Introduction to Transfusion Medicine

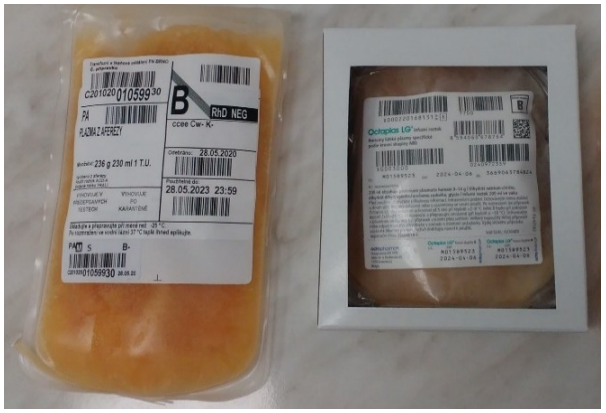
Blood component

- 1 – 10 donors
- ↑ risk of infection transmission

- Blood establishments (within ČR)
- *Red Blood Cells, Platelets, Plasma, Granulocytes*

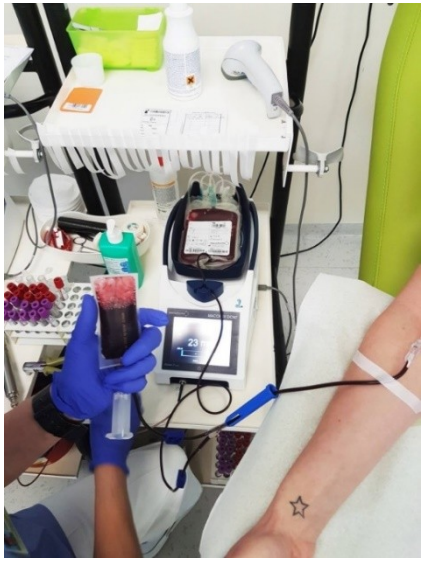
Blood derivative

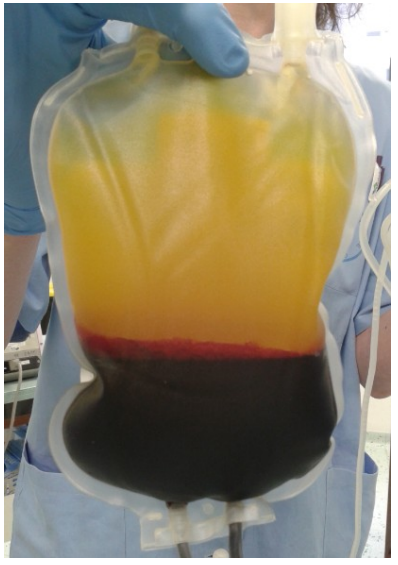
- pooled plasma (thousands donors)
- ↓ risk of infection transmission – **P**athogen **R**eduction **T**echnology
- Plasma fractionation centers (abroad)
- *Solvent/detergent-treated plasma, Coagulation factor concentrates, Immunoglobulins, Albumin…*



Blood components may be obtained:

- **whole blood donation**
  - → centrifugation
  - → separation into its constituent elements





- **apheresis**
  - only the desired component is collected, while the remaining blood is returned to the donor
  - usually further processing not needed

BLOOD COMPONENTS

Whole Blood

- source material for component preparation
- not used for transfusion (usually)
  - storage conditions and shelf life are specific for each component type
  - patients should receive only the component required to correct their specific deficiency
- whole blood may be indicated in limited clinical settings

Red blood cells

- Shelf life: 42-49 days
- Storage temperature: 2-6°C
- ABO/Rh(D) compatibility between donor and recipient necessary, pre-transfusion testing

Decision to transfuse
…is complex:

- Cause of anaemia
- Severity of anaemia
- In case of haemorrhage: the rate and amount
- Ability to compensate for the blood loss
- Presence of comorbidities affecting compensatory mechanisms

Indication

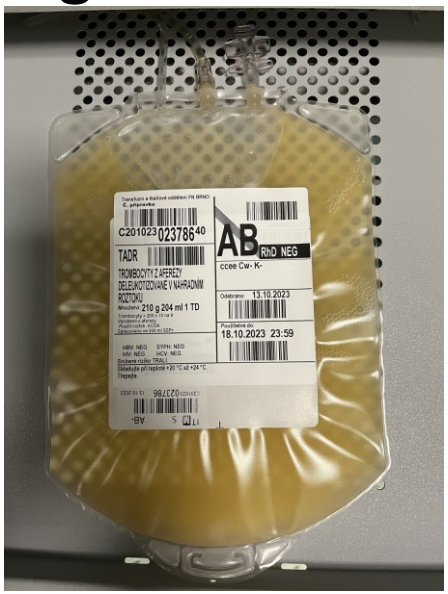
The aim of red blood cell transfusion is to provide **oxygen delivery** to organs and tissues when there is evident hypoxia caused by severe ***anaemia***.

