Alternative Therapeutics Substitutes

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LifeServe BLOOD CENTER

Your Blood. Your Hospital. Your Neighbors.

Preface

- Introduction
- Mechanism
- Advantages and Limitations
- Conclusions

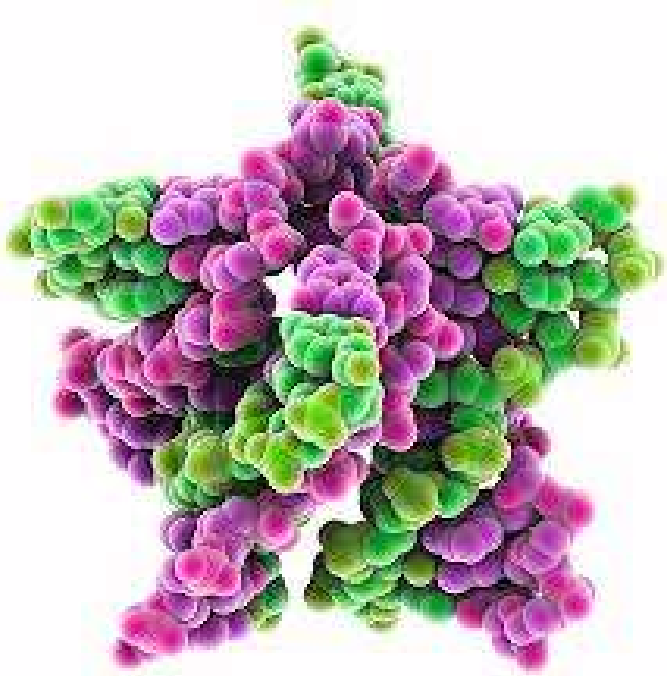
Prothrombin Complex Concentrate

Tranexamic Acid

RhoGam

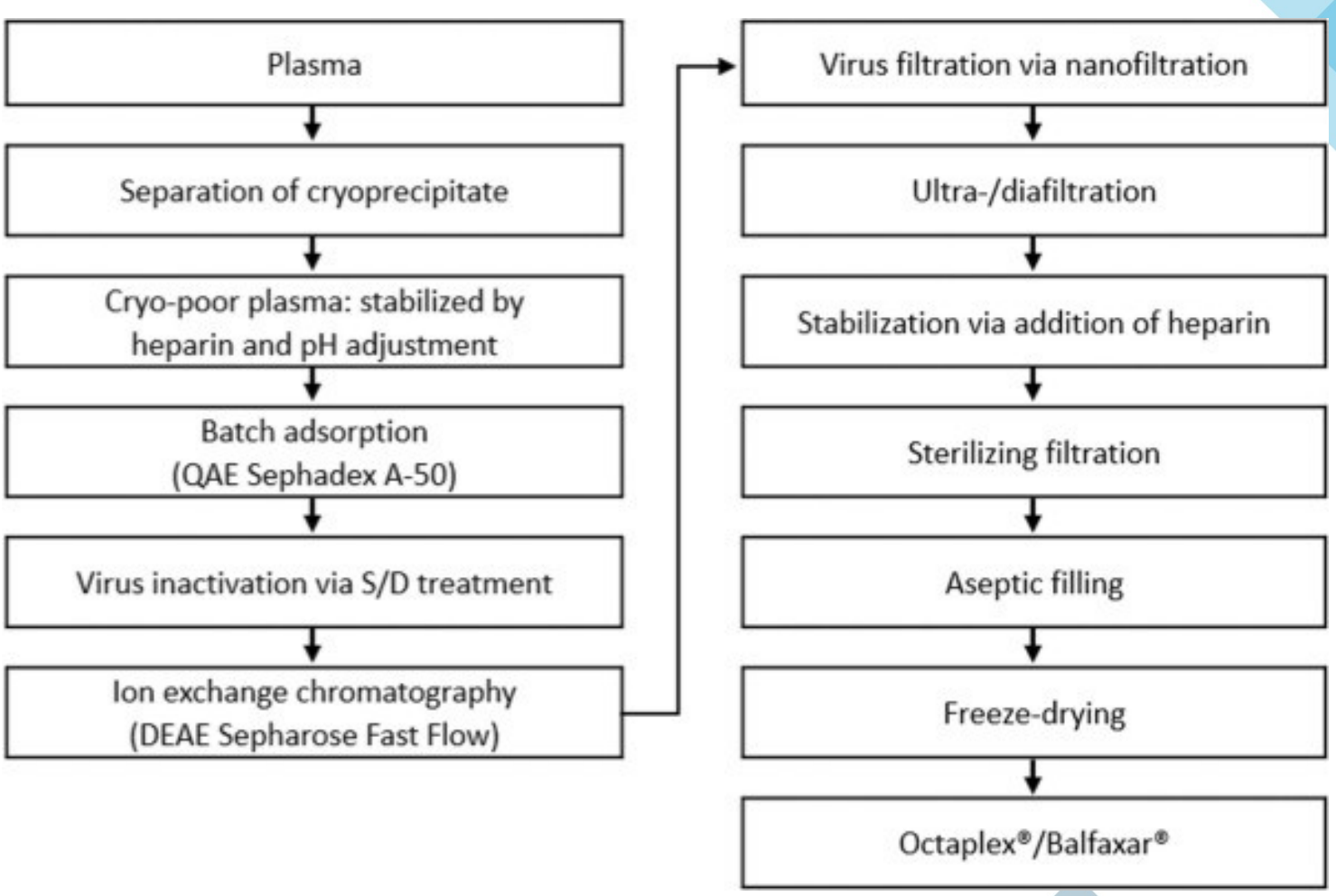
Prothrombin Complex Concentrate


NDC 63833-386-02
500 U Range
Prothrombin Complex Concentrate (Human)
Kcentra®
One single-dose vial containing 400 – 620 units of lyophilized Factor IX concentrate for reconstitution. Also contains Factors II, VII, X and proteins C and S.
For Intravenous Administration Only
Because Kcentra® is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.
See package insert Warnings and Precautions section.
CSL Behring
octaplex® 500 IU
Powder and solvent for solution for injection
Human Prothrombin Complex
One vial contains:
Name of ingredient
Total protein:
Active substances
Human coagulation factors II, VII
Factor II 280 - 760 IU
Factor VII 180 - 480 IU
Factor IX 500 IU
Factor X 360 - 600 IU
Protein C 260 - 620 IU
Protein S 240 - 640 IU
MENGANDUNG RAM
octaplex® 500 IU
HARUS DENGAN RESEP DOKTER
No. Reg. DKI1409300544A1
MENGANDUNG RAM



Prothrombin Complex Concentrate (PCC):

- Used to support clot formation and aid in treatment of bleeding
- Two forms:
  - Three factor which includes factors II, IX and X
