

Inflammation

What's inflammation(التهاب)?

--> Its an immuno-vascular response of the living vascular tissue against harmful factors.

هو عبارة عن استجابة النسيج الحي المناعية ضد اي عامل ضار.

-->Its the way by which the body defense mechanisms come outside the blood to fight the causing factor.

يعتبر الالتهاب هو الطريقة التي عن طريقها بتخرج عوامل الدفاع من الدم لمنطقة الاصابة.

طب ليه بيحصل الالتهاب؟

The puposes of inflammation are:-

- Elimination of the causing factor
- Clear out the necrotic tissue (الانسجة الميتة)
- Initiate the tissue repair

الالتهاب بيحصل عشان، التخلص من العامل الضار، التخلص من الانسجة الميتة، و تهيئة النسيج المصاب للتصلح.

اسباب الالتهاب

Causes of inflammation:-

1- living agent:

- Bacteria or their toxins
- Viruses , parasites or fungi

2- Non-living agent:

- physical agent: burn and radiation (اشعاع)
- Chemical irritant
- Mechanical agents : wounds or fractures

3- Antigen-antibody reaction and autoimmune diseases.

تفاعل الأنتيجين مع الجسم المضاد بتاعه، و امراض المناعة الذاتية.

4- Necrotic tissue.

ايه اعراض inflammation ؟

Cardinal signs of inflammation.(only appears in acute inflammation):

1- Redness and hotness: due to vasodilatation.

الدم اللي بيصل المنطقة المصابة بيسبب احمرار و سخونة (الدم سخن)

2- Swelling: due to inflammatory exudate

بيحصل تورم ف منطقة الالتهاب بسبب الافرازات الالتهابية التي هتشرح حالاً

3-pain: due to irritation of nerve endings by toxins , histamine and bradykinin, or mechanically due to swelling.

بنحس بالألم لما يحصل اضطراب في النهايات العصبية و دا بيحصل عن طريق يا اما السموم (من البكتيريا مثلاً) او بسبب افراز الهستامين او بسبب الضغط اللي بيحصل نتيجة تورم المنطقة.

4-loss of function.

Vascular Phenomenon

Its the process by which the blood cells and plasma come out the blood vessels to the area of inflammation and form the “inflammatory exudate”.

***steps of inflammatory exudate:**

1. Transient vasoconstriction by the toxins or the trauma.

ضيق مؤقت ف الأوعية الدموية

2. Vasodilatation due to:
Histamine and stimulation of the vasodilator nerve.

3. Slowing of circulation:(stasis) due to:

- Vasodilatation
- swelling of endothelial cells
- Hemo-concentration(زيادة تركيز الدم)

سريان الدم بببطاً بسبب

- توسع الشرايين

- و تورم الخلايا المبطنة للشرايين و بالتالي بيزيد الاحتكاك

- كما ان بسبب ان مونت الخلايا خارج الوعاء الدموي بيزيد من تركيز البروتين خارج الوعاء الدموي عن داخله و بالتالي هتنتقل البلازما من داخل الوعاء لخارجه، و كذا هيزيد تركيز الدم و لزوجته.

4. Escape of plasma and formation of the inflammatory exudate.

عرفنا ليه البلازما بتطلع خارج الوعاء و يكون الافرازات الالتهابية و دي بتكون السبب ف ورم المنطقة الملتهبة.

5. Leukocytes extravasation:

Its the movement of blood leukocytes outside the blood vessel to the area of inflammation(**Diapedesis**).

6. RBCs movement outside the blood vessels by **sliding movement**.

Leukocytes extravasation

1. Chemoattraction:

--> recognition of pathogen by the leukocytes , then , the leukocytes release cytokines(IL1-TNF α)

--> Endothelial cells near the infection release selectin.

2. Rolling adhesion:

--> leukocytes bind to selectin by its receptors

3. Tight adhesion:

--> The macrophage cytokines activate integrin in the surface of the leukocytes.

