Pediatric Patient Blood Management

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Faculty Disclosure

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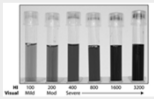
Outline

- Background
  - Transfusion indications, safety and risks
  - Patient blood management introduction: decreased costs and transfusion risks, improved patient outcomes, better utilization of limited resources
- Patient blood management initiatives
  - Transfusion thresholds
  - Information technology (physician orders, electronic cross-match)
  - Maximal surgical blood ordering schedule (MSBOS)
  - Umbilical cord milking
  - Preserving universal donor inventory (O negative RBCs, AB plasma)
  - Massive transfusion
  - Point of care coagulation assays to guide transfusion
  - Pharmacologic agents
- Summary
  - Multidisciplinary team approach

Blood Products in Children

Component	Collection	Indication	Pediatric Dose	Notes
RBCs	Whole blood or apheresis	Oxygen delivery	5-15 mL/kg (increase in hemoglobin of 1-3 g/dL)	Hematocrit varies from 60-80% with different storage solutions.
Plasma (FFP)	Whole blood or apheresis	Coagulation factor replenishment	15-20 mL/kg	Increased factor content: - Shorter time interval between collection and freezing - Shorter time between thawing and use
Platelets	Apheresis or whole blood	Hemostasis	Equivalent units (1 eu = 0.55 x 10^10 platelets) 1 eu/10 kg	Single apheresis donor typically contains 6 eu
Cryoprecipitate	Derived from plasma	Fibrinogen, factor 8, von Willebrand factor repletion	1 bag/10 kg	Smaller volume than FFP may benefit patients with fluid overload
Granulocytes	Apheresis	Refractory fungal/bacterial infection	> 1 x 10^{10} PMN or more	

What Causes Adverse Outcomes Associated with Transfusion?

Entities	Notes	
Infectious diseases (HIV, hepatitides, CMV, Zika, Babesia, parvovirus, emerging) Old, new, unknown	- Global economy - Processing/testing inadequate - Lag between discovery and mitigation/prevention	
Wrong blood in tube	Acute hemolytic transfusion reaction (never event)	

Rates 1/75,000 (bacteria in platelets), 1/250,000 (bacteria in RBCs), 1/750,000 (Hepatitis B), 1/1,000,000-1/1,500,000 (HIV, Hepatitis C)

http://www.eclinpath.com/chemistry/interference-indices/print-10/

Katz, LM and Dodd, RY, "Transfusion Transmitted Diseases" Chapter 71 in Shaz BH, Hillyer CD, Roshal M, Abrams CS. Transfusion Medicine and Hemostasis 2nd Edition, 2013 Elsevier Publishing

What Causes Adverse Outcomes Associated with Transfusion?

Entities	Notes	
Non-infectious sequelae	- Transfusion-related immunomodulation - HLA/RBC antigen allo-immunization - Future risk of HDFN	
Transfusion reactions	- Febrile, allergic reactions - Transfusion-associated graft-vs-host disease - Circulatory overload (TACO) - Acute lung injury (TRALI)	

Katz, LM and Dodd, RY, "Transfusion Transmitted Diseases" Chapter 71 in Shaz BH, Hillyer CD, Roshal M, Abrams CS. Transfusion Medicine and Hemostasis 2nd Edition, 2013 Elsevier Publishing

Pediatric Transfusions - Adverse Outcomes

According to the **UK Serious Hazards of Transfusion (SHOT)** scheme analysis published in 2007, the estimated incidence of an adverse outcome per red cells issued is:

- 18 per 100,000 for <18 years of age
- 37 per 100,000 for infants <12 months of age
- 13 per 100,000 for adults

Incorrect blood component transfused was the single largest adverse event: the majority of pediatric reports (58%) were related to human error, with even higher rates of error in the infant age group (82%)

Vanderbilt study in 2015:

- 6.2 reactions per 1000 transfusions within the pediatric (age < 21 years) population
- 2.4 reactions per 1000 transfusions within the adult population.

Increased incidences of:

- allergic transfusion reactions (2.7/1000 vs. 1.1/1000, p < 0.001)
- febrile nonhemolytic transfusion reactions (1.9/1000 vs. 0.47/1000, p < 0.001)
- hypotensive transfusion reactions (0.29/1000 vs. 0.078/1000, p < 0.05).

