Blood transfusion

Dr. Klara Vezendi

Szeged University

Transfusiology Department

Blood transfusion

is the process of transferring blood or blood-based products from one person into the circulatory system of another.

It can be grouped into two main types depending on their source:

- **Homologous transfusion**
- **Autologous transfusion**

HISTORY

- **1492: first historical attempt of blood transfusion.**

It was believed that the transfusion of blood from a young, healthy person into the aged or delibitated would restore youth and health.

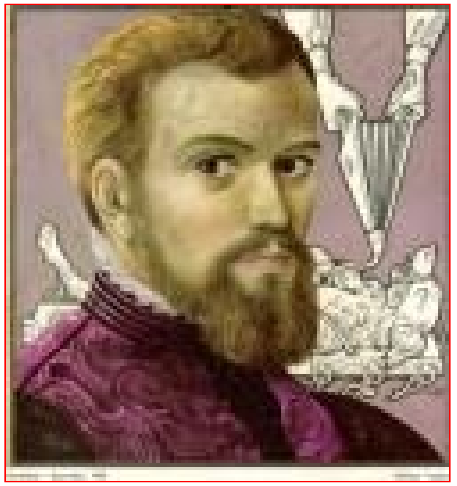
Pope Innocent VIII sank into a coma, the blood of three boys (10 years old) was infused into the dying pontiff (through to mouth – concept of circulation and methods for iv. access did not exist at that time!).

The boys had been promised a ducate each.

All four involved died.

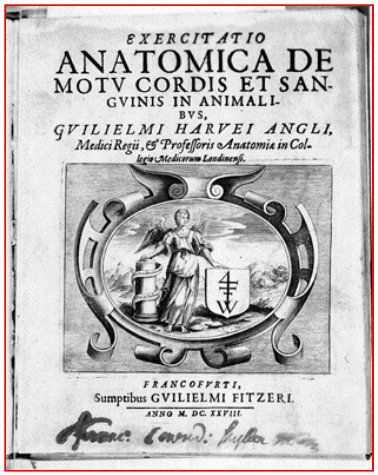
- **1555: Andreas Vesalius** (1514-1564, Italy)

broke with medieval ideas about the anatomy of the circulatory system.



- **1628: William Harvey** (1578-1657, England)

Discovered the circulation of the blood.
He published his treatise :
***De Motu Cordis* (1628).**


EXERCITATIO
ANATOMICA DE
MOTV CORDIS ET SAN-
GVINIS IN ANIMALI-
BVS,
GVILIELMI HARVEI ANGLI,
Medici Regii, & Professoris Anatomia in Col-
legio Medicorum Londinensi.

FRANCOFVRTI,
Sumptibus GVILIELMI FITZERI.
ANNO M. DC. XXVIII.

- **1665: Richard Lower** (1631-1690, England)

He performed the first documented blood transfusion *between animals* (dogs).

He connected the jugular vein of a dog to the neck arteria of a second dog. He recognised the appropriateness of transfusional replacement of blood in severe hemorrhage: *an exsangiunated dog could be completely restored by transfusion.*

- **Nov. 23, 1667. London: he transfused some ounces blood from a gentle lamb into an agitated man, Arthur Coga.**

- **1667 (Jun. 15):**

Jean-Baptiste Denis (1635-1704, France) performed the first documented human transfusion *(animal blood into human)*.

He transfused the blood of a sheep into a 15-year-old boy with a febrile illness, *who recovered.*

Denis used the procedure on several other patients.

Denis recorded the *first case of hemolytic transfusion reaction:*

„ As soon as the blood began to enter into his veins, he *felt… heat* along his arm, and under his Arm pits…*His pulse rose* presently, and soon after we observed a *plentiful sweat over all his face.* His pulse varied extremly at this instant, and he complained of a great *pain in his kidneys*, and that *he was not well in the stomach,* and that he was ready to choak unless they gave him his liberty…When he awakened… He made a great glass full of *urine*, of a color *as black, as if it had been mixed with the soot of chimneys".*

Denys perfomed several transfusions into Mr. Antoine Mauroy (a 34-year-old man with severe „phrensy”), who on the third account had died.

Denys was accused of his murder. *(In fact, Mr. Mauroy's wife poisoned her husband with arsenic).*

The Faculty of Medicine of Paris stated: the procedure of transfusion was a criminal act.
1678: French parliament forbade transfusion in France, it also was outlawed by Royal Society in London.
1679: the pope joined the outcry and banned the procedure.

Only sporadic efforts at transfusion were during the 17th and 18th century.

Transfusions of animal blood into humans (in the 1600's)

1667

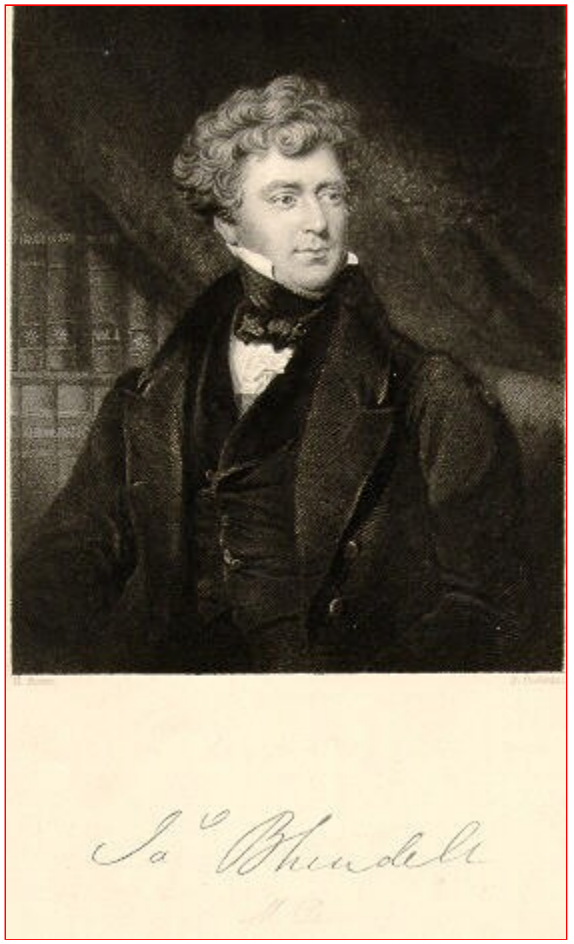
Armamentium Chirurgiae, 1693

Transfusion in the 19th century

- **1818:**

James Blundell (1790-1877, obstetrician, England)

performed the first successful transfusion of *human blood*.
He transfused a 35-year-old man with gastric carcinoma. 4 oz of blood was administered by syringe in small amounts at intervals of 5-6 minutes.
Despite temporary improvement, *the patient died* 56 hours later.



Subsequently he transfused several women with postpartum hemorrhage. He used the patient's husband as a donor.

He offered the use of human rather than animal blood for transfusion.

- **1840: Samuel Armstrong Lane (1802-1892)**

performed the first successful whole blood transfusion to treat hemophilia.

(St. George's Hospital Medical School, London)

Transfusion in Paris – 1874

(Hopital de la Pitie)

THE TRANSFUSION OF BLOOD—AN OPERATION AT THE "HÔPITAL DE LA PITIÉ," AT PARIS.—[See Page 569.]

