An introduction to Blood Components and component Therapy

July 11, 2006

Objectives

- Preparation of blood components
- Types of blood components
- Indications for component therapy
- Transfusion triggers
- Dose
- Red blood cell substitutes (artificial blood)

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First blood transfusion ?

Pope Innocent VIII

1492 - Pope Innocent VIII, in Rome, had an apoplectic stroke; became weak and went into a coma. His physician advised a Blood transfusion as a therapeutic measure for the Pope's illness. Employing crude methods, the Pope did not benefit and died by the end of that year.

http://www.bloodbook.com/trans-history.html

Highlights of Transfusion Medicine History

1665 The first recorded successful blood transfusion occurs in England: Physician Richard Lower keeps dogs alive by transfusion of blood from other dogs.

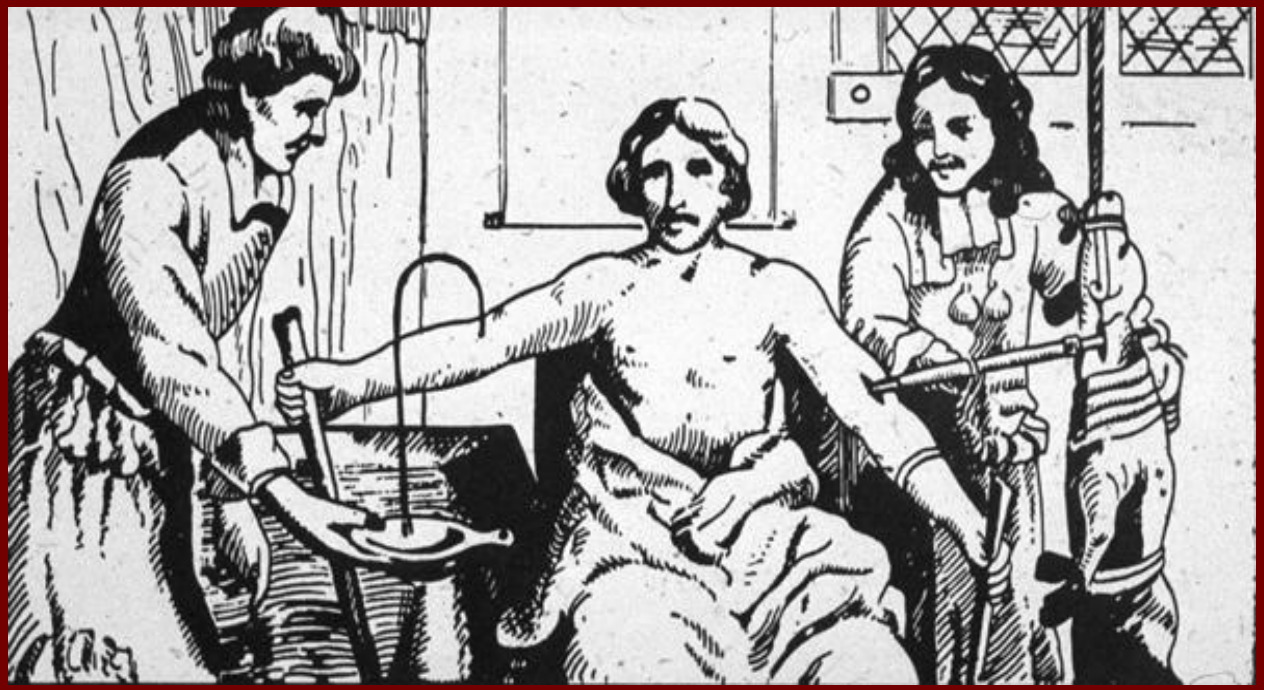
1667 Jean-Baptiste Denis in France and Richard Lower in England separately report successful transfusions from lambs to humans. Within 10 years, transfusing the blood of animals to humans becomes prohibited by law because of reactions.

1795 In Philadelphia, American physician Philip Syng Physick, performs the first human blood transfusion, although he does not publish this information.

1873-1880 US physicians transfuse milk (from cows, goats, and humans).

Early history of transfusion

- Involved transfusion of animal blood to humans



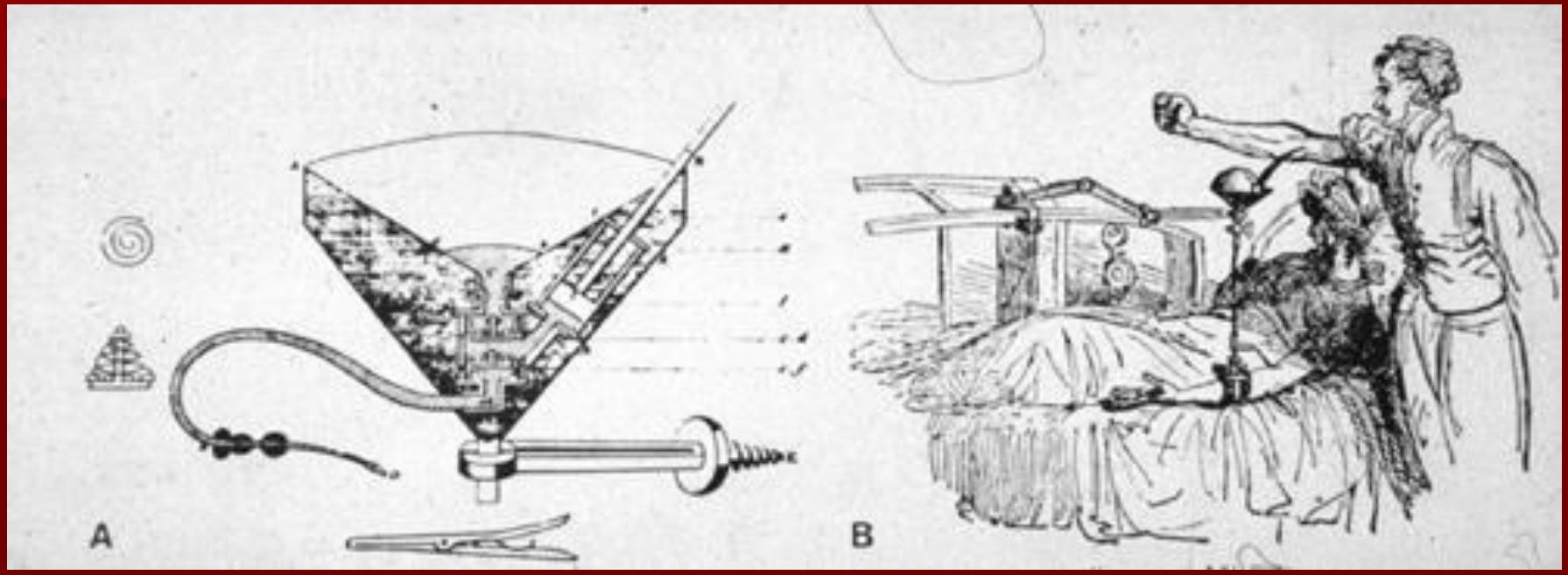
This really was a Red cell exchange!

