Whole Blood: Blood Center Perspective

Hoxworth Blood Center
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David Oh, MD
Chief Medical Officer/Co-Chair & CEO
Hoxworth Blood Center
Clinical Associate Professor
University of Cincinnati College of Medicine

Blood is Essential in Modern Healthcare

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- Blood transfusion occurs every 2 seconds in US
- One in 7 hospital admissions involves blood transfusion
- Annually
  - 10,852,000 RBC Tx
  - 2,243,000 Platelet Tx
  - 2,185,000 Plasma Tx

Blood Doesn't Grow on Trees

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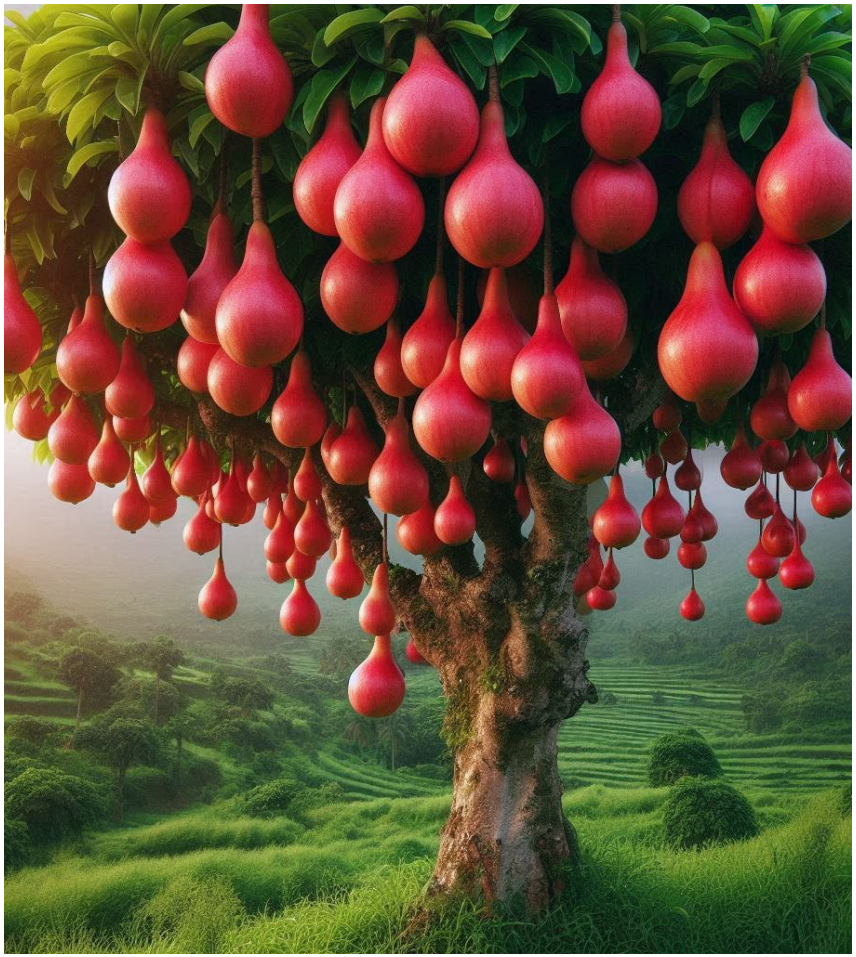

Whole Blood Donation

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Whole Blood = RBC + Plasma

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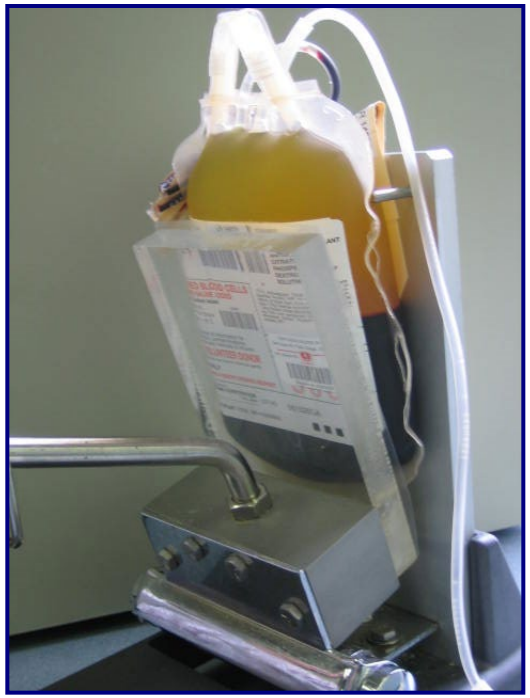

