



EM CASES SUMMARY

Episode 152 The 7 Ts of Massive Hemorrhage Protocols

With Drs. Jeannie Callum, Andrew Petrosoniak & Barbara Haas

Prepared by Saswat Deb & Priyank Bhatnagar, edited by Anton Helman, February 2021

When a patient is exsanguinating, having a standardized massive hemorrhage protocol (MHP) enables rapid and coordinated delivery of life-saving blood products, medications. *Every one-minute delay in receiving the first pack red blood cells (pRBC) in a bleeding trauma patient is associated with a 5% increase in mortality.*

Why Massive Hemorrhage Protocol instead of Massive Transfusion Protocol?

The classic definition of massive transfusion protocol is 10 units of pRBC over 24 hours and only focuses on the number of blood products transfused. Instead, the **emphasis should be placed on hemorrhage control** which not only includes transfusions, but

also monitoring blood work/considering targets, administration of other medications including tranexamic acid, keeping the patient warm and source control of the bleeding.

The 7 Ts of Massive Hemorrhage Protocols: Trigger, Team, Testing, TXA, Temperature, Target, Termination

Trigger: indications for MHP prehospital, at initial ED assessment and during resuscitation

The decision to active a MHP should be guided by clinical judgement, decision tools and response to treatment.

Prehospital indications for MHP include a concerning mechanism of injury (eg., fall from ≥ 3 stories) and/or a shock index ≥ 1 .

Initial ED assessment indications for MHP include clinical judgement incorporating clinical decision tools, resuscitation intensity and pitfall conditions.

1. **Clinical judgement** (obvious shock state or else incorporating *shock index* >1 , *delta shock index* ≥ 0.1 , *RABT Score* ≥ 2 , AND
2. **Pitfall conditions** – consider a lower threshold for activating MHP
 - o Older
 - o On anticoagulants or dual anti-platelet therapy – patients taking anticoagulants are not well

- represented in MHP studies; have a lower threshold for calling for blood
- Medications that may blunt hemodynamic parameters despite bleeding out (ie., beta-blockers)

Indications for MHP during resuscitation include [resuscitation intensity](#) (see below) or requiring >2u pRBCs

The Revised Assessment of Bleeding and Transfusion (RABT) Score – 1 point each

1. Shock index > 1.0
2. Pelvic Fracture
3. Positive FAST
4. Penetrating Injury

A 2018 study showed that RABT score ≥ 2 performed better than ABC score in predicting need for MHP.

Resuscitation intensity to help guide the decision to activate a MHP

If hemorrhagic shock is not obvious clinically, consider the resuscitation intensity: patients who **require 3 units of any combination of crystalloids or blood** products to maintain adequate perfusion are considered to have high resuscitation intensity which predicts higher mortality, and should be considered for activation of the MHP.

2:1:1 or 1:1:1 blood product ratio?

Our experts recommend a 2:1:1 ratio of blood products based on their interpretation of the PROPPR trial which found that

among patients with severe trauma and major bleeding there was no significant difference in 24hr or 30 day mortality in patients who received a 1:1:1 ratio compared to a 2:1:1 ratio, and because of practical considerations that allow faster administration of blood products using the 2:1:1 ratio. They therefore recommend:

- The first case of blood products should contain 4 units uncrossmatched pRBCs, be at the bedside in under 10 minutes, and IV running via rapid transfuser shortly thereafter
- Then the next case of blood products contains 4 RBC and 4 plasma (FFP) which should run simultaneously

“European” Fibrinogen +/- PCCs up front vs “North American” plasma strategy

Using fibrinogen concentrates with or without PCCs up front in the hemorrhaging trauma patient is common in many European countries. The small randomized studies suggest that this strategy is at least as good as the classic North American plasma strategy at 1:1. There are some benefits to the concentrate strategy – you can keep these products at room temperature in a near patient location, a blood group is not necessary, it avoids the need for AB plasma that is often in short supply, they are pathogen-reduced, small volumes, injected over minutes, and fibrinogen/PCCs do not cause transfusion related acute lung injury [TRALI](#).

Optimal threshold for replacement of fibrinogen?

There are only a few small poorly controlled studies that compare low vs. high threshold of fibrinogen level for controlling blood loss. The studies do suggest higher might be better. Guidelines recommend a **fibrinogen threshold for transfusion of fibrinogen or cryoprecipitate of <1.5-2.0 g/L.**

Team: prepare your gear, yourself and your team

Early **notification** and **preparation** of the extended team, including the ED team, laboratory team, blood bank and surgical team is essential to ensure rapid delivery of blood products and bleeding source control. Based on the limited data you gather from EMS, brief the ED team, prioritizing objectives (e.g. may require tourniquet before securing airway, priority to administer blood products) and adapt a [shared mental model](#). Team members should have roles assigned including which gear they each need to get to the bedside before the patient arrives, if time permits.

Testing: initial baseline tests and repeated testing

Having a **standardized order set** for laboratory investigations in MHP can help reducing cognitive burden and prevent missed diagnoses of coagulopathy or metabolic dysfunction in hemorrhage.

