

## Microscopic Anatomy: Blood

[See online here](#)

**Blood (Latin: sanguis, Greek: haima) is a suspension of cells in a saline solution containing protein. It makes up 6-8 % of the total body weight and has a pH value of 7.4. The blood carries out many essential functions and is the pivotal point of the whole organism. The following article provides, at a glance, the most important facts about this vital body fluid called blood.**

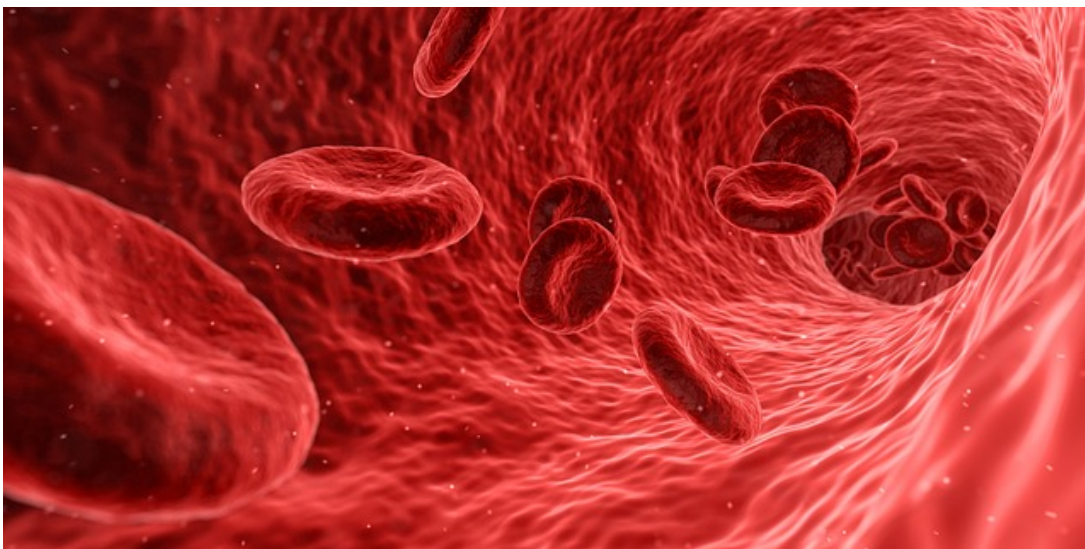
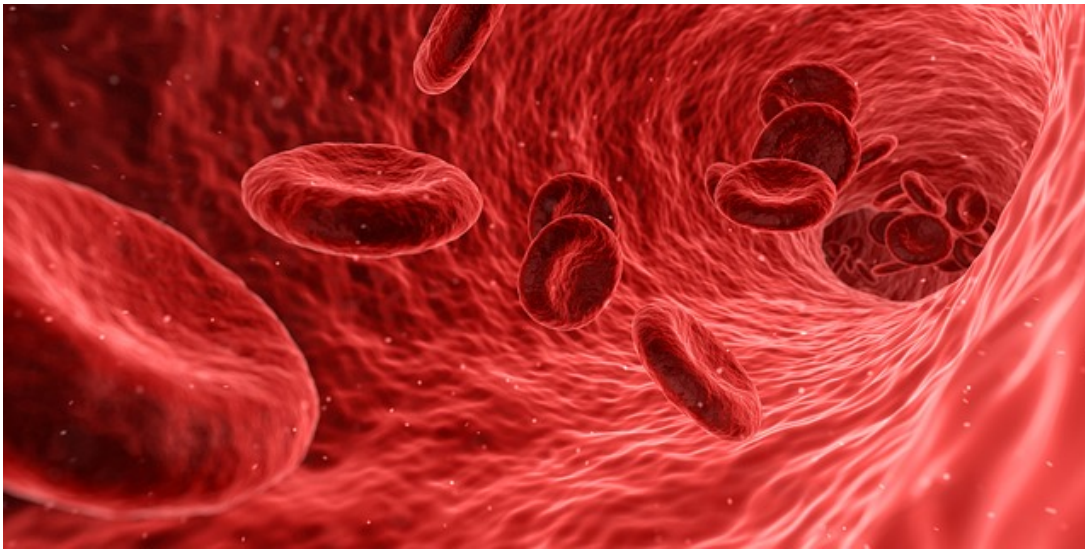


