
بسم الله الرحمن الرحيم

Plasma products

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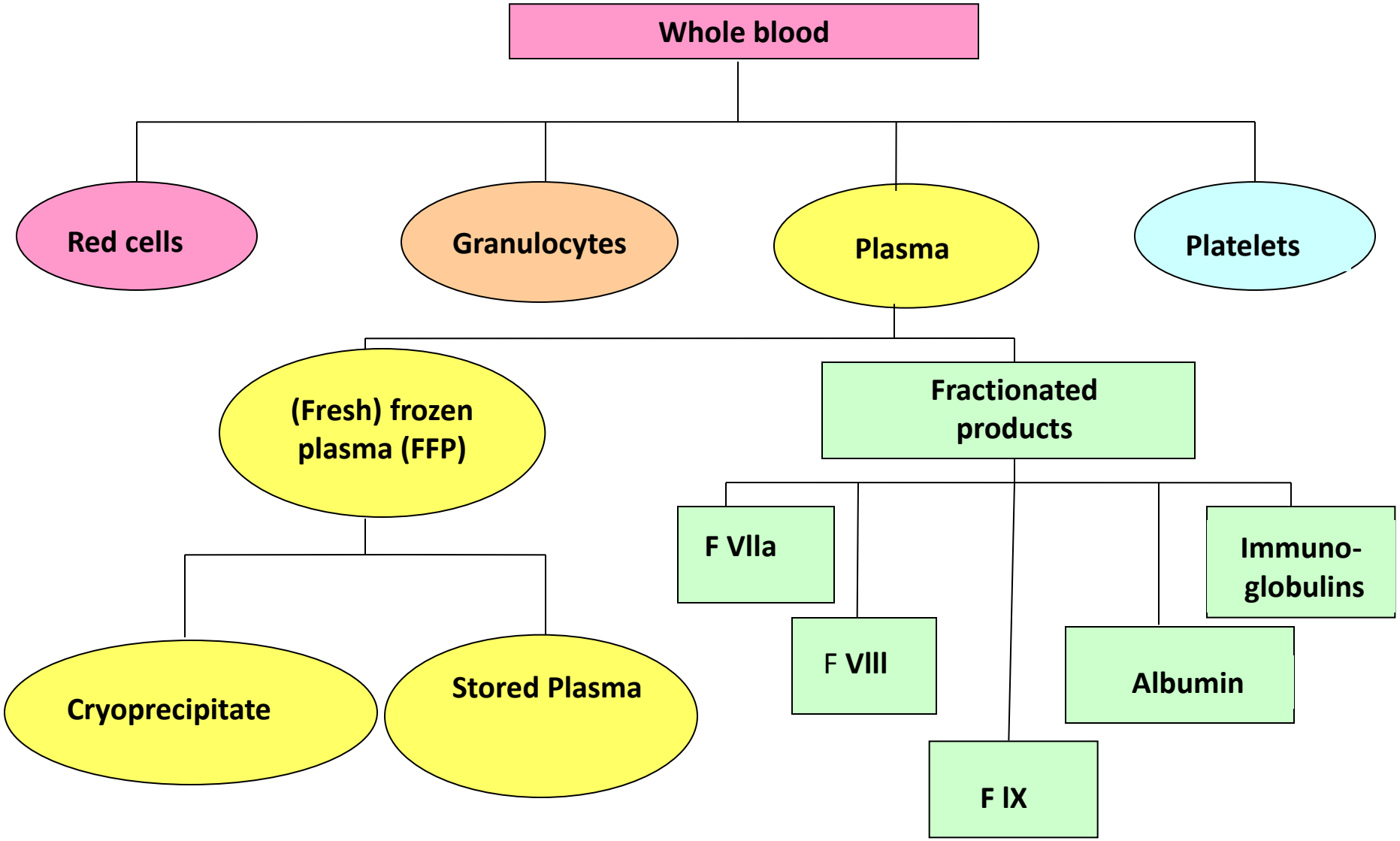
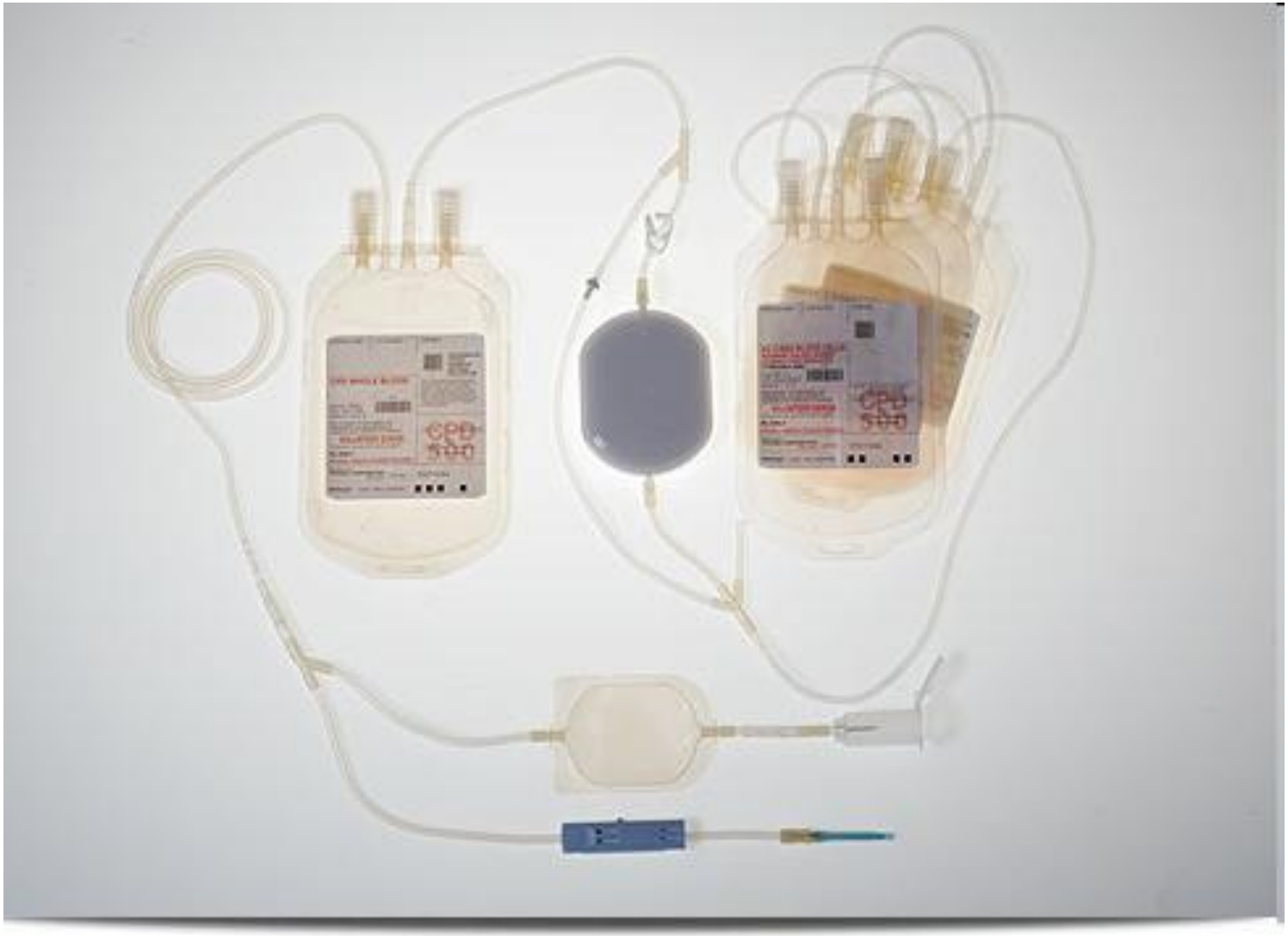
- In the United States and developed countries, whole blood is rarely used.
- Within a few hours or days, some coagulation factors, especially V and VIII, and platelets decrease in quantity or lose viability in stored whole blood.

Preparation of Components

- Summary – One unit of whole blood can produce:
  - Packed RBCs
  - Fresh frozen plasma (FFP)
  - Cryoprecipitate (CRYO)
  - Single donor plasma (SDP) – cyro removed
  - Platelets


Whole blood
Red cells
Granulocytes
Plasma
Platelets
(Fresh) frozen plasma (FFP)
Fractionated products
Cryoprecipitate
Stored Plasma
F VIIa
F VIII
F IX
Albumin
Immuno-globulins



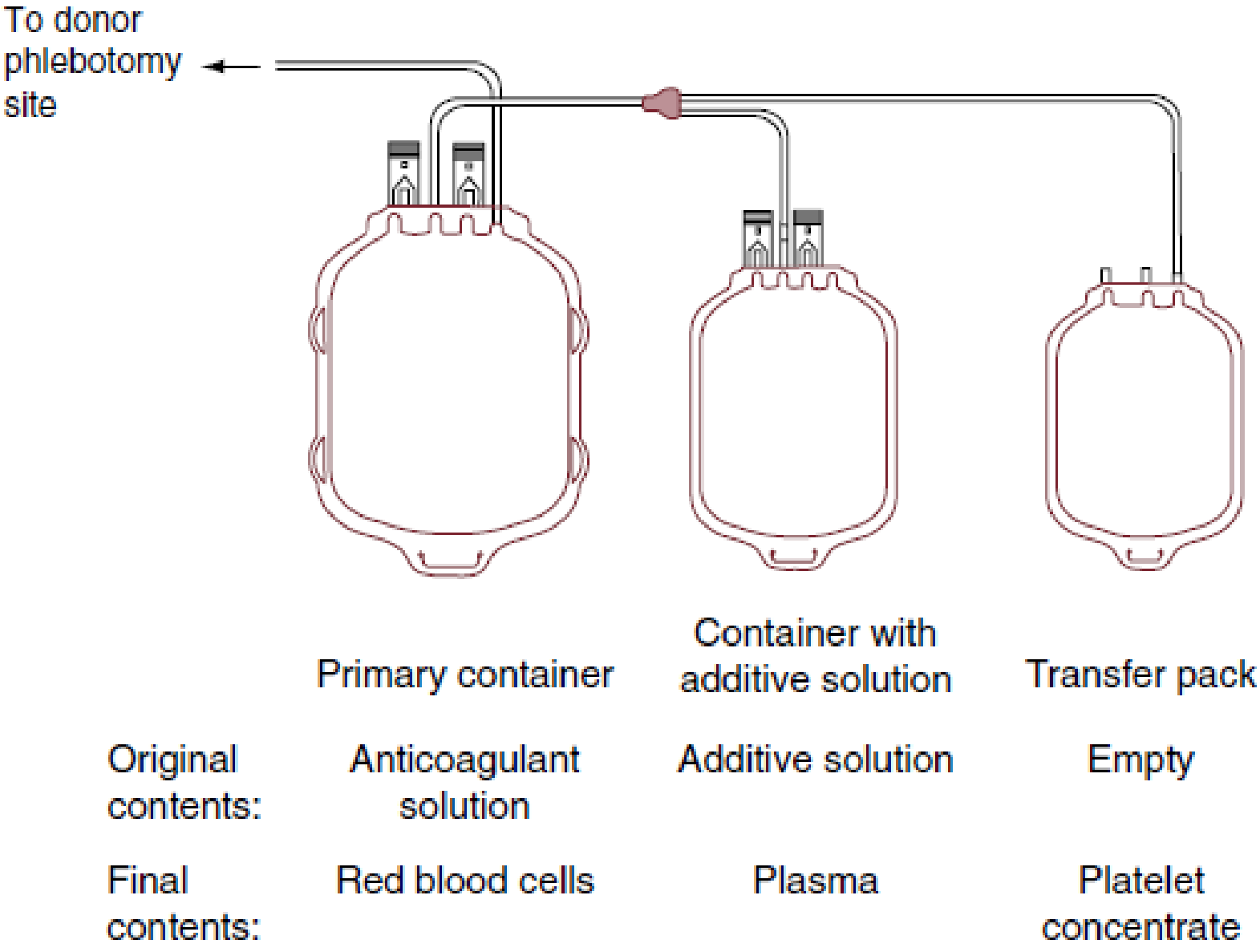


Figure 5.1 Diagram showing unit of whole blood and integral plastic bag system used for preparing blood components.

