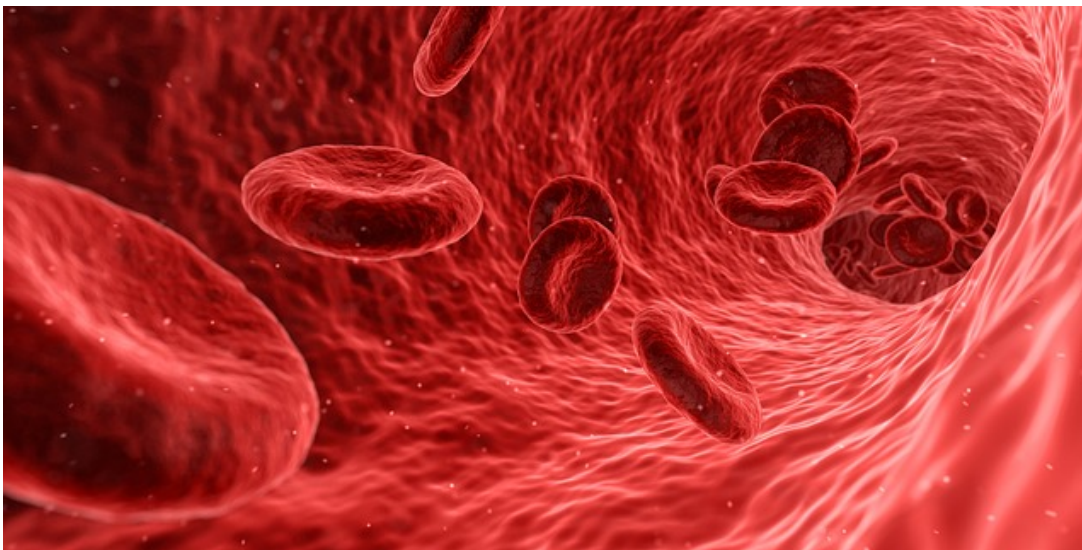


Macroscopic Anatomy of the Blood

[See online here](#)

Blood (Latin: sanguis, Greek: haima) is a suspension of different cells in a saline solution containing proteins. It makes up approximately 6-8 % of the body weight and has a pH value of 7.4. The blood is responsible for numerous essential functions and is a crucial point of the whole organism. This article provides an overview of the important facts, in order to better understand the whole concept of the "organ" blood.



Blood Components

If a centrifuge is used for a blood sample, a more or less cloudy liquid (depending on the blood's fat content) can be seen from which the red sediment has settled. The liquid component represents the blood plasma and the sediment, the cruor of the blood cells. The hematocrit indicates the ratio of plasma to blood cells. Physiologically, it is 42% for women and 45% for men.

Blood plasma

The plasma makes up approx. 55% of the blood. It contains water, proteins, ions, hormones, and physically dissolved gases. Furthermore, the serum can be extracted from the blood plasma, which is free of clotting factors.

