ABO Compatibility and Blood Products

Transfusion Support of the HSCT Patient

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Overview

- Blood Product Manufacturing
- Modifying the Component
- ABO Compatibility
- HSCT Product Processing on Day of Transplant
- Adverse Transfusion Events
- Transfusion Support Issues

Blood Processing Laboratory

- Whole Blood
- Centrifuge
- 1 Unit PRBC
- Platelet Rich Plasma (PRP)
- Centrifuge
- 1 U Platelets
- Freeze, Thaw, Centrifuge
- 1 Bag
- 1 Bag Cryoprecipitate

Whole Blood Unit after first centrifuge spin

Blood

- RBC
- Monocyte
- Platelet
- T-Lymphocyte

Red Blood Cells, Platelets (stained purple), a T-lymphocyte white cell (stained green), and a Monocyte white cell (stained gold) as seen through a scanning electron microscope. ©2000 Dennis Kunkel, Ph.D.
Express off Platelet Rich Plasma into Satellite Bag

Express off majority of plasma into satellite bag to make FFP with platelet concentrate remaining

Pre-Storage Pooled Platelets
- Leukoreduced
- Pooled
- Bacterial Tested
- Closed system - Expiration 5 days
- Volume Reduction - 4hr expiration
- Adult Platelet dose – Equivalent to Apheresis Platelets
- Returnable if stored/handled properly

Components from Whole Blood

• Red Blood Cells
  - Small amount of WBC’s and Plasma
• 1 Unit Platelet Concentrate
  - 2-5 U pooled into one bag for transfusion
  - Contain viable WBC’s
• Fresh Frozen Plasma
  - No viable WBC’s
• Cryoprecipitate
  - 5 unit pools used for adult transfusion
  - No viable WBC’s

Apheresis

Plasma-Stored versus PAS-Stored Platelets

• The primary difference between plasma-stored and PAS-stored platelets is that a fraction of the plasma volume has been removed.
• Platelet product yield, final product concentration, and final volume are the same.
PAS Platelets
(Platelet Additive Solution)

- Reduced risk of allergic transfusion reactions
- May reduce Febrile reactions and TRALI

- May substitute for Reduced Volume platelets for:
  - ABO compatibility
  - Allergic transfusion reactions – Mild to Moderate
- NOT a substitute for Circulatory Volume Overload or Fluid Issues

Inactivated (smooth) platelet (stained blue) among spiky, activated platelets as seen through a scanning electron microscope. ©2000 Dennis Kunkel, Ph.D.
Platelet Expiration

- Platelets good for 5 days after collection
  - Midnight of the 5th day
  - Available 24hr after collection
- Four hours after processing for release from blood bank.
  - Volume Reduction
  - Pooling (if not done in closed system)

Red Blood Cells

Distribution of blood groups in the USA

Platelets

- **Pooled** Whole Blood Derived
  - AKA “6 Pack” (or 5 Pack or Pre-Storage Pooled)

- **Apheresis** Machine Derived
  - Random Donor
    - AKA - RAP - Random Apheresis Platelet
    - SDR - Single Donor Random
  - HLA Directed Donor (HLA Selected)
    - AKA - MAP - Matched Apheresis Platelet

Platelet Expiration

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**Pediatric RBC Options**

- **Pedi Pack** — Discontinued 1/27/15
  - 1 RBC unit is divided into 50-80ml bags

- **Assigned Aliquot**
  - 1 RBC unit is divided into 30-43ml bags, all dedicated for a particular patient

- **Syringe**

**Blood Component Attributes**

**Modifying the Blood Product**

**Irradiation**

- Inactivates Lymphocytes that cause Transfusion Related Graft vs. Host Disease (tGVHD)

**Leukoreduction**

- **Leukoreduction**
  - Removes WBC that may cause alloimmunization against platelets
  - Reduce unwanted effects caused by WBC’s releasing cytokines during storage

- **CMV Negative/Safe**
  - Virus exists in WBC, therefore Leukoreduced blood products are considered CMV Safe

