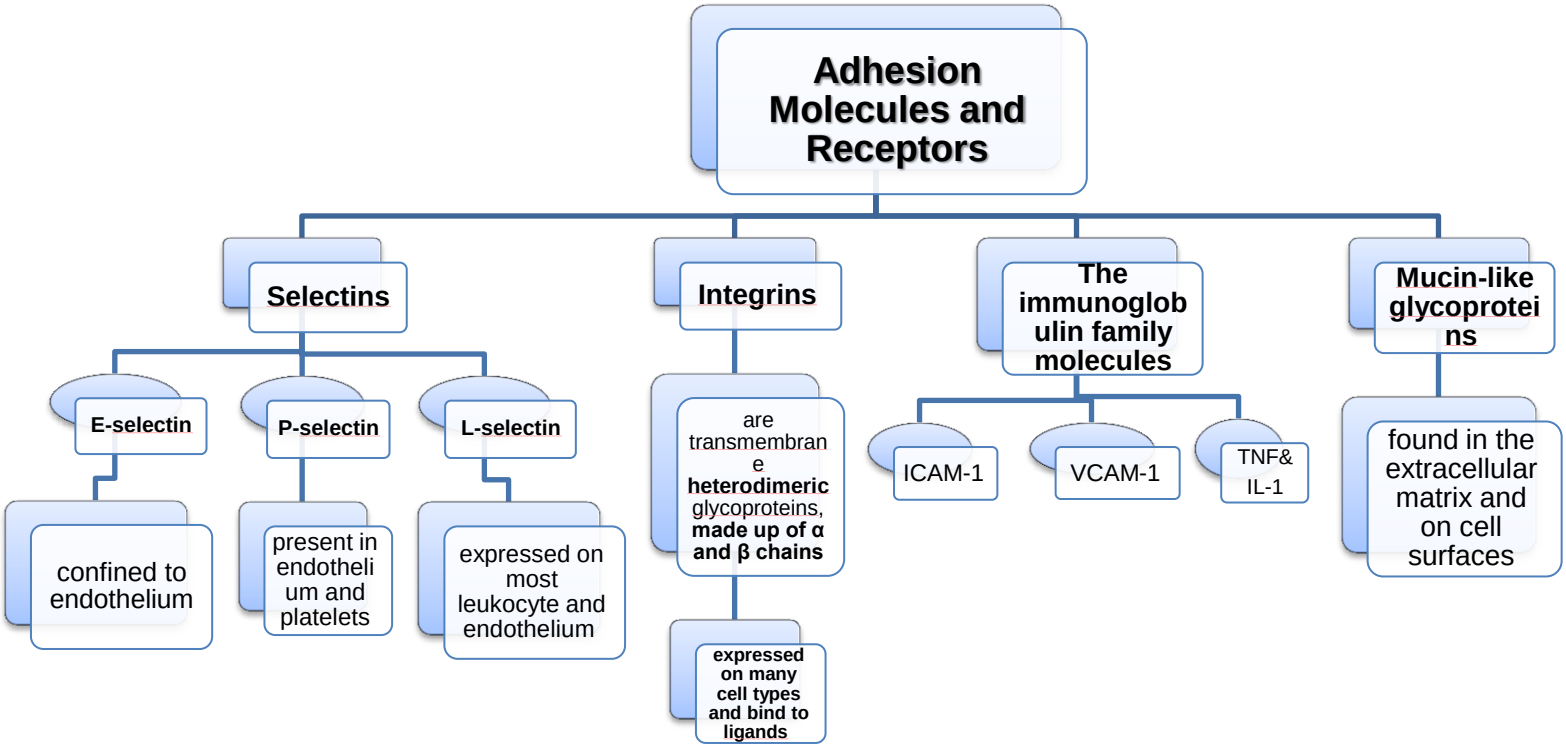
Leukocytes may induce tissue damage and prolong inflammation to host, while its destroys the microbs.

