General pathology

Inflammation lecture 1

Dr. Bushra Al-Tarawneh, MD

Definition

Inflammation:- complex process

Inflammation is a protective response involving host cells, blood vessels, and proteins and other mediators that is intended to eliminate the initial cause of cell injury, as well as the necrotic cells and tissues resulting from the original insult, and to initiate the process of repair.

the first step to initiate the immune response

Causes of inflammation

1. Infections: any type of organism that cause infection

Most common causes of inflammation (bacterial, virual, fungal, parasitic).

2. Physical agents:

Excessive heating, cooling, mechanical trauma, ultraviolet light or ionizing radiation.

3- Chemical agents: Organic and inorganic chemicals including toxins of bacteria.

Causes of inflammation

4- Immune reaction

Hypersensitivity reaction: Reaction of antibody or sensitized lymphocytes with antigenic materials like invasive bacteria or inhaled organic dusts or reaction against self tissues.

It may lead to death

5- Surgery:

Bad sterilization, foreign body like splinters, dirts or sutures.

6- Tissues necrosis:

Result from ischemia as occurred in myocardial infarction.

Significance of inflammation:

1 –Isolation & removing of the injurious stimuli.

2 –Destroying the invading microorganisms.

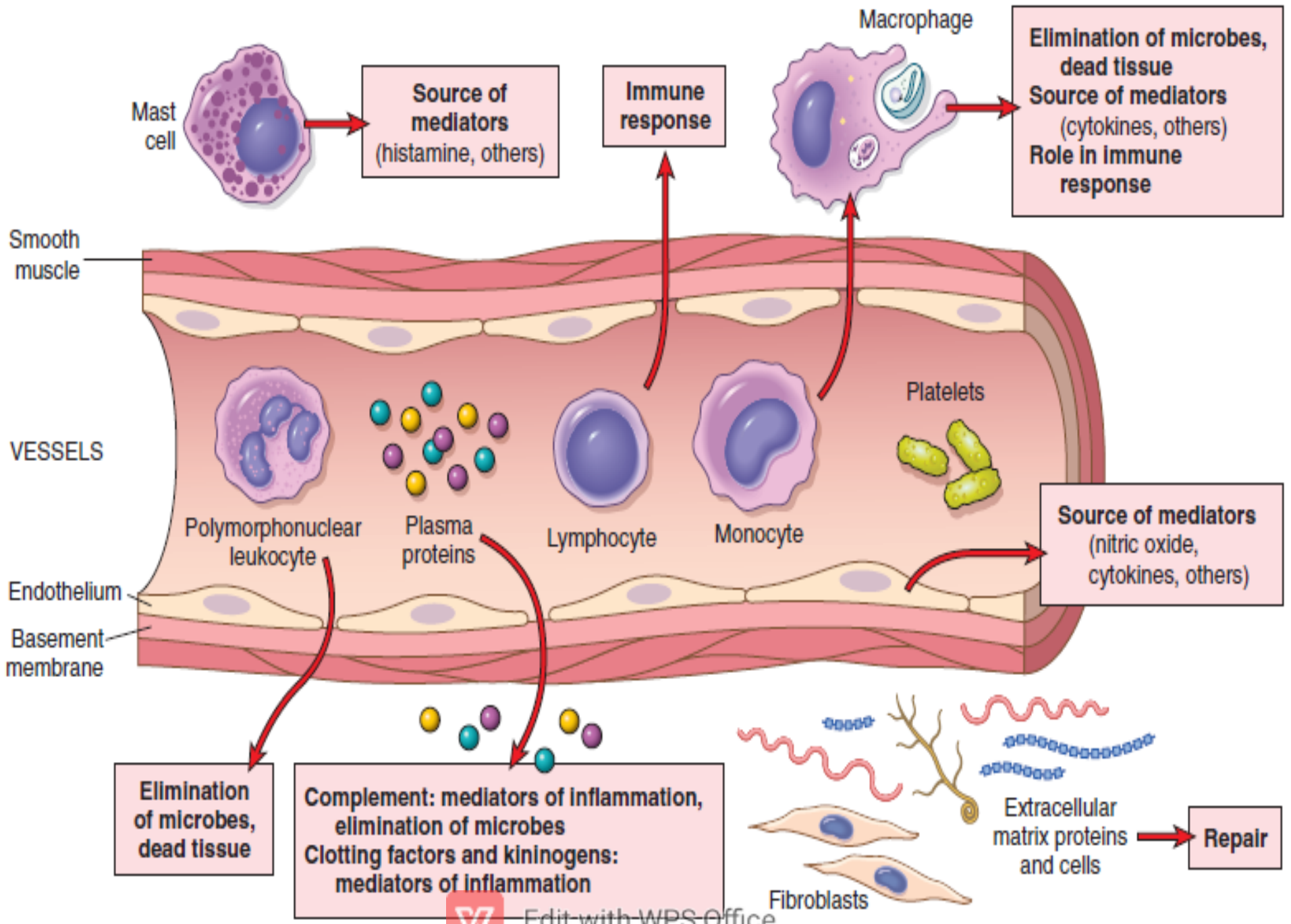
3 –Inactivation of toxins.

4 –Preparing the tissue for healing and repair.

So it is a protective response of the body

In the absence of inflammation:

Wounds & infections would never heal so lead to progressive destruction of the tissues affecting the survival of living tissues.



The components of acute and chronic inflammatory responses and their principal functions.

تبييض الرسمة

- Polymorphpnuclear leukocytes → also called neutrophils and its multinuclear cells
- Extracellular matrix proteins and cells → it eliminates microbe and damaged cells
- Cytokines →signaling molecules causes processes leads to kill the pathogen
- Mediator → in all steps we have a mediator

Harmful effect of inflammation

1- It can cause anaphylactic shock which is life-threatening hypersensitivity reaction.

