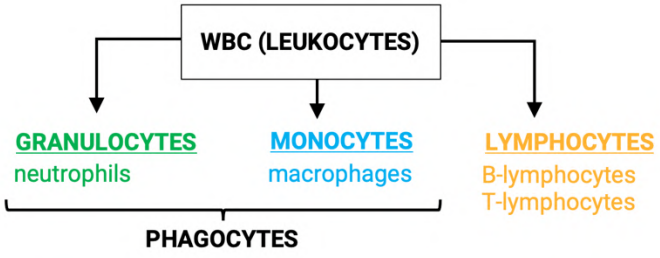
11 Immunity

11.1 The immune system



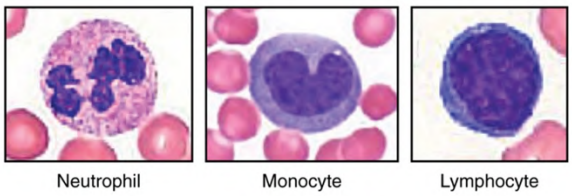


Image: Regents of University of Michigan Medical School © 2012

Phagocytes (neutrophils & macrophages)

- originate in bone marrow
- they're scavengers – removing any dead cells and invasive microorganisms

Neutrophils

- have a lobed nucleus and granular cytoplasm
- short-lived cells

Macrophages

- larger than neutrophils
- travel in blood as monocytes which develop into macrophages once they leave blood and settle in organs, removing foreign matter there
- long-lived cells
- do not destroy pathogens completely, they're cut up and their antigens are displayed, hence it becomes an antigen presenting cell (APC)

Phagocytosis

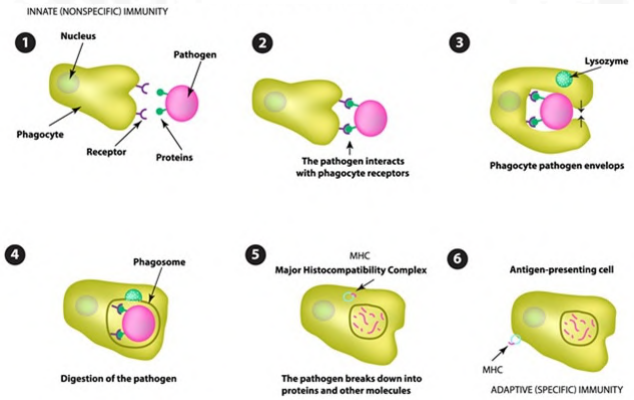


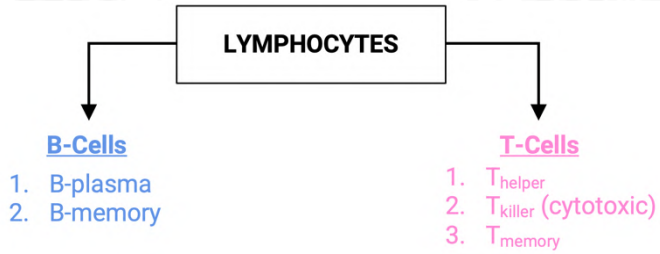
Image: Timonina / Shutterstock

- during an infection (caused by pathogens invading the body), cells under attack respond by releasing chemicals called histamines
- these attract neutrophils
- this movement towards chemical stimulus is called chemotaxis

General steps of phagocytosis

1) attraction (chemotaxis)
2) recognition and attachment
3) endocytosis
4) bacteria trapped within a phagocytotic vacuole
5) fusion of lysosomes and phagocytotic vacuole
6) killing and digestion

Lymphocytes



B-cells

- made and mature in the bone marrow
- travel to the spleen for final stages of maturation

1) B-plasma cells
- short-lived
- produce antibodies

2) B-memory cells
- form the immunological memory of the body
- responsible for 2° response

T-cells

Made in the bone marrow but mature in thymus.

