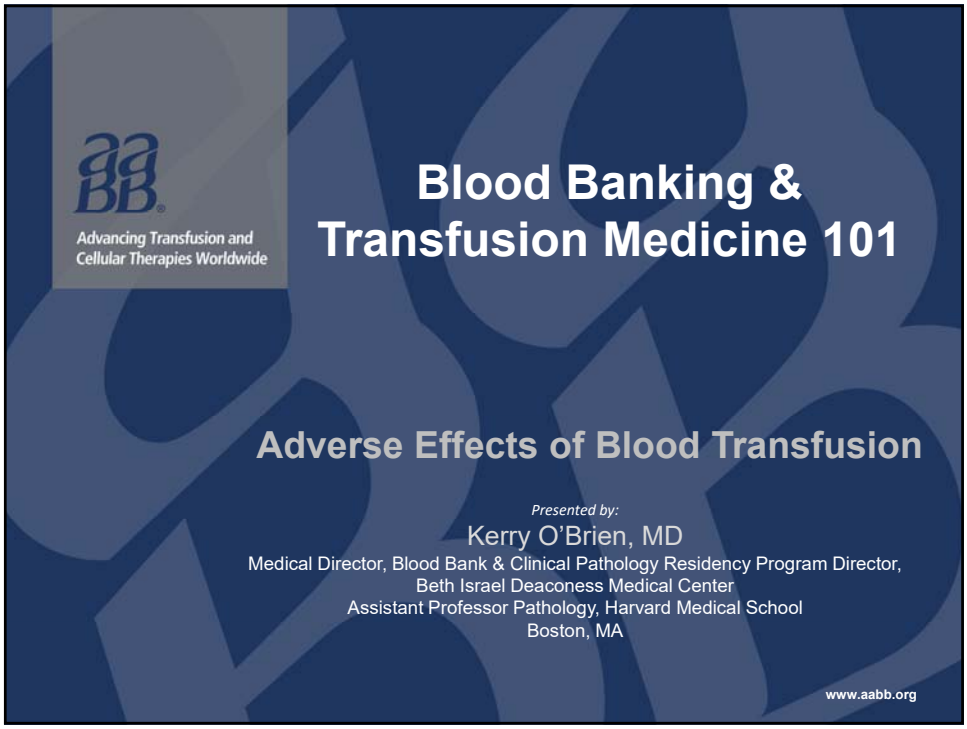

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Learning Objectives

After participating in this program you should be able to….

- Review the latest SHOT and FDA data as a framework
- Detail the main infectious risks of blood transfusion
- Explain the non-infectious adverse effects of transfusion:
  - Detail the acute transfusion reaction types:
    - Allergic
      - Mild - moderate
      - Anaphylactic
    - Acute hemolytic
    - Febrile non-hemolytic
    - Transfusion associated circulatory overload (TACO)
    - Transfusion related acute lung injury (TRALI)
    - Acute hypotensive

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2

Learning Objectives Continued

- Explain the non-infectious adverse effects of transfusion continued:
  - Describe the delayed transfusion reaction types:
    - Delayed hemolytic
    - Delayed serologic
    - Transfusion associated graft versus host disease (TA-GVHD)
    - Post-transfusion purpura (PTP)
    - Iron overload
  - Reveal the most common acute transfusion reactions:
    - Allergic
    - Febrile non-hemolytic
    - Transfusion associated circulatory overload (TACO)

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3

ANNUAL SHOT REPORT 2018

SHOT is affiliated to the Royal College of Pathologists
This report is produced by SHOT working with MHRA

MHRA SHOT Serious Hazards of Transfusion

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4

Table 2.2: Total issues of blood components from the Blood Services of the UK in the calendar year 2018

