Massive Transfusion Support of PPH: A Lab Perspective

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Disclosure

- I have no conflict of interest in relation to this presentation

Objectives

- Explain how a MHP works using the six Ts
  - Triggering and talking
  - Testing
  - Tranexamic acid
  - Temperature
  - Transfusion
  - Termination

Incidence

- PPH is the leading cause of maternal death worldwide
  - Occurs in 6% of all deliveries in Canada
- Rates of PPH are increasing in Canada

Management

CMQCC

Obstetric Emergency Management Plan: Flow Chart Format

Release 2.0 7/9/2014

Pre-Admission / Time of admission

Identify patients with special consideration: Placenta previa/accreta, Bleeding disorder, or those who decline blood products → Follow appropriate workups, planning, preparing of resources, counseling and notification

Screen All Admissions for hemorrhage risk: Low Risk, Medium Risk and High Risk → **Low Risk:** Draw blood and hold specimen; **Medium Risk:** Type & Screen, Review Hemorrhage Protocol; **High Risk:** Type & Crossmatch 2 Units PRBCs; Review Hemorrhage Protocol

Verify Type & Screen on prenatal record; if positive antibody screen on prenatal or current labs (except low level anti-D from Rhogam), Type & Crossmatch 2 Units PBRCs

Stage 0 — All Births

All women receive active management of 3rd stage
Oxytocin IV infusion or 10 Units IM, 10-40 U infusion

→ **Ongoing Evaluation:** Quantification of blood loss and vital signs

→ **Cumulative Blood Loss** >500 ml Vag; >1000 ml CS; >15% Vital Sign change -or- HR ≥110, BP ≤85/45, O_2 Sat <95%, Clinical Sx

- NO → Standard Postpartum Management Fundal Massage
- INCREASED BLEEDING → YES → Activate Hemorrhage Protocol CALL FOR EXTRA HELP

Blood Loss: >500 ml Vaginal >1000 ml CS — Stage 1 — Activate Hemorrhage Protocol

- Increase IV Oxytocin Rate
- Methergine 0.2 mg IM (if not hypertensive)
- Vigorous Fundal massage; Empty Bladder; Keep Warm
- Administer O_2 to maintain Sat >95%
- Rule out retained POC, laceration or hematoma
- **Order Type & Crossmatch 2 Units PRBCs if not already done**

Ongoing Cumulative Blood Loss Evaluation

Continued heavy bleeding

- NO → Increased Postpartum Surveillance
- YES → CALL FOR EXTRA HELP
  Give Meds: Hemabate 250 mcg IM -or- Misoprostol 600-800 SL or PO
  Transfuse 2 Units PRBCs per clinical signs
  Do not wait for lab values
  Consider thawing 2 Units FFP
  → Increased Postpartum Surveillance

Blood Loss: 1000-1500 ml — Stage 2 — Sequentially Advance through Medications & Procedures

Vaginal Birth:
- Bimanual Fundal Massage
- Retained POC: Dilation and Curettage
- Lower segment/Implantation site/Atony: Intrauterine Balloon
- Laceration/Hematoma: Packing, Repair as Required
- Consider IR (if available & adequate experience)

Cesarean Birth:
- Continued Atony: B-Lynch Suture/Intrauterine Balloon
- Continued Hemorrhage: Uterine Artery Ligation

Cumulative Blood Loss >1500 ml, 2 Units Given, Vital Signs Unstable

- NO → Increased Postpartum Surveillance
- → **To OR (if not there);**
  Activate Massive Hemorrhage Protocol
  Mobilize Massive Hemorrhage Team
  TRANSFUSE AGGRESSIVELY
  RBC:FFP:Plts → 6:4:1 or 4:4:1
  - **Unresponsive Coagulopathy:** After 10 Units PBRCs and full coagulation factor replacement, may consider rFactor VIIa
  - **Conservative Surgery**
    B-Lynch Suture/Intrauterine Balloon
    Uterine Artery Ligation
    Hypogastric Ligation (experienced surgeon only)
    Consider IR (if available & adequate experience)
  - **Fertility Strongly Desired**
    - YES → HEMORRHAGE CONTINUES
    - NO → **Definitive Surgery** Hysterectomy
  - CONTROLLED → Consider ICU Care; Increased Postpartum Surveillance

Blood Loss: >1500 ml — Stage 3 — Activate Massive Hemorrhage Protocol

California Maternal Quality Care Collaborative (CMQCC), Hemorrhage Taskforce (2009) visit: www.CMQCC.org for details
This project was supported by funds received from the State of California Department of Public Health, Center for Family Health; Maternal, Child and Adolescent Health Division

