Dr. Zachary Liederman, Bleeding Assessment and Approaches to Coagulation Testing

Key points

- The bleeding history is the most important component of bleeding assessment
  - Bleeding location
    - head to toe approach, focus on mucocutaneous vs. deep bleeding
  - Bleeding characteristics
    - frequency and onset, focus on provoked vs. spontaneous bleeding
  - Bleeding severity
    - In addition to amount of bleeding, consider any complications that have occurred and medical attention/ interventions received

Bleeding assessment tools like the Condensed MCMDM1 combine these factors into a single score. These are highly sensitive screening tests for ruling out a significant bleeding disorder

- Laboratory tests assist in diagnosing and risk stratifying patients **with** high risk bleeding histories
- In unselected patients abnormal coagulation tests are neither sensitive nor specific for predicting bleeding risk

Screening coagulation tests to consider in high risk patients:
PT/INR, aPTT, VWF profile (VWF antigen, VWF activity/ ristocetin cofactor assay, factor 8), platelet function analysis (PFA)

Simplified appro

<table>
<tr><td colspan="2">+ bleeding history</td><td rowspan="2">Further assessment required

Consider hematology consult</td></tr>
<tr><td rowspan="2">⌀ bleeding history but other risk factors, assessment limitations or high risk procedure</td><td>abnormal coag testing</td></tr>
<tr><td>normal coag testing</td><td rowspan="2">Bleeding disorder unlikely

Ok to proceed to OR</td></tr>
<tr><td colspan="2">⌀ bleeding history</td></tr>
</table>

Dr. Rita Selby, Direct Oral Anticoagulants (DOACs) and Antiplatelet agents: Monitoring, Peri-op management, Reversal

- DOACs are now first line therapy for most arterial and venous thromboembolic indications. Knowledge of the 3-4 main DOACs and considerations for choosing a DOAC based on age, indication, renal function and drug interactions is important for front line clinicians from all disciplines.

- Although routine coagulation tests are not needed to monitor DOAC therapy, DOACs affect routine coagulation tests since they inhibit key clotting factors. Knowledge of the impact of DOACs on routine coagulation tests is helpful when assessing patients for urgent reversal or management of DOAC-associated bleeding. Quantitative assessment of DOAC levels and interpreting peak and trough levels may help as well but access to these tests is limited.

- Elective interruption of DOAC therapy for procedures and surgery is based on type of DOAC, bleeding risk associated with surgery and renal function of patient.

- Strategies to manage DOAC-associated bleeding depend on whether the bleeding is minor, major but non-life threatening, or life-threatening, timing of last dose and renal function. Specific antidotes are currently not available for most DOACs with the exception of dabigatran so non-specific therapy must be optimized.

- Antiplatelet agents are broadly classified based on the receptors and pathways by which they act on platelets and whether the action is reversible or irreversible.

- Elective peri-operative management of anti-platelet drugs are based on mechanisms of action and reversibility of drugs, inherent thrombotic risk (of patient and procedure), bleeding risk associated with procedure and whether the antiplatelet therapy is monotherapy or dual therapy (cardiac stents).

- Platelet transfusions are NOT INDICATED for urgent reversal or major bleeding except in rare circumstances. Non-specific therapies like desmopressin and tranexamic acid must be optimized.

Dr. Wendy Lau, Neonatal and Pediatric Transfusions

Proposed NICU RBC Transfusion Thresholds

Respiratory status	Age of neonate	Hemoglobin Threshold
Ventilated	Age < 1 wk Age > 1 wk	Hgb < 120 g/L Hgb < 110 g/L
On O_2/ CPAP	Age < 1 wk Age > 1 wk	Hgb <100 g/L Hgb < 90 g/L
Stable and off O_2	Age > 1 wk	Hgb < 75 g/L

BJH 2013; 160: 421–433

RBC Threshold Guidelines for Children

Pediatric Patient type	Threshold	Evidence grade
PICU (stable, non-cyanotic)	70 g/L	1B
Oncology	70 g/L (typical practice) Insufficient literature	2C
Perioperative non-cardiac surgery (stable, non-bleeding)	70 g/L	1C
Chronic anemia (Diamond Blackfan anemia)	80 g/L Consensus based	2C

* Hemoglobinopathies

The following should be considered for children undergoing surgery with significant risk of bleeding:

Tranexamic acid (1B)
Red cell salvage (2C)

