Transfusion Medicine

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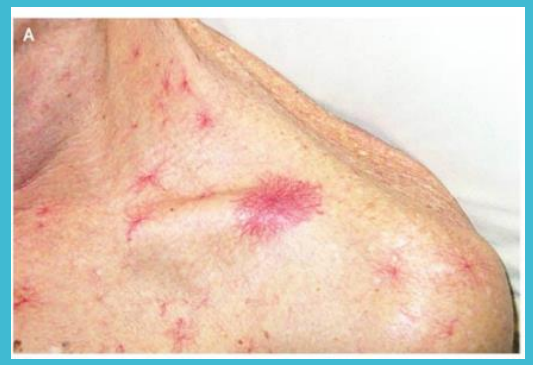
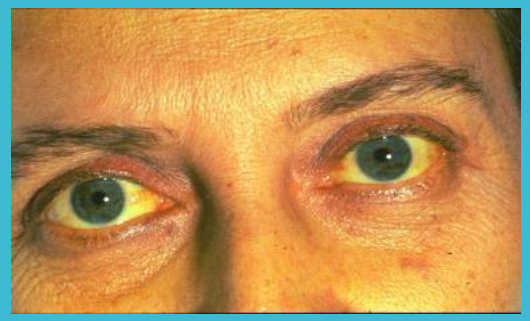
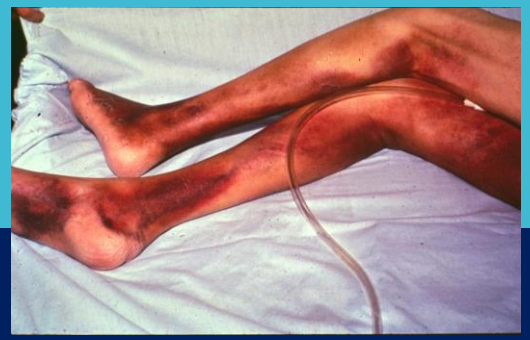
Banner MD Anderson Cancer Center
Making Cancer History®

Case 1







A 62-year old retired Navy commander with a history of chronic alcohol abuse presents to the VA hospital with 2 days of black tarry stools and hematemesis.

On physical examination, his vital signs reveal orthostatic hypotension and a pulse of 120. His oxygenation and temperature are normal. His sclera are icteric, his chest reveals spider angiomata, and his abdomen reveals ascites.He has ecchymosis of the extremities bilaterally. Rectal exam reveals black stool.

Which of the following therapies is best to initially address this patient's hypovolemia?

Laboratories are as follows:
Hemoglobin: 6.3 g/dL
Hematocrit: 19%
Peripheral smear: Poikilocytosis, macrocytosis, and decreased platelets
Platelets:42,000/uL (150,000-400,000/uL)
Prothrombin time: 20 sec (INR 3.0) (11-13.6 sec)
Partial Thromboplastin time: 67 sec (24-36 sec)
Thrombin time: 32 sec (18-28 sec)
Fibrinogen 390 mg/dL (150-400 mg/dL)

- A. Red blood cells
- B. Platelets
- C. FFP
- D. Cryoprecipitate
- E. None of the above

Which of the following therapies is best to initially address this patient's hypovolemia?

- A. Red blood cells
- B. Platelets
- C. FFP
- D. Cryoprecipitate
- E. None of the above – isotonic IV fluid (NS, LR) remains the best choice for initial volume resuscitation

GI is consulted and wants to perform endoscopy…

- Your patient is appropriately resuscitated and ready for endoscopy. Which of the following blood components will you transfuse?

- A. Red blood cells
- B. Platelets
- C. FFP
- D. Cryoprecipitate
- E. None of the above

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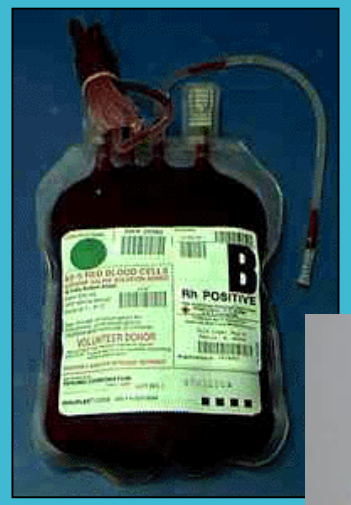

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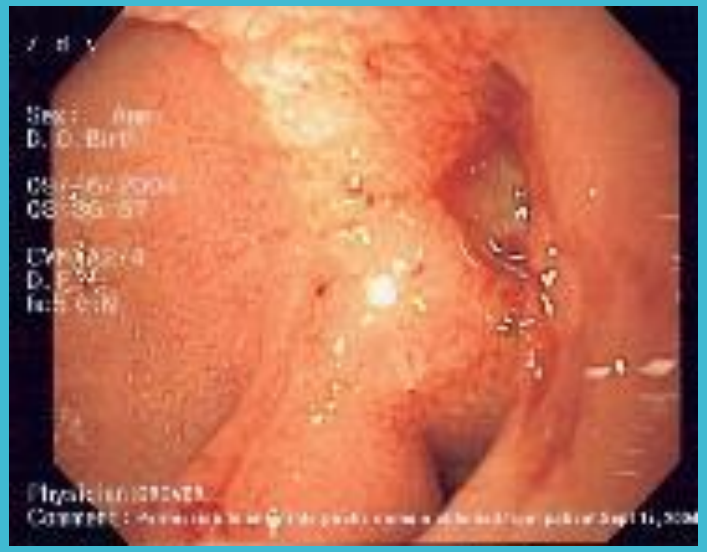
- B. Platelets
- C. FFP
- D. Cryoprecipitate

  E. None of the above

Cryoprecipitate contains:
- Fibrinogen
- Von Willebrand Factor
- Factor VIII
- Factor XIII
- Fibronectin

Defect	*Therapy*
Hypovolemia	IVF
Oxygen-carrying capacity	RBC
Primary Hemostasis	Platelet
Secondary Hemostasis	FFP and Cryo

On Endoscopy…

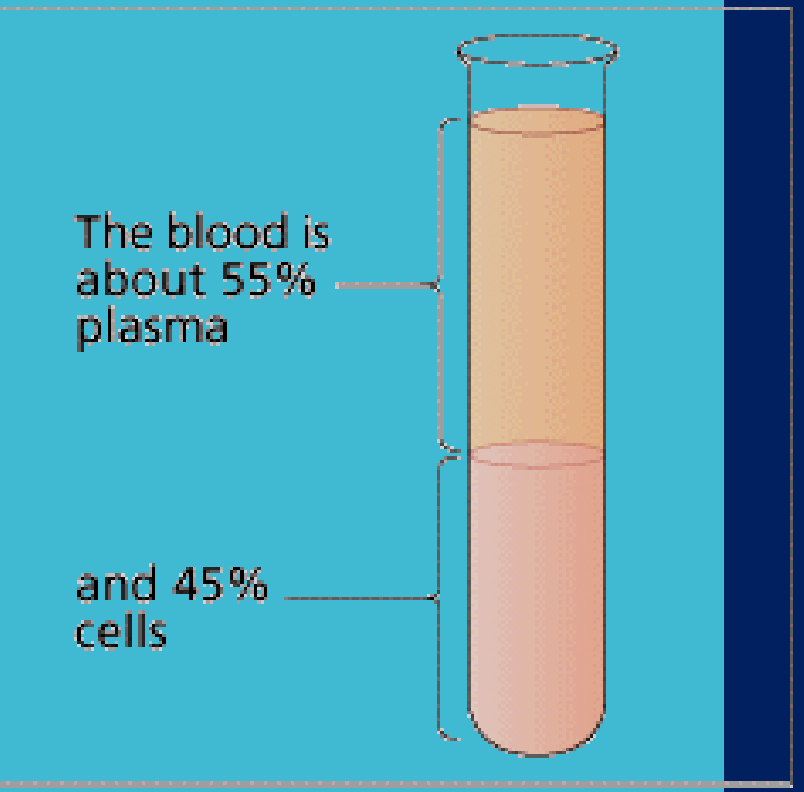


On endoscopy: a briskly bleeding ulcer!

You transfuse your patient with FFP at 6am and his INR improves to 1.5 on 7am lab check. However, a multi-trauma casualty arrives at the ED and the case is bumped. What do you expect the INR will be at 2pm?

- A. 1.5
- B. 1.0
- C. 3.0

Plasma



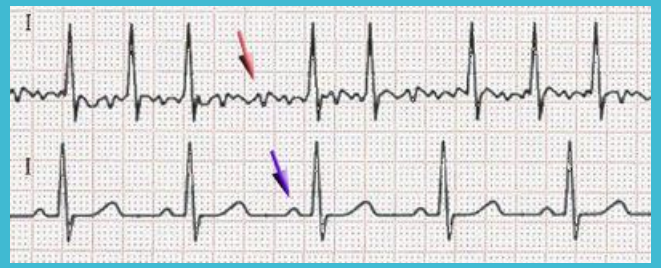
- Appropriate Use
  - Correct coagulopathy
    - Multiple factor deficiencies
  - Patients facing hemostatic challenge
    - Liver disease
    - DIC
    - Warfarin reversal
    - Massive transfusion
- Do Not Use
  - Specific factor deficiencies **(!)**
  - Volume expansion
  - Enhance wound healing
  - Hypogammaglobulinemia

Duration of effect ~ 4hrs due to half life of Factor VII!

Indication for plasma transfusion

- Documented factor deficiency
  - **AND** active bleeding
  - **OR** about to have procedure
    - PT or PTT x 1.5 times normal, or INR ≥ 1.6
- Warfarin Reversal or Vitamin K deficiency
  - Significant bleeding or procedure imminent
  - How long does it take to get plasma for transfusion?
  - Is there something faster for life-threatening bleeding?

Case 2



A 68 yo man with atrial fibrillation on metoprolol and apixaban presents with bright red blood per rectum (BRBPR).

On examination, you confirm maroon stool. BP 100/55. HR 130s and irregular. He continues to have maroon stool x 4 overnight.

CBC 8.2>10.1<182

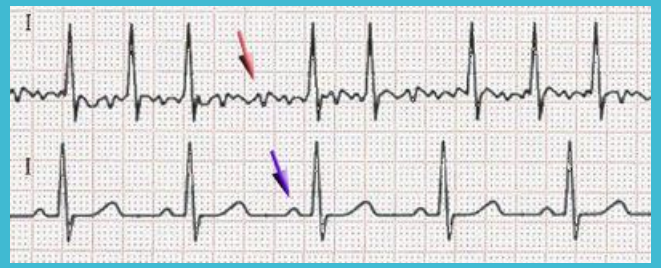
Platelet count = 182,000/µl (150-400k/ µl)

- Prothrombin time = 19 (INR=2.8) (11 – 13.6 sec)
- Partial Thromboplastin Time = 57 (24 – 36 sec)
- Fibrinogen = 390 mg/dl (150 – 400 mg/dl)

- **Which of the following do you want to transfuse?**

A. Red blood cells
B. Platelets
C. FFP
D. Cryoprecipitate
- E. None of the above

Case 2



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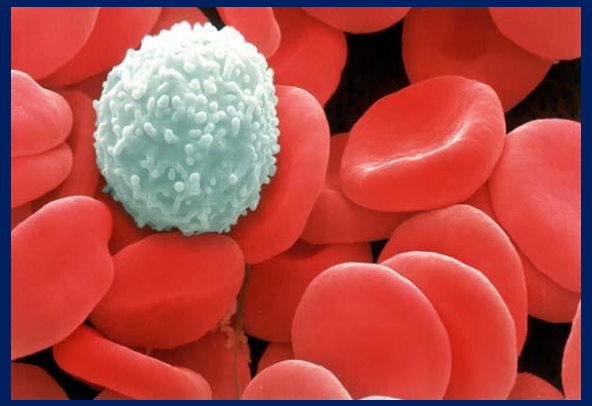
LOOKS LIKE HE'S GONNA PULL THROUGH, BUT IT MUST'VE BEEN A PRETTY VICIOUS ATTACK... HE'S LOST A LOT OF CANDY.
TOOTSIE ROLLS
4/7
©Scott Hilburn/Distributed by Universal Uclick via CartoonStock.com
SCOTT HILBURN

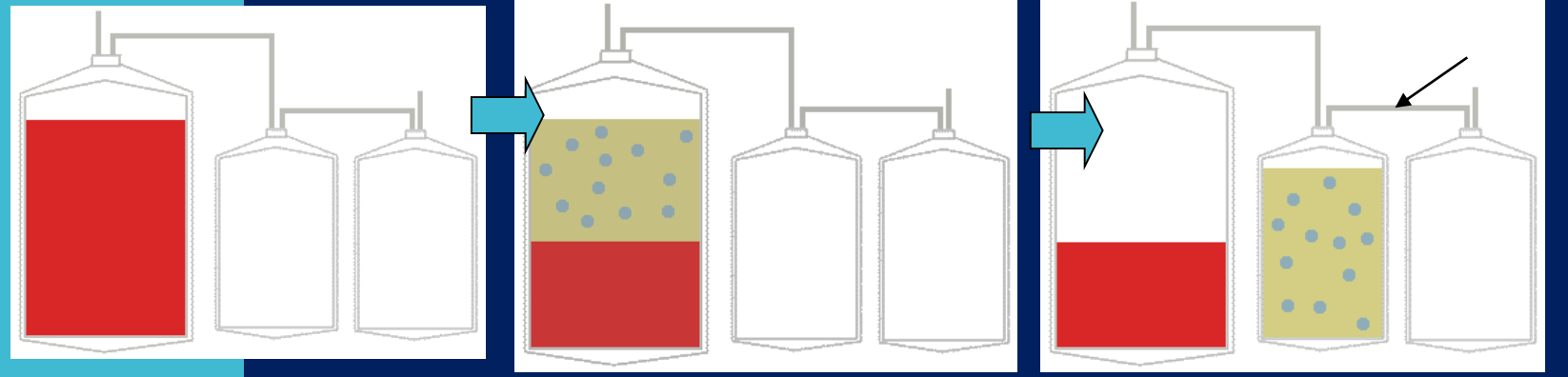
https://www.vitalant.org/Home.aspx#

You can donate too!!



