

The Immune System

The immune system consists of all the tissues, cells (functioning in those tissues and in the blood) and chemicals produced by those cells.

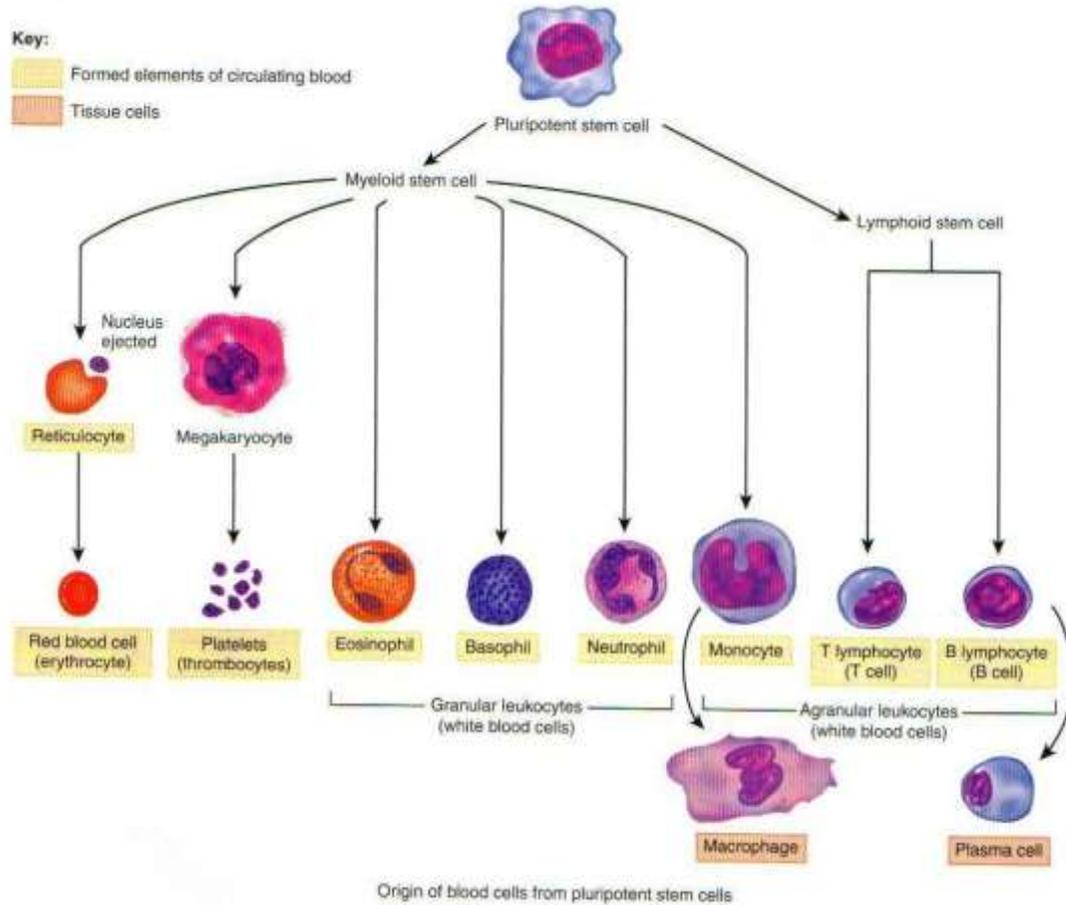


Figure 1 - Origin of Blood Cells

Tissues involved in the immune system

Lymphoid tissue:

Bone Marrow:

- Red marrow – found mainly in flat bones (skull, sternum, ribs) and the ends of long bones
- Yellow marrow – found in shafts of long bones; consists primarily of fatty tissue, but can change in red if required (e.g. in anaemia when more red blood cells are needed)

Stem cells:

- These occur in the bone marrow
- These can do anything they need to do
- They have unlimited capacity to reproduce to produce
 - More stem cells
 - Specialised replacement cells (i.e. another specific type of cell)
 - All the red and white blood cells
- Stem cells are present in all tissues and reproduce and specialise as required
- They persist throughout

Thymus:

The thymus is a lymphoid gland that produces T-cells. These are concerned with removal of abnormal cells :intracellular infection, grafts, viruses

