Confusion with Transfusions

Gregory W. Hendey, MD, FACEP
Professor of Clinical Emergency Medicine
UCSF Fresno

Objectives
- To discuss transfusion indications
- High Risk transfusion reactions
- To discuss fancy new products such as recombinant Factor VII
- To discuss new approaches to Massive Transfusion

The players
- PRBC
- Platelets
- FFP
- Cryoprecipitate
- Factor VIII and IX
- Prothrombin Complex Concentrates
- Factor VII

Components
1 Donor Unit of Whole Blood
500 cc

1 Unit of PRBC’s
225 cc
1 Unit of FFP
250 cc
1 Unit of Platelets
25 cc

Or
1 Unit of Cryoprecipitate
25 cc

Testing
- Anti-HIV-1 and 2, anti-HTLV-I and II,
- HBsAg, HBcAb, anti-HCV
- Nucleic acid amplification tests (NAT) for HIV, HCV
- Syphilis
- West Nile Virus

Storage
- RBC’s:
  - Stored at 4°C
  - Maintain function 35-42 days
- Clotting factors:
  - Lose 50% activity within 1 week
  - 1 year frozen (FFP)
- Platelets:
  - 3-5 days at room temp
**When do I transfuse PRBC’s?**

- Hematocrit < ??
  - One PRBC should increase Hct by 3
- Hemodynamics
- Host Factors
  - Symptoms
  - Age, co-morbidities
- Estimate of Ongoing Blood Loss

**Screen or Cross?**

- Type and Screen
  - “possibly”
  - Type/Rh, test plasma for unusual Ab
- Type and Crossmatch (for “x” units)
  - “probably”
  - T&S, match blood against actual units

**O-negative or O-positive?**

- When you just can’t wait
- O-neg to women of childbearing age
  - Alloimmunization
    - Hemolytic disease of newborn
- O-positive to men, older women
  - Tiny chance of hemolysis if Rh negative
  - Use if O-neg limited

**High Risk to give O+ blood?**

- Dutton, *J Trauma*, 2005:
  - Maryland Shock Trauma, one year
  - O- to young women, O+ all others
  - 581 units type O to 161 patients
  - No transfusion reactions
  - One Rh- male developed Ab

**Transfusion reactions**

- Immediate
  - Rare, life-threatening
  - Common, mild
- Delayed (infectious)
- Other considerations
Immediate, rare, life-threats:
- Acute hemolysis
  - ABO error
  - 1 in 250K
- Anaphylaxis
  - Congenital IgA deficiency
  - 1 in 150K
- Bacterial contamination
  - Platelets
  - 1 in 2.5 million

Common, minor reactions
- Simple febrile
  - Antibody vs donor Leukocyte antigens
  - 1%
- Simple allergic
  - Antibody vs donor plasma proteins
  - 0.1%

Delayed infectious risk:
- HIV
  - 1 in 900K
- Hepatitis B
  - 1 in 137K
- Hepatitis C
  - 1 in 1 million

Other considerations:
- Volume Overload
- Graft vs Host disease
- TRALI

Transfusion-related acute lung injury (TRALI)
- 1 in 5K, especially FFP
- 50% transfusion related deaths
- Immune-related, donor antibodies vs patient WBC’s → cytokines
- Non-cardiogenic pulmonary edema
- Female donors (pregnancy)
- Male-only plasma donors

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Blood substitutes

- Perflourocarbons
  - Oxygen carrying solutions—no good
- Hgb-based O2 Carriers (HBOC)
  - Single, linked, polymerized molecules
  - Human, Bovine, Recombinant
  - Free, or Liposome encapsulated

Problems:

- Renal failure
- Coagulopathy
- Hypertension
- Short half-life
- Expensive

Future trend:

- Enzymatic removal of A/B antigens
- Blood type won’t matter

Platelets

- Random donor Plt unit = 25-50cc
- Room temp, 5 days
- Increase Plt count by 5-8K
- Typical dose: 6-10 units

Apheresis platelet unit

- Collected from one donor
- Equal to about 6 random donor units
- Increases Plt count by 30-50K
- Exposure to only one donor
  - Anti-platelet antibodies

Indications for Platelets

- Plts < 50K, with active bleeding
- Massive transfusion
- Plts < 10K
  - If due to underproduction
FFP

- Approximately 250 cc
- Frozen, shelf life = 1 year
- Dose = 10 cc/kg (2-3 units)
- Apheresis (Jumbo FFP)
  - 500 or 750 cc, single donor
  - Thawing time

Is Type and Cross necessary to transfuse FFP and Platelets?

