Massive Transfusion

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Take home points

1. Blood is always available. Requests for massive transfusion or emergency release typically only require a patient name, MRN and location.

2. The blood bank will help prepare for complicated or high-risk patients (e.g., patients with RBC alloantibodies or specific coagulopathies).

3. There are unique changes in hematologic and coagulation parameters during pregnancy, and it is unclear if post-partum hemorrhage and coagulopathy are identical to hemorrhage and coagulopathy in trauma.

4. The pathophysiology of post-partum coagulopathies are poorly understood and the optimal role for blood product transfusion (i.e., which products and when) has not been studied adequately.

5. Massive transfusion for post-partum hemorrhage should address all hematologic and coagulation deficiencies, ***including cryoprecipitate for fibrinogen replacement.***

What are the goals of transfusion?

- **Red blood cells:** Increase oxygen-carrying capacity in the blood to facilitate oxygen delivery to tissues
- **Platelets:** Prevent (or stop) bleeding in the setting of thrombocytopenia or platelet dysfunction
- **Plasma:** Replenish *coagulation factors* to promote hemostasis
- **Cryoprecipitate:** Replenish *fibrinogen* to promote hemostasis

When is transfusion indicated?

- **Red blood cells:** Hb 7g/dL (or symptomatic anemia)
  - Caveat: Largely based on ICU and orthopedic surgery patients who were not acutely bleeding
- **Platelets:** <10000/microliter (or bleeding in the setting of thrombocytopenia or platelet dysfunction)
  - Caveat: Prophylactic threshold, largely based on heme/onc patients
- **Plasma:** Unclear, no RCTs (outside of specific clinical scenarios, e.g., TTP or coagulation factor deficiencies)
- **Cryoprecipitate:** Unclear, no RCTs (outside of specific clinical scenarios, e.g., bleeding in the setting of hypofibrinogenemia or factor XIII deficiency)

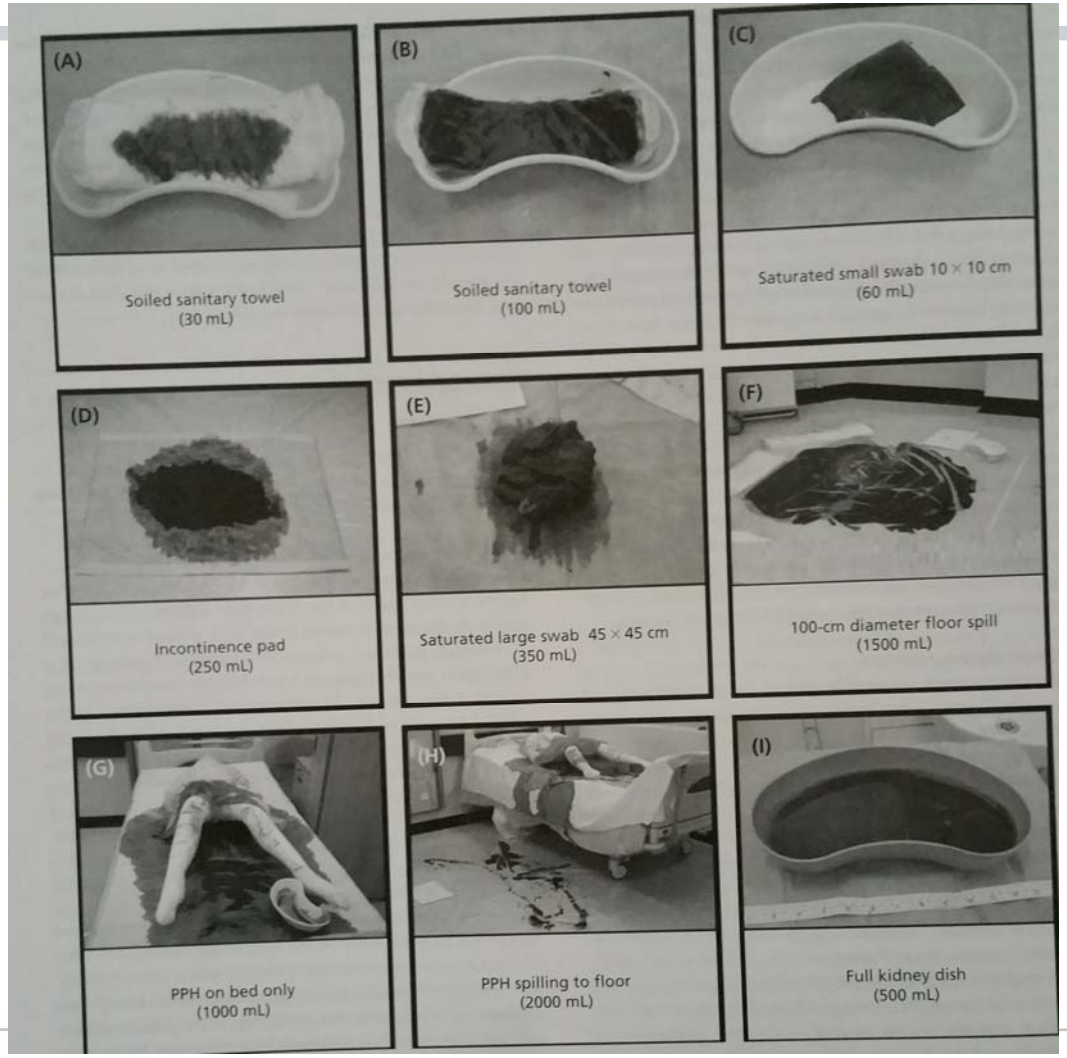
When is transfusion indicated in the obstetric setting?