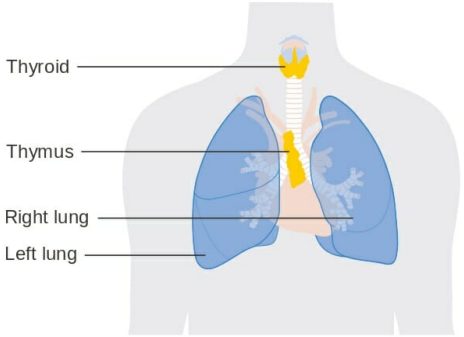


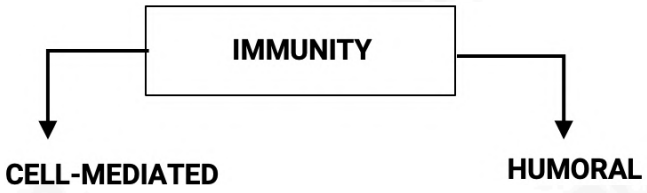
Image: https://biologydictionary.net/thymus-gland/

T_{helper}
- produce interleukins
- interleukins stimulate:
  1) B-cells to make antibodies
  2) other T-cells to divide
  3) macrophages to enhance the effect of phagocytosis

T_{killer} (cytotoxic)
- destroys cells by releasing perforin which makes holes in the cell surface membrane

T_{memory}
- leads to immunological memory of antigen
- responsible for 2° response

Immunity



a) Cell-mediated immunity

This is where T-lymphocytes respond to altered cells (APC, cancer cells, cells that've been infected by viruses)

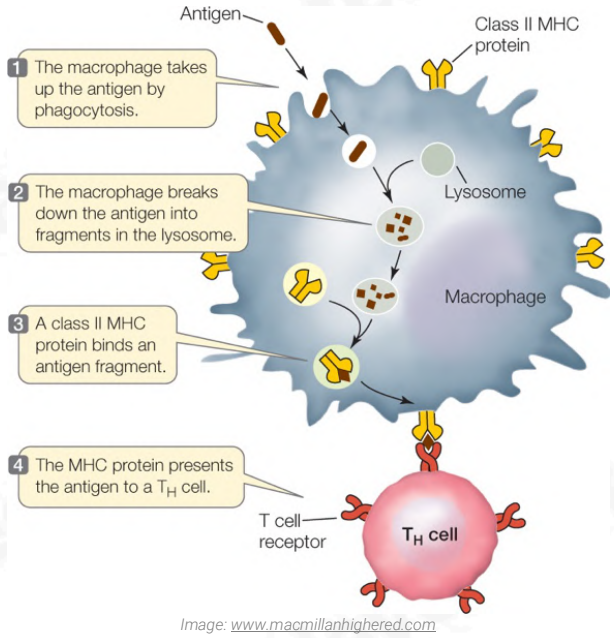


Image: www.macmillanhighered.com

1) macrophage engulfs pathogen and becomes an APC
2) T_{helper}'s cell receptor, which is complementary to the antigen, binds to antigen on APC
3) T_{helper} then releases interleukins
   - interleukins stimulate B-cells to divide into plasma cells and produce antibodies in the humoral response
   - they can also increase the effect of phagocytosis

⇒ **T-lymphocytes can only recognise antigens on an APC surface**

b) Humoral immunity

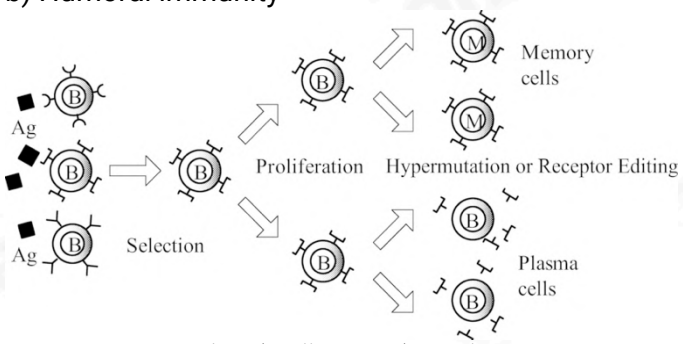


Image: https://www.researchgate.net/

a) Clonal selection

Process by which an antigen selectively binds to and activates only those lymphocytes bearing receptors for the antigen. In short, this is basically recognising and choosing which B-cells to use.

