

Transfusion Therapy 2009

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Transfusion Indications

- Relieve symptomatic anemia
 - improve O₂ delivery
- Replacement of rapid blood loss
- Correction of clotting abnormalities
 - in a bleeding patient
 - prophylaxis for a planned procedure

Packed Red Blood Cells

- Replace O₂ carrying capacity
- ABO/Rh compatible
- No Platelets, Coagulation factors

Hemoglobin Level and Symptoms

Hemoglobin (gram %)

Symptoms

9.0 - 11.0

Little to no dysfunction

7.5

Exertional dyspnea

6.0

Some Weakness

3.0

Dyspnea at rest

2.0 - 2.5

Cardiac failure

Effect of ↓ Hematocrit on Hemodynamics

	<u>Before Dilution</u>	<u>After Dilution</u>	<u>% Change</u>
<u>Hematocrit (%)</u>	33	15	-55
<u>Arterial O₂ content</u>	14	6.4	-55
<u>O₂ Delivery</u>	18.9	11.1	-41
<u>Heart Rate</u>	110	141	+28
<u>Cardiac Output</u>	2.5	3.3	+32
<u>O₂ Extraction (%)</u>	38.2	59.9	+57

To Transfuse or not to transfuse...

A 17 year old vegetarian female of British/German descent walks into your office complaining of fatigue. She denies chest pain, but has dyspnea when she walks up the 3 flights of stairs to her apartment.

Her hct is 17%, MCV 76. All other blood counts are Normal. You order a ferritin level and reticulocyte count.

To Transfuse or not to transfuse...

A 72 y.o. woman c/o gradual onset SOB, palpitations and fatigue over a 5 month period.

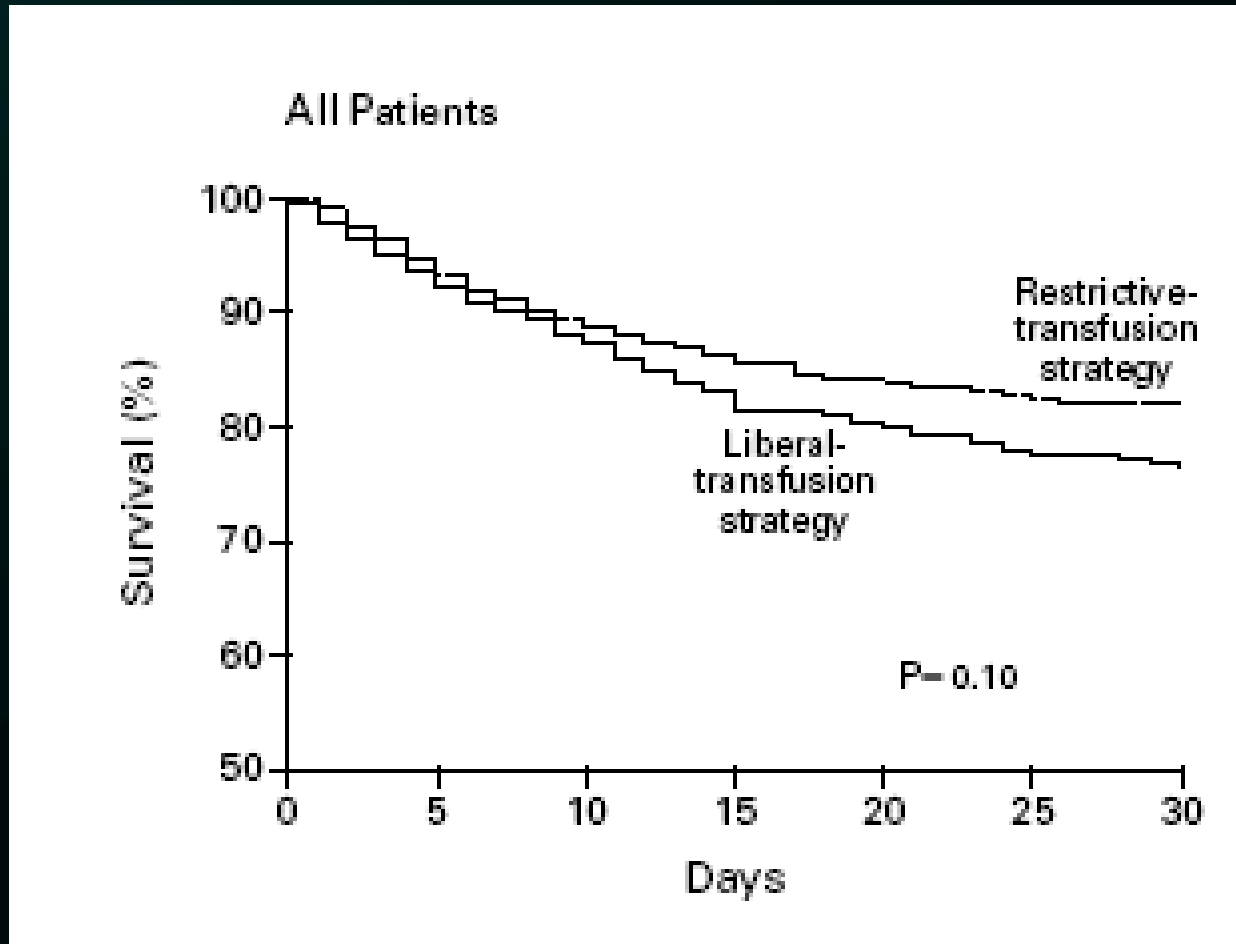
She denies bleeding but reports some increase in bruising.

On exam she is pale and has a few small bruises on her legs. The spleen is very mildly enlarged.

WBC 3.1, Hct 25%, Plts 65,000

Bone marrow shows myelodysplastic changes and classified Refractory Anemia with Excess Blasts (RAEB).