James Blundell

In 1818, James Blundell attempted human-to human transfusion of a man suffering from gastric carcinoma.

“What is to be done in such an emergency? A dog might come when you whistled, but the animal is small; a calf might have appeared better suited for the purpose, but then it has not been taught to walk properly up the stairs.”

James Blundell



Blundell's transfusion devices included the impellor (A), which consisted of a cup, tube , and syringe; and the gravitator (B), consisting of a receptacle held high above the patient with an attached tube through which the blood was injected into the patient.

Development of Plastic storage containers

1950 Carl Walter and W.P. Murphy, Jr., introduce the plastic bag for blood collection.

- Replacing breakable glass bottles with durable plastic bags allows for the evolution of a collection system capable of safe and easy preparation of multiple blood components from a single unit of whole blood.

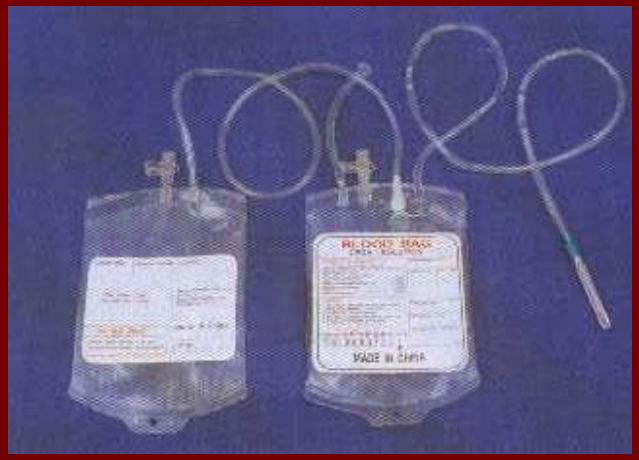
- Development of the refrigerated centrifuge in 1953 further expedites blood component therapy.

Blood Collection

Blood centers and transfusion services depend on volunteer donors

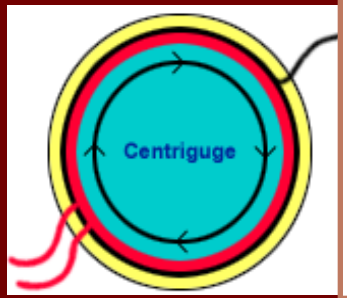
- Donors:
  - Are identified
  - Screened:
    - questionnaire, physical exam
  - Give written consent

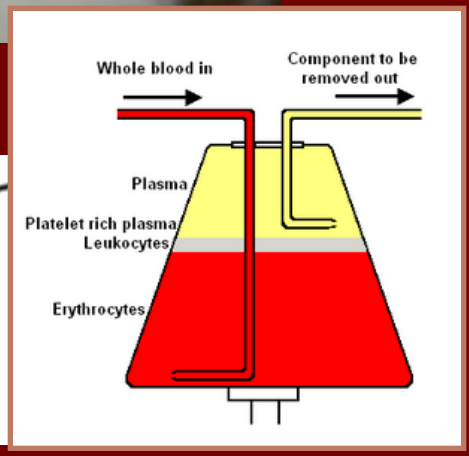
Blood collection



- Blood is collected into a sterile bag
  - Whole blood
  - Apheresis
- The bag contains anticoagulant and preservatives
- Anticoagulant-prevents clotting, citrate binds to calcium thereby inhibiting some Ca dependent steps in the coagulation pathway
- Preservatives contain phosphate, dextrose and adenine which help prolong the shelf life of blood

Apheresis collection (Collection of specific components)