CMQCC

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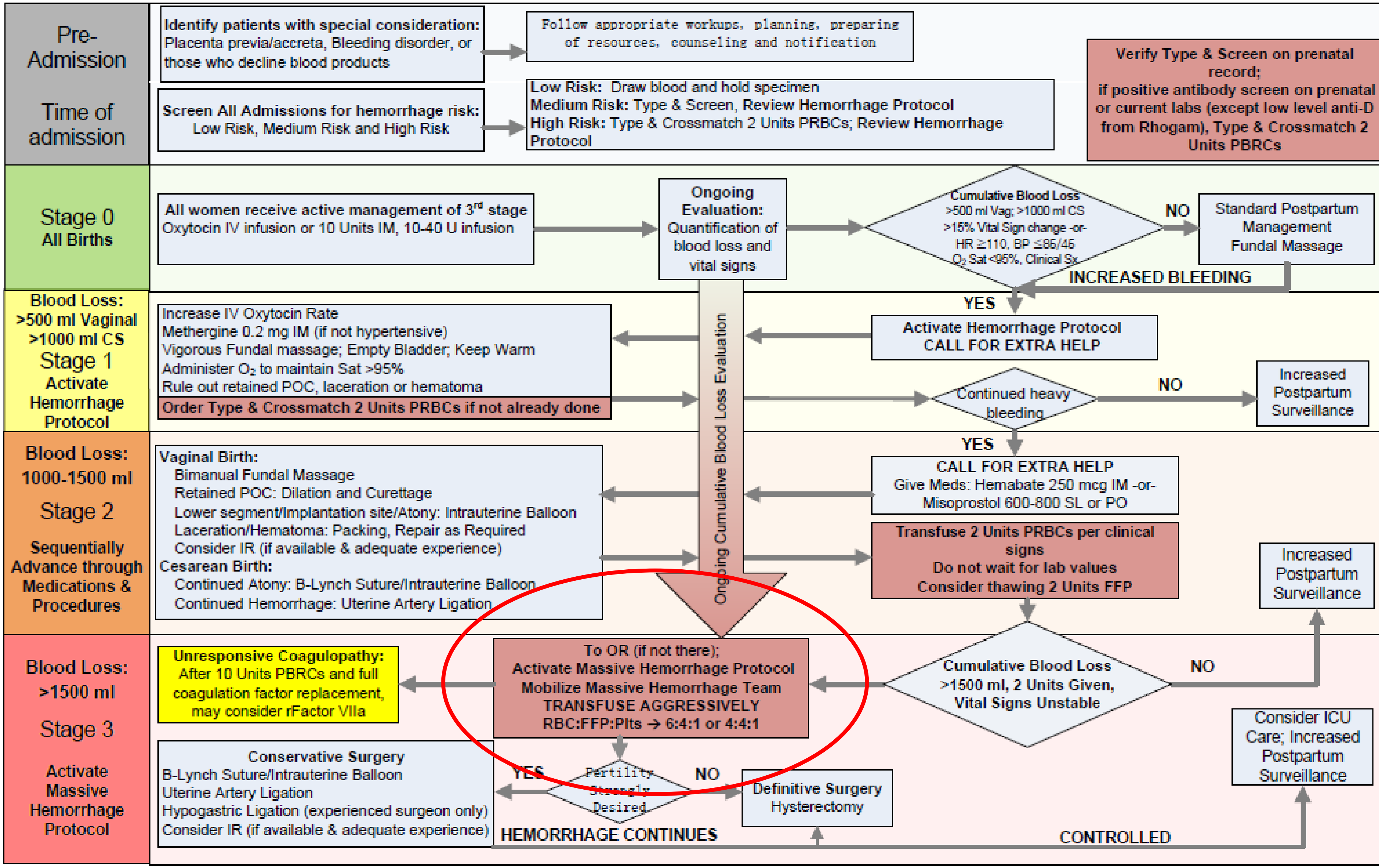

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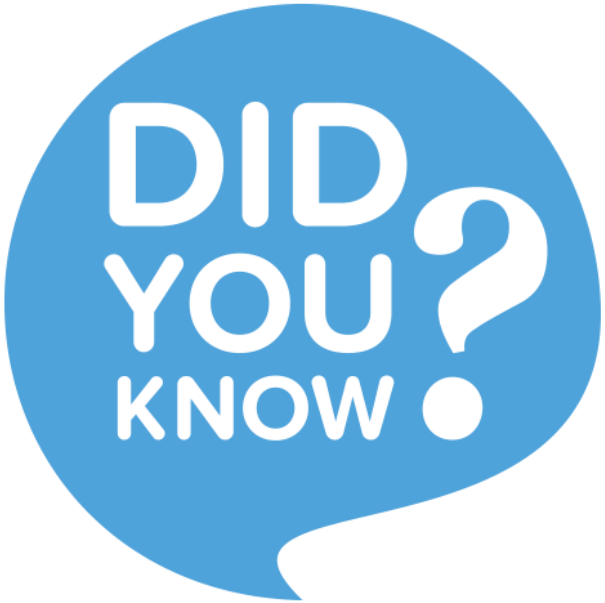


- It is forbidden to release blood components / products without patient identifiers
  - Unknown patient identifiers are acceptable

When?

When?

CMQCC obstetric hemorrhage toolkit March 24, 2015

Stage 0: All Births – Prevention & Recognition of OB Hemorrhage
Prenatal Assessment & Planning

STAGE 1: OB Hemorrhage

Cumulative Blood Loss >500ml vaginal birth or >1000ml C/S with continued bleeding -OR-
Vital signs >15% change or HR ≥110, BP ≤85/45, O2 sat <95% -OR-
Increased bleeding during recovery or postpartum

STAGE 1: BLOOD LOSS › 500 mL vaginal OR blood loss › 1000 mL cesarean with normal vital signs and lab values

American Congress of Obstetricians and Gynecologists obstetric hemorrhage checklist December 2016

When?