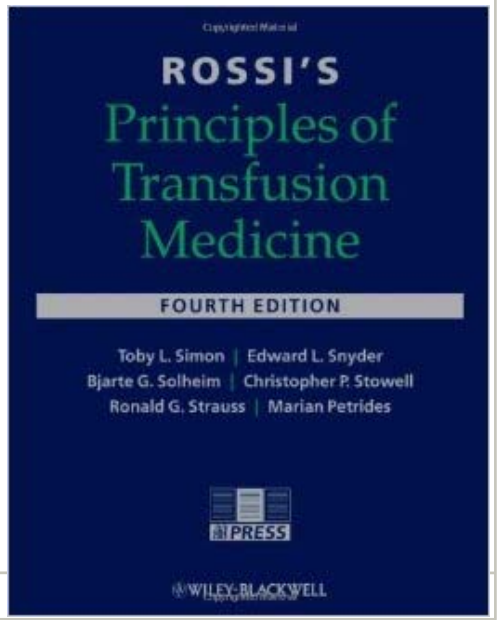
- **Red blood cells:** Hb 7-8g/dL
- **Platelets:** <50000-75000/microliter
- **Plasma:** PT/aPTT >1.5x normal
- **Cryoprecipitate:** <150-200mg/dL
- Based on consensus, expert opinion or extrapolation from other clinical situations
- No RCTs

When is massive transfusion indicated?

When massive blood loss has occurred or is anticipated to occur

How is blood loss measured?





Take home point #1

- There will be blood.
- The blood bank does not question the clinical indication for massive transfusion (or emergency release).

Take home point #2

- The blood bank can/should help prepare for deliveries with anticipated massive blood loss (e.g., placenta accreta/increta/percreta) or complicated blood product needs (e.g., antigen-negative RBCs or specific coagulation factors)

We have a bleeding patient. Her MRN is 12345678. Please activate the massive transfusion protocol.

A

- 6U RBCs
- 6U Plasma
- 1 dose Plts

B

- 8U RBCs
- 4U Plasma
- 1 dose Cryo
- *RiaSTAP is available on the crash cart*

C

- 4U RBCs
- 2U Plasma
- *Followed by…*
- 4U RBCs
- 2U Plasma
- 1 dose Plts
- 1 dose Cryo (per hour)

D

- 4U RBCs
- *Please order…*
- 10U RBCs
- 10U Plasma
- 1 dose Plts
- *Please consider using Amicar or TXA*

We have a bleeding patient. Her MRN is 12345678. Please activate the massive transfusion protocol.

