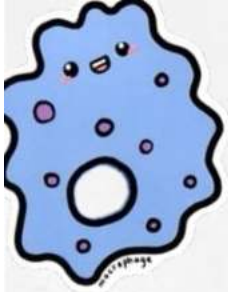
Immunology

Title : Principles Of Immunology

Lec no : One

Done By : Johainah Taha

وَقُل رَّبِّ زِدْنِي عِلْمًا




السلام عليكم 🧡 حأكون معكم هاد الفصل بتفريغ و تلخيص مادة الimmunology إن شاء الله

اللون الأسود للسلايدات، اللون الأحمر أي نوتات إضافية ✨

بأول التفريغ حتلاقوا روابط لفيديوهات مفيدة، و بنهاية التفريغ بتلاقوا كويز بيتكون من أسئلة من عدة كتب و مواقع 🧡

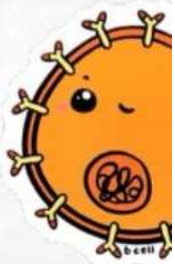
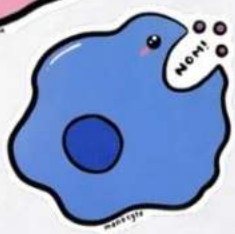
بالتوفيق يارب

Useful Links ⬇️⬇️

شرح دكتور أشرف

https://youtube.com/playlist?list=PLjOn5TM7IzhogGWGYZa7R5oEDDoUr7A4-

ملاحظة : لا يوجد كويز لهذه المحاضرة لأنها مقدمة 🧡
و كل ما فيها سيكرر بالتفصيل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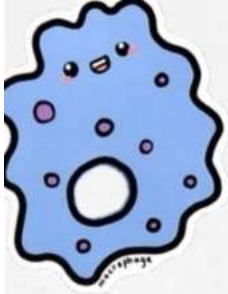


Introduction

• Immunology stems from
– Latin - immunis = "exempt;"
– English = protection from disease. Or protection of invading foreign antigen

• Immunology is the study of our protection from foreign macromolecules or invading organisms and our responses to them.

Our immune system does not response to self-antigen, it can recognize it; and that is called tolerance
↳ antigen present in our cells.
Tolerance : is the prevention of an immune response against a particular antigen

Functions of Immune System

1. Immune defense: Protection from harmful environmental antigens.

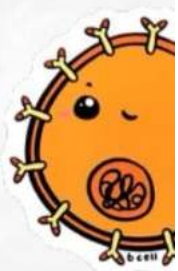
   Such as viruses, Bacteria, Fungi, Parasite...etc

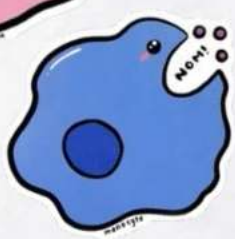
2. Immune homeostasis: Regulate and maintain the steady state of organisms.

   Such as having bad pathogens and good pathogen.
   When talking about good pathogen; we're talking about the microbiota which inhabits (تعيش في) our body in huge numbers but it is living in a peaceful situation with the human cells and immune cells, because the immune cells can differentiate the good bacteria from the harmful

3. Immune surveillance: Search and destroy neoplastic cells.

   The immune cells remain working all the time searching and destroying the invading pathogens and once there is any transformation of the human cells into a cancerous or neoplastic cells then it is going to be targeted by the immune system





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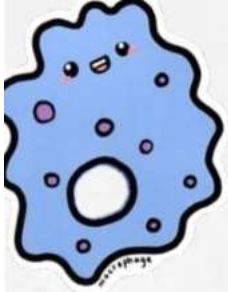
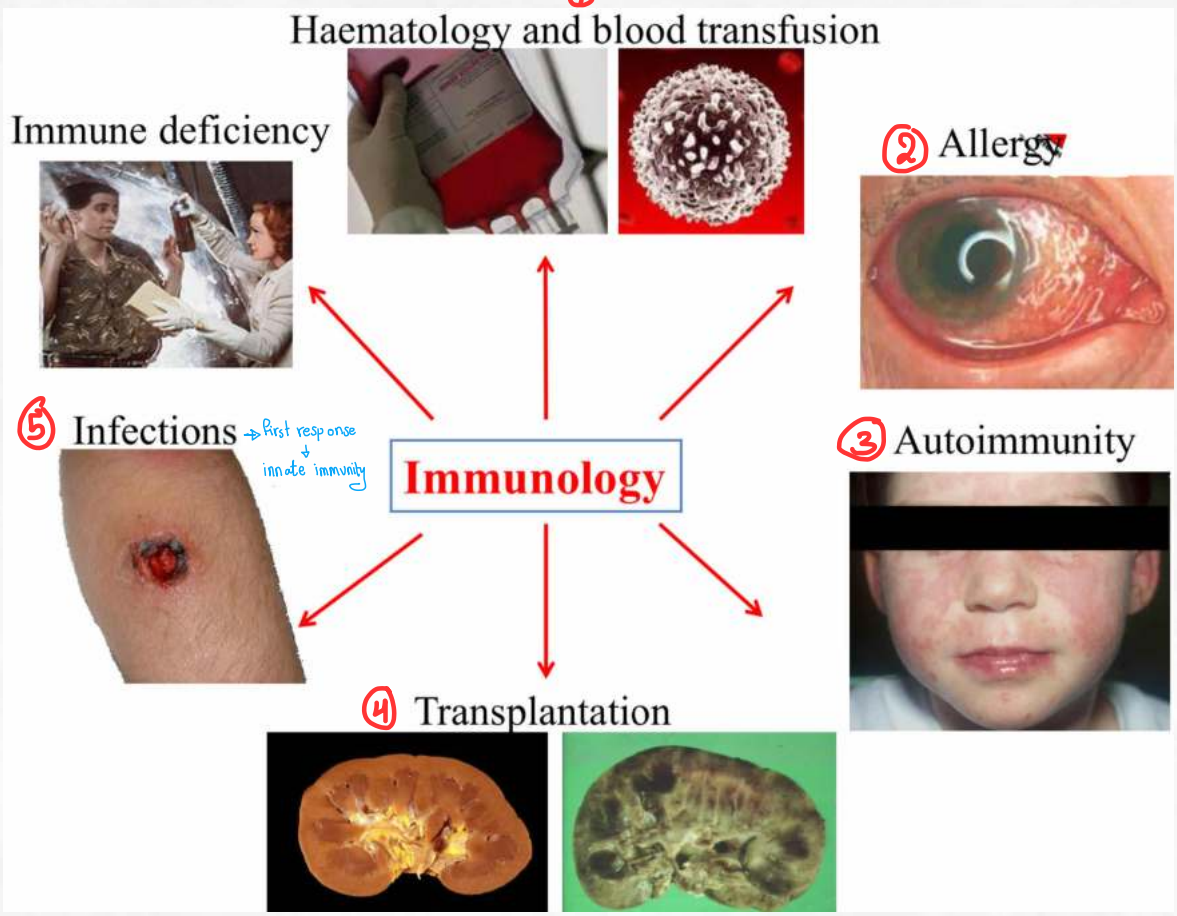
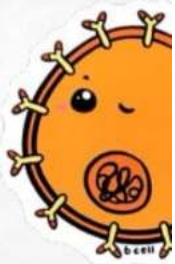
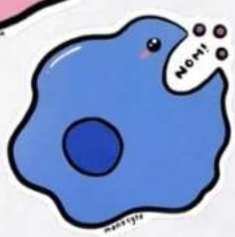


