Pediatric transfusion practice

Focus on product modification +MTP

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Transfusion Medicine and hematology

Objectives

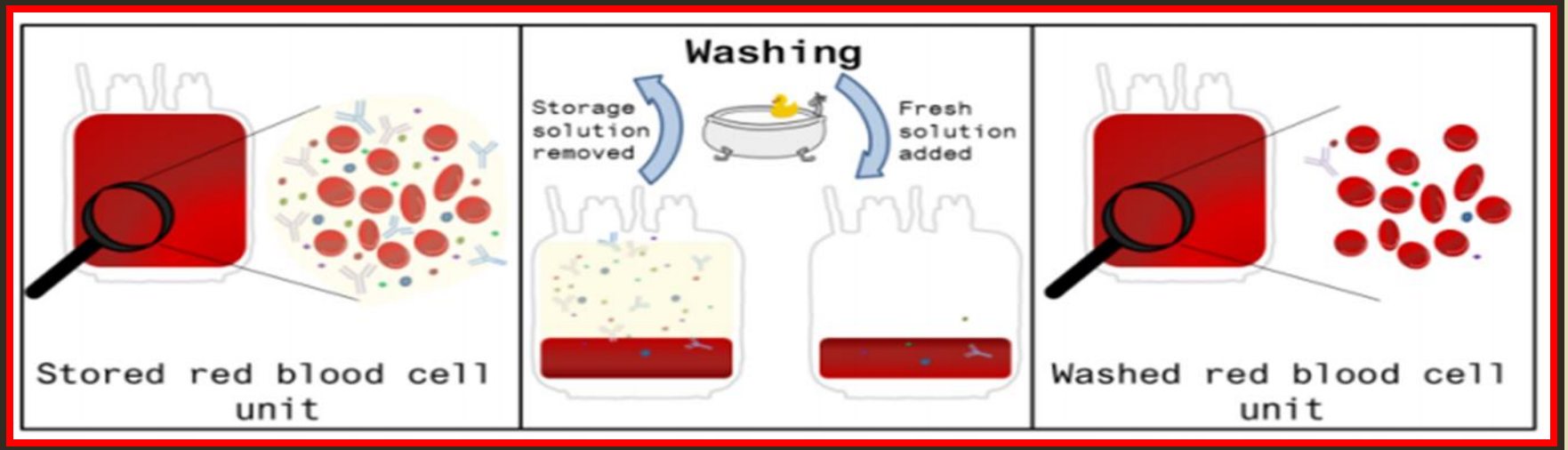
- Review indications for blood product modification (neonates and pediatrics)
  - Washing
  - Irradiation
  - CMV negative
  - Others (Hpa matched platelets)
- Transfusion in special populations
  - Sickle cell
  - Thalassemia
- Pediatric MTP update

Blood product modification for neonates

Case 1

- You receive a call from NICU for PRBC transfusion for a 650 gm. Ex-24 weeks, 2 day old neonate for hemoglobin of 70. He also has anuria with hyperkalemia. What product will you select
  1. 14 days old PRBCs'. Irradiated
  2. 10 days old PRBCs' washed and irradiated
  3. 25 days old PRBCs washed
  4. He does not need a transfusion

