Haemovigilance Report

2017

Danish **R**egistry of **T**ransfusion Risks (DART)

DSKI
Danish Society for Clinical Immunology

Member of the Haemovigilance Committee

Bitten Aagaard (Corresponding author)
M.D.
Dept. of Clinical Immunology; Aalborg University Hospital
Email: biaaj@rn.dk

Betina Sørensen
M.D.
Dept. of Clinical Immunology, Aarhus University Hospital

Rune Larsen
M.D.
Department of Clinical Immunology, Næstved Hospital

Helene Martina Paarup
M.D.
Dept. of Clinical Immunology, Odense University Hospital

Christina Mikkelsen
M.D.
Dept. of Clinical Immunology, Copenhagen University Hospital

Christina Mønster Byskov
Biomedical Laboratory Scientist
Dept. of Clinical Immunology, Copenhagen University Hospital

Mie Topholm Bruun
M.D.
Dept. of Clinical Immunology, Odense University Hospital

Table of contents

Abbreviations

AHTR	Acute hemolytic transfusion reaction
Anti-HLA	Antibodies against HLA (human leucocyte antigen)
Anti-HNA	Antibodies against HNA (human neutrophil antigen)
APP	Approximately
AR	Allergic reaction confer paragraph "Allergic Reaction" page 12
BNP	Brain natriuretic peptide
CABG	Coronary artery bypass grafting
CF	confer
DART	Danish Registry of Transfusion Risks
DAT	Direct antiglobulin test
DHA	Danish Health Authority
DHTR	Delayed hemolytic transfusion reaction
DTSR	Delayed serologic reaction
ECG	Electrocardiogram
FNHTR	Febrile non hemolytic transfusion reaction
IBCT	Incorrect blood component transfused
ISBT	International Society of Blood Transfusion
PTP	Post transfusion purpura
RC	Red cells
SHOT	Serious Hazards of Transfusion (UK Haemovigilance)
TACO	Transfusion associated circulatory overload
TAD	Transfusion associated dyspnea
Ta-GVHD	Transfusion associated graft-versus-host disease
TR	Transfusion reaction
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection

Introduction

DART is the Danish National Haemovigilance Committee. Since 1999, the committee has received and analyzed data for serious adverse events and reactions associated with transfusion of blood components.

DART is a member of the Nordic Haemovigilance Group and IHN. DART reports the Danish annual results of adverse events and reactions associated with transfusion of blood components to IHNs haemovigilance Database (ISTARE).

In 2017, 5,5 adverse events and reactions per 100,000 transfused blood components were reported to DART. The number is app. the same as the recent years, though a further decrease in transfused RC conceded in 2017, (2016: 7.1; 2015: 8.0 and 2014: 5.6/100,000 transfused blood components).

In tables representing 2017 data, only the adverse events and reactions reported in 2017 are mentioned, which means IBCT (wrong patient), AHTR, DHTR, TTI, hypotensive TR, TAD, Ta-GVHD and PTP are excluded.

As a standard procedure, since 2014, DART has validated the submitted reports according to ISBTs definitions of adverse event and reaction and imputability. The validation resulted in reclassification of one adverse reaction - and exclusion of two reports, (one DHTR, which is not represented in the tables; and one report, did not fulfil the definitions of adverse event and reaction according the ISBT definition.

The formula for reporting serious adverse events and reactions associated with transfusion of blood components to DART, and the guide to DART reporting are to find in the following links:
[Formula to report errors associated to transfusion] Formular til indberetning af fejltransfusion
[Formula to report reactions associated to transfusion] Formular til indberetning af transfusionskomplikationer
[Guide to DART reporting] Vejledning til DART indberetning

As in the recent years (2014-2016) the transfused platelets and total transfused blood components are stated as number of components, (in 2013 and previous annual reports the number of transfused platelets and thereby total transfused components are stated as single units). In tables containing data from 2013 and previous years, a note will tell if the transfused platelets and total transfused blood components are stated as single units.