Anaphylactic shock → hyper immune response

2- It can cause progressive and irreversible organ damage from chronic inflammation and fibrosis like in:

Rheumatoid arthritis. →chronic destruction of bone

Atherosclerosis. →like myocardial infraction

(السبب الأول للوفاة عالميا)

Classification of inflammation

1. Acute inflammation.
2. Chronic inflammation.

Chronic inflammation	Acute inflammation
Later onset (days)	Early onset (sec. – min.)
Longer duration (wks – yrs)	Short duration (min. - days)
Inducing B.V. proliferation and scarring (fibrosis) Lymphocytes, macrophages. (mono nuclear cells) like rheumatoid	Fluid exudation =vascular changes (edema) & polymorphonuclear leukocyte emigration. (neutrophil)

Acute inflammation:

rapid / sharply started

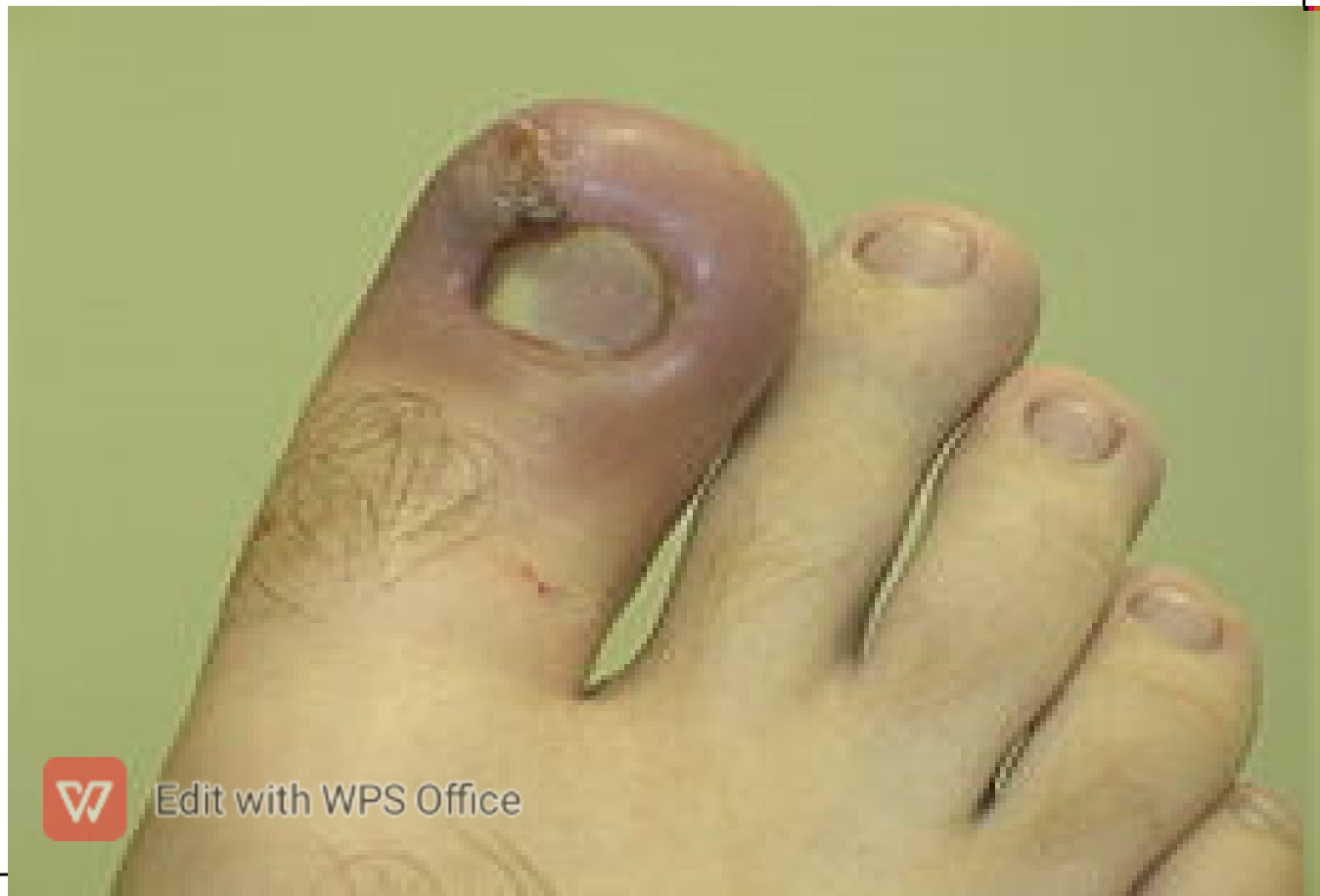
- It is immediate response of living body to injury.
- Nonspecific and may be evoked by any injury of short duration.
- Occurs before the immune response becomes established.
- Occurs to remove the injurious agent and limiting the extent of tissue damage.

Acute inflammation

Classical clinical signs & symptoms of acute inflammation is called

Cardinal signs

- Redness
- Swelling
- Heat
- Pain
- Loss of function



Causes of cardinal signs of acute inflammation:

↑ Vascular caliber (Vasodilation) → ↑ Blood flow → Heat & redness

↑ Permeability of B.V. → Leakage of plasma proteins & leukocytes → Exudates → Edema

Leukocyte emigration → Edema & Release of Inflammtory Mediators → Pain → Loss of function

General characters of Acute inflammation:-

A- It is characterized by two main component:

1. Vascular wall response.
2. Inflammatory cell response.

B- The effects of inflammation is mediated by inflammatory mediators:

1- Circulating plasma proteins.