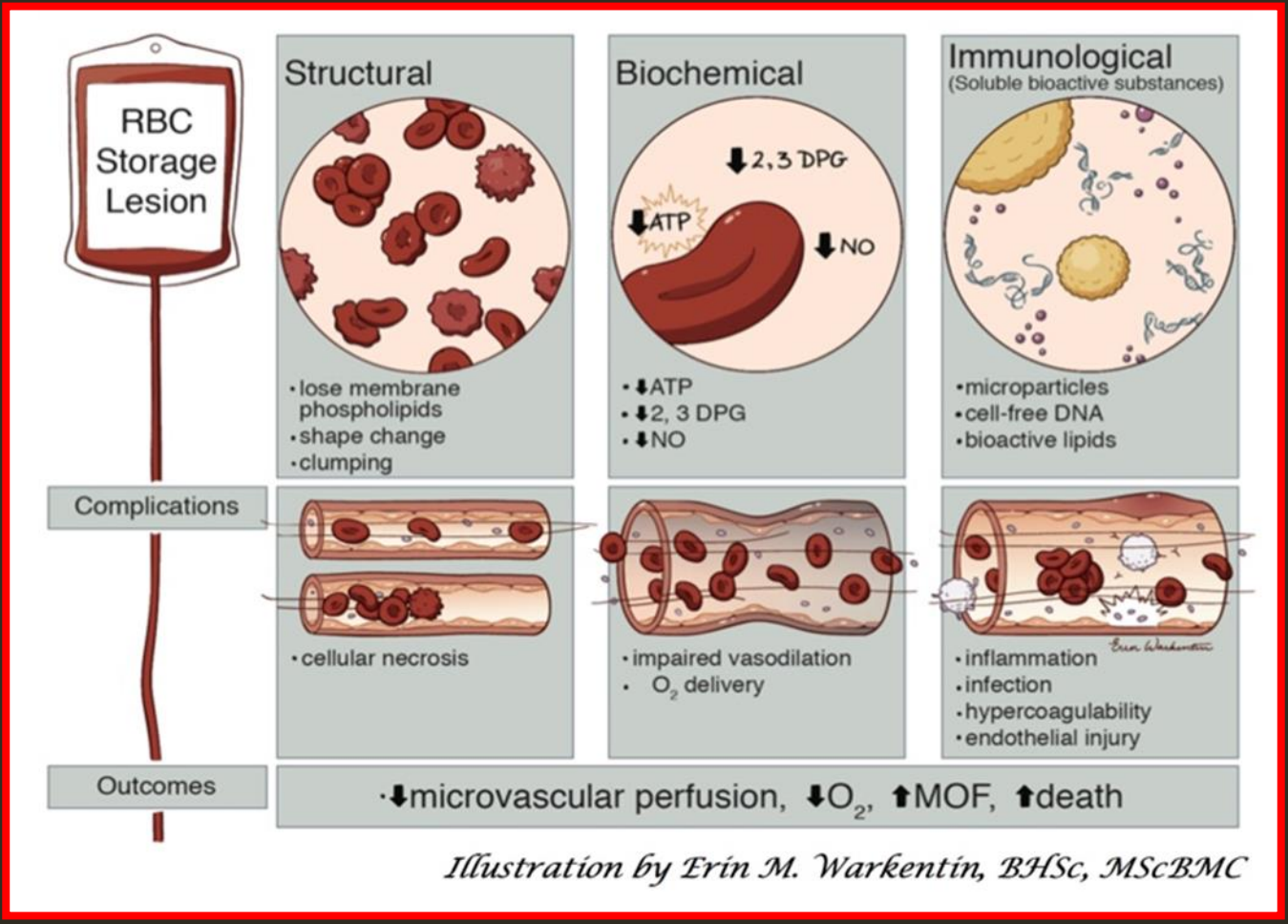
Explanation



- Neonates
  - Exchange transfusion
  - High potassium (renal failure etc)
- Not indicated for neonates
  - As a routine for small volume transfusions

Clinical guide to transfusion; Chapter 15

Red cell storage lesion



Age of red cells for neonatal/infant transfusions

TOTAL trial

N= 260 (age 6-60 months)

New (age 1-10 D) vs. old (25-35 D) red cell units

No difference in lactate levels, adverse events and 30 day survival

ARIPI trial

N=377 (ELBW premature infants)

New (0-7 D) vs. old (7-14D) RBC units

No difference in rates of infection and organ dysfunction

Fergusson DA, Hébert P, Hogan DL, et al.: Effect of fresh red blood cell transfusions on clinical outcomes in premature, very low-birth-weight infants: the ARIPI randomized trial. JAMA. 2012; 308(14): 1443–51.

Dhabangi A, Ainomugisha B, Cserti-Gazdewich C, et al.: Effect of Transfusion of Red Blood Cells With Longer vs Shorter Storage Duration on Elevated Blood Lactate Levels in Children With Severe Anemia: The TOTAL RandomizedClinical Trial. JAMA. 2015; 314(23): 2514–23.

Conclusion

- No indication for washing OR selecting a <5 day old RBC unit in neonates UNLESS
  - Massive/exchange transfusion
  - Concern for renal dysfunction and high potassium levels

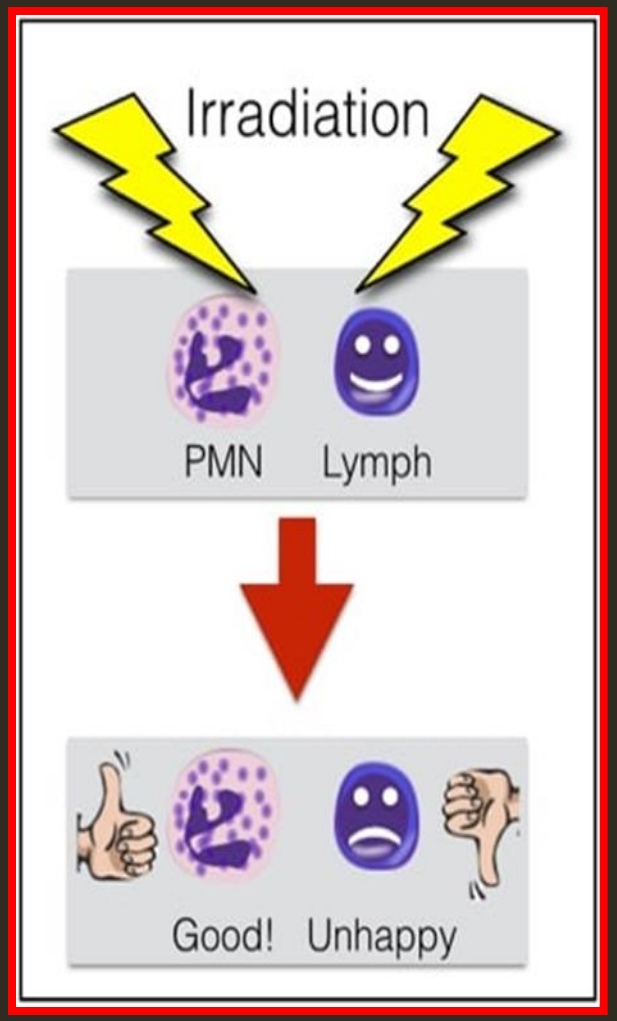
Clinical guide to transfusion; Chapter 13

Case 2

- You receive a call from bedside NICU nurse asking for irradiated platelet product for a full term neonate. Patient is admitted with a ‘syndrome’ and complex heart defect. What is your next step?
  1. Deny irradiated PRBCs
  2. Talk to your on call transfusion medicine physician
  3. Issue irradiated Platelets for concern of immunodeficiency
  4. Issue irradiated PRBCs for concern for CMV transmission

Irradiation of cellular blood products

- Damage to viable T-lymphocytes in blood product by Irradiation
  - Prevention of TA-GVHD in individuals at risk
- Effects on PRBC unit
  - Hemolysis and Hyperkalemia
  - Shelf life reduced (28D)
  - Additional wash
    - if irradiated >24 hours before transfusion
    - Large volume or IUT



Clinical guide to transfusion. Chapter 15

Indications for irradiation in neonates

- Dysfunctional or absent immune system
  - Severe Combined immunodeficiency
  - Di George syndrome (heart defects with T-cell defects)
  - Very premature infants (weight <1200gm) till 4 months of age
  - Neonate who received Intra uterine transfusions till 6 months post delivery