Stainsby et al.. British Journal of Haematology, 141, 73–79.
Oakley FD, Woods M, Arnold S, Young PP. Transfusion. 2015 Mar;55(3):563-70.

Decreased Exposure versus Fresh Blood?

Previously:

- Minimize donor exposure by using dedicated units (neonates received aliquots from same bag over time)
- Directed donations to avoid infectious risks from random donors

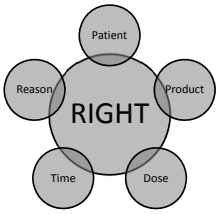
Nowadays:

- Improved random donor screening and testing
- Directed donors do not have greater safety than community donors (in some cases, may see higher rates in parental donors).
  - Maternal directed donor carries risk of hemolysis
- Dedicated type-specific units may result in wastage
  - Decreased blood use (patient blood management)
- At CNMC, we use O positive and O negative units for neonates
  - Flexible inventory to provide blood needs
  - Avoid having older blood for neonates

Jacquot C, et al. Transfusion. 2017;57(11):2799-2803.

Patient Blood Management

- Definition: "Timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome"
- Employs a multidisciplinary team approach
- Optimizes red cell mass
- Minimizes blood loss
- Exploits a patient's physiological tolerance to anemia



Murphy MF, Goodnough LT. Transfus Clin Biol. 2015;22(3):90-6.

Transfusion Overuse

Summary of the inappropriate use of blood from audits of blood use in England [2].

Audit	Year	N° of hospitals	N° of cases audited	Inappropriate use	Relevant guidelines for audit standards
Red cell transfusion	2002	All 13 hospitals in Northern Ireland	360	19% of patients inappropriately transfused and 29% overtransfused	BCSH, 2001: the clinical use of red cell transfusion
Red cells in hip replacement	2007	139/167 (83%)	7465	48% of patients	British Orthopaedic Association, 2005
Upper gastrointestinal bleeding	2007	217/257 (84%)	6750	15% of RBCs, 42% of platelets, 27% of FFP	British Society of Gastroenterology, 2002
Red cell transfusion	2008	26/56 (46%) hospitals in two regions	1113	19.5% of transfusions	BCSH, 2001: the clinical use of red cell transfusion
Fresh frozen plasma	2009	186/248 (75%)	5032	43% of transfusions to adults, 48% to children, 62% to infants	BCSH, 2004: guidelines for the clinical use of fresh frozen plasma, cryoprecipitate and cryosupernatant
Platelets in haematology	2011	139/153 (91%)	3296	27% of transfusions	BCSH, 2003: guidelines for the use of platelet transfusions
Cryoprecipitate	2012	43/82 (52%) from 3 regions	449	25% of transfusions	BCSH, 2004: guidelines for the clinical use of fresh frozen plasma, cryoprecipitate and cryosupernatant

BCSH: British Committee for Standards in Haematology (guidelines available on http://www.bcshguidelines.org).

Why?

- Reduce blood use
- Improve outcome
- Reduce hospital costs (decrease LOS, readmissions, etc.) and transfusion-associated adverse events

Importance:
Blood transfusions are one of the most over-used therapies in the US and UK
Considerable variation in use among providers

Murphy MF, Goodnough LT. Transfus Clin Biol. 2015;22(3):90-6.

Patient Blood Management Initiatives

Transfusion Thresholds

- Goal is to standardize practice based on evidence from studies
- AABB guidelines published for RBC, platelet transfusions
- Recommend restrictive transfusion thresholds
- Pertain primarily to adults and hematology/oncology patients with hypoproliferative thrombocytopenia
- Caveats
  - Guidelines are not a substitute for clinical judgment taking into account variation among patients and full assessment
  - Applicability to children/neonates may be limited

Carson JL, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. JAMA. 2016;316(19):2025-2035.
Kaufman RM, et al. Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern Med. 2015;162(3):205-13.
Roback JD et al. Evidence-based practice guidelines for plasma transfusion. Transfusion. 2010;50(6):1227-39.