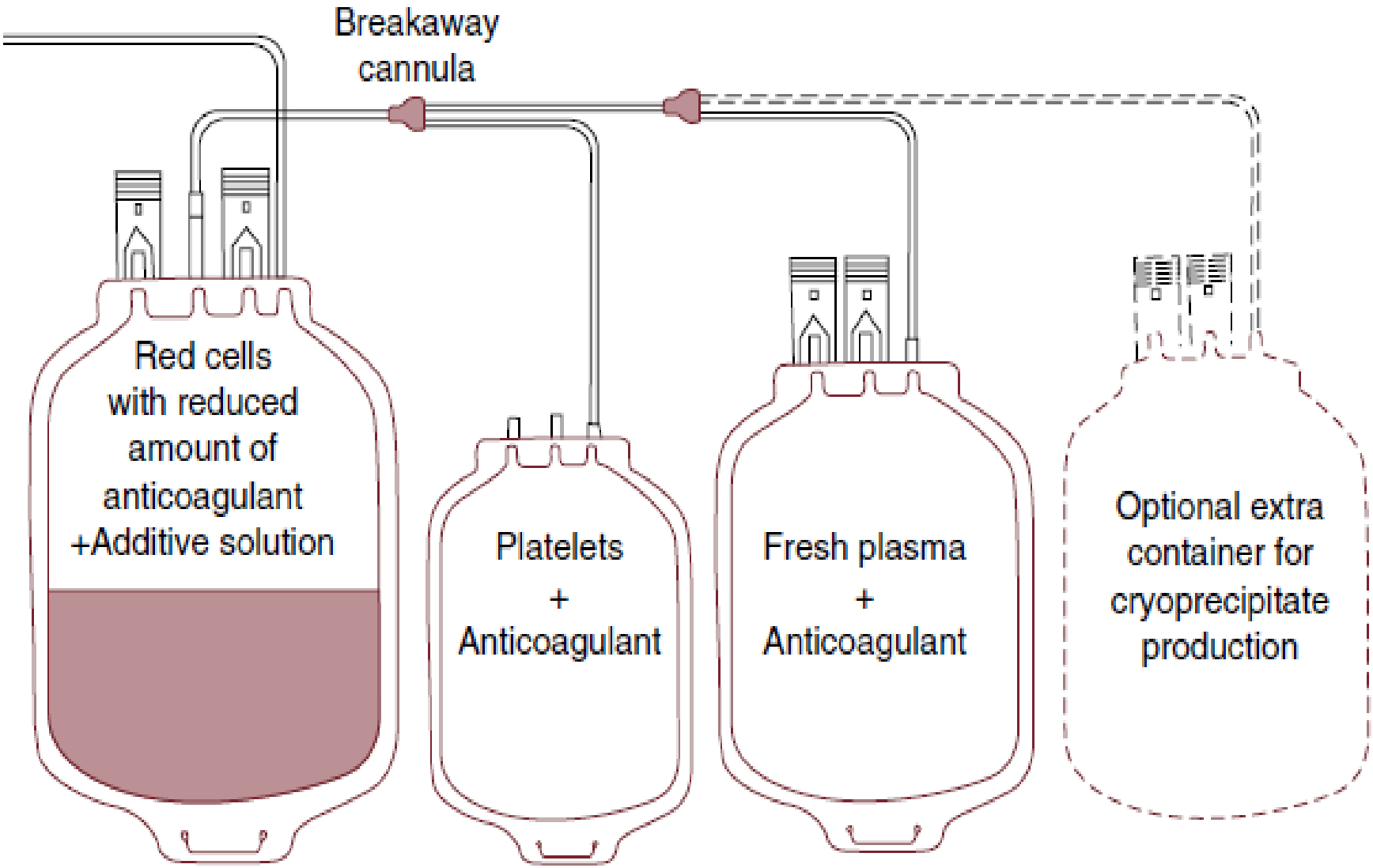
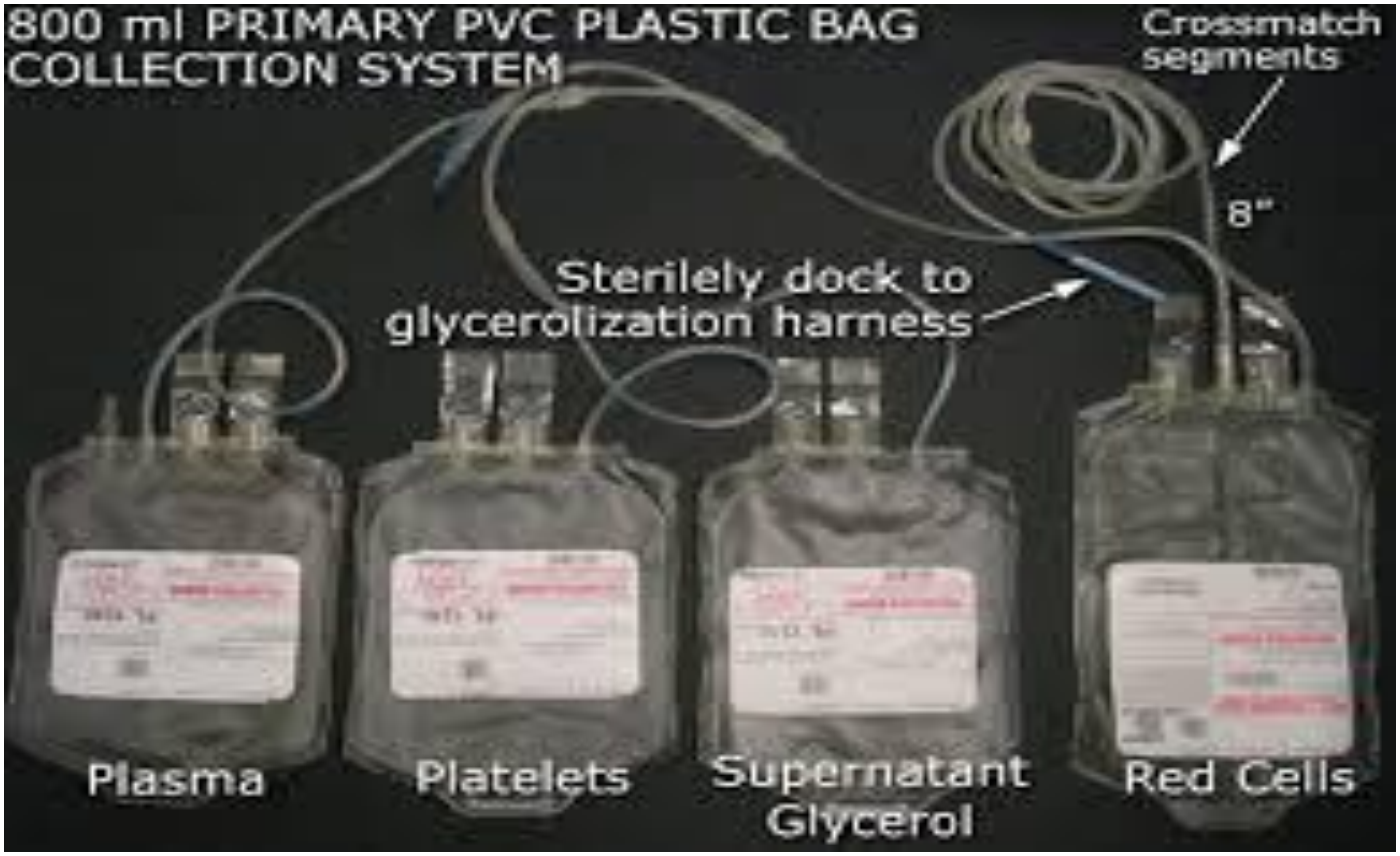
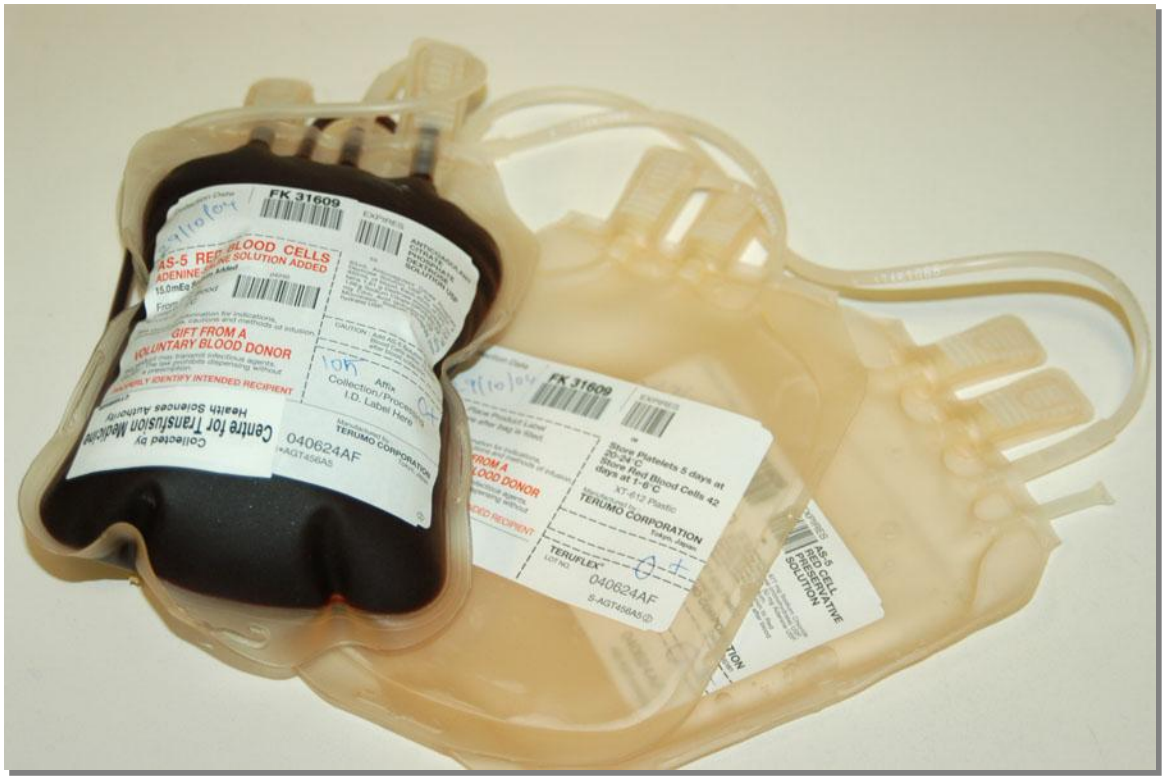
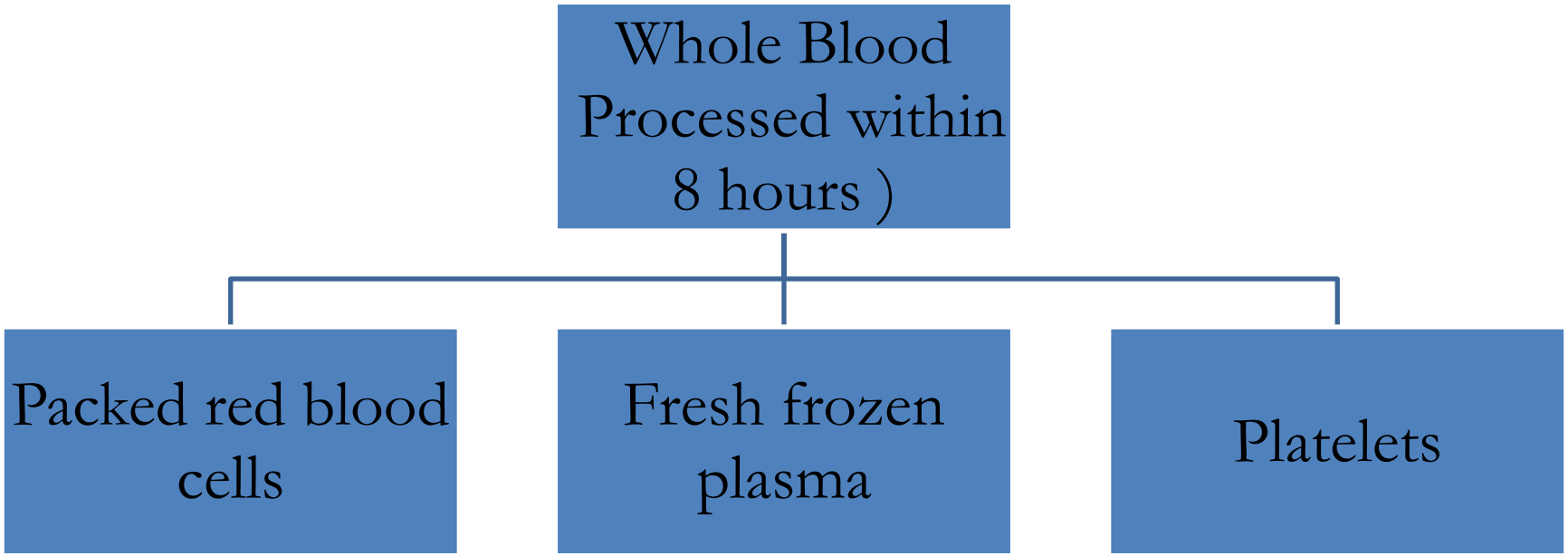


Figure 5.2 Diagrammatic illustration of the separation of whole blood into red cells, plasma, and platelet concentrate.

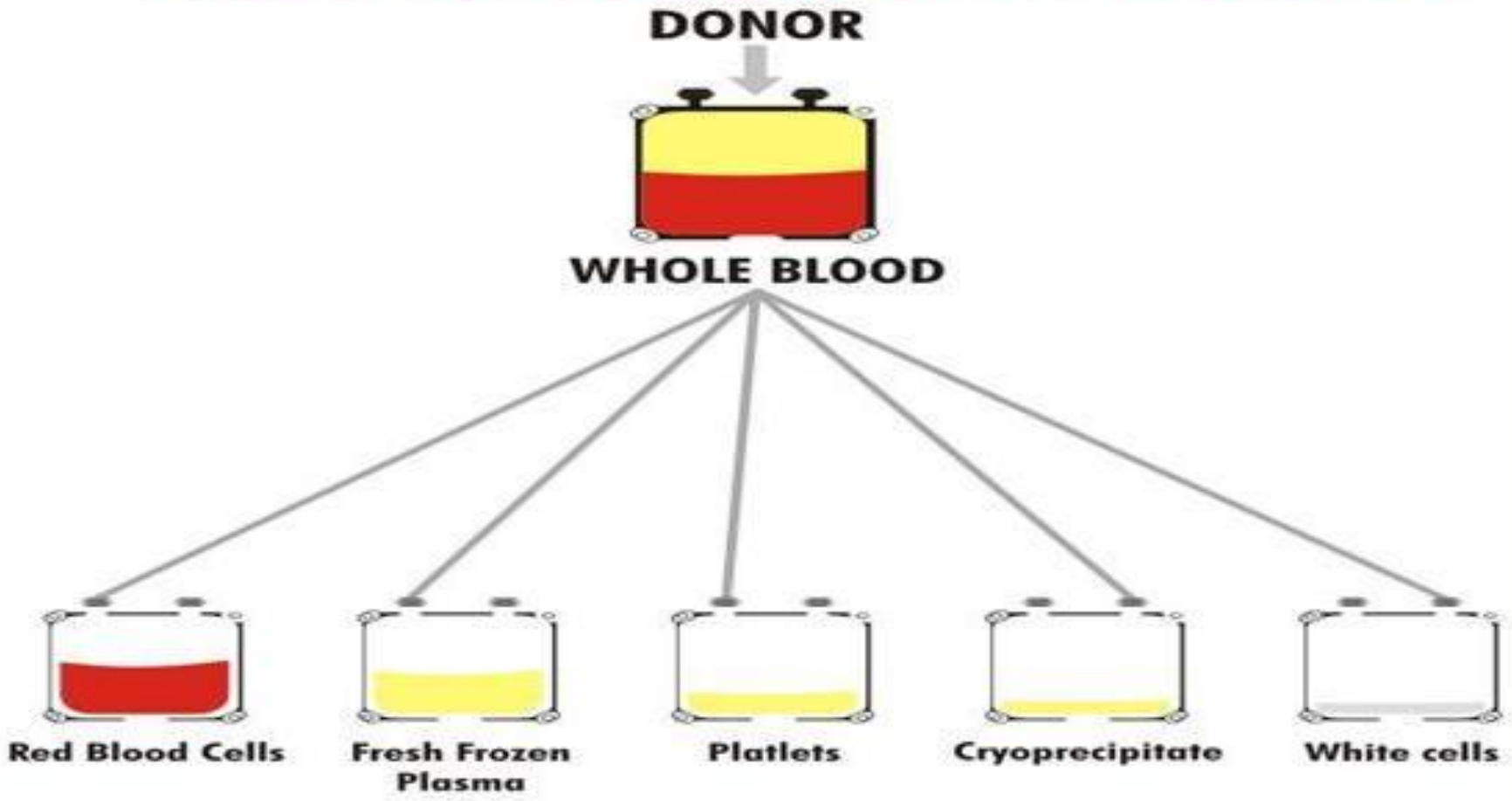

800 ml PRIMARY PVC PLASTIC BAG
COLLECTION SYSTEM
Crossmatch segments
8"
Sterilely dock to glycerolization harness
Plasma
Platelets
Supernatant Glycerol
Red Cells


GRIFOLS


FK 31609
GIFT FROM A VOLUNTARY BLOOD DONOR
Affix Collection/Processing I.D. Label Here
040624AF
TERUMO CORPORATION
Store Platelets 5 days at 20-24°C
Store Red Blood Cells 42 days at 1-6°C
TERUFLEX
AS-5 RED CELL PRESERVATIVE SOLUTION


Whole Blood
Processed within
8 hours)
Packed red blood cells
Fresh frozen plasma
Platelets

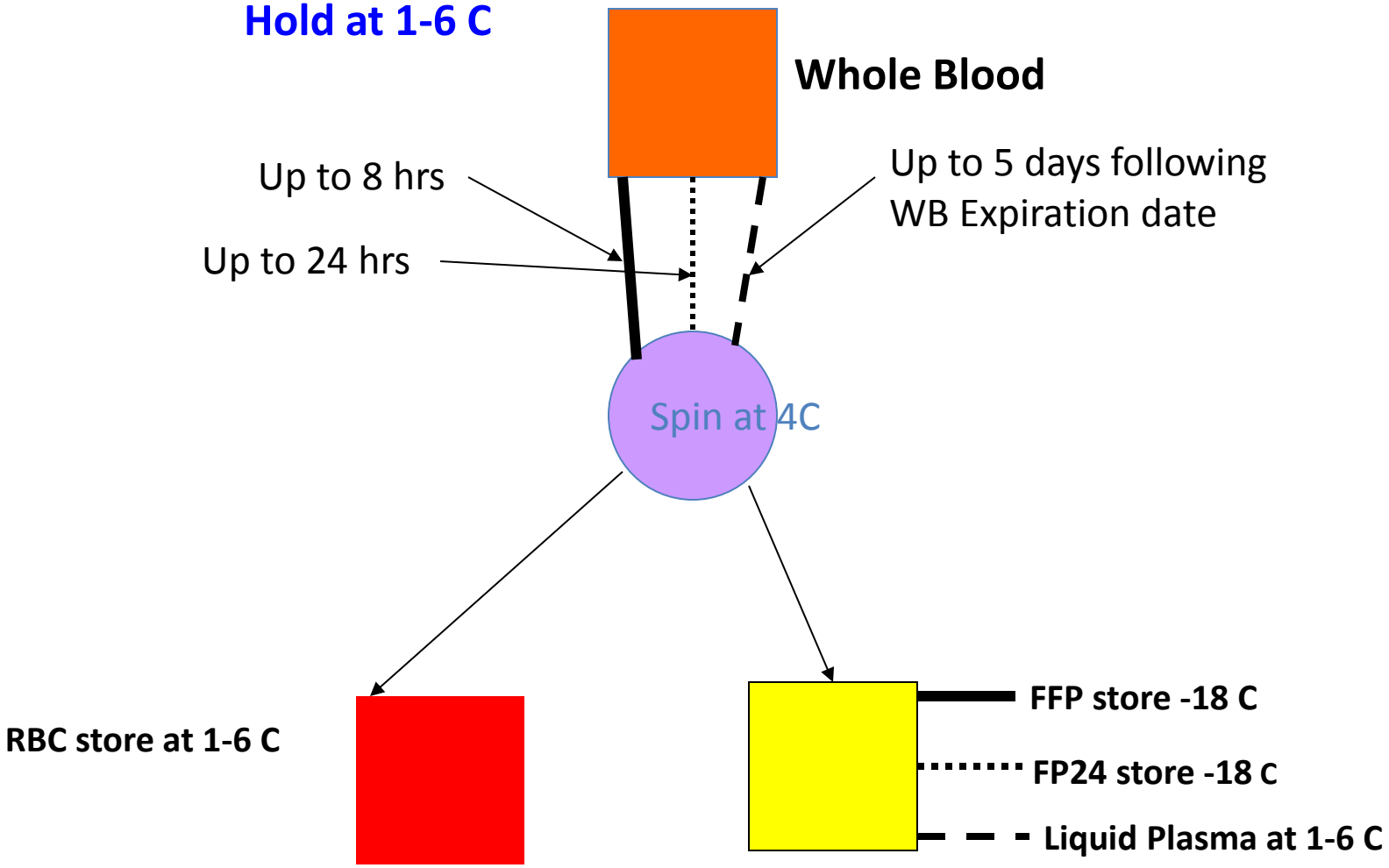
Your blood can save 4 lives.