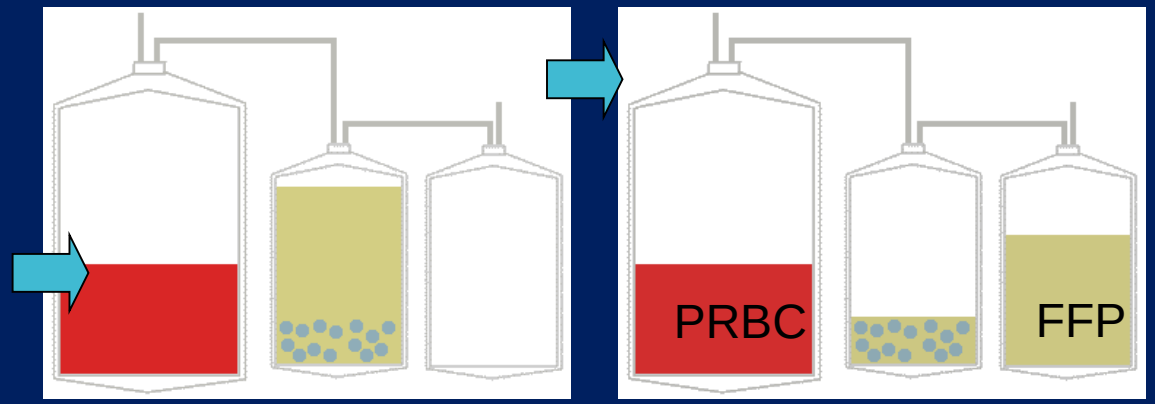
Whole blood fractionation

Centrifuge



Platelet rich plasma

Centrifuge

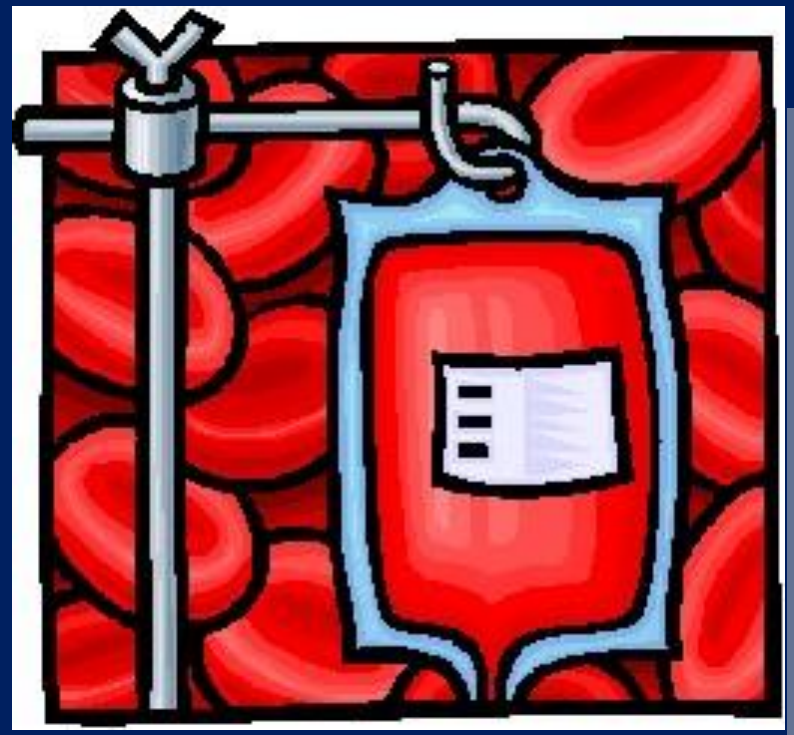


Platelets

www-medlib.med.utah.edu

www.biologycorner.com

One red cell unit =



- 200 mL red blood cells
- 100 mL storage solution
  - 42 days, 4°C
- 30 mL plasma
- 250 mg/dL iron

- Donor & Recipient
  - ABO, RhD and crossmatch compatible

- Effect
  - ↑HgB 1g/dL or Hct 3%

Case 1 update

After endoscopy, the patient's blood pressure stabilizes and his bleeding has stopped. HR 108 BP 108/52.

Repeat labs reveal:
WBC 2.3
Hb 7.7/Hct 23%
Plt 38k

Which of the following therapies do you recommend?

A. Red blood cells
B. Platelets
C. FFP
D. Cryoprecipitate
E. None of the above

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A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

RBC Transfusion Thresholds

838 ICU Patients
Hgb < 9, euvolemic

Random

This trial excluded patients with chronic anemia and active blood loss

Restrictive Transfusion
pRBC if Hgb <7 (7
N=418– 9)

Liberal Transfusion
pRBC if Hgb <10 (10 – 12)
N=420

30 day mortality 18.7%

Mortality during hospitalization 22.2%

30 day mortality 23.3%

Mortality during hospitalization 28.1%

P = 0.11

P = 0.05

TRICC, Herbert, NEJM 1999; 340: 409

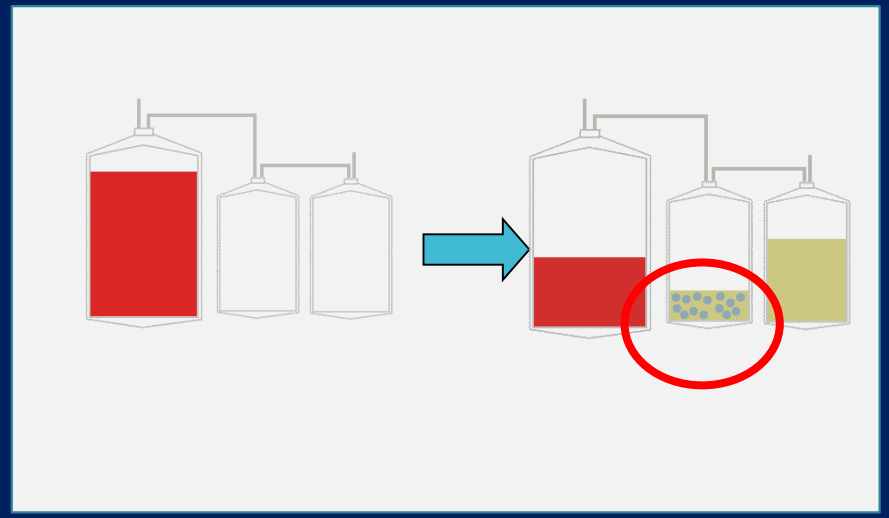
Platelet Targets

Clinical Situation	Target Platelet Count
"Lower risk" procedure = lumbar puncture, paracentesis, central line	>30,000 – 50,000
Higher risk = Biopsy of internal organs	>50,000
Neurosurgical procedure	>75 – 100,000
Bleeding patient (major - GI)	>50,000
Bleeding patient (minor – mucosal)	>30,000
Prophylaxis	>10,000

Slichter SJ. Evidence-based platelet transfusion guidelines. Hematology Am Soc Hem Educ Program 2007:172-8.

2 Types of Platelet Products

- Whole blood platelets



- 4 – 6 donors combined together to make 1 adult dose

- Apheresis Platelets

- Single donor
- Equivalent to 4-6 pooled units

Cryoprecipitate

- Prepared by slowly thawing FFP in the cold
  - Insoluable precipitate
    - Factors VIII, XIII, vWF, fibrinogen
  - One "pool" = 6-10 donor units = one adult patient dose

Indications for Cryoprecipitate Transfusion:

1. Hypofibrinogenemia
   < 100 - 150 mg
2. Obstetrical bleeding
3. DIC
4. Massive transfusion


HAGEN©2006
I agree O-positive is rather nice,
but my favourite by far is AB-negative...

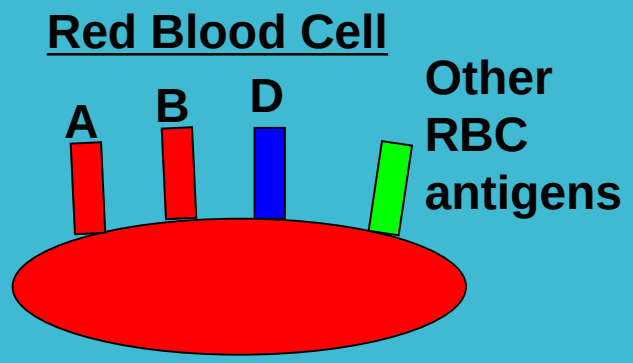
Case 3

A 42yo man has hematemesis and Hb of 5.2 g/dL. He is short of breath with exertion.
His blood type is A+. You request RBC for transfusion. The type and screen is positive.

Which of the following blood types do you transfuse?

- A. A-
- B. B+
- C. AB-
- D. O+
- E. None of the above

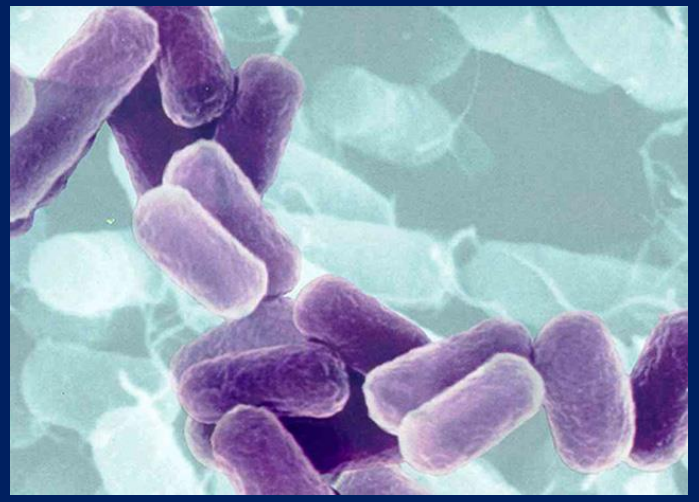
Blood Groups



- Genetically related antigens on red blood cell surface
- There are 29 blood groups systems
  - >300 different antigens
- ABO Discovered in 1901 by Karl Landsteiner
- Antigens
  - A, B, AB, none = O
- Chromosome 9q
  - ABO genetic loci codes for enzymes
  - O is recessive allele