Restrictive RBC Thresholds - Adults

- Meta-analysis of 19 trials – 6264 patients
  - Restrictive strategy
    - reduced hospital mortality but not 30 day mortality
    - did not appear to impact rate of adverse events (mortality, cardiac events, MI, stroke, pneumonia, thromboembolism) compared to liberal strategy
    - was associated with lower relative risk of infectious complications
    - led to lower proportion of patients transfused and lower number of units transfused
  - No trials in patients with acute coronary syndrome (ACS)
- AABB guidelines
  - Stable, non-bleeding: <7 g/dL (British Committee for Standards in Haematology, American College of Critical Care Medicine)
  - Cardiovascular history: <8 g/dL (Society of Thoracic Surgeons, Society of Cardiovascular Anesthesiology)
  - ACS: no recommendation
- Single unit policy recommended in non-bleeding patients

Hébert PC. Vox Sang. 2000;78 Suppl 2:167-77.
Carson JL, et al. Cochrane Database Syst Rev. 2012;4:CD002042.
Carson JL, et al. Annals of Internal Medicine. 2012;157(1):49-58.

Neonatal Studies

- Premature infants in need of transfusion (PINT):
  - No advantage for liberal transfusion practices
  - But a post-hoc analysis at 18 to 21 months' corrected age showed a significant cognitive difference favoring the liberal threshold group
- Iowa study:
  - Restrictive transfusion was associated with more apneic episodes, intraparenchymal brain hemorrhage, and periventricular leukomalacia
  - But the liberal transfusion group performed poorer on visual memory, reading, and associative verbal fluency measures at school age
- Meta-analysis in 2016 concluded: Statistically significant differences in a range of harmful outcomes between neonates exposed to restrictive and liberal RBC transfusion practice were not found.

Bell EF, Strauss RG, Widness JA, et al. Pediatrics. 2005;115(6):1685-1691.
Kirpalani H, Whyte RK, Andersen C, et al. J Pediatr. 2006;149(3):301-307.
Keir A et al. Adverse effects of red blood cell transfusions in neonates: a systematic review and meta-analysis. Transfusion. 2016;56(11):2773-2780.

Neonatal/Pediatric Thresholds

- Disclaimer: There is a paucity of evidence-based guidelines for these practices.

Neonate Condition	Hematocrit	Pediatric Condition	Hemoglobin
Stable anemia	<20-25%	Stable patient	<7 g/dL
Major surgery	<30-35%	Hemorrhage/sepsis	<8 g/dL
Moderate cardiopulmonary disease	<30-40%	Respiratory failure	<7-8 g/dL
Severe cardiopulmonary disease	<40-45%	Pre-invasive procedure/surgery	<8 g/dL
		ECMO	<12 g/dL

Strauss RG. How I transfuse red blood cells and platelets to infants with anemia and thrombocytopenia of prematurity. Transfusion 2008;48:209-217.

Platelet Thresholds – Children and Adults

Condition	Threshold
Stable, non-bleeding (standard prophylaxis)	<10,000/µL
Mucositis, fever, bleeding, central venous catheter	<20,000/µL
Invasive procedure, lumbar pursuit, post-operative	<50,000/µL
Intracranial, intraocular bleeding or procedure	<100,000/µL

- Note: guidelines are not a substitute for clinical judgment taking into account variation among patients and full assessment

Kaufman RM, et al. Ann Intern Med. 2015;162(3):205-13.

Neonatal Platelet Thresholds

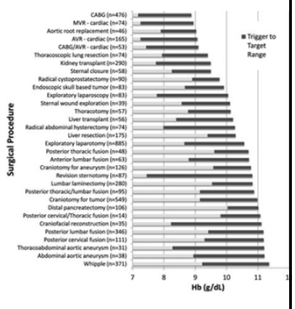
- No bleeding, including neonatal alloimmune thrombocytopenia (NAIT) without bleeding or family history of ICH
  - Platelet count < 25 x 10^9/L
- Bleeding, current coagulopathy, surgical prophylaxis, or NAIT with a family history of intracranial hemorrhage in an affected sibling
  - Platelet count < 50 x 10^9/L
- Major bleeding or requiring major surgery (e.g. neurosurgery)
  - Platelet count < 100 x 10^9/L

