Types and indications of blood products

Rudiments of Blood Transfusion
for IV. grade medical students

Dr. Csernus Zita
National Blood Transfusion Service
Regional Blood Transfusion Centre Pécs

http://aok.pte.hu/index.php?page=egyseg&egy_id=1910&menu=okt_anyag&nyelv=eng

The meaning of the word transfusion

trans (lat.) trans, through, across, over

fusio (lat.) pouring, merger, associacion, fusion, assimilation

Transfusion - blood transfusion from one person to another

Why do we need blood transfusions?

The physiological role of blood!

Absence

Function impairment

Dilution

It should be substituted

The function of blood

Blood

Stem cell – bone-marrow transplantation

Plasma
(55 - 60 %)

— Fluid portion of blood
— Contains:
91 - 92% of water
albumin & globulin
crucial hormones &
clotting factors

Red Cells
(40 - 45 %)

— Transports oxygen from the lungs to all tissues of the body and return carbon dioxide back to the lungs

White Cells

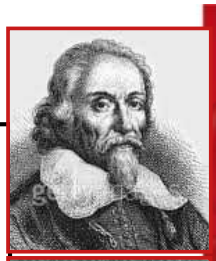
— Protect against diseases & infections

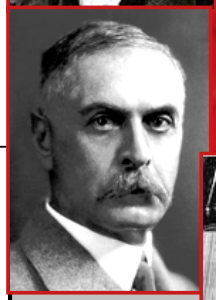
Platelets

— Small plate-shaped cells that cluster together to help form blood clots when bleeding occurs

First steps of blood transfusion

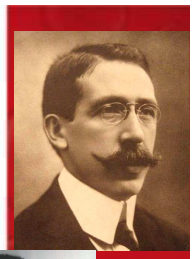
1628	English physician **William Harvey** described the functions of the heart and the **circulation of Blood**.
1667	**Jean-Baptiste Denis** in France reported successful transfusions from **sheep to humans**.
1814	**James Blundell** performed the first successful **transfusion from human to human.**
1901	**Karl Landsteiner**, an Austrian physician, discovers the first three human **blood groups ABO**
1940	The **Rh blood group** system was discovered by **Karl Landsteiner** and **Alexander Wiener**

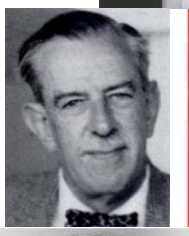
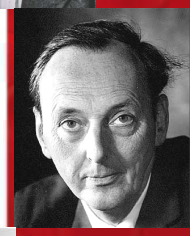


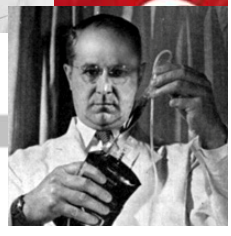




MILESTONES IN BLOOD PRESERVATION HISTORY

1914	Albert Hustin and Luis Agote using **citrate** kept blood for 48 hours in the liquid state
1933	Max M. Strumia developed **frozen storage of plasma**
1943	John F. Loutit and Patrick L. Mollison : introdution of **acid – citrate - dextrose** preservative, the still used method in blood preservation
1951	**deep freezing of red blood cells** was developed - Audrey Smith reports the use of glycerol cryoprotectant for red blood cells
1950 **1963 - 1973**	Carl Walter inventioned **first plastic blood bag** **closed blood bag systems** has made possible to ensure the sterility - introducing of it safer blood products manufacturing and storage became possible (In Hungary, it was introduced from 1984.)



BLOOD PRESERVATION

Blood preservation is called the procedures that allow the blood viable without damage to the biological condition to be kept in a sterile condition.

Aim: the transfused blood in the patient's body remain **viable**

Types: 1. use of blood preservative solutions
2. deep freezing

RBC metabolism

Substrate is glucose

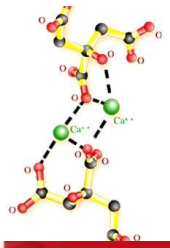
Aerob glycolysis 10%

- ribose-5-phosphate – nucleotide synthesis

Anaerob glycolysis 90% - **ATP excess**

- **2,3-diphospho glicerate shunt**
  oxygen to tissue
- ion transport
  high K^+ level in RBCs
- cell membrane integrity
  osmotic resistance
- **lactate** – pH ↓ -
  damage of RBC metabolism

I-1. CPD PRESERVATIVE SOLUTION FOR BLOOD



Storage time : 28 days

glucosum pro inf.	25,5 g
natrium citricum	26,3 g
acidum citricum	3,27 g
natrium phosphoricum acidum	2,22 g
aqua destillata	ad 1000 cm^3

Ratio: **1 : 6** 63ml CPD + **450ml** blood 1 U

2. Additive Solution / ADSOL /

Storage time: **35 days**

dextrose	111,0 mM/l
adenine	2,0 mM/l
mannitol	41,2 mM/l
natrium clorid	154,0 mM/l

