

# Transfusion Triggers

Anesthesiology and Critical Care  
Clerkship

Department of Anesthesiology

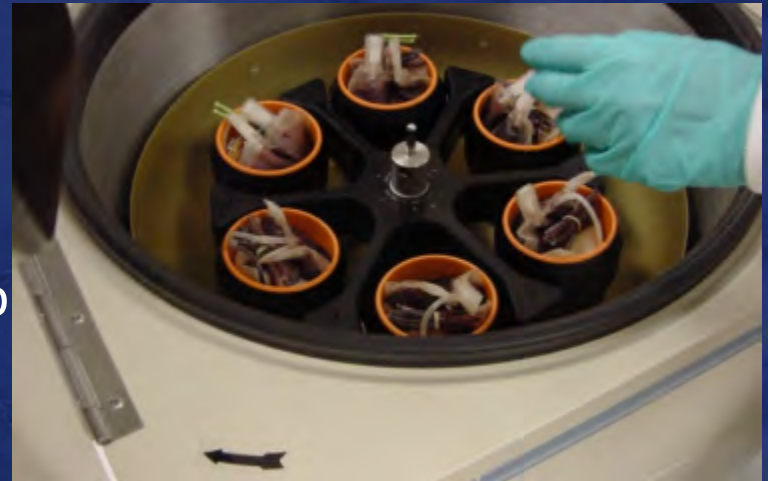
# Blood Banking Process

- 450-500cc blood removed from donor
- *Preservative = CPDA*
  - Anti-coagulated with Citrate
  - Buffered by Phosphate
  - Metabolism provided by Dextrose
  - Adenine for ATP synthesis
- Blood grouped : ABO & Rh
- Screened for Viruses



# Blood Component Separation

- Whole blood not transfused in USA
- Donation separated by centrifuge:
  - Packed Red Blood Cells (PRBC)
  - Platelets—stored at room temp
  - Fresh Frozen Plasma (FFP)
    - Frozen after separated
    - Then thawed to precipitate out cryoproteins
    - A 2<sup>nd</sup> Centrifugation separates the FFP and cryoprecipitate



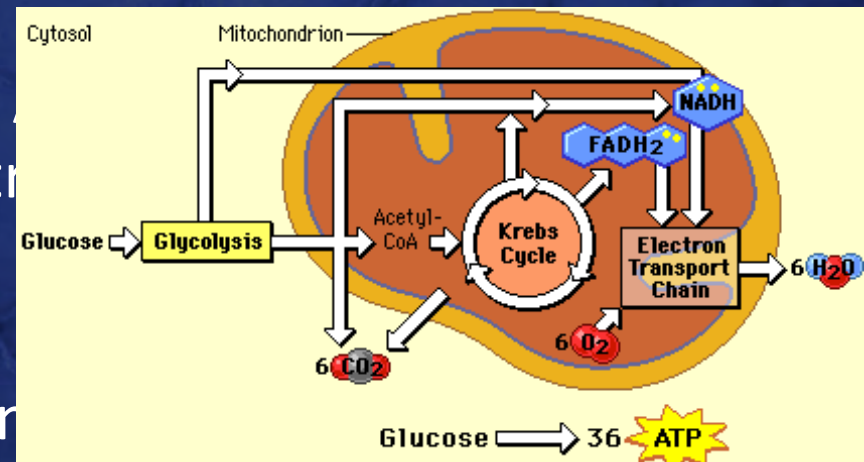
# Packed Red Blood Cells

- Stored at 4°C in CPDA-AS
- AS = additive solution
  - Basically more preservatives
  - Adds 7 days of preservation
- Stored up to 42 days
- Donor and Recipient
  - Typed for ABO compatibility
  - Screened for 20 common RBC antibodies
  - Only cross-matched if “+” screen



# When to transfuse PRBC?

- The goal is to maintain Aerobic respiration
- Cells need oxygen to create energy in the Krebs cycle and Electron Transport Chain within mitochondria
- Transfusion trigger is a balance to optimize oxygen delivery while minimizing transfusion risks



