

Massive Hemorrhage Protocol 2.0: Pediatric Considerations

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Faculty Disclosure

- I have no financial interests or conflicts to disclose.
- I do work with the **Ontario Regional Blood Coordinating Network (ORBCoN)**, a Ministry of Health-funded organization, but I receive no financial support.
- I will mention the “off-label use” of **tranexamic acid (TXA)**, **fibrinogen concentrate**, and **prothrombin complex concentrate (PCC)** in pediatric trauma.



Objectives

- Define *massive hemorrhage* (MH) in a child
- Discuss the *implications* of a child's *size, anatomy, and physiology* in relation to MH
- Highlight a few **relevant topics** with the pediatric **MHP 2.0**



MCQ Pre-test

1. Which one of the following statements is false regarding the management of traumatic massive hemorrhage in children?

- A. Validated tools specifically for MHP activation in children are available
- B. 10 ml/kg is a standard dose for RBCs, plasma and platelets
- C. Hypothermia ($\leq 36^{\circ}\text{C}$) is part of the “Lethal Triad”
- D. $\text{INR} \geq 1.8$ & base-deficit $>$ minus 6 are associated with \uparrow mortality in trauma
- E. Administering TXA within 3 hr of MHP activation is evidence-based



Why are we talking about pediatric MHPs?



Massive hemorrhage can be life-threatening...

- Leading cause of **preventable death** in adult/pediatric **trauma**
- **Firearm-related injury** is leading cause of death in children/teenagers (United States)