Immunology's Subdivisions







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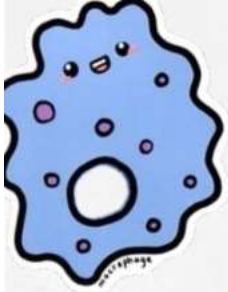


ما تركزوا على أسماء العلماء و التواريخ

History Of Immunology

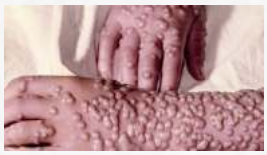
Most of them were found by a coincidence

* 430 B.C.: Philosophers noted resistance to plague by those who recovered "Only those who had recovered from plague can nurse for sick people because they would not contract the disease a second time"

Plaque used to kill huge number of population in communities, they found that only the one who infected and survived can take care of those who are sick without the risk of death, (this was the simplest form of thinking of vaccine generation)

* 15th century: Chinese and Turks use dried crusts (قشور) of smallpox by inhalation or introduction into small cut of skin in order to prevent the disease.

The first experiment of giving a killed virus vaccine was recorded in the 15th century
Note that the crust (قشرة) contain killed viruses

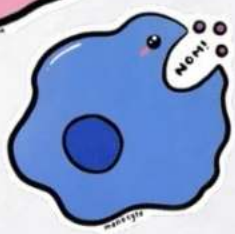


* 1796: Edward Jenner discovered that cowpox vaccination protected against smallpox. He inoculated an 8 years boy with fluids from a cowpox pustule and then intentionally infected the boy with smallpox, but the child did not develop the disease

They have noticed that the women who are milking cows which are infected by the cowbox, they have conferred immunity against smallbox, and they were not infected by smallbox. 1796 was the start of thinking of the vaccination as a protective tool against infections
So they completely eradicate smallbox by this intervention

* In 1880: Pasteur discover Anti-cholera live-attenuated vaccine. He noticed that old cultures in his lab did not kill chicken after inoculation and that chicken become immune to cholera. He applies the same principle for anthrax and rabies vaccine.

He has noted that old cultures of cholera when given to chicken, they give the chicken immunity against the illness, and the did not became sick with the bacteria, then he tries it with anthrax and rabies for vaccination purposes.



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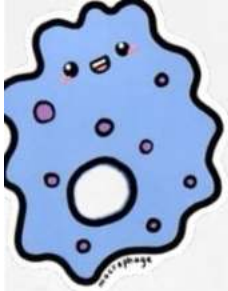



* In 1890: Von Behring and Kitasato discover diphtheriae antitoxin. They notice that serum from animals previously immunized to dipthteria could transfer the immune state to unimmunized animals.

By having the serum of animals previously immunized to diphtheria, this serum would have the anti-diptheria toxin, so when we take the serum, we give the the preformed antibodies to other sick animal, and that what we call nowadays : passive immunity

Active immunity : if someone get infected[1] by the bacteria or the virus and confers immunity or if you take the vaccine[2]. (الجسم بصنع الأنتي بودي بنفسه)
Passive immunity : is giving the serum which contain antibodies against this specific pathogen

الصفحة القادمة فيها توضيحات و تفاصيل هامة عن هالموضوع

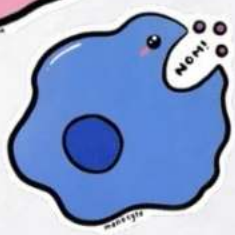
إذاً للآن اكتشفنا :- Killed virus → live-attenuated → anti-toxin

* 1883 Ellie Metchinkoff that cells like phagocytes contribute to the immune state of animals

At the beginning of the late 1800s and beginning of 1900s, scientists start looking into the cells of the immune system, and they started noticing the role of phagocytes (component of innate immunity, they phagocyte, break down, eradicate the foreign pathogen and they are antigen presenting cells (to activate specefic immunity or adaptive immunity))

ال concentration لل antigen بتصير في ال spleen و lymph node الي بنسميهم (peripheral lymphoid organs)
The Spleen drains blood, Lymph nodes drain Lymph
و بالتالي ال antigen لما يكون موجود بال blood حيصير اله concentration بال spleen
و ال antigen الموجودة بال lymph بصير الها concentration بال lymph nodes
ال lymph nodes فيها مواقع بتتركز فيها B cells و أماكن أخرى تتركز فيها T cells
فلما يدخل ال concentrated antigen ل spleen او lymph node ، بصير هناك random encounter or screening of the lymph and the blood
فلو لقى foreign antigen حيتعرف ال B او T عليه و تبدأ عملية الهجوم
لو صار عنا activation ل T cells ، بتترك مكانها و بتتحرك لمكان ال infection
و لكن ال Bcell ، حتنتج plasma cell و الي حتنتج antibodies , حتلف عبر الدم و حتعمل مجموعة من الشغلات ابسطها neutralization