- Recent RCT showed premature infants (n = 660) with higher transfusion threshold (50 x 10^9/L) had higher occurrence of a new major bleeding episode or death than those at a lower threshold (25 x 10^9/L) (26% versus 19%, p = 0.02).
  - Of note, patients with bleeding history were excluded and low number of screened infants were enrolled

New HV et al. Guidelines on transfusion for fetuses, neonates, and older children. Brit J Haematol 2016;175:784-828.
Curley A et al. Randomized Trial of Platelet-Transfusion Thresholds in Neonates. N Engl J Med. 2018

Blood Product Utilization Review

- Prospective
  - Real-time review of transfusion requests
  - More effective
  - Requires more work
  - Can lead to friction with clinical services
- Retrospective
  - Full information may not be available anymore
  - More passive, less effective
- Blood product use also helps inform ordering and appropriate inventory levels in the BB



Tuckfield A, et al. Med J Aust. 1997;167(9):473-6.
Frank SM, et al. Anesthesiology. 2012;117(1):99-106.

Clinical Decision Support

- Best practices alert
  - Interface with most recent laboratory results (hemoglobin, platelets, PT/INR)
  - Notify ordering provider when guidelines are not met
  - Data collection of override reasons
  - Use to monitor evolving clinical practices
- Alert fatigue
  - The five rights of CDS: right information to the right person in the right intervention format, through the right channel, at the right time in workflow
  - For example, operating rooms exempt from RBC notifications

Goodnough LT, et al. Transfusion. 2014;54(5):1358-65.

Electronic Cross-Match

- Virtual compatibility testing in which blood products are issued based on prior ABO/Rh testing and antibody screening
  - Must be validated prior to use
- Bypasses need to perform in vitro formal serologic XM
  - Saves time/reagent use
  - Can extend active type and screen for pre-surgical patients
  - Gives comfort to clinicians who ask for products "on hold"
  - During downtime, must perform standard serologic XM
- However, some patients are not eligible
  - E.g. BMT, ABO discrepancy, presence of antibodies
- Enables rapid cross-match upon blood order
  - Reduce allocated blood for more flexible inventory
- High yield, low cost intervention, but not universally implemented

Chapman JF, et al. Transfusion medicine. 2000;10(4):251-6.

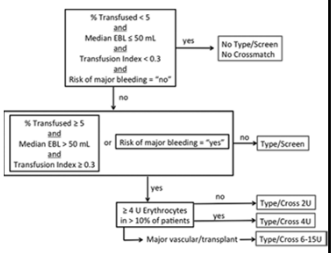
Maximal Surgical Blood Ordering Schedule

- Pre-allocation of defined number of blood products for surgical procedure
- Allows blood bank to plan and assess inventory at the beginning of day
  - Order additional units as needed to supplement inventory
- MSBOS must be updated with new techniques
  - New laparoscopic techniques may require less blood
  - Consult with surgeon/anesthesiologist to tailor settings
- Special allowance if RBC antibodies are detected
  - Higher number of units may need to be crossmatched because compatible units may be difficult to obtain
- Eliminate blood orders for low-blood-loss procedures, which reduce costs
- **Reduce unnecessary blood draws in pediatrics (which have high iatrogenic blood loss)**
- Improve OR efficiency by decreasing delays waiting for blood
- Improve compliance by not starting surgery without blood available (JCAHO guideline)
- Improve patient safety by reduction of processing multiple samples and units in the blood bank

Frank SM, et al. Anesthesiology. 2013;118(6):1286-97.
Richardson NG, et al. Ann R Coll Surg Engl. 1998;80(4):262-5.

MSBOS Algorithm

- Identify surgical procedures
- Categorize by specialty and anatomic site
- Analyze
  - # of patients transfused
  - # of units transfused
  - Median estimated blood loss
  - Transfusion index (mean number RBC units/patient)
- Calculate the Transfusion to Crossmatch ratio for each group



Frank SM, et al. Anesthesiology. 2013;118(6):1286-97.