	Red cells	Platelets	FFP	SD-FFP	MB-FFP	Cryo	Totals
NHS Blood and Transplant	1,422,742	252,951	166,462	90,500	6,336	41,386	**1,980,377**
Northern Ireland Blood Transfusion Service	41,352	8,229	3,505	1,110	299	955	**55,450**
Scottish National Blood Transfusion Service	142,670	23,881	16,203	3,580	425	3,135	**189,894**
Welsh Blood Service	85,570	10,343	8,460	4,000		421	**108,794**
Totals	**1,692,334**	**295,404**	**194,630**	**99,190**	**7,060**	**45,897**	**2,334,515**

FFP=fresh frozen plasma; SD=solvent detergent-sterilised; MB=methylene blue-treated; Cryo=cryoprecipitate

SD-FFP data supplied by Octapharma

Paediatric/neonatal MB-FFP are expressed as single units; Cryoprecipitate numbers are expressed as pools and single donations as issued; all other components are

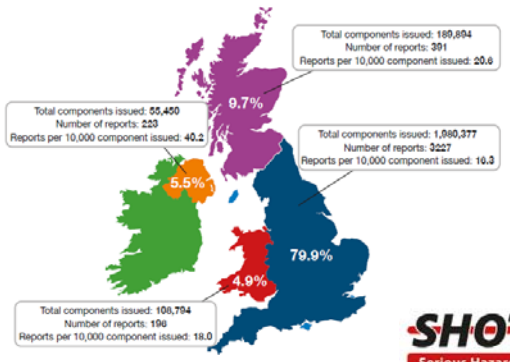

Figure 2.4: Percentage of SHOT reports submitted by UK country

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5

5

Deaths where transfusion was implicated n=20

This number includes deaths definitely, probably and possibly related to the transfusion. Delays in transfusion and pulmonary complications were the main causes of reported transfusion-related deaths in 2018. Transfusions with pulmonary complications contributed most to both deaths and major morbidity.

Major morbidity n=109

Most major morbidity was caused by febrile, allergic or hypotensive transfusion reactions and pulmonary complications. These are further detailed in the respective subject chapters in this report.

Major morbidity is defined as:

- Intensive care or high dependency admission and/or ventilation, renal dialysis and/or renal impairment
- Major haemorrhage from transfusion-induced coagulopathy
- Evidence of acute intravascular haemolysis e.g. haemoglobinaemia or severe haemoglobinuria
- Life-threatening acute reaction requiring immediate medical intervention
- Persistent viral infection

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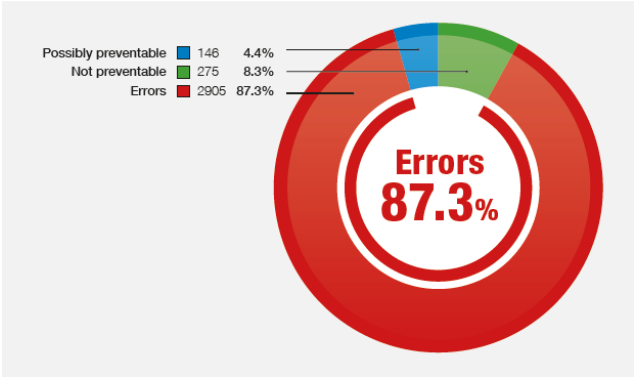
6

Figure 3.1: Errors account for the majority of reports: 2905/3326 (87.3%)



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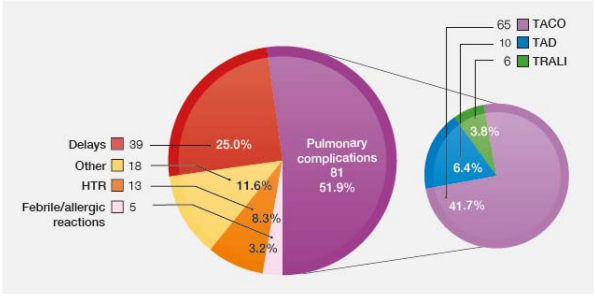
7

7

Transfusion related deaths in the UK 2010-2018 (n = 156)



HTR=haemolytic transfusion reaction; TRALI=transfusion-related acute lung injury; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea

