Pathophysiology and Management of Coagulopathy in Postpartum Hemorrhage

Current understandings, future research needs

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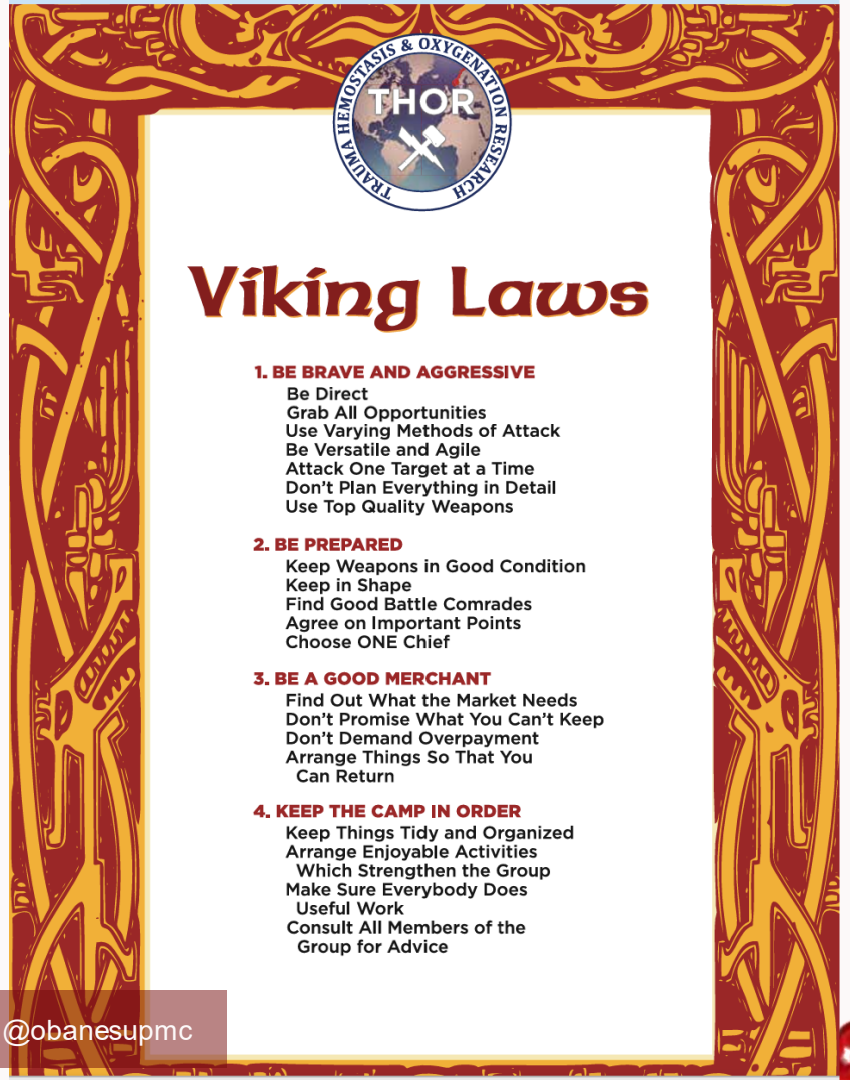
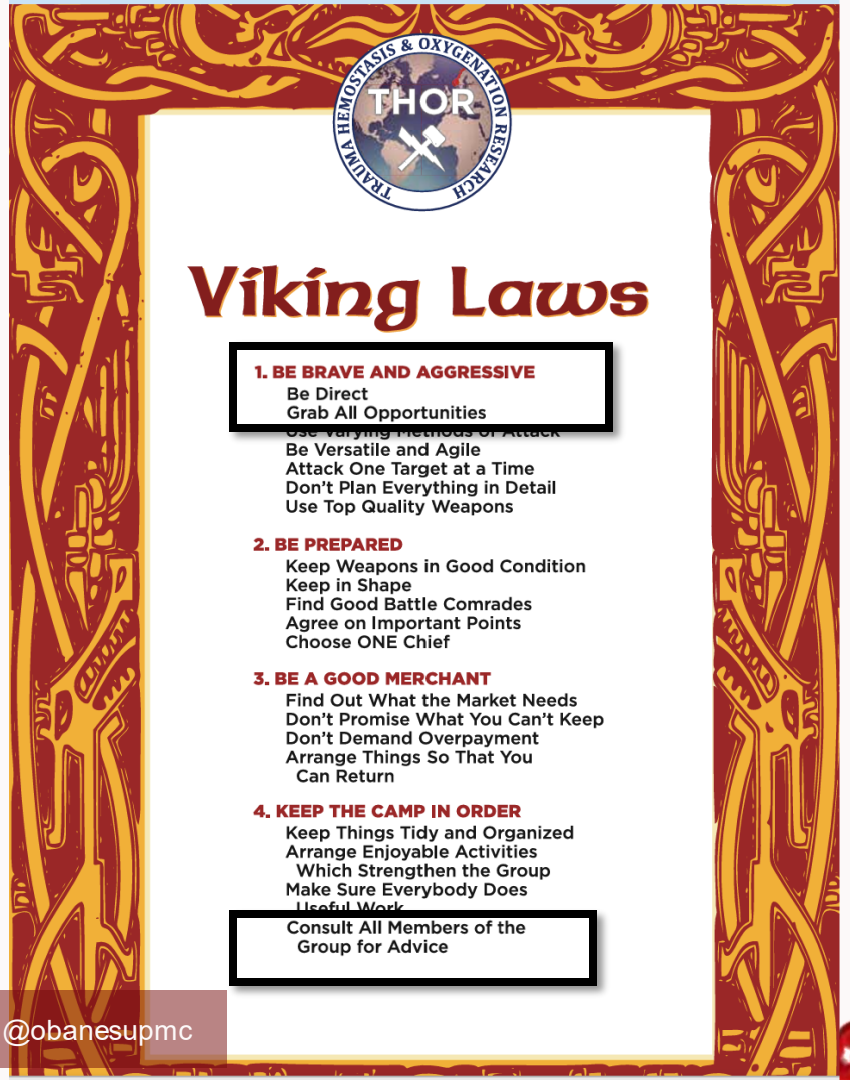




Grace's Quotes from THOR 2025 thus far

"THOR is not just about blood"

Pregnancy physiology is relevant to PPH management

"Do No Harm… Know when not to do things"

(…to plasma or not to plasma in PPH?)

"Aliens vs. Mad Max"

(…are they really mutually exclusive?)

Quote

Image credit: Gemini

Aliens + Mad Max

This may be the real power of

THOR
TRAUMA HEMOSTASIS & OXYGENATION RESEARCH

Disclosures

Salary	NIH UH3CA261067
Salary, Research	NIH R01MH134538
Salary	NIH R01DA054513
Salary, Research	PCORI # EASCS-34606
Research	Octapharma
Advisory Board	Octapharma
Advisory Board	Grifols
Consulting	Heron Pharmaceuticals
Research	Edwards Lifesciences
Research materials	Haemonetics; Werfen
Medical Expert Testimony	Ad hoc
Royalties	Cambridge University Press (Textbook)
Board of Directors	SOAP, Society for Obstetric Anesthesia and Perinatology
Research Committee	SOAP, Society for Obstetric Anesthesia and Perinatology
Consultant	ACOG, American College of Obstetricians and Gynecologists Voluntary Review of Quality of Care (VRQC) Program

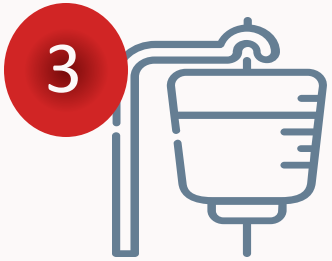
Objectives

Intro to PPH

Define, health impact

Pathophysiology

Mechanisms, triggers, distinct features in obstetric patients, compare/contrast with trauma induced coagulopathy



Treatments, Knowledge Gaps

Current treatment strategies; Current unknowns; Future & ongoing research directions

Intro to Postpartum Hemorrhage (PPH)

