



Dr. Jeannie Callum, Massive Hemorrhage: Pathophysiology & Evidence Based Management

Summary

Massive Hemorrhage Protocols are designed to ensure every patient receives coordinated, standardized and evidence-based care. The protocol should be activated promptly when faced with a massively bleeding patient – every 1 minute delay to the first RBC is associated with a 5% increase in mortality. But on the flip-side, activation is not required for every bleeding patient. Activation results in deployment of portering, critical care, and laboratory resources. Over-activation will result in unnecessary blood product wastage. Activate the protocol when faced with a patient with a critical injury (high speed collision, penetrating trauma, post-partum hemorrhage) and with marked hemodynamic instability. Most gastrointestinal hemorrhages can be managed with a call to the blood bank for uncrossmatched red blood cells. The protocol should be activated through a coordinated communication process similar to other patient emergencies. Once the trained team has been assembled, a physician lead should be explicitly designated and a communication lead designated (to coordinate care with portering and the laboratory). Once activated, the system should be fast enough to ensure the first red cell is commenced within 15 minutes. Tranexamic acid should be administered within 60 minutes of injury/activation, with the exception of gastrointestinal hemorrhage where it has been proven to be ineffective (and increases thromboembolic complications). Tranexamic acid is of no value after 3 hours. Blood work should be done at baseline and then every 1 hour and/or 4 units of red cells. Wherever possible, transfusions should be guided by the results of laboratory testing. Use blood warmers and active warming blankets to maintain patient temperature over 36°C at all times. Monitor the temperature either continuously or at a minimum of every 30 minutes. Terminate the protocol when hemorrhage control has been achieved, hemodynamics are improving, coagulation tests are trending in the right direction, and the rate of transfusion has slowed. Ensure blood is packed as delivered by the blood bank throughout resuscitation and return all blood products promptly as soon as they are no longer needed.

Objectives

1. Explain the coagulation derangement seen with acute coagulopathy of trauma
2. Understand the key components of a Massive Hemorrhage Protocol
3. Review the science behind how we manage hemorrhaging patients



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

<https://transfusionontario.org/en/provincial-massive-hemorrhage-toolkit/>

Large/Academic Hospital Setting Adult Appendix B

NEED A MASSIVE HEMORRHAGE PROTOCOL?

NO NOT YET

- ORDER 4 UNCROSSMATCHED RBC
- REASSESS NEED FOR MHP

YES NEED IT NOW

- MASSIVE BLOOD LOSS
- HYPOTENSION
- 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 <i>All others receive OPos</i>
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

- Deactivate as per local policy
- Perform bedside termination checklist
- Inform family member and SDM of needing MHP
- 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 <small>*Less than 2.0 for postpartum hemorrhage</small>	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**

- Control rapidly bleeding site (tourniquet)
- IV/IO access
- Tranexamic acid total dose of 2g IV / IO
- 4U RBCs with rapid infuser
- Limit use of crystalloids
- Calcium chloride 1g IV
- Keep patient temperature above 36°C
- Obtain MHP blood work
- Reverse anticoagulation
- Call for definitive bleeding control (OR, angio, endoscopy)

EVERY HOUR REASSESS

- Can MHP be turned off?
Can laboratory guided transfusion be used instead?
Is bleeding controlled?
Stable hemodynamics?
- Do we need to call for the next cooler?
- Patient temperature >36°C
- Collect q1h blood work
- CaCl₂ 1g IV for every 4 RBC or ionized calcium < 1.15
- Monitor for complications (hyperkalemia, volume overload)
- Is resuscitation adequate? (hemodynamics, lactate, VBG)
- Switch to group specific blood products, when able



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Dr. Justyna Bartoszko, Albumin

Disclaimer: This evidence may be low quality and does not replace clinical judgement

LIVER PATIENTS

- **Spontaneous bacterial peritonitis** - 25% albumin 1.5 g/kg within 6 hours of diagnosis, then 1 g/kg on day 3
- **Large volume paracentesis** - 25% albumin, 6-8 g for every litre removed, administer soon after procedure to avoid procedural complications (hypovolemia, hyponatremia, renal impairment)
- **Acute Onset Hepatorenal syndrome Type 1** – If eligible for liver transplant, 25% Albumin 1 g/kg on Day 1, 100-200 ml on days 2-14

SPECIAL POPULATIONS

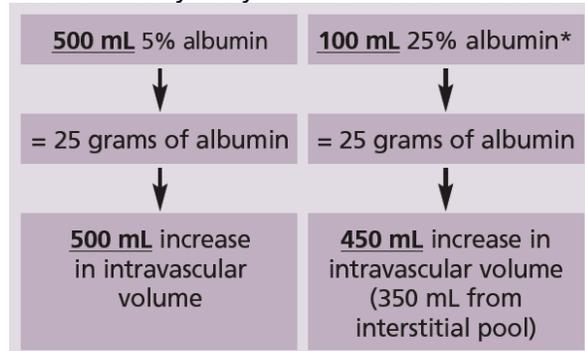
- **Ovarian Hyperstimulation Syndrome** – Treatment, not prevention. 25% albumin, 50-100 g over 4 hours, q4-12 h prn
- **Plasma exchange** - 5 % albumin, titrated to plasma volume removed
- **Burns > 50% TBSA** – In general poor quality evidence supporting use and not routinely recommended. Historically was used if unresponsive to crystalloid, 5% albumin at 0.3-0.5 ml/kg/BSA (50-100 mL/hour).