GRIFOLS

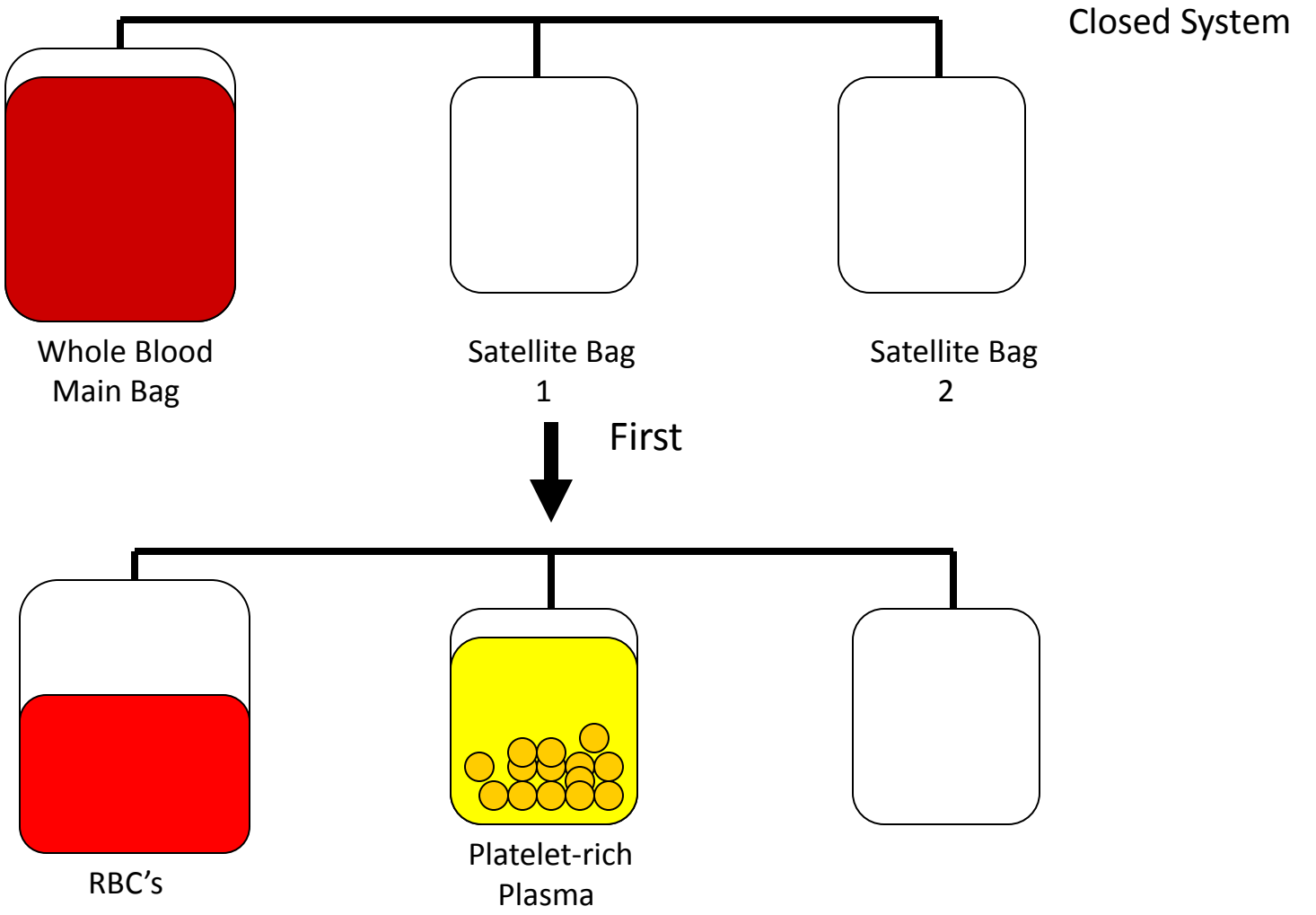

BECKMAN
13

Preparation of RBC, FFP, FP24, and Liquid Plasma

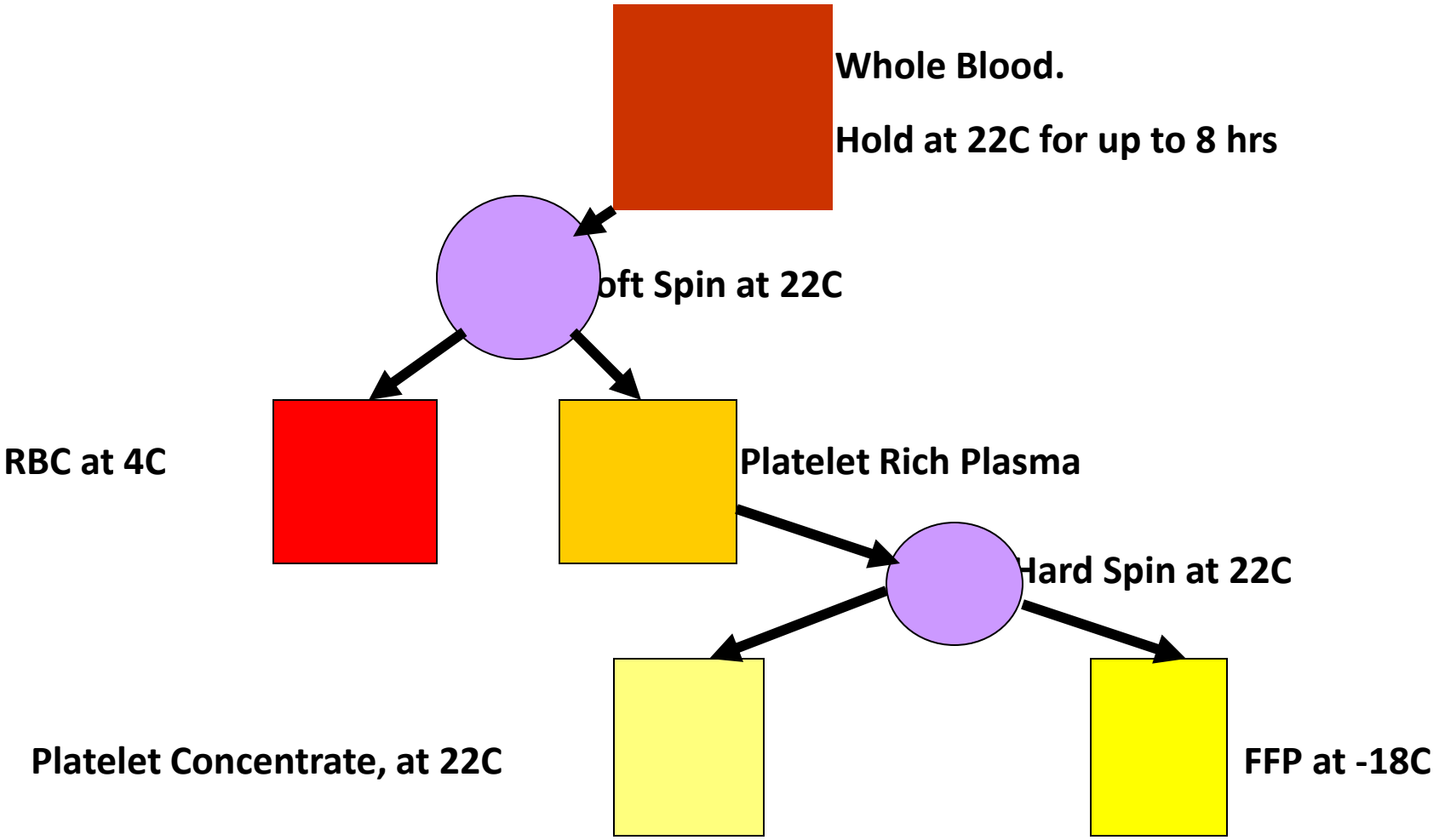


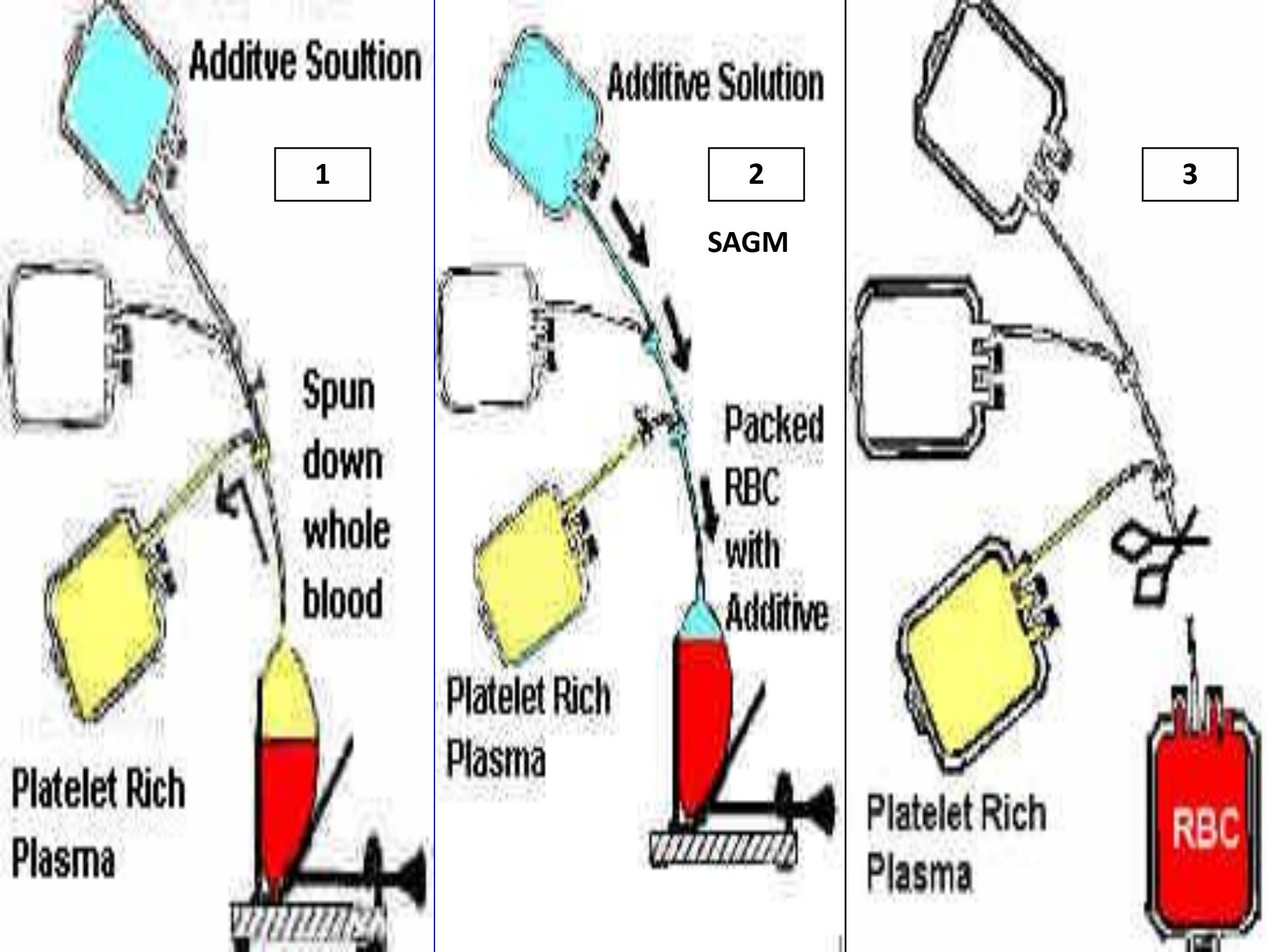
Differential Centrifugation

First Centrifugation



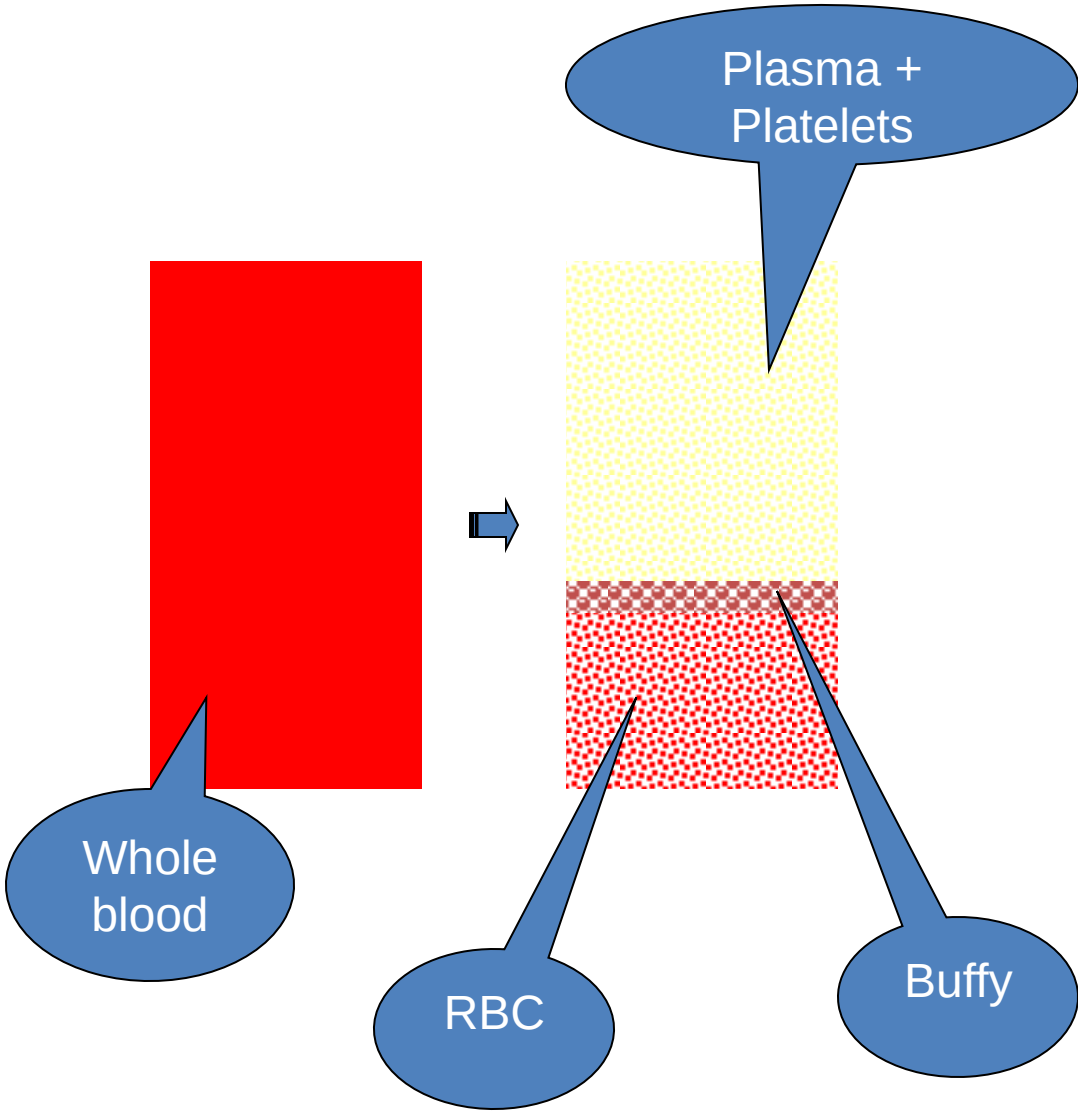
Preparation of RBC, FFP, and Platelets




Additve Soultion
1
Spun down whole blood
Platelet Rich Plasma
Additive Solution
2
SAGM
Packed RBC with Additive
Platelet Rich Plasma
3
Platelet Rich Plasma
RBC

