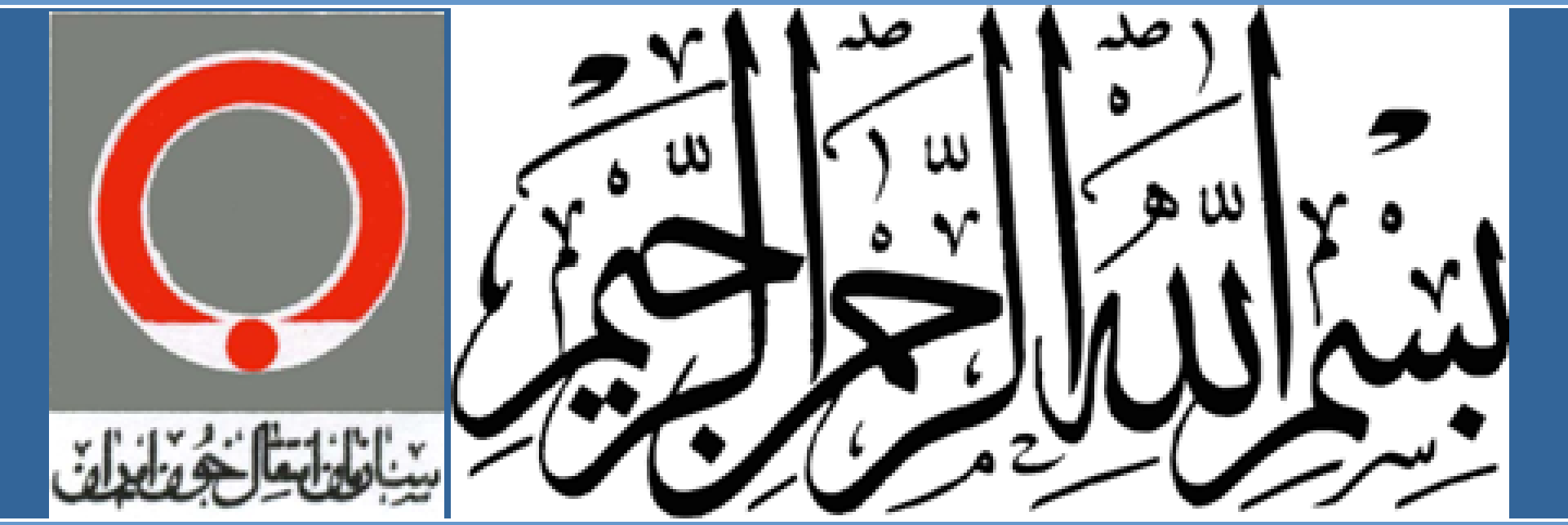
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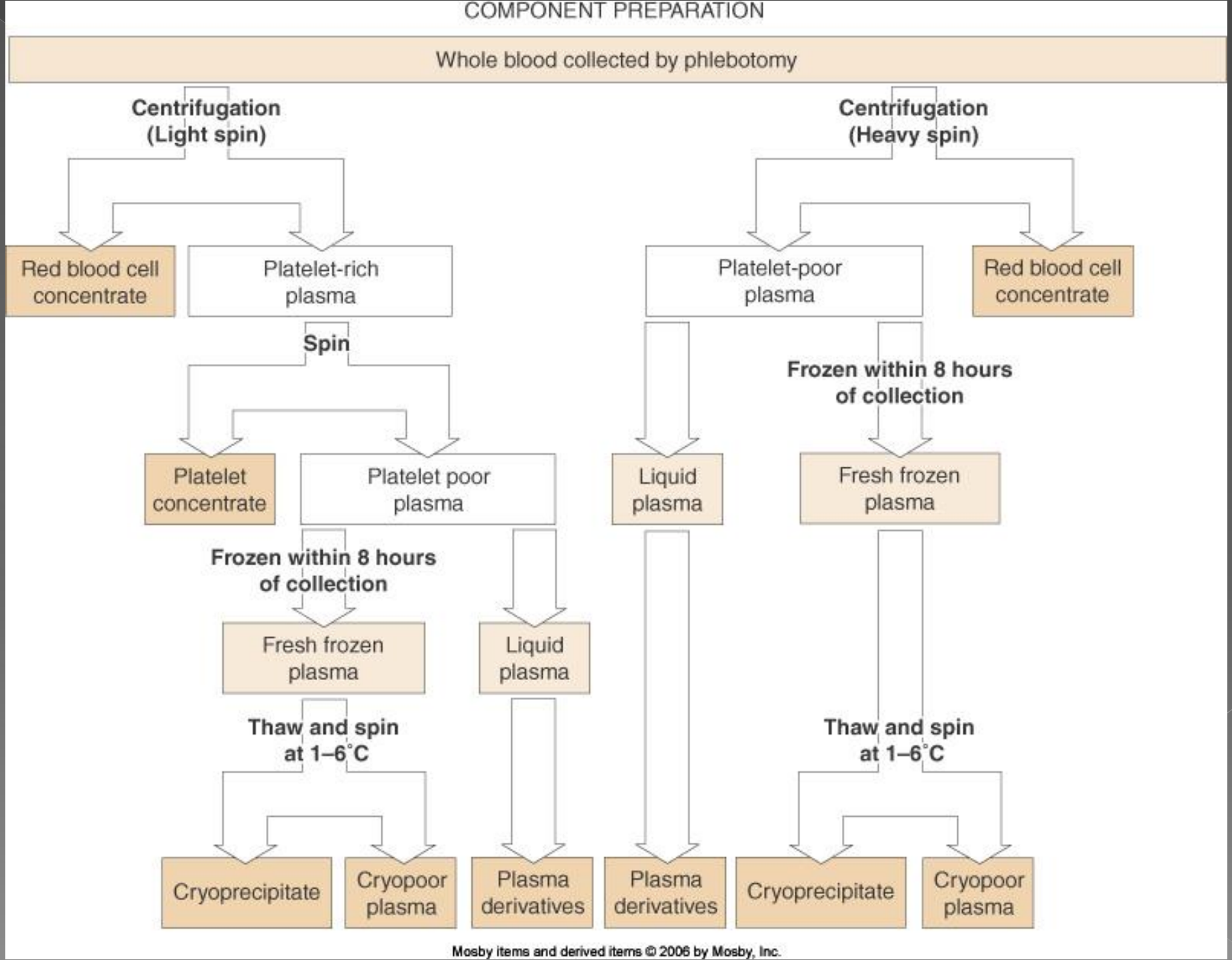
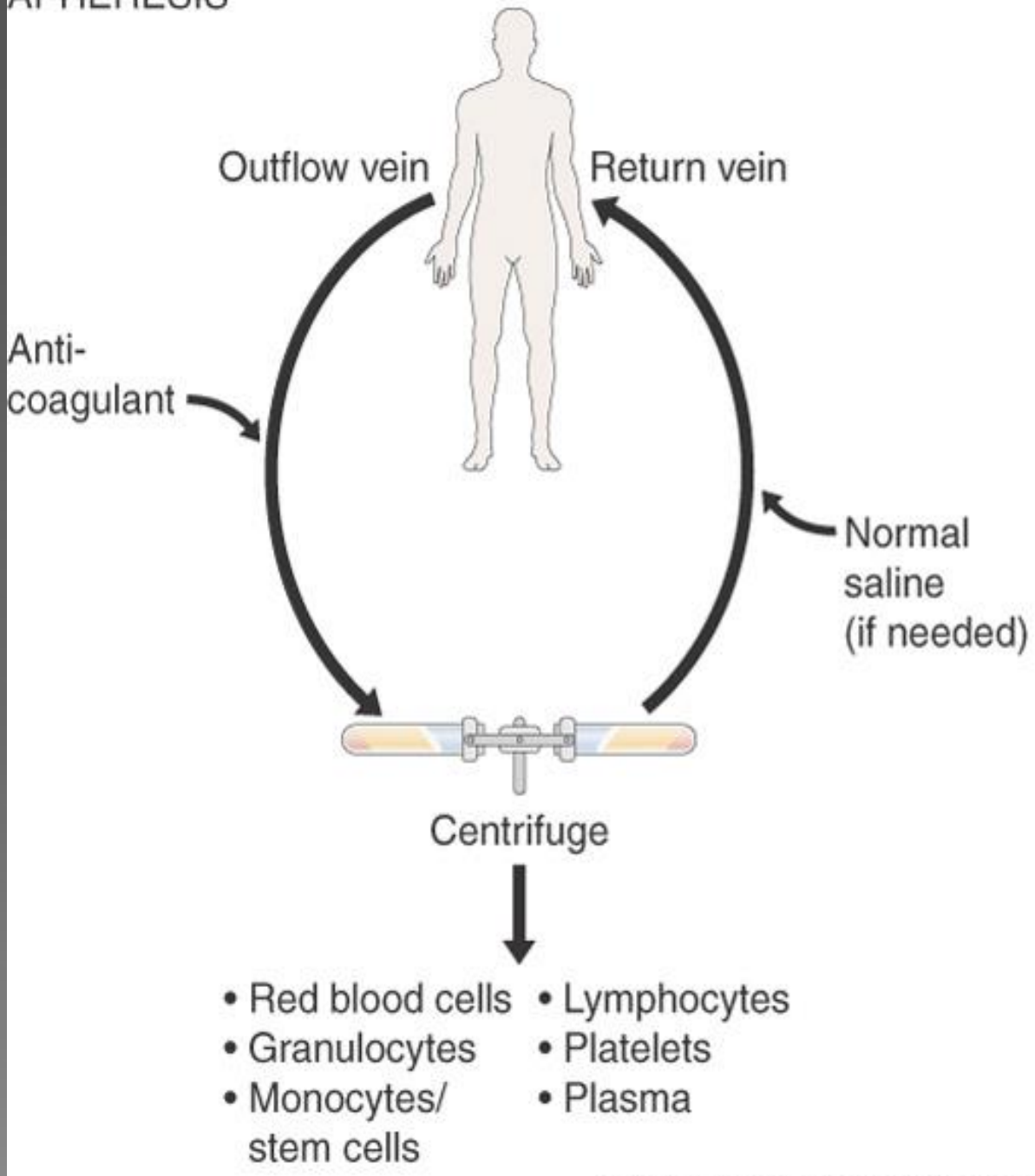
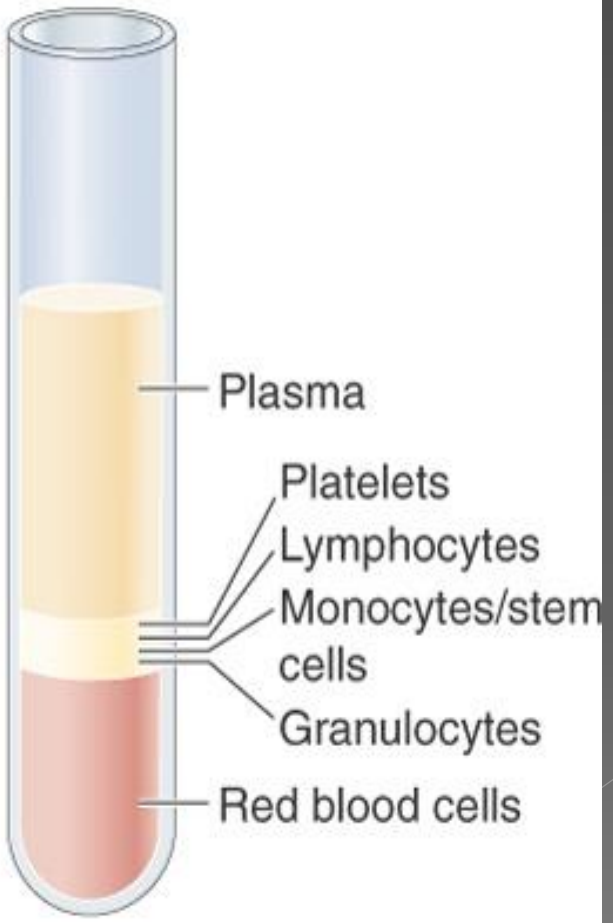
BLOOD products & Their Outcomes




JMS
TRANSFER
150 ml CAPACITY
JMS SINGAPORE PTE LTD
1JM8114410
JMS
TRANSFER
150 ml CAP
JMS SINGAPORE PTE LTD
1JM8114410
JMS
CPDA-1 - 63 m
FOR COLLECT
Do not use unless solution is clear and container is intact and undamaged. Do not supply air into bag. Store filled pack in refrigerator at 2-6°C.
CPDA-1 Solution U.S.P.
Each 100ml CPDA-1 contains:
Citric Acid (anhydrous) 0.299 g
Sodium Citrate (dihydrate) 2.63 g
Monobasic Sodium Phosphate (monohydrate) 0.222 g
Dextrose (monohydrate) 3.19 g
Adenine 0.0275 g
Water for injection q.s.
DONOR NO.
ABO BLOOD TYPE
RH TYPE
JMS SINGAPORE PTE LTD
2011-02
1JM8114410

APHERESIS





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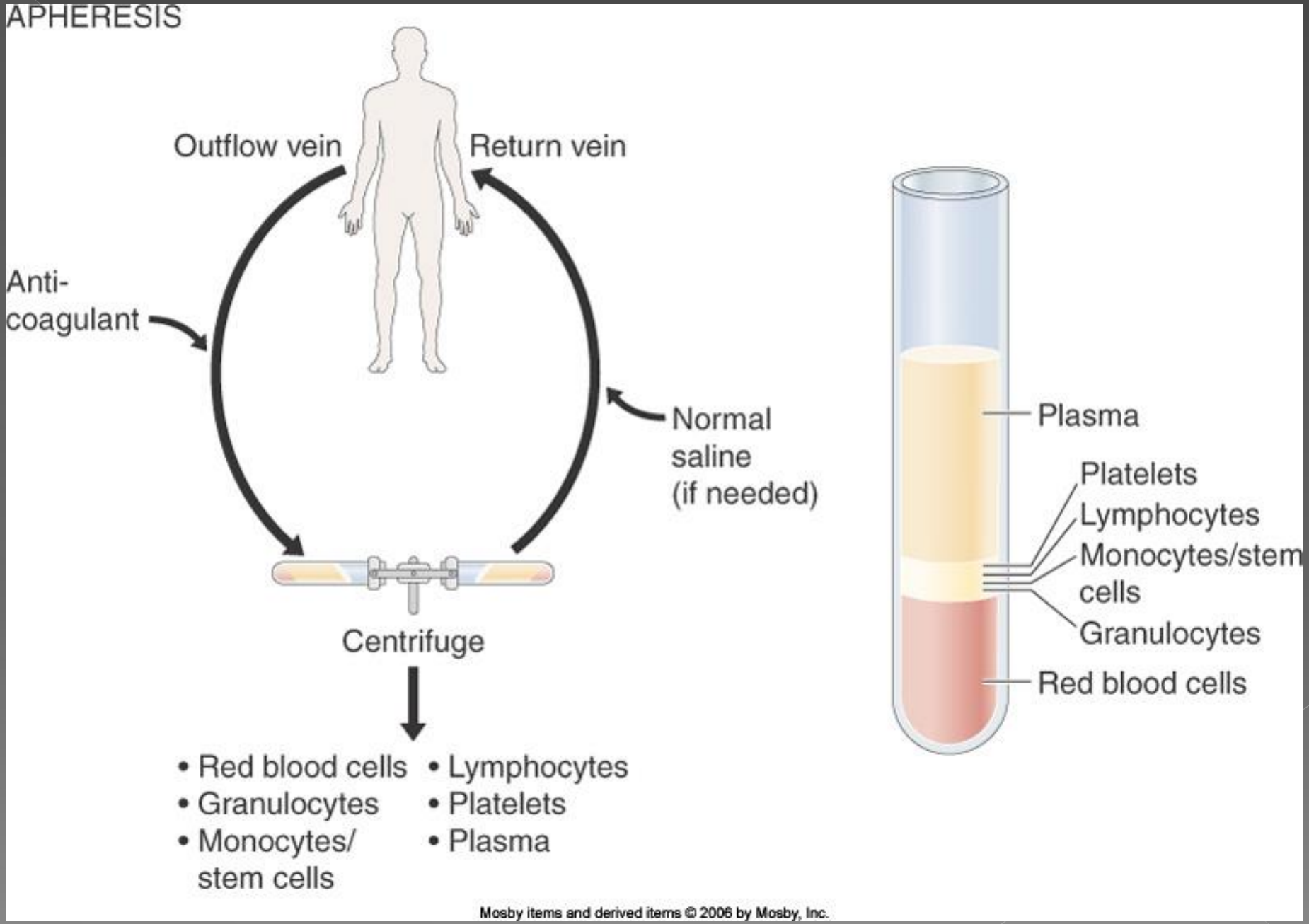
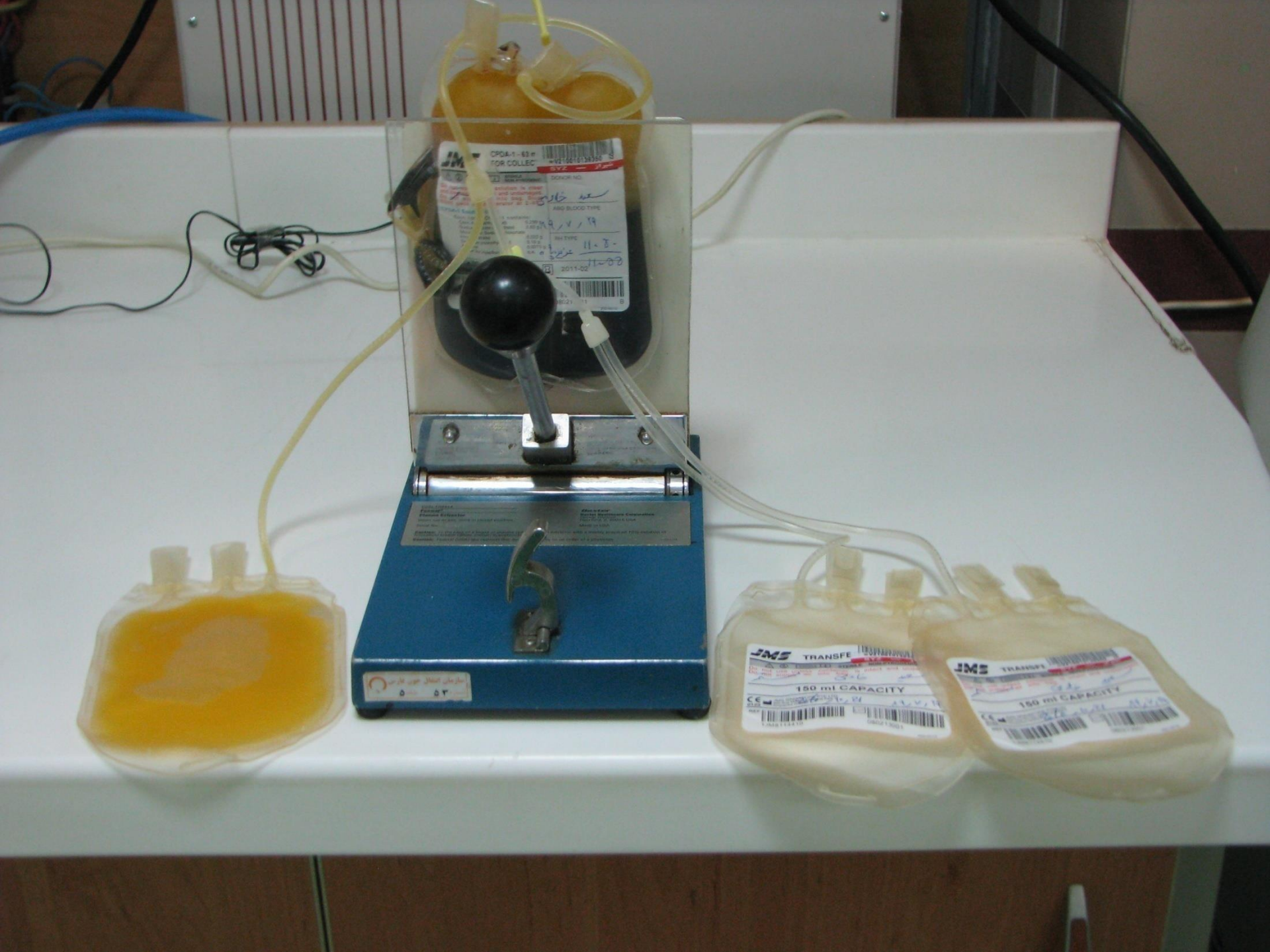