Na-**C**itrate anticoagulant Acid. **citr**. pH
Phosphate ATP production, pH **mannito**l RBC membrane integrity
Dextrose substrate
Adenine red blood cell regeneration

3. HEPARINE

Only anticoagulant effect: antithrombin cofactor

Storage time: max . 6-8 hours

II. DEEP FREEZING (CRYOPRESERVATION OF RED CELLS)

PRODUCTION: within 24 hours from fresh blood
STORAGE: for years
TYPES: 1. SLOW FREEZING:
Temperature: -80 - -90 C° Freezing time: 7 - 8 hours
2. RAPID or ULTRARAPID FREESING:
Temperature: - 196 C° Freezing time: 1 - 3 minutes

CRYOPROTECTIVE AGENTS: glycerine, DMSO

Type of PRODUCT: repeatedly washed blood product

Quality: RBC-s K^+, ATP and 2,3 DPG levels similar to fresh blood

ADVANTAGE: - long term storage of blood or autolog blood before surgery or transplantation
- reduction in transmission of the virus and leukocytes
- decreased risk of immunization

DISADVANTAGE: - high RBC loss / short storage time after washing
- expensive

STORAGE OF BLOOD PRODUCTS

1. Storage times depends on: 1. storage **temperature**
2. blood **preservative** solution

CPD - adenine preservative solution

Storage temperature	Blood product	Storage time
+ 22 °C	Platelets	5 days
	Granulocytes	24 hours
+ 4 °C	Red blood cells	35 days
	RBC washed	24 – 48 hours
	RBC irradiated	14 days
- 18 -25 °C	FFP	3 months
under - 30 °C	FFP	2 years
- 30 °C	RBC frozen	1 year
- 80 °C	PLT, RBC	2 years
- 196 °C	RBC, PLT, FFP	> 10 years

Not in routine practice

ORSZÁGOS VÉRELLÁTÓ SZOLGÁLAT

Sterile conditions for blood collection and preparation! **Quality control !**

Right blood storage:

Components storage on optimal temperature

(+20℃, +4℃, -30℃)

Under continuously controlled standard conditions ensuring the sterility of the preparation is done!

+ 4 °C

+ 20 °C

There is no single optimum method for all blood components.

- 30 °C

ORSZÁGOS VÉRELLÁTÓ SZOLGÁLAT

CHANGES IN QUALITY INDICATORS OF CPD-adenin BLOOD DURING STORAGE

I . ***Essential components reduced:***

FROM 10. DAYS - ↓

1. **ATP** content of red cells
2. 2,3-**DPG** content of red cells

oxygen transport !
massive transfusion
neonatal blood exchange
cardiopulmonary diseases

PROGRESSIVELY -↓

3. lifetime of **cellular components** / granulocyte, thrombocyte
   red blood cell /
4. labile **anticoagulant factors** / VIII, V /

NOT CONTAINS -

5. **Ca ions-** citrate effect *tetany !*
   (larger amounts of plasma transfusion)

II. ***Toxic substances get into into the plasma:***

FROM 5-6. DAYS -

1. **K^+** efflux from RBC / approx. 1 mmol/day /
   risk of potassium *intoxication!* Kidney insufficiency
   Newborns

FROM 7. DAYS -

2. rising of **ammonia** level
   risk of *intoxication !* Severe liver demage

PROGRESSIVELY increase

3.**microaggregates** - filtration !
4. free **Hb** - < 43g/U

Criteria for RBC concentrate:

Administered RBCs on the last day of storage should be detectable in the circulation of patients after 24 hours of 70-75%.

This is ensured if the red blood cell ATP content is 40-45% of baseline.

Preserved red blood cells can be detected in the circulation for 100 days. Elimination of them is 1% / day.

Decreased in vivo survival:
- auto-/izoimmun hemolysis
- fever - increased RBC destruction
- splenomegaly
- aplastic anemia

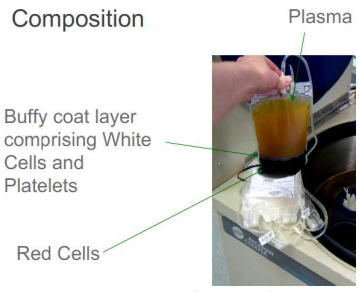
Normal RBC survival but **no Hb increase** :
- severe bleeding

Preparation of blood components

Whole blood – row material for the manufacture (450 ml -CPD 1:6)

1 U = blood component volume prepared of one blood collection bag

1. Blood components



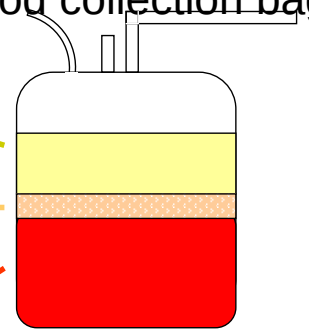
Plasma – albumin, globulin, coagulation factors etc.

