HOW IMMUNE SYSTEM IS ACTIVATED BY INFECTIOUS AGENTS

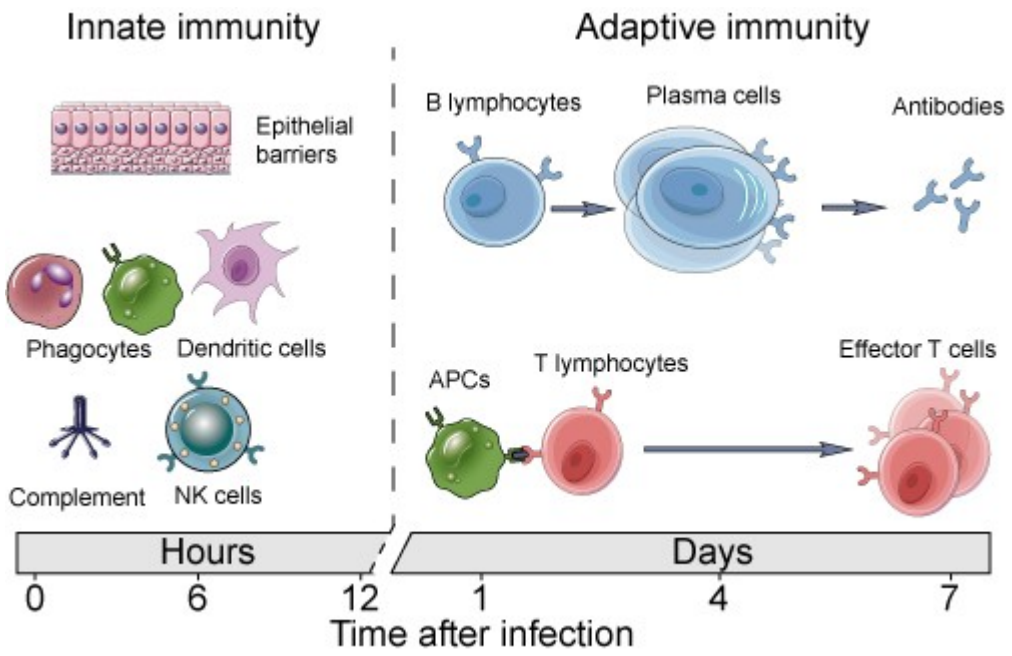
DR. ZAHID ULLAH KHAN
ASSISTANT PROFESSOR MICROBIOLOGY

Objective:

- At the end of the session .
- The 3rd year MBBS student will be able to describe;
- **Mechanism of activation of immune system of the human body by infectious agents**

- Can you describe immune system…..????
- How many types are there of immune system….????
- Can you classify major infectious agents?

- The ability of an organism to resist a particular infection or toxin by the action of specific antibodies or sensitized T lymphocytes.
- Two types.