570 HARPER'S WEEKLY. [SUPPLEMENT, JULY 4, 1874.

First photo about blood transfusion

1870. Bellevue Hospital, New York (O.S. Mason)

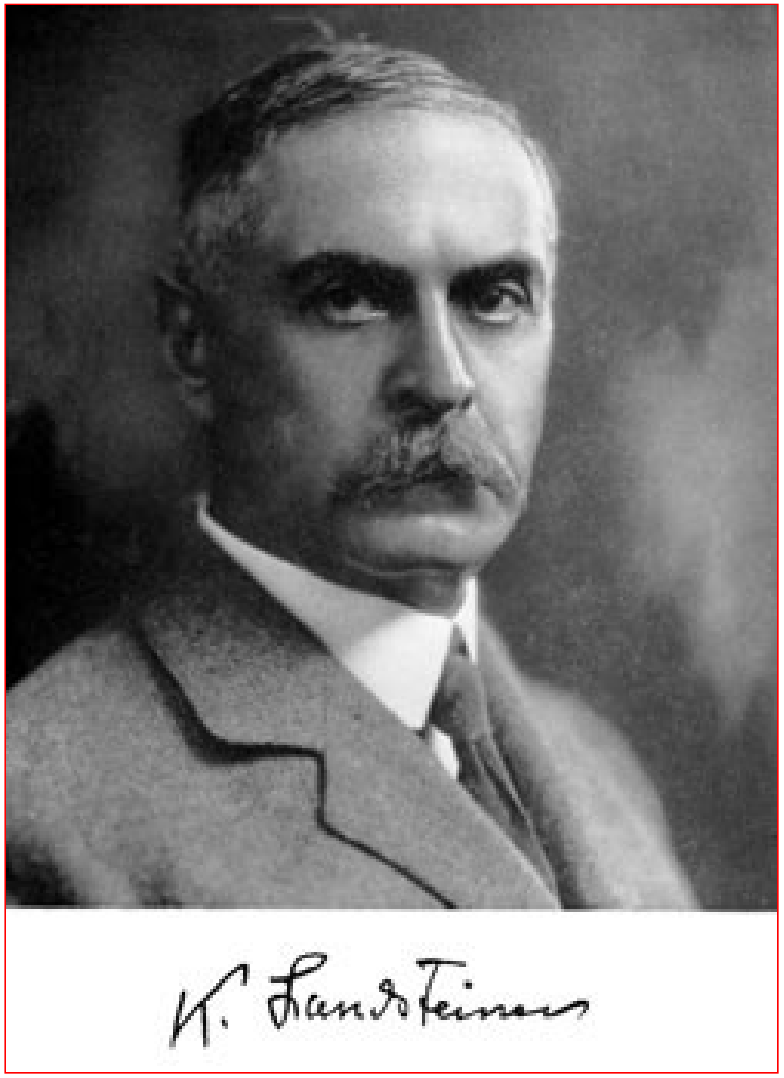
- **1901: Karl Landsteiner**

(1868-1943, Vienna)

Discovered of the three main human blood groups: A, B, C (later changed O)

(Wiener klinische Wochenschrift, 14, 1132, 1901)

The basis of modern transfusion was established.



A Nobel Medal

For his discovery he got the Nobel Prize in Physiology or Medicine (1930)

- **1902: De Castello and Sturly descovered the fourth blood group: AB**

- **1907: Ludvig Hektoen (Chicago) recommends checking the blood of donors and recipients for signs of incompatibility (cross matching) prior to transfusion.**

- **1907: Reuben Ottenberg (New York) performs the first transfusion using cross matching (compatibility testing).**

These procedures enhanced the safety of transfusion.

- **1940: Landsteiner and Wiener discovered the Rh blood group system.**

Rh factor was determined to be the cause of most remaining incompatibility reactions.

BLOOD GROUPS

Blood group systems

A total of 29 human blood group systems are now recognized by the *International Society of Blood Transfusion (ISBT).*

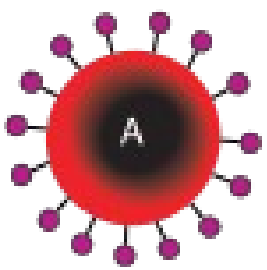
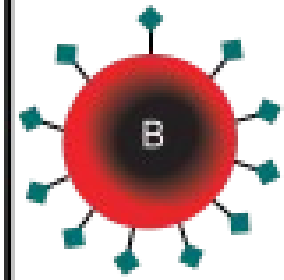
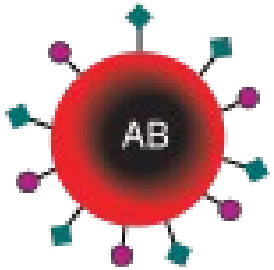
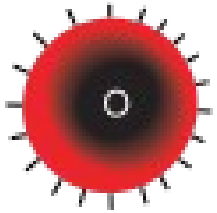
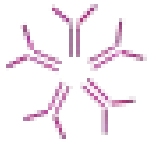
Across the 29 blood groups, over 600 different blood group antigens have been found, but many of these are very rare or are mainly found in certain ethnic groups.

The ABO and the Rh systems are the most important blood group systems in human blood transfusion.

AB0 blood grouping system

According to the AB0 blood typing system there are four different kinds of blood types: A, B, AB or 0 (null).

- ***Antigens*** **on the surface of red cells: A, B**
- ***Antibodies*** **in the plasma (IgM): anti-A, anti-B (natural antibodies)**

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens present	A antigen	B antigen	 A and B antigens	No antigens

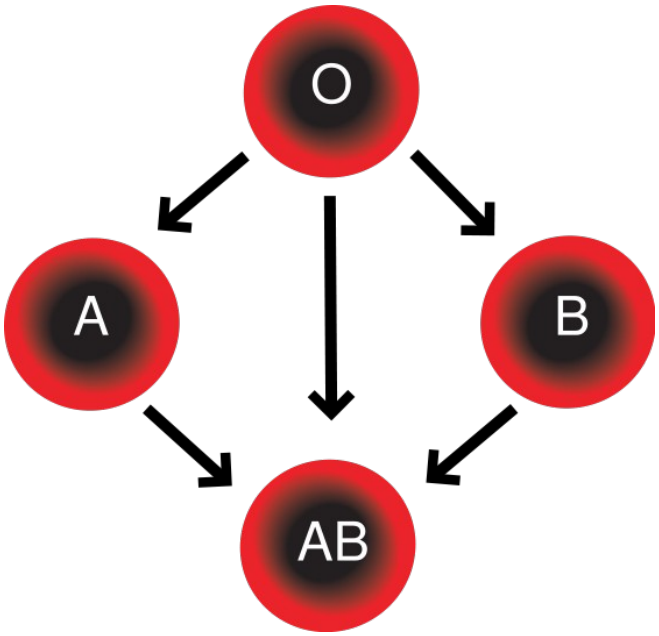
There are *reciprocal relation* between antigens (agglutinogens) and antibodies (agglutinins):

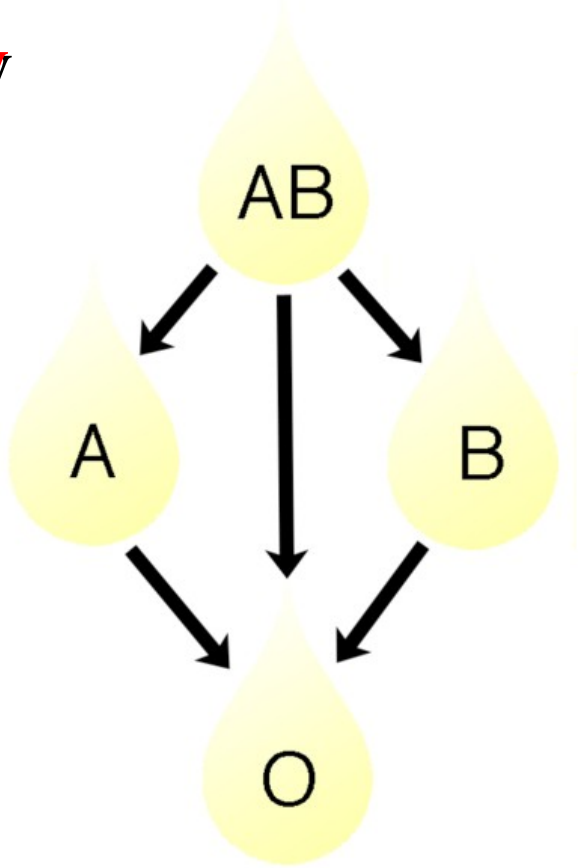
Landsteiner's rule states that if a given antigen is present in one individual its corresponding agglutinin should be absent.