CPDA-1 - 63 ml
FOR COLLEC
DONOR NO.
ABO BLOOD TYPE
RH TYPE
2011-02
JMS
TRANSFE
150 ml CAPACITY
JMS
TRANSFE
150 ml CAPACITY


A
C
D
EX4
JMS
150 ml CAPACITY

TABLE 20-1. Signs and Symptoms of Anemia vs Acute Blood Loss

Symptom	Anemia	Hypovolemia
Tachycardia	X	X
Palpitations	X	X
Cooling of extremities		X
Pallor	X	X
Hypotension		X
Reduced arterial pressure		X
Reduced central venous (jugular) pressure		X
Acidosis		X
Increased respirations		X
Decline in urinary output		X
Mental status changes		X
Weakness	X	
Headache	X	
Dizziness	X	X
Disorientation	X	X
Dyspnea	X	
Angina	X	

TABLE 20-2. Selection of ABO-Compatible Red Blood Cell Units

Recipient Group	Compatible Red Blood Cells (additive solution units)
A	A, O
B	B, O
AB	AB, A, B, O
O	O

ABO group selection for RBC Transfusion

Recipient ABO Group		Component	ABO Group	
	1st Choice	2nd Choice	3rd Choice	4thChoice
A	A	O	None	None
B	B	O	None	None
AB	AB	A	B	O
O	O	None	None	None
Oh (Bombay Group)	Oh	None	None	None

O group selection for Plasma/FFP Transfusion

Recipient ABO		Component	ABO	
	1st Choice	2nd Choice	3rd Choice	4thChoice
A	A	AB	None	None
B	B	AB	None	None
AB	AB	None	None	None
O	O	AB	A	B

ABO group selection for Platelet Transfusion

Recipient ABO		Component	ABO	
	1st Choice	2nd Choice	3rd Choice	4thChoice
A	A	AB	B	O
B	B	AB	A	O
AB	AB	A	B	O
O	O	A	B	AB

TABLE 19-3. ABO Matching

Recipient ABO Type	ABO-Compatible RBC Units	ABO-Compatible Plasma or Platelet Units
O	O	A, B, O, AB
A	A, O	A, AB
B	B, O	B, AB
AB	A, B, O, AB	AB

RBC = Red Blood Cell.

Threshold level in Acute Anemia (2)

-End-stage Renal disease ;

Anemic & on Erythropoietin :

Target Hb 30% or 42%

HCT 42% ↑ death of MI → Hb<10 transfused

-Elective Orthopedic Surgery :

Hgb 8 g% or presence of symptomatic anemia

-Preop. probability of > 500ml blood loss :

Hb<9 transfused

-Trauma Patient :

tolerate HCT 30 & 40% (↑O2 extraction)

-Blood Volume Loss >25% (Hb<6, HCT < 20%)

Massive transfusion Goals

Laboratory data	Short –term coagulation goals	Long –term coagulation goals
HCT	20-24%	>24%
Platelet	>50,000 >100,000 in CNS & multiple high energy trauma	>100,000
Fibrinogen	>100 mg/dL	>150 mg/dL
APTT	<45 seconds	<40 seconds
PT	<18 seconds	<17 seconds

Threshold Level (3)

-*Critically ill patient*

(Atherosclerotic disease) ; Hb 7g%

lower threshold reduced morbidity & mortality significantly

threshold 7g% for all critically ill patients except ;

Unstable cardiac situation Hb<8g%

→increased mortality :

x2.5/every 1g% Hb drop

-Acute coronary syndromes:

Transfusion when the admission HCT<30% : improved outcome

Transfusion at HCT 30%: X mortality

-Hb<6g% almost always requires transfusion &

-Hg >10g% rarely

(but occasionly) requires intervention

Disease	Hb	HCT
Severe cardiopulmonary failure	<13	<40%
Mild to moderate Failure	<10	
Acute coronary syndromes	< 8	
Symptomatic Anemia	< 7	
Preop with probability of >500ml blood loss in op	< 9	
Uremia & bleeding due to thrombocytopenia	< 10	
Blood volume loss>25%	< 6	<20%
Sickle cell anemia - Acute splenic sequestration crises	< 5	
- Acute chest syndrome & CVA	10	HbS <30%
- General Anesthesia	10	HbS <60%

Physicians' Hemotherapy decision making

-21% of preop RBC transfusion in Hb>10g%

-1:3 Medical transfusion in Hb>8g%

- Assemblage of experience & knowledge must still be blended; Art of medicine

-***Patient's symptoms & previous pt's Hb :***

Tolerance up to 2 gr%

Out of bed ; orthostatic change

Symptomatic anemia

Signs & Symptoms of Acute Blood Loss

Tachycardia
Palpitations
Cooling of extremities
Pallor
Hypotension
Reduced arterial pressure
Reduced central venous (jugular) pressure
Acidosis
Increased respiratory rate
Decline in urinary output
Mental status changes

Transfusion in Patients with Chronic Anemia (1)

- Transfusion is much less commonly indicated ; persisted anemia for weeks or months : compensatory mechanisms.
- Longerterm anemias : best treated by addressing their etiologies, supplementation to treat a nutritional deficiency (eg, of iron) or reducing the rate of autoimmune hemolysis.
- Congenital hemoglobinopathies, such as sickle cell disease, are treated according to disease-related protocols for purposes that are not necessarily related to oxygen delivery.
- Hypoproliferative anemias secondary to chemotherapy or end-stage renal disease are often treated with marrow stimulants ; rEPO.

Transfusion in Patients with Chronic Anemia (2)

- ***Transfusion dependent patient :*** *inability to create & maintain an adequate red cell mass.*
- *These patients often "declare" the hemoglobin at which their symptoms are best controlled.*
- ***The symptomatology not generally correlate well with laboratory values*** *in different patients but often corresponds well with these values in an individual over time.*

The most appropriate hemoglobin threshold for transfusion is a patient - specific,& even situation-specific, parameter.

- **Hb<6 g/ dL almost always requires a transfusion, whereas a level >10 g/dL rarely does so.**
- Many **between** these limits, & many have one or **more comorbidities** that affect their **tolerance of anemia.**
- **Art of medicine** to address this need.
- **In addition to symptoms**, identify **consistent signs**, such as venous oxygen saturation, that **reflect how an individual patient is tolerating anemia.**

Physiologic Approach

Packed cell : 3 ml / kg → Hb rise 1g%
Whole Blood : 6 ml / kg → Hb rise 1g%

Required Packed RBCs =
3 (desired Hb- observed Hb) Wt

D. Hb = 8g%
O.Hb = 5g%
Wt = 50kg

} 3 (8-5) 50 = 450ml

Required WB = 6(d.Hb-observed Hb) Wt.

D Hb = 10g%
O Hb = 6g%
Wt = 20kg

6 (10-6) 20 = 480ml

For Adults : 2 units regardless of patient size & usually without regard to desired target Hb

PC VS WB

Prevent TACO (Transfusion assossiated circulatory overload) ;

Headache , Cough , engorged neck veins

Routine Infusion Rate 2-4ml/kg/Hr→
1ml/kg/Hr + Diuretics

Fresh WB ; Cardiac surgery

Adequate level of ***Coagulation Factors***

Concomitant acute anemia & ***volume loss***

Blood products

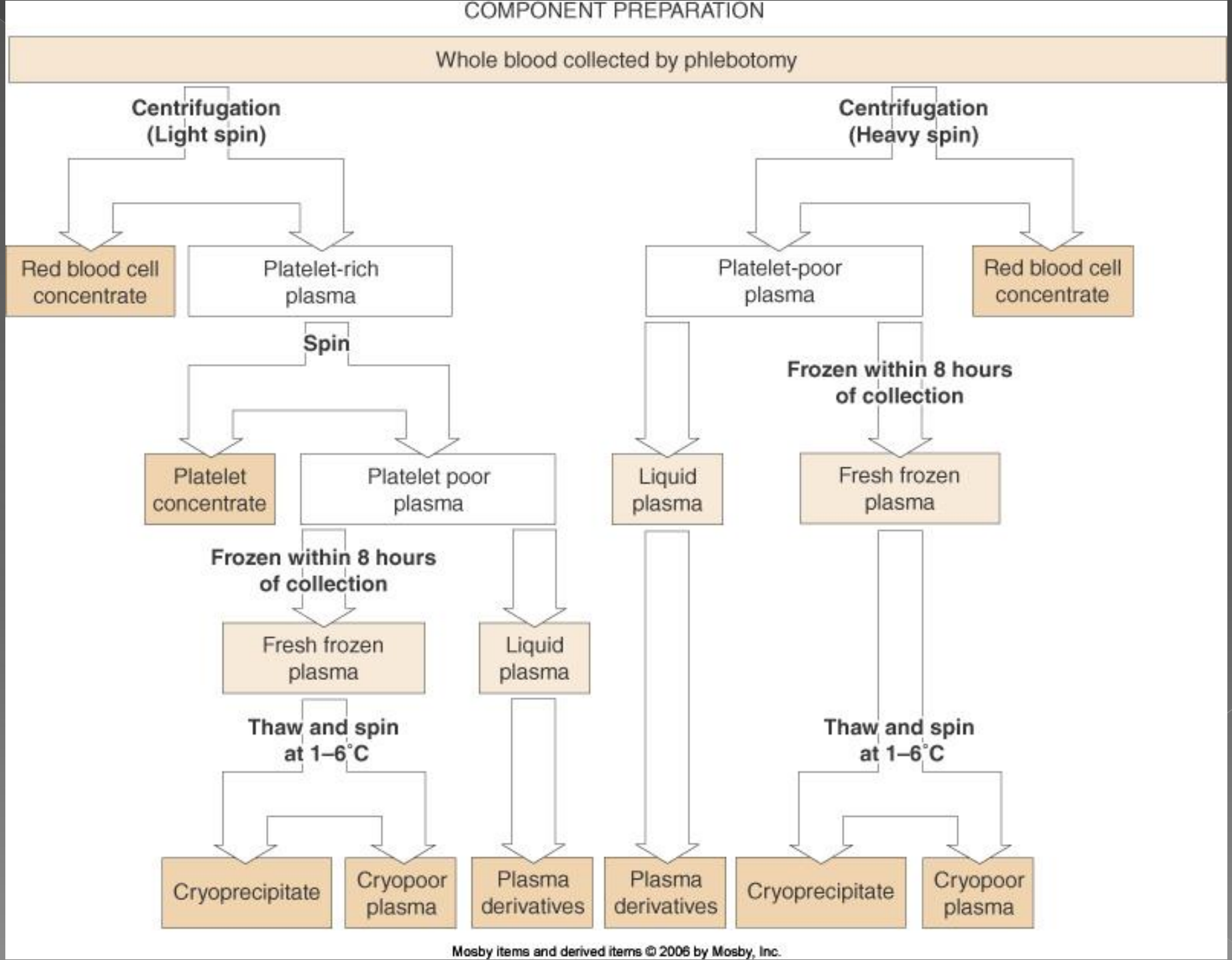
Exception : M.I. & unstable Angina in which liberal

Cellular components :

RBC
Platelet
Granulocyterategy is preferable

Acelluler Components :

FFP
Cryoprecitated AHF
Fibrin sealant (glue)
IGIV
Antiprotease concentrates
Protein C & S
Colloid solutions (Alb & PPF)



Whole Blood

O2 – Carring capacity

- Stable coagulation factors (except factor V &VIII)
- Blood Volume expansion
- Major use in the u.s today is for autologous transfusion
- For pt with concomitant red cell & volume deficits

Active bleeding

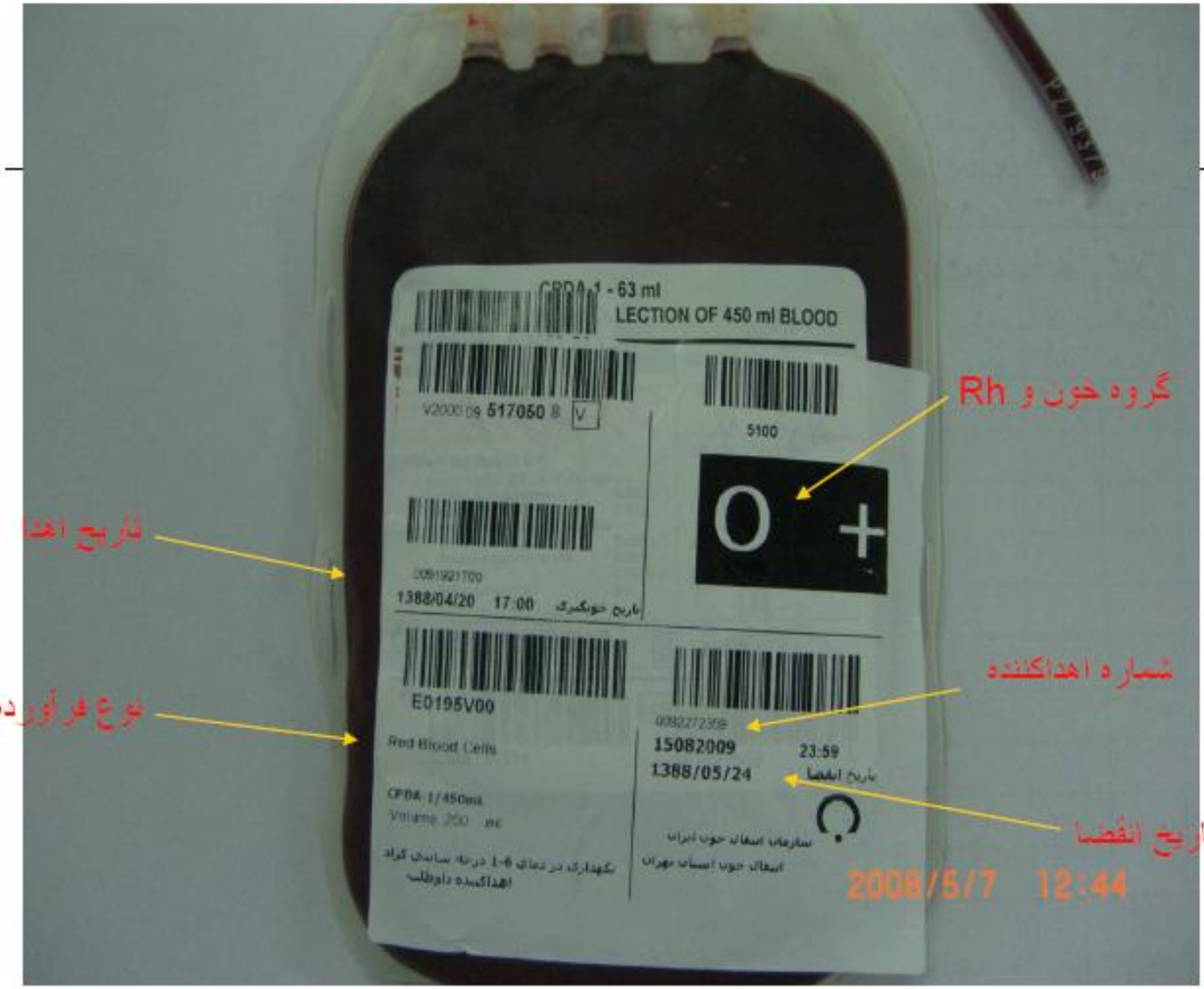
Liver transplantation

Red Blood Cells

Packed cells : Increated O2 carring capacity

Increated RBC Mass in pt who at risk of circulatory overland.

گلبول قرمز(RBC)



Selection of WB & PC

- ABO Identical but must be compatible with ABO Antibodies in recipient s plasma

Indication for transfusion

Blood loss & perioperative transfusion

- The goal for active bleeding

a- Prevent Hypovolemic shock

b- Restoration of O2 – carring capacity

Transfused pt who have lost ≥ 30-40% blood volume

- With cardiac or other dis . transfused sooner
- Sick neonate when ≈ 10% blood removed
- Resting Healthy Adults tolerate acute isovolemic hemodilution up to 5 g %

(Below 5 or 6 g/dl increased mortality)

Transfusion triggers :

89% in C.V. surgery/ orthopedic surgery / Acute GI bleeding

Summary of PC transfusion

- *Acute blood loss >15% Blood Volume*
- *Hb < 7 gr% in ill pts with symptomatic anemia*
- *Hb < 8 gr% in coronary artery disease*
- *Hb < 9 gr% before surgery & expectation of > 500 ml blood loss*
- *Hb < 10 gr% in Uremia with bleeding or thrombocytopenia*

" Task force " of the college of American pathologists

- Similar conclusion
- Several objective Measures for Hb 6-10 g%

  --Tachycardia

  - *Hypotension in normovolemic state*
  - *Mixed Venous PO2 < 25 torr*
  - *O2 extraction ratio > 50 %*
  - *Total O2 Consumption < 50 % of baseline*

TABLE 98–3. Compatibility of Recipient Blood with Donor Blood Components

Patient ABO Group	Whole Blood	Red Blood Cells	Platelets	Plasma	Cryoprecipitate
O	O	O	Any (O preferred)	O, A, B, AB	N/A
A	A	A or O	Any (A preferred)	A or AB	N/A
B	B	B or O	Any (B preferred)	B or AB	N/A
AB	AB	AB, A, B, or O (in order of preference)	Any (AB preferred)	AB, A, or B	N/A

Modified from Brecher ME (ed): Technical Manual (ed 14). Bethesda, MD: AABB Press, 2003, pp 454, 467.

TABLE 98–4. Suggested Blood Component Administration Guidelines

	Whole Blood*	Packed RBC	Granulocytes	Platelets	Plasma
Adults					
First 15 min	2 mL/min	2 mL/min	2 mL/min	2–5 mL/min	2–5 mL/min
Subsequently	100–230 mL/hr	100–230 mL/hr	75–100 mL/hr	200–300 mL/hr	200–300 mL/hr
Children					
First 5 min	N/A	N/A	N/A	5% of total volume† ordered for transfusion	5% of total volume† ordered for transfusion
First 15 min	5% of total volume† ordered for transfusion	5% of total volume† ordered for transfusion	5% of total volume ordered for transfusion	N/A	N/A
Subsequently	Variable (as tolerated)	2–5 mL/kg/hr	Over 2–3 hr (for a 200-mL product)	As tolerated	1–2 mL/min

*Generally unavailable and rarely used.