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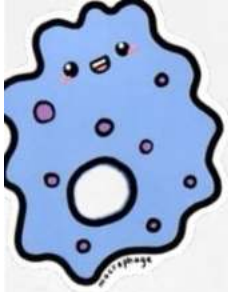

Active immunity VS Passive immunity

مهمة جداً العنحة

محظط من النت ولكنا مفيد ت مها

Active immunity	Passive immunity
Active immunity refers to immunity, which results from the production of antibodies by the person's own immune system in response to a direct contact of an antigen	Passive immunity refers to a short-term immunity which results from the introduction of antibodies from the outside
Mediated by the antibodies produced by the person's own cells	Mediated by the antibodies produced outside the body
The pathogen has direct contact with the body	The pathogen doesn't have direct contact with the body
Does not generate a rapid response	Generates a rapid response
May last for a long time	May not last for a long time
Generates an immunological memory	Does not generate an immunological memory
Side effects are very low	The body may react to antisera
Does not work in immunodeficient hosts	Works in immunodeficient hosts

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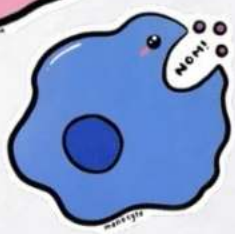
* الدكتور سأل سؤال، مين أفضل و ليش ؟ الجواب هو الActive
١. لأنه بيعمل memory بينما الpassive ما بيعمل و السبب انه الimmune system ما اشتغل عالantibody بنفسه بل استلمه جاهز
٢.بالpassive احنا بس بنعطي antibody، بينما بال active احنا عم نعمل cellular و humoral immunity، و لهيك بكون عنا memory في B+T cells
٣.الpassive بتضل لshort time

* و الدكتور كمان طلب أمثلة على أمراض بنعطيهم Antibody :
١. Covid 19 , خصوصاً بفترة عدم وجود vaccine، فكانوا يوخدوا بلازما أشخاص مصابين و تشافوا و من ثم بعطوه لشخص crtically ill عنده الviral load عالي، و بالتالي بعمل neutralization و بساعد الmacrophages و dendritic cells ليقوموا بوظيفتهم
٢. RSV، الي بستهدف الأطفال بعمر ٦ شهور
٣.snake bite

و لكن مشكلتهم انهم short lived + very expensive



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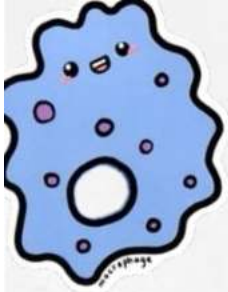


Blood Grouping and Immunology

• Experiments with blood transfusions have been carried out for hundreds of years with out any success.

• In 1901, Karl Landsteiner discovered human blood groups, and blood transfusions became safer.

• He found that mixing blood from two individuals can lead to blood clumping. The clumped RBCs can crack and cause toxic reactions. This can be fatal.

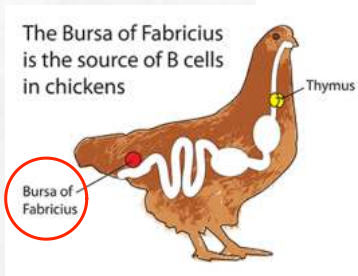
• Karl Landsteiner work on blood grouping has discover the fundamental principles of Immunology

Modern Immunology

1. Study on immune system

* In 1957,Glick Fabricius and Xianguang Zhang: Chicken without bursa can not produce Ab by B cells

* In 1961,Good and Miller: cell mediated immune of new born mice whose thymus were taken away are defective of T cells

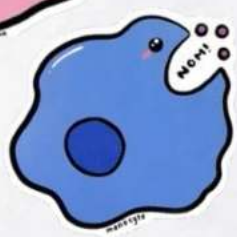


Bursa was the source of B cells
And the thymus is the source of T cells
So by depriving those organs you would deprive the animal from forming the humeral or the cellular immunity

2. Study on monoclonal antibody In 1975, Kohler and Milstein

3. Study on immune genetics in 1978, genetic control of antibody diversity

The immune genetics has to do with certain illnesses that have a genetic component and at the same time they can also be precipitated or caused by immune reaction or autoimmunity where the human body attacks itself



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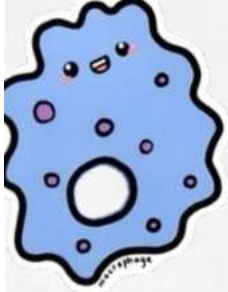


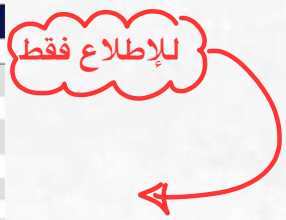
4. Study on molecular mechanism of T/B lymphocyte activation and signal transduction

5. Study on effective mechanisms of immune cells

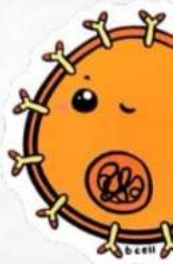
6. Clinical and transplantation Immunology

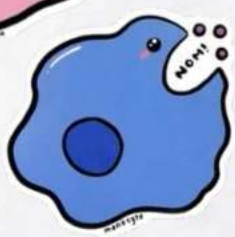
TABLE 1-2 Nobel prizes for immunologic research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Bordet	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler Niels K. Jerne	Great Britain Germany Denmark	Monoclonal antibodies Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by T cells
2002	Sydney Brenner H. Robert Horvitz J. E. Sulston	S. Africa United States Great Britain	Genetic regulation of organ development and cell death (apoptosis)



• Immunology act as an independent subject: (In 1971, International Conference of Immunology, in USA)