•http://www.mar.med.navy.mil/BloodBank

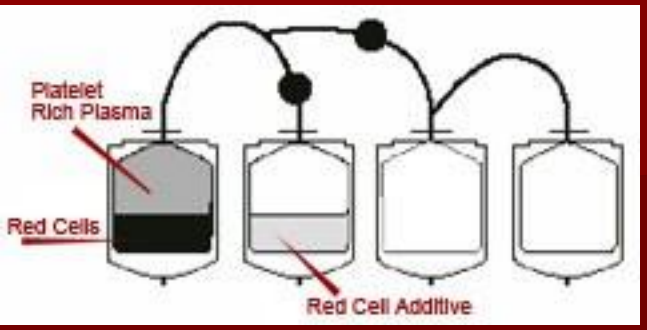
Whole blood collection

http://www.mar.med.navy.mil

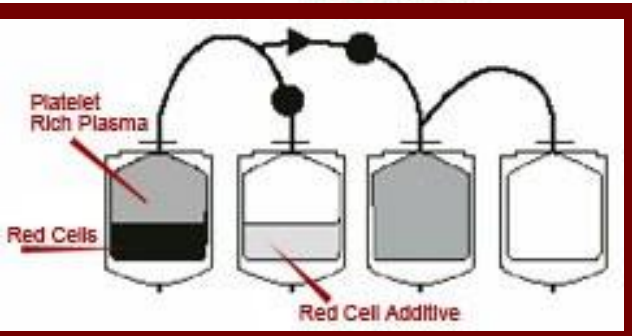
Component separation

- Whole blood can be separated into different components.
- This allows the use of one donation for at least three different transfusions
- Achieved by differential centrifugation

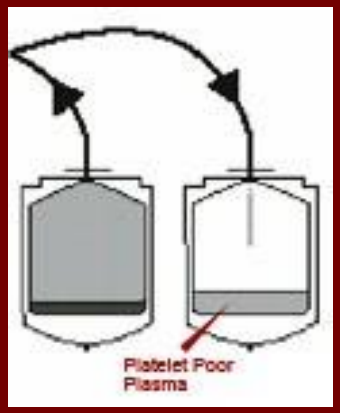
Component preparation



The whole blood (WB) donation is centrifuged at room temperature to separate red cells from plasma. Centrifugation at room temperature (20-24° C) is required to prevent the platelets from aggregating. A “light spin” is used to keep the platelets suspended in plasma.



Approximately 190-260 mL of donor plasma is expressed into the satellite bag. The RBC unit is sealed and stored at 1-6o C for varying shelf lives.



The PRP is centrifuged at room temperature using a “hard spin” to concentrate the platelets.
All but approximately 50 mL of plasma is expressed into the second satellite bag.

Preparation of cryoprecipitate

After collection of plasma, Donor plasma is rapidly frozen within eight hours of collection to preserve Factor VIII.

Donor plasma is thawed slowly at 1-6°C to the slush stage. Plasma is then centrifuged to separate the cryoprecipitated portion (i.e., cryoprecipitate) from the liquid portion (cryosupernatant plasma).

Packed RBC

Stored at 1-6^{o}C for 42 days

Whole blood

Stored at 1-6^{o}C

Plasma

Stored at -18^{0}C for 1 year

Platelets

Stored at room temp for 5 days

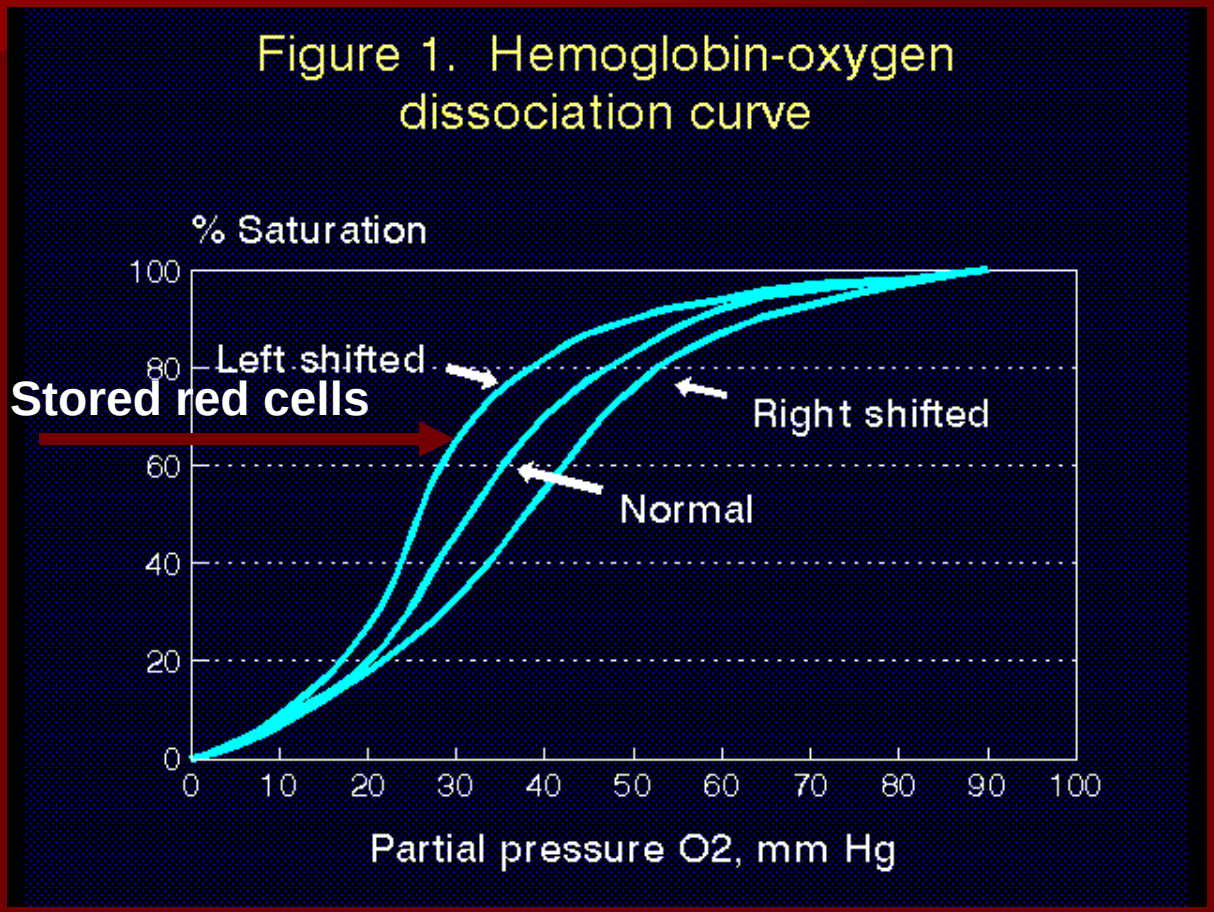
Cryoprecipitate

Stored at -18^{0}C for 1 year

The “storage lesion”

