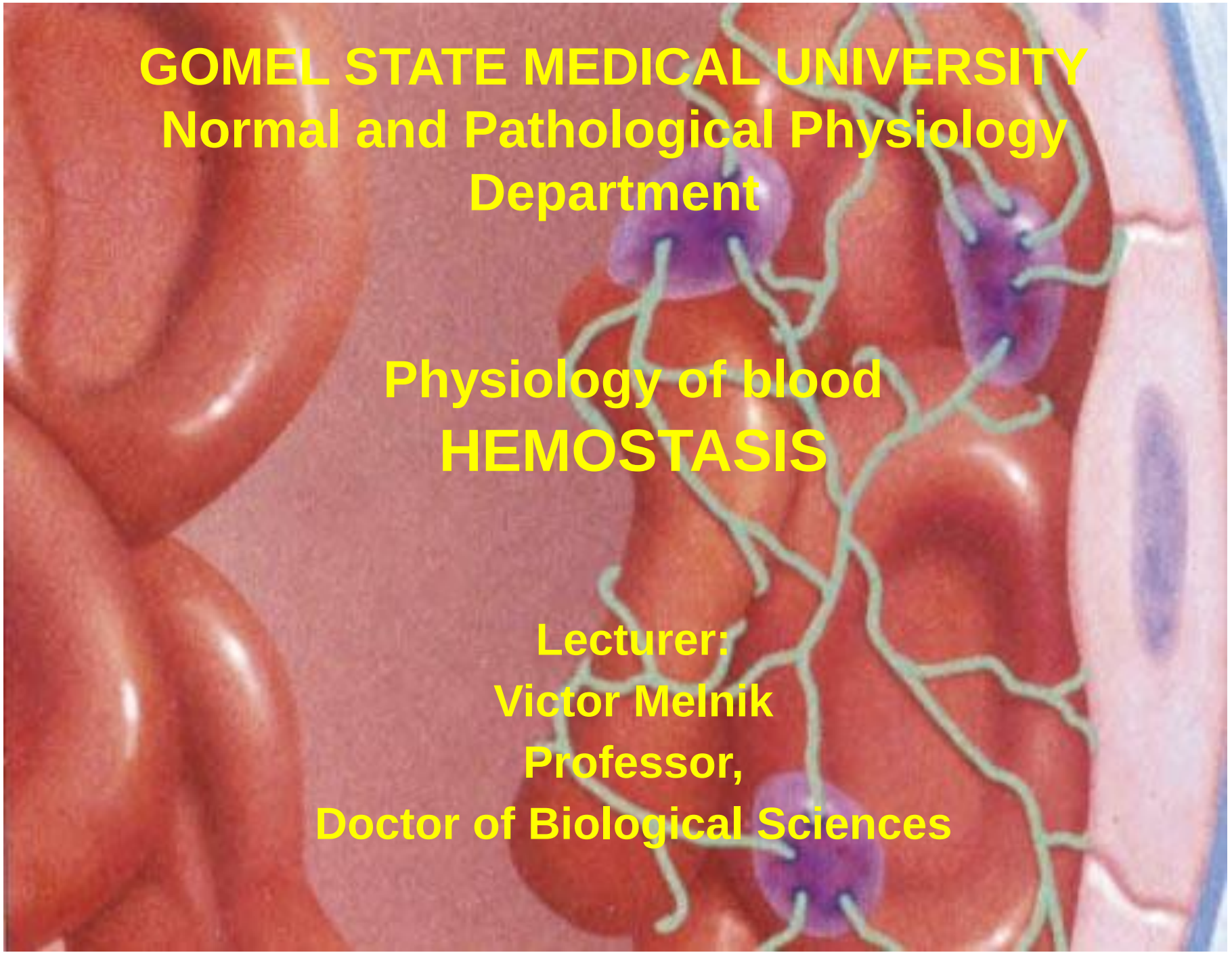

GOMEL STATE MEDICAL UNIVERSITY
Normal and Pathological Physiology Department

Physiology of blood
HEMOSTASIS

Lecturer:
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Lecture plan

1. Blood coagulation system

a. Vascular platelet (initial, primary) hemostasis.

в. Secondary hemostasis.

2. Blood anticoagulation system. Fibrinolysis. Regulation of the aggregate state of blood.

3. Blood groups (types). Rhesus-factor. Fundamentals of blood transfusion.

4. Regulation of the blood system.

5. Blood-substituting solutions.

1. Blood coagulation system

The maintenance of blood in a fluid state and its ability to circulate in the blood vessels within the confines of the circulatory system is a necessary condition for the organism`s homeostasis.

It is ensured by the system regulating the fluid state of blood (Figure).

This system includes:

- **Coagulation system of blood** (microvascular and coagulation hemostasis).
- **Anticoagulation system of blood** (anticoagulants and fibrinolysis).
- **Mechanisms of regulation.**

Blood coagulation disorders lead to severe human diseases.

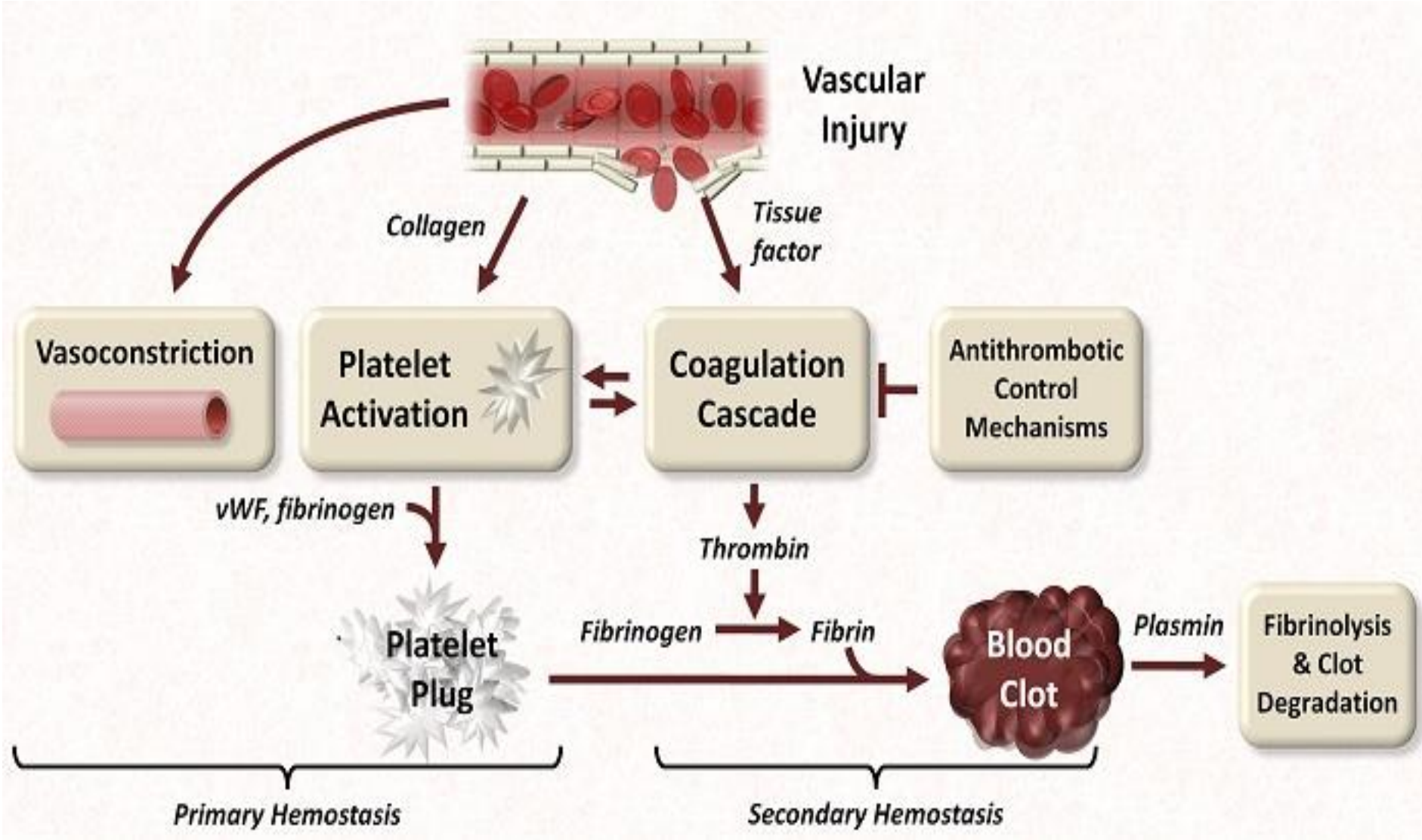

Figure — The system regulating the fluid state of blood

Hemostasis (termination of bleeding) — is caused by:

- Vascular spasm.
- Blood coagulation and formation of a blood clot (thrombus).

The system of hemocoagulation includes:

- Blood and tissues which produce and secrete substances participating in the above process.
- Neuro-humoral regulatory mechanisms.

Vascular platelet (initial, primary) hemostasis

In a healthy person the **termination of bleeding in the microcirculatory** flow with low arterial pressure is caused by the realization of the processes including:

1. Reflex spasm of the damaged blood vessel (the constriction of the vessel is caused by the release of noradrenalin, adrenalin, serotonin due to stimulation of receptors). It is known as *the initial angiospasm*.

2. Adhesion (attaching) of thrombocytes to the damaged surfaces (the injured area becomes positively (+) charged and thrombocytes have a negative electrical charge (-)). With participation of receptors they are attached to collagen in the damaged area of the blood vessel.