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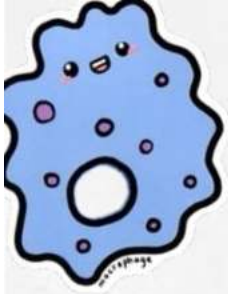
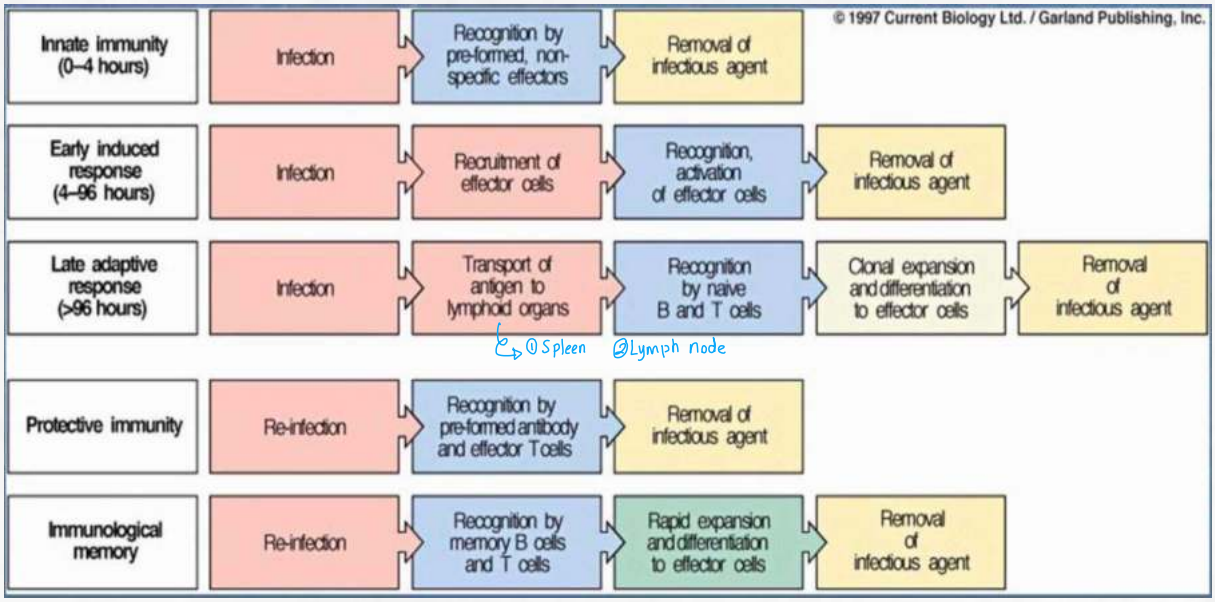


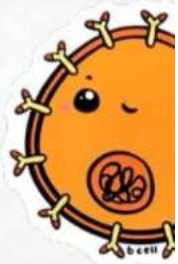
Response to initial infection

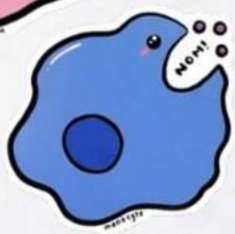


1- The response starts with innate immunity that kicks in very quickly, just seconds or minutes after the introduction of the pathogen.
The infection is going to be recognized and removed by the preformed non-specific effector cells (such as macrophages, dendritic cells and antigen presenting cells).
By phagocytes.

2- Then from 4 hours to 4 days, the specific immunity starts, Lymphocytes (B and T cells) remove the infection.(شرحنا بالسلايدات الي فوق كيف)

3- More than 4 days, the invading pathogen is going to be recognized by specific B and T cells which are going to target specifically this pathogen or antigen, and then it is going to lead to clonal expansion and differentiation to effector cells (التوضيح الصفحة القادمة)





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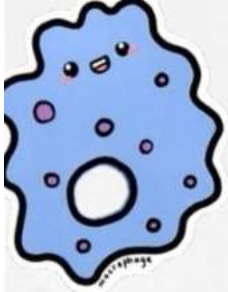


**When we talk about clonal expansion, we need to know that each B and T cells has a code for only single antigen and our bodies are built on having codes for millions of antigen even before their encounter with these cells, so these cells that have these codes but have never encountered these antigens are called naive B and T cells.

Naive B or T cells : stem cells that has not exposed to an antigen

Once they are exposed to antigen, they become activated, leading to colonal expansion

Clonal expansion : if we have antigen x then a single B and a T cell is going to have the antigen x, once naive B and T cell encounter the x antigen, this is going to lead to colonal expansion which means that it is going to produce hundreds, even millions of copies depending on the size of the invading pathogen of the same specefic antigen, this is called clonal expansion

يعني تصنيع نسخ اضافية كثيرة، حتى يستطيع الجسم مقاومة هذا الantigen الي دخل عليها

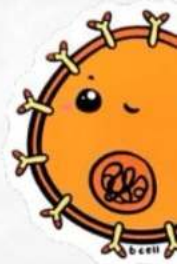
هو بكون built in من ربنا بكون اله كود بس بكون naive ، يعني have never be exposed to this antigen

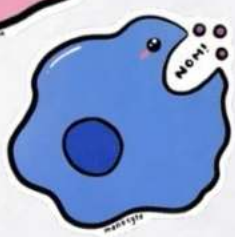
And then this naive cell is going to differentiate into effector cells

(B cell -> plasma cells -> antibodies)

(T cell -> T helper,cytotoxic, regulatory)

