

Blood Bank I

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I. Here we go!

A. Blood Bank I

- Component Therapy

B. Blood Bank II

- Blood Groups

C. Blood Bank III

- Transfusion Reactions
- Hemolytic Disease of the Newborn

D. Blood Bank IV

- Blood Donation
- Pretransfusion Testing

E. Blood Bank Practical

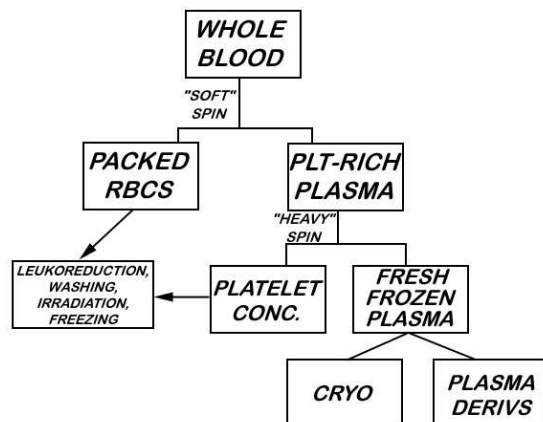
- Real Life Stuff, Calculations, Antibody ID, and sample questions

Blood Bank I

I. Nuts and Bolts

A. Basic Concept of “Component Therapy”

1. Allows for more efficient and effective use of products by giving a patient specifically what he lacks and not what he doesn't.
2. Made possible by advent of plastic bags around 1950.
3. Single unit may be made into numerous components (see figure below).



B. Anticoagulant/Preservative Solutions

1. Allows blood to be stored for extended periods without drastic effects on most metabolic and therapeutic qualities
2. Traditional anticoagulant/preservatives
 - a. Citrate-phosphate-dextrose (CPD) and citrate-phosphate-dextrose-dextrose (CP2D)
 - 1) Allows 21 days of RBC/Whole Blood storage
 - 2) Used before additive solutions
 - b. Citrate-phosphate-dextrose-adenine (CPDA-1)
 - 1) Very similar to CPD but with 17.3 mg of adenine (no adenine in CPD)
 - 2) Allows 35 days of RBC/Whole Blood storage
3. Additive solutions
 - a. Increases shelf life of RBCs to 42 days
 - b. Most common types
 - 1) AS-1 (Adsol®)
 - 2) AS-3 (Nutricel®)
 - 3) AS-5 (Optisol®)
 - c. Specifics vary, but all add more dextrose and adenine to increase blood shelf life
 - d. AS-1 and AS-5 also have mannitol
4. Critical to know storage details for various products (see Table1 below)

Product	Storage	Product	Storage
PRBCs / Whole blood	35 days (CPDA-1) 42 days (Additives) 1-6 C	WBCs	24 hours; 20-24 C (no agitation)
		Fresh Frozen Plasma	1 year; -18 C OR 7 years, -65 C 24 hours at 1-6 C after thaw
Frozen RBCs	10 years; -65 C 24 hours after thaw	CRYO	1 year at -18 C 6 hours at 20-24 C after thaw (4 hours if pooled)
Washed RBCs	24 hours; 1-6 C		
Platelets	5 days; 20-24 C (gentle agitation)		

C. Quality Control of Blood Products

1. Blood is a controlled product that is tightly regulated by the Food and Drug Administration (with many regulations from the American Association of Blood Banks and College of American Pathologists)
2. Very specific and detailed requirements for process and product acceptability

Table 2: Quality Control for Blood Products			
Product	QC	Product	QC
RBCs	HCT < 80% (all)	Apheresis platelets	$\geq 3.0 \times 10^{11}$ and pH ≥ 6.2 in 95%
RBCs leukoreduced	$\leq 5 \times 10^6$ WBCs in 95%, retain 85% of RBCs	Apheresis platelets leukoreduced	Above + < 5.0×10^6 residual WBCs in 95%
Platelets (PC)	$\geq 5.5 \times 10^{10}$ and pH ≥ 6.2 in 90%	CRYO	Factor VIII ≥ 80 IU (all) Fibrinogen ≥ 150 mg (all)
Platelets (PC) leukoreduced	Above + < 8.3×10^5 WBCs in 95%	Granulocyte concentrate	$\geq 1.0 \times 10^{10}$ in 75%