- Haemoglobin > 100 g/l: no indication
- Haemoglobin 70-100 g/l: individual evaluation
- Haemoglobin < **60 - 70 g/l**: indication almost sure

1 TU of RBCs is expected to raise haemoglobin by 10 g/l

Platelets

- Shelf life: 4 to 5 days
  - 7 days in case of sterility control or use of PRT
- Storage conditions: at 20-24°C with continuous agitation
- ABO/Rh(D) compatibility recommended
- no pre-transfusion testing



Indications

- ***Thrombocytopenia or thrombocytopathy***
  - Therapeutic: active platelet-related bleeding
    - platelet count trigger for transfusion is not strict: evaluate bleeding severity, cause, suspected dynamics
  - Prophylactic: as prevention of bleeding
    - < **10 x 10^9/l** to prevent spontaneous bleeding
    - < 50 x 10^9/l in case of invasive and major surgical procedures, cardiac or intracranial surgery 80-100 x 10^9/l

1 TD increases platelet count by 20-40 x $10^{9/l}$

Plasma

- Storage: 36 months at -25°C
  3 months at -18°C
- balanced amount of coagulation factors and coagulation inhibitors (and other plasma proteins)
- ABO compatibility necessary
- RhD not relevant
- no pre-transfusion testing

Indications

- use of plasma (FFP) less frequent - replaced:
  - coagulation factor concentrates
  - pooled plasma solvent detergent treated (OctaplasLG)
- ***massive bleeding***
- ***DIC with active bleeding***
- ***TTP (plasma exchange)***
- ***Vitamin K deficiency associated bleeding*** *(+ vit K)*

Dosage: 10 – 15 ml/kg

Granulocytes *(rare use)*

- Shelf life: short – administrated as soon as possible
- Storage temperature: 20-24°C
- ABO/Rh(D) compatibility between donor and recipient necessary, pre-transfusion testing
- Indication: severe inf. + neutropenia
- Irradiation always

BLOOD COMPONENT ADJUSTMENT

Leucocyte depletion

- *without indication limitation (safer)*
- leucocytes < 1x 10^6
- prevention/reduction
  - ↓ adverse transfusion reactions
  - ↓ alloimunisation
  - ↓ haemotherapy-associated immunosuppression
  - ↓ pathogen transmission (EBV, CMV) - alternative of CMV negative blood component

Irradiation

- prevention of **TA-GvHD**
- γ rays of 25-50 Gy inactivate T lymfocytes
- *indications:*
  - immature or altered immune system
  - transfusions from relatives / of HLA-matched blood components
- doesn´t replace leucodepletion neither destroys pathogens

Washing

- *indications:*
  - repeated severe allergic reactions due to plasma proteins
  - selective IgA deficiency
- shortened shelf life
- anaphylactic reaction prevention
- performed by additive solution or saline
- goal: total protein < 0,5 g / TU

Smaller amount needed?
- blood component may be divided

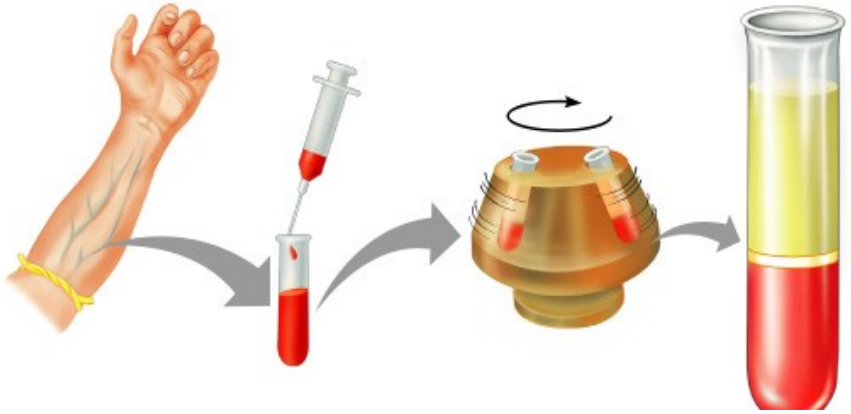
- *Red blood cells* – according to childs weight
- *Platelets* – standard pediatric dose = 1/2 of adult TD
- *Plasma* – production of pediatric dose possible, usually not cost effective

IMMUNOHAEMATOLOGY

(JUST BASICS..)

