Blood facts

- Approximately 8% of an adult's body weight is made up of blood.
- Females have around 4-5 litres, while males have around 5-6 litres. This difference is mainly due to the differences in body size between men and women.
- Its mean temperature is 38 degrees Celcius.
- It has a pH of 7.35-7.45, making it slightly basic (less than 7 is considered acidic).
- Whole blood is about 4.5-5.5 times as viscous as water, indicating that it is more resistant to flow than water. This viscosity is vital to the function of blood because if blood flows too easily or with too much resistance, it can strain the heart and lead to severe cardiovascular problems.
- Blood in the arteries is a brighter red than blood in the veins because of the higher levels of oxygen found in the arteries.
- An artificial substitute for human blood has not been found.

Functions of blood

Blood has three main functions: transport, protection and regulation.

Transport

Blood transports the following substances:

- Gases, namely oxygen (O_2) and carbon dioxide (CO_2), between the lungs and rest of the body
- Nutrients from the digestive tract and storage sites to the rest of the body
- Waste products to be detoxified or removed by the liver and kidneys
- Hormones from the glands in which they are produced to their target cells
- Heat to the skin so as to help regulate body temperature

Protection

Blood has several roles in inflammation:

- Leukocytes, or white blood cells, destroy invading microorganisms and cancer cells
- Antibodies and other proteins destroy pathogenic substances
- Platelet factors initiate blood clotting and help minimise blood loss

Regulation

Blood helps regulate:

- pH by interacting with acids and bases
- Water balance by transferring water to and from tissues

Composition of blood

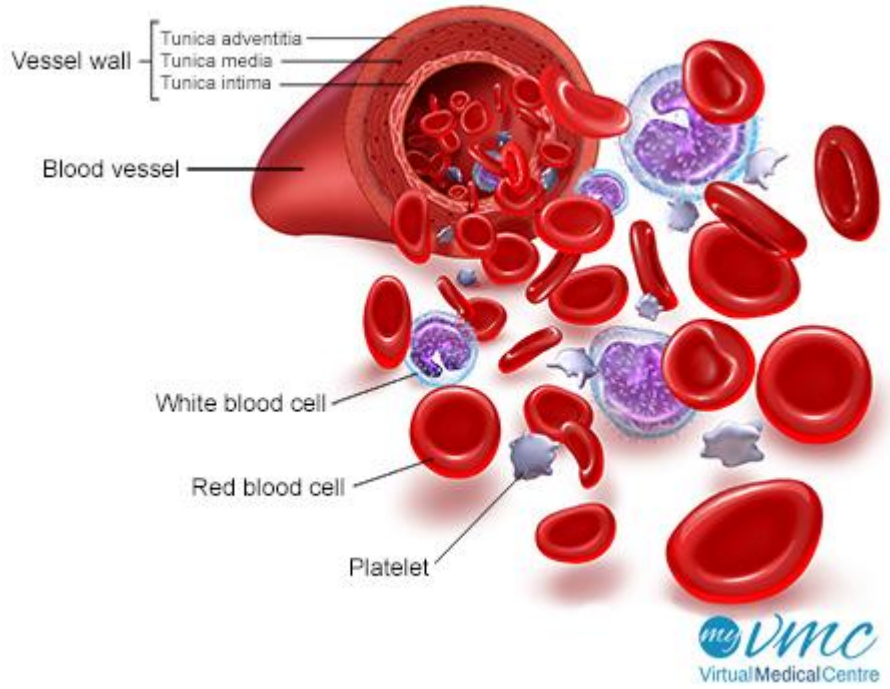
Blood is classified as a connective tissue and consists of two main components:

1. Plasma, which is a clear extracellular fluid
2. Formed elements, which are made up of the blood cells and platelets

The formed elements are so named because they are enclosed in a plasma membrane and have a definite structure and shape. All formed elements are cells except for the platelets, which are tiny fragments of bone marrow cells.

Formed elements are:

- Erythrocytes, also known as red blood cells (RBCs)
- Leukocytes, also known as white blood cells (WBCs)
- Platelets



Information on re-publishing of our images

Leukocytes are further classified into two subcategories called granulocytes which consist of neutrophils, eosinophils and basophils; and agranulocytes which consist of lymphocytes and monocytes.

The formed elements can be separated from plasma by centrifuge, where a blood sample is spun for a few minutes in a tube to separate its components according to their densities. RBCs are denser than plasma, and so become packed into the bottom of the tube to make up 45% of total volume. This volume is known as the haematocrit. WBCs and platelets form a narrow cream-coloured coat known as the buffy coat immediately above the RBCs. Finally, the plasma makes up the top of the tube, which is a pale yellow colour and contains just under 55% of the total volume.

Blood plasma

Blood plasma is a mixture of proteins, enzymes, nutrients, wastes, hormones and gases. The specific composition and function of its components are as follows:

Proteins

These are the most abundant substance in plasma by weight and play a part in a variety of roles including clotting, defence and transport. Collectively, they serve several functions:

- They are an important reserve supply of amino acids for cell nutrition. Cells called macrophages in the liver, gut, spleen, lungs and lymphatic tissue can break down plasma proteins so as to release their amino acids. These amino acids are used by other cells to synthesise new products.

- Plasma proteins also serve as carriers for other molecules. Many types of small molecules bind to specific plasma proteins and are transported from the organs that absorb these proteins to other tissues for utilisation. The proteins also help to keep the blood slightly basic at a stable pH. They do this by functioning as weak bases themselves to bind excess H+ ions. By doing so, they remove excess H+ from the blood which keeps it slightly basic.
- The plasma proteins interact in specific ways to cause the blood to coagulate, which is part of the body's response to injury to the blood vessels (also known as vascular injury), and helps protect against the loss of blood and invasion by foreign microorganisms and viruses.
- Plasma proteins govern the distribution of water between the blood and tissue fluid by producing what is known as a colloid osmotic pressure.

There are three major categories of plasma proteins, and each individual type of proteins has its own specific properties and functions in addition to their overall collective role:

1. **Albumins**, which are the smallest and most abundant plasma proteins. Reductions in plasma albumin content can result in a loss of fluid from the blood and a gain of fluid in the interstitial space (space within the tissue), which may occur in nutritional, liver and kidney disease. Albumin also helps many substances dissolve in the plasma by binding to them, hence playing an important role in plasma transport of substances such as drugs, hormones and fatty acids.
2. **Globulins**, which can be subdivided into three classes from smallest to largest in molecular weight into alpha, beta and gamma globulins. The globulins include high density lipoproteins (HDL), an alpha-1 globulin, and low density lipoproteins (LDL), a beta-1 globulin. HDL functions in lipid transport carrying fats to cells for use in energy metabolism, membrane reconstruction and hormone function. HDLs also appear to prevent cholesterol from invading and settling in the walls of arteries. LDL carries cholesterol and fats to tissues for use in manufacturing steroid hormones and building cell membranes, but it also favours the deposition of cholesterol in arterial walls and thus appears to play a role in disease of the blood vessels and heart. HDL and LDL therefore play important parts in the regulation of cholesterol and hence have a large impact on cardiovascular disease.
3. **Fibrinogen**, which is a soluble precursor of a sticky protein called fibrin, which forms the framework of blood clot. Fibrin plays a key role in coagulation of blood, which is discussed later in this article under Platelets.

Amino acids

These are formed from the break down of tissue proteins or from the digestion of digested proteins.

Nitrogenous waste

Being toxic end products of the break down of substances in the body, these are usually cleared from the bloodstream and are excreted by the kidneys at a rate that balances their production.

Nutrients

Those absorbed by the digestive tract are transported in the blood plasma. These include glucose, amino acids, fats, cholesterol, phospholipids, vitamins and minerals.

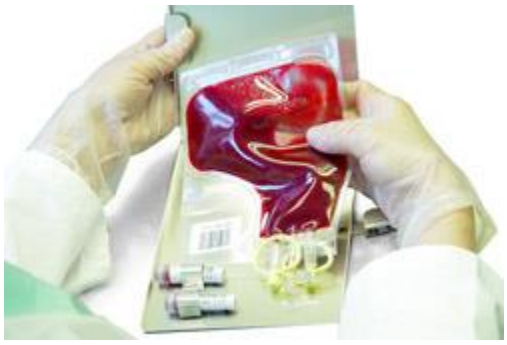
Gases

Some oxygen and carbon dioxide are transported by plasma. Plasma also contains a substantial amount of dissolved nitrogen.

Electrolytes

The most abundant of these are sodium ions, which account for more of the blood's osmolarity than any other solute.

Red blood cells



Red blood cells (RBCs), also known as erythrocytes, have two main functions:

1. To pick up oxygen from the lungs and deliver it to tissues elsewhere
2. To pick up carbon dioxide from other tissues and unload it in the lungs

An erythrocyte is a disc-shaped cell with a thick rim and a thin sunken centre. The plasma membrane of a mature RBC has glycoproteins and glycolipids that determine a person's blood type. On its inner surface are two proteins called spectrin and actin that give the membrane resilience and durability. This allows the RBCs to stretch, bend and fold as they squeeze through small blood vessels, and to spring back to their original shape as they pass through larger vessels.