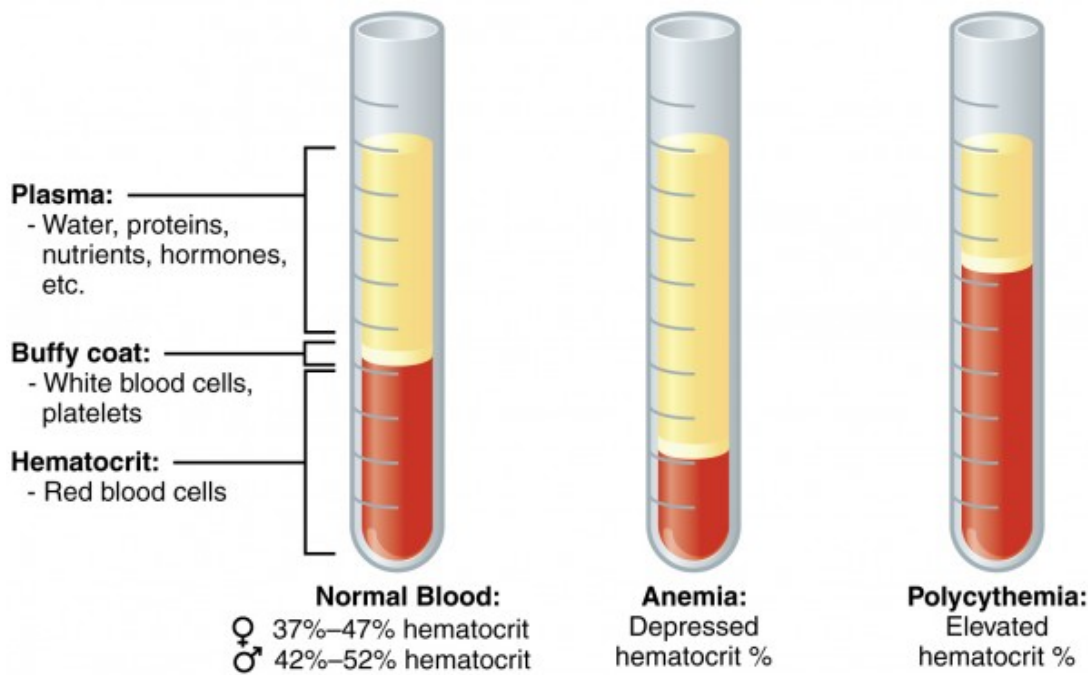


Image: Composition of blood. By Phil Schatz, License: [CC BY 4.0](https://creativecommons.org/licenses/by/4.0/)

Normal values of the plasma electrolytes:

- Na⁺ 140 mmol/L
- K⁺ 4.5 mmol/L
- Ca²⁺ 2.4 mmol/L
- Cl⁻ 105 mmol/L
- HCO₃⁻ 24 mmol/L

Therefore, plasma has an osmotic pressure of 5.6 mm Hg and an osmolarity of 290 mOsm/L. **Plasma proteins** represent the largest part of the plasma, around 75 g/L. They barely contribute to the osmolarity but play an important role in the colloid osmotic (or oncotic) pressure, meaning the osmotic pressure between plasma and interstitium. At 25 mm Hg, it is significantly higher than that of the interstitium (5 mm Hg). It prevents diffusion of too much plasma water from the blood vessels into the tissue.

Albumin is the most common plasma protein (54–60 %). Therefore, it is essential for the oncotic pressure. Albumin is produced in the liver and is one of the smallest plasma proteins. It serves as a carrier for cations, bilirubin, fatty acids, and cholate.

Other important plasma proteins are the globulins, which are classified as **α, β, and γ**. Just like albumin, α- and β-globulins act as carriers. Thus, for example, low-density lipoproteins (LDL) that carry fat and high-density lipoproteins (HDL) are important representatives of globulins.

γ globulins contain immunoglobulins (Ig) and have immunological functions. They are divided into 5 chemically different Ig classes, whereby the immunoglobulins IgG, IgA, and IgM are mainly present in the plasma.

Blood components in %	Blood subcomponents in %	Type in % (if any)	Place of production	Major functions