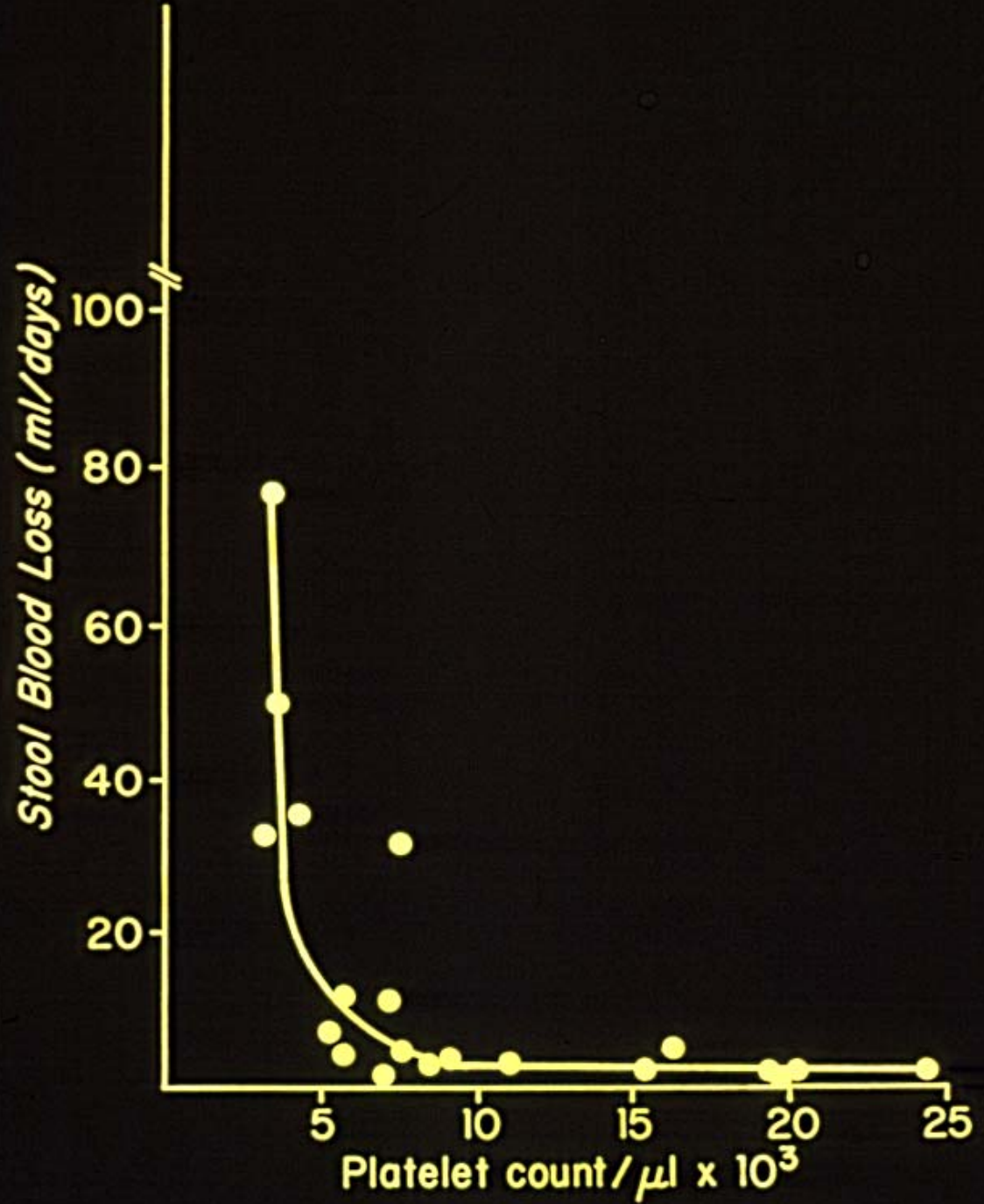
Transfusion in the Critical Care Patient



Six months later...

she is requiring 3 units of prbc every 3 weeks. She reports some mild bruising but denies any bleeding. Exam shows multiple echymoses over arms and shins, few petechiae. Stool is guiac negative.

Hct 22%, WBC 2800, Platelets 12,000

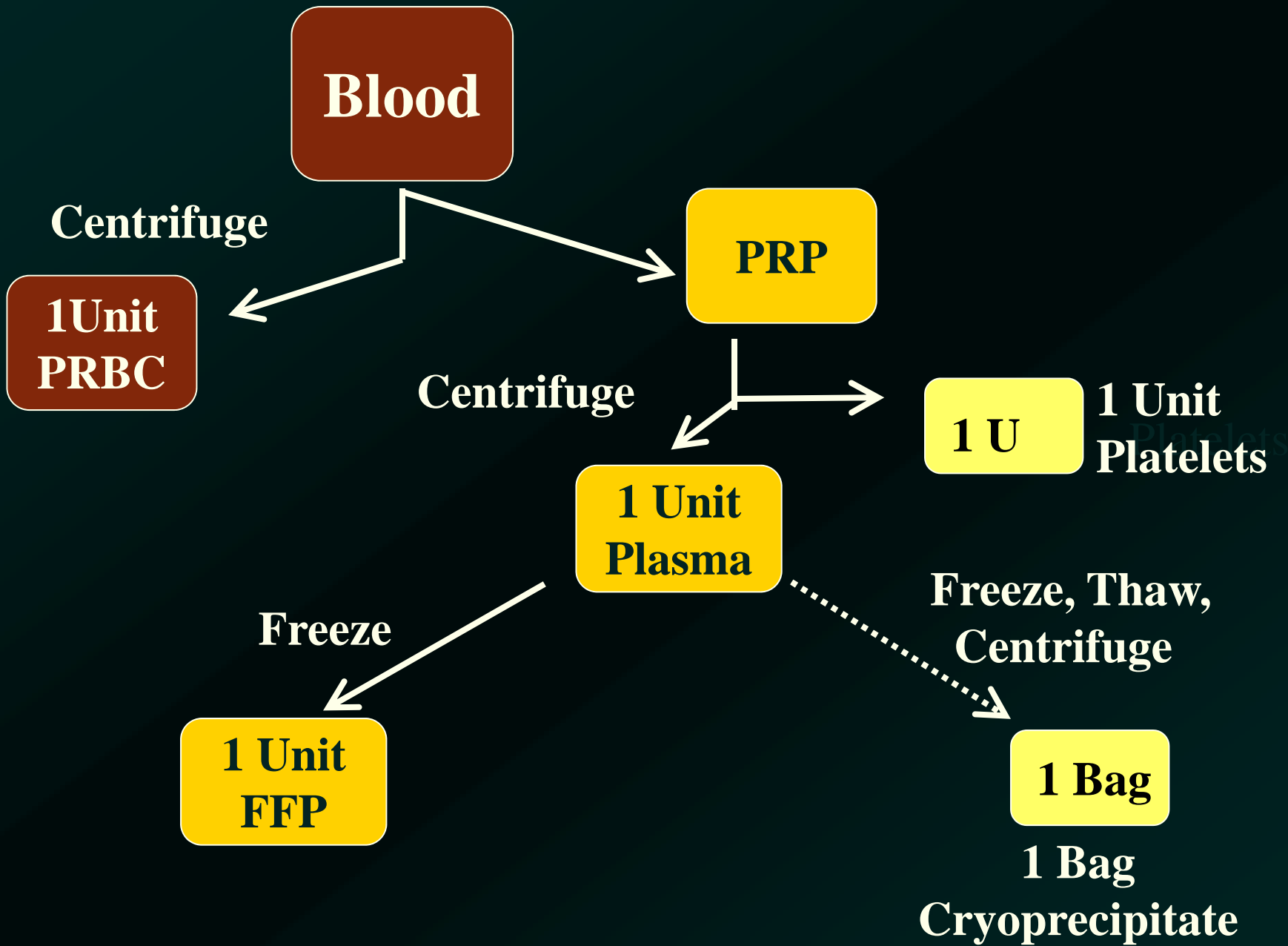


Slichter & Harker

Six weeks later...

she presents to the emergency room with severe epistaxis. She now has petechiae on the soft palate and lower extremities. Stool is guiac positive.