MSBOS Example

Provincial Blood Coordinating Program

Newfoundland Labrador

Sub-total Gastrectomy	2	**Vascular Surgery**	
Thoractomy/ Lung Resection	4	Abdominal Aneurysm (Elective)	4
Thoroscopy	4	Abdominal Aneurysm (Emergency)	4 FFP & 6 units
Total Colectomy	4	Abdominal Aortic Aneurysm	6
Total Gastrectomy	4	Aortic Grafts	2
Total Proctocolectomy	4	Aorto-Bifemorial Graft	4
Transhiatal Esophagectomy	4	Aorto- Femoral Bypass Graft	6
Tumor Pancreatectomy	4	Aorto- Iliac Bypass Graft	6
Vagoyomy/ Antrectomy	2	Aoto-Popliteal Bypass Graft	6
Wedge Resection of Liver	4	Axillo- Bifemeral Bypass Graft	6
Wedge Resection of Lung	4	Balloon Angioplasty	2
Whipple's Procedure	6	Cardiovascular Surgery	6
		Coronary Artery Bypass Graft	6
Head & Neck/ Oral Surgery			
Commando Procedure	4	Elective Aneurysm Repair	6
Laryngectomy	4	Embolectomy/ Endarterectomy/ Thrombectomy	4

- T&S alone may be sufficient for surgeries where blood usually not needed
- Some MSBOS may also provide suggested platelet orders, whether to perform coagulation screen

https://www.health.gov.nl.ca/health/bloodservices/pdf/max_surgical_blood_order.pdf

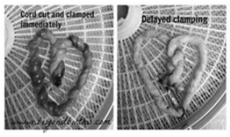
Crossmatched/Transfused Ratio

- High number shows many units are allocated but few transfused
- Strains inventory, requiring excessive blood ordering -> surplus and wastage
- Ideal C/T ratio is 1, <2 is desirable, <1.5 is optimal
- Use MSBOS to plan ahead and electronic cross-matching to provide blood rapidly without the need for excessive allocation
- Ensure an in-date type and screen sample is available if there is possibility of a blood transfusion

Novis DA, et al. Arch Pathol Lab Med. 2002;126(2):150-6.

Delayed Cord Clamping

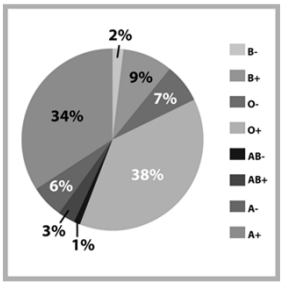
- Delayed umbilical cord clamping (30-120 seconds) increases RBC mass and circulating blood volume during the first 24 hours of life
- An alternative, "milking" or "stripping" the cord, is done by holding the placental end of the cord, and gently moving blood within the vessels toward the neonate (3-4 times) prior to clamping and cutting the cord.
- Cochrane review in 2012 showed that delayed cord clamping up to 180 seconds or umbilical cord milking versus immediate cord clamping resulted in:
  - 39% fewer transfusions for anemia
  - 41% fewer patients with IVH
  - 38% fewer patients with NEC
- The American College of Obstetricians and Gynecologists currently recommends a delay in umbilical cord clamping in vigorous term and preterm infants for at least 30-60 seconds after birth



Rabe, H., et al. Cochrane Database Syst Rev, 2012(8): p. CD003248.
ACOG, Committee Opinion No. 684. Obstet Gynecol, 2017. 129(1): p. e5-e10.

Universal Donors – Limited Resource

- To address limited availability of O negative RBCs and AB plasma, may consider:
- Expanded use of A plasma
- Issue of O positive RBCs in emergency release/massive transfusion in males
- Use of thawed plasma to extend shelf-life to 5 days



http://kybloodcenter.org/why-donate/about-blood-types/

Group A Plasma

- A plasma compatible with ~85% of patients (O and A); incompatible with 15% (B or AB)
- **2013 study:** 14% of patients received ABO-incompatible transfusions (total n = 254)
- Overall complications similar between groups – no hemolytic reactions
- Group AB plasma use reduced by 96.6%
- **2014 study** of emergency release:
- No hemolytic transfusion reaction or other adverse event in 23 patients who received incompatible blood (n = 385)
- **2017:** Multi-institution study of trauma patients who received at least 1 unit of group A plasma.
- Group A patients (identical) and group B/AB patients (incompatible) were compared.