RBCs are incapable of aerobic respiration, preventing them from consuming the oxygen they transport because they lose nearly all their inner cellular components during maturation. The inner cellular components lost include their mitochondria, which normally provide energy to a cell, and their nucleus, which contains the genetic material of the cell and enable it to repair itself. The lack of a nucleus means that RBCs are unable to repair themselves. However, the resulting biconcave shape is that the cell has a greater ratio of surface area to volume, enabling O_2 and CO_2 to diffuse quickly to and from Hb.

The cytoplasm of a RBC consists mainly of a 33% solution of haemoglobin (Hb), which gives RBCs their red colour. Haemoglobin carries most of the oxygen and some of the carbon dioxide transported by the blood.

Circulating erythrocytes live for about 120 days. As a RBC ages, its membrane grows increasingly fragile. Without key organelles such as a nucleus or ribosomes, RBCs cannot repair themselves. Many RBCs die in the spleen, where they become trapped in narrow channels, broken up and destroyed. Haemolysis refers to the rupture of RBCs, where haemoglobin is released leaving empty plasma membranes which are easily digested by cells known as macrophages in the liver and spleen. The Hb is then further broken down into its different components and either recycled in the body for further use or disposed of.

White blood cells

White blood cells (WBCs) are also known as leukocytes. They can be divided into granulocytes and agranulocytes. The former have cytoplasms that contain organelles that appear as coloured granules through light microscopy, hence their name. Granulocytes consist of neutrophils, eosinophils and basophils. In contrast, agranulocytes do not contain granules. They consist of lymphocytes and monocytes.

Granulocytes

1. **Neutrophils:** These contain very fine cytoplasmic granules that can be seen under a light microscope. Neutrophils are also called polymorphonuclear (PMN) because they have a variety of nuclear shapes. They play roles in the destruction of bacteria and the release of chemicals that kill or inhibit the growth of bacteria.
2. **Eosinophils:** These have large granules and a prominent nucleus that is divided into two lobes. They function in the destruction of allergens and inflammatory chemicals, and release enzymes that disable parasites.
3. **Basophils:** They have a pale nucleus that is usually hidden by granules. They secrete histamine which increases tissue blood flow via dilating the blood vessels, and also secrete heparin which is an anticoagulant that promotes mobility of other WBCs by preventing clotting.

Agranulocytes

1. **Lymphocytes:** These are usually classified as small, medium or large. Medium and large lymphocytes are generally seen mainly in fibrous connective tissue and only occasionally in the circulation bloodstream. Lymphocytes function in destroying cancer cells, cells infected by viruses, and foreign invading cells. In addition, they present antigens to activate other cells of the immune system. They also coordinate the actions of other immune cells, secrete antibodies and serve in immune memory.
2. **Monocytes:** They are the largest of the formed elements. Their cytoplasm tends to be abundant and relatively clear. They function in differentiating into macrophages, which are large phagocytic cells, and digest pathogens, dead neutrophils, and the debris of dead cells. Like lymphocytes, they also present antigens to activate other immune cells.

Platelets

Platelets are small fragments of bone marrow cells and are therefore not really classified as cells themselves.

Platelets have the following functions:

1. Secrete vasoconstrictors which constrict blood vessels, causing vascular spasms in broken blood vessels
2. Form temporary platelet plugs to stop bleeding
3. Secrete procoagulants (clotting factors) to promote blood clotting
4. Dissolve blood clots when they are no longer needed
5. Digest and destroy bacteria
6. Secrete chemicals that attract neutrophils and monocytes to sites of inflammation
7. Secrete growth factors to maintain the linings of blood vessels

The first three functions listed above refer to important haemostatic mechanisms in which platelets play a role in during bleeding: vascular spasms, platelet plug formation and blood clotting (coagulation).

Vascular spasm

This is a prompt constriction of the broken blood vessel and is the most immediate protection against blood loss. Injury stimulates pain receptors. Some of these receptors directly innervate nearby blood vessels and cause them to constrict. After a few minutes, other mechanisms take

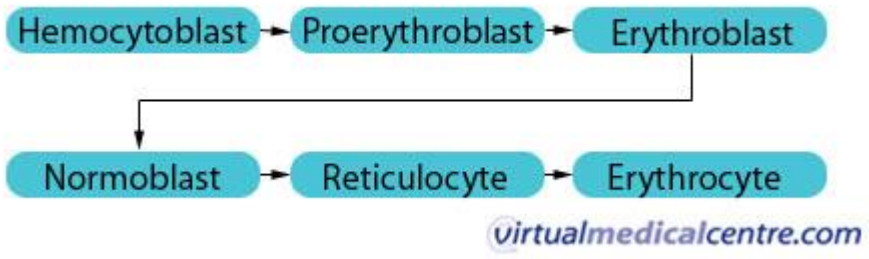
over. Injury to the smooth muscle of the blood vessel itself causes a longer-lasting vasoconstriction where platelets release a chemical vasoconstrictor called serotonin. This maintains vascular spasm long enough for the other haemostatic mechanisms to come into play.

Platelet plug formation
Under normal conditions, platelets do not usually adhere to the wall of undamaged blood vessels, since the vessel lining tends to be smooth and coated with a platelet repellent. When a vessel is broken, platelets put out long spiny extensions to adhere to the vessel wall as well as to other platelets. These extensions then contract and draw the walls of the vessel together. The mass of platelets formed is known as a platelet plug, and can reduce or stop minor bleeding.

Coagulation
This is the last and most effective defence against bleeding. During bleeding, it is important for the blood to clot quickly to minimise blood loss, but it is equally important for blood not to clot in undamaged vessels. Coagulation is a very complex process aimed at clotting the blood at appropriate amounts. The objective of coagulation is to convert plasma protein fibrinogen into fibrin, which is a sticky protein that adheres to the walls of a vessel. Blood cells and platelets become stuck to fibrin, and the resulting mass helps to seal the break in the blood vessel. The forming of fibrin is what makes coagulation so complicated, as it involved numerous chemicals reactions and many coagulation factors.

Production of blood
Haemopoiesis
Haemopoiesis is the production of the formed elements of blood. Haemopoietic tissues refer to the tissues that produce blood. The earliest haemopoietic tissue to develop is the yolk sac, which also functions in the transfer of yolk nutrients of the embryo. In the foetus, blood cells are produced by the bone marrow, liver, spleen and thymus. This changes during and after birth. The liver stops producing blood cells around the time of birth, while the spleen stops producing them soon after birth but continues to produce lymphocytes for life. From infancy onwards, all formed elements are produced in the red bone marrow. Lymphocytes are additionally produced in lymphoid tissues and organs widely distributed in the body, including the thymus, tonsils, lymph nodes, spleen and patches of lymphoid tissues in the intestine.

Erythropoesis
Erythropoiesis refers specifically to the production of erythrocytes or red blood cells (RBCs). These are formed through the following sequence of cell transformations:



The proerythroblast has receptors for the hormone erythropoietin (EPO). Once EPO receptors are in place, the cell is committed to exclusively producing RBCs. The erythroblasts then multiply

and synthesise haemoglobin (Hb), which is a red oxygen transport protein. The nucleus from the erythroblasts is then discarded, giving rise to cells named reticulocytes. The overall transformation from haemocytoblast to reticulocytes involves a reduction in cell size, an increase in cell number, the synthesis of haemoglobin, and the loss of the cell nucleus. These reticulocytes leave the bone marrow and enter the bloodstream where they mature into erythrocytes when their endoplasmic reticulum disappears.

Leukopoiesis

Leukopoiesis refers to the production of leukocytes (WBCs). It begins when some types of haemocytoblasts differentiate into three types of committed cells:

1. B progenitors, which are destined to become B lymphocytes
2. T progenitors, which become T lymphocytes
3. Granulocyte-macrophage colony-forming units, which become granulocytes and monocytes

These cells have receptors for colony-stimulating factors (CSFs). Each CSF stimulates a different WBC type to develop in response to specific needs. Mature lymphocytes and macrophages secrete several types of CSFs in response to infections and other immune challenges. The red bone marrow stores granulocytes and monocytes until they are needed in the bloodstream. However, circulating leukocytes do not stay in the blood for very long. Granulocytes circulate for 4-8 hours and then migrate into the tissues where they live for another 4-5 days. Monocytes travel in the blood for 10-20 hours, then migrate into the tissues and transform into a variety of macrophages which can live as long as a few years. Lymphocytes are responsible for long-tern immunity and can survive from a few weeks to decades. They are continually recycled from blood to tissue fluid to lymph and finally back to the blood.

Thrombopoiesis

Thrombopoiesis refers to the production of platelets in the blood, because platelets used to be called thrombocytes. This starts when a haemocytoblast develops receptors for the hormone thrombopoietin which is produced by the liver and kidneys. When these receptors are in place, the haemocytoblast becomes a committed cell called a megakaryoblast. This replicates its DNA, producing a large cell called a megakaryocyte, which breaks up into tiny fragments that enter the bloodstream. About 25-40% of the platelets are stored in the spleen and released as needed. The remainder circulate freely in the blood are live for about 10 days.

