Microbiology

◉ Sheet ○ Slides

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Subject: Virology (Immunology)

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Immunology: (introduction to immune system)

Hi every one ✋… as you know , our main source for studying virology is the slides . Anyways , this notes have been written to explain some confusing points , giving more examples to make sure that you fully understand your lectures …

Let the party begin ✌ …. BTW , Mohammad is back 😎😎

- **SLIDE 1 :**

The process of **haematopoiesis** starts from Hematopoietic stem cells (HSCs)

Hematopoietic stem cells (HSCs) : are the stem cells that give rise to all the other blood cells through the process of haematopoiesis. They are derived from mesoderm and located in the red bone marrow. (bla bla bla …)

HSCs give rise to both the **myeloid progenitor** and **lymphoid progenitor**.

Myeloid cells include :

a) **megakaryocytes** (which generates thrombocytes –platelets-) ,
b) **Erythrocytes** (RBCs)
c) Mast cells
d) and **myoblast** (gives raise to 4 types of WBCs : **neutrophils, basophils, eosinophils** and **monocytes** that circulate in the blood and become **macrophages** once they enter the connective tissue –oop .. oopa histology style :p-)

Lymphoid cells include :

a) **small lymphocytes** : **T lymphocytes** (could differentiate into plasma cells) + **B lymphocytes** (the 5th type of WBCs)
b) Neutral killer cells

*Note : leukocytes (WBCs) : are neutrophils, basophils, eosinophils , monocyte and lymphocytes .

- **Slide 2 :**

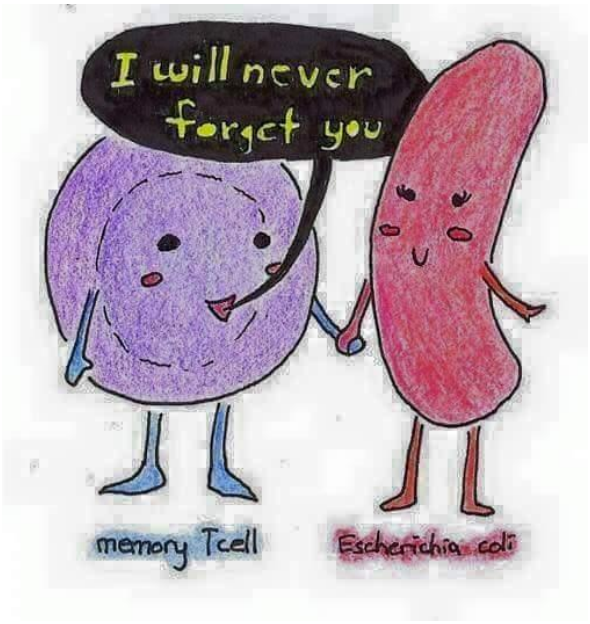
Phases of immune responses :

Immune response begin by **naïve cells** (cells that have no experience , unspecialized cells)

We have two major types of this response

1- Once **Naïve T cell** face a microbe , it differentiates into **effector T cells** , that destroy this microbe , some of these cells will further differentiate to **Memory T cells** .

2- Meanwhile , **Naïve B cells** differentiate into **plasma cells** (that secrets antibodies – immunoglobulins- to combat the foreign body) , some of these cells will further differentiate to



Memory B cells .

❖ **Slide 3**

We have two major types of immunity :

1-innate (non-specific) immunity is so named because it is present at birth and does not have to be learned through exposure to an invader. It thus provides an immediate response to foreign invaders .

However , many pathogens can resist this immunity . in these situations the innate immunity is going to send “help me “ messages to activate adaptive immunity (these messages are called cytokines)

-pathology ,is that you ? -

2-Acquired (adaptive or specific) immunity is not present at birth. It is learned.

- **Slide 4**

Our body is exposed to millions of pathogens daily , but our immunity still able to combat these pathogens ,

Our body is going to fight extracellular pathogens by : **antibodies** , **phagocytes** and **TH1 (T-helper cells 1** , **notice that we have two types of TH**) .On the other hand , intracellular pathogens are fought by **phagocytes , T-helper cells 1** and **cytotoxic cells** .