Plasma 43-63%	Water 92%	Liquid	Resorbed by the intestinal tract or produced during metabolic processes	Transport medium
	Plasma proteins 7%	Albumin 54-60%	Liver	Maintains the osmotic balance; transports lipid molecules
		Globulin 35-38%	α -globulins-Liver	Transport functions; maintains the osmotic concentration
			β -globulins-Liver	Transport functions; maintains the osmotic balance
			γ -globulins (Immunoglobulins)-Plasma cells	Immune response
	Fibrinogen 4-7 %	Liver	Blood clotting during hemostasis	
	Regulatory Proteins < 1%	Hormones and enzymes	Various places	Regulate various bodily functions
Other dissolved substances 1%	Nutrients, gases, and waste substances	Resorbed by the intestinal tract, exchanged into the respiratory tract, or produced by cells	Numerous different functions	
Form elements 37-54 %	Erythrocytes 99%	Erythrocytes	Redbone marrow	Transport gases, mostly oxygen and some carbon dioxide
	Leukocytes < 1%, platelets < 1%	Granular leukocytes: neutrophils, eosinophils, and basophils	Redbone marrow	Unspecific immunity
		Agranular leukocytes: lymphocytes, monocytes	Lymphocytes: bone marrow and lymphatic tissue	Lymphocytes: specific immunity
			Monocytes: red bone marrow	Monocytes: unspecific immunity
	Platelets < 1%	Megakaryocytes red bone marrow	Hemostasis	

The blood cells

Erythrocytes

In a blood smear specimen, the red blood cells are easily recognizable by their **biconcave shape**. Their diameter is about 7.5 μm , and they are the most common blood cells with $4.5 \times 10^6/\mu\text{L}$ in women and $5.2 \times 10^6/\mu\text{L}$ in men. Erythrocytes contain hemoglobin. They have neither a cell nucleus nor cell organelles and, therefore, only have a lifespan of about 120 days before being broken down in the [spleen](#).

Erythrocytes are generated in the red bone marrow and are stimulated by erythropoietin, which is secreted by the kidneys. Reticulocytes are immature cells that have no nucleus. It can be detected in blood smear specimens in cases of increased new synthesis (i.e. after heavy blood loss).

Erythrocytes have a larger diameter than some capillaries. Therefore, the malleability of red blood cells is extremely important, and this is due to their special red cell membrane

cytoskeleton made of ankyrin, spectrin, and actin.

Thrombocytes

With a diameter of only 2.5 μm , platelets are significantly smaller than erythrocytes and **biconvex** in their free-floating form. The blood of a healthy human contains 150,000–400,000 thrombocytes/ μL blood. These cell fragments without cell nuclei are produced by megakaryocytes of the bone marrow and circulate within the blood for approx. 10 days if they are not activated for blood clotting.

Leukocytes

Leukocytes are the blood's immune cells. Their number varies from between 4,000 to 10,000/ μL blood. They are divided into monocytes, granulocytes, and lymphocytes.

1. **Monocytes** stand out in blood smear specimens because of their size (15–20 μm). They usually have a kidney-shaped nucleus, and their cytoplasm appears pale gray under the optical microscope. Monocytes are very rare (6% of the leukocytes) and circulate only between 1 and 3 days in the blood. During this time, they mature to macrophages, which then migrate into the tissue. Therefore, they can barely be detected in the blood smear specimen.
2. **Granulocytes** have a size of 10–12 μm and are produced in the red bone marrow like all blood cells. They are divided into 3 groups:
 1. **Neutrophil granulocytes** represent the largest part of leukocytes and mostly have a segmented cell nucleus. Therefore, they are called segmented neutrophils. Only 8% of the neutrophil granulocytes are banded (banded neutrophils). The granules of the neutrophils appear pale pink in the Pappenheim stain.
 2. **Eosinophil granulocytes** constitute only 3% of leukocytes and have a cell nucleus consisting of 2 segments. Their granules stand out in blood smear specimens because of their brick-red coloring.
 3. **Basophil granulocytes** are the least common in blood smear specimens. The granules mostly cover the cell nucleus and are dark blue.
3. **Lymphocytes exhibit a round, purple-dyed nucleus** that is surrounded by a thin, pale-gray cytoplasm layer. They are classified as natural killer cells as well as B (bone marrow) lymphocytes and T (thymus) lymphocytes. However, the 3 types are not distinguishable using the light microscope.

Functions of the Blood

Erythrocytes are responsible for transporting gases

The oxygen content of a healthy person's arterial blood is about 200 mL O_2 /L of blood. Hemoglobin (Hb) binds 85% of the oxygen. The remainder is physically dissolved in the plasma.