--> integrin binds the leukocytes tightly to the endothelium by receptors for integrin.

4. Transmigration:

--> leukocytes show pseudopodia(زوائد)

--> They pass through gaps between the endothelial cells , towards the site of infection.

https://youtu.be/HiJ_tcQJUwM الفيديو دا موضح الآلية

Inflammatory exudate(edema):(الافرازات الالتهابية)

– Its the fluid formed of plasma and blood cells that came outside the blood vessels by the vascular phenomenon.

بيتكون السائل دا من بلازما و خلايا الدم و بيقوم بوظيفة دفاعية في حالات الالتهاب.

ايه هي وظيفته؟

Functions of inflammatory exudate:

1- functions of cellular part: (netrophil)

They phagocytose and kill the microbes by ROS and lysosomal enzymes. If they die they change into pus cells(خلايا صديد).

خلايا النوتروفيل بتبلع الميكروب الضار دا و تحلله ، و لو ماتت تتحول لخلايا صديد.

2-Functions of fluid part(plasma):

1-Dilution of toxins

2- It contains fibrinogen which forms fibrin threads to localize the infection.

3- It contains the antibodies that have the following functions:

a) Neutralization: Antibodies prevent the adhesion between pathogens and mucosa and block the active site of toxins. (بتفقد السموم وظيفتها)

b) **Opsonization**: the antibodies surround the bacteria and help their phagocytosis.

العملية دي اسمها opsonization

c) Agglutination: Antibodies cause gathering of bacteria together ; to limit their spread , and help their phagocytosis.

d) Antibody-mediated cell cytotoxicity: Antibodies attach themselves to the target cells and cause their destruction by nonspecific immune cells

بيكون الوسيط ما بين الجسم الضار و خلايا المناعة القاتلة.

e) Activation of complement system

هيتشرح دلوقت

f) Inflammation (chemotaxis)

* **Chemotaxis:**

Its the attraction (انجذاب) of the leukocytes toward the site of infection by chemicals like, bacterial toxins, necrotic tissue or complement system.

* **Complement system:**

Its a part of the immune system consisting of number of small proteins circulating in the blood.

-- Its formed by the liver , and found normally in the inactive form.

مجموعة من البروتينات موجودة في بلازما الدم في حالة غير نشطة تحت الظروف الطبيعية .

Functions of complement system:

1- inflammation: **C3a-C5a** (anaphylatoxins) which stimulate the release of histamine. **C5a** attracts the leukocytes.

2- cell lysis: its achieved by **C5b**

3- opsonization: its achieved by **C3b**

Phagocytosis:

Its the engulfing (ابتلاع) of the foreign bodies as bacteria and debris (بقايا البكتيريا).

- These cells are called phagocytes. They are **Neutrophil & Macrophage**.
- It aims to clean the area for the repair.

بتنظيف المنطقة وتجهزها عشان تتجدد و تتصلح.

Histamine:

Its a nitrogenous compound produced by mast cells and basophils, during of antigen antibody reactions.

هو مركب بيطلق بسبب اتحاد الالتيجن بالجسم المضاد.

–It causes vasodilatation , and increases the capillary permeability to the leukocytes and plasma.

–It can act as a neurotransmitter , and plays a role in allergies and hypersensitivity reactions.

ليها الدور ف اعراض الحساسية.