Hct 18%, WBC 2300 with 15% blasts, Platelets 13,000



Expected Platelet Increment

	1 unit 1.0×10^{11}	4 units 4.0×10^{11}	6 units 6.0×10^{11}
50 lb/ 23 kg	22,000/ul	88,000/ul	132,000/ul
100 lb/ 45 kg	11,000	45,000	66,000
150 lb/ 68 kg	7,400	30,000	44,000
200 lb/ 91 kg	5,500	22,000	33,000

Available Platelet Components

- Pooled Whole Blood (2 – 8 U)
- Apheresis
 - Standard (4-6)
 - Large (6-8)
- Family Donor
- HLA Selected Donor

Blood Component Modification

- Leukocyte depletion
- CMV screened (CMV negative)
- Gamma irradiation
- Volume depletion
- Cell “washing”

Leukocyte Reduction: Indications

Direct Evidence

Febrile transfusion reactions

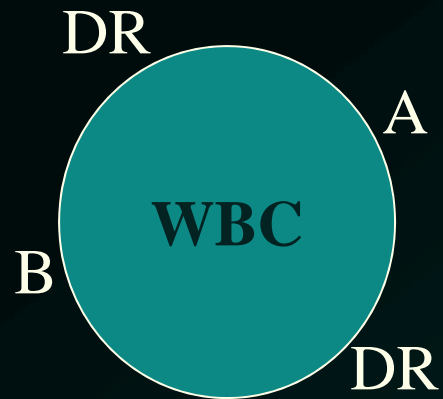
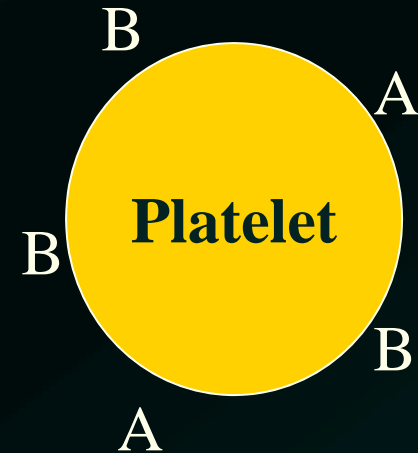
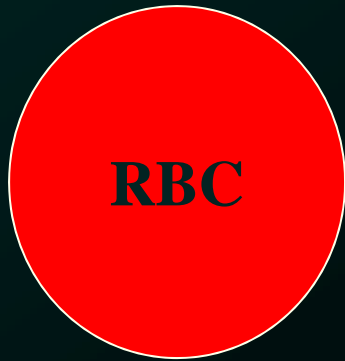
Prevention of CMV transmission

Prevention of alloimmunization to platelets

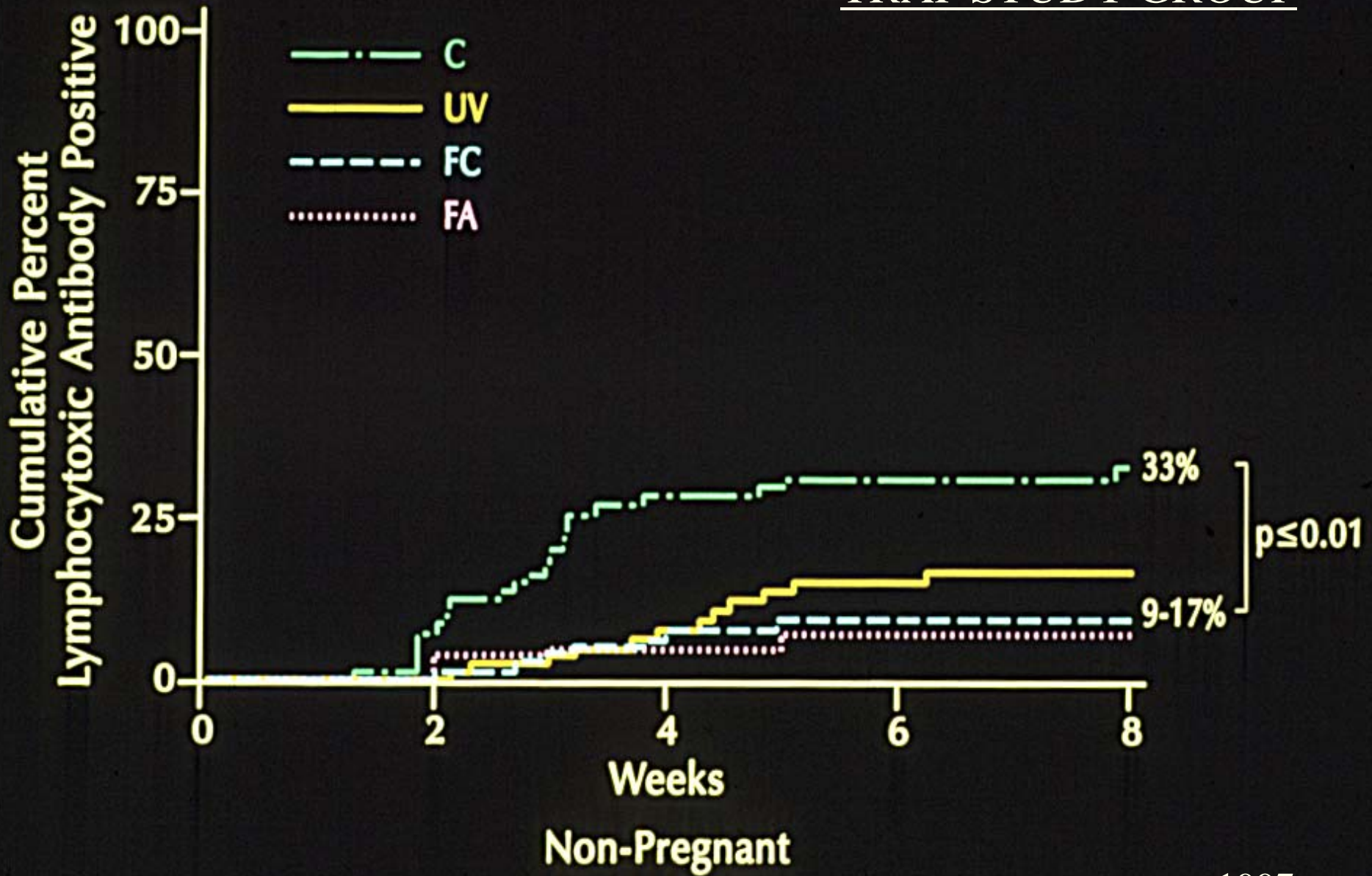
Indirect Evidence

Prevention of alloimmunization for organ transplant

HLA Antigens on Transfused Cells



TRAP STUDY GROUP



Transfusion Transmitted CMV in the Immunocompromised Patient

- Disseminated disease more common
- Pneumonitis, retinitis, hepatitis, graft loss
- Groups at risk
 - Neonates
 - HIV/AIDS
 - Stem Cell transplant recipients/candidates
 - Organ transplant recipients/candidates
 - Splenectomized patients

