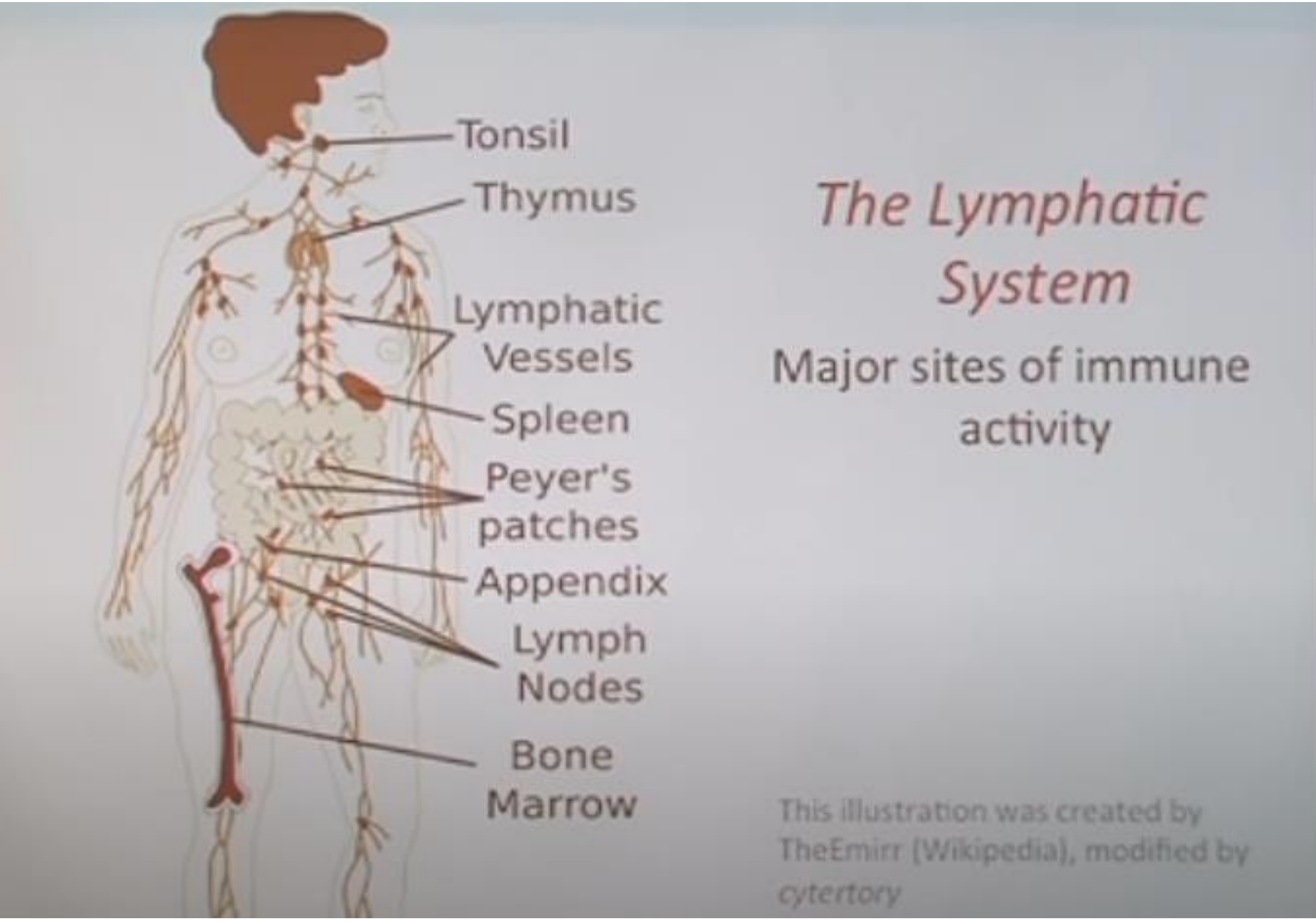
IMMUNOLOGY

IMMUNOLOGY describe

- Macroscopic entities = lymphatic system (organs, which are active in filtration of lymph and blood, pathogen capture or immune-cell generation in body)
- Microscopic entities (Immune Cells and macromolecules IMMUNOGLOBLINS, cytokines andothger moelcules)

- Macroscopic entities : Anatomy of the lymph system, showing the lymph vessels and lymph organs including lymph nodes, tonsils, thymus, spleen, and bone marrow. Lymph (clear fluid) and lymphocytes travel through the lymph vessels and into the lymph nodes where the lymphocytes destroy harmful substances. The lymph enters the blood through a large vein near the heart.

Macroscopic entities :



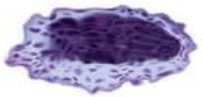
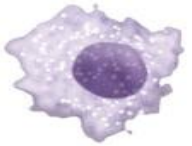
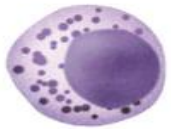
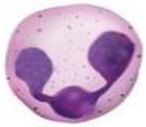
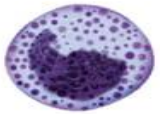
How lympfatic system is designed?

The fluid and proteins within the tissues begin their journey back to the bloodstream by passing into tiny lymphatic capillaries that infuse almost every tissue of the body. Only a few regions, including the epidermis of the skin, the mucous membranes, the bone marrow, and the central nervous system, are free of lymphatic capillaries, whereas regions such as the lungs, gut, genitourinary system, and dermis of the skin are densely packed with these vessels. Once within the lymphatic system, the extracellular fluid, which is now called lymph, drains into larger vessels called the lymphatics. These vessels converge to form one of two large vessels called lymphatic trunks, which are connected to veins at the base of the neck. One of these trunks, the right lymphatic duct, drains the upper right portion of the body, returning lymph to the bloodstream via the right subclavian vein. The other trunk, the thoracic duct, drains the rest of the body into the left subclavian vein. Lymph is transported along the system of vessels by muscle contractions, and valves prevent lymph from flowing backward. The lymphatic vessels are punctuated at intervals by small masses of lymph tissue, called lymph nodes, that remove foreign materials such as infectious microorganisms from the lymph filtering through them.

Role in immunity

- In addition to serving as a drainage network, the lymphatic system helps protect the body against infection by producing white blood cells called lymphocytes, which help rid the body of disease-causing microorganisms. The organs and tissues of the lymphatic system are the major sites of production, differentiation, and proliferation of two types of lymphocytes—the T lymphocytes and B lymphocytes, also called T cells and B cells. Although lymphocytes are distributed throughout the body, it is within the lymphatic system that they are most likely to encounter foreign microorganisms.

Microscopic entities (Immune Cells)

Cell type	Characteristics	Location	Image
Mast cell	Dilates blood vessels and induces inflammation through release of histamines and heparin. Recruits macrophages and neutrophils. Involved in wound healing and defense against pathogens but can also be responsible for allergic reactions.	Connective tissues, mucous membranes	
Macrophage	Phagocytic cell that consumes foreign pathogens and cancer cells. Stimulates response of other immune cells.	Migrates from blood vessels into tissues.	
Natural killer cell	Kills tumor cells and virus-infected cells.	Circulates in blood and migrates into tissues.	
Dendritic cell	Presents antigens on its surface, thereby triggering adaptive immunity.	Present in epithelial tissue, including skin, lung and tissues of the digestive tract. Migrates to lymph nodes upon activation.	
Monocyte	Differentiates into macrophages and dendritic cells in response to inflammation.	Stored in spleen, moves through blood vessels to infected tissues.	
Neutrophil	First responders at the site of infection or trauma, this abundant phagocytic cell represents 50-60 percent of all leukocytes. Releases toxins that kill or inhibit bacteria and fungi and recruits other immune cells to the site of infection.	Migrates from blood vessels into tissues.	
Basophil	Responsible for defense against parasites. Releases histamines that cause inflammation and may be responsible for allergic reactions.	Circulates in blood and migrates to tissues.	
Eosinophil	Releases toxins that kill bacteria and parasites but also causes tissue damage.	Circulates in blood and migrates to tissues.	

Starting overview

- Specific and unspecific Immunity

What is Nonspecific Immunity?

Non-specific immunity, as the name suggests, is not specific to a certain group of micro-organisms. These defense mechanisms act against each and every invader of the body. It is very important to understand that this non-specific immune response is so formidable that only a minute amount of infections penetrates this first line of defense.