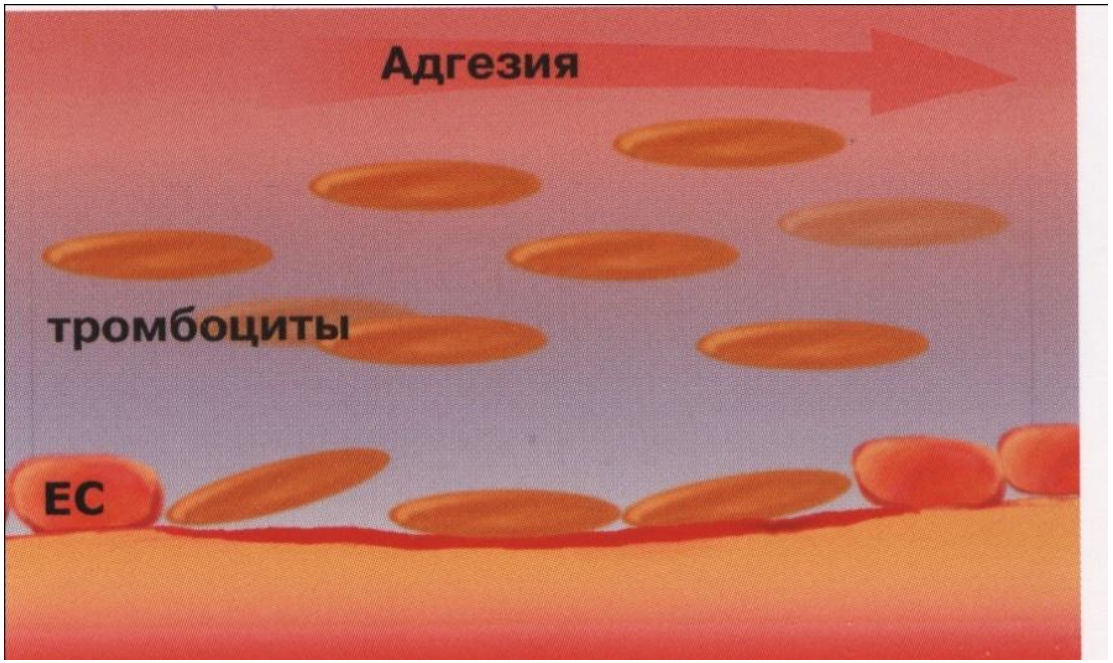

Figure — Adhesion (attaching) of thrombocytes to the damaged surfaces

3. Accumulation and aggregation of thrombocytes on the damaged area. The stimulators of the given process are adrenalin, thrombin, Ca^{++}, thromboplastin, released from thrombocytes and erythrocytes (*internal system*), and collagen, released from the tissue cells of the damaged blood vessel (*external system*). As a result, the platelet plug is formed. The aggregation of thrombocytes at this stage is a reversible process.

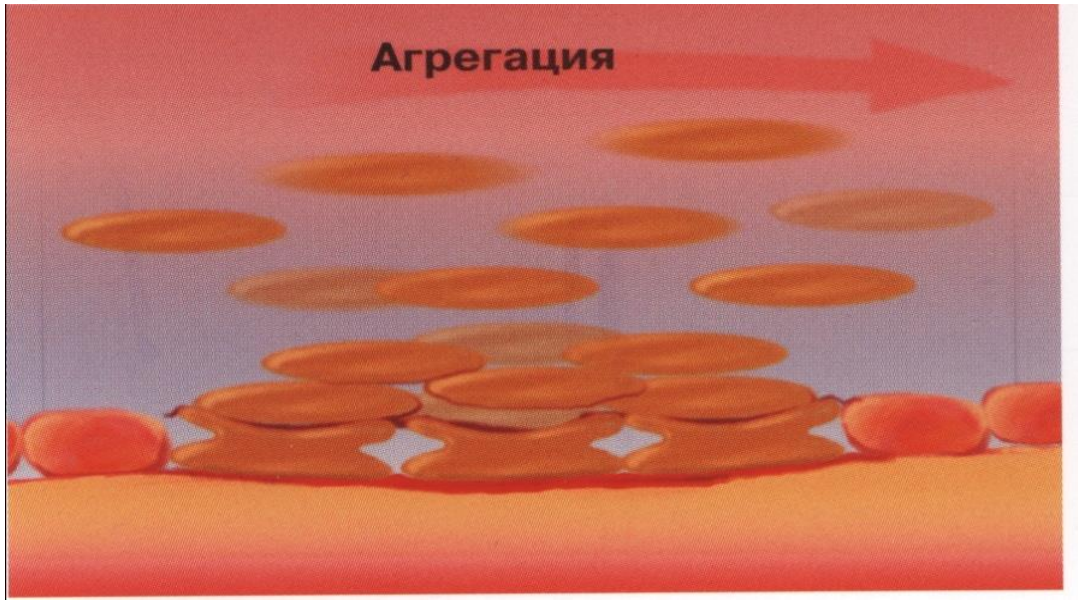

Figure — Accumulation and aggregation of thrombocytes on the damaged area.

4. Irreversible aggregation of thrombocytes. Thrombocytes flow into uniform mass, forming a thrombus, which is not permeable to blood plasma. The reaction is influenced by thrombin. The destruction of thrombocytes results in the release of physiologically active substances: adrenalin, noradrenalin, serotonin, nucleotides, coagulation factors (or clotting factors). They promote *a secondary vascular spasm*. Secreted in such a way, F3-platelet thromboplastin (thrombo-plastic factor) triggers the mechanism of coagulating hemostasis. A small amount of fibrin is produced.

5. Compression of the platelet plug. The compression of the platelet plug (thrombus) is ensured by the proteins of thrombocytes — thrombostenin (F6) and fibrin. It results in the termination of the bleeding.

In small blood vessels, the process of hemostasis stops at this stage. This hemostasis is called initial, or microvascular hemostasis.

In large blood vessels with high blood pressure, the platelet plug is not able to stop hemorrhage. In these vessels a stronger thrombus is formed as a result of other mechanism — **coagulation cascades, or secondary hemostasis.**

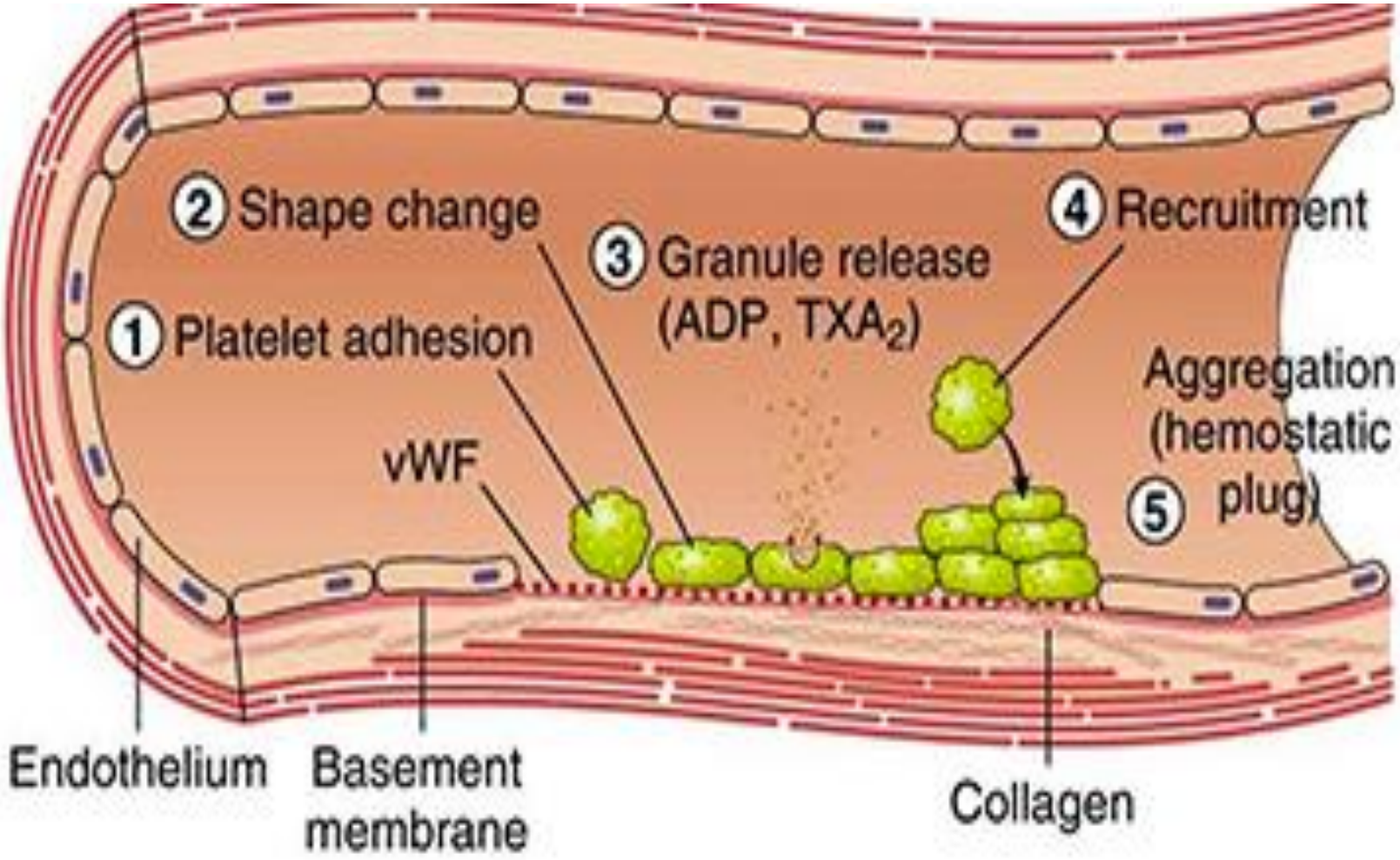

Figure — Vascular-platelet hemostasis

Secondary hemostasis

Secondary hemostasis includes the following:

- **Plasma blood-coagulation factors.**
- **Blood-coagulation factors of the formed elements of blood.**
- **Tissue blood-coagulation factors.**

I. Plasma factors (marked chronologically in the Roman numerals).

- **FI** — *fibrinogen*, the protein of plasma. Its concentration in the blood is **3 g/L**, and it is produced in the liver. It is used as a basis for thrombus formation.
- **FII** — *thrombinogen (prothrombin)*. It is synthesized in the liver with the presence of vitamin K.
- **FIII** — *thromboplastin*. It is a phospholipoprotein, which is the part of the membranes of blood and tissue cells.