†Volume ordered for pediatric transfusion should be based on the child's weight (10–15 mL/kg); excludes granulocyte transfusion.

Abbreviations: N/A, not applicable; RBC, red blood cells.

Modified from Blood Product Administration Procedure Manual, Nursing and Patient Care Services, Clinical Center, October 2004 revision. Bethesda, MD: National Institutes of Health, 2004.

TABLE 21-1. Suggested Infusion Rate of Components in Nonemergency Settings*

Component	Suggested Infusion Rate	
	Adult	Pediatric
Red Blood Cells	150-300 mL/hr	2-5 mL/kg/hr
Fresh Frozen Plasma	200-300 mL/hr	60-120 mL/hr
Platelets	200-300 mL/hr	60-120 mL/hr
Cryoprecipitated AHF	As rapidly as tolerated	As rapidly as tolerated
Granulocytes	75-100 mL/hr	65-100 mL/hr

*Transfusion must be completed in <4 hours.

hr = hour; kg = kilograms; mL = milliliter.

TABLE 98–8. Alternatives to Allogeneic Blood Transfusion

Preoperative	Intraoperative	Postoperative
Autologous Blood Collection The donor's hemoglobin should meet or exceed 11 gm/dL. The donor must be at no increased risk of bacterial infection. Donations can take place up to every 5 days with the last collection no later than 72 hr prior to the procedure. Autologous blood is subject to the same shelf-life limitations as allogeneic blood components. *The unit may be frozen until the time it will be used.* Transfusion-transmitted disease (e.g., viral), red cell alloimmunization, and some transfusion reactions are prevented. *Risk of bacterial contamination and of clerical error leading to transfusion of ABO incompatible units is not decreased significantly.*[108]	**Blood Salvaged from a Sterile Surgical Field** Blood is salvaged by devices that collect, centrifuge, wash, and concentrate the red blood cells. Blood collected in this manner may be stored at room temperature for 4 hr from the end of the collection and at 1°–6°C for up to 24 hr if refrigeration began within 4 hr from initiation of collection.[109] *Use of intraoperative blood recovery in oncologic procedures is controversial.* *Gross contamination of the surgical field with malignant cells constitutes a relative contraindication to the use of this technique.*	**Blood Recovered from Drainage** This procedure has been used primarily with cardiac and orthopedic surgery.[108] Blood recovered in this manner is generally dilute (hematocrit of approximately 20%) and may be partially hemolyzed. Transfusion with blood recovered in this manner should start within 6 hr of initiation of collection.[109]
Erythropoietin Therapy To improve hematocrit prior to elective surgery	**Acute Normovolemic Hemodilution (ANVH)** In cases in which intraoperative transfusion is likely, ANVH may be considered if the patient has a preoperative hemoglobin level of ≥12 gm/dL, is not infected or bacteremic, and does not have clinically significant cardiovascular, pulmonary, renal, or liver disease. Whole blood is collected from the patient during surgery, prior to anticipated significant blood loss, and the volume replaced with crystalloid (3 mL crystalloid for 1 mL whole blood withdrawn) or colloid (1 mL colloid for 1 mL whole blood withdrawn). Blood collected in this manner may be kept at room temperature for up to 8 hr or stored at 1°–6°C for up to 24 hr from the time of collection (if refrigeration started within 8 hr of collection)[109] and reinfused (usually in the operating room) after cessation of major blood loss or sooner if indicated.[110]	
Correction of Nutritional Anemias Iron, vitamin B_{12}, folate, etc. therapy prior to elective surgery		

اندیکاسیون های مهم تزریق گویچه های قرمز

*آنمی علامتدار در یک بیمار با حجم خون طبیعی(علایمی مانند نارسایی احتقانی قلب، آنژین و ...)

*ازدست دادن حاد خون بیشتر از ۱۵٪ حجم خون تخمین زده شده
Acute Blood loss>15%

* **Hb<9** قبل از عمل جراحی وانتظار از دست دادن بیش از **500 ml** خون در عمل جراحی
* **Hb<7** در یک بیمار بدحال و بحرانی
* **Hb<8** در بیمار مبتلا به سندرم حاد عروق کرونر
* **Hb<10** همراه با خونریزی ناشی از اورمی یا ترومبوسیتوپنی

Henry's Clinical Diagnosis & Laboratory Management By Laboratory Methods. 2007 chapter 35 page:669-684

اندیکاسیون های مهم تزریق گویچه های قرمز- ادامه

* موارد زیر در بیماری سلول داسی شکل(**SCA**)

الف – احتباس حاد: **Hb<5** یا افت **Hb** به میزان بیشتر از ۲۰٪ از **Hb** پایه

ب – سندرم حاد قفسه سینه که در این حالت **Hb** هدف (مطلوب)برابر ۱۰ است و **HbS** کمتر از ۳۰٪ بشود.

ح – پیشگیری از سکته مغزی **(stroke) : HbS <30%** بشود.

د- بیهوشی عمومی : **Hb= 10** هدف و **HbS <60%**

Henry's Clinical Diagnosis & Laboratory Management By Laboratory Methods. 2007
chapter 35 page:669-684

TABLE 19-2. The Use of RBC Transfusion for Sickle Cell Disease Complications*

Complication	Transfusion Method (strength of recommendation)
Symptomatic severe acute chest syndrome (defined by an oxygen saturation <90% despite supplemental oxygen)	Exchange (strong)
Acute splenic sequestration and severe anemia	Simple (strong)
Acute stroke in children and adults: Initiate a program of monthly transfusions	Simple or exchange (strong)
Hepatic sequestration	Simple or exchange (moderate)
Intrahepatic cholestasis	Exchange or simple (consensus)
Multisystem organ failure	Exchange or simple (consensus)
Aplastic crisis	Simple (consensus)
Symptomatic anemia	Simple (consensus)
Child with transcranial Doppler reading >200 cm/s	Exchange or simple (strong)
Adults or children with previous clinically overt stroke	Exchange or simple (moderate)

*Adapted from Yawn et al.[24]

سایر فرآورده های گلبول قرمز

- گلبول قرمز شسته شده
- گلبول قرمز کم لوکوسیت
- گلبول قرمز اشعه داده شده
- گلبول قرمز منجمد شده

Important notes for Lab.

- **Sterility:** Blood donation sites; Isopropyle alcohole 70% & Iodine (for allergy to iodine: Chlorohexidine 2%) …. 1st 20 ml of blood drained into separated bag…. For test tubes.
- **Blood products preparation:** WB store in 20-24C & in < 8 hours all products such as plt & FFP & PC should be prep. & store in proper Temp.
- **BB refregerators:** 1-6C (4C) : Record & control Refreg.Temp. / 4 h in manual method.
- **Temperature monitoring:** The least volume of bags : glycerol bottle with thermometer.
- **The PC bags transportation:** in 1-10C with ice separated by aluminum foil or plastic foil.
- **Don't put PC bags in RT >30 min.** (metabolic damage)
- **Repeated checking the PC bags in refrigerator :** to detect **gas, hemolysis,clots, brown or purple discoloration, turbid plasma**.

گلبول قرمز کم لوکوسیت

Contains : at least 85% of original red cells

WBC < 5 x 10^6 → Prevention of

HLA alloimmunization,

CMV, Repeated FNHTR

(Leukocyte depleted red blood cells)

- AABB TECHNICAL MANUAL 2008 chapter6 PAGE:189-225

Indications for Leukoreduced Blood Components

1-Reduce rate of recurrent febrile nonhemolytic transfusion reactions (FNHTRs)

2-Reduce rate of HLA alloimmunization among hematologyoncology patients

3-Reduce rate of Cytomegalovirus transmission to susceptible recipients

Blood Banking and Transfusion Medicine;D.Hillyer;Second Edition;2007:Table 26-1;Page:361

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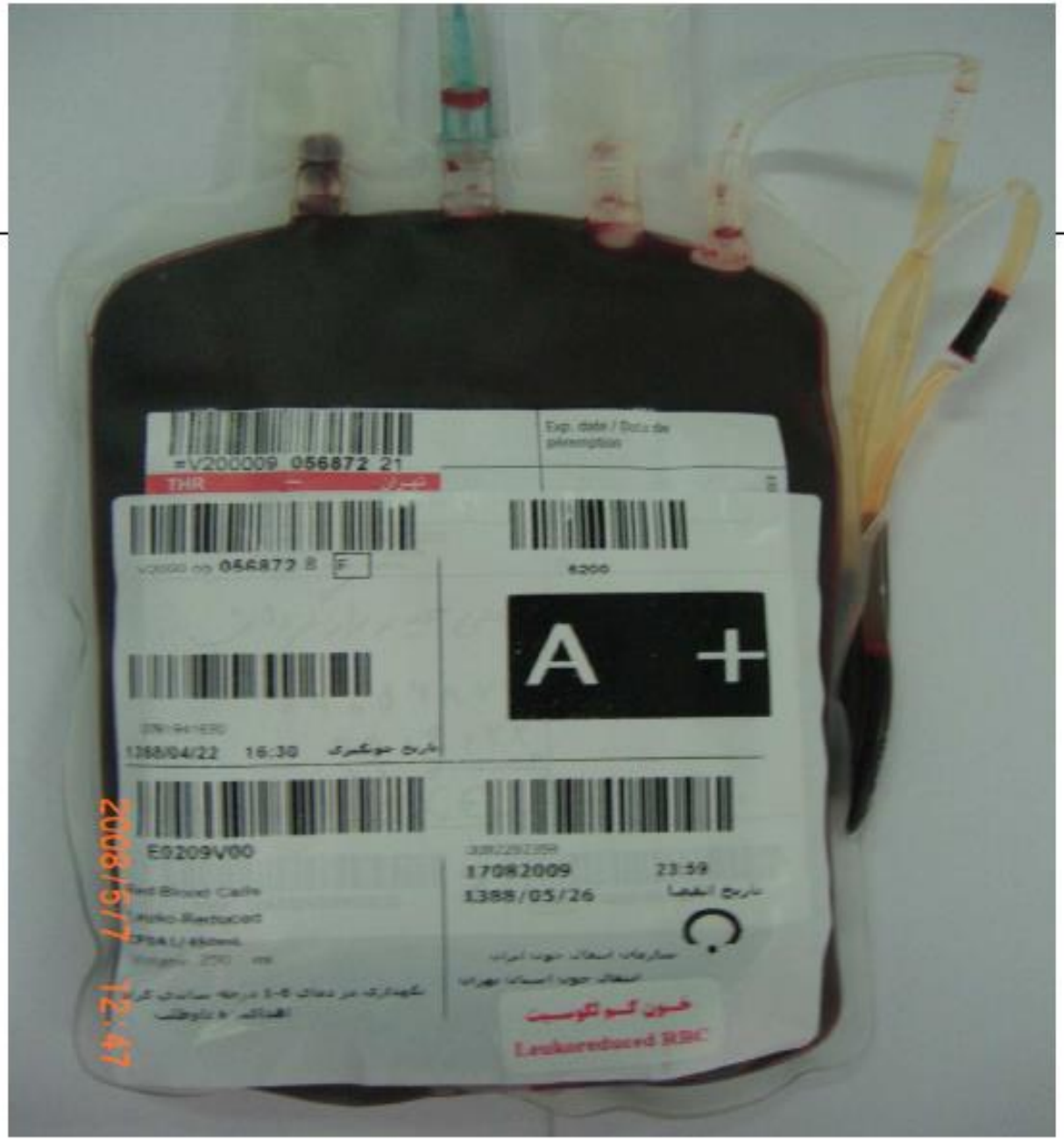
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17082009 23:59
1388/05/26
Leukoreduced RBC
2008/5/7 12:47

TABLE 20-5. Approximate Leukocyte Content of Blood Components (per unit)

Component	Leukocyte Content
Whole blood	10^9
Red Blood Cells	10^8
Washed Red Blood Cells	10^7
Deglycerolized Red Blood Cells	10^6 to 10^7
Red Blood Cells Leukocytes Reduced (by filtration)*	$<5 \times 10^6$
Apheresis Platelets	10^6 to 10^8
Apheresis Platelets Leukocytes Reduced	$<5 \times 10^6$
Platelets†	10^7
Platelets Leukocytes Reduced	$<8.3 \times 10^5$
Pooled Platelets Leukocytes Reduced	$<5 \times 10^6$
Thawed Plasma	$<0.6 \times 10^6$ to 1.5×10^7

*Leukocyte reduction with third-generation leukocyte adsorption filter.

†Derived from one unit of Whole Blood through the platelet-rich plasma process.

TABLE 23-9. Irradiation Guidelines for Neonates and Older Children Who Require Cellular Blood Components[23,26]

1. Premature infants weighing <1200 g at birth.
2. Any patient with:
a. Known or suspected cellular immune deficiency.
b. Significant immunosuppression related to chemotherapy or radiation treatment.
3. Any patient receiving:
a. Components from blood relatives.
b. HLA-matched or crossmatched platelet components.

TABLE 20-8. Coagulation Factor Half-Lives

Factor	In-Vivo Half-Life	Percent Needed for Hemostasis
I	3-6 days	12-50
II	2-5 days	10-25
V	5-36 hours	10-30
VII	2-5 hours	>10
VIII	8-12 hours	30-40
IX	18-24 hours	15-40
X	20-42 hours	10-40
XI	40-80 hours	20-30
XIII	12 days	<5

RBC	Products	Volume (ml)	HCT (%)	WBC	Adminstration Dose	Shelf life (CPDAI)
Whole blood	WB	500	40	10^9	6ml/kg/ every Hb	35
Packed cell	PC	250	75	10^8	3ml/kg/ every1gr Hb	35 days
LR - PC		225	75	$< 5\times10^6$	3ml	35d
Washed - PC		180	75	$< 5\times10^8$	3ml	24 Hr in 1-6 4 Hr in RT
RBC in As (SAGM)	SAGM	350	55-65			42 days
Rejuvenated RBCs	PIPA	300		$< 5\times10^8$		42days in closed system& 24 Hr at 4°c in open syst
Apheresis RBCs		300-350	55	$< 5\times10^6$		
Double RBC Collection		380-500	55			
Irradiated RBC	PC	250	75	10^8	3ml	28 days

Shelf – life lesions

1- K leak into ECF (Plasma) :

(***Na- K Atpase***) pump failure especially post – irradiation due to membrane ICF **K** leak

2- Decreased 2,3 DPG:

After 7-10 day: ↓ P50

27→ 16 : ***shift to the Lt.*** in Hb – O2 dissociation curve

-Decreased 2,3 DPG: 1.39ml O2 carring / gr

Met.Hb= 1.34ml O2 Carrying/gr Hb

Fresh blood with adequate **2,3 DPG** in massive transfusion & neonatal transfusion

Shelf – life lesions (cont.)

3- Decreased ATP & RBC membrane lipid release (Microvesicular release); Ecchinocytosis & Spherocytosis .

Mannitol : membrance stabilizer & prevent lipid release

DEHP plasticizer : Membrane stabilizer

Prevent lipid release DEHP plasticizer : Membrane stabilizer & ***Prevent lipid release***
DEHP plasticizer : membrance stabilizer & decreased hemolysis.

4- Increased plasma Free Hb

5- ↓ ***PH*** *& Metabolic pathway enzymes block*

6- ↑ ***Ammonium ; not suitable for pt with liver failure***

7- Accumulation of cytokines & Biologic materials ;
Histamine peroxidase , IL – 1β , IL – 8 ,

VEGF (in multiple transfusion ; **risk of Tumor growth & tumor relapse , ? Increased metastatic potential**)

Complications of WBC in PC & Plt

1-Immune modulation: decreased IL-2 & TH2>TH1…. Decreased immunity in pt.

2-Increasd CMV infection: HPS transplantation; CD 34+ HSC & CD13+ & CD14+ monocytes are the dormant sites of CMV

3-Increased prevalence of CA: recurrence & in repeated transfusion such as colorectal CA & Melanoma.

4-Increased HTLV 1,2 & perion infection by WBC

5-Increased surgical infection: related to number of units transfused & admission days.

6-Refractoriness or resistant to PLT transfusion due to HLA immunization.

7-Increased cytokines : IL-1, 8 & TNF-a…..FNHTR

Important Notes

1- **Every Blood bags** should be **checked for ABO** ***blood group again***

2- **Every change in appearance** :

Dark discoloration , Purple ,

greenish discoloration , clot particles whitish or cheesy material formation , gas in bag , light or dark discoloration of cord color ***may be due to*** ***Psychrophilic bacterial growth*** ***; discard the unit, send it to blood center.***

Important Notes (Cont.)

3- If the **hermatic seal** of the bag is **opened** ; shelf life is only 6 Hr in Rt & up to 24 Hr in 1-6°c

4- All blood products should be ***transfused*** through ***filter*** set with ***170-260 micron pores*** ***(trapping of small clots & cell debris)***
For some other conditions , ***smaller pores for microaggregate filter ; 20 microns***

5- ***First 10-15 min*** of transfusion should be under close observation with ***2-5ml/min infusion rate***

Important Notes (Cont.)

6- *No any drugs or crystalloid solution* should be infused concomitantly in to bag or through the set , especially Ringer or Dextrose 5% , *except NL saline & Albumin 5% or compatible plasma.*

7- *Warming :* plastic bag for RBC units , in water bath ***T.≤ 42°c , to prevent hemolysis***

8- *Additive solution (AS) such as SAGM ; 100 ml saline, adenine, glucose & Manitol ; immediately or Max upto 3 days post-donation…35: 42 days & HCT 70-80:55-65%*

AS1(Adsol), AS5(Optisol) & AS7 contain Manitol in neurosurgery & neonates….. Brain edema

9- *Rejuvesol:* *50ml* ***PIPA****(pyruvate, inosine, phosphate & adenine)* ***> 6 days …. upto 3 days after EXP.date …1 Hour/37 C****….Washing of Hypoxanthine, Uric acid, Inosine & inorganic phosphate….* ***High 2,3 DPG…***

Best O2 Transport

Important Notes

10- K+ content in old PC :

1st day of storage in CPDA-1: 4.2 mmol/lit.

In last day of storage in CPD-A1: 80 mmol/lit.

In Additive solution: 50 mmol/lit.

PC : 70 ml plasma in last day of storage :

K content 5.6mmol in CPDA1 & 5 mmol in AS.

Neonate transfusion rate & risk of HyperK+ :

15 ml/kg/h: 2-3 gr Hb with 0.3 mmol K+ tolerable, but if > 15 ml/kg/h or if Acidosis or RF….arrhythemia & cardiac arrest… …. So that the Washing the RBCs (PC)

11-Rhogam :

A- Prevention of Rh immunization of Rh Neg pregnant women: when Rh + platelet or PC Rh+, the plateletpheresis.

B- IVIG in not splensctomized ITP pt.

Infusion sets

1- Standard administration tubing :

170-260 micron filter Microaggregate filters:

Not used for routine blood administration

2- 2nd generation: 20-40 micron

Remove leukocytes & Platelets< 10^3 log reduction

3- 3rd generation (Leukotrap filter) :

20-40 micron pores: >10^3 log reduction

Adherence of WBCs due to ; charge (methylacylate polymers) stronge positive charge, the surface morphology, several filters layers of different pore size:

Properties of diverse cells :

diameter , density, deformability, & adhesiveness.