- Retrosternal (behind sternum)
- Described as the immune university
- Is present at 8th week of foetal gestation
- Here, immune cells are taught to recognise antigens (Ag)
- Antigens can't get in to the thymus; they (or fragments of them) need to be presented by other immune cells

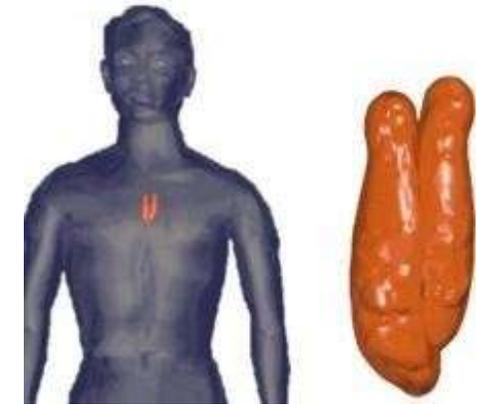


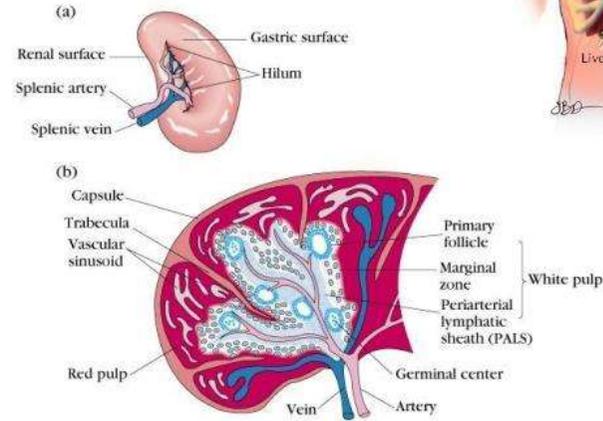
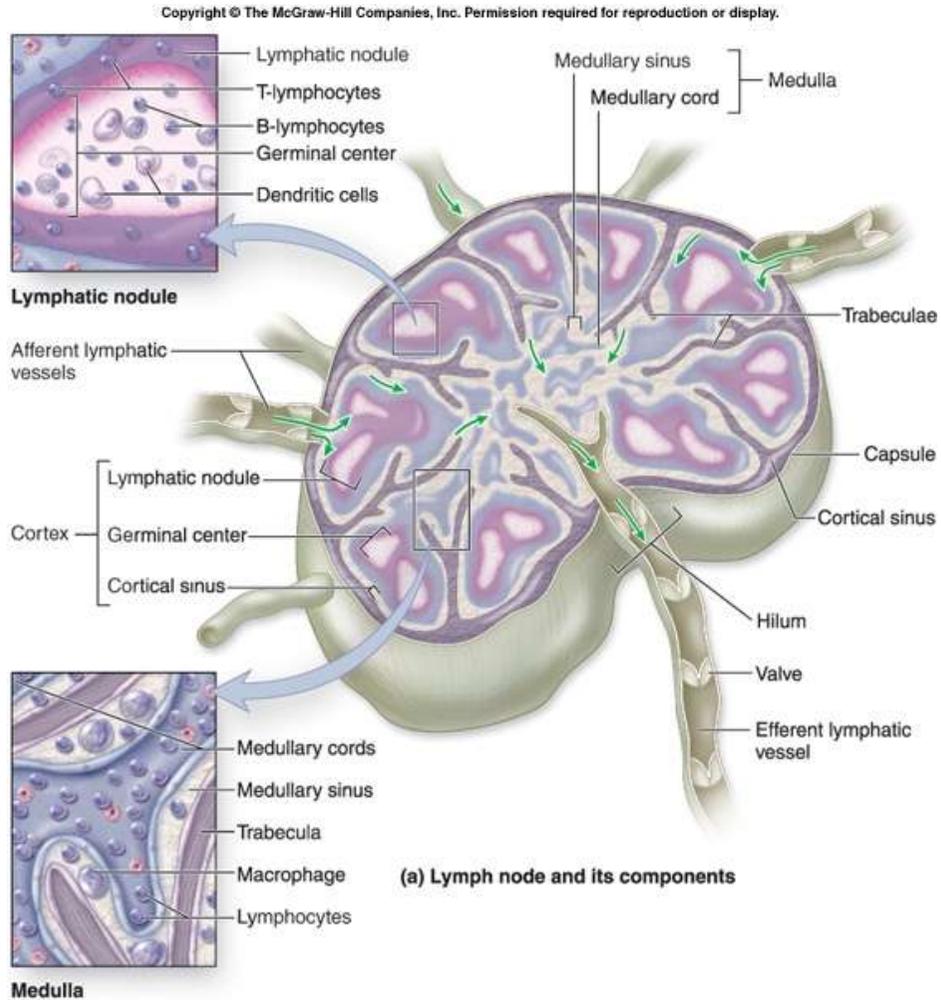
Figure 2 - Thymus Gland