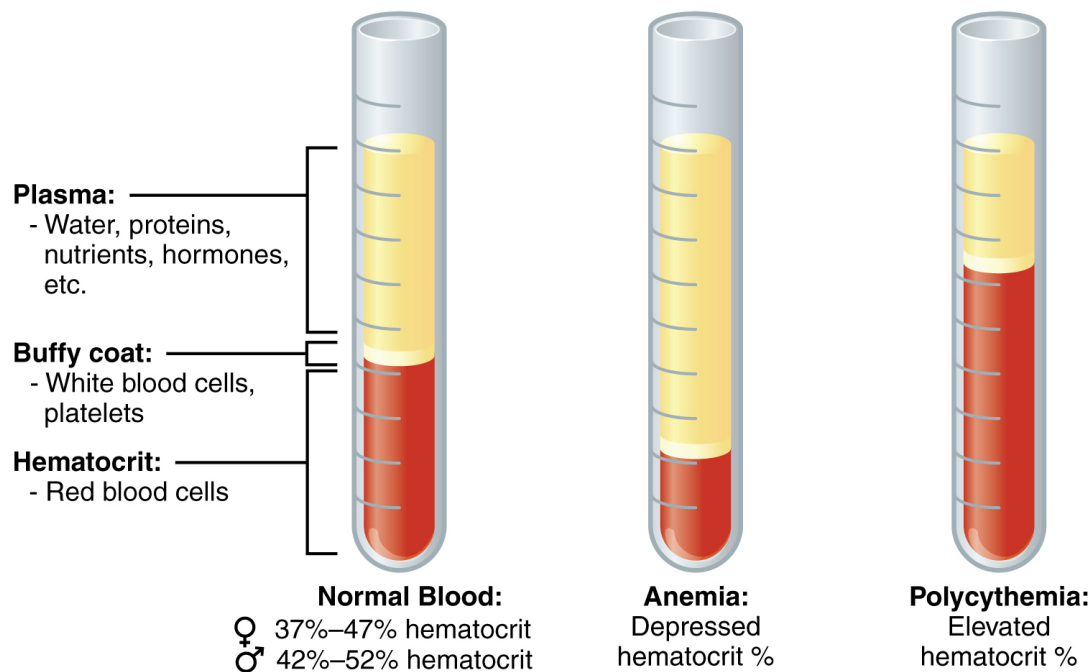
Image: "Blood" by qimono. License: [CC BY-SA 0](#)

# Blood Components

The average 70 kg human being has approximately 4.2L of blood. If a blood sample is centrifuged, a more or less turbid liquid (depending on the fat content of the blood) becomes visible with a red sediment set off against it. The liquid component represents the blood plasma; the sediment is the so-called blood clot made out of blood cells. The ratio of plasma to blood cells is indicated by the hematocrit. This is physiologically at 42% for women and 45% for men.

## Blood Plasma

The plasma represents approximately 55% of the [blood](#). It contains water, proteins, ions, hormones and physically dissolved gases. Serum free of coagulation factors can be obtained from the blood plasma.



Picture: "Composition of Blood" by Phil Schatz. License: [CC BY 4.0](#)

### Normal values of plasma electrolytes:

- $\text{Na}^+$  140 mmol/l
- $\text{K}^+$  4.5 mmol/l
- $\text{Ca}^{2+}$  2.4 mmol/l
- $\text{Cl}^-$  105 mmol/l
- $\text{HCO}_3^-$  24 mmol/l

This yields an osmotic pressure of 5,600 mmHg and an osmolarity of 290 mOsm/l for the plasma. The largest part of the plasma with 75 g/l are plasma proteins. They hardly contribute to osmolarity but do play an important role for the colloid osmotic (or oncotic) pressure, i.e. the osmotic pressure between plasma and interstitium. It comes to 25 mmHg and is thus significantly higher than that of the interstitium (5 mm Hg), which prevents too much plasma fluid from diffusing from the blood vessels into the tissue.