When RBCs carrying one or both antigens are exposed to the corresponding antibodies, they agglutinate (clup together).

Blood transfusion should be of the same ABO type as the recipient.
In urgent situations, or when the correct ABO type is doubt, type O RBCs *(not whole blood!)* may be used.

Compatibility





RBC compatibility chart: type O blood donors can give to A, B and AB; blood donors of types A and B can give to AB.

Platelet = RBC

Plasma compatibility chart: plasma from type AB can be given to A, B and O; plasma from types A and B can be given to O.

Blood group compatibility /ABO, Rh(D)/ :

Rh(D) positive:

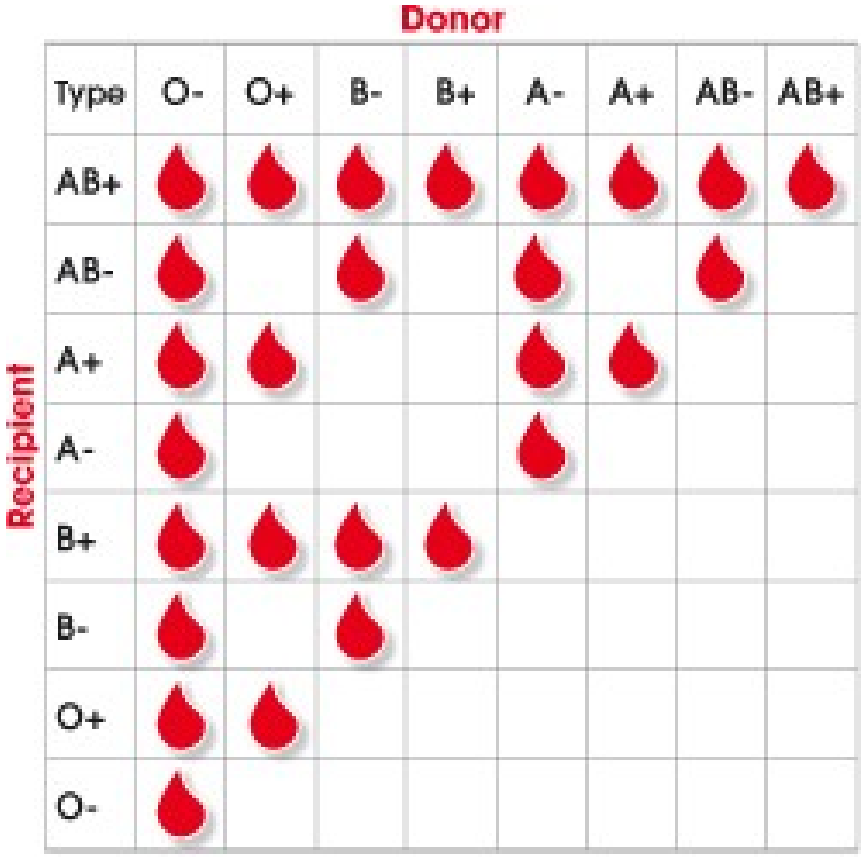
Rh(D) pos.,
Rh(D^{u}),
Rh(D) neg.

Rh(D) negative:

Rh(D)neg.

Rh(D^{u}):

Rh(D)pos.,
Rh(D^{u}),
Rh(D) neg.



Avoid Rh(D) pos. blood to Rh(D)neg. women in reproductive ages and girls!

Rh factor blood grouping system

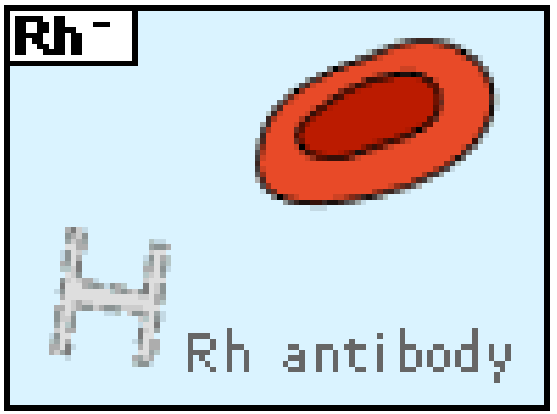
Antigens:

D: the major Rh antigen
(85 % of the population is Rh+).
Others: > 55 other antigens
(C,c,E,e…)

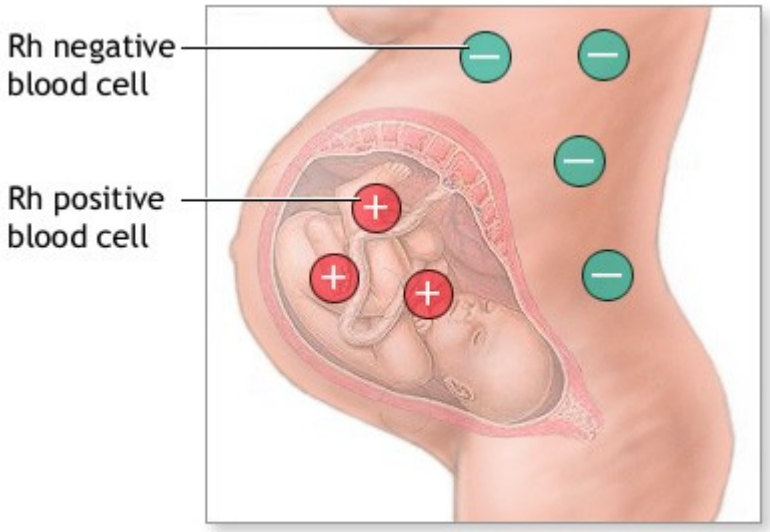
Antibody: immun (IgG)

A person with Rh- blood does not have Rh antibodies naturally in the blood plasma. But a person with Rh- blood can *develop* Rh antibodies (anti-D) in the blood plasma if he or she receives blood from a person with Rh+ blood.

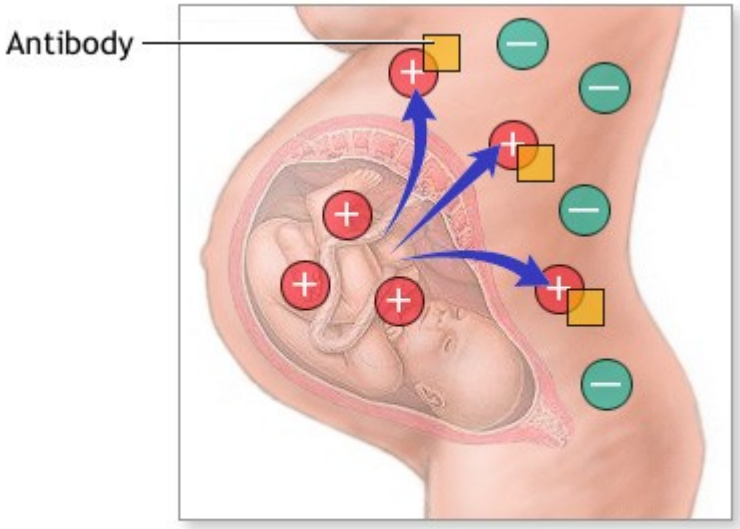
A person with Rh+ blood can receive blood from a person with Rh- blood without any problems.