# Oxygen Delivery

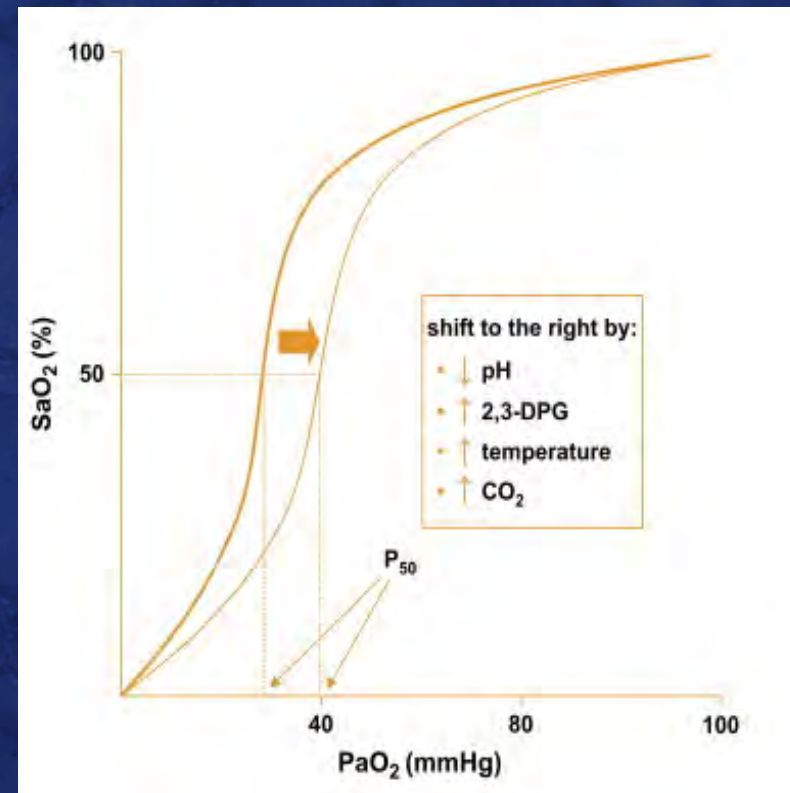
- $DO_2$  (delivery of oxygen) =  $CO \times CaO_2$ 
  - $CO$  (cardiac output) =  $HR \times SV$
  - $CaO_2$  (carrying capacity of oxygen) =  
 $(Hgb \times 1.34 \times SaO_2) + (PaO_2 \times .003)$
- $DO_2 = 800-1200\text{mL} / \text{min}$  (average 70kg person)
- $VO_2$  (oxygen consumption) =  $200-300\text{mL} / \text{min}$  (resting 70kg person)
- $ERO_2$  (extraction ration of oxygen) = 25%
  - $= VO_2 / DO_2$

# Additional Considerations Affecting Oxygen Delivery

- RBC characteristics
  - Affinity to O<sub>2</sub> (O<sub>2</sub>-Hgb curve)
  - Assist in O<sub>2</sub> on- / off-loading
- Intracellular O<sub>2</sub> consumption
  - VO<sub>2</sub> varies on metabolic activity
- Rheology
  - Flow characteristics of blood effect blood transport
  - “viscosity”
- Value of PaO<sub>2</sub>
  - Controversial impact due to low value

# Oxygen-Hemoglobin Curve

- Saturation of Hgb based on the partial pressure of O<sub>2</sub> in the blood
- **Right** shift indicates that a larger partial pressure of oxygen is needed to maintain a 50% Hgb saturation
  - Hgb with less affinity for oxygen
  - More O<sub>2</sub> delivered to the tissues
- **Left** shift indicates that a smaller partial pressure of oxygen is needed to maintain a 50% Hgb saturation
  - Hgb with a high affinity for oxygen