Spleen:

- Under diaphragm; on the left, up and behind the stomach
- It filters the blood and, if abnormal cells/chemicals are detected, they are removed
- Detects blood infections
- It collects and moves lymph from the tissues back to the venous system for
- En route, the lymph passes through the lymph nodes/tissue
- Lymph nodes contain white blood cells which scan and check the lymph as it flows
- Any infection (draining from the infection site) will create a reaction in the lymph

- Lymphoid tissue in the Gastrointestinal Tract are localised in areas called **Peyer's patches** (about 70% of the body's immune system is in the gut)

Figure 3 - Spleen



Lymph nodes:

These are swelling found along the course of the lymphatics

- They are found as part of lymphatic system circulation (entering the blood system at the subclavian veins)
- They through nodes resulting in swelling (lymphadenopathy)
- They occur in the gut as Peyer's patches (aka MALT – mucosal associated lymphoidal tissue), which helps deal with ingested infections.

Figure 4 - Lymph Node

The lymph node receives lymph via the afferent lymph vessels. It then passes through the follicles, which contain the leucocytes. It is here where the immune cells are found. These are very 'touchy-feely' cells, 'scanning' for any foreign matter and an immune reaction takes place to prevent it spread to the general body. Here, though, can be included the appendix and tonsils also.

The overall **function** of the immune system is to help maintain homeostasis by **protecting** the internal environment of the body from **invading organisms** or potentially **toxic chemicals**.

Before the immune system becomes involved, the body has physical barriers:

- **Skin** - 2 square metres
- **Mucous membranes** - 400 square metres

If anything does invade the internal environment of the body, an immune reaction will occur. The function of this immune reaction is to remove the foreign substance and re-establish homeostasis.

There are two stages of the immune reaction:

- Innate
- Adaptive

Innate

This is a general non-specific reaction, i.e. acute inflammation, and occurs external to the cells. It is immediate (i.e. within seconds), and is the beginning of a chain of events. Effectively, something has happened to the body; the body doesn't know what has happened and has to find out what that is and to elicit the appropriate healing reaction.

This has five symptoms:

- a) Redness**
- b) Heat**
- c) Swelling (oedema)**
- d) Pain**
- e) Loss of function**

What chain of events now happens to cause this:

- The blood vessels to the area dilate – more blood to the area
- The blood vessels away from the area constrict - keeping any foreign cells and material in the area, and causing swelling to dilute any potential toxins
- Immune cells are there and send out chemical messengers for more specific cells

- Activation of immune cells there
- Identifies the intruders (foreign cells, material, chemicals) and takes information to the thymus gland (for example) for educational purposes
- This reaction is self-limiting (or should be)

The cells involved here are mainly the phages; macrophages and dendritic cells in the peripheral tissues and monocytes and neutrophils in the blood. The act of 'eating' foreign matter is called phagocytosis (see later)

Adaptive

This is a specific response, i.e. it identifies the invading organism (virus, bacteria and parasites), attacks and removes it via phagocytosis and antibody and chemical production

