



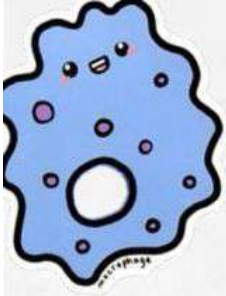
Immunology

Title : Inflammation and leukocyte migration

Lec no : 5

Done By : Laith

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السلام عليك ❤️

تفريغ المحاضرة ال ٥ بين ايديكم لكن قبل ما ندخل لازم تعرف انه

الكلام اللي باللون الاسود ← السلايدات

الكلام اللي باللون الاحمر ← كلام الدكتور

الكلام اللي باللون الازرق ← من شرح دفعة أثر ومن النت

- حضرت شرح نينجا نيرد لمحاضرة ال inflammation ورسمت وراه وفرغت كلامه فحببت اضيفه بالتفريغ اخر اشى ورح احطلكم الفيديو اذا حاب تشوفه بس فش داعي ترجع للفيديو لاني فرغت كل اشى ممكن يتفرغ 😊



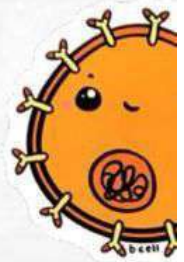
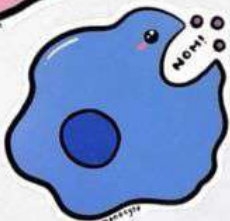
Immunology | Inflammation: Vascular Events: Part...

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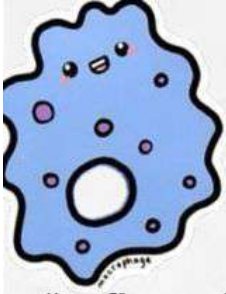
youtu.be

وهسا بنقدر نحكي

بسم الله نبدأ...



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Introduction



“Inflame” –to set fire (بالعامية نولعها)

Inflammation is “A dynamic response of vascularised tissue to injury.”

Inflammation: Local defense and protective response against cell injury or irritation or local vascular and cellular reaction, against an irritant.

It is a protective response.

It serves to bring defense & healing mechanisms to the site of injury.

Inflammation is designated by adding the suffix (itis) to the end of the name of the inflamed organ or tissue.

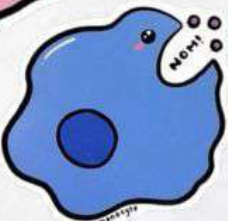
-like : osteomyelitis(inflammation of Bones)

Sinusitis(inflammation of nose)

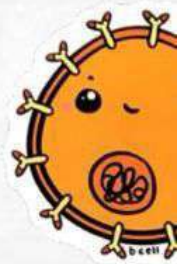
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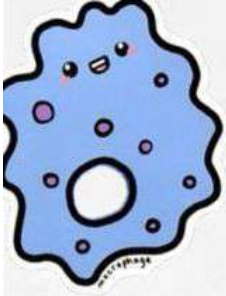
- the benefit of inflammation : It is a protective response

فكرة inflammation هي contains invading micro organisms and destruct them



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Etiology

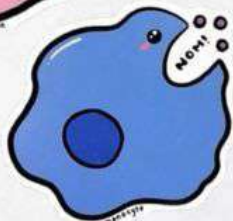


(What can cause infalmmatin ?)

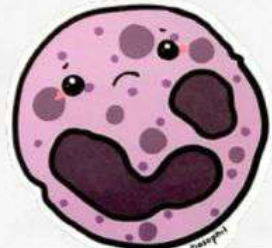
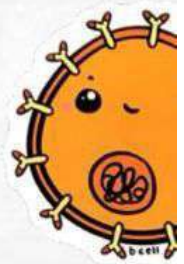
- Microbial infections: bacterial, viral, fungal, etc.
- Physical agents: burns, trauma—like cuts, radiation
- Chemicals: drugs, toxins, or caustic substances like battery acid.
- Immunologic reactions: rheumatoid arthritis. ↴

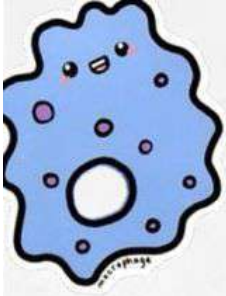
- بصير عندي hyperactivation of immune system وهاض الاشي رح
يأثر على ال joints وبعلمي التهاب بالمفاصل يسمى بال Rheumatoid

- هون ال inflammatin غير مرغوب فيه لانه صار chronic



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Types

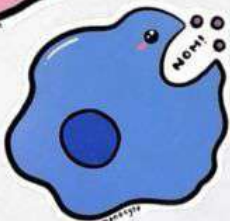


•Time course

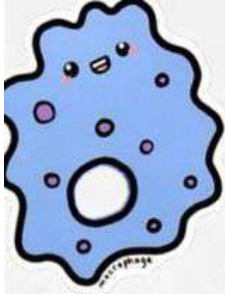
- Acute inflammation: Less than 48 hours
- Chronic inflammation: Greater than 48 hours (weeks, months, years) like : rheumatoid arthritis

•Cell type

- Acute inflammation: Neutrophils
- Chronic inflammation: Mononuclear cells (Macrophages, Lymphocytes, Plasma cells).



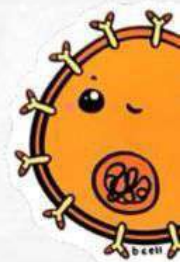
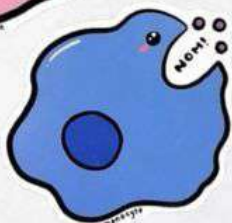
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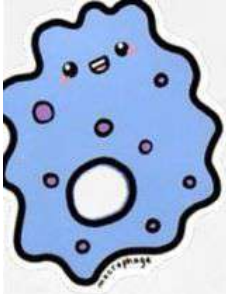
Cardinal Signs of Inflammation



- Redness : Hyperemia.
- Warm : Hyperemia
 - Redness and warm will cause vasodilatation that mean more perfusion
- Swelling : Exudation
 - swelling due to leakage of fluid (VD)
- Pain : Nerve, Chemical mediators.
- Loss of Function: Pain
 - There are 2 reasons for pain :
first reason is mechanical (edema then pressure on nerves)
the second is release chemical mediators



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Pathogenesis



The vascular & cellular responses of inflammation to an inflammatory stimulus.

are mediated by chemical factors (derived from blood plasma or some cells) & triggered by

Three main processes occur at the site of inflammation, due to the release of chemical mediators :

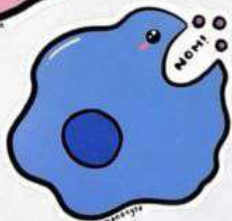
1. Increased blood flow (redness and warmth).
2. Increased vascular permeability (swelling, pain & loss of function).
3. Leukocytic Infiltration.

cellular response :

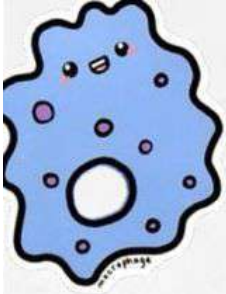
chemoattractant and cytokines يحدث نتيجة حدوث ضرر بالخلية مما ينتج افراز

من شرح الدكتور لأثر

- what are the difference between cytokine and chemokine ?
 - Cytokine : signal molecules that might mediate the inflammatory process that might help in complement activation and it has different function .
 - Chemokine : they are specific signal molecules that attract with the immune system to the injured site .