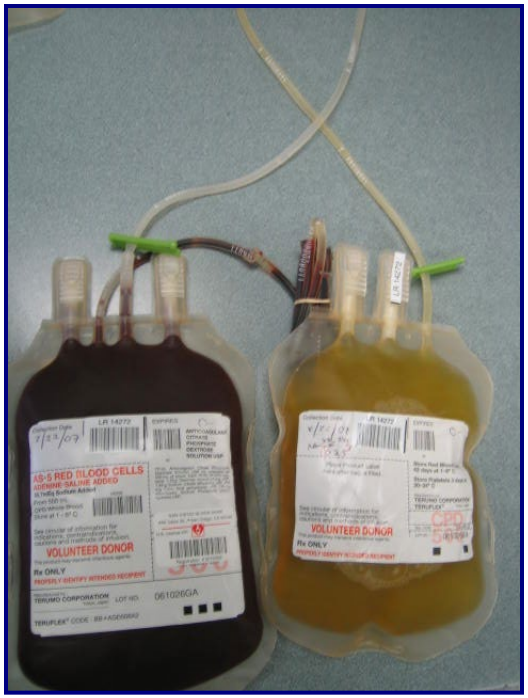

Steps required with WB manufacture

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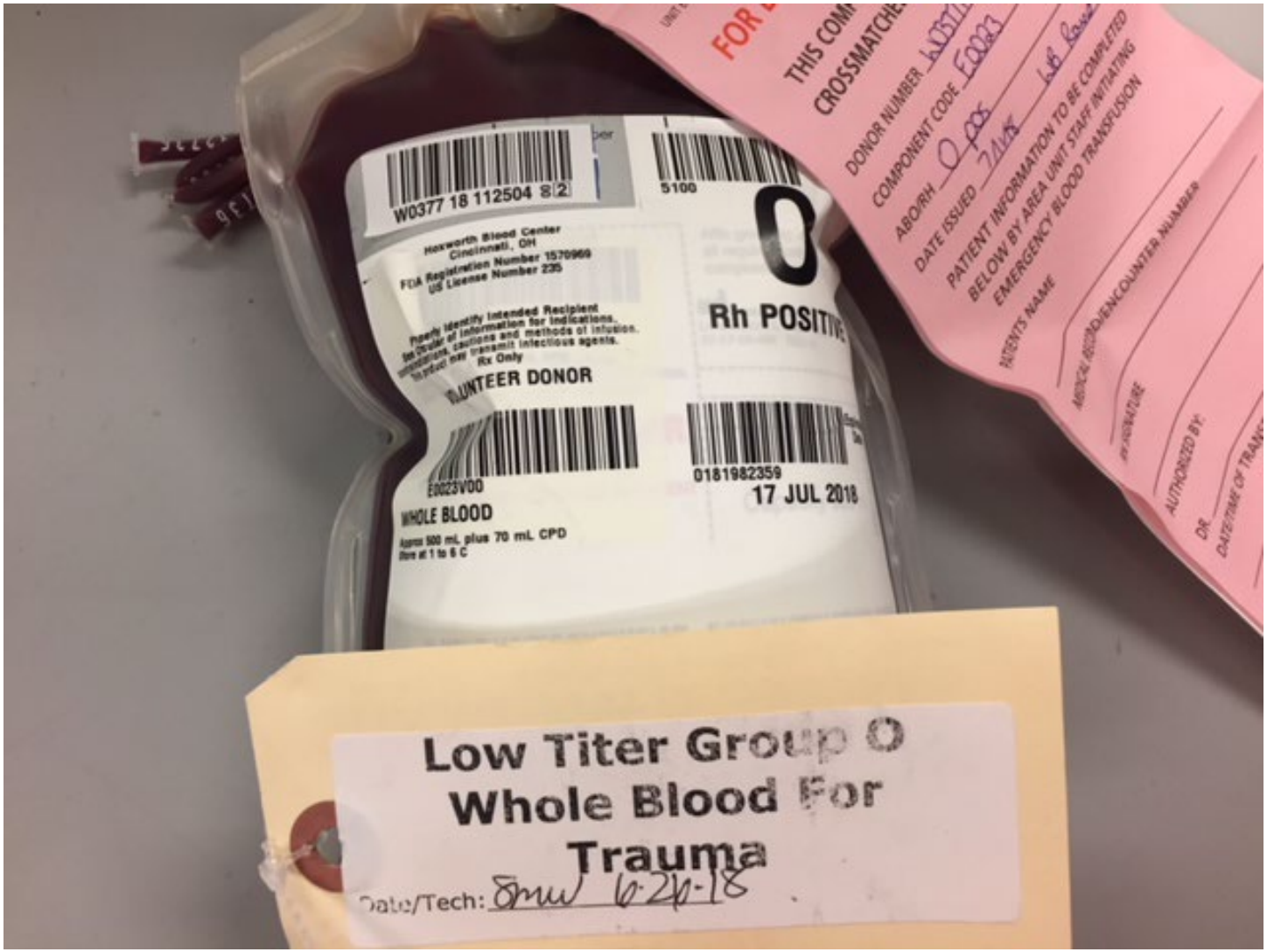
- Receive orders for WB from Hospital Transfusion Service
- Identify O-positive WB units prior to processing into components
  - Male donors
  - Donors previously typed as O-positive
    - (repeat donors only)
- WB segregated for titration
  - Only low-titer units labeled as WB
- Transfer to sterile bag with transfusion port
- IDM and other screening tests
- Label
- Distribute to ordering Hospital Transfusion Service
- Available for ordering physicians