A

- 6U RBCs
- 6U Plasma
- 1 dose Plts

Hospital A (General)

B

- 8U RBCs
- 4U Plasma
- 1 dose Cryo
- *RiaSTAP is available on the crash cart*

Hospital A (OB)

C

- 4U RBCs
- 2U Plasma
- *Followed by…*
- 4U RBCs
- 2U Plasma
- 1 dose Plts
- 1 dose Cryo (per hour)

Hospital B (General/OB)

D

- 4U RBCs
- *Please order…*
- 10U RBCs
- 10U Plasma
- 1 dose Plts
- *Please consider using Amicar or TXA*

Hospital C (General/OB)

We have a bleeding patient. Her MRN is 12345678. Please activate the massive transfusion protocol.

A

- 6U RBCs
- 6U Plasma

1:1

- 1 dose Plts

Hospital A (General)

B

- 8U RBCs
- 4U Plasma

2:1

- 1 dose Cryo
- *RiaSTAP is available on the crash cart*

Hospital A (OB)

C

- 4U RBCs
- 2U Plasma

2:1

- *Followed by…*
- 4U RBCs
- 2U Plasma
- 1 dose Plts
- 1 dose Cryo (per hour)

Hospital B (General/OB)

D

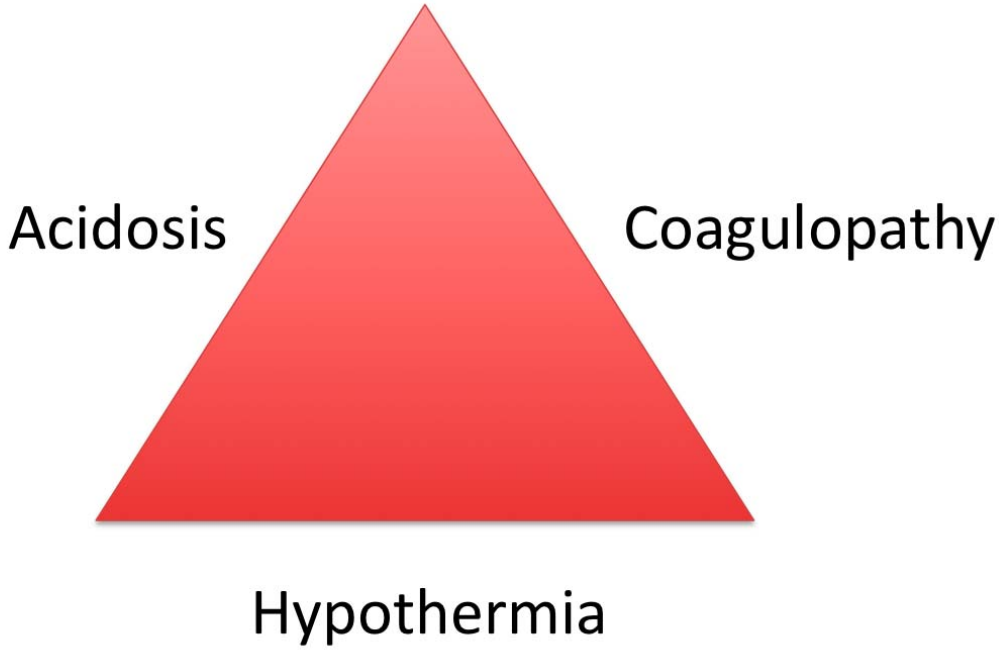
- 4U RBCs
- *Please order…*
- 10U RBCs
- 10U Plasma

1:1

- 1 dose Plts
- *Please consider using Amicar or TXA*

Hospital C (General/OB)