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Local Vascular Changes



- Initial temporary vasoconstriction for few seconds.

- Active vasodilatation of arterioles and capillaries by chemical mediators like histamine and passive dilatation of venules.

- Slowing of the circulation: outpouring of albumin rich fluid into the extravascular tissues results in the concentration of RBCs in small vessels and increased viscosity of blood (stasis).

-نتيجة خروج البروتينات و ال fluids بسبب حدوث VD هاض بجعل تركيز ال RBC كبير وييب في بطئ في الحركة في هاي المنطقو او المناطق المجاورة

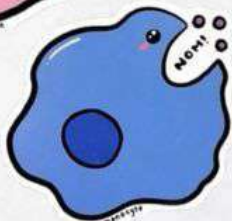
- Pavmentation: the margination of leukocytes. Neutrophils become oriented at the periphery of vessels and start to stick.

- Pavmentation:

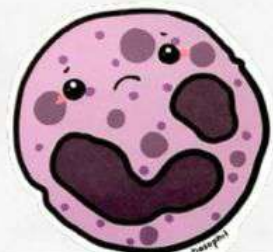
It's margination of leukocytes to site of infection

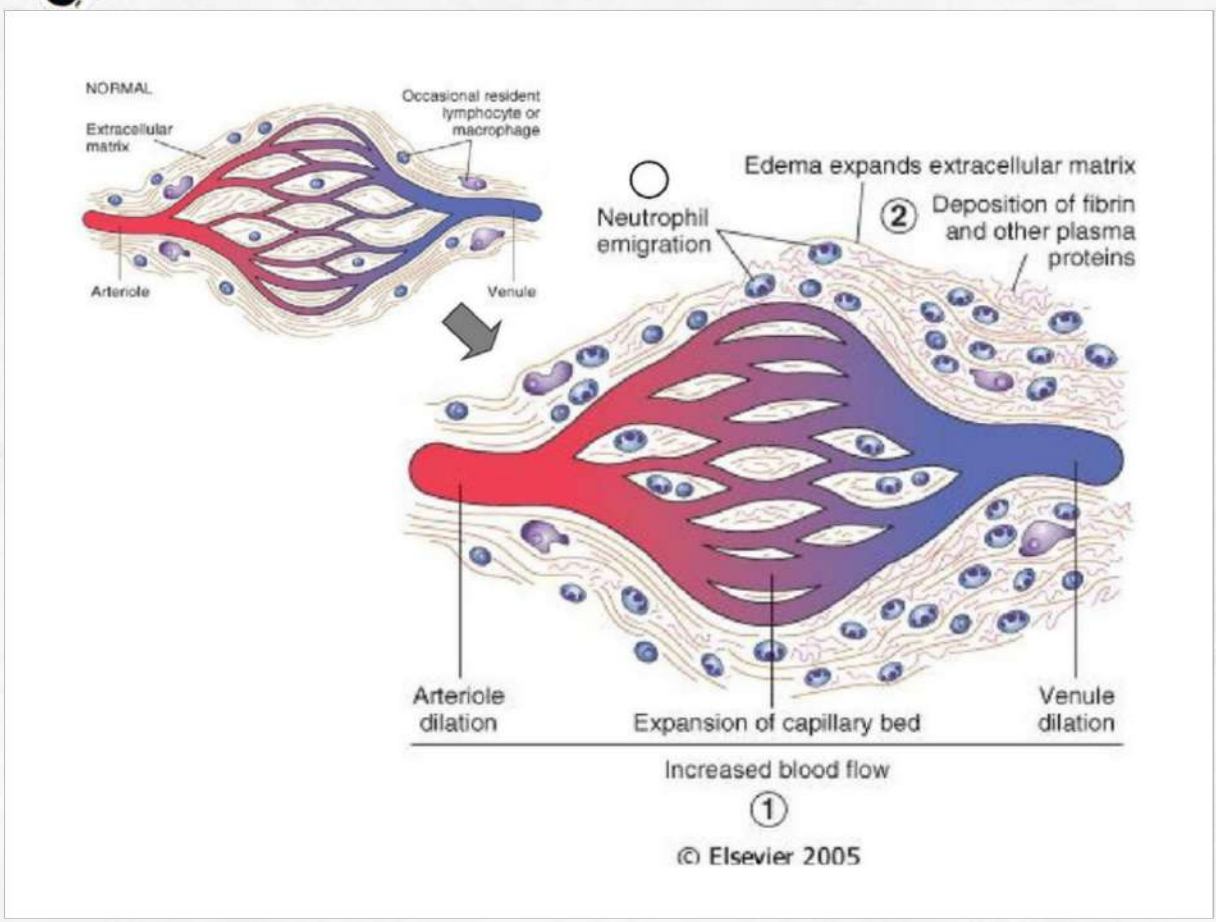
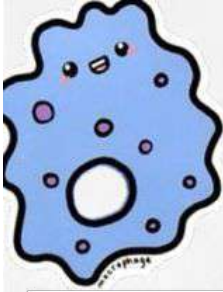
وذلك يحدث عن طريق حدوث slowing

و التصاق ال leukocytes بال epithelium ثم الذهاب لل site of infection

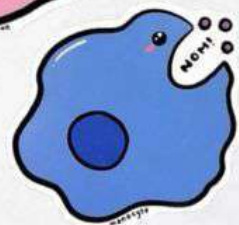


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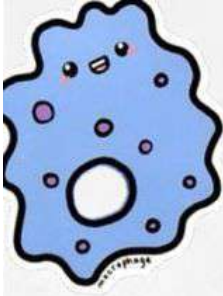




هاي الرسمة تمثل التغيرات التي سوف تحدث في ال
site of infection



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Leukocyte Exudation



- Leukocytes (PMN's , Mphages, lymphocytes, mainly T) circulate in the blood, but often do their work in tissues.