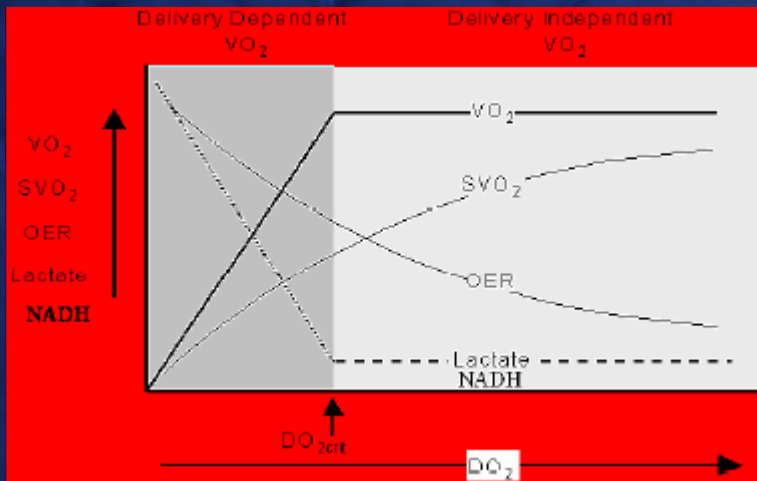




# Oxygen Delivery Compensatory Mechanisms

- Increase ERO2
  - Extract more than 25% of oxygen from each Hgb
- Sympathetic surge
  - Redistribution of intravascular compartments
    - Augments preload by recruiting more blood
  - Positive chronotropic and inotropic effect on CO
- Renin-Angiotensin-Aldosterone / ADH
  - Redistribution of intravascular compartments
  - Fluid retention augments preload
- RBC characteristics
  - 2,3-DPG decreasing Hgb affinity for oxygen

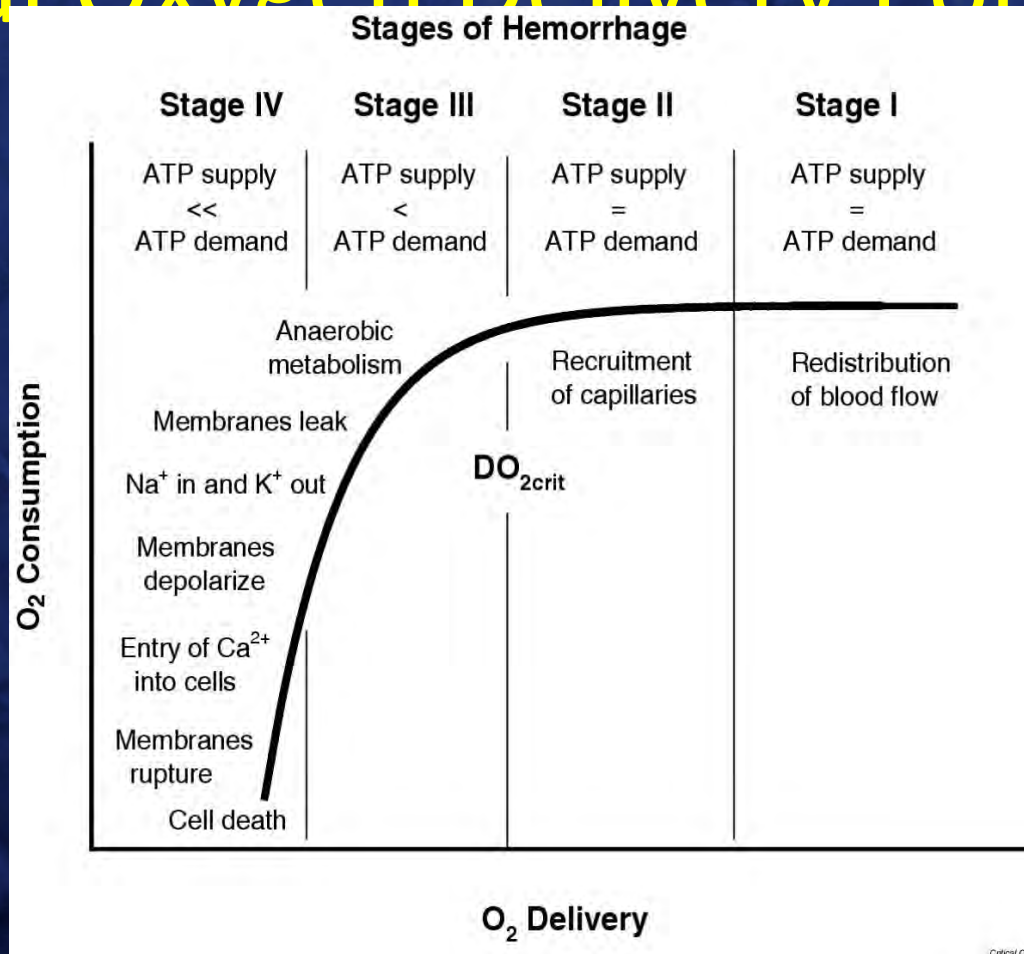
# Critical Oxygen Delivery Point



(Read Right to Left)