Hemoglobin is present in erythrocytes, and the adult Hb consists of **2 α and 2 β subunits**. Each subunit has a Fe^{2+} ion that binds to O_2 . Thus, 1 Hb can transport 4 oxygen molecules. The Hb concentration is 16 g/dL in men and 14 g/dL in women.

In the periphery, Hb delivers the oxygen to the tissue and accepts a part of the carbon dioxide. The majority of carbon dioxide, however, is transported by erythrocytes as bicarbonate and exhaled via the lungs.

Thrombocytes ensure the clotting of the blood

The clotting of the blood is called **hemostasis** and is divided into **primary and secondary hemostasis**.

Primary hemostasis

Primary hemostasis is triggered by damage to the vascular endothelium when thrombocytes come into contact with collagen located outside the vessel. Thereby, the von Willebrand factor in collagen binds to its receptor, the glycoprotein Ib of the thrombocytes, which leads to the adhesion of the thrombocytes to the damaged endothelium.

Simultaneously, Ca^{2+} activates the platelets, which means that the tubulin ring within the thrombocytes contracts, thus creating pseudopodia. Together with adenosine diphosphate (ADP), which is released from damaged cells, a thrombocyte aggregation takes place. A blood clot is formed. In addition, the activated thrombocytes secrete serotonin, fibrinogen, and thromboxane A_2 . The latter also causes vasoconstriction, and this promotes the closure of the vessel opening.

The endothelium releases prostacyclin, which inhibits the aggregation of thrombocytes to prevent the clot from clogging the entire vessel. Thus, a targeted clot formation at the damaged endothelium is assured.

Secondary hemostasis

Secondary hemostasis is divided into **extrinsic and intrinsic systems**.

The extrinsic system intervenes in cases of tissue destruction and is very fast, with a speed of about 14 seconds of thromboplastin time (quick test). The tissue factor from vascular muscle cells forms a complex with phospholipids called thromboplastin. It binds to the coagulation factor VII which activates factor X in the presence of Ca^{2+} .

In the intrinsic system, factor XII encounters negatively charged surfaces, such as collagen (or glass), and is thereby activated. After that, factor XI and factor IX are activated. Factor IX forms an enzymatic complex with phospholipids and Ca^{2+} ions, which, in turn, activates factor X (thrombokinase) via limited proteolysis. This process can be accelerated rapidly by factor VIII activated by thrombin. In this case, the partial thromboplastin time is 40–50 seconds.

After activation of factor X, the intrinsic and extrinsic systems converge. Factor X, together with factor V, phospholipids, and Ca^{2+} ions, form the prothrombin activator, which splits factor II (prothrombin) into thrombin. Thrombin, in turn, splits factor I (fibrinogen) into soluble fibrin, which turns firm via factor XIII and Ca^{2+} ions and forms a red thrombus.

The process of preventing blood clots is called fibrinolysis. Plasminogen is activated by blood factors and becomes plasmin. It splits fibrin into individual peptides. Furthermore, it splits the clotting factors I, II, V, VIII, IX, XI, and XII and thus decrease the clotting ability of the blood.

Leukocytes ensure the defense of foreign bodies

Neutrophil granulocytes function as fast defense mechanisms in cases of infections and, thus, belong to the unspecific defense of the immune system. In an infection, the


number of neutrophils increases quickly by pulling the reserves from the marginal pool (at the endothelium of large veins) or the bone marrow. They fight bacteria and can break down debris of the body's cells. The suspension of dead neutrophils and tissue debris in the lymph is called pus.