NAC: recommendations for use of irradiated blood components in Canada

Special neonatal/fetal populations

Intrauterine transfusion and Neonatal alloimmune thrombocytopenia

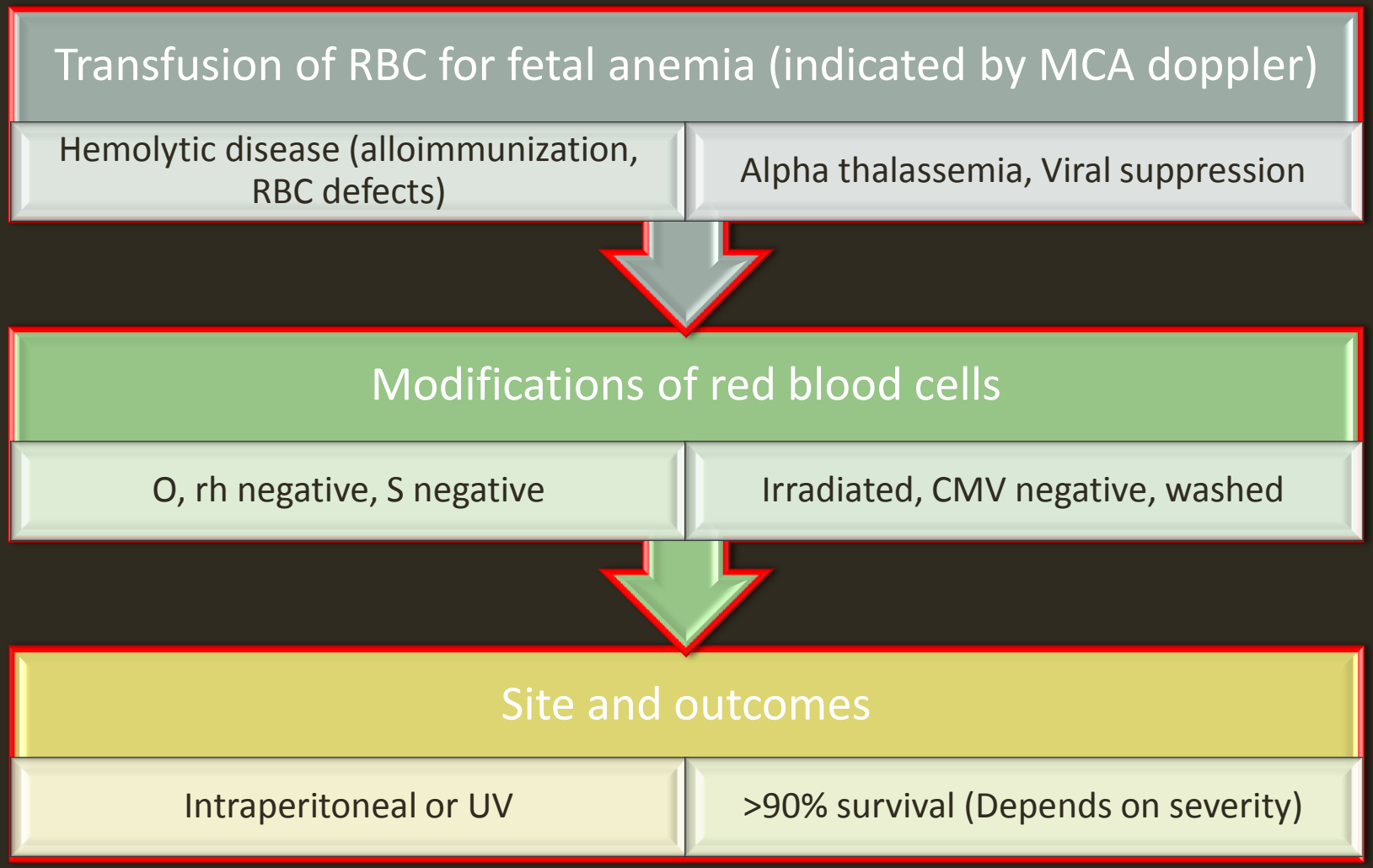
Case 3

- You are a technologist in Winnipeg who just received a call from OB about an intrauterine red cell transfusion happening today for a mother coming from Saskatoon SK (anti Kell). What are the indications for IUT
  1. Severe fetal anemia
  2. Mother has history of IUT in the past
  3. Mother has anti D alloimmunization with rising titers
  4. Mother has anti Kell

Case 4

- You are asked to get PRBCs' ready for IUT. What product will you select
  1. O negative, rh negative, kell negative CMV safe unit
  2. O negative, rh positive, Kell positive, CMV negative unit
  3. O negative, rh negative, Kell negative, CMV negative, washed unit, irradiated
  4. O negative, rh negative, Kell negative, CMV negative, irradiated unit

Intra uterine transfusion



Yinon Y, Visser J, Kelly EN, et al. Early intrauterine transfusion in severe red blood cell alloimmunization. Ultrasound Obstet Gynecol 2010; 36:601.