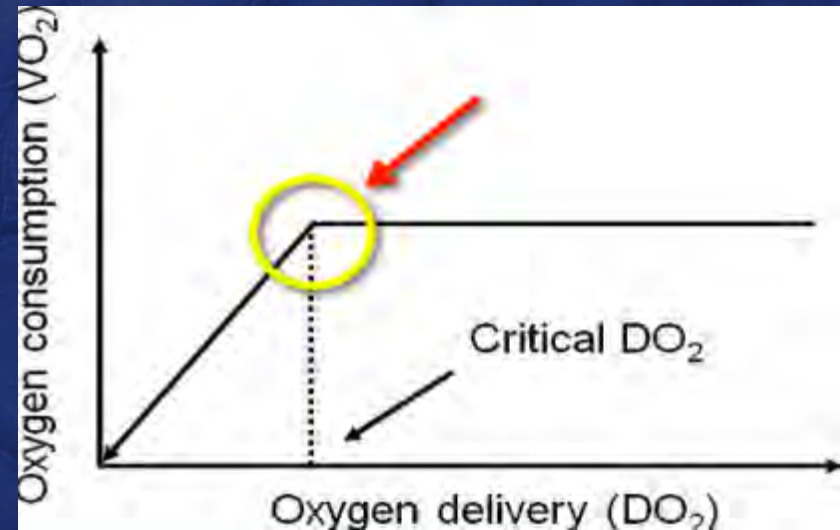
- As you deliver less Oxygen:
  - Consume same O<sub>2</sub>
  - Return to heart less O<sub>2</sub>
  - Extract more from each Hgb
- Critical Delivery Inflection point:
  - O<sub>2</sub> consumption becomes delivery dependent
  - No more “luxury perfusion”
  - Anaerobic oxygenation begins

# Critical Oxygen Delivery Point



# PRBC Trigger Threshold

- Decision to transfuse PRBC is based on understanding the  $DO_{2crit}$  inflection point
- Too far from this point and you are exposing the patient to all the risks associated with blood transfusions without any benefit
- Too far into this point you have begun anaerobic respiration



# Indications of $DO2_{crit}$

- Decreased Mixed oxygenation value from pulmonary artery catheter
- Increased Lactic Acid
  - Decreased Bicarbonate value (reflecting lactic acid)
  - Decreased pH (reflecting lactic acid)
- Evidence of end-organ ischemia
  - ECG changes
  - Regional Wall Motion changes on Echo
  - Chest pain
  - Confusion and dizziness

# What about...?

- Vital Signs
  - Changes Indicate compensatory mechanisms
  - Are those changes detrimental to patient?
- Urine output
  - Fluid conservation is key to maintaining CO
  - How long / severe is the kidney being underperfused?
- Hemoglobin or Hematocrit is low?
  - Need to consider the overall CO, CaO<sub>2</sub>, and VO<sub>2</sub>, not just one number.

# Question #6

- Regarding the detection of inadequate oxygen delivery
  - Vital signs reliably show end-organ ischemia
  - Urine output reveals end-organ ischemia
  - Regional Wall motion abnormalities reveals end-organ ischemia
  - A low hct reliably shows end-organ ischemia
  - A low pH reliably shows end-organ ischemia

# First....

- Make sure the patient is euvolumic
- Animals can tolerate major blood loss as long as their intravascular storage compartment is replete
- Have you attempted to replace the intravascular system with crystalloids?