Boundary layer (buffy coat)

Platelet concentrate

White blood cell concentrate

Red blood cell concentrate

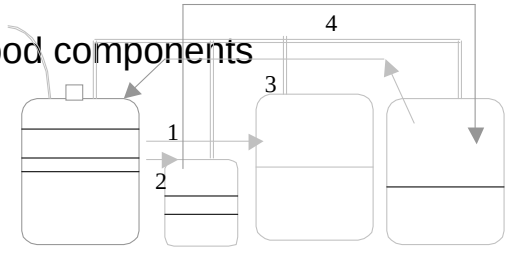


2. Blood separation

Differencial centrifugation – specific weigh difference – closed plastic bag system

Apheresis – instrumental method of obtaining blood components

Autotransfusion – preparation of whole blood or blood components



Types of blood components

Basic components: RBC, PLT, Plasma

Special components: washed, filtered, irradiated basic components or their combinations

Unstable blood components — **Non virus inctivated**

basic and special types of
- **red blood cell concentrates**
- **platelet concentrates**
- **white blood cell concentrate**
- some **plazma products** - **FFP** /fresh frozen plasma/,

cryoprecipitate/cryosupernatant

- **hemopoetic stem cell -** autologous or allo

Stabile blood components — **Virus inactivated**

Plasma fractions prepared from human plasma pool

- albumin solutions
- immunglobulins
- clotting factors
- other isolated plasma fractions or their combinations
- haemopoietic growth factors /rHu Epo, rHu IL-3, rHu IL-6, GM-CS/

I. WHOLE BLOOD AND THEIR INDICATIONS

Row material

	Preservative	Storage temperature	Storage time
I.	**1.CPD**	+4 C°	**28 day**
	2. CPD-A	+4 C°	35 day

EFFECT: 1. volume replacement
2. restoration of oxygen-carrying capacity

Similar effect can be achived! - **RBC. conc. + FFP and/or albumin**

INDICATION: *very limited*

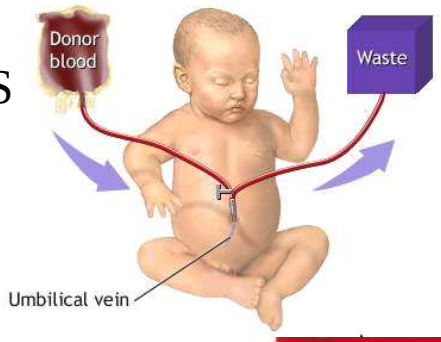
1. **acute blood loss** (the loss of 30-40 % the total blood volume, or the amount of the circulating blood volume within 24 hours) /masszive transzfusion > 10U blood /
2. **exchange transfusions**
3. **emergency conditions**, when there is no other option

Red blood cell transfusion

2. *EXCHANGE TRANSFUSIONS*

I. **ADULT** EXCHANGE TRANSFUSIONS

1. severe acute **liver failure**
2. **poisoning** / mushrooms, CO, chemicals /



II. **NEONATAL** EXCHANGE TRANSFUSIONS

a. partial: 1. rapid correction of **severe anemia**

2. **hyperviscosity** induced polycythemia

b. total : 1. haemolytic disease of newborn / **HDN** /

2. severe **RDS** 3. **DIC**

4. **harmful substances** transferred from the maternal circulation to the fetus /toxic substances, pharmaceuticals, antibodies/

5. **haemolytic crisis** of sickle cell anaemia

BLOOD PRODUCT FOR TRANSFUSION:

RBC **under 7 days** old

The blood **chrossmatch** have to be performed on the **mother's serum** also up to 4 moths of age

AMOUNT: 180 - 200 ml /kgBW

Complications due to the white blood cell and platelet content of blood products:

1. *febrile nonhemolytic transfusion reactions*
2. *HLA alloimmunisation*
3. *GVHD /irradiation! /*
4. *mikroaggregate transmission /RDS, pyrogens .../*
5. *virus transmission*

Buffy coat removing

White blood cell (WBC) content of blood products

filtered (leucocyte reduced) RBC concentrate	**< 1 x 10^6**
whole blood	2 - 3 x 10^9
RBC concentrate -resuspended buffy coat free	**1-5 x 10^8**
plasma	2 x 10^7
platelet concentrate	0,5 x 10^8

WBC removal methods	***WBC** removal rate*
• **spin and buffy coat removal**	~ 80%
• **wash – physiological saline** – plasma removal	~ 70 - 90%
• **filtration -** special filter /d = 40µ / WBC maximum removal of **99,995%**	