Ageing changes in the blood

The properties of blood change as we grow older. It is thought that these changes might contribute to the increased incident of clot formation and atherosclerosis in older people. Some of the most prominent findings on these changes include:

1. Rise in fibrinogen
2. Rise in blood viscosity
3. Rise in plasma viscosity
4. Increased red blood cell rigidity
5. Increased formation of fibrin degradation products
6. Earlier activation of the coagulation system

The increased level of plasma fibrinogen is thought to be due to either its rapid production or slower degradation. As age progresses, fibrinogen and plasma viscosity tend to be positively correlated, with the rise in plasma viscosity being largely attributed to the rise in fibrinogen.

The viscosity of blood depends on factors such as shear rate, haemocrit, red cell deformability, plasma viscosity and red cell aggregation. Although there are many factors involved, hyperviscosity syndrome can be generated by a rise in only one factor. A state of hyperviscosity causes sluggish blood flow and reduced oxygen supply to the tissue.

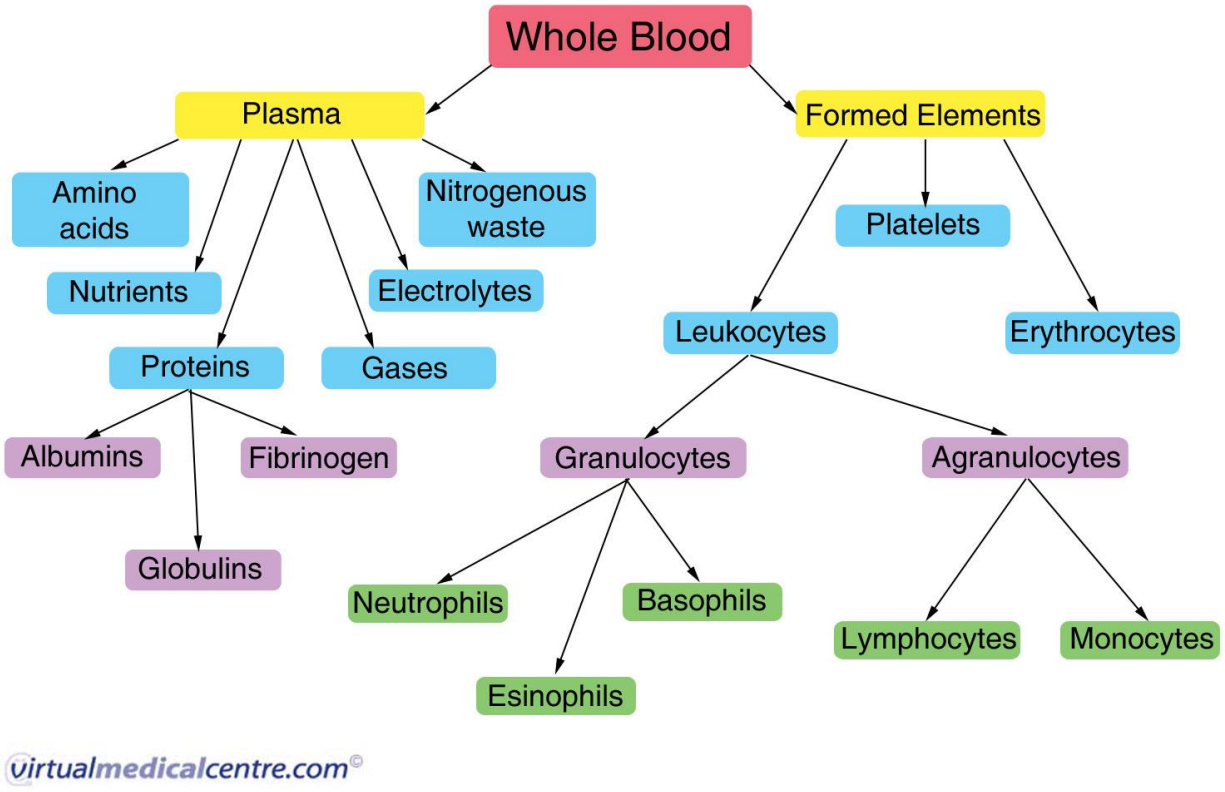
An age-dependent increase in various coagulation factors, a positive correlation with fibrinogen and a negative correlation with plasma albumin has also been found. Both platelet and red cell aggregation increase with age, with red cell aggregation appearing to be the primary factor responsible for a rise in blood viscosity at low shear rates.

The decrease in red cell deformability (increase in rigidity) refers to its ability to deform under flow forces. Less deformable cells offer more resistance to flow in the microcirculation, which influences the delivery of oxygen to the tissues. Studies have found that older people have less fluid membranes in their red cells.

Blood H^+ has also been found to be positively correlated with age, making the blood slightly more acidic as we age. This results in a swelling of the cell, making the red cells less deformable. This sets up a cycle for further increase in blood viscosity and worsening of blood flow parameters.

Since ageing causes a reduction in total body water, blood volume decreases due to less fluid being present in the bloodstream. The number of red blood cells, and the corresponding haemoglobin and haemocrit levels, are reduced which contributes to fatigue in the individual. Most of the white blood cells stay at their original levels, although there is a decrease in lymphocyte number and ability to fight off bacteria, leading to a reduced ability to resist infection.

Overall, the rise in fibrinogen is the most common and significant change in blood during ageing because it contributes to a rise in plasma viscosity, red blood cell aggregation and a rise in blood viscosity at low shear rates. Increased age is associated with a state of hypercoagulation of blood, making older people more susceptible to clot formation and atherosclerosis.



Hemoglobin variants

Hemoglobin variants are mutant forms of hemoglobin in a population (usually of humans), caused by variations in genetics. Some well-known hemoglobin variants such assickle-cell anemia are responsible for diseases, and are considered hemoglobinopathies. Other variants cause no detectable pathology, and are thus considered non-pathological variants.

Some normal hemoglobin types are; Hemoglobin A (Hb A), which is 95-98% of hemoglobin found in adults, Hemoglobin A2 (Hb A2), which is 2-3% of hemoglobin found in adults, and Hemoglobin F (Hb F), which is found in adults up to 2.5% and is the primary hemoglobin that is produced by the fetus during pregnancy.

Hemoglobin variants occur when there are genetic changes in specific genes, or globins, that cause changes or alterations in the amino acid. They could affect the structure, behavior, the production rate, and/or the stability of that specific gene. Usually there are four genes that code for alpha globin and two genes that code for beta globin. If the genes for alpha chains is mutated, the most common condition that occurs is alpha thalassemia, which causes a decrease in production of that gene. The level of severity of alpha thalassemia is determined by the number of genes that are affected.

Hemoglobin variants are most often inherited characteristics. First, abnormal beta gene can be inherited in an autosomal recessive fashion. This means that the person who inherits this will have two copies of the altered gene. Both of these genes can be passed to offspring. The next way they can be inherited is in a heterozygous fashion. This means that the person has one normal beta gene and one abnormal beta gene. This person is considered to be a carrier of

whichever hemoglobin variant is inherited. Only the abnormal gene can be passed on to offspring in this case. Carriers also do not have to deal with having symptoms or any health concerns. Another way that beta genes can be inherited is in a homozygous fashion. This means that the person has two abnormal beta genes. In this case the person produces the associated hemoglobin variant and may have the symptoms and complications that are associated with they specific hemoglobin variant they have. The severity of the conditions mainly depend on the genetic mutationand it may vary from person to person. The copies of the abnormal beta genes would more than likely be passed to offspring.

Along with lengthy list of common hemoglobin variants, there are some variants that are less common. These variants are considered silent, which means that they have no signs or symptoms. They usually affect the functionality and/or the stability of the hemoglobin molecule. With most of these variants are mutations in the alpha globin gene that result in an abnormally long alpha chain and an unstable hemoglobin molecules.

Hemoglobin F is the primary hemoglobin produced by the fetus. The hemoglobin transports oxygen efficiently in a low oxygen environment. The hemoglobin production stops at birth and decreases to adult levels by the age of one or two. The levels can be normal to increased in beta thalassemia. Hemoglobin F frequently increases in individuals withsickle cell anemia and sickle cell-beta thalassemia. Individuals with sickle cell and increase of Hb F have a milder case of the disease. There are situations where the Hb F is increased. This rare condition is called Hereditary Persistence of Fetal Hemoglobin (HPFH). This is a group of disorders where the Hemoglobin F is increased without signs or clinical features of thalassemia. Some different ethnic groups have different mutations that cause HPFH. Hb F can also be increase by acquired conditions that involve the red blood cells. Elevated Hemoglobin F levels are also associated with Leukemia and myeloproliferative disorders.