Removed Fibrin strands & clumps of dead cells; specially in Heart surgery,even particles 1-30µ

http://doi.org/10.1590/1806-9282.20210383:
Rev Assoc Med Bras 2021;67(7)1056-1060

Infusion sets

Leukoreduction :

LR- PC < $5x10^6$ WBC /unit ,

LR-Plt < $8.3x10^6$

Prevention of :

FNHTR , HLA alloimmunization , CMV ,

Leaky syndrome after 5 days of storage

Pre–storage versus post -storage LR:

Bedside filters LR:

Dramatic Hypotension with ACE inhibitors

Red blood cells leukocytes reduced

PC-LR ; RBC units leukocytes : 1-3 $\times 10^9$

AABB standard :

-LR : <5 $\times 10^6$ leukocytes /unit

- 95% of original RBCs retaining

-Best method : *Prestorage filtration* & or laboratory filtration

(< 10^6 leukocyte /unit)

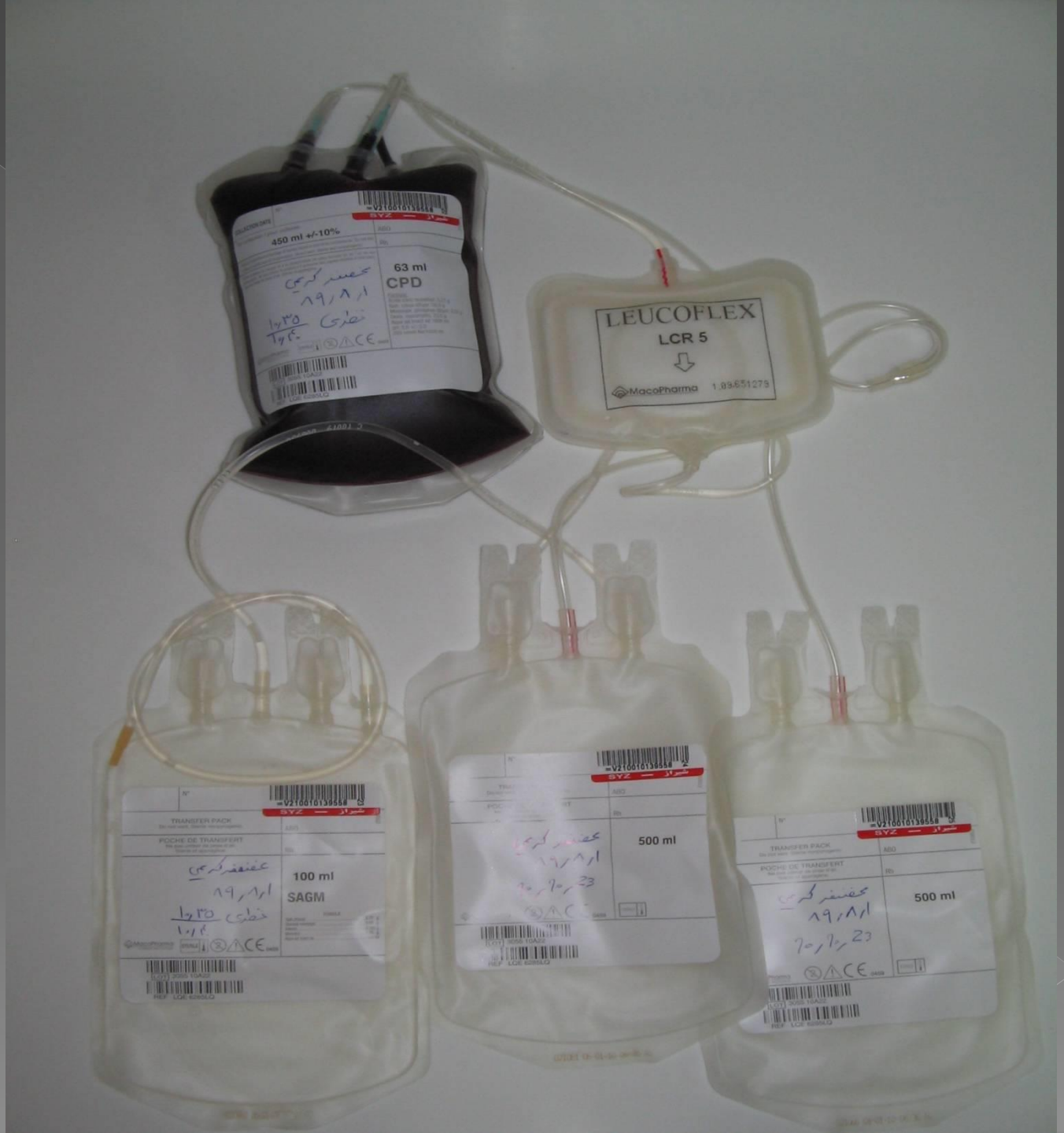
Pyrogenic Cytokine generation during storage;

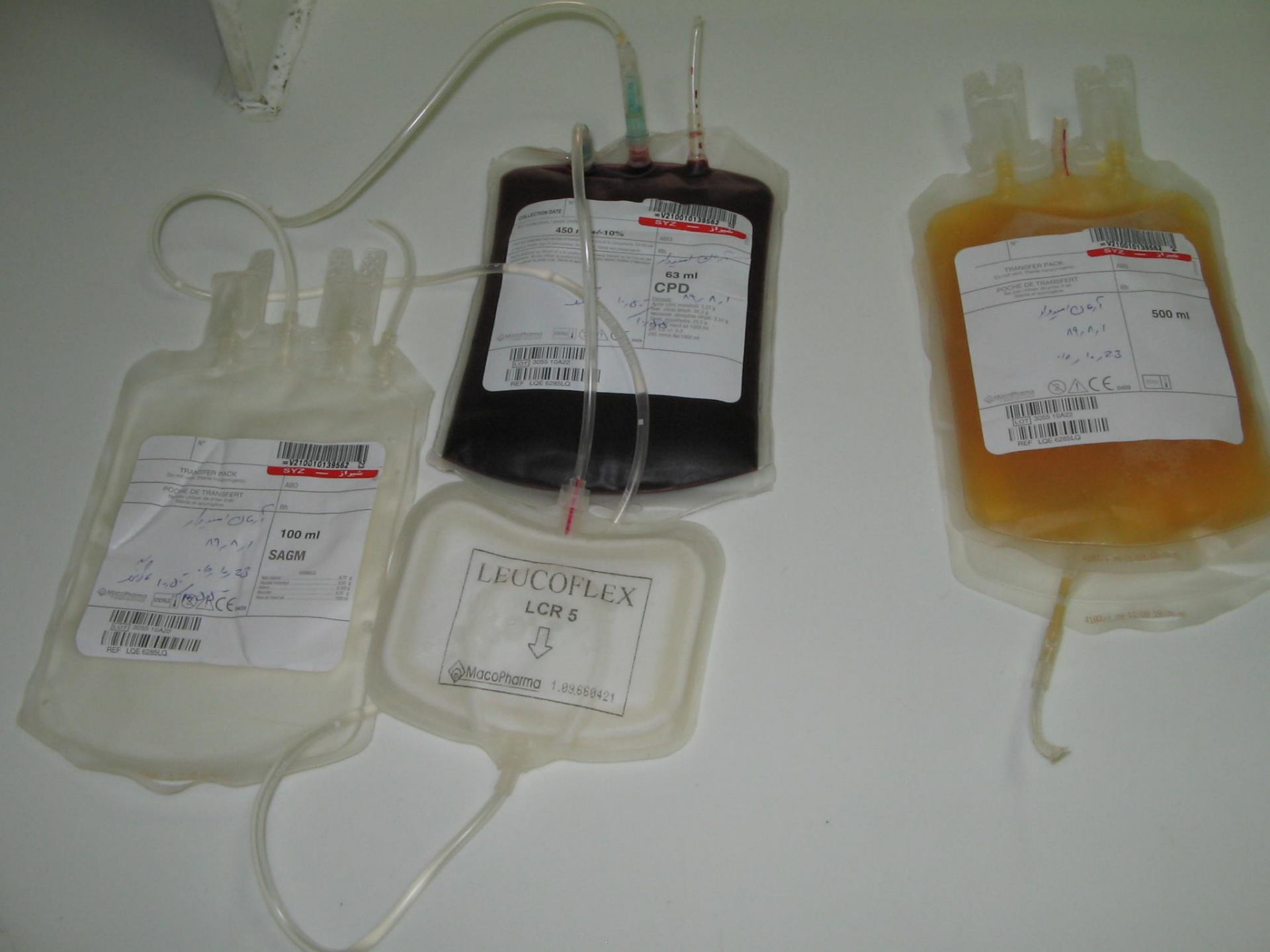
Febrile nonhemolytic transfusion reactions ; FNHTR

- Beside filtration < 5 $\times 10^6$ WBC / unit

Unit storage time ; Cytokine generation

Not the preferred method


450 ml +/-10%
63 ml
CPD
LEUCOFLEX
LCR 5
MacoPharma
TRANSFER PACK
POCHE DE TRANSFERT
100 ml
SAGM
500 ml
500 ml


TRANSFER PACK
POCHE DE TRANSFERT
100 ml
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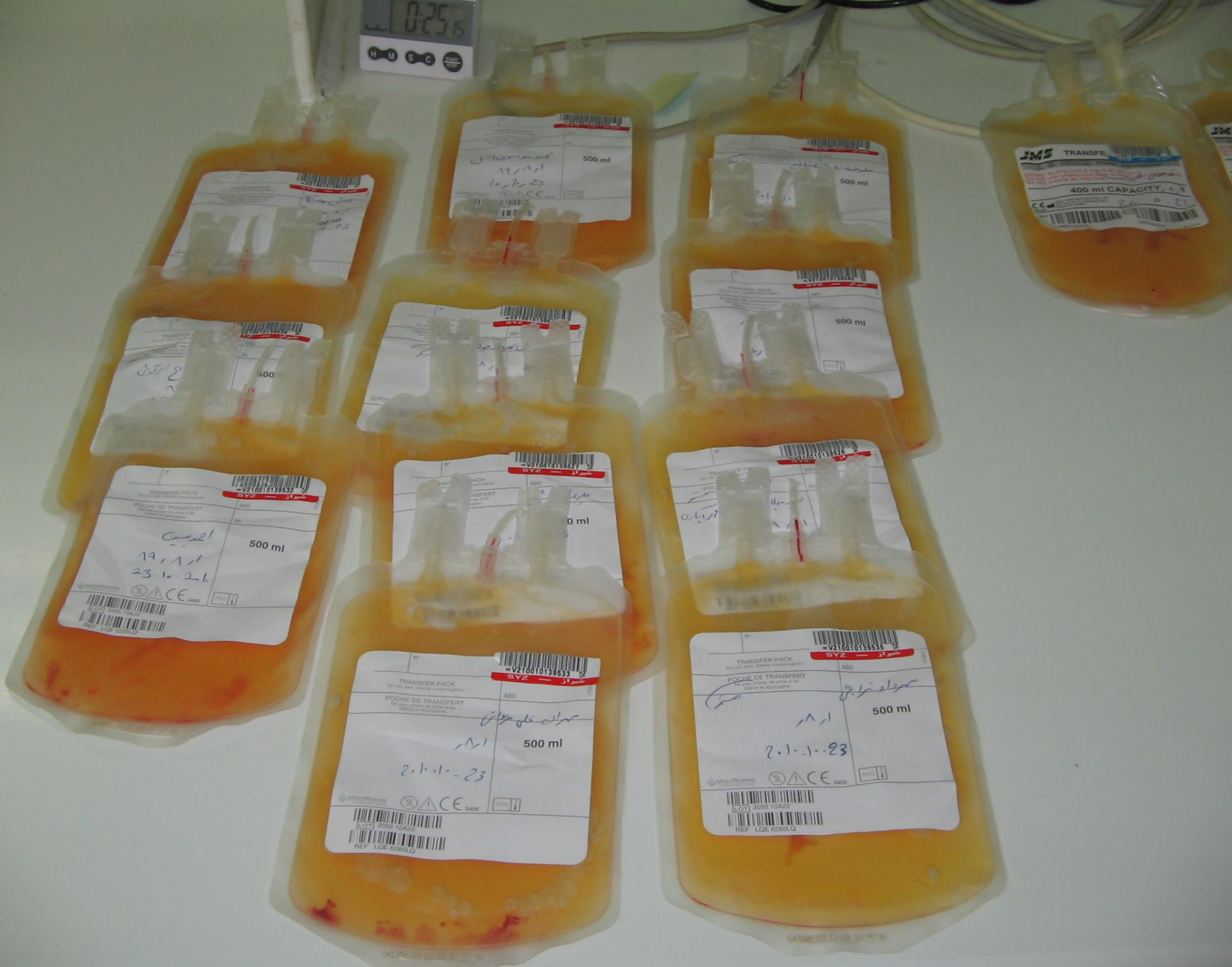
LCR 5
MacoPharma 1.09660421


500 ml
400 ml CAPACITY
TRANSFER PACK
POCHE DE TRANSFERT

Indications

1- Repeated febrile reactions with ;

long-term RBCs or plt. hemotherapy
Frequent transfusion , Female ,
Multiple pregnancies
Leukocyte alloimmunization prediction
(Anti-HLA AB) & FNHTR.
conditions : Cytokins: IL-2

2- Refractoriness to plt transfusion

Allogenic leuk.→ HLA alloimmunization
Antibodies to leuk. Ags→
Recurrent Febrile Reaction
Antibodies to plt specific Ags (PSA)
….Refractoriness

Indications(cont.)

3-Prophylaxis against alloimmunization with

chronic transfusion requirements
before the first blood transfusion
LR-platelets as well as LR-RBCs

4-CMV-Seronegative immunosuppressed with

HSC transplantation; CD 34+ HSC & CD13+ & CD14+ monocytes are the dormant sites of CMV. **High RISK:** ↓immunity, LBW or immature neonate, Intrauterine transfusion, Seronegative pregnant & Seronegative donors (HSC transplantation, Solid organ)

5-Cellular blood component transfusion in

-Immunomodulated recipients
- Prolonged survival of renal allograft
- Improved immunosuppressive drug therapy
- Decreased wound infection incidence in selected surgical patients

Indications

6-Decreased TRIM, Post-Op infection, Cancer recurrent , Prevention of leakage from anastomosis from GIT or decreased pulmonary complications after Heart surgery ..... Decreased Hospital admission time

Universal leukocyte reduction remains controversial

Voluntary universal leukocyte reduction of cellular components has been implemented by many blood centers

Contraindications & Precautions

- Volume –Related hazards

5-10 % fewer RBCs (loss in the filters)

-Incompetent filter : Sickle cell (heterozygous) & overt leukocytosis or hyperleukocytosis SX

-Not indicated to prevent post –transfusion TA-GVHD

TA-GVHD not prevented by LR-PC

Only irradiated cellular components approved

Complication in Bed-side LR....

1- ↓BP in patients use ACE drugs.

2-Red eye syndrome 3-FNHTR

Dose & Administration

Transfusion of LR-component by blood administration filter (Beside filtration)

Washed cellular products

- RBC: Normal saline 4C 1-2 lit & PLT: NS 20-24C
- X3-5 , Centrifugation …. 99.9% plasma removed

85% WBC & 20% RBCs lost , HL:24 h./4C , RT/4 h.

-Indications for Prevention of :

1-Allergic reaction , 2-Acute anaphylactic Rx; due to IgA or Haptoglobin def. ,

3- TRALI 4-Irridiated PC to decreased K+

5-Washing of juvenating RBCs from inosine or AS or Manitol 6-Rapid infusion of old PC

7-Washing of mother RBCs for her neonate in ER

8-Washing of mother Plt. for her neonate in ER

9-Washing of RBCs & Plt. With active T Ag due to bacterial infections. 10-FNHTR

11-Transfusion of non compatible product in neonates. 12-Transfusion in PNH.

Washed RBC & Plt ; pits

- Washed PC: **24 hours/1-6C** ; Hct 57% & WBC<5X10^7
- **Washed Platelet: 4hours/RT**
- Washing has **not effect on Blood group Ags & on incompatible Cross match.**
- **In IgA defiecent Pt:** washing with 4-6 lit NS or X5 washing **(the prevalence of IgA defiecency :1/1200)**
- If in **transfusion… mild allergic RX**(such as local pruritus)…transiently stop transfusion , **Antihistaminic** : if symptoms disappeared…. Continue transfusion .
- If the symptoms is **severe or diffuse** (Wheezing , bronchial spasm , diarrhea or tinismus)…. **stop the transfusion**

Frozen RBC

- **Water crystals** damaged to the RBCs …. Hemolysis ; Cryoprotectant**(Glycerol, DMSO for plt, Hydroxy starch:HES)**
- **Glycerol & DMSO:** intracellular water binding ….. prevent freezing damage , **HES** surround the RBCs similar to pearls)
- **Glycerol : low & high concentration : Hypertonic 15-20%(wt/V) & rapid freezing -100C/Min.** by immersion in liquid nitrogen tank (-197C): **-120.**
- **Glycerol 40% & slow freezing (-1C/Min):-80C** , in this condition the glycerol: 400 ml, 6.2 molar
- **PC< 6 days old or rejuvenated PC…. Freezed up to 10 years.**
- **Deglycerized before use :** to become **isotonic ; 24 hours in 4C & if closed system 14 days for AS1**
- **Recovery: 80% RBCs, at least 70% of transfused RBCs should be alive after 24 hour post-transfusion.**
- **The sickle cells should not be select for freezing…gelatinous**
- **99.9% of plasma removed during washing; Safe for IgA def.**
- **DMSO for Plt freezing: up to 2 years. Recovery: 1:3 of original**
- **Rare blood group such as Bambay**

Massive transfusion

Massive bleeding ; Replace blood loss>50% in 3 H, bleeding>150ml/min

8-10 RBC unit tranfused<24h **or** >4 PC/1H…continue

-***Na citrate toxicity ;***

Hypocalcemia & Hypo-Mg

-Cardiac dyscontractility & arrhythmia

-Liver transplantation

-**Transfusion infusion rate>30ml/Kg/H:** Ca++/EKG QT interval …. Ca / Mg infusion

- ***Hyperkalemia (specially with old PC)***

-Renal failure

-Neonate & Pediatric age group

-Hypovolemic shock

-Lactic & Metabolic Acidosis: Hyperkalemia

-*Hypothermia ; blood warmer*

Core temp < 34°c

-Platelet dysfunction.

-Slow metabolic Pathway Rate.

Core temp < 30°c

-Tachycardia & ventricular fibrillation

-*Decreased 2,3 DPG ; Shelf – life lesion*

Blood unit **>14 days ; 2,3 DPG:0**

P50 :27→16 : Shift to the Lt.

24-48 h for restoration

Massive transfusion : PC< 14 days old

Dilutional Coagulopathy

-Wash – out & dilution of plt & CF

- Plt drop to 1:3 (210,000 → 70, 000)

-PT & PTT > ×1.5 NL → Capillary bleeding

CNS , Lung & Retina ;

Microvascular bleeding

→ PT & PTT >1.3 ULN → FFP

- PT > x1.5 NL ≃ INR2 (ISI:2)

-Fibrinogen level >100mg% Plt >75-100×10^3

2 unit Cryo/10kg : 50-100mg↑ Fibrinogen level

- To Initiate massive transfusion :

10 RBC units/6 RDP or 1SDP+2FFP

Compatibility Testing in Massive Transfusion

-ABO & RH Typing : 10-15 min

-Cross match : 45-60 min

-Immediate spin cross match

-PC: Group O Neg. + FFP: AB+

-Rh IG : 72 h after D+ transfusion in D-patient

Use of whole blood

-Decreased Factor V & VIII During storage

- Useful for concomitant red cell &
  Volume deficits &
  Active bleeding as liver transplantation

Warmer for prevention of arrhythmia & SA node cooling & cardiac arrest

Hypothermia <34C… Slow metabolic pathway & Platelet activity. Temp<30C…Tachyarrythmia & VF

1- Exchange transfusion in neonates.