to get rid off infectious agent





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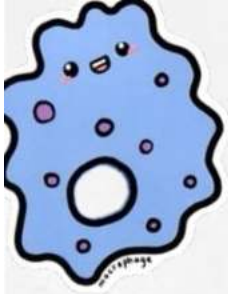
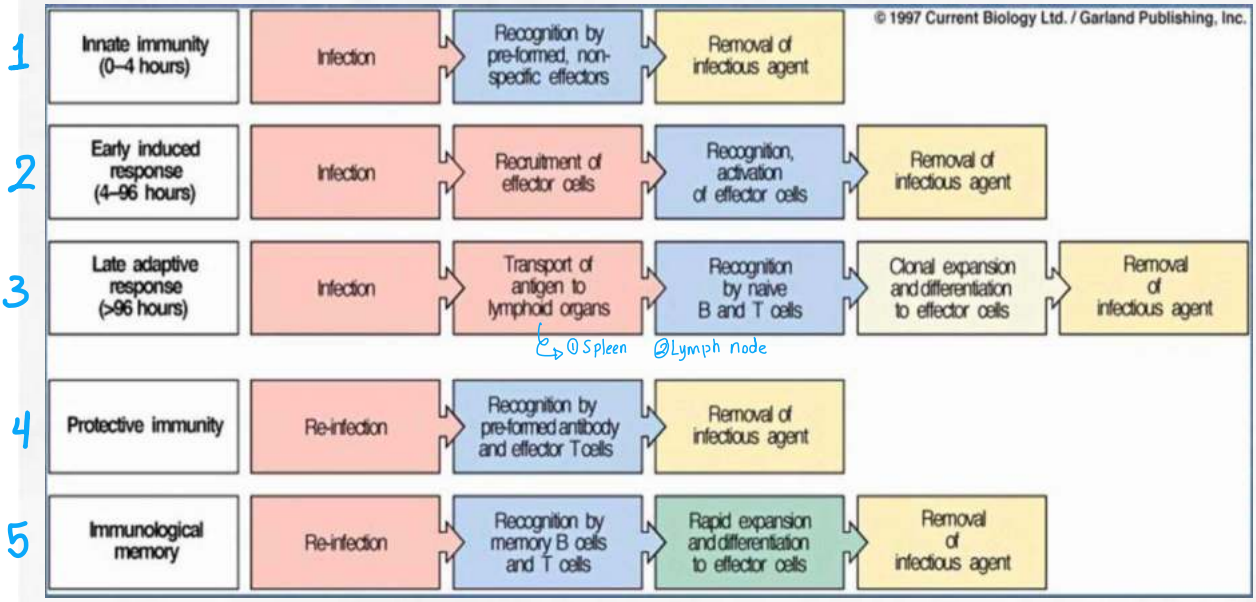
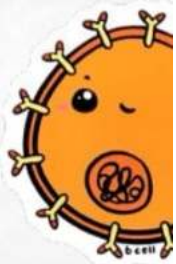


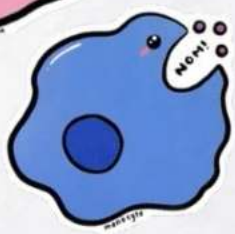
Response to initial infection



4- protective immunity : along with these steps we have memory for bcells and t cells and that is going to be protective upon re infection, so once huamn body is infected with the same antigen (x), it is going to be recognized by the preformed antibody and effector cells, and it is going to remove the infectious agent in a shotrter period of time because clonal expansion differentiation is not going to take as long as the first time

(Upon second exposure -> faster recognetion, faster clonal expansion, faster response)





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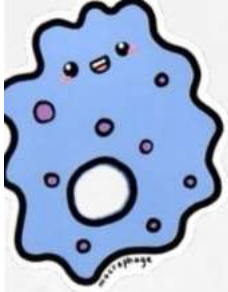


Immune system

Innate (non-specific) immunity

- Anatomic barriers (Skin,mucous membranes) ,cilia, tears, gastric juices
- Physiological barriers (temperature, pH)
- Phagocytic Barriers (cells that eat invaders) Macrophages, dendretic cells, natural killer cells
- Inflammatory barriers (redness, swelling, heat and pain)

Adaptive (specific) immunity

- Antigen specificity
- Diversity
- Immunological memory
- Self/nonself recognition

Humoral

Cellular

Infalmation signs help the patient to know that there is something wrong to seek medical help and to start the treatment

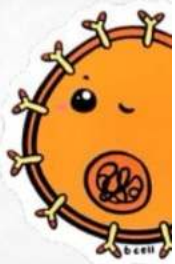
Adaptive immunity is :

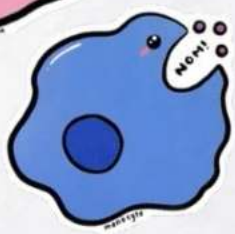
1- antigen specific (it is recognized by specefic clone which is specefic to that antigen)(شرحتلكم فكرته فوق)

2- It is diverse (can recognize different shapes or structures or sequence of antigen)

3- Immunological memory (which is formed after the removal of an acute infection)

4- Self - non self recognition (and when it fails in recognizing the self antigen; autoimmune disease occure)





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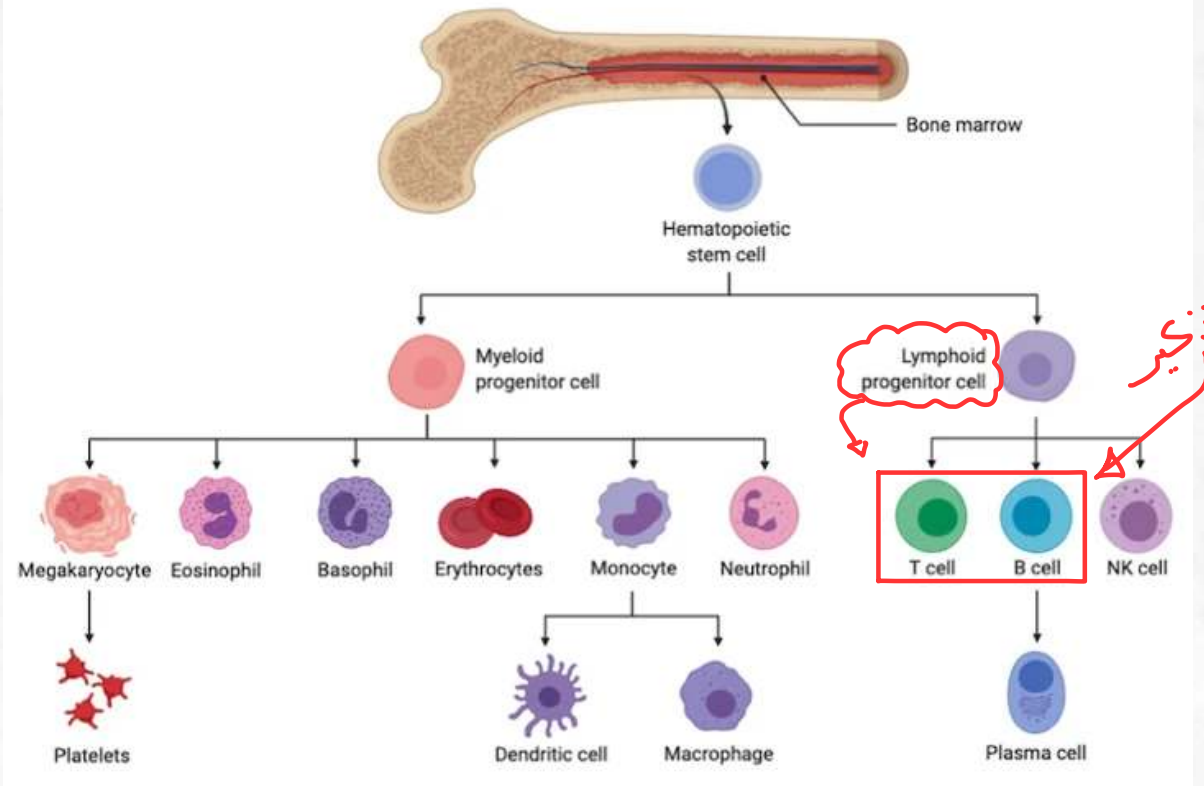
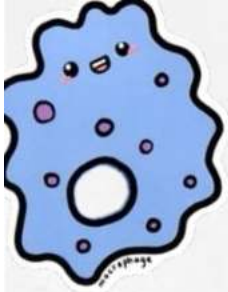