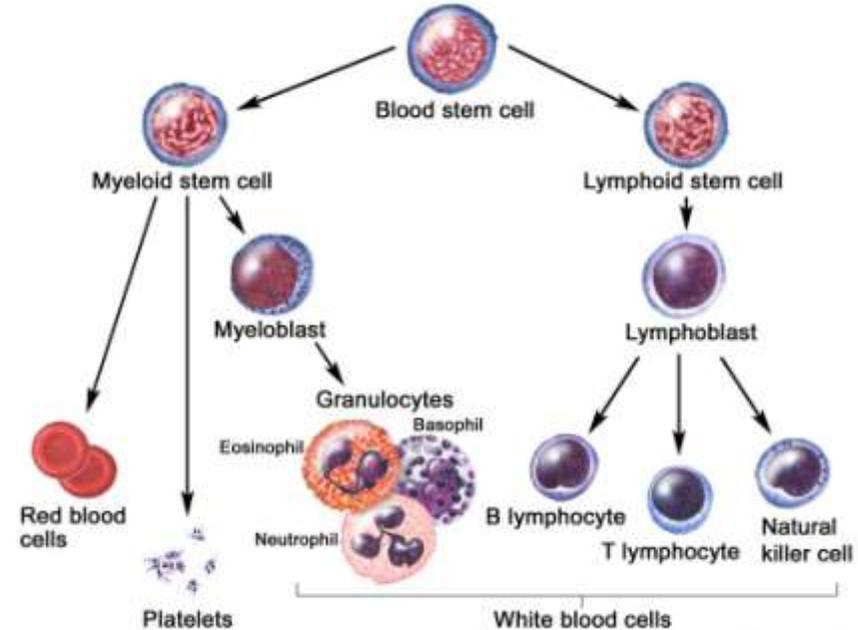
All cells need things. They have binding sites on the cell surface to bind with whatever it needs; then a channel opens up, takes it in and then the channel is closed again.

Viruses – Bind to a cell. To do this they must have a 'key' and achieve this by having a site that binds with the surface binding site on the cells. It then injects its DNA into it and then **takes over the cell**. They then use that cell to make more viruses. They can remain dormant for months/years until the conditions are 'right', however the body can't see this because they are inside the host cell. For viruses to survive they need to keep the host alive.

Innate and adaptive responses are supposed to work hand in hand; therefore they need good and clear communication.

Figure 5 - Cells of the Immune Response

Innate	Adaptive
Macrophages	B-cells
Dendritic cells	T-cells
Natural Killer Cells	
Monocytes	
Mast cells	
Eosinophils	
Basophils	
Neutrophils	
Complement System	



Cells have intelligence, as do proteins; they can make decisions and the ability to act upon them. This action depends upon what their function is

Phagocytosis

Phagocytosis is the ability of certain cells to engulf other and destroy them internally.

Cells that phagocytose:

- Macrophages
- Dendritic cells
- Neutrophils
- Monocytes

Phagocytosis consists of:

- **Attachment** (of the phagocyte with the bacteria)
- **Engulfment** (ingestion – in a capsule/vesicle)
- **Digestion** - by lysosomes
- **Excretion** – occasionally bits can be recycled, else excreted. Also pieces of antigenic material are taken to the thymus for education
 - Some bacteria can avoid destruction by upsetting the system, e.g. Pneumococcus – resists attachment, therefore no breakdown
 - **Staphylococcus Aureus** – resists digestion; the lysosomal enzymes eventually cause the death of the phagocyte, which then lyses and releases the Staph again.

White Blood Cells

White blood cells couldn't be identified at first under the microscope, they were first identified by the type of stain they took up. The names stuck, but it gives us no information as to their function:



Neutrophils (take up neutral stain)

First line of defence against bacterial infection

- Phagocytosis
- Phagocytose Ag/Ab complexes
- Enzyme production (lysozyme) - bacterial destruction

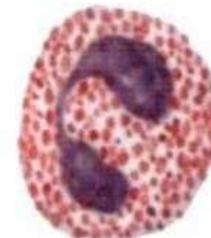
Eosinophils (take up eosin [acid] stain)

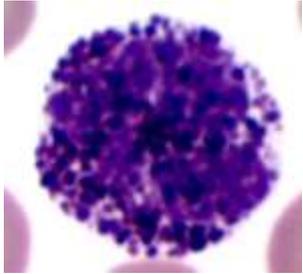
Leave blood capillaries and enter interstitial fluid

Combats inflammation in allergic responses

Effective against parasites

High Eosinophils count suggests allergic reaction or parasitic infection





Basophils (take up alkaline stain)

These are also involved in allergic reaction and inflammation.