'Other' includes 1 each for post-transfusion purpura (PTP), transfusion-associated graft-versus-host disease (TAGvHD) and anti-D immunoglobulin related; there were 6 in the avoidable, over or undertransfusion (ADU) category, 2 transfusion-transmitted infections (TTI), and 7 deaths related to other unclassified reactions

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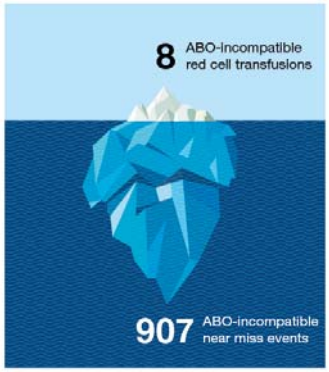
8

8

ABO-incompatible RBC transfusions in the UK 2016-2018



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9

9

What infectious diseases are donors screened for with tests?

HIV
HCV
HBV
HTLV-I/II
WNV
Syphilis
Zika virus
Trypanosoma cruzi
Babesia

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10

10

What are the major non-infectious risks of transfusion?

Transfusion reactions

- **Acute**
- **Delayed**

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11

What are the acute transfusion reactions?

- Allergic - mild to moderate to severe
- Febrile non-hemolytic
- Acute hemolytic
- Transfusion associated circulatory overload
- Transfusion related acute lung injury
- Sepsis
- Acute hypotensive reactions

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12

What are the delayed transfusion reactions?

- Delayed hemolytic
- Delayed serologic
- Transfusion associated graft versus host disease (TA-GVHD)
- Post-transfusion purpura (PTP)
- Iron overload

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13

Acute Acute Hemolytic Febrile Non-hemolytic Sepsis TRALI	**Delayed** Delayed Hemolytic TA-GVHD
Acute Allergic – mild to severe TACO Acute hypotensive	**Delayed** Delayed serologic Post-transfusion Purpura Iron Overload

Fever

No Fever

14

Acute reactions

15

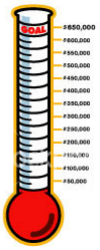
Allergic reactions

- Very common
- Type I hypersensitivity to donor plasma
- If occurs during a transfusion, stop the transfusion, treat with diphenhydramine and if hives go away, may restart transfusion slowly
- **Only** indication for re-starting transfusion after a transfusion reaction is suspected

16

Febrile Non-hemolytic reactions

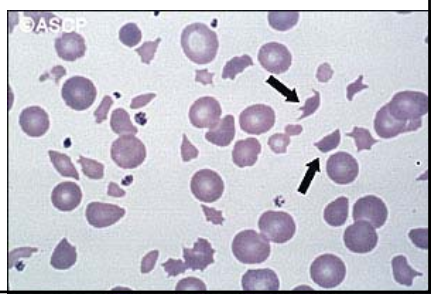
- Most frequently reported reaction (1%).
- Increase in temperature of 1°C or 1.8°F with no other explanation.
- Negative lab tests for hemolysis
- Symptoms: fever and chills (generally not rigors)
- Treatment: Symptomatic



17

Acute Hemolytic reactions

- Disastrous, may be **FATAL**
- Clerical errors (zero tolerance policy)
- Intravascular or extravascular (ABO usually intravascular)
- Signs/symptoms:
  - Fever and chills
  - Back or infusion site pain
  - Hypotension/shock
  - DIC/increased bleeding
  - Hemoglobinuria



18

Hemolysis

NORMAL (NO HEMOLYSIS) ***ABNORMAL (HEMOLYSIS)***

Negative for Hemolysis:
- Clear, yellow

Positive for hemolysis:
- Red, pink or cola-colored

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19

Transfusion associated circulatory overload (TACO)

New onset or exacerbation of ≥3 **within 6 hours** of cessation of transfusion

- Acute respiratory distress
- Elevated BNP
- Elevated CVP
- Evidence of left heart failure
- Evidence of positive fluid balance
- Pulmonary edema on imaging

www.cdc.gov/nhsn

20

Transfusion Related Acute Lung Injury (TRALI)