1. Bacteria
2. Viruses
3. Fungi
4. Protozoa
5. Helminths

- **Borders**

Physical barriers of innate immunity

- **Police and Rangers**

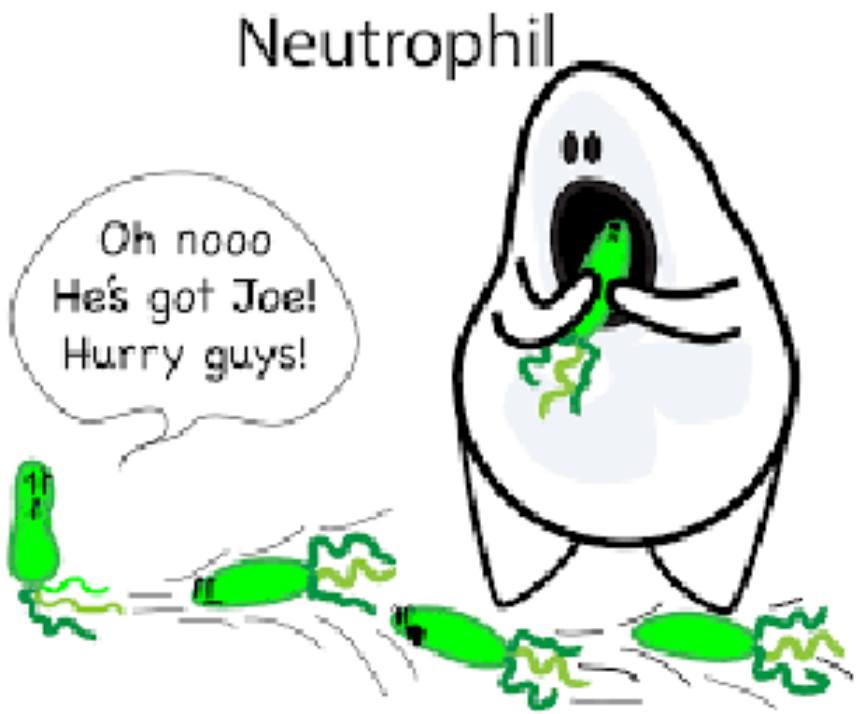
Innate immunity

- **Army and Intelligence**

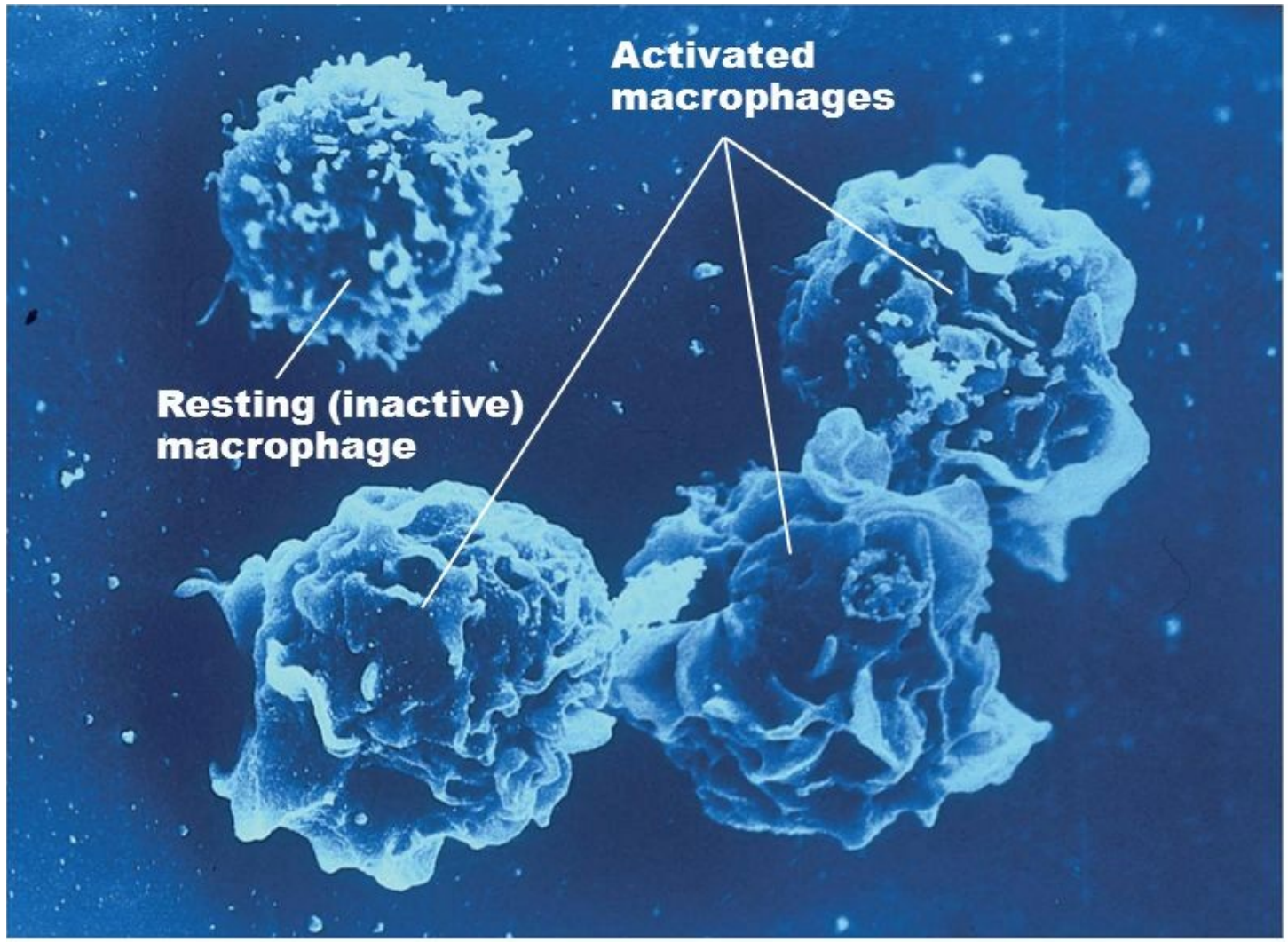
Acquired immunity


Infectious agent

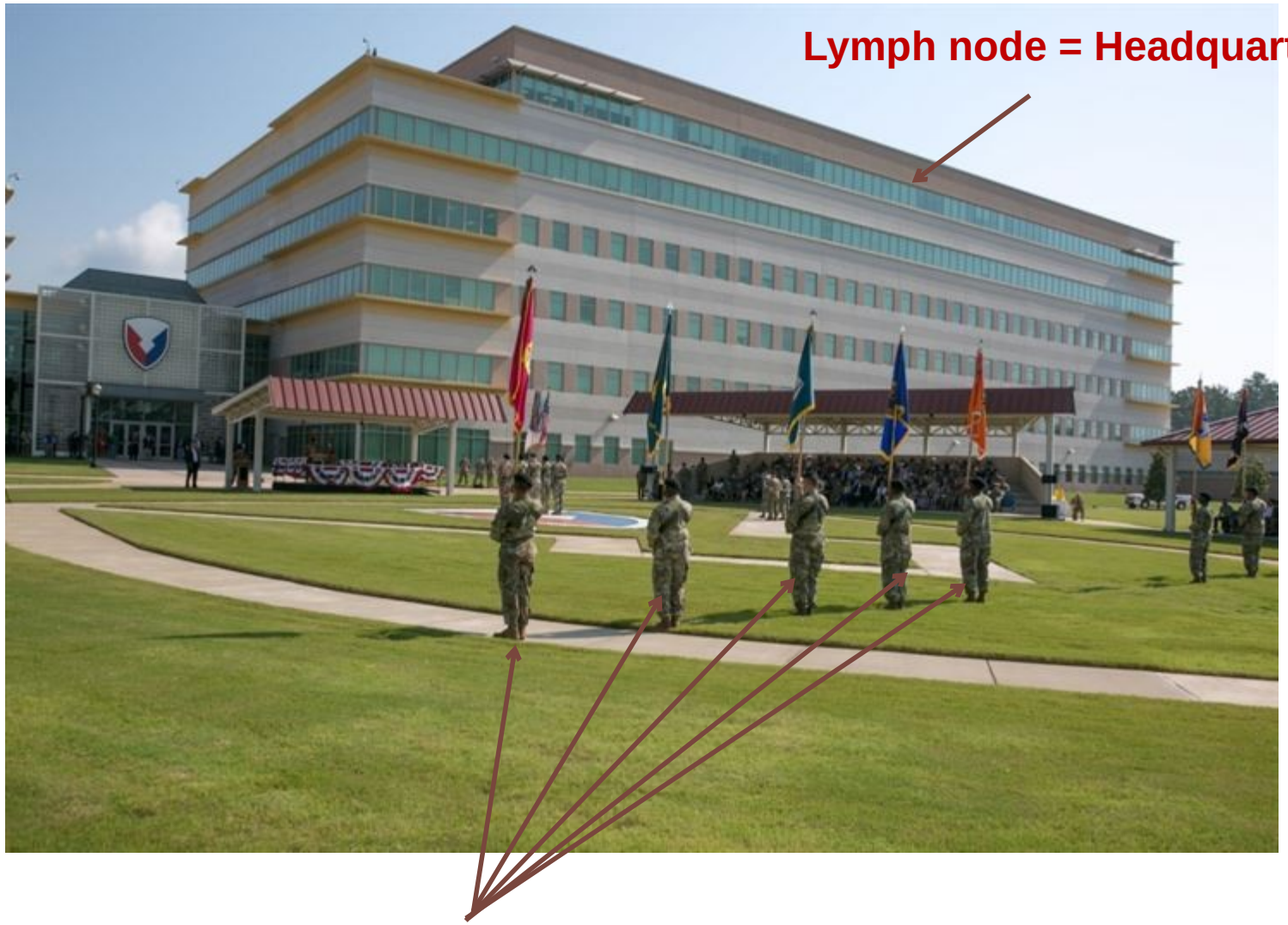

Neutrophils
Infectious agent


Neutrophil
Oh nooo
He's got Joe!
Hurry guys!

Macrophages