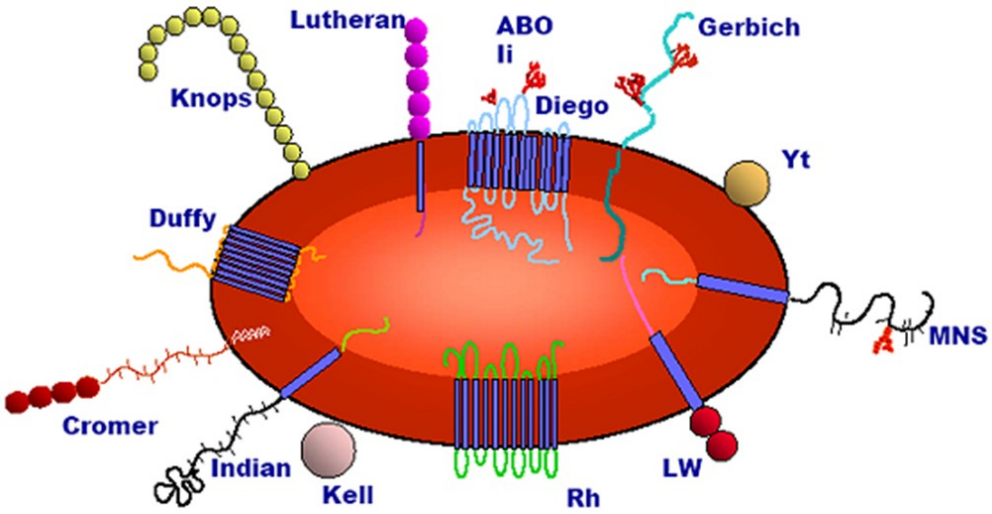
Pre-transfusion testing

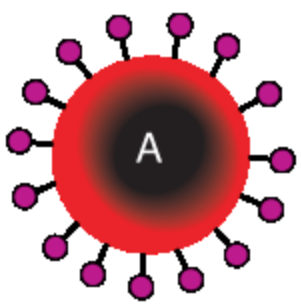
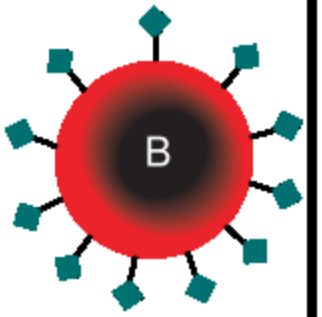
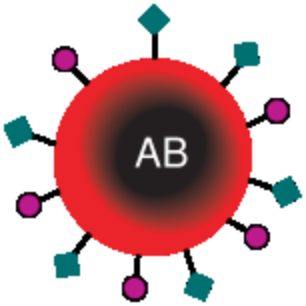
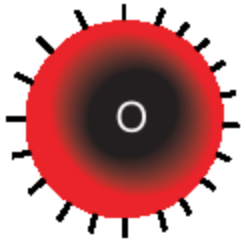
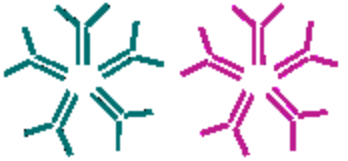
- compulsory serological tests done before erytrocyte blood component administration
- valid for 3 days
- 100% safety not guaranteed



Pre-transfusion testing comprises:

- blood group testing: ABO and RhD
- screening for red cell antibodies (non-ABO)
- compatibility test



	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

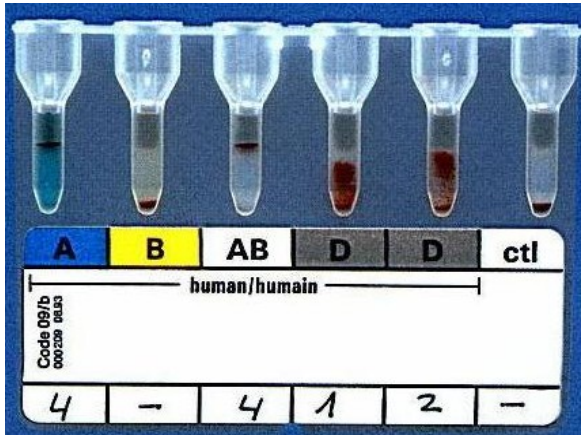
ABO and RhD testing of recipient

ABO

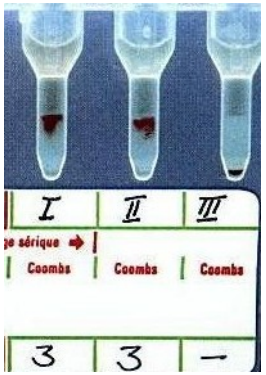
- ABO antigens (aglutinogens)
  - monoclonal anti-A and anti-B diagnostic serum
- ABO antibodies (aglutinins) – *reverse grouping*
  - diagnostic A1 and B erytrocytes