II. Blood and Components

A. Whole Blood

1. The original blood product!
2. Not stocked in most Blood Banks today
3. Specifics:

Volume:	450-500 ml
Contents:	RBCs (200 ml) Plasma (250 ml) WBCs (10^9) and platelets Anticoagulant (63 or 70 ml)

4. Potential indications:
 - a. Rapid hemorrhage of over 30-40% of blood volume
 - a. Especially trauma
 - b. Whole blood should be ABO identical, making it tougher to use in emergencies
 - b. Exchange transfusions in neonates
 - c. Some autologous transfusions (at request of MD)
5. Contraindications:
 - a. Anything where something more specific to the patient's needs would be better.
6. Storage Time and Conditions
 - a. Length depends on anticoagulant/preservative used
 - b. 1-6°C.

B. Blood Components

1. **Packed Red Blood Cells/Additive Solution Red Blood Cells**
2. **Platelets**
 - a. Platelet Concentrate
 - b. Apheresis Platelets
3. **Modified RBCs and platelets**
 - a. Leukocyte reduced products
 - b. Irradiated products
 - c. Frozen products
 - d. Washed products

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4. **Plasma and Derivatives**

- a. Fresh frozen plasma (FFP)
- b. FFP alternatives
- c. Cryoprecipitate (“Antihemophilic Factor”)
- d. Factor concentrates
- e. Other plasma derivatives

5. **Miscellaneous products**

- a. Granulocyte concentrate (not discussed in lecture)
- b. DDAVP

C. Red Blood Cells with and without additives

1. Made from whole blood by centrifugation and removal of most of plasma layer.
 - a. May be transfused without modification after preparation or may use additive solution
 - b. Units intended for use with additive solutions are collected into CPD (NOT CPDA-1), spun, then mixed with 100 cc of additive solution
 - 1) This gives a product with more volume and less plasma (HCT usually 55-65%)
2. Specifics:

Volume:	~250 ml (350 ml with additive solutions)
Contents:	RBCs (~200 ml); HCT \leq 80% Plasma (50 ml with CPDA-1) WBCs (10^8) and platelets Anticoagulant Additive solution (if applicable) 200 mg iron

3. Indications

- a. Need for increased oxygen-carrying capacity
 - 1) How do you decide?
 - a) Hemoglobin levels are only a part of the oxygen delivery process
 - b) Cardiac factors and oxygen demand often overlooked
 - c) Measuring mixed venous pO_2 and saturation and comparing to arterial levels gives an estimate of current oxygen use
 - Example: arterial saturation 100%, venous saturation 75% is normal; same patient with venous saturation 50% has a problem
 - Oxygen extraction ratio (ratio of arterial sat to arterial minus venous sats) of 0.5 or more is deemed “critical”
 - d) All factors (including increasing cardiac output and decreasing O_2 requirements) should be addressed in addition to considering transfusion

- 2) Situations that *may* require red cell transfusion:
 - a) Acute or chronic hemorrhage (over 30% of blood volume acutely)
 - b) Hemolysis
 - c) Marrow failure
- b. Important Studies/Publications:
 - 1) *NEJM* 1999;340:409-17; Critical care study showing that “conservative” transfusion strategy was as good (or better) than liberal strategy
4. Contraindications
 - a. Acute hemorrhage <20-30% of blood volume
 - 1) Crystalloids are adequate in most of these cases, but many get transfused anyway
 - b. Nutritional anemias
 - c. “Almost never” needed for HGB > 10 g/dl
5. Expected effect (per unit)
 - a. Hematocrit increased 3%, hemoglobin 1 g/dl (if not acutely bleeding or hemolyzing).
 - b. Rapid initial effect, maybe ~24 hours for full effect.
6. ABO compatibility
 - a. Always protect the **transfused** cells! (See chart)

		DONOR			
		A	B	AB	O
RECIPIENT	A	✓			✓
	B		✓		✓
	AB	✓	✓	✓	✓
	O				✓

7. Storage and shipping
 - a. Same as for whole blood with CPD, CPDA-1
 - b. 42 days at 1-6 C with additive solutions
 - c. Shipping temperature 1-10 C
8. Compatible fluids
 - a. Normal saline (0.9%)
 - b. ABO compatible plasma
 - c. 5% albumin
 - d. Red cells should not contact Lactated Ringer’s solution, D5W, 0.45% NS, antibiotics/other drugs, or TPN
 - 1) The reasons for this are primarily osmotic; hypotonic solutions like 0.45% saline will lead to red cells swelling and bursting, while hypertonic solutions like TPN and antibiotics will lead to shrinkage
 - 2) LR has enough calcium to counteract the citrate anticoagulant in blood (LR has 3 mEq Ca²⁺/L)