Definitions

The terms for blood components RC, platelets and plasma are defined by IHN (ISTARE nomenclature).
Adverse events and reactions is used as a headline for:
An adverse event
An incident
An adverse reaction
ISBT

The type of adverse events and reactions are defined by ISBT ISBT proposed standard definitions as in DARTs "Vejledning til DART indberetning" [Guide to DART reporting] Vejledning til DART indberetning.
Severity (grade 1 – 4) and imputability (five grades) of adverse events and reactions are categorized according to ISBTs standards cf. the hyperlink above.

Specifications for blood components

In Denmark blood components are produced in respect to "Guide to the preparation, use and quality assurance of blood components", EDQM 19th Edition 2017. Council of Europe
RC: Red Cells, Leucocyte depleted in Additive Solution derived from whole blood donation. This include a very few number of RC washed and – cryopreserved.
Platelets: Platelets, recovered, pooled, leucocyte-depleted, in additive solution derived from whole blood AND platelets, apheresis, leucocyte-depleted, in additive solution obtained by apheresis of a single donor. About seven percent (one region) used pathogen reduction (Intercept®) in both type of platelet products.
Plasma: Plasma, Fresh frozen prepared either from whole blood or from plasma obtained by apheresis of a single donor and frozen within 24 hours. Liquid plasma as the above mentioned plasma but never frozen (shorter shelf life).

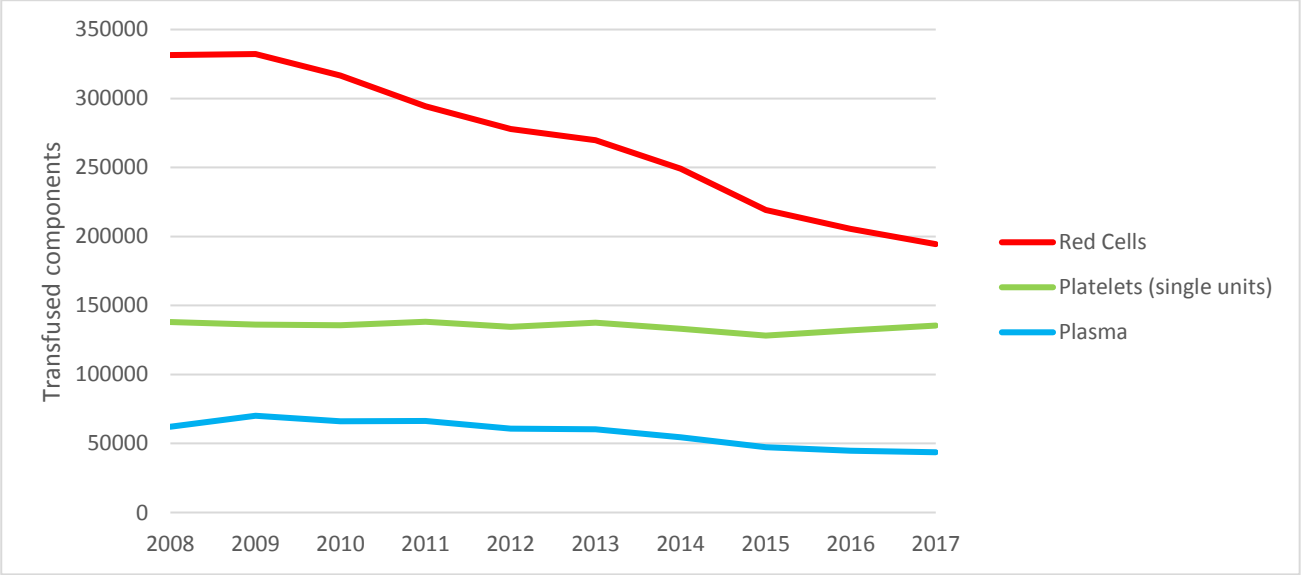
Blood Components Transfused

2017

Data of transfused blood components have been reported from the five regions. Three regions used four buffycoats/pool platelets (one of those has for seven months used three buffycoats/pool) and one region seven buffycoats/two pools.