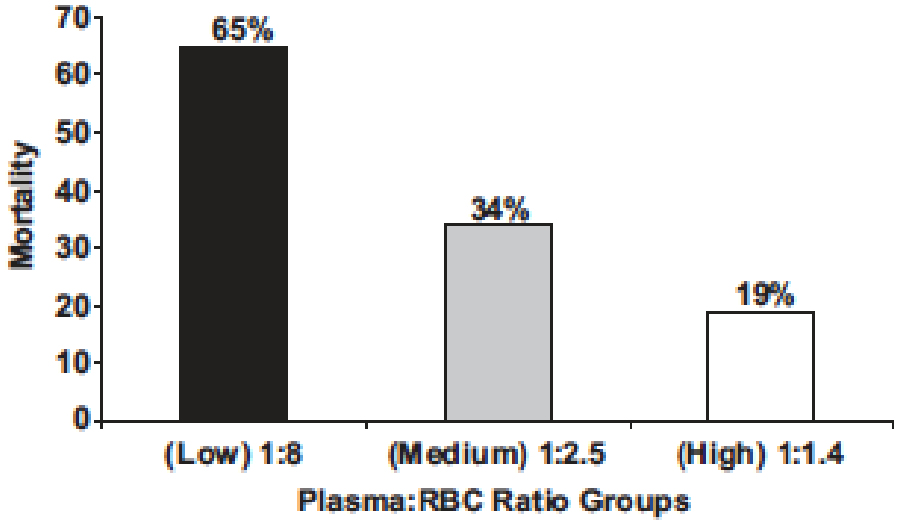
Does the ratio of plasma to RBCs affect clinical outcomes in trauma?



Hypothermia and acidosis, together with coagulopathy form the 'Lethal Triad'

Does the ratio of plasma to RBCs affect clinical outcomes?

- Retrospective study by Borgman et al., 2007
- 246 patients at US Army combat hospitals (all massively transfused, i.e., ≥10 RBC units over 24 hours)
- Grouped by low, medium and high plasma:RBC transfusion ratios
- Compared mortality



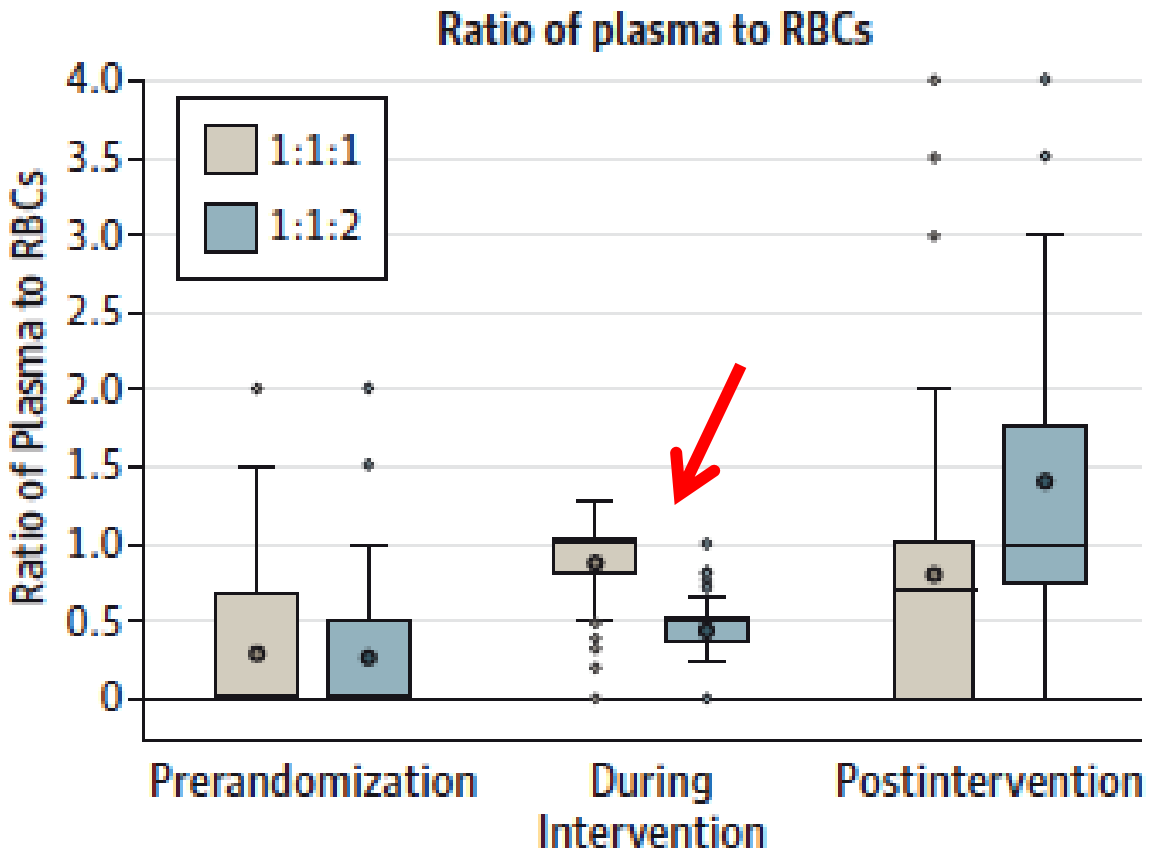
Median survival	2hrs.	38hrs.