Low-Titer Group O-Pos Whole Blood



Advantages of Whole Blood

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Simple to Administer

- In massive transfusion environment, one bag instead of separate red cell, platelet, and plasma provides value

More Potent

- Red cell dose not diluted in Additive Solution (AS – 110 mL)
- Platelets not removed from red cells by component separation and WBC-leukoreduction
- Coagulation factors in platelets are diluted if collected in apheresis platelets are in Platelet Additive Solution instead of Plasma

Fewer Donor Exposures

- Red cell and plasma and platelets are from one donor

Concerns with Whole Blood

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O Plasma to A and B recipients

- Possible hemolysis of red cells
- Low-titer requirement

Rh(D) Alloimmunization

- HDFN prevention

Inventory Management

AABB 5.27.1

Recipients whose ABO is not known or has not been confirmed shall receive

O Red Blood Cells

or

Low-titer O Whole Blood

What is LOW-TITER?

Concerns in the Use of Whole Blood

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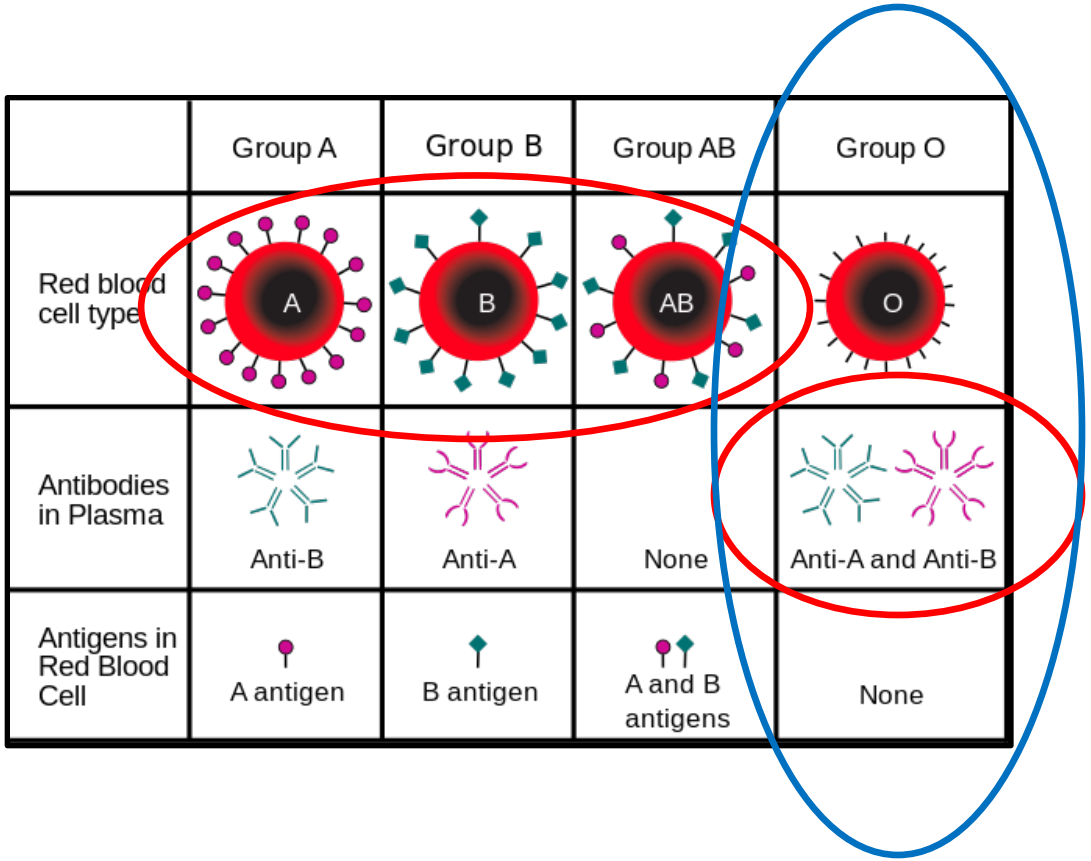
ABO Incompatiblility for Non-O Recipients