Leave capillaries and enters tissues

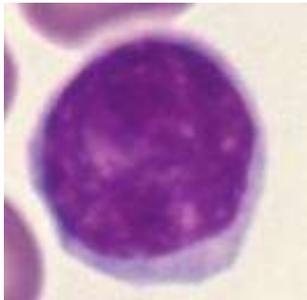
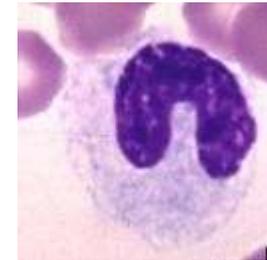
Liberates heparin, histamine, serotonin (5HT), which intensify the allergic reaction, therefore involved in allergic reactions

Monocytes

Take longer to get there, compared to Neutrophils, but arrive in larger numbers. Develop into macrophages and pass out into the peripheral tissues:

Their primary function is Phagocytosis

- Bacteria etc
- Clear up cellular debris



Lymphocytes

Types: B, T and Natural Killer Cells (NKC) –all major combatants in immune response:

- **B cells** change into plasma cells; produce **antibodies** against bacteria and toxins
- **T cells**; attack intracellular infections, viruses, fungi, transplanted cells, cancers and some bacteria
- **Natural Killer Cells**; attack wide variety of infectious microbes and certain spontaneously arising tumour cells

Natural killer cells

The vesicles in their cytoplasm have chemicals that promote blood clotting
Their life spans are 5 –9 days and are removed by macrophages in the liver



WBC and other nucleated body cells have proteins called Major Histocompatibility (MHC) antigens, protruding from the surface plasma membrane out into the extracellular fluid cell identity markers. These are unique to each person (except identical twins). RBC have blood group antigens, but don't have MHC antigens.

The MHC define whether a transplant is rejected or accepted.

WBC can only phagocytose a certain amount of material before it interferes with its own metabolic activities, hence its life span is only a few days; with a bacterial infection, but a few hours. Some B and T cells remain in the body for years.

Leucocytosis

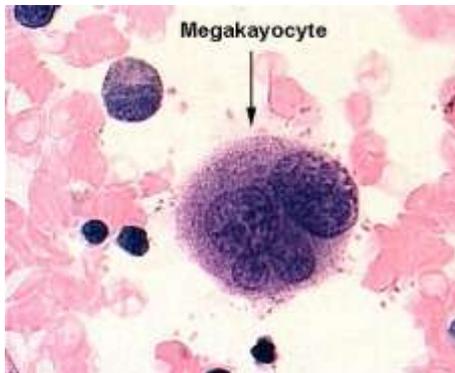
This is an increase in the numbers of WBC with a normal protective response to stresses: invading microbes, stress, exercises, anaesthesia and surgery; hence it indicates infection or inflammation. Because each cell has a different function, assessing relative numbers indicates what sort of infection it is.

Leucopenia

An abnormally low WBC count. Never beneficial; because of radiation, shock, chemotherapy.

WBC develop in red bone marrow:

- Lymphoid stem cells – T and B cells



Platelets

From Pluripotent stem cells

Myeloid stem cells develop into megakaryoblasts, which then develop into megakaryocytes. These are huge cells the splinter and fragment into 2-3000 fragments and enter the bloodstream as platelets. They have no nucleus. They are involved in blood clotting by creating a platelet plug from where the blood clot forms. This seals the wound and stops bleeding

Oedema

This is an excess of fluid in the tissues and arises because there is an increase of fluid leaking out of circulation. It occurs in inflammation

Causes of oedema:

1. Increased capillary permeability from:
 - a. Allergy, general or local. If general, it tends to be in the upper half of the body.
 - b. Other symptoms: runny nose, sneezing, wheezing, diarrhoea, urticaria.
 - c. Inflammation