صحيح انهم يكونوا في الدم ولكن حتى يقوموا بشغلهم لازم يكون في ال
tissue and site of infection

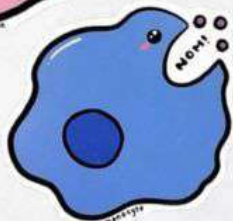
- For T and B cells, circulation increases the chances that you'll meet your antigen.

ال T and B cells يكونوا في الدم للبحث عن أي Ag وتذكر انه العملية هاي
عشوائية

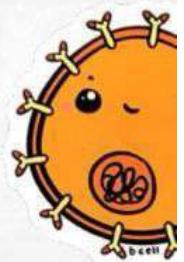
- For both to do their jobs, however, you often have to leave the blood to enter either the lymph node or the site of damage.

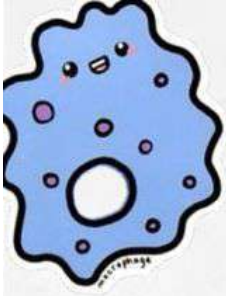
- Once at the site of damage, you want to kill microbes, control the damage, and repair it.

(وهاض الهدف من العملية كلها)



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Leukocytes Extravasation



Neutrophils are usually the first cells to move to site of infections or inflammations

1. Rolling: mediated by selectines
2. Activation by chemoattractant stimuli
3. Arrest and adhesion mediated by Integrins binding to Ig-family members
4. Transendothelial migration

Neutrophil extravasation involves 4 main stages:
lec5. Inflammation-and-leukocyte-migration.pdf

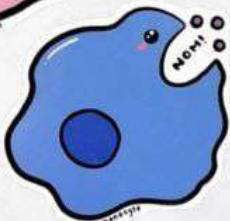
في هاي الحالة لازم نركز على التغيرات اللي بتصير على ال tissue that injured وكمان ايش التغيرات اللي بتصير على ال leukocytes نفسها اللي رح تساعدنا في عملية ال Leukocytes Extravasation وانتقالها من extravascular → intravascular

- which are the first cytokines that initiate the process of Leukocytes Extravasation????

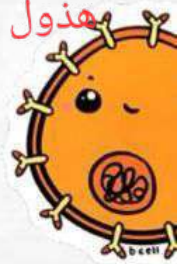
- 1) TNF
- 2) interleukins 1

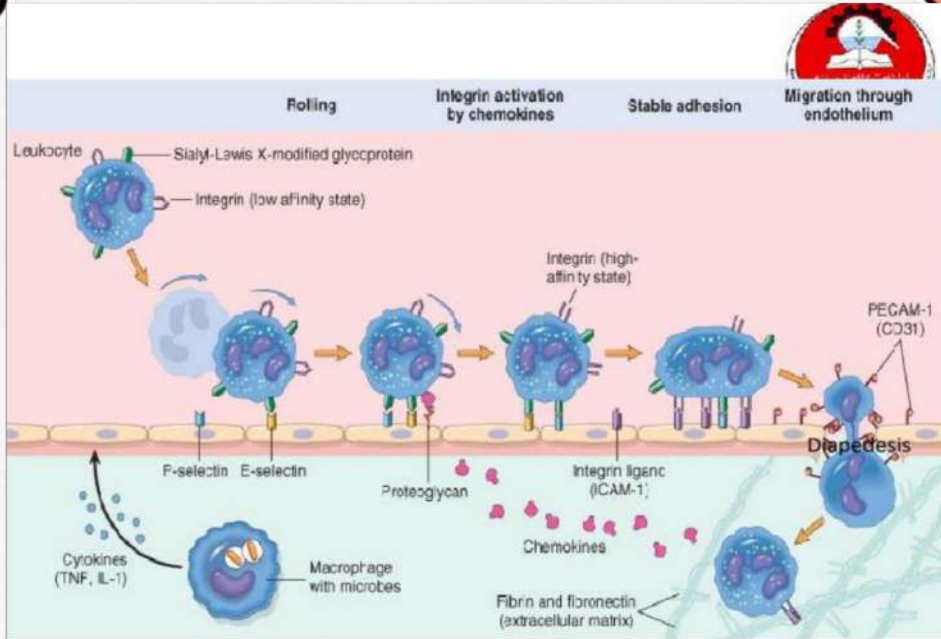
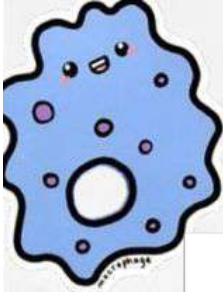
هذول يتم افرازهم عن طريق ال macrophage عند ابتلاع ال microbe

الرسمه الجاي مهمة جدا



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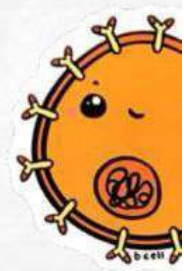
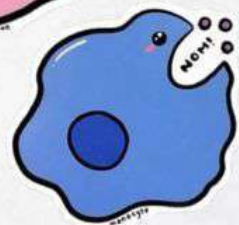


• بالبداية رح يصير عندي VC بعدين VD ثم بصير عندي leakage of fluid and protein
 • Leukocytes Extravasation ال تمبدا عملية

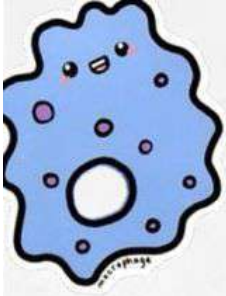
• بعد افراز ال TNF and IL-2, هذه رح يحفز ال epithelium على عمل
 • expression ل (E,P) selectins

-selectins (E,P) : they are receptors to carbohydrates Ag that located on surface of leukocytes (they are sialyl lewis (x) and integrin)

ال integrin بمروا في مرحلتين اللي هما ال low affinity ang high affinity



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بعدين بصير عندي slow of circulation ثم تبدأ عملية ال rolling process ويحدث هناك ارتباط بين ال (integrins with selectins) بعدين بصير production of chemokines from macrophage and chemoattractants ثم يتم إفراز endothelium surface of vessels الذي بدورها ترتبط مع proteoglycan receptors on the inside of endothelium ونتيجة لهاض الارتباط فان ال integrin تتحول من ال low الى ال high affinity