D. Platelets

1. **Platelet Concentrate (PC, “random platelets”)**
 - a. Prepared via centrifugation (“soft” spin then “hard” spin in the US) from a single whole blood unit.

b. Specifics

Volume:	50 ml
Contents:	Platelets ($\geq 5.5 \times 10^{10}$ in 90% tested) Plasma (including ~80 mg fibrinogen) WBCs (10^7) pH at or over 6.2

c. Indications

1) **Thrombocytopenia**

- a) Most data supports a threshold of < 10,000 in uncomplicated patients
- b) Some use a 20K threshold if febrile or septic, 50K if bleeding or undergoing major surgery
- c) Near 100K likely necessary for neurosurgery
- d) Avoid the prophylactic transfusion if possible!

2) **Thrombocytopathy**

- a) Congenital defects
- b) Drugs (ASA, Ticlopidine, Abciximab)
- c) External agents
 - Cardiac bypass machine
 - ECMO
- d) Metabolic effects (renal or hepatic failure)
 - Remember, though, that platelets are *not* first-line defense against platelet-related bleeding in renal failure! (Think DDAVP, Cryo, conjugated estrogens, etc)

d. Contraindications

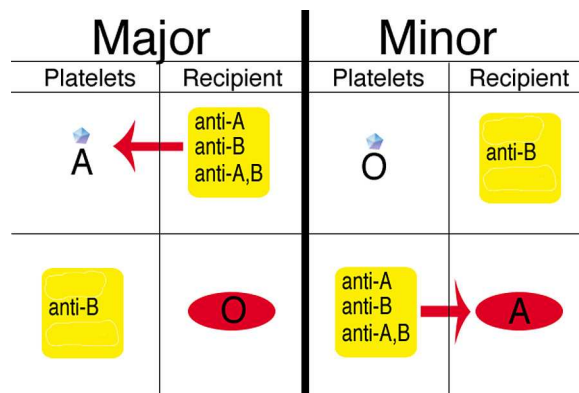
1) **Thrombotic Thrombocytopenic Purpura**
(near absolute)

- a) Protein deficiency that leads to large von Willebrand's factor multimers and subsequent platelet microthrombi
- b) More platelets = more thrombi
- c) Generally accepted contraindication, but some have reported successful transfusions
- d) Hemolytic-Uremic syndrome (HUS) is similar to TTP but lacks neurologic symptoms; similar contraindication

2) **Heparin-induced Thrombocytopenia, Type II**
(near absolute)

- a) Antibody vs. Heparin/platelet factor 4 complex
- b) Adding platelets may toss more fuel on the fire and lead to more microthrombi

- 3) **Immune/idiopathic Thrombocytopenic Purpura** (relative)
 - a) ITP is a relative contraindication because it usually just doesn't help!
- e. Dose
 - 1) 1 unit per 10 Kg body weight
 - a) Typically six to ten at a time in adults
 - 2) 10-15 mL/Kg in neonates
- f. Expected effect
 - 1) Current studies lacking (5-10K per bag?)
 - 2) Formulas (CCI, etc.) have some value in determining refractoriness (lack of response); generally used more with apheresis platelets
 - 3) One-hour post-transfusion count is standard
- g. Storage and shipping
 - 1) **5 days at 20-24 C** (with gentle agitation)
 - 2) Should not go more than 24 hours without agitation during shipping
- h. ABO and Rh
 - 1) ABO but not Rh antigens present on platelets
 - a) Platelet preparations may contain a few contaminating RBCs with Rh antigens.
 - b) Consider Rh prophylaxis with Rh incompatibility (1 vial RhIG per 30 units Rh+ PC; 1 per 3 Rh+ apheresis units)
 - 2) Platelet ABO incompatibilities
 - a) Major = Platelet ABO antigens incompatible with recipient plasma (like A plts to O recip)
 - Cleared from circulation faster; less effect
 - b) Minor = Donor ABO *antibodies* incompatible with *recipient RBCs* (like O plts to A recipient)
 - More of a concern in children and neonates (“reverse” hemolytic reactions)



2. **Apheresis platelets (“single donor” platelets)**
 - a. Made from one donor via apheresis procedure.
 - 1) Apheresis = removing whole blood from body, taking what you want, then returning the rest.