  - Four factor which includes factors II, VII, IX, X, protein C and S *(most effective at decreasing INR)*
- Stored at 2-25 C for up to **36 months** from date of manufacture
- Created from cryo-poor plasma to final product which maintains a ratio of clotting factors II, VII, IX, X to an optimum of 1:1:1:1
- Approved in states by FDA in 2013
- Popular product brand also known as Kcentra or Octaplex


Plasma
Separation of cryoprecipitate
Cryo-poor plasma: stabilized by heparin and pH adjustment
Batch adsorption (QAE Sephadex A-50)
Virus inactivation via S/D treatment
Ion exchange chromatography (DEAE Sepharose Fast Flow)
Virus filtration via nanofiltration
Ultra-/diafiltration
Stabilization via addition of heparin
Sterilizing filtration
Aseptic filling
Freeze-drying
Octaplex®/Balfaxar®

FFP vs PCC
& Managing Blood Loss

Administration and Limitations of FFP:

- Thawing (30 + min)→ delaying availability in ER situations
- Infusing large fluid volumes → fluid overload, pulmonary edema, increased cardiac strain
- Infections
- Allergic reactions
- TRALI
- (*Cardiology in Review, study; 2025*)

PCC Advantages:

- Contains **specific** vitamin K-dependent clotting factors (better choice for warfarin reversal)
- Administered in smaller volumes
- Less preparation is needed
- More rapid and targeted approach to correcting coagulopathies
- Has advantages in time sensitive surgical scenarios
- Shortens bleeding time
- Reduces transfusion requirements
- Lower risks of adverse events