- Biochemical changes occur during the storage of red blood cells and platelets
  - Some are reversible
  - Some changes rarely have clinical significance

Biochemical Changes in red blood cells



http://www.dr-amy.com/rich/oxygen/

Storage of RBC leads to:

Decreased 2,3-DPG

Poor ATP function

Increased potassium in supernatant

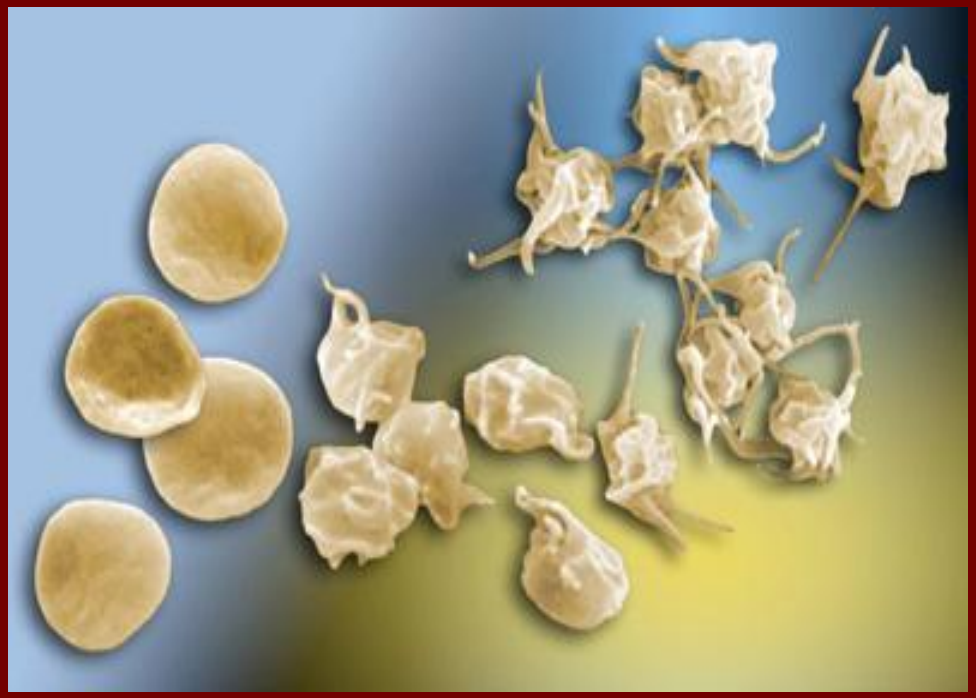
Decreased cellular potassium

Increased plasma hemoglobin

Decreased pH

Decreased % viable cells

The platelet storage lesion



http://www.uphs.upenn.edu/news/News_Releases/may02/Laser.html

- Decreased recovery and survival
- Altered morphology- decreased MPV, loss of disc shape, fragments
- Altered glycoprotein Ib
- Decreased content of α granules and dense bodies (due to platelet activation)
- Decreased function
- Lactic acid generated from glycolysis
- Decreased pH

Blood component Quality Control

- All equipment must be validated before implementation and monitored periodically
- Staff must be appropriately trained and their competency evaluated
- Contents of final products should be periodically assessed.
- Need to consider AABB and FDA requirements

Equipment

- Blood refrigerators and freezers
  - Most have built in temperature monitoring sensors and alarm systems
- Thermometers
  - Need to be placed properly and verified and calibrated periodically
- Alarm systems
  - Electrical source must be separate
  - Cause of temperature must be determined

QC of red blood cells

- RBCs prepared without additive must have a hematocrit of <80%
- Leukocyte reduced RBCs should contain < 5x 10^6 residual leukocytes
  - 95% units sampled must meet this specification

QC of platelets

- Culture for bacterial contamination or pH check
- At least 5.5 x 10^{10} platelets in random donor units
- At least 3.0 x 10^{11} platelets in apheresis units

Component Therapy

Whole Blood

- RBC and plasma + anticoagulant
- approximate volume 520ml
- Commonly used for component production
- indications are limited
  - massive transfusion (always has to be group specific)
  - ***Hb increased by 1gm/dl***

Red Blood Cells

- Packed red cells with reduced plasma volume, + additive
- Hematocrit is 55- 65%
- Volume 260 - 340ml
- Stored at 1-6^{o}C for 42 days
- Indications
  - symptomatic anemia in normovolemic patients

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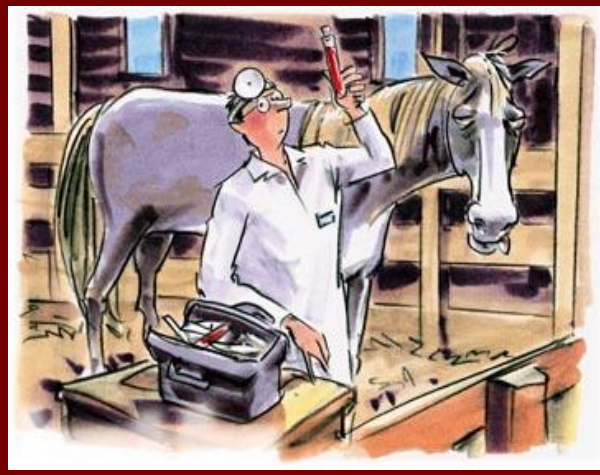
When should I transfuse Red Blood Cells?

