Immunity

Department of Biology, Medical Faculty,
Medical University of Sofia

What is immunity

- We are surrounded by pathogens trying to exploit us as a resource.
- To survive and prosper, we must fight them back. Our successful resistance against pathogens is called immunity.
- Organs and cells providing immunity form the immune system.
- Immunity is two types – innate and adaptive.

What is innate immunity

- Some of our defenses are ready to act with full force against the pathogen even before it has appeared. They are called natural or innate immunity.
- The innate immunity is non-specific, because it is directed against pathogens in general, rather than against any particular pathogen.
- It will not become more efficient after the first encounter with the pathogen.

Adaptive immunity

- Innate immunity has limited efficiency. Being broad-spectrum, it is often not effective enough against a particular pathogen.
- For that reason, specific immunity has evolved. It is based on “lock and key” recognition between macromolecules.
- Specific immunity is called adaptive or acquired, because it develops only after the pathogen is encountered and is much more efficient at the second encounter.
- The organs responsible for adaptive immunity are called lymphoid system or adaptive immune system.

Without adaptive immunity (e.g. in severe combined immunodeficiency), life expectancy is up to 1 year.

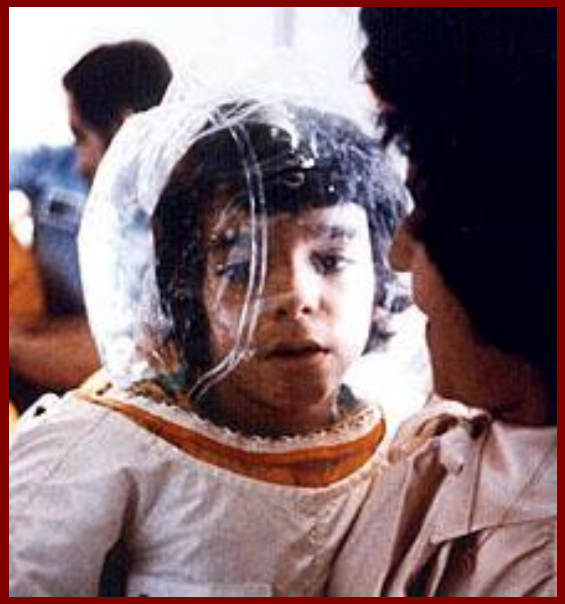
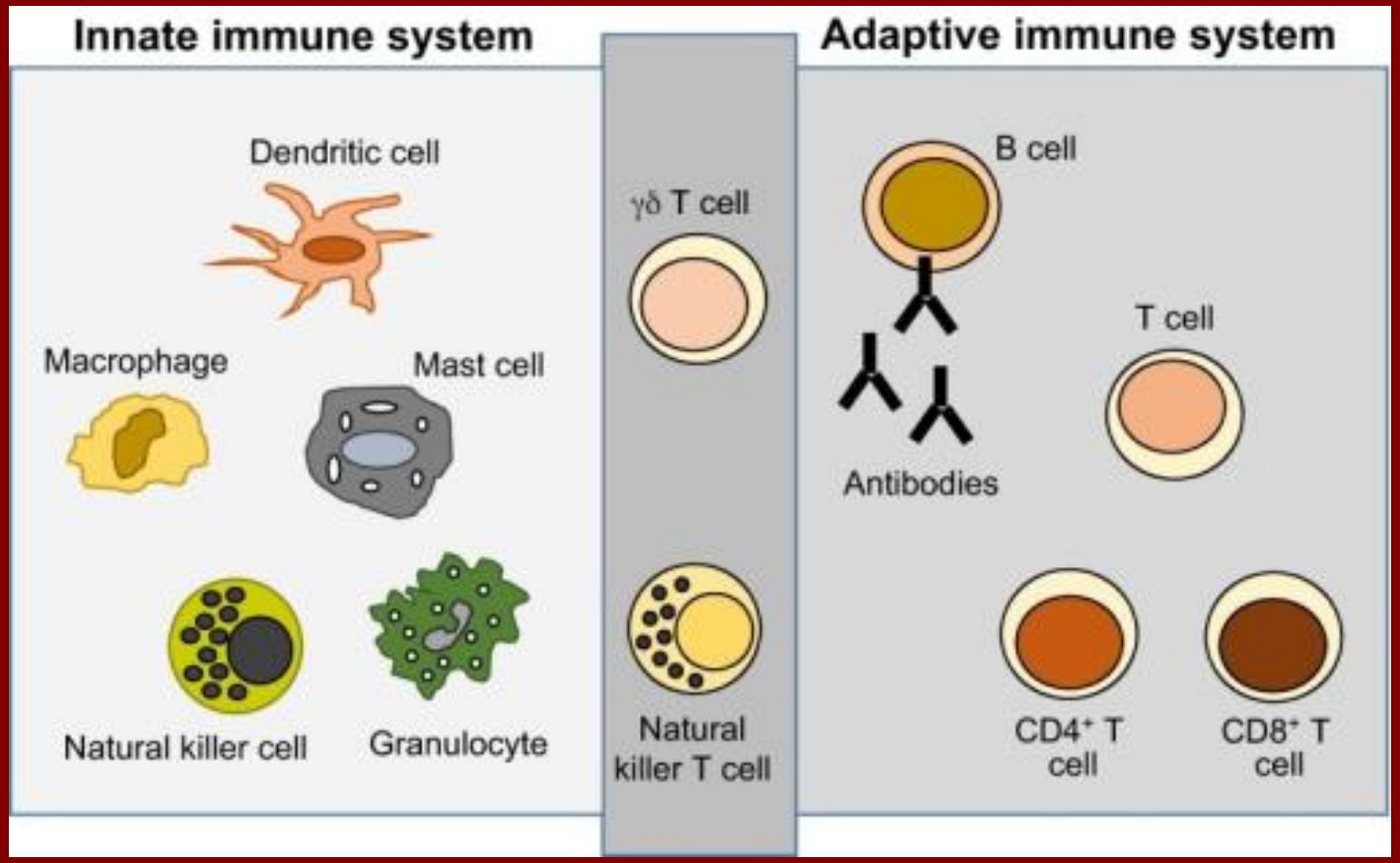


Photo: “the bubble boy” David Vetter (1971 – 1984), born with this condition, had to spend his life in a sterile environment. Source: Baylor College of Medicine Archives