- **Slides 5 + 6**

Innate immunity :

1-**skin** : imagine yourself without skin , you'd be a mess. It's not very pleasant to imagine yourself without skin. You'd have muscles and organs moving about, sticking out, and falling all over the place. (on the other hand , you can study for anatomy exams well :p) . Any microbe is going to invade your body and cause serious problems .

Furthermore , if you removed the skin barrier (by cut wound for example) , even normal flora will become pathogenic and cause infections as it reaches our internal tissues .

2-**respirotery tract** : by mucus + movement of cilia .

3-**gastrointestinal tract** : remember , ph of the stomach = 2 , (acid , bile , lymphoid tissue)

4-**urinary tract** : when someone get urinary tract infection , we advise him to drink plenty of water to flush this microbe out the tract .

5-**conjectiva**

6-**phahocytosis** : we have many scavenger cells that phagocyte microbes :

a) Neutrophils (polymorphonuclear leukocytes) (PMN)
b) Macrophages (free or fixed)

Remember the structure of antibody (FAB , FC portions) , FC portion is responsible for opsonization with the help of the complement ..

Simply talking ..

Infection → cytokines (by T-lymphocytes) → chemotaxis → macrophages

- **Slide 8 :**

Cytokines : (read from the slides , or refer to pathology sheets :p)

*Note : neutrophils are the first cells that respond to chemokines and reach the infected tissue , because neutrophils are circulating in the blood waiting for any "SOS" signal . Unfortunately , they are short lived , their life span is only 6 hours ☹ .

Major types of cytokines :

A)**Interleukins** : IL1 , IL6 and TNF → fever

B) **TNF**

C)**Interferons** : very important to combat Viral and bacterial infections .

- **Slides 9 + 10**

Interferons , are signals produced by the infected cells , telling nearby cells to be ready to combat this virus , by preventing viral gene expression .

- **Slide 11**

We finished talking about innate immunity , now we will focus on specific immunity , it's divided into two types :

A)**Humoral (non-cellular)** : it's a preventive immunity , so it attacks the virus before infection .

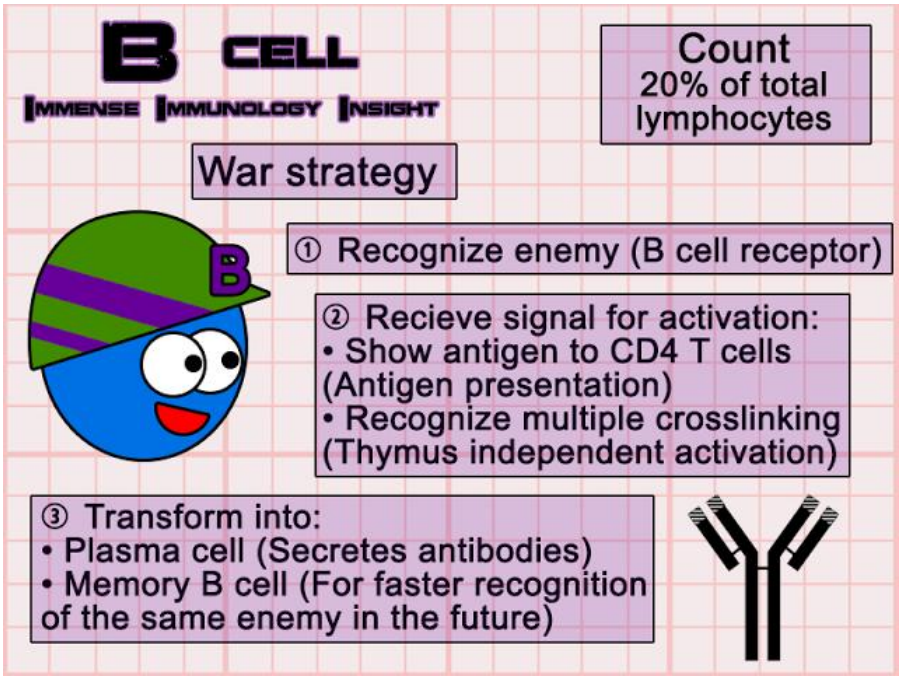
B)**cellular :** after infection , our immune system fights this microbe by cells (Cell to Cell fight ✌ - إذا كنت زلمة بتنزل تطاوش زي الزلام مش متخبيلي ورى الأجسام المضادة) , it's done mainly be T-lymphocytes .