Region	RC	Platelets (pool)	Platelets (apheresis)	Plasma (whole blood)	Plasma (apheresis)	Total
Capital Region of Denmark	66,612	14,761	372	17,002	2,682	101,429
Region Zealand	25,784	2,391	458	2,571	1,485	32,689
Region of Southern Denmark	40,751	6,642	391	7,032	0	54,816
Central Denmark Region	42,728	6,119	318	8,880	656	58,701
North Denmark Region	18,590	2,224	204	3,366	0	24,384
Total	**194,465**	**32,137**	**1,743**	**38,851**	**4,823**	**272,019**

2008-2017



Source: 2008-2013 Danish Health Authority SST, 2014 - 2017 The Regions.

The number of transfused platelets and plasma is quite stable through the last ten years. A furthermore reduction in the number of transfused RC continues the trend beginning in 2008, - one year after the publication of ”Vejledning om Blodtransfusion edition no. 1” by the

DHA. The publication was revised in 2015 at the latest edition no. 2: Danish Health Authority [Guidance - Blood Transfusion]

The Reduction in RC transfused is app. 6 % from 2016 to 2017.

Adverse events and reactions

2017

Adverse events and reactions	Number	Number/100,000 transfused components
IBCT (wrong component)	1	0.4
AR	3	1.1
TRALI	3	1.1
TACO	4	1.5
FNHTR	3	1.1
UCT	1	0.4
Total	15	5.5

2017 - Regionally

Region	Number	Number/100,000 transfused components
Capital Region of Denmark	4	3.9
Region Zealand	1	3.1
Region of Southern Denmark	3	5.5
Central Denmark Region	6	10.2
North Denmark Region	1	4.1
Total	15	5.5

The Central Region of Denmark has - as in 2015 and 2016 - a higher ratio of adverse events and reactions/100,000 transfused components than all other regions in Denmark.
The reason is most likely a general increased attendance on acknowledgement of adverse events and reactions and execution by reporting to DART.