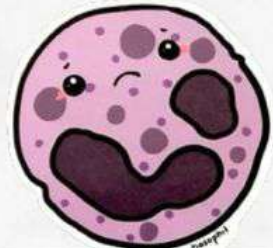
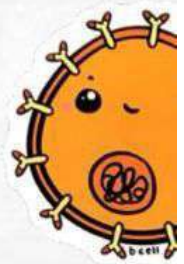
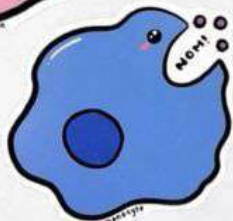
- example of low affinity (LFA-1 , VLA4) receptors

وبنفس الوقت ال chemokines (TNF,IL-1) بحفزوا تصنيع integrin ligand of high affinity (ICAM-1 , VCAM-1) بعد ارتباطهم مع ال leukocytes تبدأ مرحلة ال sticking ثم تبدأ مرحلة ال Diapedesis (by gaps btw the endothelium cells)

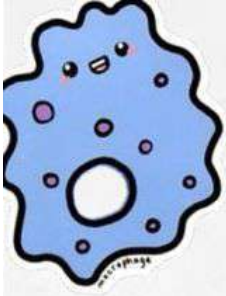
-what are the substances that make leukocytes attract to the site of infection ????

- 1)microbial peptides
- 2) complement protein like ; (C3A ,C5A)
- 3)Leukotriene B4

وبالنهاية رح يصير عندي Engulfment and killing لل microbes



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Lymphatics in Inflammation



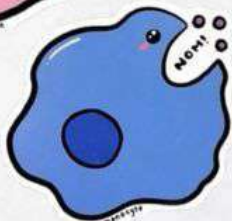
- Lymphatics are responsible for draining edema.
- Edema: An excess of fluid in the interstitial tissue or serous cavities; either a transudate or an exudate

- Transudate: An ultrafiltrate of blood plasma
 - 1) permeability of endothelium is usually normal.
(increase in hydrostatic pressure)
 - 2) low protein content (mostly albumin).

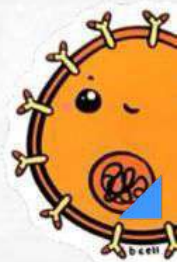
- Exudate: A filtrate of blood plasma mixed with inflammatory cells and cellular debris.
 - 1) permeability of endothelium is usually altered.
(increase in hydrostatic pressure)
 - 2) high protein content.

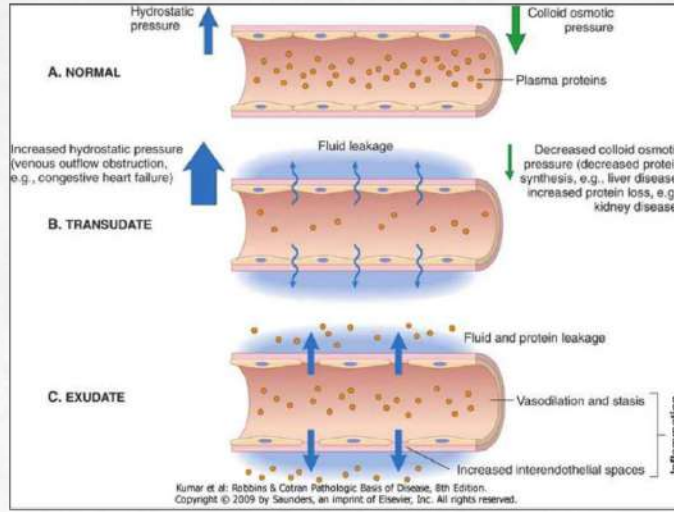
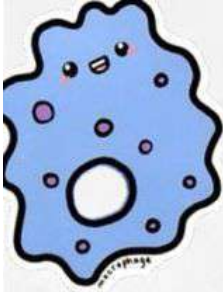
- Pus: A purulent exudate: an inflammatory exudate rich in leukocytes (mostly neutrophils) and parenchymal cell debris.

- من ناحية ال fluid ال exudate بتكون ال turbid
، اما بالنسبة لل transudate بتكون clear



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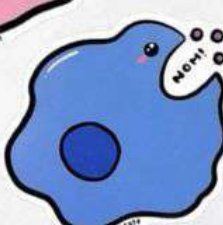




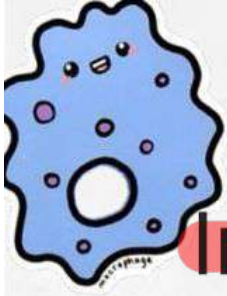
بال transudate يكون فيه زيادة hydrostatic pressure ونقصان
بال colloid osmotic pressure وهذه ما يسبب ال fluid leakage

اما في حالة ال exudate بتكون المشكلة بال permeability (لاحظ
الزيادة بال gaps بالرسمه)
وبنتج نتيجة لذلك :

- 1) تسرب لل protein and fluid
- 2) وبصير عندي VD and stasis
وبنشوف كمان cellular debris and leukocytes



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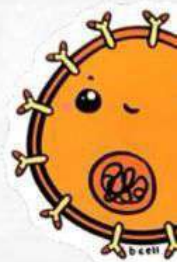
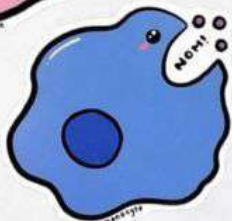
Function of



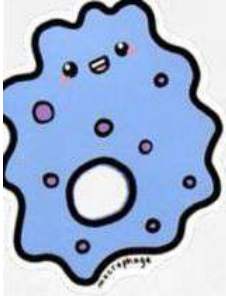
Inflammatory Exudates

- Dilute the invading microorganism and its toxins.
- Bring antibodies through the plasma to the inflamed area.
- Bring leukocytes that engulf the invading microorganisms.
- Bring fibrinogen through the plasma, which is converted, to fibrin mesh, helping in trapping the microorganism and localize the infection

-fibrin mesh: prevent the movement of organisms



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Inflammatory Mediators



•Chemical substances synthesised or released and mediate the changes in inflammation.

1.Histamine by mast cells -vasodilatation.

2.Prostaglandins –vasodilation, fever, and pain.

3.Bradykinin -induce vasodilation, increase vascular permeability, cause smooth muscle contraction, and induce pain.