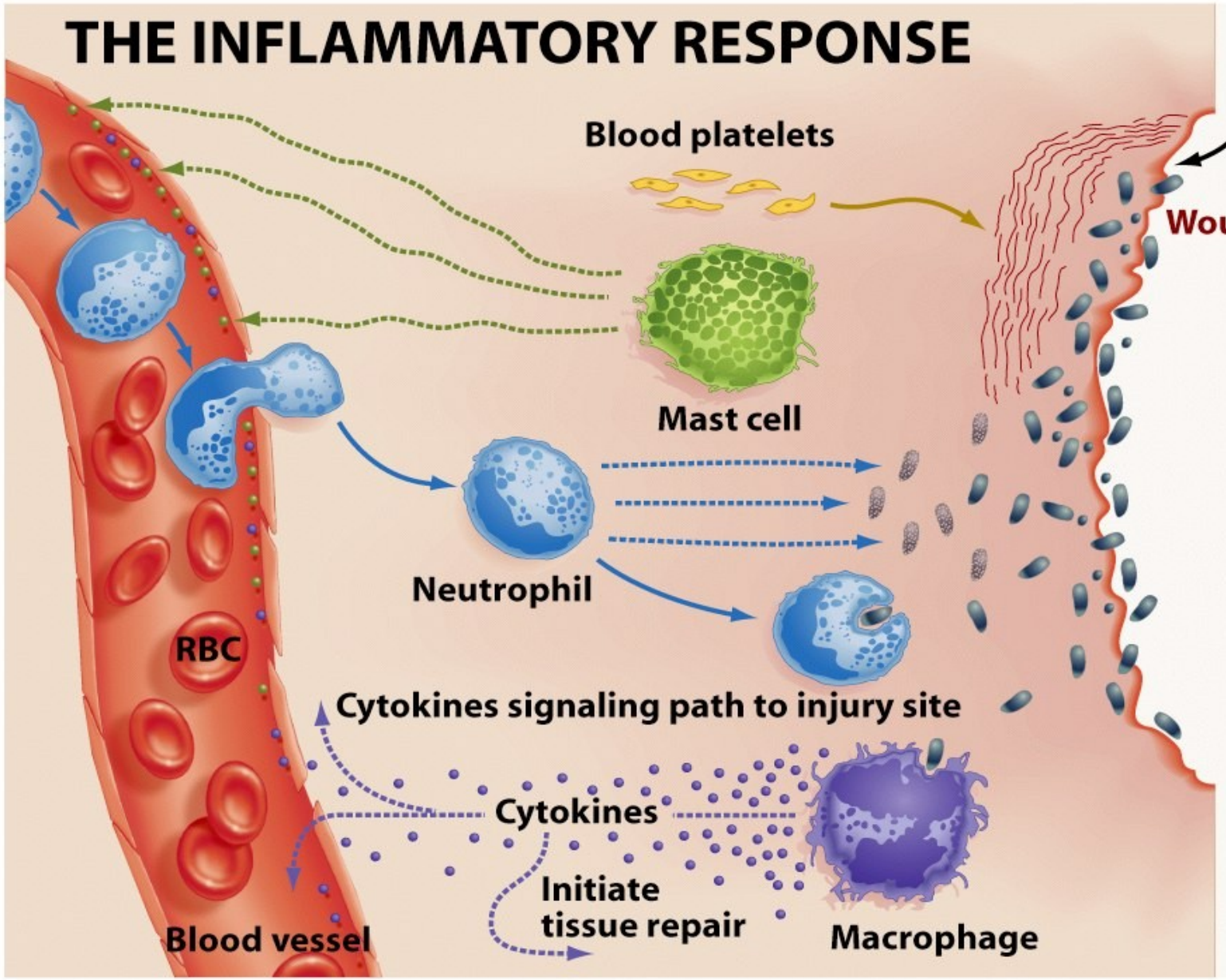

Activated
macrophages
Resting (inactive)
macrophage

Infectious agents phagocytozed by macrophage


Lymph node = Headquarter
Different clones of T cells having different TCRs

- The infectious agent transmits from the source to the human body
- Adherence occurs with the mucus membrane
- The infectious agent invades the mucosa
- Release of toxin occurs that results in inflammation