II. RED BLOOD CELL CONCENTRATE (packed RBC)

Preservative	Storage temperature	Storage time
CPD + adenin	+4 C°	35 day

HEMATOCRIT: 55 - 65 % VOLUME : ~ 200 ml

EFFECT: **restoring oxygen carrying capacity**

ADMINISTRATION: in normovolemia 1E / 3/4 - 1 hours

in hypovolemia it depends on the patient's circulation and volume

INDICATIONS: anemic conditions with hypoxia

/ symptoms: tachycardia, dyspnoea, cyanosis /

Explain the cause of anaemia ! Patients must be cured, not the lab. findings!

acut blood loss - at 20 % Htc (90 Hb) is vital indication

*With chronic anaemias there is compensation - **clinical picture** !* **Hb 70g/l**

CONTRAINDICATIONS:

- drug-treatable deficiency anaemia / Fe, folic acid, B_{12} /
- renal failure - eritropoetin / second choice -transfusion /
- AIHA - primarily steroid /tr. only in **case of vital indication**/
- physiological anaemia of newborn- and premature infant

III. WASHED RBC CONCENTRATE

Aim: **removal of plasma**

Resuspension solution	Storage temperature	Storage time
SAGM or salin(0,9%)	+4C°	48 or 24 hours

protein content: minimal 0.3 g

HEMATOCRIT: < 70% VOLUME: 150 ml

EFFECT: restoration of oxygen-carrying capacity

ADMINISTRATION: depends on patient's syndromes and circulation

Continuous monitoring is required.

INDICATIONS: 1 sensitivity to plasma proteins

/ anaphylaxis /

2. IgA deficient patients

(3. PNH / removal of complement factors! /)

IV. FROZEN RBC CONCENTRATE
Several times washed Product

Preservative	Storage temperature	Storage time
CPD, **glycerol** Volume: ~ 200ml Content: minimal WBC and plasma protein	- 30, -80, -196 °C + 4 °C	6 month, 1-2 years unlimited after thawing and washing: 24 hours

for allogen or autologous transfusion

INDICATIONS: alloimmunization to many common RBC antigens

DISADVANTAGE: expensive, high red blood cell loss

ADVANTAGE: less risk of infection and immunogenic effect long-term storage

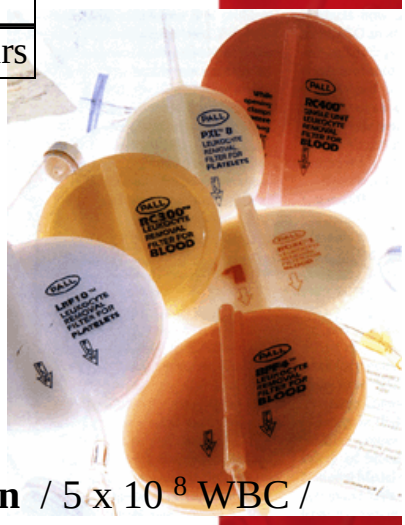
Advantages of packed RBC compared with whole blood:

1. much smaller volume
2. low plasma protein content
3. low citrate, K^+, Na^+, and NH_3 content
4. low WBC and platelet content

V. PLATELET, WBC DEPLETED, FILTERED PACKED RBC

/ 4 log filter / ***WBC content of 1 U RBC conc.*** : 1 - 2 x **10^9/U**

Preservative	Storage temperature	Storage time	Filtration
CPD-A	+4°C	35 nap	within 48 hours



WBC CONTENT: **1-2 x 10^5 / U**

EFFECT: restoration of oxygen-carrying capacity

INDICATIONS: **prophylaxis of complications due to WBC and platelet content of RBC products**

1 prevention of HLA **alloimmunization** /5 x 10^6 WBC /

2 prevention of **febrile non haemolytic transfusion reaction** / 5 x 10^8 WBC /

3 avoidance **ARDS** /**microaggregates** - platelet+WBC+fibrine- 40 - 170 µ /

4 reduction **virus transmission** /**CMV** ! - 1 x 10^7 WBC/

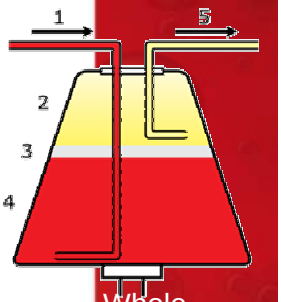
5 **intrauterine- or perinatal** transfusions

avoidance **GVHD** – ***only with irradiation* !*** */ 1x10^4 WBC /*

Currently this is the safest RBC product

Blood donation with apheresis

The apheresis RBC is leucodepleted blood product



Whole blood enters the centrifuge (1) and separates into plasma (2), leukocytes (3), and erythrocytes (4). Selected components are then drawn off (5).