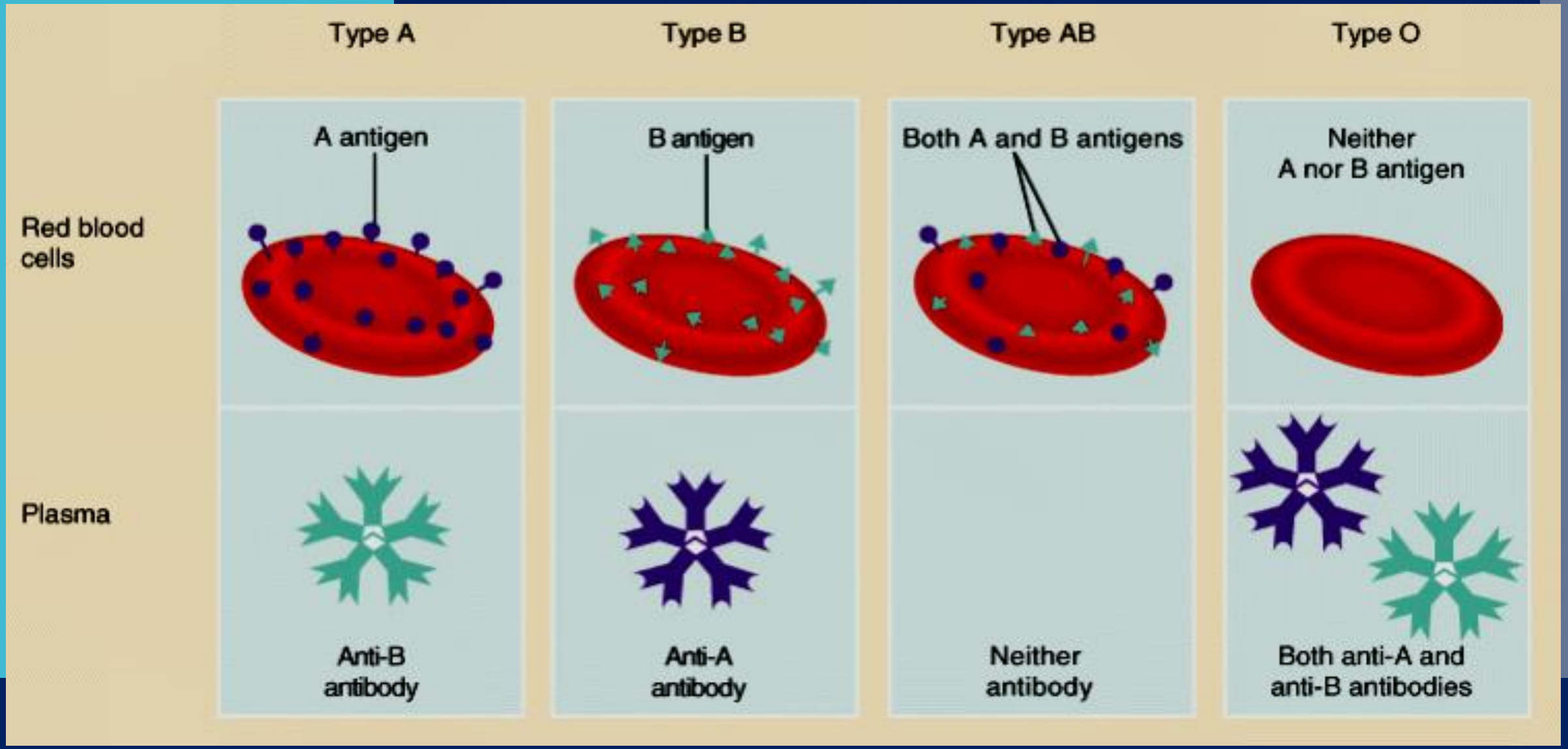
DAD \ MOM	A	O
B	AB	BO
O	AO	OO

Why is ABO so important? It's the plasma!

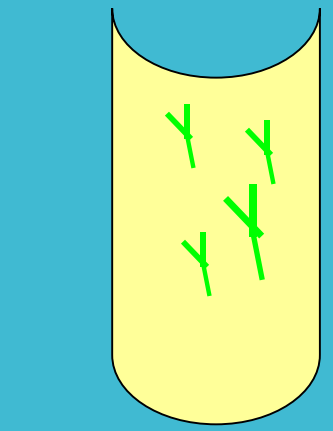


- Plasma = Anti-ABO antibodies are NATURALLY OCCURRING
  - Antibodies made in first 6 months of life
  - Only blood group system where antithetical antibodies predictably present
  - Gut bacteria contribute to antigen exposure

ABO System

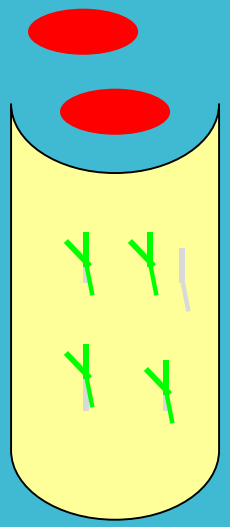


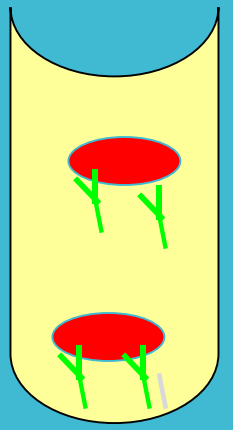
Antibody Screen = Indirect Coombs = Indirect Antiglobulin test (IAT)



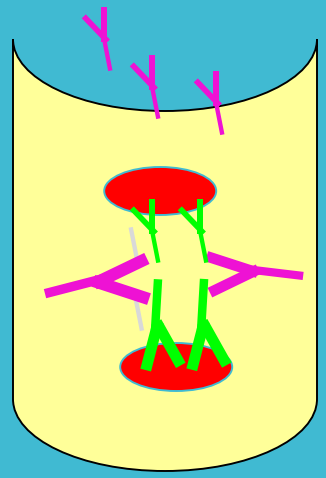
Patient plasma:
Antibodies present?

Add
Reagent
Red Cells

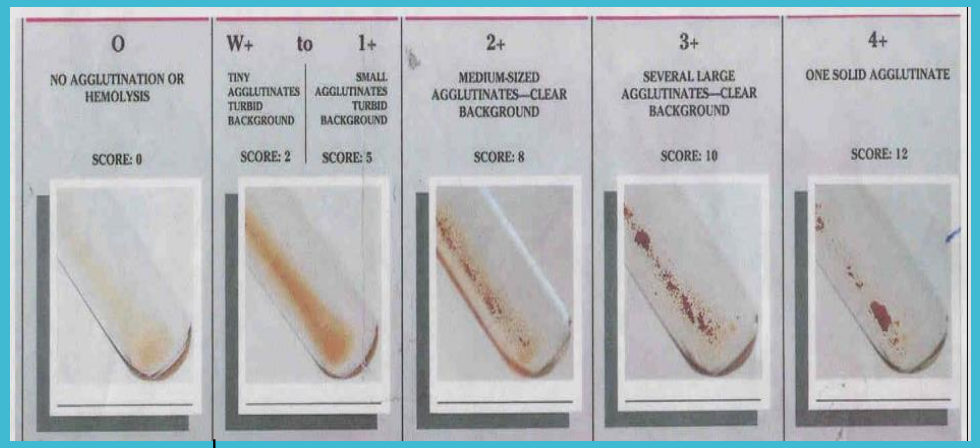




Add
Coombs
Reagent
(anti-IgG)

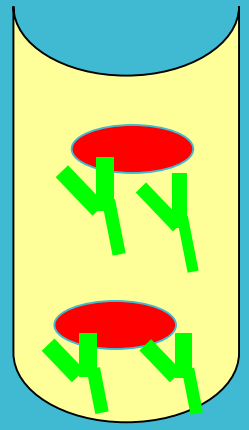


Check for
agglutination



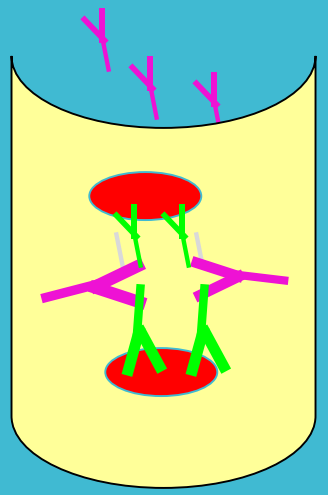
NEGATIVE | POSITIVE →

Direct Coombs = Direct Antiglobulin Test = DAT



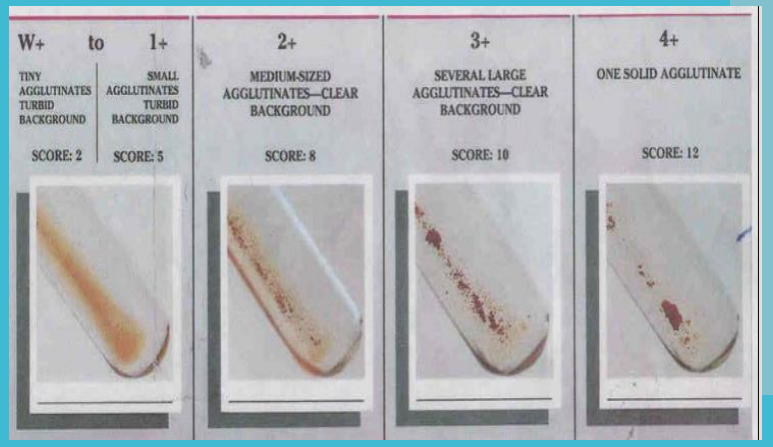
Patient RBC's:
Are they coated with Antibodies?

Add Coombs Reagent (anti-IgG)



Check for agglutination

NEGATIVE



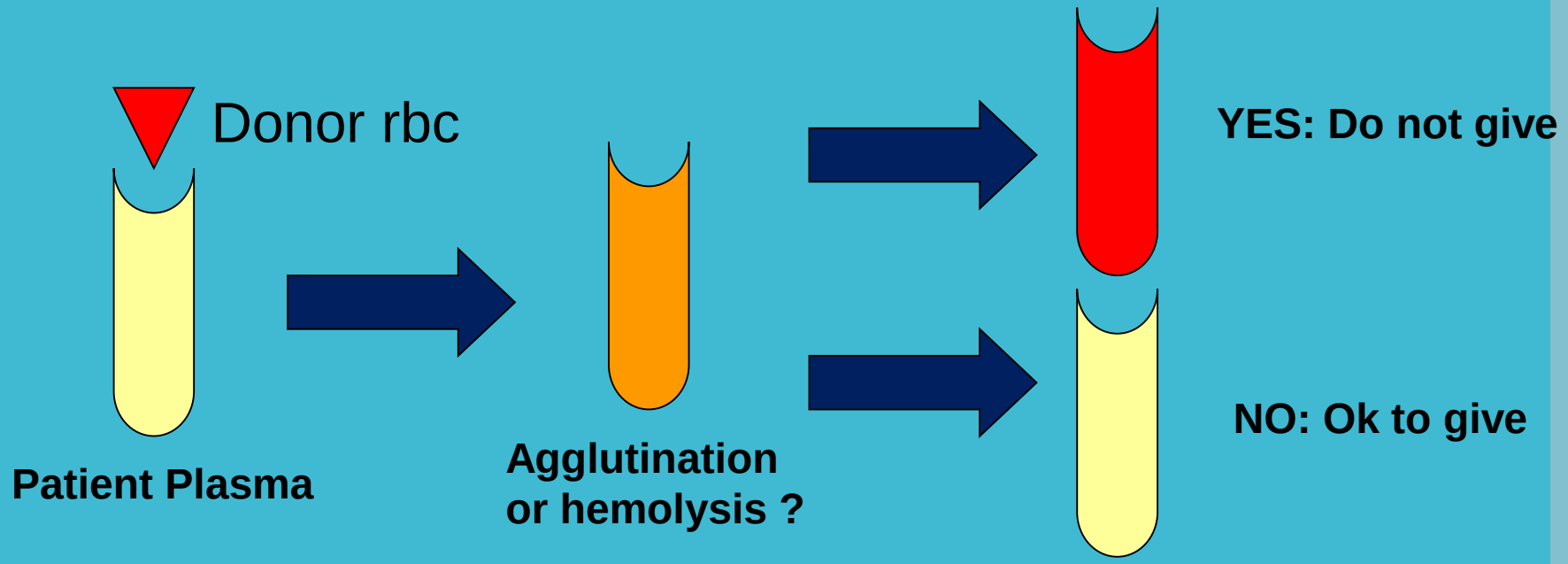
POSITIVE →

"Type and Screen"

- Blood Type
  - ABO and RhD typing
- Antibody Screen
  - Test patient plasma for presence of red cell *allo*antibodies
    - Anti-D, Anti-E, Anti-e, Anti-C, Anti-c, Anti-K,
    - Anti-Jka, etc….
  - Ab screen positive = O- may not be safe

"Type and Cross"

Crossmatch



TYPE & CROSS: Includes ABO, RhD type, antibody screen and crossmatch

Case 5

A 42yo woman is 8 months s/p allogeneic SCT for AML. Her Hb is 6.9.

Which of the following modifications do you recommend to decrease the risk of CMV transmission?

- A. Irradiation
- B. Volume Reduction
- C. Leukocyte Reduced
- D. Washed
- E. Directed Donation

Case 5

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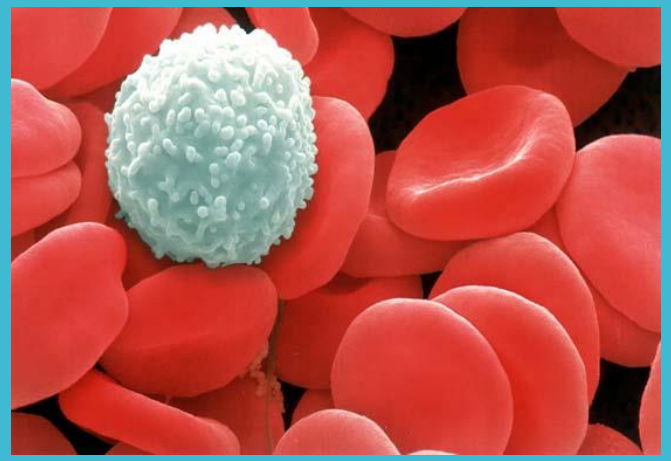
Which of the following modifications do you recommend to decrease the risk of CMV transmission?