- Actively bleeding patients
  - When 30-40% of blood volume is lost
- Anemia
  - Most healthy resting adults will tolerate a hemoglobin as low as 5g/dL
  - Increased mortality when Hb is below 5-6g/dL

Acute or chronic

  - symptomatic
  - Use transfusion Trigger guidelines



http://www.americanhorserider.coml

Transfusion trigger?

- Based on multiple studies
- Refers to the hemoglobin level at which red blood cell transfusion should be considered
- <7-8g/dL for most patients

- < 10g/dL for patients with cardiovascular or pulmonary disease.

Dose

- One unit of RBC will increase hemoglobin by 1g/dL

http://www.jwolfe.clara.net

Leukoreduced products

- cellular blood products with a leukocyte content of less than 5 x 10^6/unit
- currently done using filters which achieve 99.9 % reduction
- filtration is done at the blood center, laboratory or bedside.
- can also be achieved on apheresis devices.

Why Leukoreduce?

Leukocytes have been implicated in several adverse effects of transfusion

1. HLA Alloimmunization in the recipient
   - febrile non hemolytic transfusion reactions
   - Platelet refractoriness
   - Transplant rejection
2. Infections
   - CMV, HTLV, EBV
   - bacteria
   - ?prion disease transmission
3. Immunosuppression

Fresh Frozen Plasma

- Contains all coagulation factors, other proteins and anticoagulant
- Average unit contains ~ 1U/mL of all clotting factors
- volume 200 -600ml (jumbo units contain more plasma
- If frozen within 8 hours can be called FFP
  - Still efficacious if frozen at 24 hours
  - Once thawed, be stored at 1-6^{o}C for a total of 5 days

TABLE 1. Mean coagulation factor levels at 24-hour intervals by blood group

Coagulation factor	Level* Day 1	Day 2	Day 3	Day 4	Day 5	Mean change from Day 1 to Day 5 (%)	p values
FVIII (%)							
Blood group A	107 ± 26	76 ± 19	66 ± 18	65 ± 17	63 ± 16	41	<0.004†
Blood group B	103 ± 44	74 ± 37	71 ± 35	67 ± 36	67 ± 33	35	<0.02†
Blood group O	70 ± 16	51 ± 10	43 ± 10	43 ± 7	41 ± 8	41	<0.001†
Factor II (%)	81 ± 9	81 ± 9	81 ± 9	80 ± 10	80 ± 10	1	NS
Factor V (%)	79 ± 7	75 ± 8	71 ± 9	68 ± 9	66 ± 9	16	NS
Factor VII (%)	90 ± 18	81 ± 15	76 ± 15	72 ± 14	72 ± 15	20	NS
Factor X	85 ± 13	84 ± 13	84 ± 15	82 ± 11	80 ± 11	6	NS
Fibrinogen (mg/dL)	225 ± 12	224 ± 13	224 ± 13	224 ± 17	225 ± 12	0	NS

* Mean ± SD.

† Comparison of FVIII activity at Day 1 and that at Day 3 was statistically significant.

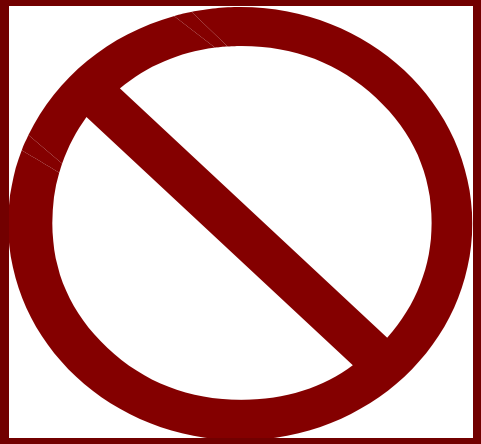
Indications for plasma transfusion

- Bleeding with multiple factor deficiencies
- Pre-op setting with multiple factor deficiencies
- Deficiency of factors V or XI, proteins C and S
- Wafarin induced coagulopathy
- Massive transfusion
- Disseminated Intravascular coagulopathy (DIC)
- Replacement fluid in plasmapheresis
- Rare specific plasma protein deficiency (e.g. C1 esterase inhibitor)

Fresh Frozen Plasma

- Dose 10- 20ml/kg will increase coagulation factors activity by about 30%
  - ***Comes to about 4 – 6 units***
  - ***Timing***
- Use cessation of bleeding and PT/PTT/INR as your endpoint

WARNING



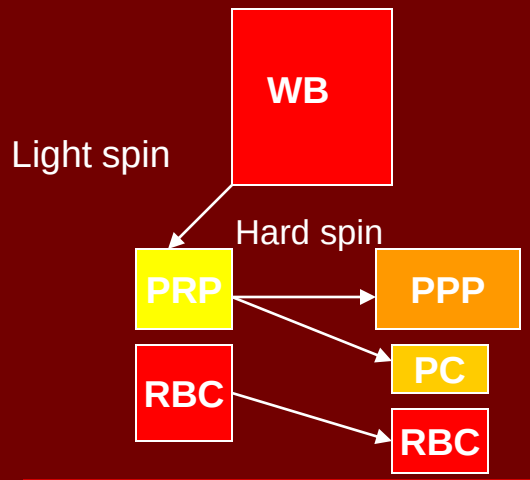
PLASMA SHOULD NOT BE USED AS VOLUME EXPANDER