CMQCC obstetric hemorrhage toolkit March 24, 2015

Stage 0: All Births – Prevention & Recognition of OB Hemorrhage
Prenatal Assessment & Planning

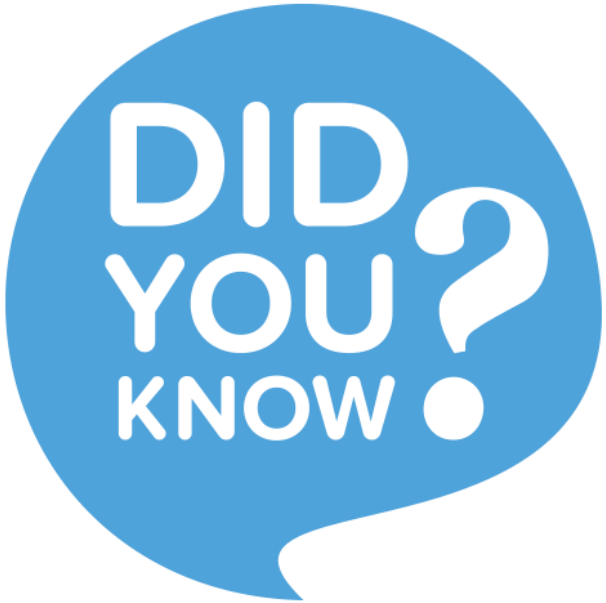
STAGE 1: OB Hemorrhage

Cumulative Blood Loss >500ml vaginal birth or >1000ml C/S with continued bleeding -OR-
Vital signs >15% change or HR ≥110, BP ≤85/45, O2 sat <95% -OR-
Increased bleeding during recovery or postpartum

Group and crossmatch 2 RBCs STAT

STAGE 1: BLOOD LOSS > 500 mL vaginal OR blood loss > 1000 mL cesarean with normal vital signs and lab values

American Congress of Obstetricians and Gynecologists obstetric hemorrhage checklist December 2016



- Group and screen
  - Aka type and screen, type and hold, etc.

- Group and cross
  - Aka type and cross, type and crossmatch, etc.

When?

STAGE 2: OB Hemorrhage

Continued bleeding or Vital Sign instability, and < 1500 mL cumulative blood loss

STAGE 2: CONTINUED BLEEDING (EBL up to 1500mL OR > 2 uterotonics) with normal vital signs and lab values

STAGE 3: OB Hemorrhage

Cumulative blood loss > 1500ml, > 2 units PRBCs given, VS unstable or suspicion for DIC

STAGE 3: CONTINUED BLEEDING (EBL > 1500mL OR > 2 RBCs given OR at risk for occult bleeding/coagulopathy OR any patient with abnormal vital signs/labs/oliguria)

STAGE 4: CARDIOVASCULAR COLLAPSE (massive hemorrhage, profound hypovolemic shock, or amniotic fluid embolism)

When?

STAGE 2: OB Hemorrhage

Continued bleeding or Vital Sign instability, and < 1500 mL cu

Transfuse 2 RBCs based on clinical signs and response; do not wait for labs

STAGE 2: CONTINUED BLEEDING (EBL up to 1500mL O with normal vital signs and lab values

STAGE 3: OB Hemorrhage

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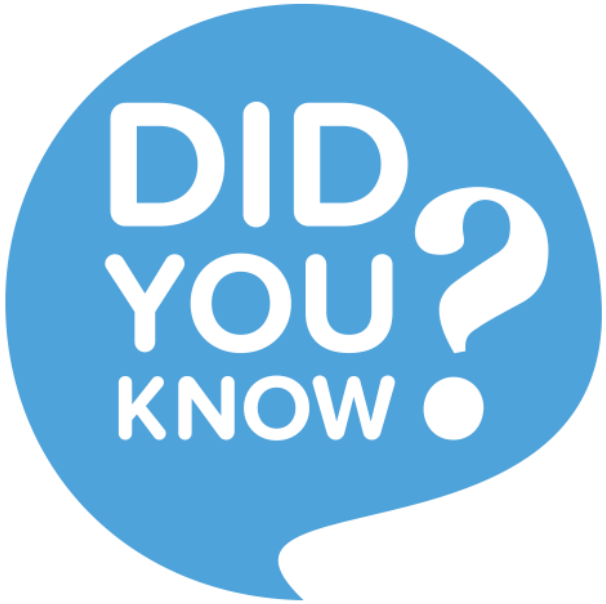
Cumulative blood loss > 1500ml, > 2 units PRBCs given, VS unstabl

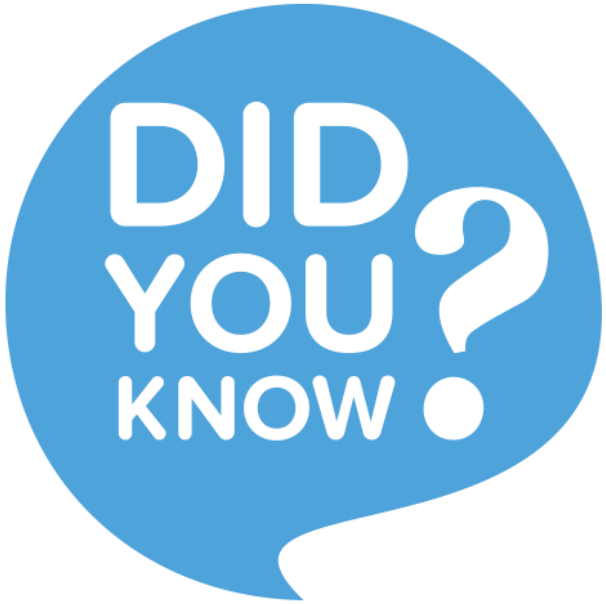
STAGE 3: CONTINUED BLEEDING (EBL > 1500mL OR > 2 RB bleeding/coagulopathy OR any patient with abnormal vital signs/labs/oliguria)

Initiate massive hemorrhage plan (MHP)