**The most common protein is albumin (54-60 %). It is, therefore, essential for the oncotic pressure.** Albumin is produced in the liver and is one of the smallest

plasma proteins. It is used as a transporter of cations, bilirubin, fatty acids and cholate.

Other important plasma proteins are the globulins. These are divided into alpha, beta and gamma. **Alpha and Beta globulins, like albumin, act as a vehicle.** For example, the fat transporting LDL (low density lipoproteins) and HDL (high density lipoproteins) are important representative of the globulins.

**Gamma globulins, by contrast, have an immunological function** and contain immunoglobulin (Ig). They can be subdivided into five Ig classes according to their different chemical structures. In the plasma, there are primarily immunoglobulins IgG, IgA and IgM present.

Blood components in %	Sub-components of the blood in %	Type in % (if applicable)	Production site	Main tasks
<b>Plasma</b> <b>43-63%</b>	Water 92%	Liquid	Absorbed through the intestinal tract or produced during metabolism	Transport medium
	Plasma proteins 7%	Albumin 54-60%	Liver	Maintains the osmotic concentration, transports lipid molecules
		Globulins 35-38%	Alpha globulins: liver	Transport, maintain the osmotic concentration
			Beta globulins: liver	Transport, maintain the osmotic concentration
			Gamma globulins (immunoglobulins): plasma cells	Immune response
		Fibrinogen 4-7%	Liver	Blood clotting during hemostasis
	Regulatory proteins <1%	Hormones and enzymes	Various locations	Regulate various body functions
	Other dissolved substances 1%	Nutrients, gases and waste	Absorbed through the intestinal tract, replacement of cells in the respiratory tract or produced in cells	Many different functions

<b>Formed Elements 37-54 %</b>	Erythrocytes 99%	Erythrocytes	Red marrow	Transports gases, primarily oxygen and some carbon dioxide
	Leukocytes <1%, Platelets <1%	Granular leukocytes: neutrophils, eosinophils and basophils	Red marrow	Non-specific immune response
		Agranular leukocytes: lymphocytes, monocytes	Lymphocytes: bone marrow and lymphoid tissue	Lymphocytes: specific immune response
			Monocytes: red marrow	Monocytes: non-specific immune response
	Platelets <1%		Megakaryocytes: red marrow	Hemostasis

## Blood Cells

### Erythrocytes/ Red blood cells

The red blood cells are easily recognized by their biconcave shape. They have a diameter of 7.5  $\mu\text{m}$ , and, with a count of  $4.5 \times 10^6 / \mu\text{l}$  in females and  $5.2 \times 10^6 / \mu\text{l}$  in males, they are the most common cells in the blood. Red blood cells contain hemoglobin. They have no cell nucleus or cell organelles and, therefore, have only a life span of approximately 120 days, before they are decomposed in the [spleen](#).

The formation of erythrocytes takes place in the red bone marrow and is stimulated by the erythropoietin released in the kidney. In the event that the marrow does not produce enough red blood cells then extramedullary hematopoiesis takes place in peripheral organs.

Red blood cells have a larger diameter than some capillaries. For this, the deformability of the red blood cells is extremely important. It is ensured through its distinctive **membrane skeleton made out of ancyrin, spectrin and actin**.

### Thrombocytes/ Platelets

Platelets in their free form have a biconvex shape, and, with a diameter of only 2.5  $\mu\text{m}$ , they are **far smaller than erythrocytes**. Healthy human blood contains 150,000–400,000 platelets/ $\mu\text{l}$  of blood. Platelets are **nucleus-lacking cell fragments are formed by shedding off of the megakaryocytes** of the bone marrow and circulate in the blood around ten days, if they do not become activated for blood coagulation.