- A. Irradiation
- B. Volume Reduction
- C. Leukocyte Reduced
- D. Washed
- E. Directed Donation

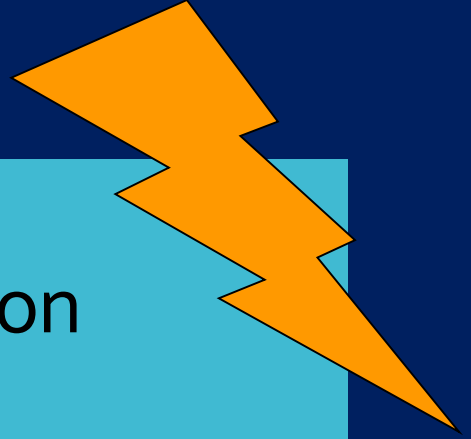
Leukocyte-reduced transfusion is considered 'CMV-safe' since CMV resides predominately within WBC

Leukoreduction



- Filtration of blood products to remove WBC
  - Decrease risk of febrile rections from 2% → 1%
  - Decrease risk of allosensitization
  - Decrease risk of CMV transmission
    - Cellular restricted pathogen

Irradiation



Protects from Transfusion Associated Graft Versus Host Disease (TA-GVHD)

- Inactivates lymphocyte division in blood product
- 2,500 cGy (cesium)
  - Fetuses / newborns
  - Bone marrow transplant patients / candidates
  - Hematological malignancy
  - Congenital immunodeficiency (DiGeorge Syndrome, etc)
  - Blood relative blood donations

Case 5

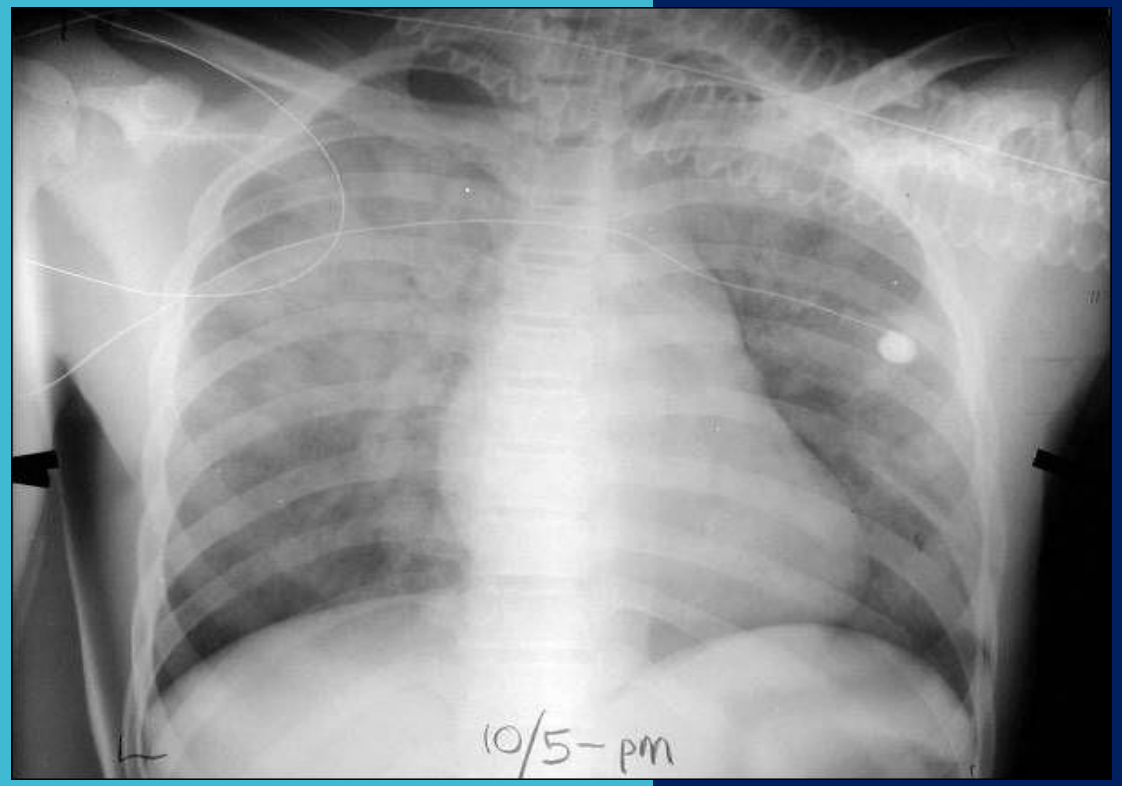
68 y.o. female restrained passenger in a high-speed motor vehicle crash is brought to BUMCP trauma bay where she is diagnosed with a pelvic fracture and requires urgent surgery. She has a history of a mechanical mitral valve replacement 10 years prior and is on warfarin.

Laboratories:
WBC = 7.9 (normal: 4.3-10k/uL)
Hct = 37% (normal :36-45%)
Platelet count = 225,000/μL (normal: 150-400,000/uL)
PT = 23 sec (normal: 10.4-12.8 seconds) INR : 2.3
PTT = 39 sec (normal: 24-36 seconds)
Fibrinogen = 175 mg/dL (normal: 150-400 mg/dL)

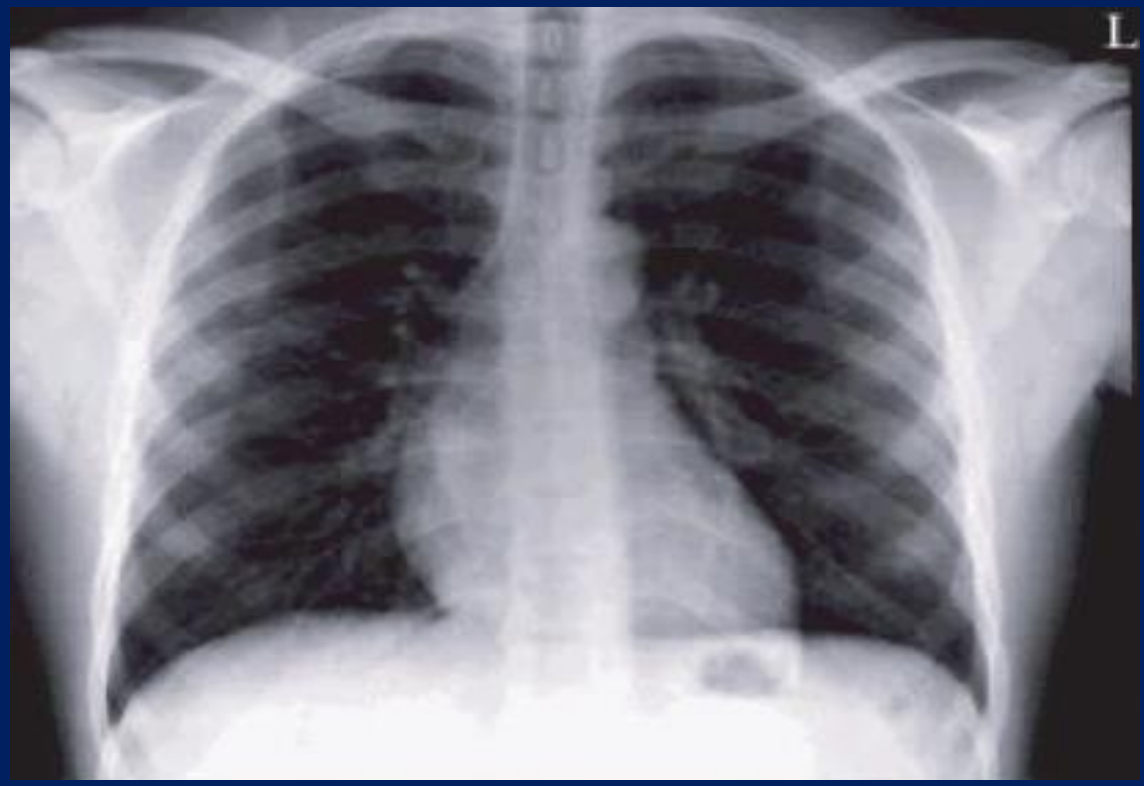
She is given IV vitamin K, 4 units of FFP and 4 units pRBCs and taken to surgery. Postoperatively, she is transfused 2 units of pRBCs + 2 more units of FFP.

One hour later, you are called to see her for trouble breathing and chest tightness. You auscultate bilateral inspiratory rales throughout. Her O2 saturations fell from 98% to 82% on room air.

Chest Xray Now



Preoperative Chest Xray



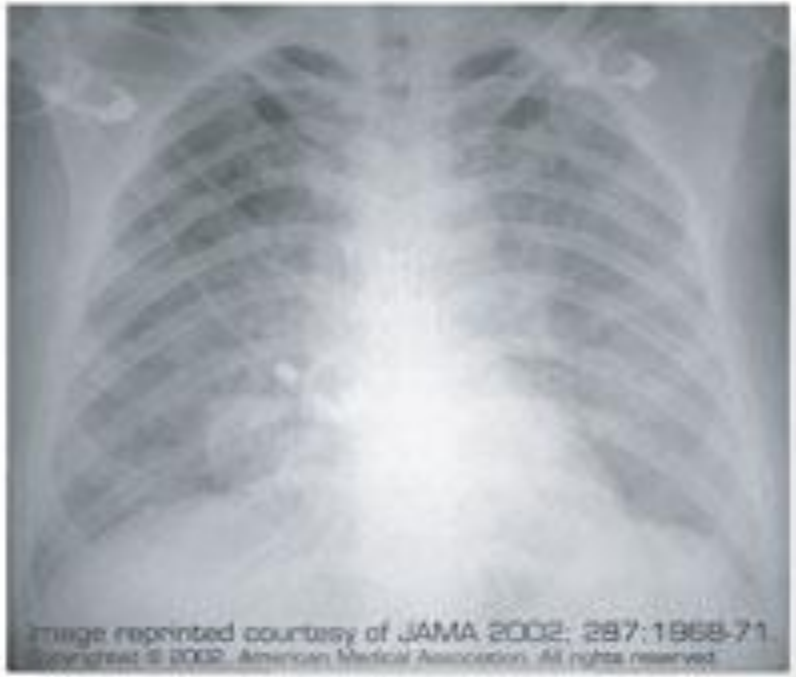
Case 5

A repeat EKG shows no ischemic changes and cardiac biomarkers are negative. Her oxygenation continues to deteriorate and despite 80 mg of IV Lasix, she requires intubation. Her urine output is 1 liter over the next 2 hours and her hematocrit remains stable. After 6 hours on the ventilator, her chest xray remains unchanged.

What is the most likely diagnosis?

A. Hemolytic transfusion reaction
B. TRALI
C. TACO
D. Sepsis
E. Diffuse alveolar hemorrhage

TRALI



Leukocyte antibodies in donor plasma

Biologic response modifiers elaborated during component storage

Predisposing recipient conditions

Possible Etiologies of TRALI

- Donor Antibodies
  - anti HLA, Class I & II
  - anti PMN
- Recipient antibodies
- Leukocyte priming activity
  - lipids increase with component storage
- Cytokines – IL6, IL8

Case 5: New Problem!

Two days later her O2 requirement is significantly decreased, her CXR has improved and she is extubated.

At that time, her laboratories showed the following:
WBC: 8.2 K/uL (4.3-10 K/uL)
Hematocrit: 32% (36-45%)
Platelets: 285 K/uL (150-400K/uL)
PT 11.2 sec (10.4-12.8 sec) INR:1.0

Today, on post-op day #4, her hematocrit is 24%. This is significantly lower, which causes a concern for bleeding, so the heparin for the mitral valve is discontinued. An abdominal/pelvic CT is negative for retroperitoneal bleed. There is no obvious GI bleeding from the NG or stool. Another 4 units of pRBCs are ordered, and you are called from the blood bank.