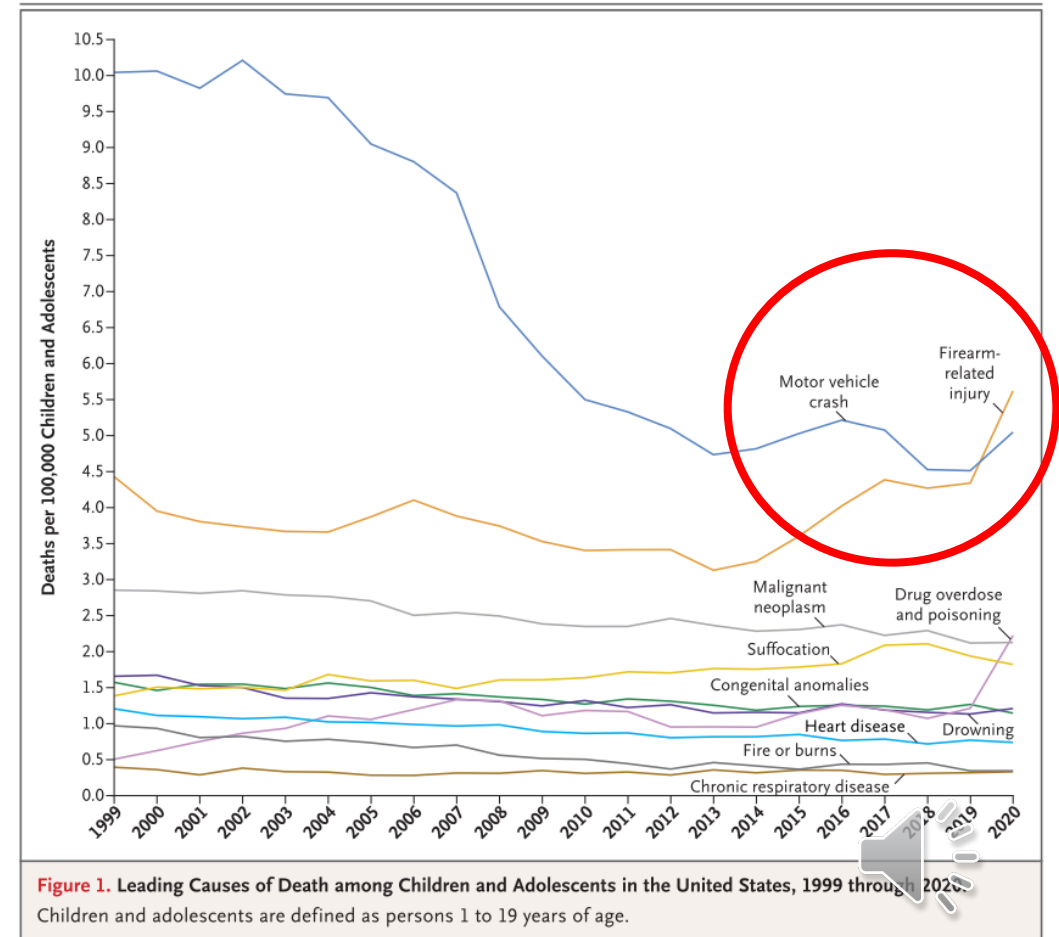
Goldstick J SM, et al. *NEJM*. 2022

- Leading cause of **intraoperative cardiac arrest** (and death) in adults/children

Dhoon TQ *APSF Newsletter* June. 2021; Bhananker SM. *Anesth Analg*. 2007

- **Placental abruption/previa** 6/10,000 live births; mortality rate 35%

Bahr TM, et al. *Transfusion*. 2019



Context of pediatric critical bleeding matters...

Prospective observational multi-center pediatric civilian **MATIC** study (N=449)

Median (IQR) age was 7.3 yr (1.7–14.7 yr)



Leonard JC, et al. *Pediatr Crit Care*. 2021

Critical Bleeding Etiology (N=449)	All-cause Mortality at 24 Hrs. (n=99)	All-cause Mortality at 28 days (n=168)
Combined	99 (22%)	168 (37.8%)
Medical (N=89)	32 (36%)	58 (65%)
Trauma (N=207)	50 (24%)	74 (36%)
Operative (N=153)	17 (11%)	36 (24%)

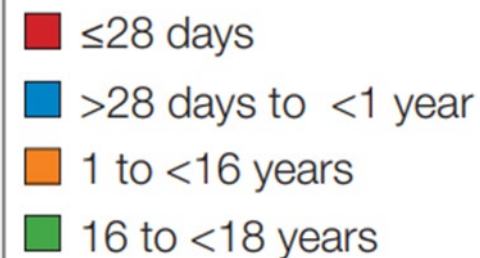
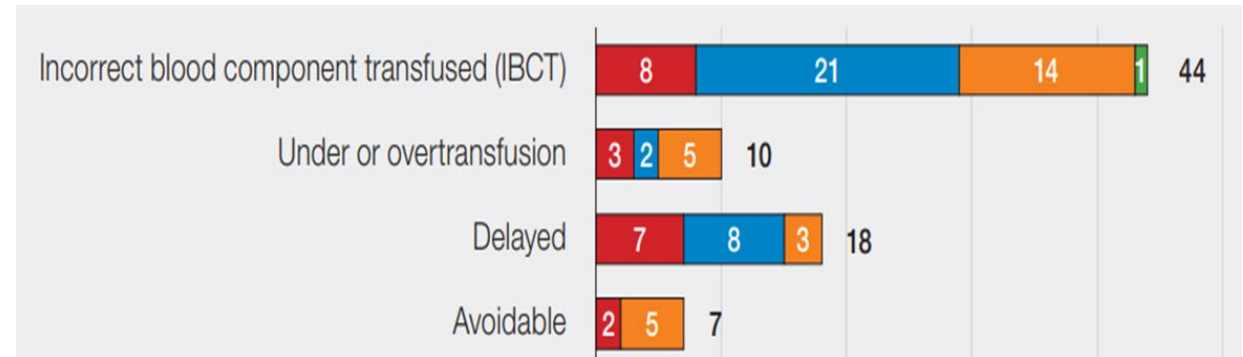


Error trap: Failure to recognize and treat massive hemorrhage in children!



