MASSIVE TRANSFUSION PROTOCOLS

EMILY ANTES RN, BSN, CCRN, EMT-B
DEFINITION OF MASSIVE TRANSFUSION

Most Commonly Accepted Definition of Mass Transfusion:

- Transfusion of $\geq 10$ units of RBCs in 24 hours.\(^6\)

Other Accepted Definitions of Massive Transfusion:

- Loss (and replacement) of one blood volume in a 70 kg pt.\(^6\)
- Transfusion of the total estimated blood volume in less than 24 hours.\(^2\)
- Transfusion of $\frac{1}{2}$ the total estimated blood volume in 1 hour.\(^2\)

https://thetraumapro.com/2017
CAUSES OF MASSIVE TRANSFUSION

- Cardiac Surgery
- Trauma
- Obstetric Hemorrhage
- Aortic Aneurysm Rupture
- Surgical Bleeding
- GI Bleeding

https://dailytimes.com
WHY USE A MASSIVE TRANSFUSION PROTOCOL?

• Massive Transfusion Protocols optimize & standardize the process of massive transfusion.\(^7\)
• Improves patient outcomes.\(^7\)
  – ↓ 24-hour and 30-day mortality\(^7\)
• Earlier delivery of components\(^2\)
• ↓ Intra-operative crystalloids\(^7\)
• ↓ Post-operative transfusion requirements\(^7\)
MTPs were developed for the resuscitation of hemorrhage in trauma patients.
  – Specifically in the military.
• Current recommendations are based on research primarily done on trauma patients.
• Clinically starting to apply these recommendations in non-trauma settings (OR/surgical & OB) although there is not an abundance of research/evidence on MTP outcomes in these areas.10
  – Anybody looking for a DNP project 😊
ABCD OF MASSIVE TRANSFUSION

- **A** → Activation
- **B** → Blood Components
- **C** → Complications
- **D** → Discontinuation & Drugs
ACTIVATION
ACTIVATION OF MASSIVE TRANSFUSION PROTOCOL

• Most sources advocate the use of an algorithm for initiation of MTP.

• Scoring Systems & Tools (Primarily Based on Trauma Patients).
  – *Assessment of Blood Consumption (ABC)*
    • 4 components, each component met receives 1 point.
      – 1. Penetrating trauma,
      – 2. SBP ≤90 mmHg,
      – 3. HR ≥120,
      – 4. + FAST exam.
    • *Score of ≥2 = likely MT.*
ACTIVATION OF MASSIVE TRANSFUSION PROTOCOL

• Research
  – Study by Hsu et al. (2013)\textsuperscript{10}
    • Base deficit $\geq 5$, INR $\geq 1.5$, & Hemoperitoneum at laparotomy as the most significant predictors of MT.
  – Study by Callcut et al. (2013)\textsuperscript{10}
    • Transfusion Triggers $\rightarrow$ INR $>1.5$, SBP $<90$ mmHg, Hgb $<11$ g/dL, base deficit $\geq 6$, positive FAST, HR $\geq 120$ bpm.
    • 2 or more triggers = 85% sensitivity predicting massive transfusion.
ACTIVATION OF MASSIVE TRANSFUSION PROTOCOL

• **Massive Transfusion Score (Revised)**

  – Nearly identical to the Cincinnati Individual Transfusion Trigger
  – Components
    • SBP<90mmHg
    • Base Deficit ≥6
    • Temp<35.5 °C
    • INR>1.5
    • Hgb <11g/dL
  – Each component receives 1 point if met.
  – *In research, 82% of patients presenting w/ MTS score ≥2 received a MT w/in 24 hours.*

• Although ABC score is more widely used and a more simplistic scoring system, new research shows the Massive Transfusion Score is a better predictor for MT at 24 hours and neither scoring system was accurately predictive of MT at > 24h.
ACTIVATION OF MASSIVE TRANSFUSION PROTOCOL

• Surgical Settings
  – ≥ 4 units of PRBCs in one hour.
  – Ongoing hemorrhage (major surgical/obstetric bleeding).
  – Continued instability r/t hemorrhage.

• CLINICAL JUDGEMENT!!!!!
BLOOD COMPONENTS/TRANSFUSION

https://www.gocomics.com/
A NOTE ON TRANSFUSION COMPATIBILITY

• If you must transfuse uncrossmatched O negative Blood…..