adaptive immunity is devided into

- Humoral
  - B-cell
    - Plasma cells
      - Anti-Body
- Cellular
  - T-cell
    - helper
    - Cytotoxic.
    - Regulatory

وقل رب زدني علماً




Antibodies Functions :

1- Neutralization

بحيث انه بيرتبط مع viral spike و بالتالي بمنعه الفايروس يرتبط على receptor تبع target cellال

2- opsonization

To make the foreign antigen more recognizable for phagocytic cells by making a complex with it

3- complement system activation

There are three pathways of complement activation: the classical pathway, which is triggered directly by pathogen or indirectly by antibody binding to the pathogen surface; the MB-lectin pathway; and the alternative pathway, which also provides an amplification loop for the other two pathways.

الدكتور سأل، متى بصير عنا cellular لل activation و متى للhumoral؟

Humoral immunity can recognize and attack extracellular pathogens, but it has no role to the intracellular pathogen.

حشره لبعين بالتفصيل

ال cellular بحفز الhumoral، كيف ؟ عبر الT helper cells ، اسمهم هيلبر اذا هم مساعدين

الT helper 0 cell عليها مستقبل اسمه CD4 و هو بروتين بتعرف على الفايروس او ال antigen عن طريق ما هو موجود على antigen presenting cell

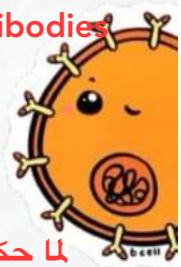
و بعد ما يتعرف على الفايروس بتحول الى TH2 cell الي بدورها بتحفز انتاج ال Ab

لو في فايروس جديد دخل الجسم حتمسكه ال phagocyte or antigen presenting cell ، حتكسره و تعمل اله presentation و بعدها بتيجي الT-cellالي عليها مستقبل الcd4 الي حيتعرف على الpathogen، و هاي الخطوة بنسميها early phase of infection

هسا لما الcd4 يتعرف عليها حيعمل activation ل T helper 1 او T helper 2

TH1 favors the activation of cell mediated Immunity.

TH2 favors the activation of humoral immunity -> production of antibodies

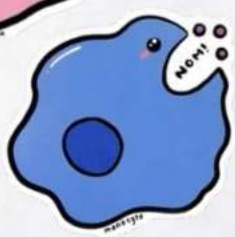



لنفهمها بشكل اوضح، في عندي antigen صار اله recognization عبر CD4، مما يؤدي الى activation ل T helper cells

لما حكينا عن مطعوم strep pneumonia، حكينا لما نعطيه للاطفال الاقل من سنتين ما رح يستجيبوا اله و السبب هو انه ال

T cells recognize only proteins

B cells rcognize proteins, lipids, carbs...ets



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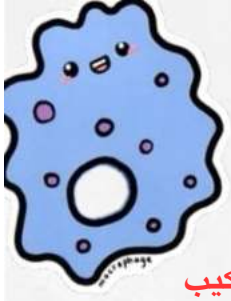


فقط للمعرفة

بالنسبة لمثال الvaccine، لازم نرجع نتوفة للRS (اذا بدكم اعملوا سكيب عن الصفحة لأنها معلومات فقط للمعرفة)

*ال B-cells هي المسؤولة عن إنتاج ال Ab, هي بتستجيب و بتكون Ab لأي شي بالدنيا، مثل polysaccarides,proteins,lipids,DNA...

*بالvaccine وظيفة الT-cell هي دعم الB-cell لحتى ينتج Ab أكثر، ولكن هدول الT-cells مشكلتهم ما بستجيبوا الا للبروتينات

*هسا الB-cell الها طريقتين لتنتج Ab

T-cell independent Ab production

مثال دخلت بكتيريا strep pneum على جسمي و من ثم نحو الlymph node لمنطقة الB-cells و الي هي الfollicles، الي حتحفز الB-cells لتنتج plasma cells الي حتعطيني Ab ضد كبسولة البكتيريا بدون مساعدة الT-cells

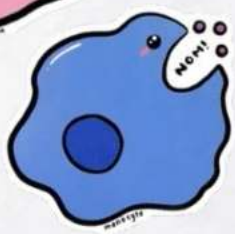
مشكلة هدول الAb انهم ضعاف و weak و ما بضلوا لفترات طويلة

T-cell dependent Ab production

لهيك بتيجي الmacrophage or dendritic cells الي بكسروا البكتيريا لأجزاء صغيرة و بالتالي بعرض البروتين على T-cell فبالتالي بتتحفز و بتحفز معها الB-cell لتنتج Ab أكثر في الfollicles و بتكون قوية و عددها أكبر و بتستمر لفترة طويلة

بالنسبة للvaccine لو كان polysaccaride لعمر سنتين و اقل فقط حيصير عندهم T-cell independent Ab
و بالتالي عدد Ab قليل و بستمروا بعملهم لفترة قصيرة

لهيك العلماء فكروا بشي ذكي، و مسكوا جزء الpolysaccaride و لصقوا فيه بروتين لحتى نحفز الB-cells و T-cells، بالتالي صار عنا T-cell dependent Ab production
و هاد الvaccine اسمه conjugated لانه ربطنا بروتين مع polysac.