- **FIV** — *calcium ions* (Ca^{++}). About 1/2 Ca^{++} are not connected with the protein and 1/2 are in the complex with plasma proteins. FIV is necessary for all the phases of blood coagulation. It promotes the aggregation of thrombocytes and binds heparin.
- **FV** — *proaccelerin*. It is produced in the liver. It participates in the 1^{st} and 2^{nd} phases of blood coagulation.
- **FVI** — it has been excluded from the classification.
- **FVII** — *proconvertin*. This is a glycoprotein which is produced in the liver with the presence of vitamin K. It is necessary for the formation of thromboplastin (tissue factor).
- **FVIII** — *antihemophilic globulin A.* It is produced in the liver, spleen, and leukocytes. It activates prothrombin. It ensures the optimum conditions for the interaction of factors IX and X. It is necessary for the adhesion of thrombocytes and activation of prothromboplastin. If this factor is absent, hemophilia develops.

- **FIX** — *antihemophilic globulin B*, a plasma protein (glycoprotein) and a vitamin K-dependent factor. The absence of this factor causes hemophilia B.
- **FX** —*Stuart-Prower factor*, a vitamin K-dependent factor. It is a part of tissue and blood thrombokinase.
- **FXI** — *Antihemolytic factor C (plasma thromboplastin antecedent)*. It is necessary for the activation of thromboplastin and FIX. The absence of this factor results in hemophilia C.
- **FXII** — *Hagemun factor* — is activated during contact with an alien surface (for example, a site of the damaged blood vessel), that is why it is named the contact factor. It is the initiator of the formation of blood thromboplastin and all the processes of hemocoagulation. The absence of this factor results in hemophilia D.
- **FXIII** — *Fibrin-stabilizing factor*. It is contained in plasma, cells, and tissues. It is necessary for the formation of final or unsolvable fibrin. It is activated by thrombin and Ca^{++}. If the given factor was absent, wounds would heal very badly.

The phases of secondary hemostasis

1st phase — formation of **active thromboplastin** (tissue and blood). The process goes with the participation of the tissue and plasma factors: IV, V, VII, VIII, IX, X, XI, XII. The formation of thromboplastin takes place as a result of the interaction of the lipid factor with plasma factors. Blood thromboplastin is produced from destroyed blood cells (*internal system*). Tissue thromboplastin is released from the damaged cells of the walls of the blood vessels and tissues (*external system).* Active thromboplastin is necessary for the activation of thrombinogen.

II phase — activation of inactive thrombinogen into the active form — **thrombin**. This process is influenced by FV — proaccelerin (accelerin**),** FX, Ca^{++} and some factors of thrombocytes.

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III phase — the process of the transformation of soluble fibrinogen into its unsoluable form — **fibrin**. Thrombin is necessary for the proteolysis of a fibrinogen molecule, transforming it into fibrin. Fibrinogen is produced in the liver. Vitamin K is necessary for its synthesis. Under the influence of thrombin with the presence of Ca^{++} the process of the formation of insoluble fibrin goes in 3 stages:

1. Influenced by thrombin, fibrinogen is splitted into fibrin-monomers.

2. After the polymerization of fibrin-monomers, the molecule of the soluble fibrin-polymer «S» is formed. For the polymerization the presence of calcium ions is necessary.

3. Under the influence of the fibrin-stabilizing factor (FXIII) insoluble fibrin («I») is formed.

The formed elements of blood get stuck in the fibrin nets, thus forming a blood thrombus. This thrombus is subjected to compression under the influence of the protein trombostenin. During the compression of the thrombus the wound closes.

The time of blood coagulation is 5–7 min.

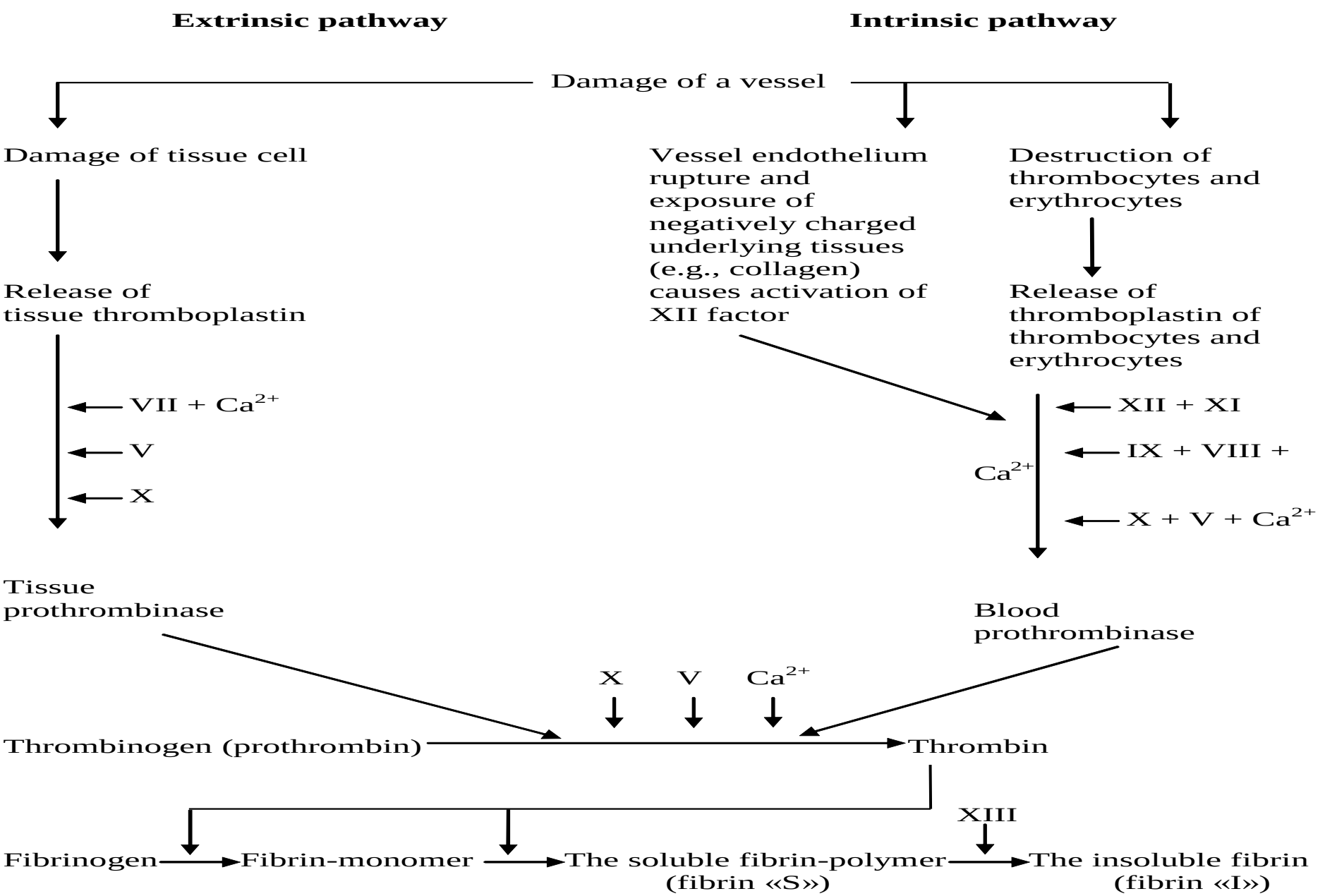


Figure — Secondary hemostasis (coagulation)