Case 5

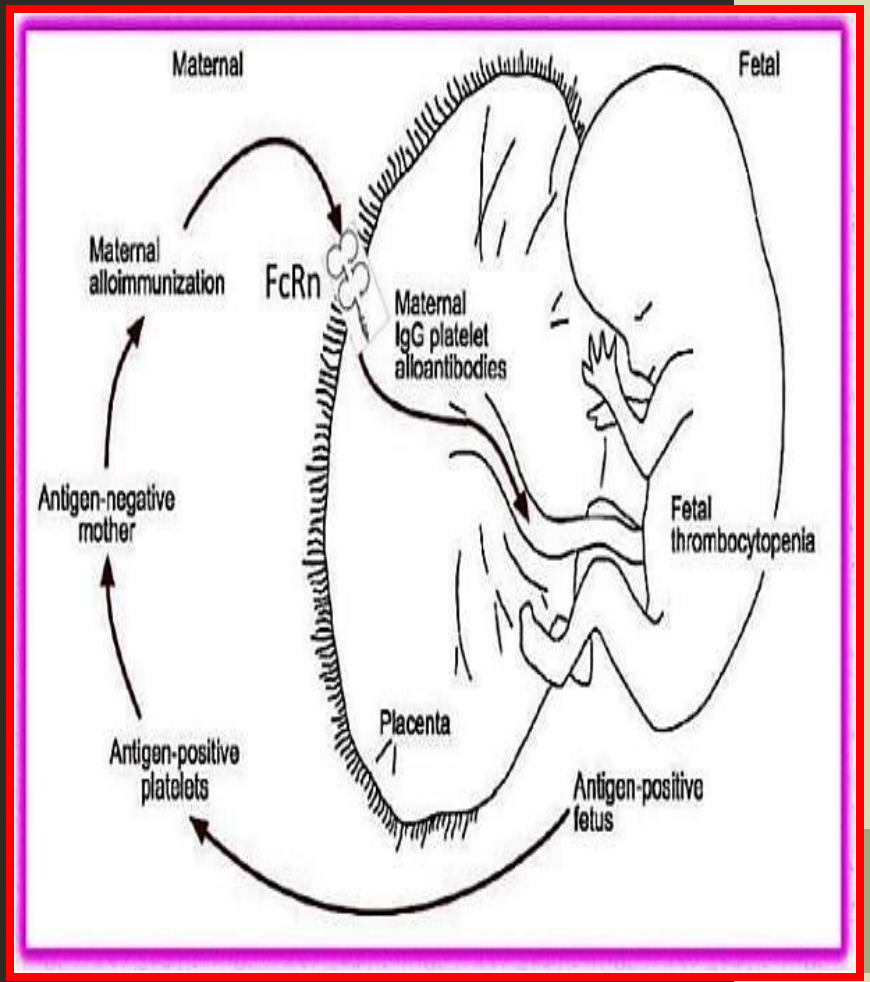
- You receive a request in the blood bank for platelet product for a full term healthy neonate with a platelet count of 20 and neonatal alloimmune thrombocytopenia. Which of the following platelet products is optimal for the patient?
  1. Random donor platelet
  2. Maternal *unwashed* platelet
  3. Apheresis platelet
  4. Hpa-matched platelet from CBS

Fetal and neonatal alloimmune thrombocytopenia

Maternal fetal platelet incompatibility

Maternal antibodies (anti-Hpa/1a) → destroy fetal platelets

Mild to severe thrombocytopenia (ICH and fetal death)



Case 6

- The neonatal nurse calls you asking for emergent platelets as infant is having a nosebleed and dropped hemoglobin. Mother is in ICU. Which product will you select
  1. Washed maternal platelets
  2. Random donor platelet followed by IVIG
  3. Do not give platelets as they will be destroyed
  4. Call CBS for emergent Hpa matched platelets (haha!)

Letsky, E. A., and M. Greaves. "Guidelines on the investigation and management of thrombocytopenia in pregnancy and neonatal alloimmune thrombocytopenia. Maternal and Neonatal Haemostasis Working Party of the Haemostasis and Thrombosis Task Force of the British Society for Haematology." British journal of haematology 95.1 (1996): 21-26.

Blood product modifications for pediatric transfusions

Case 7

- You receive a call in blood bank about a 15 year old female with leukemia receiving red blood cells. 15 minutes into transfusion, she develops anaphylactic reaction. Previous history of allergic reactions to platelets. What is the modification required for future transfusions
  1. Washed
  2. ABO compatible
  3. Volume reduced
  4. No modification needed. Only pretreat

Indications for washing in children

- Only applicable to cellular products
  - Severe anaphylactic reactions despite pre treatment
  - IgA deficiency (where donations from IgA deficient donors is not available and severe allergic reactions have occurred)
- Effects on shelf life
  - RBC→24 hours
  - Platelets→4 hours

Clinical guide to transfusion: Chapter 15

Case 8

- You get a request for irradiated PRBCs for a patient with aplastic anemia undergoing transfusion. What can be the possible reason for irradiated blood
  1. Low WBC count and immune compromise
  2. Use of T-cell inhibitors (ATG) as treatment for aplastic anemia
  3. Known pediatric marrow failure syndrome
  4. Prior history of HIV infection

Irradiation indications

- Patients with congenital T-cell immunodeficiency, including:
  - Severe combined immunodeficiency disease (SCID)
  - Di George syndrome
  - Wiskott-Aldrich syndrome
  - Cell-mediated immune deficiency of unspecified etiology
- Selected patients with acquired immunodeficiency:
  - Hodgkin lymphoma
  - Receiving or having received treatment with purine antagonists
  - Receiving or having received treatment with potent T-cell inhibitors
- Stem cell transplant recipients

NAC: recommendations for use of irradiated blood components in Canada

Case 9

- You receive a request in blood bank for minor antigen matched red blood cells for an 8 year old patient. Which of the following is NOT an indication for upfront minor antigen matching?
  1. Sickle cell disease/Thalassemia
  2. Aplastic anemia
  3. Chronic transfusion for bone marrow failure
  4. Presence of anti-Kell antibody in an otherwise healthy child

Blood products for special pediatric populations

Sickle cell disease and thalassemia

Case 10

- You receive a request of PRBCs for a 10 year old sickle cell patient admitted with anemia due to viral suppression. His antigen typing showed a U negative (Sneg, sneg) phenotype. How will you approach this patient?
  - Rh and Kell matched units since patient has no antibodies
  - Ask the physician to not transfuse the patient
  - Initiate request for U negative units for CBS AND collaborate with clinical team to determine transfusion needs/urgency

Indications for transfusion in sickle cell

- Exchange transfusion
  - Acute stroke
  - Acute Chest syndrome
  - Multi-Organ Failure
- Simple transfusion
  - Aplastic crisis
  - Splenic sequestration
  - Pre-operative
  - Anesthesia >30minutes
  - Anemia with VOC
  - Acute chest crisis