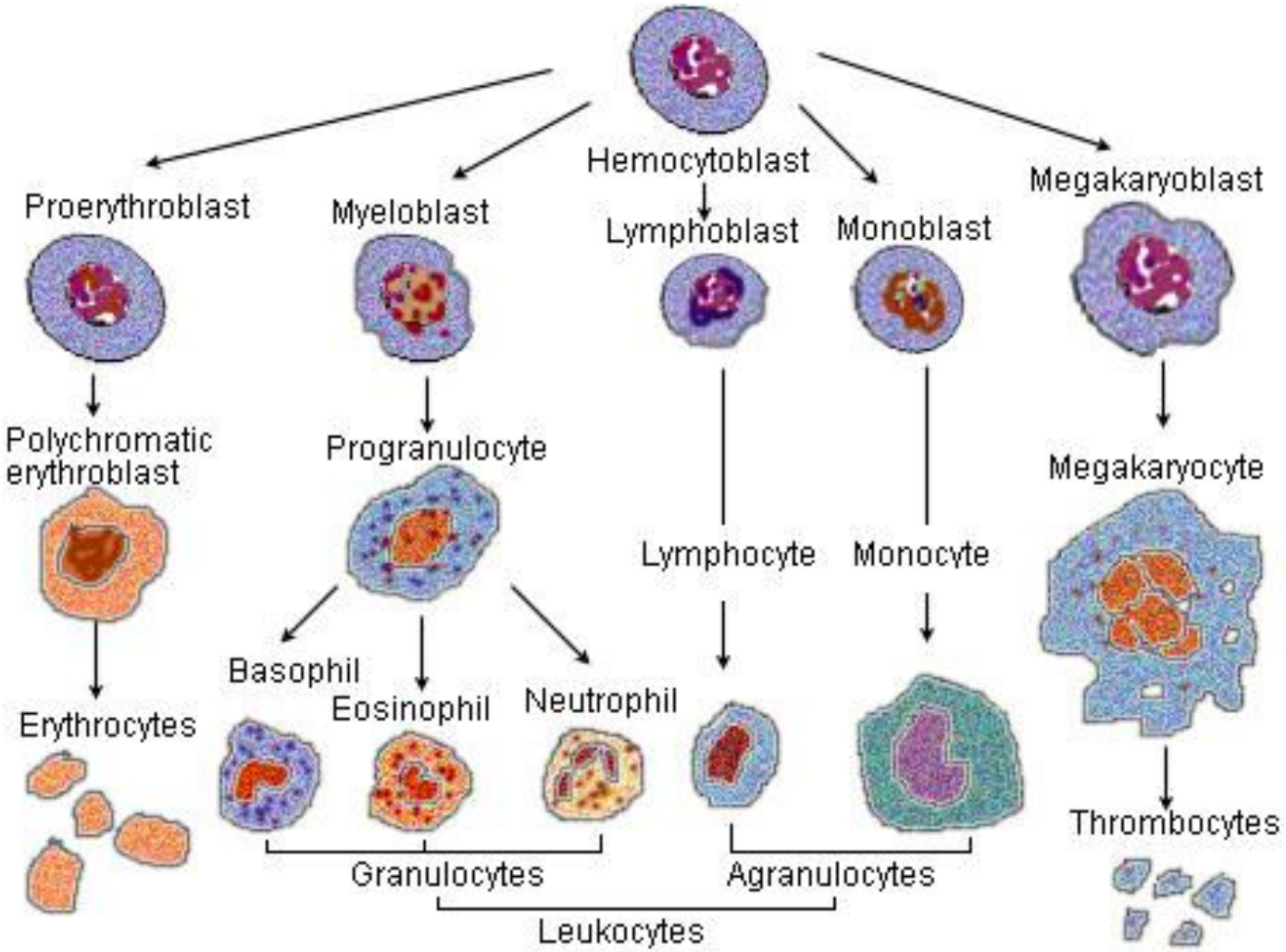
Skin is the first barrier and the first mechanism of non-specific defense. Skin is a multilayered structure that contains dead cells on the outer surface and live cells in deeper layers. Thus, many organisms find it impossible to penetrate this physical barrier. Skin cells are made by cell division at the deep basal layer. As cells reach the outer surface, they lose their vitality and finally detach themselves and shed. This outward migration of cells acts against the influx of invasive organisms. Skin contains various glands. Sebaceous glands secrete sebum which has antibacterial properties. Moreover, sweat washes infections off as the high salt content of sweat dries micro-organisms off.

Tears and saliva are secretions that wash the cornea and mouth continuously. Many epithelial surfaces in the body contain cilia. These cilia beat rhythmically to transport matter out of the body (respiratory epithelium). Saliva contains anti-bacterial properties due to lysozymes. Some epithelia produce mucus which also acts as a barrier against infections. If and when micro-organisms penetrate these defense systems they meet the lymphocytes, macrophages which phagocytose foreign matter non-specifically. This may or may not lead to the generation of a specific immune response.

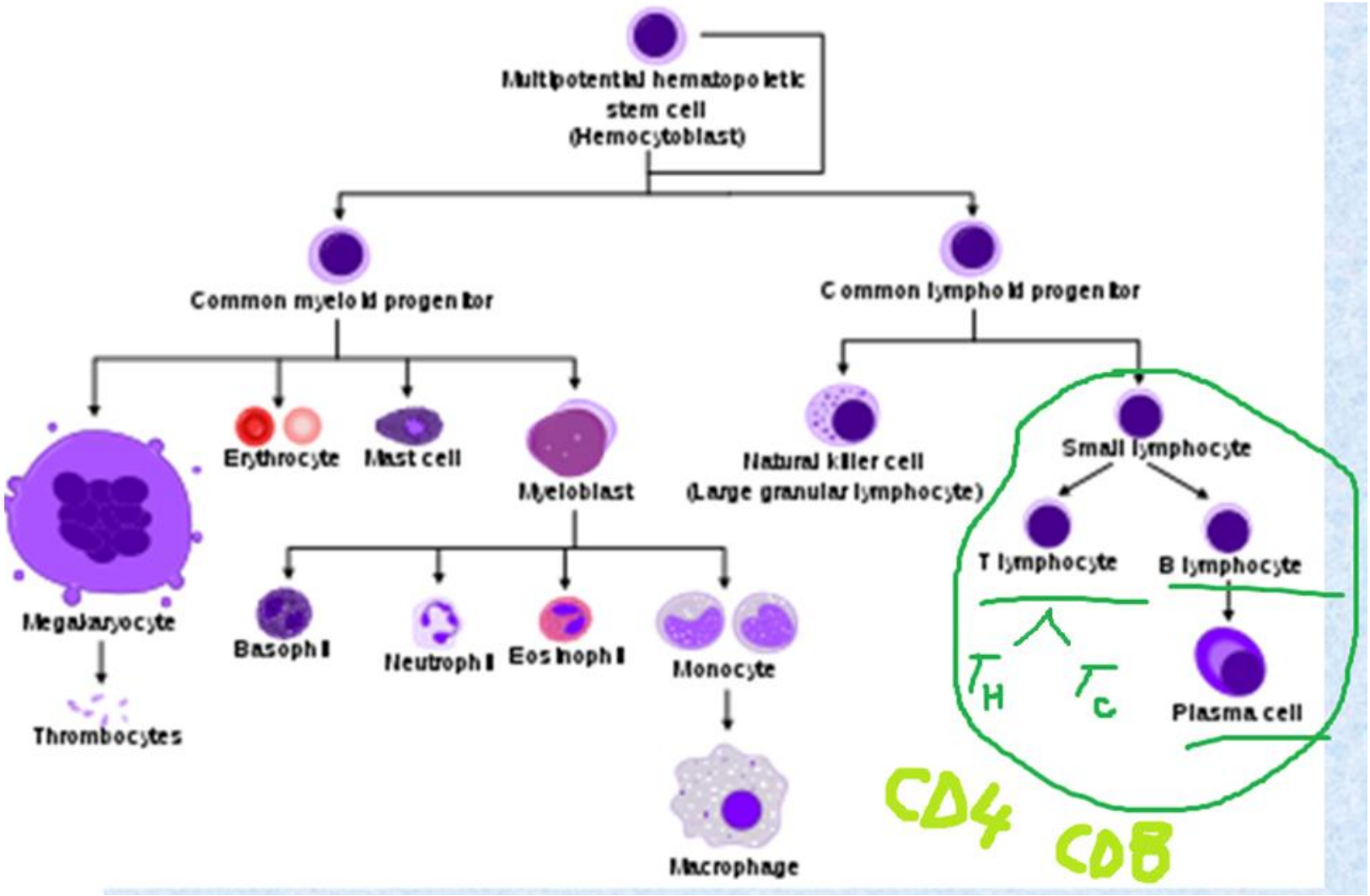
- **What is Specific Immunity?**

When a foreign substance is phagocytozed by a macrophage, a white blood cell, or an antigen presenting cell, it gets processed inside the host cell. There are antigen binding receptors called major histocompatibility complexes (MHC type 1 and 2). MHC 1 crosslinks with CD8 type lymphocytes while MHC 2 crosslinks with CD4 type lymphocytes. There is an enormous variation among antigen receptors in both T cells and B cells. CD4 T Lymphocytes get activated by this receptor cross-linkage, and they produce cytokines which promote proliferation of selected lymphocytes, the formation of new lymphocytes with selected receptor types, and activation of B cells to form antibodies. These mechanisms culminate in the destruction of the foreign organisms phagocytozed previously.

Erythropoiesis (from Greek 'erythro' meaning "red" and 'poiesis' "to make") is the process which produces blood cells



The similar scheme with details of lymphocyte subset:



HOW to eliminate the pathological entities ? (bacteria, virus, cancer-cell, infected-cell)

neutralizating or killing

T-lymphocyte
has ability to switch CELL DEATH

B-lymphocyte
has ability to produce IgM and IgG to

Phagocytic cell has ability to uptake of bacteria and kill (desintegrate in lysosome)

neutralisating

killing

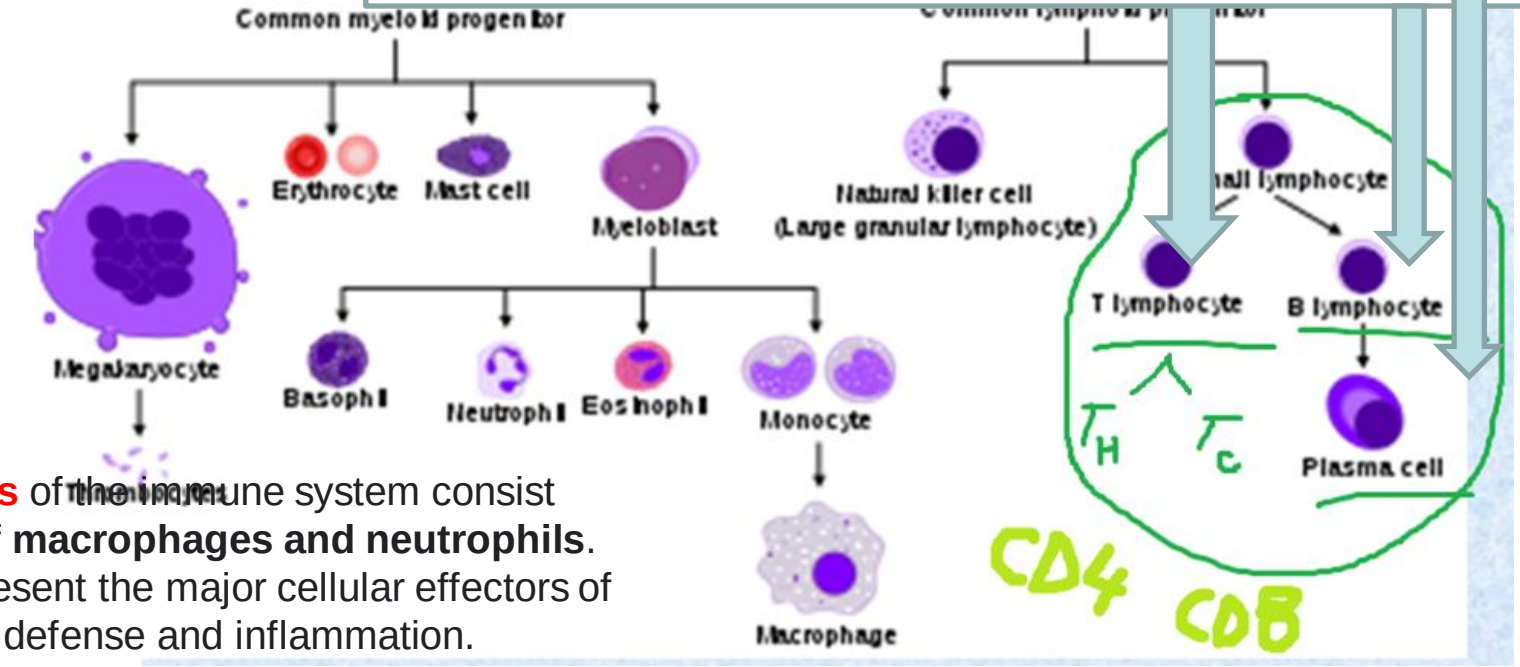
Some detail definition…

- **T cells** are one of the important white blood cells of the immune system and play a central role in the adaptive immune response. T cells can be distinguished from other lymphocytes by the presence of a T-cell receptor (TCR) on their cell surface.

- **B lymphocytes – two mains type**:

- Memory B cell – Dormant B cell arising from B cell differentiation.[1] Their function is to circulate through the body and initia a stronger, more rapid antibody response (known as the anamnestic secondary antibody response) if they detect the antig that had activated their parent B cell (memory B cells and their parent B cells share the same BCR, thus they detect the sa antigen).[23] Memory B cells can be generated from T cell-dependent activation through both the extrafollicular response a the germinal center reaction as well as from T cell-independent activation of B1 cells.[23]

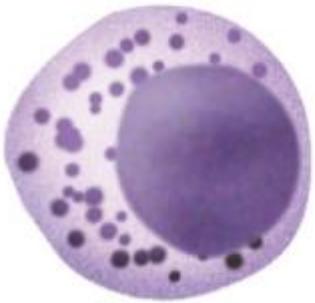
- Plasma cell – A long-lived, non-proliferating antibody-secreting cell arising from B c differentiation.[1] There is evidence that B cells first differentiate into a plasmablast- e cell, th differentiate into a plasma cell.[14] Plasma cells are generated later in an infection a , compared to plasmablasts, have antibodies with a higher affinity towards their targe antigen due to affinity maturation in the germinal center (GC) and produce more antibodies Plasma cells typically result from the germinal center reaction from T cell-dependent activat of B cells, however they can also result from T cell-independent activation of B cells.[21]



Phagocytic cells of the immune system consist predominantly of **macrophages and neutrophils**. These cells represent the major cellular effectors of nonspecific host defense and inflammation.

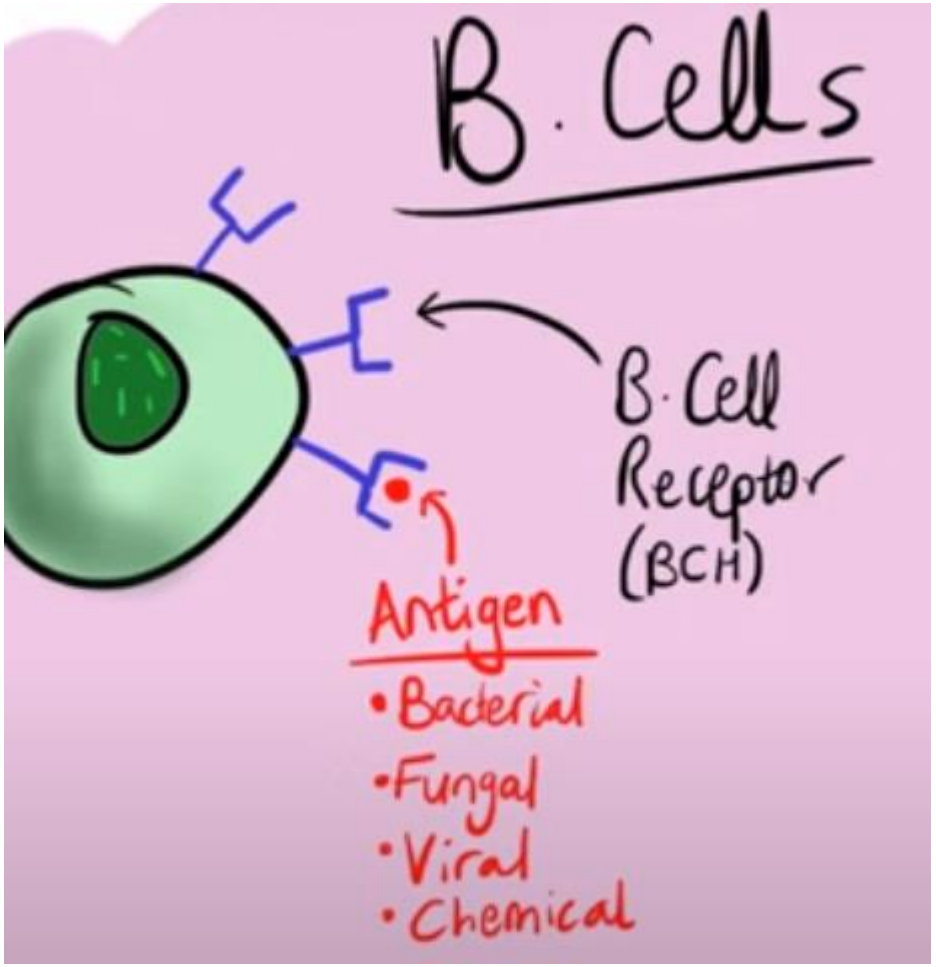
Natural killer cells (CD57 cells) and are developer from of T cell progenitor, representing a significant component of the innate immune system.

They do not produce antibodies against a foreign pathogen, but rather, are activated by chemical messenger molecules derived from macrophages including: interleukin- 2, 12, 15 and 18, and interferon. Natural killer cells circulate in the blood and possess cytotoxic properties whereby their primary responsibility is to "kill" viral and bacterial pathogens.