### Leukocytes/White blood cells

White blood cells are the immune cells of the blood. Their number varies between 4,000 and 10,000/ $\mu\text{l}$  in blood. White blood cells are divided into monocytes, granulocytes and lymphocytes.

1. **Monocytes** stand out in the blood smear due to their size (15–20  $\mu\text{m}$ ). Monocytes

typically have a kidney-shaped nucleus, and the cytoplasm appears pale grey under a light microscope. Monocytes are very rare (6% of the leukocytes) and circulate only one to three days in the blood. During this time, **they mature to macrophages, which then migrate into the tissue**. Accordingly, monocytes are sparse in peripheral blood smears.

2. **Granulocytes** are 10–12  $\mu\text{m}$  in size; like all blood cells, granulocytes develop in the red bone marrow and are divided into three groups:
  - **Neutrophils:** constitute the largest proportion of white blood cells and usually have a segmented nucleus. These are called segmented neutrophils. 8% of the neutrophil granulocytes are banded neutrophils (or stab neutrophils) whose nucleus is not segmented but rather curved. In the Pappenheim stain, the granules of the neutrophils appear as a faint pink.
  - **Eosinophil granulocytes:** make up only 3% of the white blood cells and have a nucleus that consists of two lobes. Their granules stand out in a blood smear by their brick-red coloration.
  - **Basophil granulocytes** are the least frequent in the blood smear. The granules usually cover the cell nucleus and are colored dark blue.
3. **Lymphocytes** have a round, purple-colored cell nucleus which is surrounded by a thin, pale gray cytoplasmic border. They are classified as natural killer cells, B cells (bone marrow) and T cells (thymus). Under the light microscope, however, the three types cannot be distinguished.

## Functions of the Blood

### Erythrocytes: Transport of Gas

**The oxygen content in the arterial blood of a healthy person is about 200 ml  $\text{O}_2/\text{l}$ .** Hemoglobin (Hb) binds 85% of the oxygen; the rest is physically dissolved in the plasma.

Hemoglobin is located in the erythrocytes. In an adult, Hb consists of 2  $\alpha$ - and 2  $\beta$ -subunits. Each subunit has a  $\text{Fe}^{2+}$  ion, which binds  $\text{O}_2$ . Thus, one Hb can transport four oxygen molecules. **The Hb concentration in men is 16 g/dl and in women—14 g/dl.**

**In the periphery, Hb releases the oxygen into the tissue and also takes up a portion of the carbon dioxide.** The majority of the  $\text{CO}_2$ , however, is carried in the erythrocyte in the form of bicarbonate and is exhaled in the lungs.

### Platelets (Thrombocytes) and Clotting

Blood clotting is also called hemostasis and is divided into primary and secondary hemostasis.

**Primary hemostasis** occurs when the vascular endothelium is damaged and platelets come into contact with collagen located outside the vessel. **The Von Willebrand factor** in the collagen binds the **glycoprotein Ib** of the platelets to its receptor, and the **platelets** anchor on the damaged endothelium.

At the same time,  $\text{Ca}^{2+}$  activates the platelets. This means that the tubule ring within the platelet contracts and pseudopods emerge. Together with **adenosine diphosphate (ADP)**, released from the injured cells, **thrombocytes** stick together and a so-called **platelet plug** is formed. The **activated platelets** also secrete serotonin, fibrinogen and

thromboxane A<sub>2</sub>. The latter causes, among other things, vasoconstriction, which supports closure of the vessel.

In order for the platelet plug not to block the whole vessel, **the endothelium** releases **prostacyclin which inhibits platelet aggregation**. This way, a targeted plug formation at the damaged endothelium is guaranteed.

**Secondary hemostasis** is divided into the **extrinsic** and **intrinsic** systems or pathways.

**The extrinsic system** comes into action when tissue is destroyed. With a prothrombin time of about 14 seconds (Quick test), it acts very fast. The tissue factor from the vascular smooth muscles forms a complex with phospholipids. This is called tissue thromboplastin and binds the **coagulation factor VII**, which then activates **factor X** with Ca<sup>2+</sup> present.