Components

Product	Component(s)	Volume
Packed red blood cells (pRBC)	RBCs	1 unit = 300 mL
Single donor platelets (SDP)	Platelets	1 pack = 6 units = 300 mL
Fresh frozen plasma (FFP)	Factors II, VII, VIII, IX, X, XI	1 unit = 250-300 mL
Prothrombin complex concentrate (4-factor PCC/Kcentra)*	Factors II, VII, IX, X, proteins C & S	1000 units = 40 mL • Empiric = 1500-2000 units • INR 2-4 = 25 units/kg • INR 4-6 = 35 units/kg • INR >6 = 50 units/kg
Cryoprecipitate	Factors VIII, XIII, fibrinogen, von Willebrand Factor (vWF)	1 unit = 10-15 mL • 1 unit increases fibrinogen by ~7-10 mg/dL in a 70 kg patient • Typical dose is ~10 units with a target fibrinogen of ≥100-150 mg/dL

*3-factor PCC lacks factor VII and proteins C&S; it is primarily indicated for bleeding events in patients with hemophilia B and is still rarely used in comparison to targeted factor IX replacement or 4-factor PCC.

Table 2. FFP vs. PCC

	Fresh Frozen Plasma	PCC
Components	All clotting factors (in low doses) Plasma proteins & Protein C/S	Concentration factor X, IX, VII, II, Protein C/S
	Fibrinogen	No Fibrinogen
Administration	Requires ~30 min thaw time	Within ~10 min (formulated as a powder)
	Large volume (15-30ml/kg, ~1.5-2L/patient)	**Small volume**
Adverse Events	Transfusion reactions/thrombotic events*	Risk of thrombotic events* Risk of HIT (small amounts of Heparin)
Cost	$1,500-2,000	$2,000

*The 3-4% risk of thrombosis within 14 days must be interpreted with the understanding that most of these patients are critically ill and will require prolonged ICU/hospital stay, surgical procedures and prolonged immobilization and so a subset will have thrombotic complications even without reversal. Overall, the risk of thrombosis is low compared to the benefit of achieving early hemostasis.

The cost of Kcentra per patient typically ranges from approximately $4,000 to over $11,000 for the medication alone, depending on the specific hospital's pricing, the patient's weight, dosing strategy and the patient's insurance coverage.
The price per unit of Kcentra is approximately $7.33, but a patient requires many units per dose.

Disadvantages of PCC:

Thromboembolic events:

- (studies show no significant increase when dosed appropriately)
- Stroke
- Heart attack
- Deep vein thrombosis
- Pulmonary embolus

Anaphylaxis (rare)

HIT- some concentrates contain Heparin

Conclusions:

- While PCC offers rapid, concentrated and standardized coagulation factor replacement with reduced fluid load and faster INR normalization, FFP remains in use when a broad spectrum of clotting factors is needed (liver disease) or PCC is unavailable.
- Clinicians weigh bleeding severity, underlying pathology, patient volume status and product availability in choosing one over the other

Typical Clinical Scenarios:

Use FFP:

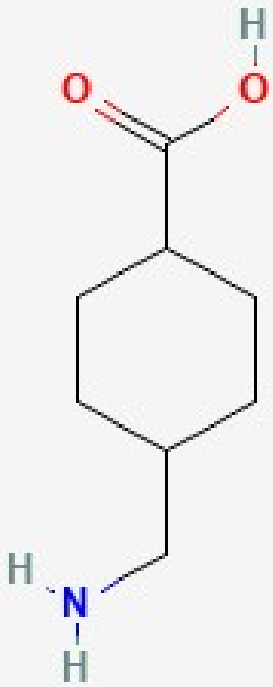
- Massive transfusion
- Liver disease patients with broad coagulopathy
- Disseminated intravascular coagulation
- Conditions requiring factors beyond II, VII, IX, X

Use PCC:

- Urgent reversal of warfarin anticoagulation
- Cardiac surgery with isolated deficit of vitamin K–dependent factors
- Patients at risk of volume overload

Traneximic Acid


NDC 0013-1114-20
10 mL Vial
Cyklokapron®
(tranexamic acid injection)
1,000 mg/10 mL
(100 mg/mL)
Intravenous Use Only
Single-Dose Vial
Discard Unused Portion