Hemoglobin H increases the affinity for oxygen. This means that it holds onto the oxygen instead of releasing it into tissue and cells. Hb H usually occurs in some alpha thalassemia and is composed of four beta globin (protein) chains. This variant is usually produced in response to a severe shortage of alpha chains, and usually cause beta chains to function abnormally.
Anemia Types

The most common types of anaemia are

- Iron deficiency anaemia
- Thalassaemia
- Aplastic anaemia
- Haemolytic anaemia
- Sickle cell anaemia
- Pernicious anaemia
- Fanconi anaemia

Iron Deficiency Anaemia

Overview

The most common form of anaemia is iron deficiency anaemia which is usually due to chronic blood loss caused by excessive menstruation. Increased demands for iron, such as foetal growth

in pregnancy, and children undergoing rapid growth spurts in infancy and adolescence, can also cause iron deficiency anaemia.
This condition is treated with iron supplementation as well as the treatment of the underlying cause of the iron deficiency.

Causes
Iron deficiency occurs when the rate of loss or use of iron is more than its rate of absorption and use. The reasons for this are

- Chronic blood loss: Most commonly due to excessive menstruation or bleeding into or from the gut as a result of a peptic ulcer, gastritis, haemorrhoids or in children, worm infestation.
- Increased use of iron: In pregnancy, due to the growth of the foetus or children undergoing rapid growth spurts in infancy and adolescence.
- Decreased absorption of iron
    - after a partial or total removal of the stomach;
    - lack of stomach acid;
    - chronic diarrhoea; or
    - malabsorption.

Signs and symptoms
The most common symptoms of chronic anaemia include tiredness, weakness, shortness of breath and sometimes, a fast heartbeat. The tongue may also become smooth, shiny and inflamed - this is called glossitis. Angular stomatitis (erosion, tenderness and swelling at the corners of the mouth) may also occur. In some instances, the patient also suffers from pica, a craving for strange foods such as starch, ice and clay.
The symptoms of the underlying cause of the iron deficiency may be present such as heavy menstrual bleeding or abdominal pain due to peptic ulceration.

Treatment
Treatment for iron-deficiency anaemia will depend on the cause and severity of the condition. Treatments may include dietary changes and supplements, medicines, and surgery. Severe iron-deficiency anaemia may require treatment in hospital, blood transfusions, iron rejections, or intravenous iron therapy.

Risk
Infants and young children, women, and adults who have internal bleeding are at highest risk for iron-deficiency anaemia.

Aplastic Anaemia

Overview
Aplastic anaemia is a blood disorder in which the body's bone marrow doesn't make enough new blood cells. This may result in a number of health problems including arrhythmias, an enlarged heart, heart failure, infections and bleeding.
Aplastic anaemia is a rare but serious condition. It can develop suddenly or slowly and tends to worsen with time, unless the cause is found and treated.

Causes
Damage to the bone marrow's stem cells causes aplastic anaemia. In more than half of people who have aplastic anaemia, the cause of the disorder is unknown.
A number of acquired diseases, conditions, and factors can cause aplastic anaemia including

- Toxins, such as pesticides, arsenic, and benzene
- Radiation and chemotherapy
- Medicines such as chloramphenicol
- Infectious diseases such as hepatitis, Epstein-Barr virus, cytomegalovirus, parvovirus B19, and HIV
- Autoimmune disorders such as lupus and rheumatoid arthritis

Inherited conditions, such as Fanconi anaemia, Shwachman-Diamond syndrome, dyskeratosis congenital and Diamond-Blackfan anaemia may also cause aplastic anaemia.

Signs and symptoms

The most common symptoms of aplastic anaemia are

- Fatigue
- Shortness of breath
- Dizziness
- Headache
- Coldness in your hands or feet
- Pale skin, gums and nail beds
- Chest pains

Treatment

Treatment for aplastic anaemia includes blood transfusions, blood and marrow stem cell transplants, and medication. These treatments can prevent or limit complications, relieve symptoms, and improve quality of life.

In some cases, a cure may be possible. Blood and marrow stem cell transplants may cure the disorder. Removing a known cause of aplastic anaemia, such as exposure to a toxin, may also cure the condition.

Risk

People of all ages can get aplastic anaemia. However, it is most common in adolescents, young adults and the elderly. Men and women are equally likely to have it.

A person's risk for aplastic anaemia is higher if you have

- Been exposed to toxins
- Taken certain medicines or had radiation or chemotherapy treatment
- Certain infectious diseases, autoimmune disorders, or inherited conditions

Haemolytic Anaemia

Overview

Haemolytic anaemia is a condition in which red blood cells are destroyed and removed from the bloodstream before their normal lifespan is up. A number of diseases, conditions and factors can cause the body to destroy its red blood cells. Haemolytic anaemia can lead to various health problems such as fatigue, pain, arrhythmias, an enlarged heart and heart failure.

There are many types of haemolytic anaemias – some of which are inherited and others that are acquired.

Inherited haemolytic anaemias include

- Sickle cell anaemia

- Thalassaemias
- Hereditary spherocytosis
- Hereditary elliptocytosis
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Pyruvate kinase deficiency

Acquired haemolytic anaemias include

- Immune haemolytic anaemia
  - Autoimmune haemolytic anaemia
  - Alloimmune haemolytic anaemia
  - Drug-induced haemolytic anaemia
- Mechanical haemolytic anaemias
- Paroxysmal nocturnal haemoglobinuria
- Certain infections and substances can also damage red blood cells and lead to haemolytic anaemia

Causes

The immediate cause of haemolytic anaemia is the early destruction of red blood cells. A number of diseases, conditions, and factors can cause the body to destroy its red blood cells. These causes can be inherited or acquired. Sometimes, the cause of haemolytic anaemia isn't known.

- In **inherited haemolytic anaemias**, the genes that control how red blood cells are made are faulty. Different types of faulty genes account for the different types of inherited haemolytic anaemias. In each type of inherited haemolytic anaemia, the body makes abnormal red blood cells. The problem with the red blood cells may involve the haemoglobin, cell membrane, or enzymes that maintain healthy red blood cells.
- In **acquired haemolytic anaemias**, the body makes normal red blood cells, however, some disease, condition, or factor destroys the cells too early. Examples include immune disorders, infections and reactions to medicines or blood transfusions.

Signs and Symptoms

The most common symptom of all types of anaemia is fatigue. A low red blood cell count can also cause shortness of breath, dizziness, headache, coldness in your hands or feet, pale skin, gums and nail beds, as well as chest pain.

Symptoms of haemolytic anaemia include

- Jaundice
- Pain in the upper abdomen
- Leg ulcers and pain
- A severe reaction to a blood transfusion

Treatment

Treatments for haemolytic anaemia include blood transfusions, medicines, plasmapheresis, surgery, blood and marrow stem cell transplants and lifestyle changes.

People who have mild haemolytic anaemia may not need treatment, as long as the condition doesn't worsen. People with severe haemolytic anaemia usually need ongoing treatment.

Risk

Haemolytic anaemia can affect people of all ages, races and sexes.

Thalassaemia

Overview

Thalassaemias are inherited blood disorders which cause the body to make fewer healthy red blood cells and less haemoglobin (an iron-rich protein in red blood cells).

The two major types of thalassaemia are alpha- and beta thalassaemia. The most severe form of alpha thalassaemia is known as alpha thalassaemia major or hydrops fetalis, while the severe form of beta thalassaemia is known as thalassaemia major or Cooley's anaemia.

Thalassaemias affect both males and females and occur most often in people of Italian, Greek, Middle Eastern, Asian, and African descent. Severe forms are usually diagnosed in early childhood and are lifelong conditions.

Causes

Haemoglobin in red blood cells has two kinds of protein chains: alpha globin and beta globin. If your body doesn't make enough of these protein chains, red blood cells don't form properly and can't carry enough oxygen.

Genes control how the body makes haemoglobin protein chains. When these genes are missing or altered, thalassaemias occur.

Thalassaemias are inherited disorders – they are passed on from parents to their children through genes. People who get abnormal haemoglobin genes from one parent but normal genes from the other are carriers. Carriers often have no signs of illness other than mild anaemia. However, they can pass the abnormal genes on to their children.

Signs and symptoms

Symptoms of thalassaemias are caused by a lack of oxygen in the blood stream. This occurs because the body doesn't make enough healthy red blood cells and haemoglobin. The severity of symptoms depends on the severity of the disorder:

- People who have alpha or beta thalassaemia can have mild anaemia, which can make you feel tired.
- People with beta thalassaemia intermedia have mild to moderate anaemia. They may also have other health problems including: slowed growth and delayed puberty; bone problems; and an enlarged spleen.
- People with haemoglobin H disease or beta thalassaemia major have severe thalassaemia. Symptoms occur within the first two years of life and include severe anaemia and other serious health problems
    - Pale and listless appearance
    - Poor appetite
    - Dark urine
    - Slowed growth and delayed puberty
    - Jaundice
    - Enlarged spleen, liver and heart
    - Bone problems

Treatment

Treatment for thalassaemias depends on the type and severity of the disorder. People who are carriers or who have alpha or beta thalassaemia need little or no treatment.