2- Rapid Blood transfusion in neonates >15 ml/kg/Hours.

3- Rapid Blood transfusion in adults > 50 ml/kg/H.

4- Transfusion in patient with Active Cold Agglutinine.

5- Transfusion via Central line.

To warming : PC in plastic bag…Water bath Temp. < 42C or Warmer, T > 42C….. Hemolysis & K leak.

TABLE 27-1. Categories of Adverse Transfusion Reactions and Their Management*

Type	Incidence	Etiology	Presentation	Diagnostic Testing	Therapeutic/Prophylactic Approach
Acute (<24 hours) Transfusion Reactions—Immunologic					
Hemolytic	ABO Rh mismatch: 1 in 40,000 AHTR: 1 in 76,000 Fatal HTR: 1 in 1.8 million	Red cell incompatibility	Chills, fever, hemoglobinuria, hypotension, renal failure with oliguria, DIC (oozing from IV sites), back pain, pain along infusion vein, anxiety	Clerical check DAT Visual inspection (free Hb) Repeat patient ABO, pre- and posttransfusion sample Further tests as indicated to define possible incompatibility Further tests as indicated to detect hemolysis (LDH, bilirubin, etc)	Keep urine output >1 mL/kg/hr with fluids and IV diuretic (furosemide) Analgesics (may need morphine) Pressors for hypotension (low-dose dopamine) Hemostatic components (platelets, cryoprecipitate, or FFP) for bleeding
Febrile, nonhemolytic	0.1 to 1% with universal leukoreduction	Accumulated cytokines in platelet unit Antibody to donor WBCs	Fever, chills/rigors, headache, vomiting	Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO) Rule out bacterial contamination WBC antibody screen†	Leukocyte-reduced blood Antipyretic premedication (acetaminophen, no aspirin)
Urticarial	1:100-1:33 (1%-3%)	Antibody to donor plasma proteins	Urticaria, pruritis, flushing	Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO)	Antihistamine, treatment or premedication (PO or IV) May restart unit slowly after antihistamine if symptoms resolve

Type	Incidence	Etiology	Presentation	Diagnostic Testing	Therapeutic/Prophylactic Approach
Anaphylactic	1:20,000-1:50,000	Antibody to donor plasma proteins (includes IgA, haptoglobin, C4) Cytokines	Hypotension, urticaria, bronchospasm (respiratory distress, wheezing), local edema, anxiety	Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO) Anti-IgA IgA, quantitative	Trendelenburg (feet-up) position Fluids Epinephrine (adult dose: 0.2-0.5 mL of 1:1000 solution SC or IM; in severe cases, 1:10,000 IV, initial rate 1mcg/minute) Antihistamines, corticosteroids, beta-2 agonists IgA-deficient blood components
TRALI	1:1,200-1:190,000	WBC antibodies in donor (occasionally in recipient), other WBC-activating agents in components	Hypoxemia, respiratory failure, hypotension, fever, bilateral pulmonary edema	Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO) Rule out cardiogenic pulmonary edema WBC antibody screen in donor and recipient. If positive, antigen typing may be indicated WBC crossmatch Chest X-ray	Supportive care until recovery Deferral of implicated donors

Transfusion-associated sepsis	Varies by component (see Infectious Disease Screening, Chapter 8)	Bacterial contamination	Fever, chills, hypotension	Gram's stain Culture of component Patient culture Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO)	Broad spectrum antibiotics (until sensitivities completed) Treat complications (eg, shock)
Hypotension associated with ACE inhibition	Dependent on clinical setting	Inhibited metabolism of bradykinin with infusion of bradykinin (negatively charged filters) or activators of prekallikrein	Flushing, hypotension	Rule out hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO)	Withdraw ACE inhibition Avoid albumin volume replacement for plasmapheresis Avoid bedside leukocyte filtration
Circulatory overload	<1%	Volume overload	Dyspnea, orthopnea, cough, tachycardia, hypertension, headache	Chest X-ray Rule out TRALI	Upright posture Oxygen IV diuretic (furosemide) Phlebotomy (250-mL increments)
Nonimmune hemolysis	Rare	Physical or chemical destruction of blood (heating, freezing, hemolytic drug or solution added to blood)	Hemoglobinuria, hemoglobinemia	Rule out patient hemolysis (DAT, inspect for hemoglobinemia, repeat patient ABO) Test unit for hemolysis	Identify and eliminate cause
Air embolus	Rare	Air infusion via line	Sudden shortness of breath, acute cyanosis, pain, cough, hypotension, cardiac arrhythmia	X-ray for intravascular air	Place patient on left side with legs elevated above chest and head

Type	Incidence	Etiology	Presentation	Diagnostic Testing	Therapeutic/Prophylactic Approach
Hypocalcemia (ionized calcium; citrate toxicity)	Dependent on clinical setting	Rapid citrate infusion (massive transfusion of citrated blood, delayed metabolism of citrate, apheresis procedures)	Paresthesia, tetany, arrhythmia	Ionized calcium Prolonged Q-T interval on electrocardiogram	PO calcium supplement for mild symptoms during therapeutic apheresis procedures Slow calcium infusion while monitoring ionized calcium levels in severe cases
Hypothermia	Dependent on clinical setting	Rapid infusion of cold blood	Cardiac arrhythmia	Central body temperature	Employ blood warmer
Delayed (>24 hours) Transfusion Reactions—Immunologic					
Alloimmunization, red cell antigens	1:100 (1%)	Immune response to foreign antigens on RBCs	Positive blood group antibody screening test	Antibody screen DAT	Avoid unnecessary transfusions Leukocyte-reduced blood
Alloimmunization, HLA antigens	1:10 (10%)	WBCs and platelets (HLA)	Platelet refractoriness, delayed hemolytic reaction, hemolytic disease of the newborn	Platelet antibody screen HLA antibody screen	Avoid unnecessary transfusions Leukocyte-reduced blood
Hemolytic	1:2500-11,000	Anamnestic immune response to red cell antigens	Fever, decreasing hemoglobin, new positive antibody screening test, mild jaundice	Antibody screen DAT Tests for hemolysis (visual inspection for hemoglobinemia, LDH, bilirubin, urinary hemosiderin as clinically indicated)	Identify antibody Transfuse compatible RBCs as needed

Graft-vs-host disease	Rare	Donor lymphocytes engraft in recipient and mount attack on host tissues	Erythroderma, maculopapular rash, anorexia, nausea, vomiting, diarrhea, hepatitis, pancytopenia, fever	Skin biopsy HLA typing Molecular analysis for chimerism	Corticosteroids, cytotoxic agents Irradiation of blood components for patients at risk (including components from related donors and HLA-selected components)
Posttransfusion purpura	Rare	Recipient platelet antibodies (apparent alloantibody, usually anti-HPA-1a) destroy autologous platelets	Thrombocytopenic purpura, bleeding 8-10 days after transfusion	Platelet antibody screen and identification	IVIG HPA-1a-negative platelets Plasmapheresis
Delayed (>24 hours) Transfusion Reactions—Nonimmunologic					
Iron overload	Typically after >100 RBC units	Multiple transfusions with obligate iron load in transfusion-dependent patient	Diabetes, cirrhosis, cardiomyopathy	Serum ferritin Liver enzymes Endocrine function tests	Iron chelators

*For platelet refractoriness, see chapter on platelet and granulocyte antigens and antibodies; for septic transfusion reactions, see chapter on transfusion-transmitted diseases. For a recent summary of transfusion reactions, see Popovsky.[4]

†Blood group antibody screening test.

AHTR = acute hemolytic transfusion reaction; HTR = hemolytic transfusion reaction; DIC = disseminated intravascular coagulation; DAT = direct antiglobulin test; IV = intravenous; Hb = hemoglobin; LDH = lactate dehydrogenase; CRYO = cryoprecipitated antihemophilic factor; FFP = fresh frozen plasma; WBC = white blood cell; PO = by mouth; SC = subcutaneous; IM = intramuscular; IgA = immunoglobulin A; ACE = angiotensin-converting enzyme; TRALI = transfusion-related acute lung injury; RBC = Red Blood Cell; IVIG = intravenous immunoglobulin; HPA = human platelet antigen.

Platelet transfusion

RDP / SDP

Random & Single donor platelet

1- Whole Blood Derived Platelets

Random-donor platelets ; **RDP**

Platelet concentrate

50-70 ml : 5.5 – 6 $\times$ 10^{10}

- European: Buffy coat method

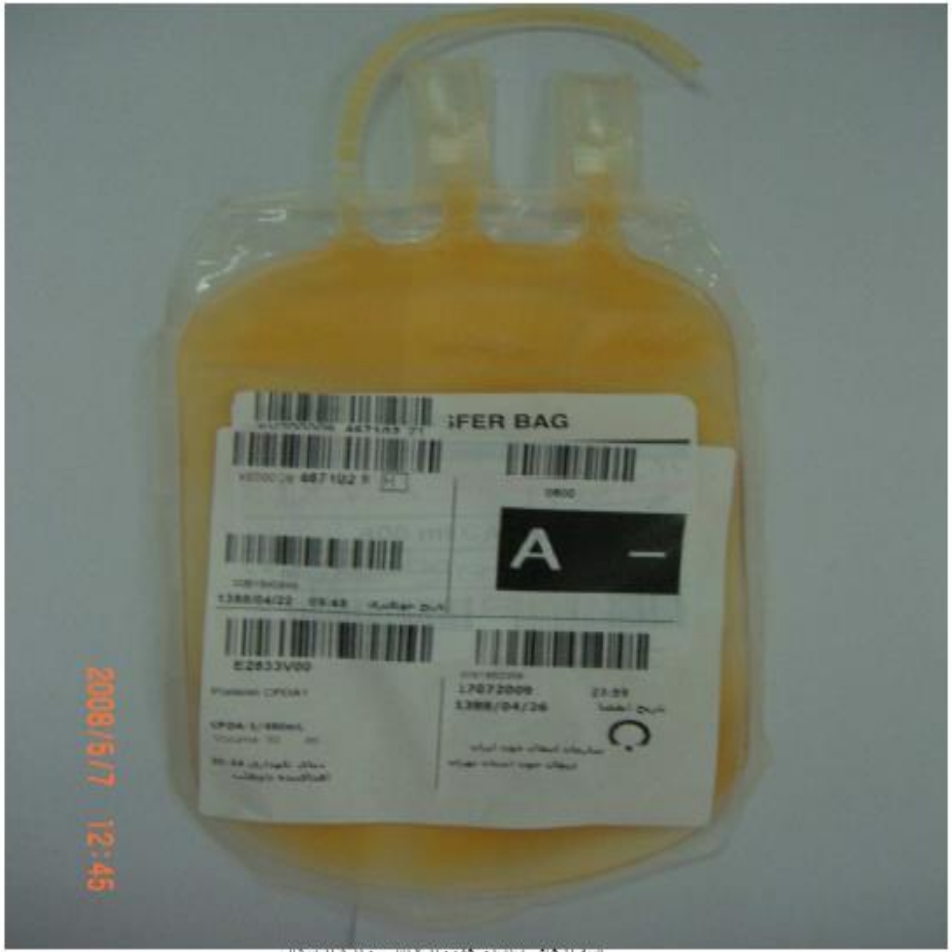
WBC contamination: 10^{8}

↑ 1 Unit → ↑ 5000/µl

↑ 1 Unit / 10kg → ↑ 30,000-50.000/µl

Random Donor Platelet

Volume 50 – 70 ml


A

2- Apheresis Platelet

Single Donor Platelet ; SDP (Plateletpheresis)

100-500 ml (300 ml) ≈ 3×10^{11}

≈ 4-6 RDP

Thrombopoietin prior apheresis ?!

- Reduced rate of Alloimmunization & transfusion reaction
- Reduced donor exposure & less risk of infection

WBC Contamination= 10^6/ bag

Single Donor Platelet

Volume ~ 300 ml

Platelet Storage Technique

Shelf life : 5-7 days , but now released < 3 days

In vitro ‹ Platelet Activation › ; prevention

PH>6 T= 20-24° gas permeable storage bag

(Second generation containers)

DEHP ≈ 72h

Fenwal PL 732 ≈ 5 Days

PL 1240 ≈ 7 Days

Gentle agitation.

Platelet Transfusion

Normal Hemostasis in four phases

- Vascular phase
- Platelet plug
- Fibrin clot
- Clot lysis

Plt are essential for 1 primary hemostatic plug
provide surface upon which fibrin forms

B.T. Measure both the Vascular & platelet phase

Although ***B.T.*** may be useful diagnostic test , but is a poor predictor of surgical bleeding

- *Plt life span 10.5 days in vivo*
  Plt life span 4 - 5 days in vito (in IRAN 3 d.)
  Plt life span decreased with progressive thrombocytopenia

Response to Plt transfusion is best assessed :

Observing bleeding stops
Measuring of
Post-transfusion platelet increment (10 min – 1 h)
CCI or Percent recovery

RDP

- WB 20-24C < 8h….RDP, 2 methods:
- 1-Soft spin:PRP:Hard spin: platelet concentrate Plt= 5.5X10^10 in 40-70 ml , WBC= 1X10^9, Small volume proper for pediatric age, activate & aggregate in sediment, slow spin in 1st stage ….. plasma & plt trap between RBCs
- 2-Buffy coat (BLC) ; Hard spin…WBC & Plt in BC …. Remove plasma…. BC of 4-6 units…. Soft spin….WBC sediment….. PRP….. Leukotrap filter ; Platelet=24X10^10 in 300ml , European method: less plt activation , better quality , needs special instrument for sterility, large volume inappropriate for neonates & RBCs loss.

Quality control

Swirling : Possibility of bacterial contamination: PH<7 , glucose<250 in Boxter PL732 or CLX glucose<500 ,
Acridine orange or gram stain : 10^4-5 CFU/ML
Direct culture with BacT/Alert : CO2 production : 10 CFU/ML in 12-36 h
LR-Plt : Prevent refractory & CMV, FNHTR , WBC<5x10^6
UV or ϒ-ray Irradiated Plt : 2500 rad ; Prevent TA-GVHR
Sterility during Donation : Asymptomatic Bacteremia in donors; dental extraction , GI infection , Enterocolitis & Colonoscopy.

Platelet transfusion thresholds

Prophylactic VS Therapeutic Transfusion

-Hypoproliferative thrombocytopenia (80%)

-Standard Prophylactic successful transfusion ≥10.000

-Already bleeding or undergo a hemostatic challenge (surgical procedure) ≥ 50.000

-Intracranial , pulmonary & ophthalmic hemorrhage ≥ 100.000

-Higher cut points might also be used in ; Massive transfusion or DIC, where the platelet count may drop rapidly specially in trauma (1:1:1 or 1:1:2).

-Role of Anemia ; reducing HCT: 41% →35%

B.T. × 2, *correction of anemia may be an additional tool to use for bleeding prevention, particularly in patients with ⬇ Plt. ADP release & PL generating IIa (phosphatidyl serine)& pushing plt from central core in laminar blood flow toward the endothelium*

Platelet transfusion thresholds (Cont.)

Febrile Pts: Plt<20,000
Invasive procedures: Colonoscopy / BM<50,000
Acute bledding: Plt<50,000
Severe bleeding & Risks of CNS, Lung & Ophthalmic Hemorrhage : Plt<100,000
Platelet dysfunction disorders
Massive transfusion without trauma : Plt<50,000
Massive transfusion with trauma : Plt<100,000
Mature newborn : Plt<50,000
Immature newborn : Plt<100,000
Pt. without fever, DIC or coagulation disorders, infections, & acute bleedings: Plt<10,000
Aspirin HL : 15-20 minutes….. Few hours after use… Plt transfusion.
Inhibitors or Blockers of GP IIb/IIIa : Abciximab, Trofiban & Eptifibatide, like Glanzman thromboasthenia.
Blockers of ADP receptor : Clopidogrel , Ticlopidine
Heart bypass surgery (Oxygen pump) : often plt dysfunction
Heparin neutralization after Heart Op.

TABLE 20-4. Current Prophylactic Platelet Transfusion Thresholds

Patient Category	Platelet Count
All patients	10,000/μL
- or -	
Stable patient	5,000/μL
Patient with fever or recent hemorrhage (now stopped)	10,000/μL
Patient with coagulopathy, on heparin, or with anatomic lesion likely to bleed[98]	20,000/μL

Note: These levels are most commonly applied to inpatients. Adjustment of the transfusion threshold may be necessitated by unusual clinical situations.

Platelet transfusion

-*Significant Renal dis (Cr > 3);*

Red cell transfusion & erythropoietin → ↑ HCT in uremia → Improved Hemostasis

→ *Plt. transfusion has low value because they, too, rapidly succumb to the same metabolic derangement.;*

1- DDAVP &

2- Cryo. (for tachyphylaxis to DDAVP) provide VWF &

3- Dialysis

-*Bleeding in congenital Plt dysfunction*

(Glanzmann, Bernard Solier)

-*Acquired Plt abnormality* (Drugs, MDS) :

Up to adequate hemostasis

Platelet transfusion

-***Extracorporeal circulation*** (pump) ;

Decision based on the pt's clinical status rather than Plt count

-***Irreversible plt antagonists*** (Clopidogrel) ≥ 1 doses of Plt during cardiac catheterization

-***After cardiac surgery***; if excessive blood loss postop, despite reversal of heparin effect

-***Bleeding due to Aspirin*** consumption , espicially in " ***hyper-responders*** "

TABLE 20-6. Comparison of Platelet Units Available in the United States

Characteristic	Whole-Blood-Derived Platelets		Apheresis Platelets
	Individual Unit	Prestorage Pooled*	
Cost of preparation	Lower	Lower	Higher
Ease of bacteria testing	Lower	Higher	Higher
Ease of leukocyte reduction	Lower	Higher	Higher
Hospital preparation required	More	Less	Less
Donor exposures	Greater	Greater	Fewer
HLA selection possible	No	No	Yes
Platelet content known	No	No	Yes

*Storage of pools of platelets beyond 4 hours requires bacteria detection by an FDA-approved culture technique.