In margination, endothelium can be lined by white cells (PAVEMENTATION)



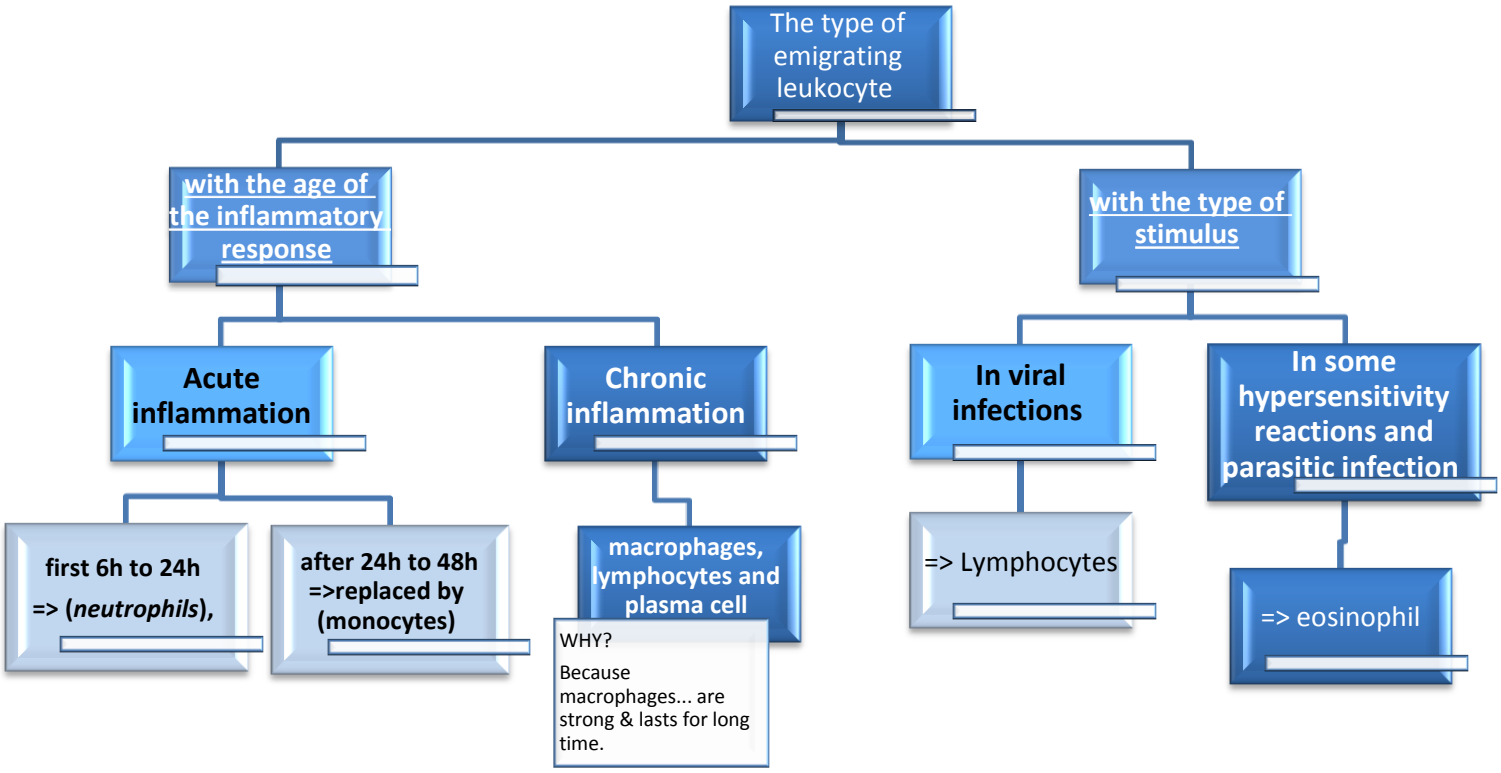
When inflammation occurs (Weibel-Palade bodies) are redistributed in site of inflammation by (Histamine & Thrombin).

These Weibel-Palade bodies effect (4 receptors) which are:



All these receptors are INACTIVE except when there is inflammation.

Neutrophils, monocytes, lymphocytes, eosinophils, and basophils all use the same pathway to migrate from the blood into tissues.



