

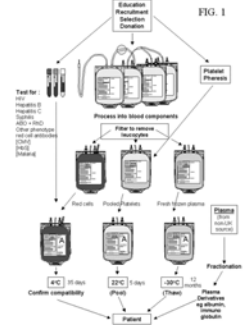
Blood Component Therapy

Jeffrey Jhang, MD
*Assistant Professor of Clinical Pathology
 College of Physicians and Surgeons
 New York, NY*

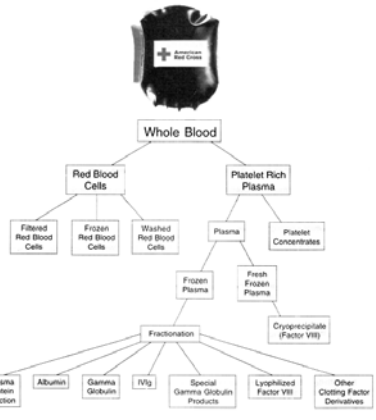
Learning Objectives

1. Know how components are prepared by whole blood separation and apheresis.
2. Most common storage methods for packed red blood cells, plasma, cryoprecipitate and platelets
3. Indications for platelet, plasma, granulocyte and cryoprecipitate transfusion
4. Indications for activated VIIa and adverse effects of recombinant VIIa

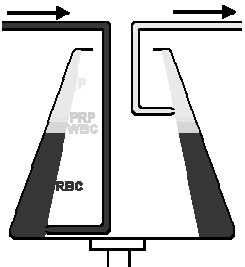
Blood Component Therapy



- Transfusion of specific parts of blood, rather than whole blood
- One donated unit can help multiple patients
 - Conserves resources
 - Optimal method for transfusing large amounts of a specific component
- Sterile, disposable, integrally associated bag, needle and satellite bags



Apheresis Technology



- Single Donor
- Multiple units per collection (Red/Plt, Red/plasma, Double Platelet, Double Red, etc)
- Platelets leukoreduced
- Used to collect granulocytes
- But anticoagulation, HES, time

Red Cells



- Homologous
- Autologous
- Directed
- Whole Blood
- Packed Red Cells
- Leukoreduced
- Irradiated
- CMV negative
- Antigen Negative
- Sickle negative
- Frozen thawed
- Washed

Packed Red Blood Cells

- Made by spinning whole blood and expressing off the supernatant
- Hct 60% (AS-1) and 80% (CPDA-1)
- 300-350 ml
- Stored at 1-6 degC
- Shelf-life:
 - 21 days (CPD)
 - 35 days (CPDA-1)
 - 42 days AS-1

Packed Red Blood Cells

- Must be ABO compatible
- Rh neg should receive Rh neg.
- One unit \uparrow Hgb by 1 g/dl or \uparrow Hct 3% (in absence of bleeding or hemolysis);
- Peds: 8-10cc/kg should \uparrow Hgb by 2 g/dl
- Restore or maintains oxygen carrying capacity to meet tissue demands
 - E.g. anemia in normovolemic patient
- Transfusion indications and triggers later in this talk

Leukoreduced



- Non-LR RBC contain $1-3 \times 10^9$ WBC
- LR contain $< 5 \times 10^6$ WBC and retains 85% of the original cells
- All Columbia PRBC units are leukoreduced
- Reduces febrile reactions
- Reduces HLA immunization (e.g. transplant)
- Effective in reducing CMV transmission (CMV-safe)
- Cellular immune function preservation
- Does NOT prevent GVHD!!!
- Prestorage vs. Bedside Filtration

CMV negative

- All neonates (up to 4 months old)
- Intrauterine Transfusions
- High risk lung transplant (-ve to -ve)
- Allogeneic stem cell transplants (-ve to -ve)
- DiGeorge Syndrome

- LR 4% vs CMV neg 1.7%

Irradiated

- Prevents Transfusion Associated Graft vs. Host Disease
- Irradiation for:
 - Units from blood relatives
 - Allo/Auto HPC Transplant Recipients
 - Intrauterine transfusion
 - Neonates undergoing exchange transfusion or ECMO
 - Hodgkin's Disease
 - Cellular immune deficiency
 - Solid Organ Transplants