Innate and adaptive immunity



https://openi.nlm.nih.gov/detailedresult.php?img=PMC4381333_DMM018036F1&req=4

Innate immunity is partly due to the barriers of the body

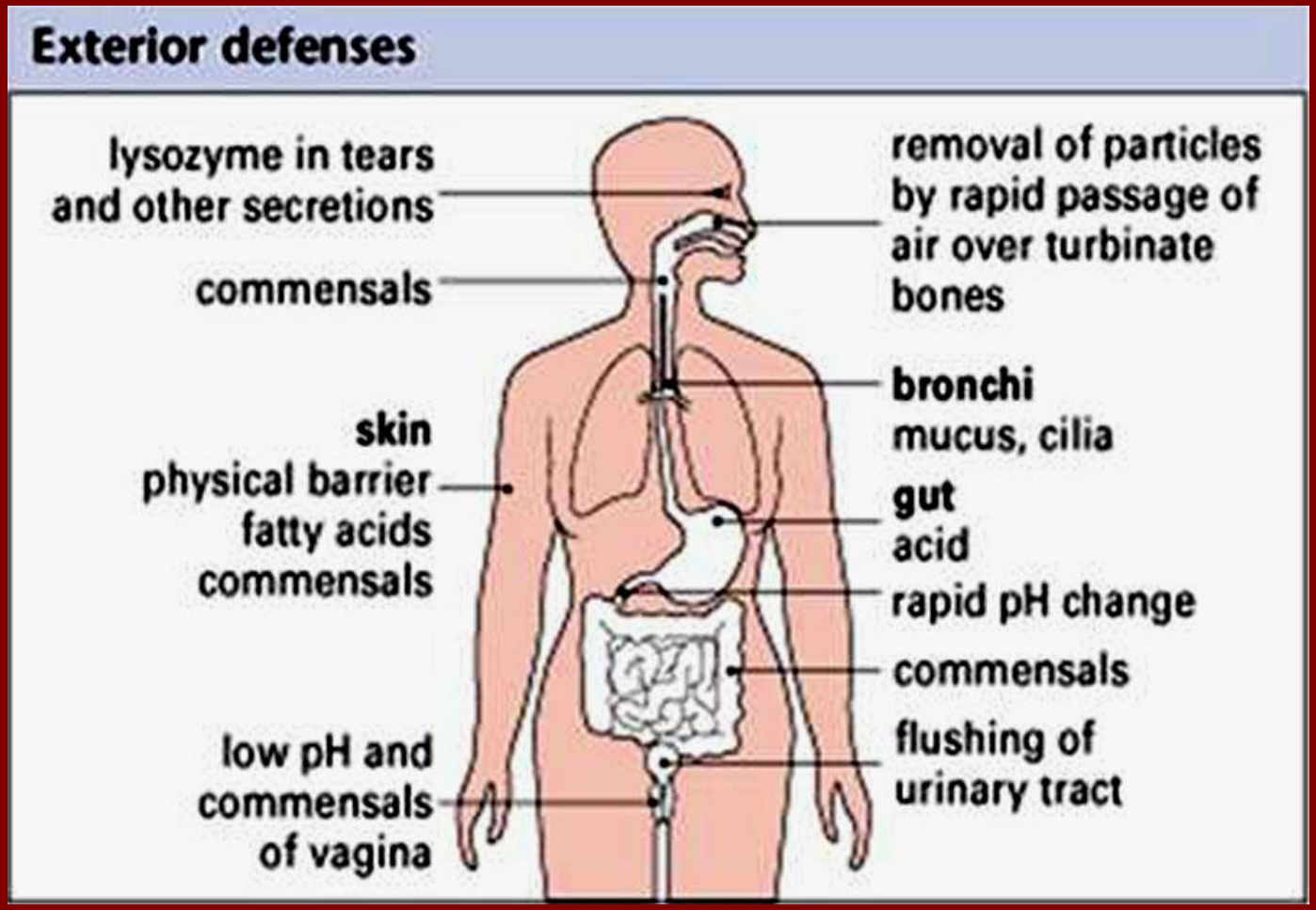
First barrier against pathogens is healthy skin. Microorganisms can not overcome the skin. The sweat, saliva, tears and urine wash pathogens away. If the skin is injured, pathogens reach mucosal surfaces. Mucus traps pathogens and protects epithelial cells. Low pH in the stomach kills microbes. The large intestine and the vagina possess normal microflora which prevent development of pathogens.

Anatomical barriers of the innate immunity	
1. Physical barrier	• Skin, washing actions, etc.
2. Chemical barrier	• Low pH, fatty acids secretion, etc.
3. Biological barrier	• Competition by other normal flora on skin surface; secretion of bactericidal agents from other micro-organisms

Table from http://www.acad.polyu.edu.hk

Barriers mapped

Barriers are NOT part of the immune system. They are just borders which limit the access of pathogens to the body. If microbes overcome the barriers, immune response starts.



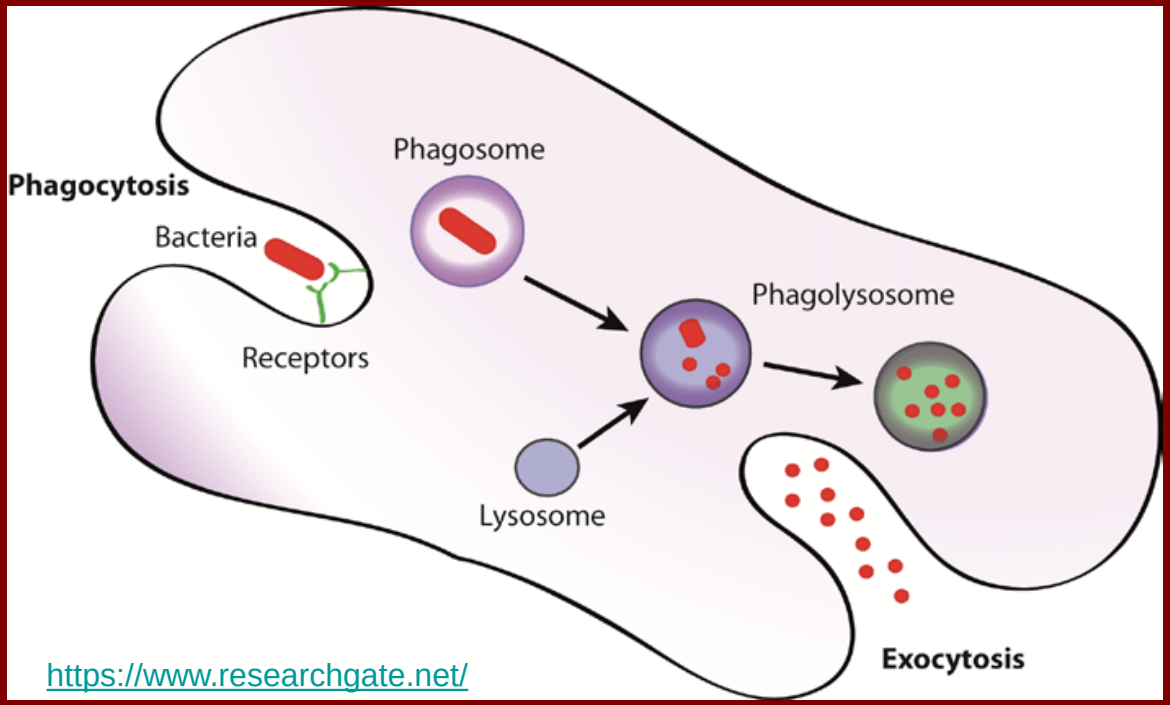
Drawing from http://www.acad.polyu.edu.hk

Phagocytosis

Phagocytosis is a way innate immunity deals with pathogens that pass the barriers. Phagocytes are the first cells interacting with foreign substances.

Phagocyte recognizes a microorganism and forms pseudopodia to surround it. The cell engulfs the pathogen and digests it by lysosomes. Later the wastes are ejected by exocytosis.

Phagocytosis is a primitive trait of eukaryotic cells. It is used by unicellular eukaryotes for feeding. For multicellular organisms phagocytosis loses its role of feeding mechanism. Multicellular animals utilize it for immunity. That's why few types of cells in multicellular organism are able to make phagocytosis.

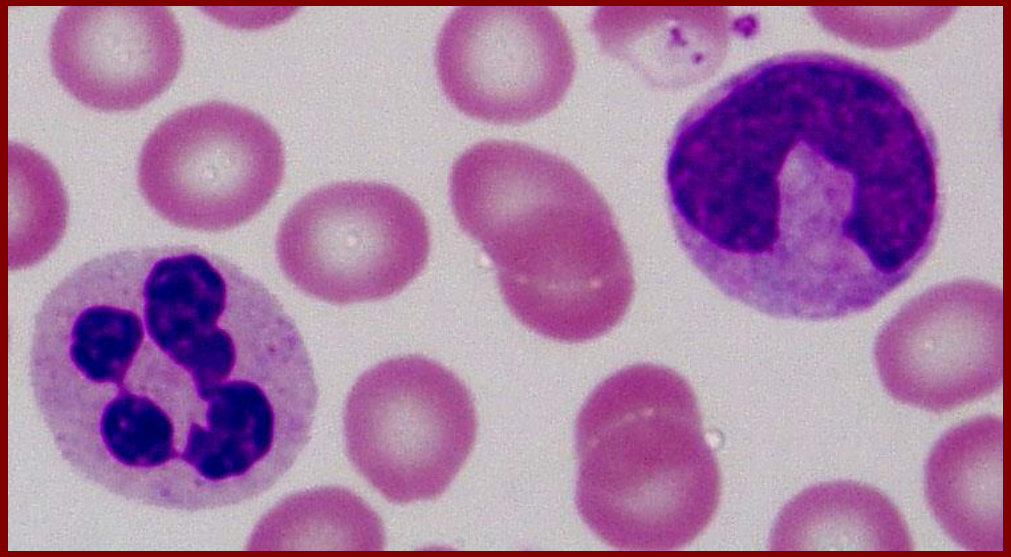


https://www.researchgate.net/

The phagocytes

Two cell types are phagocytes: the neutrophils and the macrophages.