0.9% sodium chloride

filter

ADSOL™ Red Cell Preservation Solution

ACD-A anticoagulant

Alyx Machine – machine used for **double red cell donation**

IRRADIATION OF BLOOD PRODUCTS

- **Aim:** **immunologically competent lymphocyte proliferation ihibition**

prophylaxis of GVDH >10^4 WBC

GVHD (graft versus host disease): caused by donor lymphocytes in immunodeficient states of recipient

therapy: **irradiating of blood products** (RBC, PLT, plasma)

- **Source of radiation:** γ-ray / Cs^{137}, Co^{60}
- **Dose:** 2500 - 4000 rads

Storage time: 14 days, for neonates 48 hours

INDICATIONS:

- congenital or aquired immunosuppression conditions
- blood transfusion of relatives

VI. AUTOTRANSFUSION

TRANSFUSION OF THEIR OWN BLOOD

USED: from 12 to 70 years
donor eligibility criteria
pregnancy is not reason for refusal
iron supplementation

FORMS: 1. preoperative blood collection / 2- 5 U /
2. preoperative haemodilution /better tissue oxygenation /
3. intraoperative blood salvage / cell savers /
4. postoperative blood salvage

ADVANTAGES:

1. decreased risk of infection and immunization
2. better tissue oxygenation / HTC 30% / - hemodilution
3. sparing of blood products

CONTRAINDICATIONS:

1. not correct cardiac or haematological status of patient's
2. the blood transfusions are not suitable for the patient / tumor, infection /

VII. HEMATOPOIETIC STEM CELL TRANSFUSION / TRANSPLANTATION

BONE MARROW TRANSPLANTATION

Allogenic or autologous

HARVESTING OF STEM CELLS FROM:

1. crista
2. **periferal blood with apheresis**
3. umbilical cord blood
4. fetal liver

Enrichment and freezing of stem cells

REQUIREMENTS FOR ADMNISTRATION OF BLOOD PRODUCTS CONTAINING RED BLOOD CELLS

- **ABO and Rh D GROUP IDENTICAL BLOOD TO RECIPIENT SHOULD BE ADMINISTERED IF IT POSSIBLE UNLESS** OTHERWISE SEROLOGICAL PROPOSAL **/e.g.**: exchange transfusion, irregular antibodies/
- **ABO COMPATIBILITY IS MANDARORY**
- **REQUIRED PRETRANSFUSION TESTING:**

1. **ABO and RhD grouping of patient and blood to be administered**
2. **crossmatch is performed by Blood Bank if recommended**

THE PLETHORA INHIBITS, THE ANAEMIA STIMULATES THE ERYTHROPOESIS.

Should never be increase Hb concentration with transfusion to literary value.

THE AMOUNT OF BLOOD TO BE ADMINISTERED:

$$\text{blood volume /ml/} = \frac{\textbf{TBV /ml/kg/ x / Hb}_2 \textbf{ - Hb}_1 \textbf{ / g/l}}{\text{blood product Hb g/l}}$$

TBV = total blood volume = circulating blood volume x body weight
/adult-70 ml/kg, neonate-90 ml/kg, immature new-born-100ml/kg/
Hb_1 = Hb patient's prior to transfusion
Hb_2 = Hb concentration desired after transfusion

Hb concentration of blood products: (whole blood - 120 g/l)
RBC concentrate - 220 g/l
washed RBC concentrate - 300g/l

E.g.: 70 kg patient's Hb of 80g/l to 120g/l was rised

70 x 70 x 40 = 120
220 or 300 (depending of blood product)

890 ml packed RBC ~ 4U
650 ml washed RBC c. ~ 4U

Whole blood administration is contraindicated in normovolem[illegible]!

VIII. PLATELET CONCENTRATE

2. Platelet transfusion

TYPES:	
1. Random donor platelet concentrate /4 pooled donor /	**2.** Apheresis single donor
VOLUME: 50 - 70 ml/U	200 - 500 ml/ apherezis
PLT CONTENT: 0,5-1,0 x 10^{11} /U	2,0-6,0 x 10^{11} /l/apheresis
RBC CONTENT: 0,5- 6,0 /100 PLT	small
WBC CONTENT: 1 x 10^{6} - 10^{8} /U	5 x 10^{8} / 10U apheresis
STORAG TIME: 5 days	
DEPARTMENT STORE PROHIBITED!	