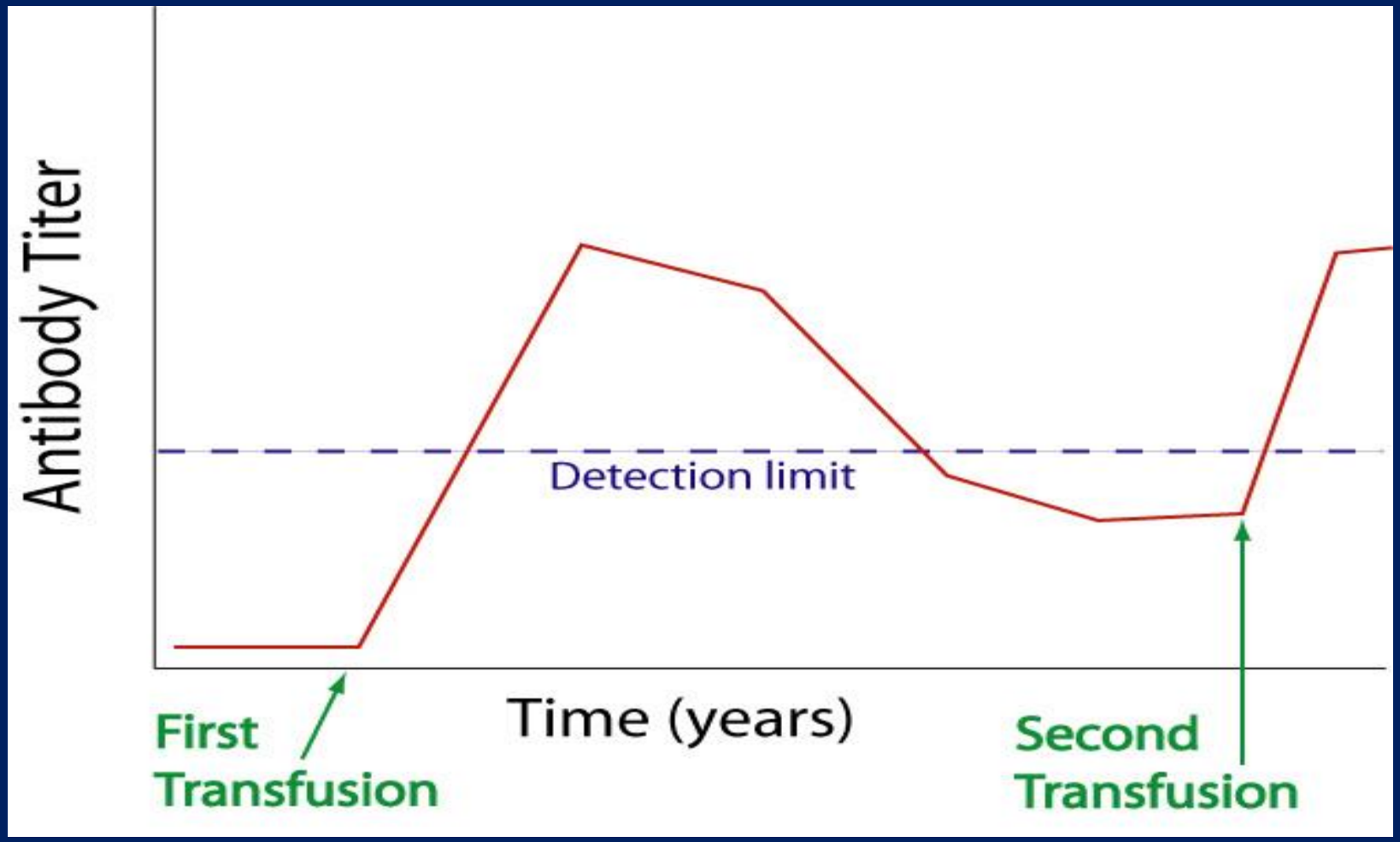
What is the most likely mechanism of the patient's drop in Hct?

A. Operative site bleeding
B. Fluid overload
C. Immune-mediated
D. Bone Marrow dysfunction

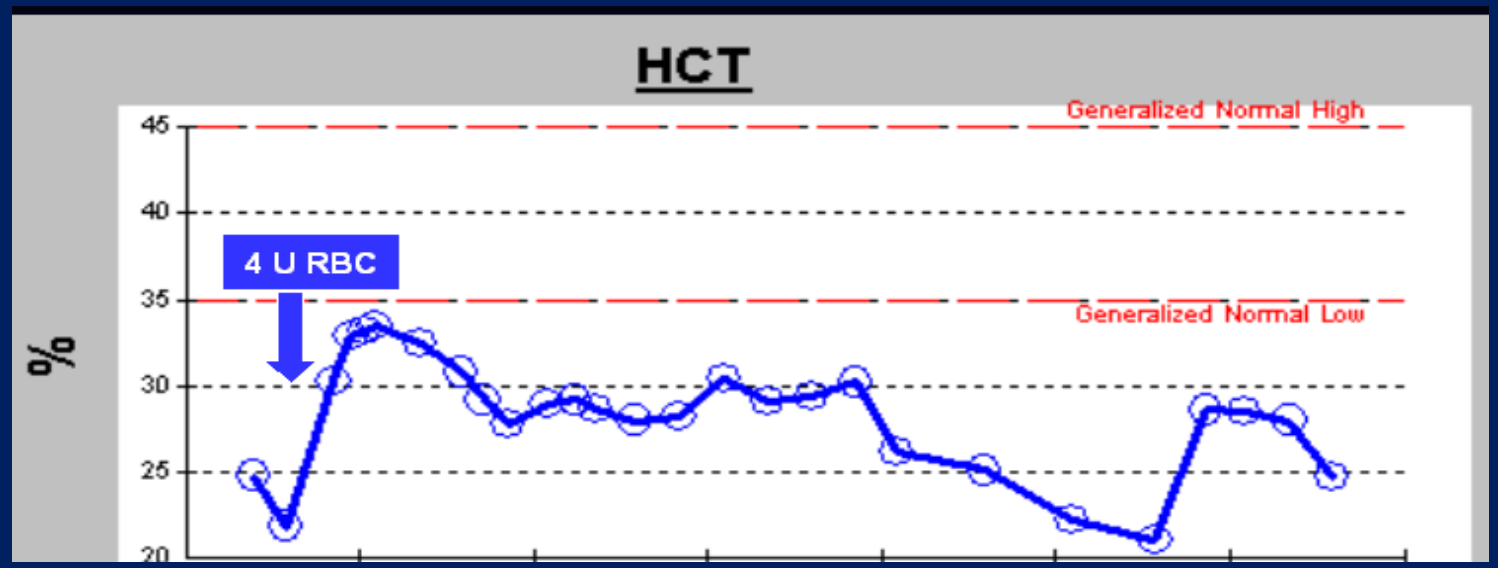
Delayed Hemolytic Transfusion Reaction

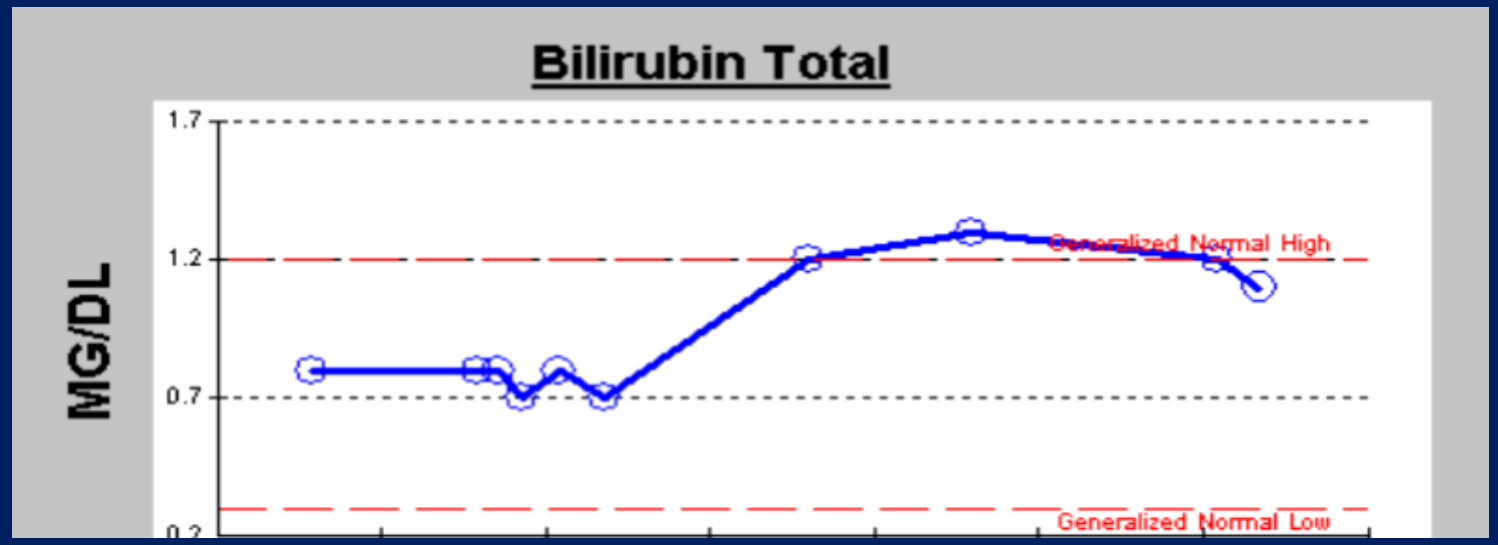
- Falling Hct 3 – 7 days after transfusion
- Fever
- Mild jaundice, hyperbilirubinemia
- Increased lactate dehydrogenase (LDH)
- + Direct and Indirect Antiglobulin Tests
  - Mixed field
  - IgG
- Renal failure and DIC are rare

Delayed Hemolytic Transfusion Reaction



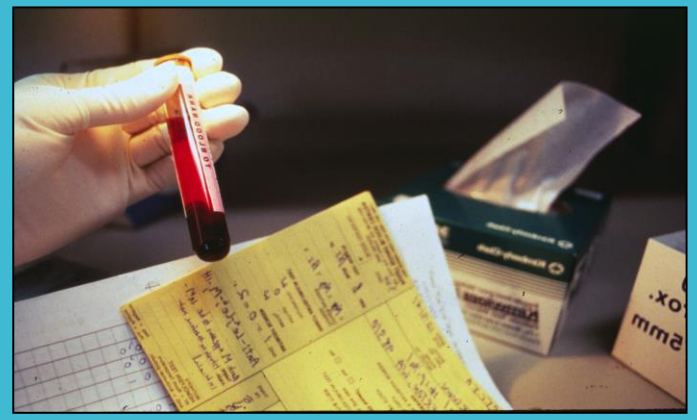
Hematocrit and Bilirubin in Delayed Hemolytic Transfusion Reaction





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

Case 6



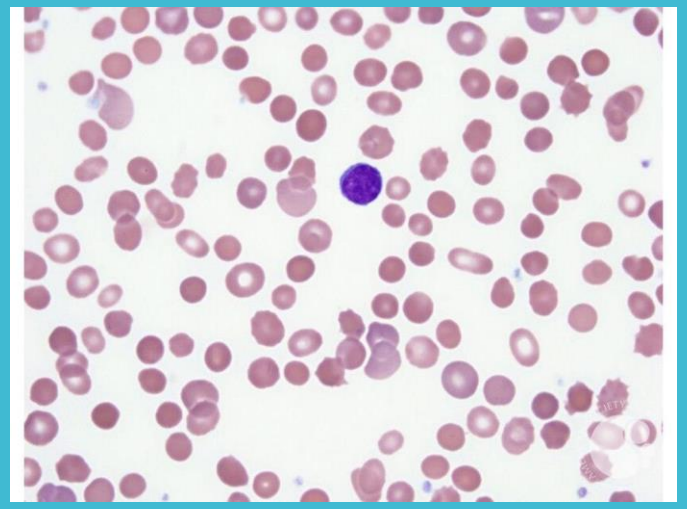
73 yo man admitted for routine hip replacement. He was typed and cross matched for 2 units RBC. On admission, his hematocrit was 40%. On post-op day 1, he is doing well with tolerable pain at the incision site and mild swelling of the hip. His vital signs are stable. His hematocrit returns at 26%. Transfusion of one unit of pRBCs is ordered.

Ten minutes after the transfusion begins, he complains of “feeling funny” and appears flushed. He begins to rigor and has a measured temperature of 40^0 C.

The paperwork is re-examined and both donor and the patient are recorded as A Rh+.

The patient’s urine is dark and a centrifuged specimen of the patient’s blood reveals a bright red plasma.

Case 7



The patient's pre-transfusion blood sample and the donor's blood sample are retyped as A Rh+, and are negative for antibodies.

A repeat crossmatch is done and the blood is compatible.

Three hours later, the patient's labs are as follows:

WBC 15,000/ ul (80% neutrophils)
Hematocrit: 22%
Platelets: 73,000/uL
PT: 17/13 sec (INR - 1.8)
TT: 20/15 sec
Fibrinogen: 105, D-Dimer >2500
BUN: 18
Bilirubin: 2.3 (2.0 indirect)
Urine dipstick: 4+ Hemoglobin

Which of the following is the most likely cause of this patient's symptoms?

A. Sepsis
B. ABO incompatibility
C. Retained surgical device
D. Babesiosis
E. TRALI

Post Transfusion Blood Typing

- Post transfusion blood sample from patient types O Rh+
- No type A cells identified.
- Direct Coombs= negative; no antibodies detected

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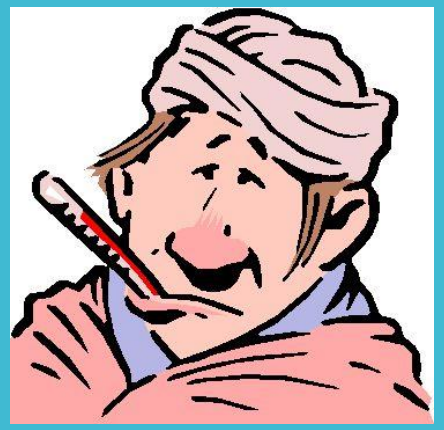
Transfusion Reactions



Most importantly, what do you do?