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b. Specifics

Volume:	~ 100 ml
Contents:	Platelets ($\geq 3.0 \times 10^{11}$ in 90% tested) Plasma (incl ~150 mg fibrinogen) WBCs (10^6 - 10^8)

c. Indications (aside from those listed in the PC section above)

1) Limiting exposure

- a) For infectious disease transmission
 - One donor exposure vs. at least six for PC decreases risk of viral transmission
 - Also decreases risk of bacterial contamination
- b) For HLA immunization?
 - Traditional thought: Fewer donor exposures mean less immunization
 - Not true! Risk more dependent on number of foreign antigens (not donors) seen; so leukoreduction is more important
 - “TRAP” study: NEJM 1997; 337, No. 26, 1861-9.

2) Platelet refractoriness (see BB Practical)

- a) Lack of response to platelet transfusion (immune and nonimmune causes)
- b) May be used as HLA-matched or crossmatched doses for immune refractoriness.

d. Storage and shipping

- 1) Same as for PC; 5 days at 20-24 C.

e. Effect

- 1) Dose dependent
- 2) Similar to PC

f. **NEW ISSUE WITH PLATELETS (both apheresis and platelet concentrate)**

- 1) As of March 1, 2004, *AABB Standards* requires that we utilize methods to both *limit* and *detect* bacterial contamination of platelets (both apheresis and platelet concentrate)
 - a) Needed because bacterial contamination is now the #1 transfusion infection risk
- 2) Limiting contamination
 - a) Careful skin preparation
 - b) Discarding initial 20-30 cc of blood
 - c) Exclusive use of apheresis platelets
- 3) Detecting contamination
 - a) Culture-based methods
 - Bacterial Detection System (Pall)

- BacT/ALERT (bioMerieux, Inc)
- b) Less sensitive methods
 - Gram stain, swirling, glucose checks by dipstick

E. Modifications to Red Cells and Platelets

1. Leukocyte reduction

- a. Definitions (*AABB Standards*, 21st ed.)
 - 1) Leukocyte Reduced Red Cells
 - a) At least 85% of original RBCs and $< 5 \times 10^6$ white cells in 95% of tested units
 - 2) Leukocyte Reduced Platelet Concentrate
 - a) At least 5.5×10^{10} platelets in 90% of units tested, and $< 8.3 \times 10^5$ WBCs in 95% of tested units
 - 3) Leukocyte Reduced Apheresis Platelets
 - a) At least 3.0×10^{11} platelets in 90%, and $< 5 \times 10^6$ WBCs in 95% of tested units
- b. Methods
 - 1) Leukocyte reduction filters
 - a) 99.99% removal of white cells
 - b) Several manufacturers and types
 - 2) Apheresis methods
 - a) Most apheresis machines have built-in leukoreduction methods available
 - 3) Other less used and less efficient methods
 - a) Washing or deglycerolizing
 - b) Centrifugation
- c. Types
 - 1) "Prestorage" leukocyte reduction
 - a) Done as early as possible; generally within 72 hours of collection (no set guideline; use package insert info)
 - b) May use inline filters at time of collection or post collection filters for red cells
 - c) Apheresis machines have filters or other leukoreduction methods built in
 - 2) "Pretransfusion" leukocyte reduction
 - a) Done prior to transfusion
 - b) "Bedside" leukoreduction uses product-specific filters at time of transfusion
 - Probably the least desirable way to leukoreduce using filters
 - c) Better done in transfusion service before issuing
 - Recent FDA memo mandates Quality-controlled leukocyte reduction
- d. Why Bother?
 - 1) **Prevention of HLA immunization**
 - a) Very effective means of preventing antibody formation against foreign HLA antigens