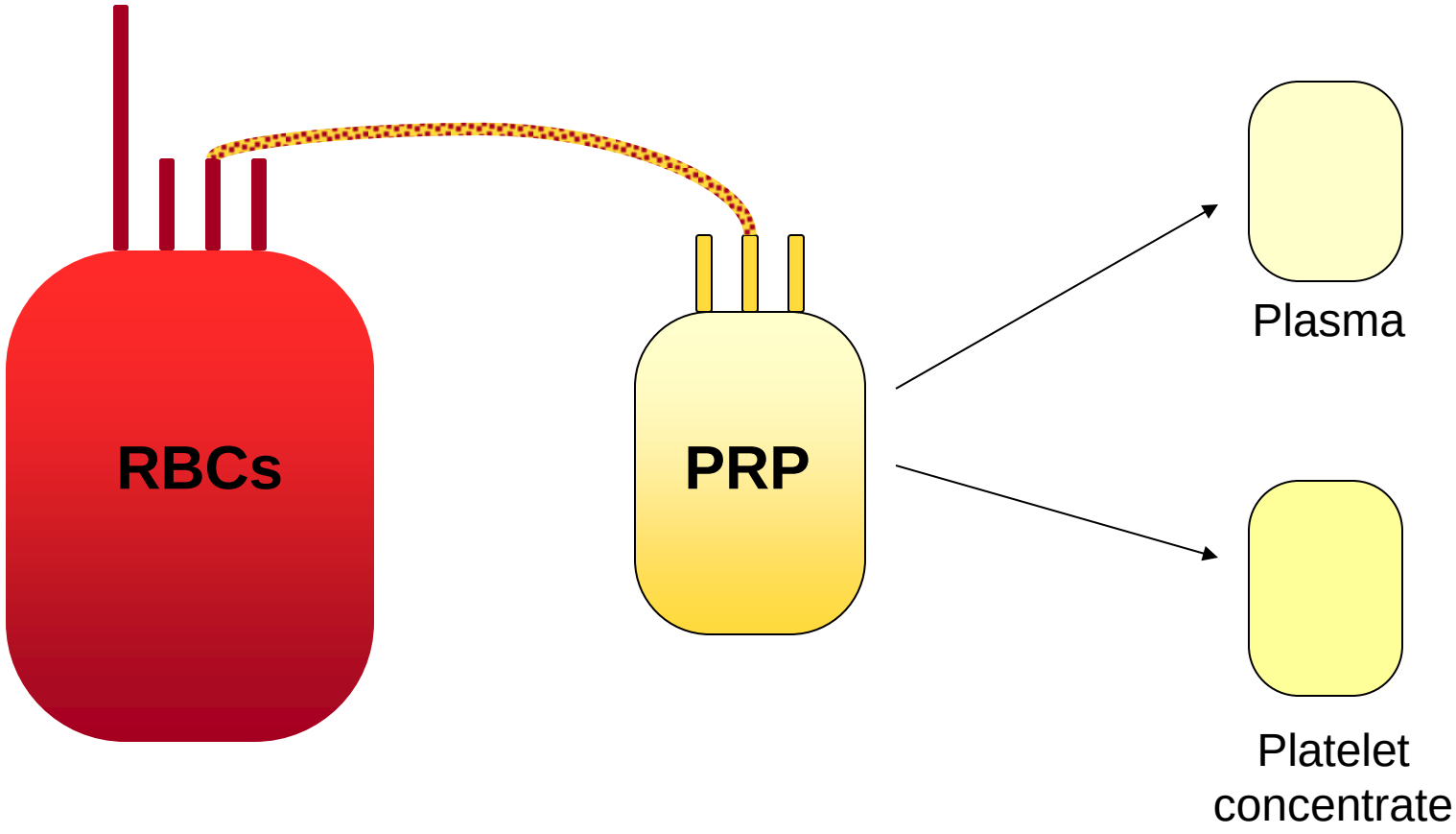
Component preparation

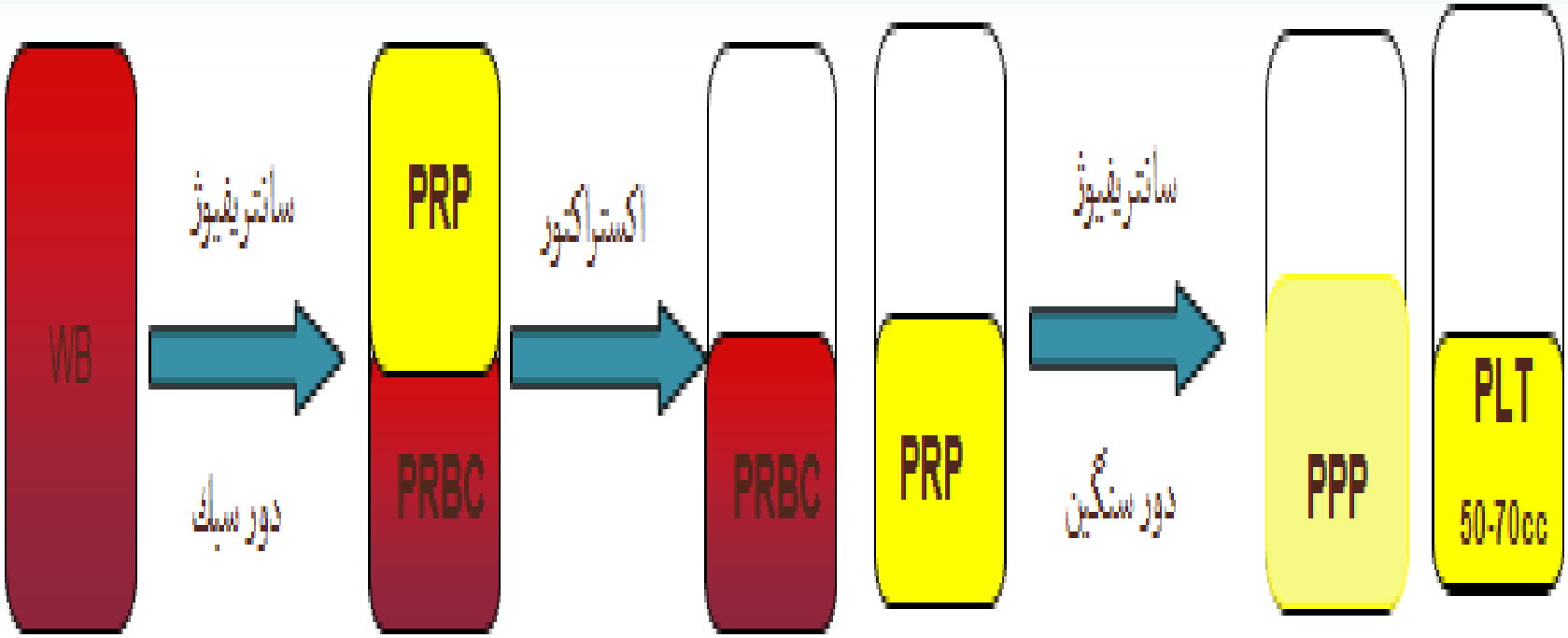
- Principle - Differential centrifugation
- Red cells
  - Packed cells
  - Red cells + additive
- Plasma
  - Bank plasma
  - Fresh frozen
  - Cryo supernate
- Platelets
  - Platelet rich concentrate
  - Platelet rich plasma
- Cryoprecipitate

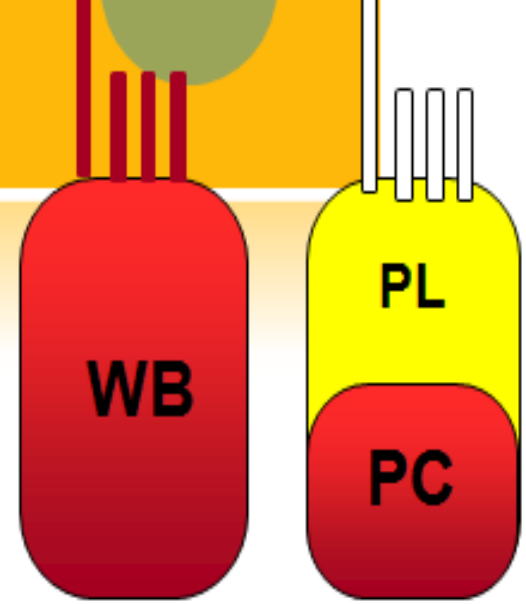



lmb
A
D

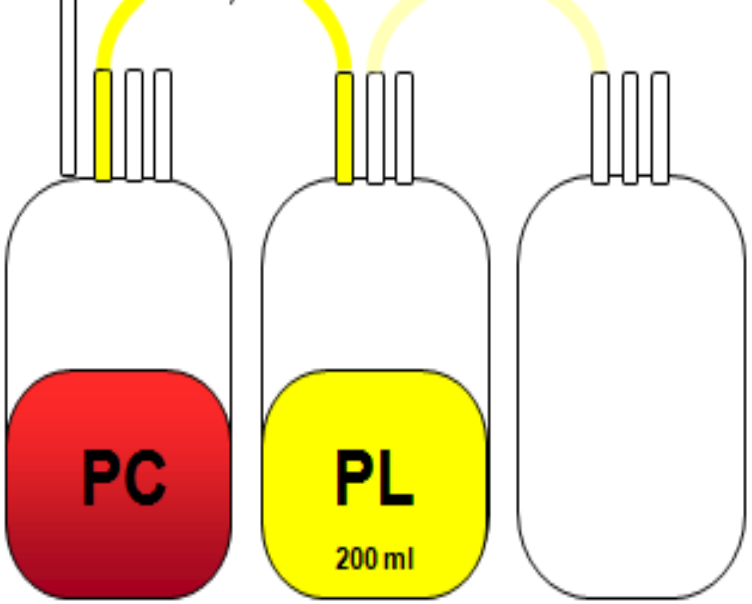
Preparation of platelet concentrate

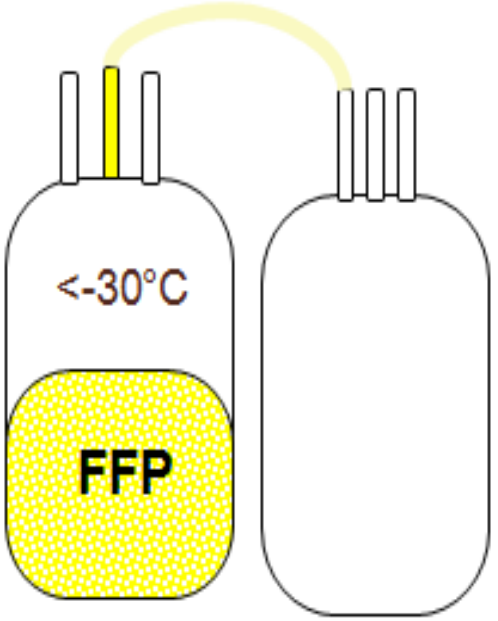


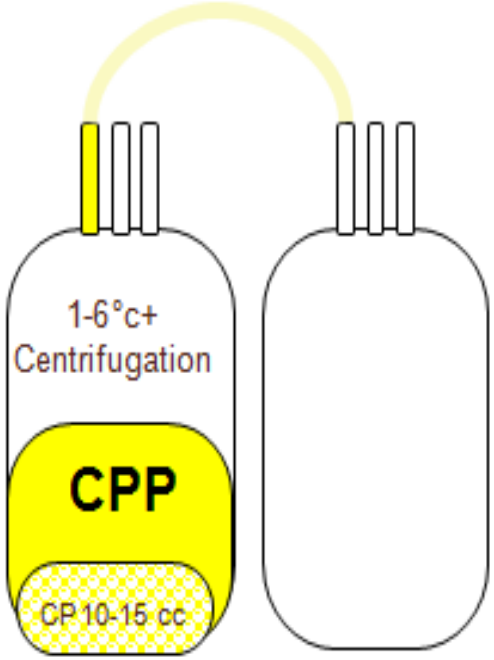

WB
سانتریفیوژ
دور سبک
PRP
PRBC
اکستراکتور
PRBC
PRP
سانتریفیوژ
دور سنگین
PPP
PLT
50-70cc