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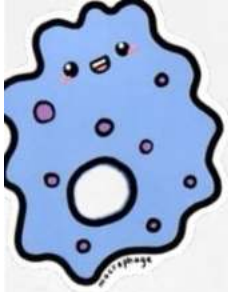
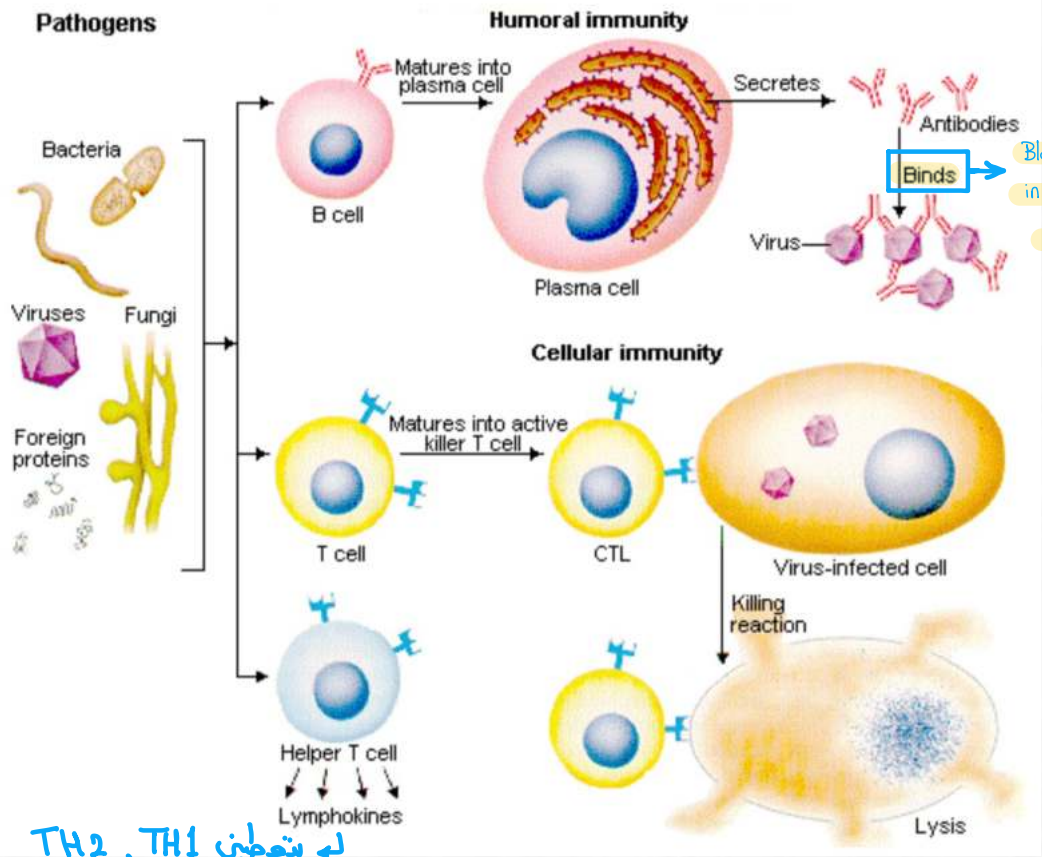


Humoral and Cellular Immunity



Block viral glycoprotein in a process called neutralization.

لـ بتعطيني TH2 , TH1

T-cells

Hepler

1- activate B cells to secret antibodies
2- activate macrophages to destroy ingested microbes
3- activate cytotoxic T cells to kill infected target cells

↓

. Express CD4 protein

Cytotoxic

Targets intracellular pathogen (infected cells (viral))

↓

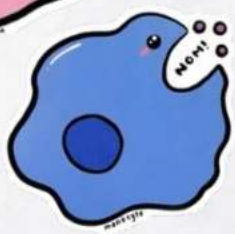
Production of perforins granzyme

↓

Cell lysis (killed cells)

↓

Express CD8 protein



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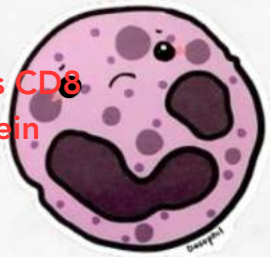
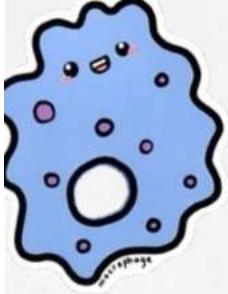
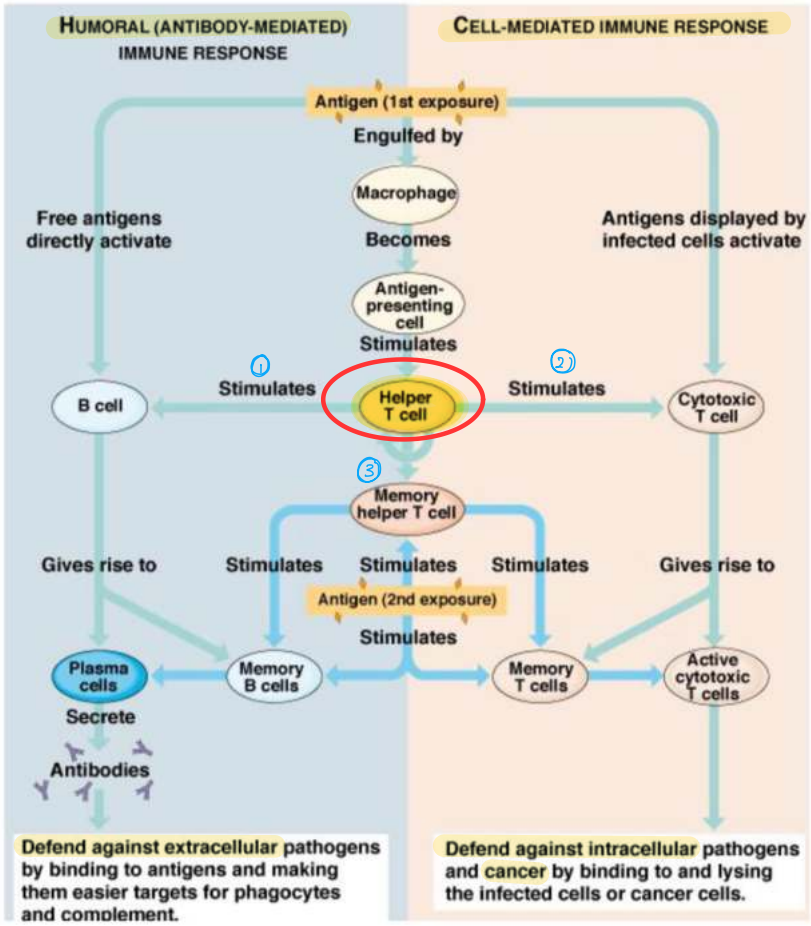