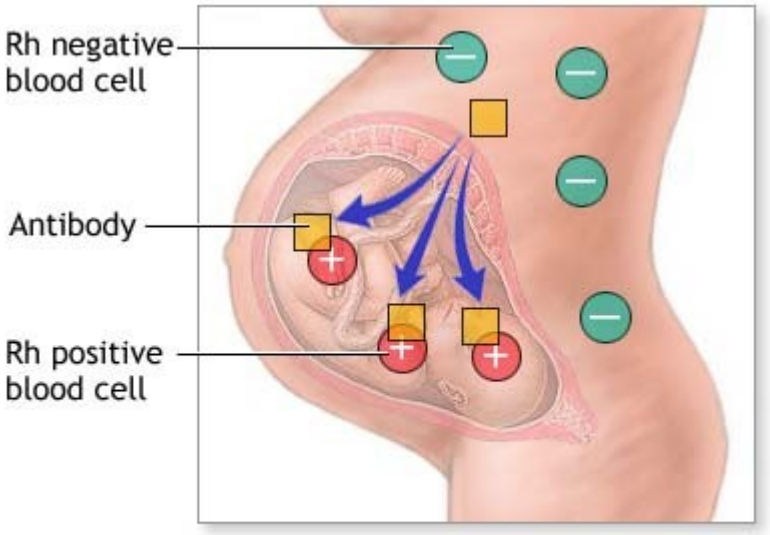
Rh incompatibility is the major cause of hemolytic disease of the newborn.



Rh incompatibility occurs when the mother's blood type is Rh- and her fetus's blood type is Rh+.

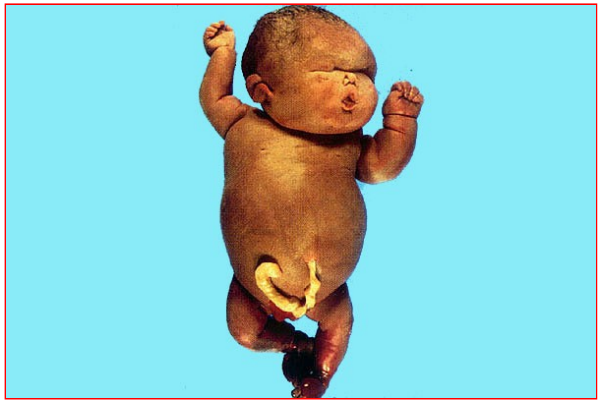


If some of the fetal blood gets into mother's blood stream, her body will produce antibodies.



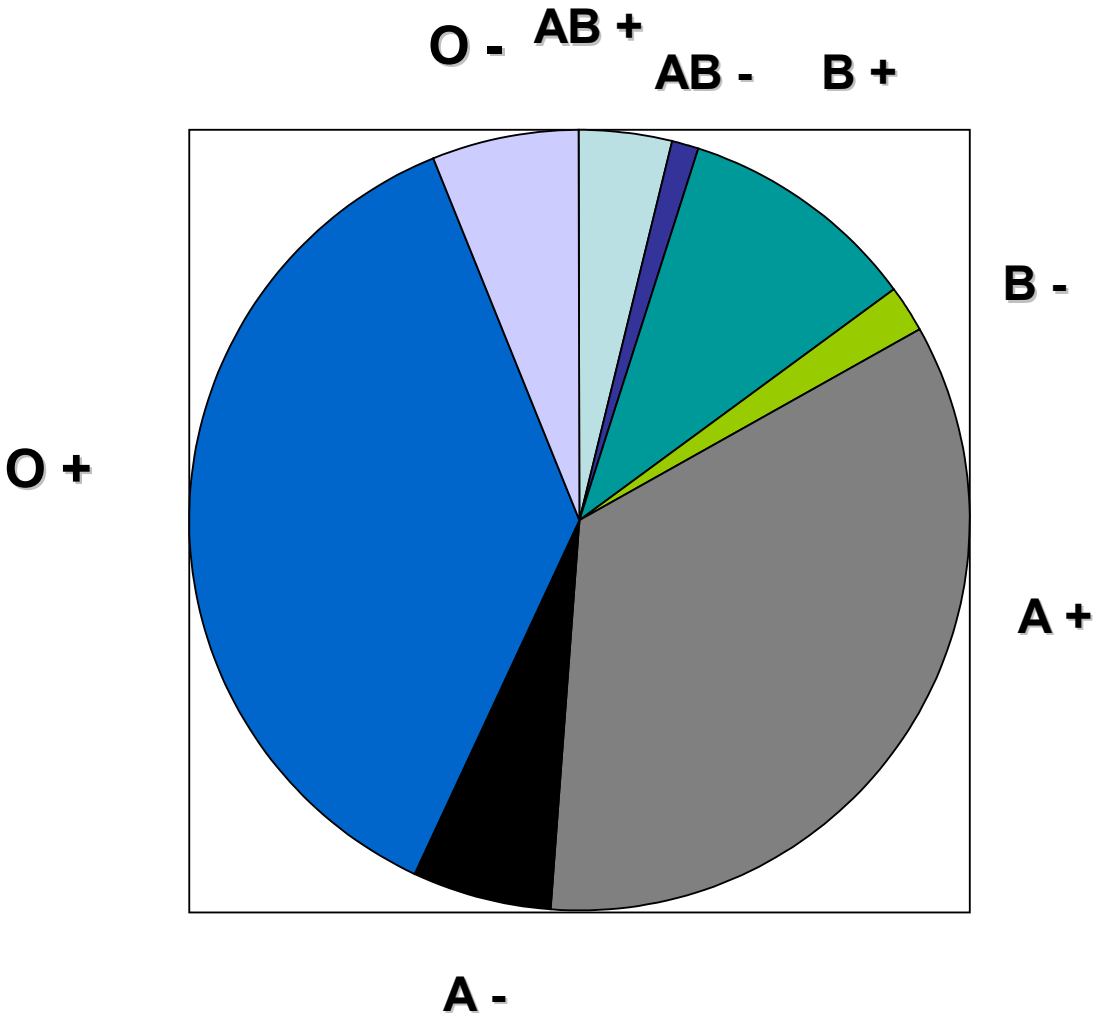
These antibodies could pass back through the placenta and harm the developing baby's red blood cells, causing very mild to very serious anemia in the fetus.

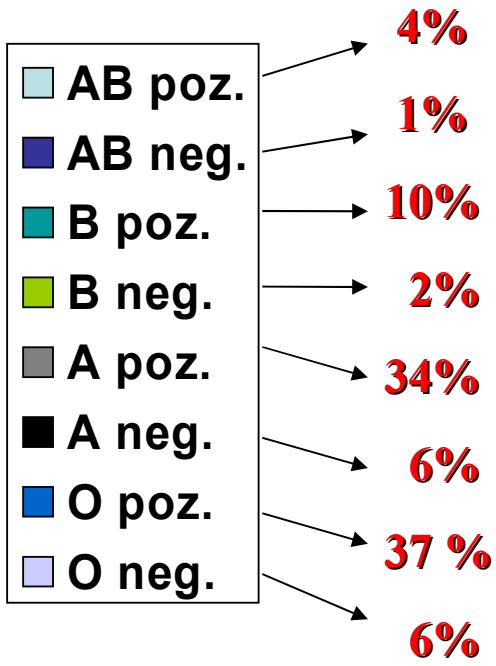
First baby is usually safe, because fetal and maternal blood usually do not mix until delivery.



If the second baby is also Rh+, there's a risk that antibodies will attack her blood cells and cause problems (anemia, jaundice, hydrops).