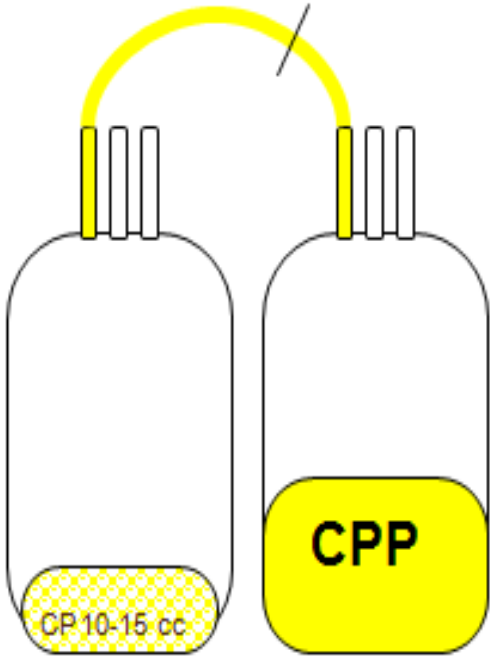

WB
PL
PC

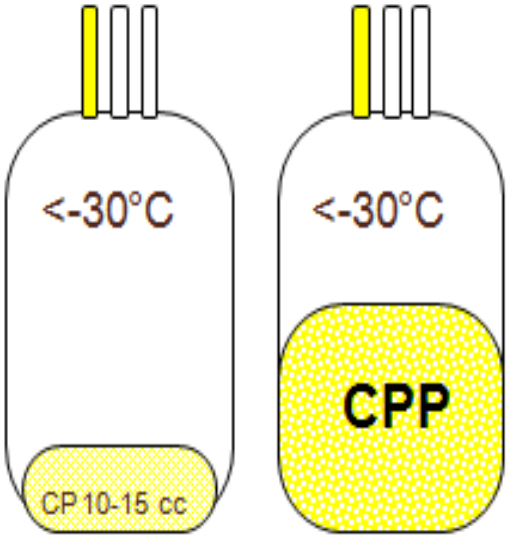
High spin


PC
PL
200 ml


<-30°C
FFP


1-6°c+
Centrifugation
CPP
CP 10-15 cc


CP 10-15 cc
CPP


<-30°C
<-30°C
CP 10-15 cc
CPP

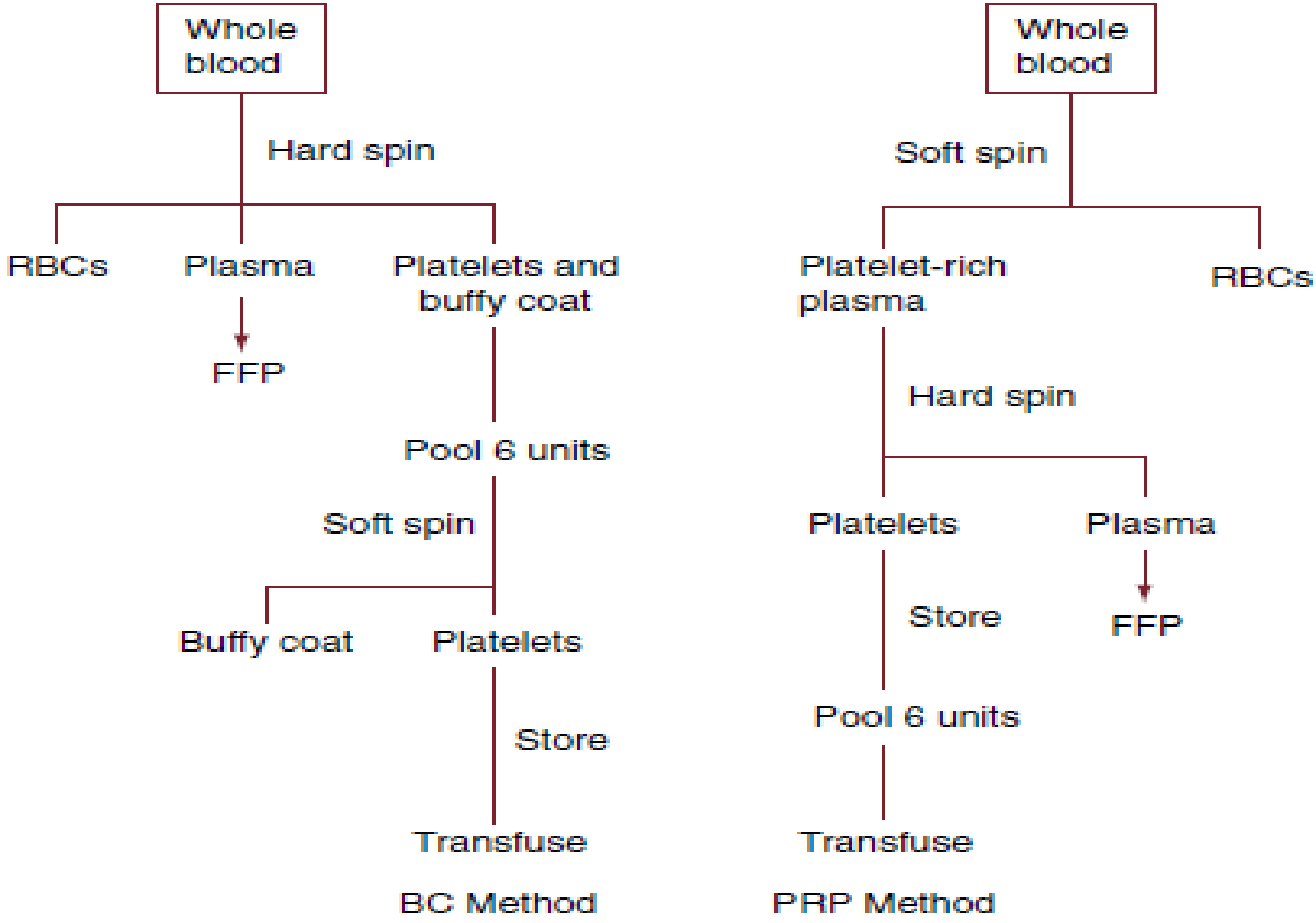
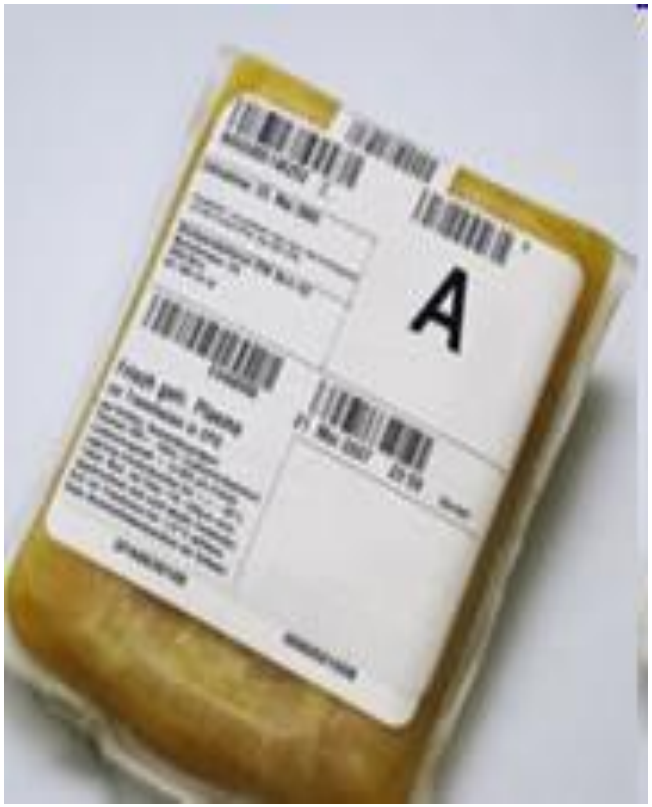


Figure 5.3 Comparison of platelet-rich plasma (PRP) and buffy coat (BC) methods of platelet preparation

Plasma


A


Blood Bank
25790
AHMED MOHAMMED LAB
KAUH
PLASMA BAG
UNIT ID: 25790R
FFP
A Rh "D" P
Taken : 14 – DEC – 03
Expires : 13 – DEC – 04
This unit was tested and found non reactive to :
HIV 1&2 , HCV , HbsAg
P24 Antigen, HTLV 1&2
Syphilis, Core Antibodies
3PA0030271
KAUH - Haematology Department

PLASMA TRANSFUSION

- Plasma Prophylaxis for Invasive Procedures
- Before performing invasive procedures physicians often transfuse plasma to patients with modest abnormalities in coagulation tests [eg,theprothrombin time/international normalized ratio (PT /INR) or activated partial thromboplastin time (aPTT)], with the goal of reducing the bleeding risk

- In most cases, this practice exposes patients to all the risks of plasma transfusion without providing a real benefit.
- This is because
- 1) mild-to-moderate abnormalities in test results like the INR fail to predict bleeding in non bleeding individuals;
- 2) modest elevations in the INR are usually not corrected to normal by plasma transfusion;
- 3) prior RCTs and observational studies failed to show that prophylactic plasma transfusions affect bleeding outcomes

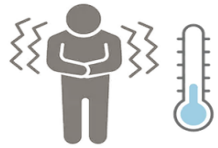
Plasma Transfusions to Treat Bleeding

- Plasma transfusion is indicated for bleeding patients with multiple coagulation deficiencies (eg, liver disease, DIC).
- It is also indicated to manage patients with specific plasma protein deficiencies (eg, Factor XI deficiency) for which a licensed coagulation factor concentrate is not available

1. **T**rigger plan 

2. **T**eam 
3. **T**ranexamic acid 

4. **T**est hourly 

5. **T**ransfuse to target 
6. **T**emperature management 
7. **T**erminate the code 

Massive Transfusion Protocols

- "Massive transfusion" is most often defined as transfusion of adults with 10 or more RBC units in a 24-hour period, although other definitions (eg, 4 RBC units in 1 hour) are also used
- In the past, trauma patients with substantial blood loss were typically treated with RBC transfusions plus crystalloid, with hemostatic products such as platelets, plasma, and cryoprecipitate administered based on laboratory test results.
- In recent years, this approach was largely superseded by a more aggressive and empiric approach, whereby the initial resuscitation of trauma patients is focused on early transfusion with plasma, platelets, and RBCs in a fixed ratio (eg, 1:1:1; note: for platelets, the "1" refers to a single whole-blood derived platelet concentrate and not 1 apheresis platelet unit).
- These fixed ratios are intended to approximate the transfusion of whole blood through a combination of components in order to prevent dilutional coagulopathy.
- The fixed ratio or "formula-based" approach was devised by military physicians during the Iraq and Afghanistan wars of the 2000s.
- Currently, it is common for blood banks to incorporate fixed ratios of blood components (ie, 1:1:1 or 1:1:2) into their local massive transfusion protocols (MTPs).

Massive Transfusion Protocols

- Laboratory based, targeted transfusion of specific components is often used after the patient has stabilized.
- It is important to note that although much of the data on MTPs relates to trauma, in civilian hospitals, massive transfusions are actually more likely to occur among other patient populations (eg, solid-organ transplant patients and cardiac surgical patients).

Massive Transfusion Protocols

- Group AB plasma is a preferred blood component in trauma MTPs before blood group determination because it lacks anti-A and anti-B. However, because AB plasma is in short supply due to the low frequency of type AB donors (-4%), group A plasma has been used in several centers as an alternate to AB plasma.
- Studies of group Band AB trauma patients who have received group A plasma support the safety of this practice, although the data are limited.

THE 7 Ts OF MASSIVE HEMORRHAGE PROTOCOL

EMERGENCY MEDICINE CASES

Adapted from
EM Cases Episode 153:
The 7 Ts of Massive Hemorrhage Protocols
Infographic by Pouria Rezapour

1 TRIGGERS for activation

Guided by **clinical judgement** and **decision tools**

Prehospital
- Concerning mechanism
- Shock index ≥1

Initial ED Assessment
- RABT score ≥2
- ABC score ≥2
- Shock index ≥1
- Δ Shock index >0.1

During Resuscitation
- Requiring >2u pRBC

Have a lower threshold for activation in **elderly**, **anticoagulation**, **meds** blunting hemodynamic response (eg. beta blockers)

2 TEAM

Early **notification** and **preparation** of extended team:

- ED team
- Lab
- Blood Bank
- Surgery

3 TESTING

Hourly:
- Hgb
- INR
- **Fibrinogen**
- **Ca**
- K
- Lactate
- VBG

(Temp, below)

Initial:
- Above plus:
- Group & screen
- PTT

4 TRANEXAMIC ACID

Trauma

Initiate within 3h
1g IV over 10min then
1g over 8h
Alternative: 2g over 20min

GI Bleed

No evidence of mortality benefit with possible risk of harm

5 TEMPERATURE

Target ≥36°C, ↑ bleeding risk per 1°C decrease

Remove wet clothing and cover appropriately

Provide **warmed** intravenous products

Monitor check temp at least **hourly**

6 TARGETS

Hematologic	Metabolic
Hgb >80	pH >7.3
Plt 50*	Lactate <4
INR 1.8	Ca_i >1.15
Fibrinogen 1.5–2	

*In head injury target Plt 100

7 TERMINATION of MHP

General requirements:

1. Normalizing **hematologic & metabolic** targets
2. Normalizing **hemodynamic** parameters

Take care to avoid common pitfall of **premature MHP termination**.
Significant trauma may cause **peri-trauma vasoplegia** despite appropriate resuscitation.

SJRH 2013 MASSIVE TRANSFUSION (MT) FLOW DIAGRAM

MASSIVE BLOOD LOSS

Any one or more of the following:
- Potential for bleeding >150 mL/min (~2L/15 mins)
- Potential for loss of >50% of blood volume in 3h
- Requirement of >4RBCs in 4h in an adult and 40 mL/kg in a child

TRAUMA PATIENTS CONSIDER EARLY FOR ADULTS:
Tranexamic acid 1000 mg IV over 10 mins then 1000 mg IV over 8 hours (*IF <3HOURS SINCE TIME OF INJURY*)

ACTIVATE MT PROCEDURE

MT PHYSICIAN

re-draw q 30-60 mins

- ORDER Routines, Coags Mg, Ca, Fibrinogen, ABO, Rh, and AB detection, VBG & lactate
- Sign for uncrossmatched blood

LIMIT CRYSTALLOID

MAINTAIN NORMOTHERMIA - keep temp >35^{o}C

MAINTAIN SBP ~90 mmHg (or if Head Injury, 100 mmHg)

Adjust management if patient is anticoagulated or has a known bleeding disorder (PCC, Factor, etc) - SEE REVERSE

MT NURSE

- Level 1 Rapid Transfuser READIED
- Patient armband with TWO identifiers
- Bloods drawn, labelled & sent
- Maximize room temperature
- Notify TM when ABO, Rh and AB detection specimen sent
- Notify TM STAT if change in patient location or deactivation of MT procedure
- Complete TM product acknowledgement orders

TM TECHNOLOGIST

TM technologist can be reached at ext 7154 or 6535

ADULTS**
- RBCs 4 UNITS
- PLATELETS 1 DOSE
- PLASMA 500 mL

PEDIATRICS**
- RBCs 15 mL/kg
- PLATELETS 5-10 mL/kg
- PLASMA 10-15 mL/kg

prepare and send q30 mins

**Dosing requirements @ discretion of MT Physician

LAB GOALS:

INR ≤ 1.7	Hgb 70-100 g/L
Fibrinogen ≥ 1g/L	pH ≥ 7.1
pTT ≤ 45s	Ca ≥ 1.15 mmol/L

PLTs >75x10^{9}/L (or >100x10^{9}/L if CNS bleed)

ANTICIPATE THESE COMPLICATIONS
Hypothermia
Hyperkalemia
Hypocalcemia
Transfusion reactions
Abdominal compartment syndrome

Warfarin Reversal

- During clot formation, several coagulation factors such as Factors II, VII, IX, and X associate with the surface of activated platelets via hydrophobic protein domains called gammacarboxyglutamic acid (Gla) domains.
- Gla domains help ensure that when activated, coagulation factors localize where they are needed to provide full hemostatic function. To form Gla domains, specific glutamic acid (Glu) residues must undergo posttranslational gammacarboxylation.
- The reduced form of vitamin K is required to contribute electrons to these carboxylation reactions. In the process, vitamin K becomes oxidized. Enzymes called vitamin K epoxide reductases serve to recycle vitamin K back to its "useful" reduced form sogammacarboxylation reactions

- Warfarin, which is structurally similar to vitamin K, competitively inhibits the epoxide reductases.
- Thus, warfarin intake causes a deficiency of reduced vitamin K, which in turn causes decreases in the functional activity of Factors II (thrombin), VII, IX, and X, as well as antithrombotic factors: proteins C and S.

Types of Plasma

- Several varieties of plasma are available for transfusion, including Fresh Frozen Plasma (FFP), Plasma Frozen Within 24 Hours After Phlebotomy (FP24), and solvent/ detergent treated plasma (SD plasma) .
- By definition, FFP is frozen within 8 hours of collection and transfused within 24 hours of thawing, to preserve levels of the most heat -labile coagulation factors, Factors VIII and V. Many transfusion services provide Thawed Plasma, which is plasma that has been thawed and maintained in a closed system at l to 6 C for 24 hours

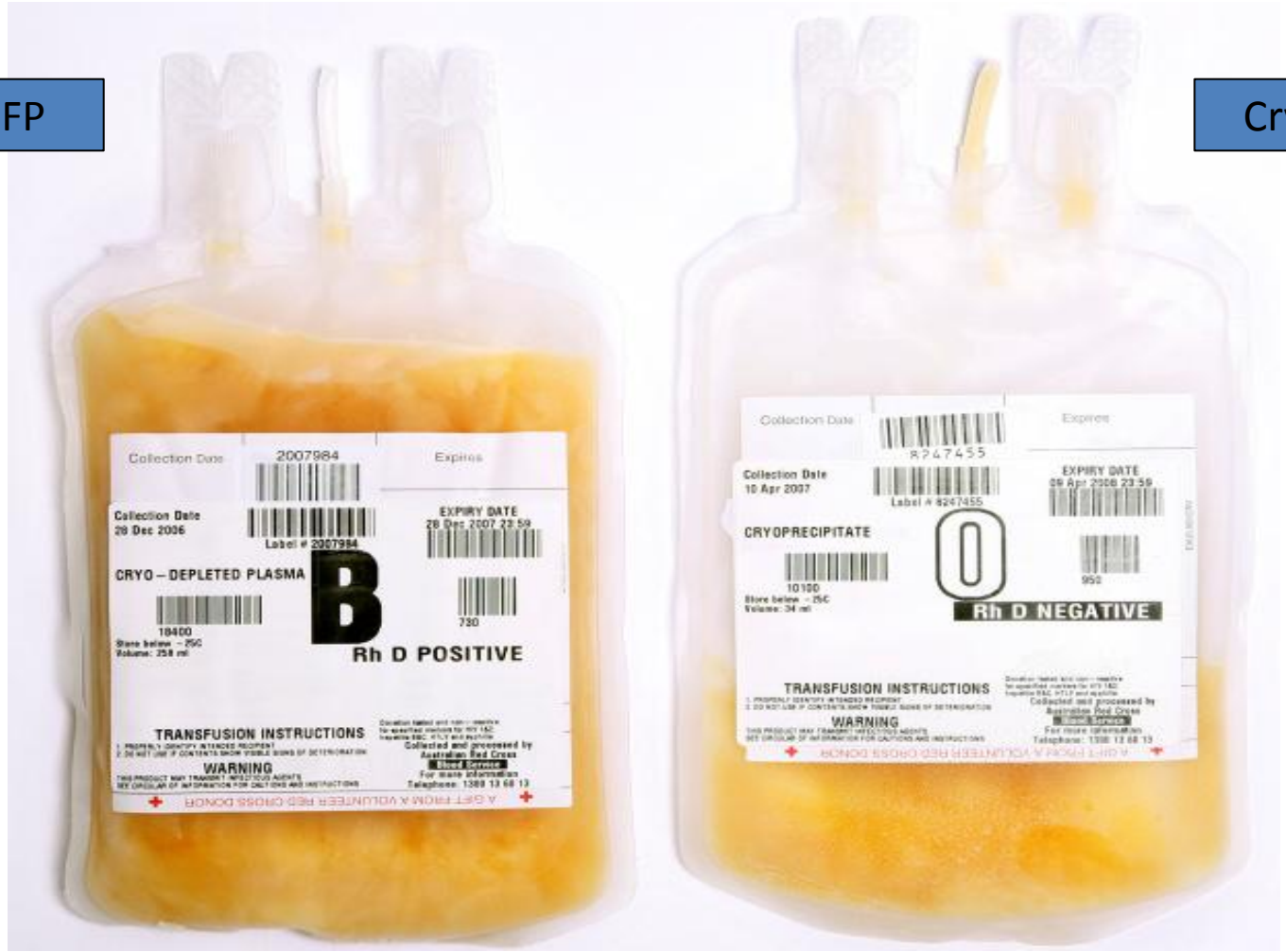
CRYOPRECIPITATE TRANSFUSION

- Cryoprecipitate is a plasma derivative that is relatively enriched for fibrinogen, Factor VIII, von Willebrand Factor (vWF), fibronectin, and Factor XIII.
- There are limited indications for cryoprecipitate, as there are pathogen reduced products and recombinant products available for several of the indications where cryoprecipitate was used previously