2- Factors produced locally by vessel wall or inflammatory cells.

C- Termination of inflammation occurs when:

1. Injurious agents and secreted mediators are removed.
2. Release of active anti-inflammatory mechanism.

like transforming beta factor / interleukin (IL)

Vascular wall changes:

Initial transient vasoconstriction

On the cell wall

Followed by: ↓ By mediator

Vasodilitation & Increased vascular permeability

↓

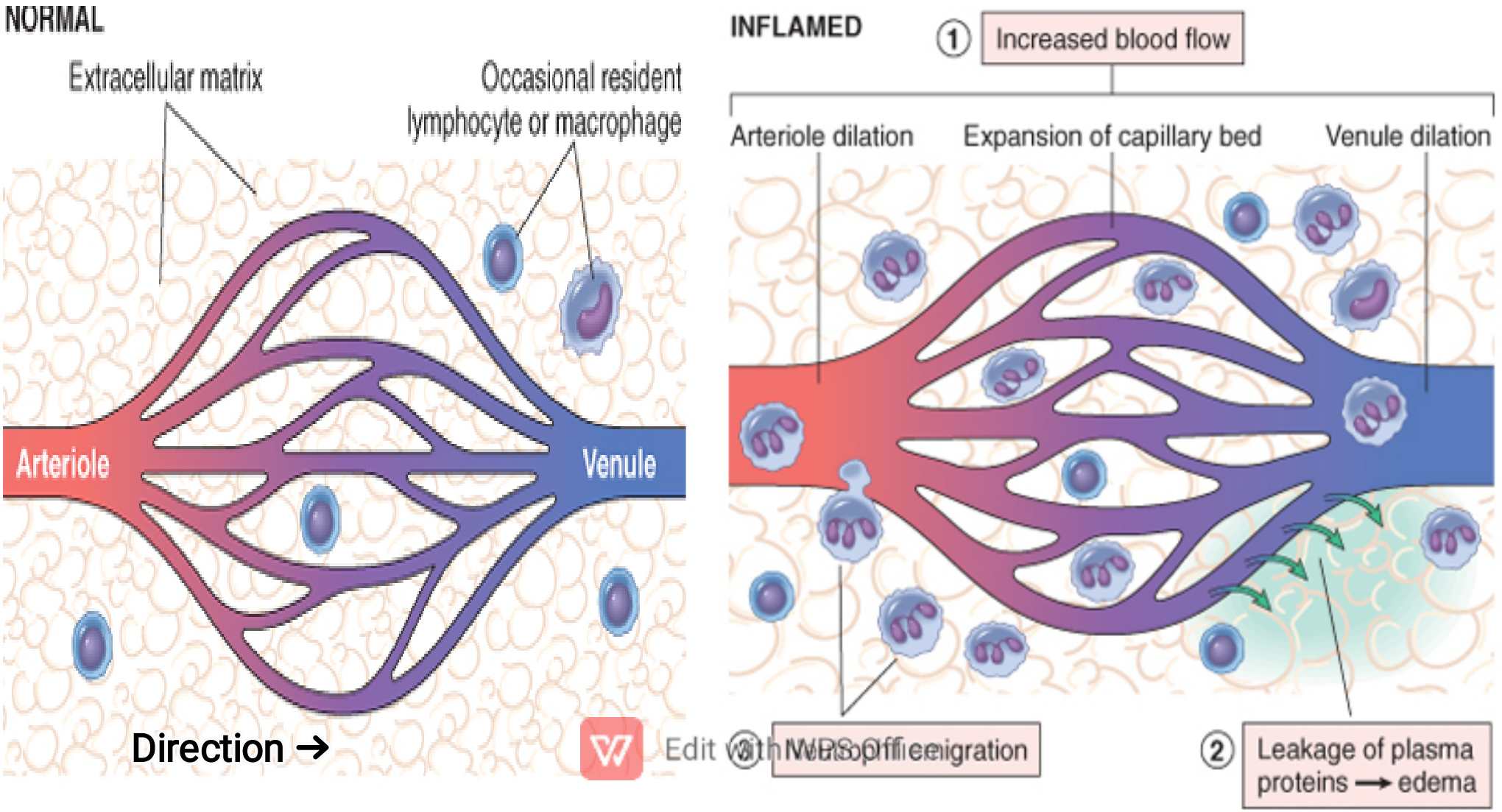
That lead to:

Marked outflow of blood content & edema formation

Alteration in vascular caliber:

1- Vasodilatation

2- Increased vascular permeability



تبييض الرسمة

There is no Neutrophile in the normal conditions

Vasodilatation (x2)ضعف التوسع

Neutrophils → extracellular area → edema

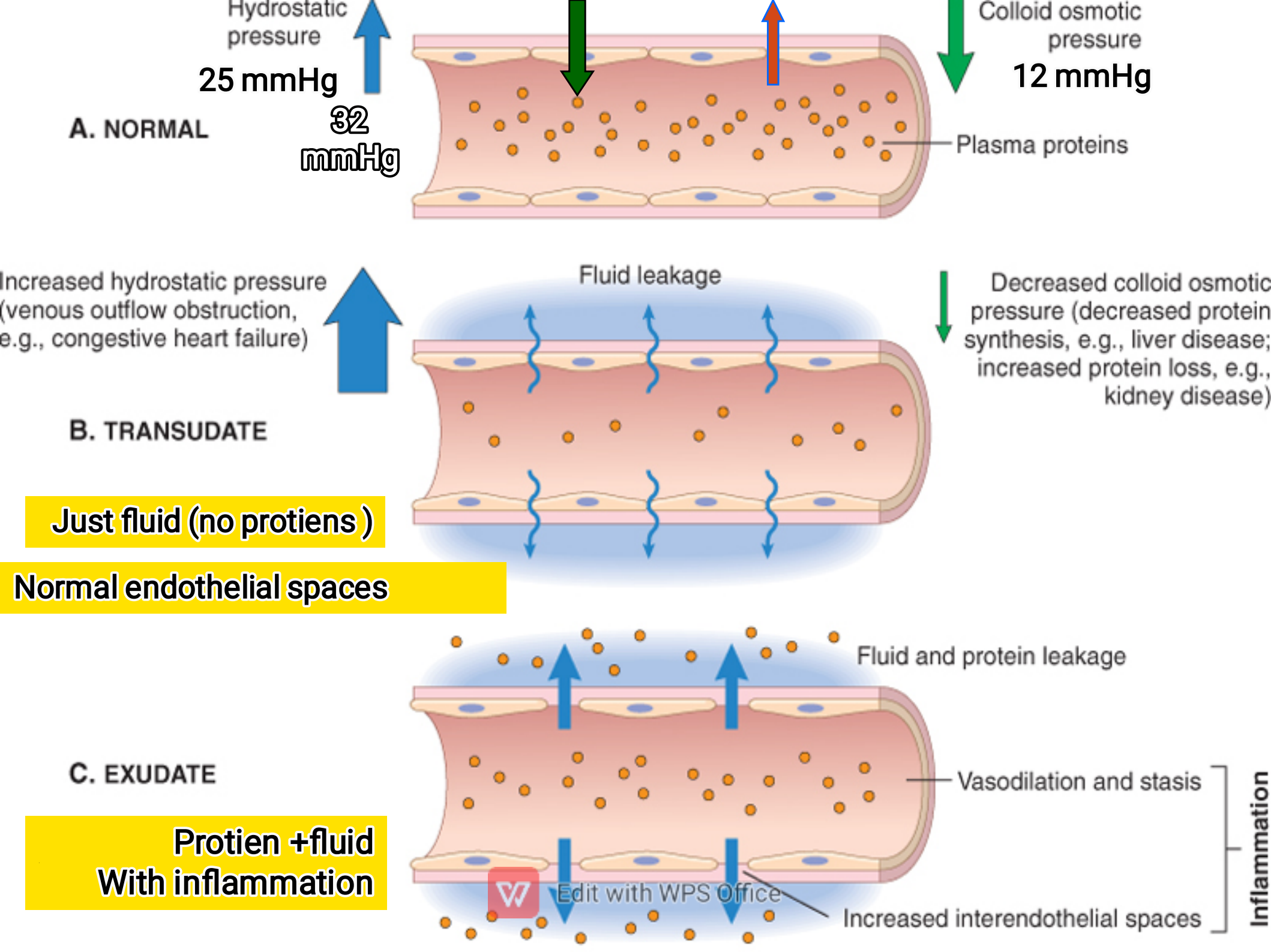
Terminology

Transudate: (Fluid leakage).

An extra-vascular fluid with low protein content & low specific gravity.

Exudate: An inflammatory extravasation of fluid that has a high protein concentration & cellular debris with high specific gravity .

Edema: Excessive fluid in the interstitial tissue or body cavities which is either exudate or transudate.


Hydrostatic pressure
25 mmHg
32 mmHg
A. NORMAL
Colloid osmotic pressure
12 mmHg
Plasma proteins
Increased hydrostatic pressure (venous outflow obstruction, e.g., congestive heart failure)
Fluid leakage
Decreased colloid osmotic pressure (decreased protein synthesis, e.g., liver disease; increased protein loss, e.g., kidney disease)
B. TRANSUDATE
Just fluid (no protiens)
Normal endothelial spaces
Fluid and protein leakage
C. EXUDATE
Protien +fluid
With inflammation
Vasodilation and stasis
Increased interendothelial spaces
Inflammation
Edit with WPS Office

Beneficial effects of fluid & cellular exudate:

1- Dilution of bacterial toxins to be carried away by lymphatics.

2- Entry of antibodies which help in lysis or phagocytosis of the microorganisms and neutralization of toxins.

3- Transport of drugs to the site where the bacteria are multiplying.

4- Exudative fibrinogen will form fibrin that trap the bacteria to facilitate phagocytosis & help in formation of granulation tissue.

5- Delivery of nutrients and oxygen essential for neutrophils which have a high metabolic activity.

6- Stimulation of immune response:
Drainage of inflammatory exudate into lymphatics, reaching lymph node will stimulate
the immune response.

Cellular changes:

Extravasation of leukocyte & phagocytosis

Extravasation:

Delivery of leukocyte to site of injury. The sequence of events in extravasation is divided into:

1- Margination:-.
Rolling & adhesion of leukocyte to the endothelium.
2-Transmigration of leukocytes across the endothelium.

3- Emigration :-
Movement of WBC in the interstitial tissues toward a chemotactic stimuli.(Chemotaxis)
4- Phagocytosis: Engulfment of invading microorganism.