Neutrophil



Monocyte (blood macrophage)

Source: Blue Histology

Neutrophils

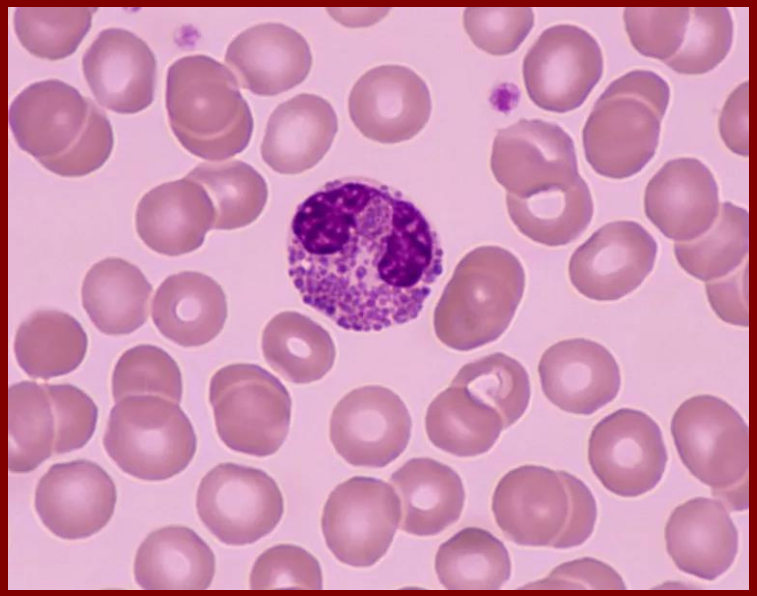
They are small cells with segmented nuclei. Neutrophils are restricted to the blood. They are short – lived cells (1-2) days.

Macrophages

They are larger cells. Nucleus is non-segmented. Macrophages are longed-lived cells in the blood and in tissues.

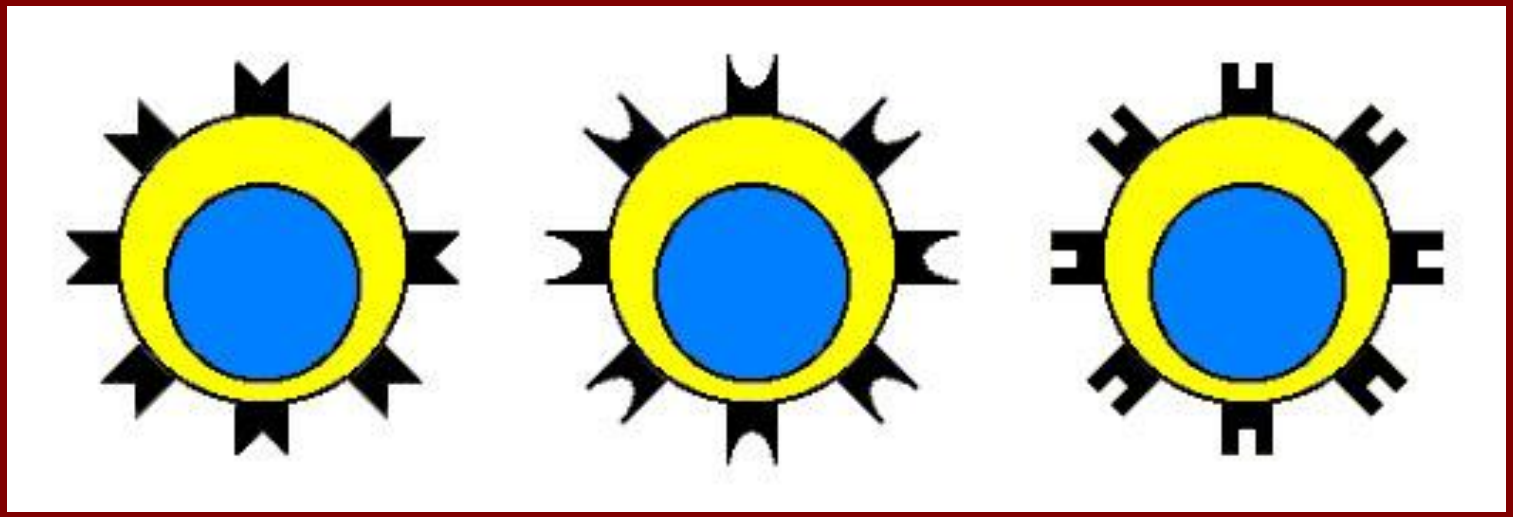
Eosinophils

Eosinophils kill their victim by extracellular degranulation. If the pathogen is too large to be engulfed, eosinophils release their granules by exocytosis. These granules contain lysosomal enzymes to digest the victim extracellularly. Eosinophils are the major innate defense against parasitic worms. They are found in blood and submucosal tissues, where parasite invasion is most likely to happen.



Eosinophil in a blood smear
https://www.verywellhealth.com/

Adaptive immunity is based on B and T lymphocytes. They have specific surface receptors for antigen

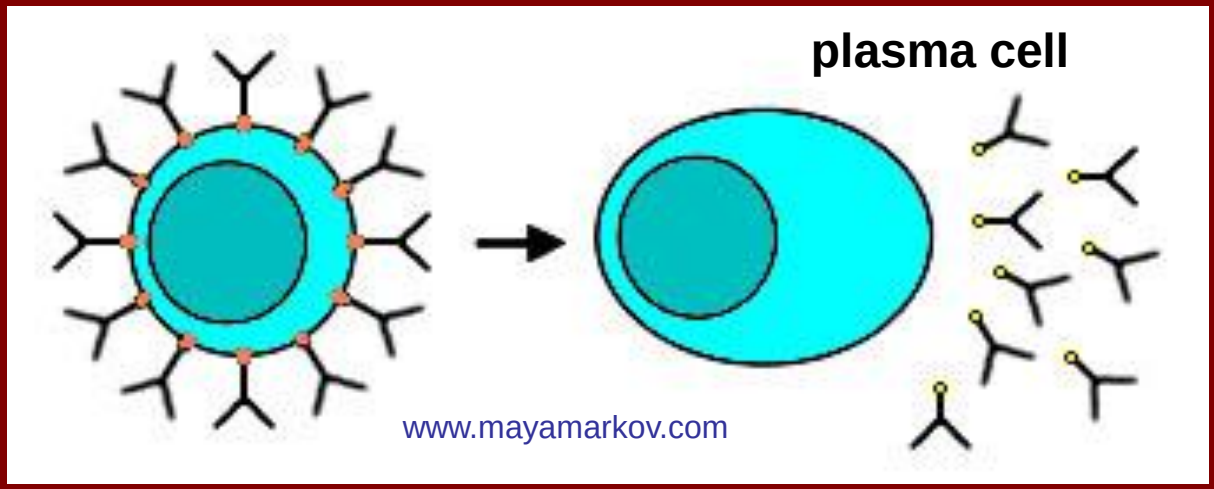


www.mayamarkov.com

B cells synthesize antibodies (immunoglobulins)

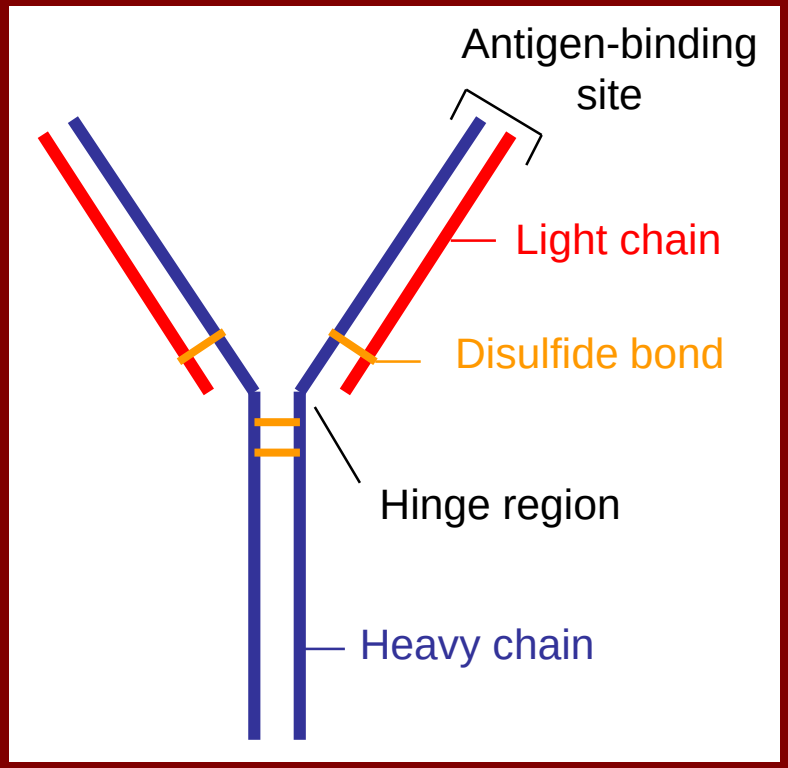
They are initially receptors, i.e. cell membrane proteins, and later are produced in a secretory (soluble) form to work.