Cryoprecipitate

FFP

Cryo



Cryoprecipitate

Quality Control

5.1 Storage and shelf life:[9.1]

Component	Shelf life when frozen	Shelf life when thawed
Cryoprecipitate (CRYO)	12 months at -18°C or colder	Pooled/Open system: Up to 4 hours stored at 20-24°C if pooled. Must not be re-frozen

Thawing and Pooling Cryoprecipitate

5.2 The temperature of the waterbath/ thawing device used to thaw cryoprecipitate must be checked and documented each time the equipment is used.[9.2]

5.3 The waterbath/thawing device used for thawing blood components should be cleaned on a regular basis and whenever there is a risk of contamination (i.e., leaking of a blood product container).

5.4 Cryoprecipitate is thawed in a plastic over-wrap to prevent contamination of the ports.[9.2]

5.5 Waterbaths and other heating devices used to thaw blood products shall not be used for incubation of tests containing biological specimens.[9.2]

5.6 Cryoprecipitate must be thawed at a temperature of 30 to 37°C. or by use of an approved thawing device.[9.2]

5.7 Automated thawing devices may be used for thawing cryoprecipitate. The manufacturer's instructions must be followed.

6.1	Check level of water in waterbath. If the water level is low, add warm water and allow the temperature to equilibrate to an acceptable temperature (30°C-37°C).
6.2	Remove the number of cryoprecipitate units from the freezer as requested. One unit of cryoprecipitate contains approximately 285g of fibrinogen. An order for 10 units of cryoprecipitate for an average sized adult patient is typical at many hospitals (1-2 units of CRYO per every 10kg body weight)[9.1]
6.3	Carefully inspect each bag for signs of cracking or breakage, especially around the ports at the top of the unit.
6.4	Place units in a plastic over-wrap bag. Each over-wrap bag should contain no more than 2 units. See Procedural Notes 8.1.

6.5	Compress the bag around the cryoprecipitate to remove as much air as possible. Secure the top of the bag with a clamp or a hemostat, if desired.	
6.6	Read and record the temperature of the waterbath/thawing device. The temperature must be 30°C to 37°C.	
6.7	Place the wrapped cryoprecipitate into the waterbath/thawing device.	6.7.1 Weights may be placed on top of the units to keep them submerged and speed thawing.
		6.7.2 Keep the end of the plastic bag above the water level to prevent contamination of the ports.
6.8	Check the cryoprecipitate every 5 minutes. Gently knead the thawed units to re-suspend the cryoprecipitate. Thawing time should not exceed 10 minutes. For automated heating devices, set timer for 5 minutes.	
6.9	Remove the cryoprecipitate bag(s) from the waterbath/thawing device when thawing is complete.	
6.10	Inspect each unit(s) for evidence of leaking and perform visual inspection. See IM.003 – Visual Inspection of Blood, Blood Components and Fractionated Products.	6.10.1 If the container(s) is not intact or does not meet visual inspection criteria, discard as per IM.005 - Final Disposition of Blood, Blood Components and Other Related Products Not Suitable for Transfusion Manual Procedure. Select a different unit from the freezer.
6.11	Assemble materials in designated pooling area. See Quality Control 5.8.	
6.12	Re-suspend the thawed cryoprecipitate carefully and completely, either by kneading it into the residual 10 -15 mL of plasma or by adding approximately 10 mL of 0.9% sodium chloride (normal saline for IV use) and gently re-suspend.	6.12.1 Wearing clean gloves remove a plasma transfer set from its package and close the clamp on the line.
		6.12.2 Using aseptic technique, loosen but do not remove the cap from one end of the transfer set.
		6.12.3 Remove the protective cap from one port of the IV saline bag.
		6.12.4 Remove the cap from the transfer set and insert into the port of the IV saline bag.
		6.12.5 Remove the protective cap from one port of one of the cryoprecipitate bags.
		6.12.6 Using a similar technique, insert the other end of the plasma transfer set into the first cryoprecipitate bag.

	6.12.7 Elevate the saline bag and open the clamp of the transfer set and allow 10 mL of saline to flow into the first cryoprecipitate bag. Clamp the transfer set and mix thoroughly to resuspend the precipitate.
6.13	Transfer the contents of the first bag to the next bag and each subsequent bag using the ever increasing volume to flush the dissolved cryoprecipitate until all contents are in the final bag.
6.14	Use a tubing stripper to ensure as much as possible of cryoprecipitate mixture flows into the last bag.
6.15	Close the clamp. Use a tube sealing method (heat sealer or hand sealer and clips) to seal the tubing three times. See Procedural Notes 8.2.
6.16	Cut the tubing, leaving two seals close to the cryoprecipitate bag.
6.17	Record the lot number and expiry date of 0.9% sterile IV saline added.
6.18	Prepare the label for the pooled cryoprecipitate bag with the following modified component information:[9,2] • Product name (e.g., pooled cryoprecipitate) • Number of units in pool • Name of facility preparing component • Unique numeric or alphanumeric identification of pooled component. See Procedural Notes 8.3 • ABO of pooled component (if all units of same ABO) • Approximate volume of pooled component • Date and Time of expiry of pooled component Label the pooled cryoprecipitate bag with the following recipient information: • Recipient's family and given name(s) • Recipient's identification number(s) • ABO group of recipient
6.19	Attach the compatibility/component label to the bag of pooled cryoprecipitate.
6.20	Issue product. If there is no computer system used to issue blood components, write the patient and product information onto the Issue/Transfusion record. See Procedural Notes 8.4 and IM.004-Manual Issuing of Blood, Blood Components and Other Related Products Using the Issue/Transfusion Record.
6.21	Store at 20-24°C until issue

Cryoprecipitate

- Cryoprecipitate is suggested for fibrinogen replacement for acquired hypofibrinogenemic conditions such as liver transplantation and postpartum hemorrhage Pathogen reduced concentrates are standard-of-care to treat Factor VIII deficiency, congenital hypofibrinogenemia, dysfibrinogenemia, and von Wille brand disease. Congenital Factor XIII deficiency, associated with a delayed bleeding phenotype, is extremely rare, and there is now a recombinant Factor XIII concentrate available.
- Fibronectin is not currently used as a therapeutic agent. Thus, cryoprecipitate is primarily used to replace fibrinogen in patients who are bleeding or having invasive procedures

Cryoprecipitate

- Plasma, cryoprecipitate, and fibrinogen concentrate are all sources of fibrinogen. However, the volume of plasma needed is considerably larger than that of cryoprecipitate to achieve the same replacement dose of fibrinogen (eg, 300- 400 mg of fibrinogen can be replaced with 250 mL of plasma or with only 10-15 mL of cryoprecipitate) .
- Fibrinogen concentrate is also a low-volume option, and it has the additional advantages of being pathogen reduced and requiring no thawing time. To date, cryoprecipitate and fibrinogen concentrate have not been directly compared in clinical studies.

Cryoprecipitate

- Cryoprecipitate is prepared from single-donor plasma by gradual thawing of rapidly frozen plasma.
- This process causes precipitation of proteins rich in fibrinogen, as well as factor VIII.
- Each unit of cryoprecipitate typically yields 100 to 250 mg of fibrinogen, 80 to 100 units of factor VIII, and 50 to 60 mg of fibronectin.
- Cryoprecipitate is a plasma product and therefore requires ABO compatibility
- The volume of each bag unit is approximately 15 to 18 mL.

Transfusion Therapy : Blood and Blood Products James R. Roberts MD, FACEP, FAAEM, FACMT, in Roberts and Hedges' Clinical Procedures in Emergency Medicine and Acute Care, 2019

Cryoprecipitate

- Cryoprecipitate is indicated for the treatment of patients with
- fibrinogen deficiency,
- congenital afibrinogenemia,
- dysfibrinogenemia,
- and factor XIII deficiency
- and in some patients with hemophilia A or von Willebrand's disease.
- It can also be used as a second-line treatment to correct a deficiency in coagulation factor VIII (in hemophilia A) when factor VIII concentrates are not readily available.
- Because cryoprecipitate contains no factor IX, it is of no value in the treatment of factor IX deficiency (hemophilia B).

Transfusion Therapy : Blood and Blood Products James R. Roberts MD, FACEP, FAAEM, FACMT, in Roberts and Hedges' Clinical Procedures in Emergency Medicine and Acute Care, 2019

Cryoprecipitate

- Mild deficiencies in factor VIII are defined as 10% to 30% of normal activity and severe deficiencies as less than 3% of normal activity.
- When treating bleeding, the goal depends on the site and severity of hemorrhage, but in general one should aim for at least 50% of normal factor VIII activity.
- For life-threatening hemorrhage, aim for 100% activity.
- The amount of cryoprecipitate required to correct coagulation defects ranges from 10 to 20 units/kg for minor bleeding, such as hemarthrosis, to 50 units/kg for control of bleeding in surgery or trauma.
- Guide specific replacement by laboratory assay of factor VIII activity.
- The half-life of factor VIII in plasma is 8 to 12 hours.

Transfusion Therapy : Blood and Blood Products James R. Roberts MD, FACEP, FAAEM, FACMT, in Roberts and Hedges' Clinical Procedures in Emergency Medicine and Acute Care, 2019

- Cryoprecipitate may be required to correct significant hypofibrinogenemia (<100 mg/dL). A typical adult dose of approximately 10 bags of cryoprecipitate raises the fibrinogen level by up to 1 g/L (60 to 100 mg/dL). In cases of severe bleeding after the use of a fibrinolytic agent such as tissue plasminogen activator, cryoprecipitate can be used to help control the bleeding. A consensus on dosing has not been reached, but many sources recommend between 10 and 12 bags

  Transfusion Therapy : Blood and Blood Products James R. Roberts MD, FACEP, FAAEM, FACMT, in Roberts and Hedges' Clinical Procedures in Emergency Medicine and Acute Care, 2019

PLASMA PRODUCTS FOR TRANSFUSION

Fresh Frozen Plasma (FFP)

Thawed Plasma

Plasma Frozen within 24 hours of Collection (FP24)

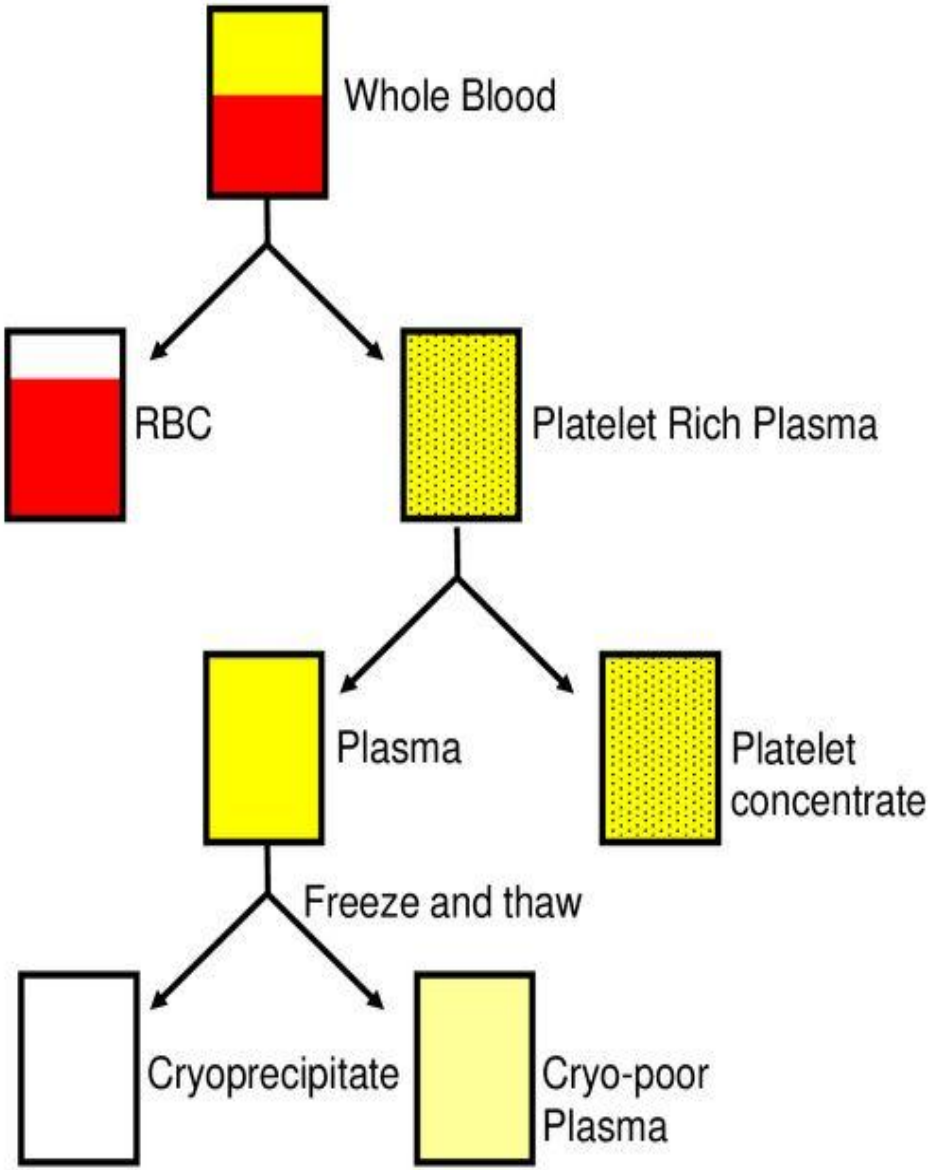
Liquid Plasma

Plasma, Cryoprecipitate Reduced (Cryo-poor Plasma)

Cryoprecipitated AHF (Cryoprecipitate, Cryo)