In the **intrinsic system**, **factor XII** comes into contact with negatively charged surfaces, such as collagen (or glass), and becomes activated. Subsequently, **factor XI** and then **IX** are activated. Factor IX along with phospholipids and Ca<sup>2+</sup> ions form an enzymatic complex, which activates **factor X (thrombokinase)** by limited proteolysis. This process can be greatly accelerated with the **thrombin activated factor VIII**. The partial thromboplastin time comes to 40-50 seconds.

With the activation of factor X, **intrinsic and extrinsic system converge**. Factor X, in combination with factor V, phospholipids and Ca<sup>2+</sup> ions, forms the prothrombin activator, which splits factor II (prothrombin) to thrombin. **Thrombin**, in turn, divides factor I (fibrinogen) to soluble **fibrin**, which by means of factor XIII and Ca<sup>2+</sup> ions becomes solid, so that a red thrombus is formed.

The process of breaking down coagulation is called **fibrinolysis**. This activates plasminogen to **plasmin** by blood factors. The latter then splits fibrin into individual peptides. In addition, it splits the coagulation factors I, II, V, VIII, IX, XI and XII, thus lowering the clotting ability of the blood.

## Leukocytes: Defense against Foreign Bodies

**Neutrophils granulocytes** act as rapid action force for **inflammation** and thus belong to the non-specific immune system. During an infection, the number of neutrophils increases quickly by using the reserves from the marginal pool (on the endothelium of large veins) or the bone marrow. They fight bacteria and can remove debris of endogenous cells. The suspension of dead neutrophils and tissue debris in tissue fluid is called pus.


Eosinophil granulocytes serve to defend against worm parasites.

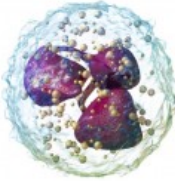
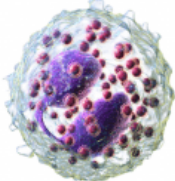
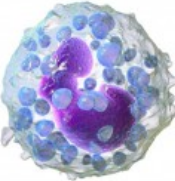
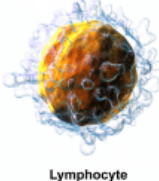
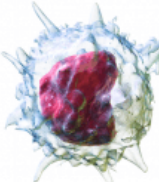
**Lymphocytes**, except for natural killer cells, are part of the **specific immune system**. In the thymus, T-lymphocytes are trained to distinguish the body's own antigens from foreign antigens and to respond accordingly. Hereby, T-helper cells and cytotoxic lymphocytes develop. T-helper cells support the mechanisms of the specific and non-specific defense; the cytotoxic lymphocytes recognize virus-infected or degenerated cells based on their antigens and kill them.

**B-lymphocytes** can be activated to **plasma cells**, which produce **free antibodies** that bind foreign antigens and neutralize them. This means that B-lymphocytes belong to the **humoral component** of the **specific immune** response. When activated, part of the B-

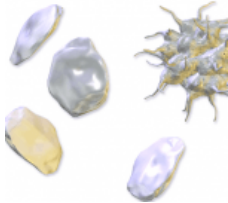
lymphocytes differentiate to become memory cells that remain in the body for many years. When contact occurs with a known antigen, they already know which antibodies are required.

**Natural killer cells** are part of the non-specific immune system, and, through their cytolytic granules, they are able to trigger apoptosis in degenerated cells.