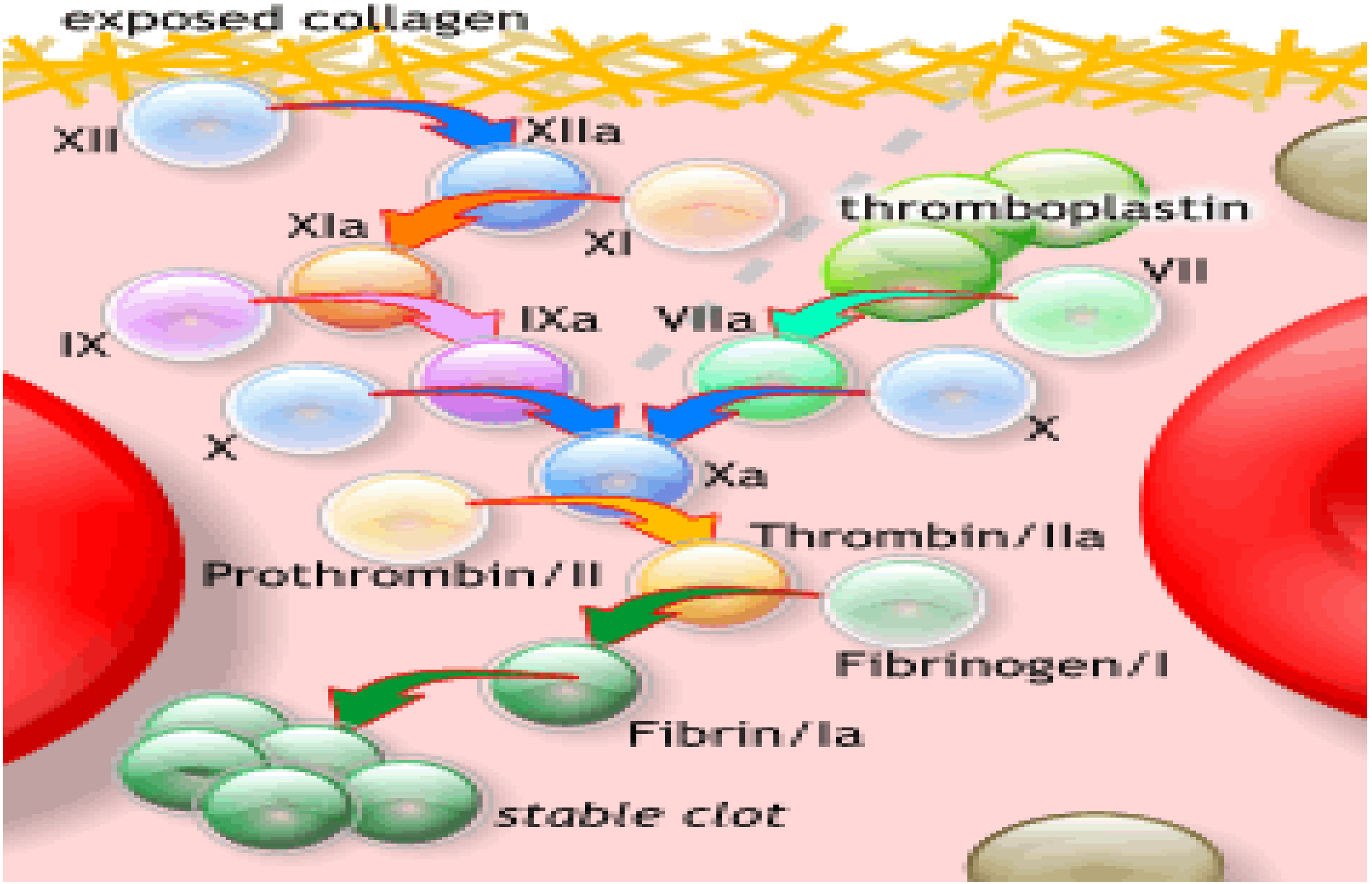


Figure —Coagulating hemostasis

2. Blood anticoagulation system

Despite the fact that all the factors necessary for blood coagulation constantly circulate in the bloodstream, it remains fluid. It is one of the parameters of homeostasis.

The mechanisms of the maintenance of blood fluidity:

- **Smooth surface of the blood vessels (prevents the activation of the Hagemun factor and aggregation of thrombocytes).**
- **Negative charges of the vessel wall and the formed elements of blood which provide their repulsion from each other.**
- **The blood vessel wall is coated with the thin layer of soluble fibrin, having the ability to adsorb active blood-coagulation factors.**
- **High blood flow rate (interferes the concentration of the coagulation factors).**
- **Presence of natural anticoagulants.**

There are **2 groups of anticoagulants** in the organism:

1. *Initial* (they are present in the blood constantly).

2. *Secondary* (they are formed during coagulation or fibrinolysis).

Initial anticoagulants — antithromboplastins, antithrombins:

- **Antithrombin II (heparin)**. It inhibits all the phases of hemocoagulation.
- **Antithrombin III** — plasma factor of heparin. It transforms thrombin into inactive metathrombin.
- **Antithrombin IV.**
- **Protein C** — vitamin K-dependent protein. Activates fibrinolysis.
- **Prostacyclin** — inhibits thrombocyte aggregation.

Secondary anticoagulants**.** The function of secondary anticoagulants consists in restriction of intravascular coagulation.

- **Antithrombin I (fibrin)** is capable to bind with significant (up to 90 %) amounts of thrombin.
- **Anticoagulants formed during fibrinolisis** (products of degradation of thrombinogen, fibrinogen, and fibrin).

The anticoagulants which are used in laboratory clinical practice are:

1. **Heparin.**
2. **Citric acid and its 0.5 % salt solutions.**

The factors accelerating blood coagulation:

- Damage of the blood vessel walls.
- Augmentation of thromboplastin formation.
- Augmentation of vitamin K absorption.
- Augmentation of fibrinogen formation.
- High temperature.
- Increased amounts of amino acids in the blood.
- Decreased fibrinolysis.

The factors decreasing coagulation:

- Decreased thromboplastin formation.
- Decreased vitamin K absorption.
- Increased development of anticoagulants.
- Decreased fibrinogen formation.

Types of hemophilia

Type A hemophilia — terminated phase I of coagulation (disturbance of thromboplastin formation). If FVIII is absent, phases II and III are also terminated.

Type B hemophilia — absence of FIX.

Type C hemophilia — absence of FXI (plasma predecessor of thromboplastin).

Type D hemophilia — absence of FXII.

Hemophilia occurs more commonly in males than in females.

Fibrinolysis

Fibrinolysis is the process of dissolution of a blood thrombus. It is considered that in the blood there is constant transformation of a small amount of fibrinogen into fibrin, which is exposed to dilution — fibrinolysis.

During the damage of tissues the process of fibrin formation dominates over fibrinolysis and local blood coagulation takes place. The main function of fibrinolysis is the restoration of the lumen of the blood vessel.

Fibrinolysis starts immediately upon thrombus compression in **2 phases** (Figure):

I phase — plasminogen transformation into *plasmin*.

II phase — plasmin-influenced dissolution of fibrin (thrombus) with the formation of peptides and amino acids.

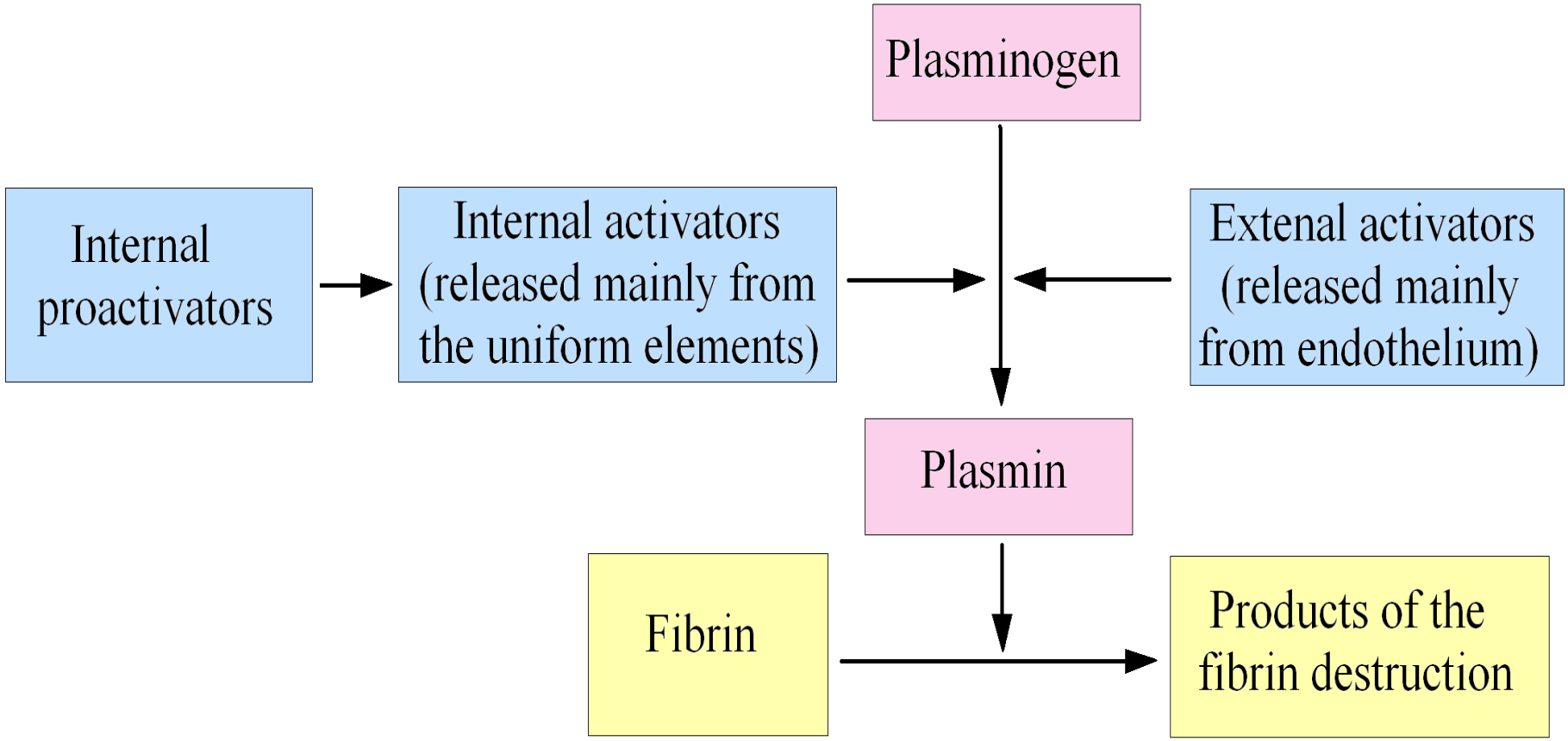


Figure — The activation of fibrinolysis

The factor providing fibrinolysis is plasminogen, which under the influence of tissue and blood factors transforms into the active form — **plasmin**.

