The ABC’s of Blood Components

Terry Downs, MT(ASCP)SBB
Administrative Manager
University of Michigan Hospitals
Blood Bank and Transfusion Service
Objectives

- Describe three additives used in blood components.
- List the indications for five blood components.
- Review whole blood donations versus apheresis collections.
Whole Blood Donation

- Collection of one 450-500 mL of whole blood into a bag
- Bag then processed into components
- Additive solutions may be added
- Takes about 10 minutes to collect 500 mL
Apheresis Collection of Blood

- Whole blood is separated into components during collection
- Desired component if removed
- Remaining components are returned to donor
- Centrifugal technique primarily used in US
- Allows for “double-red” or multiple plasma
- Apheresis platelets
- Granulocytes
Collection and Storage Systems

- Different configurations based on intended processing method
  - Manual processing
  - Automated processing
  - Platelet processing method

- Approved anticoagulants
  - ACD-A
  - ACD-B
  - CPD
  - CP2D
  - CPDA-I
## Contents of Anticoagulant-Preservative Solutions

<table>
<thead>
<tr>
<th></th>
<th>ACD-A</th>
<th>CPD</th>
<th>CP2D</th>
<th>CPDA-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisodium Citrate</td>
<td>22.0 g/L</td>
<td>26.3 g/L</td>
<td>26.3 g/L</td>
<td>26.3 g/L</td>
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<tr>
<td>Citric Acid</td>
<td>8.0 g/L</td>
<td>3.27 g/L</td>
<td>3.27 g/L</td>
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<tr>
<td>Monobasic Sodium Phosphate</td>
<td>0</td>
<td>2.22 g/L</td>
<td>2.22 g/L</td>
<td>2.22 g/L</td>
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<tr>
<td>Dextrose</td>
<td>24.5 g/L</td>
<td>25.5 g/L</td>
<td>51.1 g/L</td>
<td>31.9 g/L</td>
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<tr>
<td>Adenine</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.275 g/L</td>
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<tr>
<td>Shelf Life (days)</td>
<td>21</td>
<td>21</td>
<td>21</td>
<td>35</td>
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</tbody>
</table>

ACD-A: Anticoagulant citrate-dextrose A  
CPD: Citrate-phosphate-dextrose  
CP2D: Citrate-phosphate-dextrose-dextrose  
CPDA-1: Citrate-phosphate-dextrose-adenine
Additive Solutions

- Extend the shelf life to 42 days.
- Approved additive solutions in US
  - AS-1
  - AS-3
  - AS-5
Content of Additive solutions (in mg/100 mL)

<table>
<thead>
<tr>
<th></th>
<th>AS-1 (Adsol)</th>
<th>AS-3 (Nutricel)</th>
<th>AS-5 (Optisol)</th>
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<tr>
<td>Dextrose</td>
<td>2200</td>
<td>1100</td>
<td>900</td>
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<tr>
<td>Adenine</td>
<td>27</td>
<td>30</td>
<td>30</td>
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<tr>
<td>Monobasic Sodium Phosphate</td>
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<td>0</td>
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<td>Mannitol</td>
<td>750</td>
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<td>525</td>
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<td>Sodium Chloride</td>
<td>900</td>
<td>410</td>
<td>877</td>
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<tr>
<td>Sodium Citrate</td>
<td>0</td>
<td>588</td>
<td>0</td>
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<tr>
<td>Citric Acid</td>
<td>0</td>
<td>42</td>
<td>0</td>
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<tr>
<td>Shelf Live (days)</td>
<td>42</td>
<td>42</td>
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</tbody>
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Circular of Information, 2009
History of Storage Solutions

- In the beginning...
  - No storage solutions at all
  - Donor and recipient remained together

- Rous & Turner developed 1st RBC storage solution for rabbit RBCs
  - Heterophile agglutination test for syphilis
  - Mixture of citrate and glucose
  - Raised hematocrit when injected back into rabbits