• You have to stick with it!!!

• If a patient has received > 2 units of O negative blood, subsequent transfusion of their own blood type (A, B, or AB) may cause hemolysis.6
  – This is due to the trace amounts of Anti-A & Anti-B antibodies found in transfused type O RBCs.

• Therefore, transfusion of > 2 units of O negative uncrossmatched blood precludes the transfusion of type specific blood until Anti-A & Anti-B titers are drawn.6

• Blood bank will determine, from these titers, when the residual circulating Anti-A & Anti-B antibody levels are low enough to safely transfuse type-specific blood.6
## RED BLOOD CELLS

<table>
<thead>
<tr>
<th><strong>PACKED RED BLOOD CELLS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
</tr>
</tbody>
</table>
| **Transfusion Trigger**   | \( Hgb < 7 \text{ g/dL} \) (ASA says <8g/dL), \( Hct < 25\% \)  
  **Goal:** Hgb 7-10g/dL   |
| **Contents in 1 Unit**    | Hct 65\%, RBCs, small amounts of plasma, & WBCs. |
| **Volume of 1 Unit**      | \textit{Total Volume: 300 mL}  
  \textit{RBC Volume: 200 mL}  
  \textit{CPDA Volume: 100 mL} |
| **Effect of 1 Unit**      | ↑\textit{Hgb by 1g/dL}, ↑\textit{Hct by 3\%}  |
| **Dose**                  | \textit{Adults: Goal Directed}  
  \textit{Pediatrics: 20mL/kg} |
| **Shelf-Life**            | 35-42 days |

1. \( g/dL \) stands for grams per deciliter.
2. \( Hct \) stands for hematocrit.
3. \( CPDA \) stands for citrate, phosphate, dextrose, and adenine.
4. \( \uparrow \) indicates an increase.
5. The values are approximations and may vary.
6. The percentages are approximate and may vary.

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**CLINICIAN JUDGEMENT**
# PLASMA PRODUCTS

## FRESH FROZEN PLASMA

<table>
<thead>
<tr>
<th>Purpose</th>
<th>To replenish coagulation factors, prevention &amp; treatment of coagulopathy, and to promote hemostasis.</th>
</tr>
</thead>
</table>
| Transfusion Trigger | *PT/PTT > 1.5 x the mean control*<sup>1</sup>  
*INR > 2.0*<sup>1</sup> |
| Contents in 1 Unit | All coagulation factors & inhibitors, complement, fibrinogen, albumin, & globulins.  
<sup>6</sup> |
| Volume of 1 Unit | *Total Volume:* 250 mL |
| Effect of 1 Unit | Goal to achieve minimum 30% factor activity.<sup>1</sup>  
*Each unit increases each clotting factor 2-3%* |
| Dose | *Initial Dose:* 10-15 mL/kg.  
- Repeat dosing guided by coagulation tests (PT, INR, aPTT). |
| Shelf-Life | 1 year at -18°C & 24 hours at 1-6°C once thawed<sup>6</sup> |
PLASMA PRODUCTS

<table>
<thead>
<tr>
<th>CRYOPRECIPITATE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
</tr>
<tr>
<td><strong>Transfusion Trigger</strong></td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td><strong>Contents in 1 Unit</strong></td>
</tr>
<tr>
<td><strong>Volume of 1 Unit</strong></td>
</tr>
<tr>
<td><strong>Effect of 1 Dose</strong></td>
</tr>
<tr>
<td><strong>Dose</strong></td>
</tr>
<tr>
<td><strong>Shelf-Life</strong></td>
</tr>
</tbody>
</table>
### Table 17-5 from Barash: Indications for Platelet Transfusion

<table>
<thead>
<tr>
<th>Indication</th>
<th>Platelet Count (x10^3/μL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable patients w/o evidence of bleeding or coagulopathy</td>
<td>&lt;10,000/μL</td>
</tr>
<tr>
<td>Prophylaxis for central venous catheterization</td>
<td>&lt;20,000/μL</td>
</tr>
<tr>
<td>Prophylaxis for invasive procedure such as LP, neuraxial anesthesia, endoscopy w/ biopsy, or major non-neuraxial surgery</td>
<td>&lt;50,000/μL</td>
</tr>
<tr>
<td>Stable patients w/ clinical evidence of bleeding or coagulopathy including DIC.</td>
<td>&lt;50,000/μL</td>
</tr>
<tr>
<td>Patients undergoing massive transfusion</td>
<td>&lt;75,000-100,000/μL</td>
</tr>
<tr>
<td>Patients having surgery at critical sites (eye or CNS)</td>
<td>&lt;80,000-100,000/μL</td>
</tr>
<tr>
<td>Microvascular bleeding attributed to platelet dysfunction (uremia, liver disease, post CPB)</td>
<td>Clinician Judgment</td>
</tr>
</tbody>
</table>