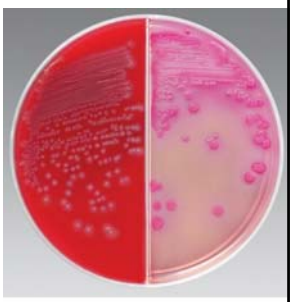
- Respiratory insufficiency with CXR that looks like bilateral pulmonary edema
- +/- Fever, chills, hypotension
- Usually **within 6 hours** of transfusion
- May be fatal (5-10%)

21

Bacterial Contamination

- Most common platelets: room temperature storage
  - Gram Positive Cocci
- Red cells: cold loving bugs like Yersinia
- Rapid onset high fever
- Rigors
- Abdominal cramping
- Nausea/vomiting
- Shock

Treatment: Immediate IV antibiotics and pressure support



22

Brief Report

SALMONELLA SEPSIS CAUSED BY A PLATELET TRANSFUSION FROM A DONOR WITH A PET SNAKE

MEHRDAD JAFARI, M.D., PH.D., JEAN FORSBERG, M.D., RONALD O. GILCHER, M.D., JAMES W. SMITH, M.D., PH.D., JAMES M. CRUTCHER, M.D., M.P.H., MICHAEL MCDERMOTT, B.S., BRENT R. BROWN, M.D., AND JAMES N. GEORGE, M.D.

N Engl J Med, Vol. 347, No. 14 · October 3, 2002

23

Staphylococcus aureus sepsis from one cocomponent of a "triple" apheresis platelet donation

Richard M. Kaufman and William J. Savage

TRANSFUSION Volume 54, July 2014

A 29-year-old asymptomatic woman with chronic thrombocytopenia, in Week 38 of pregnancy, received 1 unit of apheresis platelets (PLTs) in clinic. During the transfusion, she developed bilateral flank pain and coughing. The transfusion was stopped, and she was admitted to the hospital. She became febrile to 102.8°F and was transferred to intensive care with severe sepsis. She was treated with intravenous antibiotics. The baby was delivered by cesarean section; mother and baby were discharged home in good condition on Hospital Day 10.

24

Hypotensive Reaction

- All other adverse reactions presenting with hypotension (low blood pressure) are excluded ***AND*** hypotension occurs during or within 1 hour after cessation of transfusion

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25

Delayed reactions

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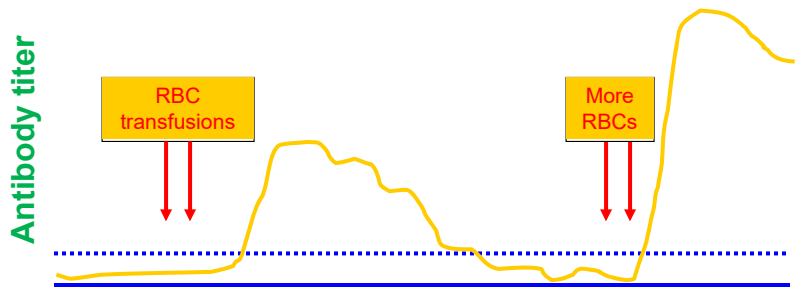
26

Delayed Hemolytic Transfusion Reactions

- Involves anamnestic antibody production
- Occur when preformed antibody is absent (or present in an amount insufficient for detection by routine methods) in the recipient's pretransfusion blood sample
- Recipient previously sensitized and thus has lymphocytes that are primed and ready to produce (anamnestic) antibodies upon rechallenge by the same antigen

27



1992: the recipient is immunized to a foreign antigen, but antibody is present only transiently

2008: the recipient is transfused with cells bearing the same antigen

28

Delayed Hemolytic Transfusion Reactions

- Treatment is supportive
- Transfuse antigen negative red blood cells as needed for symptomatic anemia
- Patients should be educated to inform all providers of their antibody history as antibodies may sometimes not be detected depending on reagents and methods used