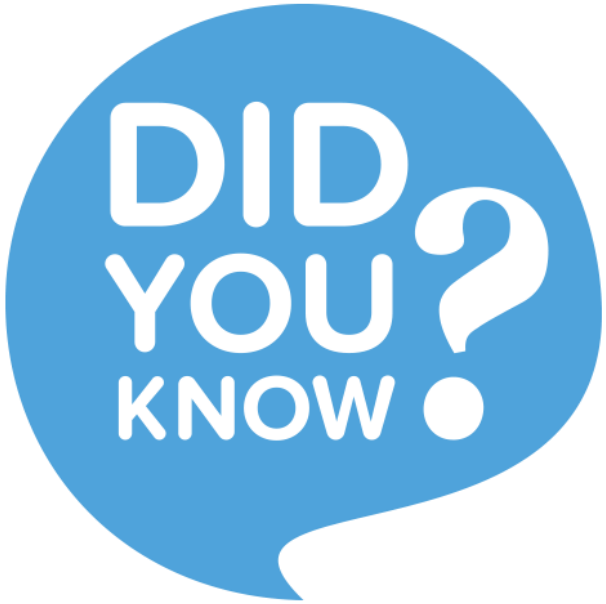
STAGE 4: CARDIOVASCULAR COLLAPSE (massive hemorrhage, profound hypovolemic shock, or amniotic fluid embolism)



- There is a big difference between:
  - emergency release components (aka trauma units, unmatched blood, etc.)
  - massive hemorrhage plan



- There is a big difference between:
  - emergency release components (aka trauma units, unmatched blood, etc.)
    - No current sample in lab / testing not complete
    - Get what you ask for in “universal donor” group
  - massive hemorrhage plan



- There is a big difference between:
  - emergency release components (aka trauma units, unmatched blood, etc.)
    - No current sample in lab / testing not complete
    - Get what you ask for in “universal donor” group
  - massive hemorrhage plan
    - Patient may or may not have been thoroughly tested
    - Get blood components automatically in a set ratio

MHP

- Outlines the entire process for supporting a massively hemorrhaging patient
  - It's not just a ratio of blood components!

MHP

- Triggering and talking
- Testing
- Tranexamic acid
- Temperature
- Transfusion
- Termination

MHP

- Triggering and talking
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Transfusion

- Initiating the MHP turns on a tap
  - MHP packs sent as fast as they can be produced
  - Keep coming until you say “stop”
  - Each pack contains
    - RBCs, plasma +/- platelets

Transfusion

- What's in the MHP pack?
  - Recommended ratio of RBC to plasma
    - Between 1:1 and 2:1

Transfusion

Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs a 1:1:2 Ratio and Mortality in Patients With Severe Trauma
The PROPPR Randomized Clinical Trial

John B. Holcomb, MD; Barbara C. Tilley, PhD; Sarah Baraniuk, PhD; Erin E. Fox, PhD; Charles E. Wade, PhD; Jeanette M. Podbielski, RN; Deborah J. del Junco, PhD; Karen J. Brasel, MD, MPH; Eileen M. Bulger, MD; Rachael A. Callcut, MD, MSPH; Mitchell Jay Cohen, MD; Bryan A. Cotton, MD, MPH; Timothy C. Fabian, MD; Kenji Inaba, MD; Jeffrey D. Kerby, MD, PhD; Peter Muskat, MD; Terence O'Keeffe, MBChB, MSPH; Sandro Rizoli, MD, PhD; Bryce R. H. Robinson, MD; Thomas M. Scalea, MD; Martin A. Schreiber, MS; Deborah M. Stein, MD; Jordan A. Weinberg, MD; Jeannie L. Callum, MD; John R. Hess, MD, MPH; Nena Matijevic, PhD; Christopher N. Miller, MD; Jean-Francois Pittet, MD; David B. Hoyt, MD; Gail D. Pearson, MD, ScD; Brian Leroux, PhD; Gerald van Belle, PhD; for the PROPPR Study Group

- Prospective, multicentre trial showed no difference in mortality at 24 hours or 30 days in severe trauma patients with major bleeding treated with either a 1:1:1 ratio or 1:1:2 ratio

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
  - 1 platelet

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet

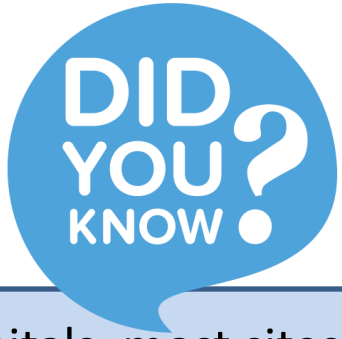
Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet

This amount of plasma contains ~2.5 g of fibrinogen

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet



Except for large hospitals, most sites can only thaw 4 units of plasma (**or** cryoprecipitate) at a time

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet
    - 1 bag (pooled platelet)
    - 1 bag (apheresis platelet)

The pool is four individual donations combined; the apheresis platelet is an equivalent number of platelets collected from a single individual (~30 x 10^{10} platelets)

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet
    - 1 bag (pooled platelet)
    - 1 bag (apheresis platelet)

Depending on the size of your hospital, you may or may not get a platelet automatically with every MHP pack.

Transfusion

- What is in the MHP pack?
  - 4 RBCs
  - 4 units of thawed plasma
    - 4 bags of FP
    - 2 bags of AFFP
  - 1 platelet
    - 1 bag (pooled platelet)
    - 1 bag (apheresis platelet)

The platelet will NOT be inside the MHP pack.

Don’t expose platelets to the cold!