Does survival increase the likelihood of receiving a higher plasma:RBC ratio?

PROPPR RCT (1:1 vs. 1:2 Plasma:RBC)

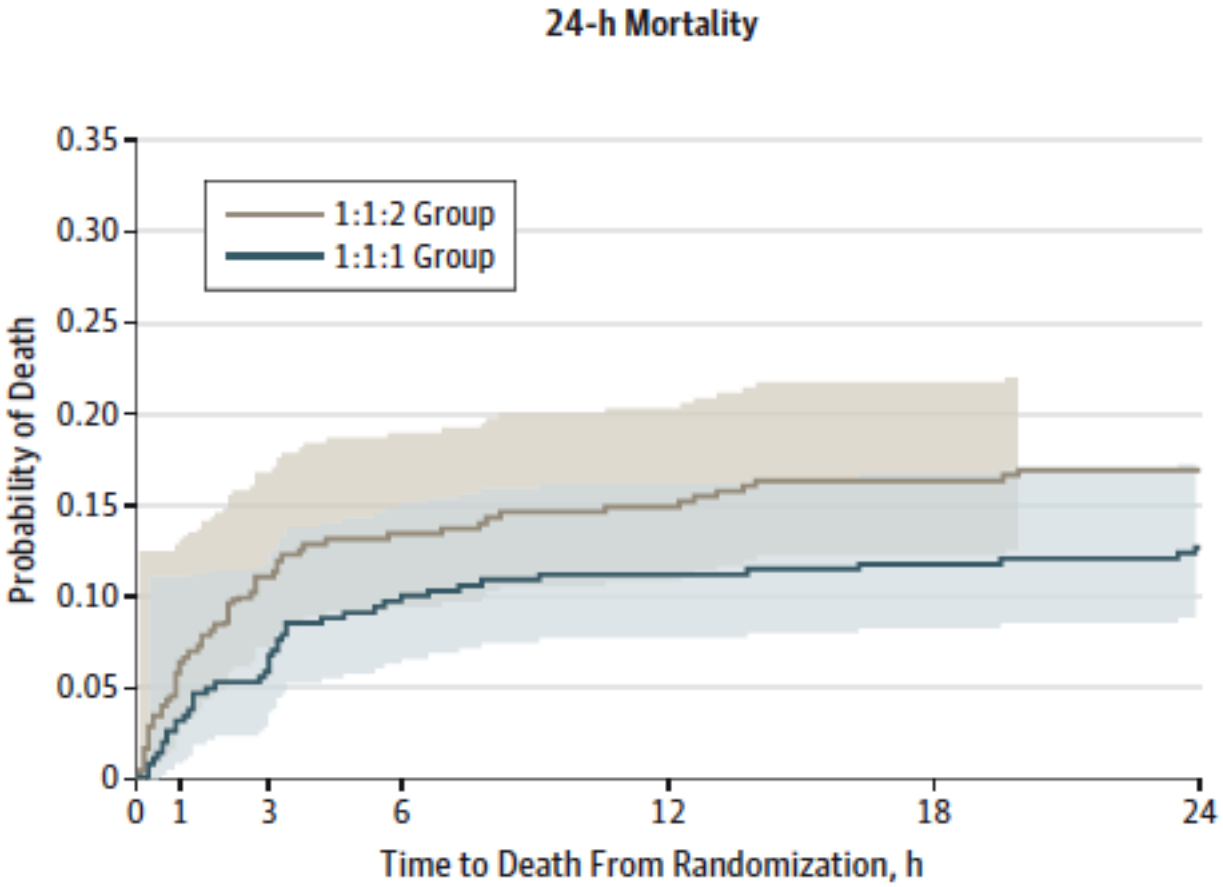
- 680 trauma patients at 12 level I centers in North America
- 338 randomized 1:1 Plasma:RBC
- 342 randomized to 1:2 Plasma:RBC
- No statistically significant differences between groups
- Primary outcomes: Mortality at 24-hours (95% power to detect 10% difference) and 30-days (92% power to detect 12% difference)

PROPPR RCT (1:1 vs. 1:2 Plasma:RBC)



Holcomb et al., *JAMA*, 2015

PROPPR RCT
(1:1 vs. 1:2 Plasma:RBC)



No statistically significant difference in 24-hour (or 30-day) mortality between groups

Holcomb et al., *JAMA*, 2015

Can we apply the results of PROPPR to obstetric patients?

