ABO blood products transfused not identical: a problem or the solution?

Carla Luana Dinardo, MD, PhD
Fundação Pró-Sangue
Universidade de São Paulo

Case I

- SBL, 45 years old, female
- ALL in chemotherapy induction
- 5,000 platelets/mm 3
- Hb 6.8 g/dL
- Low Digestive Hemorrhage

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- Transfusion of platelet and red blood cells was requested

Available blood products

Anti-C; anti-E, anti-Jka, anti-S

Patient typed as **A**

Doubts?

- What to transfuse?
  - O or B types for platelets?
  - O or A for red blood cells?
- What are the risks of non-ABO identical transfusions?
- What tests can help in choosing the ideal blood component?

GENERAL PRINCIPLES

Defining ABO non-identical

Platelets / Plasma

RBCs

Donor AB → Patient A, B and O

Donor O → Patient A, B and AB

Donor A → Patient B and AB

Donor B → Patient A and AB

Donor O

↓

Patient A, B and AB

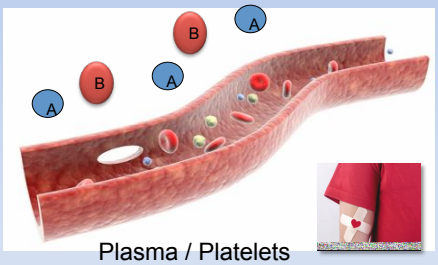
ABO non-identical transfusions

Platelets

Plasma

RBCs

ABO non-identical transfusions

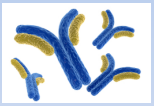


Plasma / Platelets
AB

- 80% of the population is secretor
- Substances A and/or B In plasma and secretions

Patient O

ABO non-identical transfusions



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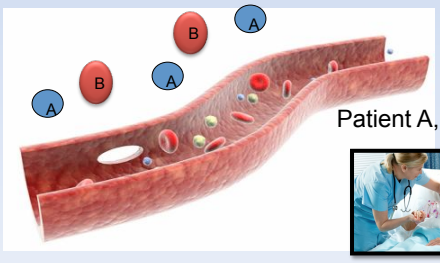
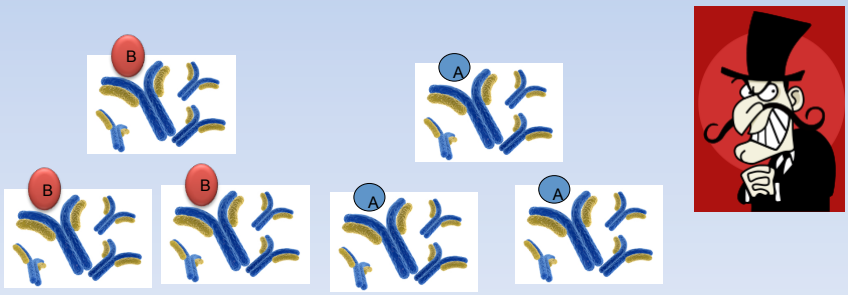