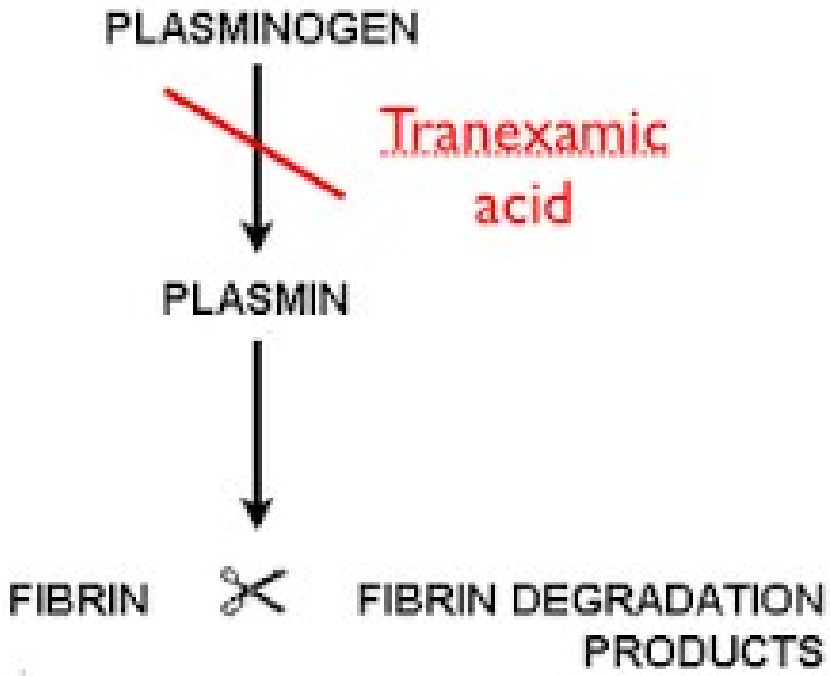

H
O
O
H
N
H

Overview:

- AKA clotting acid→ anti-fibrinolytic action
- Derived from the amino acid lysine
- Stable at room temperature and does not require cold chain storage
- Stored for up to 12 weeks at temperatures ranging from –20°C to 50°C
- Administration is usually IV injection, over 10 minutes (no faster than 1 mL/minute, if undiluted, to avoid hypotension); It's diluted in a solution with normal saline
- Approved by FDA Nov 2009

Uses:

- Short periods of bleeding in hemophiliacs after tooth extraction; other types of oral surgery
- Severe nose bleeds
- Severe menstrual hemorrhaging
- Postpartum hemorrhage
- Ulcerative colitis
- Bleeding associated with prostate, bladder, cardiac, orthopedic surgery
- Excessive bleeding in trauma patients


PLASMINOGEN
Tranexamic acid
PLASMIN
FIBRIN
FIBRIN DEGRADATION PRODUCTS

Tranexamic Acid Cont:

Effectiveness: Studies consistently show that TXA significantly reduces surgical bleeding and the need for blood transfusions across various surgeries, including cardiac and orthopedic

Trauma: In trauma patients, early administration of TXA (within 3 hours of injury) has been shown to reduce all-cause mortality and death due to bleeding, with studies suggesting it improves survival even in resource-limited settings

Safety: TXA does not appear to increase the risk of thrombotic events (blood clots) when used appropriately; some evidence suggests it may even reduce the risk by mitigating the need for pro-thrombotic blood transfusion

Crash-2 Trial (Published 2010):

CRASH-2 Trial:

- Randomized, placebo-controlled trial
- Tranexamic acid administered: 1 g loading dose/10 min followed additionally by 1 g infusion/8h)
- Used in adult trauma patients with or at risk of significant bleeding, who were within 8h of trauma
- Total of 20,211 adult trauma patients with or at risk of significant bleeding, who were within 8 h of their injury; 274 hospitals in 40 countries; enrollment began 5/2005
- Recruited patients from high, middle and low-income settings; Beneficial effect of TXA on mortality did not vary by geographic region
- Patients were administered either TXA or a matching placebo
- The primary outcome was death within 4 weeks
- Findings:
  - **TXA significantly reduced death due to bleeding with no increase in vascular occlusive events**

Summary:

TXA demonstrates the ability to curtail blood loss and reduce transfusion requirements by controlling bleeding

Used in conjunction with blood component-based resuscitation, shows improved measures of coagulopathy and survival within patients requiring massive transfusion

Disadvantages of TXA:

- Rare risk of **thromboembolic events**
- **Vision/Eye Problems:** changes in vision, including impaired color vision or retinal issues, requiring regular eye exams
- **Allergic Reactions:** Rare: Severe allergic reactions (anaphylaxis)
- **Seizures:** There is an increased risk of seizures, particularly with high doses or improper administration (e.g., intrathecal injection)
- **Kidney Impairment:** primarily excreted by the kidneys; individuals with kidney impairment may require dose adjustments or be unable to use it.
- **Tranexamic acid is generally contraindicated for people with a history of a previous clot (HRT)**

Common Side Effects:

Rare side effects can occur; usually mild:

- **Headache**
- **Nausea, vomiting, and diarrhea**
- **Abdominal or stomach pain/discomfort**
- **Back, muscle, or joint pain**
- **Nasal and sinus symptoms** (e.g. stuffy or runny nose)
- **Fatigue or weakness**

Conclusions:

- Tranexamic acid (TXA) and fresh frozen plasma (FFP) are **complementary treatments** in trauma, not alternatives
- They address different aspects of traumatic coagulopathy:

  •**Tranexamic acid (TXA)** is an **antifibrinolytic drug** that prevents the breakdown of blood clots, helping the body preserve the clots it forms naturally

  •**Fresh frozen plasma (FFP)** is a **blood product** that replaces lost coagulation factors and other proteins in the blood, helping to improve clotting function

Conclusion continue:

- In essence, TXA acts as a preventative measure against clot degradation, while FFP acts as a replacement therapy for the components needed to form a clot in the first place.
- The best treatment approach involves **using both** appropriately within a structured major hemorrhage protocol

Summary:

Co-administration of FFP with TXA is superior in improving acidosis, coagulopathy and clotting time than using either agent alone

Early administration of TXA can reduce the overall requirement for FFP and other blood products during a massive transfusion

TXA helps the body make the most of the clotting factors (whether naturally present or supplied via FFP/cryoprecipitate) by preventing their premature breakdown

Robust evidence suggests that TXA can diminish blood loss, lower transfusion rates, reduce complications and improve hemoglobin and hematocrit levels in surgical patients