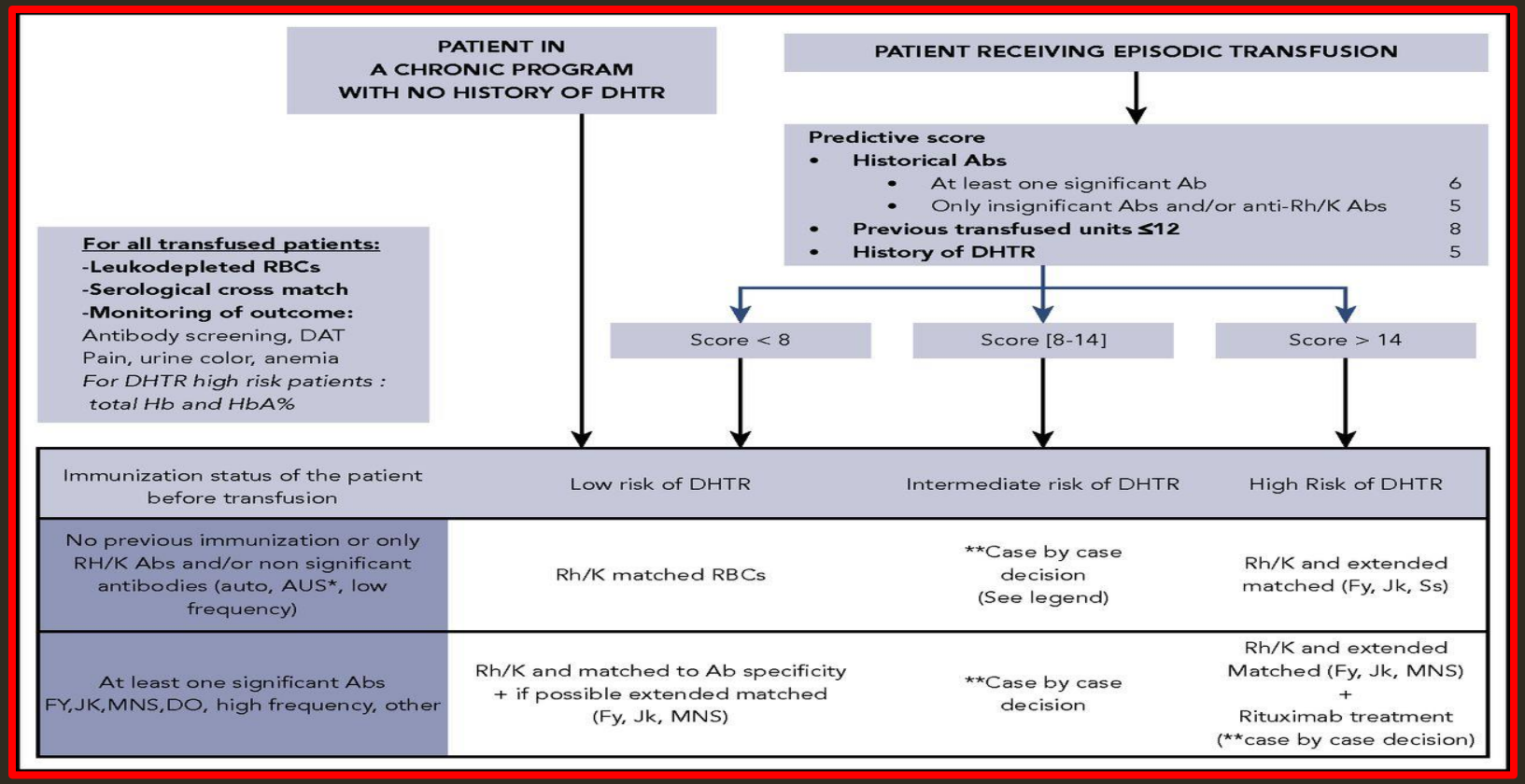
Wun, Ted, and Kathryn Hassell. "Best practices for transfusion for patients with sickle cell disease." *Hematology Reviews* 1.2 (2009).

Why is transfusion of sickle cell patients complicated?

- Donor and recipient pool are genetically different
  - Variants in RHCE genes in African population which are highly immunogenic
- High burden of transfusion
  - Stroke (chronic transfusion)
  - Multiple ACS (chronic transfusion)
- Inflammatory condition
  - Responders vs. non-responders based on genetic makeup

Pirenne, France, and Karina Yazdanbakhsh. "How I safely transfuse patients with sickle-cell disease and manage delayed hemolytic transfusion reactions." *Blood* 131.25 (2018): 2773-2781.