Cumulated table of reports

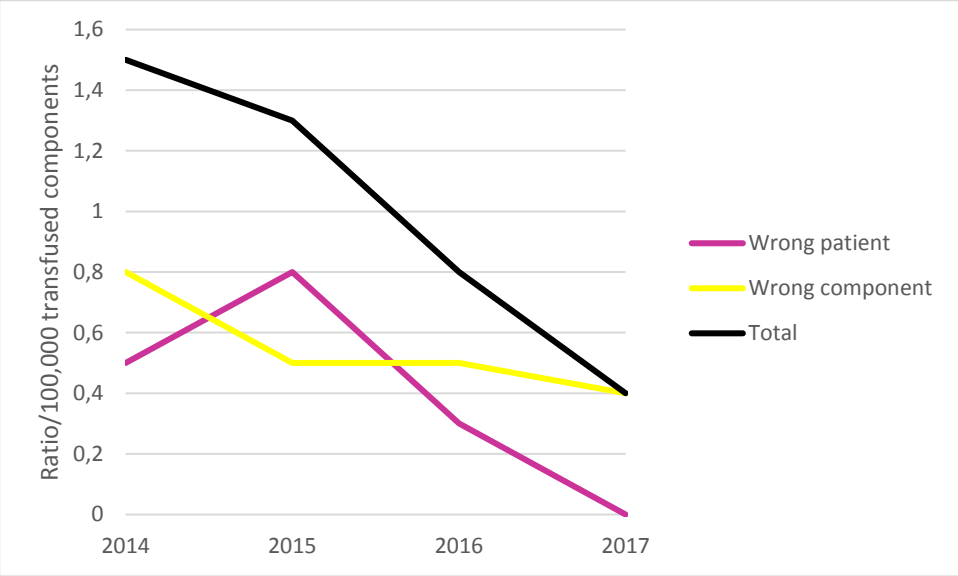
2014-2017

adverse events and reactions	Number/100,000 transfused components (absolute)				
	2014	2015	2016	2017	2014-17
Wrong patient	0.5 (2)	1.0 (3)	0.4 (1)	0	0.5
Wrong component	0.8 (3)	0.7 (2)	0.7 (2)	0.4 (1)	0.7
AHTR	0.3 (1)	0.3 (1)	0.4 (1)	0	0.3
DHTR	0.5 (2)	2.0 (6)	1.4 (4)	0	1.0
AR	0.8 (3)	1.0 (3)	2.1 (6)	1.1 (3)	1.3
TRALI	0.5 (2)	0.3 (1)	1.1 (3)	1.1 (3)	0.8
TACO	0.5 (2)	0.3 (1)	0.4 (1)	1.5 (4)	0.7
TTI	0	0.3 (1)	0	0	0.1
FNHTR	0	0.3 (1)	0.7 (2)	1.1 (3)	0.5
Hypotensive TR	0	0.7 (2)	0	0	0.2
TAD	0	0.3 (1)	0	0	0.1
UCT	1.1 (4)	0.7 (2)	0	1.1 (1)	0.6
Total	5.6 (19)	8.0 (24)	7.1 (20)	5.5 (15)	6.6

Adverse events and reactions listed by type

Incorrect blood component transfused (IBCT) - wrong patient/wrong component

Year	Number/100,000 transfused components (absolute)		
	Wrong patient	Wrong component	Total
2014	0.5 (2)	0.8 (3)	1.5 (3)
2015	0.8 (3)	0.5 (2)	1.3 (5)
2016	0.3 (1)	0.5 (2)	0.8 (3)
2017	0	0.4 (1)	0.4 (1)



The fraction of IBCT in 2017 is the lowest ever registered (only 7% of all reported adverse events and reactions), in the time DART has made annually reports, (2001). The reduction in the reported errors happens as the electronic validation of transfusion is implemented in some regions of Denmark.

Region	Fraction of transfused blood components validated electronically (%)
Capital Region of Denmark	0
Region Zealand	45
Region of Southern Denmark	38
Central Denmark Region	95
North Denmark Region	0
Mean	36

Acute hemolytic transfusion reaction (AHTR) and Delayed hemolytic transfusion reaction (DHTR)

Neither AHTR nor DHTR were reported to DART in 2017. Never before, we have had no reports of AHTR and DHTR. Most likely, it is a result of lack in reporting to DART, alternatively an effect of fewer errors (wrong patient/wrong component).

Erythrocyte antibodies detected in blood from patients with AHTR and DHTR in 2014-2017

Year	Number/100,000 components transfused (absolute)	
	AHTR	**DHTR**
2014	0.3 (1)	0.5 (2)
2015	0.3 (1)	2 (6)
2016	0.4 (1)	1.4 (4)
2017	0	0

Erythrocyte antibodies detected in blood from patients with AHTR and DHTR in the period 2001-2016.

Antibody	**Jk^a**	**S**	**C**	**E**	**K**	**Jk^b**	**Fy^a**	**c**	**e**	**Fy^b**	**Lu^a**	**Bg**	**B**	**Cw**	**Wr^a**	**Other***
AHTR	3		1		2	2		1				1	1		3	3
DHTR	6	2	1	11	4	5	5	7	1	2	1			1		

- Two reactions where detected antibodies had unknown specificity, and one reaction where the only antibody identified was cold agglutinin.

Allergic Reaction (AR)

This year the term "allergic reaction" is used according to ISBT and DART terminology.
In previous annual reports the term "anaphylactic reaction" is applied. There is no difference in the severity of adverse events and reactions this year compared to previous years.
As in former reports "allergic reactions" refer to grade 2-4 allergic reactions ISBT and the clinical presentation is an anaphylactic reaction cf. ISBTs definition.