Antibodies mediate humoral immunity.



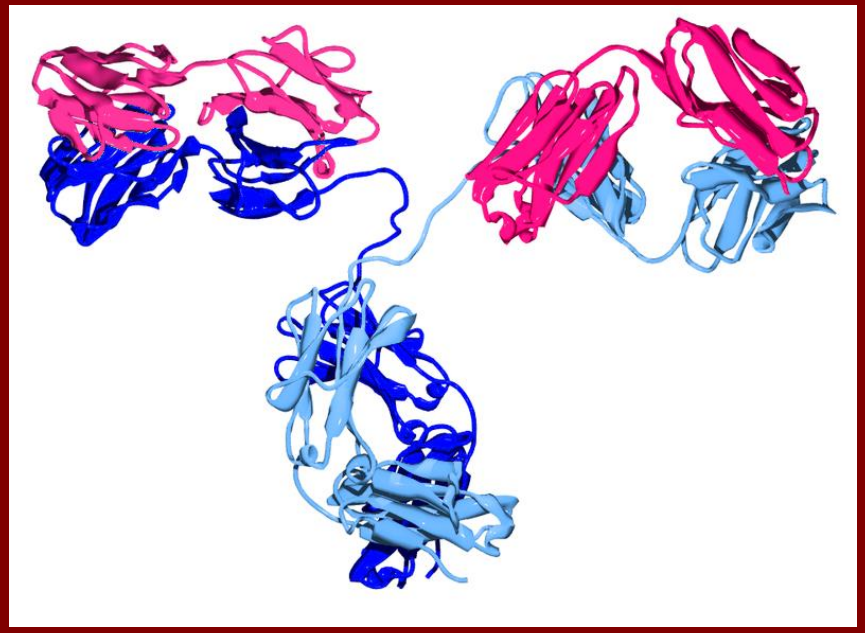
Antibody structure

The antibody is a protein in quaternary structure. It consists of two types of polypeptide chains. Each chain has two copies in the antibody monomer. Shorter chains (in red on the left picture) are called light chains. Longer polypeptides (in blue) are called heavy chains. These four protein molecules are bound together by disulfide bonds. Light and heavy chains together form two antigen-binding sites. Antigen and antibody are bound by week NON-COVALENT BONDS. Their connection is made because of spatial affinity, electrostatic and hydrophobic interactions etc.



Molecular model of IgG

(by Tim Vickers, adapted)



T cells are responsible for cell-mediated immunity

They have a surface receptor recognizing antigen.

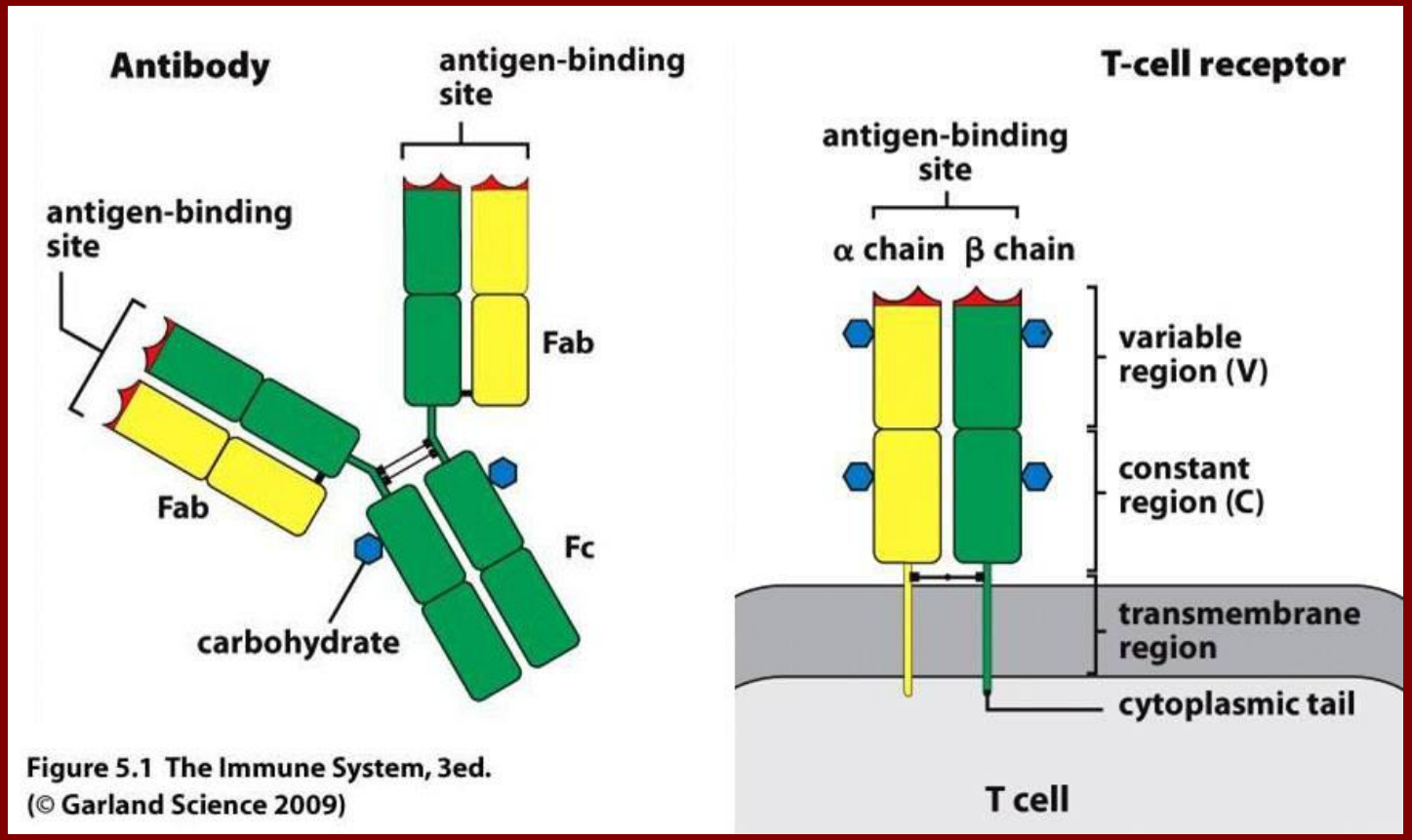
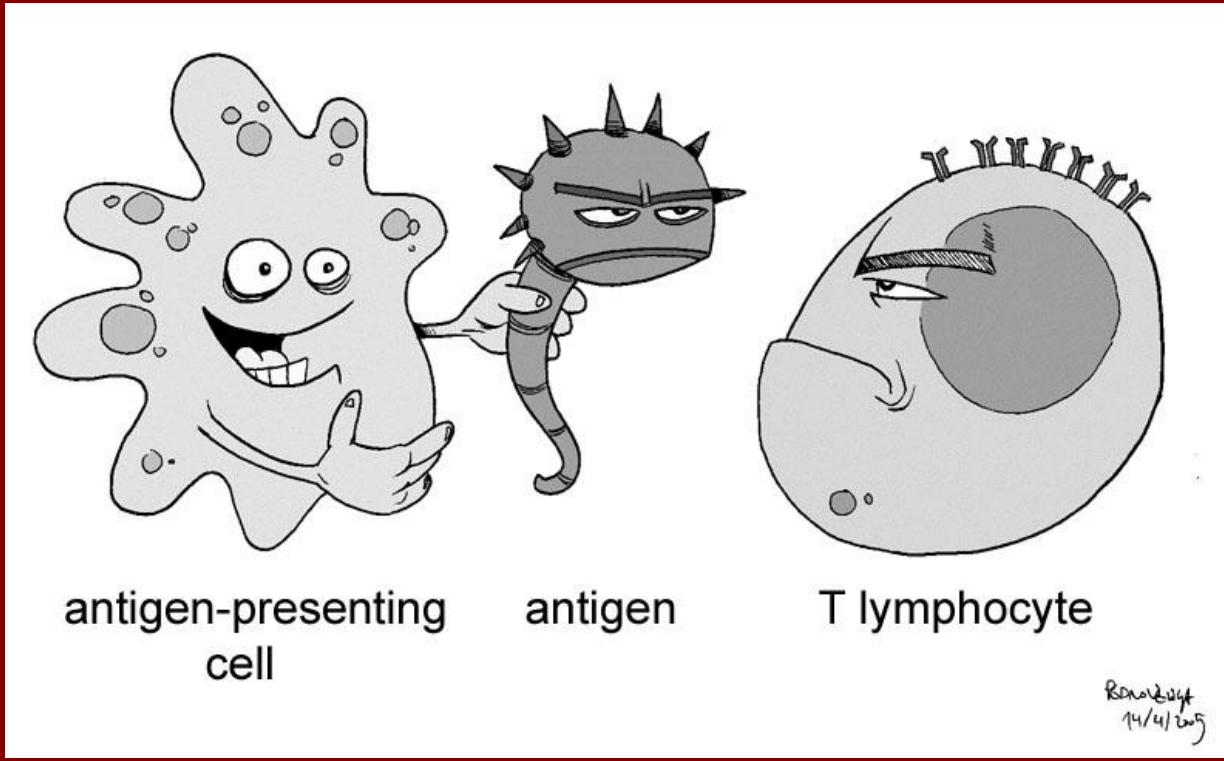