USE AVAILABLE CONCENTRATES FOR CONGENITAL DEFICIENCY OF FACTORS OTHER THAN V AND XI

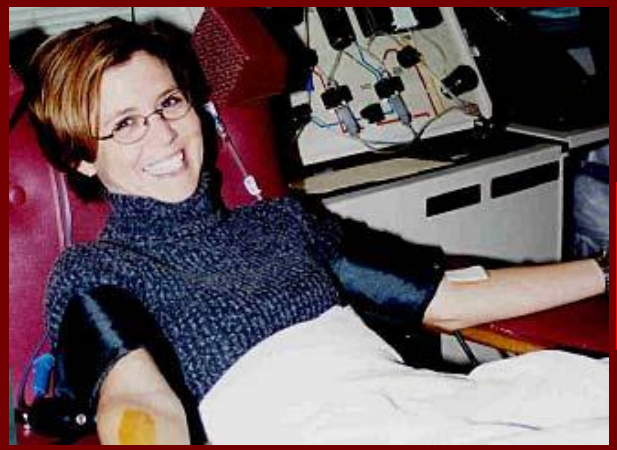
TREAT THE PATIENT, NOT THE NUMBERS

The platelet product

- 2 basic types
  - Whole blood derived (random donor platelets)
  - Platelet pheresis (single donor platelets)



Whole blood derived platelets



Apheresis platelets

http://www.bloodntissue.org/blooddonation_platelet.asp

Content

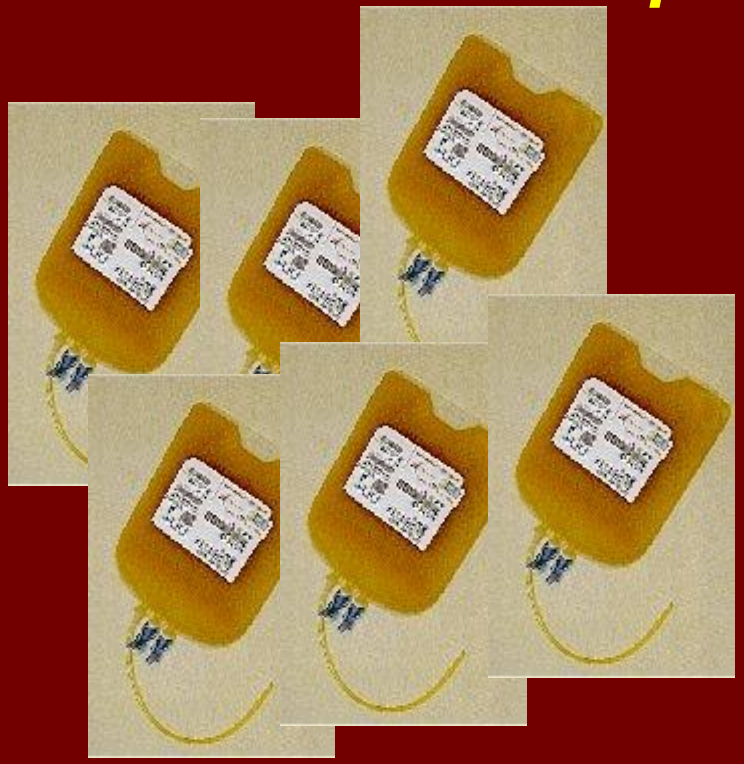
1 apheresis platelet

Volume ~ 400ml

Minimal RBC and WBC

=

6-8 random donor platelets

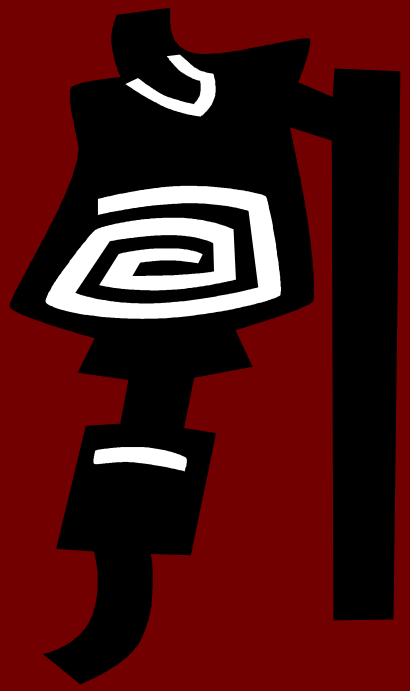


Volume ~ 50-70ml

Minimal RBC and WBC

Indications for Platelet transfusion

- Prophylactic transfusion
  - Severe thrombocytopenia
  - Before invasive procedure if thrombocytopenia is present
- Thrombocytopenic bleeding
- Dilutional thrombocytopenia
- Thrombocytopathy
  - Congenital or Acquired



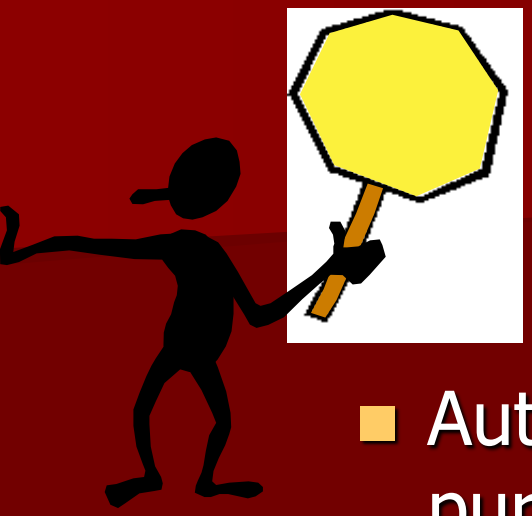
Transfusion Triggers for Platelet transfusion