Initial baseline tests: CBC, coags (INR, PTT, fibrinogen), electrolytes (including calcium), VBG, lactate +/- BhCG

Q1h tests: Hb, INR, lactate, VBG, fibrinogen

Calcium plays an important role in regulating coagulation and hemostasis. The citrate preservative in blood products binds to serum calcium making it inactive. It is thus vital to monitor serum calcium and to consider administering calcium every 3 to 4 blood products that are administered.

Fibrinogen is often forgotten in lab orders and is impacted by both coagulopathy of trauma and dilution from administered blood products. It requires careful monitoring and replacement with cryoprecipitate or fibrinogen concentrate.

A high **INR** has been shown to predict poor outcomes for massively hemorrhaging patients and correcting it with FFP +/- PCCs (see below) is vital. It should also be used to assess the trajectory of the resuscitation and should be checked every hour or every 3 to 4 units of pRBCs along with Hb, fibrinogen and lactate.

PTT is a one-time screening test – no need for repeating. A single measurement of PTT early in the resuscitation helps screen for congenital bleeding disorders or on-board anticoagulants, such as DOACs, that may need to be co-managed.

***Pitfall:** Calcium and fibrinogen are the blood tests that are most often forgotten in severely hemorrhaging patients; use a checklist/order set that includes these to avoid this pitfall*

Tranexamic Acid (TXA) indications, contraindications and dosing

The decision to give TXA should be made at the same time as the decision to give blood products in the hemorrhaging trauma patient – early!

Our experts recommend TXA for all trauma patients in whom you suspect life-threatening hemorrhage within 3 hours of the time of injury who are receiving blood products for hemorrhaging, and in patients with initial SBP<90 or HR >110 based on the CRASH-2 trial. Give TXA ASAP – observational data suggests that every 15 min delay decreases its mortality benefit by 10%.

For isolated head injured patients the CRASH-3 trial did not show a clinically significant benefit for early administration of TXA.

Relative contraindications to TXA

- History of coronary stent(s)
- Active hematuria (it is thought that administration of TXA in the patient with hematuria may cause clot formation resulting in obstructive uropathy)
- History of venous thromboembolic disease

Pitfall: TXA is sometimes forgotten; if you are transferring a patient to a trauma center with concern for active hemorrhage, be sure to administer TXA prior to transport within 3 hours of the time of injury (the earlier the better).

TXA dosing

Observational data suggests that about 50% of the time the second bolus or infusion of TXA after the initial 1g bolus is not given at all in trauma patients, likely because the infusion is associated with logistical problems of requiring a dedicated IV. Some patients will not be adequately reversed with 1g alone.

Our experts recommend a **one-time 2g IV dose up front** to ensure all patients receive an adequate dose of TXA.

Temperature: hypothermia increases mortality in trauma patients

Hypothermia, which results from the trauma itself as well as the administration of blood products, is sometimes overlooked in the management of polytrauma patients. Hypothermic patients have poor outcomes because of the negative effects of hypothermia on coagulation. It is important to employ early temperature measurement in a systematic way by incorporating it into a trauma checklist and repeating the measurement q1h, or more frequently if the patient was initially hypothermic. Simple methods to keep the patient warm include removing wet clothing, placing warm blankets, administering warmed IV products and monitoring temperature q1h and more often in patients who present hypothermic.


Targets: clinical, hematologic and metabolic resuscitation targets

There are clinical and laboratory resuscitation targets that should be used to help monitor patient stability, response to resuscitation efforts and for prognostication. Laboratory targets are more important to assess trajectory of MHP and other resuscitation efforts rather than initial assessment and can be divided into hematologic and metabolic.

Clinical targets to consider include HR <100, MAP >55-70 (depending on baseline BP) GCS >15 (if no head injury/intoxication), urine output >30mL/hr and normal [IVC diameter/collapsibility](#)

Hematologic	Metabolic
Hgb >80	pH >7.3
Plt 50*	Lactate <4
INR 1.8	Ca _i >1.15
Fibrinogen 1.5-2	

*In head injury target Plt 100



Hematologic and metabolic targets in trauma patients in whom a massive hemorrhage protocol has been activated

Termination of MHP

The decision to stop a MHP is nuanced and based on hemodynamics and resuscitation targets outlined above. It is important to involve both the ED and inpatient teams in the decision to terminate MHP to avoid a second wave of bleeding and instability. Ideally, MHP termination conversations should happen when both patient hemodynamics and resuscitation targets are normalized or at least trending in the right direction.

General requirements for termination of MHP include

1. Normalizing hematologic and metabolic targets
2. Normalizing hemodynamic parameters

Pitfall: take care to avoid the common pitfall of premature MHP termination; significant trauma may cause peri-trauma vasoplegia despite appropriate resuscitation

Special Considerations in Massive Hemorrhage Protocols

Smaller hospitals with challenging access to blood products

In rural/remote hospital settings where blood products may not be available, the use of prothrombin concentrate complex (PCCs) and fibrinogen should be considered. In most European centres, red cells along with fibrinogen with or without PCC (instead of FFP and platelets) have become common practice (see above).