Figure 5.1 The Immune System, 3ed.
(© Garland Science 2009)

T cells need a phagocyte to present the antigen

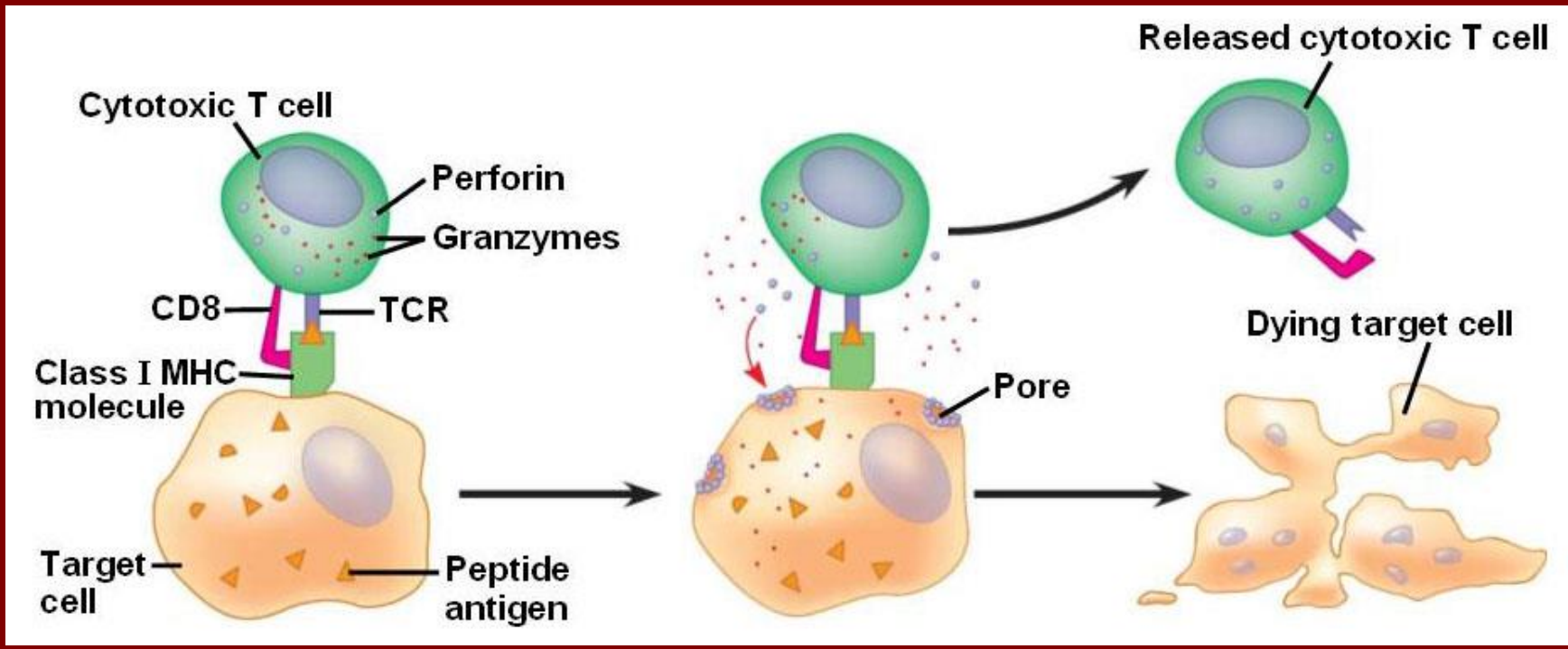
T cells do not recognize natural antigen. T cells require antigen presentation from other cells in the body. A cell like a phagocyte engulfs the pathogen and digests it. Later the phagocyte expresses pieces of the digested pathogen on its surface. These pieces of the microbe are bound with special cell surface molecules. T cell recognizes the complex of the pathogen and cell surface molecule as a whole structure – an antigen. Because of this recognition, T cell is activated.



http://dict.space.4goo.net

T killers lyse virus-infected cells and cancer cells

T killers are adapted to react against our own cells. If a cell from our body is infected whit a virus or is transformed to a cancer cell, it starts to produce strange proteins. The cell will express pieces of these unusual proteins on its surface. These short peptides are bound to the special cell surface molecules. T killer recognizes these complex and release toxic granules. These granules contain enzymes which provoke dead of the target cell. T killer instructs our cell to kill itself in order to eliminate the virus.