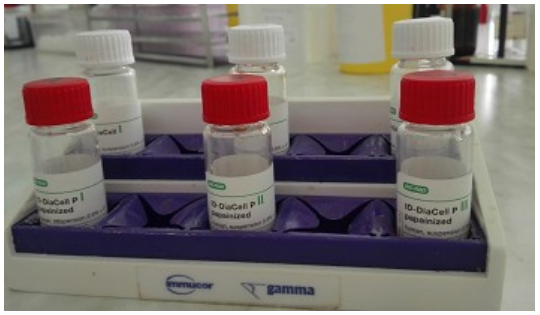
RhD

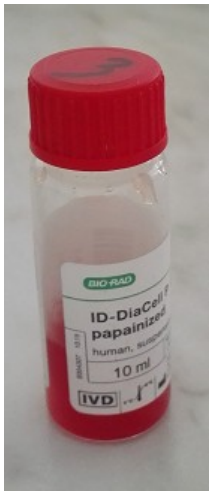
- using 2 different diagnostic anti-D (IgM) sera

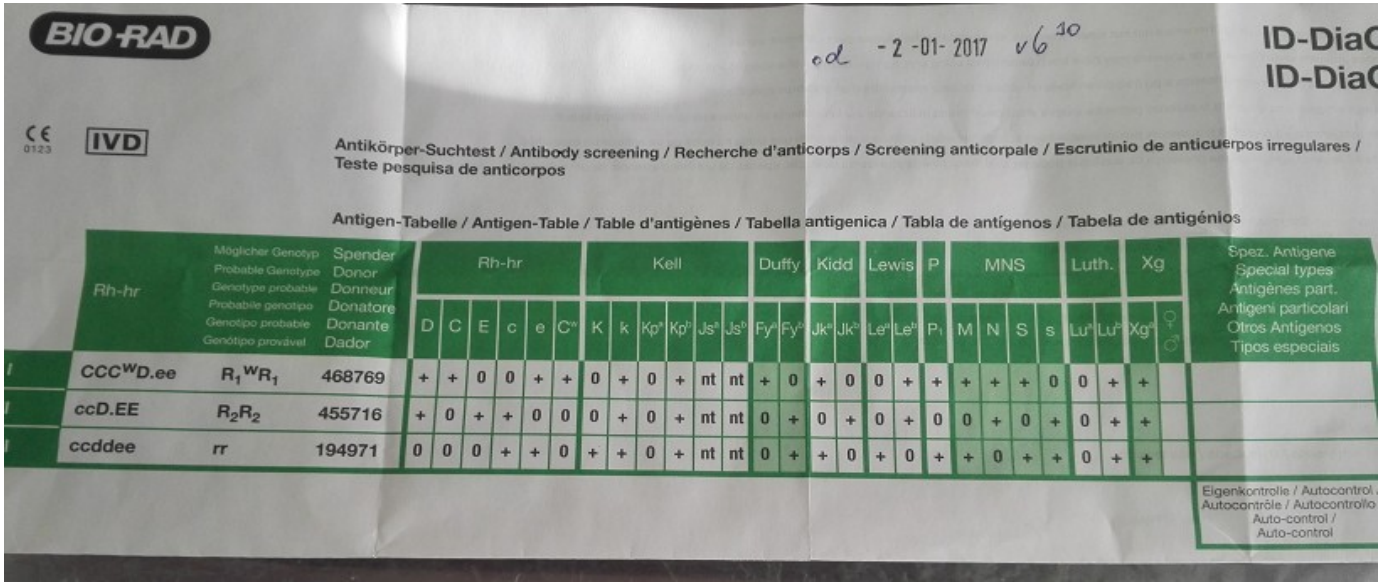


Screening for red cell allo-antibodies

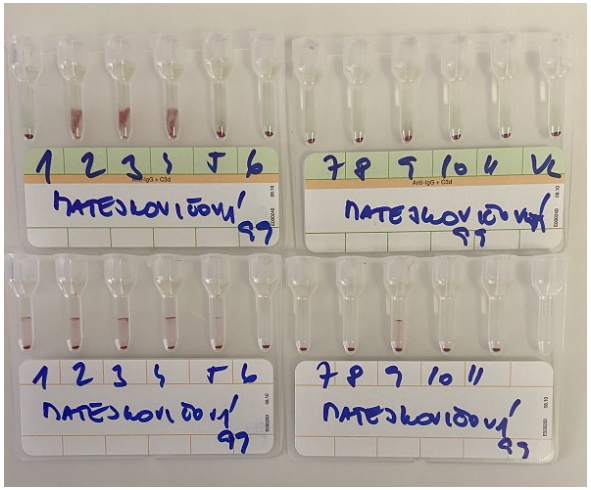








Antibody identification



BIO-RAD

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05361.01.x – 05461.01.x (Japan: 0536.01.xx – 0546.01.xx)

2017.02.27 (Japan: 27.02.17)
V.I.P. Software: P90

ID-DiaPanel
ID-DiaPanel-P

Antigen-Tabelle / Antigen-Table / Table d'antigènes / Tabella antigenica / Tabla de antígenos / Tabela de antigénios
Antikörper-Identifizierung / Antibody identification / Identification d'anticorps / Identificazione anticorpale / Identificación del anticuerpo / Identificação do anticorpo

	Rh-hr: Möglicher Genotyp / Probable Genotype / Genotype probable / Probabile genotipo / Genotipo probable / Genotipo provável		Spender / Donor / Donneur / Donatore / Donante / Dador	Rh-hr: D	C	E	c	e	C^{w}	Kell: K	k	Kp^{a}	Kp^{b}	Js^{a}	Js^{b}	Duffy: Fy^{a}	Fy^{b}	Kidd: Jk^{a}	Jk^{b}	Lewis: Le^{a}	Le^{b}	P: P$_{1}$	MNS: M	N	S	s	Luth.: Lu^{a}	Lu^{b}	Xg: Xg^{a}	♀	♂	Spez. Antigene / Special types / Antigènes part. / Antigeni particolari / Otros Antigenos / Tipos especiais	