- **STOP** the transfusion
- Keep the IV line open
- Perform clerical check of product and patient
- Signs & Symptoms
  - Follow and document vital signs
  - Supportive treatment
    - Anti-pyretics, anti-histamines, anti-inflammatories
  - Send for pertinent labs
- Note type of product
- Notify and send patient tube and product to blood bank

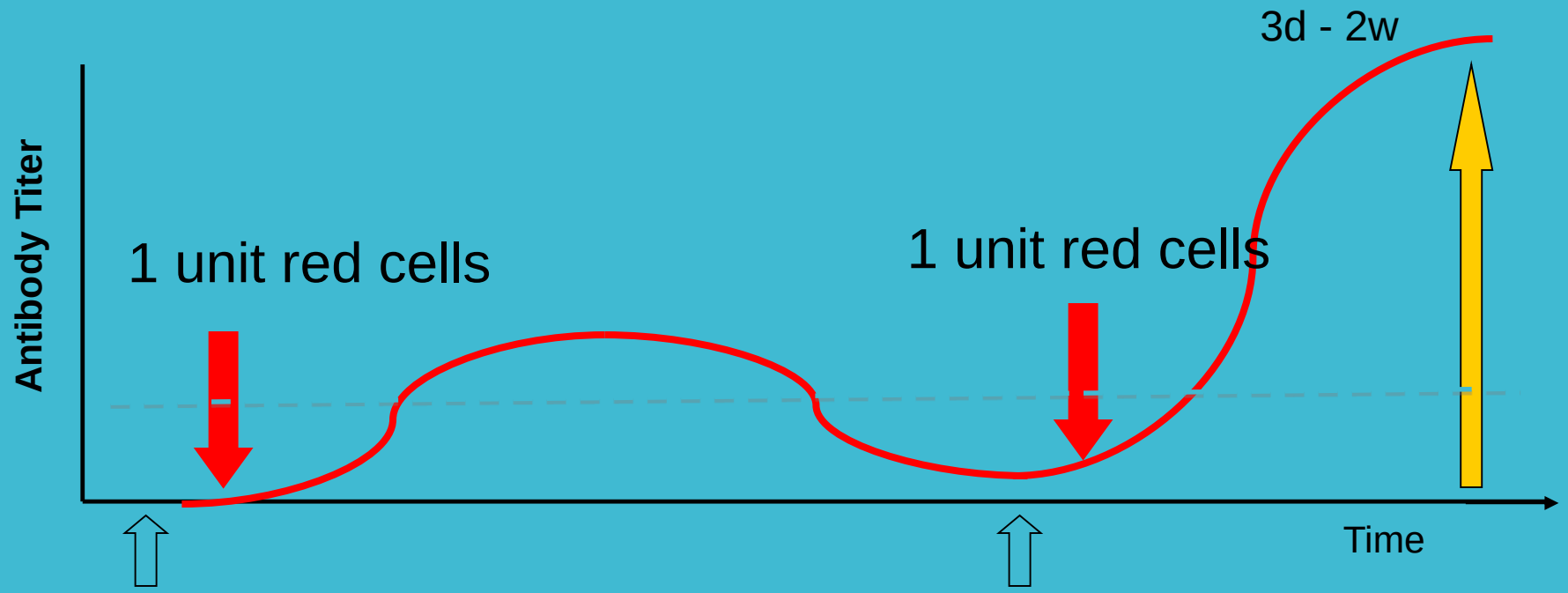
Acute Hemolytic Transfusion Reaction

- Signs & Symptoms
  - Fever, hypotension
  - Flank and transfusion site pain
  - Nausea, vomiting
  - Renal failure
  - DIC
- Laboratories
  - Hemoglobinemia
  - Hemoglobinuria
  - LDH elevated
  - DAT +

Questions and thanks

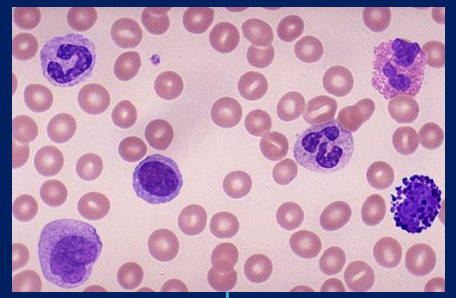
Delayed Hemolytic Transfusion Reaction (DHTR)

Hemolytic Anemia
- Low Hgb
- High bilirubin, LDH
- Spherocytosis
- Reticulocytosis
- Positive Ab Screen
- Positive DAT



Febrile (Non-Hemolytic) Transfusion Reaction

- Relatively common
- Cause
  - Cytokines from donor leukocytes
- Signs & Symptoms
  - Fever (2°F), chills within a few hours of transfusion
  - N/V, hypotension
- Action
  - Discontinue transfusion
  - Support & monitor
  - Ok to give next transfusion if no hemolysis



- Leukoreduction decreases incidence from 2% to 1%

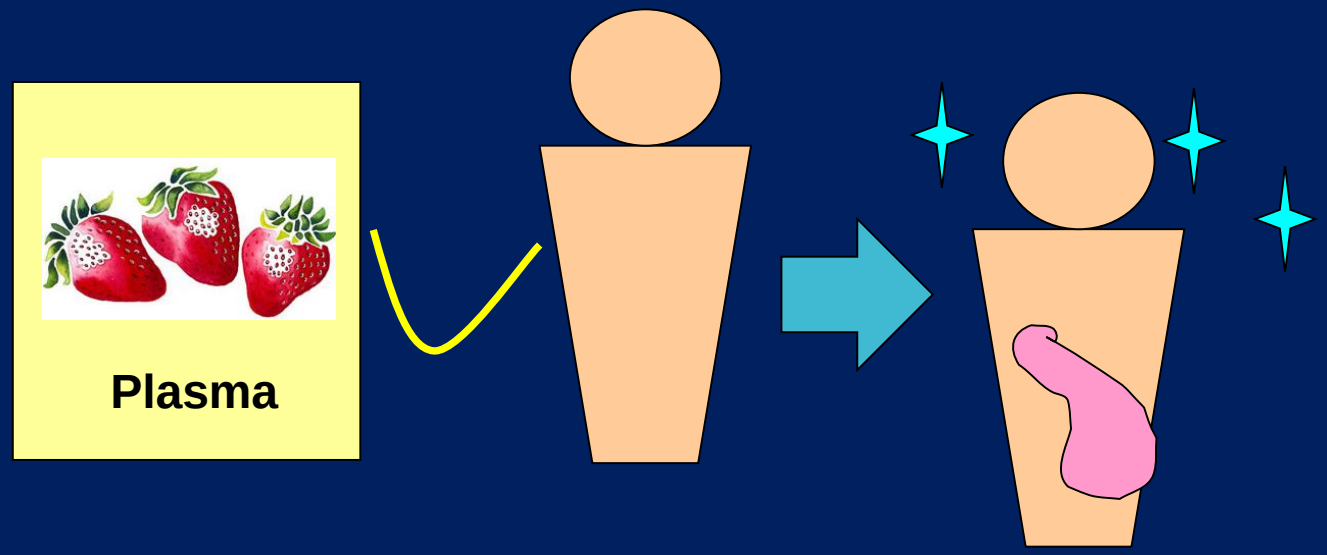
Urticarial, Allergic & Anaphylaxis

URTICARIAL ***(Common)***

ANAPHYLACTIC ***(Rare)***

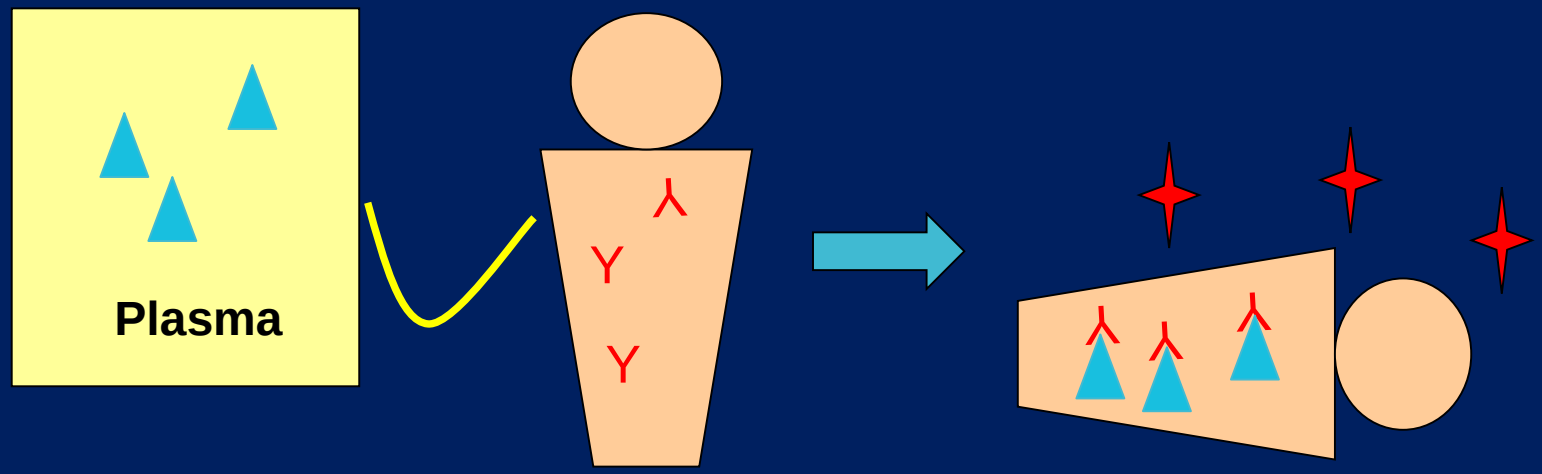
- Hypersensitivity Reactions
  - Proteins in donor plasma cause hypersensitivity reaction in recipient
  - IgA deficient patient
  - Washed RBC (plasma removed)

Urticarial / Allergic Reaction



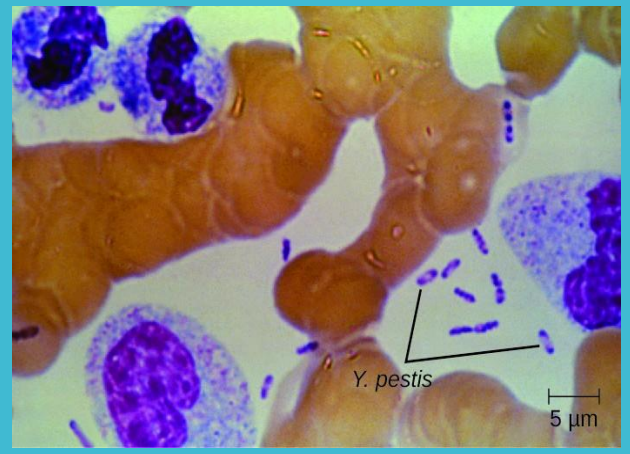
- Donor proteins cause IgE mediated histamine release in patient
  - Flushing, pruritis, urticaria
  - Usually no temperature
- Treat with anti-histamines
- Ok to re-start transfusion at slower rate if symptoms subside or stabilize

Anaphylaxis & Anaphylactoid



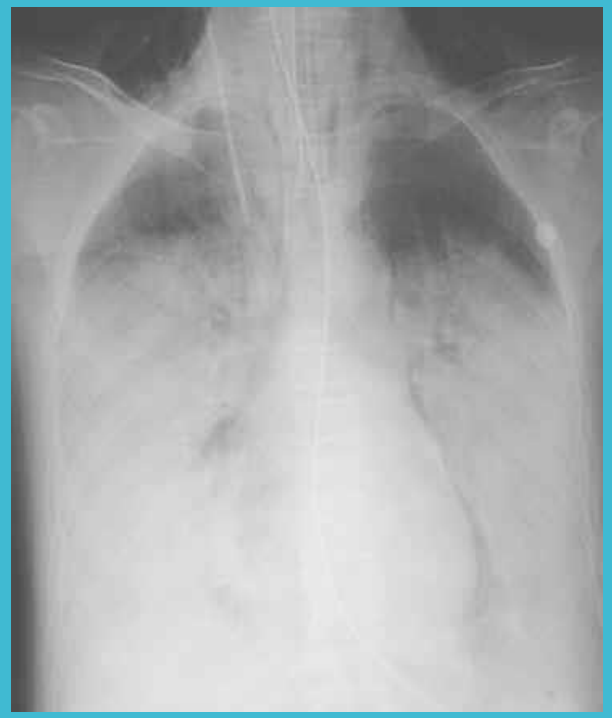
- Hypotension, dyspnea, airway edema, anxiety, larger rash
- Requires emergent care
  - Anti-histamines
  - Epinephrine, corticosteroids, pressors and intubation if necessary
  - May have to wash platelets or rbc's (blood products) for future