Transfusion

- Wh
  - 4
  - 4
  - 1
  - 1
    - 1

Beth Israel Deaconness Medical Center (Boston) BTS uses:

RBC plasma ratio of 2: 1

Includes cryoprecipitate ~q1 hour

DT be ack.

<u>elets to the cold!</u>

Transfusion

- Wh
  - –
  - –
  - –
    - •

Beth Israel Deaconness Medical Center (Boston) BTS uses:

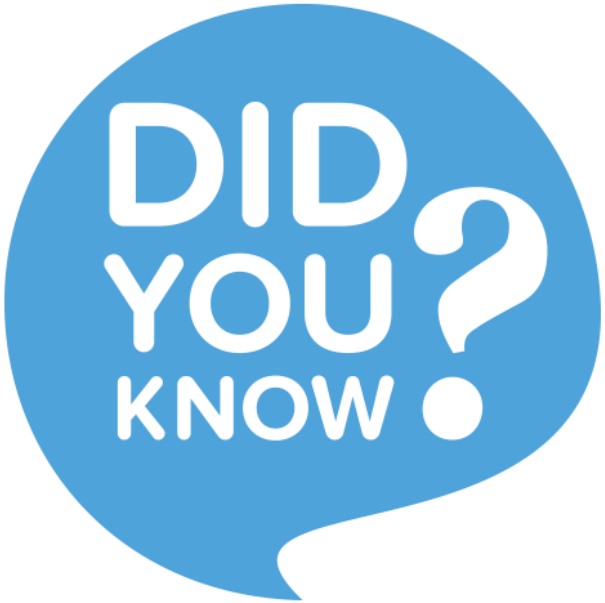
RBC plasma ratio of 2: 1

Includes cryopr

The cryoprecipitate will NOT be inside the MHP pack.

<u>Don't expose cryo to the cold!</u>

- The BTS must have a current sample from your patient to issue group-specific RBCs



Transfusion

- Initiating the MHP turns on a tap
  - MHP packs sent as fast as they can be produced
  - Keep coming until you say “stop”
  - Each pack contains
    - RBCs, plasma +/- platelets

Transfusion

- RBC
  - 5 minutes
- Plasma
  - 30 minutes
- Cryoprecipitate
  - 45 minutes

Transfusion

- RBC
  - 5 minutes
- Plasm
  - 30
- Cryoprecipitate
  - 45 minutes

Therefore, optimally could expect a pack to be arriving every ~ 30 minutes.

Transfusion

- .
- P
- C

Except for the very largest hospitals, thawed plasma / cryo is not kept on hand. Therefore, the first MHP will contain just RBCs (+/- platelets).

Expect to wait ~30 minutes from request for plasma, and ~45 minutes for cryoprecipitate.

Transfusion

- [illegible]
- P[illegible]
- C[illegible]

Except for the very largest hospitals, thawed plasma / cryo is not kept on hand. Therefore, the first MHP will contain just RBCs (+/- platelets).

Expect to wait ~30 minutes from request for plasma, and ~45 minutes for cryoprecipitate.

Fibrinogen

- Pregnant women have higher “normal” levels of fibrinogen
  - As high as 4-5 g/L
  - Low values may represent a more severe coagulopathy compared with nonpregnant individuals
    - In Charbit’s study, serum fibrinogen below 200 mg/dL (2 g/L) had a PPV for severe hemorrhage of 100%
- Keep fibrinogen >2 g/L

Pacheco LD et al. An update on the use of massive transfusion protocols in obstetrics. American Journal of Obstetrics & Gynecology March 2016;340-344.

How?

How?

Cryoprecipitate

- Plasma derived component rich in factor VIII, fibrinogen and vWF

Fibrinogen concentrate

- A pasteurized, lyophilized concentrate of fibrinogen produced from a pool

Which is better?

- One head-to-head comparison
  - 63 bleeding, hypofibrinogenemic (<1 g/L) pediatric cardiac surgery patients
    - Primary outcome: postoperative blood losses during the 48 hours after surgery

Which is better?

- One head-to-head comparison

Hemostatic effects of fibrinogen concentrate compared with cryoprecipitate in children after cardiac surgery: A randomized pilot trial

Filomena R. B. G. Galas, MD, PhD, Juliano P. de Almeida, MD, PhD, Júlia T. Fukushima, MSc, Jean Louis Vincent, MD, PhD, Eduardo A. Osawa, MD, PhD, Suely Zeferino, RN, Lígia Câmara, RN, Vanessa A. Guimarães, MD, Marcelo B. Jatene, MD, PhD, and Ludhmila A. Hajjar, MD, PhD