ABO and Rh distribution by nations





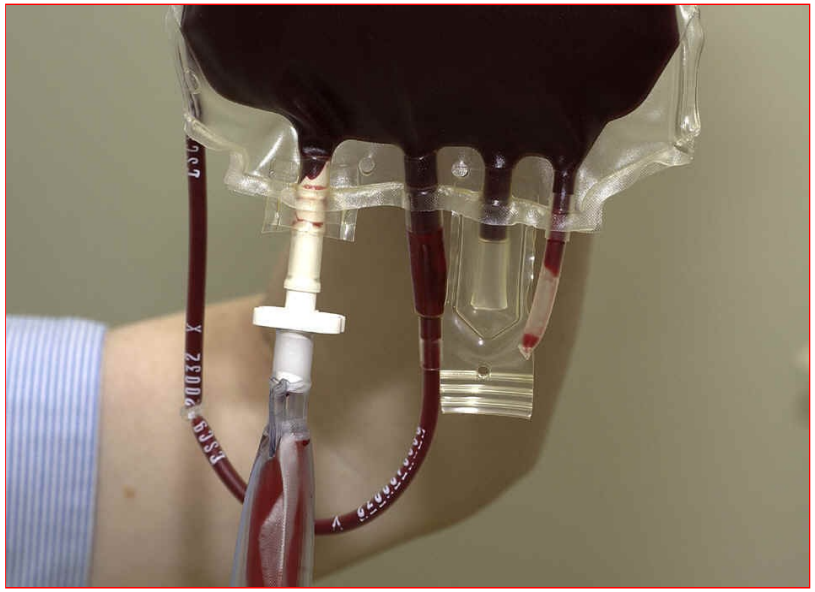
Hungary: A: 44%, 0: 32%, B: 16%, AB: 8%

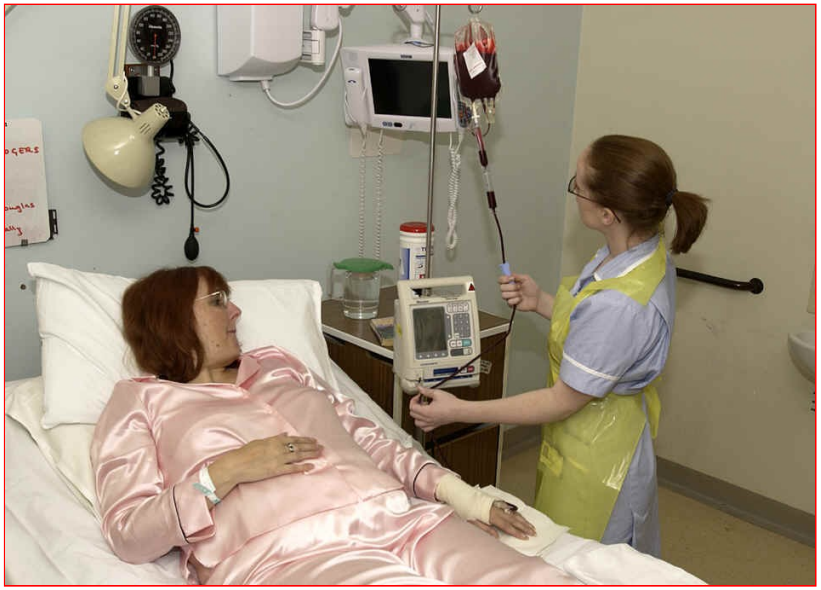
Some other clinically important blood group system

Blood group:	Antigen:	Antibody frequency: %
Kell:	K, k	9 / 99,8
Duffy:	Fy^a, Fy^b	66 / 83
Kidd:	Jk^a, Jk^b	77 / 72
Lewis:	Le^a, Le^b	22 / 72
MNSs:	M, N, S, s	78 / 72 / 55 / 89
Ii:	I, i	Fetal RBCs: i, adult RBCs: I
P:	P1, P2	P1 poz:79

BLOOD TRANSFUSION

The decision to transfuse is a *clinical judgment* that requires weighing the possible benefits and known hazards against alternative treatments.





The transfusion trigger

- For years: - hemoglobin (Hb) should be maintained at the level of 10 g/dl (100 g/l)
  - hematocrit (Hct) greater than 30 %.

- Nowadays: **Hb or Hct alone is poor transfusion trigger.**

Many patients with anemia do not need transfusion (pharmacologically treatable anemias: iron deficiency, B12 vitamin deficiency…; chronic anemias are generally well tolerated)

Indication: low Hb, Hct levels with inadequate tissue oxygen delivery.

As a general rule: **Hb level of 70 g/l is an indication for transfusion.**

Hb > 100 g/l: transfusion is not necessary.

Each patient needs to be looked at individually.

Recipients in risk:

In these cases carefully selected blood products have to be administered.

- **Polytransfused patients**
- **Multiparous women**
- **Recipients suffering from certain diseases:**
  - **Autoimmune hemolytic anemia (AIHA)**
  - **Malignant diseases**
- **Age:**
  - **Premature infant**
  - **Newborn**
  - **Elderly individual**

Pretransfusion testing: three steps

- **ABO and Rh(D) typing:**
  - Routine testing for **ABO and Rh(D)** is necessary:
    - other antigens rarely cause problems
    - they can never cause a problem until after the first exposure
- **Antibody screening:**

  for unexpected anti-RBCs antibodies is routinely done
  - **negative result:** any unit of red cells of the same ABO and Rh type of the patient may be transfused
  - **positive result:** transfused blood must be selected that does not contain the corresponding red cell antigen
- **The cross-match:**
  - Is a direct mixing experiment between the **recipient's serum and the donor red cells** to detect the incompatibility of the donor blood.

Forward (clinical) ABO typing:

patient's blood (RBCs) is mixed with test serum contains antibodies against type A or type B blood.

Antibodies:			Patient's own sera:	Blood group:
Anti-A	Anti-B	Anti-A,- B		
+	-	+	-	A
-	+	+	-	B
-	-	-	-	O
+	+	+	-	AB

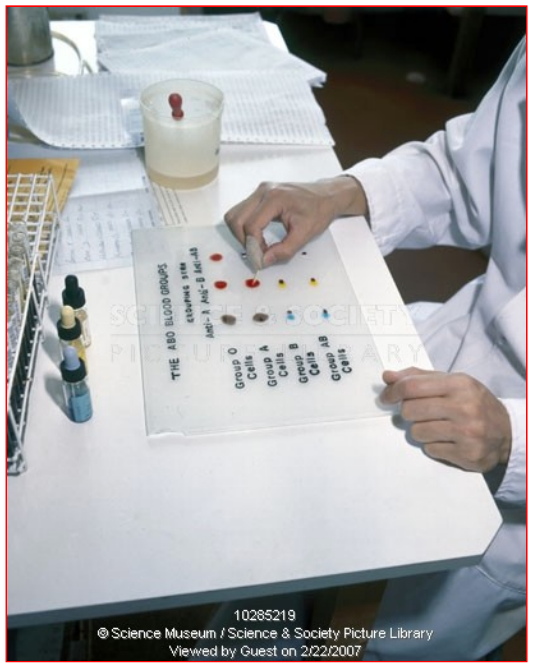
Anti-A	Anti-B	Anti-D	Control	Blood Type
●	●	◌	●	O-pos
●	●	●	●	O-neg
◌	●	◌	●	A-pos
◌	●	●	●	A-neg
●	◌	◌	●	B-pos
●	◌	●	●	B-neg
◌	◌	◌	●	AB-pos
◌	◌	●	●	AB-neg
◌	◌	◌	◌	Not valid