TABLE 3. Outcome data between groups*

	Identical (n = 809)	Incompatible (n = 354)	p value
In-hospital mortality			
Survival to discharge	572 (71)	253 (71)	0.83
In-hospital death	237 (29)	101 (29)	
Early mortality (<24 hr)			
Yes	114 (14)	59 (17)	0.28
No	695 (86)	295 (83)	
Hospital LOS (days)	14 (0-111, 17)	14 (0-128, 18)	0.89

* Categorical data are reported as number (%), and continuous data are reported as mean (range, SD).

Zielinski MD, et al. J Trauma Acute Care Surg. 2013;74(1):69-74.
Chhibber V, et al. Transfusion. 2014;54(7):1751-5.
Dunbar NM et al. Transfusion. 2017;57(8):1879-1884.

Use of Emergency O Positive Blood

- High rate of alloimmunization in healthy volunteers (80%)
- However, rates are lower in patients with AIDS, liver disease, malignancy and trauma (reported ranges 4-22%)
  - Possibly result of immunosuppression
  - In cases of heavy bleeding, D+ RBCs may not persist long enough to sensitize
- 2017 study:
  - Emergency patients with unknown blood type transfused with O RhD+ red blood cell concentrates had a low risk of forming anti-D antibodies (3-6%).
  - Approach saved more than 10% of the total O RhD- red blood cell concentrate demand
- In massive transfusion protocols, recommendation to save O negative units for women of child-bearing age and children
- In surgeries with high blood use (e.g. liver transplant), patients are switched to D-positive units until bleeding subsides
- Anti-D typically does not bind complement
  - Leads to extravascular hemolysis (delayed hemolytic reaction)

Yazer and Triulzi. Transfusion 2007; 47: 2197-2201.
Meyer E, Uhl L. Transfusion. 2015;55(4):791-5.
Selleng K, et al. Lancet Haematol. 2017;4(5):e218-e224.

Massive Blood Transfusion

- **Indications**
- Clinical massive hemorrhage in hard to control area
- Ongoing blood loss greater than 150 mL/min
- Loss of more than half of the patient's estimated blood volume in two hours
- **Goals**
- Rapid release of blood products from blood bank
- Balanced ratio to re-approximate whole blood to achieve hemostasis (evidence drawn from trauma literature)
- Laboratory testing may help assess efficacy (e.g. coagulation testing)
- Protocol continues until deactivated by clinical team

	Packages to Transfuse (in order below:)	0-4 kg Neonate (85 mL/kg)	5-9 kg Infant (85 mL/kg)	10-24 kg Young Child (75 mL/kg)
	Emergency Release (A)	1/2 RBC	1 RBC	2 RBC
	B	1/2 RBC 1/2 FFP 2 eu Plt	1 RBC 1 FFP 3 eu Plt	2 RBC 2 FFP 4 eu Plt
Exceeds Total Blood Volume No Crossmatch Required	C	1/2 RBC 1/2 FFP 2 Cryo	1 RBC 1 FFP 3 Cryo	2 RBC 2 FFP 4 Cryo
	B	1/2 RBC 1/2 FFP 2 eu Plt	1 RBC 1 FFP 3 eu Plt	2 RBC 2 FFP 4 eu Plt
	C	1/2 RBC 1/2 FFP 2 Cryo	1 RBC 1 FFP 3 Cryo	2 RBC 2 FFP 4 Cryo
	B	1/2 RBC 1/2 FFP 2 eu Plt	1 RBC 1 FFP 3 eu Plt	2 RBC 2 FFP 4 eu Plt
	C	1/2 RBC 1/2 FFP 2 Cryo	1 RBC 1 FFP 3 Cryo	2 RBC 2 FFP 4 Cryo

Children's National Medical Center MBTP Packet.
Diab YA, Wong EC, Luban NL. Br J Haematol. 2013 Apr;161(1):15-26.