Key Pediatric SHOT Messages:

- **Massive blood loss** in children is **uncommon** and hospitals should have **protocols in place**
- **Communication/Education** regarding blood component dosing and indication is **vital**
- **Education and training resources** should be provided for those administering (neonatal) transfusions **to reduce errors**



Annual UK *Serious Harm of Transfusion* (SHOT) Report 2020: Paediatric Cases



Inequities in pediatric MHP care...

- **MHPs have variable content**, and are either **adult-based** and/or **underutilized in non-trauma settings** in some Canadian pediatric tertiary care hospitals

Arsenault V, Lieberman L, Akbari P, Murto K, COPTN, et al. *Can J Anesth.* 2023

- **↑ risk of MHP overactivation and higher mortality rate in trauma**

Roque DF, Murto K, Grimm D, McVey M, Ly M, Thompson T, Leung E, Pavenski K, Petrosoniak A, Callum J. (*ASA. 2023. Abstract A3098*)

- **MHPs lack pediatric-specific content** in 45% of Ontario hospitals caring for children

Grant C, Hajjaj OI, Murto K, Cope S, Petrosoniak A, Thompson T, Pavenski K, Callum JL. *Can J Emerg Med.* (in press)



“So let me get this straight, in children...”

- Massive hemorrhage (MH) is a leading cause of death and cardiac arrest
- Can be “traumatic” or “non-traumatic”



- Ch
- tra *“It should be mentioned that all studies have to be interpreted with caution because of retrospective and observational study designs, varying definitions of massive transfusion, varying age groups included, relatively small sample sizes, nonrandom treatment allocation, and high potential for confounding.”*

Steinbicker AU, Wittenmeier E, Goobie SM. Curr Opin Anesthesiol. 2020; 22: 259



Kamyszek RW. J Trauma Acute Care Surg. 2019



What specific factors predispose children to errors in diagnosis and treatment of massive hemorrhage?

Tan GM, Murto K, Downey LA, Wilder MS, Goobie SM. *Pediatr Anesth.* 2023



Define pediatric MH: “Lost” vs “Administered”

Traditional:

Blood volume (BV) lost

- > 1BV in 24 hrs
- > 0.5 BV in 3 hrs
- > 10% BV every 10 mins.

Mortality rate?

Hardy JF, et al. *Can J Anesth.* 2004
Barcelona SL, et al. *Pediatr Anesth.* 2005
Diab YA, et al. *Br J Haematol.* 2013

Clearly defining pediatric massive transfusion: Cutting through the fog and friction with combat data

Lucas P. Neff, MD, Jeremy W. Cannon, MD, Jonathan J. Morrison, MRCS, Mary J. Edwards, MD, Philip C. Spinella, MD, and Matthew A. Borgman, MD, *San Antonio, Texas*

**40 ml/kg ANY blood product < 24 hrs
(combat-injured)**

J Trauma Acute Care Surg. 2014

BLOOD MANAGEMENT

Relationship between transfusion volume and outcomes
in children undergoing noncardiac surgery

Susan M. Goobie, James A. DiNardo, and David Faraoni

**40 ml/kg RBCs in-hospital
(civilian non-cardiac surgery)**

Transfusion. 2016



Shorter time-based definitions of adult MH and mortality prediction in trauma...

- **Traditional:**
 - > 10 U RBCs in 24 hrs
- **Critical administration threshold (CAT):**



Recent definition in Pediatrics 38 ml/kg of ALL blood components in 1st 4 hrs

Rosenfeld E, et al. *J Pediatr Surg.* 2019

0.5-2 hrs of injury

Moren A, et al. *J Trauma Acute Care Surg.* 2015; Meyer DE, et al. *J Trauma Acute Care Surg.* 2018; Wong HS, et al. *Transfusion.* 2020



A 20 ml/kg critical administration threshold..?