*Barash: Table 17-5, Chapter 17, p. 433*
**PLATELETS**

<table>
<thead>
<tr>
<th><strong>Purpose</strong></th>
<th>To correct thrombocytopenia or impaired platelet function &amp; prevent hemorrhage. Prophylaxis to decrease bleeding during certain procedures.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transfusion Trigger</strong></td>
<td>See table in slide 16.</td>
</tr>
</tbody>
</table>
| **Contents in 1 Unit** | 1 Unit random donor platelets: $\geq 5.5 \times 10^{10}$ platelets/unit<sup>6</sup>  
1 Unit apheresis platelets: $\geq 3 \times 10^{11}$ platelets/unit<sup>6</sup> |
| **Volume of 1 Unit** | 1 Unit random donor platelets: 50 mL<sup>6</sup>  
1 Unit apheresis platelets: 300-400 mL<sup>6</sup> |
| **Effect of 1 Dose** | 1 dose of random donor platelets or 1 dose of apheresis platelets increases platelet count by 30,000-60,000 u/L<sup>1</sup> |
| **Dose** | 1 “6-pack” of random donor platelets<sup>6</sup>  
1 unit of apheresis platelets<sup>6</sup> |
| **Shelf-Life** | 5 days at 20-24°C<sup>1</sup> |
GOALS OF MASSIVE TRANSFUSION

• Improve oxygenation of tissues
• Correct hypovolemia
• Correct existing/prevent further coagulopathy
• Avoid acidosis
• Avoid hypothermia
• Avoid complications such as citrate toxicity & hyperkalemia
**TRANSFUSION RATIOS**

- This method of transfusing blood components is called *damage control resuscitation*.\(^2\)
- Products should be transfused in a 1:1:1 ratio.
- **1 Unit FFP: 1 Unit Platelets: 1 Unit PRBCs:**
  - *Note:* 1 UNIT of random donor platelets not one DOSE of platelets.
  - *Example:* 6 Units FFP: 1 platelet apheresis (1 apheresis = 6U): 6 Units PRBCs
TRANSFUSION RATIOS

• **Physiology behind the 1:1:1 Ratio**
  
  – Goal is to replicate whole blood.
  
  – When a patient requires massive transfusion they have lost a significant portion of their total blood volume.
  
  – Administration of crystalloid for the treatment of shock in combination with blood progresses rapidly to >50% dilution of coagulation factors.
  
  – When administering blood in a 1:1:1 ratio you get dilution of each product by the others.
  
  – If you are transfusing ONLY blood in a 1:1:1 ratio, although the products dilute one another, the content of what you are transfusing maintains levels above traditional transfusion triggers.
  
  – Changing this ratio by increasing any one product would dilute the other two products to less than effective levels.
## Transfusion Ratios

### 1:1:1 Ratio

<table>
<thead>
<tr>
<th>Component</th>
<th>Transfused 1:1:1</th>
<th>% Non-Circulated</th>
<th>Functional Cells</th>
<th>Transfusion Trigger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulation Factor</td>
<td>65%</td>
<td>-</td>
<td>65%</td>
<td>1.5x normal (66%)</td>
</tr>
<tr>
<td>Platelets</td>
<td>88 x 10⁹</td>
<td>10%</td>
<td>55 x 10⁹</td>
<td>&lt;50 x 10⁹</td>
</tr>
<tr>
<td>RBC’s (Hct)</td>
<td>29%</td>
<td>30%</td>
<td>26%</td>
<td>25%</td>
</tr>
</tbody>
</table>

