

Pirogov Russian National Research Medical University
Department of General surgery

Transfusion therapy

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Definition

- **Transfusiology** - section of medical sciences (hematology) on the management of the body's functions by acting the morphological composition of blood through the transfusion of whole blood and blood products as well as blood-substituting solutions and other means.
- **Transfusion** - a method aimed to correct the functions of the body through infusion of whole blood and it's components.

History of transfusion: empiric period

- From the ancient times people suggest the blood as a miracle cure.
- The ancient Egyptian army was followed by the herds of sheep whose blood was taken orally in case of bleeding.
- Roman patricians drank the fresh blood of the fallen gladiator, believing in its anti-aging effect.
- Hippocrates recommended to mix the blood of healthy people with biological juices of ill ones and take orally in patients with epilepsy and mental disorders.
- German physician and chemist Andreas Libau in 1615 described in his writings a blood transfusion from one person to another via thin silver tubes, but evidence of the procedure was not found.

History of transfusion: physiologic period

- 1628 - **William Harvey** discovered the circulation laws.
- 1666 - English physiologist **Richard Lower** described a series of experiments on the intravenous administration of various solutions into the bloodstream of dogs using thin silver tubes, including the first successful experience of direct blood transfusion from one dog to another that helped to save her life.
- 1667 - **Jean-Baptiste Denis** in France and Richard Lower in England independently make a record of successful blood transfusions from sheep to the man. JB Denis had saved the life of mentally ill boy suffering from severe anemia due to often medical bloodletting.

History of transfusion: physiologic period

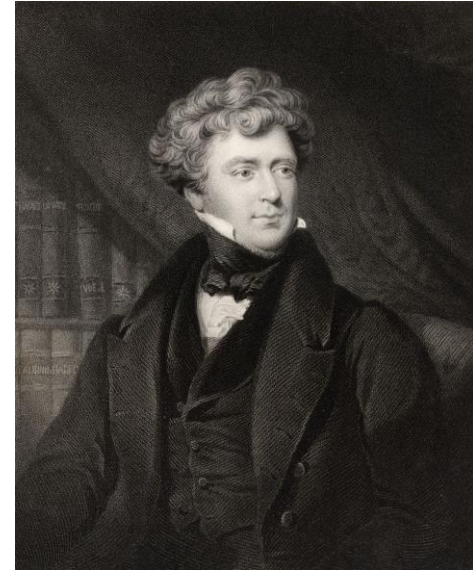
- The other two transfusions from the sheep to the man were successful, but the third experiment led to death of the patient, so the JB Denis was imprisoned.
- 1675 - The Vatican issued an edict prohibiting blood transfusions
- 17th century - a total of 20 blood transfusions throughout Europe



Jean-Baptiste Denis - the personal physician of King Louis XIV, made the first documented successful transfusion of blood from the animal to man

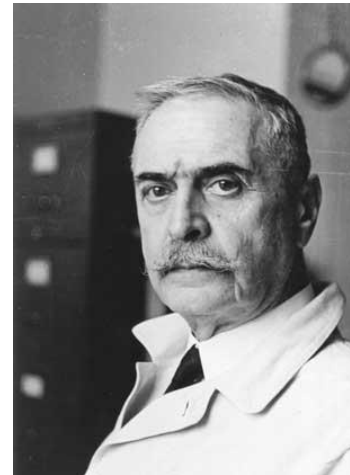
History of transfusion: physiologic period

- 1829 - English physiologist and obstetrician **James Blundell** held a number of successful blood transfusions from one person to another: he with his students transfused the blood taken from relatives to 11 bloodless women in labor. Also, they have documented adverse reactions and suggested the use of some kind of **biological compatibility test** to prevent them. He invented the first machine for transfusion.



History of transfusion: scientific period

- 1901 - Vienna bacteriologist **Karl Landsteiner** discovered the phenomenon of (iso-) hemagglutination and allocated 3 blood groups: A, B, C
- 1902 - Landsteiner officers found a group of people that do not fit into the standard three groups of blood
- 1907 - Czech physician **Jan Jansky** found that the deviants from the scheme of Landsteiner are the independent blood group (gr. 4)
- 1910-1915 – blood stabilization by sodium citrate



Karl Landsteiner,
1930 - Nobel Prize in
Physiology



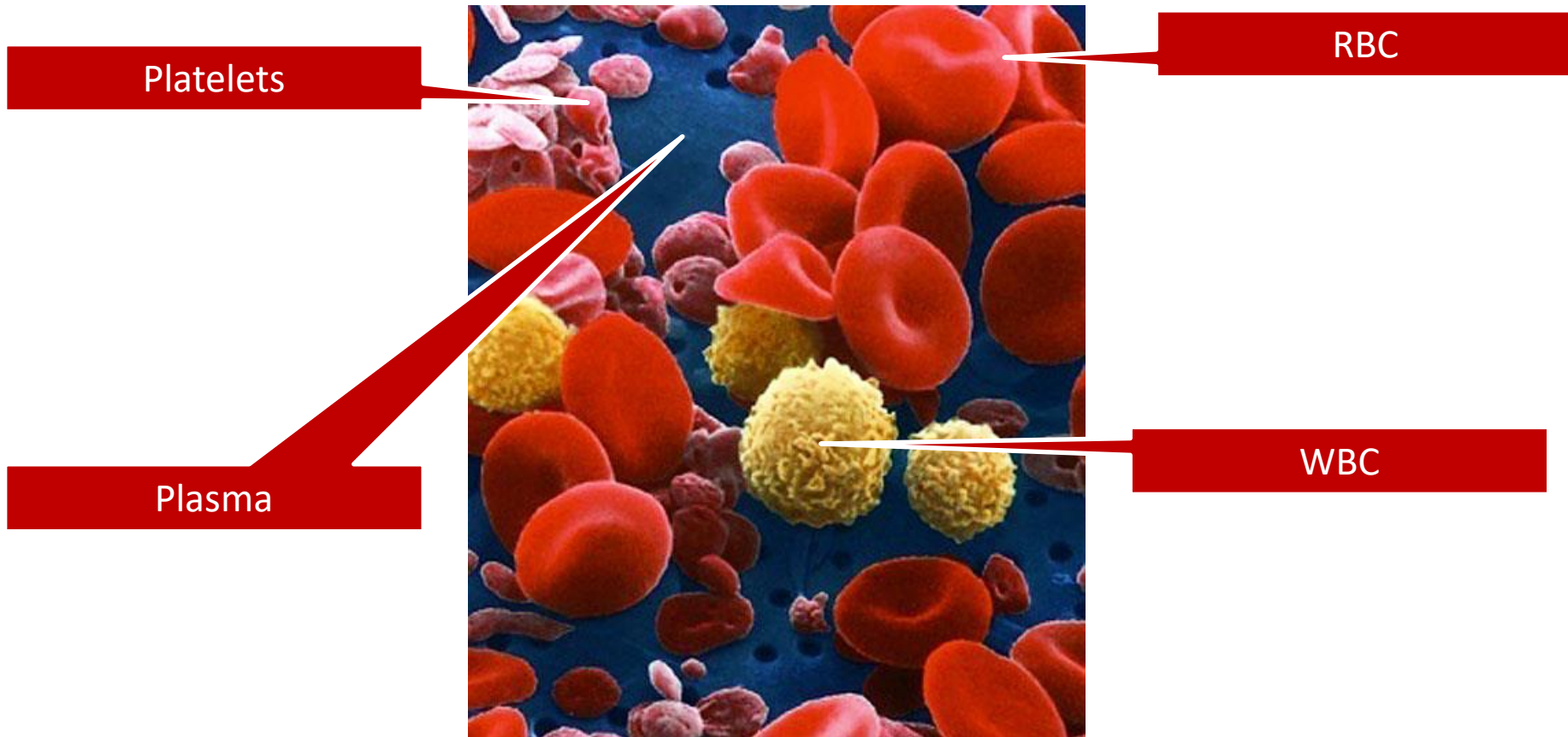
Jan Jansky



History of transfusion: scientific period

- 1919 - VE Shamov, EN Elansky, IR Petrov received the first isohemagglutination serum for the determination of blood groups by ABO system
- 1927-29 - Karl Landsteiner and his students **A. Wiener** and **F. Levin** discovered antigen system MN and P on the RBC.
- 1929 - in Moscow, created the world's first Institute of Blood Transfusion and Blood transfusion service
- 1939-42 - **Alexander Wiener** with the participation of Karl Landsteiner discovered The Rh antigen of RBC
- Active investigating of blood antigens worldwide

Blood antigens



Today there are more than 500 blood antigens, forming more than 40 antigenic systems

Blood group



- hereditary determined combination of antigens on the surface of the blood cells and in plasma, as well as the corresponding antibodies in plasma, which are formed by 3-4th month of the fetal development and do not change throughout life.
- infinite number of antigen-antibody combinations, the same blood group can only have persons with identical genotype (monozygotic twins)

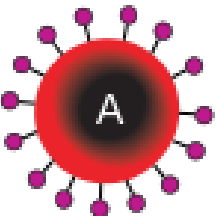
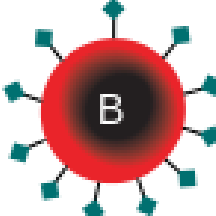
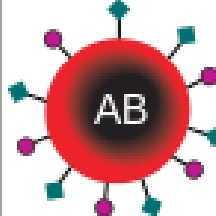
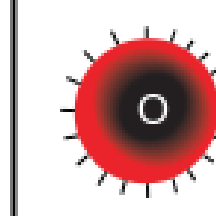
From a clinical point of view the main importance have only a few antigenic system:

- ABO
- Rh-factor (CcCwEeD)
- Kell (QC)

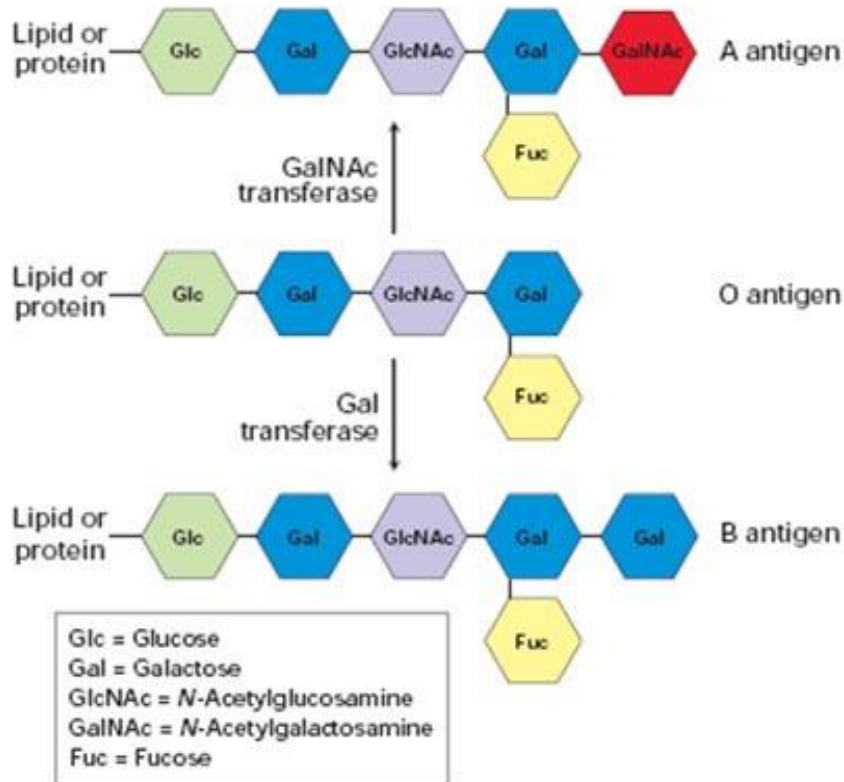
From a clinical point of view, the blood group is a combination of RBC antigen systems ABO, Rh (and Kell) and corresponding plasma antibodies.

ABO system

- Hereditary determined combination of antigens on the surface of RBC (A, B, O), and antibodies in the plasma (anti-A/ α , anti-B/ β)
- 4 combinations: $O\alpha\beta$ (I), $A\beta$ (II), $B\alpha$ (III), AB (IV)
- Meeting relevant antigens and antibodies leads to agglutination and hemolysis

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red Blood Cell	 A antigen	 B antigen	 A and B antigens	None

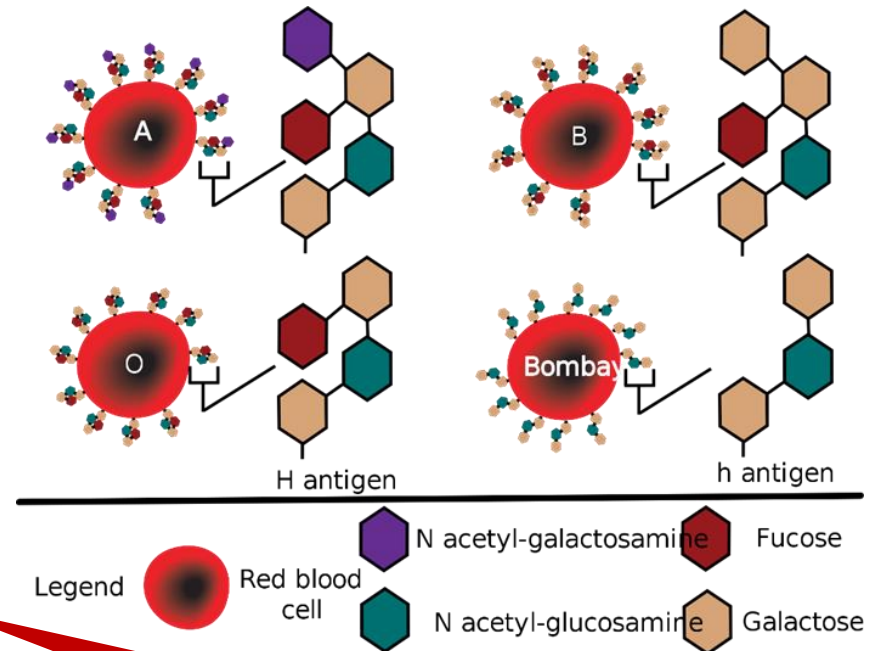
Genetics of blood groups



- Genes A and B encode two different glycosyltransferases that transfer N-acetyl-galactosamine or D-galactose to the common precursor of the erythrocyte antigen (substance H).
- With the O blood group, the gene regions do not encode any enzymes, and substance H with the presence of terminal fucose (O-antigen) is expressed on the surface of erythrocytes.

Antigens ABO

- Antigen A:
 - **Subtype A₁** (88%) - strong, rapidly react with corresponding antibody and gives a visible agglutination,
 - The blood of the A₁ rarely contains of anti-A₂ antibody (α_2)
 - **Subtype A₂** (12%) - a weak, slowly react with corresponding antibody and gives a delayed agglutination
 - Blood A₂ often contains of anti-A₁ antibody (α_1): A₂ $\beta\alpha_1$ or A₂B α_1
- The anti-B antibody is clinically homogeneous
- Substance H antigen and O - precursor of all antigens

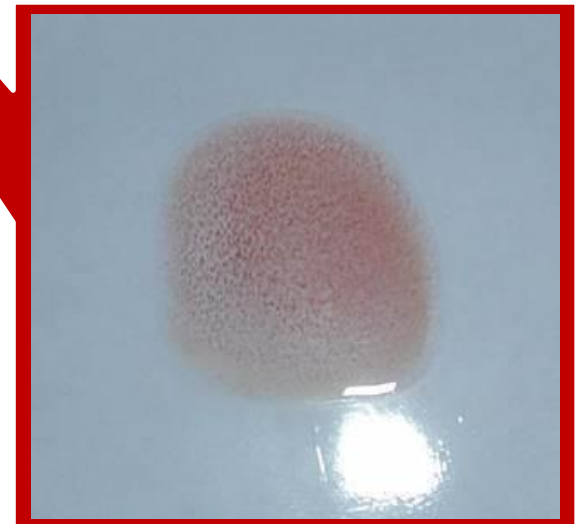
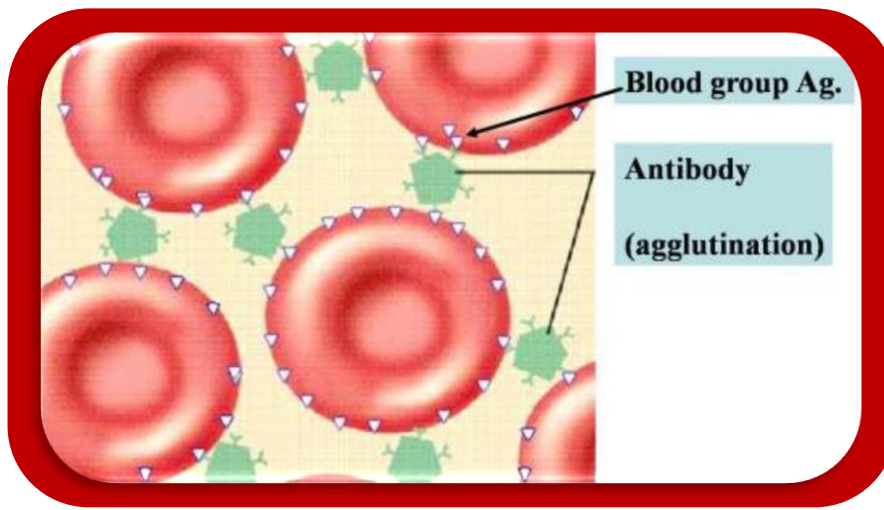
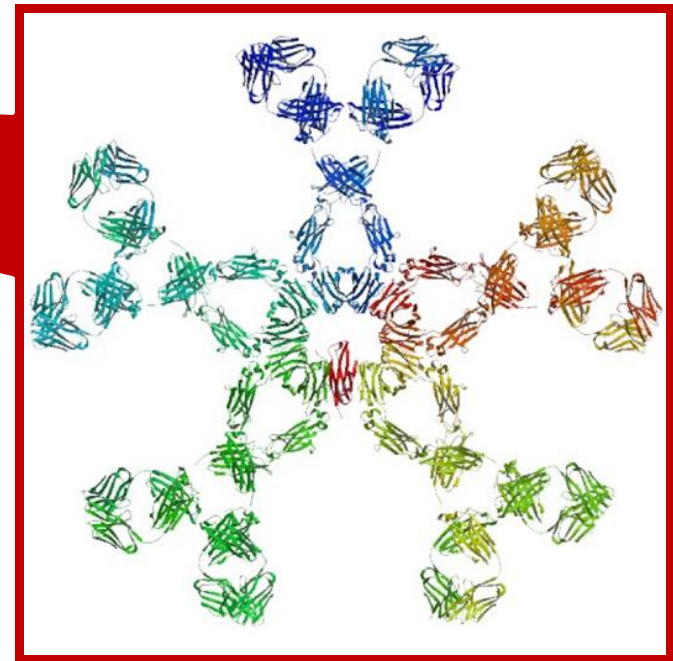


Blood group A₂: later gives a visible agglutination in the test, so it is associated with a high risk for error; Transfusion of A₁ blood to the A₂ recipient may lead to hemolysis by the presence of α_1 in 20% of cases, so individual compatibility test is required!