1

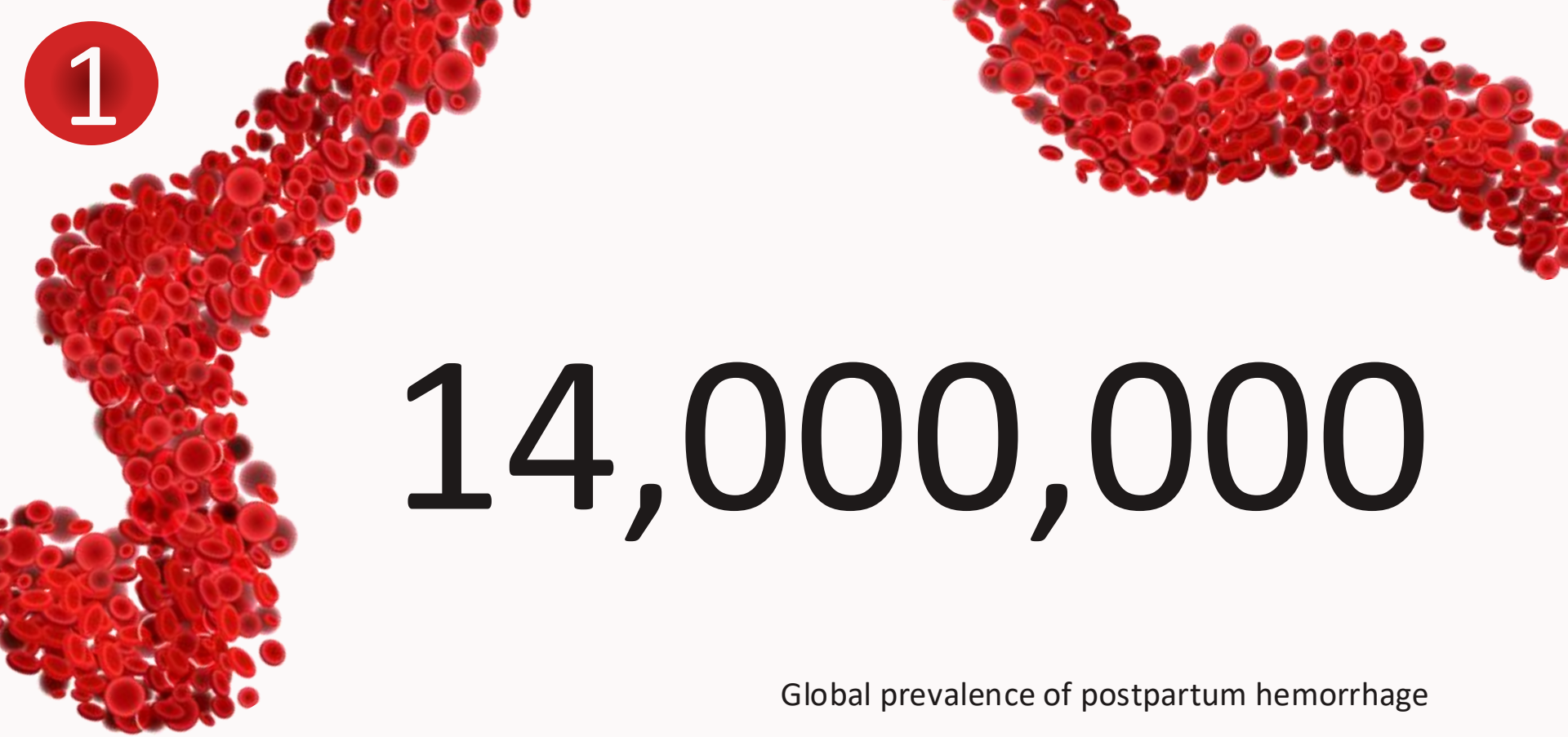
Definition of PPH

- Blood loss 500mL (vaginal) or ≥1,000 mL (cesarean) with associated morbidity/mortality

Coagulopathy prevalence

- *Low!* Clinically significant in ~3% of PPH cases, rising with blood loss >2,000 mL
- Distinct subtypes: *hyperfibrinolysis*, *dysfibrinogenemia*, and *dilutional coagulopathy*

Evensen A. Am Fam Physician. 2017. PMID: 28409600.
Hofer S. Eur J Anaesthesiol. 2023. PMID: 36131564
de Lloyd L. J Thromb Haemost. 2023. PMID: 36696216.
Collins PW. Blood Adv. 2025. PMID: 39913691



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14,000,000

Global prevalence of postpartum hemorrhage

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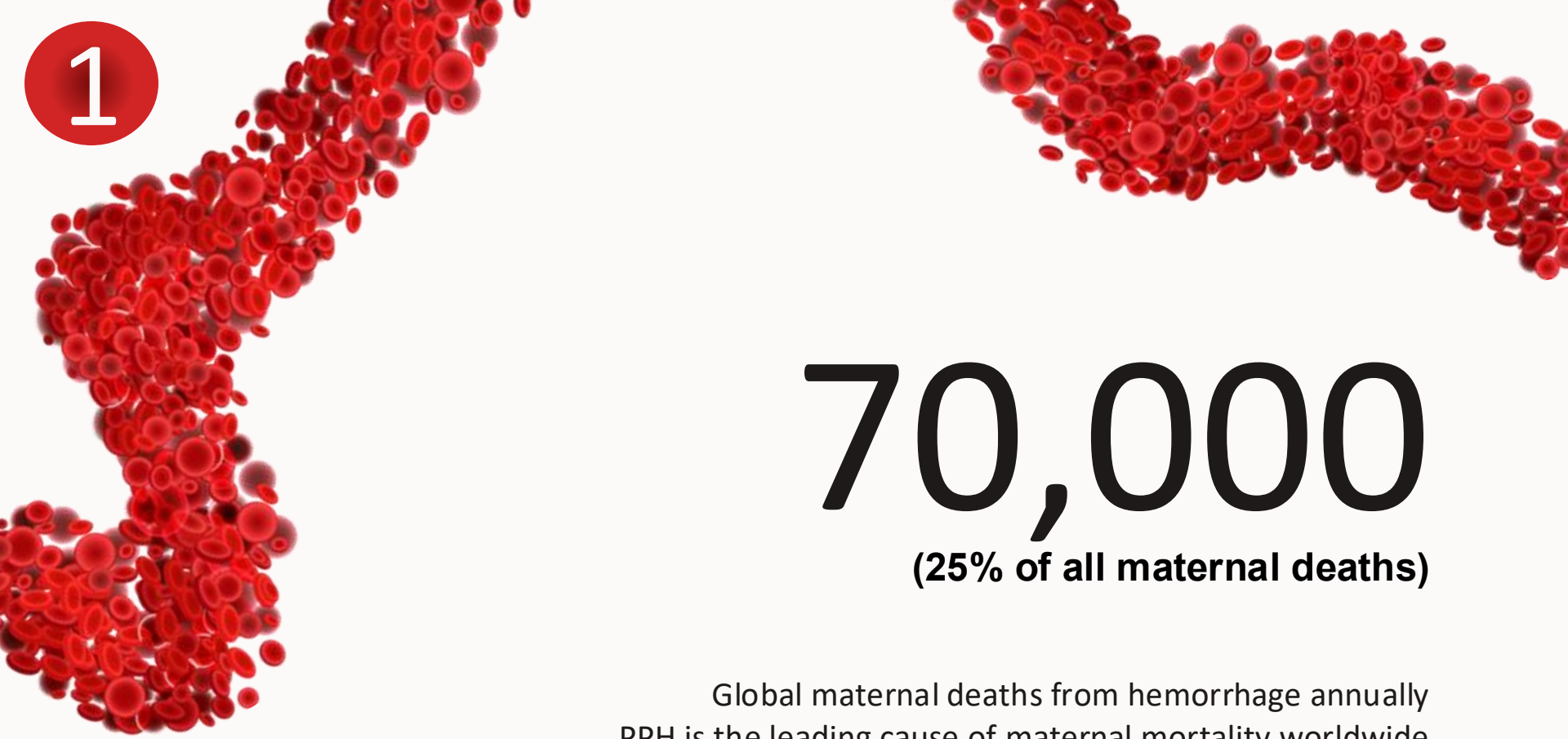
Source: WHO



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70,000

(25% of all maternal deaths)

Global maternal deaths from hemorrhage annually
PPH is the leading cause of maternal mortality worldwide