# Always keep in mind...

- Transfusion triggers varying widely across patient populations
  - Consider differences:
    - A Healthy 20yo
    - A 75yo with severe CAD
    - A single ventricle neonate
    - A critically ill mechanically ventilated patient
  - Need to understand the complex pathophysiology of these different populations in order to appropriately transfuse them



# Transfusion Considerations

- Is the patient Euvolumic?
- Is the patient critically ill / mechanically ventilated?
- Does the patient have coexisting comorbidities?
  - Cardiac
  - Pulmonary
  - Cerebral vascular
- Is this Acute or Chronic anemia?
- The decision to transfuse never rests solely on a Hgb value!
  - That being said, the Hgb value is usually between 6-9g/dL prior to transfusing depending on patient idiosyncrasies

# Clinical practice guideline: Red blood cell transfusion in adult trauma and critical care\*

Crit Care Med 2009 Vol. 37, No. 12

## A. Recommendations Regarding Indications for RBC Transfusion in the General Critically Ill Patient

1. RBC transfusion is indicated for patients with evidence of hemorrhagic shock. (Level 1)
2. RBC transfusion may be indicated for patients with evidence of acute hemorrhage and hemodynamic instability or inadequate oxygen delivery. (Level 1)
3. A "restrictive" strategy of RBC transfusion (transfuse when Hb < 7 g/dL) is as effective as a "liberal" transfusion strategy (transfusion when Hb < 10 g/dL) in critically ill patients with hemodynamically stable anemia, except possibly in patients with acute myocardial ischemia. (Level 1)
4. The use of only Hb level as a "trigger" for transfusion should be avoided. Decision for RBC transfusion should be based on an individual patient's intravascular volume status, evidence of shock, duration and extent of anemia, and cardiopulmonary physiologic parameters. (Level 2)
5. In the absence of acute hemorrhage RBC, transfusion should be given as single units. (Level 2)
6. Consider transfusion if Hb < 7 g/dL in critically ill patients requiring mechanical ventilation (MV). There is no benefit of a "liberal" transfusion strategy (transfusion when Hb < 10 g/dL) in critically ill patients requiring MV. (Level 2)
7. Consider transfusion if Hb < 7 g/dL in resuscitated critically ill trauma patients. There is no benefit of a "liberal" transfusion strategy (transfusion when Hb < 10 g/dL) in resuscitated critically ill trauma patients. (Level 2)
8. Consider transfusion if Hb < 7 g/dL in critically ill patients with stable cardiac disease. There is no benefit of a "liberal" transfusion strategy (transfusion when Hb < 10 g/dL) in critically ill patients with stable cardiac disease. (Level 2)
9. RBC transfusion should not be considered as an absolute method to improve tissue oxygen consumption in critically ill patients. (Level 2)
10. RBC transfusion may be beneficial in patients with acute coronary syndromes (ACS) who are anemic (Hb  $\leq$  8 g/dL) on hospital admission. (Level 3)

# What's the Big Deal?

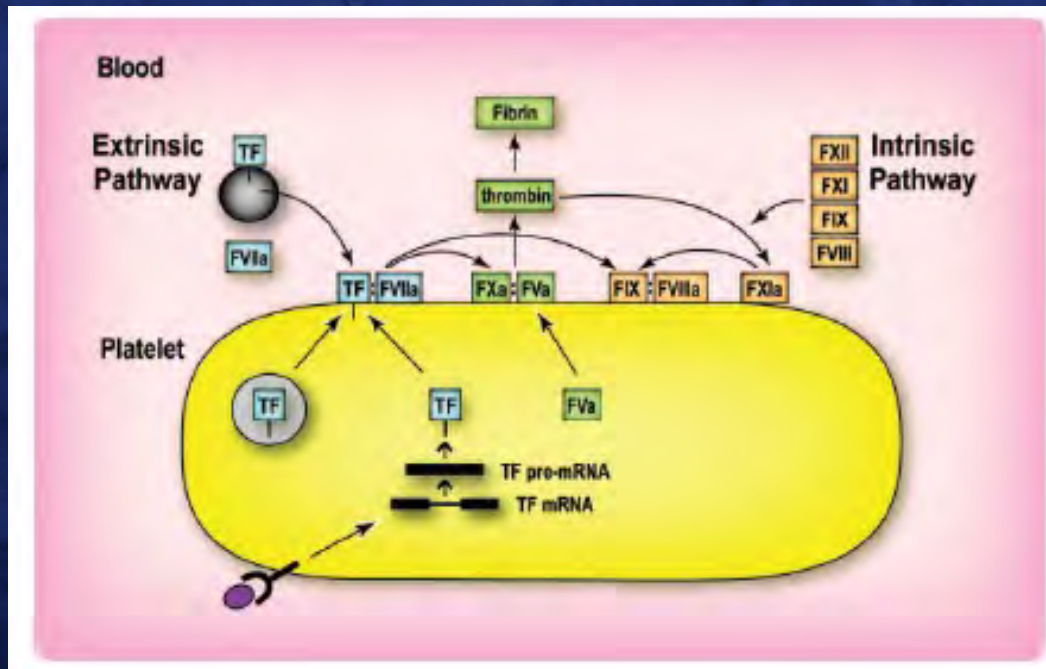
## Just give 2 Units!