Year	Number/100,000 components transfused (absolute)			
	RC	**Platelets**	**Plasma**	**Total**
2014	0	3.0(1)	3.7(2)	0.8(3)
2015	0	3.1(1)	4.2(2)	1.0(3)
2016	0.5(1)	3.0(1)	8.9(4)	2.1(6)
2017	0	3.0(1)	4.6(2)	1.1(3)

Lung associated transfusion reaction

Some haemovigilance organizations tend to use a collective header for the next two reactions to transfusion. As the two reactions can be difficult to separate in the clinical ward it makes sense to regard them as close related.

Transfusion-related acute lung injury (TRALI)

Year	Number/100,000 components transfused (absolute)			
	RC	Platelets	Plasma	Total
2014	0.4 (1)	0	1.8 (1)	0.5
2015	0.5 (1)	0	0	0.3
2016	1.0 (2)	0	2.2 (1)	1.1
2017	0.5 (1)	3(1)	2.3 (1)	1.1

Transfusion associated circulatory overload (TACO)

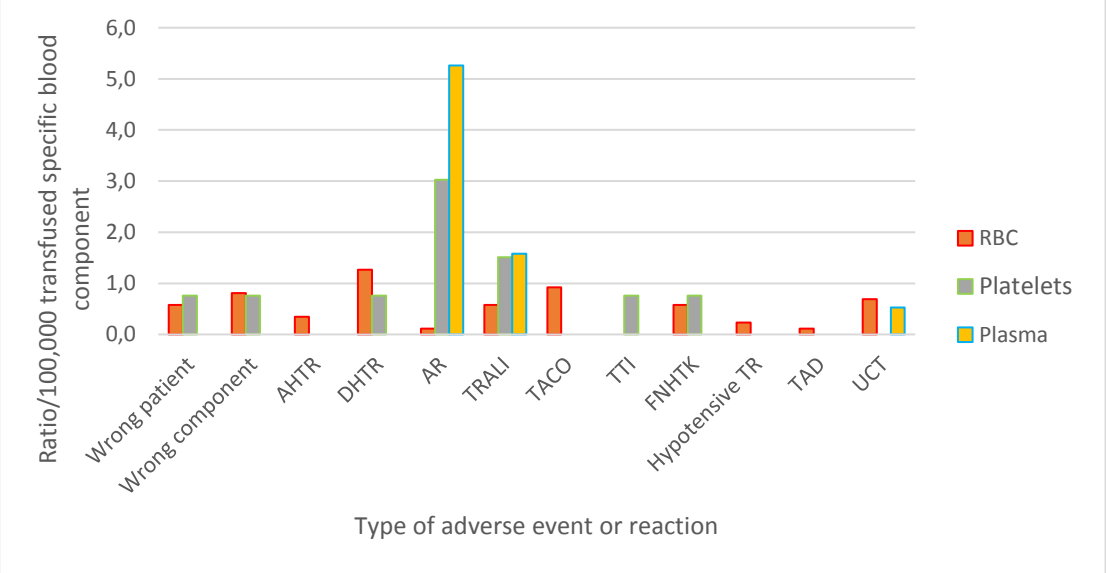
Year	Number/100,000 components transfused (absolute)			
	RC	Platelets	Plasma	Total
2014	0.8 (2)	0	0	0.5
2015	0.5 (1)	0	0	0.3
2016	0.5 (1)	0	0	0.3
2017	2.1 (4)	0	0	1.5

Adverse events and reactions in relation to blood component

2017

Adverse events and reactions	Number/100,000 components transfused (absolute)		
	RC	Platelets	Plasma
IBCT (wrong component)	0.5 (1)	0	0
AR	0	3 (1)	4.6 (2)
TRALI	0.5 (1)	3 (1)	2.3 (1)
TACO	2,1 (4)	0	0
FNHTK	1.5 (3)	0	0
UCT	0.5 (1)	0	0
Total	5.1 (10)	5.9 (2)	6.7 (3)