### 1:1:2 Ratio

<table>
<thead>
<tr>
<th>Component</th>
<th>Transfused 1:1:2</th>
<th>% Non-Circulated</th>
<th>Functional Cells</th>
<th>Transfusion Trigger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulation Factor</td>
<td>52%</td>
<td>-</td>
<td>52%</td>
<td>1.5x normal (66%)</td>
</tr>
<tr>
<td>Platelets</td>
<td>55 x 10⁹</td>
<td>10%</td>
<td>37 x 10⁹</td>
<td>&lt;50 x 10⁹</td>
</tr>
<tr>
<td>RBC’s (Hct)</td>
<td>40%</td>
<td>30%</td>
<td>36%</td>
<td>25%</td>
</tr>
</tbody>
</table>
RESEARCH ON TRANSFUSION RATIOS

• Two major studies validating the 1:1:1 ratio.
• PROMMT (Prospective Observational Multicenter Major Trauma Transfusion) Study\textsuperscript{10}
  – “1\textsuperscript{st} multi-center prospective study examining timing & sequence of MT product delivery in the civilian trauma setting.” (Holcomb et al., 2013)
  – Findings: Higher ratios of Plasma and Platelets to RBCs associated w/ ↓ 30-day mortality.

• PROPPR (Pragmatic, Randomized Optimal Platelet and Plasma Ratios) Study\textsuperscript{8}
  – Findings:
    • 1:1:1 ratios were associated with decreased mortality d/t exsanguination in the 1\textsuperscript{st} 24h.
    • ↑ hemostasis w/ 1:1:1 ratio
    • No difference in mortality between 24h & 30 days.
THE ROLE OF CRYSTALLOID IN MASSIVE TRANSFUSION

- Damage control resuscitation (1:1:1) helps to avoid complications associated with the infusion of large volumes of resuscitative crystalloids during hemorrhage.¹
  - Complications: Pulmonary edema, ARDS, coagulopathy, MODS, & abdominal compartment syndrome.¹
  - Large volume crystalloids cause additional bleeding via coagulation factor dilution, hypothermia, and ↓ blood viscosity.¹

- Recommendations for crystalloid infusion during massive transfusion is that it be limited to carrier solutions for blood products.¹
THE ROLE OF CRYSTALLOID IN MASSIVE TRANSFUSION

• A study by Bickell et al. comparing fluid resuscitation strategies, found that patients in which fluid resuscitation was delayed until surgical control of bleeding had improved rates of survival.¹

• Shreiber et al. compared a standard (2L) crystalloid resuscitation strategy to a restrictive strategy w/ permissive hypotension in victims of penetrating trauma in a pre-hospital setting.¹
  – Findings: Lower mortality w/ restrictive fluid strategy.¹

• Note: Permissive hypotension is absolutely contraindicated in some disease processes such as TBI & SCI.¹

• Bottom Line: Be thoughtful w/ crystalloid administration in massive transfusion.
MONITORING DURING MASSIVE TRANSFUSION

• Obtain baseline labs: CBC (w/ H&H and Platelet count), CMP, ABG, PT, PTT, INR, & Fibrinogen.
• UpToDate recommends coagulation tests after every 5-7 units of RBCs.\(^5\)
  – This is considered either PT, PTT, & platelet count or TEG.
  – Fibrinogen is also helpful to determine need for cryoprecipitate.
• Major complications of massive transfusion include acid-base imbalance, citrate toxicity, and hyperkalemia.\(^2\)
  – Monitor ABGs, Calcium, & Potassium levels on an ongoing basis.
• H&H should be evaluated on an ongoing basis.
MONITORING DURING MASSIVE TRANSFUSION

• Base deficit & lactate are good parameters to evaluate organ perfusion and effectiveness of resuscitative efforts.

• Base deficit reflects oxygen delivery/debt and effectiveness of fluid resuscitation.¹
  – -2 to -5 mild shock
  – -6 to -9 moderate shock
  – > -10 severe shock
  – Base deficit > -5 to -8 on admission is predictive of increased mortality.

• Elevated lactate is reflective of organ hypoperfusion.¹
  – Normal lactate 0.5-1.5 mmol/L
  – >5 mmol/L = significant lactic acidosis.
  – ½ life of lactate 15-30 minutes (rapid decrease w/ correction of cause).
  – Continued elevation at 24 hours = predictor of increased mortality.