Transfusion in sickle cell disease



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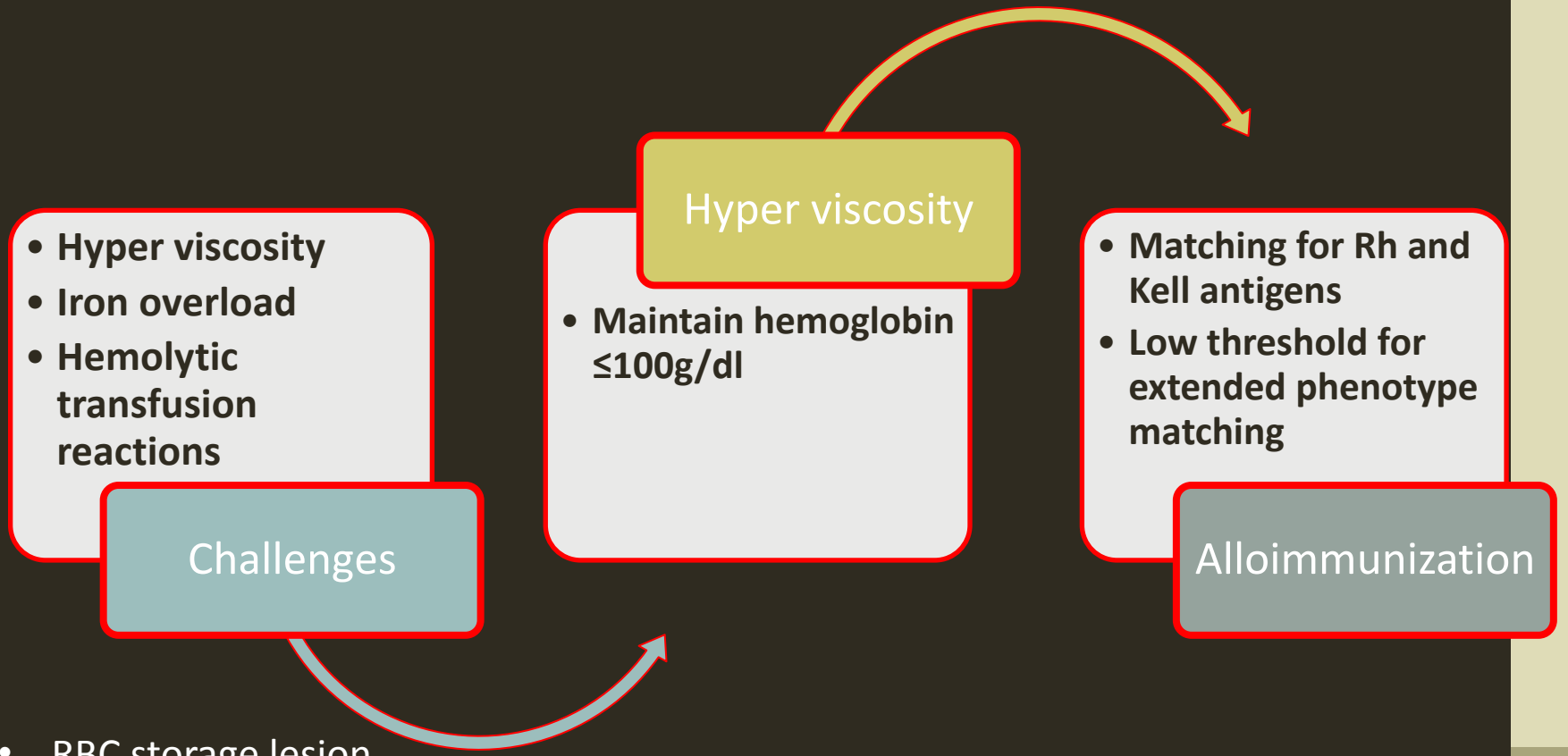
In conclusion



- RBC storage lesion
  - No consensus.
  - Most centers use RBC <15D for exchange

Pirenne, France, and Karina Yazdanbakhsh. "How I safely transfuse patients with sickle-cell disease and manage delayed hemolytic transfusion reactions." *Blood* 131.25 (2018): 2773-2781.

Best practices in sickle cell disease

- Use of HU to prevent transfusions
- Avoid transfusions for simple pain crisis
- Avoid transfusions for simple anemia
- Low threshold for introducing iron chelation

Wun, Ted, and Kathryn Hassell. "Best practices for transfusion for patients with sickle cell disease." *Hematology Reviews* 1.2 (2009).

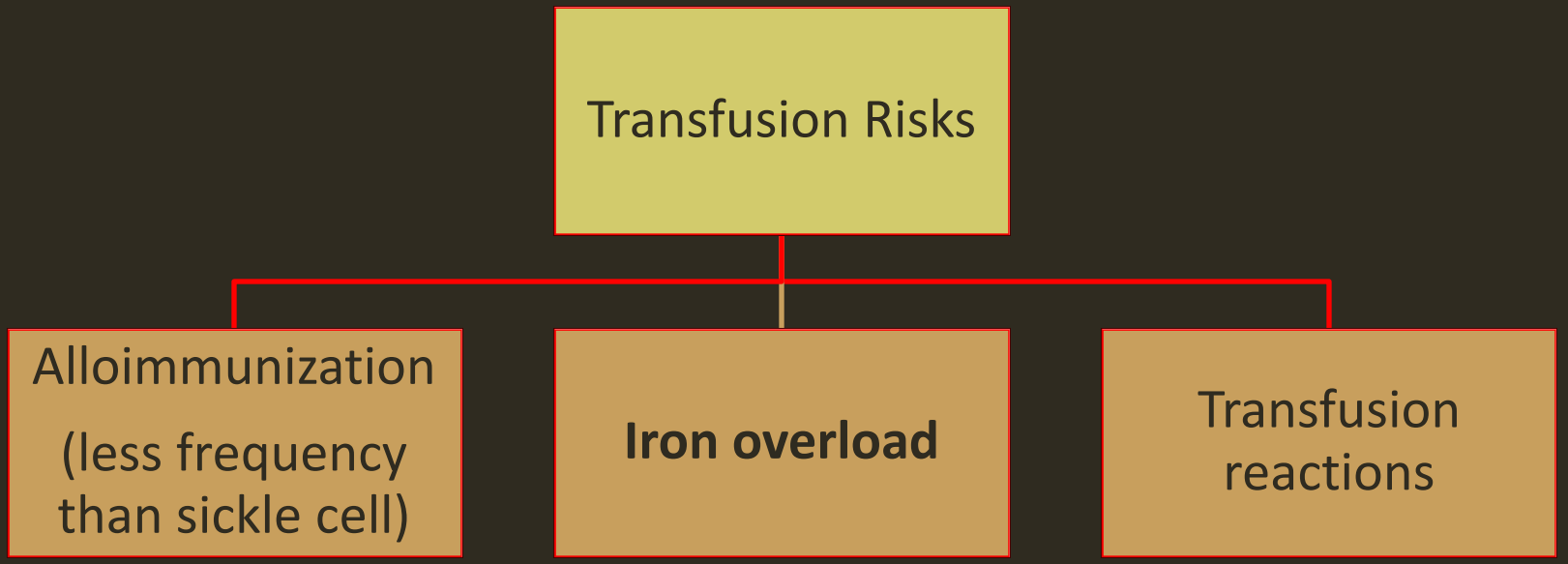
Thalassemia

- Hemoglobinopathy leading to reduced/abnormal B or A globin chains
- Highly variable phenotypes
  - Based on number of genes deleted
  - Type of mutation
- Transfusion Dependent
  - Hgb ≤7, poor growth, large spleen, symptomatic anemia
- Non transfusion dependent
  - Moderate hemolytic anemia but maintaining a hemoglobin (Hb) level that is sufficient for growth and development

