Pathology

INFLAMMATION

LECTURE (3)

As a doctor you should know what can threaten your patient's life
you should know what makes your patient suffers from pain
THAT'S WHY YOU LEARN PATHOLOGY

Definition: BLUE Examples:GREEN Important: RED Extra explanation:GRAY Disease names: **UNDERLINE**.

Lecture(3) Outlines

- Definition of chemical mediators.
- The types of chemical mediators.
- Cell derived chemical mediators.
- Plasma derived chemical mediators.(complement system and kinin system)
- The chemical mediators effects.

Definition of chemical mediators

- Chemical mediators are responsible for the vascular and cellular events in acute inflammation.

- 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).

Types of chemical mediators

Chemical meditators are divided into two types :

A- Cell derived: (مشتقه من الخلايا)

- Mast cells
- Macrophages
- Platelets
- Lymphocytes
- Basophils
- Endothelial cells

B- Plasma protein derived:

(Proteins that are usually manufactured by the liver and released to the circulation)

- complement system
- kinin system

Cell derived chemical mediators : Histamine + Serotonin

Histamine	Serotonin *(5 hydroxytryptamine)*
secreted by basophils, mast cells and platelets. *it causes Endothelial activation. *mast cells+basophils have granules that contain histamine. *increases vascular permeability especially in allergic reactions. e.g. when a bee stings you its antigen will cause allergic reaction (redness - pain or death) this will stimulate the immune globulin " IgE " which is responsible for allergic reaction . IgE is coated the outer surface of mast cell , the antigen will site on the FC part . after this binding the mast cell will release its granules so the histamine will be released.	**secreted by platelets** *it comes from metabolized amino acid called tryptophan. **it causes: vasoconstriction.* *platelets play a major role in coagulation. *when we have platelets aggregation, that means we have a clot; when the platelets disaggregate that means the blood flows freely (we don't have a clot) .*
***Both cause vascular dilatation and increased vascular permeability**	

Cell derived chemical mediators : Prostaglandins+Leukotrienes

Prostaglandins	Leukotrienes
***Are metabolites of Arachidonic Acid (found in cytoplasmic membranes of inflammatory cells (cell membrane phospholipids)** *** they both are secreted by : mast cells and leukocytes**	
***Cause vascular dilation, fever, pain and it sometimes increase vascular permeability.** **all medicines* (المضادة للحراره و الالم) are (anti-prostaglandin) ***The enzyme (phospholipase) influences the phospholipids in the cell membrane of inflammatory cell** *neutrophils,macrophages and others.* ***Phospholipase will make arachidonic acid** (two enzymes act on it) : **Cyclooxygenase, lipoxygenase** ; as a result of this, Leukotrienes, Thromboxane A2,Prostacyclin,Prostaglandins	*** 4 types : A_4 - B_4-C_4-E_4** **A_4-C_4-E_4 :** ***bronchospasm** ***increase vascular permeability.** **B_4 :** **Is chemotactic; (makes chemotaxis) → (directional migration of inflammatory cells from blood vessels to site of injury (site of antigen)** ***leukotriene causes :** **-increased vascular permeability** **- chemotaxis** **-leukocyte adhesion and activation.**

More details on Prostaglandins

Cyclooxygenase		Lipoxygenase	
COX-1 , COX-2 **=formation of prostaglandin G2 , H2** **this will transform into:** **thromboxane A2 and prostacyclin PGI2**		***Formation of** **lipoxin and leukotriene**	
thromboxane A2	**prostacyclin PGI2**	**lipoxin**	**leukotriene**
***vasoconstriction** ***aggregation to platelets** **platelets contribute in thrombosis (coagulation)* **platelets are different from coagulation factor; because : platelets are cells coagulation factor is a substance*	***vasodilation** ***inhibits platelet-aggregation**	***antagonize the prostaglandins** "anti-prostaglandins" **inhibit neutrophil adhesion and chemotaxis*	*** C_4 ,D_4 ,E_4 ,B_4** **C_4 ,D_4 ,E_4 :** ***bronchospasm** *(major symptom in asthma)* ***increased vascular permeability** **B_4 :** ***chemotactic**

you need to know: the source of these chemical mediators - how to inhibit them - action of each one of them

If this metabolic pathway CONTINUED we will have ...
Prostaglandins E_2 , D_2 ; which cause vasodilation, increase vascular permeability that we see in inflammation.