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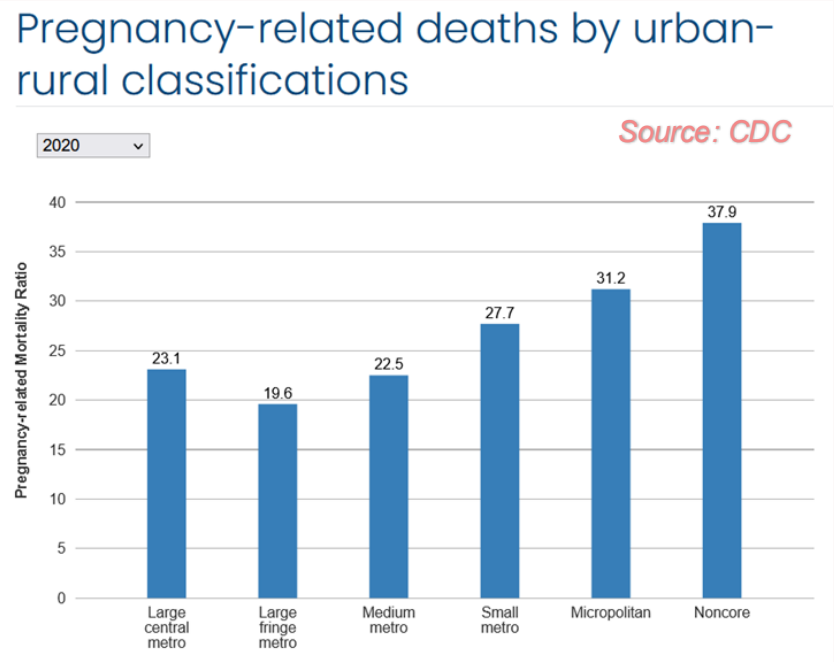
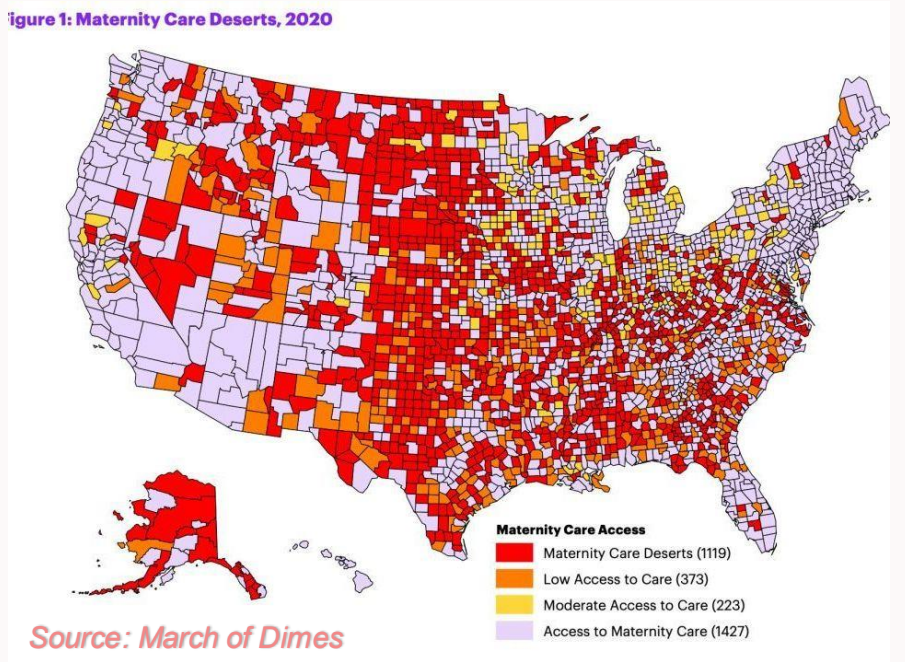
Source: WHO

Disproportionate Effects by Rurality

Lowest MMR worldwide, 1.7 - 2 per 100,000
3.4x higher in rural/small units





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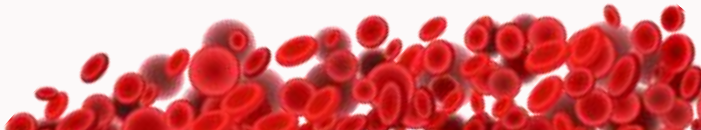
2

Pathophysiology

of PPH-Associated Coagulopathy



“Four Ts” : Causes of PPH

RISK FACTORS

Antepartum hemorrhage
Augmented labor
Chorioamnionitis
Fetal macrosomia
Maternal anemia…
Maternal obesity
Multifetal gestation
Preeclampsia
Primiparity
Prolonged labor
…

Tone

Uterine atony

Tissue

Retained placenta

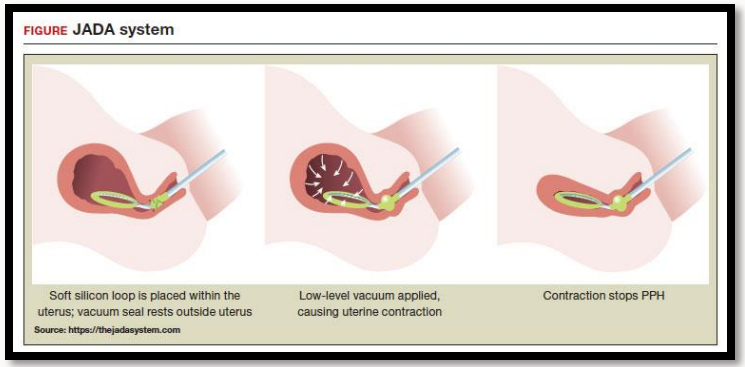
Trauma

Genital tract laceration

Thrombin

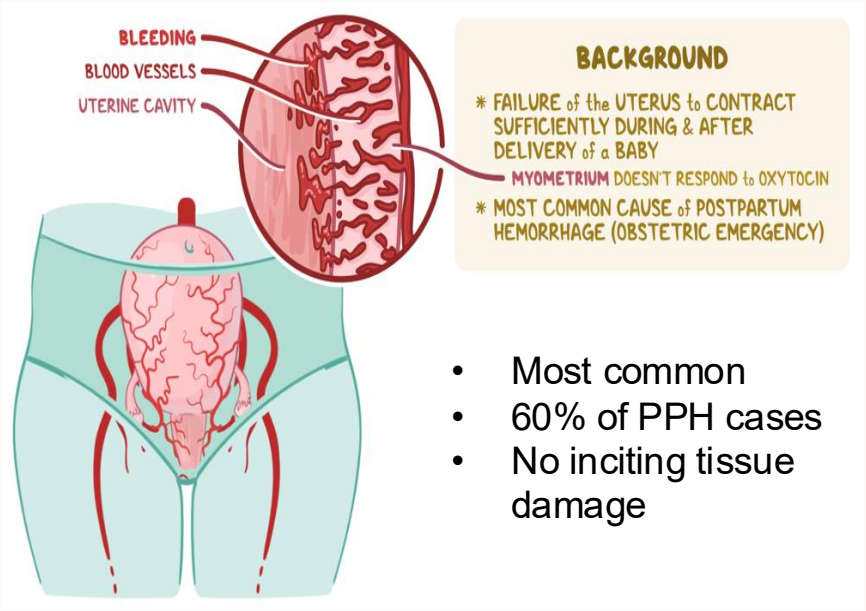
Coagulopathy, disseminated intravascular coagulation

“Four Ts” : Causes of PPH



Tone

Uterine atony, inversion



- Most common
- 60% of PPH cases
- No inciting tissue damage

Treatments:
Uterine massage, Oxytocin/Uterotonics, Tamponade Devices, Artery embolization, Hysterectomy

“Four Ts” : Causes of PPH

RISK FACTORS	
Antepartum hemorrhage	Maternal obesity
Augmented labor	Multifetal gestation
Chorioamnionitis	Preeclampsia
Fetal macrosomia	Primiparity
Maternal anemia…	Prolonged labor
	…

Tone

Uterine atony

Tissue

Retained placenta, placenta accreta spectrum

Trauma

Genital tract laceration

Treatments:
Uterine evacuation; antibiotics for endometritis

“Four Ts” : Causes of PPH

RISK FACTORS

Antepartum hemorrhage
Augmented labor
Chorioamnionitis
Fetal macrosomia
Maternal anemia…
Maternal obesity
Multifetal gestation
Preeclampsia
Primiparity
Prolonged labor
…

Tone

Uterine atony

Tissue

Retained placenta, placenta accreta spectrum

Trauma

Genital tract laceration

Treatments:
Repair lacerations; surgery if uterine rupture

“Four Ts” : Causes of PPH

RISK FACTORS

Antepartum hemorrhage
Augmented labor
Chorioamnionitis
Fetal macrosomia
Maternal anemia…
Maternal obesity
Multifetal gestation
Preeclampsia
Primiparity
Prolonged labor
…

Tone

Uterine atony

Tissue

Retained placenta, placenta accreta spectrum

Thrombin

Coagulopathy, disseminated intravascular coagulation

Treatments:

Replace coagulation factors…
Research opportunities

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Key Mechanisms of Coagulopathy

⚡**Triggers**: Placental abruption, amniotic fluid embolism (AFE), massive hemorrhage

Hyperfibrinolysis

Excess plasmin generation cleaves fibrinogen/fibrin, ↑D-dimer, plasmin-antiplasmin complexes