THE INFLAMMATORY RESPONSE

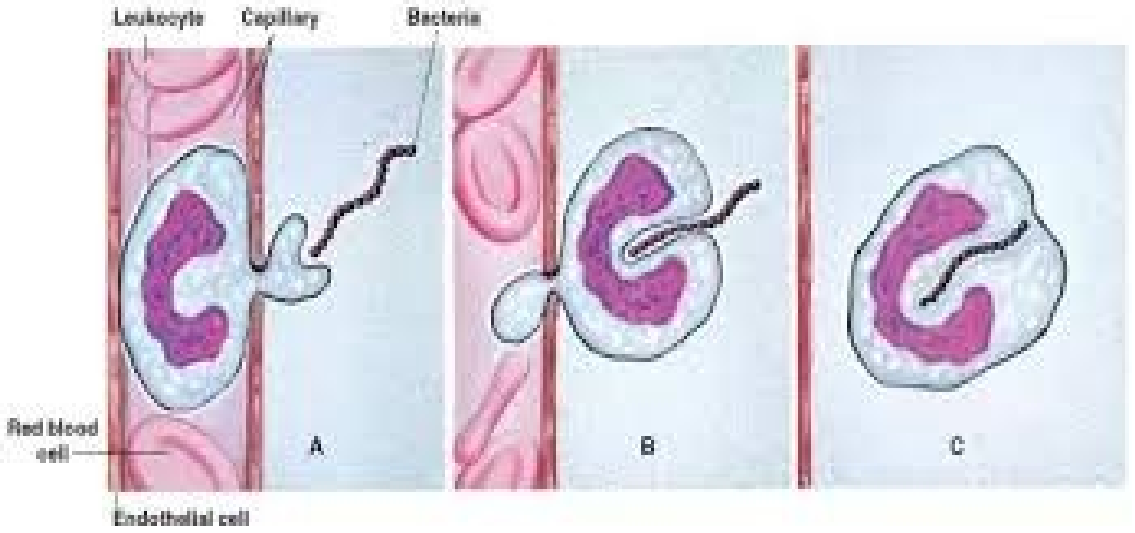


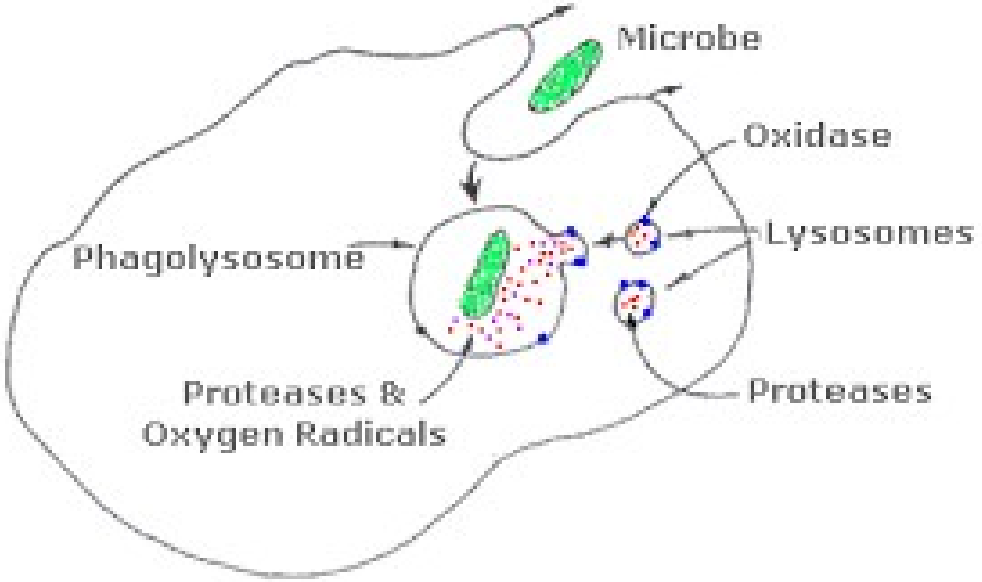
1. Bacteria and other pathogens enter wound.
2. Platelets from blood release blood-clotting proteins at wound site.
3. Mast cells secrete factors that mediate dilation and constriction of blood vessels. Delivery of blood, plasma, and cells to injured area increases.
4. Neutrophils secrete factors that kill and degrade pathogens.
5. Neutrophils and macrophages remove pathogens by phagocytosis.
6. Macrophages secrete cytokines, which attract immune system cells to the site and activate cells involved in tissue repair.
7. Inflammatory response continues until the foreign material is eliminated and the wound is repaired.