- b) “TRAP” Study: NEJM 1997, 337; No 26, 1861-9.
- 2) **Prevention of febrile nonhemolytic transfusion reactions**
- a) Benign reactions, but mimic early hemolysis
- b) First type: White cells secrete pyrogenic cytokines in bag *before* transfusion
- Seen more commonly with platelet transfusions
- c) Second type: Patient reacts to transfused white cells, pyrogenic cytokines secreted *after* transfusion
- Seen more commonly with red cell transfusions
- d) Pretransfusion reduction works fine for second type, prestorage usually necessary to prevent first.
- 3) **Prevention of CMV transmission**
- a) Virus carried only in white cells (probably monocytes).
- b) *Blood*, Vol. 86, No 9, 1995: pp. 3598-3603.
- Suggested filtered products are equivalent to CMV seronegative in preventing CMV seroconversion.
 - Early not yet published 2003 study from Hutchinson Center in Seattle casts doubt on this; implications not clear yet
- c) Be sure staff is trained in proper use (if used wrong, why bother?)
- 4) **Prevention of immunosuppressive effects of transfusion**
- a) Transfusion probably immunosuppresses recipient
- Many studies show increased post-op infections and increased cancer recurrence in transfused patients (but other studies do not show the same effect)
- b) If it does, WBCs may be the culprit
- c) Not universally accepted, in fact, quite controversial
- 5) **Reduction of bacterial contamination**
- a) Some studies suggest reduction in bacterial load (especially *Yersinia enterocolitica*) with leukoreduction
- 6) **Reduction in the risk of prion disease**
- a) One of the reasons for universal leukoreduction in Europe
- b) REALLY, REALLY controversial
- e. Leukocyte reduction is NOT indicated for:
- 1) Prevention of graft vs. host disease

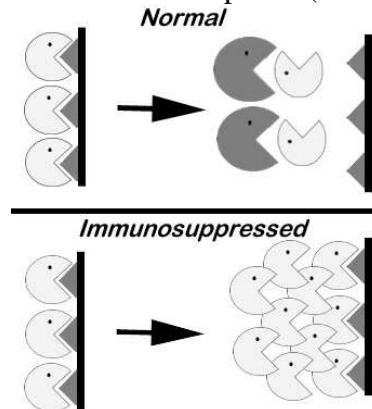
- 2) Transfusion of previously frozen products (FFP, cryo, etc)
- f. Potential complications
 - 1) Anaphylactoid reactions
 - a) Seen in patients taking ACE inhibitors (captopril, enalapril, etc), which block breakdown of cytokines induced by interaction with the filter surface
 - b) More in transfusion reaction section
2. **Washing**
 - a. 1-2 L of saline removes about 99% of plasma
 - b. Generally takes one to several hours (automated)
 - c. Shelf life
 - 1) Red cells: 24 hours post-wash
 - 2) Platelets: 4 hours post-wash
 - d. Why Bother?
 - 1) **Removal of plasma proteins (RBCs and Platelets)**
 - a) Classic example: IgA deficiency
 - Few IgA deficient patients develop anti-IgA; exposure leads to anaphylaxis
 - Requires more washing (3L or so)
 - IgA-deficient donors are alternative
 - b) Removal of unwanted antibodies
 - ABO antibodies (neonatal transfusions)
 - Other antibodies (white cell and platelet)
 - 2) **Neonatal Alloimmune Thrombocytopenic Purpura (Platelets)**
 - a) Severe congenital thrombocytopenia usually due to maternal anti-PL^{A1} (HPA-1A); analogous to HDN
 - Mom exposed through pregnancy or transfusion
 - Re-exposure leads to antibody re-activation
 - Antibody crosses placenta and trashes baby's platelets
 - b) Washed maternal platelets are treatment of choice (lack the offending antigen and antibody)
 - 3) **Repeated febrile nonhemolytic reactions (RBCs and Platelets)**
 - a) Removes cytokines and WBCs
 - b) It works, but seems like overkill
 - e. NOT adequate to prevent graft vs. host disease
4. **Freezing**
 - a. Cryopreservative agents protect component while freezing and thawing
 - 1) Glycerol used for red cells in either 40% or 20% concentrations (40% most common)

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- 2) Dimethyl sulfoxide (DMSO) used for platelets, but recovery isn't great
- b. Why Bother?
 - 1) **Storage of rare or autologous units**
 - 2) **Plasma hypersensitivities (as with washed)**
 - 3) **Repeated febrile reactions (as with washed)**
- c. Storage
 - 1) Red Cells
 - a) 10 years at -65°C (40% glycerol) or -120°C (20% glycerol)
 - b) 24 hours at $1-6^{\circ}\text{C}$ after thawing/deglycerolizing
 - 2) Platelets
 - a) No defined storage times (probably 4 hours post-removal of DMSO, though)

5. Irradiation

- a. Irradiation is effective in deactivating lymphocytes without significantly damaging anything else
- b. The normal response:
 - 1) Transfused lymphs (CD4 and CD8) mount an immune response against HLA incompatible host tissues
 - 2) Normally, host lymphs counterattack and neutralize the response (see top of figure below).