Dysfibrinogenemia

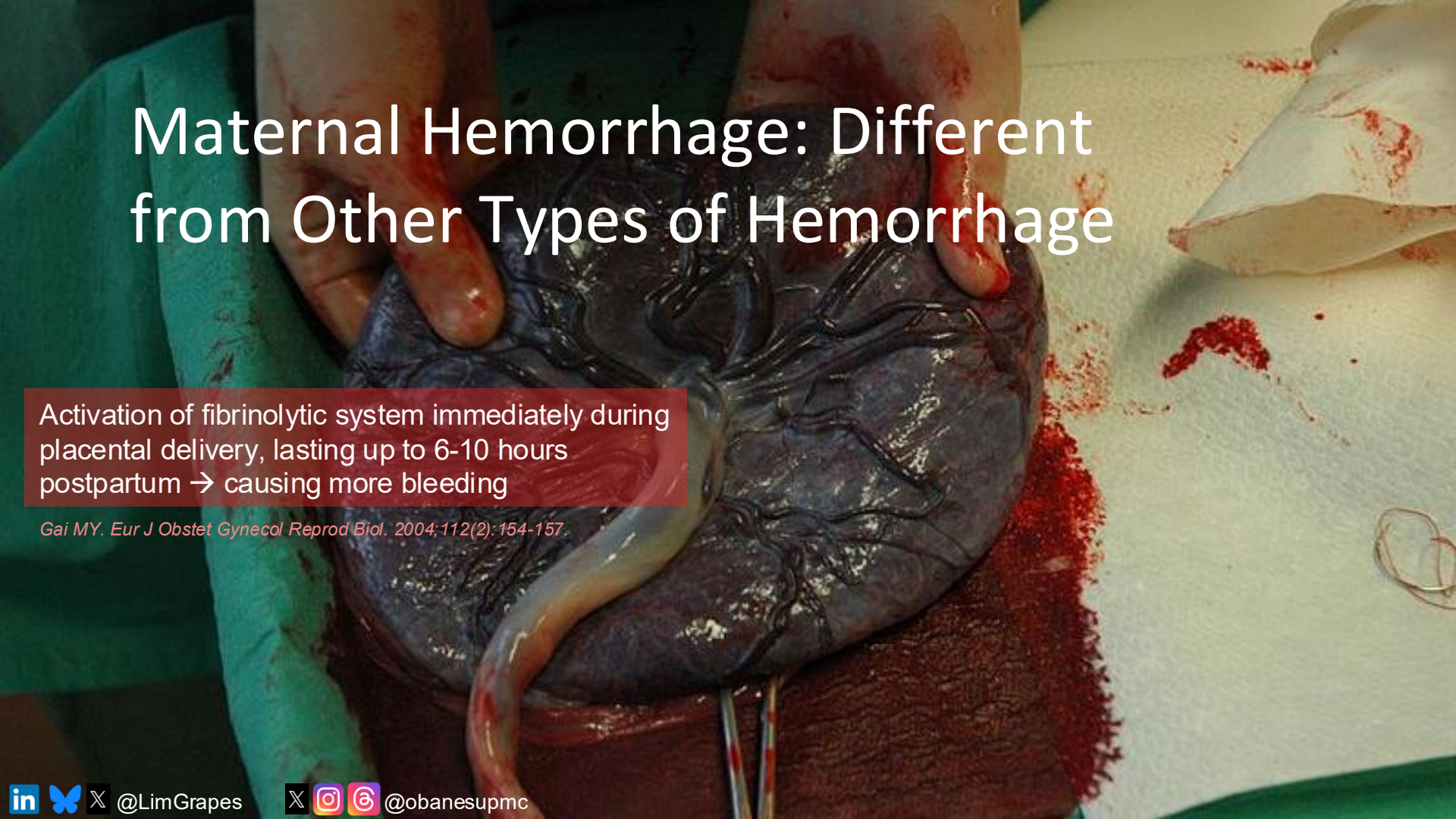
Abnormal fibrinogen structure (Clauss/antigen ratio <0.7)

Factor depletion

Low fibrinogen (<2g/L), factor V, VIII in severe cases

de Lloyd L. J Thromb Haemost. 2023. PMID: 36696216
Collins PW. Blood Adv. 2025. PMID: 39913691
Collins P. Thromb Haemost. 2016. PMID: 27028301

Maternal Hemorrhage: Different from Other Types of Hemorrhage



Activation of fibrinolytic system immediately during placental delivery, lasting up to 6-10 hours postpartum → causing more bleeding

Gai MY. Eur J Obstet Gynecol Reprod Biol. 2004;112(2):154-157.

Maternal Hemorrhage: Different from Other Types of Hemorrhage

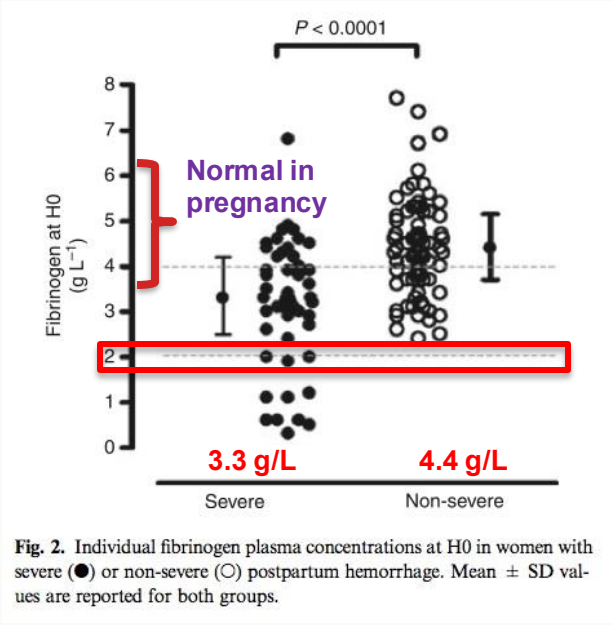


Fig. 2. Individual fibrinogen plasma concentrations at H0 in women with severe (●) or non-severe (○) postpartum hemorrhage. Mean ± SD values are reported for both groups.

Charbit B. J Thromb Haemost. 2007 Feb;5(2):266-73.

Fibrinogen is the best predictor for severe postpartum hemorrhage.

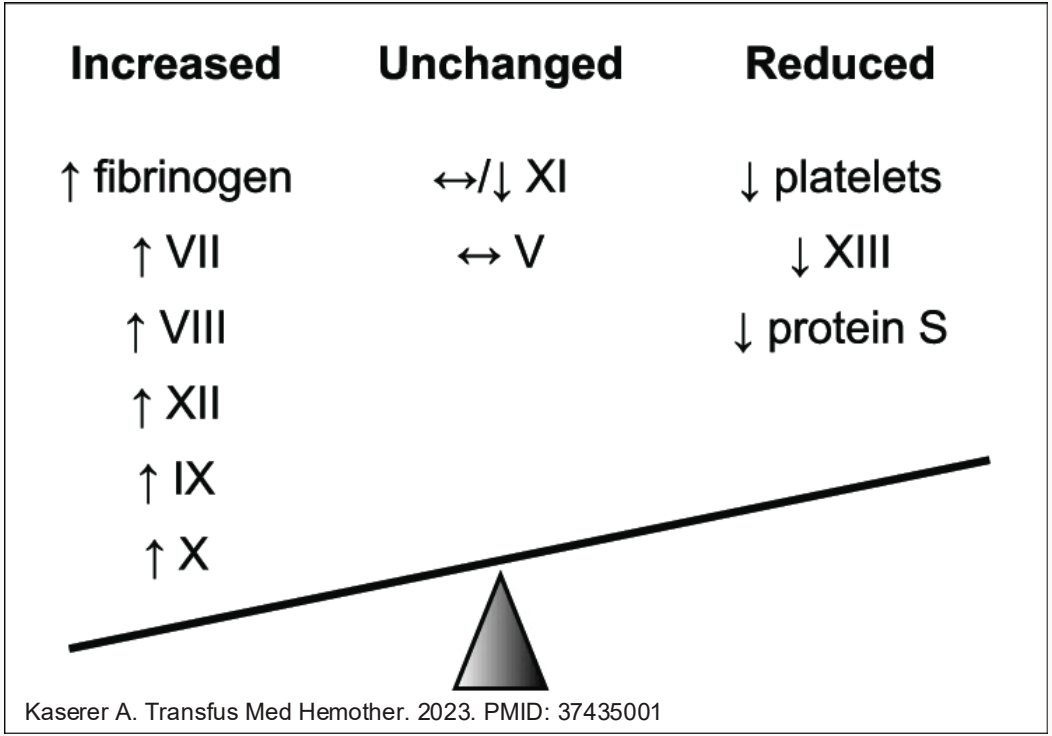
Severe PPH Definition:
- Decrease in Hb by 4g/dL
- Transfusion of at least 4 RBC units
- Hemostatic intervention (angiography, arterial ligation, hysterectomy)
- Death

Risk for severe PPH was 2.6-fold higher for each 1 gL^{-1} ▼fibrinogen

NPV of fibrinogen concentration >4 gL^{-1} was 79%
PPV of fibrinogen concentration ≤2 gL^{-1} was *~100%*

These findings indicate that a simple Clauss fibrinogen measurement can anticipate the risk of severe bleeding in PPH

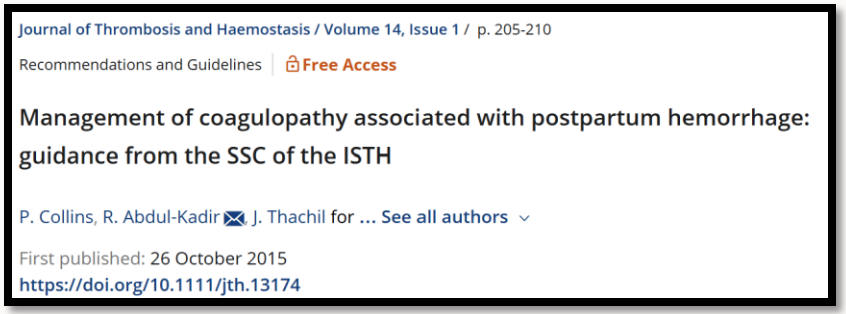
Coagulation Factor Changes in Pregnancy



Kaserer A. Transfus Med Hemother. 2023. PMID: 37435001

PPH Guidelines: Early fibrinogen replacement, POCT + algorithm

Recomends point of care testing for PPH management



Journal of Thrombosis and Haemostasis / Volume 14, Issue 1 / p. 205-210

Recommendations and Guidelines | Free Access

Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH

P. Collins, R. Abdul-Kadir, J. Thachil for ... See all authors

First published: 26 October 2015

https://doi.org/10.1111/jth.13174

Transfusion Medicine and Hemotherapy

Review Article

Transfus Med Hemother
DOI: 10.1159/000528390

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Patient Blood Management in Pregnancy

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The appropriate fibrinogen intervention trigger or target level is unknown.