ADVANTAGE: good survival 8-10 days /HLA compatible donor
COST: random platelet - low / apheresis - significant

STORAGE: in plastic bag on 20 - 22 ° C with gentle shaking
pH: 6.8 - 7

EFFECTIVE DOSE: **2.4 x 10^{11} platelets**

1U /10 kg BWT (4-8 U) or 1 apheresis (10 U)

INCREMENT : 5-10 000 / µl (5-10 G/l) - 1U
1 hour after transfusion 20 – 40 G/l - 4 U

VERIFYING THE EFFICACY OF PLATELET TRANSFUSIONS:

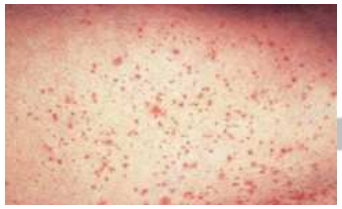
Corrected platelet count incement (CCI):

$$\frac{\text{No of PLT after transfusion - No of PLT before transfusion}}{\text{number of units transfused}} \times \text{BSA}$$

Effective PLT increment 1 hour after transfusion is
> 7,5 x 10^{9} /l PLTs

INDICATIONS:
1. amegacaryocytic thrombocytopenia
2. platelet dysfunction
3. dilutional thrombocytopenia
4. DIC
5. immunisation

Platelet function inhibitor medication is contraindicated.
E.g: acetyl-salicylic



Clinical signs !

PLATELET SURVIVAL:

1. **normal**: 8-10 days - 50% detectable 1 hour after transfusion
2. **decreased:** lifetime is hours or minutes
   1. ***immunization*** - **allogen**-: pregnancies, transfusions, transplantations
      refractory status: no effect of random donor PLTs
      therapy: crossmatched HLA compatible, filtered apheresis PLTs
      - **autologous**: ITP **therapy:** primarily **steroid!**
   2. ***DIC*** /consumption /
   3. ***sepsis***
   4. ***splenomegaly***
   5. ***febrile conditions***

*In case **protein allergy** washed PLTs can be given*

Avoidance of ***GVHD*** with **irradiation** of PLT

IX. WHITE BLOOD CELL PRODUCTS

TYPES: 1. pool from 10 units **buffy coat** using fresh whole blood	2. single apheresis
VOLUME: 300 ml / pool	200 - 300 ml / apheresis
GRANULOCYTE CONTENT: 0,5-0,60 x 10^9 /E /70% gr. 30 % ly/ high red blood cell and platelet contamination	**ADVANTAGE:** 1 x 10^{10} / apheresis 1. higher granulocyte content 2. HLA compatible
STORAGE TIME: max. 24 hours - **Prohibited store in department !**	
METHOD OF STORAGE: 20 - 24 C° /room temperature /	

Donor stimulation before apheresis:

steroid or growth factors

EFFECT: ***questionable***

DOSAGE:

1 x 10 ^{10} granulocyte / day = (10 - 15 E buffy coat)
1 apheresisWBC product

INFUSION: very slowly, in several portions
high lymphocyte content – GVHD – **irradiation!**
RBC content - **crossmatch**

3. White blood cells

LIFETIME IN CIRCULATION: some hours

SURVIVAL: shortened by antibodies against HLA and/or granulocyte anigens

INDICATION: **rare** **ALWAYS INDIVIDUALLY**

1. SEVERE BACTERIAL OR FUNGAL INFECTION with antibiotic/antimicotic resistence even after 48 - 72 hours treatment with WBC count: 0.2 x10^9 /l
2. NEONATAL SEPSIS / irradiated, CMV, toxoplasma negative! /

COMPLICATIONS: **FREQUENT !**

1 febrile nonhemolytic reaction / 5 - 10% /
2 anaphylaxis
3 RDS
4 Multiple immunizations / TCT. RBC. contamination /
5 Infections transmission / CMV, toxoplasma, HTLV-I ... /
6 GVHD / correlation with the lymfocyte count/

Remains in the background against haemopoetic growth factors – G-CSF , GM-CSF

4. Plasma transfusion

PLASMA FRACTIONATION:

Source: **1. whole blood** **2. apheresis**

plasma

/180-200 ml/ /600-1000 ml/

fresh frosen plasma / within 6-24 hours /

cryoprecipitate

VIII.f. concentrate
and other
clotting factors

cryo-supernatant

albumin
immunoglobulins
and other factors
pl: antitrombin - III. f.
protein S
protein C
fibronectin . . .

5% protein content - 50–60% albumin 10-15% globulins

the other protein fraction concentrates are in mg quantities

I. FFP /FRESH FROSEN PLASMA/

Preservative	Storage temperature	Storage time
CPD	-30 C°	2 years

Freezing must be completed within 6-24 hours of receiving the blood!

Not disinfected PRODUCT!