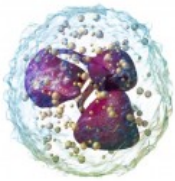
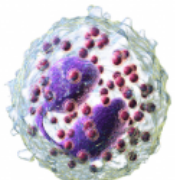
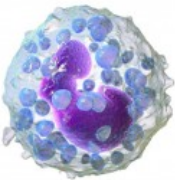
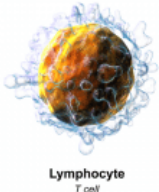
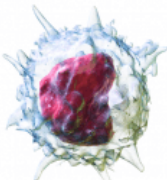

Eosinophil granulocytes function as defense against parasites.

Lymphocytes, except for natural killer cells, belong to the specific immune system. In the thymus, **T lymphocytes** are trained to differentiate between foreign antigens and endogenous antigens and react accordingly. In the process, helper T cells, as well as cytotoxic lymphocytes are developed, which support the mechanisms of the specific and unspecific immune defense, and which recognize virus-infected or degenerated cells and kill them.

B lymphocytes can be activated as plasma cells that produce free antibodies that bind the foreign antigens and render them harmless. Thus, B lymphocytes belong to the humoral component of the specific defense. During the activation process, a part of the B lymphocytes differentiates themselves as memory cells that remain in the body for many years. In case of renewed contact with the antigen, they already know which antibodies are needed.

Natural killer cells are part of the unspecific immune system and can cause apoptosis in degenerated cells because of their cytolytic granules.

Formula elements	Main subtypes	Amount per microliter and importance (scale)	Appearance in the standard blood smear specimen	Summary of functions	Comment
	Erythrocytes (red blood cells) 	5.2 million (4.4-6.0 million)	Flattened biconcave shape; no nucleus; light-red color	Transports oxygen and carbon dioxide between tissue and lungs	Lifespan of about 120 days.
	Leukocytes (white blood cells)	7000 (5000-10,000)	Significantly dark-colored nucleus	All functions of the immune system	Exiting the capillaries and migrating into the tissue; lifespan of usually a few hours or days

Leukocytes	Granulocytes	4360 (1800- 9950)	Plenty of granules in the cytoplasm; usually capped nucleus	Unspecific disease resistance	Classified by membrane-bound granules in the cytoplasm
	Neutrophils 	4150 (1800-7300)	Number of nuclear lobes increases with age	Phagocytic cells; particularly effective against bacteria, releasing cytotoxic chemical from granules.	Most common leukocyte; lifespan: minutes up to days
	Eosinophils 	165 (0-700)	Nucleus is generally two-lobed; bright, red-orange granules	Phagocytic cells; particularly effective with antigen-antibody complex; releasing histamines	Lifespan: minutes up to days
	Basophils 	44 (0-150)	Nucleus is generally two-lobed but difficult to detect due to heavy, dense, and dark purple granules	Promote infections	Rarest leukocyte; lifespan: unknown
	Agranulocytes	2640 (1700- 4950)	Lack of granules in the cytoplasm; have a simply shaped nucleus that can be indented	Immune defenses	Group consists of 2 major cell types of different origin
	Lymphocytes 	2185 (1500- 4000)	Spherocytes with a single, often large nucleus, making up a large part of the cell volume; dark spots; appears as a large (natural killer cells) and a small (B cells and T cells) variant	Primary specific (adaptive) immunity; T cells directly attack other cells (cellular immunity); B cells release antibodies (humoral immunity); natural killer cells are like T cells but unspecific	Initial cells originate in the bone marrow; secondary production takes place in the lymphoid tissue; several different subtypes; memory cells form after contact with a pathogen and ensure a faster reaction; lifespan: many years
	Monocytes 	455 (200-950)	Largest leukocyte with an indented or hoof-shaped nucleus	Particularly effective phagocytes engulf pathogens or damaged cells. They also serve as antigen-presenting cells for other components of the immune system	Produced in the red bone marrow; designated as macrophages after leaving the circulation system
Platelets 	350,000 (150,000-500,000)	Cell fragments which are surrounded by the plasma membrane and contain granules; violet spot	Hemostasis and release of growth factors to repair and heal tissues	Derived from megakaryocytes which remain in the red bone marrow and release platelets in the circulatory system	

Blood Diseases

Inflammatory values in the blood

Inflammatory values play an important role in diagnosis. They are obtained by examination of the blood. Here, the erythrocyte sedimentation rate, the C-reactive protein, and the number of leukocytes are mostly determined. In addition, a differential blood count can be made as well.