TABLE 18-1. Blood Component Transfusions in Nonemergent Settings

Component	Suggested Adult Flow Rates		Special Considerations	ABO Compatibility	Filter
	First 15 Minutes	After 15 Minutes			
Red Blood Cells (RBCs)	1-2 mL/min (60-120 mL/hour)	As rapidly as tolerated; approximately 4 mL/minute or 240 mL/hour	Infusion duration should not exceed 4 hours. Generally administered over 1-2 hours for hemodynamically stable recipients. For recipients at risk of fluid overload, may adjust flow rate to as low as 1 mL/kg/hour.	Whole blood: ABO identical RBCs: ABO compatible with recipient's plasma Crossmatch required	In-line (170-260 micron) Leukocyte reduction if indicated
Platelets	2-5 mL/min (120-300 mL/hour)	300 mL/hour or as tolerated	Usually given over 1-2 hours. For recipients at risk of fluid overload, use slower flow rate (see RBCs).	Crossmatch not required ABO/Rh compatibility preferable but not required May be HLA matched	In-line (170-260 micron) Leukocyte reduction if indicated
Plasma	2-5 mL/min (120-300 mL/hour)	As rapidly as tolerated; approximately 300 mL/hour	Time for thawing may be needed before issue. For recipients at risk of fluid overload, use slower flow rate (see RBCs).	Crossmatch not required ABO compatibility with recipient red cells	In-line (170-260 micron)
Granulocytes	1-2 mL/min (60-120 mL/hour)	120-150 mL/hour or as tolerated	Over approximately 2 hours. Infuse as soon as possible after collection/release of component; irradiate.	Crossmatch required ABO/Rh compatibility required May be HLA matched	In-line (170-260 micron) Do not use leukocyte reduction or microaggregate filters
Cryoprecipitated AHF	As rapidly as tolerated		Infuse as soon as possible after thawing; pooling is preferred.	Crossmatch and ABO compatibility not required	In-line (170-260 micron)

TABLE 19-5. Summary of AABB Recommendations for Prophylactic Platelet Transfusion in Adults[56]

Clinical Setting	PLT Transfusion May Be Indicated for:	Strength of Recommendation	Quality of Evidence
Therapy-related hypoproliferative thrombocytopenia	PLT count ≤10,000/μL	Strong	Moderate
Central venous catheter placement	PLT count <20,000/μL	Weak	Low
Diagnostic lumbar puncture	PLT count <50,000/μL*	Weak	Very low
Major elective nonneuraxial surgery	PLT count <50,000/μL	Weak	Very low
Cardiac surgery with bypass	Perioperative bleeding with thrombocytopenia and/or evidence of PLT dysfunction. Routine PLT prophylaxis not recommended.	Weak	Very low
Intracranial hemorrhage on anti-PLT therapy	Insufficient evidence for recommendation	Uncertain	Very low

*Clinical judgment should be used for patients with PLT counts between 20,000 and 50,000/μL.
PLT = platelet.

TABLE 19-6. Causes of Platelet Refractoriness[81]

Nonimmune	Immune
Fever	HLA antibodies
Medications (eg, amphotericin, vancomycin)	ABO incompatibility
Splenomegaly	Human platelet antigen (HPA) antibodies
Sepsis	Drug-dependent autoantibodies
Disseminated intravascular coagulation	
Hemorrhage	
Veno-occlusive disease	
Graft-vs-host disease	
Prolonged platelet storage	

Complications of plt transfusion

1- Febrile & Allergic plt transfusions

(two most common)

- Group O donor plasma from 6-8 pooled donor

2- Acute hemolysis (passive isoagglutinins)

-Plasma compatible donor prevents such reactions; espicially important in neonate , young children & Adult with multiple transfusion each day

3- Volume overload (Plasma -reducted plt units) or volume reduction technique

- *4- Immunization to Rh (D)*
- *5- Thrombosis in TTP*
- *6- Bacterial contamination*

  (10% ; 2/1000)
- *Endotoxic shock in gram negative*
- *Transfusion - Associated sepsis*
- *Chills fever Hypotension & hypoxia*
- *Shortening the storage shelf life*
- *Especial care for neutropenic pts*

Systemic reactions to Plt transfusions

- **Acute –Rx:** 2% 1/3 reactions in the first transfusion
- Rash , wheezing , fever , chills , dyspnea , urticaria & hypotension .
- **Cytokine generation** during the in vitro storage (TNF, IL-1, 6 & 8*).
- Transfusion reaction x4 with platelet , older & higher **WBC contaminated**

Leukocyte Reduction ; LR

Whether *all cellular components* should be LR ;
Controversial

-Decreased the transmission of *prions*

-Reduce the risk of *postoperative infection* especially CMV

-*Improve post transfusion survival*
(transfusion – related immunomodulation)
TRIM

-Reduced *alloimmunization*

-Decreased episodes of *refractoriness to platelet transfusion*

-Fewer febrile reactions ; *FNHTR*

Leukocyte Reduction ; LR

AABB Standards for blood banks & Transfusion services:

$<5\times10^{6}$ residual donor leukocytes/units (SDP & Pooled Plt) $<8.3\times10^{5}$ in RDP

FDA quality control :

95% confidence

European guidelines standards:

$<1\times10^{6}$ leukocytes ,

QC : 90% Confidence , <10% failure rate

TABLE 20-3. Approximate Leukocyte Content of Blood Components (per unit)

Component	Leukocyte Content
Whole Blood	10^9
Red Blood Cells	10^8
Washed Red Blood Cells	10^7
Deglycerolized Red Blood Cells	10^6 to 10^7
Red Blood Cells Leukocytes Reduced (by filtration)*	$<5 \times 10^6$
Apheresis Platelets	10^6 to 10^8
Apheresis Platelets Leukocytes Reduced	$<5 \times 10^6$
Platelets†	10^7
Platelets Leukocyte Reduced	$<8.3 \times 10^5$
Pooled Platelets Leukocytes Reduced	$<5 \times 10^6$
Fresh Frozen Plasma (thawed)	$< 0.6 \times 10^6$ to 1.5×10^7

*Leukocyte reduction with third-generation leukocyte reduction filter.

†Derived from 1 unit of Whole Blood via platelet-rich plasma process.

Dosage of plt transfusion

-Many blood centers now report mean contents 20-40% above required minimum (5.5×10^{10}) plt/unit from WB

-*Fewer units need*

-*Acceptance of lower plt count*

-*Progressive reduction in standard dose*

10→8→6→ even 4 units

-*Platelet – Apheresis*

3×10^{11}/unit with early instruments

-*Corrected count increment (CCI)*

CCI (10min-1Hr) < 7500	CCI (24Hr) < 4500
Immune Refractoriness	Non-Immune

TABLE 20-5. Determination of Platelet Response

Corrected count increment (CCI)

$CCI = (CI \times BSA)/\text{unit content} (\times 10^{-11})$

Platelet recovery

$$\text{Platelet recovery (\%)} = \frac{CI \times (1000\ \mu L/mL) \times \text{blood volume in mL} \times 100}{\text{unit content}}$$

Sample calculations

Patient mass = 80 kg: blood volume = 80 kg × 75 mL/kg = 6000 mL

Patient body surface area: 2.0 m^2 (determined from a table or nomogram)

Pretransfusion platelet count:	5000/μL	→ CI = 20,000/μL
Posttransfusion platelet count:	25,000/μL	

Platelet count in unit:	1.5×10^6/μL	→ Unit content = 4.0×10^{11} platelets
Volume of unit:	267 mL	

$CCI = (20{,}000/\mu L \times 2.0\ m^2)/4.0 = 10{,}000$

Successful transfusion:	≥7500
Refractory patient:	Two or more transfusions with CCI <5000

Recovery = $(20{,}000/\mu L \times 1000\ \mu L/mL \times 6000\ mL \times 100\%)/(4.0 \times 10^{11}) = 30\%$

Maximum achievable if patient has spleen: 65% to 70%

$$CCI = \frac{\text{Platelet count increment} \times BSA}{\text{Number of platelets transfused } (\times 10^{11})}$$

BSA = body surface area (m^2).

Example:

Pretransfusion platelet count = 8000/μL

Post-transfusion platelet count = 36 000/μL

BSA = 1.5 m^2

Platelet dose = 3.0×10^{11}

$$CCI = \frac{24\,000 \times 1.5}{3} = 12\,000$$

A CCI > 7500 at 1 hour or a CCI > 4500 at 24 hours

CCI calculation example

- An adult patient ; BSA=2.0 m^2, platelet count rose from 5,000/pL to 25,000/pL after a platelet transfusion containing 4.0 x 10^{11} platelets , the CCI would be:

(Count increment x BSA) /unit content=

(20,000/pL x 2.0 m^2)/4.0 = 10,000

- **A CCI > 7500 :** Successful transfusion.
- **2 times of CCIs 1 h < 7500 :** refractoriness.

-Low-dose prophylactic platelet transfusion
(Half the standard dose): 1.5×10^{11}

-SToP & PLADO studies ;
Hypoproliferative thrombocytopenia secondary to chemotherapy for hematologic malignancies or undergoing either autologous or allogeneic stem cell transplantation were randomly assigned to a prophylactic platelet transfusion dose of 1.1 (low dose), 2.2 (medium dose), or 4.4 x $10^{11}/m^2$ platelets (high dose).

Not statistically different between bleeding episodes in 1272 pts who received at least one plt transfusion for WHO Grade 2 or higher bleeding

Platelet Life span

-*Abnormally short life span*
in severe thrombocytopenia ≃ 2 days

-*In normal subjects ; 5-7 days*

-*Fixed loss of platelets from the circulation* ≃
7100/µl/day

- *" Storage lesion "*

Apheresis platelets(SDP)

Platelets collection 1-2 hour

Cytopheresis procedure

Plt donor selecton as blood donors

>3 ×10^{11} plt/bag

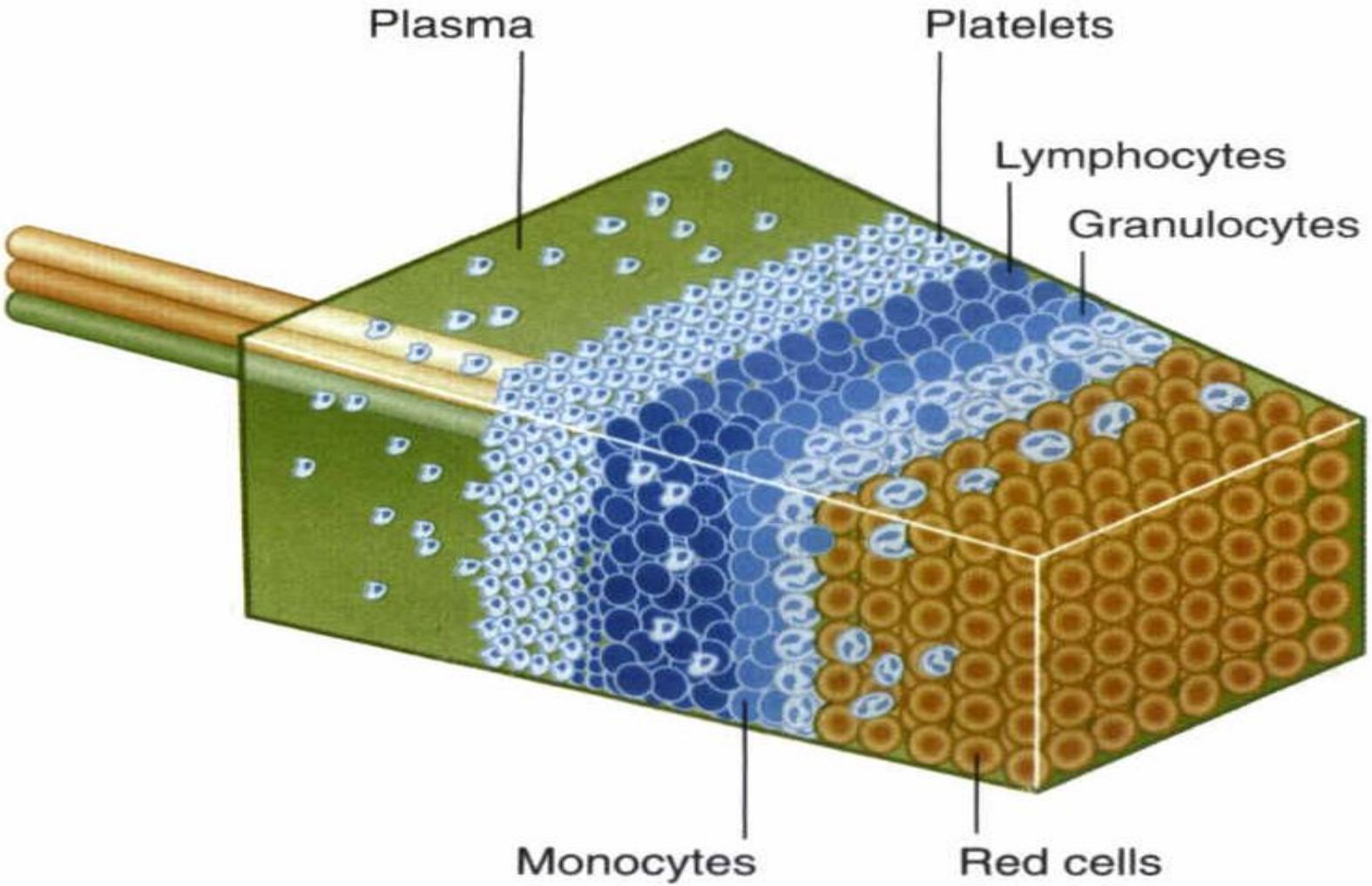
≈ 5-6 & now 6-7 units of routine plt concentrate bag

volume 200-400 ml

Leukocyte reduction technique < 5 ×10^{6} / unit ,

Shelf life : 3-5 days

Currently, about 90% of platelet transfusions in the U S are derived from apheresis collections,& the usage of these platelets has increased in a steady, linear manner for the past two decades.



-Donor apheresis

-Therapeutic apheresis ;

Cytoreduction for hyperviscosity or risk - factors

Plasmapheresis versus plasma exchange

-Peripheral blood hematopoietic progenitor cell collection

Indications

- Limit donor exposures
- Unresponsive to WB derived plt (RDP)
- *Immune ;*

CCI 1 h < 5000

Nonimmune ; CCI 24 h :

return to baseline (< 4500)

- HLA alloimmunization
- HLA-matched /HLA selected
- Cross matched- compatible
- Refractory to platelets

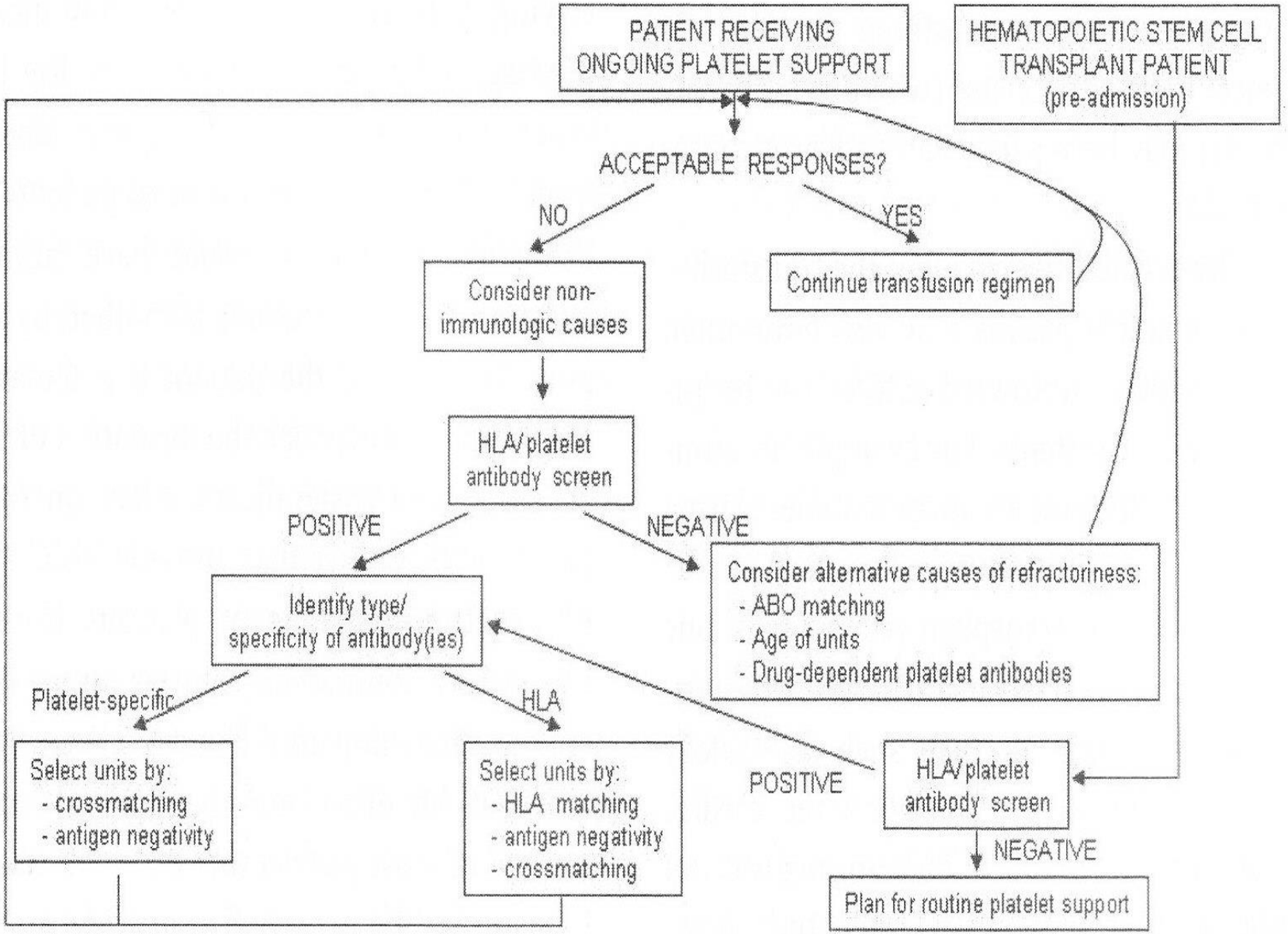

PATIENT RECEIVING ONGOING PLATELET SUPPORT
HEMATOPOIETIC STEM CELL TRANSPLANT PATIENT (pre-admission)
ACCEPTABLE RESPONSES?
NO
YES
Consider non-immunologic causes
Continue transfusion regimen
HLA/platelet antibody screen
POSITIVE
NEGATIVE
Identify type/ specificity of antibody(ies)
Consider alternative causes of refractoriness:
- ABO matching
- Age of units
- Drug-dependent platelet antibodies
Platelet-specific
HLA
Select units by:
- crossmatching
- antigen negativity
Select units by:
- HLA matching
- antigen negativity
- crossmatching
POSITIVE
HLA/platelet antibody screen
NEGATIVE
Plan for routine platelet support

Table 35–5 Platelet Transfusion Guidelines

Thrombocytopenia due to decreased production

- Stable patent: Platelet count < 10 000/μL
- Fever: Platelet count < 20 000/μL
- Bleeding, invasive procedure or surgery: Platelet count < 40 000–50 000/μL
- Retinal or CNS bleeding: platelet count < 100 000/μL

Microvascular bleeding due to platelet dysfunction

TABLE 98–5. Guidelines for Platelet Transfusion per National Institutes of Health Practice

Patient Population	Threshold
Stable aplastic anemia patient	<5000/μL or bleeding
General oncology patient	<10,000/μL
Stable non-oncology patient	<10,000/μL
Post–hematopoietic stem cell transplant	<10,000/μL
Aplastic anemia patient receiving ATG	<20,000/μL
Patients undergoing invasive procedures	<50,000/μL
Neurosurgery patients	<100,000/L

Abbreviation: ATG, antithymocyte globulin.