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OBSTETRICS & GYNECOLOGY

Journal of Obstetric, Gynecologic, & Neonatal Nursing JOGNN Scholarship for the Care of Women, Childbearing Families & Newborns

Journal of Midwifery & Women's Health

OBSTETRIC ANESTHESIOLOGY: RESEARCH REPORT

National Partnership for Maternal Safety

Consensus Bundle on Obstetric Hemorrhage

Main, Elliott K. MD; Goffman, Dena MD; Scavone, Barbara M. MD; Low, Lisa Kane PhD, CNM; Bingham, Debra DrPH, RN; Fontaine, Patricia L. MD, MS; Gorlin, Jed B. MD; Lagrew, David C. MD; Levy, Barbara S. MD

Author Information

Anesthesia & Analgesia 121(1):p 142-148, July 2015. | **DOI:** 10.1097/AOG.0000000000000869

Obstet Gynecol. 2015 Jul;126(1):155-62.
Anesth Analg. 2015 Jul;121(1):142-148.
J Midwifery Womens Health. 2015 Jul-Aug;60(4):458-64.
J Obstet Gynecol Neonatal Nurs. 2015 Jul-Aug;44(4):462-470.

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The 4 R's of PPH

- READINESS
- RECOGNITION & PREVENTION
- RESPONSE
- REPORTING & SYSTEMS LEARNING

ANESTHESIA & ANALGESIA
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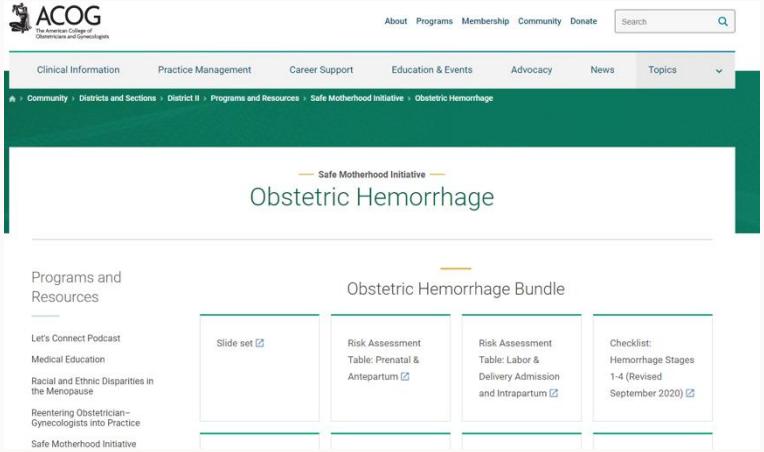
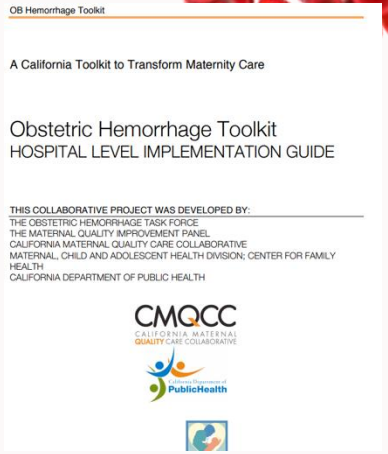
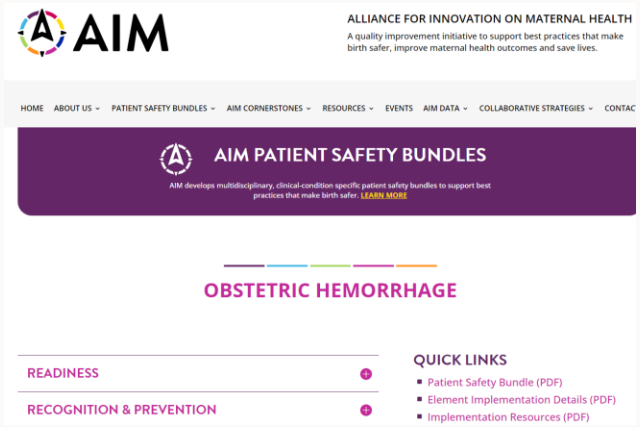
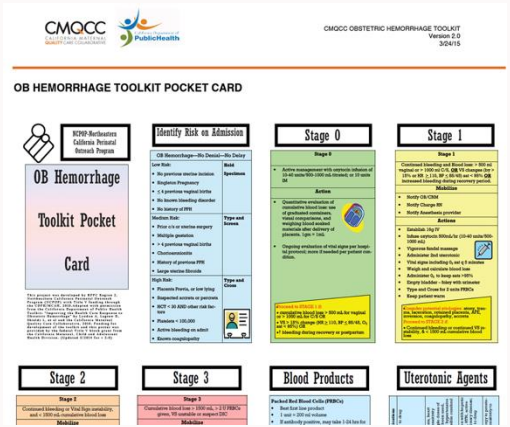
READINESS

PPH Protocols & Toolkits









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OB Hemorrhage Checklist

Affix Label

Postpartum hemorrhage is defined as cumulative blood loss of greater than or equal to 1000mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours. However, blood loss >500mL in a vaginal delivery is abnormal and should be investigated and managed as outlined in Stage 1.

0

Recognition: ☐ Call for RN assistance ☐ Notify Charge Nurse ☐ Notify Provi

☐ Obtain Hemorrhage Cart ☐ Notify Anesthesia

Designate: ☐ _____ ☐ _____

Announce Assessments (q 5-15 minutes): ☐ QBL ☐ Vital signs / LOC / SpO2

☐ Determine stage

Signs & Symptoms of Hypovolemia or Hemodynamic Instability

HR ≥ 110 O2 sat < 95 Respiration > 28

SBP < 90 DBP < 50 Oliguria

Pallor, dizziness, or altered mental status

STAGE 1: Blood loss >1000mL after delivery with normal vital signs and lab values. Vaginal delivery 500-999mL should be treated as in Stage 1.

1

Initial Steps:

☐ Ensure 16G or 18G IV access / Consider 2nd IV site

☐ Increase IV fluid (crystalloid without oxytocin)

☐ Assess VS: T____ P____ R____ BP____ Pain____

☐ Assess SpO2 ____ ☐ Apply O2 via FM if < 95%

☐ Assess LOC

☐ Fundal massage / assess height, position, tone

☐ Assess bladder, catheterize as necessary

☐ Keep Warm

Medications:

☐ Increase oxytocin, consider additional uterotonics, not

☐ Analgesic (dose & time[s])_____

Blood Bank:

☐ Confirm active Type and Screen and consider Type and Crossmatch of 2 units PRBCs

Action:

☐ Determine etiology and treat

☐ Prepare OR (optimize visualization / examination)

☐ Start collecting blood loss and anticipate cell salvage

☐ Consider a higher level of care

Draw labs, including viscoelastic testing (VET)

Oxytocin (Pitocin) **Time(s)**

30 units in 500mL diluent

10 units IM _____

Methylergonovine (Methergine):

IM X 1 (avoid with HTN) _____

emabate)

s IM (avoid with asthma)

15 minutes, max 8 doses) _____

Cytotec)

800-1000 micrograms PR

600 micrograms PO or 800 micrograms SL _____

Tranexamic Acid (TXA)

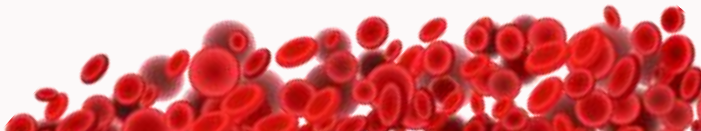
1 gram IV push over 10 min; may be repeated once after 30 minutes OR add 1-gram vial to 100mL NS and give IV over 10 min; may be repeated once after 30 min; do not exceed 2-grams _____

Tone (i.e., atony)
Trauma (i.e., laceration)
Tissue (i.e., retained products)
Thrombin (i.e., coagulation dysfunction)