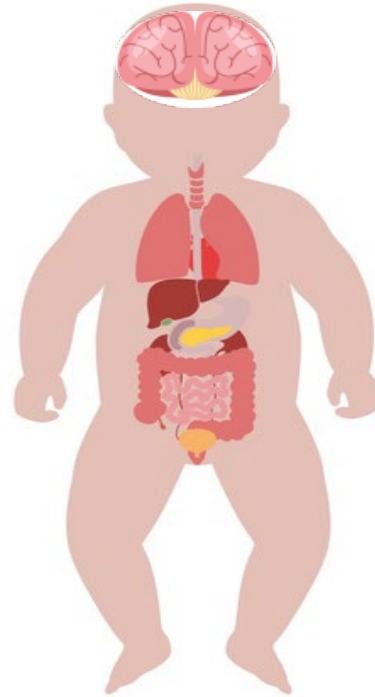
Feature	Hanna K, et al. 2019 <i>J Trauma Acute Care Surg.</i>	Morgan K, et al. 2023 <i>J Trauma Acute Care Surg</i>
Threshold	≥20 mL/kg RBCs in 24 hrs	>20 mL/kg any component in 1 hr (CAT)
<p><i>BUT...is 20-40 ml/kg of blood components in 1-4 hrs applicable as an MHP trigger in non-trauma settings? (e.g., elective surgery or ICU)</i></p>		
Odds of In-hospital Mortality (If threshold met)	OR 3.8 (95% CI, 2.9-4.9)	OR 3.4 (95% CI, 1.67-6.89)
Clinical Implication	Risk stratification	Actionable early trigger for intervention



Errors in diagnosis and treatment of MH...



Size



Anatomy



Physiology



Massive Hemorrhage: Size and Anatomy

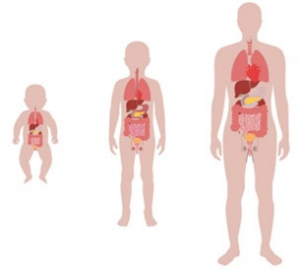
- **Size**

- Blood volume & delayed recognition
- Vascular access
- Ease of rapid blood component or crystalloid administration
- Weight-based dosing

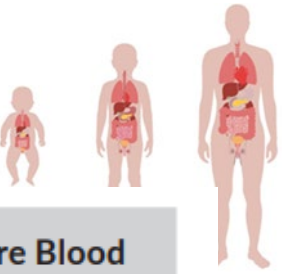


- **Anatomy**

- Disproportionate larger head/reduced control
- Tightly packed internal organs
- Pliable skeleton
- Large body surface area: volume ratio-prone to hypothermia (< 36°C)



Massive Hemorrhage: CV Physiology..



Organ System	Class I. Minimal Blood Volume Loss "Subclinical" (<15% total blood volume)	Class II. Mild Blood Volume Loss "Occult" (15%–30% total blood volume)	Class III. Moderate Blood Volume Loss "Overt" (31%–45% total blood volume)	Class IV. Severe Blood Volume Loss "Very obvious" (>45% total blood volume)
Cardiovascular				
Heart Rate	↔	↔, ↑	↑	↑↑ or ↓
Systolic Blood Pressure	↔, ↑	↔	Low ↔, ↓	↓↓
Pulse Pressure ^a	↔	↔	↓ (<40mmHg)	↓ (<20mmHg)
Presence of Palpable Pulses	Weak peripheral pulse Strong central pulse	Thready peripheral pulse Weak central pulse	Absent peripheral pulse Weak central pulse	Absent peripheral pulse Thready/absent central pulse
Central Nervous System				
Mental Status	Mild anxiety	↑ Anxiety/irritable	Confusion/lethargy	Comatose
Glasgow Coma Scale	↔	↔	↓	↓↓
Temperature	↔	↓	↓	↓↓
Renal				
Urine output (mL/kg/h)	↔	↓	↓↓	–



Tan GM, Murto K, Downey LA, Wilder MS, Goobie SM. *Pediatr Anesth.* 2023



Massive Hemorrhage: “Blood Failure” and ...