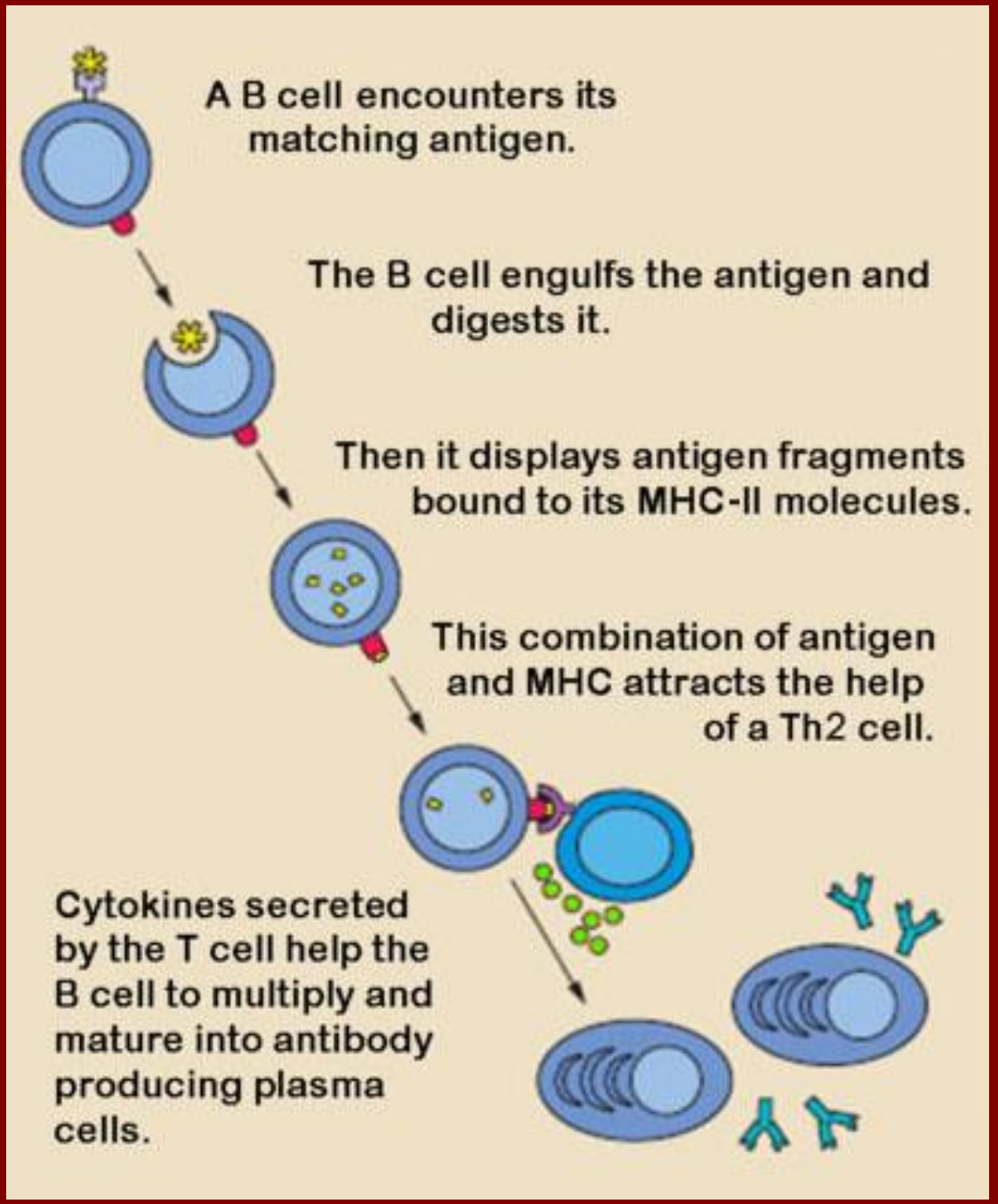
http://bio1152.nicerweb.com

T helpers are needed to activate both T killers and B cells

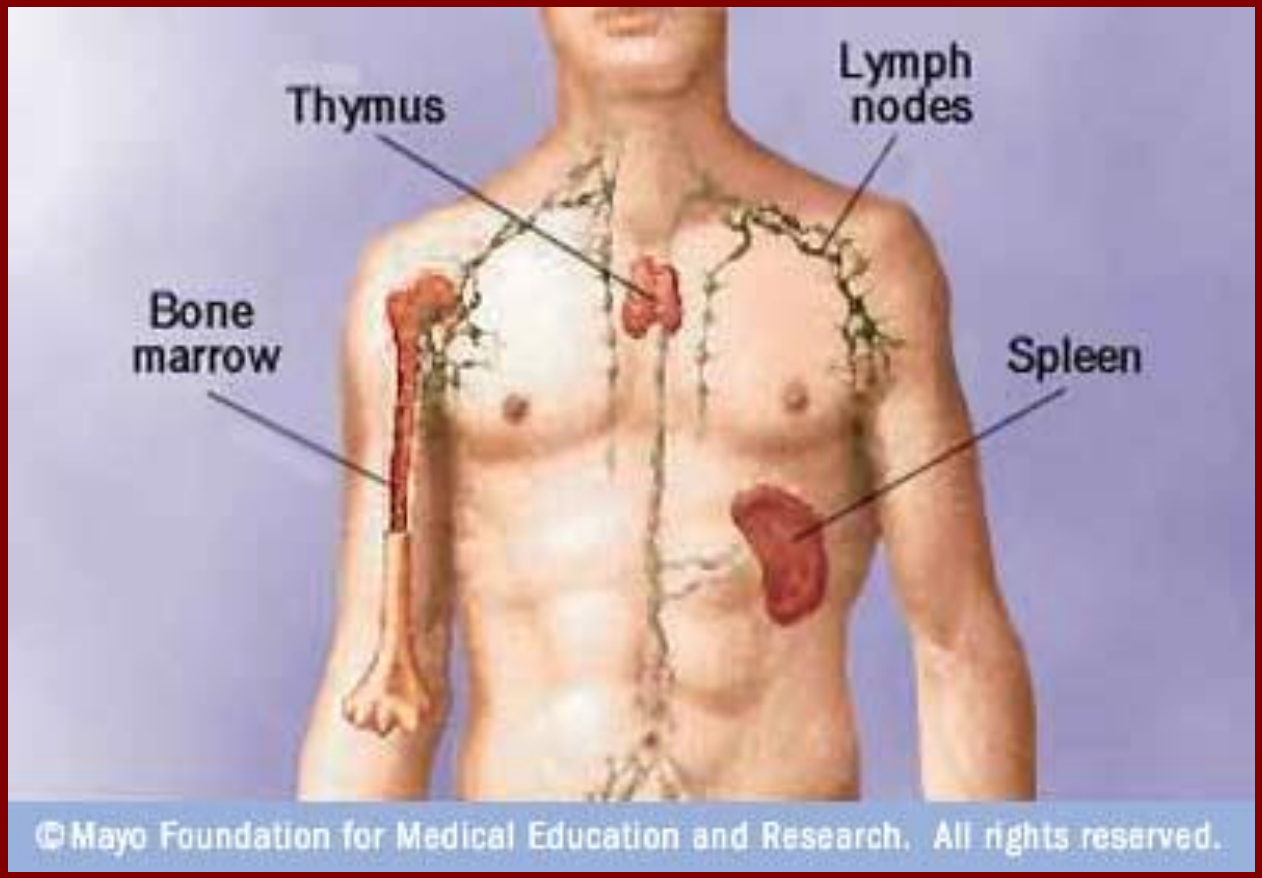
T helpers are the basic regulators of the immune system. They help the activity of other immune cells by releasing T cell cytokines. These cells help suppress or regulate immune responses.

HIV virus specifically recognize and attack T helper cells. When helpers are killed, whole immune system is eliminated.

Modified from www.niaid.nih.gov



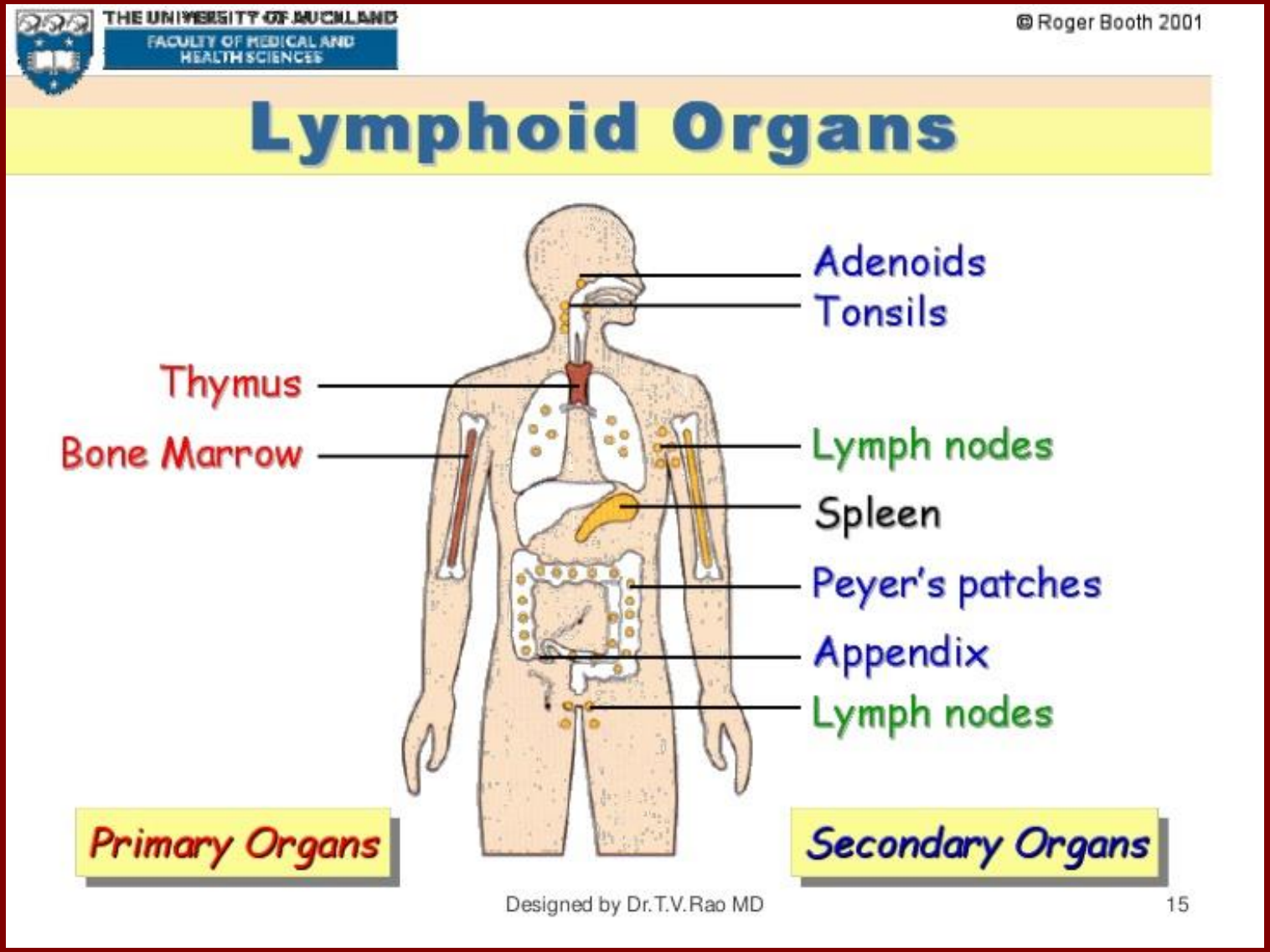
The immune system includes central and peripheral organs



In central organs, lymphocytes become able to recognize antigen

P. Calabresi (2006), http://myelitis.org

In peripheral organs, immune response is developed



Secondary immune response is better than primary (immunological memory)

When the pathogen comes for the first time in our body, our immune system requires time to react. There are single immune cells which recognize it. These cells have to multiply in order to react against the antigen. Mitotic divisions require time and our immune system reacts 5 - 7 days after pathogen recognition.