Antigen-negative

- More transfusions, the higher the likelihood of alloimmunization
- Gets more difficult to find compatible units for patients with antibodies against high frequency antigens (e.g. anti-e) or multiple antibodies
- Calculate the availability based on the incidence of the antigen in the general population
 - anti-E, 70% of donors are E negative; 7/10 units will be compatible
 - anti-e where $<1\%$ of donors are compatible (need to screen 100 units to find one that is compatible)
- If multiple antibodies, multiply the frequencies
 - E.g. anti-K and anti-E; $.7 \times .9 = 63\%$ units antigen neg

Guidelines for Red Cell Transfusion

RBC Transfusion Trigger Why NOT to give PRBC

- Volume expansion
- Wound healing
- Religious objection
- Based solely on a number

Acute Blood Loss

- Loss of TBV
 - 15-30%
 - give crystalloids, colloids in young, healthy patients
 - 30-40%
 - Rapid volume replacement
 - RBC transfusion likely needed
 - >40%
 - Life-threatening bleeding
 - Requires rapid volume replacement
 - Requires RBC transfusion

Acute Blood Loss

- Hgb and Hct
 - Hgb >10, rarely needed
 - Hgb <6, usually needed
 - Hb 6-10 and Co-morbid Conditions
 - indications for transfusion should be based on the patient's risk of inadequate oxygenation from ongoing bleeding and/or high-risk factors.
 - CHF, CAD, pulmonary disease, cerebrovascular insufficiency, chemotherapy, sickle cell disease, thal major, tachycardia, weakness, h/a, dizziness, SOB

- Don't transfuse based on "transfusion trigger"

**American Society of Anesthesiologists Task Force
On Blood Component Therapy 1996*

Chronic Anemia

- Compensatory mechanisms such as increasing 2,3-DPG may allow greater tolerance for anemia
- Treat the underlying cause (e.g. iron, folate, B12)
- Try EPO trial if the patient can be observed rather than treated immediately
- Acute blood loss or perioperative therapy apply
- In general:
 - Hgb >10, rarely needed
 - Hgb <6, usually needed
 - Hb 6-10 and Co-morbid Conditions

Preoperative Usage

- Each case should be evaluated individually
- Avoid transfusion by treating pre-existing anemia, stopping antiplatelet drugs and anticoagulants; consider EPO
- Asymptomatic Anemia with Hgb <7 g/dL and scheduled surgery expected to produce significant blood loss
- In actively bleeding patient with a change in vital signs

Special Circumstances

- Severe thalassemia or congenital anemia
 - Suppress endogenous erythropoiesis by maintaining Hgb >9-11 g/dL
- Sickle Cell Disease
 - Simple Transfusion or RBC Exchange
 - Transfusion may be indicated to reduce Hgb S to <30%

MSBOS

- Shelf life decreases when blood is held or crossmatched
- Common elective procedures
 - Recommends T/S order to a maximum number of units that can be ordered initially

Intraoperative Usage

- 20% blood volume loss can do well without transfusion
- Change in vitals signs not due to anesthesia (may not be reliable)
- Decreased Urine Output
- Estimated blood loss > 1000 ml
- Laboratory Values (Hgb/Hct may not be reliable)

Uncrossmatched Blood

- Used in exsanguination
- Prefer type specific (takes 5 min)
- If no time for typing:
 - O+ for males
 - O+ for females beyond childbearing years
 - O neg for females of childbearing years
- Crossmatching is done retrospectively

Plasma



- Fresh Frozen Plasma
- Thawed Plasma
- Plasma Frozen within 24 hours
- Donor Retested Plasma
- Solvent Detergent Plasma
- Repletion of all known clotting factors
- Also contains antithrombin, plasma proteins
- 200-300 ml per unit