Three standard treatments are used to treat moderate and severe forms of thalassaemia, these include blood transfusions, iron chelation therapy, and folic acid supplements.

Risk
Family history and ancestry are the two risk factors for thalassaemias.

Sickle Cell Anaemia

Overview
Sickle cell anaemia is a serious disease in which the body makes sickle-shaped ("C"-shaped) red blood cells. Normal red blood cells are disk-shaped and move easily through your blood vessels. Red blood cells contain the protein haemoglobin (an iron-rich protein that gives blood its red colour and carries oxygen from the lungs to the rest of the body).
Sickle cells contain abnormal haemoglobin that causes the cells to have a sickle shape, which don’t move easily through the blood vessels – they are stiff and sticky and tend to form clumps and get stuck in the blood vessels.
The clumps of sickle cells block blood flow in the blood vessels that lead to the limbs and organs. Blocked blood vessels can cause pain, serious infections, and organ damage.
In sickle cell anaemia, a lower-than-normal number of red blood cells occurs because sickle cells don't last very long. Sickle cells usually die after about 10 to 20 days and the body can't reproduce red blood cells fast enough to replace the dying ones, which causes anaemia.

Causes
Sickle cell anaemia is an inherited, lifelong disease. People who have the disease inherit two copies of the sickle cell gene – one from each parent.

Signs and Symptoms
The most common symptoms of sickle cell anaemia are linked to anaemia and pain.
Common symptoms for anaemia include

- Fatigue
- Shortness of breath
- Dizziness
- Headache
- Coldness in the hands and feet
- Pale skin
- Chest pain

Sudden pain throughout the body is a common symptom of sickle cell anaemia. This pain is called a "sickle cell crisis", and often affects the bones, lungs, abdomen, and joints.

Treatment
Sickle cell anaemia has no widely-available cure. However, treatments can help relieve symptoms and treat complications. The goals of treating sickle cell anaemia are to relieve pain, prevent infections, eye damage and strokes, and control complications.
Bone marrow transplants may offer a cure in a small number of sickle cell anaemia cases.

Risk
Sickle cell anaemia is most common in people whose families descended from Africa, South or Central American, Caribbean islands, Mediterranean countries, India and Saudi Arabia.

Pernicious Anaemia

Overview

Pernicious anaemia is a condition in which the body can't make enough healthy red blood cells because it doesn't have enough vitamin B12 (a nutrient found in certain foods). People who have pernicious anaemia can't absorb enough vitamin B12 due to a lack of intrinsic factor (a protein made in the stomach). However, other conditions and factors can also cause vitamin B12 deficiency.

Causes

- A lack of intrinsic factor is a common cause of pernicious anaemia as the body can't absorb enough vitamin B12.
- Some pernicious anaemia occurs because the body's small intestine can't properly absorb vitamin B12 which may be due to the wrong bacteria in the small intestines; certain diseases that interfere with vitamin B12 absorption; certain medicines; surgical removal of part of the small intestine; and tapeworm infection.
- Sometimes people develop pernicious anaemia because they don't get enough vitamin B12 in their diets.

Signs and symptoms

Apart from the symptoms of anaemia (fatigue, dizziness, etc.), the vitamin B12 deficiency may also have some serious symptoms such as

- Nerve damage
- Neurological problems such as confusion, dementia, depression, and memory loss.
- Symptoms in the digestive tract include nausea and vomiting, heartburn, abdominal bloating and gas, constipation or diarrhoea, loss of appetite, and weight loss.
- An enlarged liver
- A smooth, beefy red tongue
- Infants who have vitamin B12 deficiency may have poor reflexes or unusual movements, such as face tremors.

Treatment

Pernicious anaemia is treated by replacing the missing vitamin B12 in the body. People who have this disease may need lifelong treatment.

Risk

You are at higher risk for pernicious anaemia if you

- Have a family history of the condition.
- Have had part or all of your stomach removed.
- Have certain autoimmune disorders that involve the endocrine glands, such as Addison's disease, type 1 diabetes, Graves' disease, and vitiligo.
- Have had part or all of your small intestine removed.
- Have certain intestinal diseases or disorders that prevent your body from properly absorbing vitamin B12.
- Take medicines that prevent your body from properly absorbing vitamin B12.

- Are a strict vegetarian who doesn't eat any animal or diary products and doesn’t take a vitamin B12 supplement, or if you eat poorly overall.

Fanconi Anaemia

Overview

Fanconi anaemia, or FA, is a rare, inherited blood disorder that leads to bone marrow failure. FA is a type of aplastic anaemia that prevents your bone marrow from making enough new blood cells for your body to work normally. FA can also cause your bone marrow to make many abnormal blood cells. This can lead to serious health problems, such as leukemia.

FA is a blood disorder, but it can also affect many of the body's organs, tissues, and systems. Children who inherit FA are at higher risk of being born with birth defects, and people who have FA are at higher risk of some cancers and other serious health problems.

FA is an unpredictable disease. The average lifespan for people with FA is between 20 and 30 years. The most common causes of death related to FA are bone marrow failure, leukemia, and solid tumours.

Causes

FA is an inherited disease – it is passed on from parents to children through the genes. At least 13 faulty genes are associated with FA. FA develops when both parents pass the same faulty FA gene to their child. People who have only one faulty gene are FA carriers which means they don't have FA, but they can pass the faulty gene to their children.

Signs and symptoms

The symptoms of FA include

- Anaemia
- Bone marrow failure
- Birth defects
- Developmental or eating problems

Treatment

Treatment for FA is based on a person's age and how well or poorly the person's bone marrow makes new blood cells.

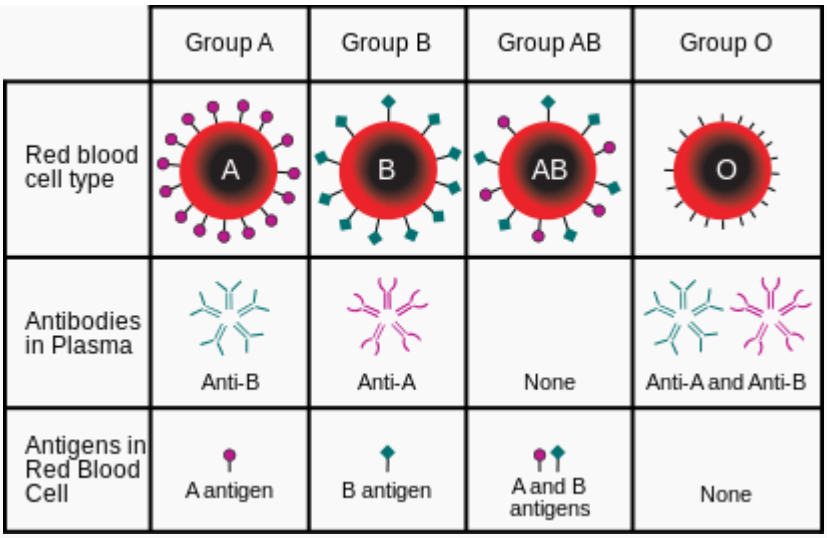
The four main types of treatment for FA are

- Blood and marrow stem cell transplant
- Androgen therapy
- Synthetic growth factors
- Gene therapy

Risk

FA occurs in all racial and ethnic groups and affects men and women equally. You are at an increased risk of developing the disease if you have a family history of FA.

Blood type



Blood type (or blood group) is determined, in part, by the ABO blood group antigens present on red blood cells.

A **blood type** (also called a **blood group**) is a classification of blood based on the presence and absence of antibodies and also based on the presence or absence of inherited antigenic substances on the surface of red blood cells (RBCs). These antigens may be proteins, carbohydrates, glycoproteins, or glycolipids, depending on the blood group system. Some of these antigens are also present on the surface of other types of cells of various tissues. Several of these red blood cell surface antigens can stem from one allele(or an alternative version of a gene) and collectively form a blood group system.[1] Blood types are inherited and represent contributions from both parents. A total of 35 human blood group systems are now recognized by the International Society of Blood Transfusion (ISBT).[2] The two most important ones areABO and the RhD antigen; they determine someone's blood type (A, B, AB and O, with +, − or Null denoting RhD status).