Hinojosa-Laborde C, et al. *Physiology (Bethesda)*. 2022

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Blood				
Hemoglobin	↔	↔	↓	↓
Lactate (mmol/L)	≤2.0	≤2.0 or >2.0	>3.0	>4.0
SVO2	↔	↔↓	↓	↓
Base Deficit (mEq/L)	0 to -2	-2 to -6	-6 to -10	> -10
pH	↔	↔, ↓	↓	↓↓
Fibrinogen	↔	↓	↓	↓↓
INR/PT	↔	↔↑	↔, ↑	↑
Platelet Count	↔	↔↓	↔, ↓	↔, ↓



Tan GM, Murto K, Downey LA, Wilder MS, Goobie SM. *Pediatr Anesth*. 2023



Approaching the problem: Strategies to improve MHP transfusion practice in children



Key elements of a pediatric MHP (“7 Ts”):

1. **TRIGGER** and **Treat** bleeding (apply **damage control resuscitation** [DCR] principles & **STOP** bleeding)
2. **Team** (including telecommunication)
3. **Tranexamic acid** & Cell salvage
4. **Temperature** ($\geq 36^{\circ}\text{C}$) & **Traumatic brain injury**
5. **TESTING**
6. **TRANSFUSION (MTP)** & **Trouble**
7. **Termination** & **Tracking** performance

Tan GM, Murto K, Downey LA, Wilder MS, Goobie SM. *Pediatr Anesth.* 2023




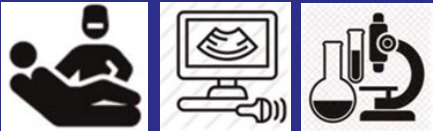

Two-Step Approach to MHP Activation...

- **Step 1:** Administer **4 U uncross-matched RBCs** (or **20–40 mL/kg** in pediatrics).
- **Step 2:** If bleeding persists, activate MHP.
- Balance urgency with resource management to minimize wastage.
- Use validated tools for early MHP activation



Validated tools predict transfusion in peds trauma

Gianola S, et al. *J Trauma Acute Care Surg.* 2022

Tool and Approach	Components	Threshold Score (Range)	Sensitivity (%)	Specificity (%)
ABC 	1. HR \geq 120 2. sBP < 90 mmHg 3. Penetrating trauma 4. FAST +	\geq 1.0 \geq 2.0 \geq 3.0	0.71-0.85 0.29-0.77 0.06-0.70	0.38-0.80 0.55-1.00 0.54-1.00
ABC-D 	1. SIPA 2. Penetrating trauma 3. FAST + 4. BD > -8.8 & Lactate > 3.5 mmol/L	Score \geq 1 Score \geq 2 Score \geq 3	97.9 87.4 77.4	40.4 52.5 78.8
SIPA 	1. HR/sBP	0-3 yr; 4-6 yr: >1.2 7-12 yr: >1.0 13-17 yr: >0.9	0.46-0.95	0.35-0.85