Gamma Irradiation - Indications

- Prevention of TR Graft vs Host Disease
 - Immunocompromised patients
 - Stem Cell Transplant patients
 - Lymphoproliferative disorders
 - Acute Leukemia
 - Premature infants
 - Others
 - Fludarabine Rx
 - Recipients & donors who share HLA antigens

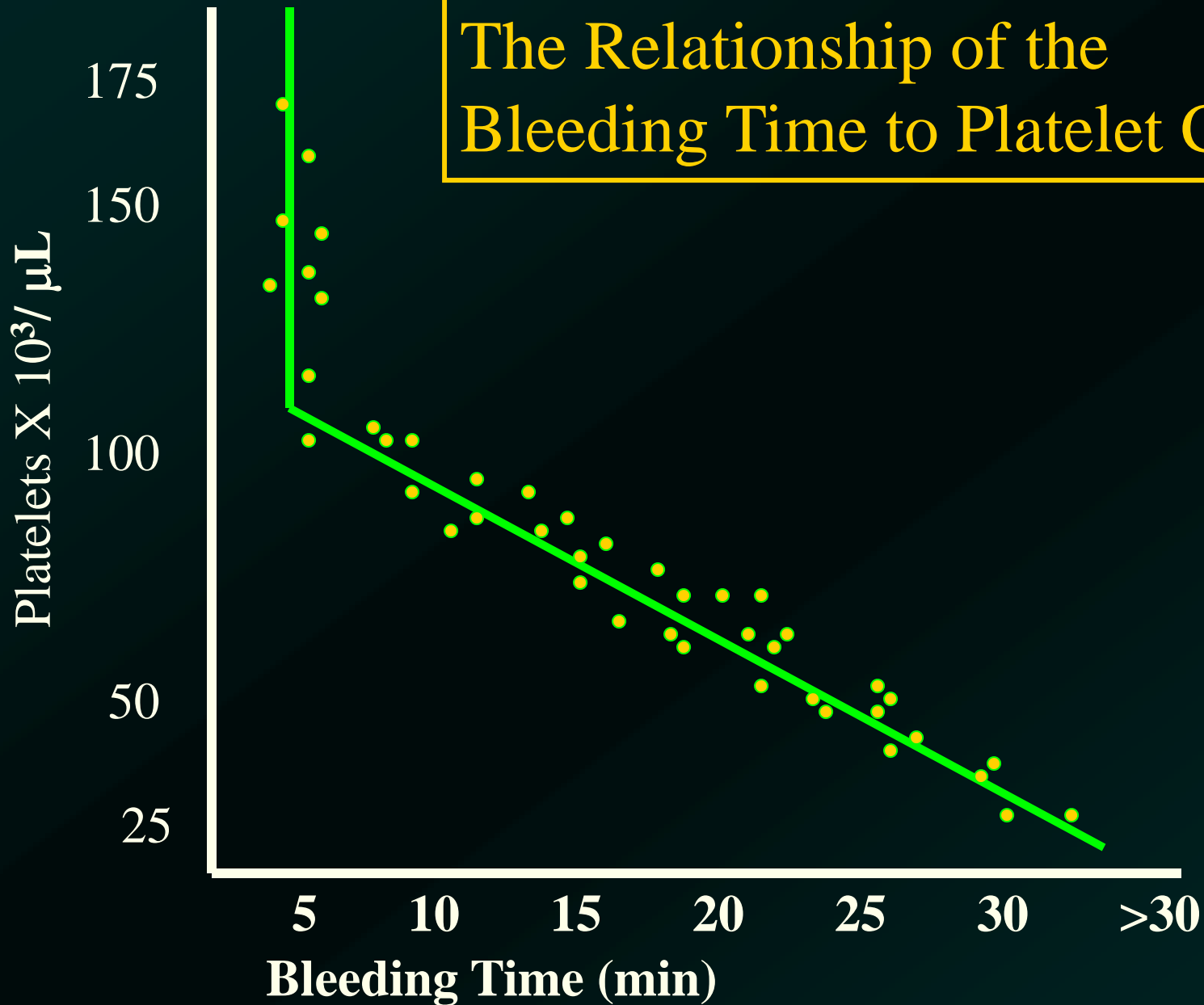
