11.0 TRANSFUSION MEDICINE / COAGULATION LABORATORY

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The Transfusion Medicine and Coagulation laboratory section will address the following recommendation statements: 27-37.

The MHP will ensure immediate notification to laboratories of an MHP activation. Uncrossmatched red blood cells shall be available at the bedside not more than 10 minutes after MHP activation and used until group-specific red blood cells are available. There shall be an uninterrupted supply of blood components to the bedside and the components shall be supplied in a validated container. The MHP will define the proportionate issue of blood components, blood products and the management of anticoagulant agent reversal.

11.1 Transfusion Medicine Responsibilities During MHP

TML should initiate internal protocols in consultation with the physician on call. The lab will follow internal blood selection, crossmatching and emergency release policies as they pertain to the MHP.

- Uncrossmatched red blood cells shall be available at the bedside within 10 minutes of MHP activation and be transfused until crossmatch compatible red blood cells are available.
- Laboratory staff will prepare all required products on a “STAT” basis to support patient clinical condition and to maintain product level ordered and dispensed.
- Communication between the TML and the MHP Team/Nurse Leader is paramount. The TML will notify the MHP Leader when blood products and components are ready, so the dedicated porter can be dispatched. They should also communicate MHP status updates to the other laboratory staff as needed to assess workload and inventory needs.
- TML should work to identify MHP patient identity as soon as possible to check for current specimens and confirm patient crossmatch history, including blood group, to support the MHP.
- The TML will continually “stay ahead” by preparing additional products so that the next pack of products is always ready.
- MHP remains in effect until deactivation has been initiated. Reassessment of need to continue with MHP should be done after each pack by the clinical team.

Preparing Blood and Components for Issue
Standard approach (Larger Community and Teaching Hospitals)

Table 1: Transfusion Packs for Adults with Massive Hemorrhage: Standard Approach

	**Pack 1:** 4 Red Blood Cells (RBCs). If the MHP patient is any aged male or female not of childbearing potential (<45), O Positive RBCs should be issued.
	**Pack 2:** 4 RBCs, 4 Frozen Plasma (FP).
	**Pack 3:** 4 RBCs, 2 FP and 4g of Fibrinogen Concentrates (FCs).
	**Pack 4 and beyond:** includes 4 units of RBC and 2 units of FP. Lab values should now be used to guide transfusion at this point.

Platelets: when stocked in the hospital transfusion laboratory, should be transfused based on the platelet count.

Fibrinogen Concentrates: transfuse 4g if Fibrinogen is <1.5g/L
*Less than 2.0g/L for postpartum hemorrhage.

Modified approach for smaller hospitals without the ability to provide plasma

Physicians should consider transferring the patient to a hospital capable of definitive hemorrhage control first. Then follow the transfusion protocol below:

Table 2: Transfusion Packs for Adults with Massive Hemorrhage: Modified Approach for TMLs that can't provide plasma

	**Pack 1:** 4 Red Blood Cells (RBCs). If the MHP patient is any aged male or female not of childbearing potential (<45), O Positive RBCs should be issued.
	**Pack 2:** 4 RBCs, 2000 IU Prothrombin Complex Concentrates (PCCs), 4g of Fibrinogen Concentrates (FCs).

If transfer is not possible then continue with the following:

	**Pack 3:** 4 RBCs, 2000 IU PCCs and 4g of FC.

Platelets: when not stocked in the hospital transfusion laboratory, should be ordered in for transfusion only if patient cannot be transferred out and will be used. If the patient is transferred out before platelets transfused, this should be communicated to the receiving hospital.

11.1.2 Inventory Management

The recommendations for the MHP state that patients should be switched to ABO group specific red blood cells as soon as is feasible to conserve group O red blood cells. A second sample must be obtained to confirm the patient's ABO group before ABO group specific red cells can be issued[1].

Communication should be maintained between the TML and the Team Leader to determine the extent of products needed (dependent upon patient condition) throughout the MHP transfusion event. The TML will execute defined protocols to obtain additional blood products from nearby area hospitals and/or CBS if stocks fall below minimum inventory level. When platelets are ordered in for patients but not transfused before patient transfer, then consider sending platelets with the patient.