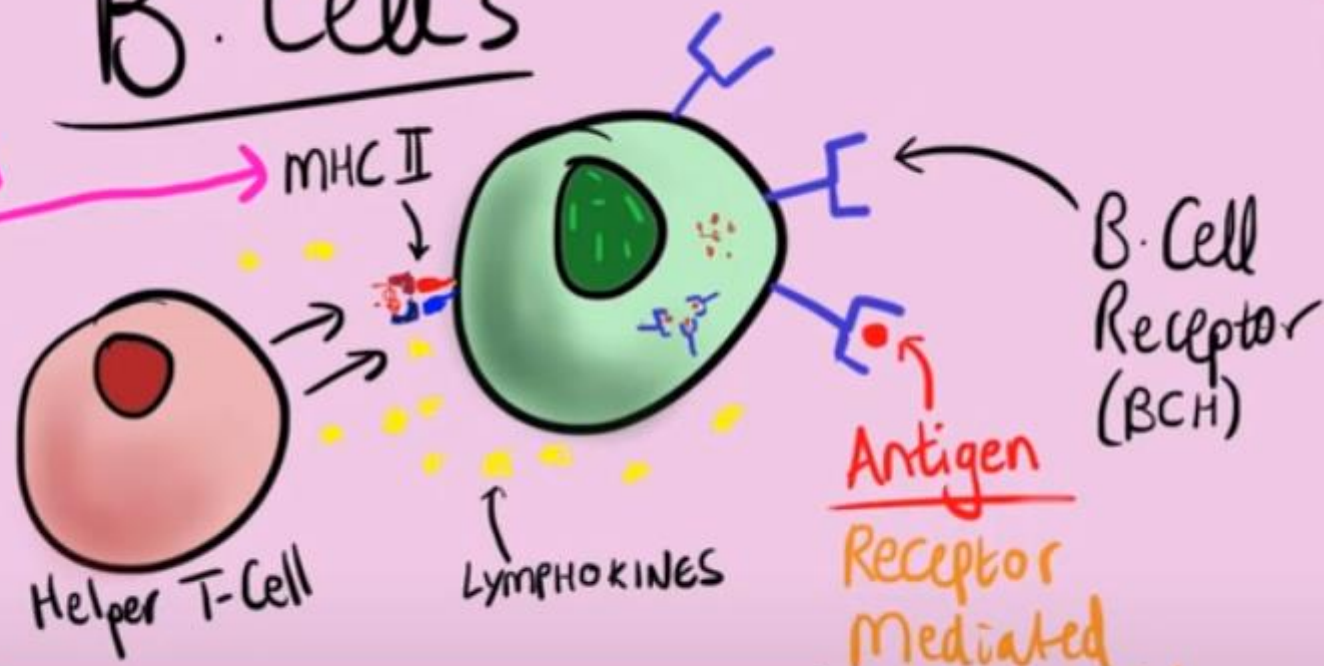
Natural killer cell

B cell


B. Cells
B. Cell Receptor (BCH)
Antigen
• Bacterial
• Fungal
• Viral
• Chemical

B Cells

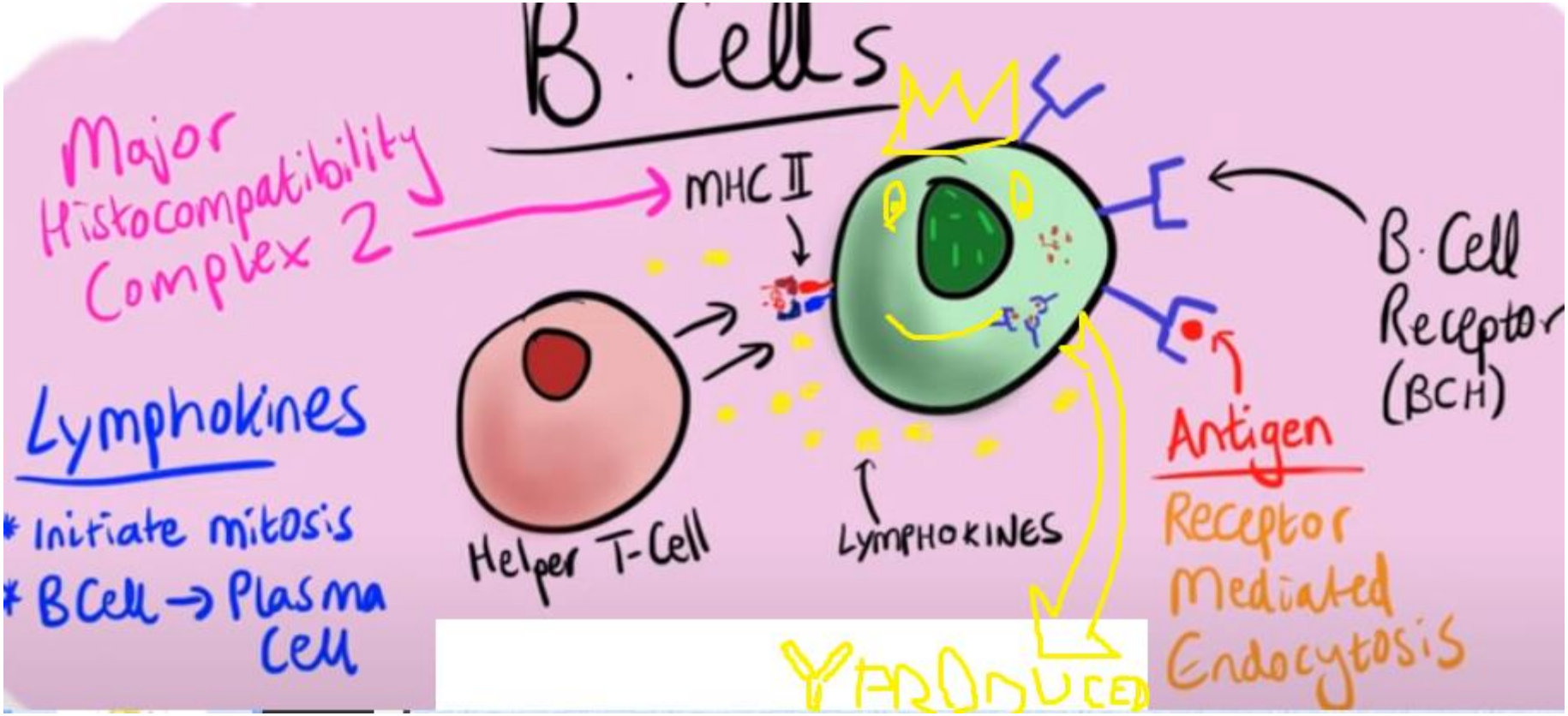
Major Histocompatibility Complex 2



Lymphokines

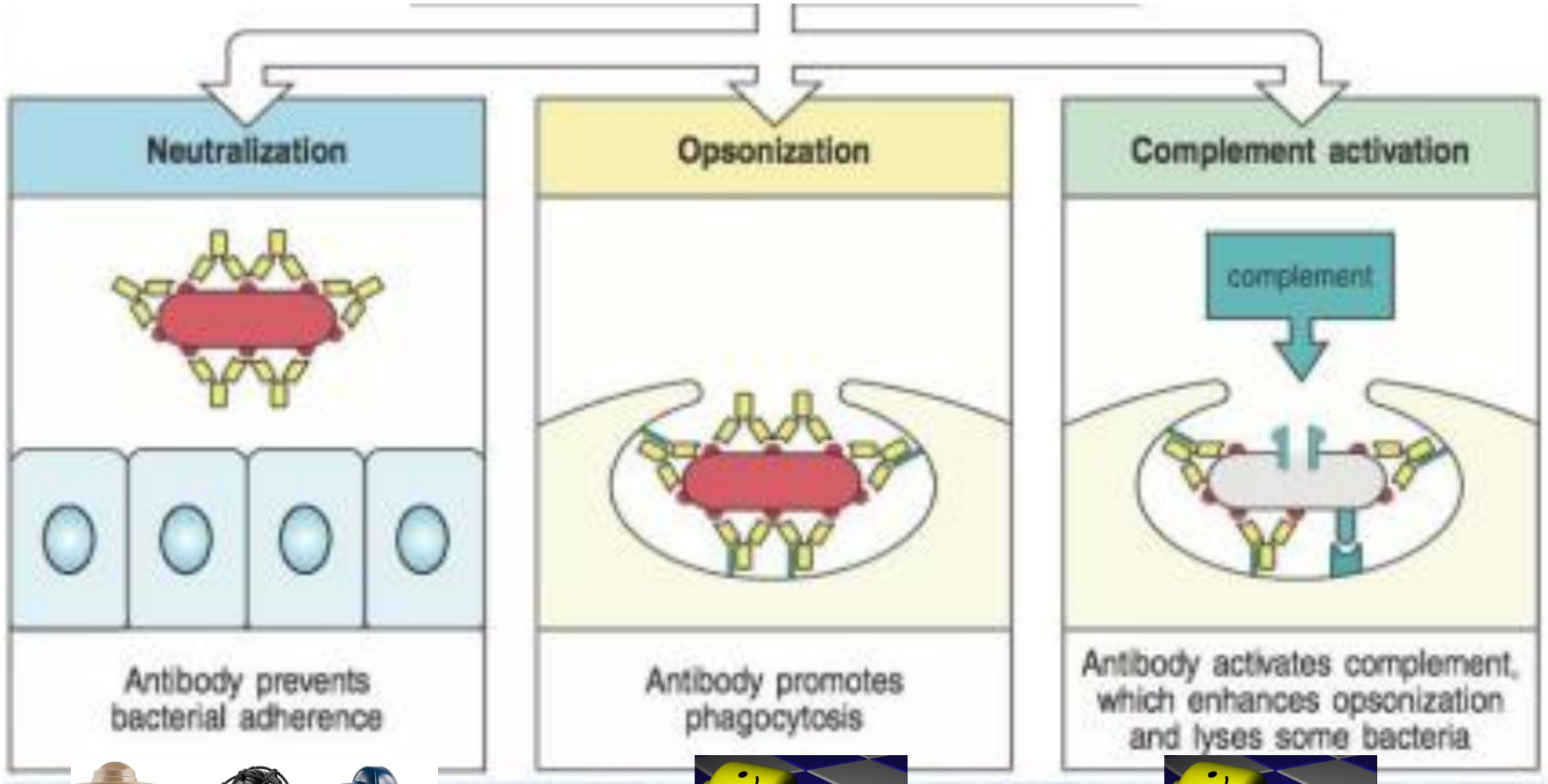
* Initiate mitosis
* BCell → Plasma Cell

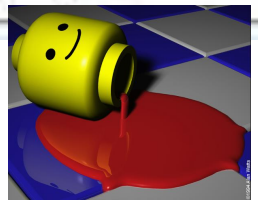
Receptor Mediated Endocytosis


B. Cells
Major Histocompatibility Complex 2
MHC II
B. Cell Receptor (BCH)
Lymphokines
* Initiate mitosis
* BCell → Plasma Cell
Helper T-Cell
LYMPHOKINES
Antigen
Receptor Mediated Endocytosis

IgM antigen

Final fight of IgM against bacteria (and other xenogenobiotica or pathogen)