CUMULATIVE QBL

Physiology of Pregnancy

and Why it is both Protective and Problematic for PPH



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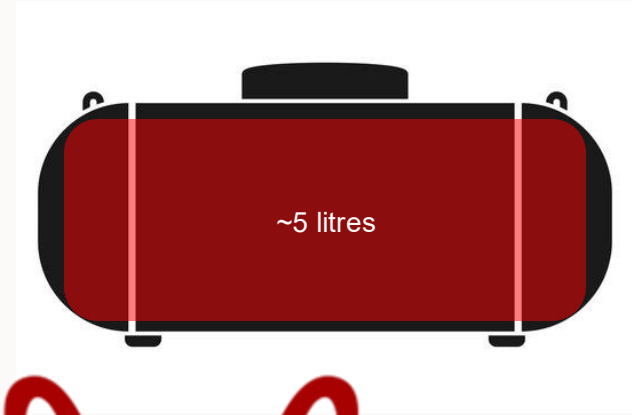
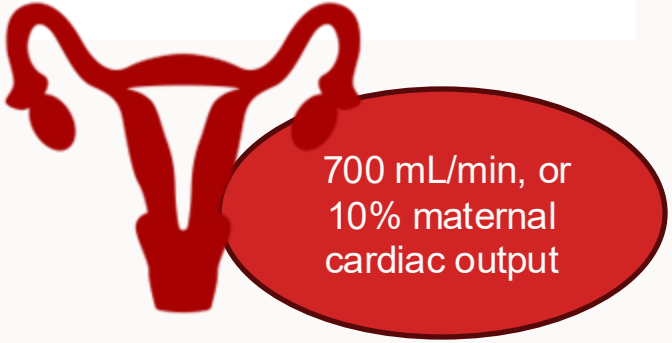
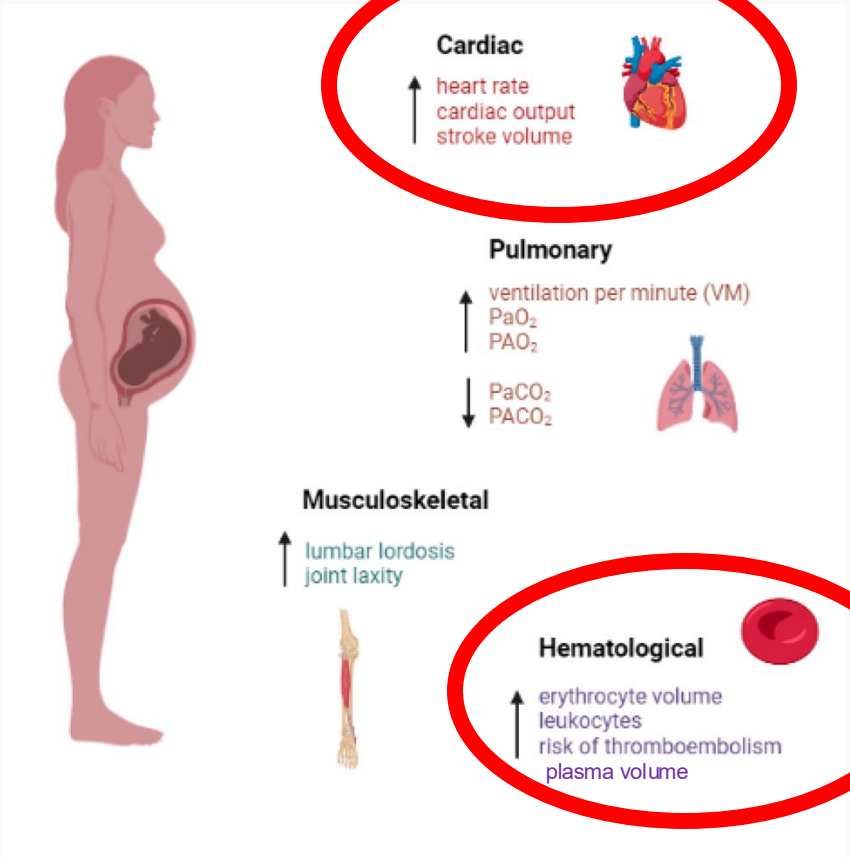
Physiology of Pregnancy