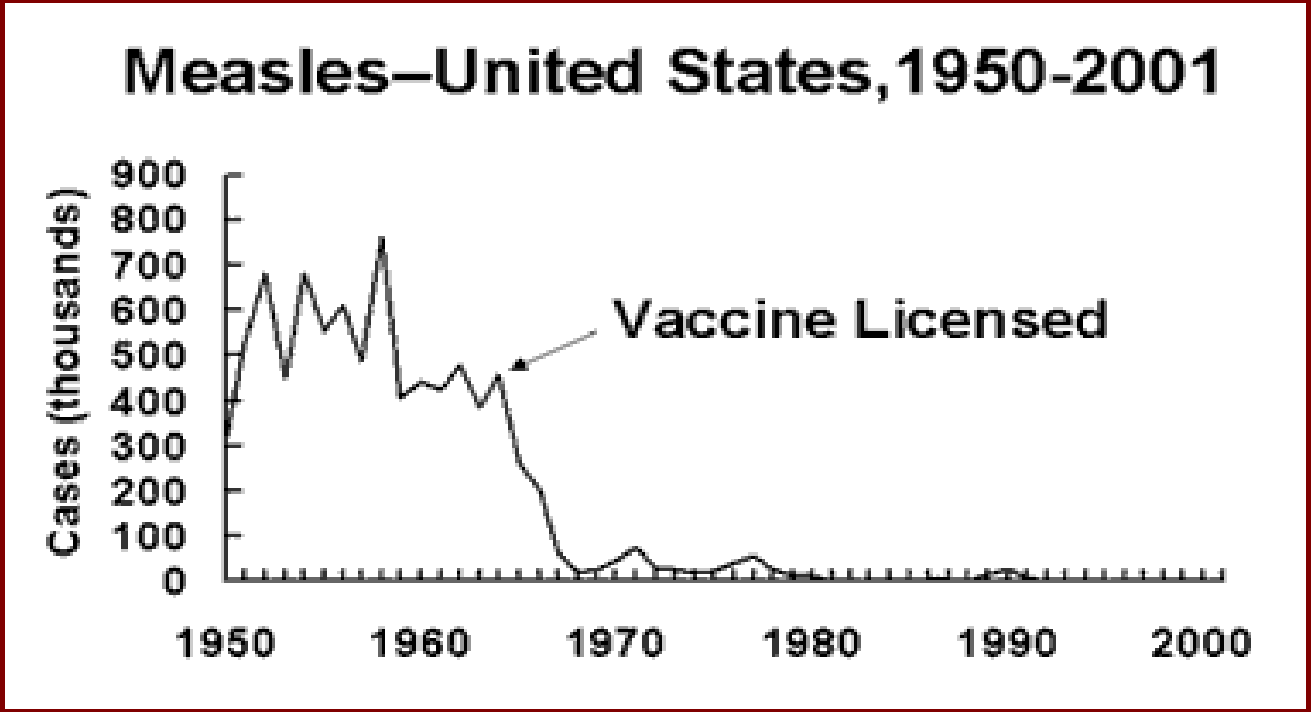
If the pathogen is coming for a second or third time, immune system has already memorized it and reacts faster.

During the first immune response part of multiplied cells react at the moment. They are called effector B and T – lymphocytes. Another portion of the cell population become memory cells. They remain dormant, waiting for a next meeting with the same pathogen. If the same antigen comes again, memory cells quickly produce new effectors. Secondary immune response start wit much more activated cells and it is faster.

Memory B cell. Cartoon by Genentech Corporate Communications Department

Secondary immune response is the base of active immunization (vaccination).

When we immunize, we supply a pathogen or its antigens in a harmless form so that the immune system can react against it. If the real pathogen comes later, the immune response will be secondary and often effective enough to prevent the disease altogether.



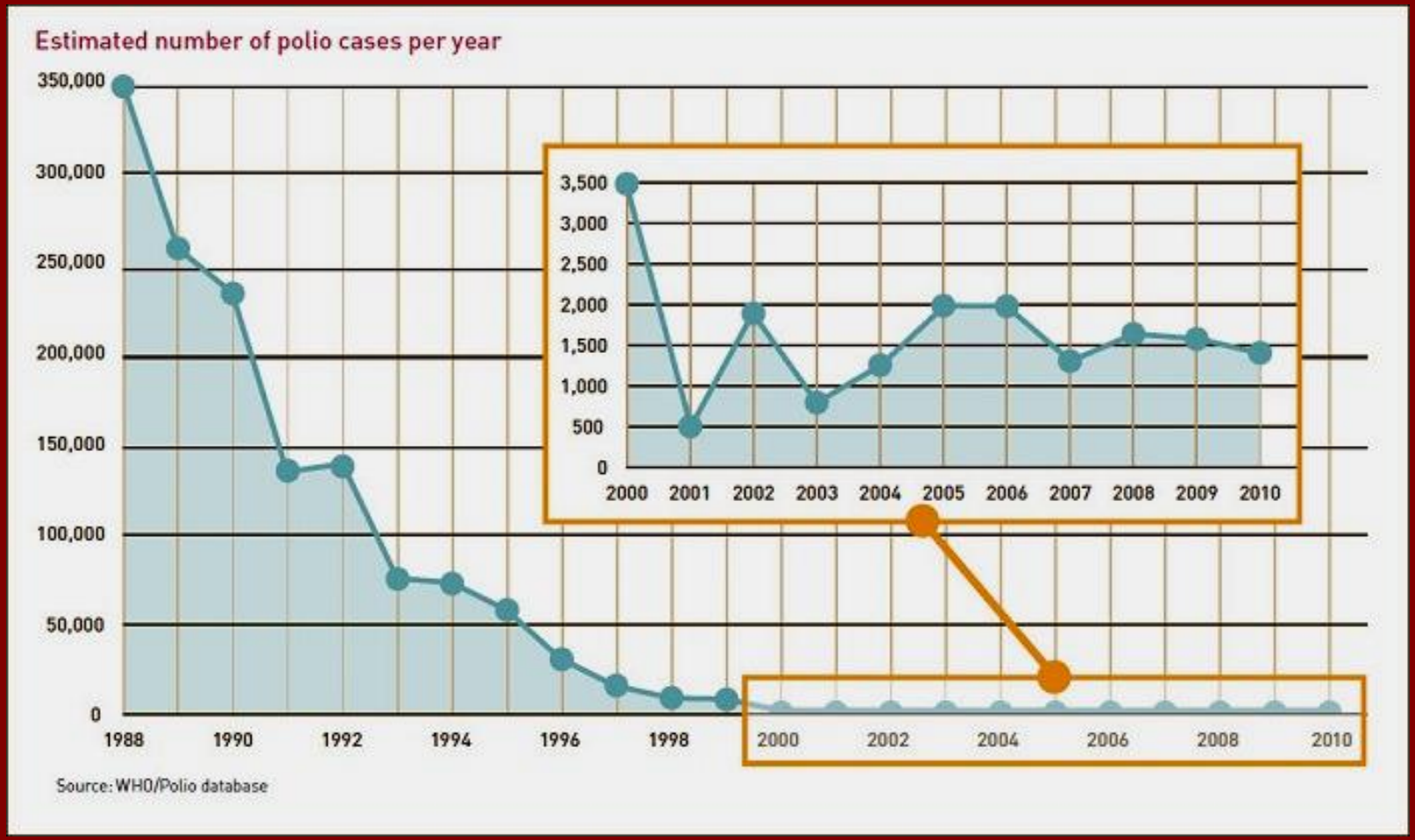
The graphic shows the eradication of measles from the USA after the licensure and wide use of measles vaccine beginning in 1963. Europe is still endemic for measles due to later start of immunization and stronger anti-vaccine prejudice.