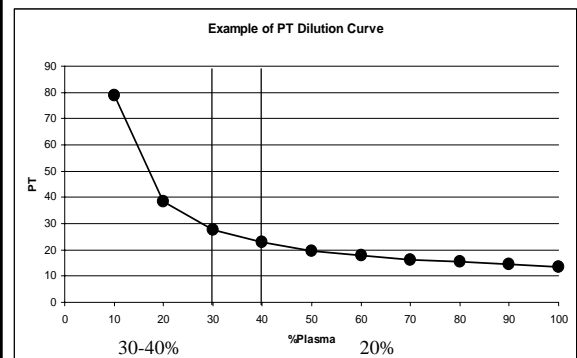
Plasma

- Short half-life of coagulation factors (some <4 hours); therefore, frozen as FFP within 8 hours
- Plasma frozen within 24 hours; loss of labile factor activity; may be a good source of AB plasma during shortage or high volume use (e.g. TTP)
- Takes approx 1 hour to thaw 6 units
- Good for 24 hours post thaw as FFP
- then it can be stored for 5 days as liquid plasma (labile factors V and VIII decreased)
- 4-6 units or 10-20 cc/kg is the appropriate dose (large volume load!)

Plasma

Recipient	Preferred	Alternate
O	O	A,B,AB
A	A	AB
B	B	AB
AB	AB	Can convert to A if absolutely necessary

PT Dilution Curve



Plasma Not indicated

- Volume expansion
- Nutritional Supplement
- Prophylactically following cardiopulmonary bypass
- To promote wound healing

Indications

- Congenital Factor Deficiency
 - Invasive Procedure or Trauma (e.g. factor XI Deficiency)
- Emergency Warfarin Reversal
 - Vit K!!
- Microvascular bleeding and elevated PT/PTT
- Loss of more than one blood volume and no lab values then give empirically

Audit Criteria

- Bleeding and/or surgery and PT >20 sec
- PT >45 sec
- PTT > 55 sec with factor deficiency, bleeding, or surgery
- Massive bleeding with no labs available
- Vitamin K is the primary therapy for Warfarin overdose

Massive Transfusion

- Usually a surgical bleed
- Try to tailor the component therapy to studies (esp. PT)
- Remember that 30% coagulation factors is surgically hemostatic
- FFP for PT >21 sec
- Platelets for Plt <50,000
- Cryo for fibrinogen <100

Drawbacks

- Donor exposures
- Volume Overload
- Allergic Reactions
- Transfusion Related Acute Lung Injury (TRALI)

Platelets



- Random vs Apheresis
- HLA-matched
- Crossmatch-compatible
- kept at room temperature with agitation (increasing risk of bacterial contamination)
- 5 day outdate; actually now 7 days because they are now cultured
- Always in short supply
- Apheresis SDP is 200-400 ml (6-8 units)

Platelets

- Columbia uses only single donor platelets
- Leukoreduced because of apheresis collection
- ABO matched platelets preferable
- Rh negative receive Rh negative platelets
- Platelet alloimmunization (XM, HLA matched)
- Bacterial contamination a problem (RT storage)
- One RDP increases platelet count by 5000
 - SDP = 6-8 units random donor platelets should raise 30-40,000

- The need for platelet transfusion is not based on a single number:
 - Type and extent of surgery
 - Ability to control bleeding
 - Consequences of uncontrolled bleeding
 - Actual and expected rate of bleeding
 - Presence of factors that interfere with platelet function

Audit Criteria

- Prophylaxis
 - Platelets <15,000 (no ITP, TTP)
 - Platelets <25,000 and neonate
- Bleeding or invasive procedure
 - Platelets <50,000
 - If neurosurgery or ECMO <100,000
- Neonates at risk of ICH
 - Platelets <50,000
- Massive bleed with no labs available
- Microvascular bleeding post CPB
 - Platelets <50,000
- Thrombocytopenia
 - Medications e.g. ASA

Platelet Refractoriness

• Incidence of alloimmunization varies in reports from 20-70% for multi-transfused thrombocytopenic pts