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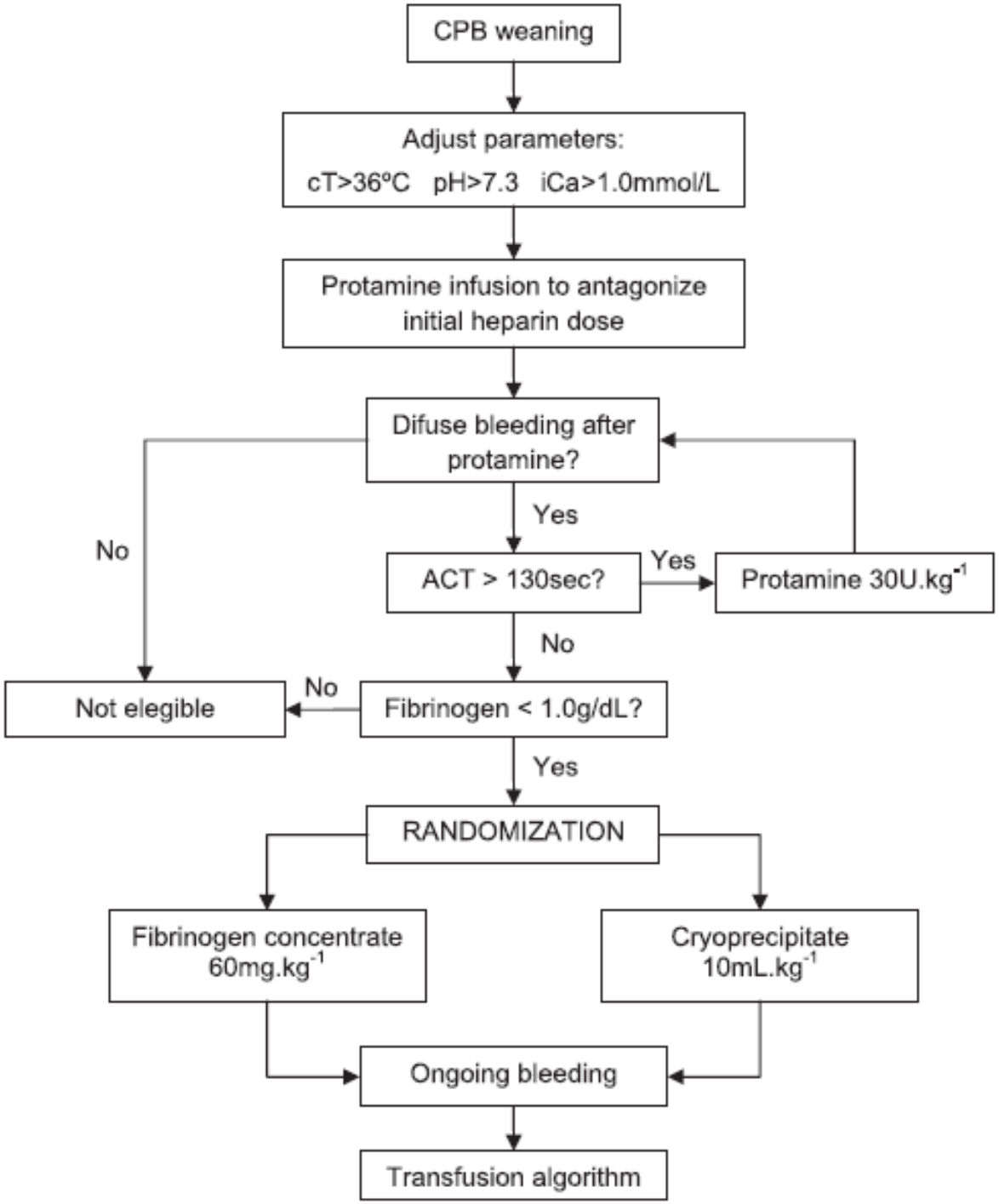
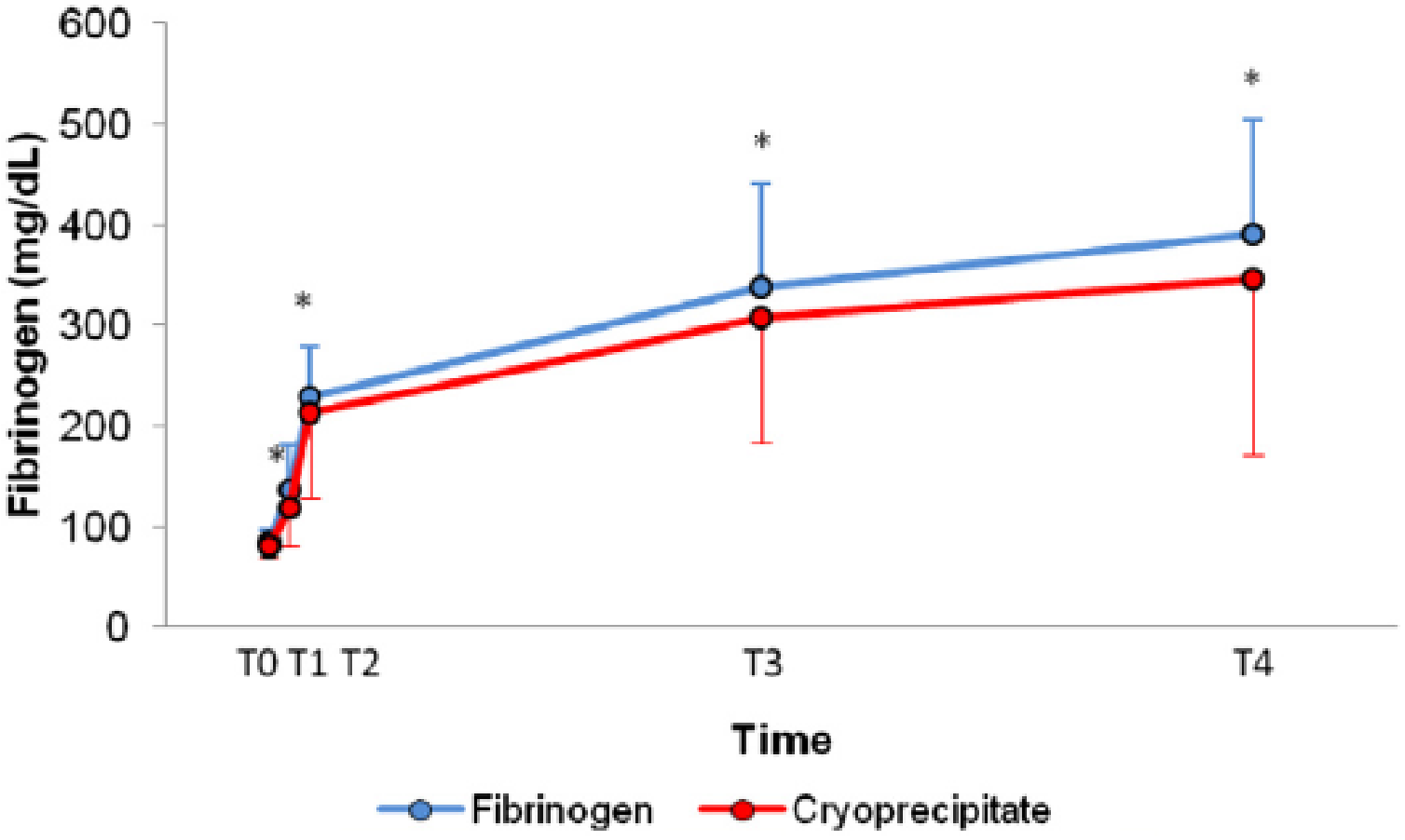