Differences between acute and chronic inflammation

	<u>Acute inflammation</u>	<u>Chronic inflammation</u>
onset (بداية ظهور) (الاعراض)	rapid	gradual
Duration	few days	months or years
Cardinal signs	present	absent (مالوش الاعراض اللي قولنا عليها ف الاول)
Toxemia	acute (مؤقتة)	chronic (مزمنة)
the inflammatory cells	Neutrophils and pus cells , eosinophils and basophils	Macrophages and lymphocytes, plasma cells , giant cells and fibroblasts
edema (تراكم) (السوائل ف الانسجة)	present	absent
blood vessels	Numerous , thin walled (due to short duration) and dilated	less numerous, thick walled and may show

		endarteritis obliterans(التهاب بطانة الوعاء الدموي لدرجة الانسداد)
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Important Cells of inflammation:

- 1- **pus cells:** they are dead neutrophils
- 2- **eosinophils:** wbc's that appear in allergic and parasitic inflammation

Biologic change in inflammation:

1- fever

2- **leucocytosis** (increase in number of leukocytes)

- neutrophils: in suppurative inflammation
- Eosinophils: in parasitic and allergic inflammation
- Lymphocytes: in chronic and viral inflammation

3- **changes in the organs:**

- hyperplasia of reticulo-endothelial system
- Reversible change in organs as cloudy swelling and fat accumulation
- Cell death (necrosis)
- Toxemia, sepsis, pyemia

Chemical mediators of inflammation:

They are chemicals that are released in cases of inflammation and responsible for vascular and cellular events.

هي مواد كيميائية تقوم بوظيفة الوسيط (mediator) التي يبحفز حدوث الاستجابات المناعية أثناء الالتهاب.

-They are either cell derived or plasma derived.

***cell derived:**

1- **prefomed mediators in granules**(مصنوعه مسبقا)

- Histamine
- Serotonin
- Lysosomal enzymes

2- **Newly synthesized**(بتتصنع بعد حدوث الالتهاب)

- Prostaglandins
- Leukotrienes
- Platelet activating factor(PAF)
- Reactive oxygen species(ROS)
- Nitric oxide
- Cytokines(TNF , IL1)

***plasma derived:**

1- **Factor XII (Hegman factor) activation**

a-kinin system: bradykinin

b-coagulation /fibrinolysis system

تنشيط Factor XII وينشط ال kinin system الكلي له وظيفة دفاعية ، و كما ان ينشط عملية التجلط .

2- complement system activation.

تنشيط ال complement system ويكون وسيط لاستجابات مناعية زي ما شرحنا .

Actions of these mediators:

- 1- Histamine: Vasodilatation, increase vascular permeability, endothelial activation.
- 2- Serotonin: Vasodilatation, increase vascular permeability
- 3- Lysosomal enzymes: proteases and hydrolases.
- 4- Prostaglandins: Vasodilatation, pain, fever.
- 5- Leukotrienes: increase vascular permeability, chemotaxis, leukocytes adhesion and activation
- 6- Platelets activating factor: Vasodilatation, increase vascular permeability, leukocytes adhesion, chemotaxis, degranulation, oxidative process
- 7- Reactive oxygen species: killing of microbes, tissue damage
- 8- Nitric oxide: Vascular smooth muscle relaxation, killing of microbes.
- 9- Cytokines (TNF, IL1): Local endothelium activation (expression of adhesion molecules), fever, pain, anorexia, hypotension, decrease vascular resistance
- 10- Hageman factor (Factor XII) activation: kinin cascade, clotting/ fibrinolytic systems, complement cascade
- 11- Kinins: increase vascular permeability, smooth muscle contraction, vasodilatation, pain.
- 12- Coagulation/ Fibrinolysis system: clotting cascade, fibrinolytic system
- 13- Complement activation: cell lysis, inflammation, opsonization

ايه تاثير ال inflammation؟

A) Beneficial effect: dilution of toxins, phagocytosis , localization of infection, and eliminate the causing agent.

B) Harmful effect:

1. Swelling of inflamed tissue that causes loss of function
2. Healing by fibrosis leads to narrowing , pressure atrophy (ضمور الخلايا نتيجة الضغط) and organ dysfunction.
3. Hypersensitivity: in cases of allergies
في حالات الحساسية يحصل استجابات الالتهاب لأسباب عادية مش محتاجة، و في الحالة دي يعتبر الالتهاب ضار بالجسم.