- Yes and no
- Need Type for FFP
  - Plasma carries anti-A/B antibodies
  - Could hemolyze patient RBC’s
- AB is universal donor
- Plts: prefer type-specific, if known
  - <0.5 cc RBC in Platelet unit

Indications for FFP

- INR > 1.5
  - With active bleeding, or
  - Prior to invasive procedure
- Massive transfusion

Cryoprecipitate

- One unit from one donor (25 cc)
- Rich in Fibrinogen, VIII, vWF
- Little indication in ED
  - Fibrinogen depletion (DIC)

Factor 8, 9 concentrates

- Hemophilia A (VIII), B (IX)
- Heat treated, purified concentrate
- Recombinant
**Concerns:**
- Clotting can occur at any abnormal endothelium
  - Stroke, MI, arterial thrombus
- Expense ($10,000)

**Dosage:**
- Moderate bleed: 50% activity
- Severe: 100%, admit, repeat
- Plasma = 50 cc/kg
- 70 kg x 50 cc/kg = 3500 u (100%)
- F8C: 1 U/kg raises activity by 2%
  - 25 U/kg = 50% = 1750 U
- F9C: 1 U/kg raises activity by 1%

**Example:**
- 20 yo Hemo A: shoulder pain
- Dx: Hemarthrosis
- No tests
- 70 kg x 50 cc/kg = 3500 u (100%)
- 50% = 1750 units FVIII conc.
- Sling, analgesics, close follow up

**Prothrombin complex concentrate (PCC)**
- Factors II, VII, IX, X
- Hemophiliacs with inhibitors
- Super-therapeutic coumadin with life-threatening bleeding
- Thromboembolic complications

**Recombinant Factor 7-activated**
- Binds tissue factor → coagulation
- Clotting via extrinsic pathway

**Concerns:**
- Clotting can occur at any abnormal endothelium
  - Stroke, MI, arterial thrombus
- Expense ($10,000)

**Indications?**
- FDA-approved:
  - Hemophilia A/B with inhibitors
- Off-label:
  - Post cardiac surgery coagulopathy
  - Coumadin tox with severe bleeding
  - Intracranial bleeding
  - Trauma / Massive transfusion
**ICB: Mayer, NEJM, 2005:**
- Phase 2 study, 399 pts with ICH
- Randomized to rF7 or placebo
- Primary outcome measure: % increase in ICH size at 24 hrs.
  - 14% vs 29%
  - Lower 90d mortality: 18% vs 29%
- But more major thromboembolic events: 7% vs 2%

**ICB: Mayer, NEJM, 2008:**
- Phase 3, randomized, 841 pts
- % increase in ICH:
  - 26% placebo; 18% and 11% rF7 groups
- 90d mortality:
  - 19% placebo; 18% and 21% for rF7
- Combined, death or severe disability:
  - 24% placebo; 26% and 29% rF7

**Trauma: Boffard, J Trauma, 2005:**
- PRDBPCT
- 277 pts, 32 hosp, 6 PRBC w/in 4 hrs
- rFVIIa or placebo
- Blunt trauma pts: 2.6 U less blood
- No diff in mortality

**Trauma: Spinella, J Trauma, 2008:**
- Retro, rFVIIa use in Iraq
- 129 pts with Massive transfusion
- 49 received FVII:
  - Given more PRBC, FFP, Cryo
  - Higher baseline BP (105 vs 92)
- Lower mortality (14% vs 35%)
- Baseline diff? Drug benefit?

**Trauma: Narayan, Neurosurg 2008:**
- PRDBPCT, Traumatic ICH
- 97 patients, 38 hospitals
- Placebo (36) vs 5 diff doses FVII (61)
- No diff in mortality (11% vs 11%)
- Trends toward less hematoma expansion but more DVTs

**Massive transfusion**
- Definition:
  - Entire blood volume in 24 hrs
    - (75 cc/kg, 5L, 10 units PRBC)
    - 5 units in 3 hrs + ongoing hemorrhage
- Problems:
  - Coagulopathy, DIC
  - Hypothermia
  - Acidosis
  - Hypocalcemia (citrate toxicity)
Coagulopathy:

- Multi-factorial
  - Dilution
  - Hypothermia, acidosis
- 2 approaches:
  - 1) treat problems as they arise
  - 2) treat prophylactically (Protocol)
    - 5 PRBC / 5 U FFP / 1 apheresis Plts
    - Approximates Whole blood

Borgman, J Trauma, 2007:

- Retro, 246 pts, > 10 U PRBC
- Higher FFP:PRBC, higher survival
- Low ratio (1:8) Survival 35%
- High ratio (1:1.4) Survival 81%
- Supports 1:1 massive transfusion

Ho, Can J Surg, 2005:

- Mathematical model
  - Ongoing loss, various ratios of transfusion
- Assumptions:
  - 30% blood loss, IVF, 2 U PRBC
  - Clotting factors already 50%
- PRBC:FFP 3:1, 2:1, 1:1
- Only way to maintain or “catch up” is 1:1 or higher (more FFP)

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Holcomb, Ann Surg, 2008:

- Retro, 466 massive transfusion pts
- High FFP:PRBC ratio (>1:2) vs low
- 30 day survival: 60% vs 40%
- Same effect with Plt:PRBC ratio
- Recommended 1:1:1

Massive Transfusion Pack

- 5 U PRBC (O-negative)
- 5 U FFP (AB, pre-thawed)
- 1 U Apheresis Platelets

Summary

- Transfusion indications
- Transfusion reactions
- New products such as Factor VII
- Massive Transfusion