1	CCC^{w}D.ee	$R_1{}^{w}R_1$	314007	+	+	0	0	+	+	0	+	0	+	nt	nt	+	0	0	+	0	0	+	+	+	+	+	0	+	0				1
2	CCD.ee	R_1R_1	489622	+	+	0	0	+	0	+	+	0	+	nt	nt	0	+	+	0	+	0	0	+	+	+	+	0	+	+				2
3	ccD.EE	R_2R_2	998942	+	0	+	+	0	0	0	+	0	+	nt	nt	0	+	+	+	0	0	+	+	+	+	0	0	+	+				3
4	Ccddee	r′r	221588	0	+	0	+	+	0	0	+	0	+	nt	nt	+	+	+	0	0	+	0	+	0	0	+	+	+					4
5	ccddEe	r″r	507795	0	0	+	+	+	0	0	+	0	+	nt	nt	+	+	+	0	0	+	+	0	+	0	+	0	+	nt					5
6	ccddee	rr	145261	0	0	0	+	+	0	+	^{w}+	+	+	nt	nt	+	0	+	+	0	+	+	+	+	+	+	0	+	+				6
7	ccddee	rr	431184	0	0	0	+	+	0	0	+	0	+	nt	nt	0	+	0	+	+	0	+	0	+	0	+	0	+	0				7
8	ccD.ee	R^{o}r	560620	+	0	0	+	+	0	0	+	0	+	nt	nt	0	0	+	0	0	0	+	+	+	0	+	0	+	0				8
9	ccddee	rr	267310	0	0	0	+	+	0	0	+	0	+	nt	nt	+	0	+	0	0	+	+	0	+	0	+	0	+	nt				9
10	ccddee	rr	352642	0	0	0	+	+	0	0	+	0	+	nt	nt	+	0	0	+	0	+	+	+	0	+	0	0	+	+				10
11	ccddee	rr	551930	0	0	0	+	+	0	0	+	0	+	nt	nt	0	+	+	0	0	+	+	+	+	0	+	0	+	0				11

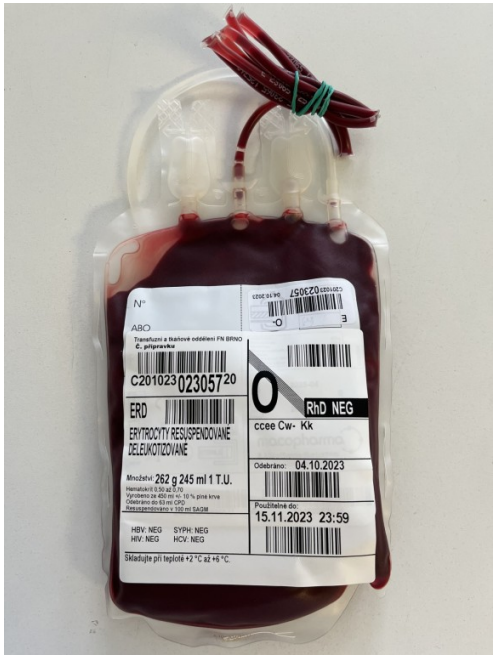
Patient / Patient / Patient / Paziente / Paciente / Paciente