TO STOP THE FORMATION OF PROSTAGLANDINS
I may give the patient steroids cortisone and this is one of the actions of cortisone;as it inhibits the action of phospholipase and stop the formation of arachidonic acid. **steroids are very important in inhibiting action of phospholipase.*

More details on Prostaglandins

مبدأ علاج الألم و الحرارة الي تسببه ال Prostaglandins يعتمد على:

anti COX-1 and anti COX 2

***they are anti prostaglandins; their role is to inhibit cyclooxygenase and stop it forming prostaglandins → pain,vasodilation,increase vascular permeability**

no vasodilation → no congestion ,

***no increased vascular permeability → no edema(**تضغط على نهاية العصب و تسبب ألم , no swelling)

***steroids are more effective in *earlier* stages.**

Cell derived chemical mediators : Nitric oxide - ROS - Lysosomal enzymes - Cytokines

Nitric oxide (NO)	Reactive O_2 species (ROS) (free radicals)	Lysosomal enzymes	Cytokines
*Secreted by endothelial cells and macrophages *Causes: - vasodilation which is *relaxation of smooth muscle cells of the blood vessels* - helps in the killing of bacteria.	*Cause tissue damage, kill bacteria	In inflammatory cells (especially in: macrophages and neutrophils) *They lyse protein and cause tissue damage as well as attacking microbes and bacteria.	secreted by: macrophages and lymphocyte *very important cytokines that play major role in inflammation :* TNF: tumor necrosis factor IL: interleukin, IL1 and IL6 *cytokines cause: 1- activate the adhesion molecules 2- promote the acute phase response 3- shock

Cell derived chemical mediators : SUMMARY

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<tr><th>Histamine</th><th>Serotonin
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Plasma derived chemical mediators

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<tr><th colspan="2">Complement</th><th>Kinin System</th><th>Coagulation protein</th></tr>
<tr><td colspan="2">*Proteins secreted by liver and found in plasma (they are acute phase proteins; which occur as a systemic manifestation of acute inflammation → C-reactive protein) and released in circulation; those proteins are activated through two pathways:</td><td rowspan="4">*They are also proteins; they are released to the circulation and they are activated by the coagulation factor (factor 12)(Hageman factor) which acts on: *kinins (proteins released by liver) *help in transformation of prekallikrein (kinin product) to kallikrein to bradykinin(end product)(bradykinin is the source of pain in inflammation)</td><td rowspan="4">------</td></tr>
<tr><td>(1)
CLASSIC PATHWAY</td><td>(2)
ALTERNATE PATHWAY</td></tr>
<tr><td colspan="2">as a result of this activation (according to inflammation) we consider three components for complement :
C3a , C5a , C3b</td></tr>
<tr><td>C3a , C5a
*a → activated

-They promote chemotaxis
- Help in recruitment and activation of leukocytes.</td><td>C3b
----
-Opsonization, because C3b is an opsonin → (an opsonin is a protein capable of coating the particle & bacteria and help in phagocytosis)
opsonins can also be immunoglobulins (5 groups) :
A , G , M , E , D
they are also capable of coating the particles and helping in phagocytosis.</td></tr>
</table>

What are phagocytic cells?

1-Macrophages
2-Neutrophils
3-Eosinophils (weakly phagocytotic)

Effects of Chemical Mediators

Cell Derived Chemicals

Mediator	*Effect*
Histamine	**both cause vascular dilatation and increased vascular permeability**
Serotonin	
Prostaglandins	**causes vascular dilation, fever, pain and sometimes increase vascular permeability.**
Leukotrienes	**increase vascular permeability.**
Reactive O_2 species (ROS)	**Cause tissue damage, kills bacteria.**
Nitric oxide	**Causes relaxation of smooth muscle cells and helps in the killing of bacteria.**
Lysosomal enzymes	**lyse protein and cause tissue damage as well as attacking microbes and bacteria.**

Plasma Derived Chemicals

Mediator	*Effect*
Complement	**CLASSIC PATHWAY:** promote chemotaxis, and help in recruitment and activation of leukocytes.
	ALTERNATE PATHWAY: opsonization, and they are also capable of coating the particles and helping in phagocytosis.
Kinin System	help in transformation of prekallikrein (kinin product) to kallikrein to bradykinin (end product) (bradykinin is the source of pain in inflammation)
Coagulation Protein	____

HOPEFULLY WE DID A GREAT JOB

ONLINE TEST

FOR ANY QUESTIONS AND SUGGESTIONS CONTACT US ...

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To make sure that all students are aware of any changes, please check out this link to know if there are any additions or changes.
The same link will be used for all of our work:
(Pathology Edit)

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- ❑ Sarah AlHussein

DIFFICULTIES IN YOUR LIFE DON'T COME TO DESTROY YOU.. BEST OF LUCK