The main activators of plasmin formation are the blood and tissue plasminogen activators. The other factors which stimulate fibrinolysis are the active plasma factor XII, kallikrein-kinin system, urokinase, acid and alkaline phosphatases, trypsin, complement C_1, streptokinase.

Excessive fibrinolysis is prevented by plasmin inhibitors (antiplasmins) and inhibitors of the plasminogen activator.

Regulation of the aggregate state of blood

Normally, there is no intravascular blood clotting or it occurs to a small extent. **The fragile process of the regulation of blood coagulation involves many factors and systems:**

- ***Presence of the inhibitors of pro-coagulants in plasma.***
- ***Many factors are in the inactive state.***
- ***The concentration of pro-coagulants decreases due to fibrinolysis. Therefore, a thrombus is not formed in the blood vessels of fast blood flow but develops in the blood vessels of low blood flow.***
- ***Pro-coagulants are inactive in the blood.***

On the whole, the mechanism of the regulation of coagulation is neuro-humoral. In the body there are special chemoreceptors reacting to the concentrations of thrombin, plasmin, and other factors of the coagulation and anticoagulation systems in the blood.

The **stimulation of the sympathetic** nervous system **increases the speed of blood coagulation** (hypercoagulation). It is pronounced in stress, pain, and is accompanied by the collateral release of adrenalin.

Under the influence of *adrenalin*:

- **Thromboplastin is released from the vascular wall.**
- **FXII (the contact factor) is induced, which activates prothromboplastin.**
- **Phospholipids are released from erythrocytes.**
- **Glucocorticoids, somatotropic hormone, antidiuretic hormone, calcitonin, testosteron, progesteron initially cause hypercoagulation but then activate fibrinolysis.**

Blood coagulation is prevented by the action of the complex anticoagulation mechanism:

- When thrombin is slowly formed in the blood vessels, it is neutralized by the plasma anticoagulants (antithrombins, heparin).
- Heparin (prevents the formation of thromboplastin and thrombin, activating fibrinolysis).

3. Blood groups (types)

In 1901 Karl Landsteiner observed that blood transfusions in different people in some cases caused erythrocyte agglutination, and in some did not. His further research and also that of J. Jansky allowed to discover the major human blood groups which differ from one another by the presence or absence of erythrocyte antigens (agglutinogens) and antibodies (agglutinins) in blood plasma (Table).

Table — Blood groups (types) of the AB0 system

Blood groups	Erythrocytes	Plasma or serum
	Agglutinogen	Agglutinin
I (0)	0	α, ß
II (A)	A	ß
III (B)	B	A
IV (AB)	AB	0

The **agglutinogens** of erythrocytes are **A** and **B**. In blood plasma there are γ-globulin-natured specific antibodies (**agglutinins α** and **ß**). They have 2 centers of linkage that provide an opportunity of the formation of bridges between two erythrocytes and formation of erythrocyte conglomerates.

Normally, there are no agglutinins corresponding to agglutinogens, and everyone has their individual panel of erythrocyte agglutinogens (Figure).

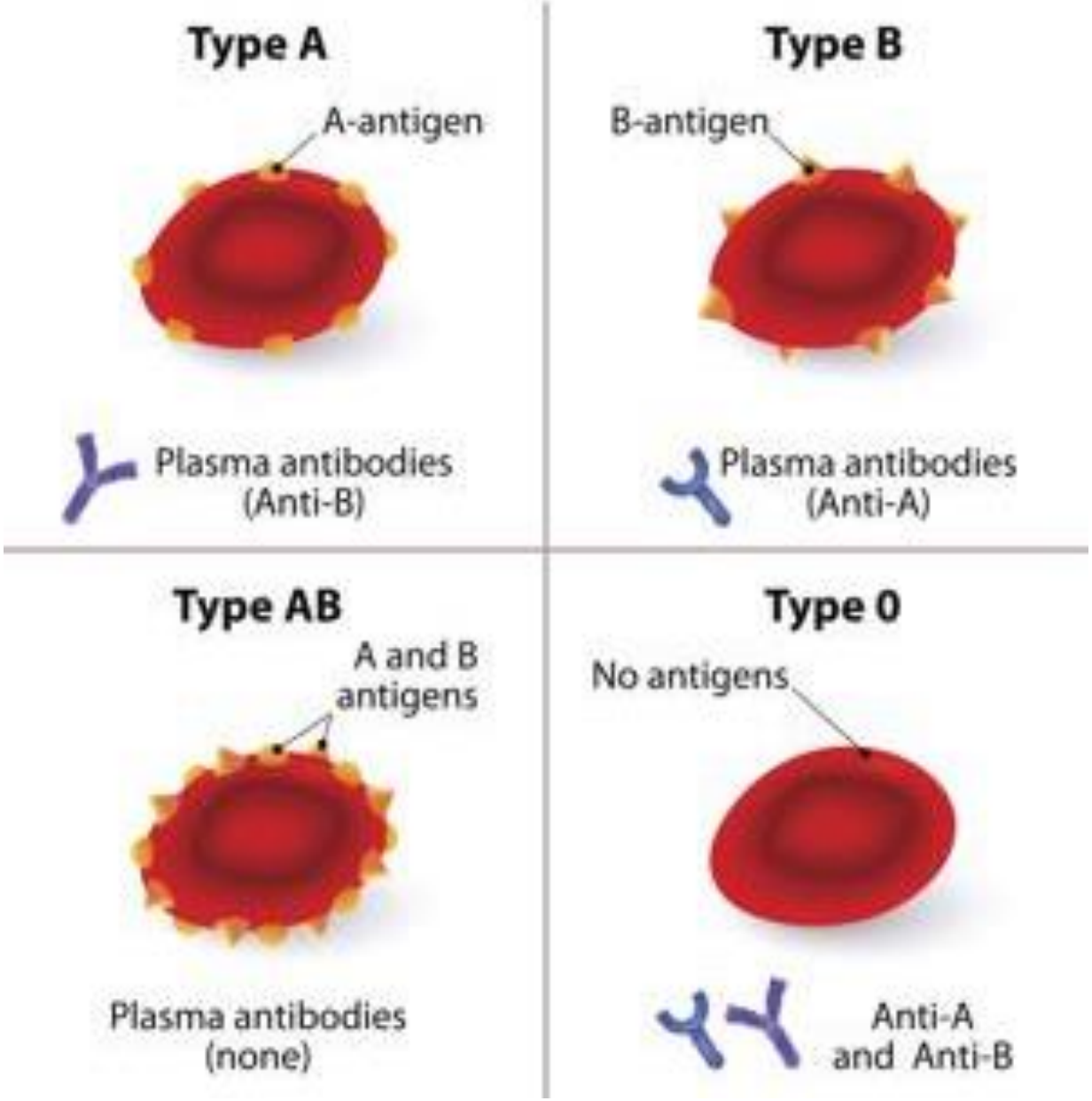


Figure — ABO blood groups

In the blood of neonates there are no antibodies of the ABO system and antigens, which are absent in newborns, are formed within the first year of life.

For blood transfusion the blood is selected to avoid meeting similar agglutinogens of the donor with agglutinins of the recipient (e. g. A and α, B and ß). Donor agglutinins are not considered since they dilute in the recipient blood and thus they cannot cause agglutination of the recipient erythrocytes (in transfusion of small amounts of blood of 200–500 mL). During transfusion of a big amount (4–5 L) of blood plasma of 0 (I), a large number of agglutinins come into the recipient blood. Thus, the dilution effect is lost and therefore the donor agglutinins may cause agglutination of the recipient erythrocytes.

As a rule, to avoid possible transfusion reactions, it is best to transfuse only matching blood types (that is, a type B+ recipient should ideally receive blood only from a type B+ donor and so on). In emergency situations, blood transfusions may be performed under the scheme (Figure) of blood groups compatibility.

Individuals with I (0) blood type are known as universal donors, those with blood type IV (AB+) are universal recipients.

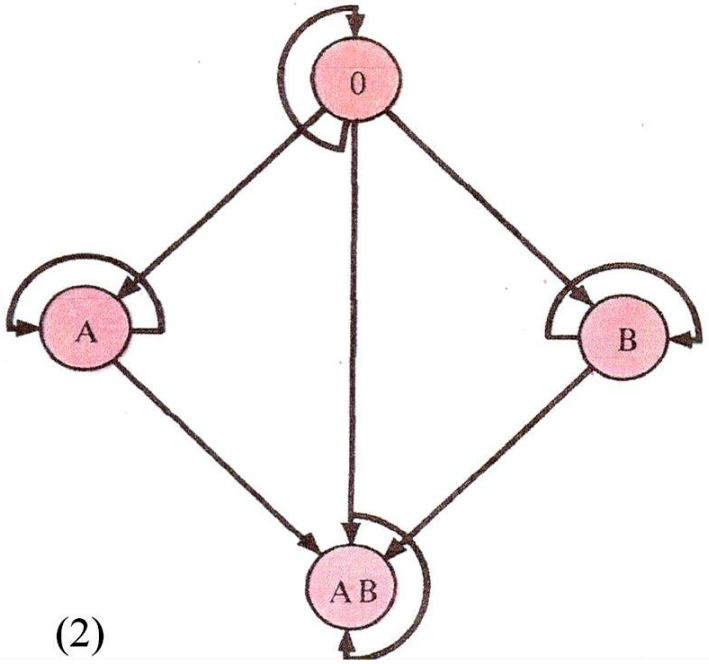


Figure — Possible variants of transfusion of blood of different groups.