29

Delayed Serologic Transfusion Reactions

- Similar to delayed hemolytic transfusion reaction, BUT there are no clinical signs or symptoms
- New antibody is identified in the Blood Bank following recent transfusion
- Treatment is supportive for symptomatic patients

30

Transfusion associated graft versus host disease (TA-GVHD)

- Extremely rare
  - 1 fatality reported to the FDA between 2011 and 2015
- Almost uniformly fatal
- Transfusion of viable lymphocytes in cellular blood products
  - Whole blood
  - Packed red blood cells
  - Platelets

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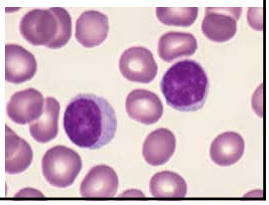
31

TA-GVHD

- If the recipient's immune system cannot recognize these cells as foreign, they may engraft in the recipient and mount an immune response against the host – destroying their bone marrow
- Irradiation of these cellular products in at-risk patients prevents this adverse event



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32

TA-GVHD

- 2 days to 2 weeks after a non-irradiated cellular transfusion in an at-risk recipient:
  - Rash
  - Diarrhea
  - Fever
  - Hepatomegaly
  - Liver dysfunction
  - Marrow aplasia
  - Pancytopenia

33

TA-GVHD

- Treatment: Largely palliative – vast majority of the time nothing helps prevent death
- > 99% fatal
- So, prevention is key

34

TA-GVHD

- Prevention: Irradiation of cellular blood products in at-risk patients
- At risk patients:
  - Congenital immunodeficiency
  - Hematopoietic stem cell recipients
  - Hematology malignancies
  - Patients on fludarabine and other drugs that affect T-lymphocyte number or function
  - Fetus and neonates

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35

Irradiator

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36

Posttransfusion Purpura

- Extremely rare complication of transfusion
- Occurs in previously pregnant women
- Occurs 2-14 days after transfusion of a blood product
  - Usually a packed red blood cell
- Results in severe thrombocytopenia
  - Platelet count < 10,000/µL

37

Posttransfusion Purpura

- Results from alloantibody to a foreign platelet antigen
  - Usually anti-HPA-1a
- Alloantibody also behaves like an autoantibody and attacks the patient's own platelets
- Patients present with unexplained purpuric rash, bruising or mucosal bleeding

38

Posttransfusion Purpura

- Disease may be self-limited – going away on its own within 21 days
- ***BUT,*** about 30% have major hemorrhage
- Mortality rate is 10%
- Treatment is high dose IVIG for 2-5 days with or without steroids
- Does not usually recur in the same patient for unexplained reasons

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39

Iron Overload from Transfusion

- An excess of systemic iron, that results in accumulation in vital organs
  - Liver
  - Heart
  - Pancreas and other endocrine organs
- Increases risk of cirrhosis, heart failure, diabetes, as well as other diseases

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40

Iron Overload from Transfusion

- Transfusion dependent patients
  - Beta-thalassemia major
  - Sickle cell disease
  - Myelodysplastic syndrome

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41

Iron Overload from Transfusion

- Symptoms are often limited until significant organ damage has already occurred
- Estimate total body iron stores in at-risk patients with
  - Serum ferritin concentration
  - Transferrin saturation
  - Heart and liver MRI
  - SQUID – superconducting quantum interface device

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42

Iron Overload from Transfusion

- Patients chronically transfused RBCs often have complications beginning in their 40's
- Treatment:
  - Therapeutic phlebotomy
  - Iron-chelating drugs

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43

You've made it to the end……

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44

Final Thoughts

- Review FDA and SHOT data
- Detail the known infectious risks of transfusion
- Detail the acute transfusion reaction types
- Describe the delayed transfusion reactions

45

Questions?

Contact
AABB eLearning Team
eLearning@aabb.org

46