www.cdc.gov

Global timeline of polio eradication

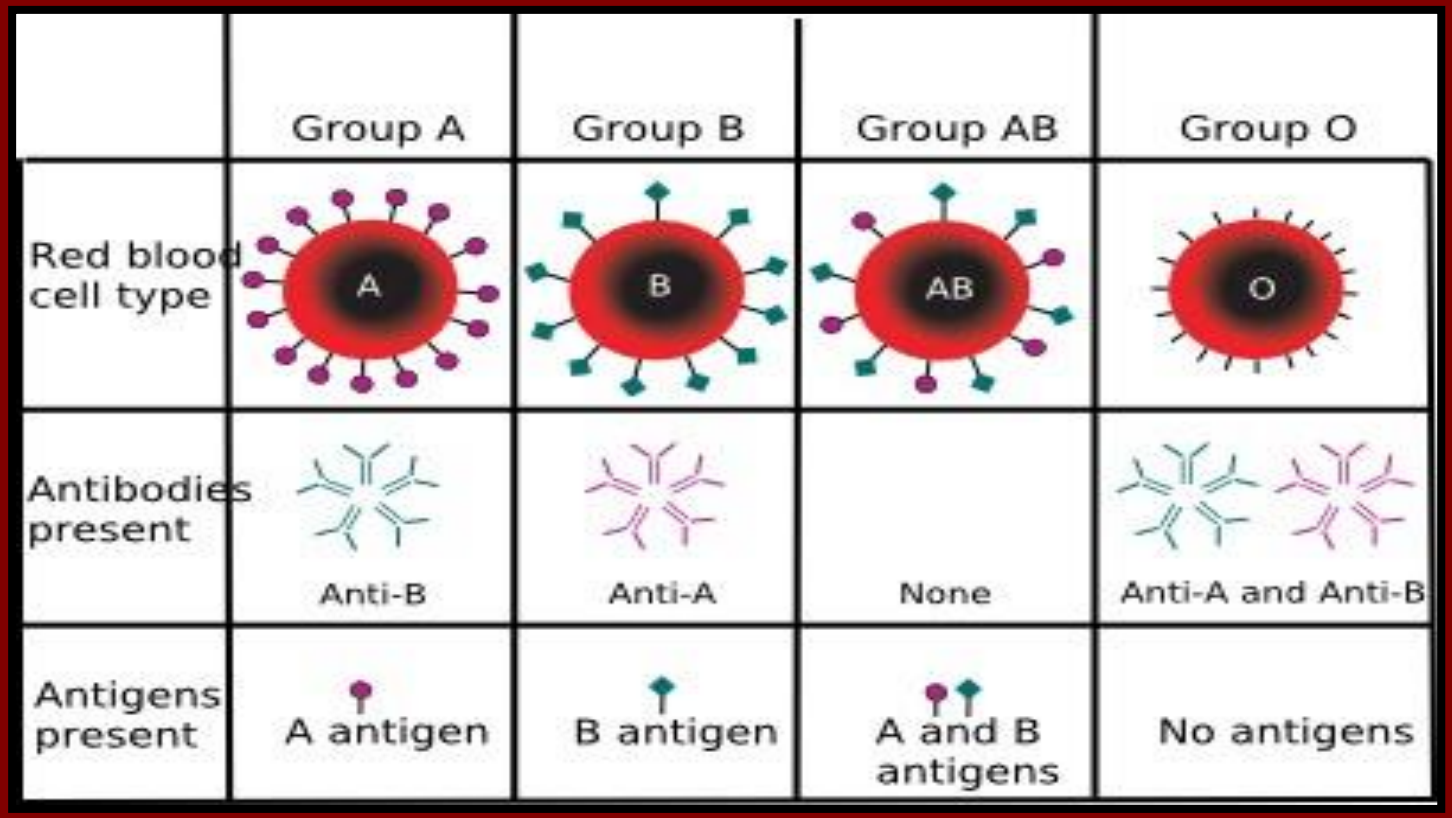
After smallpox was eradicated by vaccines, now eradication of poliomyelitis is under way.

Below: polio cases per year.



The ABO blood group system

One blood group system is based on the alleles of one gene encoding molecules on the surface of the red blood cells. The ABO blood group system consists of three alleles of the gene I – alleles A, B and O. Alleles A and B encode enzymes adding specific monosaccharides on the surface of erythrocytes producing antigen A and B respectively. Allele O encodes inactive enzyme and antigen is not produced.



en.wikipedia.org

Genotypes and phenotypes in the ABO system

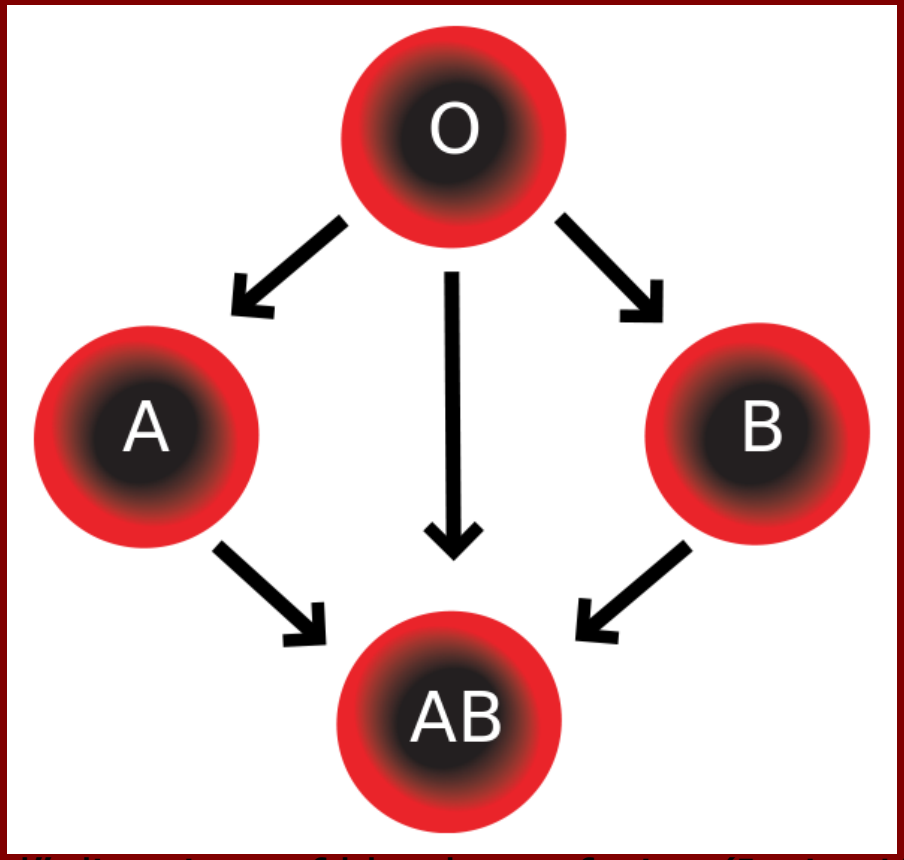
Alleles A and B are codominant. In a common combination both of them are expressed to make blood group AB. Allele O is recessive to A an B. Persons who posses two alleles O are blood group O.

Each individual produces antibodies against the foreign blood group. That's why a person, who is blood group A has anti-B antibody in his serum.

Genotype	Phenotype (blood group)	Antigens on erythrocytes	Antibodies in serum
AA, AO	A	A	anti-B
BB, BO	B	B	anti-A
AB	AB	A + B	neither
OO	O	neither (only H)	anti-A + anti-B

Compatible transfusion

According to the scheme is visible that O is universal donor and AB is universal recipient. Blood group O has no foreign antigen for no one of the other blood groups and can donate to everybody. Blood group AB has both of antigens and can accept blood from all of the other blood groups.



"Allowed" directions of blood transfusion (InvictaHog, Wikimedia)