Formed Element	Main subtypes	Number per micro liter and importance (scale)	Appearance in the standard blood smear	Summary of the functions	Comment
<p><b>Erythrocytes (red blood cells)</b></p> 		5.2 million (4.4-6.0 million)	Flattened biconcave disc; no nucleus; bright red color	Transport oxygen and some carbon dioxide between tissues and lungs	Life: approx. 120 days
<p><b>Leukocytes (white blood cells)</b></p>		7,000 (5,000 -10,000)	Clearly dark colored nucleus	All of the functions of the immune system	Leave the capillaries and move into the tissue, life: usually a couple of hours or days

<b>Leukocytes</b>	<b>Granulocytes</b>	4,360 (1,800-9,950)	Abundant granules in the cytoplasm; usually capped nucleus	Non-specific disease resistance	Classified according to membrane-bound granules in the cytoplasm
	Neutrophils	 4,150 (1,800-7,300)	Number of nucleus lobes increases with age	Phagocyte; particularly effective against bacteria, releases cytotoxic chemicals of granules	Most common leukocyte, life: minutes and up to days
	Eosinophils	 165 (0-700)	Nucleus usually two-lobed; bright, red-orange granules	Phagocytic cells; particularly effective with antigen-antibody-complex; release antihistamines; promote action against allergies and parasitic infections	Life: minutes to up to days
	Basophils	 44 (0-150)	Nucleus usually two-lobed, but difficult to detect due to heavy, dense and dark purple granules	Promote inflammation	Least frequent leukocyte, life span: unknown
	<b>Agranulocytes</b>	2,640 (1,700-4,950)	Lack of granules in the cytoplasm; has a simply shaped nucleus, which can be indented	Immune response	Group consists of two main cell types from a number of different origins
	Lymphocytes	 2,185 (1,500-4,000)	Sphere-shaped cell with a single, often large nucleus, which accounts for a large part of the cell volume; dark spots; appears as a large (natural killer cells) and small (B and T-cells) variant	Primary specific (adaptive) immune response; T-cells directly attack other cells (boost cellular immunity); B-cells release antibodies (humoral immunity); natural killer cells are similar to the T-cells, but are non-specific	Initial cells derived from the bone marrow, secondary production occurs in the lymphoid tissue; several different subtypes; memory cells are formed after contact with a pathogen and provide a faster reaction; lifetime: many years
	Monocytes	 455 (200-950)	Largest leukocyte with indented or horse shoe-shaped nucleus.	Particularly effective phagocytes, swallow up pathogens or worn cells; also serve as antigen-presenting cells for the other components of the immune system	Produced in the red bone marrow; after leaving the circuit, called macrophages



<p><b>Blood platelets</b></p> 	<p>350,000 (150,000 -500,000)</p>	<p>Cell fragments surrounded by plasma membrane, contain granules; purple spot</p>	<p>Hemostasis and release of growth factors to repair and heal tissue</p>	<p>Formed from megakaryocytes that remain in the red bone marrow and release platelets into the bloodstream</p>
---	---	--	---	---

## Diseases of the Blood

### Levels of Inflammation in the Blood

Inflammation values play an important role in diagnostics, typically obtained by the analysis of a blood sample. This usually includes the **erythrocyte sedimentation rate**, **C-reactive protein** and **white blood cell** count. In addition, there is a differential leukocyte count.

For the determination of the erythrocyte sedimentation rate, blood is stored in a narrow tube for two hours in an upright position. After one hour, the distance the red cells have traveled downwards to settle at the bottom of the tube is measured. Normal values after an hour are less than 15 mm in men and under 20 mm in women. A change in these values can indicate anemia, inflammation and even cancer.

**The C-reactive protein** is part of the immune system and is considered a marker for acute inflammation. Its concentration in the blood in a healthy person is under 10 mg/l.

The number of white blood cells is determined automatically. A very high number is called leukocytosis. If the value is very low, in turn, this is called leukopenia.