To avoid complications duiring blood transfusions:

1. A blood group is determined with the application of the standard sera of I, II and III groups by blending a drop of each serum type with a drop of the examined blood. The group compatibility is determined by the presence or absence of agglutination. To avoid mistakes, the examination is performed at a temperature of 15–25 °C. The drop of blood brought into the serum should be 3–5 times less than the serum drop. In case of indistinct results, the examination is repeated with the serum of other series.

2. ***Direct and indirect tests***.

Direct test. The donor erythrocytes are mixed on a slide with the recipient plasma or serum at 37 °C. The purpose is to determine the presence of antibodies in the recipient serum to the donor erythrocytes. If there is no agglutination, the **indirect test** is carried out. The recipient erythrocytes are placed into the donor serum in order to reveal antibodies in the donor serum to the recipient erythrocytes.

3. ***Biological test***. First, a stream intravenous introduction of 10–15 mL donor blood is performed, and after 3–5 min the recipient is examined for the presence or absence of complications (high heart and respiration rates, short-breath, heavy breathing, facial hyperemia, etc.). This introduction is repeated for *three times*. In absence of any complications, the rest of the blood is administered.

People with I (0) blood group have anti-A and anti-B immune agglutinins (ά and ß) present in blood plasma. Transfusion of large amounts of this blood is prohibited since in these cases the donor agglutinins are not diluted in the recipient plasma, which can cause agglutination of erythrocytes in the recipient. Besides, people with I (0) blood group have **antigen H** on the surface of erythrocytes which can interact with anti-H-antibodes frequently present in the blood plasma of II (A) and IV (AB) groups and less in III (B) group. In these cases blood transfusion of I (0) group to individuals having other blood groups can result in hemolytic shock (hemotransfusion shock). Therefore, **universal donors are called *dangerous* universal donors.**

The presence of H-antigen on the surface of erythrocytes ensured the name of the AB0 system as ABH.

The prevalence of the blood groups: I (0) — 40–50 %, II (A) — 30–40 %, III (B) — 10–20 %, IV (AB) — 5 %. Geography: 40 % people in Central Europe have blood group II (A), 90 % in North America — I (0), more than 20 % in Central Asia — III (B). I (0) blood group is present in all nationalities, II (A) — dominates in inhabitants of Europe, Middle East, China, Japan, IV (AB) — dominates in inhabitants of India, Central Asia.

Apart from agglutinogens A and B (systems AB0), more than 400 agglutinogens are known, 140 from which (M, N, S, P, Di, C, K, Ln, Le, Fy, Ik, etc.) make almost 20 groups or systems.

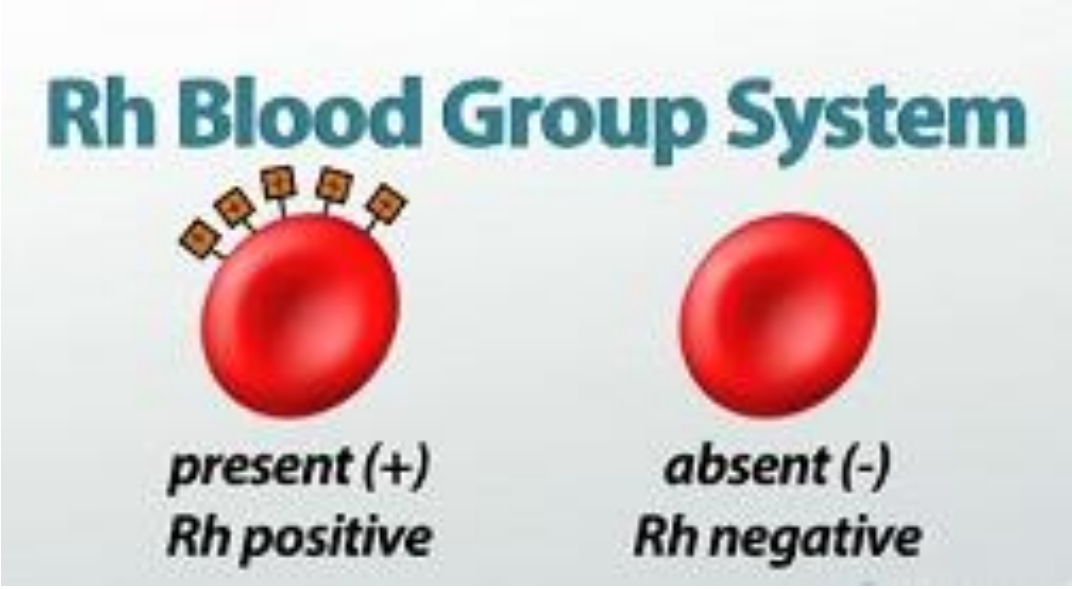
From them, it is possible to note systems: MNSS, P, Lutherans, Lewis, Kidd, etc. For example, the Kell-Cellano system consists of 2 agglutinogen K and k and forms 3 groups — KK, кк and Кк. The given system of blood is present in 100 % people.

Fortunately, the antigenic properties of the majority of these antigens are poorly expressed and neglected during blood transfusions. However, these systems matter in frequent blood transfusions. Therefore, it is not recommended to repeat blood transfusions from the same donor.

Alongside with agglutinins, blood plasma may contain ***hemolysins*** (marked agglutinins α and ß respectively).They are mainly IgM antibodies and their binding with similar agglutinogens results in erythrocyte hemolysis. Their action is revealed at a temperature of 37–40 °C and within 30–40 seconds the hemolysis of erythrocytes happens.

Rhesus-factor

The **Rh-factor (Rh)** was discovered in 1940 by Landsteiner and Wiener. The Rh-factor is an antigen located on the surface of erythrocytes. In Europe **85 % people have this factor**, in **15 % it is absent**. People whose blood has the Rh-factor are called rhesus- positive (Rh+), those who do not have it are rhesus-negative (Rh-) (Figure).



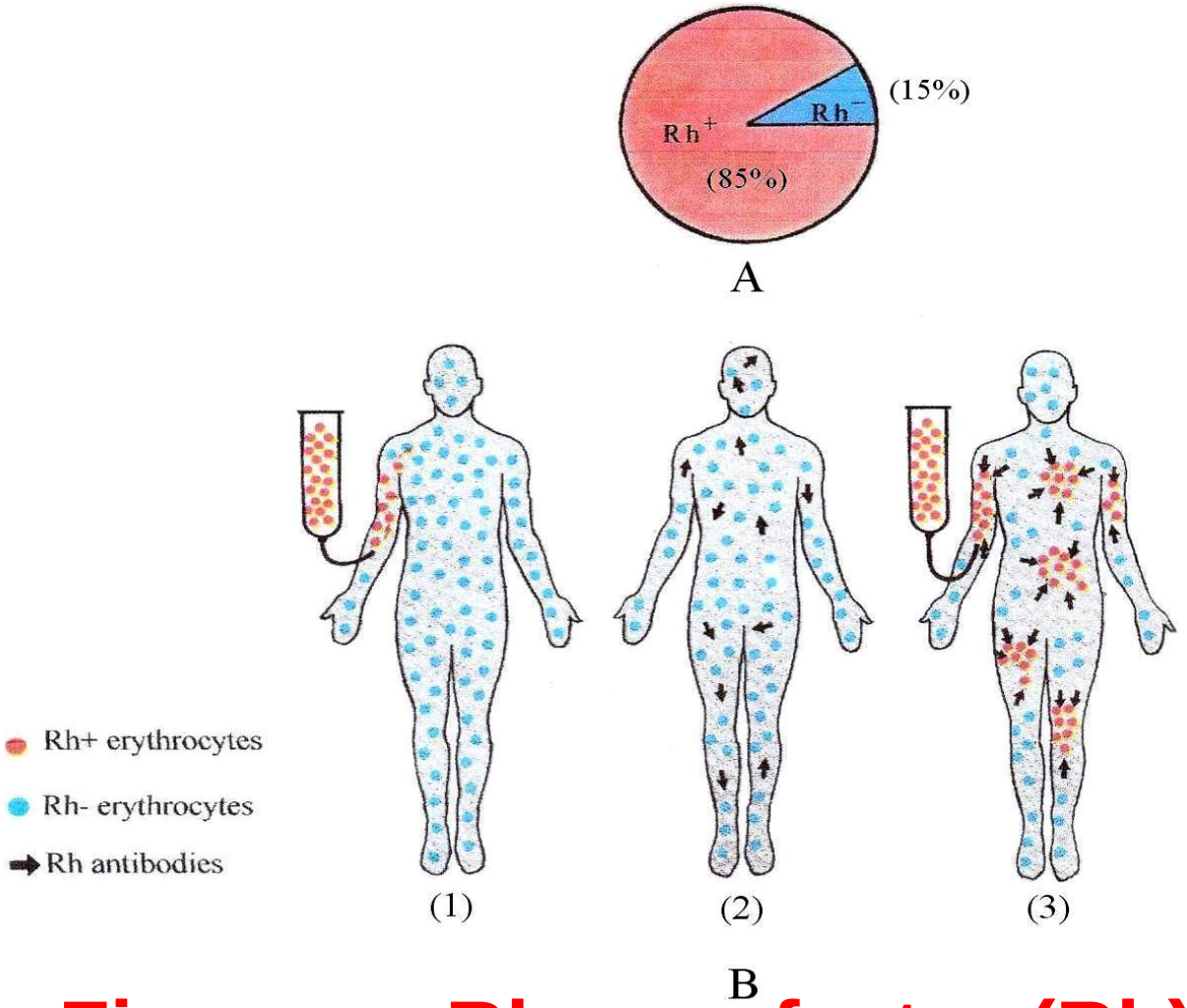


Figure — Rhesus factor (Rh)

Notes: A — frequency of Rh+ and Rh– people. B — «Rhesus conflict»:
(1) — transfusion of Rh+ blood to a Rh– recipient.
(2) — the production of Rh antibodies in the organism of the recipient.
(3) — the second transfusion of Rh+ blood to the Rh– recipient causes agglutination.