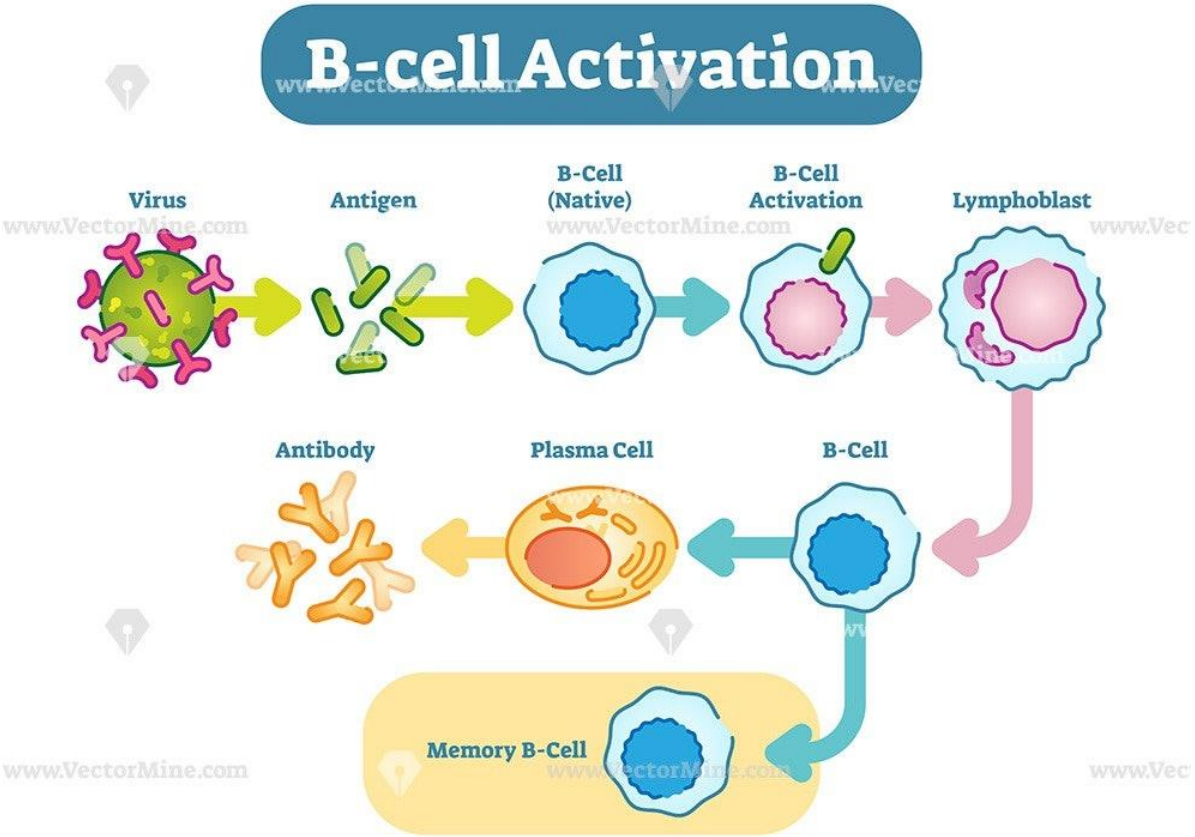




Example FOR SARS-virus neutralization see

file:///C:/Users/229576/Downloads/pathogens-10-00751-v3.pdf

Complex summary of main 2 types of B-Cells and activities



T cell

T-cells developer into two different group:

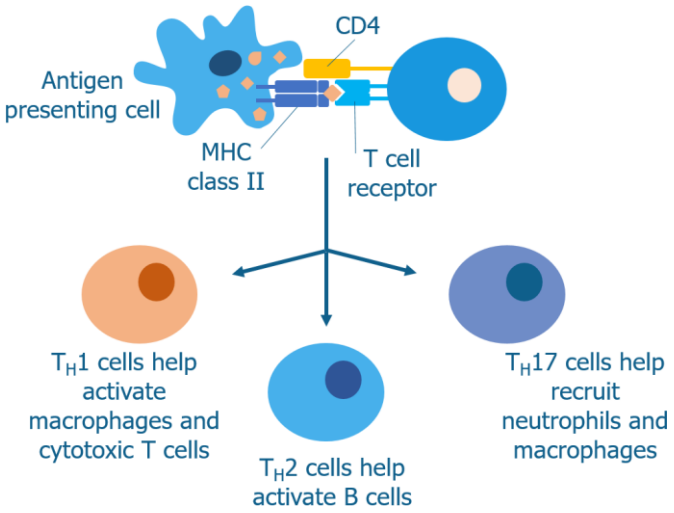
CD4 POSITIVE CELLS (so called Th or HELPER cell)

CD 8 POSITIVE CELL (so called CYTOTOXIC CELL)

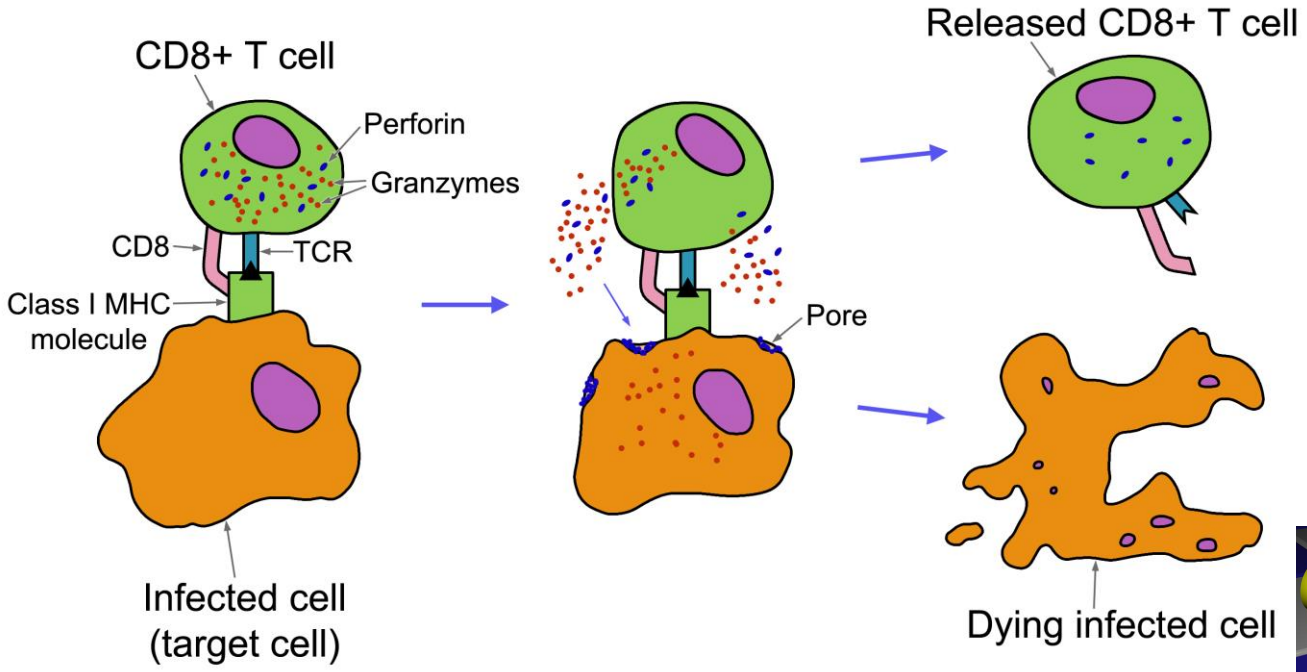
HELPER T lymphocyte have this role in the immune action:

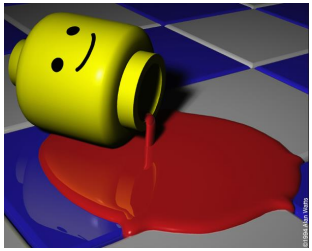
1. The T cell receptor on a CD4+ T cell recognizes the pathogen peptide displayed on the surface of an antigen presenting cell

2. Different types of helper T cells (T_H) are produced depending on the type of pathogen that is recognized

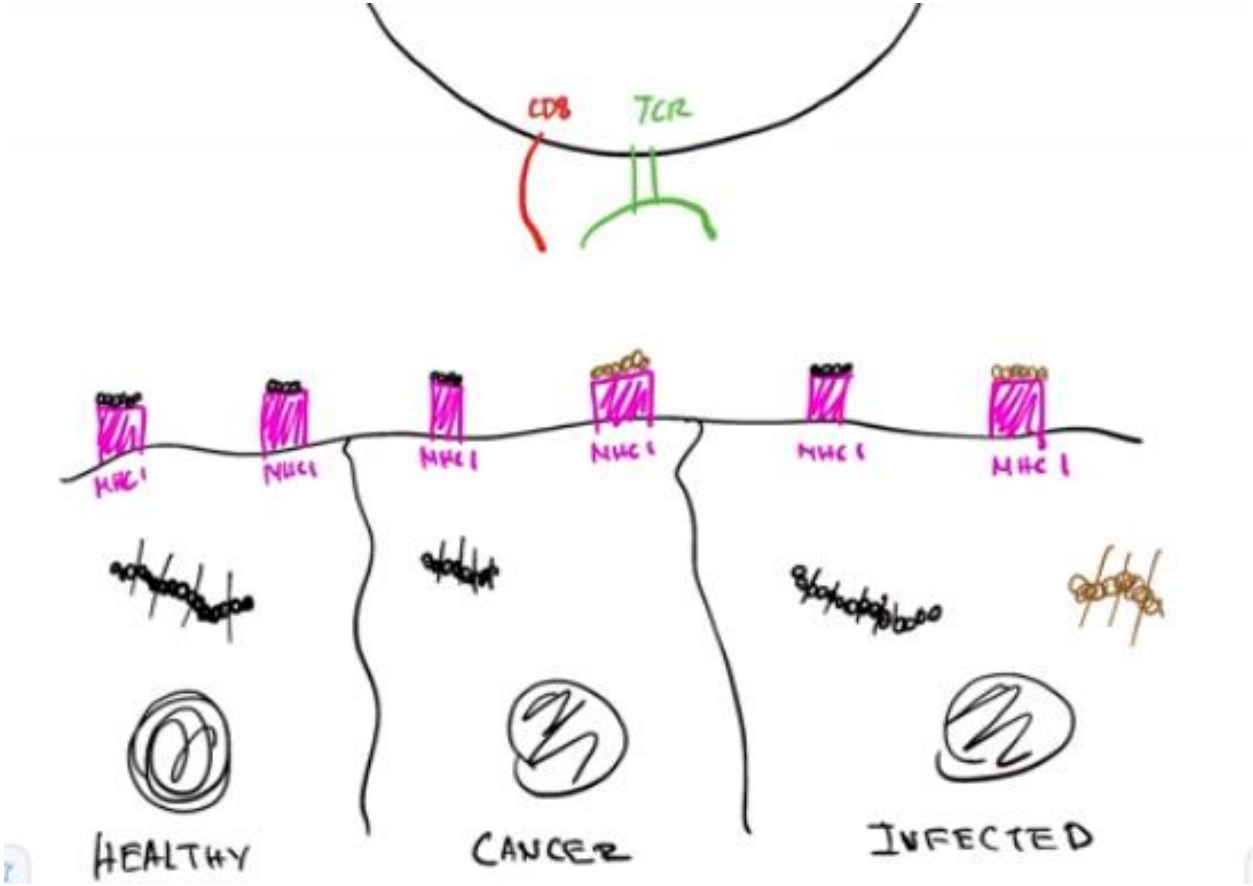


CYTOTOXIC T lymphocyte have this role in the immune action:

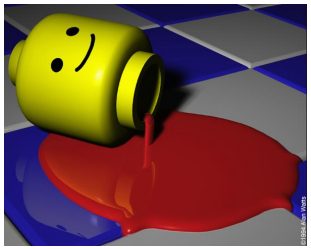


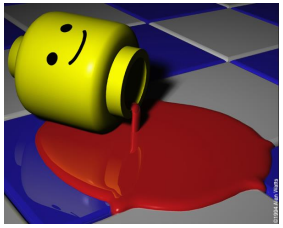


Cytotoxic T Cells and T Helper Cells - Bing video

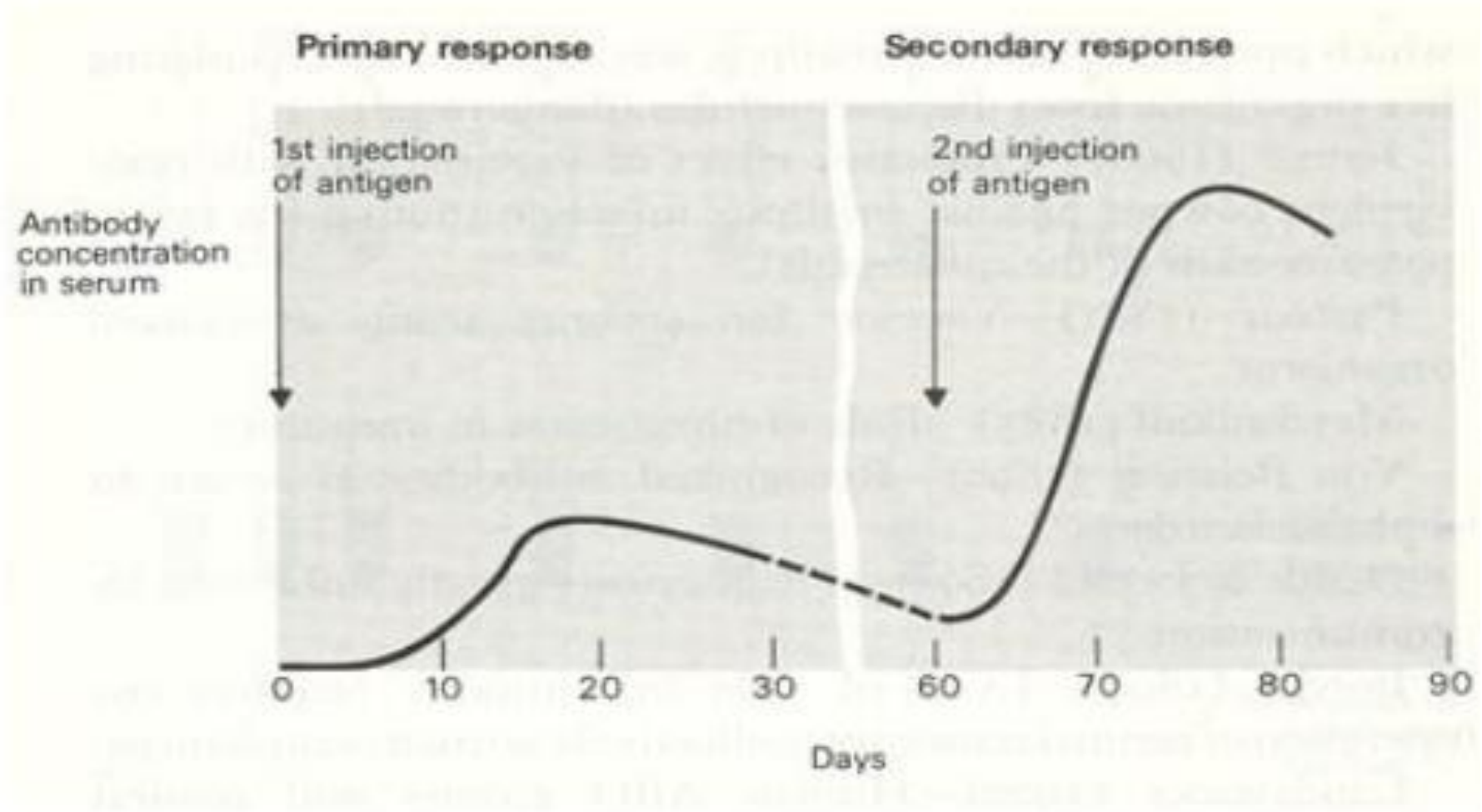


No killing by T_C cell





Imunity and memmory (cell production of ANTIBODY at first and second invasion of patogen)

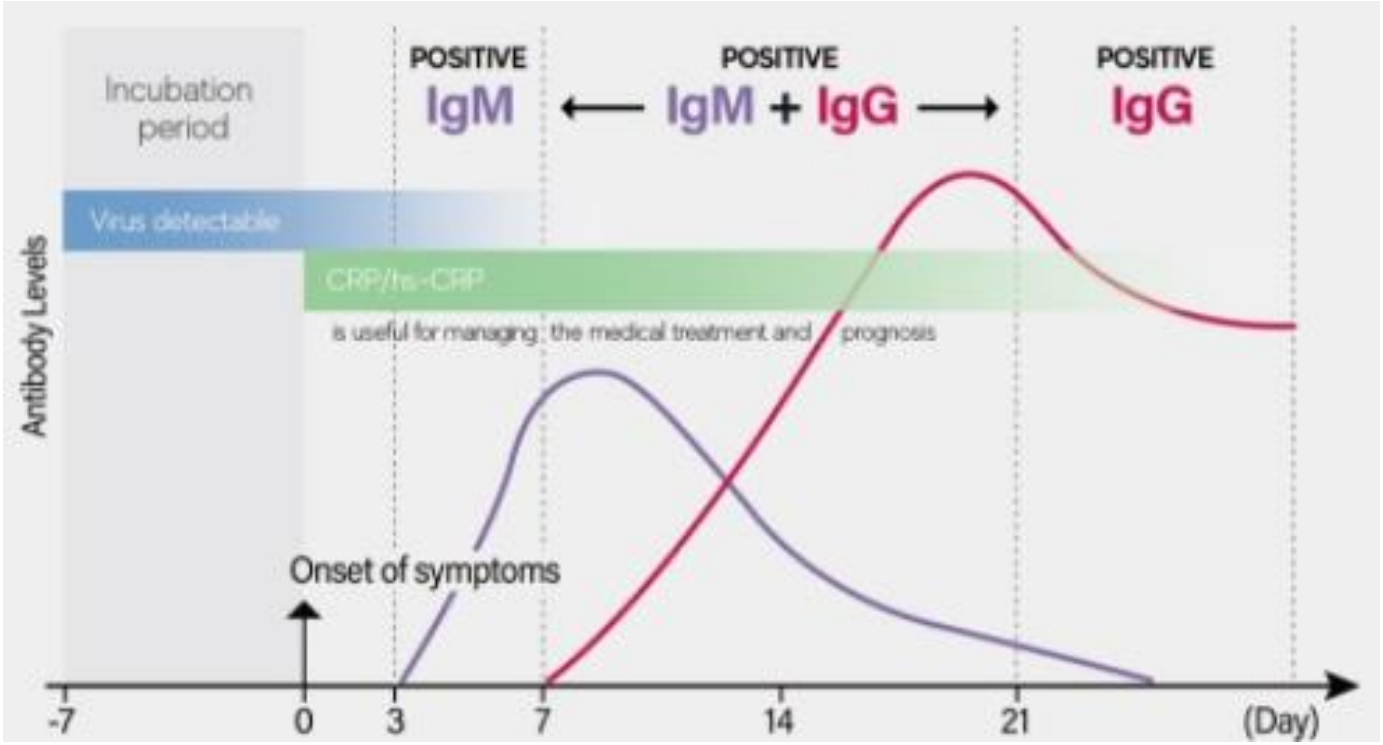


Exist only one type of antibodies?

No! Two most common are IgM and IgG.