- T_{helper} cell recognises B-APC and becomes activated, releasing interleukins to signal further actions

b) Clonal expansion (proliferation)

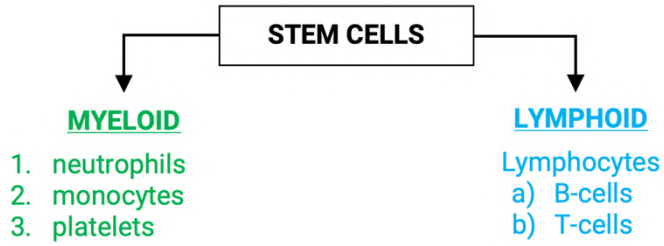
The rapid multiplication of B (or T) cell clones after activation by an antigen.

- B-APC divides and differentiates into –
  1) plasma cells to make specific antibodies
  2) memory cells to prepare for 2° response

⇒ **B-cells can respond to APC as well as pathogens directly**

Numbers of white blood cells

- Neutrophils in the blood increases during bacterial infections and whenever tissues become inflamed and die
- Lymphocyte numbers increase during viral infections and TB



- leukaemias are cancers of these stem cells
- cells divide uncontrollably to produce many cells that don't differentiate properly and disrupt production of normal blood cells

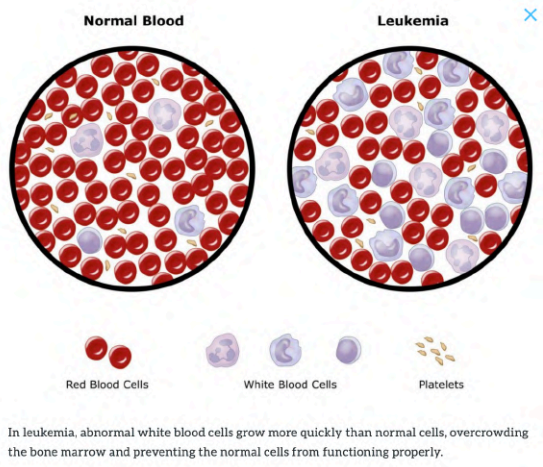


Image: https://orthoinfo.aaos.org/en/diseases--conditions/leukemia/

- immature white blood cells are produced quickly, disrupting balance of components in blood
- as a result, the body does not have enough red blood cells or platelets
- this causes anaemia and increases the risk of excessive bleeding
- the number of mature lymphocytes and neutrophils decrease, so susceptibility to infections increase
- the person is now said to be immunosuppressed

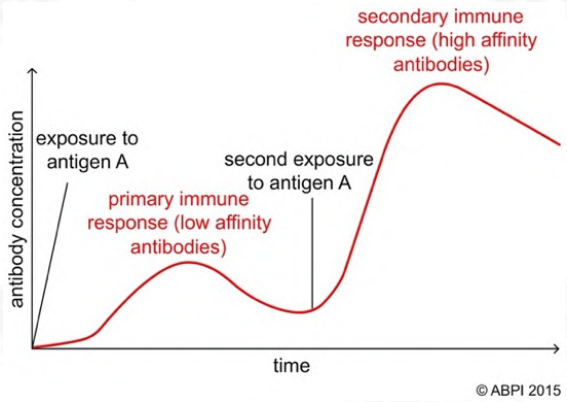
Immune response

> **immune response** – the complex series of responses of the body to the entry of a foreign antigen
  - involves the activity of lymphocytes and phagocytes

- **antigen** – substance that is foreign to the body and stimulates an immune response
- **self** – substance produced by the body that the immune system does not recognise as foreign and therefore does not stimulate an immune response
- **non-self** – any substance or cell recognised by the immune system as foreign and stimulates an immune response

Role of memory cells in long-term immunity

Remain in the blood for years and cause long-term protection.



Autoimmune diseases

Occurs when the immune system mistakenly identifies self-antigens as foreign (non-self) and mounts an immune response against them.