**Reduced Volume**

- Plasma removed from product down to 100ml
  - RV results in some platelet loss and platelet activation

- **Indications**
  - Small recipient size
  - Severe fluid restriction issues
  - ABO compatibility *
  - Allergic reactions *

*PAS platelets may substitute for RV if for:
  - ABO compatibility
  - Mild-moderate allergic transfusion reactions

**Washed**

- Rarely used (Anaphylaxis), removes essentially all plasma proteins from component
ABO Compatibility

Preventing Hemolytic Transfusion Reactions for ABO mismatched BMT Transplants

Acute Hemolytic Transfusion Reaction

Antibodies + RBC's \rightarrow \text{Complement Activation} \rightarrow \text{Antibody Coated RBC's} \rightarrow \text{Membrane Damage and Cell Death}

Key Concept:
We make antibodies to what we are not.

ABO Compatibility Concepts

- Antigens exist on the RBC Cell Wall
  - A and B antigens are expressed on the cell wall
- Antibodies exist in the Plasma
- RBC's do not have Plasma
  - (Actually not true – there is ~ 20-40ml)
- Platelets have Plasma but no RBC's
  - (Actually not true – there is ~ 1-3ml)

Case Study - Background

Mrs. Mary Jones
- 57yo, Myelofibrosis
- Scheduled for PBSC Transplant
- URD
- Her ABO type O positive
- Donor ABO type A positive
Case Study – ABO Pre-Transplant

- **O positive**
  - Antibodies to both type A and to B RBC’s
  - Anti-A and Anti-B
  - RBC’s – Give type **O positive**
  - Platelets – Give any type
  - Plasma – Give any type
  - There are no RBC’s in Platelets or Plasma.
  - There is no such thing as Anti-0

Post Transplant Blood Component Support

ABO mismatched Transplant

Give Components that are compatible with what the recipient: was, is, and will be.

- All ABO mismatched recipients get ABO type **O** RBC’s
- Give Platelets that do not have plasma with antibodies to either original or donor ABO types

Case Study – ABO Post-Transplant

Patient: **O positive**
Donor: **A positive**

- RBC’s – Give type **O positive**
- Platelets, Plasma – Give compatible with Type **A**
  (Full volume **A, AB**. Or Reduced Volume **O, B**)
  Coming soon: PAS platelets may substitute for RV
  - There are no RBC’s in platelets or Plasma.
  - There is no such thing as Anti-0

HSCT Product Processing

ABO Mismatched Transplants
Case Study – Transplant
(Patient O, Donor A)

• Mary has Anti-A titers
  – IgM 1:32
  – IgG 1:128
These titers would hemolyze type A RBC's in the HSCT Product

• Assure RBC's in HSCT Product is < 20ml
  – Hct is checked on PBSC product
  – If > 20ml RBC in product - must RBC deplete
    • PBSC done in Cellular Therapy Lab,
    • Marrow done by Apheresis

Donor Type A

Major ABO Mismatch
Patient Antibodies directed toward Donor RBC's

Patient Type O

PBSC done in Cellular Therapy Lab,
Marrow done by Apheresis

RBC Deplete

Engraftment of Donor RBC's
Patient ABO type O, Donor ABO type A

Patient Vascular Space

Major ABO Mismatch

Case Study 2 - Background

Mr. Mike North
• 45yo, AML
• Plan for Bone Marrow Transplant
• URD
• His ABO type  A positive
• Donor ABO type  O negative

Donor Type A

Major ABO Mismatch
Patient Antibodies directed toward Donor RBC's

Patient Type O

PBSC done in Cellular Therapy Lab,
Marrow done by Apheresis

RBC Deplete

Case Study 2 – Transplant
(Patient A, Donor O)

• Donor has Anti-A titers
  – IgM 1:512
  – IgG 1:256
These titers would hemolyze type A RBC's in the Patient

• Assure Plasma in HSCT Product is < 200ml
  – If > 200ml Plasma -> Plasma deplete
Minor ABO Mismatch
Donor Antibodies directed toward Patient RBC's