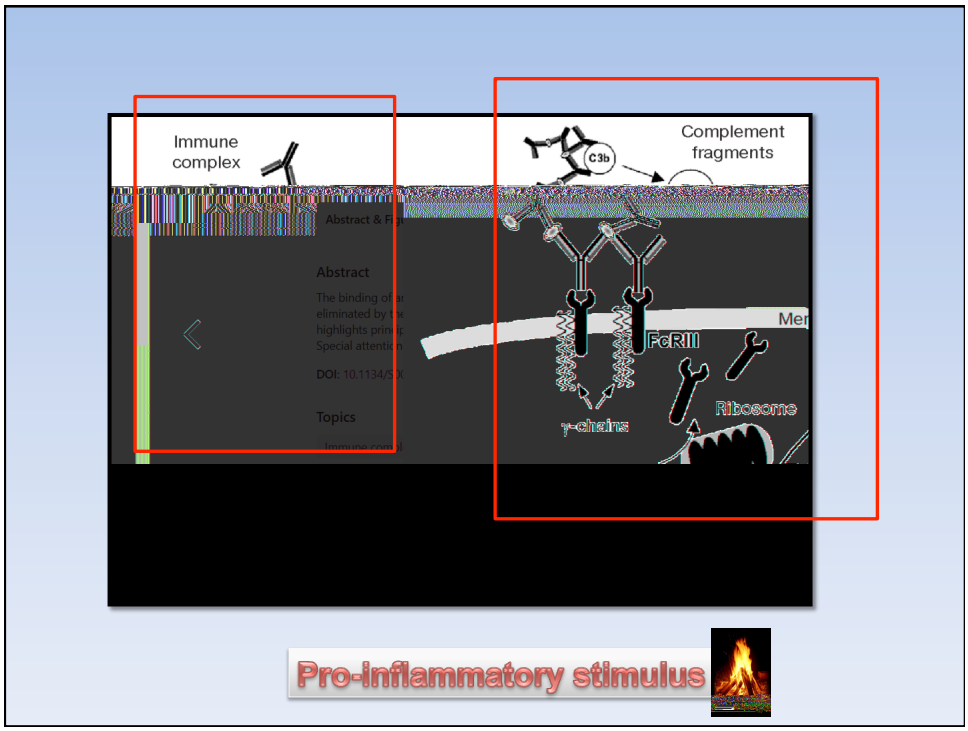
Patient A, B ou AB

Circulating Immune Complexes Villain



What are circulating immune complexes?

- Antigen-antibody complexes formed by the binding of IgG or IgM to soluble antigen
- They activate complement mainly by classical route
- They bind to activating or inhibitory FcR receptors, facilitating the immune response


Immune complex
C3b
Complement fragments
Abstract
Topics
FcRIII
γ-chains
Ribosome
Pro-inflammatory stimulus

PLATELETS

Types of Platelet Transfusions

1. ABO identical
2. Major ABO incompatibility
3. Minor ABO incompatibility

Transfusion of ABO identical platelets

- No reductions in mortality and bleeding
- Logistic is complex
  - Short shelf-life of platelet concentrates
  - Low availability of apheresis platelet donors

Shehata N, 2009

Published in final edited form as:
Transfusion. 2012 March ; 52(3): 635–640. doi:10.1111/j.1537-2995.2011.03329.x.

Providing ABO Identical Platelets and Cryoprecipitate to (Almost) All Patients—Approach, Logistics and Associated Decreases in Transfusion Reaction and Red Cell Alloimmunization Incidence

Blumberg

Transfusion of ABO identical platelets

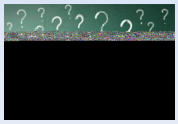
- Increased platelet increment
- Reduction of transfusion reactions
- Reduction of RBC alloimmunization
- Reduction of platelet refractoriness
- Reduced use of RBCs in massive transfusions

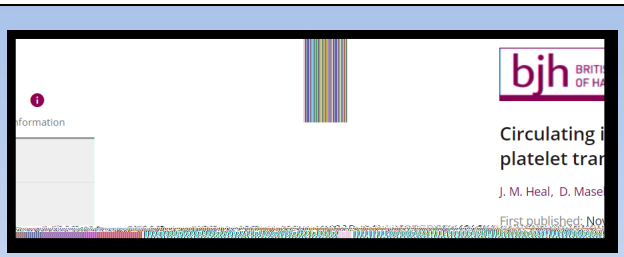
Transfusion of ABO non-identical platelets

Villain

Circulating ABO immune complexes formed by antibodies and soluble ABH antigens in plasma

Is AB the universal platelet type?





- Immune complexes circulating after transfusion of ABO non-identical platelets
- Possible justification for platelet refractoriness

[redacted]

Formation of ABO immune complexes

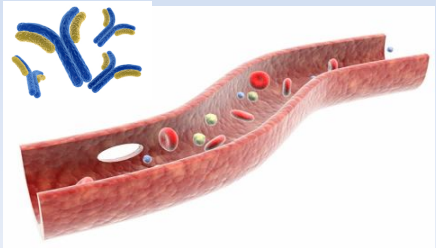
Altered platelet function ⟷ Altered clot formation