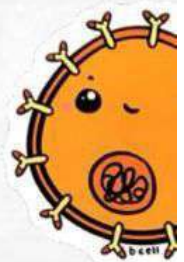
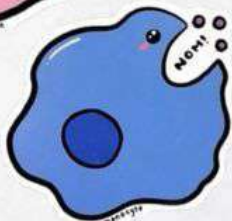
•Cytokines including TNF, IL1, IL6, IL8

•Lipid mediators: prostaglandins, leukotirns, and platelet activation factor

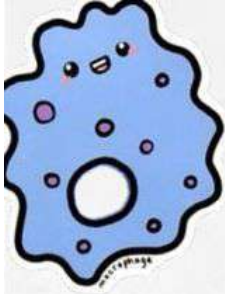
-حکینا انه جزء من ال pains بكون بسبب ال prostaglandins

-what is the mechanism of fever ??

prostaglandins will go to hypothalamus and apply new sitting of Body temperature



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Cytokines and Inflammation



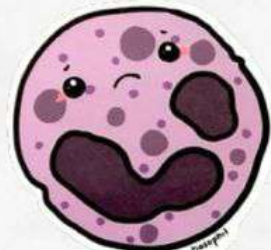
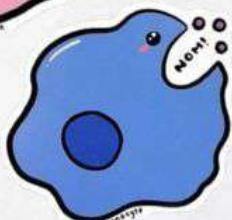
- Macrophages or DCs stimulated via innate immune receptors make pro-inflammatory cytokines, especially TNF (Tumor necrosis factor), IL-1, and IL-6
- TNF and IL-1 signal to endothelial cells to make them:
 - Leaky to fluid (influx of plasma; containing antibodies, complement components, etc.)
 - Sticky for leukocytes, leading to influx of first neutrophils, later monocytes, lymphocytes
 - IL-6 promotes fever and adaptive immune responses and has systemic effects (“acute phase response” of liver, including C-reactive protein or CRP; levels used clinically as an indication of systemic inflammation)

• Acute phase reaction:

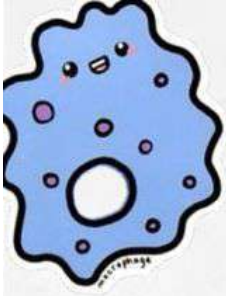
1- CRP (C-reactive protein)

(It's a test for people which gives an indication of inflammation, which is induced by IL6)

2-ESR (erythrocyte sedimentation rate)



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Inflammation Outcomes



1. Abscess formation

(if the infection become localized)

2. Progression to chronic inflammation

3. Resolution–tissue goes back to normal

4. Repair–healing by scarring or fibrosis

5. Spread through lymphatics or blood stream

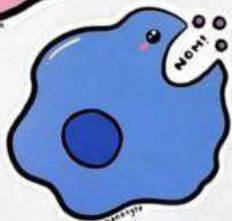
the best tretment from abscess?

1) drainage

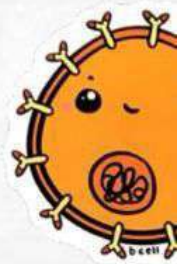
2) antibiotics

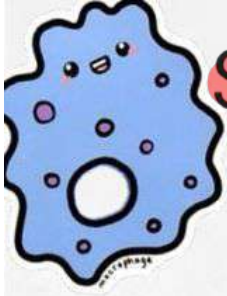
scarring or fibrosis inflammation ال ممكن ال
والتي ممكن تتطور وتظهر Keloid والتي تظهر عند ذو البشرة السمراء
اكثر اشبي

اذا صار عندي Spread through lymphatics or blood فرح
يسبب عندي systemic infection



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Suppurative or Purulent Inflammation

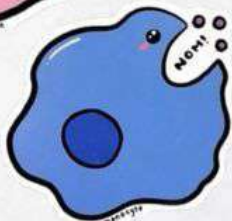


- Pus: thick fluid containing viable and necrotic polymorph and necrotic tissue
- 1. Localized: ex. Abscess: Abscess is the localized collection of pus, commonly seen solid block of tissue
- Example: dermis, liver, kidney, brain etc. Pus consists of partly or completely liquefied dead tissue mixed with dead or dying neutrophils and living or dead bacteria, formed of 3 zones .
- Small abscess is called boil or furuncle
- Large one carbuncle
- Fistula
- 2. Diffused: Spreading of pus to adjacent areas e.g.cellulites occurring in subcutaneous tissue . Usually caused by streptococci.

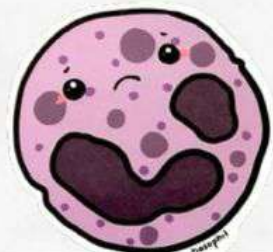
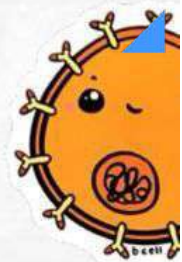


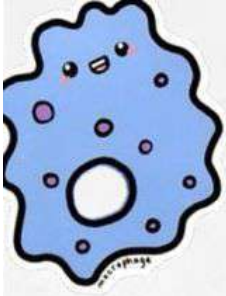
- اذا كان في inflammation in hear hair follicles هاي تسمى boil or furuncle

-Carbuncles are clusters of several boils



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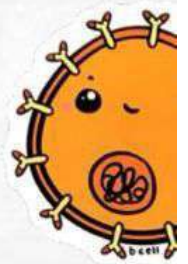
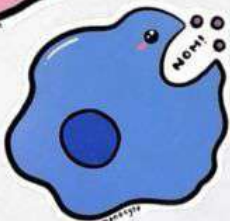
-A fistula is an abnormal connection between two body parts or two cavities (pathogen as result of infection)

-طيب ايش ابتفرق عنها ال sinuses

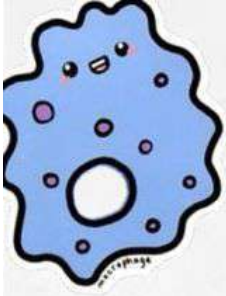
sinuses :A cavity, space, or channel in the body

واشهر مثال على ال sinuses هو (pilonidal sinus) وبصير شوفارية الترييلات (Truck drivers) بسبب الجلوس لفترات طويلة مع الاهتزاز المستمر وبتكون في منطقة اسفل الظهر وبتكون بداخلة كمية من ال pus و كتلات من الشعر

pilonidal sinus is a small hole or tunnel in the skin at the top of the buttocks, where they divide (the cleft)



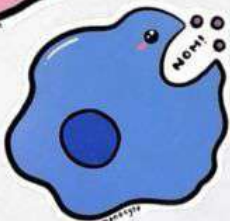
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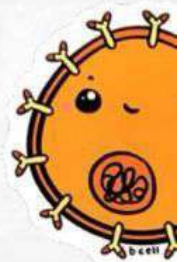
Anti-Inflammatory Therapeutics