CONTENT: - like fresh plasma

all clotting factor / VIII, V, too! –labile factors/
complement
plasma proteins

APLICATION:

Thawing in 37 C° a water bath and transfusing immediately after
Dose: 10-12 ml / kg / 4-7 U /
Administration : 3/4 -1 hour / U

AB0 compatible

EFFECT : REPLACEMENT OF PLASMA FACTORS - labiles too

CONTROL THE EFFECT: partial thromboplastin time
- Prothrombin time

Plasma transfusion

INDICATIONS of FFP:

1 severe bleeding in unknown factor defciency
2 complex coagulation factor deficiency / DIC, severe liver lesions, liver transplantation, massive transfusion, blood replacement after bleeding /
3 congenital factor deficiency, if no missing factor concentrate /Antithrombin III, C1-esterase inhibitor, Factor V /
4 TTP - plasma exchange / 3 L / day /

FILTERED PLASMA

PREPARATION specific plasma filters, repeated centrifugation, aphereis
INDICATIONS: Patients on immunosuppressive state

IRRADIATED PLASMA

PRODUCTION: fresh product - 2500-4000 rad γ irradiation
INDICATIONS: protect against GVHD

non virusinactivated product

II. CRYOPRECIPITATE

Cryoprecipitate is a precipitate formed from plasma frozen at– 30 ℃ within 4 – 6 hours, then thawed + 4 ℃.

MAIN INDICATIONS: fibrinogen and factor VIII supplementation, but **in Hungary** only **raw material** of clotting factors included in precipitate, recently.

NON VIRUS INACTIVATED PRODUCT
Prepared from 4-6 U whole bloods
Volume: 100 ml

CONTENT:

1. factor **VIII**. / 2 - 4 U/ml t 1/2: 8-12 hours /
2. fibrinogen / 6 - 10 g/l t1/2: 3 - 5 days/ 250 mg/U plasma
3. factor von Willebrand t 1/2: 12 hours
4 fibronectin t 1/2: 1 - 3 days

Specific indication of cryosupernatant : **TTP**

III. CLOTTING FACTOR CONCENTRATES

1. FACTOR VIII. CONCENTRATE

virus-inactivated lyophilized preparation from THOUSANDS OF pooled donor plasma

Volume: 10 ml
Benefits: – high content of actives substance in small volume
- suitable for home treatment
CONTENT:. VIII.f 150 IU / mg protein
Half-life: 12 hours

ADMINISTRATION: intravenously in more portions / accident, surgery /

EFFECT: stops the bleeding, prevents haemorrhage and articular lesions

INDICATIONS: Hemophilia A

HUNGARIAN **PRODUCT** / Behring License / HUMAFAKTOR – 8
Others: HAEMOCTIN 500 NE, RECOMBINATE 500 NE, KOGENATE BAYER 500 NEADVATE 500 NE, BERIATE 100 NE/m

THERAPEUTIC DOSE CALCULATION IS INDIVIDUAL:

f. VIII volume to be administered = plasma volume x (Exepted f. VIII - Starting f. VIII /

2. PROTEIN S and PROTEIN C

EFFECT: - F V. and F VIII anticoagulant factor inactivating proteins
- Plasminogen activator - fibrinolytic effect

Storage: + 4 ° C Expiery: several years

INDICATION: - **congenital factor deficit**

Symptoms
* deep vein thrombosis
* Massive neonatal venous thrombosis - purpura fulminans

3. FACTOR IX. CONCENTRATE

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INDICATION: **hemofilia B** / congenital F. IX.f./

Alphanine® SD : Monoclonal : Grifols
BeneFix® : Recombinant : Pfizer
Mononine® FS : Monoclonal : CSL Behring
Immunine Human : Baxter
Haemonine Human Biotest

Dose (units) = (factor IX desired - factor IX baseline) x total body weight (kg)

FACTOR VIIa RECOMBINANT indicated – haemophylia A or B patients with **inhibitor**

4. PROTHROMBIN COMPLEX CONCENTRATE

PCC content II,VII,IX,X

Indication: **acquired deficiency** of the prothrombin complex coagulation factors – vitamin K deficit, liver disease
overdose of vitamin K antagonists
congenital deficiency of vitmin K dependent coagulation factors II and X when purified specific coagulation factor product is not available

Products:

Octaplex PCC II,VII,IX,X + protein S and protein C

Prothromplex TIM 3 (Baxter, Vienna, Austria) (II, IX and X) TOTAL (II,VII,IX,X)

Confidex® (CSL Behring, Marburg, Germany) (II,VII,IX,X protein S and protein C + AT+ heparin)

Adverse event: allergic reaction
HIT (heparin induced trombocitopenia)
thromboembolism

IV. ALBUMIN (5% és 20%)

Viral inactivated, virus free blood fraction
Plasma concentrations of albumin: 40 - 50 g / l
Half life time: approx. 14 days **blood-derived albumin is only 12-16 hours**

Heat stabilized **Storage: 2-25 °C Storage time: several years**

PRODUCTS:

1 **5% - the same as the plasma oncotic pressure**
volume expansion effect lasts for 48 hours
2 **20% - (oncotic effect four times that of blood plasma)**

EFFECT: - **extravascular compartment mobilization - water suction effect**
1g albumin binds 18 ml water
movement of fluids from the interstitial to the circulation