Low-Titer

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- AABB Standard does not define “Low-Titer”
- No agreed upon gold standard method
- How do I implement a whole blood program for massively bleeding patients? Yazer MH, Cap AP, Spinella, Alarcon L, Triulzi DJ. Transfusion 2018;58;622-628.
  - CTS in Pittsburgh: Units <50 (immediate spin, tube)
  - Mayo Clinic: Units <200 (immediate spin, tube)
- How often should donors be tested?
  - Antibody titers appear to be relatively stable over time
  - Test every time to simplify the process of selecting units

Whole Blood Low Titer

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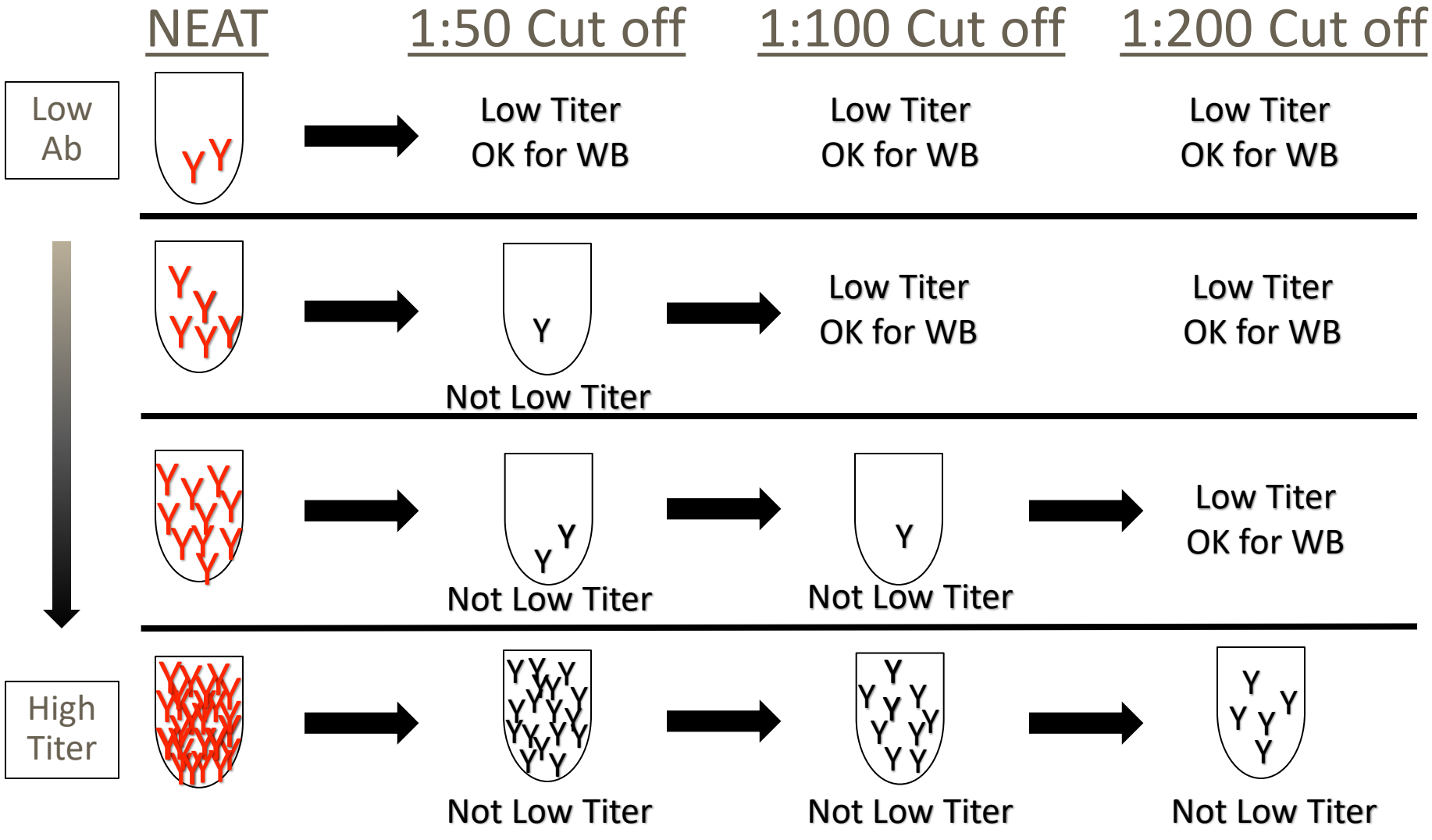