Extracorporeal Membrane Oxygenation

- **Indications**
- Maintenance of heart and lung function in the face of life threatening cardiopulmonary disease or when maximal medical therapy has failed
- Support of cardiac failure post CPB surgery with low cardiac output
- **Complications**
- Bleeding (intracranial and post-op surgical)
- Embolism / thrombosis
- Heparin-induced thrombocytopenia (HIT)
- End organ dysfunction: renal, hepatic, pulmonary and neurocognitive dysfunction
- Hemolysis

- **Examples of diseases requiring ECMO support**
- Primary pulmonary hypertension of newborn
- Respiratory distress syndrome
- Meconium aspiration syndrome
- Sepsis
- Congenital diaphragmatic hernia
- Congenital heart abnormalities

Coagulation Testing

	ADVANTAGES	DISADVANTAGES
Activated clotting time (ACT)	Point of care (POC) Cheap, run on whole blood	Direct unfractionated heparin (UFH) effect not measured
Activated partial thromboplastin time (aPTT)	Some POC devices Works for both UFH and direct thrombin inhibitors	Unreliable in critically ill patients Inter- and intra-patient variability
Anti-factor Xa activity	Measures UFH ability to catalyze AT inhibition of Xa	Hyperbilirubinemia and elevated free hemoglobin interfere
TEG / ROTEM	Can be POC Clot strength / fibrinolysis measured	Limited availability Expert interpretation needed

- Evidence suggests that anti-Xa activity (heparin) levels
  - correlate better with heparin dosing compared to aPTT and ACT
  - are also less labile

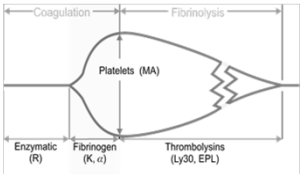
Liveris A, et al. Pediatr Crit Care Med 2014;15: e72-9.
O'Meara LC, et al. ASAIO J 2015;61: 339-44.

Analytical Testing Issues and Challenges

- Lack of correlation between coagulation results, especially in neonates and children
- Experience is limited by small, non-evidence based studies
  - variable testing
  - different blood products / derivatives
  - different pumps and oxygenators
- Extracorporeal Life Support Organization publishes guidelines:
  - ELSO Guidelines for Cardiopulmonary Extracorporeal Life Support (version 1.3, November 2013): https://www.elso.org/Portals/0/IGD/Archive/FileManager/929122ae88cusersshyerdocumentselsoguidelinesgeneralalleclsversion1.3.pdf
  - "Red Book" published in 2017
- Institutional algorithms are not evidence-based and differ with respect to coagulation assay use, blood/blood derivative transfusion guidelines

Bembea MM, Annich G, Rycus P, Oldenburg G, Berkowitz I, Pronovost P. Pediatr Crit Care Med 2013;14:e77
www.elsonet.org

Thromboelastography (TEG)/Rotational Thromboelastometry (ROTEM)



TEG	ROTEM	Represents	Affected by
Clotting time (R)	Clotting time (CT)	Time to clot initiation	Coagulation factor function/quantity
Angle (α)	Clot formation time (CFT)	Speed of clot formation	Fibrinogen function and quantity
Maximum amplitude (MA)	Maximum clot firmness (MCF)	Clot strength	Platelet count and function
Lysis at 30 min (Ly30)	Lysis index after 30 minutes (LI)	Clot breakdown	Hyperfibrinolysis

Diab YA, Wong EC, Luban NL. Br J Haematol. 2013 Apr;161(1):15-26.

Institutional Guidelines – TEG Use for Management of Cardiac Surgery Patients

TEG parameter		Intervention
Neonates ≤1 month	Infants >1 month and older children	
Hep R >8 minutes	Hep R >11 minutes	FFP 15 mL/kg
Hep K >2.5 minutes	Hep K >3 minutes	Cryoprecipitate 1 unit/5 kgs
Hep MA <55 mm	Hep MA <50 mm	Platelets 1 equiv unit/5 kgs
Delta R* >4 minutes		2nd half dose protamine (if bleeding)
LY30 >7.5%		Amicar 100 mg/kg IV (if bleeding)
Normal TEG/hep-TEG or refractory bleeding		Novoseven 90 mcg/kg IV

* Delta R=R on TEG minus R on Hep TEG.

Disclaimer: Representative excerpts from CNMC guidelines.
These may not be broadly applicable to other patient populations.