1- Margination, rolling and adhesion

- Margination occurs as a result of the release of chemical mediators:

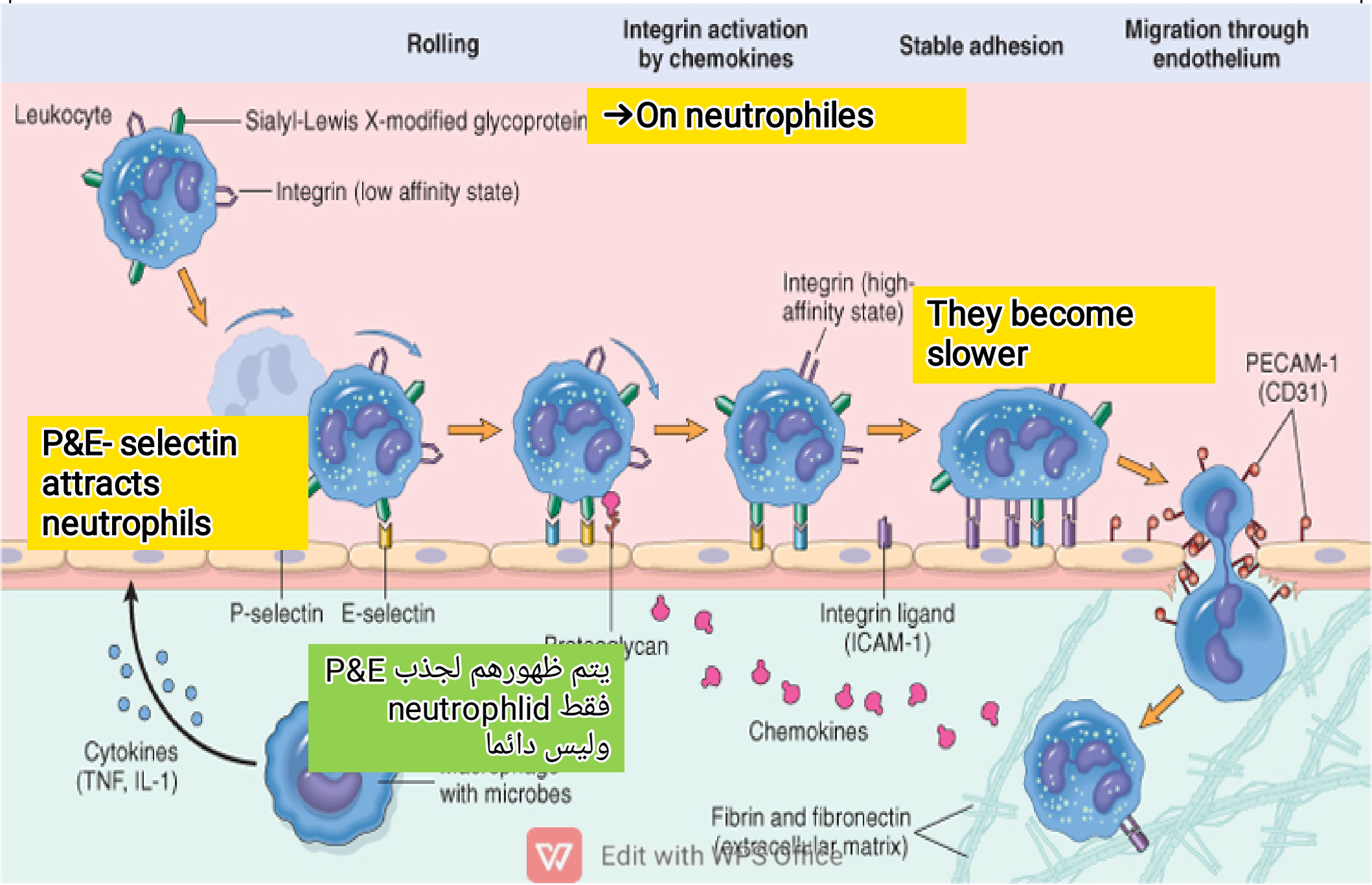
  Histamine, Leukotrienes, Kinins, Cytokines.

- These substanses will affects the endothelial cells of the capillaries and causes the leukocytes to increase their expression of adhesion molecules.

- The leukocytes begin to marginate, or move to and along the periphery of the blood vessels.

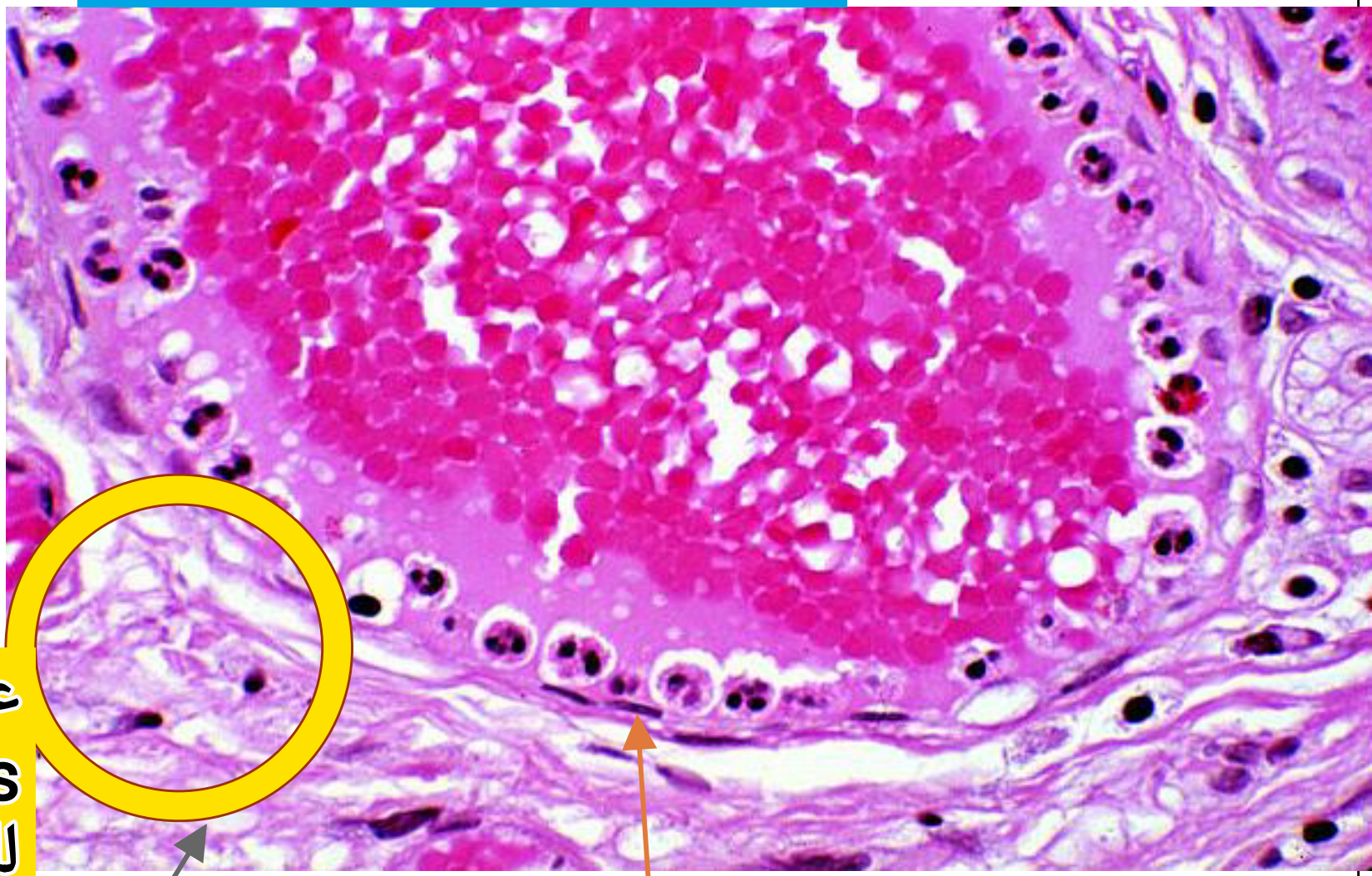
- The first leukocyte marginated is neutrophil.