- **Slide 12**

Humoral immunity is mainly by :

A)**immunoglobulins** : each IG has specific antigen , it binds to it's antigen like lock and key .

B)**Plasm cells** : B-lymphocytes bind to antigen → differentiate into plasma cells that carry specific IG on their surfaces → neutralization of the microbe .



❖ **Slides 13 + 14**

*note : FAB portion → antigen binding site / FC portion → opsinization

We have 5 types of antibodies : G , A , M , E and D (GAMED – جميد) :p

E and D have nothing to do with humoral immunity :

-**IGD** → cell bound -**IGE** → produced in allergic reactions

M , A and G are important in humoral immunity :

-**IGM** : first IG to be produced , biggest one (pentamer) → cant cross the placenta

-**IGG** : formed after IGM . However , it remains with you forever ! Simply it's the antibody which will be produced as a final response for vaccination .

-**IGA** : also called secretions antibody or surface antibody .it's found in all body secretions , as well as in mucosa of GI tract .

Clinical Note : giving some vaccines orally is safer and more preventive than IV route . For example ,it's better to give poliomyelitis vaccine orally . this vaccine is going to produce a local, mucosal immune response in the mucous

membrane of the intestines by IGA . In the event of infection, these mucosal antibodies limit the replication of the wild poliovirus inside the intestine. So giving vaccines in the normal route of infection is more preventive .

- **Slides 15→ 27**

Now , we will talk about the most confusing concept ever , cell – mediated immunity , from now I'm going to simplify some points by my way .. so please , understand what is written here well , and then go over the slides quickly ..

As we said , cell-mediated immunity depends mainly on cell-cell interaction , and it's more important than humoral immunity since children with congenital deficiency of cellular immunity develop unusually severe disease .

This type of immunity is depended on **T-lymphocytes** , which are classified into :

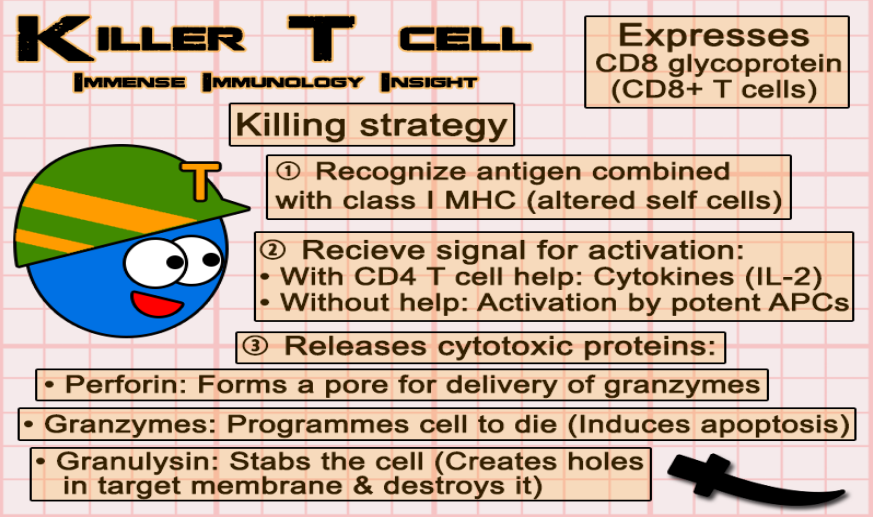
A)CD4 +Ve helper T cell B)CD8 +ve cytotoxic T cell

Each cell is activated by different type of **cellular** antigens , these antigens also called **MHC** (major histocompatibility complex) are two classes :