Hemolysis

Types of ABO incompatibilities

Major

A or B



O

Types of ABO incompatibilities

Major

Platelets express **ABH** antigens

↓

Lower platelet post-transfusion increment

Lower interval between transfusions

Types of ABO incompatibilities

Major

Platelet dysfunction

↓

Demonstrated in vitro
in the presence of isohemagglutinins in
moderate to high titres

Types of ABO incompatibilities

Major

PLADO study
(Optimal Prophylactic Platelet Dose to Prevent Bleeding in Thrombocytopenic Patients)

- ✓ **Lower** post-transfusion platelet increment (4 and 24h)
- ✓ **Shortening** of the interval between transfusions
- ✓ **No increase** in bleeding rate grade 2 or higher

In emergency situations, this type of transfusion is an option

Types of ABO incompatibilities

Minor

O

A or B

Types of ABO incompatibilities

Minor

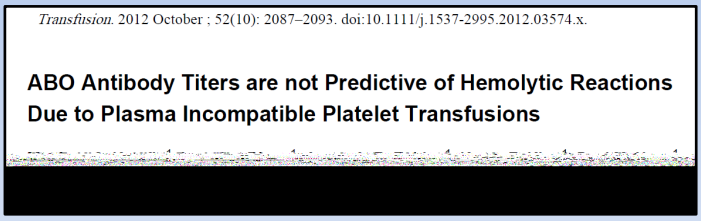
Risk of **acute hemolytic reaction**

Estimated frequency of 1/50,000 incompatible transfusions

Potentially lethal
- 6 deaths recorded between 1996-2006 *

*FDA report

Restriction of transfused volume


Transfusion. 2012 October ; 52(10): 2087–2093. doi:10.1111/j.1537-2995.2012.03574.x.

ABO Antibody Titers are not Predictive of Hemolytic Reactions Due to Plasma Incompatible Platelet Transfusions

Restriction of incompatible plasma volume transfused to 600mL

No reports of acute hemolysis

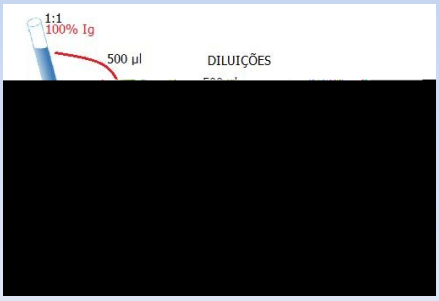
Increased rates of post-transfusion DAT+ (subclinical hemolysis)

Titration of Isohemaglutinins Rational

- **Dilution** of anti-A / anti-B antibodies
  - ABO antigens in epithelial tissues and plasma
  - Plasma volume itself
- The **lower** the titer, the **greater** the ability of most antibodies to be diluted

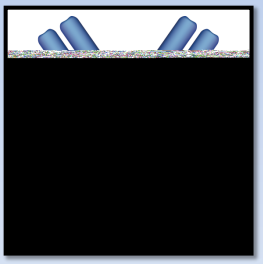
Titration of Isohemagglutinins

Gel-test or tube methods



Different
Literature varies in relation to the best technique to b**e used**

Titration of Isohemagglutinins



IgM

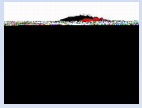
IgG

Which titer is safe? No one knows!

Hemolytic reactions described with titers ranging from

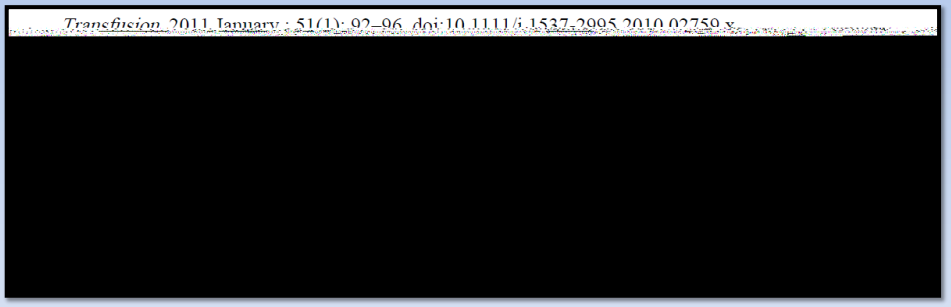
32 to 16.384 **IgM**

32 to 32.000 **IgG**



Depends on the volume of incompatible plasma (transfused) and the volume of the recipient