Why it is problematic for PPH

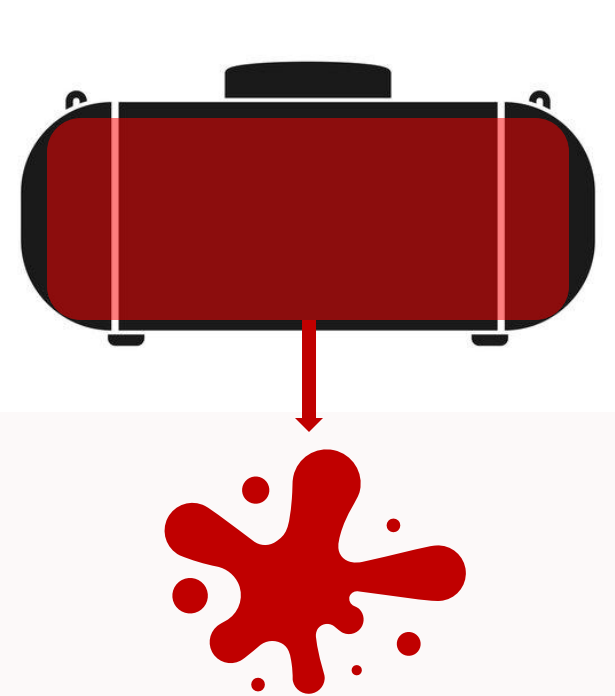


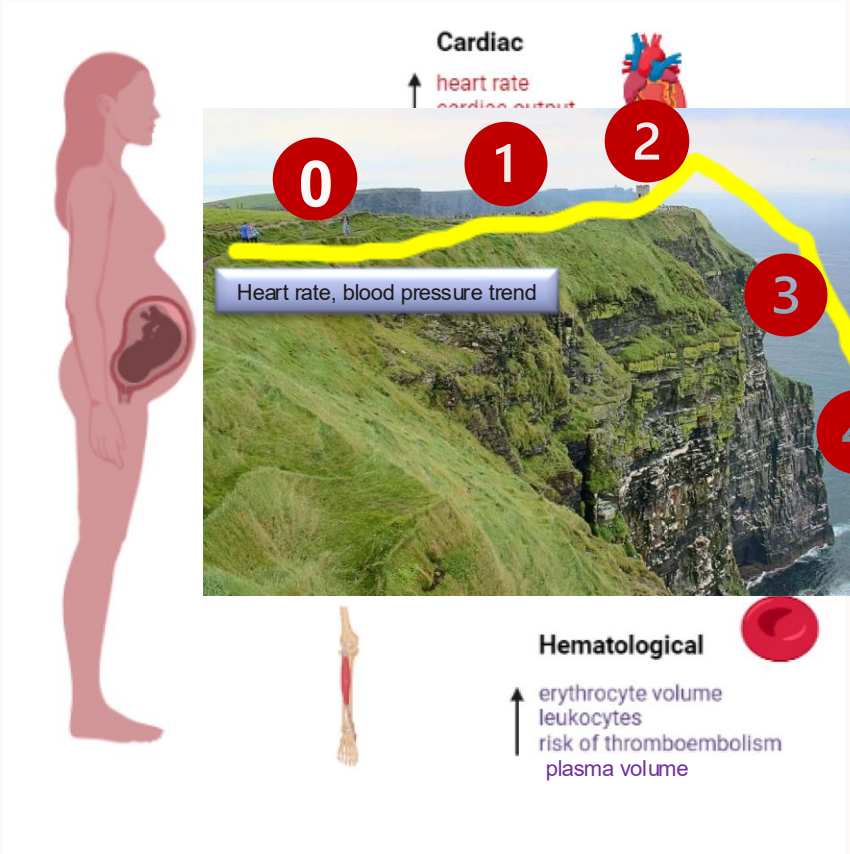




Physiology of Pregnancy

Why it is problematic for PPH

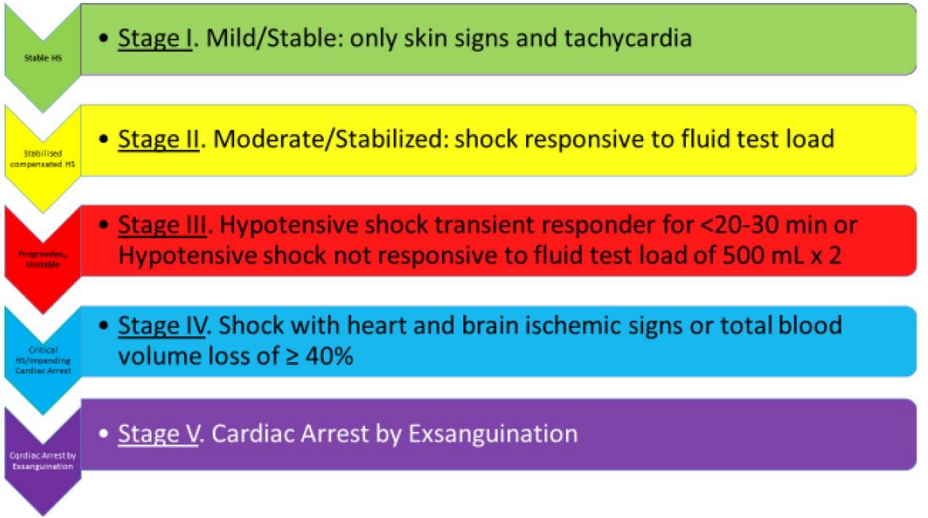




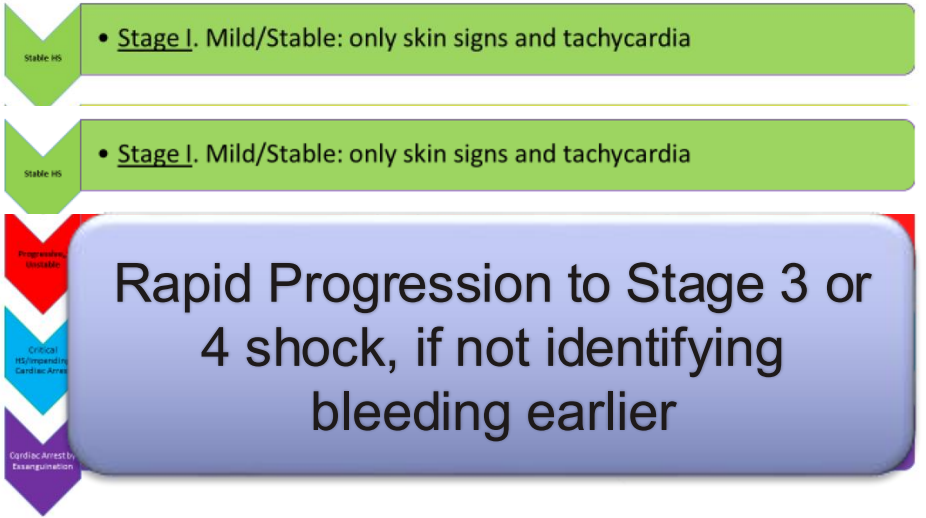
Physiology of Pregnancy

Why it is problematic for PPH

Shock: Trauma Paradigm



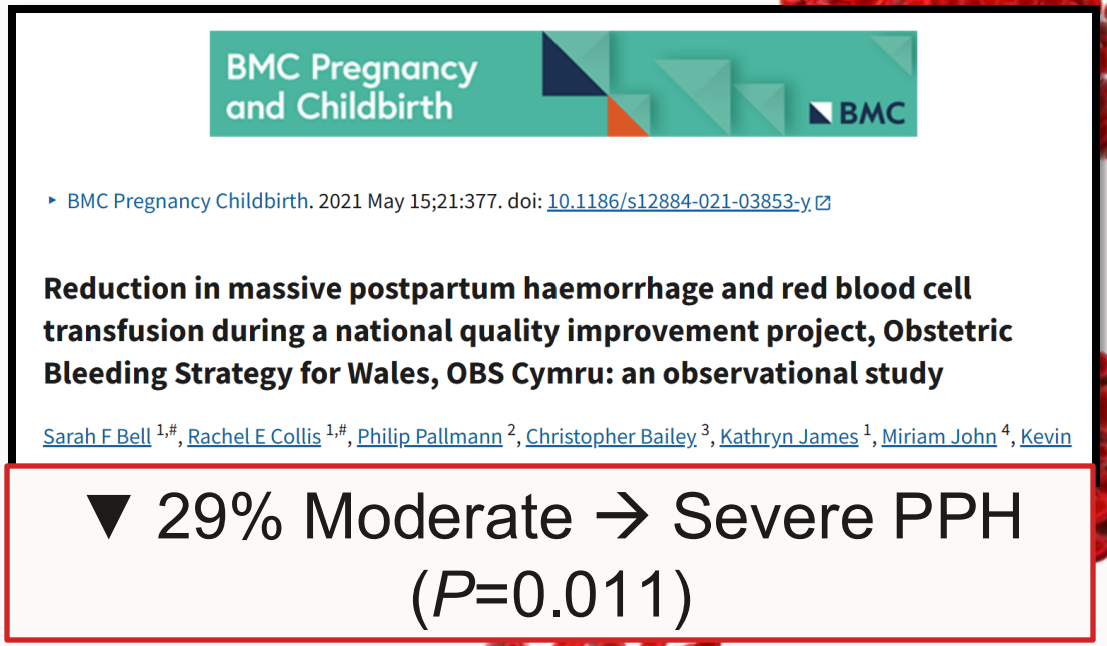
Shock: PPH Paradigm



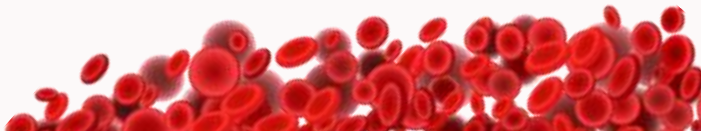
Key Point

If you're doing it right, you are preventing the progression to moderate/severe postpartum hemorrhage

1. Risk assess all mothers
2. Gravimetric cumulative blood loss
3. MDT @ 1000mL for earlier interventions
4. POC-guided product replaceemnt



Acute Obstetric Coagulopathy (AOC)



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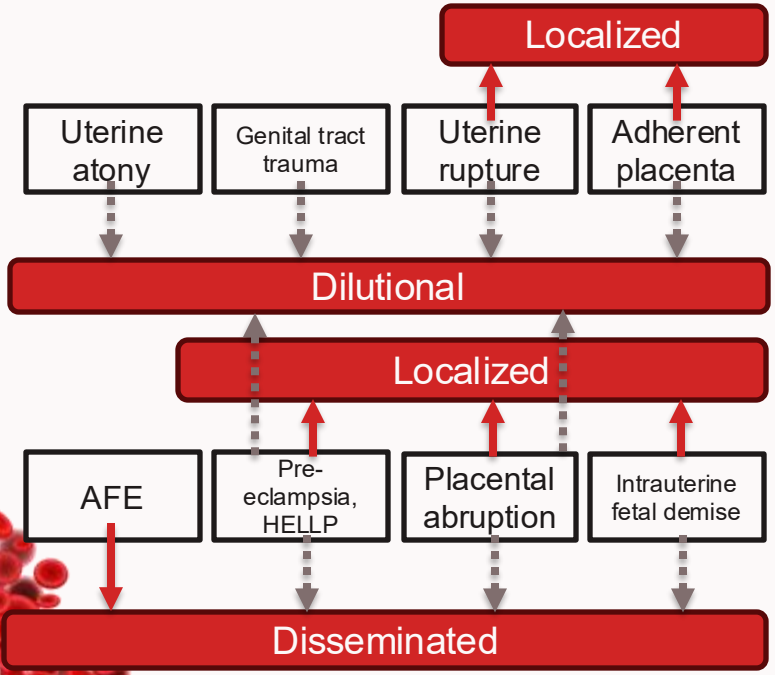
Acute Obstetric Coagulopathy (AOC)



Defining Features

- PAP >40,000 ng/mL, D-dimer >25x normal.
- Clauss fibrinogen <2g/L; Clauss/antigen ratio<0.7--functional fibrinogen deficiency

Biomarkers

- Hypofibrinogenemia, dysfibrinogenemia, and reduced factor V/VIII

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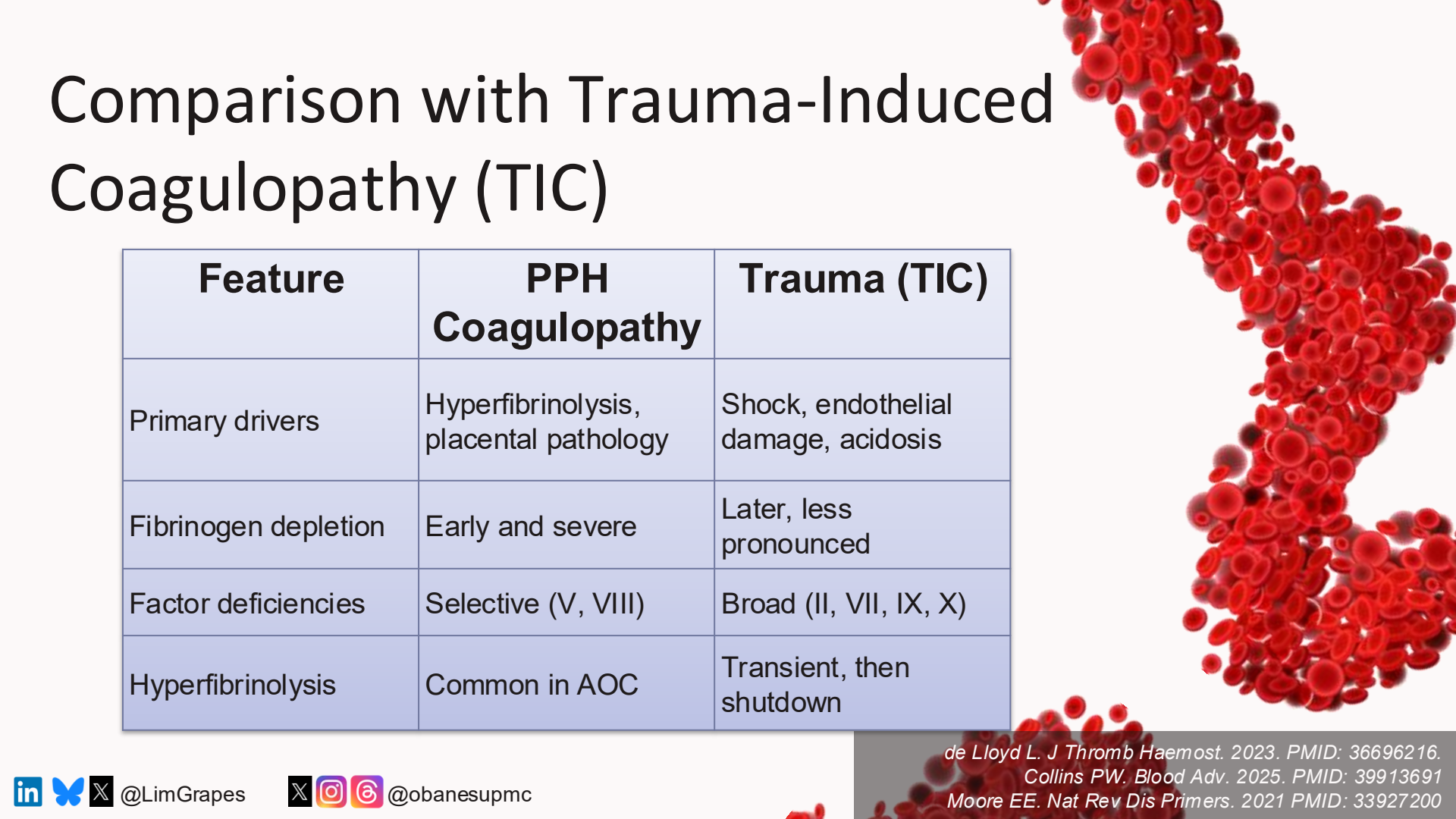
Collins P. J Thromb Haemost. 2016. PMID: 27028301
de Lloyd L. J Thromb Haemost. 2023. PMID: 36696216
Collins PW. Blood Adv. 2025. PMID: 39913691