Out- of- Group Transfusion

Many patients ; no signs or symptoms

Majority ; +DCT

Exceptions : Small pt. , Apheresis units

RDP : plasma dilution

Apheresis high volume ;

1:3000 to 1:10,000 → Hemolysis

Identify *"Dangerously- High"* titer of anti-A & or anti-B

Platelet Volume Reduction

Shortly before transfusion

Dose & administration

One apheresis unit → increased 30-60×10^3 plt/µl

If RBC ≥2ml → Compatibility testing

Donor plasma should be
ABO-compatible
with recipients' RBCs

Platelets - leukocytes reduced

Leukocytes 0.5-1 × 10^8 /unit of platelets
Not removed by the standard 170 micron blood filter
Plt-LR : < 8.3 × 10^5 WBC/unit
Pooled plt-LR : < 5× 10^6 WBC/unit
Apheresis platelets leukocytes reduced:
<5× 10^6/unit
Passage of plt through
leukocyte reduction filters>90%
Leuktrapping : 99.9%
Prestorage , Laboratory &
Bedside LR-filtration

Indications

1-Prophylaxy against HLA alloimmunization in selected pt. (long-term transfusion therapy)

2-Prevention of FNHTR & Alloimmunization before first transfusion

3-Commitment to use RBCs-LR

4-Reduction of the risk of CMV transmission

Contraindications & Precautions

1-Similar to those for plt.

ITP , TTP , DIC , HIT (Type II)

Add fuel to the Fire

2-Acute hemolytic transfusion reactions with units containing ABO-incompatible plasma

.

Irradiated cellular Products

RBCs ; PC , WB

Platelet concentrate

Granulocyte concentrate

UCB , HPC-A or M ?!

genetic diversity in the population

Indication of Irradiation cellular components (AABB)

1- Pt who At risk of TA-GVHD

2- The donor is a blood relative of the recipient

One-way haplotype match

Degree of genetic diversity in a population

Low HLA diversity in Japan TA-GVHD Risk; x20

(1:874) Versus 1:16,835 in France

3- Donor selected for HLA compatibility by HLA typing or crossmatching

TABLE 23-8. Irradiation Guidelines for Neonates and Older Children Requiring Cellular Blood Components[20,23]

1. Premature infants weighing <1200 grams at birth.

2. Any patient with:
   a. Known or suspected cellular immune deficiency.
   b. Significant immunosuppression related to chemotherapy or radiation treatment.

3. Any patient receiving:
   a. Components from blood relatives.
   b. HLA-matched or crossmatched platelet components.

Effect of irradiation of RBCs

Decreased RBC Recovery % Post-transfusion ±10%

- Increased efflux of potassium ; X2

-Irradiated components stored >24h … infants

washing

Life threatening in infants especially who received

via *CVP or an intracardiac* line ; Arrest

Expiration date for Irradiated Cellular blood components

RBC Irradiated

Original outdate or 28 days from date of irradiation, whichever is sooner whole blood irradiated… 1-6°c

Platelets Irradiated

Open system : 4 hours;
Closed system : no change from original exp. date.

Complications of plt transfusion

1- Febrile & Allergic plt transfusions
(two most common)
- Group O donor plasma from 6-8 pooled donor

2- Acute hemolysis (passive isoagglutinins)
- Plasma compatible donor prevents such reactions
- Especially important in neonate young children & Adult with multiple transfusion each day

3-Volume overload (Plasma -reducted plt units) or volume reduction technique

- *4- Immunization to Rh (D)*
- *5- Thrombosis in TTP*
- *6- Bacterial contamination (10% ; 2/1000)*
- *_ Endotoxic shock in gram negative*
- *_ Transfusion - Associated sepsis*
- *_ Chills fever Hypotension & hypoxia*
- *_ Shortening the storage shelf life*
- *_ Especial care for neutropenic pts*

Systemic reactions to Plt transfusions

- **Acute –Rx:** 2% 1/3 reactions in the first transfusion
- Rash , wheezing , fever , chills , dyspnea , urticaria & hypotension .
- **Cytokine generation** during the in vitro storage
  (TNF, IL-1, 6 & 8*).
- Transfusion reaction x4 with platelet , older & higher **WBC contaminated**

Plasma derivatives

Frozen plasma

- *FFP/PPP WB* : 200-280ml / -70ml PRP →PPP
  Apheresis : 400-600ml
- *F24*

--*Cryoreduced - plasma* (CRP) or cryosupernant

-*Solvent Detergent - treated plasma*; S/D plasma

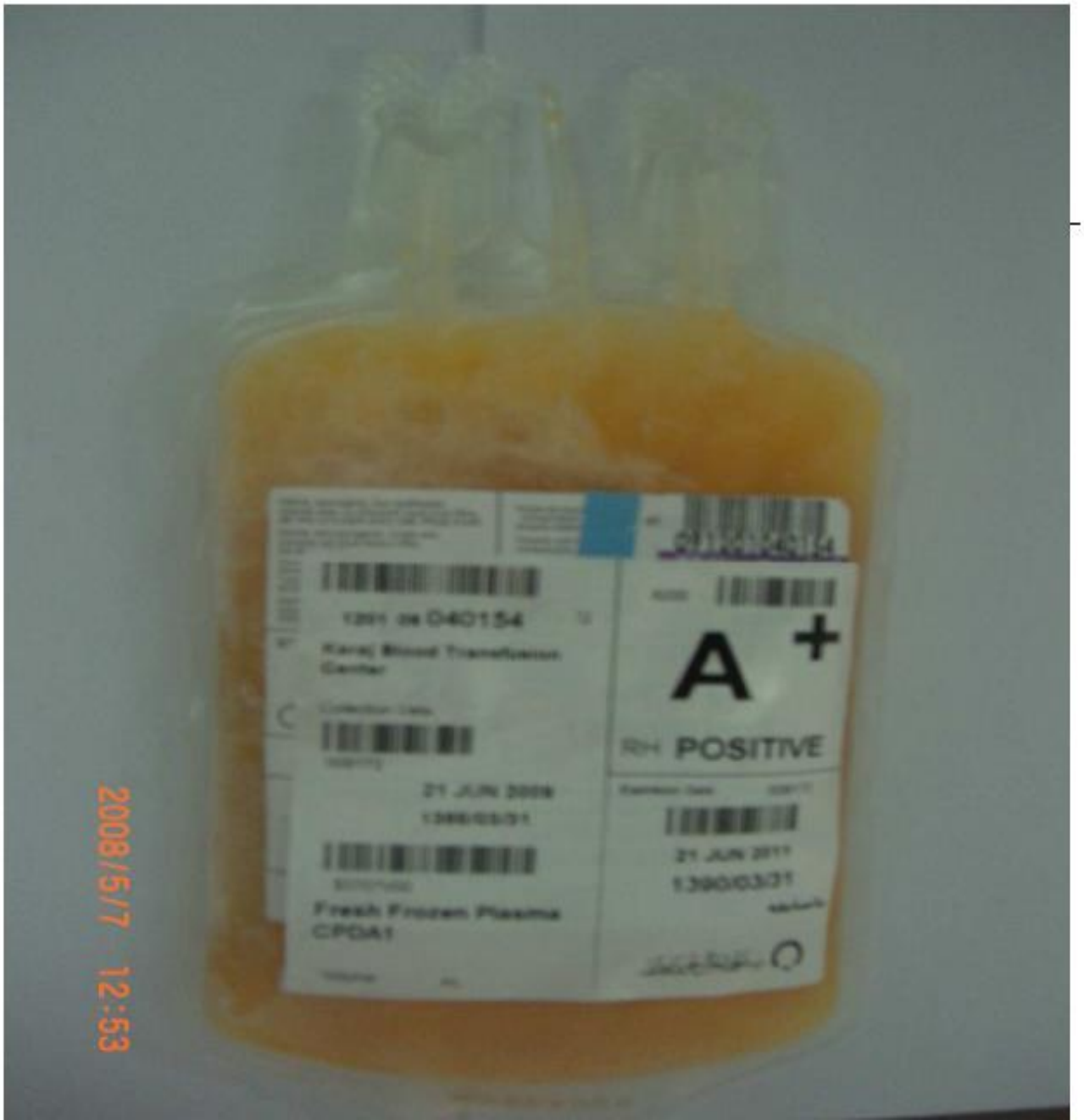
-*Liquid plasma* (stored at 1-6 °C)

--*Source plasma* (Stored at -180 ° or Colder)

- Thawed plasma
- F24
- Cryopoor plasma or CPP
- Recovered plasma
- Liquid plasma
- Platelet rich plasma or PRP
- Platelet poor plasma or PPP
- Source plasma
- Donor restricted plasma

Solvent detergent plasma; S/D

- Pooled plasma....tri-n-butyl phosphate as solvent, X-100 Non-ionic detergent.
- Slight ↓ Factor V, VIII , protein S & Anti- plasmin
- Effective on lipid envelop of viruses (HBV , HCV , HGV , HTLV 1 & 2 & CMV).
- Not effective on Parvo-virus & HAV.
- Decreased TRALI due to dilution of Anti-Leukocyte Antibodies.


A +
RH POSITIVE
21 JUN 2011
Fresh Frozen Plasma
CPDA1
2008/5/7 12:53

DR-Plasma
(Donor retested plasma)

- **FFP or F24** that keep in Quarantine
- Only use when **another sample** from the donor **after Window period** to assure the Negative results ..... **Safe Plasma products.**

The least Quarantine time : 56 days.

2. Cryoprecipitate 10-15ml
3. Albumin
4. IVIG / RhIG
5. Plasma - derived clotting factor concentrates

Administration Guidelines

Adults 8-10ml/kg :

2-5ml/min in first 15min

200 -300ml/hr subsequently

Children :

First 5min : 5% of total volume

1-2mL/min subsequently

Indications

FFP Indications

1- ***Coagulopathies*** **confirmed by PT & PTT**

PT > 16 PTT > 5s (1.5 – 1.8x) ISI : 2 → INR: 2

PT x> 1.3 in neuro & opthalmologic bleeding

2- Liver disease ;

All C.F synthesis except VWF , TPA , PI

3- ***Hereditary C.F deficiency***

4- ***Warafarin*** effect reverse

5- ***Dilutional coagulopathy (Washed out)*** in massive transfusion

6- **DIC**

7- ***Replacement fluid*** in plasmaphresis FFP/CPP, preferentially Group O : TTP : ADAMTS13

8- ***C1 estrase inhibitor deficiency***

1-Liver disease & transplantations

Portal HTN , splenomegaly with

2° thrombocytopenia

Decreased synthesis all of coagulation Factors

(except VIII, TPA & Plasminogen inhibitor),

Caboxylation of Vitamine K dependent CF ↓

Dysfibrinogenemia , Clearance & inactivation of circulatory active CF

PT>16-18 PTT >55-60 (> 1.5*upper limit).

PT & PTT is poor predictor of surgical bleeding.

FFP correct Patients for only about 4 hours.

RX of bleeding in Liver Dis.: FFP & Platelet, rFVIIa

2- Massive transfusion (Dilutional coagulopathy)

1 bag FFP & PLT : 5 whole blood, PC (1: 5)

Trauma :

thrombocytopenia developed before diluted C.F. ; **New approach 1:1 in trauma**

Elective surgery :

CF dilution before thrombocytopenia

OB & GYN :

1/2 - 4/6 & even 1:1

2- Massive transfusion (Dilution coagulopathy)

<24 Hours ; 5 liters blood transfusion or > 10 PC

1 bag FFP & PLT : 5 whole blood, PC (1: 5)

Trauma :

thrombocytopenia developed before diluted C.F. ; New approach 1:1:1 in trauma

Elective surgery :

CF dilution before thrombocytopenia

OB & GYN : 1/2 - 4/6 & even 1:1:1 ; 4 Plt=1 FFP

CNS & eye dis.; risk of bleedings : PT & PTT >1.3

In massive transfusion: platelet should > 50,000

3- Consumptive coagulopathy ; DIC

Microangiopathic hemolytic anemia ; Schistocytosis, Microvascular thrombi promote tissue ischemia.

Shock, tissue ischemia, sepsis, hemolytic transfusion reactions, disseminated cancer (esp. Mucin producing Adenocarcinoma), ***Acute promyelocytic leukemia ; AML , M3***

Tumor lysis syndrome , obstetric events

3-Consumptive coagulopathy; DIC

Consumptive CF: 1, 2, 5, 8 , 13 ↓ bleedind tendency

Microangiopathic hemolytic anemia ; Schistocytosis, Microvascular thrombi promote tissue ischemia.

D-Dimer & FDP: inhibit fibrin polymerization.

Active fibrinolysis....Thrombi solve...bleeding.

Shock, tissue ischemia, sepsis, hemolytic transfusion reactions, disseminated cancer (esp. Mucin producing Adenocarcinoma), ***Acute promyelocytic leukemia ; AML , M3***

Tumor lysis syndrome , obstetric events

4- Rapid reversal of warfarin effect & vit.K deficiency

Vit. K dependent factors
(II, VII, IX ,X & protein C & S)

Vit . K body store last only 2 wks.

ABT use , obstructive jaundice & fat malabsorption

Prolonged pT

D/C Warfarin , correct CF deficiency **48h** later

Vit. K administration correct CF def. **12-18h** later

FFP administration 10-15 ml/kg correct CF **4h** later
& INR normalized

PCC (Prothrombin complex concentrates; Factor VIII inhibitor bypassing activity) **& or rFVIIa**

TABLE 20-7. Guidelines for Correction of Excessive Oral Anticoagulation*

Clinical Situation	Guideline
INR >therapeutic but <5, no significant bleeding	Lower anticoagulant dosage.
	Temporarily discontinue drug if necessary.
INR >5 but <9, no significant bleeding	Omit 1-2 doses; monitor INR; resume when in therapeutic range.
	Alternative if patient at increased risk of hemorrhage: ◆ Omit a dose and give 1 to 2.5 mg vitamin K_1 orally. ◆ For rapid reversal before urgent surgery: give 2 to 4 mg vitamin K_1 orally; repeat dose with 1 to 2 mg at 24 hours if INR remains elevated.
INR >9, no significant bleeding	Omit warfarin; give 2.5-5.0 mg vitamin K_1 orally.
	Closely monitor INR; give additional vitamin K_1 if necessary.
	Resume warfarin at lower dose when INR is within therapeutic range.
Serious bleeding at any elevation of INR	Omit warfarin.
	Give 10 mg vitamin K_1 by slow intravenous infusion.
	Supplement with plasma or prothrombin complex concentrate depending on urgency of correction. Vitamin K_1 infusions can be repeated every 12 hours.
Life-threatening hemorrhage	Omit warfarin.
	Give prothrombin complex concentrate with 10 mg vitamin K_1 by slow intravenous infusion.
	Repeat as necessary, depending on INR.

*Adapted from Ansell et al[295]; guidelines developed and vetted by the American College of Chest Physicians.
INR = international normalized ratio.

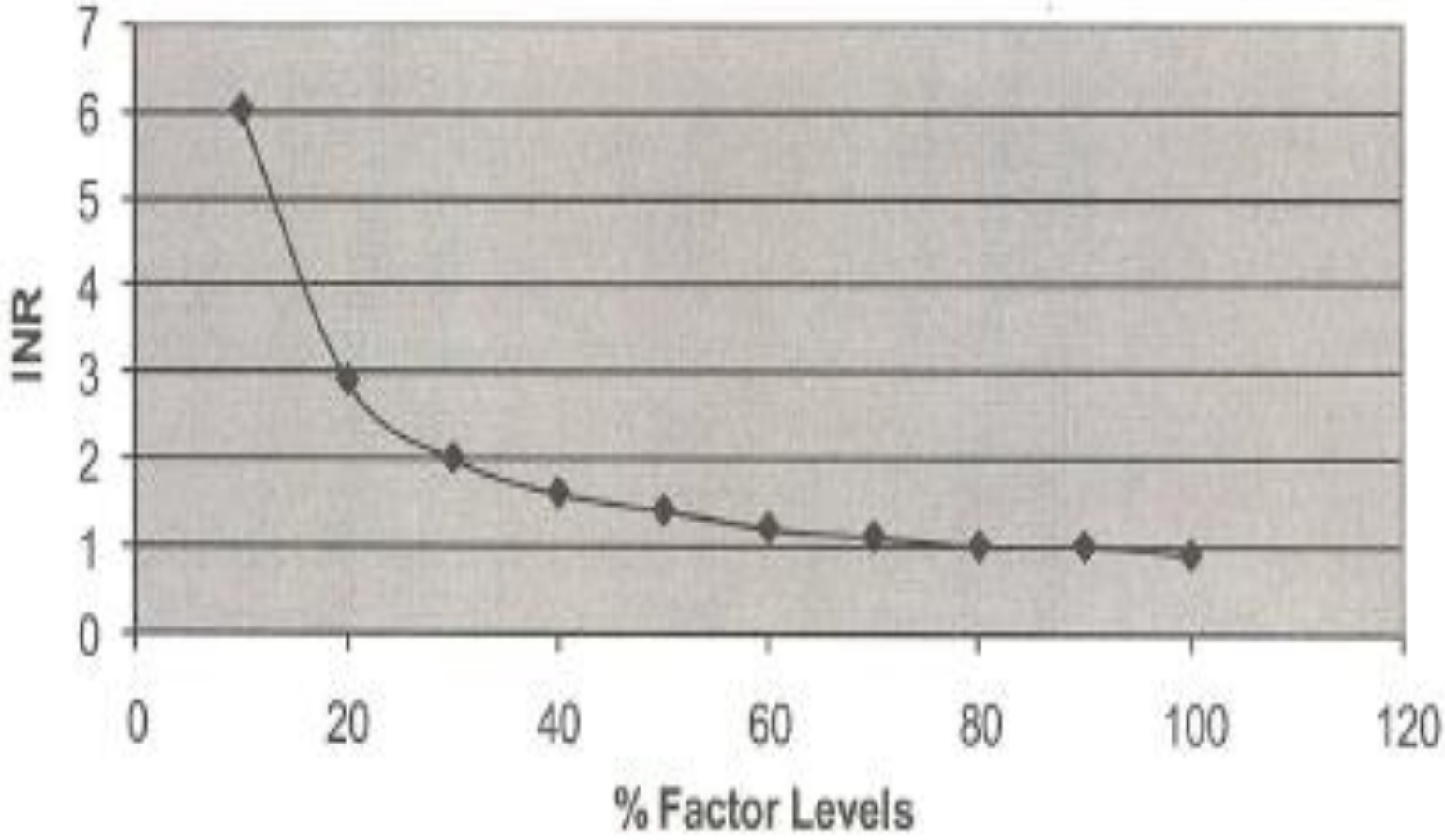


FIGURE 20-2. Exponential relationship of INR to percentages of factor levels. (Used with permission from Wayne Chandler, MD, University of Washington Department of Laboratory Medicine.)

5- TTP & HUS

FFP or plasma exchange for

Ultera large: UL-VWF clearing protease

Plasmapheresis is preferred especially in those with autoantibody acquired TTP, who at risk of volume overload such as cardiac or renal impairment

FDA : CRP (CPP for refractory TTP) ;

CRP by some authoress is the first line therapy for TTP but randomized trial show same efficacy & survival for both FFP & CRP

5- TTP & HUS

Hemolysis, ↑ LDH, thCPN, Fever,Neurologic def. & RF.

ADAMTS13 ↓ : UL-VWF..... **VWF level : AB>B>A>O**

FFP or plasma exchange for

Ultra large : **UL-VWF clearing** protease

Plasmapheresis is preferred especially in those **with autoantibody** acquired TTP, who **at risk of volume overload** such as cardiac or renal impairment

FDA : **CRP** (**CPP** for refractory TTP) ;

CRP by some authoress is the **first line therapy** for TTP but randomized trial show **same efficacy & survival for both FFP & CRP.**

6- C1 esterase inhibitor

- C1 inhibitor ..... Control complement system activity
- C1 inhibitor deficiency .....edema of mucosa & airway , GIT ..... Dyspnea & ...
- Autosomal Dominant .....
- RX : FFP & concentrated Factor.