T

Their activation time-schedule in patient after pathogen invasion is there:



Example FOR SARS-virus neutralization see file:///C:/Users/229576/Downloads/pathogens-10-00751-v3.pdf

Summary of pathogen elimination (not only by Tcell and B cell)

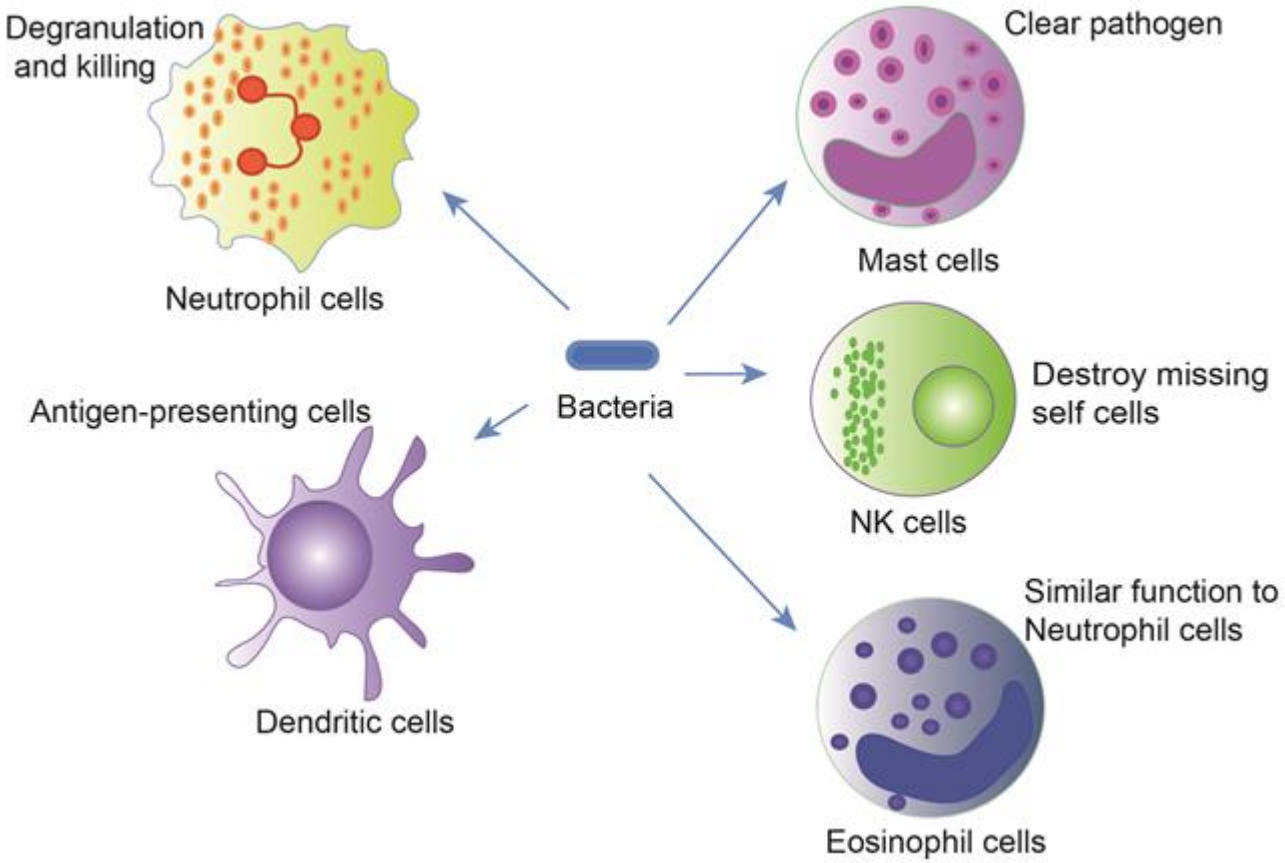
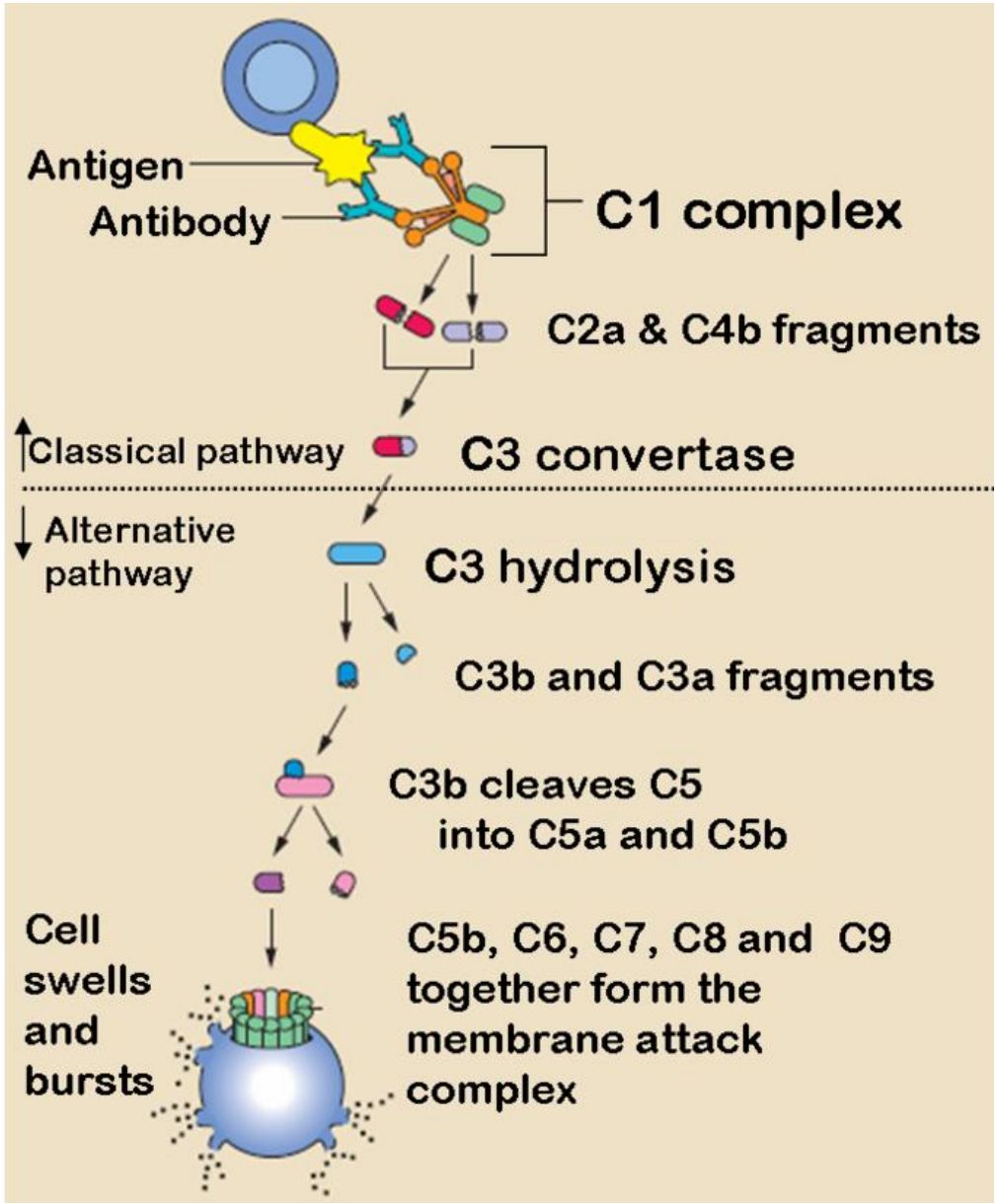


Figure 2: Phagocytosis in main innate immune cells
The innate immune cells include mast cells and natural killer cells, phagocytes (monocytes, macrophages and dendritic cells), and the granulocytes (neutrophils, eosinophils and basophils). Each cell type is equipped with different mechanisms to attack and eliminate pathogens from the host, but these innate immune cells could synergistically function to combat microbial entry.

COMPLEMENT

(additional type of immune reaction, where only molecule without blood cell play role)

- The complement system helps antibodies and phagocytic cells clear pathogens from an organism.
- The complement system consists of a number of small proteins produced by the acute phase reaction in the liver during inflammation.
- Complement was discovered many years ago as a heat-labile component of normal plasma that augments the opsonization of bacteria by antibodies and allows antibodies to kill some bacteria. This activity was said to 'complement' the antibacterial activity of antibody, hence the name. Although first discovered as an effector arm of the antibody response, complement can also be activated early in infection in the absence of antibodies. Indeed, it now seems clear that complement first evolved as part of the innate immune system, where it still plays an important role.
- The **complement system** is made up of a large number of distinct plasma proteins that react with one another to opsonize pathogens and induce a series of inflammatory responses that help to fight infection. A number of complement proteins are proteases that are themselves activated by proteolytic cleavage. Such enzymes are called zymogens and were first found in the gut. The digestive enzyme pepsin, for example, is stored inside cells and secreted as an inactive precursor enzyme, pepsinogen, which is only cleaved to pepsin in the acid environment of the stomach. The advantage to the host of not being autodigested is obvious.
- The **classical complement pathway** starts with antibody binding, which causes a cascade reaction of complement proteins that gradually form a membrane attack complex.
- The **alternative complement pathway** is usually stimulated by pathogen antigens or toxins rather than antibodies, and cleaves C3 until there is enough to continue the steps of the classical complement pathway from the C5 convertase step.
- The lectin pathway is homologous to the classical pathway, but with the opsonin, mannose-binding lectin (MBL), and ficolins, instead of C1 from the antibody. This pathway uses proteases on the MBL to form C3 convertase, which continues the steps of the classical complement pathway from the C3 convertase step.
- The complement system is regulated by complement control proteins, such as decay accelerating pathway, which prevent complement proteins from forming MAC on the body's cells.



remember:

C1

C2 andC4

C3

C5

C6 –C9

-basic picture scheme-

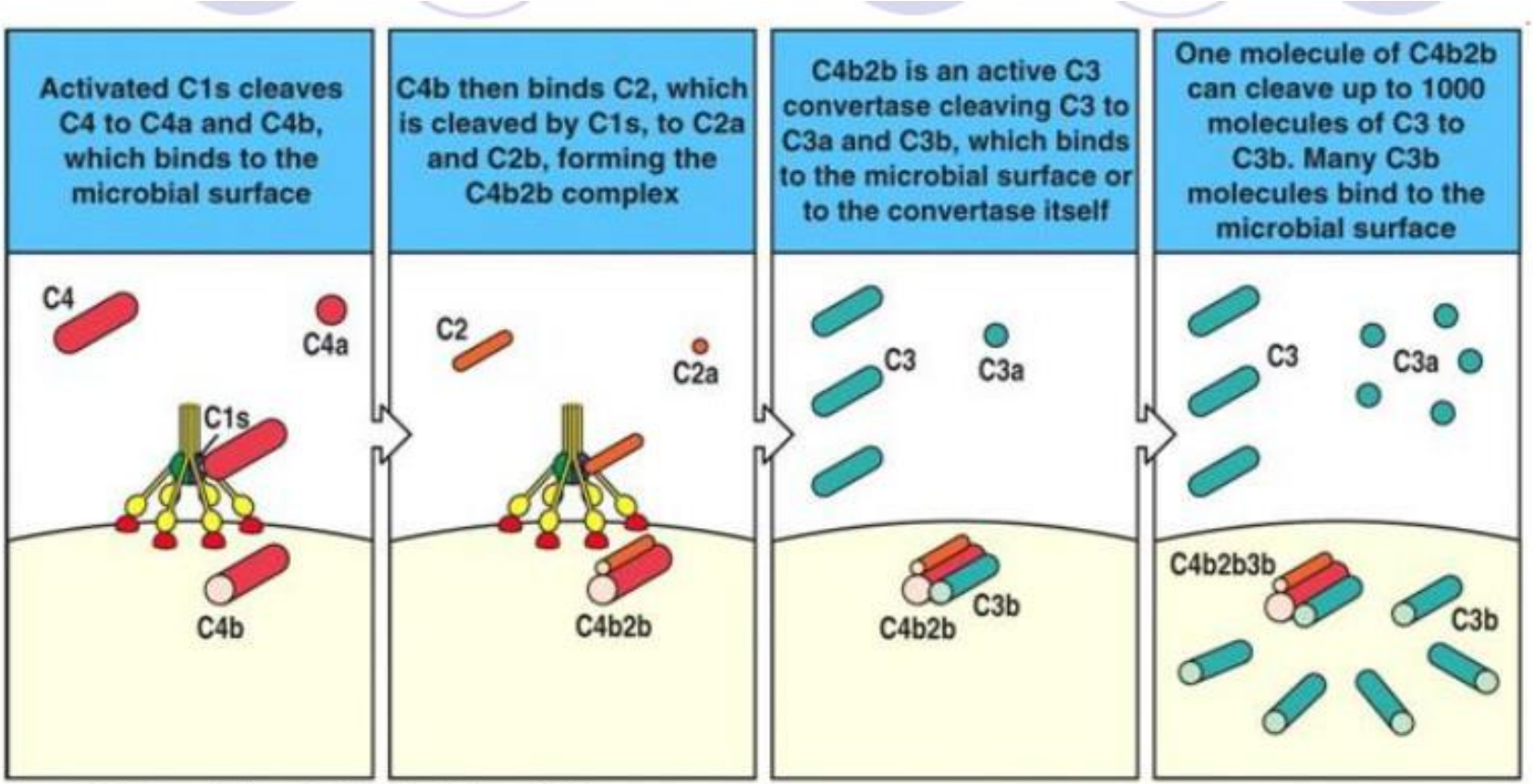
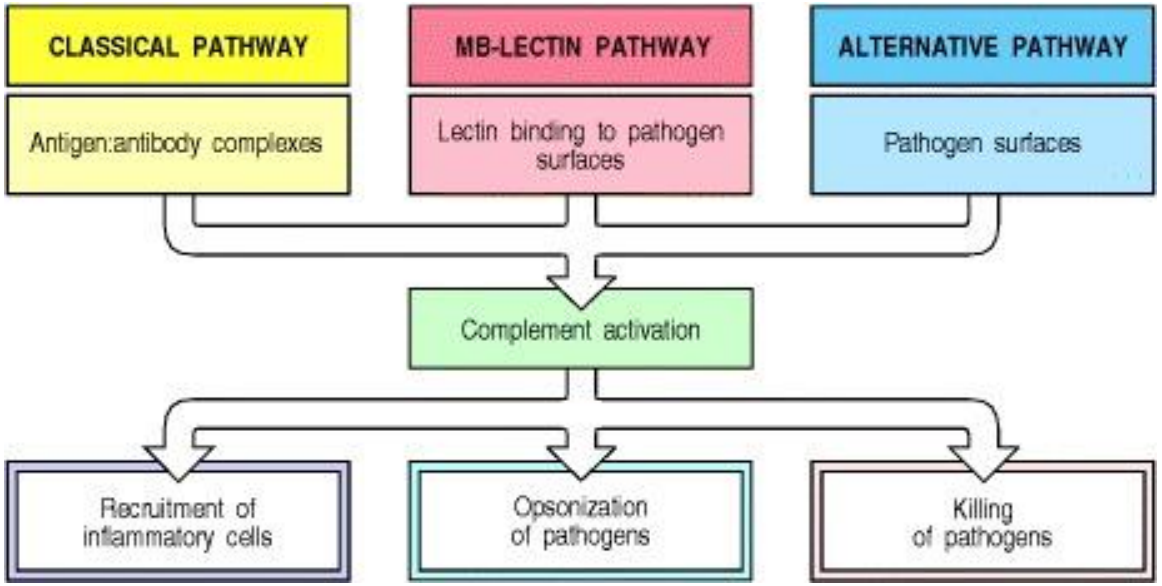


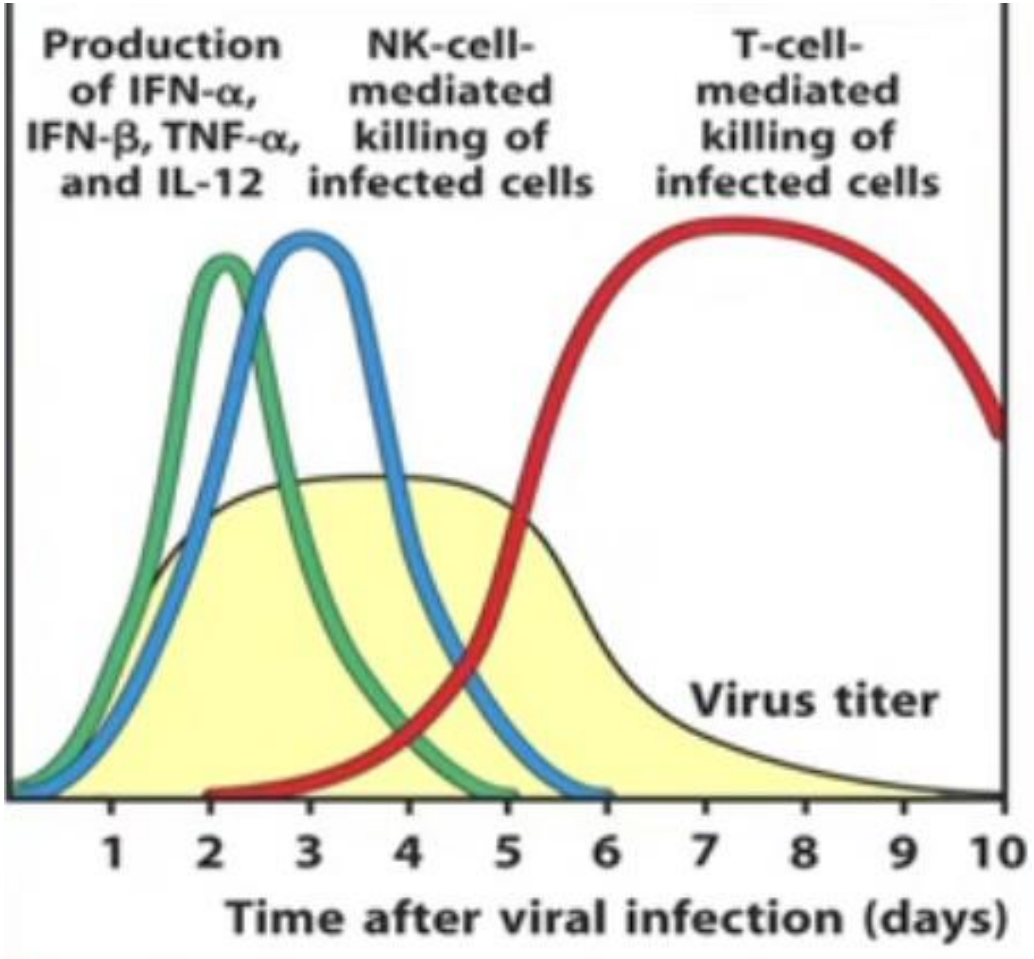
Figure 2-22 Immunobiology, 6/e. (© Garland Science 2005)

Summary of effect of classical and another COMPLEMENT pathways



TIME interval of immune action

(compare NK-cell vs. T-cell)



Described problem of decreased or increased imuno-reaction

Antigen	Co-stimulation	No Co-stimulation
Infectious agent	Protective immunity	Recurrent infection
Innocuous substance	Allergy	No Allergy
Grafted organ	Rejection	Acceptance
Self organ	Autoimmunity	Self tolerance
Tumor	Tumor immunity	Cancer

Figure 1.32 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Odkazy

- Slide 1 (vscht.cz)
- Figure 2.7, Schematic overview of the complement cascade - Immunobiology - NCBI Bookshelf (nih.gov)