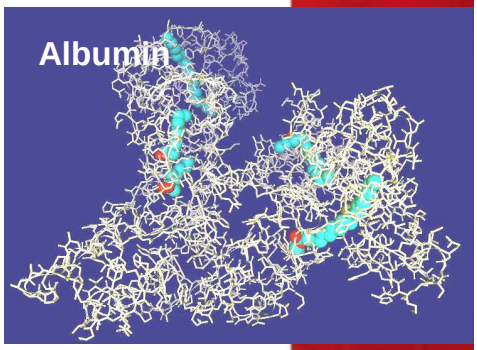
DOSE: **5%: 250-500 ml** **20% < 200-300ml/ day**
dose (g) = (2.5g/dl – actual albumin concentration) x (kg x 0.8)

2.5 g/dL: desired concentration of albumin; kg: body weight;
0.8: coefficent to calculate the volume of plasma

Administration: intravenously , infusion set for single use

INDICATIONS: Albumin is used as a **second choice** when **solutions of crystalloids or non-protein colloids non** produced a clinically adequate response and in cases in which non-protein colloids are contraindicate

1 **Acute plasma volume replacement** - albumin <25 g / l
2 Burns - **plasma protein replacement**
3 **Ascites not responsive to diuretics** - diuretic resistant edema,
hypoproteinemia 20% albumin + diuretics
4. **Haemorrhagic shock of infants**
safe and can be used without blood group properties



RISK: overdose

Tissue hypoxia - dehydration
Circulatory overload - pulmonary edema
Protein Allergies - Anaphylaxis

Contraindicated in patients with **Parenteral nutrition**
Treatment of immunodeficiencies

no better and more specific effects than other colloidal solutions
not contain essential amino acids and immunoglobulins

V. IMMUNOGLOBULINS

VIRUS FREE lyophilized **plasma fraction extracted from about 1000** DONOR plasma pool PRODUCED BY FRACTIONATION

STORAGE: + 4 °C. IgG, **T 1/2**: 21 days

Indication: restoration of te specific antibody response
enhance the body's resistance (prophylaxis)

Dose: 200-400mg/kg prophylactic: 2 - 4 weeks to years
therapeutic: 3 - 5 days

Types:

Non-specific - **polyvalent** human serum globulin (**IgG and** few **IgA,IgM)**
- **includes the average infected population antibodies**

Specific - vaccines / anti-D-HBs - CMV, -varicella, -. tetanus etc /
- **contains substantially higher concentrations of specific antibodies**
active or passive immunization
gene technological methods
- **hyperimmune gamma globulin** / anti-D etc /

COMPLICATIONS: **anaphylactic reactions, hemolysis**

Absolute contraindications: Selective IgA deficiency with anti-IgA +

ADMINISTRATION: slowly
SCIG: primer immunodeficiency - self-administration at home
IMIG: measles, gram negative sepsis
IVIG: most effective - high dose - standard blood administration set

ADMINISTRATION - slowly! -recognition of possible complications

Main areas of INDICATION - still evolving

primary immunoglobulin deficiency (X chain low immunoglobulin, familiar variable immune deficiency, immunoglobulin G secondary deficiency)
secondary immunoglobulin deficiency – infection, newborn sepsis, CLL with hypogammaglobulinaemia, toxins, drogs
autoimmune deficiency diseases - ITP, Kawasaki disease
immunocytopenia – PTP

Effect: passive immunization, immunomodulation

Products: Intragam P, Octagam, Flebogamma, Intratect, Humaglobin etc.

Characteristics of coagulation factor products

Virus inactivated blood products

1. Safe: virus-inactivated, disinfected
   extreme rare virus transmission
2. Lyophilized - solvent included
3. Storage: - 2-6 °C.
4. Expiry date: several years
5. Dosage: - Strict adherence to instructions
   - The half-life taking into account factors
   - Overdose - thrombosis

6 Disadvantage: - expensive

Recommendations:

1. **Macroscopic control** before administration
2. Dosage and administration -**manufacturer's instructions**
3. After resolution **should be given immediately**
4. When adding clotting factors **hematology consultation** is needed!

The future of transfusiology

Increase of **storage time**: red blood cells, platelets
Virus inactivation of all plasma products and cellular blood products

Red Blood Cell Transfusion

1. **EPO** : chronic kidney disease, treated HIV patients, carcinoma patients, allogeneic and autologous bone marrow donors
2. **Autologous** blood transfusions
3. **Enzymatic modification of red blood cells** (converted„0" group) or camouflaged red blood cells with mPEG
4. **Blood substitutes** : ⇨ Perfluorinated compounds
   ⇨ Hemoglobin solutions
   ⇨ Recombinant hemoglobin

Platelet transfusion:

1. **TPO** (thrombopoietin)
2. **Artificial** blood platelets

White blood cell transfusion:

1. **G-CSF**
2. **leukocyte depletion** in all blood products

Plasma and plasma product transfusion:

Rekombinant proteins (F VIII, anti-D, etc.)