The Rh-factor includes 6 basic antigens: C, D, E, c, d, e. Among them, the most powerful is D (it possesses high antigenic properties).

In Rh^+ blood transfusion to a Rh^- person the agglutinins are formed in the recipient slowly (within several months). That is why a single transfusion does not lead to any hemotransfusion complications. A repeated transfusion causes **rhesus-incompatibility (rhesus-conflict)** with serious complications: formation of erythrocyte conglomerates and their hemolysis, intensive intravascular blood coagulation, many organs are affected, the kidneys in particular.

It is important to take into account the rhesus-factor of a woman during pregnancy. If a fetus inherits the Rh-positive blood from its father, and the mother is Rh-negative, the mother's organism develops antibodies to Rh^+ erythrocytes of the fetus (Figure). Rh formation in the fetus starts only from the 3^{rd} month of the antenatal period and becomes active by the end of the pregnancy. During this period the mother`s organism has no time for Rh sensitization.

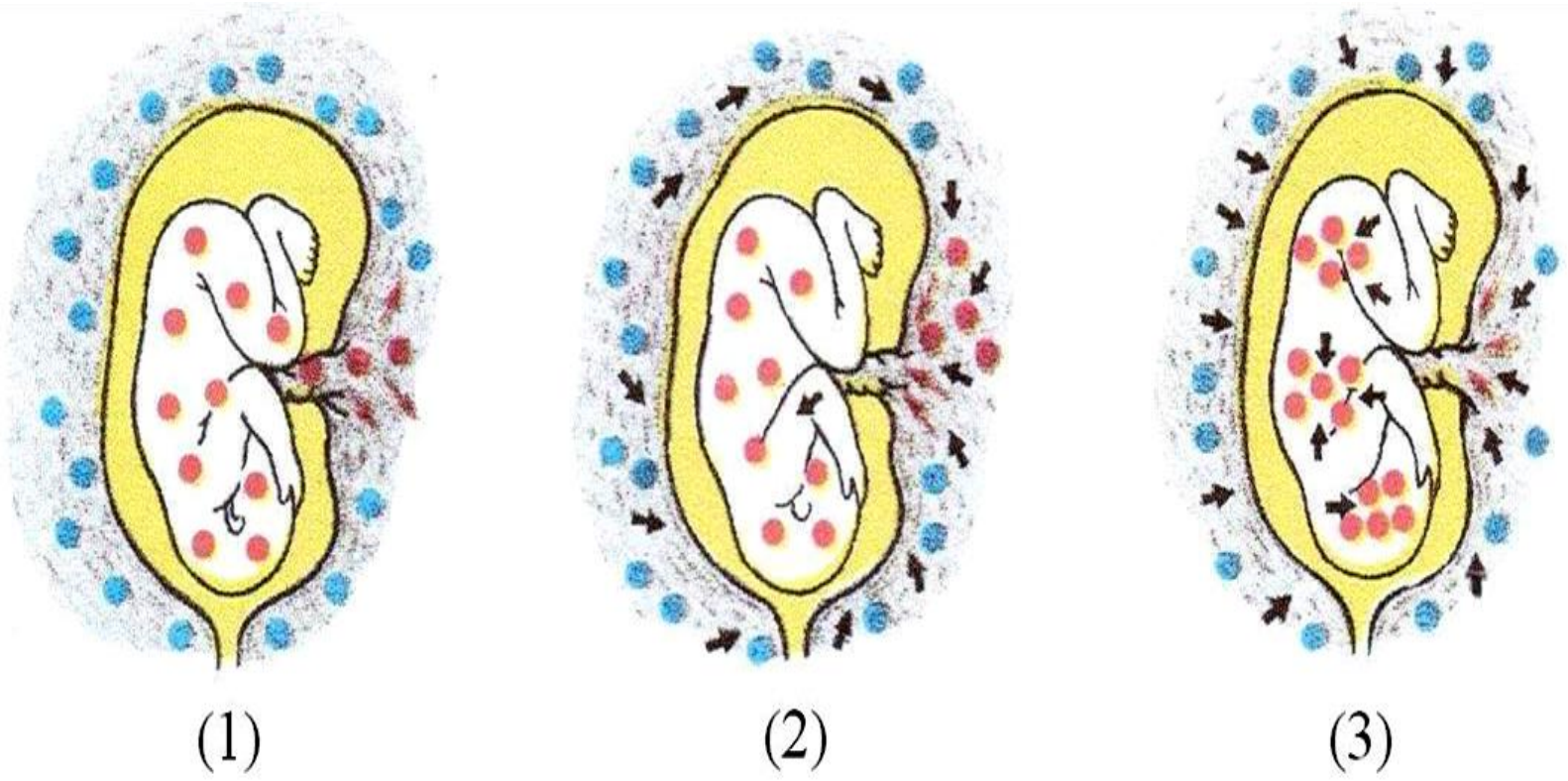


Figure — Rh incompatibility between a Rh-negative pregnant woman and a Rh-positive fetus

Notes: 1 — immunization of the Rh- mother by the Rh+ erythrocytes of the fetus.

2 — production of Rh antibodies in the mother`s organism.

3 — agglutination of the Rh+ erythrocytes of the fetus by the mother`s antibodies.

The formation of antirhesus-agglutinins lasts slowly (3–5 months). Therefore, pregnancy complications usually do not occur during an Rh-negative woman’s first pregnancy with an Rh-positive fetus, because her body does not have a chance to develop a lot of antibodies. Rh incompatibility develops in a second and further pregnancies (also Rhesus disease or Rh factor disease), which causes the antibodies in the mother`s blood attack and destroy the fetus`s erythrocytes, which can result in its severe health problems or even intra-uterine death.

The development of antibodies in Rhesus-negative women can be prevented by injections of immune serum containing ‘anti-D gamma globulin’ (anti-D administration) instantly after the delivery of a rhesus-positive baby. Anti-D gamma globulin’ destroys fetal Rh^+ erythrocytes which got into the mother`s blood, i.e. the factor causing antibody formation and their accumulation is prevented.

Regulation of the blood system

Neuro-humoral regulation of erythrogenesis. For normal erythrogenesis process (erythropiesis) adequate nutrition with sufficient amount of ***ferrous lactate*** is necessary. It is the limitation factor, and deficiency results in anemia.

Erythropoietins are manufactured in many organs (spleen, liver, bone marrow, salivary glands) but mostly in the kidneys.

The basic starting mechanism is **hypoxia** or blood loss.

Kastle's antianemic factor is the complex of vitamin B_{12} (external factor) and gastromycoproteid in the stomach (internal factor). This complex comes into the liver and from it into the bone marrow.

Ascorbic acid promotes absorption of ferrous lactose into the intestines converting it from Fe^{+++} into Fe^{++}. The daily need in ferrous lactose for normal erythrogenes is 20–25 mg.

The products of erythrocyte destruction stimulate hemopoiesis (autoregulation). The number of destroyed erythrocytes is equal to that of newly formed erythrocytes (self-control).

Hormones. **Androgens** increase and estrogens decrease erythropiesis. That is why the count of erythrocytes in men's blood is higher than in women`s.

Erythropiesis is stimulated by **adrenalin, thyroxin, somatotropic hormone.**

The role of the nervous system. The stimulation of the nerves going to the bone marrow enforces erythropiesis. Nervous and hormonal factors affect the red bone marrow through erythropoietins.

The role of the cerebral cortex. It is possible to develop a conditioned reflex resulting in the decreased formation of erythrocytes.