- c. Lack of host neutralization may lead to Transfusion-associated graft vs. host disease (TA-GVHD)
 - 1) Almost uniformly fatal
 - 2) Rash, diffuse mucositis, hepatitis, **bone marrow fibrosis and failure**
- d. Risk factors
 - 1) **Immunosuppression**
 - a) Congenital T-cell deficiencies (DiGeorge's, SCID, Wiskott-Aldrich)
 - b) Stem cell or marrow transplant recipients
 - c) **Patients taking Fludarabine (new data)**
 - 2) **Intrauterine and premature neonate transfusions**
 - 3) **Hodgkin's Disease**

- a) Patients with other heme malignancies often get zapped blood, too
- 4) **Receiving blood from a first-degree relative donor or receiving HLA-“matched” units**
 - a) HLA-heterozygous recipient getting blood from an HLA-homozygous donor
 - b) Recipient doesn't recognize transfused cells as foreign, so no counterattack.
- e. Patients probably NOT at risk
 - 1) Organ transplant recipients
 - 2) Term neonates
 - 3) Aplastic anemia
 - 4) AIDS patients
 - 5) Patients receiving previously frozen blood products (FFP, cryoprecipitate)
- f. Don't use irradiation for:
 - 1) Preventing CMV transmission
 - 2) Peripheral stem cell infusions
- g. Maximum storage: 28 days after irradiation
 - 1) K+ and free hemoglobin increase in red cells
 - 2) Doesn't change shelf life for platelets

F. Plasma Group

1. Fresh Frozen Plasma (FFP)

- a. Use (and abuse) greatly increased in recent years.
- b. Specifics:

Volume:	200-250 ml
Contents:	All coagulation factors <ul style="list-style-type: none"> • 400 mg fibrinogen • 1 IU/ml of all others Almost no <u>viable</u> cells Anticoagulant

- c. Basics notes about coagulation
 - 1) 100% levels of coagulation factors are not required for adequate hemostasis
 - a) 20-30% levels are enough in most cases
 - 2) However, factor levels at which someone will clot don't necessarily give normal PT/PTT
 - 3) Factor VII in vivo half-life is only about 4 hours
- d. Indications
 - 1) **Coagulopathy due to multiple factor deficiencies**
 - a) Liver disease
 - Decreased production of all hepatic factors; seen first with F VII (increased PT)

- b) Urgent reversal of Vitamin K deficiency from dietary factors or Warfarin use (or overdose)
 - II, VII, IX, X
 - IV or SQ vitamin K takes hours (about 12) to replenish these factors
 - In general, need at least 4-6 units initial dose to attain hemostasis in someone who is acutely bleeding and on Warfarin (usually more)
 - “Normal” PT/PTT not necessary
- c) Dilutional coagulopathy
 - Transfusion of multiple coag factor poor products (RBCs and crystalloids in massive transfusion) dilutes coag factors
 - Usually not apparent until after at least 10-15 or more units of RBCs (with accompanying fluid) in a 24 hour time span
- 2) **Protein C or S deficiency or complications**
 - a) Protein C inhibits Factors V and VIII and thereby inhibits coagulation; Protein S is a cofactor
 - b) Both are Vitamin K dependent
 - c) Deficiency of either may lead to thrombosis, which the clinicians may treat with Warfarin (not knowing about the deficiency)
 - d) When vitamin K dependent factors decline, so do proteins C and S; if they were low to begin with, the patient may become hyperthrombotic.
 - The classic finding is horrible skin necrosis caused by small vessel thrombosis
 - e) Treat the skin necrosis with FFP
- 3) **Plasma exchange for TTP/HUS**
 - a) If nonresponsive, consider “cryo-reduced” plasma (FFP with cryo removed), or Solvent/detergent-treated plasma (if you can find it)
- e. Not indicated for:
 - 1) Volume expansion
 - a) Alternatives (albumin, plasma protein fraction, crystalloids) are safer
 - 2) Heparin reversal
 - a) Supplies Antithrombin, which potentiates heparin!
 - b) Use protamine sulfate or just stop the heparin
 - 3) Factor deficiencies with specific concentrates available (like factor VIII and IX)