2014-2017



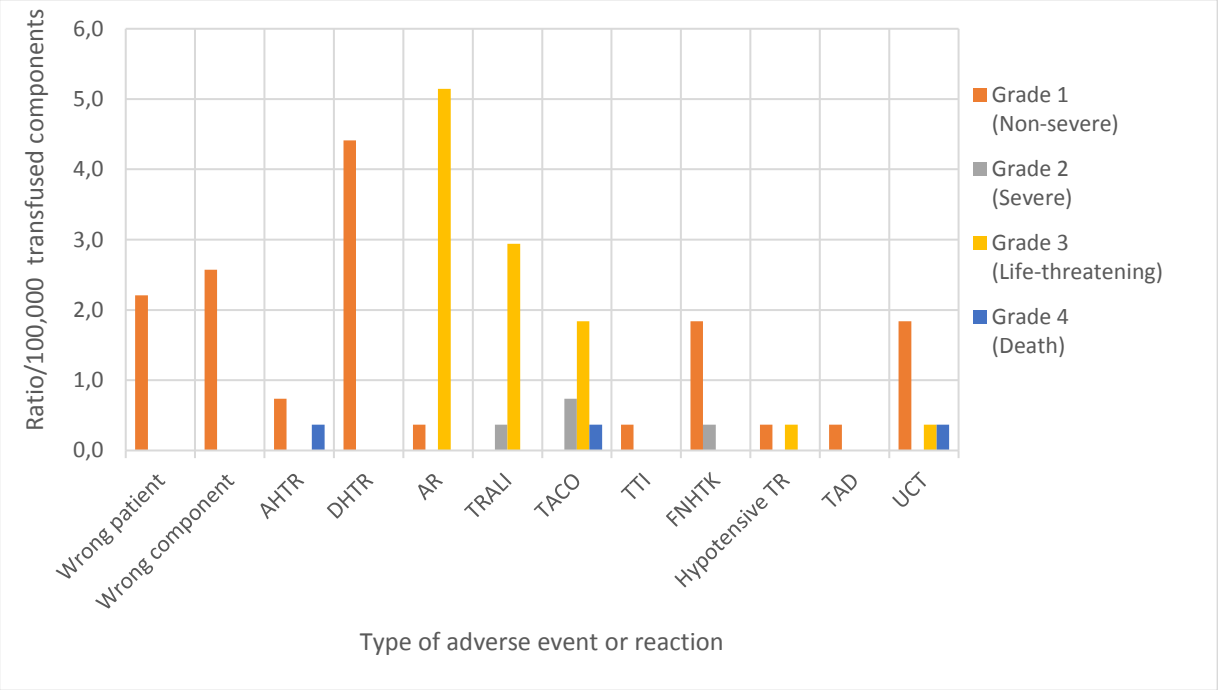
Severity

2017

Adverse events and reactions	Grade 1 (Non-severe)	Grade 2 (Severe)	Grade 3 (Life-threatening)	Grade 4 (Death)	Total
IBCT (wrong component)	1	0	0	0	1
AR	0	0	3	0	3
TRALI	0	1	2	0	3
TACO	0	2	2	0	4
FNHTR	2	1	0	0	3
UCT	0	0	0	1	1
Total	3	4	7	1	15
Ratio/100.000 components	1.1	1.5	2.6	0.4	5.5

The UCT reaction resulting in grade 4 (death) has a very low imputability cf. "Cases" page 21. Due to the severity, the Haemovigilance Committee chose to include it, because we could not for sure reject reaction to transfusion to be at least contributing to the fatal reaction.

2014-2017



Cases

Incorrect blood component transfused (IBCT) – wrong component

1) **Recipient: patient with a hematologic malignancy treated with chemotherapy**
   Transfused component: RC NOT irradiated
   Location: Region of Southern Denmark
   Severity: Non-Severe
   A transfused component, which by mistake was NOT irradiated, as the standard operation procedure prescribes. In the blood bank, the demand for irradiated blood components was missed.