Eigenkontrolle / Autocontrol / Autocontrôle / Autocontrollo / Autocontrol / Auto-controlo

Resultat / Result / Résultat / Risultato / Resultado / Resultado: LISS / Coombs	Enzyme	4°C	Bemerkungen / Remarks / Remarques / Note / Observaciones / Observações

Compatibility testing

- recipient serum x donor erytrocytes



Emergency red cells

- insufficient time for pre-transfusion testing
- blood sampling for additional testing
- **O negative** or patient´s blood group if known
- adverse transfusion reaction risk due to possibility of pre-existing antibodies!

PRINCIPLES OF HAEMOTHERAPY

General principles of haemotherapy

- Transfusion when indicated!
- Consistent compliance with guidelines
- ***effective haemotherapy and restrictive transfusion strategy*** – always consider possible alternatives to transfusion
- ***procedures to increase safety*** of haemotherapy
- ***Patient education*** about benefits and risks of transfusion

Alternatives to transfusion
Patient blood management

- **Optimization of patient´s endogenous red cell mass**:
  - screening and treating for anaemia - iron substitution, erytropoetin
  - *autotransfusion*
- **↓ blood loss and optimization of coagulation**
  - medication correction (with bleeding risk)
  - surgical techniques
  - haemostatic agents (tranexamic acid, tissue adhesives)
  - controlled intraoperative hypotension
  - reduction of diagnostic blood sampling
  - coagulation factor concentrates
- **↑ tolerance of anaemia**

Transfusion administration

- within 6 hours
- monitored (patient blood pressure, pulse, temperature before and after; adverse reactions)
- Bed side test
- administration through transfusion set (filter), separately
- rest of the blood component should be left for 24 hours

HAEMOTHERAPY COMPLICATIONS

Mandatory testing of blood donations

- **Infection markers** serologically
  - HBV (HBsAg)
  - HCV (anti-HCV)
  - HIV (dual tests)
  - Syphilis (antibodies against T.P.)
- **Imunohaematology**
  - Blood group testing (ABO and RhD typing)
  - Antierytrocyte antibody screening

Most complications are due to:

Leucocytes

solution:

- **leucocyte depletion**
- **irradiation**

Plasma

solution:

- **selection of clinical plasma donors** (without history of immunisation)
- **using of additive solutions for blood component preparation**
- **washing**
- **coagulation factor concentrates**
- **Solvent/detergent-treated pooled plasma (OctaplasLG)**

Complications of transfusion - classification

- etiology
- time-to-onset
- severity

Etiology

- **Infection transmission**
- **Cardiovascular and metabolic complications**
  - circulatory overload, hypothermia, hyperkalemia, hypocalcemia, transfusion haemosiderosis, hypotension, hypertension
- **Immune-mediated complications**
  - **Transfusion-related immunomodulation** – associated with dose of transfused leucocytes and storage time of blood component
  - **Allo-imunisation**
  - **Immune-mediated transfusion reactions**
    - acute and a delayed haemolytic reaction, FNHTR, allergic reaction, anaphylactic, TRALI, TA-GvHD, posttransfusion purpura

Transfusion complications according to time of their development

- **Acute**
  - < 24 h after transfusion
  - e.g. acute haemolytic reaction, FNHTR, TRALI, allergic, cardiovascular and metabolic complications
- **Delayed**
  - > 24h after transfusion, days to weeks
  - e.g. delayed haemolytic reaction, Ta-GvHD, infection, allo-imunisation, transfusion haemosiderosis (iron overload)

Transfusion complications according to severity

- **Nonserious**
  - mild clinical course
  - usually fade away soon after the transfusion is stopped
  - symptoms are mild and reversible
- **Serious**
  - severe symptoms, may be life-threatening
  - require vital signs monitoring

Frequent cause of transfusion complications is administrative error!