Volume Depletion - Indications

- Volume overload
- Persistent allergic or febrile reactions

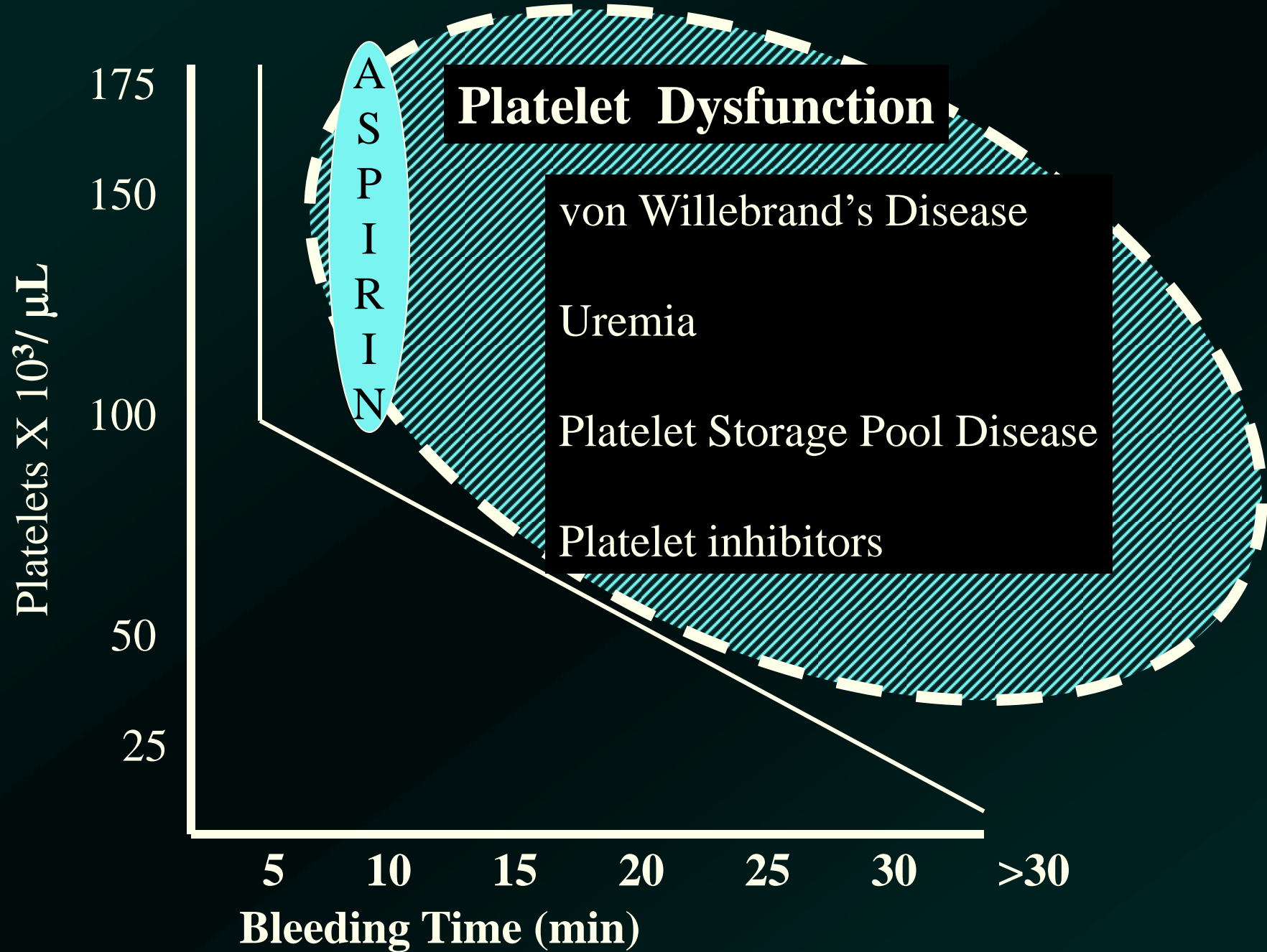
Cell Washing

- Life threatening allergic reactions

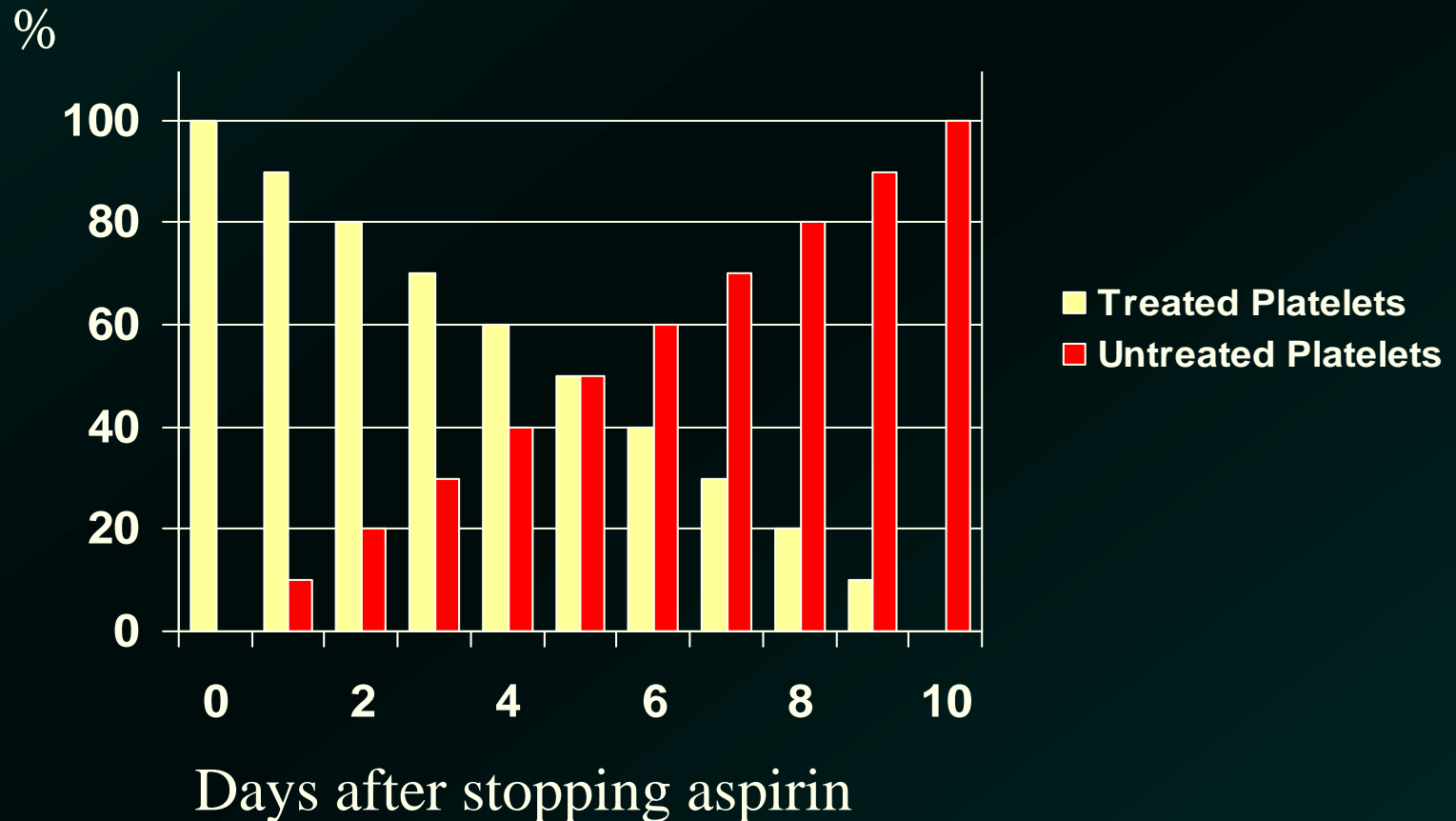
The Relationship of the Bleeding Time to Platelet Count