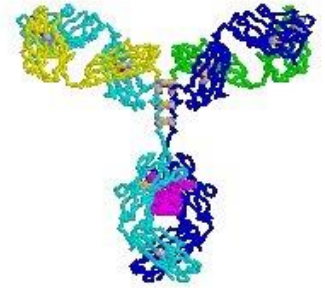
Bombay phenomenon - a rare blood type, at which RBC have no A, B, O and H antigens but anti-A, -B, -O, -H are present in plasma

Anti -A, -B Antibodies

- **IgM**
- **Congenital**
- **Complete** - give visible agglutination
- **Cold** - the optimum temperature for the reaction - 19-25 degree of Celsius
- **Do not cross the placenta**



Resus factor system



Antigens:

- First discovered in rhesus monkeys
- **85%** of people are Rh positive
- Contain of a heterogeneous group of RBC antigens in various combinations: **Cc Cw D Ee**
- **D** antigen has the most antigenicity and immunogenicity
- **Cw - Willis antigen** is a variant of antigen C that has a high immunogenicity like the D one, but rare expression
- To date, the blood of donor and the recipient required typing for all Rh antigens, except the emergency situations when it is allowed to type only D

Antibodies:

- **IgG**
- **Acquired:** produced after the first meeting with the antigen
- **Incomplete:** require special environmental conditions to detect agglutination
- **Warm:** the optimum temperature for the reaction is 37-40 degree of Celsius
- **Crosses the placenta**

Traditionally, Rh positive blood group is meant the presence of antigen D; but the complete formula of Rh-positive blood is as follows:

C + c + Cw- D + E- e +

Kell (-Cellano) antigen system

- The second after Rh antigen system of RBC, causes the development of post-transfusion complications
- Named in honor of patients whose antigens were first discovered: Ms. Kellacher and Ms. Cellano
- Presented with two antigens K (K_1 , Kell), and k (K_2 , Cellano)
- The incidence in the population - 10%
- Antibodies: acquired IgG, appearing after the first exposure of the antigen
- Every tenth "blind" blood transfusion - a transfusion of Kell (+) blood to the Kell (-) recipient
- Since 2005, subjected for mandatory determination

Blood typing

First choice:

- Monoclonal antibodies

Second choice (with uncertain results):

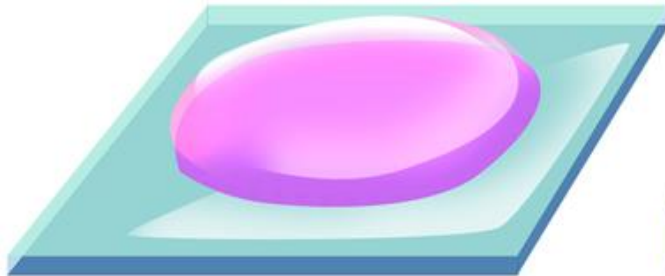
- Standard serum
- Standard erythrocytes
- Indirect Coombs test

- Antigen-antibody reaction
- Visible agglutination of red blood cells
- The correct ratio of antigen and antibody (1:10)
- Optimal temperature conditions
- Optimal environment
- The use of additional conditions for the weak antigens (colloid solution, antiglobulin antibodies)

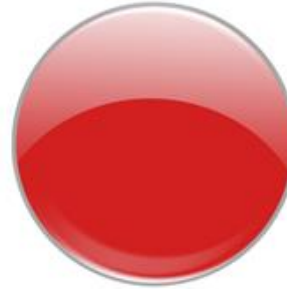
Determining of antigen-antibody interaction

S
L
I
D
E

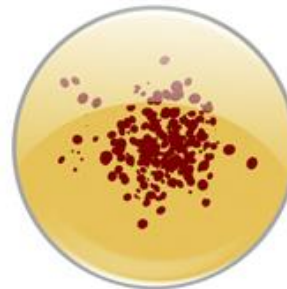
Drop of
blood



Glass slide with
drop of serum



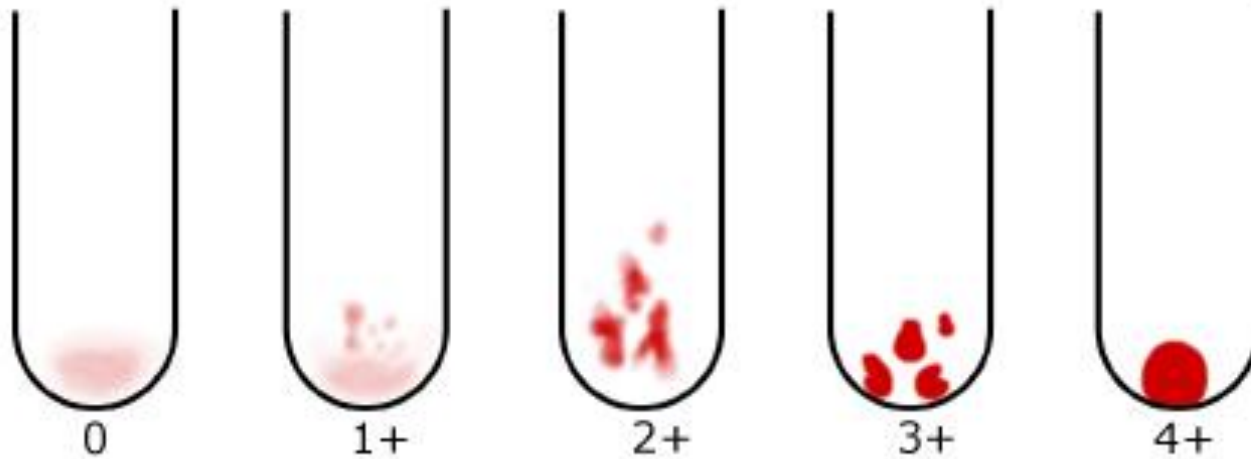
Negative agglutination
reaction



Positive agglutination
reaction (visible to the
naked eye RBC
conglomerates)

Determining of antigen-antibody interaction

A Tube method



Tube (liquid phase) testing is carried out in a test tube to which RBC and antibodies (serum) have been added in a specific ratio. Agglutination looks like an RBC aggregates on the bottom of tube.

Determining of RBC agglutination

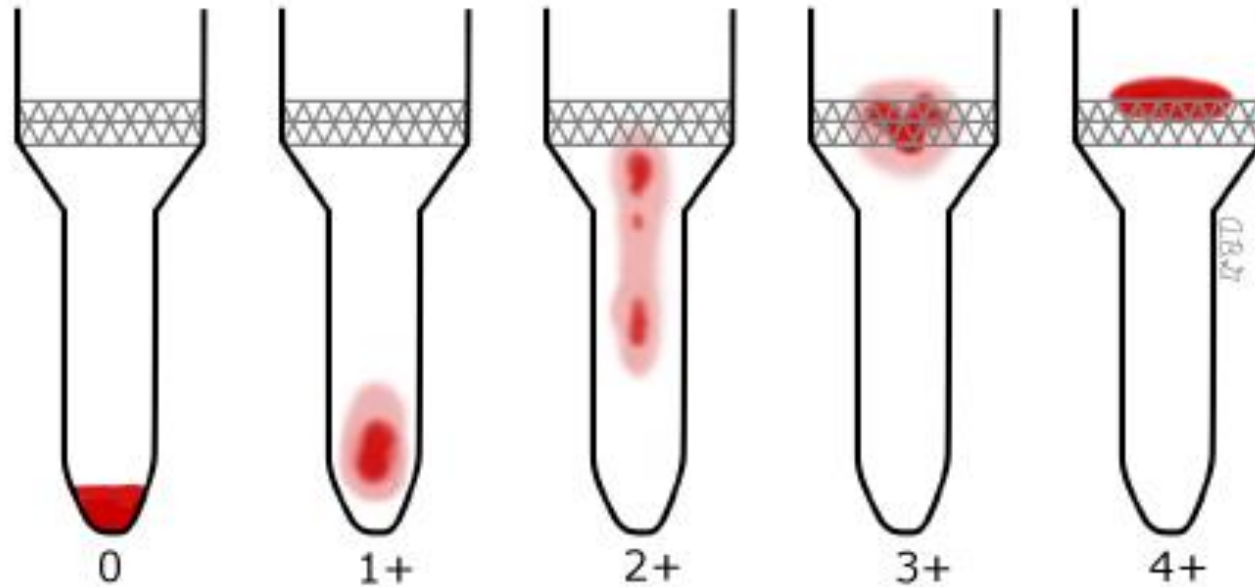
B Solid phase method



One component (antigen or antibody) is immobilized in a solid matrix affixed to a microplate well. Reaction of testing RBC with affixed antibodies produce a dispersed pattern within the well. To reveal the reaction of testing serum with RBC antigens affixed to a well special RBCs coated with anti-IgG should be added

Determining of RBC agglutination

C Column method



Column agglutination techniques employ glass beads or gel to separate agglutinated RBCs from non-agglutinated RBCs following incubation of antibodies or plasma/serum with RBCs.