• Patient fails to make a suitable increment (CCI)

$$-CCI = [PI * BSA * 10^{11}] / n$$

-CCI = corrected count increment

-BSA = body surface area

-n = number of platelets transfused

CCI

- Calculate the CCI
- $n = 4 \times 10^{11}$ platelets
- BSA = 1.8 m²
- Plt start: 8,000
- 1-hour post count: 33,000

$$CCI = \frac{25,000 \times 1.8 \times 10^{11}}{4 \times 10^{11}}$$

$$CCI = 11,250$$

*CCI < 7500 considered failure

AABB Technical Manual 14th edition

Non-immune Refractoriness

- Massive Bleeding
- Fever
- Sepsis
- Splenomegaly
- DIC
- Allotransplant
- Poor storage of plt product
- Effects of Drugs
- IV Amphotericin B
- TTP

Immune

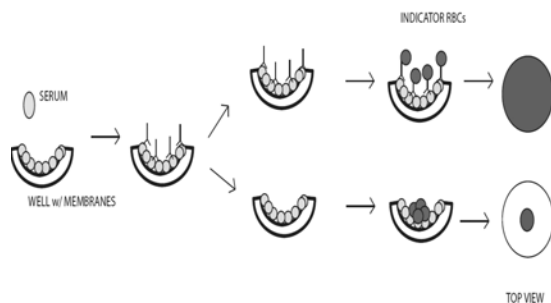
- Antibodies to HLA or platelet specific antigens
- Alloimmunization can follow transfusion, pregnancy, organ transplantation
- Reduced alloimmunization with leukoreduced products

—#leukocytes more important than #donor exposures (TRAP study NEJM 1997)

Crossmatch or HLA-matched Platelets

- Determine refractoriness with 15 minute or 1-hour post counts;
- Send off anti-platelet and HLA antibody screen; HLA type patient; inquire about family member
- r/o possible non-immune causes of thrombocytopenia
- If screen(+), then go for HLA-A,B match or crossmatched platelets (remember platelets don't express class II); monitor increments
- Remember that absolute platelet count may not be the endpoint

Anti-platelet Antibody Screen



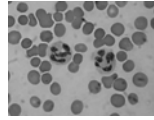
Cryoprecipitate Antihemophilic factor (AHF)



- Fraction of plasma that does not dissolve on thawing plasma at 4 degC
- Rich in fibrinogen, factor VIII, vWF, fibronectin
- 15ml/unit; adult dose is 10 units or 1U/10kg; **NOT concentrated plasma!**
- Treats low fibrinogen (\uparrow 50-100g/dl)
- Can be used to treat uremic thrombocytopenia
- No longer used to replace factor VIII or vWf

Audit Criteria

- Fibrinogen <40
- Fibrinogen <100 with bleeding or surgery
- DIC in obstetric patient
- Abnormal fibrinogen
- Fibrin glue
- Factor XIII deficiency
- vWD with bleeding or surgery



Granulocytes

- Prepared from a single donor using apheresis technology with HES as a sedimentation agent
- Should contain at least $> 1.0 \times 10^{10}$ granulocytes
- Stimulated can yield $4-8 \times 10^{10}$ granulocytes
- However, collection for us is done without stimulation (G-CSF or steroids) and rarely makes this goal
- They are stored at 24 deg C
- They must be infused within 24 hours of collection

Granulocytes

- Criteria:
 - ANC <500
 - Fever
 - Documented infection (bacterial or fungal) for 24-48 hours
 - Unresponsive to appropriate antibiotics
 - Reasonable hope of marrow recovery

Granulocytes

- Must be ordered through NYBC and depends on donor availability
- Check T&S: Must be type and Rh specific, ab screen neg
- IRRADIATE to prevent GVHD
- Transfuse within an hour of receipt in blood bank (you may have to orchestrate); infuse within 24 hrs of collection
- Transfuse through a standard blood filter (NOT A LEUKOREDUCTION FILTER; blood bank should provide)
- Hold antifungals before and after transfusion → pulmonary reaction can result otherwise
- Premedicate with Benadryl, Tylenol and Solumedrol
- Manage Reactions as they occur

Drawbacks

- Rarely yields adequate dose without stimulation; better for smaller weight peds, but they may not be able to tolerate the volume
- Must be ABO/Rh compatible; red cell alloantibodies will likely make these unavailable
- Donor testing is not available prior to infusion
 - Requires emergent medical need release
 - Pedigreed platelet apheresis donors are recruited
- these highly valued, repeat plateletpheresis donors are then deferred to 56 days because of red cell loss
- No HLA testing
- Transfusion Reactions: fever, chills, allergy, and pulmonary reactions occur frequently