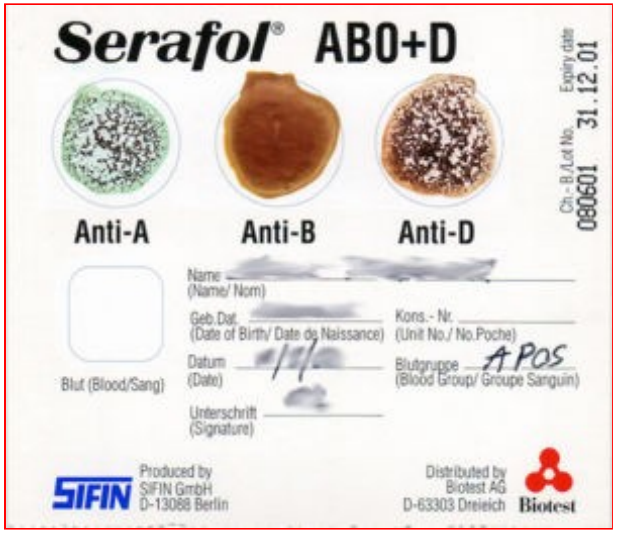
Reverse (laboratory) ABO typing:

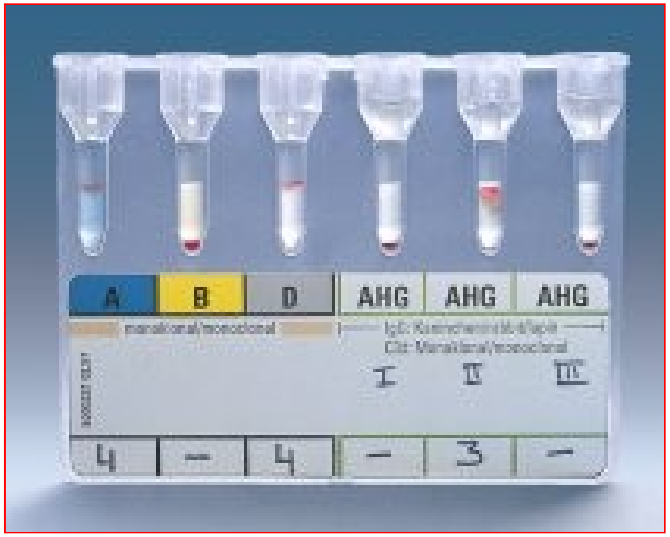
the patient's serum is mixed with blood that is known to be type A and type B.

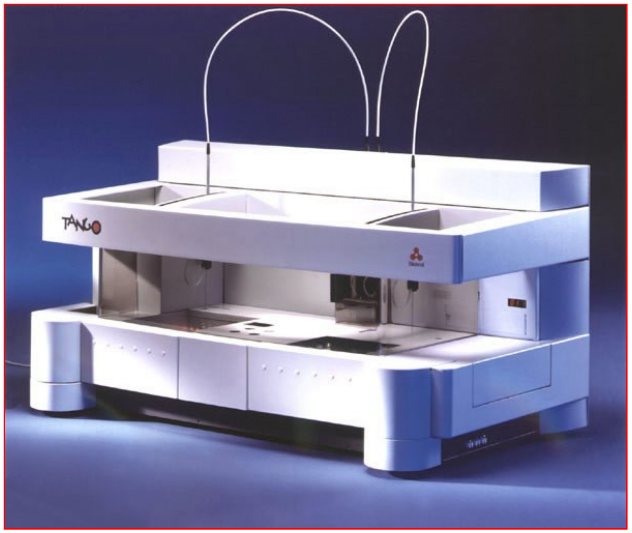
Antibodies:			Test RBCs:			Blood groups:
Anti-A	Anti-B	Anti-A,-B	A	B	O	
+	-	+	-	+	-	A
-	+	+	+	-	-	B
-	-	-	+	+	-	O
+	+	+	-	-	-	AB

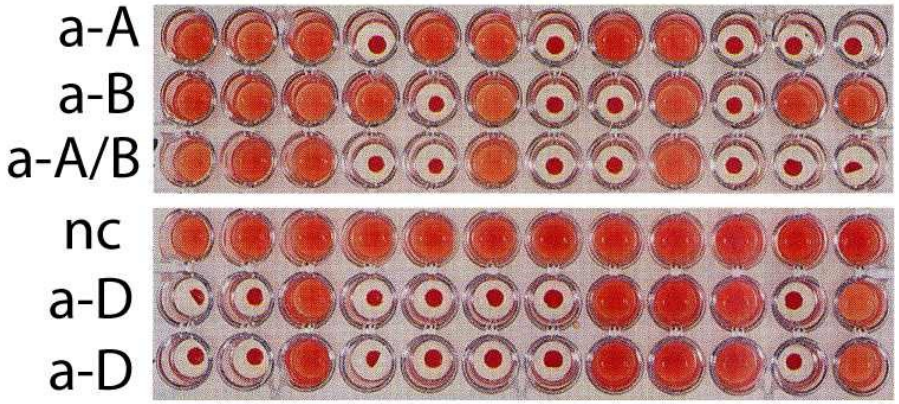
Blood grouping methods











BLOOD PRODUCTS

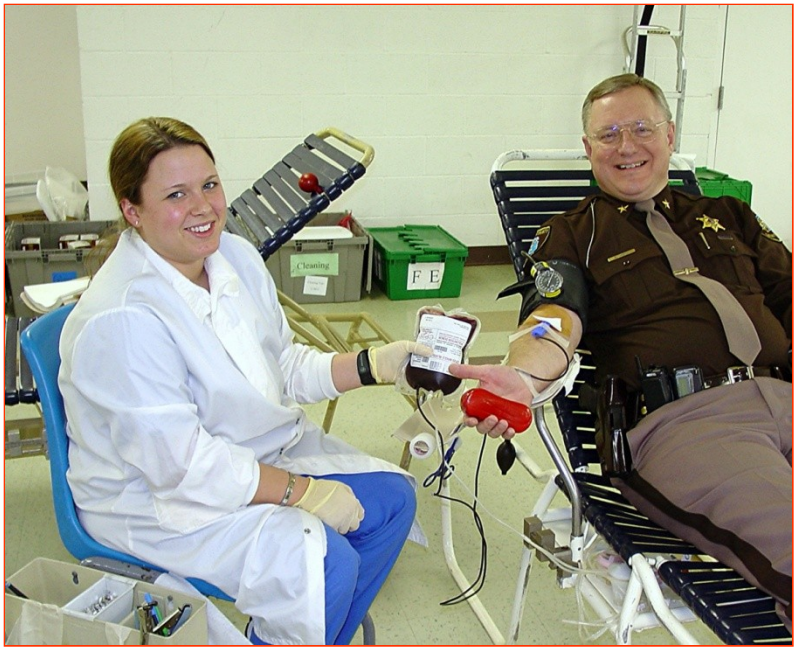
It must be decided what kind of blood components is necessary to the patient.

Blood component therapy allows a single unit of donated blood to benefit more than one patient.

Red blood cells and platelets are the most fequently transfused blood components.

Standard blood donation:

a 450 ml unit of whole blood is collected in a plastic bag that contains an anticoagulant preservative.