• **Bottom Line: Normalized base deficit & lactate are good end goals of resuscitation.**
COMPLICATIONS OF MASSIVE TRANSFUSION

https://www.trend-online.com/
COMPLICATIONS OF MASS TRANSFUSION

• *Coagulopathy*\(^2\)
  – Dilutional thrombocytopenia & coagulopathy common.
  – Limit crystalloid, monitor coagulation factors & platelets.
  – Avoid hypothermia & acidosis.

• *Citrate Toxicity*\(^2\)
  – Calcium/citrate binding has the potential to lead to clinically significant hypocalcemia.
  – Monitor calcium and replace when needed.

• *Hypothermia*\(^2\)
  – 6 U RBC’s @ 4°C decreases body temperature by 1°C (70kg adult).\(^5\)
  – RBCs & FFP should be administered on a warmer.
  – Hypothermia can lead to a myriad of complications including coagulopathy & dysrhythmias.
COMPICATIONS OF MASS TRANSFUSION

• **Acid-Base Imbalance**
  - If rate of transfusion exceeds capability of the liver to metabolize citrate, metabolic acidosis occurs.
  - Metabolic acidosis r/t compromised tissue perfusion w/ hemorrhage is common.
  - Acidosis normally resolves w/ restoration of tissue perfusion.
  - Alkalosis may occur after restoration of tissue perfusion d/t conversion of lactate & citrate to bicarb by the liver.

• **Hyperkalemia**
  - Each unit of RBC’s contains < 4 mEq of K.
  - Hyperkalemia may develop w/ transfusion rate > 100mL/min.
  - Monitor & treat if necessary.
THE LETHAL TRIAD

“Bloody Vicious Cycle” or “Lethal Triad”

Trauma → Hemorrhage → Coagulopathy
- ▼ Factor, ▼ Platelet (Loss, dilution, consumption)

Acidosis ∩ Hypothermia → Factor & platelet dysfunction

Figure 53-4 from Barash, Paul G. Clinical Anesthesia, 8th Edition (p. 1499)
DISCONTINUATION & DRUGS

https://www.emsworld.com/
DISCONTINUATION OF MASSIVE TRANSFUSION

- Discontinuation of the MTP is at the control of bleeding.
- Once control of bleeding is established, transfusion is goal directed, guided by patient assessment, lab values, and clinician judgment.
- Ratios of 1:1:1 are only indicated for patients requiring massive transfusion.\(^7\)
  - This ratio does not increase survival & may actually worsen outcomes in non-hemorrhaging patients.\(^7\)

https://www.istockphoto.com/
PHARMACOLOGIC ADJUNCTS IN MASSIVE TRANSFUSION

• **Tranexamic Acid (TXA)**
  - The use of TXA in massive transfusion is a subject of ongoing research.
  - TXA is a common adjunct in massive transfusion protocols.
  - TXA is also more commonly being used in obstetric hemorrhage.\(^9\)
  - The CRASH-2 trial associated early TXA administration with decreased mortality in massive hemorrhage.\(^10\)
  - Complication of associated thrombosis r/t TXA administration is of concern.\(^10\)
  - No specific recommendations on dosage when administered as part of a MTP.

• **Recombinant Factor VIIa**
  - In the military this is widely used for massive hemorrhage. Some MTP will suggest w/ persistent coagulopathy, but it is considered an off-label use.\(^4\)
Massive transfusion protocol (MTP) from the University of Michigan's Level I Trauma Center.
MASSIVE TRANSFUSION IN OBSTETRICS

• Obstetrics→
  – Pregnant women are hypercoagulable w/ compensatory hyperfibrinolysis setting the stage for massive bleeding.\(^5\)
  – Post partum hemorrhage is the #1 cause of maternal death.\(^9\)
  – Rapid identification of hemorrhage & activation of MTP is paramount for survival in these patients.
  – WOMEN trial supports use of TXA in PPH (1g).\(^9\)
MASSIVE TRANSFUSION IN PEDIATRICS

- Massive hemorrhage in pediatrics
  - Transfusion of >40 mL/kg or 50% of the blood volume in 24h.

- Circulating Blood Volumes
  - Infant 90 mL/kg
  - > 3 months 70 mL/kg

- Injury Severity Score is the recommended tool for activation of MTP.

- Still 1:1:1 ratio
  - 20 mL/kg RBC
  - 20 mL/kg FFP
  - 10 mL/kg Plts.

- In infants < 6 months TEG is a better measure of coagulation.
QUESTIONS???

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REFERENCES