BJH 2016; 175: 784-828

Proposed NICU Platelet Transfusion Thresholds

Clinical status	Platelet threshold	Grade Comment
Major bleeding or requiring major surgery (e.g. neurosurgery)	< 100 x 10^9/L	No RCT in prems
Bleeding, current coagulopathy, sx, exchange transfusion	< 50 x 10^9/L	
No bleeding (including NAIT if no bleeding and FHx of ICH)	< 30 x 10^9/L	Grade 2C

Special considerations for NAIT – neonatal alloimmune thrombocytopenia

BJH 2013; 160: 421–433
BJH 2019; 185(3):549-562,

Suggested platelet thresholds for platelet transfusion in children

Platelet threshold (x 10^9/L)	Clinical situation
< 10	Irrespective of signs of hemorrhage (excluding ITP, TTP/HUS, HIT)
< 20	Severe mucositis Sepsis Laboratory evidence of DIC in the absence of bleeding Risk of bleeding due to a local tumour infiltration
< 40	Prior to lumbar puncture
< 50	Moderate hemorrhage (e.g. GI bleeding) Surgery, unless minor (except at critical sites)
< 75-100	Major hemorrhage or significant post-op bleeding Surgery at critical sites: CNS including eyes

** expert opinion

BJH 2016; 175, 784-828

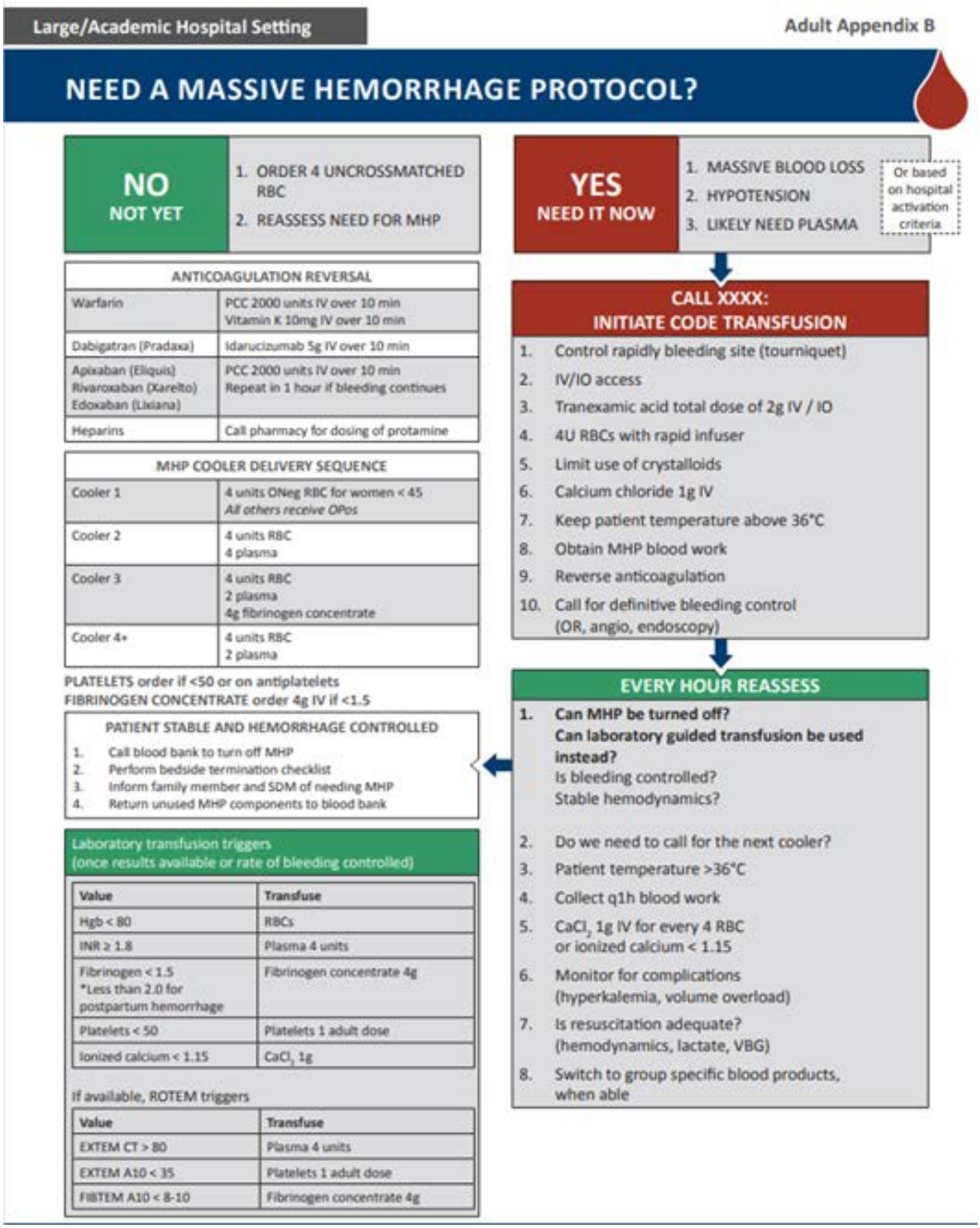
Clinical Pearls

- Laboratory reference ranges (hematology and coagulation) specific for neonates and children should be used
- Always consider the etiology of the anemia and thrombocytopenia prior to ordering a transfusion
- Order blood products using child's weight

Blood Products are ordered by weight (ml/ kg)

Product	Pediatric Dose (ml/kg)	Typical Adult Dose
RBC	10-15 ml/ kg	1 Unit ≈ 280-300 mL
Platelets	10-15 ml/kg	1 Unit ≈ 250-350 ml
Plasma	10-15 ml/kg	3-4 Units ≈ 750-1000ml
Cryoprecipitate*	1-2 U/10 kg	Adult Pool 150-200ml

Dr. Katerina Pavenski, Massive Hemorrhage Protocols: Real World Applications



Large/Academic Hospital Setting — Adult Appendix B

NEED A MASSIVE HEMORRHAGE PROTOCOL?

NO — NOT YET
1. ORDER 4 UNCROSSMATCHED RBC
2. REASSESS NEED FOR MHP

YES — NEED IT NOW
1. MASSIVE BLOOD LOSS
2. HYPOTENSION
3. LIKELY NEED PLASMA

Or based on hospital activation criteria

ANTICOAGULATION REVERSAL	
Warfarin	PCC 2000 units IV over 10 min Vitamin K 10mg IV over 10 min