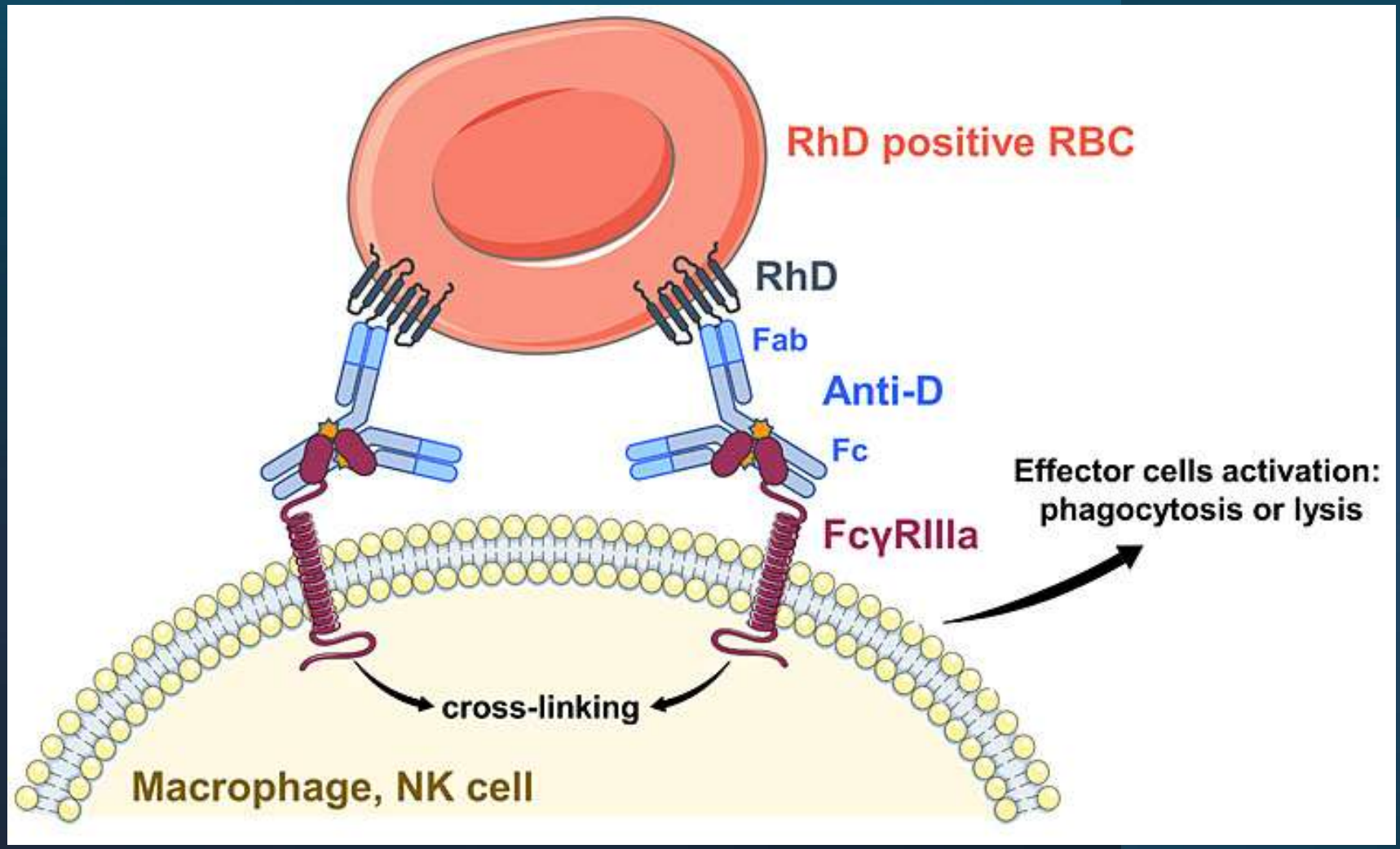
RhoGam

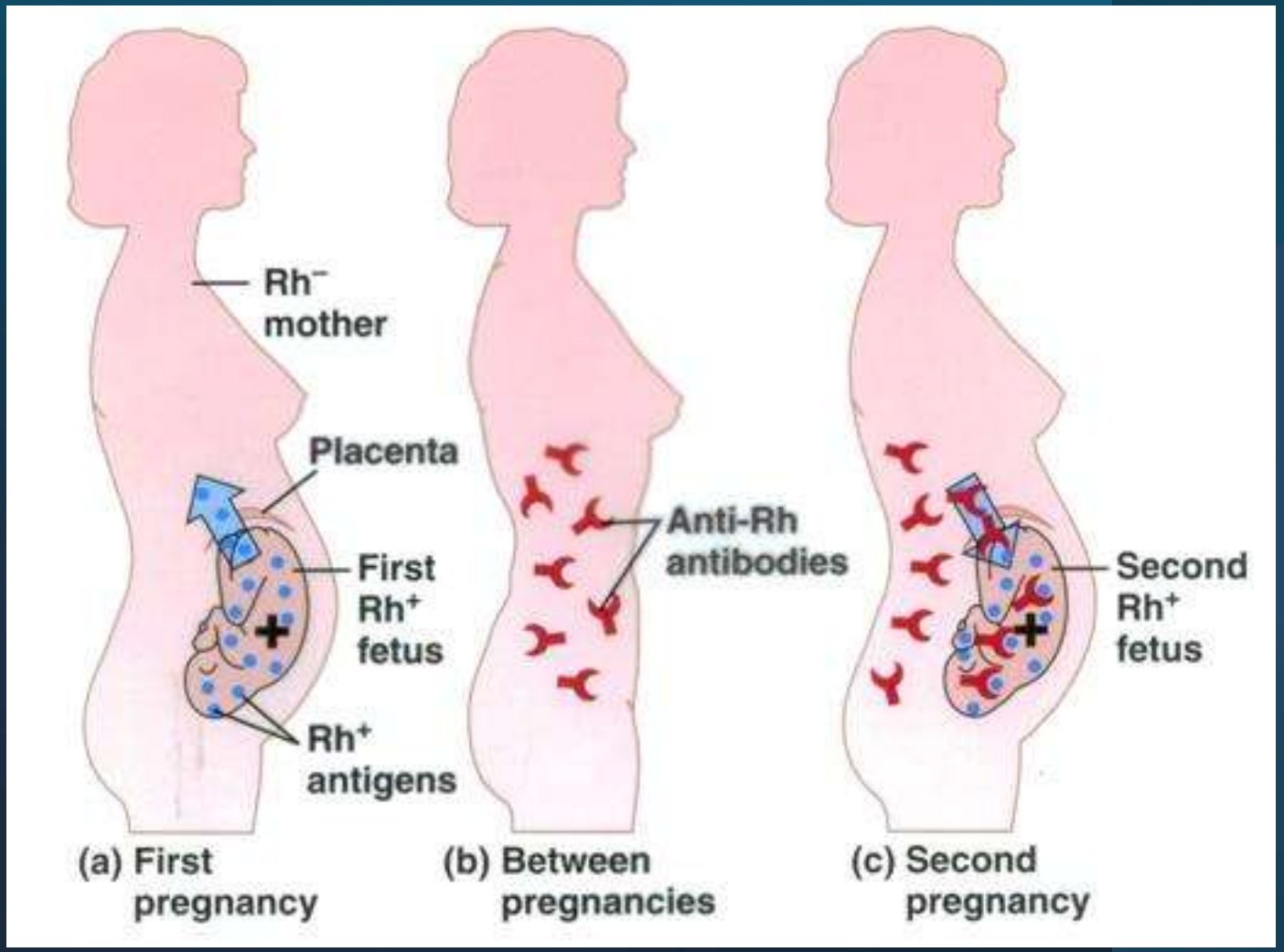

Rh(D) Immune Globulin (Human)
NDC 0662-7805-25
RhoGAM®


PRESCRIPTION ONLY MEDICINE
KEEP OUT OF REACH OF CHILDREN
Rh(D) Immunoglobulin-VF
Solution for Intramuscular Injection
625 IU in 1.3 mL
Lifeblood
CSL Behring

Mechanism of Action:

- Poorly understood mechanism....
- Purpose is to reduce the risk of RhD alloimmunization
- Pre-made Rh(D) antibodies in the RhoGAM injection quickly target and coat any Rh-positive (D+) fetal RBC that has entered the mother's bloodstream:
  - The anti-D antibodies bind to macrophages via Fc receptors, leading to destruction
  - or through splenic sequestration and circulatory elimination
- All should occur before the mother's B-cells can mount an immune response and form long-lasting antibodies and memory B-cells
- Avoid **Hemolytic Disease of the Newborn (HDN)**


RhD positive RBC
RhD
Fab
Anti-D
Fc
FcγRIIIa
Effector cells activation:
phagocytosis or lysis
cross-linking
Macrophage, NK cell


Rh⁻ mother
Placenta
First Rh⁺ fetus
Rh⁺ antigens
(a) First pregnancy
Anti-Rh antibodies
(b) Between pregnancies
Second Rh⁺ fetus
(c) Second pregnancy

Dosage:

- RhoGam is given to at-risk Rh-neg mothers carrying an Rh-pos fetus
- Rh-neg mothers who have been transfused in emergent situations with an Rh-pos RBC unit
- Dosage: 300 ug injection at 28 weeks gestation and at delivery
- Given with each future pregnancy
- Prevent Anti-D formation in >95% of cases

Non-childbearing Males?