Margination, Rolling, Emigration & Phagocytosis:-



Margination and adhesion of neutrophils to the endothelium

مصبوغة بH&E



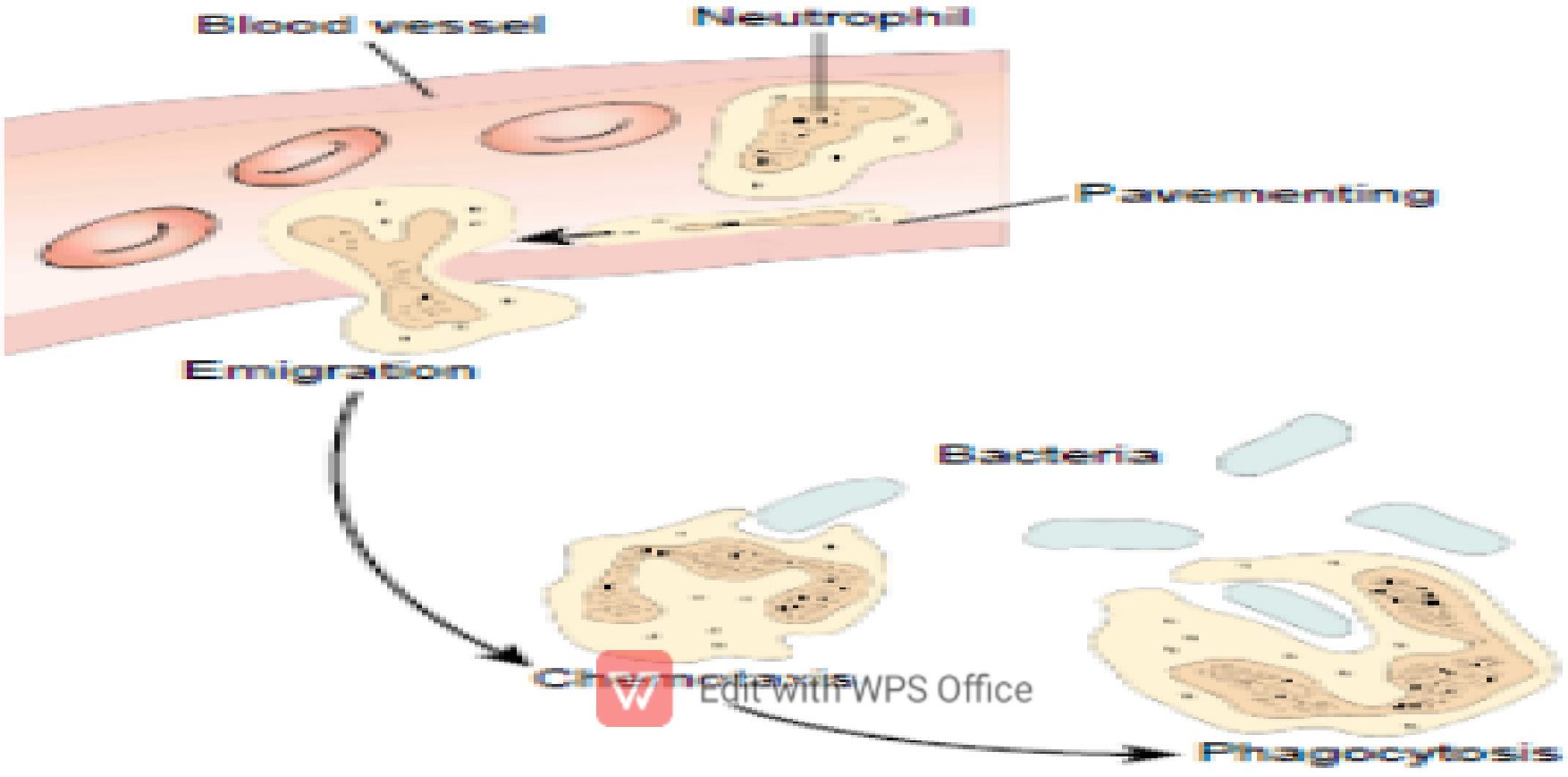
عندما تخرج neutrophils للاطراف يصبح emegration

Margination → neutrophils are attached to the B.V

2. Emigration:

CD31 facilitates

The leukocytes send pseudopodia that pass through the capillary walls then by ameboid movement migrate into the tissue spaces.