- during the maturation of T-cells in the thymus, millions of cells are destroyed as they have T-cell receptors complementary to self-antigens
- some of these cells evade destruction and are activated to stimulate an immune response against the body's own proteins
- starts as an attack involving antibodies and killer T-cells against certain parts of the body
- attack can be localised in one organ or directed against the whole body
- e.g., Myasthenia gravis, rheumatoid arthritis, type 1 diabetes, lupus, psoriasis, etc.

Myasthenia gravis (MG)

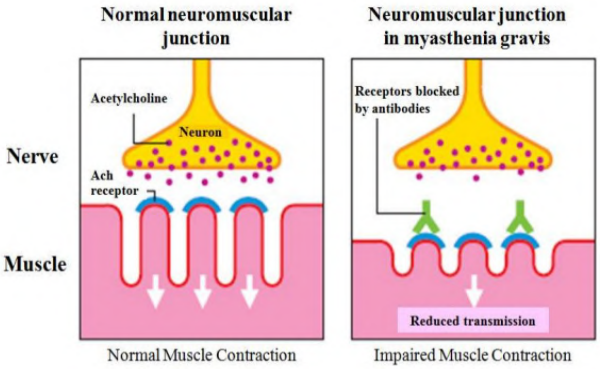


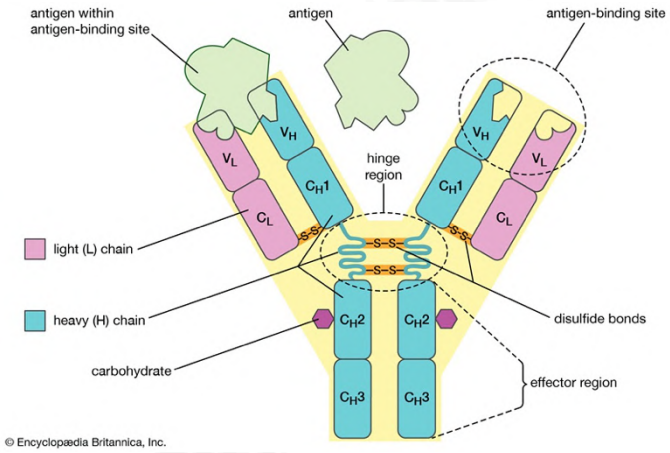
Image: https://healthjade.com/acetylcholine/

- antibodies are produced against receptors on muscle fibres for acetylcholine which is released by ends of motor neurones to stimulate muscle contraction
- people with MG have T_{helper} cells that are specific for cell surface receptors for acetylcholine
- T_{helper} cells stimulate a clone of B-cells to differentiate into plasma cells and secrete antibodies that bind to receptor blocking transmission from motor neurones
- muscle cells are not stimulated so muscle tissue starts to break down
- **symptoms** – muscle weakness
- **treatment** – drug that inhibits enzyme in synapses that breaks down acetylcholine increases its concentration so its action in stimulating muscle contraction lasts longer *or* surgical removal of the thymus gland

11.2 Antibodies and vaccination

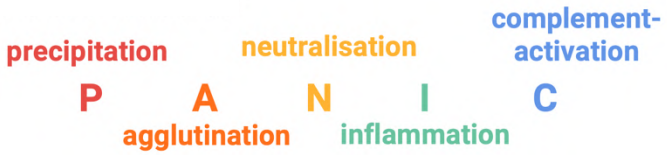
Antibodies

- globular glycoproteins
- have quaternary structure
- form group of plasma proteins called immunoglobulins



- **Hinge region** – gives flexibility to bind around antigen
- **Antigen binding sites** – sequence of amino acids in these regions make a specific 3D shape which binds to one type of antigen

Functions of antibodies



- attach to flagella of bacteria making them less active and easier for phagocytes to engulf
- cause agglutination (clumping together) of bacteria, reducing chances of spread
- punch holes in bacteria cell walls, causing them to burst when they absorb water by osmosis
- antibodies coat bacteria, making phagocytosis easier as phagocytes have receptor proteins
- combine with toxins, neutralising them (antitoxins)
- combine with viruses and bacterial toxins, preventing them from entering or damaging cells