- Maybe not – *how well does traumatic bleeding and coagulation in young male patients model severe post-partum hemorrhage?*

- Etiologies of post-partum hemorrhage
  - Uterine atony or genital tract trauma
  - Uterine rupture
  - Uterine inversion
  - Retained placenta
  - Placental abruption
  - Placenta accreta/increta/percreta

- Alterations in hematologic parameters and coagulation during pregnancy
  - Expansion of plasma volume and RCM
  - Thrombocytopenia (gestational vs. ITP vs. pre-eclampsia vs. TTP/HUS)
  - Increase in coagulation factors VII, VIII, IX, X, XII, vWF and fibrinogen
  - Decrease in protein S and increased activated protein C resistance
  - Decreased fibrinolysis (due to decreased tPA and increased TAFI and PAI)

More or less plasma?

- Compared to the plasma of a pregnant patient, donor plasma is relatively poor in coagulation factors and fibrinogen
- Should the threshold for plasma transfusion depend on the etiology of bleeding and the likelihood of a consumptive coagulopathy?

How should coagulation be monitored during management of post-partum hemorrhage?

- **Goal:** Transfuse the appropriate products and avoid unnecessary transfusions
- PT/aPTT: low sensitivity, long TAT
- Fibrinogen (Clauss): high sensitivity for hemorrhage progression (<200mg/dL), long TAT
- TEG/ROTEM: point-of-care whole blood coagulation testing (i.e., clot formation, fibrinogen, platelets and fibrinolysis); shown to reduce blood loss and blood component use in cardiac surgery patients (Ak et al., 2009)

Fibrinogen replacement

- Increase in fibrinolysis coincident with placental separation, potentially leading to sharp decline in fibrinogen levels
- Replacement (recommended at <150-200mg/dL) traditionally with cryoprecipitate, which contains predominantly fibrinogen, factor VIII, factor XIII and vWF
  - Must be thawed prior to issue
  - Expires 4-6 hours after thaw
- Fibrinogen concentrate (e.g., RiaSTAP)
  - ~20mg/mL (vs. 10mg/mL cryo or 2mg/mL plasma)
  - Lyophilized, stable RT 30 months
- Ongoing RCT (FIB-PPH) examining fibrinogen concentrate for initial management of post-partum hemorrhage

Anti-fibrinolytics

- **Rationale:** CRASH-2 RCT comparing tranexamic acid (TXA) to placebo
  - >20000 bleeding trauma patients at >250 hospitals in 40 countries
  - Statistically significant reduction in mortality with no increase in thrombotic events
- **WO**rld **M**aternal **AN**tifibrinolytic (WOMAN) Trial
  - 15000 patients with diagnosed post-partum hemorrhage
  - Effect of early TXA on mortality, hysterectomy, need for surgical intervention and transfusion

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3. There are unique changes in hematologic and coagulation parameters during pregnancy, and it is unclear if post-partum hemorrhage and coagulopathy are identical to hemorrhage and coagulopathy in trauma.

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5. Massive transfusion for post-partum hemorrhage should address all hematologic and coagulation deficiencies, ***including cryoprecipitate for fibrinogen replacement.***

Future directions

- Quantitation of blood loss
- Understanding of coagulopathies in "conventional" trauma vs. post-partum hemorrhage
  - Using the most effective blood product and minimizing unnecessary transfusions
- Real-time monitoring of coagulation at the bedside (via TEG/ROTEM)
  - Goal-directed transfusion therapy
- Evaluation of the utility of fibrinogen concentrates (FIB-PPH RCT)
- Evaluation of the utility use of anti-fibrinolytics (WOMAN RCT)
  - Minimizing blood loss and reducing the need for transfusion