Chemotaxis

After extravasation, ***leukocytes emigrate in tissues toward the site of injury (chemotaxis)*** *defined as locomotion oriented along a* ***chemical gradient.***

NOTE:

Chemotaxis*: tissue => site of injury.*

Transmigration (diapedesis):

Blood vessels => tissue (endothelium)

Chemoattractants

Chemoattractants, is the substances ***inside the cell.***

A) Exogenous => bacterial products.

B) Endogenous

1*components of the complement system, particularly C5a

2*products of the lipoxygenase pathway, mainly leukotriene B4 (LTB4)

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

They attach to G-protein receptor.

After the Leukocytes reaches to the *SITE of INFLAMMAION* they can now eat the microbs by **Phagocytosis**.

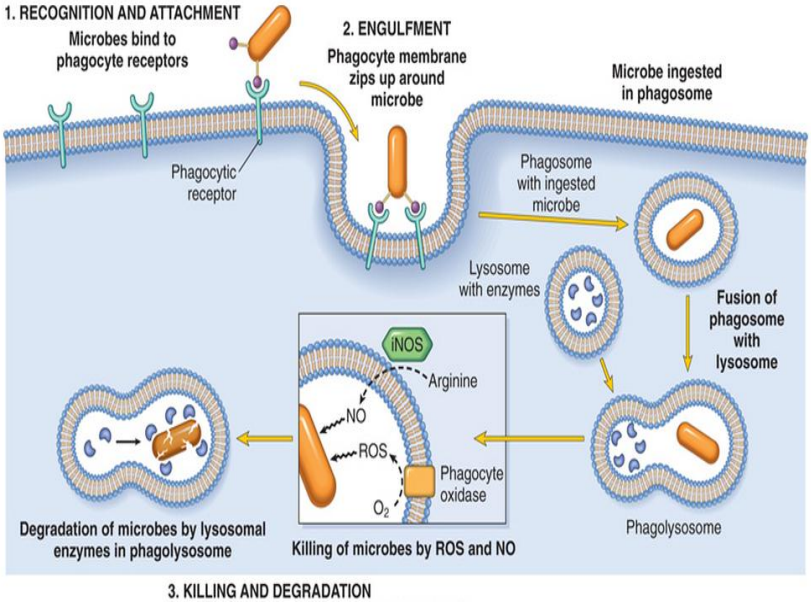
Phagocytosis

Done in 3 steps:

*(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*



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in Details,

(1) **recognition and attachment**: by ***(Opsonization)***

Opsonization **= the process of coating a particle to recognized by phagocytes.**

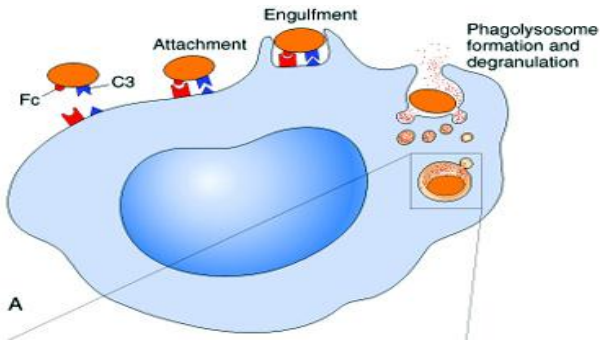
Who do the *Opsonization?!* = *opsonins*

The substances covering the particles could be:

- **antibodies (IgG)**
- **complement proteins (C3)**
- **And others: lectins (mannose-binding lectin (MBL), fibronectin, fibrinogen, and C-reactive protein**

These substances are recognized by Fc and C3b receptors on phagocytes.