While there are multiple benefits of the concentrate strategy (can be stored at room temperature, not requiring a blood group, pathogen-reduced, small volumes, injected over minutes, and avoids TRALI reactions), the benefits have only been shown in small studies. Large trials are required to further corroborate these findings.

Life threatening hemorrhage on warfarin

If the patient is known to be taking warfarin and has *imminent life-threatening bleeding* and a MHP is being activated, our experts recommend **both FFP at a minimum ratio of 1:2 and 2000 International Units (IU) PCC**, along with **vitamin K 10mg** to ensure sustained reversal in 6 hours after the PCCs wear off. It is not necessary to wait for the INR result before administering PCCs in this context.

***Pearl:** some patients who have a very high INR and/or morbid obesity, or have continued significant bleeding 1hr after the first dose may require a 2nd dose of PCC 2000 IU 1hr later, preferably in consultation with a hematologist*

Life threatening hemorrhage on Direct Oral Anticoagulants (DOACs)

While the evidence is weak with respect to clinical benefit, an acceptable regimen in the trauma patient with life threatening bleeding who has taken a DOAC within 12 hours, in whom a MHP has been activated is:

- For a patient on Dabigatran consider Idarucizumab 5g

- For a patient on a Xa inhibitor (eg., apixaban, rivaroxaban), PCC 2000 IU; if significant bleeding persists after 1 hour, a second dose of 2000 IU of PCC should be considered; while not approved in Canada, a specific antidote to Xa inhibitors, Andexanet alfa, has also been used in these situations as a continuous infusion.

Life threatening hemorrhage in obstetrical patients

Observational data has shown that a fibrinogen level below 2g/L leads to worse outcomes including maternal death, in the bleeding obstetrical patient. Our experts recommend **IV fibrinogen concentrate 4g or cryoprecipitate 10 units**, as soon as possible and then check the fibrinogen level to ensure it is >2g/L. Replacement of fibrinogen may decrease both the need for ongoing blood transfusions and associated complications such as volume overload.

***Pearl:** pregnant and postpartum patients who are hemorrhaging tend to have low fibrinogen with an increased risk for DIC, so have a low threshold to give fibrinogen in the massively hemorrhaging obstetrical patient.*

***Beware:** Blood transfusions are not benign – consider them like an organ transplant; female patients of childbearing age should receive O-negative pRBCs until crossmatch is obtained; they should also be counselled to have a group and screen completed 3 to 6 months post-transfusion due to associated alloimmunization risks.*

Blood product stewardship: practical methods to prevent wastage

Blood products are a limited resource in hospitals that require careful utilization in appropriate clinical indications. Methods to prevent blood product wastage are:

- Ensure indication for MHP is met; for example, a patient who requires transfusion of only 2 units of red cells to reach clinical and lab targets does not require ongoing MHP which included FFP and platelets
- Return unused blood products in the same package configuration within the container as they came from the blood bank to prevent damage from improper storage
- Unused blood products must be returned within 60 minutes to prevent wastage
- Do not write on the blood product package labels as this would render the product unusable if returned
- Do not return empty blood product packages with unused products as this produces risk of contamination and safety hazards for blood bank technicians

Take Home Points for the 7 Ts of Massive Hemorrhage Protocols

- Have a formalized MHP in your institution and between institutions so that bleeding patients receive state-of-the-art standardized care irrespective of which institution they are in
- Time is life! Every one-minute delay in receiving the first pRBC is associated with a 5% increase in mortality

- Trigger for MHP should take into account **clinical judgement** based on obvious shock state, *shock index* >1, *delta shock index* ≥0.1, *RABT Score* ≥2, *resuscitation intensity*), **mechanism of injury** and **pitfall conditions** (older, anticoagulants, certain drugs that alter vital signs)
- Both FFP and PCC along with vitamin K are sometimes required to reverse INR in a patient on warfarin with life-threatening hemorrhage, and repeat dosing of PCC in 1hr should be considered for patients with very high INR, morbidly obese patients and those with significant continued bleeding
- Fibrinogen is the first coagulation factor to drop in trauma and needs to be replaced and measured to assess trajectory
- Pregnant and postpartum patients who are hemorrhaging tend to have low fibrinogen with an increased risk for DIC, so have a low threshold to give fibrinogen in the massively hemorrhaging obstetrical patient
- Patients in whom a MHP is activated tend to develop hypocalcemia; it is important to monitor serum calcium levels and replace calcium accordingly
- Do not neglect to keep the patient warm by monitoring temperature, removing wet clothing, using warm blankets and warmed IV products
- TXA administered within 3 hours of injury has a significant mortality benefit – be sure to give it prior to transfer to a trauma center (the earlier the better)
- Termination of MHP is a shared decision amongst the ED and inpatient teams and should take into account both clinical and laboratory targets, taking care not to prematurely terminate the MHP (which can lead to a second wave of hemorrhage and instability)
- There are easy ways to prevent blood product wastage so that those blood products can be used to save more lives

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