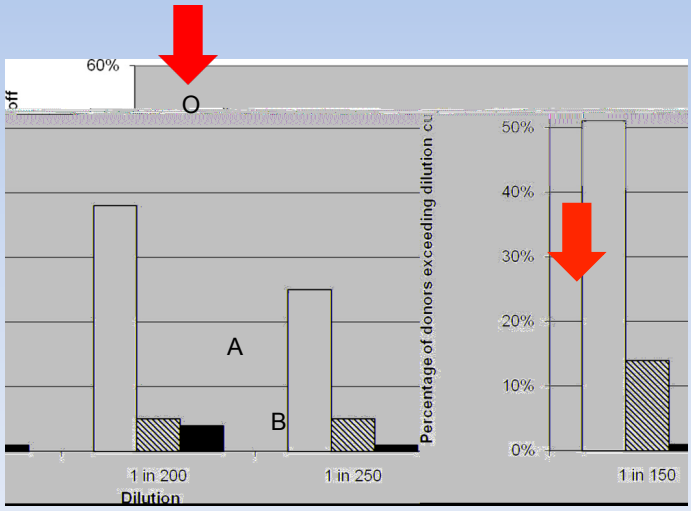
United States- NIH



Rate of hemolytic reactions without prophylaxis → 1/2.460

No new reactions after1:250 **IgM** prophylaxis

United States- NIH



Quillen K, 2011

Europe

- Scotland
  - 1:50 IgM
  - Change of threshold after hemolysis at titer 1: 100
- England
  - 1:100 IgM

Mandatory prophylaxis

Fundação Pró Sangue

- Prophylactic titer 1:100 IgM
  - For 15 years
  - No reported hemolytic reactions
- Prophylaxis titer 1:128 IgM
  - Only apheresis units
  - Manual technique
  - No hemolytic reactions

Fundação Pró Sangue

IT	Frequency	Percent
<128	211	85.8
≥128	35	14.2
<64	165	67.1
≥64	81	32.9

85% of donors with IgM titers below 1: 128

Small impact on stock considering them as hazardous

Titration of Isohemagglutinins

Benefits

Vast evidence attesting the effectiveness

Disadvantages

Large volume transfused

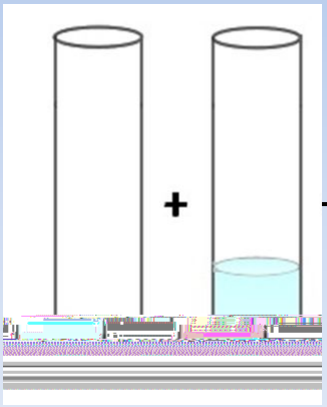
Small Recipient

No-secretor status

Qualitative Hemolysin Test Rational

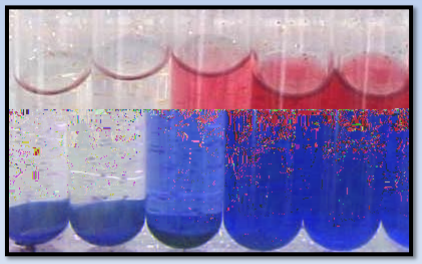
- Detect the presence, in the incompatible serum, of anti-A and / or anti-B with hemolysis capacity
- Three possible outcomes:
  - Absence of hemolysis ➡ Transfusion is safe
  - Partial hemolysis
  - Total hemolysis

Laboratory Technique



45'

RT

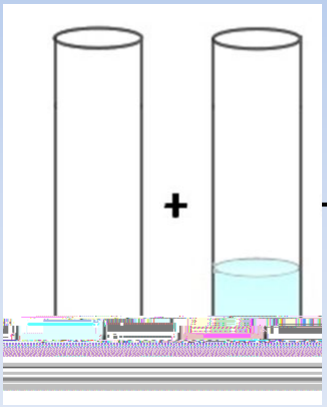


Absence of hemolysis | Partial Hemolysis | Total Hemolysis

50µL RBC suspension at 3%

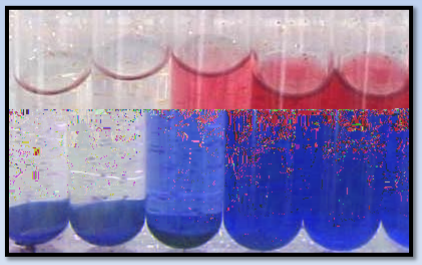
100µL of PTL serum

Laboratory Technique



15'