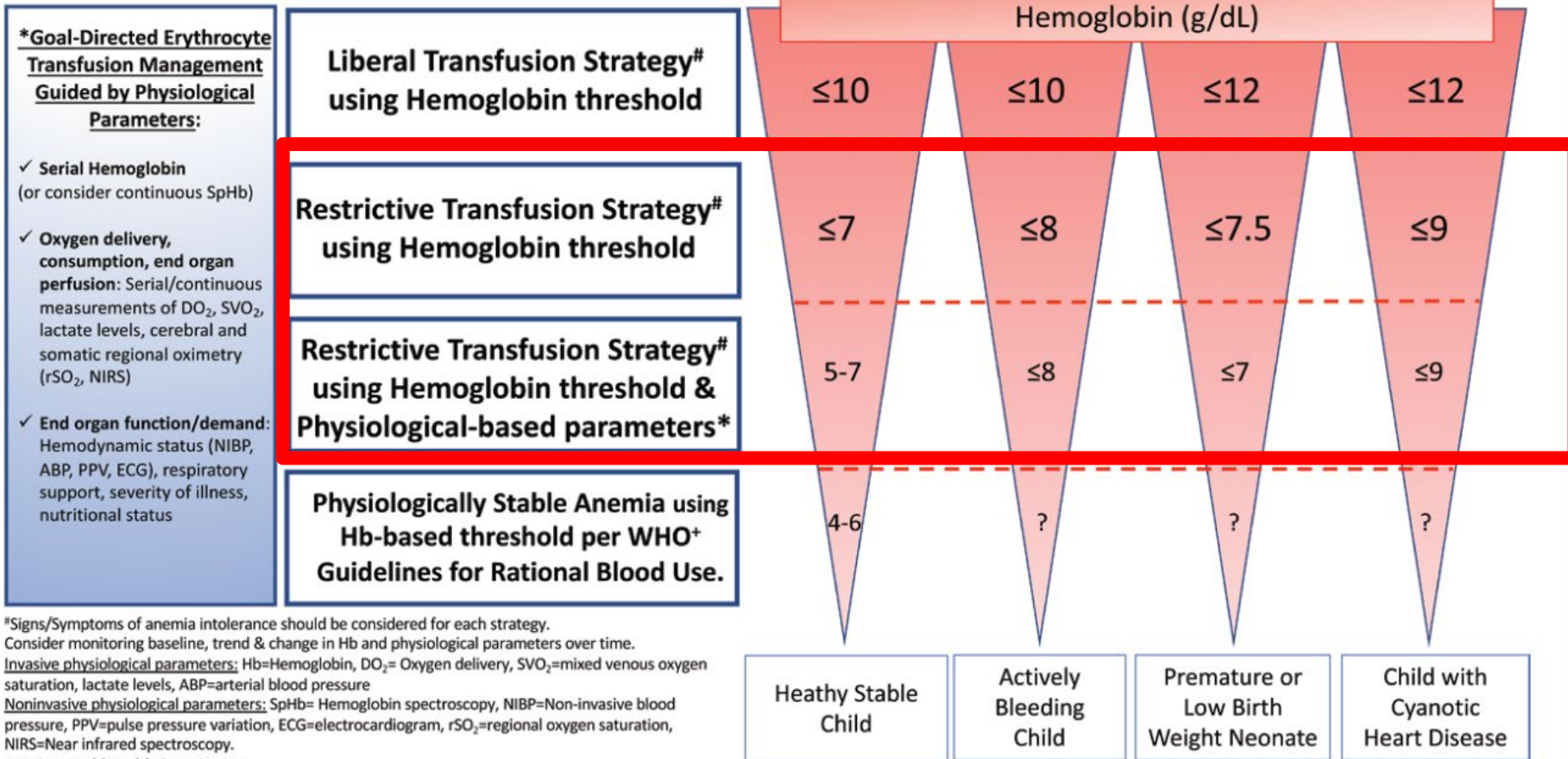
Phillips R, et al. *J Pediatr Surg.* 2020.