Indications of transfusion

- Chronic Red cell transfusion in thalassemia
  - Severe anemia
  - FTT, Growth delay
  - Hypersplenism, EM hematopoiesis
    - Decision usually made in first 3 years of life based on frequency and response of red cell transfusions
    - Maintain hemoglobin ~9-10
      - Suppress abnormal erythropoiesis
      - Improve QOL/growth/maturation

Transfusion risks in thalassemia



Transfusion best practices

- Extended antigen phenotyping of patient
- Upfront matching for Rh and Kell
  - Extended antigen matching once antibodies form
- Record of transfusions
  - Close monitoring for iron overload
  - Low threshold for starting chelation therapy

Massive transfusion in pediatrics

Chicoo!

- 12 year male
- Ulcerative colitis
- Lower GI bleed
- EMS
- eBL ~500ml

ER:

- HR:130, RR:20, BP: 90/50
- Wt: 30kg
- Hematemesis, fills tub with blood

Chicoo: Initial Management

- Trauma room
- Labs (CBC, PT,PTT, Fibrinogen,VBG)
- 60mg/kg NS bolus
- 2 Units O negative uncross matched RBC

Points to ponder

Is Chicoo having a massive hemorrhage?

Should he be managed differently from other bleeding patients and why?

Definitions: Massive Hemorrhage

Adult

- Rapid blood loss
  - 4.5 L / 30 min
  - 150ml / min
  - 3 U of PRBCs over 3 hr

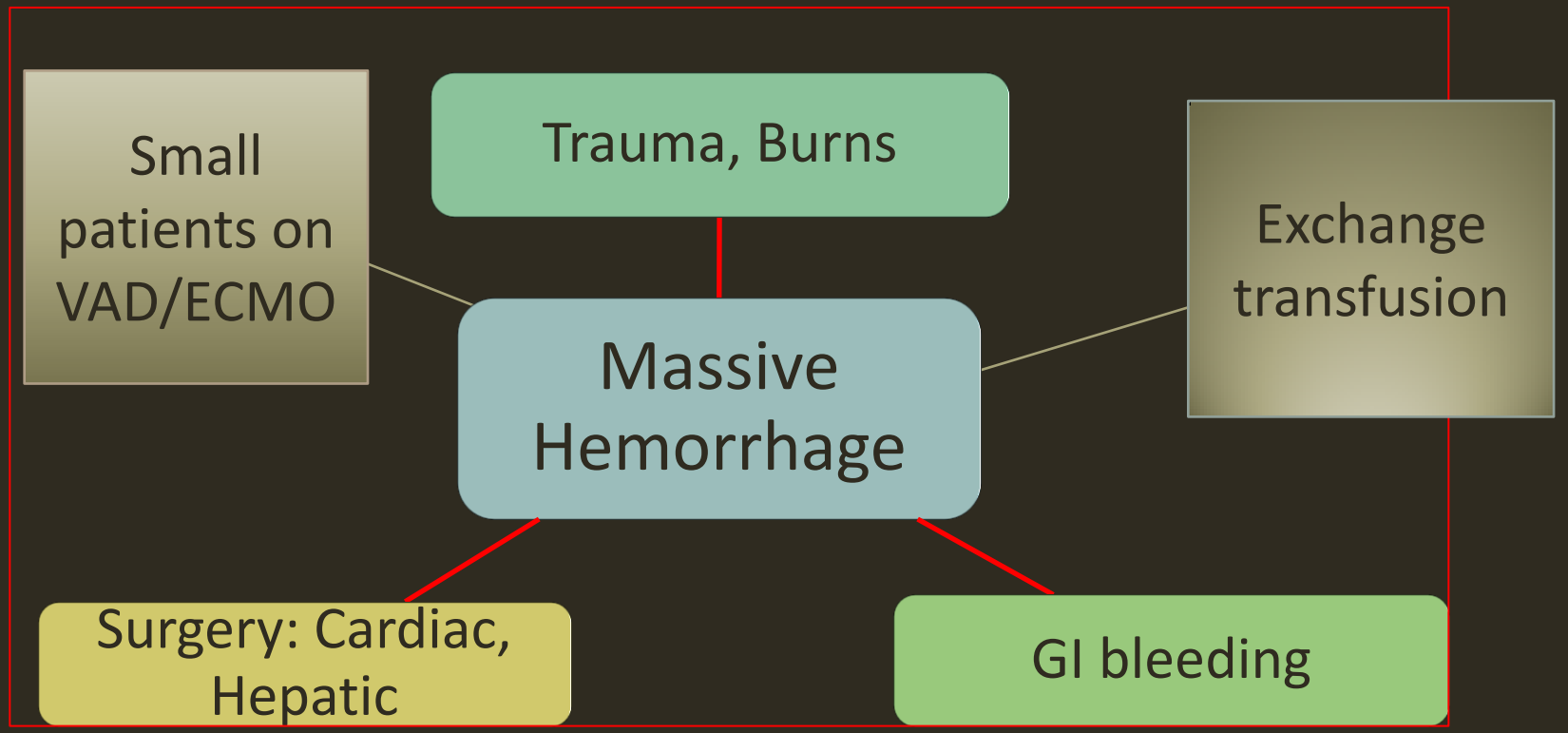
(*greater than)

Pediatric

- Rapid blood loss
  - 50% TBV in 3 hr (40ml/Kg)
  - 10% BV loss / min
- Better ability to withstand hemorrhage

Barcelona, Sandra L., Alexis A. Thompson, and Charles J. CotÉ. "Intraoperative pediatric blood transfusion therapy: a review of common issues. Part II: transfusion therapy, special considerations, and reduction of allogenic blood transfusions." Pediatric Anesthesia 15.10 (2005): 814-830.