37°C



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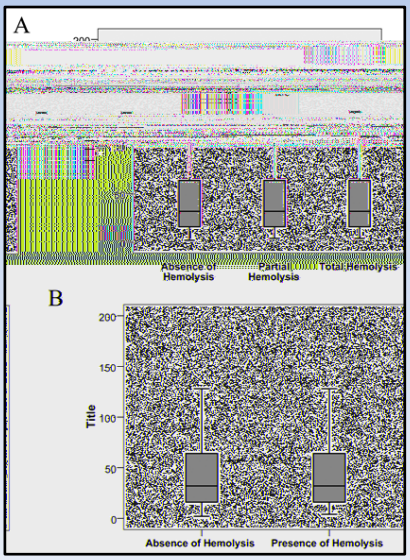
Correlation with Isohemaglutinins Titration



Lack of correlation between tests

Dinardo et al, 2015

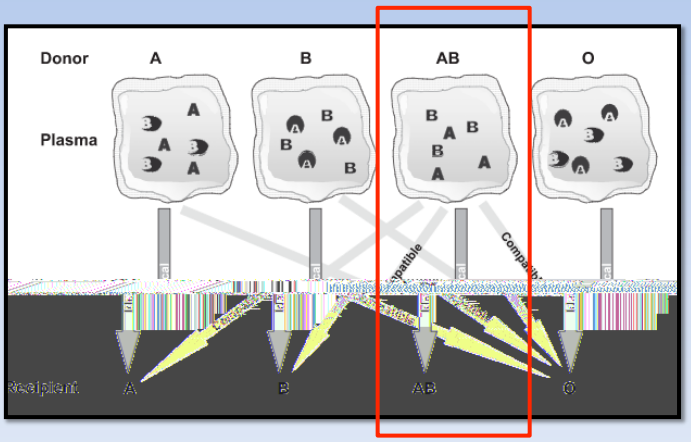
QHT - Impact on routine

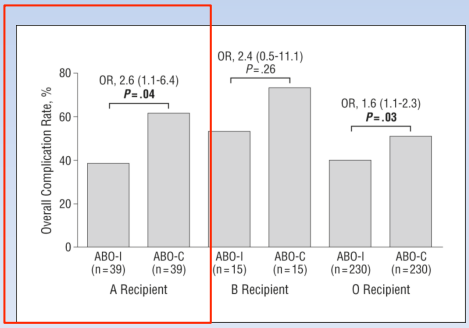
- **65%** of platelet units considered as "dangerous"
  - Difficult management of the platelet inventory

[redacted]

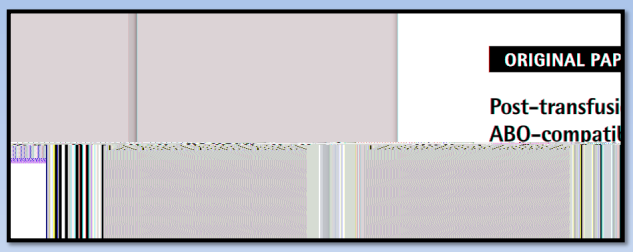
There is a lack of studies attesting the safety of QHT as a prophylactic strategy

PLASMA

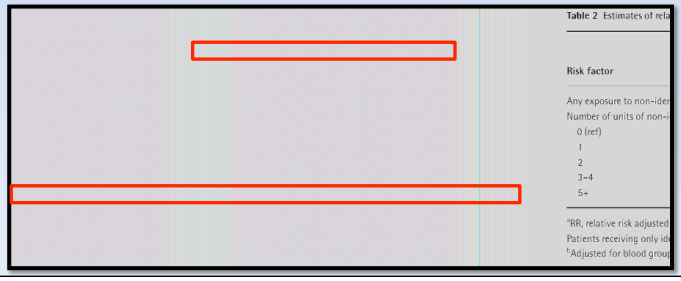




- Plasma ABO-compatible vs ABO-identical plasma
  - No differences in mortality
  - Plasma ABO identical **less complications** during hospitalization