3. Chemotaxis:-

Process by which leukocytes migrate in response to a chemical signal.

Leukocytes move through the tissue guided by secreted cytokines:-

Chemokines.

Interleukin.

Bacterial & cellular debris.

Complement fragments (C3a, C5a).

4. Phagocytosis:

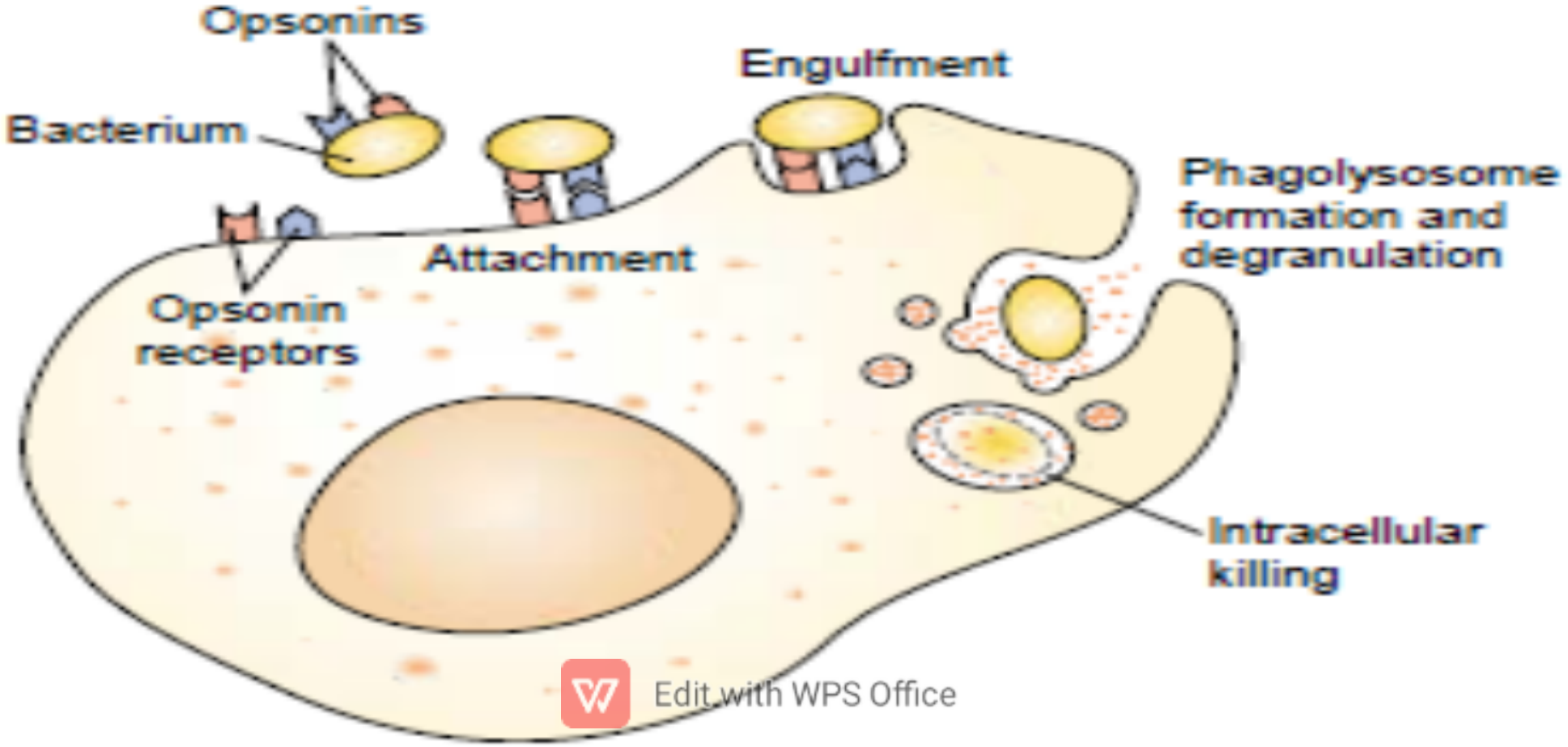
Engulfment & degradation of bacteria & cellular debris by Neutrophils & Macrophages

Phagocytosis: three steps:

1. Adherence + opsonization.
2. Engulfment.
3. Intracellular killing.

Opsonization

Coating of antigen with antibody or complement so enhance the binding of antigen to leukocytes. (Adherence)



Phagocytosis

1- Recognition of the agent as foreign leading to adherence and opsonization.

2- Cytoplasmic extensions (pseudopods) surround this foreign agent.

3- Fusion of the membrane forming phagocytic vesicle (Phagosome)

4-The phagosome merges with a lysosome that containing antibacterial molecules and enzymes that digest the microbe

Outcome of acute inflammation:

1- Resolution.

2- Progression to chronic inflammation.

3- (Pus formation).

4- Scarring and fibrosis. (with chronic inflammation)

Factors affect the Outcome of acute inflammation:

1. The nature and intensity of the injury.
2. The site and tissue affected.
3. The ability of host to mount the response.