Dabigatran (Pradaxa)	Idarucizumab 5g IV over 10 min
Apixaban (Eliquis) Rivaroxaban (Xarelto) Edoxaban (Lixiana)	PCC 2000 units IV over 10 min Repeat in 1 hour if bleeding continues
Heparins	Call pharmacy for dosing of protamine

MHP COOLER DELIVERY SEQUENCE	
Cooler 1	4 units ONeg RBC for women < 45 *All others receive OPos*
Cooler 2	4 units RBC 4 plasma
Cooler 3	4 units RBC 2 plasma 4g fibrinogen concentrate
Cooler 4+	4 units RBC 2 plasma

PLATELETS order if <50 or on antiplatelets
FIBRINOGEN CONCENTRATE order 4g IV if <1.5

PATIENT STABLE AND HEMORRHAGE CONTROLLED
1. Call blood bank to turn off MHP
2. Perform bedside termination checklist
3. Inform family member and SDM of needing MHP
4. Return unused MHP components to blood bank

Laboratory transfusion triggers
(once results available or rate of bleeding controlled)

Value	Transfuse
Hgb < 80	RBCs
INR ≥ 1.8	Plasma 4 units
Fibrinogen < 1.5 *Less than 2.0 for postpartum hemorrhage	Fibrinogen concentrate 4g
Platelets < 50	Platelets 1 adult dose
Ionized calcium < 1.15	$CaCl_2$ 1g

If available, ROTEM triggers

Value	Transfuse
EXTEM CT > 80	Plasma 4 units
EXTEM A10 < 35	Platelets 1 adult dose
FIBTEM A10 < 8-10	Fibrinogen concentrate 4g

CALL XXXX: INITIATE CODE TRANSFUSION
1. Control rapidly bleeding site (tourniquet)
2. IV/IO access
3. Tranexamic acid total dose of 2g IV / IO
4. 4U RBCs with rapid infuser
5. Limit use of crystalloids
6. Calcium chloride 1g IV
7. Keep patient temperature above 36°C
8. Obtain MHP blood work
9. Reverse anticoagulation
10. Call for definitive bleeding control (OR, angio, endoscopy)

EVERY HOUR REASSESS
1. **Can MHP be turned off?**
   Can laboratory guided transfusion be used instead?
   Is bleeding controlled?
   Stable hemodynamics?
2. Do we need to call for the next cooler?
3. Patient temperature >36°C
4. Collect q1h blood work
5. $CaCl_2$ 1g IV for every 4 RBC or ionized calcium < 1.15
6. Monitor for complications (hyperkalemia, volume overload)
7. Is resuscitation adequate? (hemodynamics, lactate, VBG)
8. Switch to group specific blood products, when able