Figure 49-3 Biological Science, 2/e

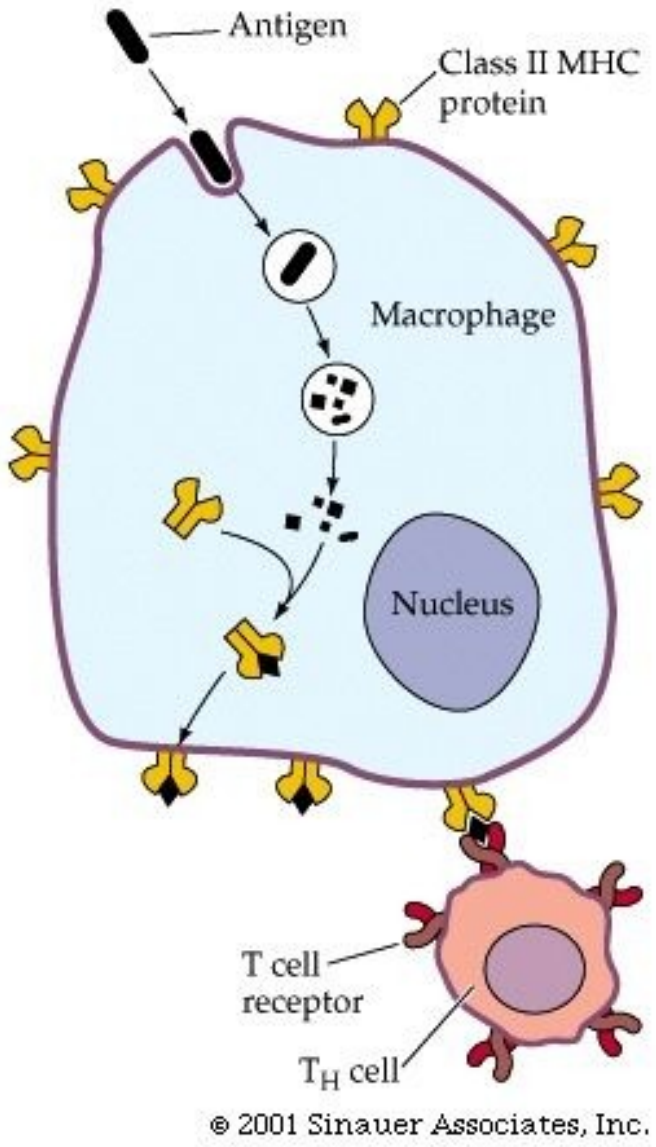
- Neutrophils phagocytose bacteria and form phagosome
- Neutrophils start emptying its lysosomal granules in this phagosome
- Lysosomal products especially destructive enzymes , start digesting the bacterial component
- Bacterial antigens are now free

  antigens
- These antigens then drain into the lymphatics and somewhere down into lymph nodes.





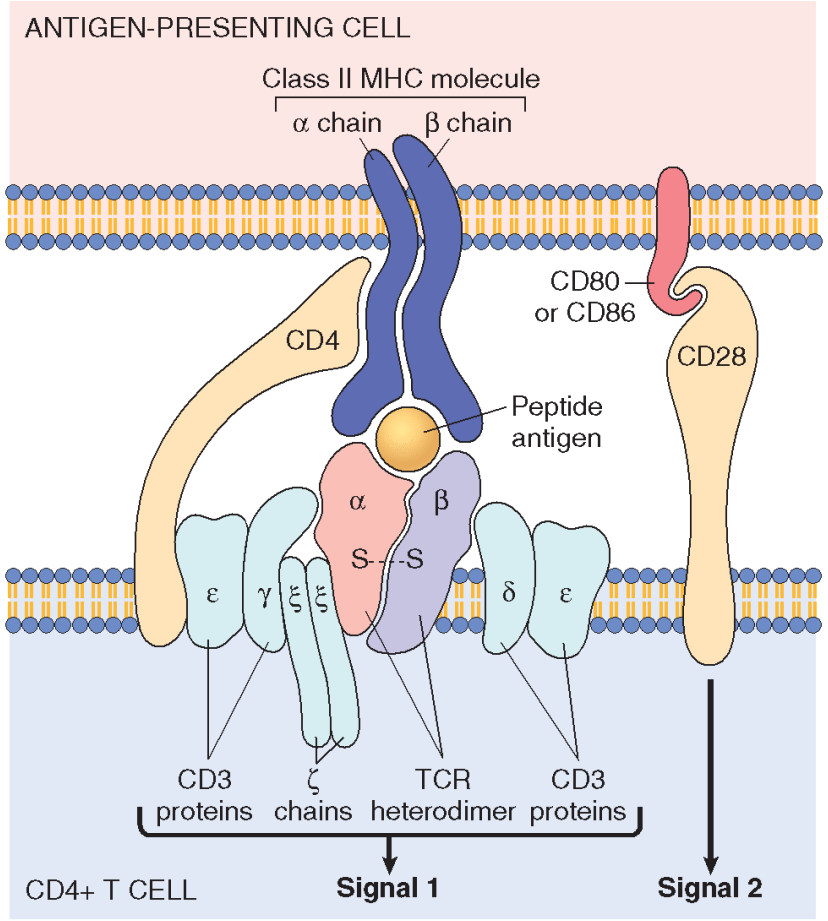
- Macrophages are more advanced types of cells than neutrophils
- Macrophages kill the bacteria and bring the antigen out of the bacteria and present it to the immune system in a very professional way
- Macrophages have 2 genes on chromosome no 6