Plasma Derivatives

Factor VIII Concentrate

Factor IX Concentrate

AT Concentrate

Humate-P

FEIBA (Factor VIII Inhibitor
Bypassing Activity)

Albumin

IVIG

RhIg



Humate-P

- Antihemophilic Factor/vWf used to treat hemophilia A or von Willebrand Disease
- Plasma derived, freeze dried, then reconstituted for IV infusion
- risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease agent, cannot be completely eliminated.
- Possible adverse events include allergic reaction, urticaria, chest tightness, rash, pruritus, and edema. Anaphylactic reactions can occur in rare instances.
- Thromboembolic events have been reported in VWD patients receiving coagulation factor replacement therapy,

RhIg



- Pooled human plasma-derived anti-D IgG
- IM or IV preparations
- Available in 50µg and 300µg doses
- Used for protection of D-negative females after abortion, miscarriage, termination of ectopic pregnancy, amniocentesis, antepartum
- Post-partum, screen for FMH, quantify FMH and calculate dose
 - One full dose can protect against a FMH of 15 ml fetal red blood cells

Recombinant Products

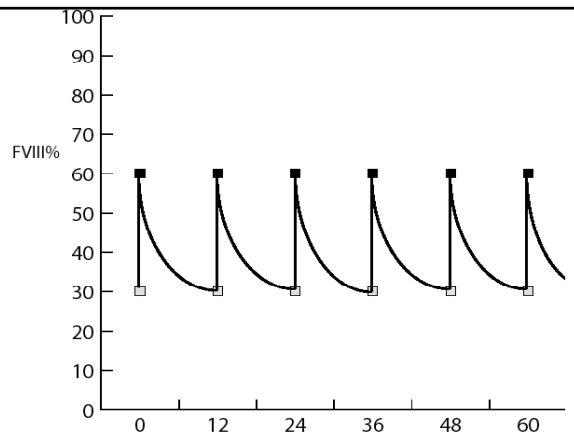
Recombinant Factor VIII

e.g. Recombinate

Recombinant Factor IX

e.g. BeneFIX

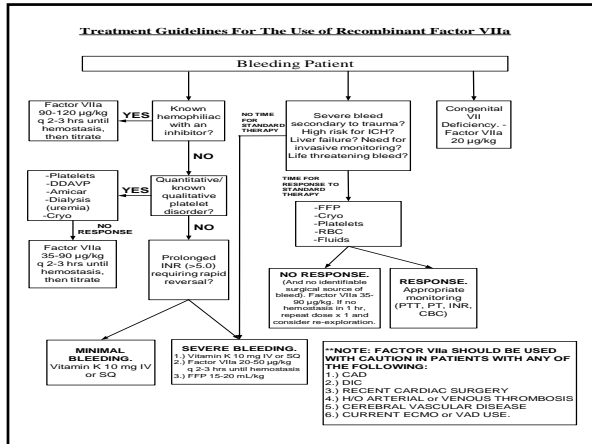
Recombinant Factor VII (Novoseven)



Recombinant Factor VII

- **Approved only for the treatment of Hemophiliacs with bleeding and known factor VIII inhibitor or congenital factor VII deficiency**
- Requests for off label indications are increasing and the BB must review each indication
 - Recent examples/some make sense, some don't: Intracranial hemorrhage, massive surgical bleeding, coumadin overdose, liver disease with volume overload, ...etc
- Appropriate dose? Frequency? Monitor?
 - 40 µg/kg, 60 µg/kg, 90 µg/kg?
 - Must be dosed every two hours with cessation of bleeding as the end point?
 - No reliable means of monitoring the efficacy; can not follow the PT/aPTT





Caution

- Risk of MI, myocardial ischemia
- Risk of CVA, CNS ischemia
- Disseminated Intravascular Coagulation
- Anaphylaxis
- Thrombophlebitis
- Arterial Thrombosis
- Deep Vein Thrombosis and Pulmonary Embolism