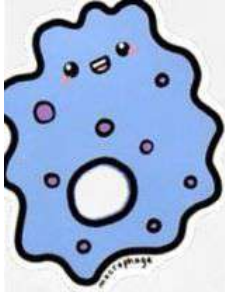


- NSAIDs: inhibitors of inflammation and fever (block prostaglandin synthesis)
- Glucocorticoids are also potent anti-inflammatory drugs
- Agents that block TNF are effective in treating rheumatoid arthritis, Crohn's disease, etc.
- Agents that block IL-1 are less effective for these diseases but are useful for some genetic inflammatory diseases (and are currently in clinical trials for more common conditions)



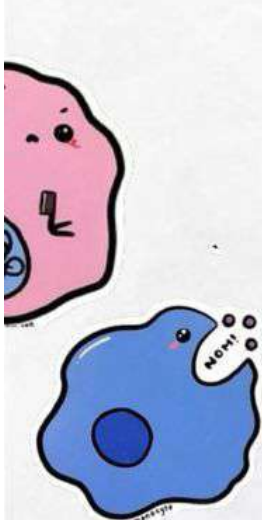
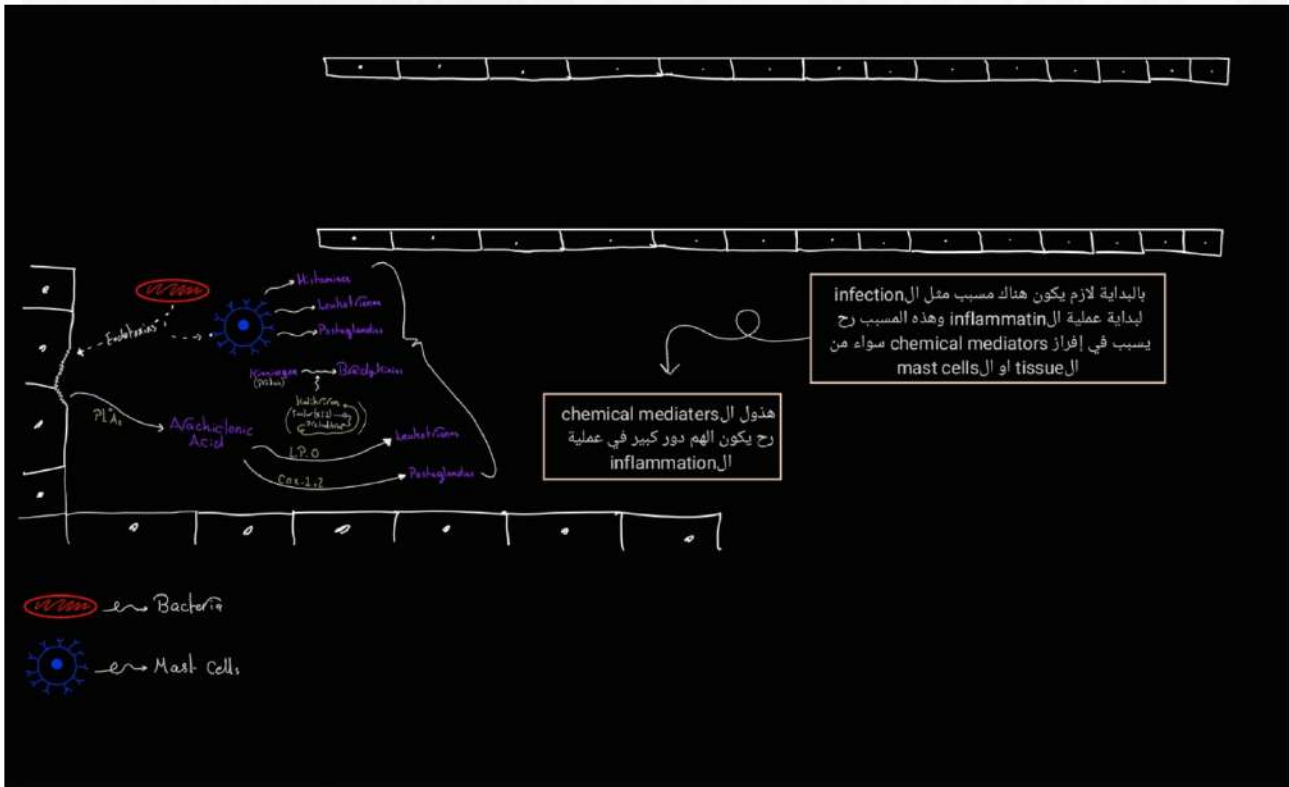
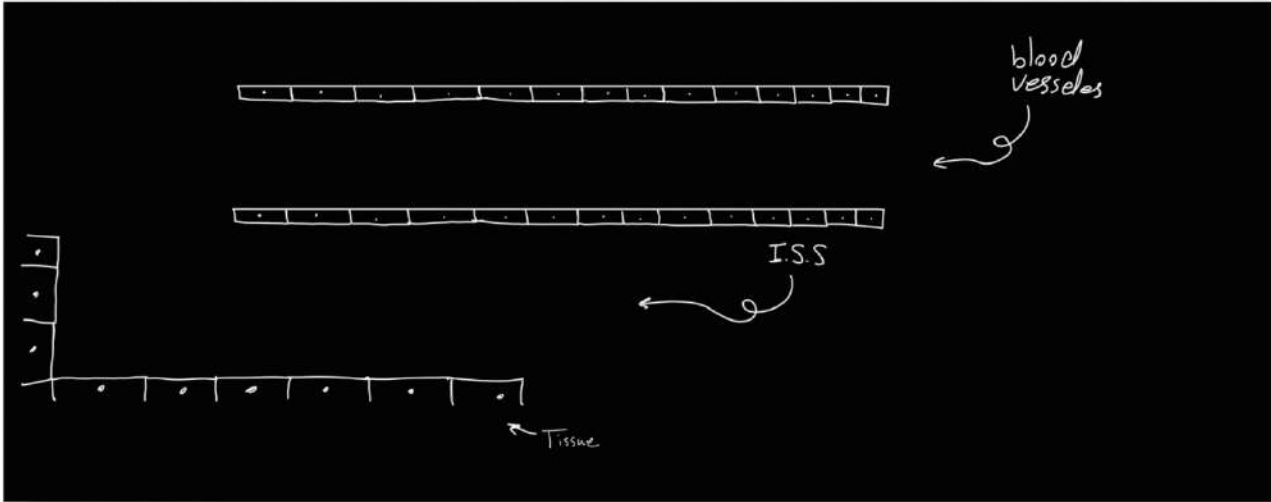
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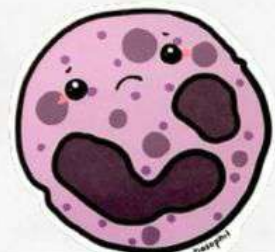
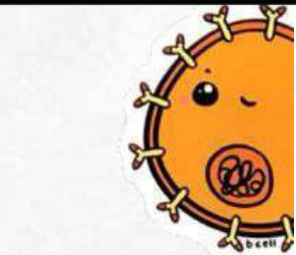