- sample change
- error in identification data
- error in blood group testing
- change of blood component
- not respecting standard procedures

Acute haemolytic reactions

- Cause:
  - Immune: incompatible transfusion – mostly administrative error!
  - **Non-immune**: temperature, mechanical, bacterial contamination
- Symptoms:
  - chills/fever, dyspnoea, back pain or chest pain, tachycardia, hypotension, shock, anxiety, vomiting
- Diagnosis:
  - ↑ bilirubin, ↑ LDH, ↓ haptoglobin, haemoglobinemia, haemoglobinuria
  - blood group verification of patient and blood component, DAT (positive), compatibility test (positive)
- Treatment/management:
  - stop the transfusion, vital signs monitoring
  - intensive care may be needed to prevent shock, kidney failure (maintain urine output, haemodialysis), DIC

Delayed haemolytic reaction

- Cause:
  - **Immunisation in the past** (prior transfusion, pregnancy)
- Symptoms:
  - fever, icterus, development of anaemia in 5 to 14 days – extravascular haemolysis, kidney failure not so often
- Diagnosis:
  - anaemia, ↑ bilirubin, ↑ LDH, ↓ haptoglobin, haemoglobinuria, positive DAT, identification of anti-erytrocyte allo-antibodies
- Treatment/management:
  - supportive
  - transfusion of compatible RBCs lacking the antigen against which is the patient immunised
- Prevention:
  - respecting standard/safe procedures *(documentation)*

Febrile non-haemolytic transfusion reaction

one of more fequent transfusion complications

- Cause:
  - cytokines released from leucocytes during storage
  - HLA antibodies
- Symptoms:
  - fever, chills, shivering during or shortly after transfusion (usually occurs in 30-60 minutes from beginning of transfusion)
- Diagnosis:
  - temperature rise ≥ 1˚C from baseline
  - FNHTR is a diagnosis of exclusion! Symptoms of FNHTR also occur in other more serious reactions – acute hemolysis, bacterial contamination, TRALI
- Treatment/management:
  - antipyretics
- Prevention:
  - leucocyte depletion (occurence in countries with widespread leucocyte depletion has significantly decreased).

Transfusion-associated sepsis

- Cause:
  - bacterial contamination of blood component
  - highest risk have platelets stored in room temperature
- Symptoms:
  - fever, chills, vomiting, diarrhoea, tachycardia, hypotension, shock
- Diagnosis:
  - blood culture (patient), sterility testing (blood component)
  - bacterial contamination should be excluded in all serious reactions with fever and hypotension
- Treatment:
  - antibiotics, symptomatic/supportive
- Prevention:
  - visual control of the blood component
  - respecting of the storage conditions

Allergic and anaphylactic

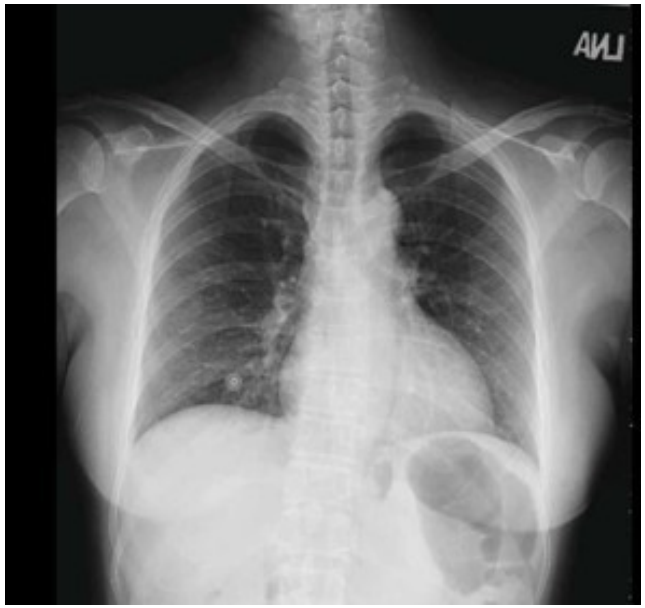
- Cause:
  - most often after blood components with plasma content
  - antibodies against plasmatic proteins in blood components
  - anaphylaxis – selective IgA deficiency patients with anti-IgA antibodies
- Symptoms:
  - urticaria, itching, vomiting, diarrhoea, hypotension, shock, dyspnoea
- Diagnosis:
  - patient´s IgA level should be examined if severe allergic transfusion reaction repeates
- Treatment:
  - symptomatic, antihistamines
- Prevention:
  - washing of cellular blood components (for patients with severe reactions), premedication with steroids and/or antihistamines