- For D-neg individuals who will not bear children and transfused only once in their lives with an incompatible unit, formation of an anti-D IgG antibody will have negligible clinical impact; The risk of a hemolytic transfusion reaction is <1%
- Only when the alloimmunized patient is **RE-EXPOSED** to D-pos RBC's through a **second transfusion**, consequences of hemolysis and a delayed transfusion reaction can occur but are manageable through supportive care
- D-neg units should always be requested if available
- If RhoGam is necessary, it is then given at a higher dose (6000ug)

Risks of high dose RhoGam (6000 ug):

- Vomiting
- Hematuria
- Neutropenia
- DIC

Medical protocols in emergent situations generally involve:

- Prioritizing survival for immediate hemorrhage
- Monitoring the patient closely for a transfusion reaction (post –transfusion labs)
- Switching to type specific, fully cross-matched blood when it becomes available

Conclusion:

- If massive hemorrhage occurs and D-neg units are **NOT** available, then RhIG should not be administered without careful consideration of the risks associated with high dose RhIG and the impact on the overall RhIG supply

Questions?

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Outreach

- Physician available 24/7
  - Practitioners with transfusion-related questions/issues
  - Blood bank-related questions/issues
  - (515) 309-4840
- Educate the medical community to keep them up to date on transfusion-related topics
  - Presentations to medical personnel
  - Contact: *alex.smith@lifeservebloodcenter.org*
- Quarterly webinars
  - *https://www.lifeservebloodcenter.org/for-hospitals/resource-guide/education*

Thank you!

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