- Robertson used this info to create the first blood bank in France during World War I
  - First time separating donor and recipient (Mollison)
Figure 2.—Clinical transfusion with Blundell gravitator for transmitting “blood in a regulated stream from one individual to another” (3).
Collected blood in citrate only (to prevent contamination and overgrowth)
- Mixtures of sodium citrate and dextrose caramelized when the solutions were heated (collection bottles)
- Healthy donor provides enough glucose to support storage for 5 days
- Thus, the use of sodium citrate and 5-days storage on ice
Figure 3.—Blood transfusion apparatus used in World War I.

A. a. Transfusion needle.
b. Rubber tube.
c. Glass tube.
d. Rubber stopper.
e. 1-liter bottle.
f. Glass tube.
g. Rubber tube.
h. Glass tube for suction, with cotton in bulb.

B. i. Transfusion needle.
j. Rubber tube.
k. Glass tube.
l. Rubber tube.
m. Glass tube.
n. Rubber stopper.
o. Glass tube.
p. Rubber tube.
q. Glass tube for exerting compression (cotton in bulb) (27).
World War II

- US revived the study of citrate and glucose solutions
- Loutit & Mollison showed citrate and glucose solutions could be autoclaved if pH was <5.8
- ACD solution manufactured in sterile vacuum bottles
- Stored for 21 days
Phosphate

- Leaks slowly during storage
- Adding sodium phosphate to ACD reduced phosphate loss (reduced the gradient in concentration between inside and outside of stored RBC)
- CPD solutions increased the fraction of RBC recovered after 3 weeks of storage
Plastic bags

- Developed in the 1950s
- Lighter weight and resistance to breakage
  - Sterilized closed collection system
  - Exclude air bubbles (embolism)
- Manufacture connected sets of bags
- Introductions of DEHP
Adenine

- Loss of RBC viability corresponds to loss of ATP
- Added adenine and inosine to restore cell shape, ATP concentration and viability
- CPDA-1 solution allowed for 35 day storage
  - 75% hematocrit
  - Ran out of glucose in tightly packed unit
- Started the move to component processing instead of whole blood
Additive Solutions

- Developed to provide additional volume and nutrients for longer storage and better flow
- Designed for component processing
- Solution added to the red cell bag only
- First additive solution SAG (saline-adenine-glucose)
  - 55% hematocrit
  - Added glucose prevent glucose loss
  - Added adenine reduced ATP loss
- Mannitol found to reduce hemolysis
Hemolysis

- Addition of mannitol reduced hemolysis by 50%
  - Works as a free radical scavenger and membrane stabilizer
- Citrate has same membrane-protective function
  - Also balances the osmotic pressure of small ion-permeable RBCs
- SAGM (Europe)
- AS-1 and AS-5 (USA) No citrate, mannitol
- AS-3 (Canada and USA) Citrate, no mannitol
Storage Lesion

- RBCs lose potassium, DPG, ATP and lipids
  - Membrane rigidity
  - Oxygen off-loading
  - Acidotic
  - Suspending fluid free hemoglobin
  - Negatively charged microvesicles with pro-inflammatory activity
  - Decreasing pH
Infant Transfusions

- Traditionally, neonates transfused with CPD, CP2D or CPDA-1 only (no additive)
- Avoid additional solutes
  - Concern for increased risk for hepatic or renal toxicity
  - Concern for large doses of dextrose in a short period of time
- Newer studies suggest blood components in additive solutions are safe and efficacious
- Clinicians need to be aware of hematocrit differences
Leukoreduction

- WBCs break down in the cold
  - Release proteases and lipases that damage RBCs
- Improve RBC recovery and reduce hemolysis
- Widely used in USA
- One unit of whole blood contains $\geq 1 \times 10^9$ white cells
- Decrease the frequency of recurrent febrile nonhemolytic transfusion reactions
- Reduce the risk of transfusion transmitted CMV
- Reduce incidence of HLA alloimmunization
Leukoreduction