TRALI
Transfusion Related Acute Lung Injury

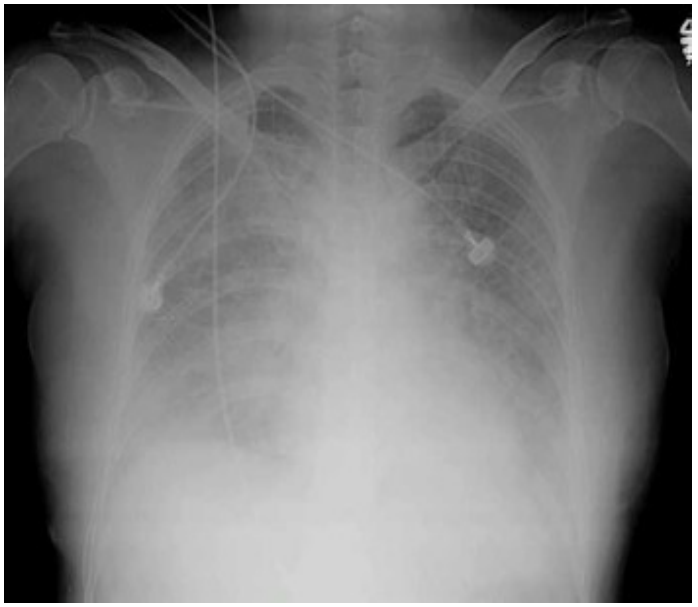
- Cause:
  - anti-HLA or anti-HNA antibodies (prior immunisation) - activating neutrophiles → sequestration in lung microcirculations - endothelium damage - capillary leakage - **ARDS**
- Symptoms:
  - fever, hypotension, respiratory failure with bilateral pulmonary infiltrates, without symptoms of circulatory overload
  - onset < 6 hours from transfusion
- Diagnosis:
  - oxygen saturation, chest X-ray, anti-HLA / anti-HNA antibodies
- Treatment:
  - oxygen, ventilation
  - leucodepleted blood components
- Prevention: restriction on female-donor plasma

TRALI

Before transfusion



After transfusion



TACO
Transfusion Associated Circulatory Overload

- Cause:
  - after high volume transfusions – acute hypervolemia
- Symptoms:
  - dyspnoea, cough, acute pulmonary oedema, tachycardia, cyanosis
  - onset < 12 hours after transfusion
- Diagnosis:
  - development of acute dyspnoea, low oxygen saturation
  - chest X-ray of cardiac decompensation
- Treatment:
  - oxygen therapy, diuretics
- Prevention:
  - transfusion rate should be 2-4ml/kg/hour, 1ml/kg/hour in high risk patient

TA – GvHD (Transfusion-associated Graft versus Host disease)

- Cause:
  - donor lymphocyte proliferation in immunocopromised or HLA similar recipient
  - rare, but usually fatal
- Symptoms:
  - fever, erythema, vomiting, diarrhoea, lymphadenopathy, hepatopathy, pancytopenia
  - onset 4 – 30 days after transfusion
- Diagnosis:
  - biopsy consistent with GvHD
  - evidence of donor and recipient lymphocyte chimerism
- Prevention:
  - irradiation, not administering transfusion from relatives

Hypothermia

- body temperature drop to 32 – 34˚C
- usually after massive transfusions (rather than single unit transfusion)
- Prevention: preheating of blood components

Hyperkalemia

abnormal increase of blood potassium level after transfusion

- fast RBCs administration (> 60 ml/min.)
- longer storage time / irradiation of RBCs

- could be serious - cardiac arrest
- fastest diagnosis - ekg

Hypotension

- blood pressure drop ≥ 30 mmHg within 4 h
- other causes should be excluded

Hypertension

- blood pressure raise ≥ 30 mmHg within 4 h with exclusion of other causes

Post-transfusion purpura

- Cause:
  - specific anti-platelet antibodies (e.g. anti-HPA 1a)
- Symptoms:
  - severe thrombocytopenia, bleeding
  - serious transfusion complication
- Diagnosis:
  - identification of anti-platelet antibodies
- Treatment:
  - IVIG

Post-transfusion hemosiderosis

- iron overload caused by multiple transfusions (transfusion-dependent patients)
- hemosiderin = large aggregates of ferritin → tissue dammage (liver cirrhosis, cardiomyopathy, endocrinopathy,…)
- 1 TU contains approx 230 mg of iron

Material for investigation of transfusion complications:

- pre-transfusion blood sample
- post-transfusion blood sample
- rest of the blood component (5-10 ml)

- transfusion reaction reporting form

Take home message

- follow guidelines
- respect indications – restrictive transfusion politics – consider bloodless alternatives
- use procedures to increase haemotherapy safety
- interdisciplinary cooperation

Thank you for your attention.