"Personalized" Transfusion Medicine: Pharmacy Products

- Reduce UFH use
- Provide consistent anticoagulation
- Reduce bleeding risk
- Reduce thrombosis risk to patient and circuit
- Delay need to change out circuit (risks, blood donor exposure, cost)

Antithrombin-III concentrate

Octaplas (solvent/detergent treated plasma)

Von Willebrand factor repletion

Prothrombin Complex Concentrates

Options for Controlling Bleeding

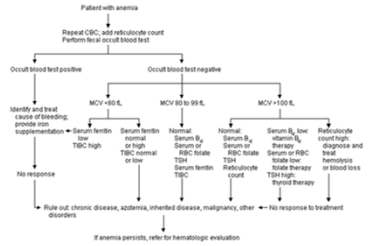
Product	Mode of Action	Indication
AT-III concentrate (ATryn®, Thrombate III®)	Heparin requires antithrombin III for anticoagulant effect	Used in ECMO patients with heparin resistance, inadequate anticoagulation
Fibrinogen concentrate (RiaSTAP®)	Heat-treated, lyophilized alternative to cryoprecipitate	Fibrinogen deficiency, DIC
Activated VIIa (Novo-Seven®)	Coagulation factor	Factor 7 deficiency, hemophilia with inhibitors. Used off-label for refractory bleeding.
Prothrombin complex concentrates (PCC)	Mixture of factors II, VII, IX, and X (vitamin K-dependent factors). Activated and nonactivated formulations exist.	Warfarin overdose reversal (alternative to FFP). Used off-label for bleeding control.
Von Willebrand / factor VIII / factor IX concentrates	Undergo manufacturing steps to remove infectious risk, safer than blood transfusion	Congenital and acquired coagulation disorders
Desmopressin	Promotes release of vWF from endothelial cells	Used for von Willebrand disease and hemophilia A
Anti-fibrinolytics (aminocaproic acid)	Inhibits plasmin, which breaks down clots	Slow degradation of fibrin clots, beneficial in trauma patients with severe injury
Topical hemostatic, agents, sealants, adhesives	Provide targeted action of pro-coagulant	Used in surgical/invasive procedures

Drawbacks: limited activity, lack of experience, cost, risk of thrombosis

Goodnough LT, Shander A. Anesth Analg. 2013;116(1):15-34.

Pharmacology – Correction of Anemia

- Optimize patient's hemoglobin level prior to elective surgery to minimize need for transfusion
- Establish etiology of anemia to determine optimal therapy
- Iron (oral or parental), erythropoietin, folate, vitamin B12
- "$5 iron pills instead of $500 blood unit"

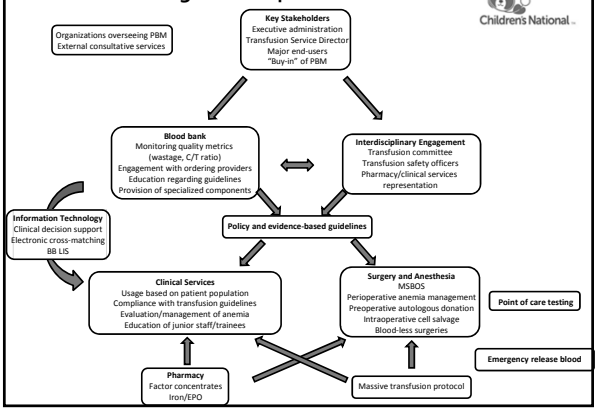


Products
Iron
Folate
Vitamin B12
Erythropoiesis-stimulating agents

Abramson SD, Abramson N. Am Fam Physician. 1999;59(4):851-8.

Putting It All Together

Program Components



Summary

- Patient blood management encompasses a wide range of interventions
  - Must tailor to institutions needs
  - **Interdisciplinary cooperation and executive support are crucial**
- AABB and other professional organizations have issued evidence-based transfusion thresholds/criteria
  - Institutional blood use is monitored by committee
- **To help decrease use, plan ahead before blood is needed**
- For surgery, optimize erythropoiesis, minimize blood loss, and manage anemia (consider iron for example)
- Order "type and screen" ahead of time and ensure blood bank sample is current
  - Blood can be rapidly issued when needed
  - Blood bank inventory meets surgical needs according to MSBOS
- Consider factors which may impact decision-making, such as age, religion, co-morbidities, when ordering blood & blood products
- **Overall patient blood management goals: decreased costs, improved patient outcomes, better use of limited resources**
  - Established for adults and applicable to children

Goodnough LT, Shander A. Anesthesiology. 2012;116(6):1367-76.

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