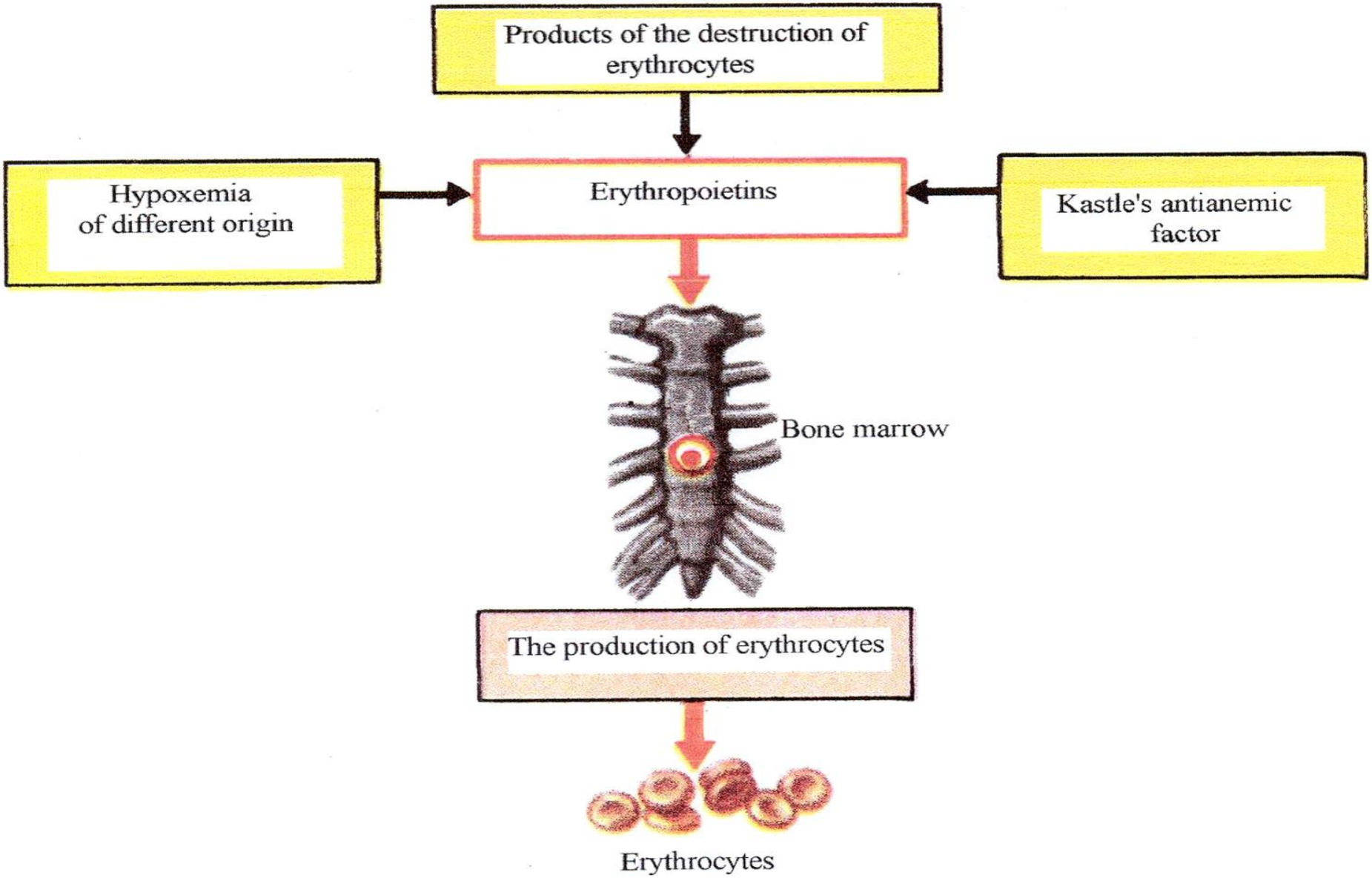


Figure — Factors which stimulate erythropoiesis

Neuro-humoral regulation of leukopoiesis.

1. Stimulation of leukopoiesis *by the products of leukocyte destruction* (self-control). The more the destruction is, the more leukocytes are produced.

2. *Stimulation by tissue destruction products*, especially by their proteins.

3. *Stimulation by microbes and their toxins*.

4. Stimulation of leukopoiesis by leukopoietins.

5. Stimulation of leukopoiesis by the colony-stimulating factors. These factors are produced by macrophages, endothelium and a number of other immune cells. The colony-stimulating factor (GM-CSF) stimulates both granulocyte and monocyte production; the other two, namely the granulocyte colony-stimulating factor (G-CSF) and monocyte colonystimulating factor (M-CSF), stimulate granulocyte and monocyte production, respectively.

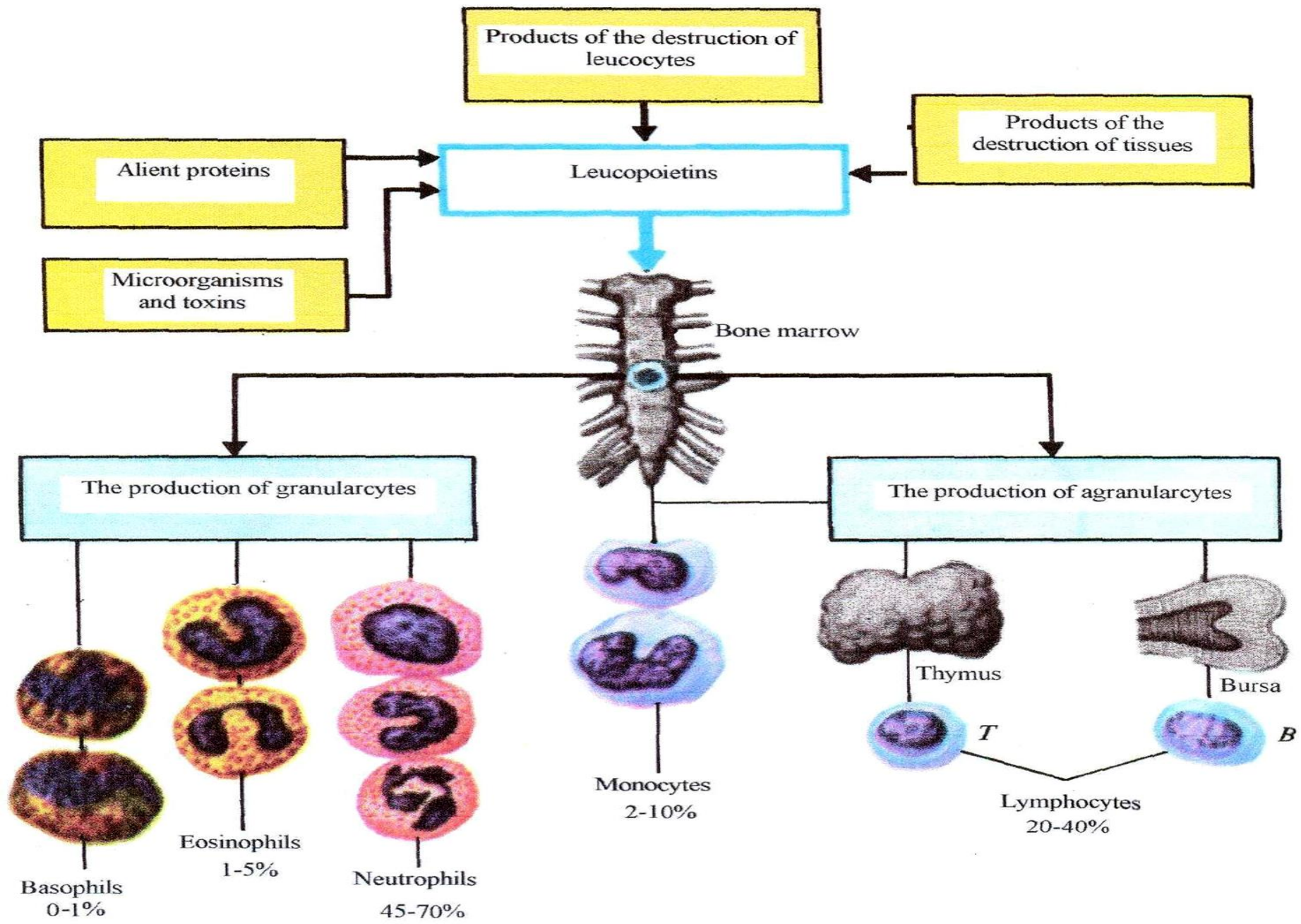


Figure — Factors which stimulate leukopoiesis

6. Interleukins (IL) are produced by leukocytes (mainly by T-helper lymphocytes and activated macrophages) and promote the development and differentiation of leukocytes and hemopoetic cells. For example, IL-3 stimulates the production of granulocytes and monocytes, IL-5 regulates the growth of eosinophils, IL-2, IL-4, IL-6 and IL-7 regulate growth and differentiation of T- and B-Lymphocytes.

7. *Hormones.* The release of adrenalin and hydrocortisone results in leukocytosis due to the release of neutrophils, monocytes, and lymphocytes from the blood depot (leukocytosis caused by stress, emotional excitation).

The role of the nervous system. The stimulation of the sympathetic nervous system increases the number of neutrophils. The stimulation of the vagus reduces the number of leukocytes in peripheral blood.

Thrombocytopoiesis

Thrombocytopoietins can be of **short or long action**. The former are produced in the spleen and stimulate the release of thrombocytes into the blood. The latter are contained in blood plasma and stimulate the formation of thrombocytes in the bone marrow.

Thrombocytopoiesis increases after blood loss. The number of thrombocytes can increase within a few hours and can exceed their normal number twice.

Blood-substituting solutions

In hemodynamic disorders caused by blood loss, apart from blood transfusion various blood-substituting solutions (blood fluids) are used

Blood-substituting solutions should conform with the following requirements:

- Their physico-chemical properties should be close to the basic parameters of blood (isotonic, isoionic, etc.).
- Absence of the influence on the basic biological properties of blood.
- Absence of toxicity.
- Long-term stay in the vascular system.
- It is possible to maintain sterilization and long storage of solutions.
- They should not produce sensitization and their reintroduction should not lead to anaphylaxis.

Salt solutions **(Saline solution, Ringer-Locke solution** and others) have a low molecular weight, compared with protein and colloid solutions and thus are quickly removed from the bloodstream, i. e. they can replace the volume of the lost blood within a short period of time (dehydration, acute blood loss, intoxication etc).

The drawback of **synthetic *colloid* solutions (plasma substitutes)** is their ability to induce allergic responses.

Protein **preparations:**

- Native, preserved and fresh frozen plasma (FFP).
- 5 % albumin solution.
- Protein — it is an albuminous preparation of isogenic human plasma.

They have a high molecular weight and are slowly removed from the bloodstream (applied in shock, blood loss, burns, and in the treatment of pathological processes accompanied by dehydration). Their introduction does not cause pathological reactions but bind toxic materials. Their intravenous introduction increases the volume of circulating blood.

Whole blood transfusions are no longer common. The **blood components** *necessary for the organism* (plasma, erythrocyte mass, etc.) are mainly used for transfusions.

Blood components: preserved blood, plasma, erythrocyte mass, washed erythrocytes, leukocytes (fresh), thrombocytes (fresh).