Many pregnant women carry a fetus with a blood type which is different from their own, which is not a problem. What can matter is whether the baby is RhD positive or negative. Mothers who are RhD- and carry a RhD+ baby can form antibodies against fetal RBCs. Sometimes these maternal antibodies are IgG, a small immunoglobulin, which can cross the placenta and cause hemolysis of fetal RBCs, which in turn can lead to hemolytic disease of the newborn called erythroblastosis fetalis, an illness of low fetal blood countsthat ranges from mild to severe. Sometimes this is lethal for the fetus; in these cases it is called hydrops fetalis.[3]

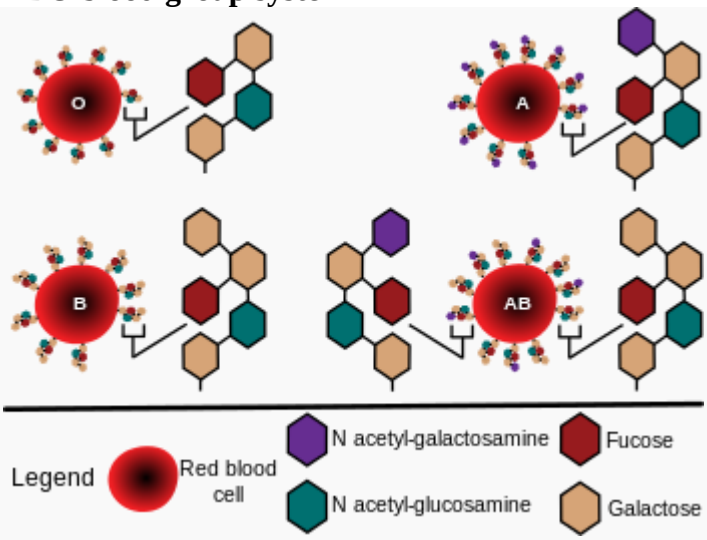
Blood group systems

A complete blood type would describe a full set of 30 substances on the surface of RBCs, and an individual's blood type is one of many possible combinations of blood-group antigens. Across the 35 blood groups, over 600 different blood-group antigens have been found, Almost always, an individual has the same blood group for life, but very rarely an individual's blood type changes through addition or suppression of an antigen in infection, malignancy, or autoimmune

disease.[6][7][8][9] Another more common cause in blood type change is a bone marrow transplant. Bone-marrow transplants are performed for many leukemias and lymphomas, among other diseases. If a person receives bone marrow from someone who is a different ABO type (e.g., a type A patient receives a type O bone marrow), the patient's blood type will eventually convert to the donor's type.

Some blood types are associated with inheritance of other diseases; for example, the Kell antigen is sometimes associated with McLeod syndrome.[10] Certain blood types may affect susceptibility to infections, an example being the resistance to specific malaria species seen in individuals lacking the Duffy antigen.[11] The Duffy antigen, presumably as a result of natural selection, is more common in ethnic groups from areas with a high incidence of malaria.[12]

ABO blood group system



ABO blood group system: diagram showing the carbohydrate chains that determine the ABO blood group

ABO blood group system

The *ABO system* is the most important blood-group system in human-blood transfusion. The associated anti-A and anti-B antibodies are usually *immunoglobulin M*, abbreviated IgM, antibodies. ABO IgM antibodies are produced in the first years of life by sensitization to environmental substances such as food, bacteria, and viruses. The **original terminology** used by Dr. Karl Landsteiner in 1901 for the classification is A/B/C; in later publications "C" became "O".[13] "O" is often called *0* (*zero*, or *null*) in other languages. The Austrian Federal Ministry of Health claims the**original terminology** used by Dr. Karl Landsteiner in 1901 for the classification is 0(Zero)/A/B/AB and that in later publications "0" became "O" in most of English language countries.[13][14]

Phenotype	**Genotype**

A	AA or AO
B	BB or BO
AB	AB
O	OO

Rh blood group system

The Rh system (Rh meaning *Rhesus*) is the second most significant blood-group system in human-blood transfusion with currently 50 antigens. The most significant Rh antigen is the D antigen, because it is the most likely to provoke an immune system response of the five main Rh antigens. It is common for D-negative individuals not to have any anti-D IgG or IgM antibodies, because anti-D antibodies are not usually produced by sensitization against environmental substances. However, D-negative individuals can produce IgGanti-D antibodies following a sensitizing event: possibly a fetomaternal transfusion of blood from a fetus in pregnancy or occasionally a blood transfusion with D positive RBCs.[15]Rh disease can develop in these cases.[16] Rh negative blood types are much less common in proportion of Asian populations (0.3%) than they are in White (15%).[17] The presence or absence of the Rh(D) antigen is signified by the + or − sign, so that, for example, the A− group is ABO type A and does not have the Rh (D) antigen.

ABO and Rh distribution by country

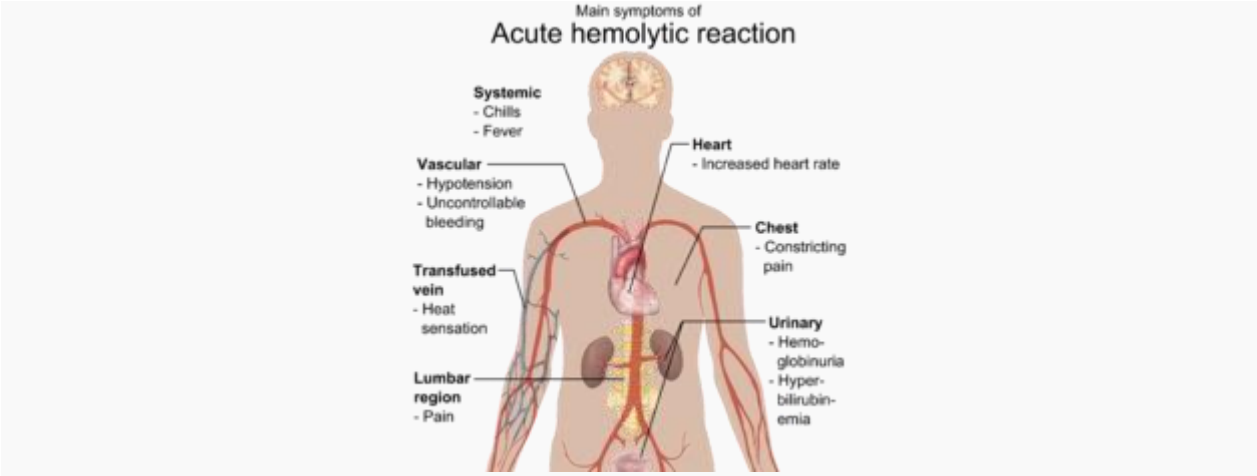
As with many other genetic traits, the distribution of ABO and Rh blood groups varies significantly between populations.

Other blood group systems

33 blood-group systems have been identified, including the ABO and Rh systems.[18] Thus, in addition to the ABO antigens and Rh antigens, many other antigens are expressed on the RBC surface membrane. For example, an individual can be AB, D positive, and at the same time M and N positive (MNS system), K positive (Kell system), Le^a or Le^bnegative (Lewis system), and so on, being positive or negative for each blood group system antigen. Many of the blood group systems were named after the patients in whom the corresponding antibodies were initially encountered.

Blood transfusion

Transfusion medicine is a specialized branch of hematology that is concerned with the study of blood groups, along with the work of a blood bank to provide a transfusion service for blood and other blood products. Across the world, blood products must be prescribed by a medical doctor (licensed physician or surgeon) in a similar way as medicines.



Main symptoms of acute hemolytic reaction due to blood type mismatch.

Much of the routine work of a blood bank involves testing blood from both donors and recipients to ensure that every individual recipient is given blood that is compatible and is as safe as possible. If a unit of incompatible blood is transfused between a donor and recipient, a severe acute hemolytic reaction with hemolysis (RBC destruction), renal failure and shock is likely to occur, and death is a possibility. Antibodies can be highly active and can attack RBCs and bind components of the complement system to cause massive hemolysis of the transfused blood.

Patients should ideally receive their own blood or type-specific blood products to minimize the chance of a transfusion reaction. Risks can be further reduced by cross-matching blood, but this may be skipped when blood is required for an emergency. Cross-matching involves mixing a sample of the recipient's serum with a sample of the donor's red blood cells and checking if the mixture *agglutinates*, or forms clumps. If agglutination is not obvious by direct vision, blood bank technicians usually check for agglutination with a microscope. If agglutination occurs, that particular donor's blood cannot be transfused to that particular recipient. In a blood bank it is vital that all blood specimens are correctly identified, so labelling has been standardized using a barcode system known as ISBT 128.

The blood group may be included on identification tags or on tattoos worn by military personnel, in case they should need an emergency blood transfusion. Frontline German Waffen-SS had blood group tattoos during World War II.

Rare blood types can cause supply problems for blood banks and hospitals. For example, Duffy-negative blood occurs much more frequently in people of African origin,[21] and the rarity of this blood type in the rest of the population can result in a shortage of Duffy-negative blood for these patients. Similarly for RhD negative people, there is a risk associated with travelling to parts of the world where supplies of RhD negative blood are rare, particularly East Asia, where blood services may endeavor to encourage Westerners to donate blood.[22]

Hemolytic disease of the newborn (HDN)

A pregnant woman can make IgG blood group antibodies if her fetus has a blood group antigen that she does not have. This can happen if some of the fetus' blood cells pass into the mother's blood circulation (e.g. a small fetomaternal hemorrhage at the time of childbirth or obstetric

intervention), or sometimes after a therapeutic blood transfusion. This can cause Rh disease or other forms of hemolytic disease of the newborn (HDN) in the current pregnancy and/or subsequent pregnancies. If a pregnant woman is known to have anti-D antibodies, the Rh blood type of a fetus can be tested by analysis of fetal DNA in maternal plasma to assess the risk to the fetus of Rh disease.[23] One of the major advances of twentieth century medicine was to prevent this disease by stopping the formation of Anti-D antibodies by D negative mothers with an injectable medication calledRho(D) immune globulin.[24][25] Antibodies associated with some blood groups can cause severe HDN, others can only cause mild HDN and others are not known to cause HDN.[3]

Blood products

To provide maximum benefit from each blood donation and to extend shelf-life, blood banks fractionate some whole blood into several products. The most common of these products are packed RBCs, plasma, platelets, cryoprecipitate, and fresh frozen plasma (FFP). FFP is quick-frozen to retain the labile clotting factors V and VIII, which are usually administered to patients who have a potentially fatal clotting problem caused by a condition such as advanced liver disease, overdose of anticoagulant, or disseminated intravascular coagulation (DIC).