Table 1. Reported Characteristics of Colloids (Albumin) vs. Balanced Crystalloids

Characteristics	Balanced Crystalloid Solution (Plasmatyte-148)	Albumin (5% or 25% Albumin)
Approximate Cost	\$2 per 1 L	\$62 per dose (25% 100 ml or 5% 500 ml)
Typical <i>in vitro</i> pH	4-6.5	6.4-7.4
Typical constituents	Sodium: 140 mEq/L Potassium: 5 mEq/L Chloride: 148 mEq/L Magnesium: 3 mEq/L Acetate: 27 mEq/L Gluconate: 23 mEq/L	Sodium: 130-160 mEq/L Chloride: 109-137 mEq/L
Oncotic Pressure Effects	Lower, with intravascular and interstitial fluid replacement effect but potential for protein dilution and greater peripheral edema	Higher, allowing for translocation of interstitial fluid into plasma volume. Less peripheral edema but potential for pulmonary edema in capillary leak states and excessive intravascular volume expansion with mobilization of fluid intravascularly.
Plasma Volume Expanding Effect	Variable depending on serum oncotic pressure	450 ml per 25 g dose
Perceived Effect on Fluid Balance	Greater interstitial edema and higher cumulative fluid balance	Lower interstitial edema and lower cumulative fluid balance
Perceived Hemodynamic Effect	Shorter lived increase in plasma volume	Sustained increase in plasma volume (likely less in critically ill patients)

Figure 1. Intravascular Volume Expansion Effect by Albumin Formulation

Source: *Bloody Easy For HealthCare Professionals*, 4th edition (new version coming soon)



Dr. Aditi Khandelwal, New Updates in Transfusion

Topic	Summary	References
Pooled pathogen reduced buffy coat platelets (PPPT)	<p>Pathogen reduced platelets (PPPT) available in Ontario</p> <p>PPPT effectively reduces transfusion transmitted infections – viruses, bacteria, T cells, protozoa parasites</p> <p>Psoralen treatment (INTERCEPT technology) is being used</p> <p>Instead of 4 for pooled platelets, 7 buffy coats are being pooled for PPPT then treated</p> <p>Shelf-life is 5 days</p> <p>Less donor plasma is present in each bag</p> <p>No viable lymphocytes, hence no irradiation required</p> <p>Considered CMV negative</p> <p>Fewer allergic and febrile reactions</p> <p>Main concern – non-immune platelet refractoriness in chronically transfused populations</p>	<p>Blais-Normandin I, Tordon B, Anani W. Pathogen-reduced buffy coat platelets [Internet]. Ottawa: Canadian Blood Services; 2022 [cited 2022 05 10]. Available from: https://profedu.blood.ca/en/transfusion/publications/pathogen-reduced-buffy-coat-platelets</p>
Tranexamic Acid (TXA) Updates – Is there an increase in CV/VTE risk?	<p>NEJM 2022</p> <p>P: N=9535 undergoing non-cardiac surgery</p> <p>I: TXA 1g bolus</p> <p>C: placebo</p> <p>O: TXA is superior to placebo in reducing bleeding (HR 0.76). <i>Non-inferiority for CV/VTE safety outcomes was not established (TXA group 14.2% vs. Placebo 13.9%)</i></p> <p>JAMA Surg 2021</p> <p>Syst review and meta-analysis with N=125550 surgical pts</p> <p>IV TXA vs. Placebo/no treatment</p> <p>No increase in TE events</p>	<p>Devereaux PJ et al. Tranexamic acid in patients undergoing noncardiac surgery. NEJM 2022 Apr 2. doi: 10.1056/NEJMoa2201171. Online ahead of print.</p> <p>Taeber I et al. Association of intravenous tranxamic acid with thromboembolic events and mortality. JAMA Surg. 2021;156(6)e210884</p>
Wrong blood in tube errors (WBIT)	<p>ABO mistransfusions can occur due to WBIT</p> <p>WBIT is detected ~ 1 in 10,000 samples</p> <p>WBIT are either:</p> <ul style="list-style-type: none"> - Intended patient + wrong label (~50%) - Wrong patient + intended label (~50%) <p>WBIT occur more frequently in EDs > inpatient wards > outpatient wards</p> <p>Most commonly, WBIT is identified during pre-transfusion testing (58%) and check sample (20%)</p> <p>Most common source of error is availability of another patient's labels or tubes when phlebotomy is being performed</p> <p>Electronic positive patient identification has not eliminated WBIT</p> <p>WBIT is preventable if all protocols/policies are followed</p>	<p>Dunbar NM et al. Factors associated with wrong blood in tube errors: An international case series – The BEST collaborative study. Transfusion 2022;62:44-50.</p> <p>Dunbar NM et al. Emergency departments are higher risk locations for wrong blood in tube errors. Transfusion 2021;61:2601-2610.</p>