Sepsis



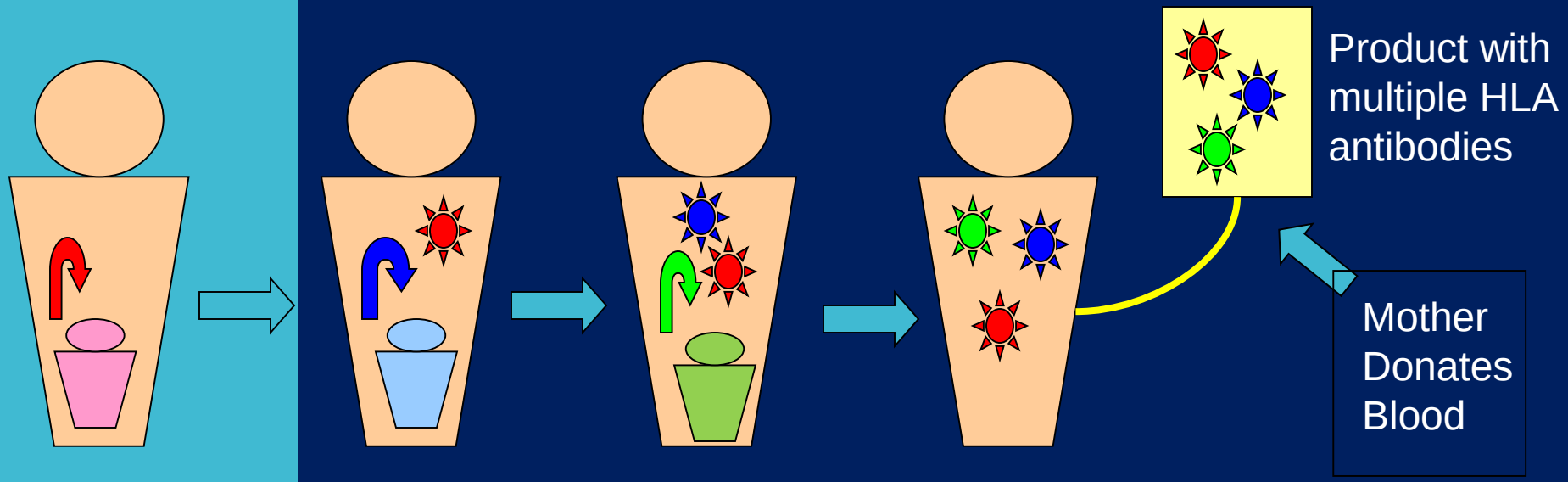
- Blood components contaminated by bacteria
  - Blood donor skin flora
  - Blood donor unrecognized bacteremia
  - Environmental or product handling during processing
- Most common in platelets because stored at room temp
  - Up to 1 in 1,300 platelet transfusions
- Always let blood bank know if septic reaction suspected so products can be cultured

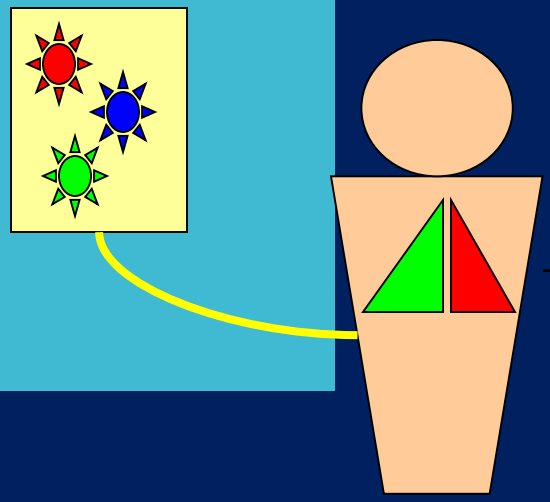
Transfusion Related Acute Lung Injury (TRALI)



- Acute onset hypoxemia
  - Within 6h of transfusion
  - Bilateral lung infiltration
  - No sign circulatory overload
- True frequency unknown
  - 1 in 2-5,000 plasma containing transfusions
  - Under diagnosed
  - 72% require mechanical ventilation
  - 5 - 10% mortality

TRALI proposed mechanism





When product infused, antibodies passively transfused.

Agglutinate with leukocytes in pulmonary microvasculature.

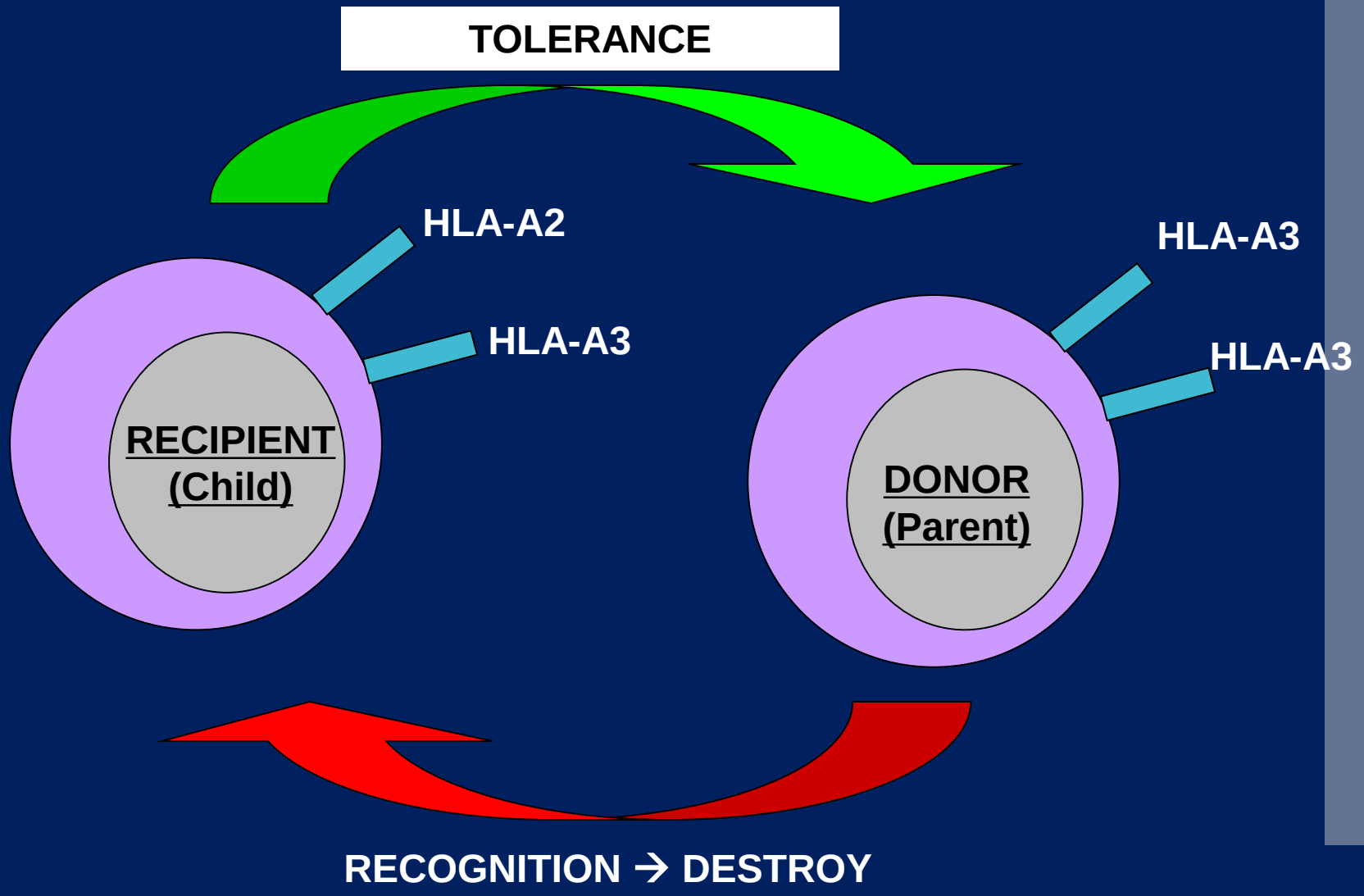
Causes respiratory distress and ARDS picture.

Important to notify blood bank so that donor-recipient testing can be done

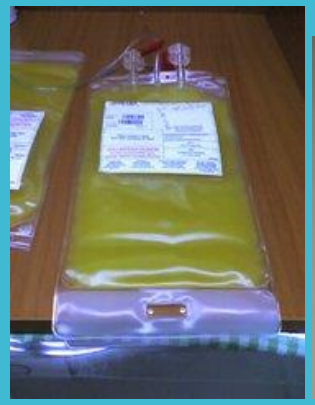
Transfusion Associated GVHD

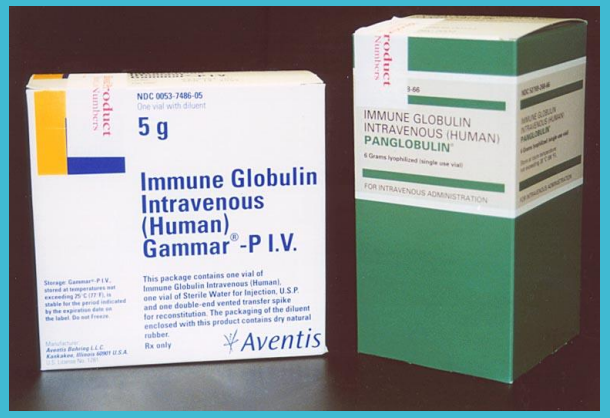
- Engraftment and proliferation of donor lymphocytes in transfusion recipient.
- Who's at risk?
  - Immunocompetent patient transfused with HLA haploidentical product (blood relative)
  - Severely immunocompromised patients
- Donor cells attack
  1. Hematopoietic cells → refractory pancytopenia
  2. Other organ systems: Fever, enterocolitis, rash, hepatitis
- **Usually fatal: 90-100%**

Blood related donor: ta-GVHD risk



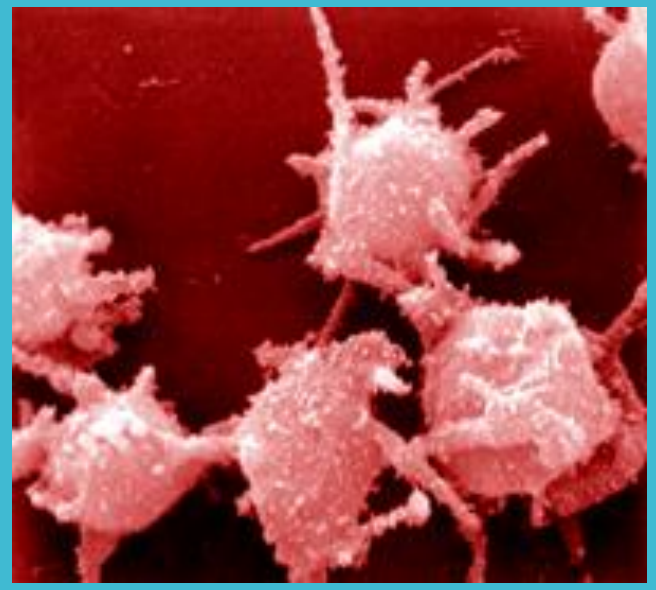
Blood Products





- Red Blood Cells
- Platelets
- Plasma
  - Cryoprecipitate
  - Albumin
  - IVIG
- Coagulation factors
  - Plasma derived or recombinant

Platelets



Activated Platelets

www.cbr.ubc.ca

- Function
  - Initial phase of coagulation
- Use
  - Treat thrombocytopenia
  - Platelet function disorders
- Not used
  - Pre-procedure prophylaxis to prevent serious bleeding
  - Expand intravascular compartment

Special Considerations

	CMV ”Safe”	Irradiated	Leukoreduced
Hematopoietic Stem Cell Transplant	X	X	X
Chemotherapy		X	X
Lymphoproliferative Disorder		X	X
Organ Transplant Candidates	X (if CMV-)		X
Neonates	X	X	X

Transfusion associated CMV

- **50% or more of** blood donors CMV are seropositive
  - ~1% thought to be infectious
  - Usually transfusion associated CMV of no clinical consequence

- Certain categories of immunocompromised patients can have progressive disease
  - Fetuses / newborns
    - Pregnant mothers
  - Bone marrow transplant patients / candidates
  - Solid organ transplant patients
  - Seronegative HIV/AIDS patients