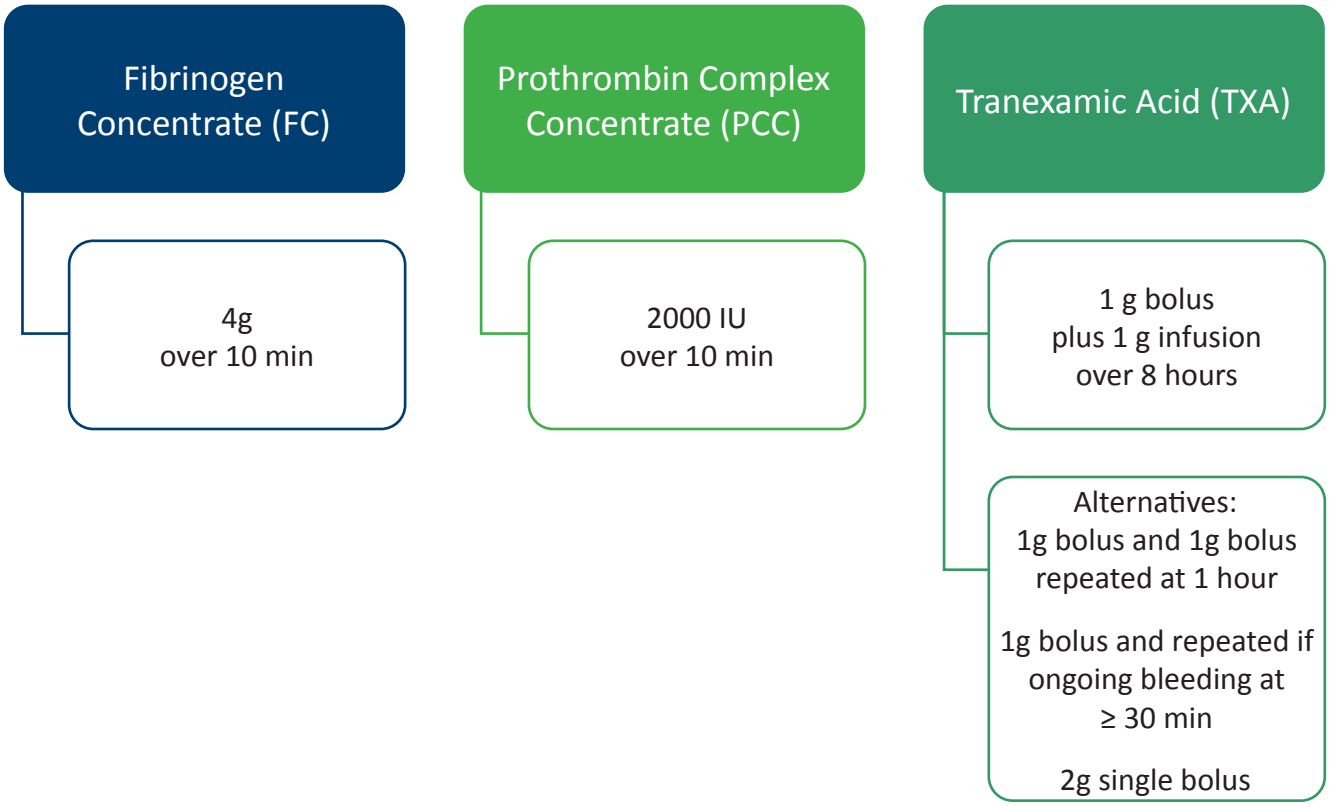
11.2 Coagulation

Patients who present with or are at risk of massively bleeding may be on anticoagulants that need to be reversed immediately. Refer to table 3 for reversal agents.

Managing Coagulopathy in the Massively Hemorrhaging Patient

Management of coagulopathy in the massively hemorrhaging patient is multifactorial and includes blood product support, administration of hemostatic agents (e.g., TXA), temperature control, acid-base management, and reversal of anticoagulant and antiplatelet agents.

Figure 1: Hemostatic Agent Dosing



Anticoagulant Reversal in the Massively Bleeding Patient

Table 3: Anticoagulant and Antiplatelet Agent Dosing

Anticoagulant	Recommended Reversal
Warfarin	Prothrombin complex concentrate PCC (Octaplex® or Beriplex®) 2000 units IV over 10 min Vitamin K 10 mg IV over 10 min
Dabigatran (Pradaxa®)	Idarucizumab (Praxbind®) 2.5g IV twice (total = 5g) over 10 min
Rivaroxaban (Xarelto®) Apixaban (Eliquis®) Edoxaban (Lixiana®)	Prothrombin complex concentrates (Octaplex ®or Beriplex®) 2000 units IV over 10 min Repeat at 1 hour if still bleeding
Heparin	**Unfractionated Heparin (UFH)** Protamine 1 mg per 100 units of UFH administered within past 4 hours 25mg IV of Protamine will reverse heparin infusions running at a rate of approx. 1,500 units/hour **Low Molecular Weight Heparin (LMWH)** If administered within 8 hours: 1 mg of protamine per 100 units anti-Xa or 1mg per 1mg of enoxaparin If administered more than 8 hours ago: 0.5 mg of protamine per 100 units anti-Xa or 0.5 mg per 1mg of enoxaparin

When antiplatelet agents (including aspirin, $P2Y_{12}$ inhibitors, and GPIIb/IIIa antagonists) are present in the setting of a massive hemorrhage, it is unclear if empiric platelet transfusions are consistently beneficial and potentially may be harmful.