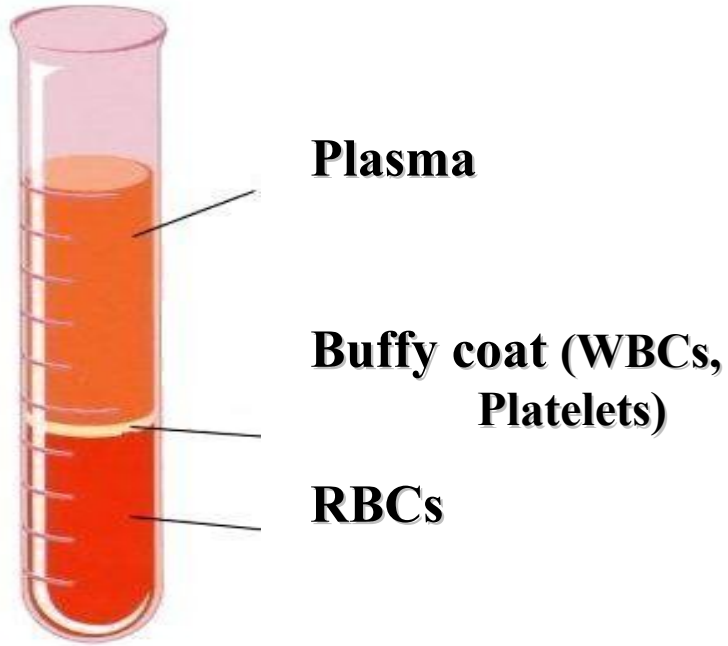


Triple or quadruple blood bags are used.

(one primary bag having anticoagulant CPDA solution and three empty satellite bags).

After collection, blood has to be centrifugated:

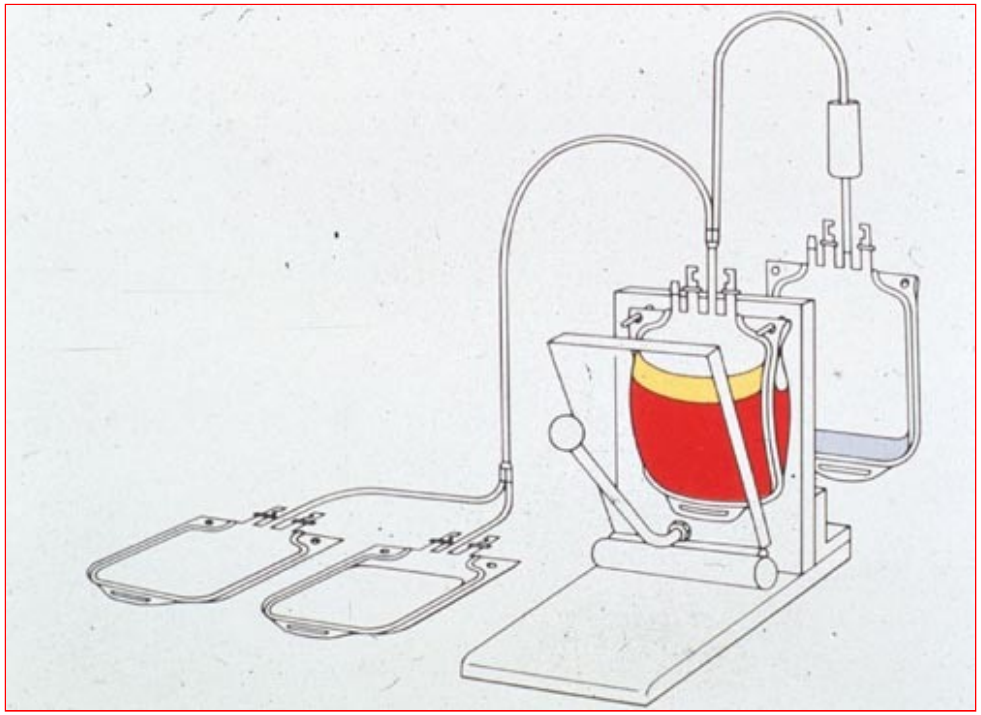
Centrifuge force makes red cells, plasma leukocytes, and platelets from different layers into the blood bag, according to their different densities.



Separation of components is happen in a closed system, using a set of plastic containers, which have been integrally connected to each other.

Microbial contamination is avoided by the closed system.

Separation procedure: plasma is expressed into an attached empty container from the primary bag in which RBCs and buffy coat are left. Buffy coat can used for platelet preparation.



RBCs plasma platelets

Separation of blood components permits their storage under optimal conditions (at different temperatures):

- **RBCs:** at +4°C
- **Platelets:** at room temperature with continuous agitation
- **Plasma:** in frozen state

Platelet agitator equipment

Blood components

- **I. Labile blood components:**
  are prepared as single units from one donor.
  - **have limited shelf life**
  - **have not been submitted to a viral inactivation step!**
- **II. Stable blood components:**
  are medicinal products prepared from pooled human plasma.
  - **shelf life longer than a year**
  - **all products are virus inactivated**

Blood products

I. Labile:

- Whole blood
- Red blood cells (RBCs)
- Leukoreduced RBCs
- Washed RBCs
- Platelet concentrates
- Granulocytes
- Fresh frozen plasma (FFP)

II. Stable:

- Coagulation factor concentrates
- Albumin
- Immunglobulin preparations (polyvalent /IVIG/, hyperimmune)
- Other proteins

Whole blood:

most countries have stopped giving whole blood!

Many disadvantages!

- whole blood is a more likely carrier of transfusion transmitted diseases

- most patients require only one particular component of whole blood

- blood products have a greater shelf life than whole blood

- blood filtration and other techniques help to make blood safer

Indication: **rapid massive blood loss.**

Red blood cells (RBCs):

A unit of RBCs is prepared from a whole blood.
After centrifugation most of the plasma is removed.

leukocyte content: normal physiological

Disadvantages:
FNHTR (febrile, non hemolytic transfusion reaction)
HLA immunisation
TA-GVHD
microaggregates transfusion transmitted
infectious diseases (CMV, EBV, HTLV I-II)

Indication: **symptomatic anemia (to increase oxygen carrying capacity).**

It is not used generally.

Buffy coat removed (leukocyte poor) RBCs:

It is the generally used RBCs product in Hungary!

After centrifugation the buffy coat layer (contains white cells and platelets) is removed.

leukocyte content: <1,2 x10^9/U

plasma content: < 3g/U

ABO antibody content: minimal

shelf life: 35 days at +4°C

Advantages:

reduction of microaggregates

FNHTR is reduced by about 2/3

it can be given as ABO compatible product

Indication: **symptomatic anemia (to increase oxygen carrying capacity).**

Leucocyte depleted RBCs:

It is prepared using special filters that remove > = 99,9% of WBCs

leukocyte content: ≤1-5 x10^6/U

plasma content: < 3g/U

shelf life: 35 days at +4°C

Advantages:

prevention of repeated FNHTR, HLA alloimmunisation and transfusion transmitted infectious diseases (CMV, EBV, HTLV I-II).

Indication:

- for patients who have had febrile transfusion reactions on > 2 occasions

- for prevention of HLA-sensitisation

- used as „CMV" negative RBCs.

Bedside filtration

Leukocyte reduction filters

Washed RBCs:

Red cells washed with 0,9% isotonic saline to remove most proteins, antibodies and electrolytes.

leukocyte content: < 5 x10^8/U
(it is should not be considered leucoreduced!)
plasma content: ≤ 0,5g/U
shelf life: with 0,9% isotonic saline: 24 hours
with adenine: 48 hours

***Advantages*: very low plasma content**
***Indication*: for patients who have severe reactions to plasma (e.g. severe allergies or IgA immunisation).**

Irradiated RBCs:

It is prepared by 25-50 Gy gamma irradiation to stop lymphocyte proliferation.

shelf life: 14 days after irradiation

Advantages: **reduces the risk of transfusion related graft-versus- host disease.**

Indication: **- for patients with immunodeficiencies**
- malignancy
- stem cell/bone marrow transplant
- intra-uterine transfusions

It is should not be considered leucoreduced product!

Platelet concentrates:

Are used in treatment of patients with thrombocytopenic bleeding associated with severely decreased platelet production or bleeding associated with functionally abnormal platelets.