- Achieved by in-process collection or filtration
  - Soon after collection (prestorage)
  - At the bedside with filter
- Subject to QC testing for prestorage
- Red cells and apheresis platelets:
  - Residual count of $<5.0 \times 10^6$
- Random platelets:
  - Residual count of $<8.3 \times 10^5$
- Washing is NOT a substitute for leukoreduction
Irradiation

- Prevent TA-GVHD
- Blood component (red cells and platelets only) exposed to a radiation dose
- Used for patients at risk for TA-GVHD
  - Fetal and neonatal recipients of intrauterine transfusions
  - Cellular components from a blood relative
  - BMT patients
  - Recipients of cellular components selected for HLA compatibility
Side Effects to Transfusion – Acute

- Hemolytic transfusion reaction
- Immune-mediated platelet destruction
  - Platelet refractoriness
- Febrile nonhemolytic reaction
  - Temp elevation
- Allergic reactions
  - Hives, wheezing
- Anaphylactoid/anaphylactic reactions
  - Hypotension, tachycardia, nausea
  - IgA deficient patients
- TRALI
  - Hypoxemia within 6 hours of transfusion
Side Effects to Transfusion – Delayed

- **Delayed hemolytic reaction**
  - Immunologic destruction of transfused red cells
  - Result of incompatibility of antigen on transfused cells with antibody in recipient circulation

- **Alloimmunization**
  - New onset of antibody causes destruction of circulating cells

- **Postransfusion purpura (PTP)**
  - Dramatic, sudden thrombocytopenia 7-10 days post txn

- **Transfusion associated graft vs host disease (TA-GVHD)**
  - Viable T-lymphocytes in transfused component engraft in the recipient and react against recipient tissue antigens
Side Effects to Transfusion – Nonimmunologic Complications

- Transmission of infectious agents
  - Viruses, parasites, vCJD, CMV

- Bacterial sepsis
  - Multiply at low temps
  - Use citrate as a nutrient

- TACO
  - Pulmonary edema from excessive volume or rapid rates

- Hypothermia
  - Massive transfusion of large volumes of cold products

- Metabolic complications
  - Citrate toxicity
  - Acidosis or alkalosis
Red Blood Cell Components Overview

- One unit contains 50-80 g of hemoglobin
- Leukoreduced
- Whole blood donation
  - Prepared from blood collected into an anticoagulant preservative solution, separated from the plasma
  - Additive solution may/may not be added
- Apheresis collection
  - Collected by apheresis procedure in an anticoagulant
  - Double-red cells may be collected
  - Red cells volume is noted on bag
Indications

- Treatment of symptomatic or critical deficit of oxygen-carrying capacity
- Used for red cell exchange transfusions
  - Fetus and infants with maternal antibody
  - Sickle-cell anemia patients on stroke prevention program
Contraindications

- Not used for anemias treatable by iron, B12, folic acid or erythropoietin
- Not used for volume expansion or to increase oncotic pressure of circulating blood
Dosage and Compatibility

- One unit will increase hemoglobin concentration by about 1 g/dL
- Smaller aliquots for pediatric/infant doses
- Donor ABO compatible with recipient ABO antibodies
- Crossmatch test performed
  - Electronic
  - Immediate spin
  - Antiglobulin
Side Effects

- Hemolytic transfusion reaction
- Alloimmunization of recipient
- TACO
- Iron overload (each unit 250 mg of iron)
- Nonimmune hemolysis
Plasma Components Overview

- Aqueous part of blood derived from whole blood donation or apheresis collection of plasma
- Albumin
- Coagulation factors
- Fibrinolytic proteins
- Immunoglobulins
- Fresh frozen plasma
- Plasma frozen within 24 hours after phlebotomy
- Plasma cryoprecipitate reduces
- Liquid plasma (never frozen)
Indications

- Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors
- Massive transfusion patients with coag deficiencies
- Patients on warfarin in need of a procedure (cannot wait for Vitamin K reversal)
- Plasma exchange in patients with TTP
- Patients with select coag factor deficiencies and no concentrate available
- Patients with rare plasma protein deficiencies and not recombinant products are available
Contraindications

- Do not use when coagulopathy can be corrected with a specific therapy
  - Vitamin K
  - Cryoprecipitate
  - Specific coag factor concentrate
- Do not use for volume expander only
Dosage, Preparation and Compatibility

- Volume transfused depends on the clinical situation, patient size and may be guided by laboratory assays
- ABO compatible with the recipient’s red cells
- Thaw plasma in waterbath
  - 24 hour outdate for FFP
  - 5 day outdate for thawed plasma
  - 26 day outdate for liquid plasma
Cryoprecipitated Antihemophilic Factor

- Prepared by thawing whole-blood derived FFP between 1-6 C and recovering the precipitate
- The cold-insoluble precipitate is refrozen
- Contains fibrinogen, Factor VIII, Factor XIII, vWF and fibronectin
  - ≥ 80 IU Factor VIII
  - ≥ 150 mg of fibrinogen
Cryo Indications

- **Uses**
  - Control bleeding associated with fibrinogen deficiency
  - Treat Factor XIII deficiency
  - 2\textsuperscript{nd} line therapy for vWF and Factor VIII therapy
Cryo Contraindications

- Contraindications
  - Do not use if other virus-inactivated concentrates or recombinant factors are available
Dosage, Preparation and Compatibility

- Formula to raise plasma fibrinogen by 50-100 mg/dL:
  - Number of bags = 0.2 x body weight in kg

- Thaw in 30-37 C waterbath
  - May be pooled or pre-pooled
  - 4 hour outdate for pool
  - 6 hours outdate for single unit

- Compatible test not required
  - ABO compatible desired
  - Rh is not considered
Platelets Overview

- Essential for normal hemostasis
- Therapeutic goal to provide adequate numbers of normally functioning platelets
- Platelets are suspended in an appropriate volume of the original plasma or additive solution
- Random platelets from whole blood donation
  - $5.5 \times 10^{10}$
- Apheresis platelets
  - $3.0 \times 10^{11}$
Platelet Indications

- Patients with
  - Thrombocytopenia
  - Dysfunctional platelet disorders
  - Active platelet related bleeding
  - Serious risk of bleeding (prophylactic use)
Platelet Contraindications

- When bleeding is unrelated to decreased numbers of or abnormally functioning platelets
- If platelet count is >1000,000/μL
- Avoid in patients with activation or autoimmune destruction of platelets (HIT, TTP or ITP) unless life-threatening hemorrhage
Dosage, Preparation and Compatibility

- One unit of platelets should increase platelet count by 5-10K/μL
- Adult dose is one 5-pack of pooled platelets or one apheresis platelet
- Pediatric doses smaller
- Pool if necessary or divide apheresis platelets for peds
- Compatibility test not necessary
- Donor plasma should be ABO compatible with recipient when transfusing to infants and large volumes to adults
- Rh neg recipients should receive Rh neg random platelets
- Apheresis platelets are red cell free and Rh matching is not necessary
Side Effects

- **Bacterial contamination**
  - Most likely component to be contaminated
  - High fever, severe chills, hypotension

- **Platelet alloimmunization**
  - HLA antibodies may develop after platelet txn
  - Become refractory to txn

- **Red blood cell alloimmunization**
  - From presence of residual red cells
  - Rh Pos platelets to Rh Neg patient, consider one dose of RhIG

- **Hemolysis**
  - Group O apheresis platelets to A, B or AB recipient
Granulocytes

- Collected by apheresis
- Contains $> 1.0 \times 10^{10}$
- Transfusion therapy is controversial
- Used for patients with documented infections unresponsive to antimicrobial therapy
- Must be ABO compatible with recipient antibodies