The antiplatelet effects of aspirin and clopidogrel can be at least partially reversed with platelet transfusions. Meanwhile, platelet transfusions appear less effective for ticagrelor reversal, as the drug and its active metabolite have a longer half life.

The decision to transfuse platelets in these patients should be individualized according to specific patient factors and the judgment of the treating clinician.

CAUTION:

A. Factor VIIa is not recommended in the case of patients with hypothermia, arterial pH less than 7, or known history of prior venous or arterial thrombotic event. In addition, strong evidence of efficacy of Factor VIIa in off-label use is lacking.

B. Prothrombin Complex Concentrate - No contraindications listed. Risk of thrombosis and DIC. No documented efficacy in the absence of pre-existing coagulopathy or INR values less than 1.5

C. TXA - contraindications include acquired defective color vision, patients with subarachnoid hemorrhage, patients with active intravascular clotting and patients with hypersensitivity to TXA or any of the ingredients.

For centers that don't normally stock idarucizumab or PCCs, the best option for a bleeding patient on anticoagulants is early transfer.

More information can be found at Thrombosis Canada at https://thrombosiscanada.ca/clinicalguides.

11.3 Approaching Patients with Bleeding Disorders with Massive Hemorrhage

Physicians should suspect that the bleeding patient may have a bleeding disorder when

- Bleeding is not in keeping with severity of injury
- Patient is not on antithrombotic therapy
- There is a history of abnormal bleeding

Healthcare professionals should look for a medical alert bracelet/tag and/or a bleeding disorder card. If a bleeding disorder is suspected, they should immediately contact the nearest Hemophilia treatment centre (HTC).

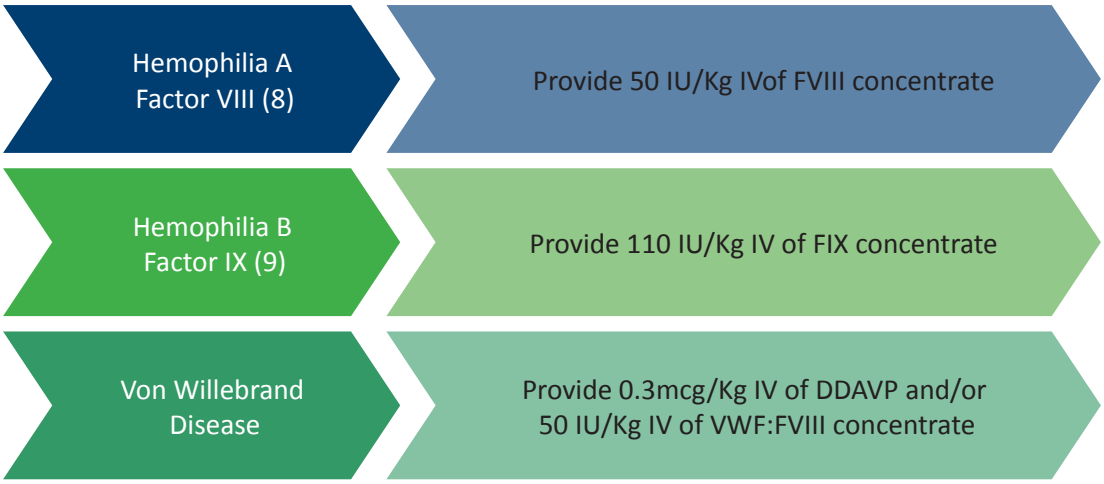
Pediatric

Please refer to Pediatric appendices for pediatric MHP blood product, factor concentrate and associated drug dosing including TXA. As current administration of non-vitamin K antagonist direct oral anticoagulants (DOACs) in children is rare, only reversal strategies for warfarin and heparin are provided. Similar to adult bleeding patients in need of red blood cell transfusion, children can be transfused group O uncrossmatched red blood cells until group specific crossmatch compatible blood cells are available. There is no threshold volume of group O red cells above which a switch to group specific red blood cells is prohibited.

Hemophilia Treatment Centres in Ontario	
Hamilton Health Sciences	Health Sciences North (Sudbury)
London Health Sciences	St. Michael's Hospital (Toronto)
Thunder Bay Regional Health Sciences Centre	Sick Kids (Toronto)
Kingston Health Sciences Centre	The Ottawa Hospital
Children's Hospital of Eastern Ontario (Ottawa)	

It is recommended that replacement therapy be given immediately for obvious or suspected bleeding or major trauma. Treat first and then investigate.

Figure 2: Replacement Therapy for the Bleeding Disorder Patients with a Massive Hemorrhage



More information can be found at www.hemophilia.ca.

References

1. Canadian Standards Association. CSA-Z902-20 Blood and Blood Components. 2020. 10.6.1.3.