Monoclonal antibodies

- Complete antibody of IgM class
- Obtained by sensitization of murine lymphocytes against specific antigen (A, B, D, E, e, C, c, Cw, K, k), followed by hybridization with lymphoma cells
- Antibody solution giving visible agglutination to a specific antigen
- “Super” antibody



Blood typing with ABO monoclonal antibodies

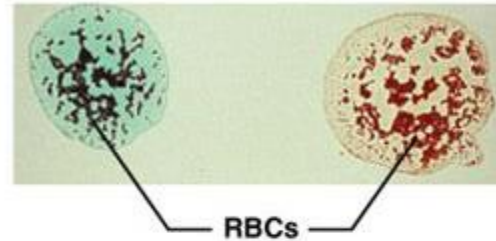
Blood being tested

Serum

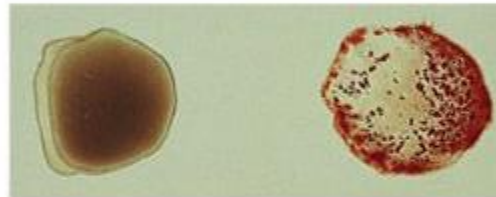
Anti-A

Anti-B

Type AB (contains
agglutinogens
A and B)



Type B (contains
agglutinin B)



Type A (contains
agglutinin A)



Type O (contains
no agglutinogens)



Blood typing with monoclonal antibodies



Blood typing with standard serums and RBC

- The standard serum and RBC from a known set of antigens and antibodies

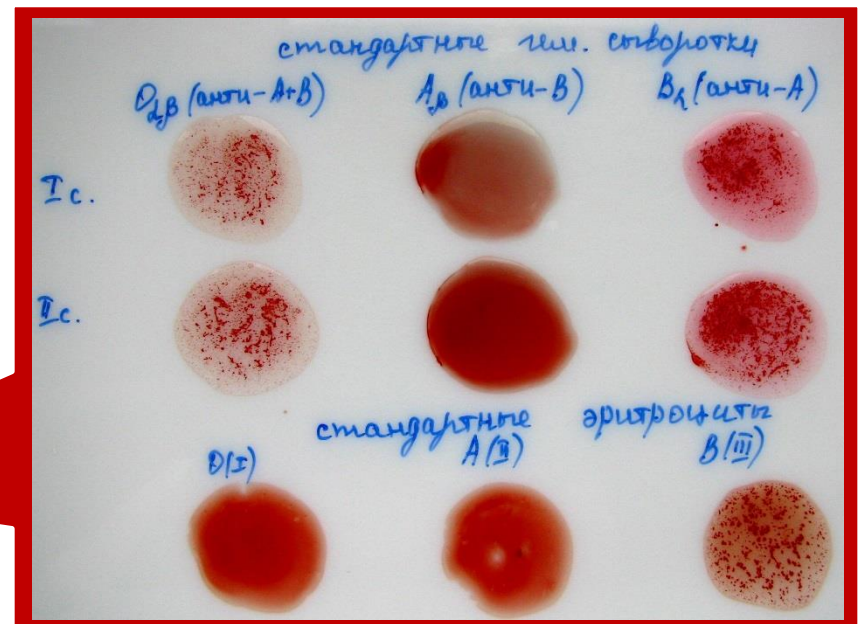
- **Serum:**

- O (I) $\alpha\beta$
- A (II) β
- B (III) α
- AB (IV) - control

- **Red blood cells:**

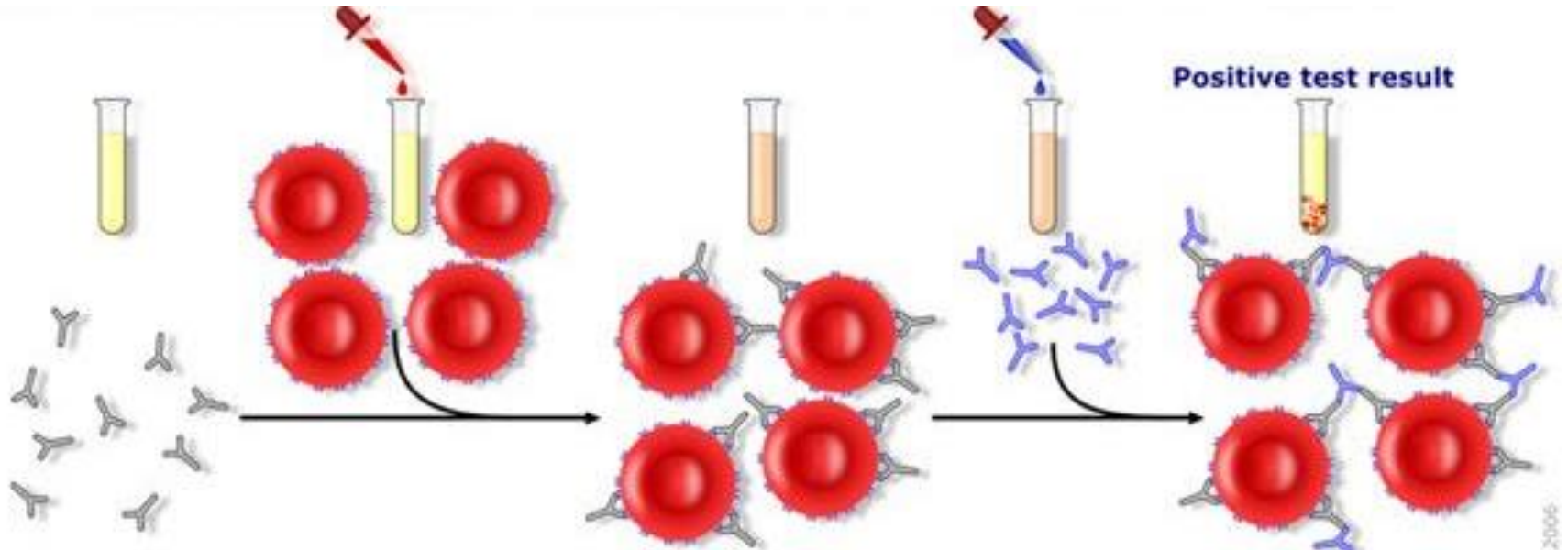
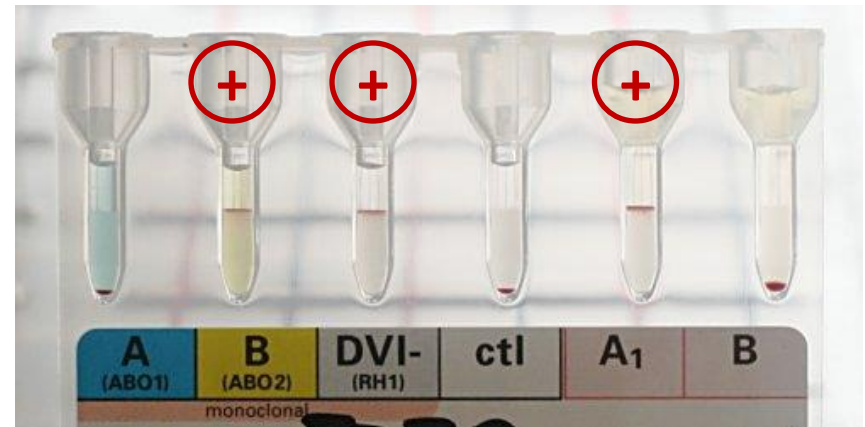
- O - control
- A
- B
- AB

- Sharing - cross method



Indirect Coombs test

- A method of determining in vitro of antibodies and antigens
- The method for the compatibility testing



Typical errors in blood typing

- **Technical errors:**

- Wrong order of the reactants
- Using of low-quality or expired reagents, improper storage, breach appearance
- Failure to comply with the temperature conditions
- Poor room lighting
- Violation of the ratio of reactants and the test RBC
- Lack of follow-up
- No addition of saline (nonspecific aggregation)

- **Errors associated with the presence of hard to define blood groups:**

- Subgroups of blood
- Non-specific agglutination of red blood cells
- Blood chimeras
- Other features

Legal regulation of blood transfusion in Russia

- **Preparation and use of blood components is regulated by MoH and the Federal Law of the Russian Federation:**
 - Russian Ministry of Health Order (Ministry of Health of Russia) on April 2, 2013 N 183n Moscow "On approval of rules for the clinical use of blood and (or) its components"
 - Federal Law of the Russian Federation dated 20 July 2012 N 125-FZ "On the donation of blood and its components"
- **Errors during transfusion entail criminal responsibility of the physician:**
 - Causing grievous bodily harm by negligence committed as a result of improper performance of their professional duties, shall be punished by **imprisonment for up to 4 years**, or imprisonment for up to one year with deprivation of the right to engage in medical practice after serving the main punishment for up to 3 years (with or without any) (ch. 2, Art. 118 of the Criminal Code)

International guidelines

- American Society of Anesthesiology
- British Committee for Standards in Hematology
- Australian and New Zealand Society of Blood Transfusion
- Eastern Association for Surgery of Trauma (EAST) and the American College of Critical Care Medicine of the Society of Critical Care Medicine (SCCM)
- European Society of Cardiology (ESC)
- Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists
- **AABB** (formerly the American Association of Blood Banks)
- American College of Physician



Principles of blood transfusion

- **Whole blood transfusion** – transfusion of whole blood contains RBC, WBC, platelets and plasma proteins
- **Blood component therapy** – transfusion of those blood components (RBC, WBC, platelets, plasma) critically low level which threatens the life.
- **Restricted blood transfusion** – using lower threshold of blood parameters as an indication for transfusion (eg Hb 7 g/dL over 10 g/dL)
- **Liberal blood transfusion** – using higher threshold of blood parameters as an indication for transfusion (eg Hb 10 g/dl over 7 g/dL)
- Blood component therapy over whole blood transfusion
- Restricted over liberal blood transfusion
- Minimal doses of whole blood and components