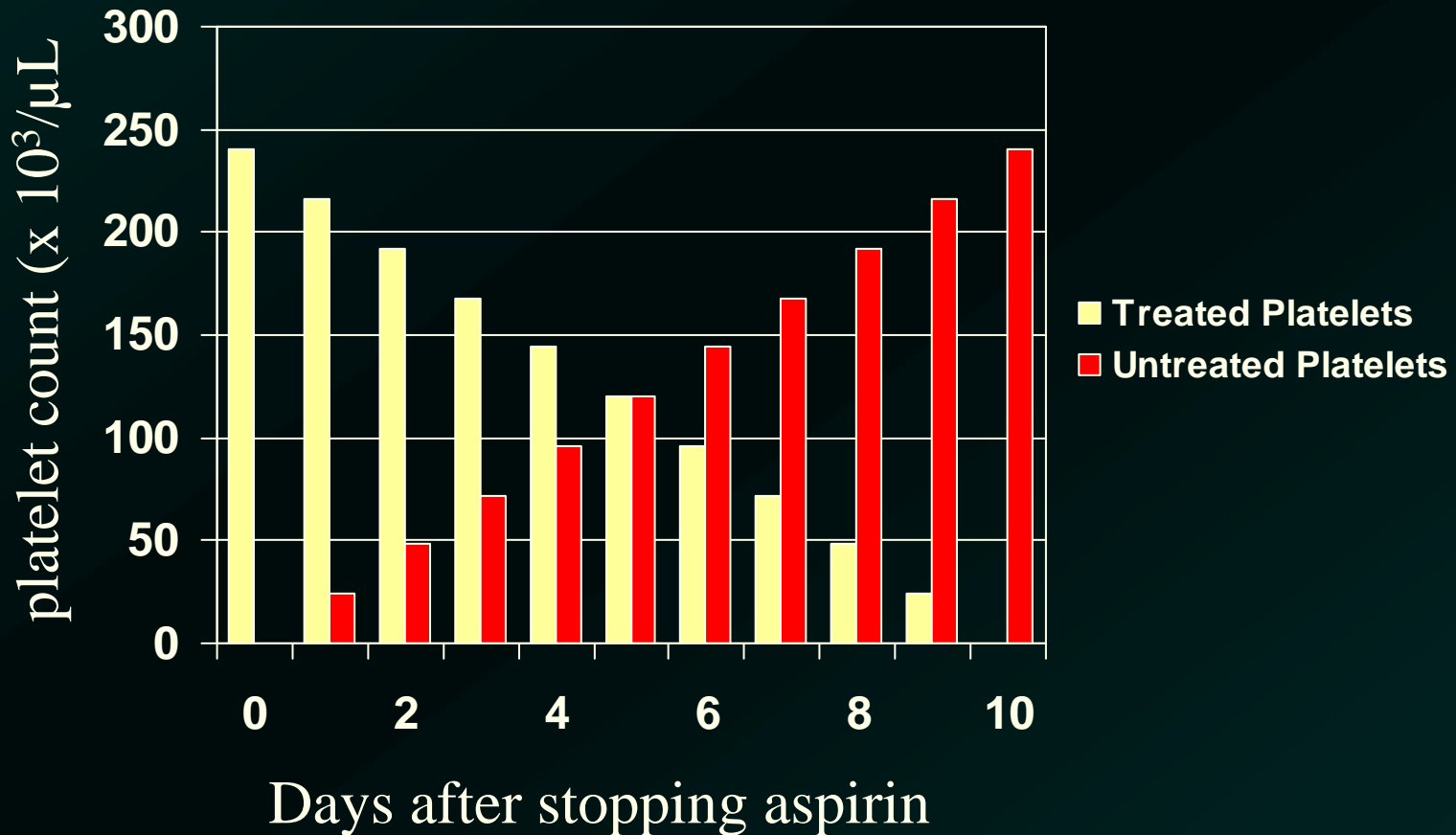
Slichter & Harker



Duration of Aspirin - Platelet Effect



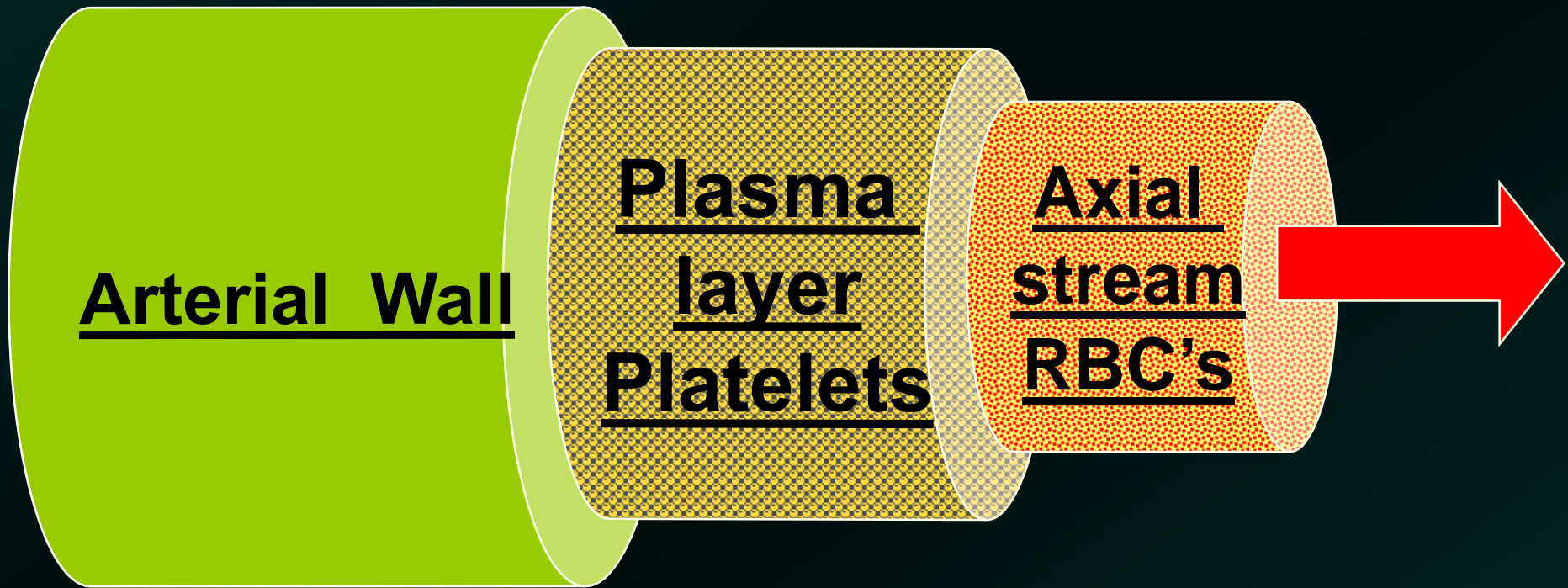
Duration of Aspirin - Platelet Effect



Effective Therapeutic Regimens for Uremic Bleeding

- Dialysis
- Red Blood Cell transfusion
- Erythropoietin
- Desmopressin (DDAVP)
- Cryoprecipitate
- Conjugated estrogens

Concentric Layers of Flowing Blood



Platelet Transfusion Trigger Recommendations

<u>Pre-procedure/Trauma</u>	<30-50,000
high risk	<50-100,000
platelet dysfunction	<50,-100,000
<u>Microvascular bleeding</u>	<50-100,000
CPB, IVAD	<100,000
massive transfusion	

58 yo M with alcoholic cirrhosis admitted to the ICU for upper GI bleeding.

CBC: WBC 5.4K, Hct 24%, Plt 44K,
INR 4.3, PTT 40, fibrinogen 82

Emergent EGD: 3 large duodenal ulcers, massive amounts of BRB, injected with epinephrine with questionable hemostasis.

Surgery consult: reverse his coagulopathy prior to any intervention.

Overnight, the patient continued to bleed briskly and required a total of 38U of PRBC.

12 U FFP for persistent coagulopathy (INR around 2)
two pools of cryoprecipitate for fibrinogen <100
three 6-pks of plts for thrombocytopenia (plt < 50K),

Patient was finally taken to angiography where his vessels were embolized w/o duodenal infarction.

Laboratory Tools

What do you really need to know?