- 86,000 general patients
- Comparison ABO-compatible plasma x only ABO identical plasma
- Mortality 14 days after plasma transfusion

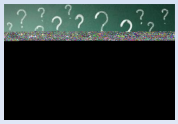


Transfusion of ABO non-Identical Plasma

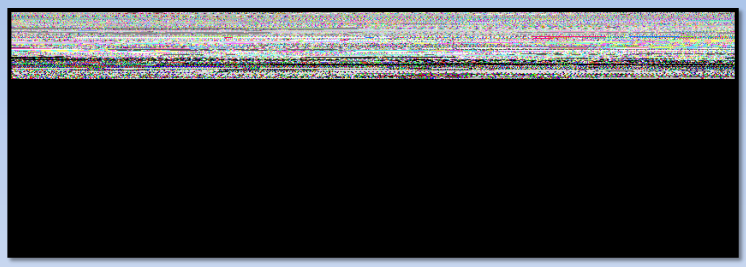
Villain

Circulating ABO immune complexes formed by antibodies and soluble ABH antigens in plasma

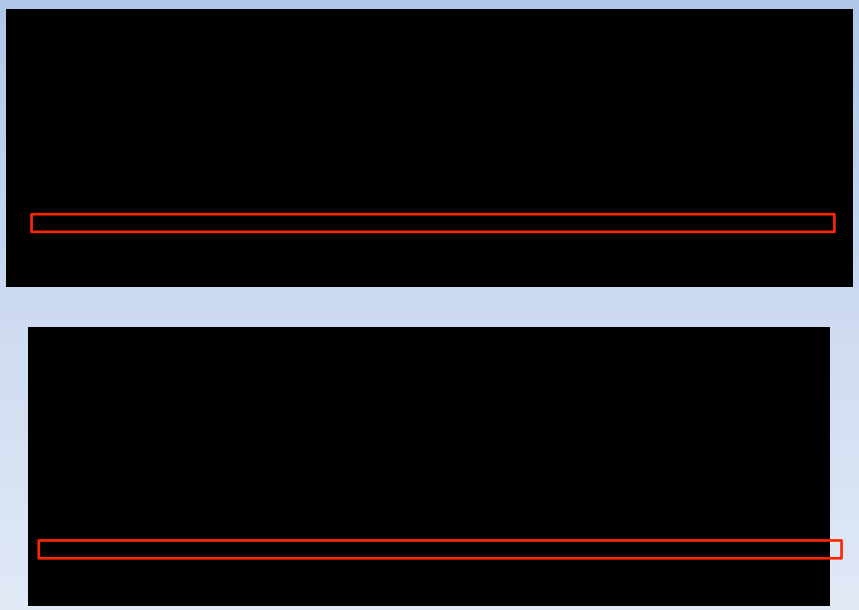
Is AB plasma universal?



RED BLOOD CELLS



- 18,843 transfusion records
- Including patients receiving at least one RBC unit
- Type A patients had an increase in in-hospital mortality
  - Receiving at least one O-type unit
- When trauma patients were excluded, the risk increased



CLINICAL CASE

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Available blood products

Anti-C; anti-E, anti-Jka, anti-S

Patient typed as **A**

Case I

- Isohemagglutinin titration of O-type platelets was performed
  - 1:128
  - 1:64
    - Unit selected for transfusion
- Type A RBC unit was transfused
  - Phenotype-identical type A donor was summoned for next transfusions

TAKE HOME MESSAGES

Transfusion of ABO non-identical blood products

- Components of high plasmatic content
  - Formation of circulating immune complexes
  - Change in the patient's inflammation status

- Platelet units
  - Major ABO incompatibility
    - Lower platelet increment
  - Minor ABO incompatibility
    - Risk of acute hemolysis
- ABO non-identical RBC units
  - Increased in-hospital mortality

Universal donor and recipient?

Perspective

Reality

Transfusion of ABO-identical blood products should be the rule

THANK YOU