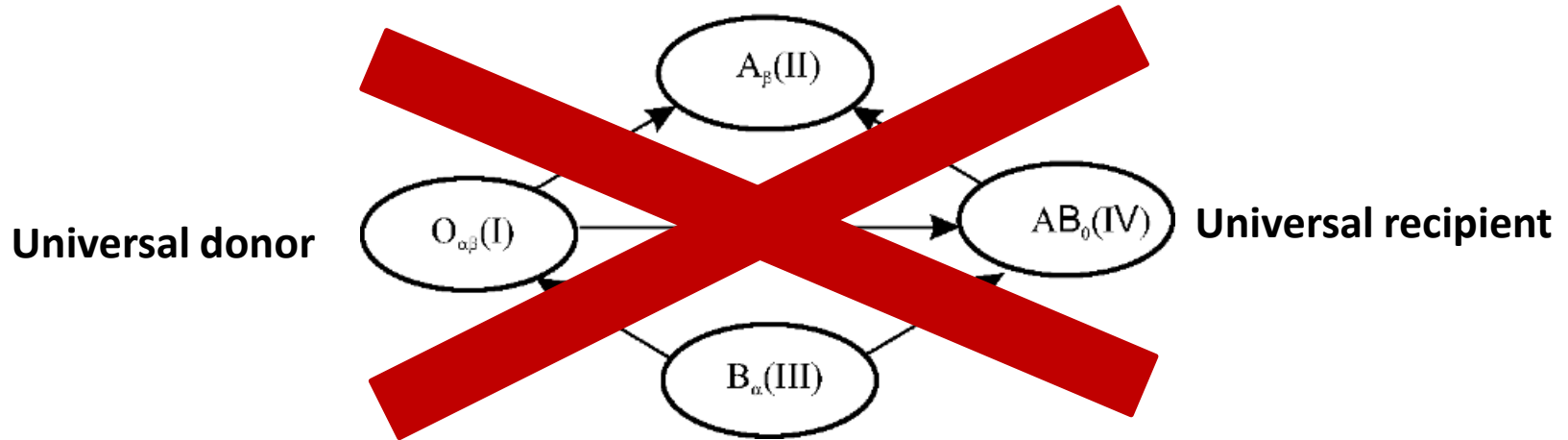
Restricted blood transfusion

- Hb level of 7 g/dL over 10 g/dL in 6264 medical and surgical patients (adults and children):
 - **A 39 percent decrease in the probability of receiving a transfusion** (46 versus 84 percent; relative risk 0.61; 95% CI 0.52-0.72)
 - **Fewer units** (1.19) transfused per patient
 - **A trend towards a lower 30-day mortality** (relative risk = 0.85; 95% CI 0.70-1.03)
 - **A trend towards a lower overall infection rate** (relative risk = 0.81; 95% CI 0.66-1.00).
 - **No difference** in functional recovery, or hospital or intensive care length of stay
 - **No increased risk of myocardial infarction** (relative risk = 0.88; 95% CI 0.38-2.04).

General rules of blood transfusion

- Predominant use of blood component therapy
- Limitations for the whole blood transfusion: vital indication in massive bleeding (Rus) / any massive hemorrhage or continued bleeding (EU, USA)
- Restricted blood transfusion
- Harvesting of the whole blood or blood components from the donor or the patient should be made by the special Transfusion service
- It is advisable to use the whole blood and components harvested from a minimum number of donors.
- Transfusion of the same blood type according to ABO and Rh with the exception of individual cases.
- Patients with a history of transfusion complications, as well as pregnancy, childbirth ended with hemolytic disease, and patients with aplastic syndrome myelodepression are required for individual selection of blood and components.

Ottenberg's rule



- **It should be used only the same-type blood according to ABO and Rh matched by phenotype, except certain situations:**
 - For healthy recipients with blood type A (II) or B (III) in emergent situations in the absence of same-type blood components may be transfused Rh-negative RBC of O (I) type, in recipients with AB (IV) can be transfused Rh-negative RBC components B (III), regardless of the recipient Rh affiliation.
 - In urgent cases the inability to determine the recipient's blood type for life-saving transfusion may be used RBC components of O (I) Rh-negative type in an amount of not more than 500 ml, regardless of the recipient blood type and Rh affiliation.
 - In urgent cases, in the absence of same-type fresh frozen plasma may be used plasma of AB (IV) type for the recipient with any blood type.

General rules of blood transfusion

- Transportation of blood and components can be carried out only by medical staff, responsible for compliance with the rules of transportation.
- Could not be utilized the results of blood typing that were obtained in other medical institution.
- The informed consent for blood transfusion must be signed by the patient before transfusion.
- It is forbidden to make transfusion of blood and components to multiple recipients from one container (unit).
- Blood transfusion is an obligation for the treating doctor or doctor on duty, who passed a special training, during surgery – for the surgeon or anesthesiologist, not directly involved in the surgery, as well as transfusiologist.

Blood transfusion step by step

1. Indications and contraindications for blood transfusion, history of blood transfusions and previous pregnancies, choice transfusion units
2. Getting the transfusion unit from the storage and assessing it's suitability for transfusion
3. Donor blood typing according to ABO, Rh and **phenotyping by CcEeCwKk**
4. Recipient blood typing according to ABO, Rh and **phenotyping by CcEeCwKk**
5. **Antibody screen in the recipient**
6. Tests for individual compatibility
7. **Biological test for individual compatibility**
8. Blood transfusion
9. Monitoring of the patient for 24 hours, evaluation of blood transfusion
10. Filling the medical records

Obligatory in children under 18 years old, women of childbearing age and pregnant, recipients with a history of transfusion complications or history of RBC antibodies, recipients that need a multiple (including repeated) transfusions of blood and (or) components

If unable to determine the antigens C, c, E, e, Cw and K, and k should be transfused same-type blood and components according to ABO and Rh antigen D.

Step 1: indications for blood transfusion

- **Whole blood:** massive bleeding in patients who are hemodynamically unstable
- **RBC units:** acute bleeding in patients who are hemodynamically stable, chronic anemia
- **WBC units:** leucopenia, agranulocytosis
- **Platelets unit:** thrombocytopenia
- **Plasma unit:** coagulopathy, active bleeding

Whole blood and RBC units

- **Whole blood:**

- Oxygen transportation
- Volume expansion
- Colloid osmotic pressure
- Hemostatic proteins

- **RBC units**

- Oxygen transportation

ACUTE BLEEDING

CHRONIC ANEMIA

The combined 30-day in-hospital mortality for patients with various postoperative hemoglobin levels



Indication for RBC transfusion in Russia

- Massive blood loss (25-30% of blood volume), accompanied by a decrease in hemoglobin levels **below 7-8 g/dL** and a hematocrit below 25% and the occurrence of circulatory disorders.
- Chronic anemia - only for the correction of the major symptoms caused by anemia and can not be the main pathogenetic therapy.

International indications for RBC and whole blood transfusion

Acute massive bleeding with hemodynamic instability – no threshold

Thresholds for other clinical situations

Condition	Hgb threshold for transfusion
Symptomatic patient*	10 g/dL
Hospitalized patient	
Preexisting coronary artery disease	8 g/dL
Acute coronary syndromes	8 to 10 g/dL
Heart failure	7 to 8 g/dL
Intensive care unit (hemodynamically stable)	7 g/dL
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL
Non-cardiac surgery	8 g/dL
Cardiac surgery	7 to 8 g/dL
Ambulatory outpatient	
Oncology patient in treatment	7 to 8 g/dL
Palliative care setting	As needed for symptoms; hospice benefits may vary

*Symptoms of anemia include symptoms of myocardial ischemia, orthostatic hypotension or tachycardia unresponsive to fluid replacement.

RBC units

- **Packed red cells:** the red cells from a donor unit are concentrated to a hematocrit of about 75%, and the volume is made to 200 ml. Storing red cells (just above freezing) allows survival for 42 days but, unfortunately, decreases the 2,3-DPG and ruins the platelets and neutrophils. Giving packed red cells is the fastest way to increase the oxygen-delivering capacity of the blood. **A unit of whole blood or packed red cells will raise the hematocrit by 3% and the haemoglobin by 1 g/dL.**
- **Washed red cells:** RBCs are washed with sterile saline using machines specially designed for this purpose. These washed RBCs are suspended in sterile saline, usually at hematocrits of 70–80%, with a volume of approximately 180 ml. **Saline washing removes all but traces of plasma (98%), reduces the concentration of leukocytes and removes platelets and cellular debris.**
- **Irradiated red cells:** packed red cells are gamma radiated to kill the lymphocytes. **The lack of T-cells prevents donor vs. host disease.** They are used for severely immunocompromised patients, lymphoma patients, stem-cell/marrow transplants and unborn children undergoing intrauterine transfusion.
- **Leukoreduced red cells** (“filtered” and/or “washed” red cells). These are packed red cells from which 99.9% of the white cells are filtered out (pre- or post-storage) or removed by freezing/thawing/washing. The use of “Leuko Poor filters” is becoming very popular. **These reduce (but do not eliminate) the risk of cytomegalovirus (CMV), Epstein-Barr, human T-lymphotropic virus (HTLV) infections and febrile reactions.**