Allergic reaction (AR)

2) **Age: 16 year old**
   Gender: male
   Transfused components: RC, platelets and plasma
   Location: Capital Region of Denmark
   Severity: life-threatening
   Imputability: probable
   Recipient admitted with fractures because of trauma, transfused with several blood components (red cells, platelets and plasma) peroperatively. During transfusion with a unit of plasma, he develops universal urticarial rash and hypotension (systolic pressure 50 mm Hg).
   Treatment: adrenaline, antihistamine and steroid was effect full. Antibiotic treatment was given more than one hour earlier.
   Delta tryptase: 14.3 µg/l (peak tryptase 25.9 µg/l; basic tryptase 11.6 µg/l), IgA not stated.

3) **Age: 59 year old**
   Gender: male
   Transfused components: platelets
   Location: Capital Region of Denmark
   Severity: life-threatening
   Imputability: probable
   During transfusion, the recipient develops universal itchy urticarial rash and afterwards hypotension (blood pressure 68/52 mm Hg, systolic pressure initially 111 mm Hg) and desaturation (99-93%).
   Treatment: antihistamine and steroid was effect full.

Delta tryptase: not stated, IgA normal (value not stated).

4) **Age: 59 year old**
   Gender: male
   Transfused components: RC, platelets and plasma
   Location: North Denmark Region
   Severity: life-threatening
   Imputability: probable
   Recipient admitted for Coronary artery bypass grafting (CABG), transfused with several blood components (red cells, platelets and plasma). During transfusion, he develops universal urticarial rash and hypotension (values not stated) and desaturation.
   Treatment: adrenaline, antihistamine and steroid were effect full.
   Delta tryptase: 30.03 µg/l (peak tryptase 38.7 µg/l; basic tryptase 8.67 µg/l), IgA: 1 g/l (normal).
   X-ray chest: normal

Transfusion-related acute lung injury (TRALI)

5) **Age: 79 year old**
   Gender: female
   Transfused components: platelets
   Location: Central Denmark Region
   Severity: life-threatening
   Imputability: probable
   During transfusion, the recipient desaturates to 65 % (saturation initially normal) and becomes cyanotic. Blood pressure stable. Admitted to intensive care unit for non-invasive ventilation (NIV) treatment.
   Treatment: diuretics and steroid with some effect.
   X-ray chest: bilateral infiltrations. 24 hours later remission in the exudative changes and one week later the chest X-ray is normal.
   Anti-HLA I and II: One donor (four donors contribute to a pool of platelets) had high levels of both anti-HLA I and II antibodies, some of which were specific to the HLA type of the patient.
   Anti-HNA: not stated neither for patient or the donors

6) **Age: 77 year old**
   Gender: female
   Transfused components: RC

Location: Region of Southern Denmark

Severity: life-threatening

Imputability: probable

Recipient admitted for pneumonia with suspicion of malignant pathology, transfused with red cells. During transfusion, she develops polypnea (40/min) and desaturates to 63 % (saturation initially normal). Admitted to intensive care unit for supporting respiratory treatment. Echocardiography shows normal ejection fraction, but estimates hypovolemia (dehydration).

Treatment: diuretics and steroid with some effect.

X-ray chest: Bilateral infiltrations.

Anti-HLA I and II: The donor had no antibodies, samples from the patient were not available.

Anti-HNA: The donor had no antibodies, samples from the patient were not available.

7) **Age: 10 year old**

Gender: male

Transfused components: Plasma

Location: Region of Southern Denmark

Severity: severe

Imputability: possible

Recipient transfused with plasma because of reduced coagulation capacity. Earlier the same day he had a successful therapeutic plasma exchange (human albumin). One and a half hour after transfusion began; he desaturates to 85 % (saturation initially normal) and becomes cyanotic. Blood pressure stable (Systolic 100 – 110 mm Hg). Rise in body temperature to 40°C. No others etiologies to acute lung injury.

Treatment: Oxygen therapy, medication (diuretics) not stated.

X-ray chest: No chest x-ray at the time of adverse reaction. 24 hours later chest x-ray is normal

Anti-HLA I and II: No detectable antibodies in a sample of the donor. No samples from the patient was available.