SIPA=shock index pediatric adjusted; ABC=Assessment of blood consumption



Goal directed therapy: RBCs

Hypothetical Strategies to Guide Perioperative Erythrocyte Transfusions in Pediatric Patients



Adopted from: Tomic Mahecic, Dunser, Meier. RCB transfusion triggers is there anything new? Transfus Med Hemother 2020 ;47:361-368



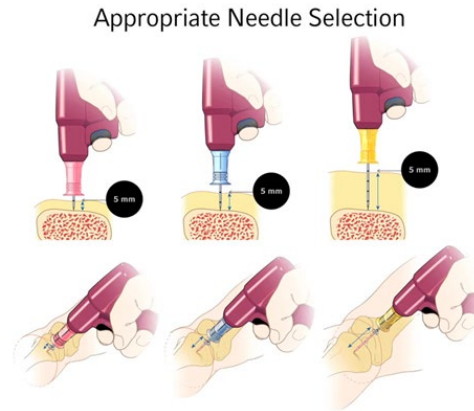
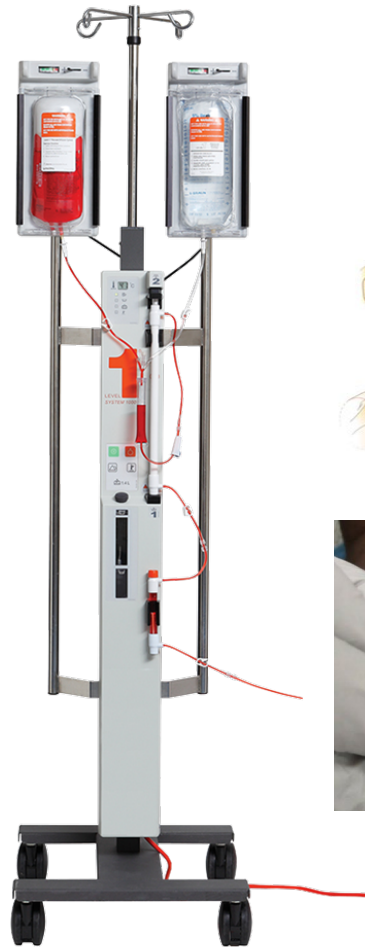
Goal directed therapy: Plasma, PLTs & fibrinogen

TABLE 2 Pediatric dosing of blood components/products and therapeutic targets for massive hemorrhage.

Blood component/ product	Dose per kg	Anticipated increase	Treatment Threshold
Red blood cells	10mL ^b	2g/dL (20g/L)	<8g/dL ^c
Frozen plasma	10mL	Coagulation factors by 20%	INR>1.8
Platelets	10mL	150×10 ⁹	<50×10 ^{9d}
Cryoprecipitate	5mL	Fibrinogen by 30mg/dL	<1.5g/L
Fibrinogen concentrate	20mg	Fibrinogen by 30mg/dL	<1.5g/L ^a



Videos: Pull-Push Method, Rapid Infuser and peripheral IV/intraosseous access in children



Pull-Push Method Video:

<https://youtu.be/jcKA7N7MNIU>

Level 1 Infuser Video:

https://www.youtube.com/watch?v=MxNs_BF3Cv8

Intra-osseous access:

<https://www.youtube.com/watch?v=mpnroZi8t0A>

Peripheral venous access:

<https://www.youtube.com/watch?v=bu5zqiZFViY>



MCQ Post-test

1. Which one of the following statements is false regarding the management of traumatic massive hemorrhage in children?

- A. Validated tools specifically for MHP activation in children are available
- B. 10 ml/kg is a standard dose for RBCs, plasma and platelets
- C. Hypothermia ($\leq 36^{\circ}\text{C}$) is part of the “Lethal Triad”
- D. $\text{INR} \geq 1.8$ & base-deficit $>$ minus 6 are associated with \uparrow mortality in trauma
- E. Administering TXA within 3 hr of MHP activation is evidence-based



Conclusions:

- ***No formal definition of massive hemorrhage in children***
- ***Inequities in pediatric transfusion therapy likely contribute to poor outcomes***
- ***Key elements of a pediatric MHP: “7Ts”***
 - **MHP triggers:** 20-40 ml/kg RBCs in 1-4 hrs; SIPA, ABC or ABC-D
 - Component/product transfusion **thresholds** & **weight-based dosing** (TAXI & TAXI-CAB)



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I ♥
DAPM, CHEO 