- 4) Mild elevations of PT/PTT
 - a) Generally become significant at about 1.5 times normal
- 5) “Wound healing” or “patient well-being”
- 6) Antithrombin deficiency
 - a) Formerly an indication for FFP
 - b) Virus inactivated concentrates now available
- f. Preparation
 - 1) **Pre-storage**
 - a) Made from a single whole blood donation.
 - b) Centrifuged, separated, and frozen at –18 C within 8 hours (kept for up to one year)
 - c) May also be kept at –65 C for up to 7 years
 - 2) **Pre-transfusion**
 - a) Thawed at 30-37 C.
 - b) Stored at 1-6 C for 24 hours.
- g. Dosage
 - 1) Generally given two bags at a time in adults.
 - 2) 10-15 ml/Kg in neonates.
- h. Effect
 - 1) Each two-unit dose increases factor levels by about 20-30% in a 70 Kg person
 - 2) Transient due to short half-lives (especially Factor VII)
 - 3) Greatly elevated PT/PTT more affected than mildly elevated
- i. ABO and Rh
 - 1) Plasma antibodies must be compatible with recipient RBCs
 - 2) Can give without regard to Rh.

		<i>DONOR</i>			
		A	B	AB	O
RECIPIENT	A	✓		✓	
	B		✓	✓	
	AB			✓	
	O	✓	✓	✓	✓

- 2. FFP Alternatives
 - a. **Solvent/detergent-treated Plasma (SDP, PLAS+[®]SD)**
 - 1) Approved by FDA in summer 1998; removed from market by Red Cross in 2002
 - 2) Pooled ABO-identical plasma from as many as 2500 donors treated to deactivate enveloped viruses (HIV, HTLV, HBV, HCV).

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- 3) Why it wasn't widely embraced
 - a) Pooled product; fear of undiscovered pathogens.
 - b) Nonenveloped viruses (Parvo, HAV) unaffected
 - c) Higher cost than FFP when introduced
- b. **Donor-retested FFP**
 - 1) Introduced about the same time as SDP
 - 2) Tries to eliminate window-period transmissions by holding plasma at least 112 days (two possible 56-day donor cycles) for re-testing of the donor
 - 3) Considered an alternative to SDP
 - 4) Not widely used due to administrative headaches and increased cost
- c. **Plasma, cryoprecipitate reduced ("cryo-reduced plasma", "cryosupernatant")**
 - 1) Residual plasma that remains after cryoprecipitate removed from FFP (see below).
 - 2) Product contains less vWD, so may be useful in TTP plasma exchanges if regular FFP doesn't work (literature shows mixed results on this)
 - 3) Storage and transfusion just like FFP
- d. **Linked Plasma**
 - 1) Ensuring that patient receives plasma and red cells from same donor
 - 2) Saves donor exposures
 - 3) Adds much complexity to process; not widely used

3. Cryoprecipitate

- a. Also has seen increased use in recent years.
- b. Specifics:

Volume:	Approximately 15 mL
Contents:	≥ 150 mg fibrinogen (us. ~250 mg) ≥ 80 IU factor VIII 80-120 IU von Willebrand's Factor 40-60 IU factor XIII Fibronectin

- c. ABO and Rh
 - 1) Same as for FFP
- d. Indications
 - 1) **Fibrinogen deficiency (congenital or acquired)**
 - a) General threshold: 100 mg/dl for adequate hemostasis post-surgery.
 - b) Calculation in BB Practical section