Platelets

number

function

[Coagulation Factor]

Fibrinolysis

= The emergency hemostasis panel

Indices Predictive of Microvascular Bleeding

	Sensitivity	Specificity	<u>Predictive value</u>	
			Positive	Negative
<u>PT ratio</u>				
1.3 (INR 1.3)	89	50	33	94
1.8 (INR 1.6)	44	96	80	84
<u>PTT Ratio</u>				
1.3	56	56	26	82
1.8	56	96	83	87
<u>Platelet count</u>				
≤ 50,000/cc	89	93	73	96
<i>or</i>				
<u>Fibrinogen</u>				
≤ 50 mg/dl				

Fresh Frozen Plasma Recommendations

Pre-procedure / Trauma

Known coagulation factor deficiency

PT >1.5 X Normal (INR >1.6)

Urgent reversal of warfarin

Microvascular bleeding

PT >1.5 X Normal (INR >1.6)

Massive transfusion with continued bleeding

Fresh Frozen Plasma - Dosage

Volume of 1 Unit FFP: 200-250 cc

1 cc plasma contains 1 u coagulation factors

1 Unit FFP contains 200 u coagulation factors

Factor recovery with transfusion = 40%

1 Unit FFP provides 80 u coagulation factors

70 kg X .05 = plasma volume of 35 dl (3.5 L)

$\frac{80 \text{ u}}{35 \text{ dl}} = 2.3 \text{ u/dl} = 2.3\%$ (of normal 100 u/dl)

In a 70 kg Patient:

1 Unit FFP increases most factors ~2.5%

4 Units FFP increase most factors ~10%

Rule of thumb: 10-15cc/kg

Cryoprecipitate Recommendations

- Fibrinogen <80-100mg/dl
- No available factor concentrates/ DDAVP
- Pre-procedure/trauma
- Bleeding patient
 - massive transfusion and microvascular bleeding
 - platelet dysfunction
 - peripartum and DIC

Cryoprecipitate – Dosing

- Pre-pooled 6 Unit packs

$$350\text{mg/Unit} = 2100\text{mg} / \text{pool}$$

In a 70kg patient:

1 pool raises Fibrinogen 40 mg/dl

Recombinant VIIa (Novo-Seven®)

- ❖ Severe Hemophilia A
 - Inhibitor patients
- Warfarin overdose
- Cerebral bleeding
- Massive trauma
- Liver disease and transplantation
- Thrombocytopenia
- Vascular surgery

Adverse Effects of Transfusion

- Transmission of infections
- Transfusion reactions
- Graft vs Host disease
- Immunomodulation

Infections that can be Transmitted by Transfusion

- HIV 1:1,900,000/ unit
- Hepatitis C 1:1,000,000/ unit
- Hepatitis B 1:500,000-750,000/unit
with PCR
- HTLV I & II 1:640,000/ unit
- CMV

Other Transfusion Transmitted Infections

- Chagas, Malaria, Babesiosis, Yersinia
<1 : 1,000,000
- Bacterial Contamination
- West Nile Virus
- Prions?

Bacterial Contamination

- Platelets
 - Normal skin flora
 - Transitory flora
 - Apheresis units tested
- Red Blood Cells
 - Cold Loving Organisms
 - Yersinia
 - Pseudomonads
 - Serratia
- Stat Gram stain/culture unit and recipient
- Notify Blood Center

Transfusion Reactions

- Febrile non-hemolytic Txn Rxn 1: 20 – 100
- Urticarial 1 : 50-100
- Bacterial Contamination <1: 2,000
- Transfusion Related Acute Lung injury (TRALI) 1: 500 -10,000
- Anaphylaxis 1 : 20,000
- Acute Hemolytic Transfusion Rxn 1: 30,000
- Delayed Hemolytic Transfusin Rxn 1: 35,000 (?)

Causes of Fever During Transfusion

- Patient's underlying condition
- Febrile non-hemolytic Txn Rxn 1:20 – 100
- Transfusion Related Acute Lung injury (TRALI) 1:500 -10,000
- Acute Hemolytic Transfusion Rxn 1:30,000
- Bacterial Contamination <1:2,000

Management of Transfusion Reactions

- Hold transfusion; Keep line open
- Clerical check
- Examine plasma for free hemoglobin
- Serologic examination
- Test for hemolysis
 - LDH, bilirubin

Intravascular Hemolytic Transfusion Reactions

Signs & Symptoms

- Chest or back pain
- Dyspnea
- Nausea
- Chills
- Flushing
- Sense of “doom”
- Fever
- Hypotension
- Tachycardia
- Hemoglobinemia
- Hemoglobinuria
- Anuria & Renal Failure
- Bleeding
- DIC

10% Mortality

Transfusion Related Acute Lung Injury (TRALI)

- 30 min to 6 hours post-transfusion
- 10 – 14% of reported transfusion fatalities
- Non-fatal reported incidence increasing
- 90% anti-HLA; anti-neutrophil
- As little as 50cc Plasma

TRALI: “2 hit” model

- 1st event: Predisposed pt, inflammatory cytokines activating pulmonary endothelium and priming neutrophils
- 2nd event: Transfusion of blood components containing Biological Response Modifiers activate neutrophils