Indication for using of Leukoreduced red cells

- Chronically transfused patients
- Patients undergoing cardiac surgery
- All potential recipients of solid organ or hematopoietic cell transplants
- Patients with solid organ or hematopoietic cell transplants
- Patients with previous febrile nonhemolytic transfusion reactions
- CMV seronegative at-risk patients for whom seronegative components are not available

Fresh frozen plasma

Indications for transfusion of fresh frozen plasma:

- **DIC**,
- **Acute massive blood loss** (more than 30% of blood volume) with the development of hemorrhagic shock and DIC;
- **Hepatic disease** associated with decreased production of plasma coagulation proteins and their deficiency in the circulation;
- **Overdosing** of VKA anticoagulants
- **Coagulopathy** due to deficiency of plasma physiological anticoagulants (AT-3, Proteins C, S)
- Therapeutic plasmapheresis

Not less than 1000 ml

Not less than 25-30% of total infusion volume (800-1000 ml)

Initially - 15 ml/kg of body weight with next transfusion of 5-10 ml/kg of body weight after 4-8 hours

The same-type of ABO and Rh (if more than 1000 ml)

Cryoprecipitate

- The plasma component containing "heavy" clotting factors:
 - **Factor VIII (100 IU)**
 - Fibrinogen
 - vWF
 - Factor XIII
 - Fibronectin
- Indications:
 - Hemophilia Type A
 - Low levels of fibrinogen
- Requires ABO compliance

Prothrombin Complex Concentrate (PTC)

- Plasma derivate
- Contains Vit-K-depending clotting factors
 - 3-component: II, IX, X
 - 4-component: II, VII, IX, X
 - Activated: II, VIIa, IX, X
- Additionally:
 - AT-3,
 - Proteins C и S
 - Heparins
- Indication:
 - VKA associated coagulopathy
 - Bleedings on DOACs

Platelet concentrate

Indications:

- Acute bleeding and increased bleeding risk in thrombocytopenia (usually at the level of platelets of 20×10^9 or less)
- Limited used for immune thrombocytopenia
- Requires ABO and Rh compliance
- In an emergency situation permitted transfusions O (I) Rh negative cells
- Dosage
- 1 dose contains of $55-60 \times 10^9$ cells per liter and increases the level of platelets in the $5-10 \times 10^9$ per liter
- To restore hemostasis, need to transfuse at least $50-70 \times 10^9$ cells per 10 kg of body weight
- The average dose is $300-500 \times 10^9$ cells per liter - ie 5-7 doses
- Evaluating the efficacy - stop bleeding and increase platelet levels in 18-24 hours

Normal count: $180-320 \times 10^9$

Restriction for surgery: $60-80 \times 10^9$

Spontaneous bleeding 20×10^9 and less

Leukocyte concentrate

- **Indications:**

- Reduction in the absolute number of granulocytes in the recipient of $0,5 \times 10^9$ per liter and lower in the presence of infection, do not respond to antibiotic therapy.
- Neonatal sepsis, uncontrolled antibacterial therapy.

- Requires ABO and Rh compliance

- The criteria for evaluating the effectiveness of transfusions of granulocytes is the positive clinical dynamics: reducing body temperature, reducing intoxication, stabilization of previously disturbed organ functions, but **not the level of white blood cells (granulocytes) in the peripheral blood!**

Step 1: history of blood transfusion

- Indication for compatibility testing and relevant underlying conditions(s) that may need to be considered when selecting blood components for the patient, such as hematologic malignancy, hemolytic anemia, hemoglobinopathy (eg, sickle cell disease or thalassemia), or pregnancy
- History of blood transfusion including red cells, platelets, or plasma; hematopoietic cell transplantation, or solid organ transplantation with incompatible blood groups
- History of RBC antibodies (eg, from previous transfusion testing)
- History of transfusion reaction(s)
- For women of childbearing potential: either current pregnancy, including the approximate gestational age; prior pregnancy; or no future pregnancy possible (eg, patient has had a hysterectomy)
- Urgency of transfusion (eg, active bleeding, routine preoperative testing)
- Special modifications required such as irradiation, leukoreduction, cytomegalovirus-safe products, or other special transfusion requirements

Evaluation of suitability of blood units for transfusion

- The label
 - Donor information
 - Information about the producer
 - Information on blood group
 - Information about infections
 - Information on quarantine
 - Expiration date
- Assessment of packaging tightness
- Macroscopic evaluation of the environment



Step 5: antibody screen in the recipient

- Antibodies that are always considered to be potentially clinically significant include those directed against the following blood group systems (antigens within the system in parentheses): ABO (A, B), Rh (D, C, c, E, e), Duffy (Fya, Fyb), Kidd (Jka, Jkb), Kell (K, k), and SsU (S, s, U).
- Screening methods (recipient's serum + known antigens of RBC):
 - Liquid phase testing (with albumin, PEG, enzymes, low ionic strength saline)
 - Solid-phase adherence method
 - Column agglutination

Compatibility testing (crossmatch)

- **Electronic (or manual) crossmatch**
 - Full phenotyping of RBC with crossmatching according to the main antigen systems
- **Immediate spin crossmatch**
 - Liquid phase testing of recipient's serum and RBC of the donor for agglutination
- **Individual compatibility test on the surface and in the tube**
 - Slide reaction and liquid phase testing of recipient's serum and RBC of the donor for agglutination
- **IgG crossmatch (full crossmatch)**
 - Indirect Coomb's reaction with recipient's serum and RBC of the donor

Compatibility testing (crossmatch)

- For a patient with a **negative** antibody screen and no history of clinically significant antibodies, crossmatching typically is straightforward; RBC unit often can be released to the recipient following an electronic or immediate spin crossmatch.
- For a patient with a **positive** antibody screen or a history of RBC antibodies, additional testing that includes indirect antiglobulin testing (indirect Coombs's testing) is used to ensure that RBCs in the selected unit do not express the antigen(s).
- For a patient whose antibody screen appears inconsistent with the results of the crossmatch, additional testing may be needed to clarify which units are safest for transfusion.

Manual crossmatch

- Transfused RBC must be comparable in terms of the ABO, Rh and phenotype:
 - For heterozygous recipients (Cc, Ee, Kk) compliant consider both heterozygous and homozygous donors: Cc, CC and cc; Ee, EE and ee; Kk, KK and kk respectively. For homozygous recipients (CC, EE, KK) are the only compatible donor homozygous
- The rest of the blood cells must be comparable in terms of the ABO and Rh
- Plasma should be comparable only according to ABO (Rh only for volumes greater than 1 liter)

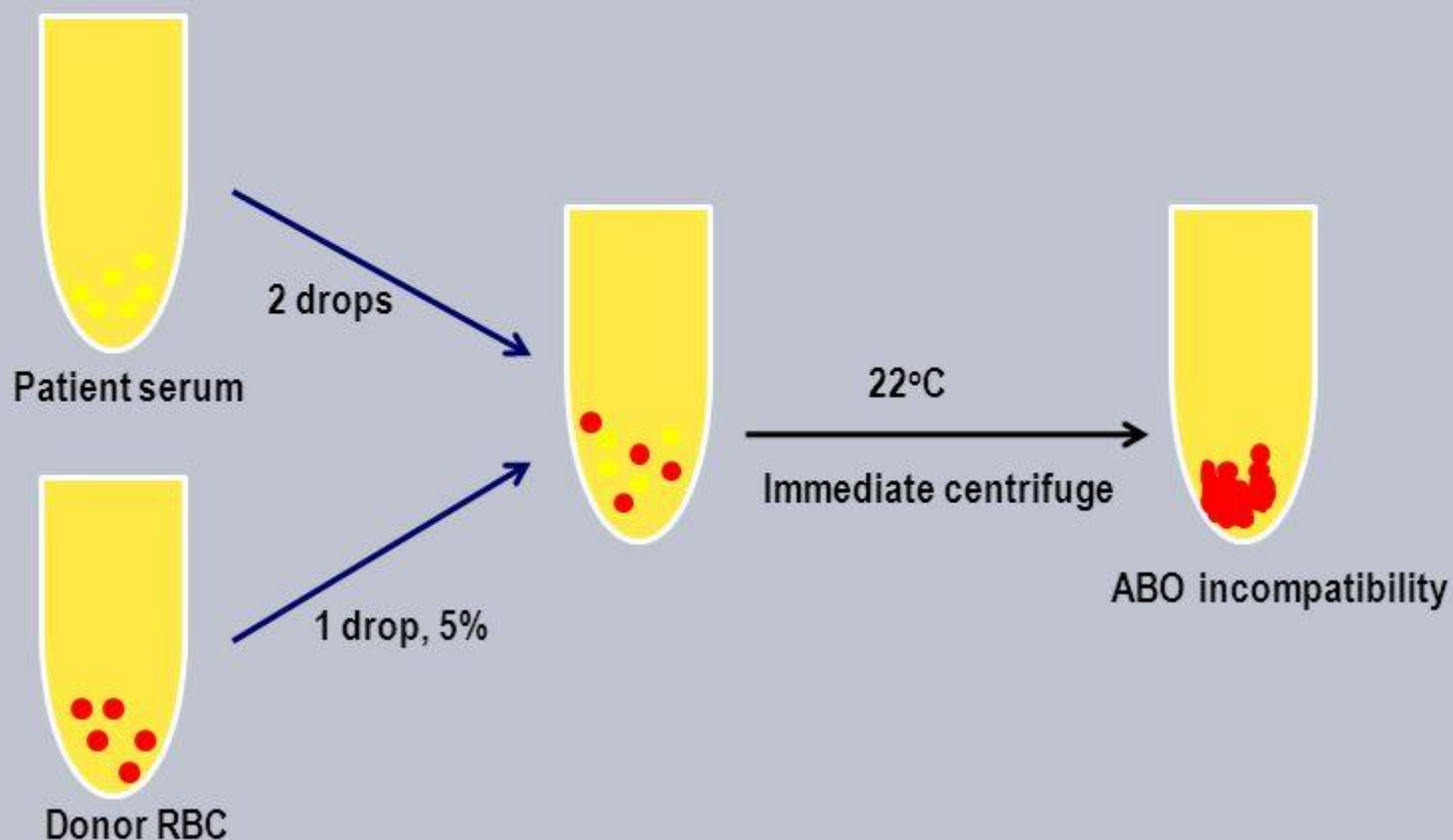
Приложение № 2

Таблица подбора доноров крови и (или) ее компонентов, совместимых с реципиентом по Rh-Hr и Kk, при трансфузии (переливании) эритроцитсодержащих компонентов