(2) **Engulfment: by using (pseudopods).** pseudopods flow around the particle to be engulfed, eventually resulting in complete enclosure of the particle within a **phagosome.**



 # phagocytic vacuole fuses with a lysosomal granule, resulting in phagolysosome

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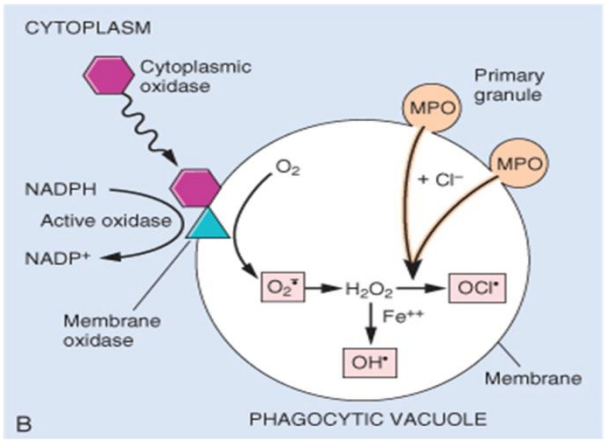
(3) **Killing and Degradation: 2 mechanisms for Microbial killing.**

1. Oxygen-dependent mechanisms

The H2O2-MPO-halide system

(معقم يستخدم في المستشفيات) is the most efficient bactericidal system in neutrophils. (very effective)

(طريقة مضمونة لقتل المايكروبات)

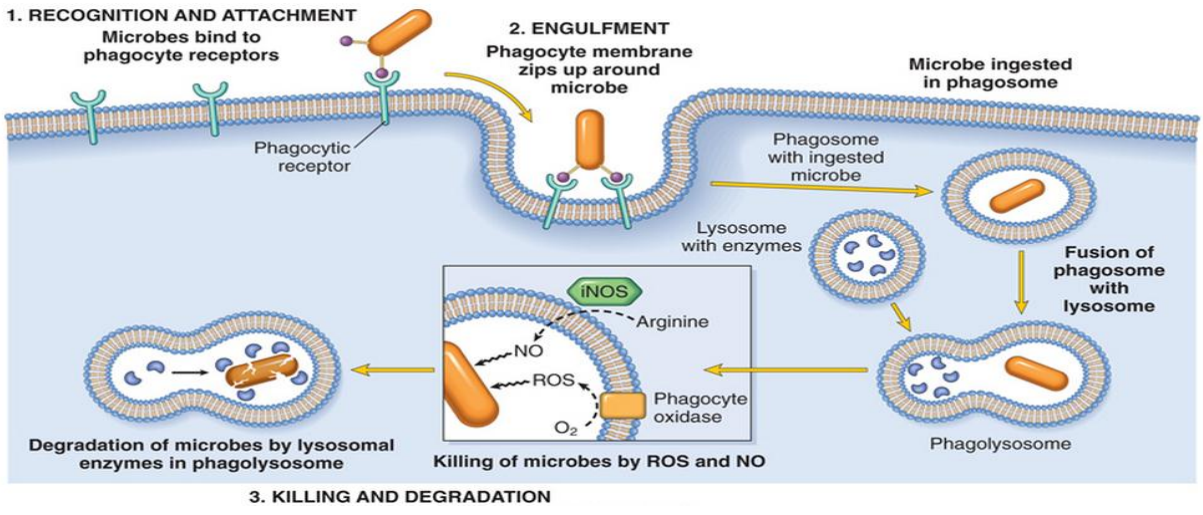


2. Oxygen-independent mechanism: **By**

***bactericidal permeability increasing protein (BPI**

***defensins *major basic protein *Lactoferrin *lysozyme**

In addition, neutrophil granules contain many enzymes, such as elastase, that also contribute to microbial killing.



***Defects in Leukocyte Function* (عيوب كريات الدم البيضاء) could be in:**

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

***They occur in both* GENETIC and ACQUIRED conditions.**

GENETIC

1) Leukocyte adhesion deficiency 1 and 2

2) Chronic granulomatous disease

*Decreased oxidative burst. **2 types**:*

1- X-linked:

***NADPH oxidase** (membrane component)*

2- Autosomal recessive:

- ***NADPH oxidase** (cytoplasmic components)*
- ***Myeloperoxidase deficiency** (absent MPO-H2O2 system)*

3) Chédiak-Higashi syndrome

Protein involved in organelle membrane fusion (no phagolysosomes)

ACQUIRED

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