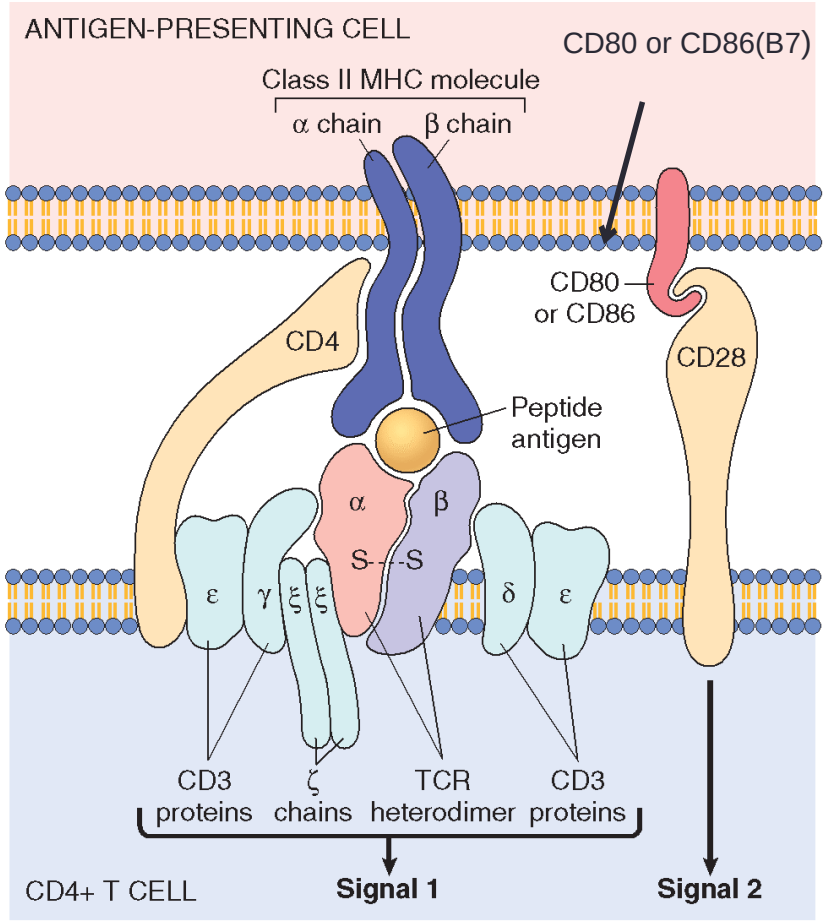
- The short arm of the chromosome has special set of genetic material
- The genetic material on the top, it keeps on shuffling while the bottom is stable
- Different mRNA will produce different shapes of peptide chains and these peptide chains have constant tails but variable heads
- The macrophage when activated they produce MHCII at chromosome 6
- These MHCII molecules shift to the phagosome to fit the antigen into its pocket

- Sooner or later by random chance some MHCII molecules will bind a specific antigen
- After binding the antigen, the macrophage brings this complex to its surface and present it to the headquarter (Lymph node)
- It is then presented to the T-lymphocytes
- T-lymphocytes are trained and educated in the thymus and are normally traced in bone marrow
- Macrophage has to present this antigen to the T-lymphocyte because some of the T-lymphocytes are T-helper that will help some B-lymphocytes to make antibodies

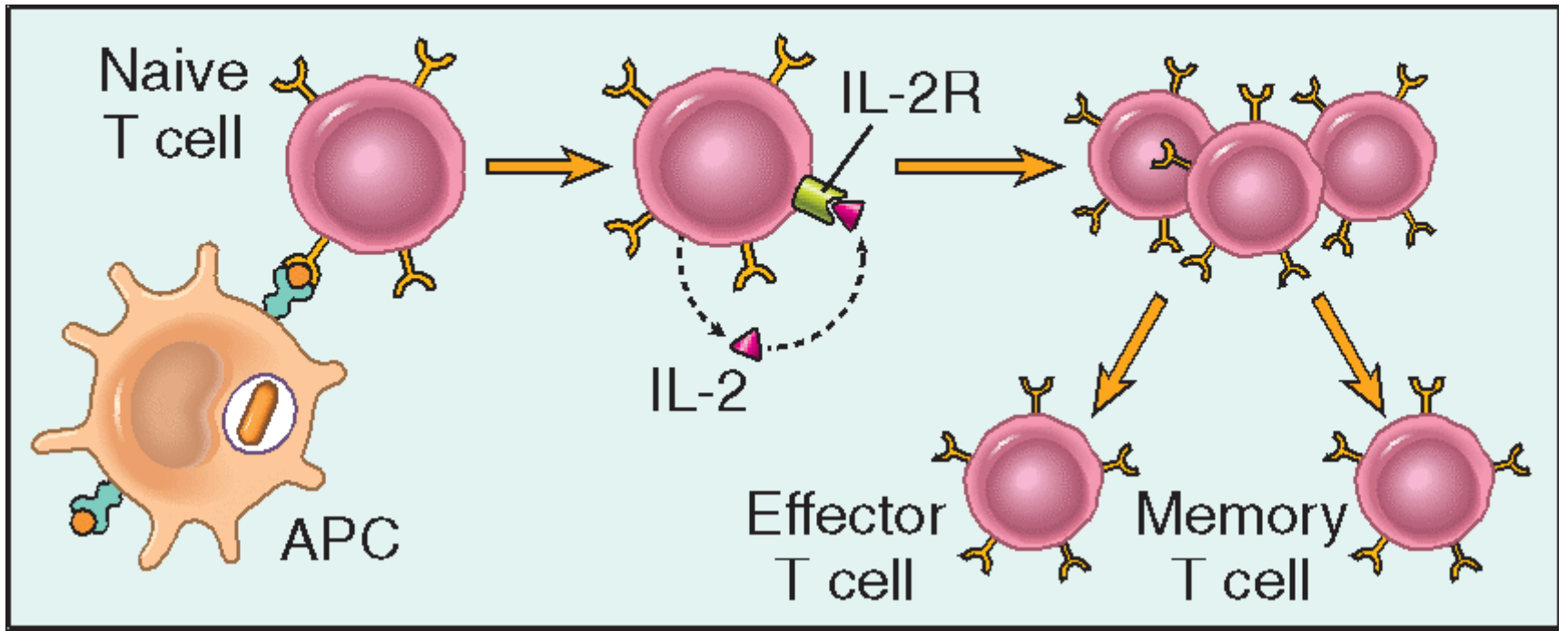
- T-lymphocytes contain TCR to recognize the antigen and CD4 to recognize MHC-2
- When the antigen along with MHC-2 molecule are presented to T-cell, it gives signal through CD3 to the nucleus
- The macrophage also send signals to the nucleus through interleukin-1