ABO Incompatible Plasma

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- Hemolytic Transfusion Reactions are rare after platelet transfusions containing ABO-incompatible plasma
  - Between 2005 and 2015
    - 7 fatalities reported to FDA implicating PLT transfusion
      - 5 cases associated with “high-titer” group O apheresis units
        - » Anti-A titer of **2048** in only case with reported titer value
      - 1 case with group A apheresis platelet to group B recipient
        - » Anti-B titer of **2048**
      - 1 case with two group O apheresis platelets from same donor to ABO recipient
        - » Anti-A and Anti-B titers of 128

Yazer MH. Who’s afraid of incompatible plasma. A balanced approach to the safe transfusion of blood products containing ABO-incompatible plasma. Transfusion. 2018. 58:532-538.

Universal Rh(D)-Positive Whole Blood

Concern: Rh-pos Red Cells

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- RhD is highly immunogenic in immunocompotent individuals
  - 80% of O-neg healthy immunocompotent male subjects exposed to <1 mL of O-pos RBCs developed antibodies
- RhD is much less immunogenic in immunocompromised recipients
  - D-neg liver transplant recipients of D-pos RBCs did not develop anti-D
- 22% of O-neg non-oncology recipients of O-pos RBCs developed anti-D
- 35% (117/335) of O-neg women (13-50 yo) receiving >= 1 unit of O-pos RBCs were sensitized (Yazer et al, Transfusion. 2021)

Yazer MH. Triulzi DJ. Detection of anti-D in D- recipients transfused with D+ red blood cells. Transfusion. 2007. 47:2197-2201.

Modeling based on a Level 1 Trauma Center Registry of Universal Rh(D)-pos LTOWB

5 Rh(D)-neg females of childbearing potential may receive Rh(D)-pos WB per year (504 over a 100-year period)

82.5% would be expected to survive acute trauma injuries

Of females of childbearing potential: Average age of 33 ± 10 years

22.1% would become Rh(D)-alloimmunized

Resulting in 67 pregnancies over 100-year period

50.7% of fetuses would become Rh(D)-pos

9.0% of fetuses would be significantly affected by HDFN

(6 Pregnancies affected from 504 transfused FCP over 100 yrs)

1-2 Potential HDFN cases per 100 potential transfusions of FCP

1-2 Potential HDFN cases every 20 years

The risk to future pregnancies of transfusing Rh(D)-negative females of childbearing potential with Rh(D)-positive red blood cells during trauma resuscitation is dependent on their age at transfusion. Triulzi, Yazer. Vox Sang. 2021