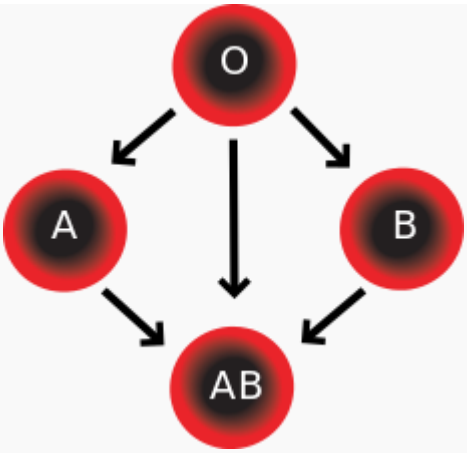
Units of packed red cells are made by removing as much of the plasma as possible from whole blood units.

Clotting factors synthesized by modern recombinant methods are now in routine clinical use for hemophilia, as the risks of infection transmission that occur with pooled blood products are avoided.

Red blood cell compatibility

- **Blood group AB** individuals have both A and B antigens on the surface of their RBCs, and their blood plasma does not contain any antibodies against either A or B antigen. Therefore, an individual with type AB blood can receive blood from any group (with AB being preferable), but cannot donate blood to any group other than AB. They are known as universal recipients.
- **Blood group A** individuals have the A antigen on the surface of their RBCs, and blood serum containing IgM antibodies against the B antigen. Therefore, a group A individual can receive blood only from individuals of groups A or O (with A being preferable), and can donate blood to individuals with type A or AB.
- **Blood group B** individuals have the B antigen on the surface of their RBCs, and blood serum containing IgM antibodies against the A antigen. Therefore, a group B individual can receive blood only from individuals of groups B or O (with B being preferable), and can donate blood to individuals with type B or AB.
- **Blood group O** (or blood group zero in some countries) individuals do not have either A or B antigens on the surface of their RBCs, and their blood serum contains IgM anti-A and anti-B antibodies. Therefore, a group O individual can receive blood only from a group O individual, but can donate blood to individuals of any ABO blood group (i.e., A, B, O or AB). If a patient in a hospital situation needs a blood transfusion in an emergency, and if the time taken to process the recipient's blood would cause a detrimental delay, O negative blood can be issued. Because it is compatible with anyone, O negative blood is often overused and

consequently is always in short supply.[26] According to the American Association of Blood Banks and the British Chief Medical Officer's National Blood Transfusion Committee, the use of group O RhD negative red cells should be restricted to persons with O negative blood, women who might be pregnant, and emergency cases in which blood-group testing is genuinely impracticable.[26]



Red blood cell compatibility chart

In addition to donating to the same blood group; type O blood donors can give to A, B and AB; blood donors of types A and B can give to AB.

Red blood cell compatibility table[27][28]

Recipient[1]	**Donor**[1]							
	O−	**O+**	**A−**	**A+**	**B−**	**B+**	**AB−**	**AB+**
O−	✓	✗	✗	✗	✗	✗	✗	✗
O+	✓	✓	✗	✗	✗	✗	✗	✗
A−	✓	✗	✓	✗	✗	✗	✗	✗
A+	✓	✓	✓	✓	✗	✗	✗	✗

B−	✓	✗	✗	✗	✓	✗	✗	✗
B+	✓	✓	✗	✗	✓	✓	✗	✗
AB−	✓	✗	✓	✗	✓	✗	✓	✗
AB+	✓	✓	✓	✓	✓	✓	✓	✓

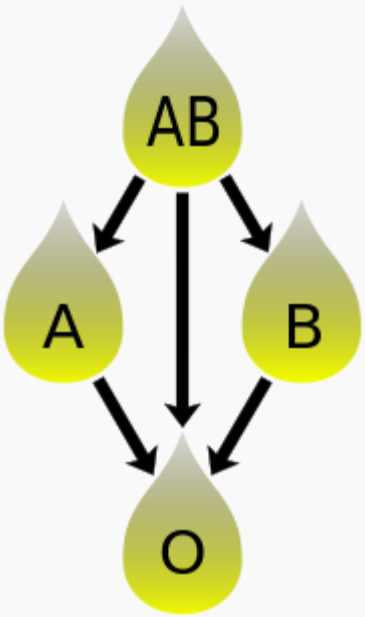
Table note

1. Assumes absence of atypical antibodies that would cause an incompatibility between donor and recipient blood, as is usual for blood selected by cross matching.

An Rh D-negative patient who does not have any anti-D antibodies (never being previously sensitized to D-positive RBCs) can receive a transfusion of D-positive blood once, but this would cause sensitization to the D antigen, and a female patient would become at risk for hemolytic disease of the newborn. If a D-negative patient has developed anti-D antibodies, a subsequent exposure to D-positive blood would lead to a potentially dangerous transfusion reaction. Rh D-positive blood should never be given to D-negative women of child bearing age or to patients with D antibodies, so blood banks must conserve Rh-negative blood for these patients. In extreme circumstances, such as for a major bleed when stocks of D-negative blood units are very low at the blood bank, D-positive blood might be given to D-negative females above child-bearing age or to Rh-negative males, providing that they did not have anti-D antibodies, to conserve D-negative blood stock in the blood bank. The converse is not true; Rh D-positive patients do not react to D negative blood.

This same matching is done for other antigens of the Rh system as C, c, E and e and for other blood group systems with a known risk for immunization such as the Kell system in particular for females of child-bearing age or patients with known need for many transfusions.

Plasma compatibility



Plasma compatibility chart

In addition to donating to the same blood group; plasma from type AB can be given to A, B and O; plasma from types A, B and AB can be given to O.

Blood plasma compatibility is the inverse of red blood cell compatibility.[29] Type AB plasma carries neither anti-A nor anti-B antibodies and can be transfused to individuals of any blood group; but type AB patients can only receive type AB plasma. Type O carries both antibodies, so individuals of blood group O can receive plasma from any blood group, but type O plasma can be used only by type O recipients.

Plasma compatibility table[28]

Recipient	**Donor**[1]			
	O	**A**	**B**	**AB**
O	✓	✓	✓	✓
A	✗	✓	✗	✓

B	✗	✗	✓	✓
AB	✗	✗	✗	✓

Table note

1. Assumes absence of strong atypical antibodies in donor plasma

Rh D antibodies are uncommon, so generally neither D negative nor D positive blood contain anti-D antibodies. If a potential donor is found to have anti-D antibodies or any strong atypical blood group antibody by antibody screening in the blood bank, they would not be accepted as a donor (or in some blood banks the blood would be drawn but the product would need to be appropriately labeled); therefore, donor blood plasma issued by a blood bank can be selected to be free of D antibodies and free of other atypical antibodies, and such donor plasma issued from a blood bank would be suitable for a recipient who may be D positive or D negative, as long as blood plasma and the recipient are ABO compatible.

Universal donors and universal recipients

A hospital corpsman with the Blood Donor Team from Naval Medical Center Portsmouth takes samples of blood from a donor for testing

With regard to transfusions of packed red blood cells, individuals with type O Rh D negative blood are often called universal donors, and those with type AB Rh D positive blood are called universal recipients; however, these terms are only generally true with respect to possible reactions of the recipient's anti-A and anti-B antibodies to transfused red blood cells, and also possible sensitization to Rh D antigens. One exception is individuals with hh antigen system (also known as the Bombay phenotype) who can only receive blood safely from other hh donors, because they form antibodies against the H antigen present on all red blood cells.[30][31]

Blood donors with exceptionally strong anti-A, anti-B or any atypical blood group antibody may be excluded from blood donation. In general, while the plasma fraction of a blood transfusion may carry donor antibodies not found in the recipient, a significant reaction is unlikely because of dilution.

Additionally, red blood cell surface antigens other than A, B and Rh D, might cause adverse reactions and sensitization, if they can bind to the corresponding antibodies to generate an immune response. Transfusions are further complicated because platelets and white blood cells (WBCs) have their own systems of surface antigens, and sensitization to platelet or WBC antigens can occur as a result of transfusion.