Fibrin Glue

Whole Blood Separation into Components



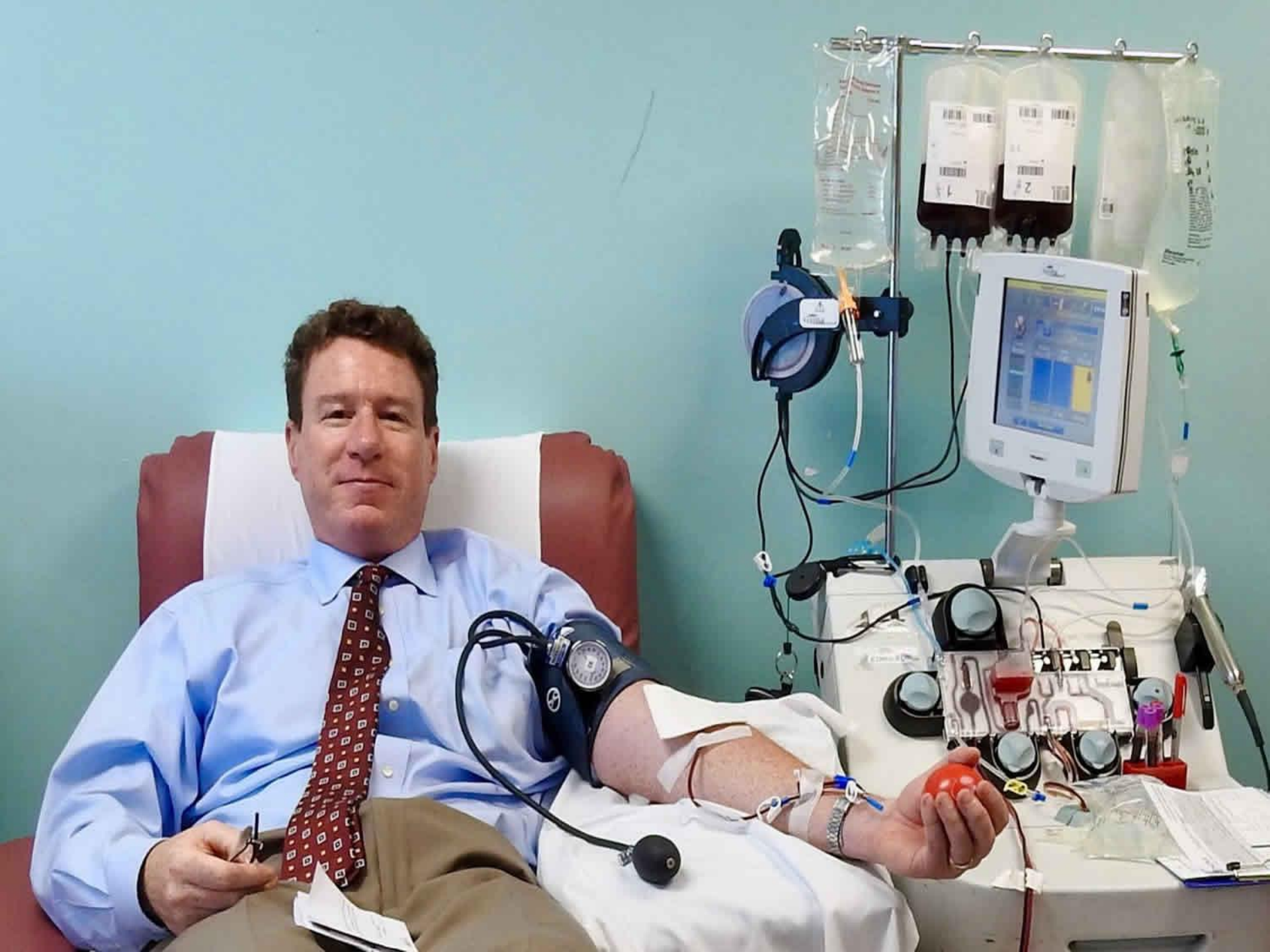
CPP


Code 4R4409
Baxter
CRYOPRECIPITATE POOR PLASMA
Fenwal®
Plasma Container Carton

Cryoprecipitate Poor Plasma

- It is a by-product of cryoprecipitate preparation.
- It lacks labile clotting factors V and VIII and fibrinogen.
- It contains adequate levels of stable clotting factors II, VII, IX & X.
- It is frozen and stored at -20^{0}C or lower

Apheresis Plasma

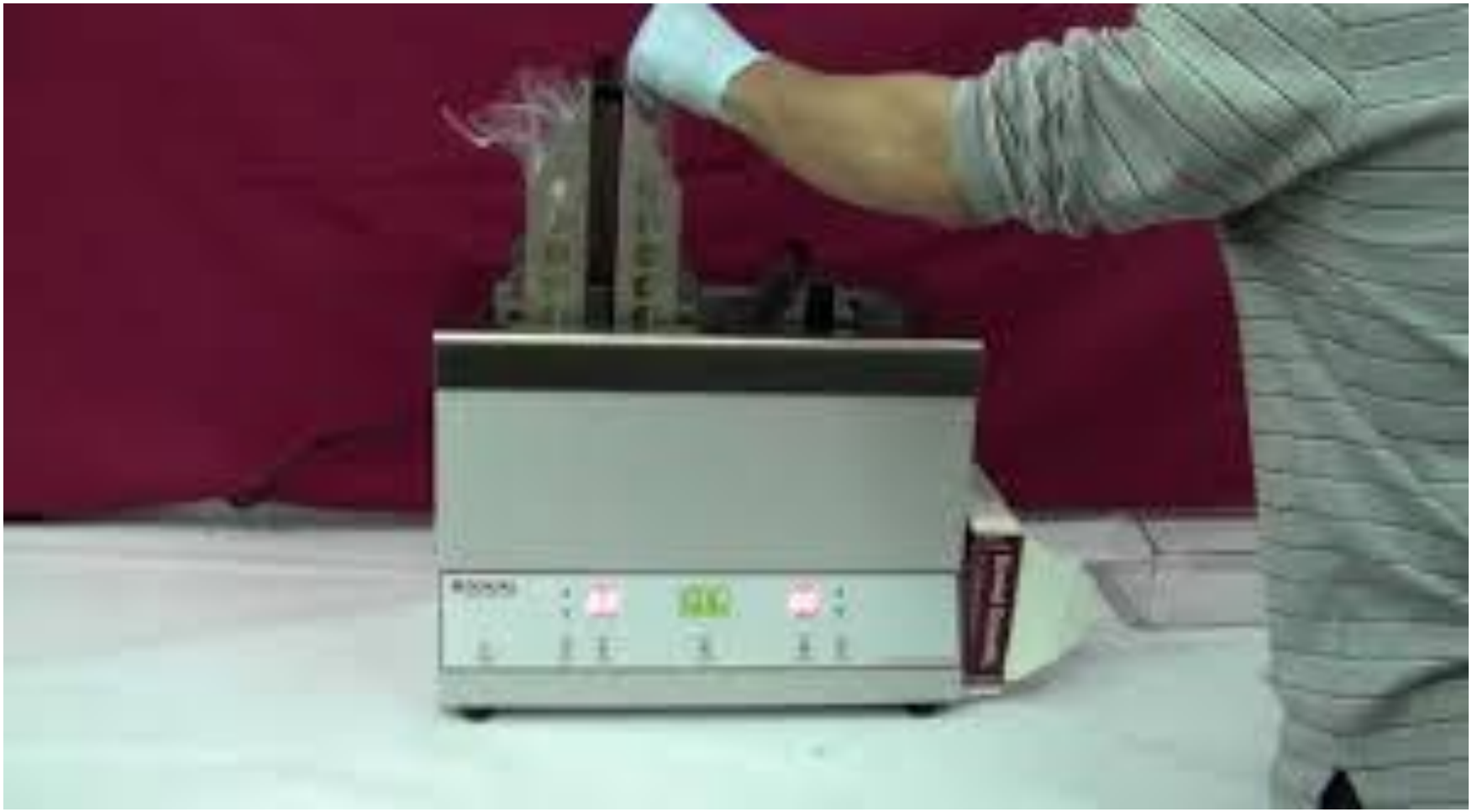


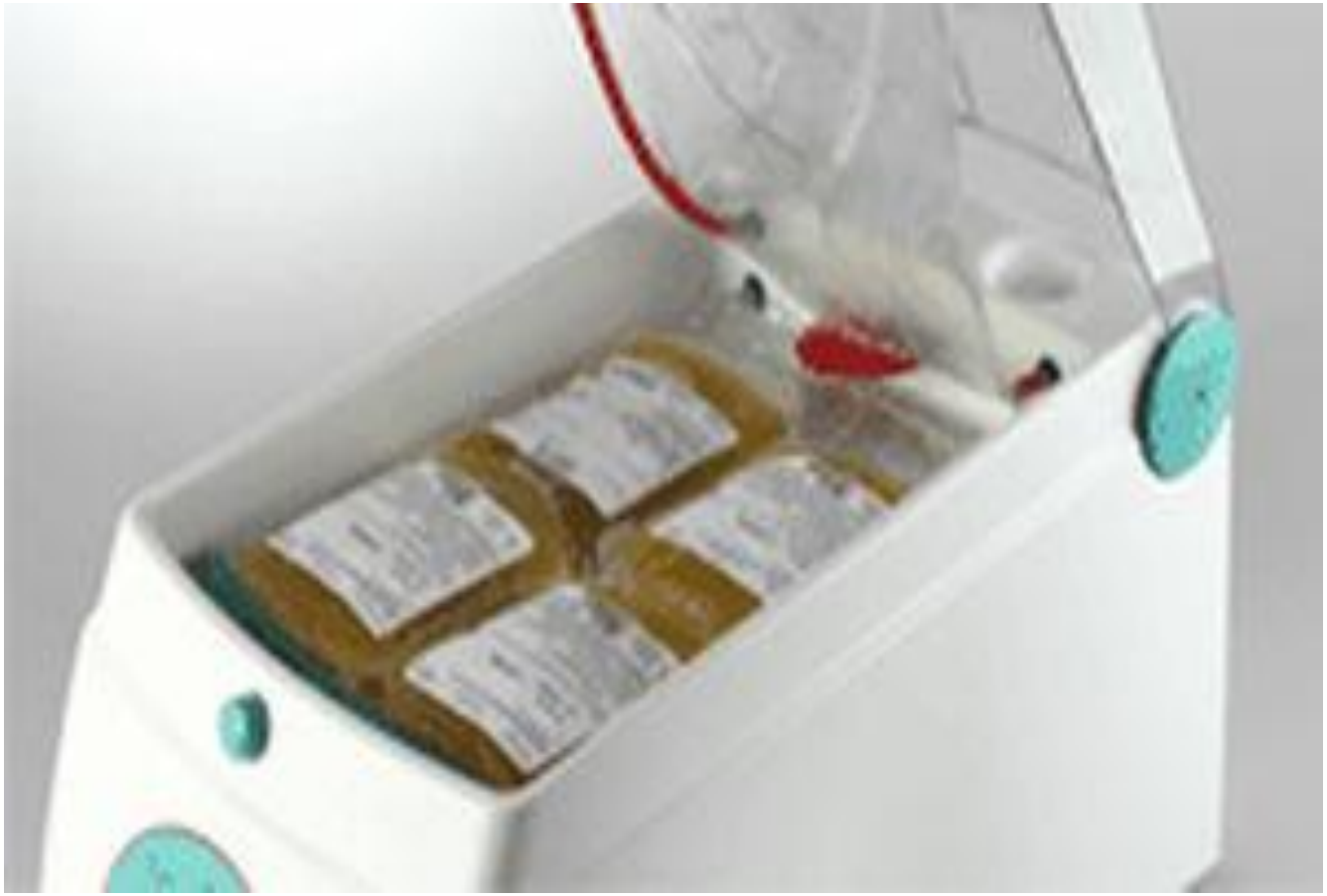
Guideline of thawing plasma

- The water bath used for thawing plasma should be cleaned on a regular basis and whenever there is a risk of contamination (i.e., leaking of a blood product container).
- Plasma is thawed in a plastic overwrap to prevent contamination of the ports
- Water baths and other heating devices used to thaw blood products shall not be used for incubation of tests containing biological specimens.
- Plasma must be thawed at a temperature of 37°C. or by use of an approved thawing device.

- The component should be thawed at 37 °C in a water bath or other equipment designed for the purpose, within a vacuum sealed overwrap bag.
- Protocols must be in place to ensure that the equipment is cleaned daily and maintained to minimize the risk of bacterial contamination

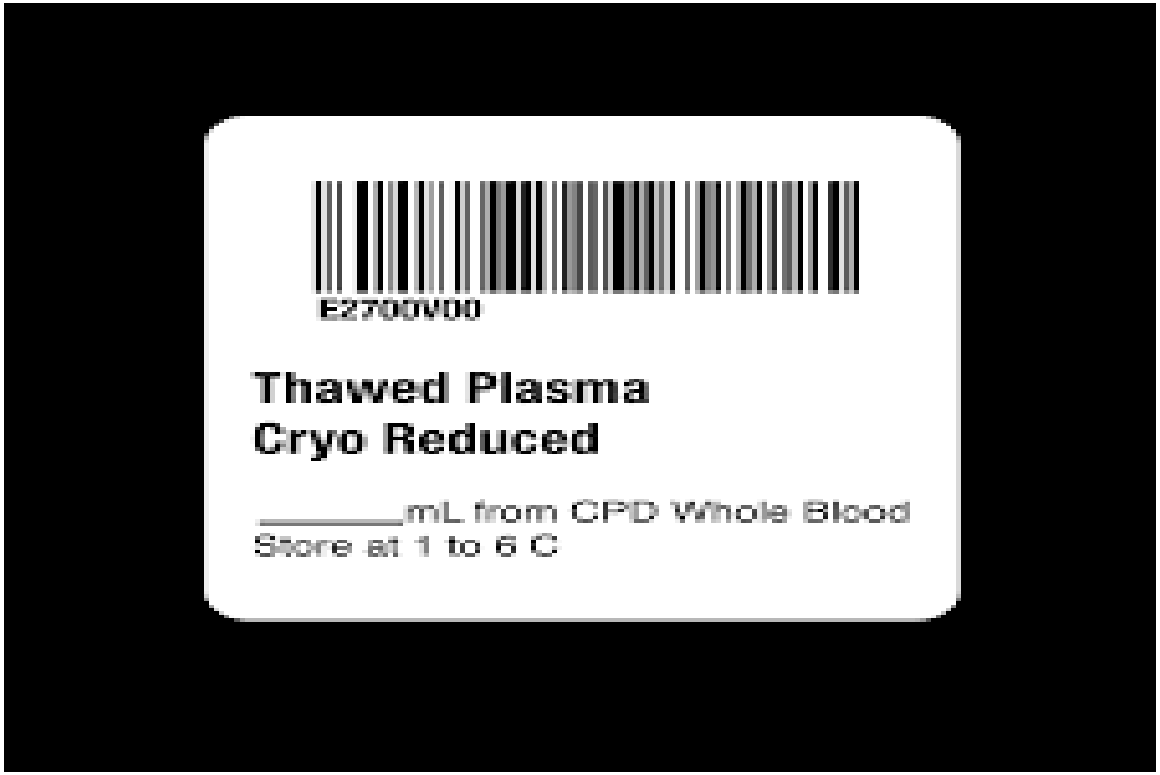
Plasma thawing






ZipThaw


TEMPERATURE
POWER
EQUATHERM
PLASMA THAWING BATH
HIGH LIMIT
HEAT
Curtin Matheson
Scientific, Inc.
MOTOR
SPEED
HEAT
WARNING
ROTATING PARTS
DO NOT OPERATE
WITH PLATFORM OFF.
INJURY MAY RESULT


E2700V00
Thawed Plasma
Cryo Reduced
_____mL from CPD Whole Blood
Store at 1 to 6 C

Clotting Factor Concentrates

- Factor VIII
- von Willebrand Factor
- Factor IX (9)
- Activated Factor VII (7) NovosevenTM
- FEIBA-NF (Factor Eight Inhibitor Bypass Agent)
- Factor XIII (13) FibrogamminTM
- ProthrombinexTM
- Factor XI (Eleven) BPLTM
- Fibrinogen Concentrate (RiaSTAP®)

Albumin

Albumin

- Significant hypoalbuminemia
- Nephrotic syndrome
- Therapeutic plasma exchange
- Cardiothoracic surgery as a pump prime for cardiopulmonary bypass
- Excessive protein losses/replacement of drain losses
- Burns fluid replacement
- Liver transplant post-operative management
- Post cardiac surgery chylothorax management

Approved First Line Uses of Albumin	
Indication	**First Line**
Type 1 (acute) Hepatorenal Syndrome	Albumin 5% (1gm/kg) on day 1, then 50gms/day
Paracentesis	Albumin 25% 25 gm x 1
Physiologically Significant Hypoalbuminemia	Albumin 25% 0.5 to 1 g/kg/dose (Max 100 g/dose)
Plasmapheresis	Albumin 5% is replacement fluid
Spontaneous Bacterial Peritonitis with Cirrhosis	Albumin 25% (1.5gm/kg)
Heart & Lung Transplantation	Albumin 5% 12.5gm PRN

Albumin

- Adverse reactions to albumin solutions are usually mild and transient.
- Mild reactions such as mild hypotension, flushing, urticaria, fever and nausea usually disappear when the infusion rate is slowed or ceased.
- Very rarely, severe allergic reactions such as anaphylaxis or significant hypotension can occur. The infusion should be stopped and appropriate treatment initiated (IV fluids for hypotension and IM adrenaline for anaphylaxis).
- Due to the colloid osmotic effect of Albumin 20%, patient should be monitored for circulatory overload.