The blood is stored vertically in a test tube for 2 hours to determine the erythrocyte sedimentation rate. After every hour, the level of the erythrocyte column is determined. Normal values for men after 1 hour are below 15 mm and for women below 20 mm.

Change of these values may indicate anemia, inflammation, and even cancer.

The C-reactive protein belongs to the immune system and is deemed to be a marker for acute inflammations. In a healthy person, its concentration in the blood is below 10 mg/L.

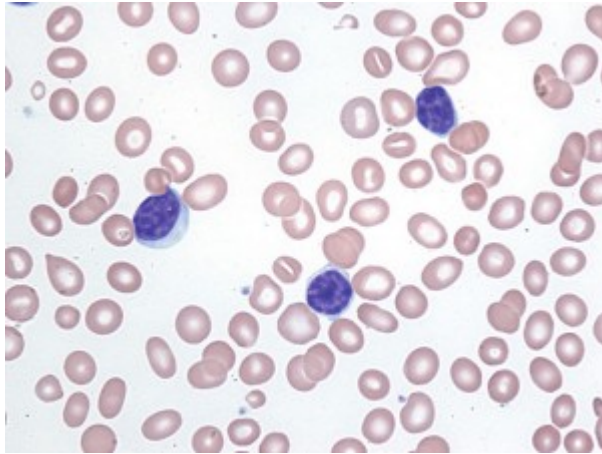
The number of leukocytes is determined by a machine. If the number is too high, it is called leukocytosis. If the value is lowered, however, it is called leukopenia.

The leukocytes are identified in subtypes in the blood smear to produce a differential blood count. In 100 leukocytes, there are normally 4 monocytes, 58 neutrophils (of which only 3 are segmented), 1 eosinophil, up to 1 basophil, and 35 lymphocytes. **If the number of banded neutrophils is significantly increased, then it is called a left shift and indicates a bacterial infection.** If there are too many hypersegmented granulocytes, there is a shift to the right, which may indicate a vitamin B12 deficiency.

Anemia

- **Iron deficiency anemia:** erythrocytes are microcytic and hypochromic; cause: chronic blood loss and insufficient iron intake.
- **Megaloblastic anemia:** erythrocytes are megaloblastic and normochromic; cause: vitamin B12 deficiency, folic acid deficiency, and alcohol.
- **Renal anemia:** erythropoietin; cause: renal failure
- **Aplastic anemia:** erythrocyte deficiency; cause: bone marrow damage
- **Hemolytic anemia:** erythrocytes are strongly degraded; cause: incorrect cytoskeleton (spherocytosis, sickle cell anemia, thalassemia), malaria, sepsis, poisoning.

Leukemia



[Image](#): Peripheral blood with chronic lymphocytic leukemia. By Gabriel Caponetti, License: [CC BY-SA 3.0](#)

Leukemia is characterized by many leukocytes, in particular their precursors. These precursors have no function in the immune defense yet. They spread in the bone marrow, the blood, and the lymphoid organs and thus, reduce their function, interfering with the formation of other blood cells. **The result is aplastic anemia, decreased blood clotting, and a dramatically weakened immune defense.**

Coagulation disorders

Coagulation disorders are either innate or acquired. An increased bleeding tendency is mostly based on malfunction or lack of a coagulation factor:

- **Hemophilia A:** Factor VIII deficiency
- **Hemophilia B:** Factor IX deficiency
- **von Willebrand disease:** von Willebrand factor deficiency
- **Vitamin K deficiency:** decreased synthesis of factors II, VII, IX and X

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