№ п/п	Реципиент	Донор крови и (или) ее компонентов	
		Совместимый	При экстренных показаниях к трансфузии (переливанию) допустим
	фенотип	фенотип	фенотип
1	CcD ⁺ ee	CcD ⁺ ee CC ⁺ D ⁺ ee ccd ⁺ dee ccD ⁺ ee Ccd ⁺ dee	—
2	CCD ⁺ ee	CCD ⁺ ee CC ⁺ d ⁺ dee	—
3	CcD ⁺ Ee	Любой фенотип, кроме C ⁺ w +	
4	ccd ⁺ dee	ccd ⁺ dee	Ccd ⁺ dee
5	ccD ⁺ Ee	ccD ⁺ Ee ccd ⁺ dee ccD ⁺ ee ccD ⁺ EE ccd ⁺ dEe	CcD ⁺ ee CcD ⁺ Ee Ccd ⁺ dee Ccd ⁺ dEe
6	C ⁺ wD ⁺ ee	C ⁺ wD ⁺ ee	CCD ⁺ ee
7	ccD ⁺ Ee	ccD ⁺ Ee ccd ⁺ dEE	ccD ⁺ Ee CcD ⁺ EE
8	C ⁺ wcD ⁺ ee	C ⁺ wcD ⁺ ee	CcD ⁺ ee CC ⁺ D ⁺ ee C ⁺ wcD ⁺ ee
9	ccD ⁺ ee	ccD ⁺ ee ccd ⁺ dee	CcD ⁺ ee Ccd ⁺ dee
10	Ccd ⁺ dee	Ccd ⁺ dee ccd ⁺ dee CC ⁺ d ⁺ dee	ccd ⁺ dEe
11	C ⁺ wcD ⁺ Ee	C ⁺ wcD ⁺ Ee ccD ⁺ Ee ccd ⁺ dee	CcD ⁺ ee CcD ⁺ EE
12	ccD ⁺ weak ⁺ ee	ccD ⁺ weak ⁺ ee ccd ⁺ dee	Ccd ⁺ dee
13	Ccd ⁺ dEe	ccd ⁺ dee Ccd ⁺ dee Ccd ⁺ dEe ccd ⁺ dEe CC ⁺ d ⁺ dee	—
14	CCD ⁺ Ee	CCD ⁺ Ee CC ⁺ D ⁺ ee CC ⁺ d ⁺ dee	—
15	ccd ⁺ dEe	ccd ⁺ dEe ccd ⁺ dEE ccd ⁺ dee	Ccd ⁺ dee Ccd ⁺ dEe
16	CcD ⁺ EE	CcD ⁺ EE ccD ⁺ EE ccd ⁺ dEE	CcD ⁺ EE Ccd ⁺ dEe ccd ⁺ dEe
17	C ⁺ wcdd ⁺ ee	C ⁺ wcdd ⁺ ee ccd ⁺ dee	Ccd ⁺ dee
18	CCd ⁺ dee	CCd ⁺ dee	Ccd ⁺ dee ccd ⁺ dee
19	CCD ⁺ EE	CCD ⁺ EE	CCD ⁺ EE CC ⁺ D ⁺ ee
20	CCd ⁺ dEe	CCd ⁺ dEe CC ⁺ d ⁺ dee	Ccd ⁺ dee ccd ⁺ dee
21	Ccd ⁺ dEE	Ccd ⁺ dEE ccd ⁺ dEE	Ccd ⁺ dEe ccd ⁺ dEe ccd ⁺ dee
22	ccd ⁺ dEE	ccd ⁺ dEE	ccd ⁺ dEe
23	CCD ⁺ weak ⁺ ee	CCD ⁺ weak ⁺ ee CC ⁺ d ⁺ dee	CCD ⁺ ee
24	CcD ⁺ weak ⁺ ee	CcD ⁺ weak ⁺ ee CCD ⁺ weak ⁺ ee ccD ⁺ weak ⁺ ee	Ccd ⁺ dee ccd ⁺ dee
25	ccD ⁺ weak ⁺ Ee	ccd ⁺ dee ccd ⁺ dEe ccD ⁺ weak ⁺ Ee	Ccd ⁺ dee Ccd ⁺ dEe
26	ccD ⁺ weak ⁺ EE	ccD ⁺ weak ⁺ EE ccd ⁺ dEe ccd ⁺ dEE	Ccd ⁺ dEe ccd ⁺ dee
27	C ⁺ wcdd ⁺ Ee	ccd ⁺ dee ccd ⁺ dEe C ⁺ wcdd ⁺ Ee	Ccd ⁺ dee Ccd ⁺ dEe
28	C ⁺ wcD ⁺ EE	C ⁺ wcD ⁺ EE ccD ⁺ EE ccd ⁺ dEE	CcD ⁺ EE
29	kk	kk	—
30	Kk	Kk kk KK	-
31	KK	KK	Kk kk

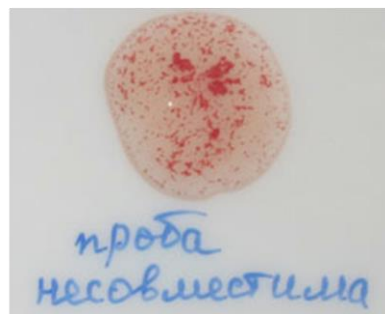
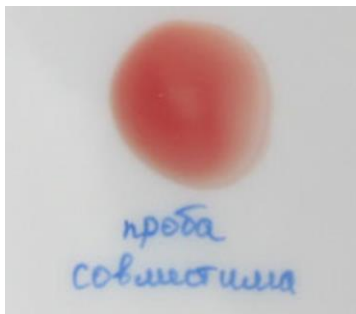
Immediate Spin Technique (IST)

- ✓ Detects only IgM antibody, reactive at 22°C.
- ✓ Clinically significant IgG antibody reactive at 37°C not detected



Individual compatibility test on the surface and in the tube

- **ABO:** red blood cells of the donor are mixed on the plane with recipient's serum at a ratio of 1:10 at room temperature.
- No agglutination means compatibility
- **Rh:** in the diagnostic tube are mixed donor's RBC and recipient's serum and PEG and dextran (poliglukin)
- No agglutination means compatibility



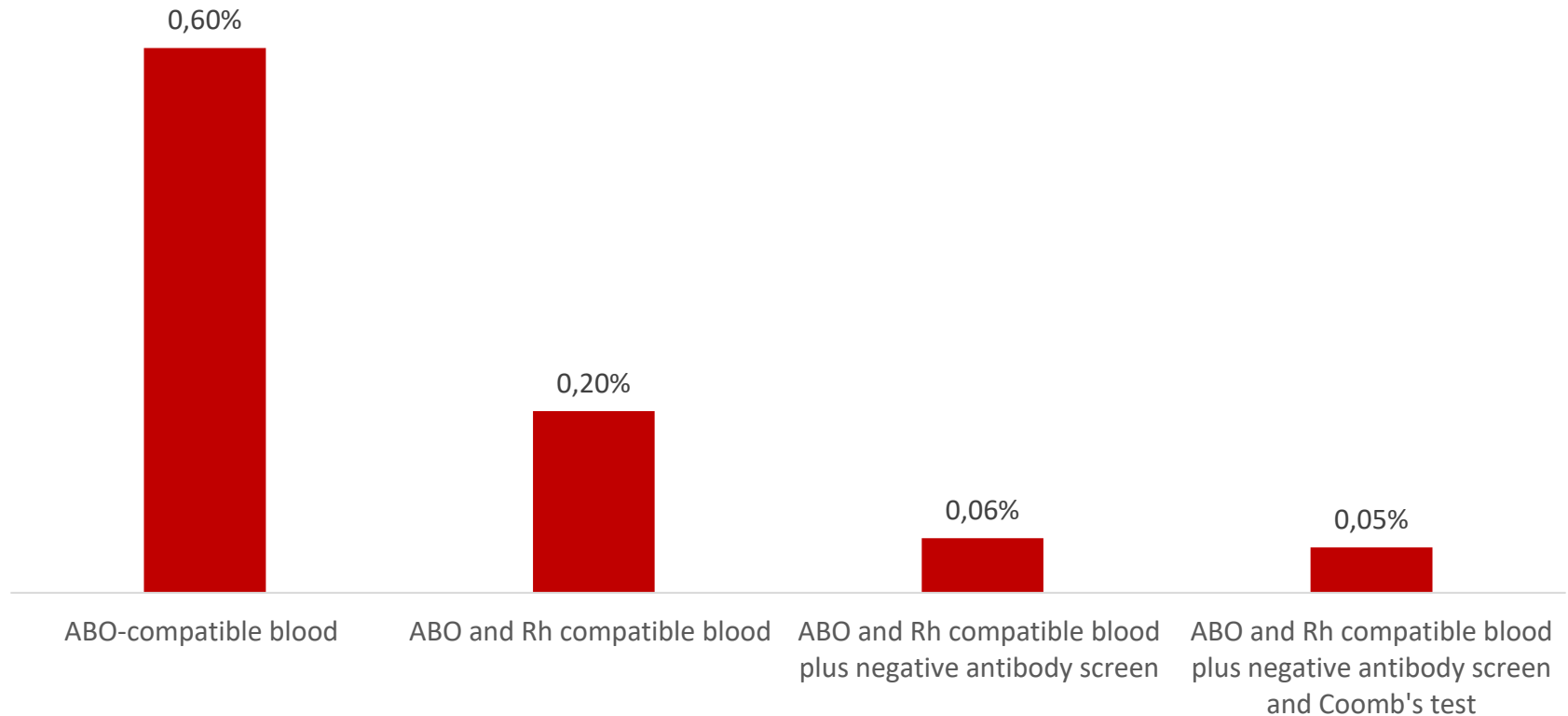
Агглютинация есть –
кровь несовместима.