Platelet count	Risk of hemorrhage
>50,000/uL	Bleeding with surgery, invasive procedures not likely
10,000 – 50,000/uL	Spontaneous bleeding unlikely but may occur with surgery or trauma
5,000-10,000/uL	Risk of spontaneous bleeding
<5,000/uL	High risk of spontaneous bleeding

Transfuse only for neurosurgical or ophthalmic procedures

Transfuse if bleeding

Prophylactic Transfusion



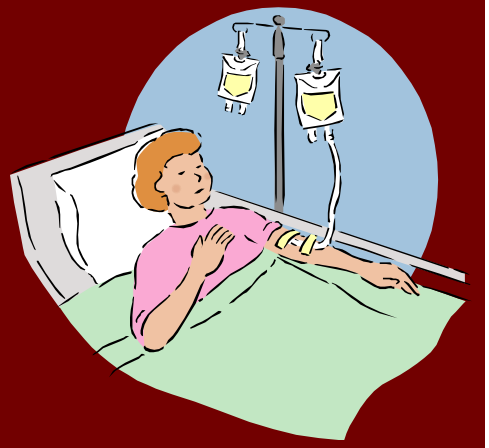
Contraindications to Platelet transfusion

- Autoimmune idiopathic thrombocytopenic purpura (ITP)
- Thrombotic thrombocytopenic purpura (TTP)
- Heparin induced thrombocytopenia (HIT)
- Coagulopathy only
- Anatomic bleeding only

Standard Platelet doses

- Infants: 5- 10ml/kg body weight
- Children: 1 unit (whole blood derived) for every 10-15kg body weight
- Adults: 4-8 units pooled or I unit apheresis platelets

Expected Increment



	1 unit	4 units	6 units
50lb	22,000/uL	88,000/uL	132,000/uL
100lb	11,000/uL	45,000/uL	66,000/uL
150lb	7,400/uL	30,000/uL	44,000/uL
200lb	5,500/uL	22,000/uL	33,000/uL

On the average, expect an increment between 30,000 – 60,000/uL

How can you assess a response to platelet transfusion?

- Cessation of hemorrhage

- Post transfusion count
  - Dependent on size
  - Initial platelet count
  - Dose given
  - One third transfused platelets will remain in the spleen

Cryoprecipitate

- Contains factors *VIII, XIII, vWF, and fibrinogen*
  - *NOT CONCENTRATED FFP*
- volume 10-15 ml
- Indications
  - congenital or acquired deficiencies of fibrinogen and factor XIII deficiency
  - Von Willibrands disease
  - uremic platelet dysfunction
- Dose 1 unit/ 10 kg

Granulocytes

- Granulocytes and other WBC, platelets, plasma
- Collected by apheresis
- volume 200 -300ml
- Indications
  - *granulocytopenia with persistent fever or infection not responding to antibiotic or antifungal therapy in patients whose bone marrow function is expected to recover*

- Dose: not well established, but should not be less than 1 x 10^{10} PMNs per dose
  - Transfuse within 24 hours of collection preferably in the first 6 hours

Red blood cell substitutes

Desirable characteristics of a blood substitute

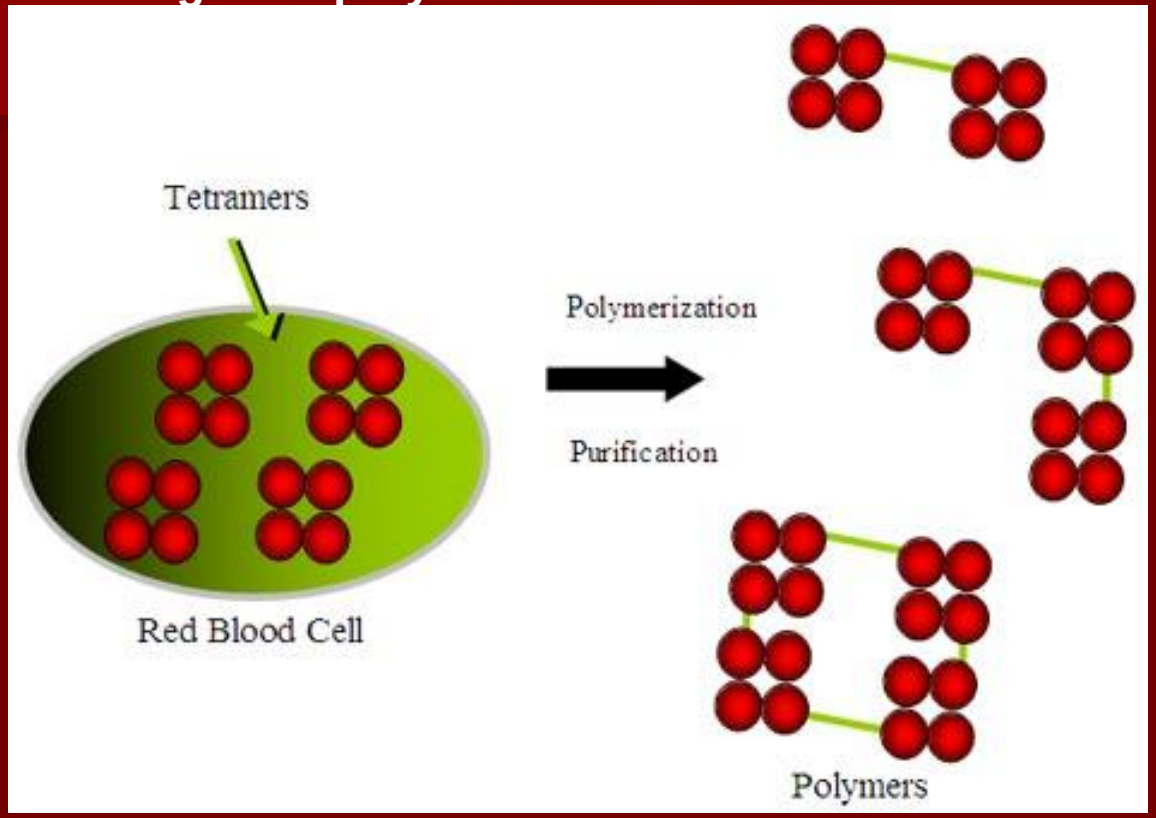
- Free of infectious complications
- Abundant supply, easy to use, low cost
- Transport high concentrations of oxygen
- Suitable intravascular half life
- Safe, minimal or no testing