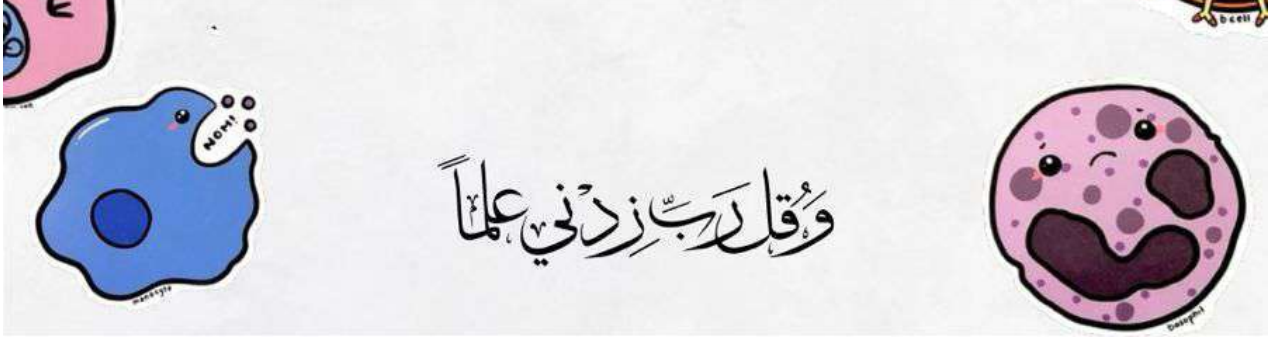
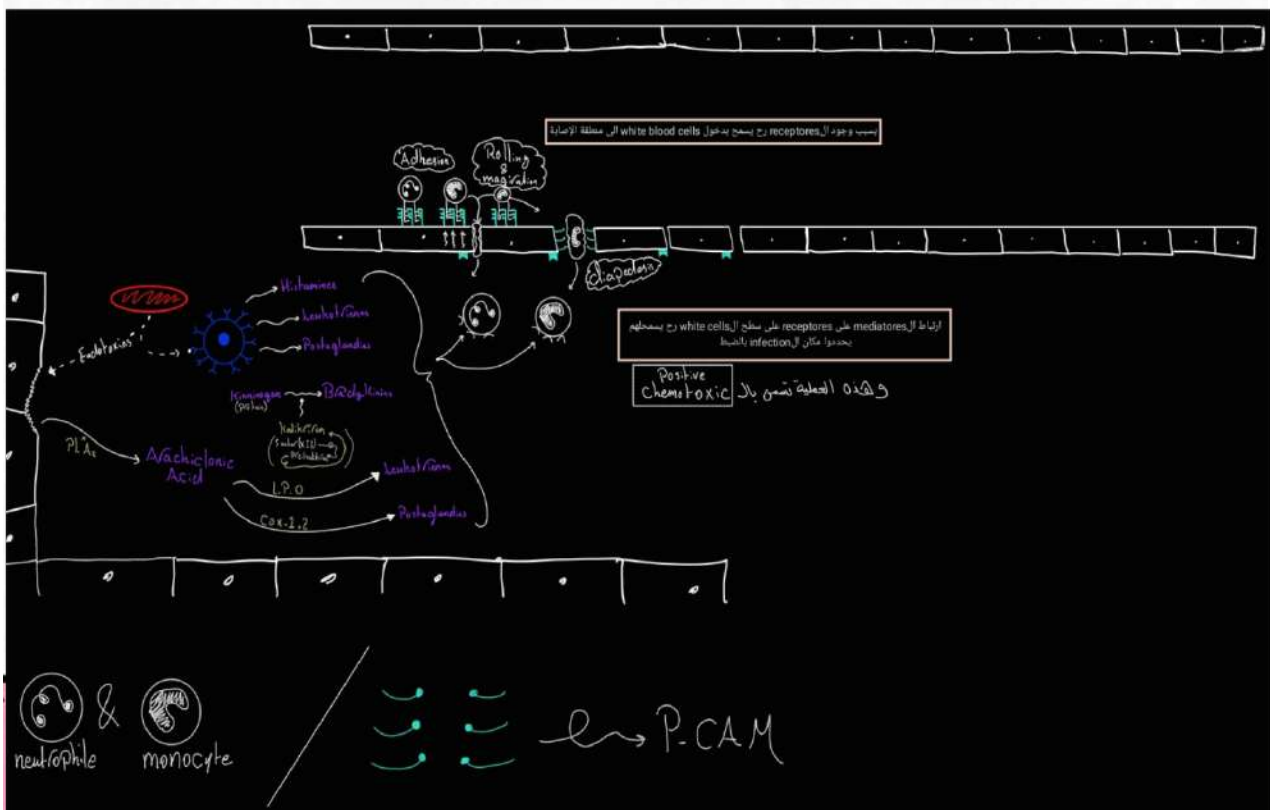
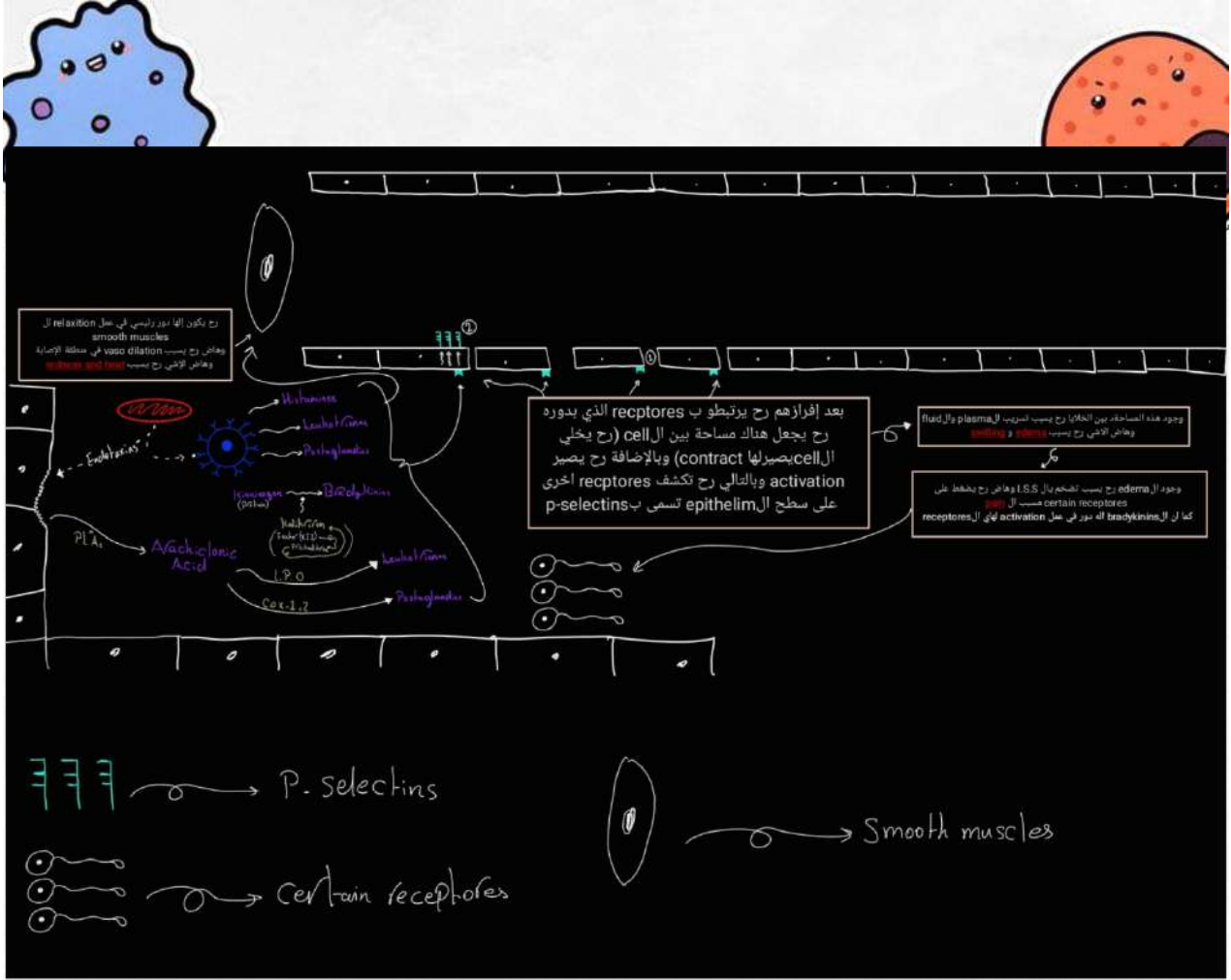
Inflammatin