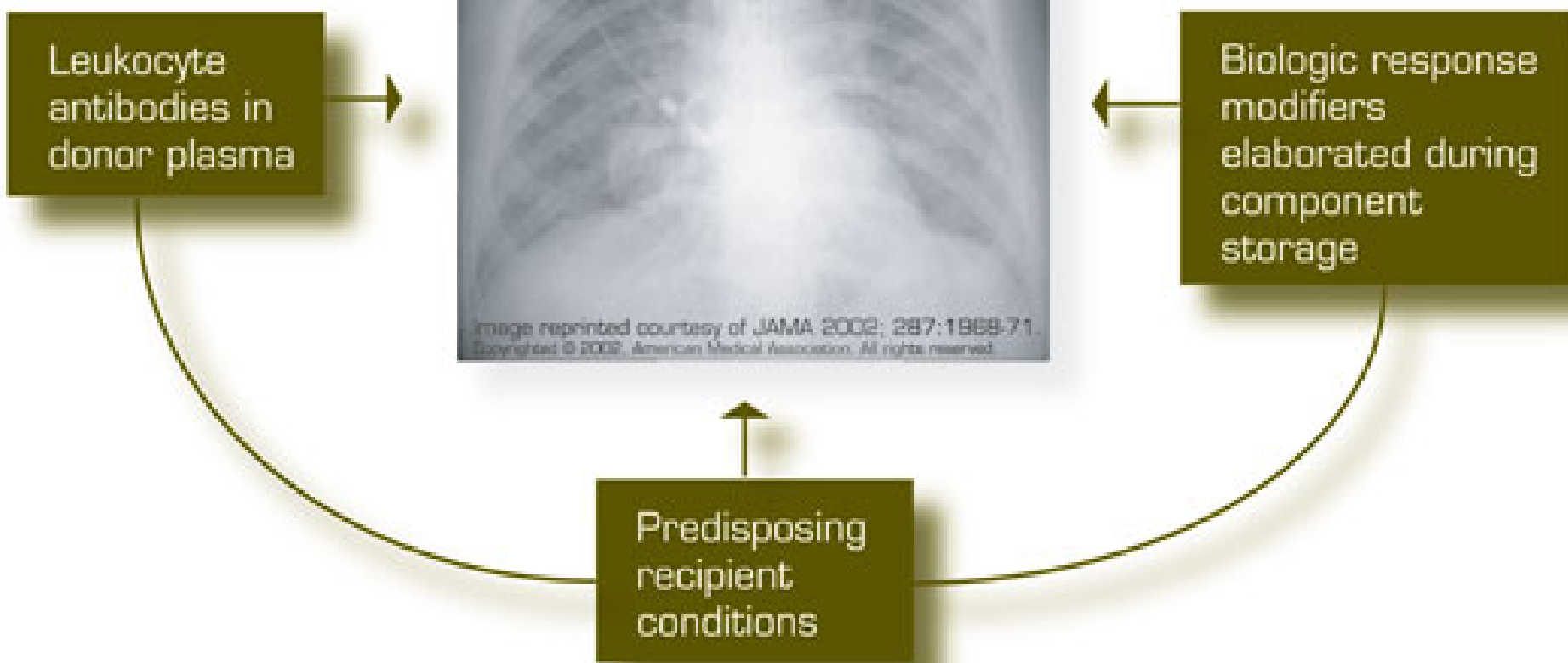
TRALI



Leukocyte antibodies in donor plasma

Biologic response modifiers elaborated during component storage

Predisposing recipient conditions



One week after the 58 yo M with alcoholic cirrhosis undergoes embolization he is cardiovascularly stable with a hematocrit of 28% and without signs of bleeding.

The following morning his hematocrit has dropped to 17%. There are no signs of bleeding and although he is tachycardic his bp is stable.

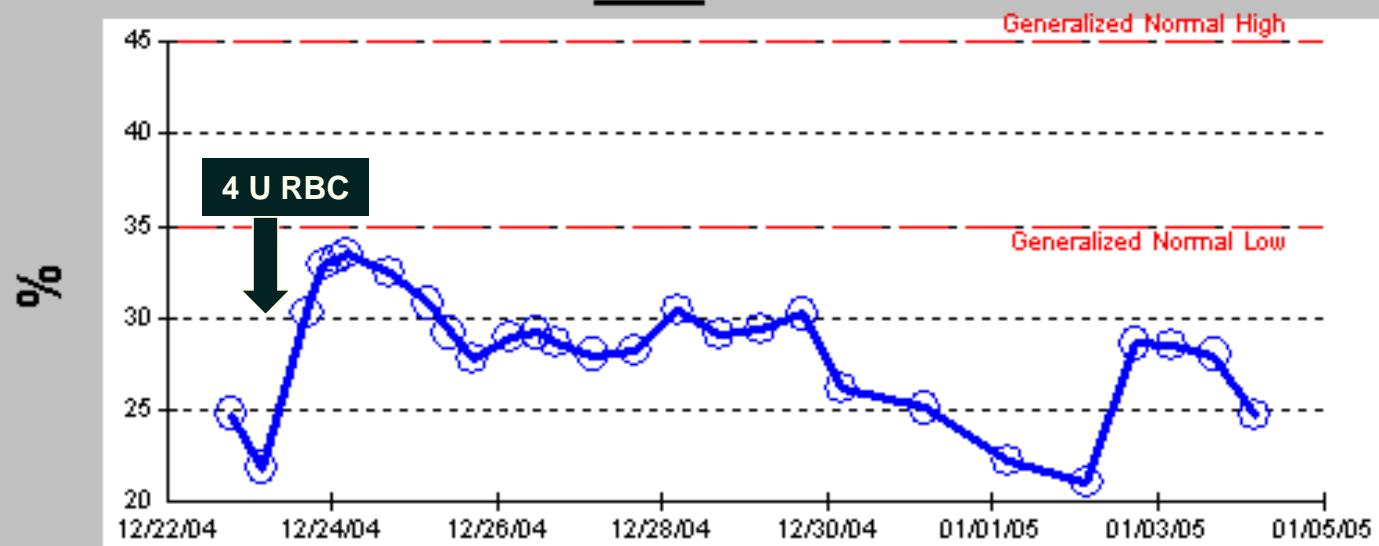
You order an emergency type and cross for 4 units of packed red blood cells.

30 minutes later you are called by a physician from the Puget Sound Blood Center.

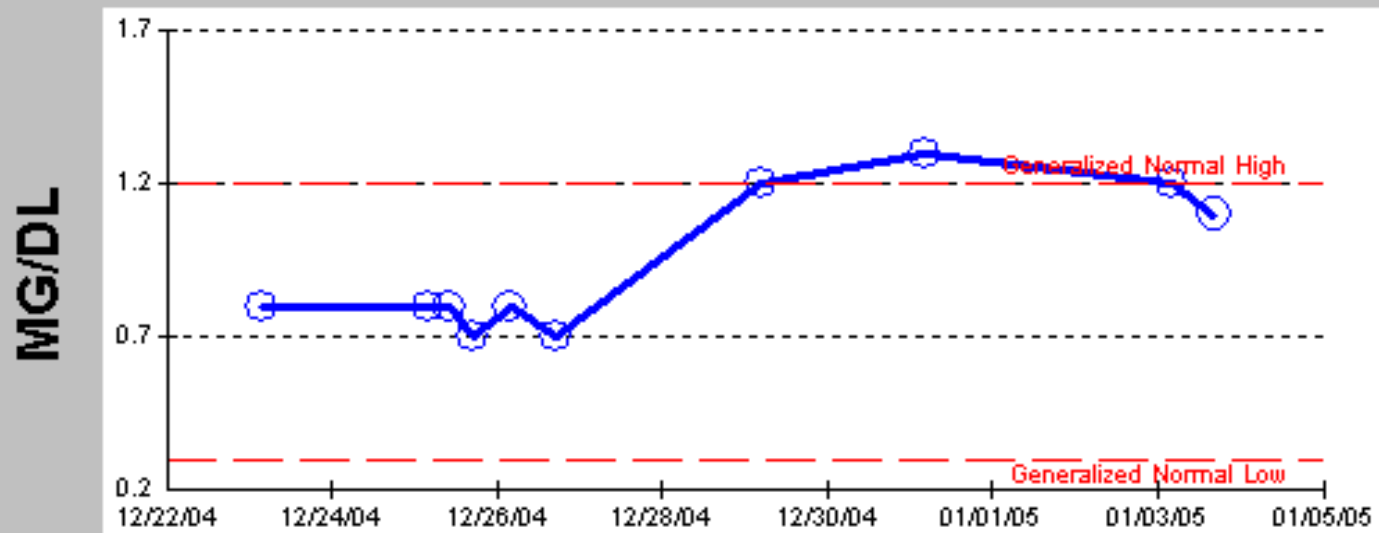
Delayed Hemolytic Transfusion Reaction

- Falling hct 3 – 7 days after transfusion
- +/-Fever
- Mild jaundice, increased LDH
- + Direct and Indirect Antiglobulin Tests
 - Mixed field
- Renal failure and DIC are rare.

HCT



Bilirubin Total



DHTR associated with anti-Jk(a) 7 days after transfusion in previous patient

Delayed Hemolytic TR