Anti-HNA: No detectable antibodies in the plasma of the donor. No samples from the patient was available.

Transfusion associated circulatory overload (TACO)

8) **Age: 54 year old**

Gender: female

Transfused components: RC, platelets and plasma (7:2:6)

Location: Central Region Denmark

Severity: life-threatening

Imputability: definite

Recipient admitted because of rectal bleeding (hemoglobin 2.5 mmol/l) transfused with several blood components. No known heart failure. During gastroscopy and transfusion with the last component, she develops respiratory distress and need of oxygen therapy. All extremities show peripheral oedema. Known positive fluid balance.

Treatment: diuretics was effect full.

X-ray chest: Bilateral infiltrations

9) **Age: 73 year old**

Gender: male

Transfused components: RC

Location: Capital Region of Denmark

Severity: severe

Imputability: probable

Known terminal heart failure, Ejection fraction 10%. Fifteen minutes from onset of transfusion, he develops respiratory distress, polypnoea (28/min) and need of oxygen therapy. No information about peripheral oedema or positive fluid balance.

Treatment: diuretics and morphine was effect full.

X-ray chest: None

10) **Age: 64 year old**

Gender: female

Transfused components: RC

Location: Central Region Denmark

Severity: severe

Imputability: definite

No information about known heart failure. Just after transfusion had finished, she develops severe dyspnoea, a rise in blood pressure (systolic pressure 187 – 270 mm Hg), tachycardia (106/min.) and desaturation to 82%. Troponin rise (value not stated). BNP not measured

Treatment: diuretics and nitroglycerin was effect full.

X-ray chest: none

11) **Age: 91 year old**

Gender: male

Transfused components: RC

Location: Region Zealand

Severity: life-threatening

Imputability: definite

Recipient admitted because of pneumonia, transfused (slowly) with two units of red cells. Known with heart failure and aortic stenosis. During transfusion with the second component, he develops respiratory distress with desaturation to 70-80%, tachycardia (118/min.) and a rise in blood pressure (151/91 – 189/119 mm Hg). No information about peripheral oedema or positive fluid balance.

Treatment: diuretics was effect full.

X-ray chest: Bilateral infiltrations

Febrile non hemolytic transfusion reaction (FNHTR)

12) **Age: 14 year old**

Gender: female

Transfused components: RC

Location: Central Region Denmark

Severity: non-severe

Imputability: possible

One hour after transfusion began; she develops a rise in temperature (> 2 °C and > 39 °C) and chills. Stable blood pressure, no headache or nausea.

Treatment: None

13) **Age: 56 year old**

Gender: female

Transfused components: RC

Location: Central Region Denmark

Severity: non-severe

Imputability: possible

Recipient admitted for Coronary artery bypass grafting (CABG), transfused with several blood components. One hour after transfusion began, she develops a rise in temperature (> 2 °C and > 39 °C (37.4 – 39.8 °C) and chills. Headache or nausea not stated. Post transfusion blood group serology negative (DAT inclusive).

Treatment: None

14) **Age: 78 year old**

Gender: female

Transfused components: RC

Location: Central Region Denmark

Severity: severe

Imputability: possible

Just after transfusion began, she develops a rise in temperature (> 2 °C and > 39 °C (37.1 – 39.2 °C), chills and marginal dyspnoea. Headache or nausea not stated. Post transfusion blood group serology shows anti-K and anti-Kp^a, the transfused component was K and Kp^a negative (as the compatible test was negative). DAT positive both pre- and after transfusion.

Treatment: None

Unclassifiable Complication of Transfusion (UCT)

15) **Age: 77 year old**

Gender: female

Transfused components: RC

Location: Central Region Denmark

Severity: death

Imputability: unlikely

Recipient admitted with sepsis. One hour after transfusion began (120 ml transfused), she had cardiac arrest. The ECG and blood samples (cardiac enzymes) at the time of complication show signs of acute myocardial infarction. The regional blood center received the information about possible complication of transfusion several days later, no samples from the patient was available.