- **Risks** of Blood product transfusion:
  - Incompatibility reactions
  - Transfusion Transmitted Infections (TTI)
  - Transfusion Related Acute Lung Injury (TRALI)
  - Transfusion Related ImmunoModulation (TRIM)
  - Transfusion Associated Cardiac Overload (TACO)
  - Electrolyte derangements
  - pH changes
  - Temperature decrease
  - Alloimmunization
  - Depressed Erythropoiesis
  - ....

# Coagulation Overview

- Primary hemostasis
  - Injured endothelium exposes tissue factor and damaged collagen
  - vWF binds to collagen and to circulating platelets
  - Plts change from spherical to spindle shaped and release granules
  - Plts aggregate to form platelet plug
- Secondary hemostasis
  - Tissue Factor (TF) on damaged endothelium activates FVII
  - Plt surface serves as platform for coagulation “cascade”
  - TF-FVII activates FX, which activates FV
  - This complex then activates Thrombin
  - Thrombin cleaves fibrinogen to fibrin
  - Platelets receptors conform to bind to fibrin
  - Platelets cross-link fibrin which cross links with factor XIII

# Coagulation



Mackman et al. Blood Coagulation in Hemostasis and Thrombosis. Arterioscler Thromb Vasc Bio 2007;1692.

# Fresh Frozen Plasma

- Traditionally isolated by centrifugation
- Apheresis is now often used
  - Plasma extracted from donor while the RBCs remain
  - Platelet rich plasma
  - Frozen after apheresis
- Needs to be ABO matched
- Remember type AB is the universal plasma donor



# Fresh Frozen Plasma Facts

- Contains all coagulation factors (enzymes)
- 1 ml has about 1 unit of each coagulation enzyme
- 1 ml has about 1 mg of fibrinogen
  - 1 unit has about 300-400 mg
  - 4 units has about 1200-1500 mg = 1 pooled cryoprecipitate bag
- Upon warming factors V and VIII deplete rapidly
  - Called “labile” factors because of sensitivity



# Indications for FFP

1. Replacement of isolated factor deficiencies
  - IF isolated recombinants are not available
2. Reversal of Warfarin effect for emergency procedure or blood loss
3. Massive Blood Transfusion
  - IF > 1-2 Blood Volumes over a few hours
  - Best strategy is to be guided by Thromboelastagram (TEG)
4. Antithrombin III deficiency
  - IF recombinant is not available
5. Treatment of Immunodeficiencies
  - IF purified Immunoglobulins are not available
6. Treatment of thrombotic thrombocytopenic purapura

# FFP dosage

- 1mL / 1 kg will give 1% of Factors (enzymes)
- Normal coagulation calls for 30% of coagulation enzymes
- For an average 70kg person with coagulopathy
  - Assume 5-10% Enzymatic activity... but could be worse or better
  - Want 20% more so need 20mL / kg = 1400mL
    - Equals 4-6units of FFP
  - 15-20mL/kg is an average dosage for FFP transfusion