Агглютинации нет –
кровь совместима.

Importance of individual blood compatibility

Risk of reaction



Biological test for individual compatibility

- The biological test for compatibility is carried out by a single infusion of blood or components of 10 ml at the rate of 2-3 ml (40-60 drops) per minute for 3 minutes. Thereafter transfusion stops for 3 minutes, and the status of recipient monitored by the pulse, number of respiratory movement, blood pressure, general condition, skin tone, body temperature. This procedure is repeated three times. If some of clinical symptoms (chills, back pain, feeling of heat and tightness in the chest, headache, nausea or vomiting) appears, the doctor immediately stop the transfusion.



Steps 9-10

- After transfusion the container with rest of donor's blood, the diagnostic tube with rest of recipient's serum and the tubes, slides or other reagents used for compatibility test should be storage for 48 hours.
- The transfusion protocol should be filled
- After transfusion the patient requires bed rest for 2 hours with hourly measuring of hart rate, arterial blood pressure and body temperature, control of urination. Laboratory test to evaluate the efficacy of transfusion should be made on the next day after transfusion.

Протокол трансфузии (переливания) донорской крови и (или) ее компонентов

1. Ф.И.О. реципиента: _____ № медицинской карты: _____
2. Дата трансфузии (переливания) донорской крови и (или) ее компонентов: _____
« ____ » _____ 20 ____ г.
3. Время начала трансфузии (переливания) донорской крови и (или) ее компонентов реципиенту: _____
4. Время окончания трансфузии (переливания) донорской крови и (или) ее компонентов реципиенту: _____
5. Группа крови реципиента: _____
6. Резус-принадлежность: _____
7. Фенотип: _____
8. Определение резус-принадлежности реципиента проводилось: _____
в лаборатории / экспресс-методом: _____
9. Исследование антигенов выявлены / не выявлены: _____
10. Медицинские показания к проведению трансфузии (переливания) донорской крови и (или) ее компонентов: _____ Hb ____ Ht ____
11. Трансфузионный анамнез: трансфузии были / не были: _____
12. Трансфузии по индивидуальному подбору в прошлом: были / не были: _____
13. Реакции и (или) осложнения, возникшие у реципиента в связи с трансфузией (переливанием) донорской крови и (или) ее компонентов: _____
14. Акушерский анамнез (количество беременностей): _____
15. Особенности течения (самопроизвольные аборты, гемолитическая болезнь новорожденного и другое): _____
16. Макроскопическая оценка крови и (или) ее компонента: пригодна к переливанию / не пригодна к переливанию: _____
17. Данные с этикетки контейнера с кровью и (или) ее компонентом: _____
18. Наименование компонента крови: _____
19. Наименование организации, заготовившей донорскую кровь и (или) ее компоненты: _____
20. Дата заготовки донорской крови и (или) ее компонентов: _____
21. Срок годности донорской крови и (или) ее компонентов: _____
22. № контейнера донорской крови и (или) ее компонентов: _____
23. Объем донорской крови и (или) ее компонентов (мл): _____
24. Код донора крови и (или) ее компонентов (ФИО донора): _____
25. Группа крови донора крови и (или) ее компонентов: _____
26. Резус-принадлежность донора крови и (или) ее компонентов: _____

Место для этикетки

27. Перед трансфузией (переливанием) донорской крови и (или) ее компонентов проведены контрольные проверки показателей:
Группа крови реципиента _____ Резус-принадлежность реципиента _____
Группа крови донора* _____ Резус-принадлежность донора* _____
28. При определении показателей использовались реактивы _____
(наименование с указанием серии и срока годности)
29. Проведены пробы на индивидуальную совместимость*: _____
указать метод, используемые реактивы (наименование, серию, срок годности),
результат проведения каждой пробы
30. Биологическая проба: _____
указать метод, результат проведения пробы
31. Способ трансфузии (переливания) донорской крови и (или) ее компонентов: _____
32. Осложнения во время трансфузии (переливания) донорской крови и (или) ее компонентов: _____
33. Наблюдение за состоянием реципиента:

	Артериальное давление, мм рт. ст.	Частота пульса, уд./мин.	Температура, °С	Диурез, цвет мочи
Перед переливанием				
Через 1 час после переливания				
Через 2 часа после переливания				
** Через 3 часа после переливания				

34. Врач, проводивший трансфузию (переливание) донорской крови и (или) ее компонентов: _____

(ФИО)

(подпись)

* Указывается при проведении трансфузии (переливания) эритроцитсодержащих сред.

** Указывается при проведении трансфузии (переливания) донорской крови и (или) ее компонентов в амбулаторных условиях.

Types of transfusion

- **Indirect transfusion** - previously harvested and preserved blood
- **Exchange transfusion** - complete replacement of total blood volume, it is rarely used, such as hemolytic disease of the newborn
- **Direct transfusion** - is prohibited !!
- Transfusion from a donor
- Autohemotransfusion

Donor in Russia

- The donor has the right to be a competent person who is a citizen of the Russian Federation or residing in the territory of the Russian Federation legally for at least one year of a foreign citizen or stateless person who has attained the age of eighteen years or has acquired full legal capacity until they reach the age of eighteen years, in accordance with Russian legislation who has expressed a desire to voluntarily donate blood and (or) components, past volunteer medical examination and has no medical contraindications for donation of blood and (or) components.
- Blood transfusion from animals and cadavers is prohibited!

Autohemotransfusion

- **Preoperative harvesting:**

- Step-phased approach
- Preoperative isovolumic or hypervolemic hemodilution (1-2 units of blood harvesting with volume replacement by saline solutions)

Baseline Hb >10 g/dL and Ht >33

Last harvesting no earlier than 3 days prior to surgery

- **Blood reinfusion:**

- The blood which flowed into the body cavity without damaging the hollow organs, amniotic membranes, without signs of tumor and infection

When normovolumic hemodilution Hb >90g/dL and Ht >28 at hypervolemic – Ht >23

Complications of blood transfusion

- Vector-borne infections
- Acute hemolysis
- Delayed hemolytic reactions
- Non-hemolytic febrile reaction
- Anaphylactic shock
- Bacterial shock
- Thrombophlebitis and cellulitis in the area of vein access
- Acute overload with the volume
- The syndrome of acute lung injury
- Embolism and Thrombosis

Acute hemolysis

- Initial symptoms of acute hemolysis:
 - Pain in the chest, abdomen or lower back,
 - Hot flashes or chills,
 - Agitation, shortness of breath, cyanosis.
- Considered pathognomonic symptom of pain in the lumbar region.
- The following manifestations:
 - Acute DIC,
 - Circulatory shock
 - Acute renal failure

Treatment:

- Immediate cessation of transfusion;
- Infusion therapy;
- Correction DIC - FFP, heparin;
- Glucocorticosteroids;
- Plasmapheresis;
- Dopamine, sodium bicarbonate, diuretics, upon the occurrence of acute renal failure - hemodialysis.

Anaphylactic shock

Symptoms:

- Nonproductive cough, bronchospasm,
- Hypotension,
- Abdominal cramping,
- Vomiting, diarrhea,
- Loss of consciousness,
- No increase in temperature

Therapy:

- Cessation of transfusion,
- Immediate introduction of adrenaline under the skin,
- Prednisolone intravenously
- Fluid management

Massive transfusion syndrome

Developed with the rapid introduction of more than 40-50% of circulating blood volume

Implication:

- Citrate intoxication:
 - Decreased Ca^{2+} level
 - Convulsions, respiratory failure, sleep apnea, asystole,
- Increased K^{+} :
 - Low heart rate, hypotension, asystole
- Hemostatic disorders:
 - DIC
- Hypothermia

Transfusion-related acute lung injury (TRALI)

- Acute respiratory distress following transfusion of plasma-contained blood products
- Infusion of donor antibodies directed against recipient leukocytes: anti-HLA (human leukocyte antigens) or anti-HNA (human neutrophil antigens) antibodies that directly cause complement activation, resulting in the influx of neutrophils into the lung, followed by neutrophil activation and release of cytotoxic agents, with subsequent endothelial damage and capillary leakage.
- Rapid onset of dyspnea and tachypnea within 6 hours after transfusion
- Fever, cyanosis, and hypotension
- Supplemental oxygen therapy, mechanical ventilation and ICU support