CPB weaning
Adjust parameters:
cT>36ºC pH>7.3 iCa>1.0mmol/L
Protamine infusion to antagonize initial heparin dose
Difuse bleeding after protamine?
No
Yes
ACT > 130sec?
Yes
Protamine 30U.kg-1
No
Not elegible
No
Fibrinogen < 1.0g/dL?
Yes
RANDOMIZATION
Fibrinogen concentrate 60mg.kg-1
Cryoprecipitate 10mL.kg-1
Ongoing bleeding
Transfusion algorithm

Which is better?

- Primary outcome:
  - median 48-hour blood loss was not significantly different between the 2 groups

- Also:
  - After treatment, plasma fibrinogen concentration increased similarly
  - there were no differences in allogeneic blood transfusion

Which is better?



Which is better?

Which is better?

	Fibrinogen concentrate	Cryoprecipitate
Is it pathogen reduced?		
Storage conditions		
Storage duration		
Time from issue until ready to use		
Issue concurrently with plasma?		
Licensed in Canada for this indication?		

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Issue concurrently with plasma?		
Licensed in Canada for this indication?		

Which is better?

	Fibrinogen concentrate	Cryoprecipitate
Is it pathogen reduced?	**Yes**	No
Storage conditions	**Room temperature**	Frozen
Storage duration		
Time from issue until ready to use		
Issue concurrently with plasma?		
Licensed in Canada for this indication?		

Which is better?

	Fibrinogen concentrate	Cryoprecipitate
Is it pathogen reduced?	**Yes**	No
Storage conditions	**Room temperature**	Frozen
Storage duration	**60 months**	12 months
Time from issue until ready to use		
Issue concurrently with plasma?		
Licensed in Canada for this indication?		

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	Fibrinogen concentrate	Cryoprecipitate
Is it pathogen reduced?	**Yes**	No
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Licensed in Canada for this indication?	No	**Yes**

MHP

- Triggering and talking
- Testing
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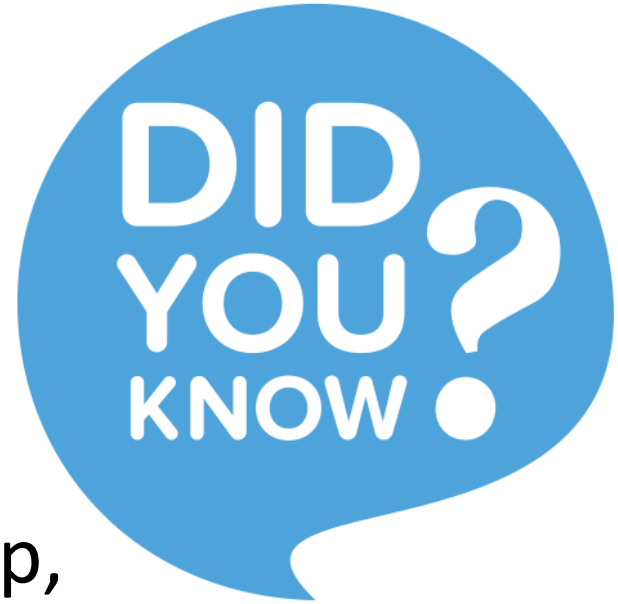
Triggering and Talking

- Who is going to trigger your MHP
  - i.e. who is the MRP?
- How to communicate this?
  - i.e. how do you notify the laboratory / BTS / porters?
    - our site has a special “red line” phone number to call
  - To minimize miscommunication, only one designated contact individual (RN) should order blood components and products.
  - Communicate early – give the BTS a heads-up if you think you are getting into trouble.



- Under circumstances of massive hemorrhage in a patient of unknown blood group, it is recommended to provide O negative RBCs to females of reproductive potential and O positive RBCs to all others
  - So don't be surprised if the tech asks you or your staff how old the patient is!

MHP

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Testing

- It is critical to collect a group and screen sample STAT, if needed
  - Need to switch patient to group specific ASAP
  - O negative RBCs are not unlimited, and there is only a limited amount of AB plasma available, even at the largest of hospitals
    - AB individuals are around 4% of the population

Testing

- It is critical to collect a group and screen sam
  - N AP
  - C re is o le, e
    - AB individuals are around 4% of the population

Group (ABO and Rh): ~15 minutes
(10 to spin sample, 5 to test)

Antibody screen: ~30 minutes (not including spin)

Testing

- Recommended q1h:
  - CBC
  - INR / PTT
  - fibrinogen
  - calcium
  - ABG
  - potassium

O'Brien KL and Uhl L. How do we manage blood product support in the massively hemorrhaging obstetric patient? Transfusion 2016;56;2165-2171.