**Never give FFP as Volume Replacement!**

# Platelets

- Traditionally from centrifugation of whole blood
- Apheresis or “single donor” now more common
  - Less risk because not pooled from multiple sources
  - Will contain some factor rich plasma
- Stored at room temperature
  - Increases bacterial growth susceptibility
- Freezing or warming will make them nonviable
- Storage time = 3-5days

# Platelet transfusion triggers

- Normal platelet count 150-350 000
- <10,000-20,000 for a nonbleeding patient without a source of potential bleeding
- <50,000 for most operations
- <70,000-100,000 for neurosurgical bleeding where any amount of bleeding is catastrophic
- Platelet count does NOT assess platelet function
  - Need to consider quality as well as quantity
  - Consider Platelet mapping or TEG

# Cryoprecipitate

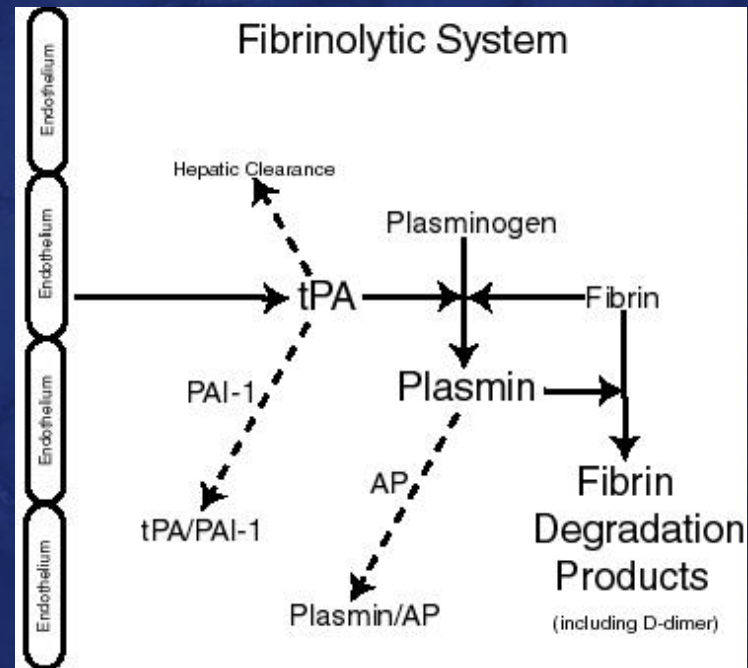
- As FFP is thawed from frozen, cryo precipitates out first
- Originally developed for hemophiliacs
  - Because Cryo is rich in Factor VIII and vWF
- Now mostly used as a source of fibrinogen
- Each pooled unit has 4 major parts
  - Fibrinogen: 1200 – 1500 mg
  - VIII: 800-1000 units
  - vWF: 800 – 1000 units
  - XIII

# Cryoprecipitate transfusion triggers

- Fibrinogen is necessary to make fibrin
  - Fibrin cross-links on platelets to form clot
  - FXIII cross-links fibrin polymers to strengthen fibrin clot
- Minimum concentration of fibrinogen needed is controversial
  - Traditionally, Fibrinogen  $< 100\text{mg/dL}$  should be replaced
  - Newer studies suggest replacing fibrinogen  $< 200\text{mg/dL}$
  - OB patients may need a level of  $> 300\text{mg/dL}$

# Clot Dissolution = Fibrinolysis

- Begins with tPA, which activates plasminogen to plasmin
- Plasmin binds to fibrin polymers at lysine residue
- Breaks fibrin polymers into two D-Dimers
- Anti-fibrinolytics
  - $\epsilon$ -aminocaproic acid & tranexamic acid
  - lysine analogs
  - Competitive antagonists





# Factor concentrates

- PCC = procoagulant concentrates
  - 3 factor types: II, IX, X, variable amount of heparin
  - 4 factor types: II, VII, IX, X, variable amount of heparin
  - Approved for rapid reversal of anti-vitamin K medications in life threatening bleeding
  - Come in 30-40cc dosage
- Recombinant fVII
  - Developed for hemophiliacs with replacement inhibitors
  - Sets off Tissue Factor pathway

The End