Table 35–6 Plasma Transfusion Guidelines

Coagulation factor deficiency, factor concentrate unavailable

Dilutional coagulopathy

Hemorrhage in liver disease

Disseminated intravascular coagulation (DIC)

Coumadin reversal

Thrombotic thrombocytopenic purpura (TTP)

Side effects of FFP

- Fever , chills & allergic reactions
-Server allergic reactions with bronchospasm &
-TRALI ; noncardiogenic pulmonary edema
(HLA Abs in donor plasma react with recipient WBC) or ; third leading cause of mortality related to transfusion ,underdiagnosed because can occur in extremely ill patients
-Anaphylactic reactions ;
IgA / Haptoglobin containg plasma infusion in to IgA def.
-Transfusion Transmitted infectious disease

Side effects of FFP

1- Fever chills & allergic reactions
2- Occasionally server allergic reactions with bronchospasm &
3-TRALI (noncardiogenic pulmonary) edema (HLA Abs in donor plasma react with recipient WBC) or reversely plasma react with donor WBC ; third leading cause of mortality related to transfusion underdiagnosed because can occur in extremly ill patients
4-Anaphylactic reactions ;
IgA containg plasma infusion in to IgA def.
5- Transmission of infectious disease

Side effects of FFP

1- Fever chills & allergic reactions

2- Occasionally server allergic reactions with bronchospasm &

3-TRALI (noncardiogenic pulmonary) edema (HLA Abs in donor plasma react with recipient WBC) or; third leading cause of mortality related to transfusion underdiagnosed because can occur in extremly ill patients

4-Anaphylactic reactions ;

IgA containg plasma infusion in to IgA def.

5- Transmission of infectious disease

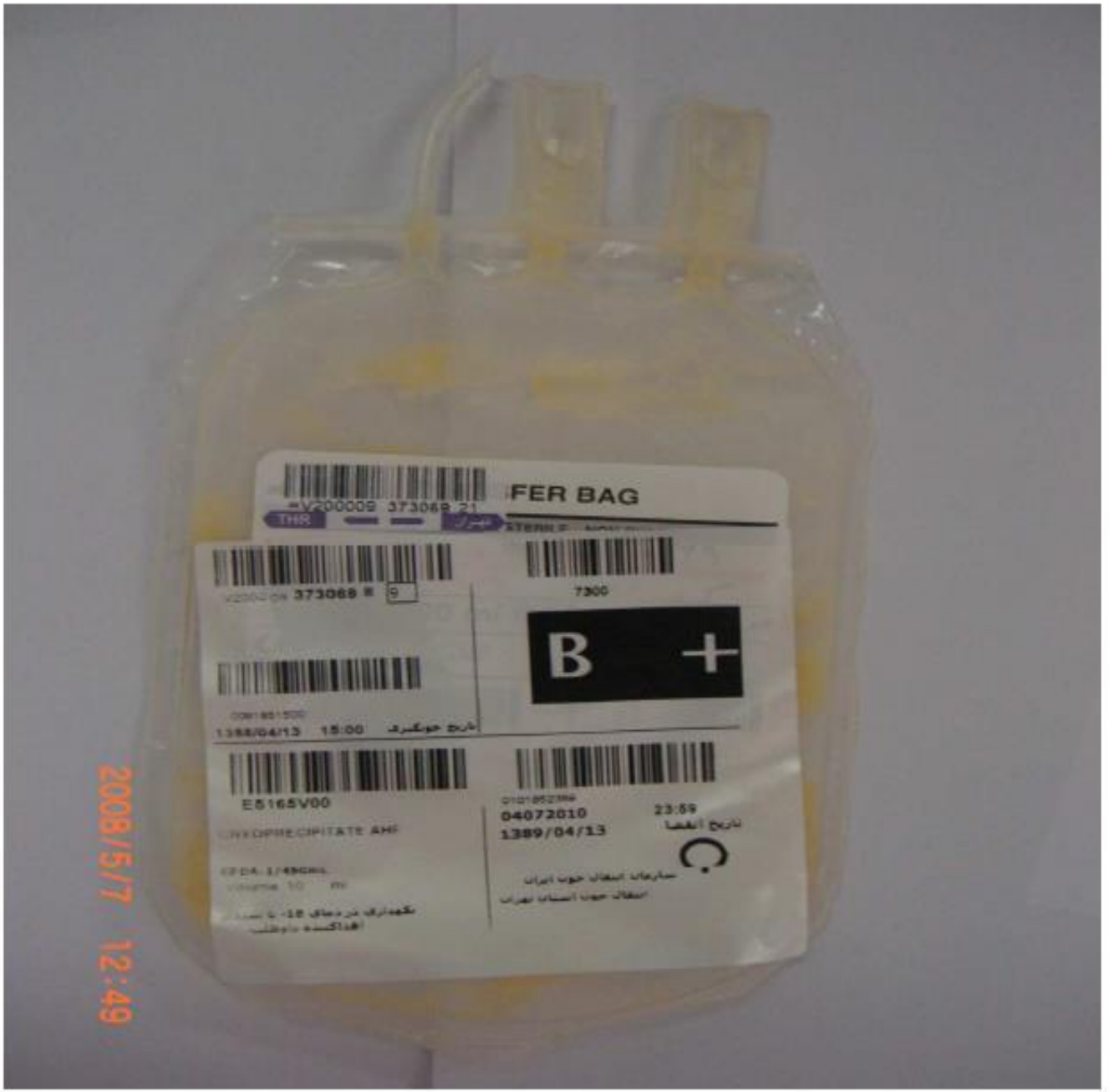
Table 57.7 FEATURES OF COMMON VARIANTS OF VON WILLEBRAND DISEASE

Features	Type 1	Type 2A	Type 2B	Type 3	Platelet Type
Inheritance	Autosomal dominant	Autosomal dominant	Autosomal dominant	Autosomal recessive	Autosomal dominant
Factor VIIIc in plasma	Normal or reduced	Normal or reduced	Normal or reduced	Markedly reduced	Normal or reduced
vWF antigen	Normal or reduced	Normal or reduced	Normal or reduced; increased affinity for platelets	Markedly reduced	Normal or reduced; increased affinity for platelets
Ristocetin cofactor activity	Normal or reduced	Reduced	Normal or reduced	Markedly reduced	Reduced or normal
vWF multimeric analysis	Normal (plasma and platelets)	Absence of large and intermediate-sized multimers in plasma	Absence of large multimers from plasma; normal in platelets	Small multimers or absent multimers in plasma and platelets	Reduction in large multimers caused by "consumption" by platelets
Ristocetin-induced platelet aggregation	Normal or diminished	Diminished	Increased aggregation at low ristocetin concentrations	Markedly diminished	Hyperaggregation with patient's platelets, normal plasma, and low concentration of ristocetin
vWF in platelets	Normal or reduced	Normal or absence of large and intermediate-sized multimers	Normal	Absent	Normal
Ancillary findings	DDAVP usually produces significant increase in plasma VIIIc and vWF	DDAVP produces rise in factor VIIIc, but functional vWF increase is variable and may be of short duration	Variable response to DDAVP, with intravascular platelet aggregation and thrombocytopenia in some cases; ristocetin-induced platelet aggregation enhanced in presence of patient's plasma; cryoprecipitate does not aggregate platelets in vitro unless ristocetin is added	Response to DDAVP lacking; endothelial vWF absent	Transfusion of vWF or DDAVP may produce intravascular platelet aggregation and thrombocytopenia; cryoprecipitate produces in vitro platelet aggregation

DDAVP, 1-deamino-8-D-arginine vasopressin; vWF, von Willebrand factor.

CRYOPRECIPITATE

Cold insoluble portion of plasma
High molecular weight glycoproteins
At R.T. for up to 6 hours
Compatibility testing: Unnecessary
10-15 ml plasma:
> 80 IU factor VIII (AHF)
> 150 -200 mg fibrinogen → one unite
→↑ 5-10 mg/dl
≈ 30% factor XIII of the original plasma
VWF


FER BAG
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Therapeutic dose

Adults 80-150 ml of cryo (8-10 units pooled)

2-5 ml/min in first 15 min , 200-300 ml/hr

Children : 5% of total volume in first 5 min → 1-2 ml/min

Dose(units)=desired fibrinogen increment mg/dl x plasma vol. / 250mg / unit

TABLE 20-8. Coagulation Factor Half-Lives

Factor	In-Vivo Half-Life	Percent Needed for Hemostasis
I	3-6 days	12-50
II	2-5 days	10-25
V	5-36 hours	10-30
VII	2-5 hours	>10
VIII	8-12 hours	30-40
IX	18-24 hours	15-40
X	20-42 hours	10-40
XI	40-80 hours	20-30
XIII	12 days	<5

- ***The fibrinogen necessary for hemostasis:*** *50-100 mg/ dL follow the pt with coagulation test results patients with such conditions*
- ***Maintaining the fibrinogen above this level*** *aids both the patient & normalize the test.*
- ***When fibrinogen levels drop;*** *eg DIC or ongoing , high-volume hemorrhage,initiate cryoprecipitate (or at least prepare it) as the critical point of 100 mg/dL is approached (eg, at ≈120 mg/dL).*
- ***Although the dosage of cryoprecipitate is often stated in tens of units*** *(eg, 10, 20, or 30 units), the dosage required to achieve the desired effect is readily calculated:*
- *Dose (units)= [desired fibrinogen increment (mg/dL) x plasma volume]/250 mg/unit*

General Factor Replacement Guidelines for Treatment of Hemophilia A & von Willebrand Disease

Indication	Minimum Desired Factor Level (%)	Factor VIII Dose (IU/kg)	Factor IX Dose (IU/kg)	Duration (days)
Hemophilia*				
Severe epistaxis, oral mucosal bleeding†	20-30	10-15	20-30	1-2
Hemarthrosis, hematoma, persistent hematuria,‡ gastrointestinal bleeding, retroperitoneal bleeding	30-50	15-25	30-50	1-3
Trauma without signs of bleeding, tongue/retropharyngeal bleeding†	40-50	20-25	40-50	2-4
Trauma with bleeding, surgery, intracranial bleeding§	100	50	100	10-14
von Willebrand Disease¶				
Major surgery	50	40-60 daily		
Minor surgery	30	30-50 daily or every other day		
Dental extractions	30	20-30, single dose		12 hours
Spontaneous bleeding	30	20-30, single dose		

*Data from US Pharmacopeia.[197] Dosing intervals based on a half-life of Factor VIII over 8-12 hours (2-3 doses/day) and half-life of Factor IX over 18-24 hours (1-2 doses/day). Maintenance doses of one-half the initial dose (as shown) may be given at these intervals. The dosing frequency depends on the severity of bleeding, with more frequent dosing used for serious bleeding.

†In addition to antifibrinolytics.

‡Painless spontaneous hematuria usually requires no treatment. Increased oral or intravenous fluids are necessary to maintain renal output.

§Factor may be administered continuously. Following the initial loading dose, a continuous infusion at a dose of 3 IU/kg per hour is given. Subsequent doses are adjusted according to measured plasma factor levels.

¶Concentrates labeled in terms of the ratio of von Willebrand factor to ristocetin cofactor. The recommended doses for adults, number of infusions, and target plasma levels are the same as those for Factor VIII.[198]

Indications

Fibrinogen deficiency

(DIC. Obstetric complications, rare congenital)

Dysfibrinogenemia (congenital or acquired) measurable by immunoassay but non functional in TT

Factor XIII deficiency

DIC

Urgent treatment of hemophilia A & VW Disease in the absence of factor VIII concentrate or rF VIII

Correction of Plt defect of uremic bleeding

(variable success)

As topical glue ; with Ca & bovine thrombine

Table 35–7 Cryoprecipitate Transfusion Guidelines

Factor VIII deficiency, factor concentrate unavailable
von Willebrand disease, factor concentrate unavailable
Hypofibrinogenemia
Factor XIII deficiency
Uremic bleeding (DDAVP preferred)
Topical fibrin sealant (commercial product preferred)

Contraindication

Absence of specific haemostatic abnormality

Specific haemostatic abnormality for which specific factor concentrates are available.

Platelet -type von willebernd disease

Contraindication of Cryo

- Absence of specific haemostatic abnormality
- Specific haemostatic abnormality for which specific factor concentrates are available.
- Platelet -type Von Willebernd disease;

Cryo infusion ….. Dangerous Plt aggregation

Dosage of Cryoprecipitate

Blood Volume =

Wt X 70 ml/kg adult

8o - 85 ml/kg infants & children < 40 kg

100 ml/kg premature

Plasma volume = Blood volume (1- Hct%)

Fibrinogen level required (mg) =

(Desired level – observed level) **X** plasma level ÷ 100 mg/dl

Bags of cryo required = required fibrinogen level ÷ 250

TABLE 20-10. General Factor Replacement Guidelines for Treatment of Hemophilia A and von Willebrand Disease

Indication	Minimum Desired Factor Level (%)	Factor VIII:C Dose (IU/kg)	Factor IX Dose (IU/kg)	Duration (in days)
Hemophilia*				
Severe epistaxis, oral mucosal bleeding†	20 to 30	10 to 15	20 to 30	1 to 2
Hemarthrosis, hematoma, persistent hematuria,‡ gastrointestinal bleeding, retroperitoneal bleeding	30 to 50	15 to 25	30 to 50	1 to 3
Trauma without signs of bleeding, tongue or retropharyngeal bleeding†	40 to 50	20 to 25	40 to 50	2 to 4
Trauma with bleeding, surgery,§ intracranial bleeding§	100	50	100	10 to 14
von Willebrand disease‖				
Major surgery	50	40 to 60, daily		
Minor surgery	30	30 to 50, daily or every other day		
Dental extractions	30	20 to 30, single		0.5
Spontaneous bleeding	30	20 to 30, single		

Issues in FFP Transfusion

- ***Administration*** Thaw at 37 ; water bath
  infuse within 4 - 6 hrs
  ABO matching must be check
- ***ABO matching***

O	O	FFP
A	A/O	FFP
B	B/O	FFP
AB	O/A/B/AB	FFP

- ***Dose*** 10-15 ml/kg
- ***Monitoring*** clinical ; bleeding stops
  Lab ; correct PT/aPTT
  Howevere ; DO NOT "TREAT" LAB LEVELS
- ***Adverse effect*** Allergic Reactions
  TRALI

Plasma Cryopercipitate Reduced ; CPP

Shelf life : 12 months

Normal level of factor :

V (85%), I , VII, VIII, X

a2-antiplasmin , antithrombin , protein C, & protein S

Fibrinogen level : 200mg/dl

Thrombotic thrombocytopenic purpura ; ***TTP***

Both Von-Willebrand Factor (VWF) antigen & VWF activity are decreased

TABLE 20-8. Coagulation Factor Half-Lives

Factor	In-Vivo Half-Life	Percent Needed for Hemostasis
I	3-6 days	12-50
II	2-5 days	10-25
V	5-36 hours	10-30
VII	2-5 hours	>10
VIII	8-12 hours	30-40
IX	18-24 hours	15-40
X	20-42 hours	10-40
XI	40-80 hours	20-30
XIII	12 days	<5

TABLE 18-1. Blood Component Transfusions in Nonemergent Settings

Component	Suggested Adult Flow Rates		Special Considerations	ABO Compatibility	Filter
	First 15 Minutes	After 15 Minutes			
Red Blood Cells (RBCs)	1-2 mL/min (60-120 mL/hour)	As rapidly as tolerated; approximately 4 mL/minute or 240 mL/hour	Infusion duration should not exceed 4 hours. Generally administered over 1-2 hours for hemodynamically stable recipients. For recipients at risk of fluid overload, may adjust flow rate to as low as 1 mL/kg/hour.	Whole blood: ABO identical RBCs: ABO compatible with recipient's plasma Crossmatch required	In-line (170-260 micron) Leukocyte reduction if indicated
Platelets	2-5 mL/min (120-300 mL/hour)	300 mL/hour or as tolerated	Usually given over 1-2 hours. For recipients at risk of fluid overload, use slower flow rate (see RBCs).	Crossmatch not required ABO/Rh compatibility preferable but not required May be HLA matched	In-line (170-260 micron) Leukocyte reduction if indicated
Plasma	2-5 mL/min (120-300 mL/hour)	As rapidly as tolerated; approximately 300 mL/hour	Time for thawing may be needed before issue. For recipients at risk of fluid overload, use slower flow rate (see RBCs).	Crossmatch not required ABO compatibility with recipient red cells	In-line (170-260 micron)
Granulocytes	1-2 mL/min (60-120 mL/hour)	120-150 mL/hour or as tolerated	Over approximately 2 hours. Infuse as soon as possible after collection/release of component; irradiate.	Crossmatch required ABO/Rh compatibility required May be HLA matched	In-line (170-260 micron) Do not use leukocyte reduction or microaggregate filters
Cryoprecipitated AHF	As rapidly as tolerated		Infuse as soon as possible after thawing; pooling is preferred.	Crossmatch and ABO compatibility not required	In-line (170-260 micron)

TABLE 19-5. Summary of AABB Recommendations for Prophylactic Platelet Transfusion in Adults[56]

Clinical Setting	PLT Transfusion May Be Indicated for:	Strength of Recommendation	Quality of Evidence
Therapy-related hypoproliferative thrombocytopenia	PLT count ≤10,000/μL	Strong	Moderate
Central venous catheter placement	PLT count <20,000/μL	Weak	Low
Diagnostic lumbar puncture	PLT count <50,000/μL*	Weak	Very low
Major elective nonneuraxial surgery	PLT count <50,000/μL	Weak	Very low
Cardiac surgery with bypass	Perioperative bleeding with thrombocytopenia and/or evidence of PLT dysfunction. Routine PLT prophylaxis not recommended.	Weak	Very low
Intracranial hemorrhage on anti-PLT therapy	Insufficient evidence for recommendation	Uncertain	Very low

*Clinical judgment should be used for patients with PLT counts between 20,000 and 50,000/μL.
PLT = platelet.

TABLE 19-6. Causes of Platelet Refractoriness[81]

Nonimmune	Immune
Fever	HLA antibodies
Medications (eg, amphotericin, vancomycin)	ABO incompatibility
Splenomegaly	Human platelet antigen (HPA) antibodies
Sepsis	Drug-dependent autoantibodies
Disseminated intravascular coagulation	
Hemorrhage	
Veno-occlusive disease	
Graft-vs-host disease	
Prolonged platelet storage	

TABLE 19-4. Summary of WHO Bleeding Scale*

WHO Bleeding Grade	Examples
1	Oropharyngeal bleeding ≤30 minutes in 24 hours
	Epistaxis ≤30 minutes in previous 24 hours
	Petechiae of oral mucosa or skin
	Purpura ≤1 inch in diameter
	Positive stool occult blood test
2	Epistaxis >30 minutes in 24 hours
	Purpura >1 inch in diameter
	Hemoptysis
	Melanotic stool
	Gross/visible hematur a
	Visible blood in body cavity fluid
	Bleeding at invasive sites
3	Bleeding requiring RBC transfusion over routine needs
	Bleeding associated with moderate hemodynamic instability
4	Bleeding associated with severe hemodynamic instability
	CNS bleeding on imaging study
	Fatal bleeding

*Modified from Kaufman et al.[56]

WHO = World Health Organization; RBC = Red Blood Cell; CNS = central nervous system.