Hybridoma method for the production of monoclonal antibodies

- B-cells that divide by mitosis do not produce antibodies and plasma cells that secrete antibodies do not divide
- **monoclonal antibodies** – identical copies of one type of antibody

1) antigen is injected into a mouse
2) spleen cells which produce lymphocytes which produce antibodies are removed
3) plasma cells from spleen are fused with cancer cells or myeloma cells forming hybridoma cells that divide indefinitely
4) they divide by mitosis and produce antibodies

Using monoclonal antibodies in diagnosis and treatment of disease

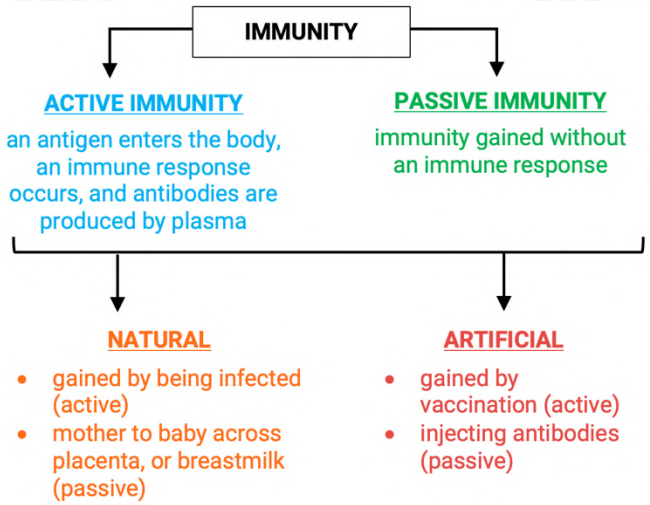
In diagnosis

- used to locate position of blood clots
- used to locate cancer cells which have different cell surface proteins and therefore can be detected by antibodies
- used to identify exact strain of virus or bacterium causing an infection, which speeds up treatment

In treatment

- treatment of breast cancer – antibody binds to cancerous cells and marks them for destruction by immune system
- treatment of rheumatoid arthritis (autoimmune) – antibody binds to proteins secreted by T-cells that causes damage to cartilage in joints and blocks its action

Types of immunity



Vaccination

Vaccines

- preparation containing antigens which is used to stimulate an immune response artificially
- it may contain antigens in the form of live or dead microorganisms, harmless (attenuated organism), toxoid (harmless toxin), surface antigens

How vaccines can provide long-term immunity

1) vaccine contains antigens that stimulate an immune response
2) macrophages take up virus by phagocytosis and act as antigen presenting cells (APC)
3) lymphocytes bind to these and under clonal selection
4) clonal expansion then occurs by mitosis
5) memory cells are formed
6) booster is used to further stimulate memory cell formation

Poor response to vaccines due to –

- suffer from malnutrition and don't have enough proteins to make antibodies or clones of lymphocytes
- defective immune system and don't develop necessary B and T cell clones

Vaccination programmes

Eradication of smallpox

- *Variola* virus was stable, it didn't mutate and change cell surface antigens
- vaccine was made from a harmless strain of a similar virus – a 'live' vaccine is more effective
- infected people can be easily identified
- vaccine was freeze-dried and can be kept at high temperatures for as long as 6 months
- didn't affect animals – easier to break transmission cycle

Herd immunity

Herd immunity interrupts transmission in a population so that those who are susceptible never encounter the infectious agents concerned.

Why measles, cholera, malaria, and TB haven't been eradicated

Antigenic variation

a) Antigenic drift – minor changes in the viral antigen, memory cells are still able to recognise them and start a secondary response

b) Antigenic shift – major changes in antigen structure

- currently there are no effective vaccines for diseases caused by protocists as they're eukaryotes with many more genes.
- e.g., malaria; each stage has its own antigen

⇒ measles – poor response by some children, needs several booster shots

⇒ cholera – many strains

⇒ malaria – too many stages (antigenic variations)

⇒ TB – symptoms may not be shown