Testing

- Recommended q1h:
  - CBC
  - INR / PTT
  - fibrinogen
  - calcium
  - ABG
  - potassium

Hgb > 80 g/L
Platelets > 50 x 10^9/L
INR ≤ 1.5
PT/PTT < 1.5x normal

O'Brien KL and Uhl L. How do we manage blood product support in the massively hemorrhaging obstetric patient? Transfusion 2016;56;2165-2171.

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Tranexamic acid

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

www.thelancet.com Published online April 26, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30638-4

Tranexamic acid

- WOMAN trial
  - 20,000 women >16 years old with a clinical diagnosis of PPH
  - 21 diverse geographical settings, including countries with some of the highest rates and absolute numbers of maternal deaths
  - randomly assigned to receive either 1 g of intravenous tranexamic acid or a matching placebo, in addition to usual care

Tranexamic acid

- Deaths from bleeding were significantly reduced by 19%
- Maternal mortality was reduced by 31% if tranexamic acid was given within 3 h of birth
- Adverse events (including TE events) did not differ

- *"Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for post-partum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset."*

MHP

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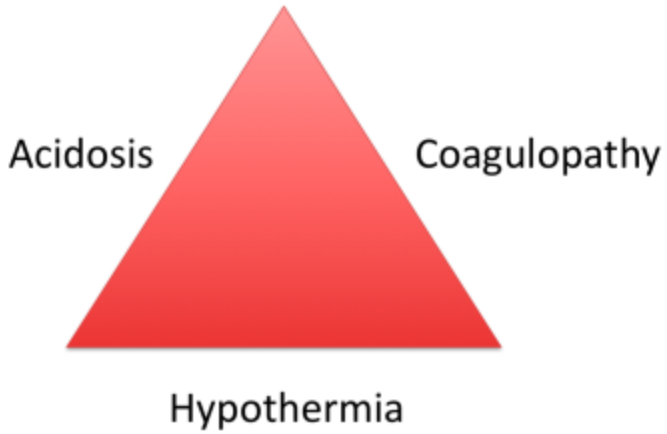
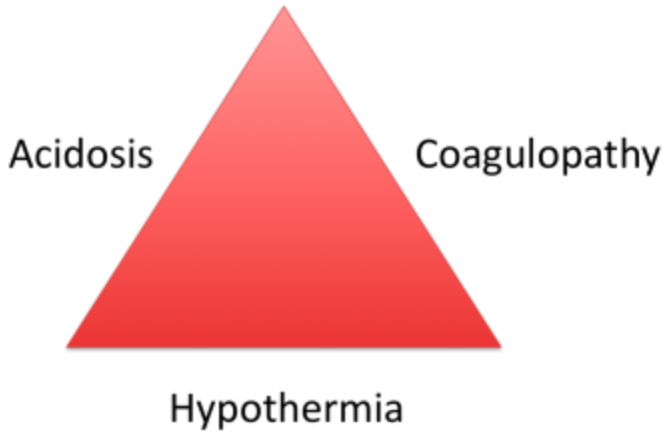
Temperature



Temperature

Coagulation is a system of complex enzymatic reactions

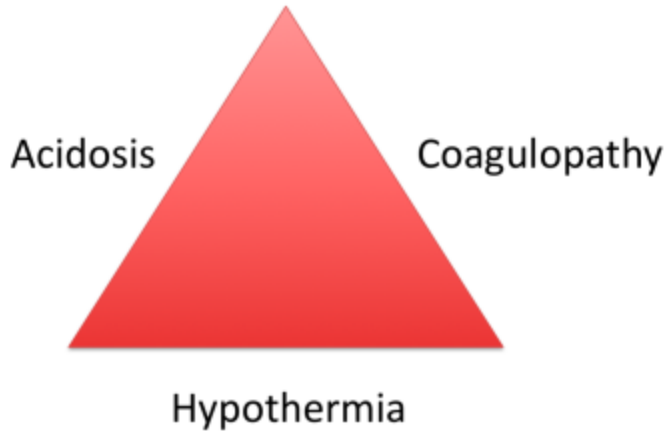


Administration of large amounts of blood components exacerbates this

Temperature

Coagulation is a system of complex enzymatic reactions

Every 1°C drop in temperature increases blood loss by 16%



Risk of clinically important hypothermia is significantly increased by infusion of 5 or more units of blood

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Other complications of massive transfusion:

Dilutional coagulopathy
Hypocalcemia / hypomagnesemia / citrate toxicity
Metabolic acidosis (rare)
Hyperkalemia

MHP

- Triggering and talking
- Testing
- Tranexamic acid
- Temperature
- Transfusion
- Termination

Termination

- Very important to notify the BTS
  - Prevent wastage
  - Deal with testing backlog

Wastage

- Send blood components and products back to BTS ASAP if not planning to use immediately
  - RBCs – until expiry
  - Plasma – 5 days
  - Cryo – 4 hours
  - Platelets – until expiry

Objectives

- Explain how a MHP works using the six Ts
  - Triggering and talking
  - Testing
  - Tranexamic acid
  - Temperature
  - Transfusion
  - Termination


Thank you