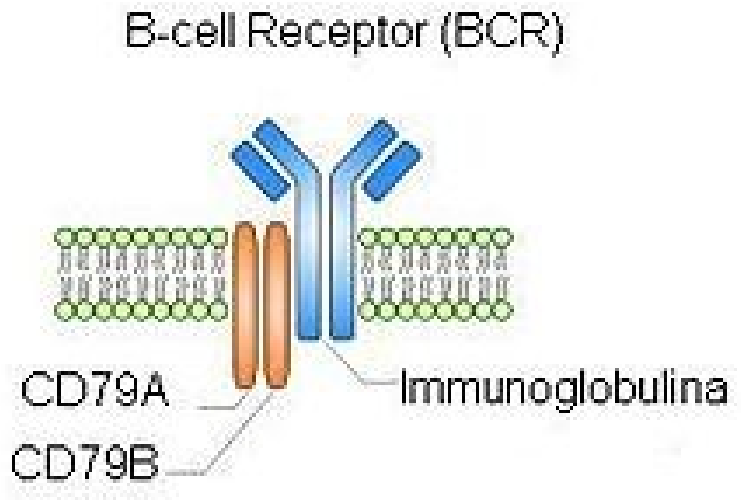
- Macrophages also give signals through B-7 to the nucleus
- The headquarter will get overwhelmed to start reacting to the situation



- In the T-lymphocyte gene 1 will be activated which form interleukin-2
- Gene 2 will be activated to form interleukin-2 receptor on T-cell which will attract interleukin-2
- The 2nd molecule interleukin-2 gives the ultimate signal to the nucleus and stimulates set of genes which are concerned with mitosis
- The T-cell starts multiplying and produces thousands and millions of T-cells, this is called **clonal expansion**