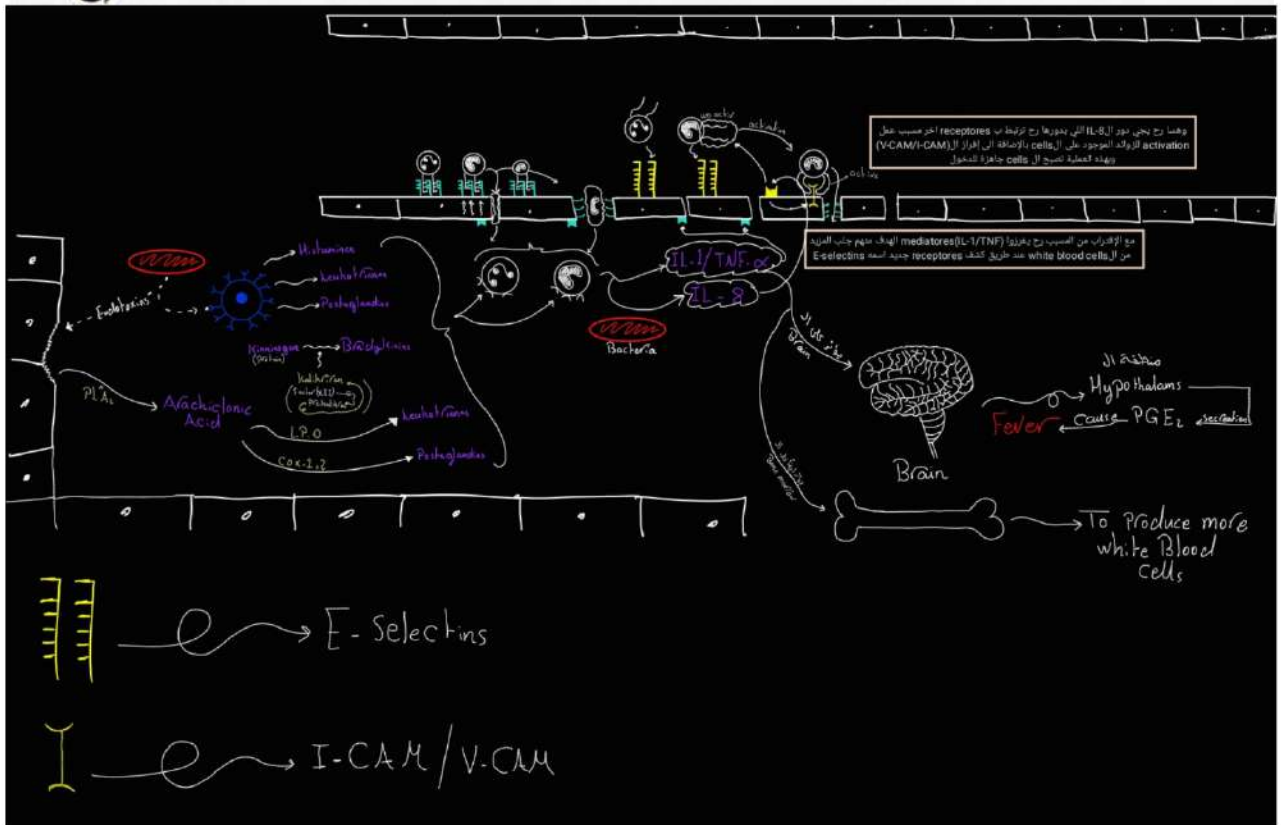
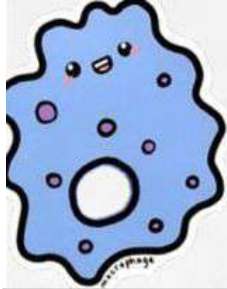
(Ninja nerd)



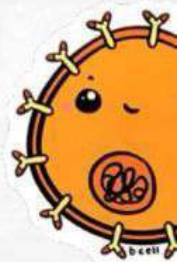
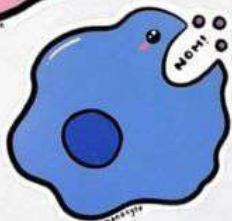
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وبالتوفيق يا رب 🙏❤️



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