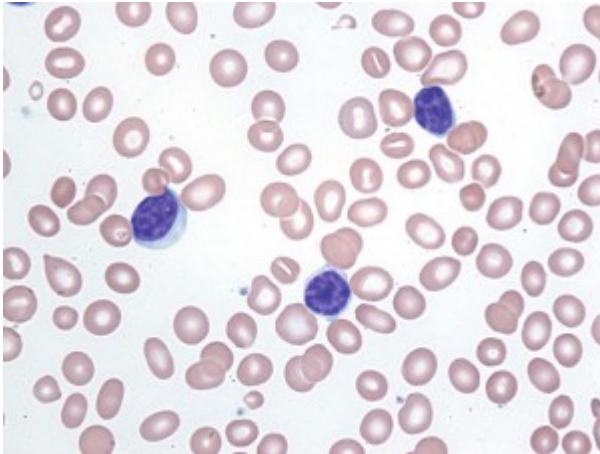
For a differential blood count, the leukocytes in the blood smear are identified by subtypes. 100 leukocytes usually comprise four monocytes, 58 neutrophil granulocytes (of which only 3 are segmented), one eosin granulocyte, up to one basophil granulocyte and 35 lymphocytes. If the number of **band neutrophils** is significantly elevated, this is called a **left shift**. It is an indication for bacterial infection. If too many granulocytes are overly segmented, this is called a right shift. This can be due to a deficiency of vitamin B12.

### Anemia

Anemia is defined as low hemoglobin level for a person's age, sex and prevailing conditions. Anemia is classified based on the cause of low hemoglobin into:

- Iron deficiency anemia: erythrocytes are microcytic and hypochromic; cause: chronic blood loss, insufficient iron intake.
- Megaloblastic anemia: erythrocytes are macrocytic and normochromic; cause: vitamin B12 deficiency, folic acid deficiency, alcoholism.
- Anemia of chronic disease such as renal anemia due to insufficient erythropoietin production; cause: renal insufficiency.
- Aplastic anemia: red blood cell deficiency; cause: damage to bone marrow.
- Hemolytic anemia: abnormal destruction of red blood cells; cause: defective cytoskeleton (hereditary spherocytosis, sickle-cell disease, thalassemia), sepsis, malaria, poisoning.

# Leukemia



Picture: "Peripheral blood with chronic lymphocytic leukemia" by Gabriel Caponetti. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

**Leukemia** is characterized by a greatly increased number of white blood cells (**leukocytes**), in particular their **precursor cells** (also called **blast cells**). Blast cells have no immune function and spread into the bone marrow, the blood and the lymphoid organs, thereby reducing their function, which also interferes with the formation of the other blood cells. Consequences include **aplastic anemia**, **reduced blood clotting** and a dramatically weakened **immune defense**.

## Coagulation Disorders

Coagulation disorders are either **inherited** or **acquired**. Increased bleeding is mostly due to a disturbed functioning or the lack of one of the coagulation factors:

- **Hemophilia A: factor VIII** deficiency;
- **Hemophilia B: factor IX** deficiency;
- Von Willebrand's disease syndrome: Von-Willebrand factor deficiency;
- **Vitamin K deficiency:** reduced synthesis of factors II, VII, IX and X.

## Popular Exam Questions on Blood

Solutions can be found below the references.

### 1. Blood plasma refers to:

1. The liquid left over after the coagulation of the blood.
2. The ionized component of the blood.
3. A saline solution isotonic to blood.
4. The supernatant liquid after centrifugation of the blood.
5. The cellular portion of the blood.

### 2. What substance is best used for platelet aggregation?

1. Factor IX
2. Factor XI
3. Fibrinogen
4. Factor X
5. Plasmin

### 3. An iron-deficiency anemia is most often caused by:

1. Chronic blood loss;
2. Vitamin B12 deficiencies;
3. Increased iron excretion due to renal insufficiency;
4. Increased alcohol consumption;
5. Damages to the hematopoietic bone marrow.

## References

Lüllmann-Rauch: Taschenlehrbuch Histologie, 4. Auflage – Thieme

Speckmann, Hescheler, Köhling: Physiologie, 6. Auflage – Urban & Fischer

Schmidt, Lang, Heckmann: Physiologie des Menschen mit Pathophysiologie, 31. Auflage – Springer

**Correct answers:** 1D, 2C, 3A

**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).

Notes