مثلا بالجلد والكبد هنالك قدرة ع التضاعف فيتم انشاء خلايا جديدة مكان التي تدمرت
لكن بالقلب والدماغ (liquefactive necrosis)يبقى المكان فارغ ولن تنمو خلايا جديدة

1- Resolution:

Regaining normal histological & functional state of the tissue.

It occurs when there is:

a. Limited or short lived injury. (simple / extreme)

b. Minimal or no tissue damage.

c. A tissue which is capable of replacing any type of injured cells.

Point 2 : the hepatocytes, skin and GI can proliferate to regenerate the damage

But the liquefative necrosis in the brain is irreversible damage because the cells cant proliferate

2- Progression to chronic inflammation:

Chronic inflammation occur if:

a. The offending agent is not removed. → like TB

b. There is extensive initial tissues injury.

c. There is decreased capacity of the affected tissue to re-grow.

Chronic inflammation may be followed by restoration of the normal structure and function or may lead to scarring.

3- Pus formation

Pus: A purulent inflammatory exudate caused by pyogenic bacteria, and it is a manifestation of healing that result in granulation & scaring.

Pus is formed of:

1. Living & dead neutrophils.
2. Bacteria.
3. Cellular debris.

Pus is surrounded by pyogenic membrane formed of capillaries, neutrophils and fibroblast led to the formation of **abscess.**

4- Scarring and fibrosis:

Acute→ chronic →scarring & fibrosis

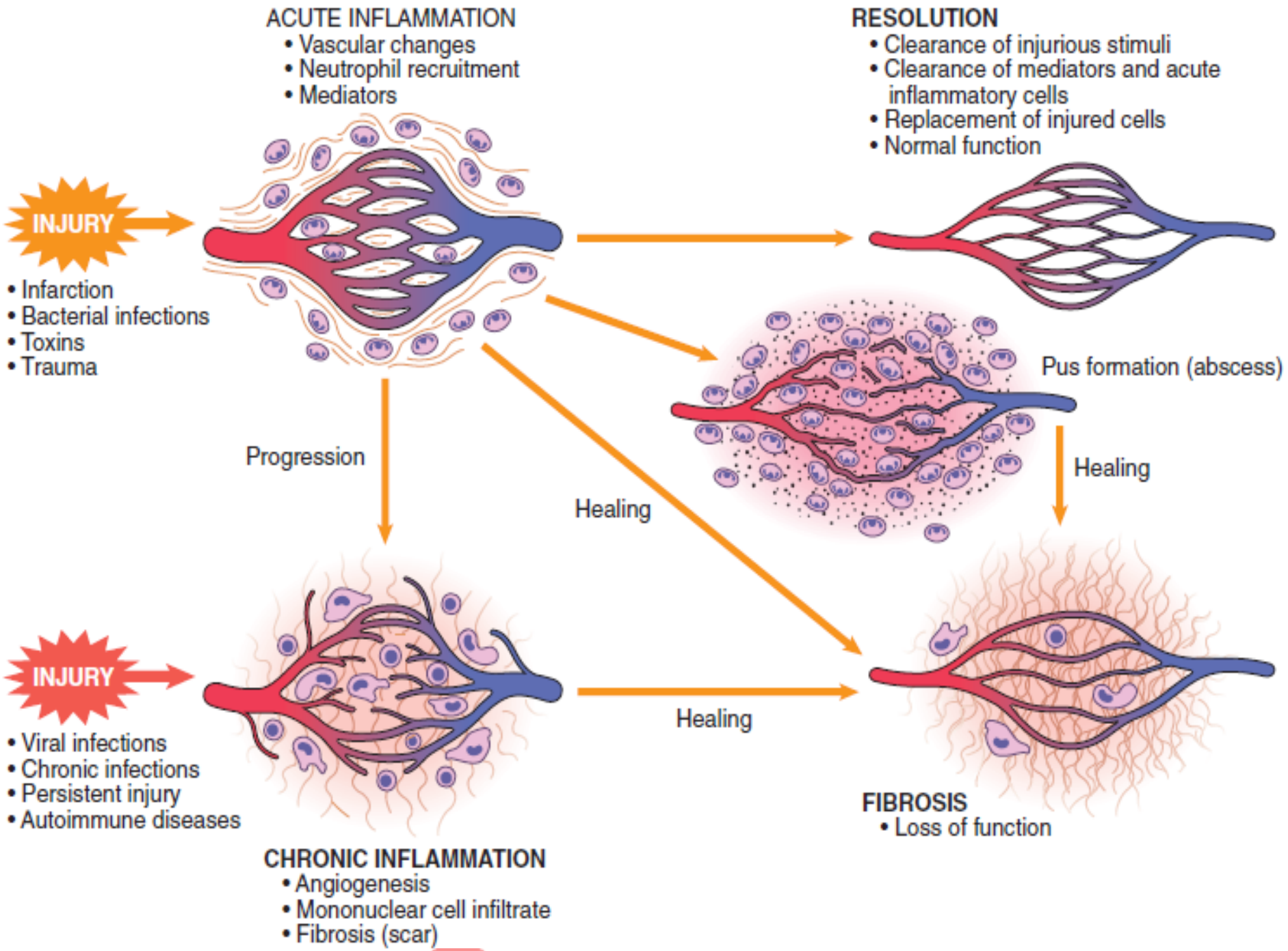
In long term injury (not capable to regenerate)

Replacement of the injured tissue by fibrous connective tissue.

This occurs:

1- If we have large tissue destruction.

2- If the inflammation occur in tissue that do not regenerate.



Outcomes of acute inflammation: resolution, scarring (fibrosis), or chronic inflammation

https://www.youtube.com/watch?v=B9Qi7we0Ynk

THANK YOU