Whole Blood Program Details

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Restrict ordering of whole blood	• TRAUMA only!!! • Component therapy for other settings
O-Positive Whole Blood	• O-Negative is too difficult to stock for this purpose • Only males (any age) and females >55 yo
Low-Titer	• WB unit: <100 (Immediate spin)
Cold Whole Blood with all IDM Screening Completed	• NOT WARM FRESH (<24 hours)
Non-Leukoreduced WB	• Concerns about platelet function with platelet sparing filter

Whole Blood Program Details

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Male only donors requested

- TRALI concerns
- Previous studies done with male only WB
- ALL WB provided are from male donors
  - NOT labeled as “male only’

No CMV serologic status requirement

- CMV status only indicated for severely immunocompromised

No irradiation requirement

- Only indicated to prevent TA-GVHD

Whole Blood Program Details

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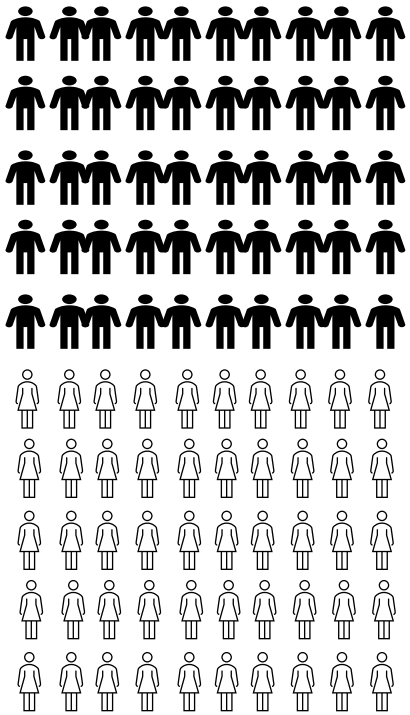
- CPD: 21 day expiration
- WB not returnable to Hoxworth Blood Center if not transfused
- 6 WB distributed at a time as massive transfusion set
- 8 WB required in inventory to enroll TROOP subjects

Availability of WB for Production



100 whole blood donors present

No female donors – TRALI mitigation
50 male donors

2/3 repeat donors = 33 male donors

40% Type O = 13-14 male donors

Remaining donors are excellent
Automated Red Cell candidates
(20% of all red cells)

TOWAR: Type O Whole Blood and Assessment of Age During Prehospital Resuscitation Trial

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- Open label, multi-center, pre-hospital randomized trial utilizing 10 level-1 trauma centers
- Determine the efficacy and safety of low titer whole blood resuscitation as compared to standard of care resuscitation in patients at risk of hemorrhagic shock
- Appropriately characterize the hemostatic competency of whole blood relative to its age.
- Subjects will receive up to 2 WB units prehospital transfusion vs standard resuscitation therapy
- Primary outcome measure: 30-day mortality
- https://clinicaltrials.gov/ct2/show/NCT04684719

TROOP: Trauma Resuscitation With Low-Titer Group O Whole Blood or Products

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- Compare the effectiveness of unseparated whole blood (referred to as Low-Titer Group O Whole Blood) and the separate components of whole blood (including red cells, plasma, platelets, and cryoprecipitate) in critically injured patients who require large-volume blood transfusions.
- Randomized to WB components vs traditional component therapy
- Only eligible if transfused 2 or less blood products prior to randomization
- Primary outcome measure: 6-hour mortality
- https://clinicaltrials.gov/ct2/show/NCT05638581

Summary

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- Advantages of Whole Blood for massive transfusion
  - Ease of Administration – conceptually appealing
  - Concurrent RBCs, plasma and platelets
    - Plasma: coagulation factors
    - Red Cell: oxygen delivery
    - Platelets: clot formation
  - Less dilution of blood components with preservatives/anticoagulants
- Concerns
  - Anti-A and anti-B antibodies may cause hemolysis
  - Rh-positive RBCs in WB may result in recipient sensitization with anti-D
  - Inventory complications with separate massive transfusion protocols for women of childbearing age
  - Expiration/product wastage

Fig. 1. The normal chaos of component massive transfusion, trying to reconstitute WB out of components versus just transfusing WB. [Color figure can be viewed at wileyonlinelibrary.com]

Holcomb JB. Get ready. Whole blood is back and it's good for patients. Transfusion 2018. 58:1821-1823.