Not indicated if platelet count is > 10000µl, unless actively bleeding.

- **Random donor platelets: are separated from a single unit of whole blood. Shelf life: 5 days at 20-24°C.**

Each unit contains 0,5-0,8x10^{11} platelets.

Dosage:1 unit/10 kg body weight.

- **Apheresis platelets: platelets are harvested from a single donor using hemapheresis equipment. It generally contains 2,5-5x10^{11} platelets per bag.**

Indications: **for patients who are refractory to platelets from unmached donors (antibodies to HLA or platelet specific antigens).**

Granulocytes:

are obtained by apheresis from an ABO and Rh compatible donor (who have been stimulated by G-CSF).

It should be always irradiated to prevent GVHD.

It should be administered as soon as possible after collection (if it is not possible, storage at +4^{o}C for no longer than 24 hours).

Indication: - for patients with severe neutropenia and a documented life-threatening bacterial or fungal infection not responsive to antibiotic therapy - neonates with clinical sepsis - patients with infections who have neutophil function defects

Therapeutic dose: 1-2x10^{10} granulocytes for an adult patient.

Fresh frozen plasma (FFP):

The plasma is removed from a unit of whole blood and frozen below - 30°C within 6-24 hours of collection.
It is an unconcentrated source of all clotting factors without platelets.

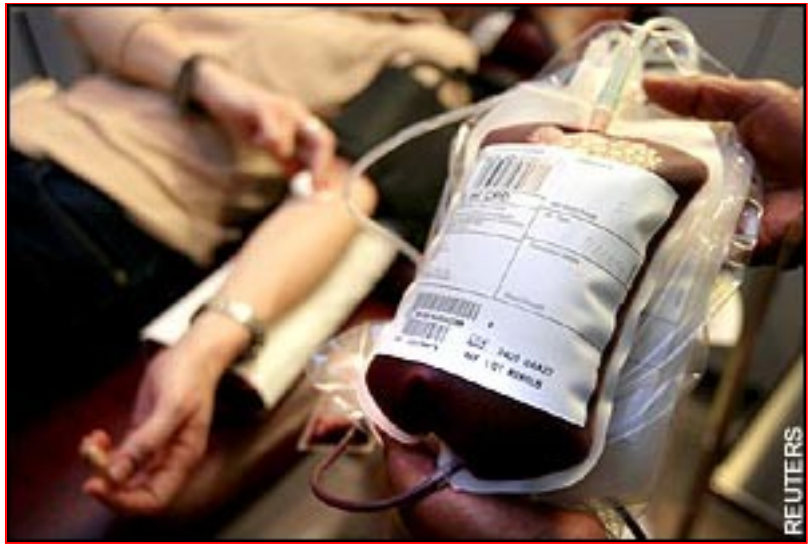
Indications: **- multiple clotting factor deficiencies with bleeding**
- severe liver disease
- urgent warfarin reversal
- massively bleeding patients along with RBCs to prevent dilution of clotting proteins

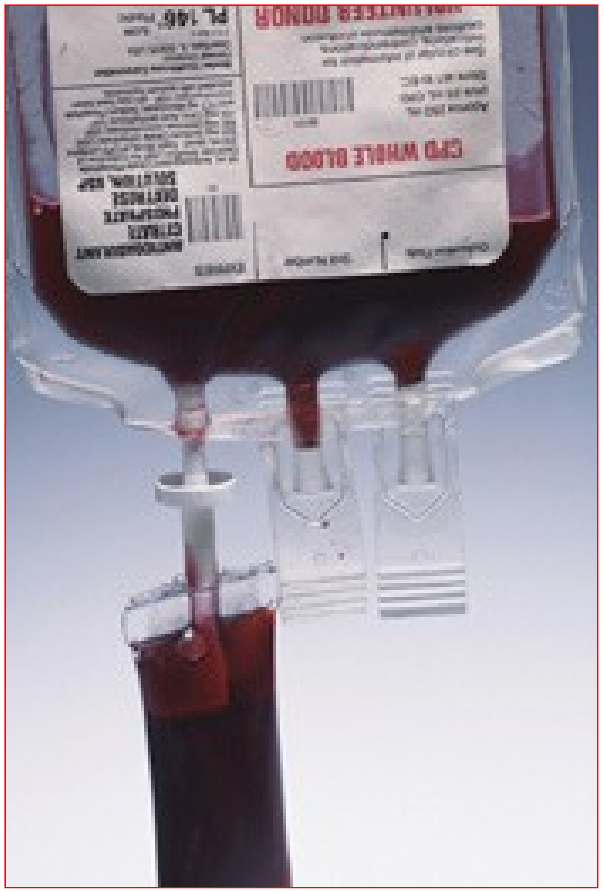
Should not be used for volumen expansion or nutritional support.

FFP must be ABO compatible with the recipients red cells.
Rh need not be considered.

Blood transfusion is a dangerous procedure!

Some risks associated with receiving a blood transfusion.





Transfusion reactions I.

- **Acute hemolytic reaction:**
  Most serious:
  ABO incompatibility
  (most commonly due to the administration of mismathed blood types)
- **Febrile non-hemolytic transfusion reaction:**
- **Allergic reactions:**
- **Anaphylaxis:** in patients with IgA deficiency

- **RBC antibodies**
- **WBC HLA-, platelet antibodies, cytokins** (released from WBCs during storage)
- **allergens in donor plasma**
- **anti IgA antibodies**

Transfusion reactions II.

- **Transfusion-associated acute lung injury (TRALI):**
- **Bacterial contamination:**
- **Transmission of viral infections:**
  HAV, HBV, HCV, HIV, HTLV, WNV, CMV
- **Other risks:**
  volumen overload, iron overload (>100 unit RBCs), K+ toxicity, GVHD, post-transfusion purpura

- **anti HLA antibodies *in donor plasma(!)***
- **1: 25-50000 platelet-, 1: 500000 red blood cell transfusion**
- **risks (2006, USA): HBV: 1: 250,000, HIV, HCV: 1: 2,000,000**

As of mid-2005, all donated blood in the United States is screened for the following infectious agents:

- **HIV-1 and HIV-2**
- **Human T-lymphotropic virus (HTLV I-II)**
- **Hepatitis C virus**
- **Hepatitis B virus**
- **West Nile virus**
- **Treponema pallidum**

Transfusion must be stopped immediately if there are any clinical symptoms and signs of biological incompatibility!

Symptoms and signs:

- malaise
- thoracic pressure
- nausea, vomiting
- diarrhoea
- pain in the lumbar region
- dyspnoea
- cold sweat
- agitation
- frequent and easily obliterated pulse
- circulatory failure
- fever
- hemoglobinuria

What to do in case of transfusion complications:

- Stop transfusion
- Preserve the vein
- Start prevention and treatment of complication
- New blood sample from the patient
- Informing head of department
- Transfusion consultation
- Blood group serology examination

Good practice points of blood transfusion I:

- Consider the cause of anemia (treat nutritional anemia with nutritional supplements - iron, vitamin B12, folic acid)
- Plan all transfusions during business hours
- Always check the identity of the patient
- DO NOT add any drugs to the blood bags
- ALL blood components must be filtered during administration

Good practice points of blood transfusion II:

- Use sterile blood giving sets and change after 12 hours or 3 units
- Blood should only be warmed using official blood warming devices
- Record observations more frequently during rapid transfusions, and in unconscious patients and young children
- Never infuse a unit for longer than four hours
- Ensure all transfusion related forms are filled in and filed away in patient notes

- **„Blood is the best thing possible to have in our veins”.**
  (Woody Allen)

- **That is certainly the case when the blood is our own!**