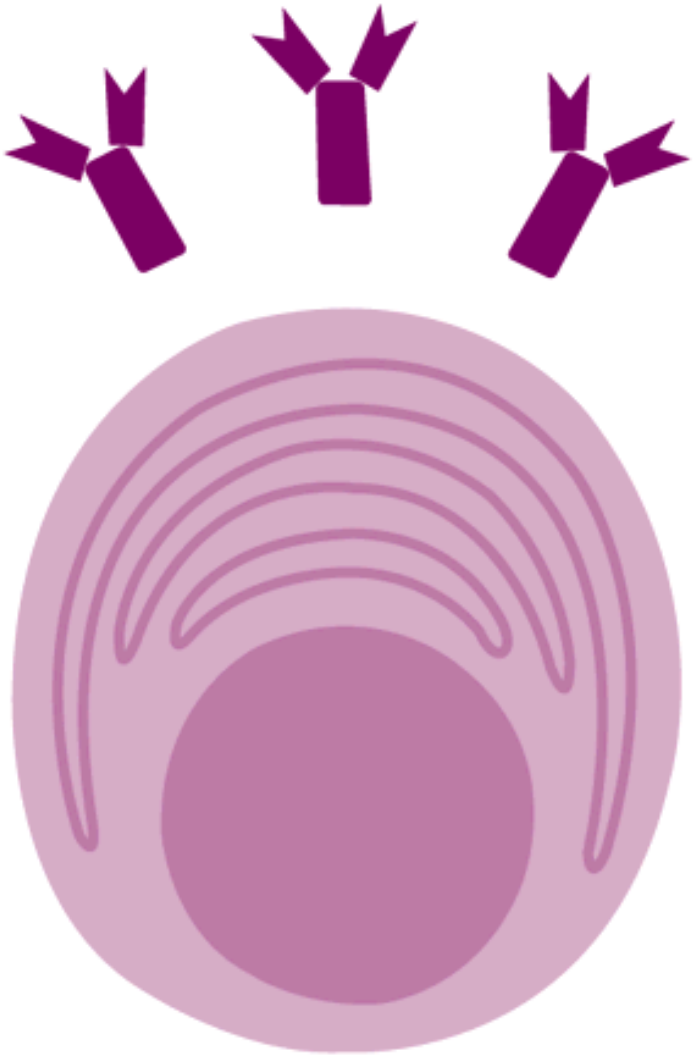


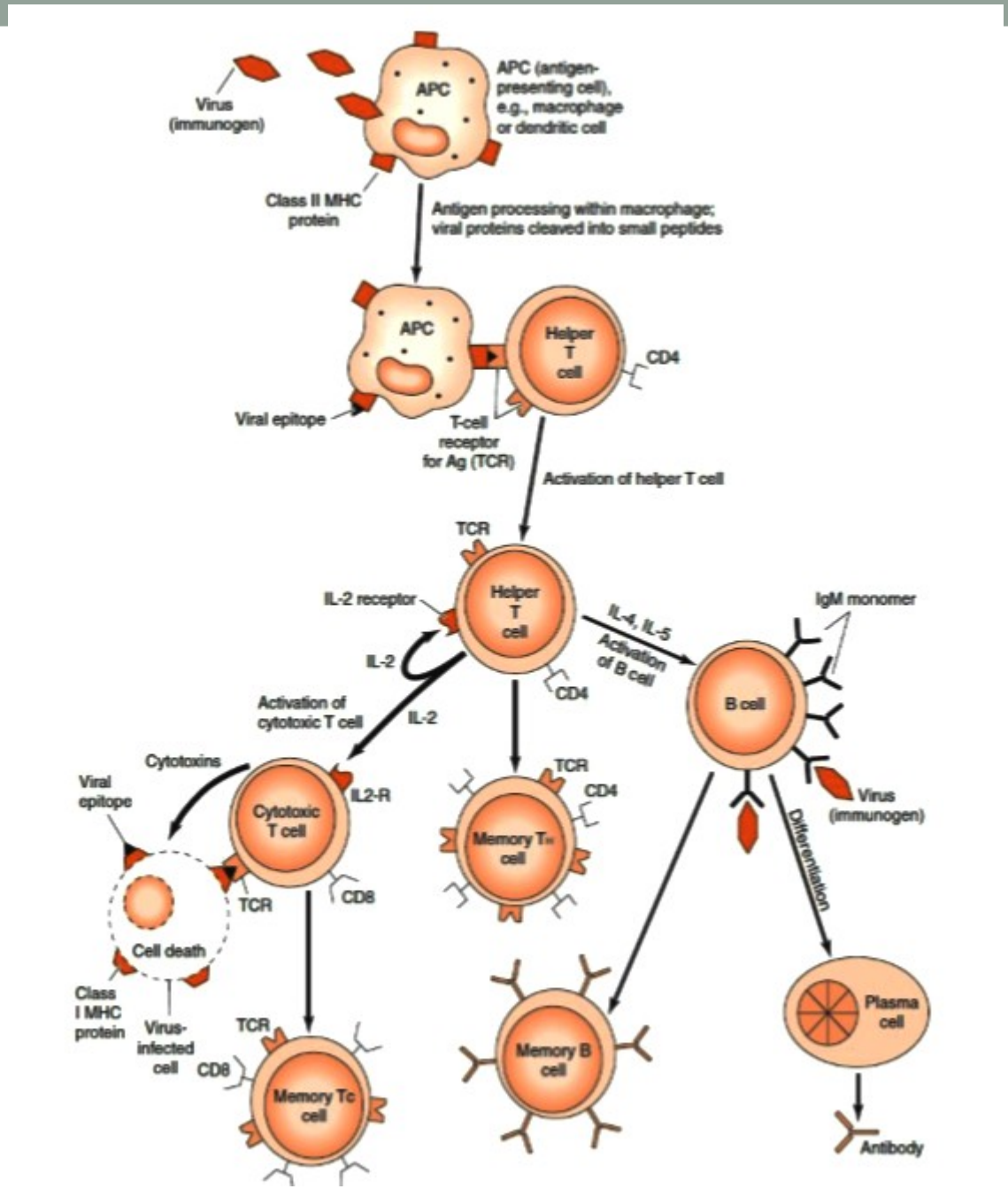
- B-lymphocytes are those which are in our bone marrow and mature into bone marrow and then they come in circulation and some settle in the lymph nodes.
- B-cell contain B-cell receptors and different BCRs are for different antigens
- These BCRs are surface Immunoglobulins (IgM and IgD)
- In the B-cell there is specialised protien called CD-79, when the surface immunoglobulins are loaded with the appropriate antigen, the immunoglobulin move tail and activates CD-79



- CD-79 gives signal to the nucleus and nucleus produces receptors expressed on the surface of the selected B-cells.
- The T-cells which were proliferated they open a new box of genes and they produce a product which are helping B-cells.
- The molecule coming from the T-cells is called B-cell growth factor and it is interleukin-4
- T-cell produced molecules bind with the B-cell and give message to the nucleus of the B-cell
- There is strong mitotic reaction to B-cell and B-cell clone starts expanding and cell number increases

- When B-cell have enough multiplication they start expressing another type of receptors
- Meanwhile other gene is activated to the T-cell and make another molecule, this molecule is called interleukin-5 or B-cell differentiation factor
- The B-cell undergoes differentiation and change into oval cell with the nucleus cart bean shaped with very prominent golgi bodies
- These will powerfully activate their machinery to produce antibodies
- Such B-cells which are actively producing antibodies are called Plasma Cells




Virus
(immunogen)
APC
APC (antigen-presenting cell), e.g., macrophage or dendritic cell
Class II MHC protein
Antigen processing within macrophage; viral proteins cleaved into small peptides
APC
Helper T cell
CD4
Viral epitope
T-cell receptor for Ag (TCR)
Activation of helper T cell
TCR
IL-2 receptor
Helper T cell
IL-4, IL-5
Activation of B cell
IgM monomer
IL-2
CD4
Activation of cytotoxic T cell
IL-2
B cell
Cytotoxins
Viral epitope
Cytotoxic T cell
IL2-R
TCR
CD4
Memory Th cell
Virus (immunogen)
CD8
Differentiation
Cell death
Class I MHC protein
Virus-infected cell
TCR
CD8
Memory Tc cell
Memory B cell
Plasma cell
Antibody

1. Why neutrophils come out first at the site of injury?
2. Enumerate the ways macrophages uses to communicate with T lymphocytes

Thank You