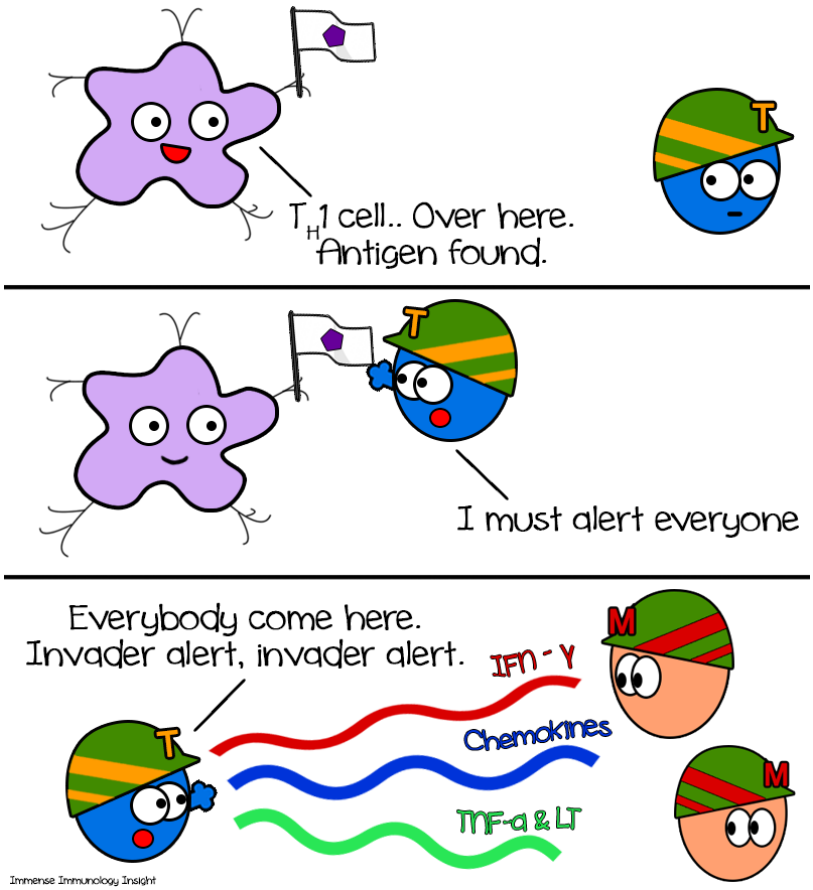
1)MHC class 1 : presented in all nucleated cells , as a response for viral infection .

2)MHC class 2 : presented in antigen presenting cells (macrophages , dendritic cells , T cells , etc ..) as a response for phagocytosis of this virus .

Now let's think about the meaning of these antigens . Class 1 is presented by infected cell to say: (I'm infected , go away from me) . So we need to kill this cell and alert other cells by **CD8 Cytotoxic cell** that binds to MHC 1 (**induce apoptosis** in infected cell by injecting granzymes and release some **cytokines**)



On the other hand , class 2 is presented by phagocytes that detect and phagocytize the virus , so it means (hi there , I found a virus , watch out) . Here we need a cell that can alarm our immune system , which is called **CD4**



helper T cells that binds to MHC 2 (**liberate cytokines** and **activate B cells**)

Notice that some of B and T cells are going to differentiate into memory cells , see slide 21 .

We have 3 major ways to deal with the virus : (slide 20)

1- **Antibodies** → neutralize the virus → prevent cell-cell spread
2- **Phagocytosis** :- antibodies → opsinizaiton "eat me " → activation of phagocyte →phagocytosis and presenting MHC 2 → binding of CD4 → kill intracellular microbe and release cytokines (activation of other T cells , B cells , phagocytes)
3- **Kill infected cells** ☹ : infected cell → present MHC 1→ binding of CD8 → killing the infected cell → release cytokines to alarm other cells

(Slide 22) **What will happen to microbe if ……**

A)It was extracellular microbe (before infection) ?

1- Antibodies → neutralize the virus → prevent cell-cell spread . **(Net result : neutralization)**

2-antibodies → opsinizaiton "eat me " → activation of phagocyte →phagocytosis and presenting MHC 2 → binding of CD4 → release cytokines → inflammation . **(Net result : phagocytosis)**

B) it was phagocytized and become intracellular microbe inside phagocyte?

1- presenting MHC 2 → binding of CD4→ kill intracellular microbe and release cytokines (activation of other T cells , B cells , phagocytes) .

2-but phagocytes also contain nuclei , (are you thinking what I'm thinking ?) , yes , sometimes it can present MHC1 →binding of CD8→ killing phagocytes ☹

C) it was an intracellular microbe ?

infected cell → present MHC 1→ binding of CD8 → killing the infected cell → release cytokines to alarm other cells .

Slide 28 , 29 → just read the slides , there's nothing to be added (NK= neutral killer cells)

سيفقدني قومي إذا جد جدهم *** و في الليلة الظلماء يفتقد البدر

و نحن أناس لا توسط عندنا *** لنا الصدر دون العالمين أو القبر

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