RBC Substitutes

- Hemoglobin based oxygen carriers
  - Polyheme: polymerized human hemoglobin
  - Hemopure: polymerized Hb from bovine RBC
  - Hemosol: partially polymerized human Hb
- Perfluorocarbon based products
  - Fluosol DA
  - Oxygent

Polyheme

Hemoglobin polymerization

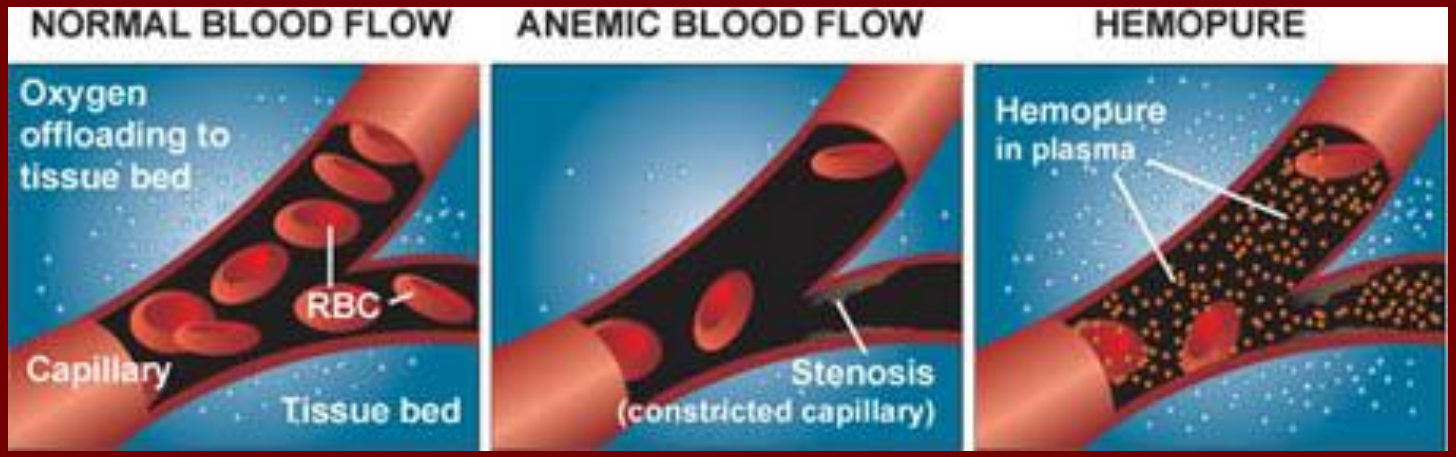


Patient sample

http://www.northfieldlabs.com/polyheme

Hemopure

CHARACTERISTICS	BIOPURE'S OXYGEN THERAPEUTICS	RED BLOOD CELLS
STORAGE	*Room temperature (2° to 30° C)*	Refrigerated
SHELF LIFE	*36 months*	42 days
PREPARATION	*Ready to use*	Testing, typing and crossmatching
COMPATIBILITY	*Universal*	Type specific
EFFECTIVENESS	*Immediate oxygen delivery*	Dependant on length of storage
PURITY	*Processed to remove infectious agents*	Tested and screened for infectious agents
RAW MATERIAL	*Bovine hemoglobin - abundant, controlled source*	Limited availability, not controlled



http://www.biopure.com

Perflurocarbon based red blood cell substitutes

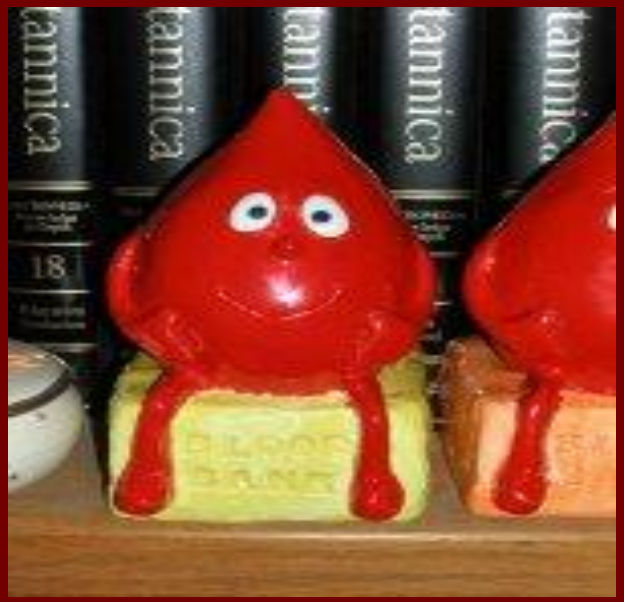
- A group of compounds that are highly soluble for gases including O2
- Must be prepared as emulsions
- Several products undergoing clinical trials

Adverse effects of red blood cell substitutes

- Renal toxicity
- vasoconstriction
- Thrombocytopenia
- Alteration of lab values
- Iron overload
- ? Potentiation of sepsis

Have you donated blood today?

"Just as one cannot draw money from a bank unless one has deposited some, so the blood preservation department cannot supply blood unless as much comes in as goes out".



Dr. Bernard Fantus