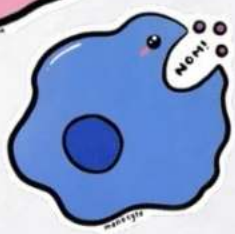
Overview of Immune Response



There is an interaction between T cell and B cell activation, once the T helper cell activate and stimulate the B helper cell this is celled (T helper cell dependent immunity) which gives more robust immunity if there is no stimulation from helper T cells

In the (T helper independent immunity) when there is only an activation by B cell, the immunity is going to be weaker than it is stimulated by the helper T cell.

The helper T cell is responsible in stimulating the production of cytotoxic T cells, memory helper T cells and plasma cells which are going to produce antibodies and memory cells



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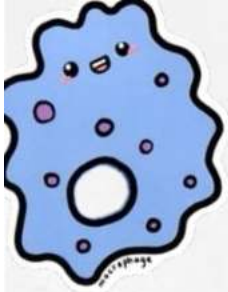


Innate Versus Adaptive Immunity

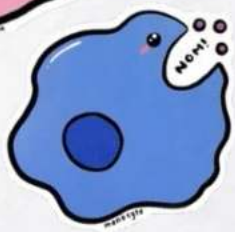
	Innate	Adaptive
Response time	Hours	Days - after 4 days -
Specificity	Limited and fixed	Highly diverse, improves during the course of immune response
Response to repeat infection	Identical to primary response	Much more rapid than primary response

The reaction of the human body to any invading pathogen or antigen whether he has encountered it for the first time or hundredth time is limit and fix.

In the second encounter, the immune response is going to be faster and more potent than the first time.
The third and the fourth are going to be more potent than the second and first time

طيب بما انه الinnate يعتبر non-specific
كيف بقدر يميز انه هاد foreign ؟ (واجب)

The surfaces of microorganisms typically bear repeating patterns of molecular structure. The innate immune system recognizes such pathogens by means of receptors that bind features of these regular patterns; these receptors are sometimes known as pattern-recognition molecules.



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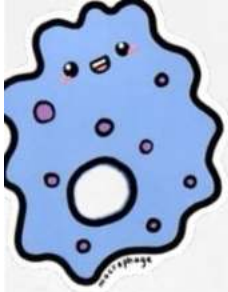
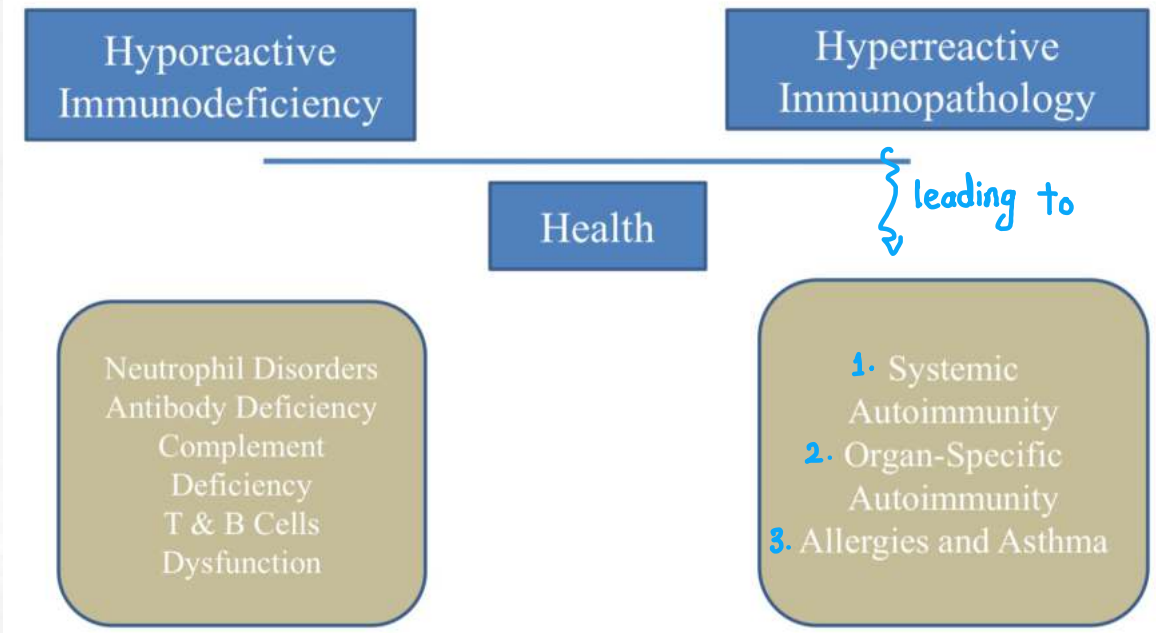
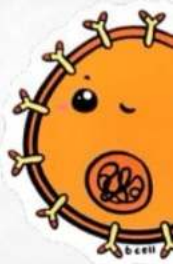
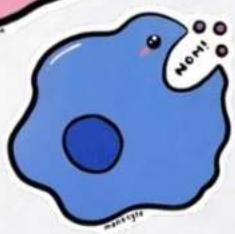


Immunology- The Balance



So Homeostasis of immune system is important because both hyper and hypo are harmful





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