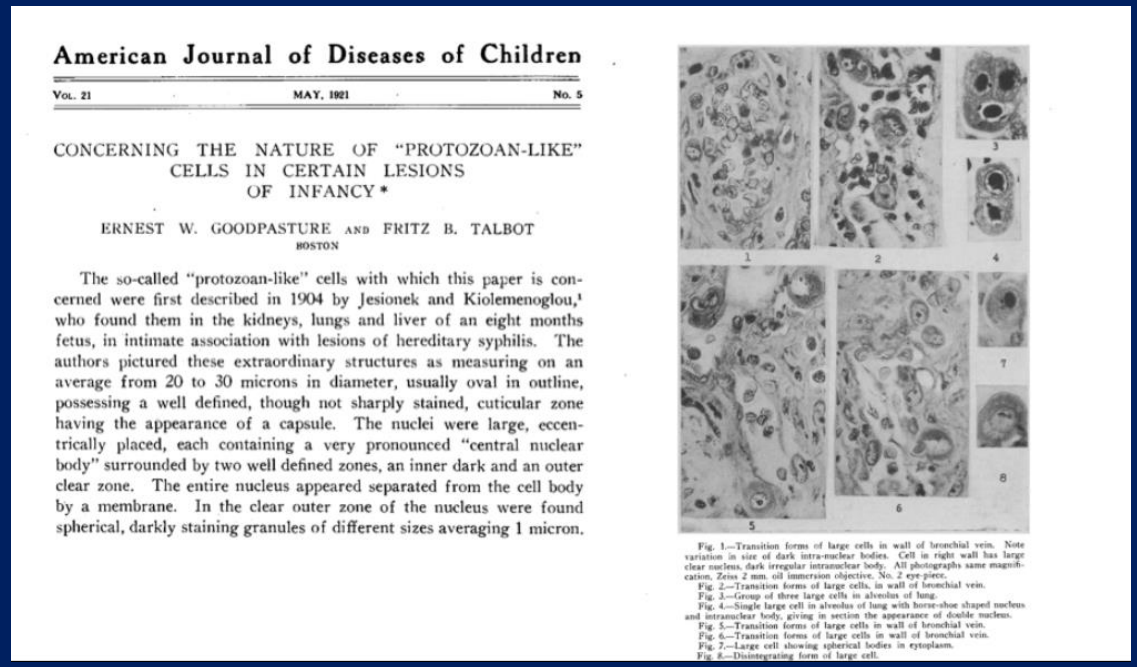
"CMV Safe" Blood Products

Prevent transfusion associated-CMV disease in patients at risk

- "CMV safe" products made by two methods
  - Donor negative for CMV antibodies (CMV negative)

OR

  - Blood product leukoreduced
    - CMV cellular restricted pathogen



American Journal of Diseases of Children

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CONCERNING THE NATURE OF "PROTOZOAN-LIKE" CELLS IN CERTAIN LESIONS OF INFANCY *

ERNEST W. GOODPASTURE AND FRITZ B. TALBOT
BOSTON

The so-called "protozoan-like" cells with which this paper is concerned were first described in 1904 by Jesionek and Kiolemenoglou,[1] who found them in the kidneys, lungs and liver of an eight months fetus, in intimate association with lesions of hereditary syphilis. The authors pictured these extraordinary structures as measuring on an average from 20 to 30 microns in diameter, usually oval in outline, possessing a well defined, though not sharply stained, cuticular zone having the appearance of a capsule. The nuclei were large, eccentrically placed, each containing a very pronounced "central nuclear body" surrounded by two well defined zones, an inner dark and an outer clear zone. The entire nucleus appeared separated from the cell body by a membrane. In the clear outer zone of the nucleus were found spherical, darkly staining granules of different sizes averaging 1 micron.

Fig. 1.—Transition forms of large cells in wall of bronchial vein. Note variation in size of dark intra-nuclear bodies. Cell in right wall has large clear nucleus, dark irregular intranuclear body. All photographs same magnification, Zeiss 2 mm. oil immersion objective, No. 2 eye-piece.
Fig. 2.—Transition forms of large cells, in wall of bronchial vein.
Fig. 3.—Group of three large cells in alveolus of lung.
Fig. 4.—Single large cell in alveolus of lung with horse-shoe shaped nucleus and intranuclear body, giving in section the appearance of double nucleus.
Fig. 5.—Transition forms of large cells in wall of bronchial vein.
Fig. 6.—Transition forms of large cells in wall of bronchial vein.
Fig. 7.—Large cell showing spherical bodies in cytoplasm.
Fig. 8.—Disintegrating form of large cell.

May 1921

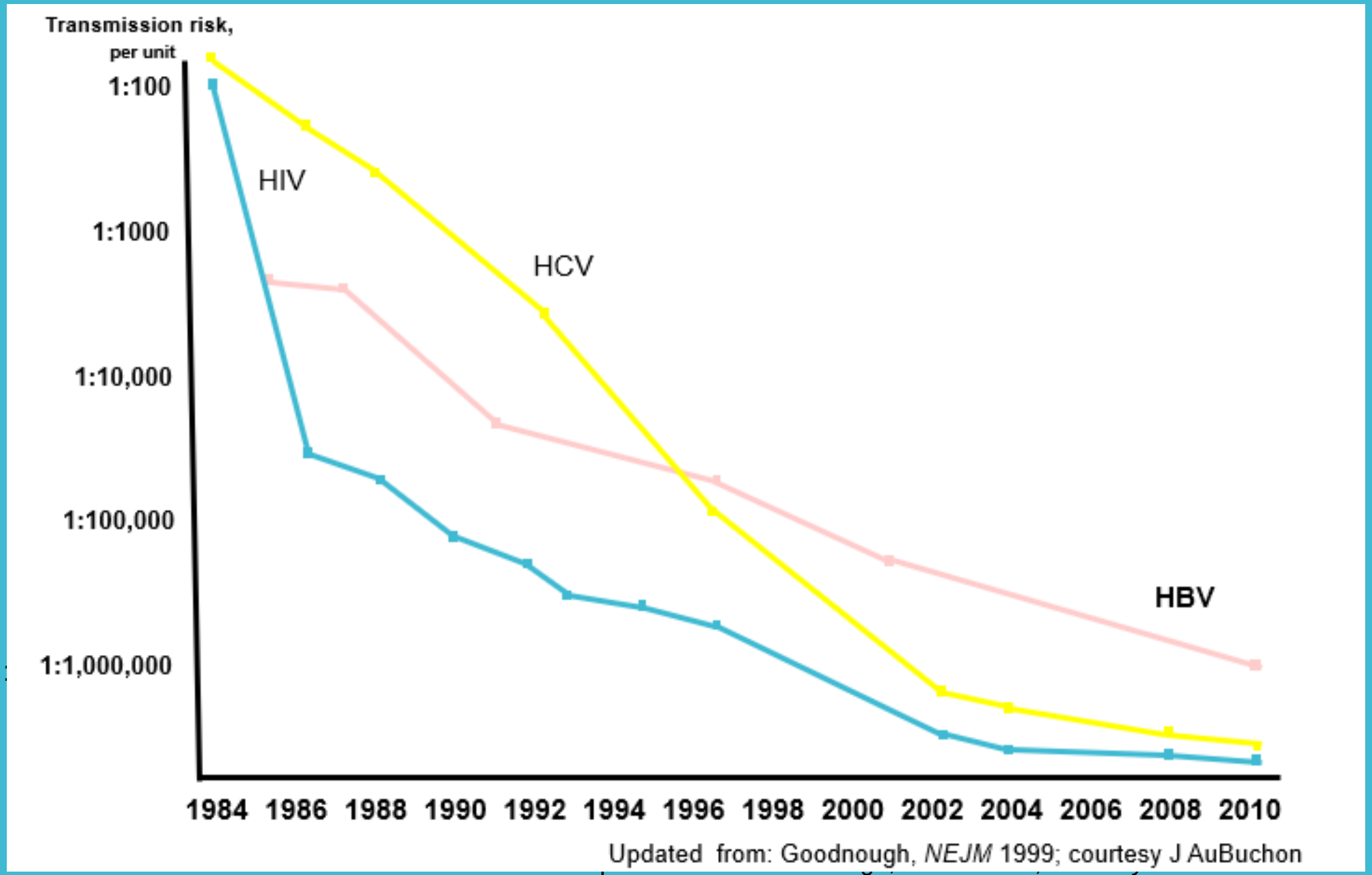
Case 4

- Type and cross is negative on repeat unit.

- RBC is about to be transfused and he asks you, "Which infectious disease am I most likely to acquire from this RBC unit?" You answer:

- A. Hepatitis A
- B. Hepatitis B
- C. Hepatitis C
- D. HIV
- E. Zika Virus

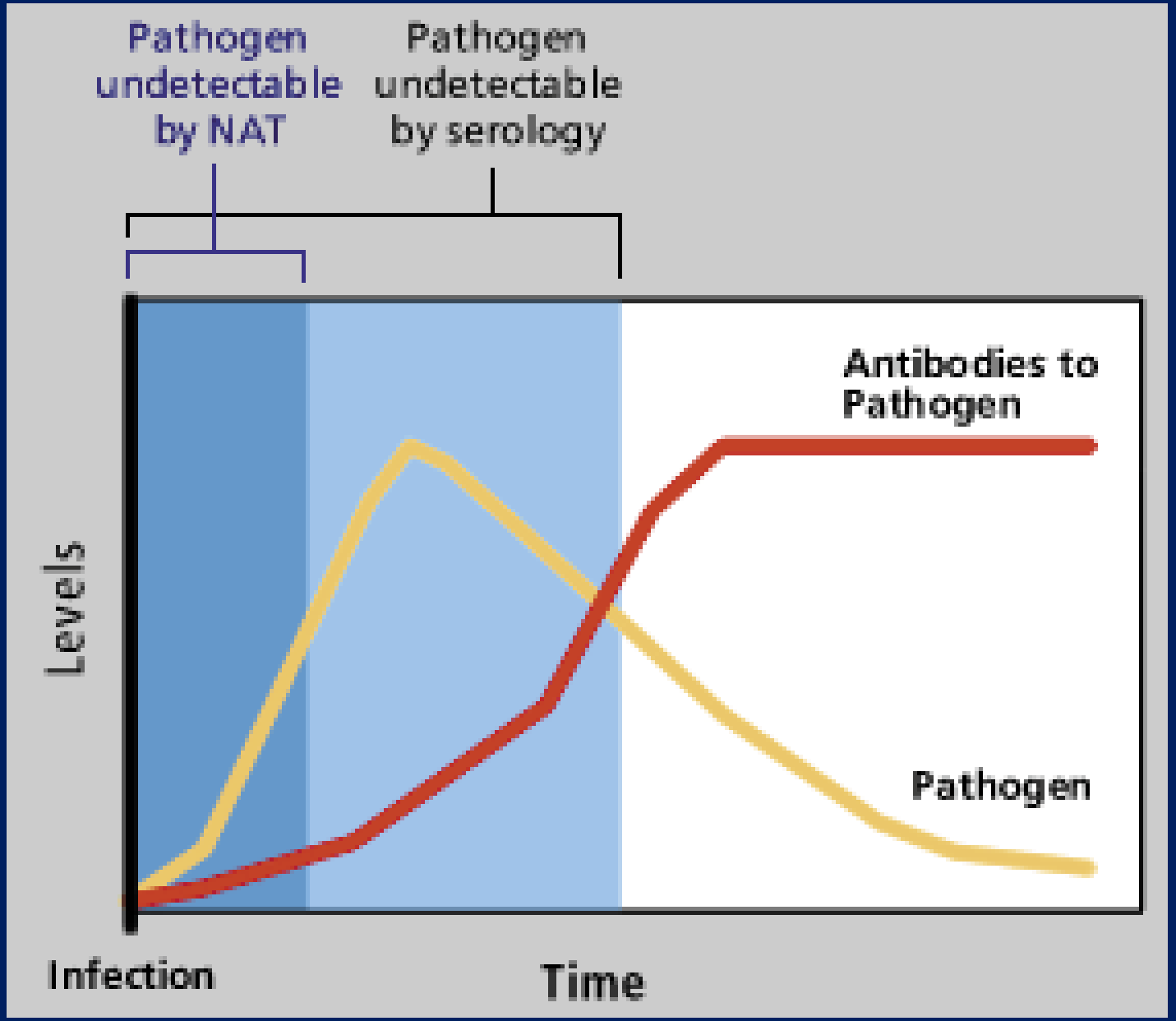
The evolution of transfusion risks



Transfusion Transmitted Disease

- Has significantly decreased over last two decades
- We make the blood supply safer using several tactics
  - Only volunteer donors
  - Blood donor questionnaire
  - Blood donor testing
- Look for donor risk factors
  1. Disease we test for
     - HIV, HBV, HCV, Syphilis, Chagas, WNV, HTLV
     - Sepsis
  2. Disease we cannot test for
     - variant Jacob-Creutzfeldt
     - "classical" Jacob-Creutzfeldt
     - Malaria (we don't test for)
     - Diseases we don't know about

Why are there *any* residual risks?



Residual risk: Test sensitivity