Causes of Massive Hemorrhage in Pediatrics

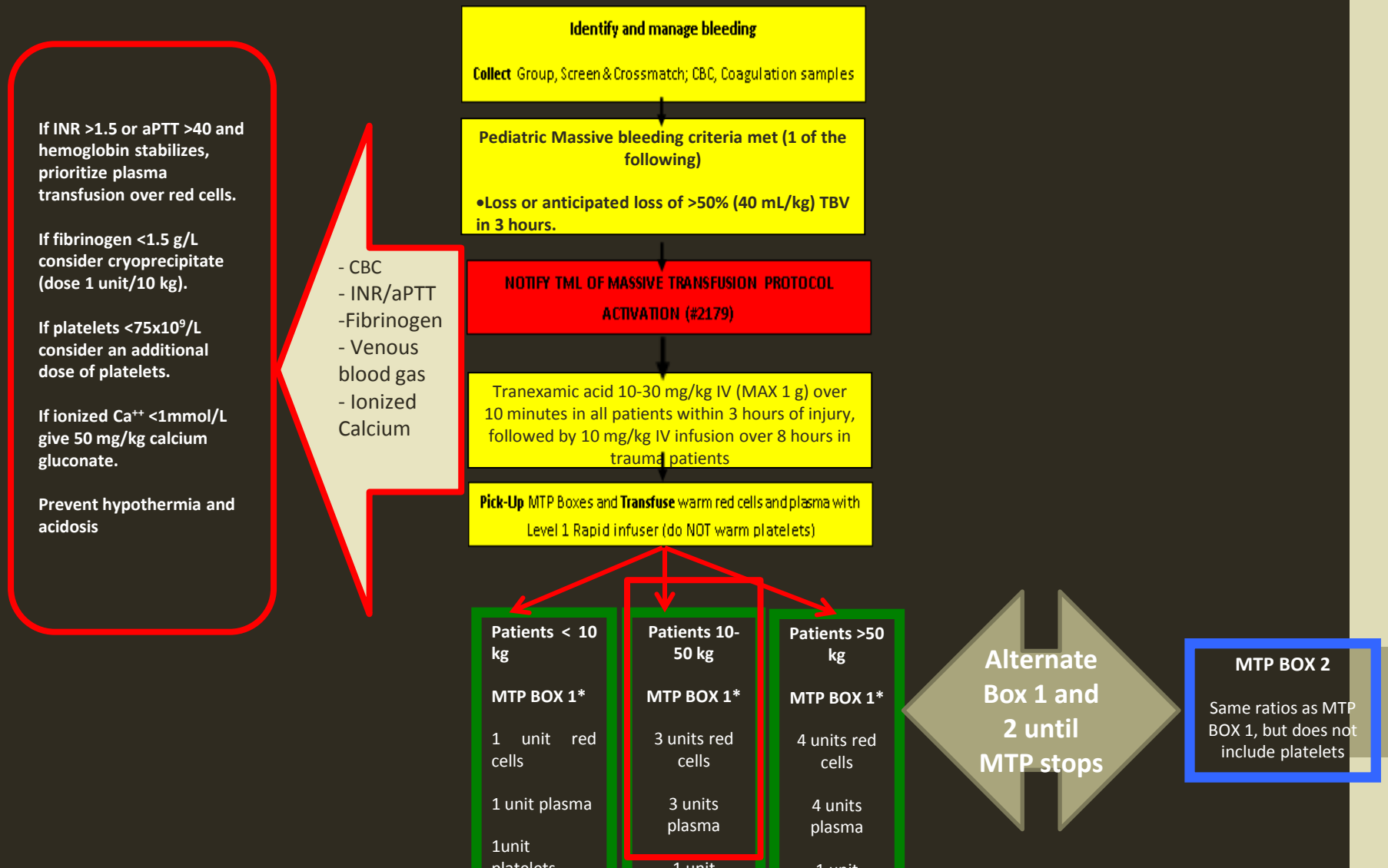


Who needs massive transfusion?

- Discretion of MRP
  - Mechanism of injury/bleeding
  - Abnormal coagulation studies
- Adult trauma patients
  - ABC score to predict who needs MTP
    - 70-86% sensitivity and specificity
    - Penetrating injury, positive US, Low BP, high HR
- No predictive tool in pediatrics

Cotton, Bryan A., et al. "Multicenter validation of a simplified score to predict massive transfusion in trauma." Journal of Trauma and Acute Care Surgery

Pediatric MTP flow sheet is hanging in ER



Update on Chicoo!

- Box 1 of product
- Cryoprecipitate + TXA
- Lower GI bleed markedly slows down
- Moves to PICU for monitoring

Pediatric MTP conclusion

- What is the optimal amount of blood product for each blood volume?
  - Weight based
  - Aliquoting abilities of blood bank
- RBC:FFP:Platelets ratio?
- What is the evidence for improved mortality?
  - No robust evidence
  - Based on adult studies

Pediatric MTP conclusion

- MTP in neonates?
  - Not validated but can be used
  - Whole blood exchange?

- Monitoring technologies
  - Currently lab based
  - Can consider input of perfusion and use of TEG/ROTEM

Thank you

- Recommendations around plasma protein products?

Conclusion