Fibrinogen concentrate

- Cardiac surgery is associated with acquired hemostatic defects secondary to cardiopulmonary bypass that lead to excess bleeding.

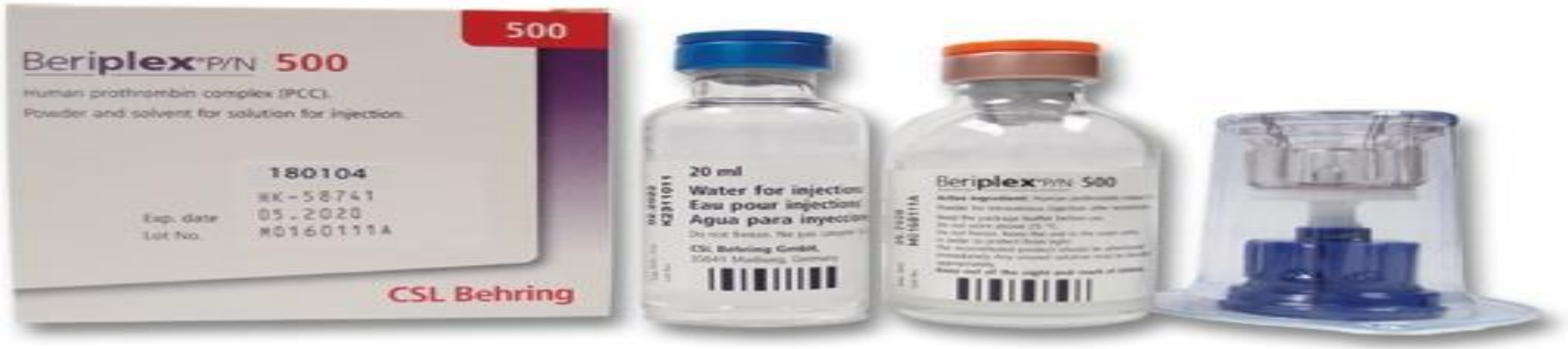
Coagulation factor concentrates

- Prothrombin complex concentrate (PCC)
- Recombinant Factor Vila (rFVIIa)
- Fibrinogen concentrate

PCC

- There are several methods available to reverse the effect of warfarin. For warfarinized patients in whom urgent reversal is needed (eg, bleeding or requiring emergency surgery), the treatment of choice is a four-factor prothrombin complex concentrate (PCC).
- PCCs contain high levels of Factors II, VII, IX, and X in the non activated state, as well as proteins C and S. A recent RCT demonstrated that warfarin reversal was more rapid and reliable in bleeding patients taking warfarin who received a PCC as compared with patients receiving plasma.
- Vitamin K administration is also recommended when reversing warfarin, to ensure a sustained effect. Plasma can also be used if PCCs are contraindicated, such as in patients who have had heparin-induced thrombocytopenia, because some PCCs contain heparin.

Prothrombin complex concentrate (PCC)



Prothrombin complex concentrate (PCC)

- 3-factor PCCs have only one approved indication : preventing and controlling bleeding related to hemophilia.
- 4-factor PCCs are approved for urgent reversal of vitamin K antagonist (warfarin) in acute major bleeding or when needed for urgent surgery or invasive procedures

Prothrombin complex concentrate (PCC)

- PCCs are derived from pooled human plasma .
- • 3-factor PCCs contain three vitamin-K dependent coagulation factors (Factors II, IX, and X) and a small amount of Factor VII.
- • 4-factor PCCs contain therapeutic levels of Factor VII, in addition to Factors II, IX, and X.

- 3-factor PCCs do not effectively lower the international normalized ratio (INR); addition of a small amount of Fresh Frozen Plasma (mean 2 units) increases the likelihood of satisfactory INR lowering.
- • 4-factor PCCs contain heparin and should not be used in patients with heparin allergies or heparin-induced thrombocytopenia .

- Efficacy and safety of 3-factor PCCs or 4-factor PCCs in the setting of patients with severe or life-threatening bleeding associated with target-specific oral anticoagulants (eg , dabigatran , rivaroxaban , apixaban, edoxaban) is unclear.

Recombinant Factor VIIa (rFVIIa)

AryoSeven™ 1.2mg - 2.4mg - 4.8mg

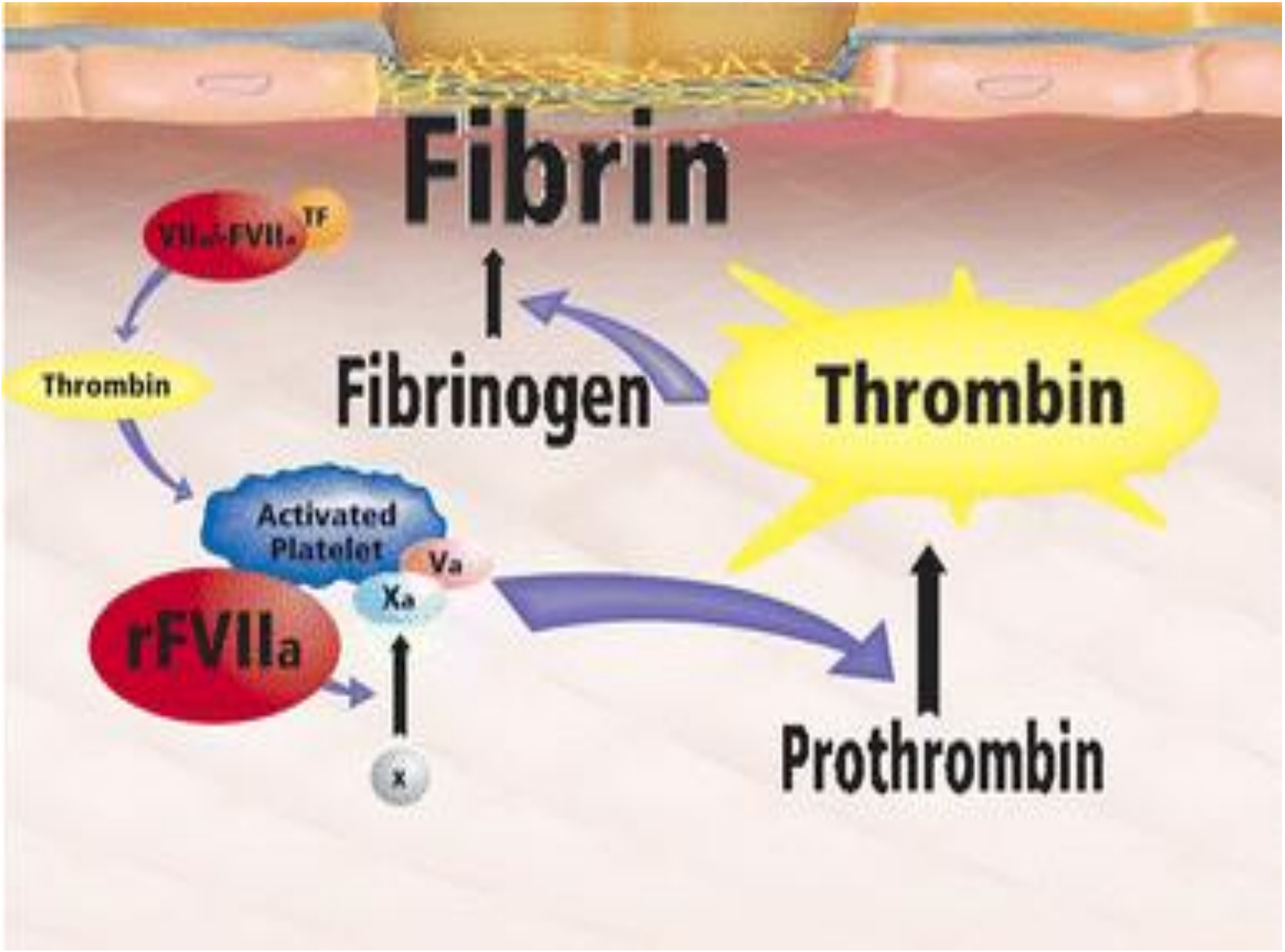
AryoSeven™ RT 1mg - 2mg - 5mg - 8mg

Recombinant Factor VIIa (rFVIIa)

- Approved by the Food and Drug Administration (FDA) hemophilia A and B with inhibitors
- Acceptable in patients with congenital Factor VII deficiency or patients with Glanzmann thrombasthenia with antibodies to glycoprotein llb/llla
- Enhances thrombin generation at the site off or treating vascular injury.

Recombinant Factor VIIa (rFVIIa)

- Black box warning issued in 2005 regarding the risk of arterial thromboembolic complications .
- • Efficacy of rFVIIa as a general hemostatic drug remains unproven
- bleeding
- with rFVIIa administration in certain conditions, such as blunt trauma and after complex cardiac surgery, clinical trial data has generally not shown efficacy, and there are data suggesting increased thrombotic risk. Therefore, off-label use of rFVIIa should be restricted to settings of ongoing refractory bleeding despite administration of all available therapies, when the benefit clearly outweighs the risk, and at the lowest dose


Fibrin
VIIa-FVIIa
TF
Thrombin
Fibrinogen
Thrombin
Activated Platelet
Va
Xa
rFVIIa
X
Prothrombin

Fibrinogen concentrate

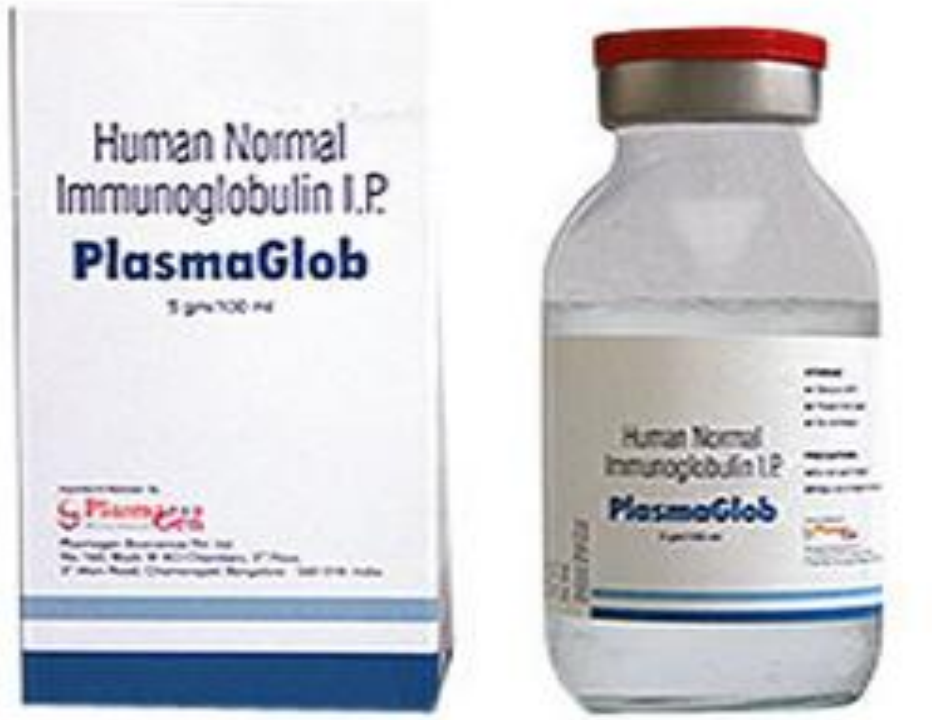
Fibrinogen concentrate

- Approved by FDA for treating bleeding only in patients with congenital fibrinogen deficiency
- Derived from pooled human plasma.
- • Precursor to fibrin; thrombin converts fibrinogen to fibrin to form soluble fibrin clot, which is then stabilized by activatedFactor X Ill.

Fibrinogen concentrate

- Adverse reactions include allergic and hypersensitivity reactions .
- • Thromboembolic events were reported.
- • Use in obstetric hemorrhage, trauma, and cardiac surgery was reported but is considered off-label, and future studies are needed to prove efficacy

IVIG


Human Normal
Immunoglobulin I.P.
PlasmaGlob
Human Normal
Immunoglobulin I.P.
PlasmaGlob

IVIG

- Intravenous immunoglobulin (IVIG) is a blood product prepared from the serum of between 1000 and 15 000 donors per batch.
- It is the treatment of choice for patients with antibody deficiencies. For this indication, IVIG is used at a ‘replacement dose’ of 200–400 mg/kg body weight, given approximately 3-weekly. In contrast, ‘high dose’ IVIG (hdIVIG), given most frequently at 2 g/kg/month.

Jolles S, Sewell WA, Misbah SA. Clinical uses of intravenous immunoglobulin. Clinical & Experimental Immunology. 2005 Oct;142(1):1-1.

IVIG INDICATIONS

Primary humoral immunodeficiency/primary immunodeficiency disease
Multifocal motor neuropathy
B cell chronic lymphocytic leukemia
Immune thrombocytopenic purpura
Kawasaki syndrome
Acute and chronic inflammatory demyelinating polyneuropathies
Bone marrow transplantation
Pediatric HIV-1 infection

TABLE 1.

FDA-Approved Uses of IVIG

- Primary humoral immunodeficiency
- Immune thrombocytopenic purpura
- Kawasaki disease
- Multifocal motor neuropathy
- B-cell chronic lymphocytic leukemia
- Chronic inflammatory demyelinating polyneuropathy

Abbreviations: FDA, US Food and Drug Administration; IVIG, intravenous immunoglobulin.

Indication with Off-label Use	Role of IVIG	Evidence	Dosing
Guillain-Barré syndrome (GBS)[4,5,6,7]	Alternate first line treatment	Consistent evidence from well-performed, randomized control trials. IVIG is recommended per AAN and EFNS guidelines.	2000/mg/kg/ treatment course divided between 2-5 consecutive days
Lambert-Eaton myasthenic syndrome (LEMS)[5,8]	May improve antibody titers and muscle strength	Evidence from observational studies and small randomized controlled trials. IVIG is recommended per AAN guidelines.	1,000 mg/kg/day for 2 days
Myasthenia gravis[4,5,9,10,11]	Short term management of acute exacerbations	Evidence from randomized controlled trials. IVIG is recommended for moderate to severe cases by AAN guidelines and only for acute exacerbations by EFNS guidelines.	2000/mg/kg/ treatment course divided between 2-5 consecutive days

FDA-approved indications	Off-label indications
Idiopathic thrombocytopenic purpura	Graft versus host disease following allogeneic bone marrow transplant or hematopoietic stem cell transplantation
Kawasaki disease	Polymyositis
Chronic inflammatory demyelinating polyneuropathy	Acute disseminated encephalomyelitis
Kidney transplant with high antibody recipient or an ABO incompatible donor	Autoimmune diabetic proximal neuropathy
Alloimmune thrombocytopenia	Central nervous system vasculitis
Autoimmune hemolytic anemia	Polymyositis
	Atopic dermatitis
	Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection
	Systemic vasculitides
	Acute antibody-mediated rejection following solid organ transplantation
	Systemic lupus erythematosus

Pooled Normal Human Plasma

Pooled Normal Human Plasma

- Pooled Normal Human Plasma is collected from single donors between the ages of 18 and 65 and pooled per FDA regulations. The material undergoes viral testing, and the final product is aliquoted to customer specifications. Each unit is tested and found negative for HBsAg, HCV, HIV-1, HIV-2, HIV-1Ag or HIV 1-NAT, ALT, and syphilis by FDA-Approved Methods.

THANK YOU FOR YOUR ATTENTION