With regard to transfusions of plasma, this situation is reversed. Type O plasma, containing both anti-A and anti-B antibodies, can only be given to O recipients. The antibodies will attack the antigens on any other blood type. Conversely, AB plasma can be given to patients of any ABO blood group due to not containing any anti-A or anti-B antibodies.

Blood group genotyping

In addition to the current practice of serologic testing of blood types, the progress in molecular diagnostics allows the increasing use of blood group genotyping. In contrast to serologic tests reporting a direct blood type phenotype, genotyping allows the prediction of a phenotype based on the knowledge of the molecular basis of the currently known antigens. This allows a more detailed determination of the blood type and therefore a better match for transfusion, which can be crucial in particular for patients with needs for many transfusions to prevent allo-immunization.

Karl Landsteiner History

Two blood group systems were discovered by Karl Landsteiner during early experiments with blood transfusion: the ABO group in 1901[34][*full citation needed*] and in co-operation with Alexander S. Wiener the Rhesus group in 1937.[35][36] Development of the Coombs test in 1945,[37] the advent of transfusion medicine, and the understanding of ABO hemolytic disease of the newborn led to discovery of more blood groups, and now 33 human blood group systems are recognized by the International Society of Blood Transfusion (ISBT),[4] and in the 33 blood groups, over 600 blood group antigens have been found;[5] many of these are rare or are mainly found in certain ethnic groups.

Czech serologist Jan Janský is credited with the first classification of blood into the four types (A, B, AB, O) in 1907, which remains in use today. Blood types have been used in forensic science and were formerly used to demonstrate impossibility of paternity (e.g., a type AB man cannot be the father of a type O infant), but both of these uses are being replaced by genetic fingerprinting, which provides greater certainty.[38]

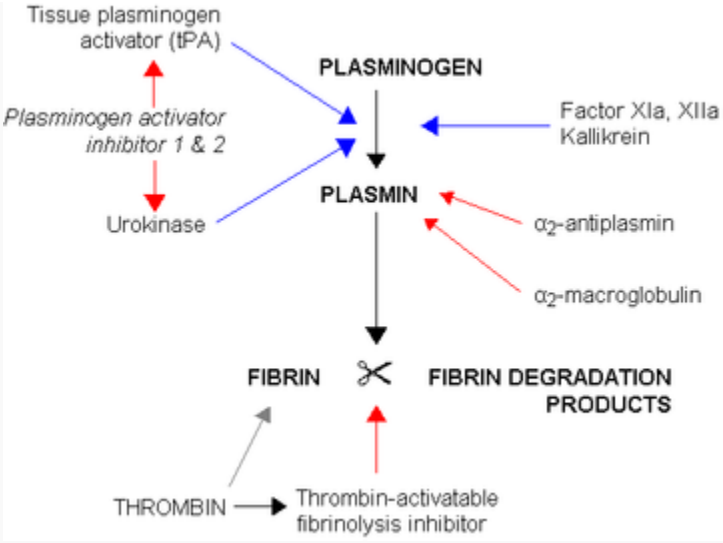
According to the Austrian Federal Ministry of Health[*full citation needed*] the original terminology used by Karl Landsteiner in 1901 for the classification is A, B and 0 (*zero*); the "O" (*oh*) you find in the ABO group system is actually a subsequent variation occurred during the translation process, probably due to the similar shape between the number 0 and the letter O.

Society and culture

A popular belief in Japan is that a person's ABO blood type is predictive of their personality, character, and compatibility with others. This belief is also widespread in South Korea[39] and Taiwan. Deriving from ideas of historical scientific racism, the theory reached Japan in a 1927 psychologist's report, and the militarist government of the time commissioned a study aimed at breeding better soldiers.[39] The fad faded in the 1930s due to its lack of scientific basis and ultimately the discovery of DNA in the following decades which it later became clear had a vastly more complex and important role in both heredity generally and personality specifically. No evidence has been found to support the theory by scientists, but it was revived in the 1970s by Masahiko Nomi, a broadcaster with a background in law who had no scientific or medical background.[39] Despite these facts, the myth still persists widely in Japanese and South Korean popular culture.[40]

Fibrinolysis is a process that prevents blood clots from growing and becoming problematic.[1] This process has two types: primary fibrinolysis and secondary fibrinolysis. The primary type is a normal body process, whereas secondary fibrinolysis is the breakdown of clots due to a medicine, a medical disorder, or some other cause.[1]

In fibrinolysis, a fibrin clot, the product of coagulation, is broken down.[2] Its main enzyme plasmin cuts the fibrin mesh at various places, leading to the production of circulating fragments that are cleared by other proteases or by the kidney and liver.



Fibrinolysis (simplified). Blue arrows denote stimulation, and red arrows inhibition.

Plasmin is produced in an inactive form, plasminogen, in the liver. Although plasminogen cannot cleave fibrin, it still has an affinity for it, and is incorporated into the clot when it is formed.

Tissue plasminogen activator (t-PA)[3] and urokinase are the agents that convert plasminogen to the active plasmin, thus allowing fibrinolysis to occur. t-PA is released into the blood very slowly by the damaged endothelium of the blood vessels, such that, after several days (when the bleeding has stopped), the clot is broken down. This occurs because plasminogen became entrapped within the clot when it formed; as it is slowly activated, it breaks down the fibrin mesh. t-PA and urokinase are themselves inhibited by plasminogen activator inhibitor-1 and plasminogen activator inhibitor-2 (PAI-1 and PAI-2). In contrast, plasmin further stimulates plasmin generation by producing more active forms of both tissue plasminogen activator (tPA) and urokinase.

Alpha 2-antiplasmin and alpha 2-macroglobulin inactivate plasmin. Plasmin activity is also reduced by thrombin-activatable fibrinolysis inhibitor (TAFI), which modifies fibrin to make it more resistant to the tPA-mediated plasminogen.

Measurement

When plasmin breaks down fibrin, a number of soluble parts are produced. These are called fibrin degradation products (FDPs). FDPs compete with thrombin, and thus slow down clot formation by preventing the conversion of fibrinogen to fibrin. This effect can be seen in the thrombin clotting time (TCT) test, which is prolonged in a person that has active fibrinolysis.

FDPs, and a specific FDP, the D-dimer, can be measured using antibody-antigen technology. This is more specific than the TCT, and confirms that fibrinolysis has occurred. It is therefore used to indicate deep-vein thrombosis, pulmonary embolism, DIC and efficacy of treatment in acute myocardial infarction. Alternatively, a more rapid detection of fibrinolytic activity, especially hyperfibrinolysis, is possible with thromboelastometry (TEM) in whole blood, even in patients on heparin. In this assay, increased fibrinolysis is assessed by comparing the TEM profile in the absence or presence of the fibrinolysis inhibitor aprotinin. Clinically, the TEM is useful for near real-time measurement of activated fibrinolysis for at-risk patients, such as those experiencing significant blood losses during surgery.

Testing of overall fibrinolysis can be measured by a euglobulin lysis time (ELT) assay. The ELT measures fibrinolysis by clotting the euglobulin fraction (primarily the important fibrinolytic factors fibrinogen, PAI-1, tPA, alpha 2-antiplasmin, and plasminogen) from plasma and then observing the time required for clot dissolution. A shortened lysis time indicates a hyperfibrinolytic state and bleeding risk. Such results can be seen in peoples with liver disease, PAI-1 deficiency or alpha 2-antiplasmin deficiency. Similar results are also seen after administration of DDAVP or after severe stress.

Role in disease

Few congenital disorders of the fibrinolytic system have been documented. Nevertheless, excess levels of PAI and alpha 2-antiplasmin have been implicated in the metabolic syndrome and various other disease states.

However, acquired disturbance of fibrinolysis (Hyperfibrinolysis), is not uncommon. Many trauma patients suffer from an overwhelming activation of tissue factor and thus massive hyperfibrinolysis.[6] Also in other disease states hyperfibrinolysis may occur. It could lead to massive bleeding if not diagnosed and treated early enough.

The fibrinolytic system is closely linked to control of inflammation, and plays a role in disease states associated with inflammation. Plasmin, in addition to lysing fibrin clots, also cleaves the complement system component C3, and fibrin degradation products have some vascular permeability inducing effects.

Pharmacology

In a process called thrombolysis (the breakdown of a thrombus), fibrinolytic drugs are used. They are given following a heart attack to dissolve the thrombus blocking thecoronary artery; experimentally after a stroke to allow blood flow back to the affected part of the brain; and in the event of a massive pulmonary embolism.

Thrombolysis refers to the dissolution of the thrombus due to various agents while fibrinolysis refers specifically to the agents causing fibrin breakdown in the clot.

Antifibrinolytics, such as aminocaproic acid (ε-aminocaproic acid) and tranexamic acid are used as inhibitors of fibrinolysis. Their application may be beneficial in patients with hyperfibrinolysis because they arrest bleeding rapidly if the other components of the haemostatic system are not severely affected. This may help to avoid the use of blood products such as fresh frozen plasma with its associated risks of infections or anaphylactic reactions. The antifibrinolytic drug aprotinin was abandoned after identification of major side effects, especially on kidney.