2. Increased sodium in extracellular space
 - a. Increased sodium in food/drugs
 - b. Disturbed sodium/potassium balance caused by some kidney disorders
3. Increased fluid volume:
 - a. Usually secondary to increased sodium levels
 - b. Water retention because of kidney problems, leading to decreased urine output
 - c. Hormonal imbalances (premenstrual water retention, HRT or oral contraceptives)
4. Decreased plasma osmotic pressure because of decreased protein in blood
 - a. Kidney disease leading to loss of blood protein (in urine). Oedema here is general
 - b. Liver disease leading to reduced protein production and low blood protein
 - c. Malnutrition – low protein intake
 - d. Malabsorption of protein, despite normal diet, e.g. coeliac disease.
5. Reduced flow in lymphatic and venous system:
 - a. Venous blockage because of thrombosis/tumour. This will cause unilateral oedema,
 - b. and with thrombosis the affected limb is painful and swollen
 - c. Varicose veins because of defective valves. This can be bilateral with blue distended varicosities. May be coloured skin over the ankles
6. Lymphatic system blockage because of tumour or parasitic infection (elephantiasis).
 - a. Here the oedema is non-pitting with possible lymphatic gland enlargement. If it a tumour, the oedema is one-sided.

Disorders

To understand disorders of the lymphatic system, it helps to:

- list the main structures of the lymphatic system
- state the main groups of lymphatic glands in the body
- describe areas that drain to these main glands
- describe the functions of the lymphatic glands as related to the immune system –lymphocyte production and development

Lymphatic gland enlargement:

Figure 6 - Tonsillitis

Mild cases

Acute inflammatory diseases, e.g. tonsillitis

Chronic inflammatory disease, e.g. glandular fever

Lymphoma: two types:

- Hodgkin's
- Non-Hodgkin's (see below)



Lymphosarcoma
Leukaemia

Severe cases

AIDS – Acquired immunodeficiency syndrome

Here a person experiences a telltale assortment of infections due to the destruction of their immune cells through human immunodeficiency virus. AIDS is the end-stage of HIV. A person with HIV could be symptom free for years, even though the virus is active. In the 20 years after the first cases were reported in 1981, 22 million people died of AIDS.

Worldwide up to 40 million people have HIV.

Allergic reactions

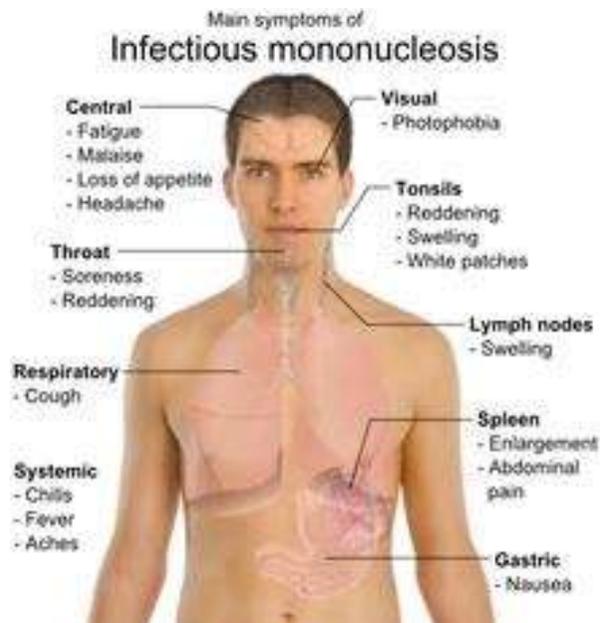
People frequently confuse allergy with intolerance; an allergic reaction will cause severe distress or be life-threatening. Common allergens include certain foods: milk, peanuts, shellfish, eggs, antibiotics, (penicillin, tetracycline), vaccines (pertussis, typhoid), venoms (bee stings, wasp, snake), cosmetics, plants chemical (poison ivy, pollen, dust, moulds) and even microbes.



Infectious mononucleosis

This is an infectious disease caused by the Epstein-Barr virus (EBV). It occurs mainly in children and a young adult via intimate oral contact – hence is also called the ‘kissing disease’.

Figure 7 - Infectious Mononucleosis



Lymphomas

These are cancers of the lymphatic organs. Most have no known cause; includes Hodgkin's disease and non-Hodgkin's lymphomas.

Systemic Lupus Erythematosus (SLE)

This is a chronic autoimmune disease affecting multiple organ systems. It mostly occurs in females between the ages of 15 –25, more often in blacks than whites. Its cause isn't known. Symptoms include joint pain, slight fever, weight loss, oral ulcers, enlargement of lymph nodes and spleen, rapid hair loss and a 'butterfly rash' across the cheeks and bridge of the nose.

**Figure 8- SLE - Systemic
Lupus Erythematosus**