Patient Type A
Donor Type O

Plasma Deplete

Engraftment of Donor RBC's
Patient ABO type A, Donor ABO type O

Minor ABO Mismatch

Adverse Transfusion Events

Transfusion Reactions
- Hemolytic ABO Incompatibility
- Allergic Plasma Proteins
- Febrile Cytokines
- Cardiac Fluid Overload Fluid Volume
- TRALI Donor Antibodies

Hemolytic Transfusion Reactions
- Rare
- Caused by incompatible blood component
  - Patient antibodies against donor RBC
  - Donor antibodies (in Plasma/Platelets) against recipient RBC
- RBC hemolysis ->
  - Fever, hypotension, nausea, vomiting, tachycardia, dyspnea, chest or back pain, flushing, severe anxiety
  - Hemoglobin induced renal failure
**Allergic Transfusion Reactions**

- **Uticaria**
  - Patient reacting to specific plasma proteins in donor plasma
    - Hives, itching, rash, swollen eyes, laryngedema, anaphylaxis, Dyspnea
  - Pre-medicate with antihistamines
  - Plasma reduce platelets (Reduced Volume)
  - Run slow
  - RBC’s already have plasma removed

**Washed Blood Components**

- **Indication**
  - Life Threatening Allergic Reactions
- **How**
  - Normal saline added to bag
  - Centrifuged -> plasma removed
- **Effect**
  - Removes donor plasma proteins
  - Adverse Effect of washing - Cell loss (~ 20% of cells)

**Febrile Transfusion Reactions**

- Caused by sensitization to antigens on cell components, particularly leukocytes and/or cytokines produced by donor lymphocytes
  - Fever, chills, rigors, hypotension
- Pre-medicate with acetaminophen
- Leukoreduction – Pre-storage

**Bacterial Contamination**

- Rare
- More common with platelets
- Sudden, severe – Usually in 1st 15min.
- High Fever, rigors, hypotension, nausea, vomiting
- Stop, notify Blood Bank, save bag for culture
  - Co-components must be sequestered

**Transfusion Associated Circulatory Overload (TACO)**

- Too much, too fast
- Slow it down
### Reactions - Actions

- **Allergic Plasma Proteins**
  - Premed with antihistamine
  - Reduce Volume Platelets
  - (or coming soon: PAS platelets)
  - Slow transfusion

- **Febrile Cytokines**
  - Premed with antipyretic
  - Slow transfusion
  - Apheresis Platelets or Pre-storage Leukoreduced

- **Cardiac Fluid Overload Fluid Volume**
  - Give less, give slow

### TRALI
Transfusion Related Acute Lung Injury

- Donor Plasma contains antibody against patient's HLA or leukocyte specific antigens.
  - Less often patient has antibodies against donor leukocytes in the component
  - Dyspnea, hypotension, fever – 30min-6hr post transfusion -> Sudden onset diffuse non-specific pulmonary infiltrates, Ventilatory support
  - Save bag for antibody identification by Blood Bank
  - Report to Blood Bank

### Transfusion Support Issues

### Platelet Refractoriness

- Enlarged Spleen
  - Platelets sequestration

- Consumption
  - Bleeding
  - Fever

- Alloantibodies against donor platelets
Case Study – Platelet Support

• Initially had marginal increments to platelets – 20-30K increments by pre and post counts
  – Review of Abdominal CT showed Splenomegaly

• After 2 weeks had increments of <5K

Case Study – Platelet Support

• Platelet Alloantibody Workup ->
  – Platelet Reactive Antibody (PRA) – 93%
    • Had Class I antibodies against HLA antigens (expressed on platelets) to 9 out of 10 platelet donors
  – MAP Referral to Blood Bank for HLA Selected Donors
  – Better increments with HLA Selected Donors

Prevention/Treatment of Bleeding in the Refractory Patient

• Scheduled platelet transfusions

• Anti-fibrolytic agent
  – Aminocaproic acid (Amicar)®
  – Tranexamic acid

• Red Blood Cell transfusions

Concentric Layers of Flowing Blood

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