- c) I personally rarely use formulas, but use 10-20 bags per dose in adults, more if fibrinogen is less than 50 mg/dl.
- d) 10 bags deliver about 2500 mg of fibrinogen in about 150 ml of volume
 - >1 liter FFP needed for same amount!
- 2) **Treatment of von Willebrand's disease**
 - a) May be used for severe forms
 - b) Some factor VIII concentrates (e.g., "Humate-P") contain vWF
 - c) DDAVP can be used for milder forms
- 3) **Treatment of uremic thrombocytopeny**
 - a) Acquired adhesion defect (probably) which may respond to vWF supplementation
 - b) Second line of defense (after DDAVP)
 - c) Also consider conjugated estrogens, increasing HCT to ~30%
 - d) Am J Med 1994;96:168-79.
- 4) **Factor XIII deficiency**
- 5) **Topical "glue"**
 - a) Mixed with bovine thrombin
 - b) New fibrin sealants are making this use obsolete.
- 6) **Treatment of Hemophilia A**
 - a) NOT done in the real world!
 - b) Calculation in BB practical section for exams
 - c) General targets:
 - For hemarthrosis: 50% F VIII level
 - For surgery: 100% F VIII level
- e. **Manufacture**
 - 1) Made from a single unit of FFP.
 - 2) Thaw FFP at 1-6 C, spin and remove liquid, re-freeze slushy precipitate within 24 hours.
- f. **Storage and preparation for transfusion**
 - 1) **-18 C for 1 year**
 - 2) After thawing (at 30-37 C, like FFP), store up to 6 hours at 20-24 C (unlike FFP)
 - 3) If units are pooled, transfuse within **4** hours.
- 4. **Factor Concentrates**
 - a. **Factor VIII concentrate**
 - 1) Used for moderate to severe hemophilia A
 - 2) Virus inactivated or recombinant
 - 3) Dosage: Discussed in BB Practical
 - 4) Target levels: as above
 - 5) May contain vWF and be used in vWD.
 - b. **Factor IX Concentrate**
 - 1) Used for hemophilia B
 - 2) Old Factor IX complex concentrate not often used anymore (risk of thrombosis)
- 5. **Albumin and Plasma Protein Fraction**

Pathology Review Course

- a. Volume expanders
- b. Virus inactivated
- c. Ridiculously expensive!
- d. Differ only in composition
 - 1) Albumin: 96% albumin, 4% globulins/others
 - 2) PPF: 83% albumin, 17% globulins/others

G. Granulocyte concentrate

1. Rarely used today.
2. Specifics

Volume:	Variable
Contents:	WBCs ($\geq 1.0 \times 10^{10}$) Platelets ($> 3 \times 10^{11}$) RBCs (> 2 ml) Plasma Anticoagulant

3. Indications
 - a. A clinical situation including:
 - 1) Fever for 24-48 hours, positive blood cultures for bacteria or fungi, or progressive parenchymal disease unresponsive to antibiotics
 - 2) Neutropenia ($< 500/\mu\text{L}$)
 - 3) *Reversible* bone marrow hypoplasia
4. Not indicated for:
 - a. Prophylactic use
 - b. Patients with no hope of marrow recovery
5. Cans and Can'ts!
 - a. **Can irradiate** granulocytes to prevent TA-GVHD
 - 1) Irradiation harms lymphocytes but doesn't really affect granulocytes greatly
 - b. **Can't filter** granulocytes to prevent CMV transmission
 - 1) This seems obvious, doesn't it? Filters remove white cells, right? Are you with me? Hello?
 - 2) To protect against CMV transmission, need CMV-negative donor
6. Storage Conditions
 - a. 24 hours at 20-24 C *without* agitation
7. Caution
 - a. Granulocyte concentrate has abundant red cells, so must be ABO and Rh compatible
 - b. Crossmatch required before transfusion, also

H. DDAVP

1. Synthetic form of ADH used initially for treatment of Diabetes Insipidus.
2. As a fortunate side effect, causes release of vWF from endothelial cell storage; seems to functionally increase Factor VIII, as well.

3. Potential indications:
 - a. Uremic thrombocytopenia
 - 1) 0.3 µg/Kg IV
 - 2) Generally should be tried before platelets or cryo.
 - b. Mild hemophilia A
 - c. von Willebrand's Disease
 - 1) Works in types without marked deficiency
 - 2) Don't use in type IIB or III
 - a) IIB: may cause clotting
 - b) III: ineffective
 - d. Hepatic failure (for improved platelet function)
4. Effect diminishes/vanishes with repeat doses ("tachyphylaxis")

I. "Blood Substitutes"

1. Popular with the press
2. Probably better termed "blood supplements" or "oxygen therapeutics" because none can do everything that blood can do
3. Various, competing technologies
 - a. Modified hemoglobin solutions (human, bovine, recombinant)
 - 1) Hemopure (Biopure)
 - 2) PolyHeme (Northfield Labs)
 - 3) HemAssist (Baxter); removed in 1998 due to concerning results in phase III trials
 - b. Perfluorocarbon solutions
 - 1) Oxygent (Alliance)
4. Biopure product ("Hemopure") recently approved in South Africa
 - a. Modified bovine hemoglobin solution
5. Potential advantages
 - a. Universal compatibility
 - b. Less stringent storage (Many are stored at room temperature)
 - c. Infectious disease risk "eliminated"
6. Uses
 - a. Trauma or other massive transfusion setting
 - b. Military settings