Comparison with Trauma-Induced Coagulopathy (TIC)

Feature	PPH Coagulopathy	Trauma (TIC)
Primary drivers	Hyperfibrinolysis, placental pathology	Shock, endothelial damage, acidosis
Fibrinogen depletion	Early and severe	Later, less pronounced
Factor deficiencies	Selective (V, VIII)	Broad (II, VII, IX, X)
Hyperfibrinolysis	Common in AOC	Transient, then shutdown



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Collins PW. Blood Adv. 2025. PMID: 39913691
Moore EE. Nat Rev Dis Primers. 2021 PMID: 33927200

Comparison with Trauma-Induced Coagulopathy (TIC)

Feature	PPH Coagulopathy	Trauma (TIC)
Primary driver		
Fibrinogen dep		
Factor deficien		
Hyperfibrinolysis	Common in AOC	Transient, then shutdown

PPH coagulopathy: fibrinogen centric; sustained hyperfibrinolysis

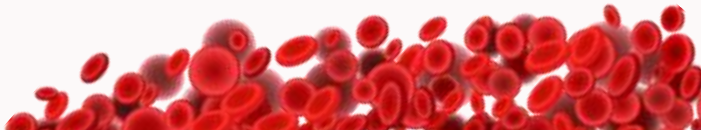
TIC: global hemostatic collapse from shock, endothelial injury

de Lloyd L. J Thromb Haemost. 2023. PMID: 36696216.
Collins PW. Blood Adv. 2025. PMID: 39913691
Moore EE. Nat Rev Dis Primers. 2021 PMID: 33927200

03

Treatment Strategies, Knowledge Gaps

Current treatment strategies; Current unknowns; Future & ongoing research directions



Treatment Strategies

Antifibrinolytics

Tranexamic acid 1-2g IVP within 3 hours of PPH: reduced mortality, morbidity (WOMAN Trial 2017)

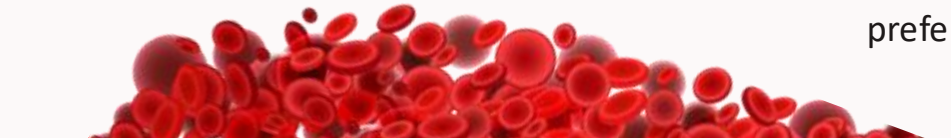
Fibrinogen replacement

Target Clauss fibrinogen ≥2 g/L or Fibtem A5 ≥12 mm

Cryoprecipitate or fibrinogen concentrate preferred over FFP

Viscoelastic testing (TEG, ROTEM)

Guides individualized transfusion, reduces unnecessary FFP, Platelets



PPH Transfusion Protocols, Factor Concentrates

Massive transfusion protocols

Balance RBC:FFP:platelets (ratios) but avoid over-reliance on FFP

But adjust based on VET

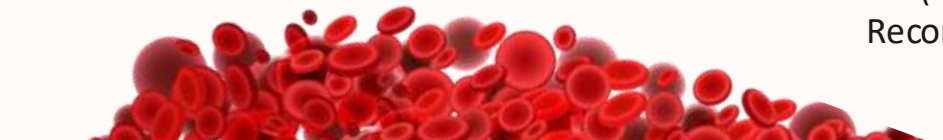
Factor concentrates

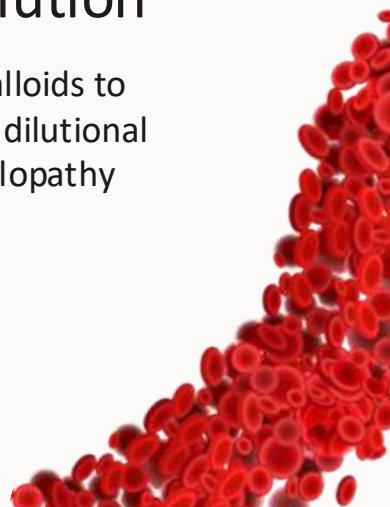
Limited evidence:
- prothrombin complex concentrate
- Factor XIII

Harm (thrombosis):
- Recombinant FVIIa

Avoid dilution

Limit crystalloids to prevent dilutional coagulopathy



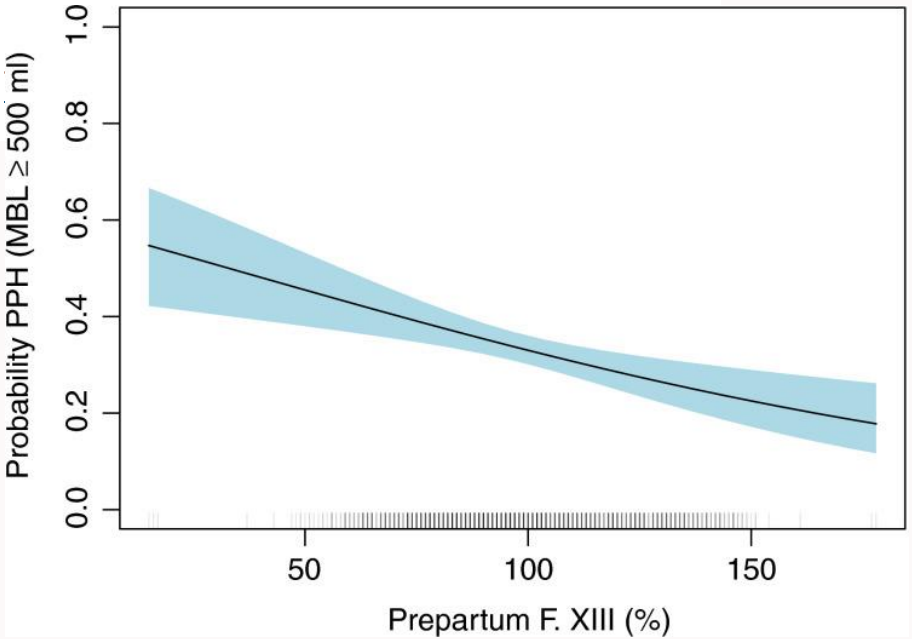


Factor XIII Could Be Interesting for PPH

The impact of prepartum factor XIII activity on postpartum blood loss

Christian Haslinger [1] · Wolfgang Korte [2] · Charles Greenberg [4] · Roland Zimmermann [1]

FXIII <50% increased probability of PPH to >50%



Haslinger C. J Thromb Haemost. 2020. PMID: 32176833.

Factor XIII Could Be Interesting for PPH

The impact of antenatal factor XIII levels on postpartum haemorrhage: a prospective observational study

Maternal–Fetal Medicine | Published: 03 December 2018

Mean pre-delivery FXIII activity:

80% women with PPH
86% women without PPH
P=0.001

Table 3 Antenatal maternal blood coagulation parameters in groups of patients without PPH (< 500 mL) and with PPH (≥ 500 mL)

Coagulation factors	Total	*n*	Blood loss < 500 mL	*n*	Blood loss ≥ 500 mL	*n*	*p* value
Factor XIII (%)	85.44 ± 14.97	548	86.45 ± 14.65	470	79.33 ± 15.50	78	< 0.001[1b]
aPTT (s)	30.5 ± 2.6	547	30.5 ± 2.6	529	31.1 ± 2.3	78	0.176[1b]
Prothrombin time (s)	108.0 (100.0; 115.0)	547	108.0 (100.0; 115.0)	469	108.0 (100.0; 115.8)	78	0.693[2a]
Platelets (/nL)	215 (178; 254)	546	217 (179; 256)	468	206 (172; 244)	78	0.067[2b]

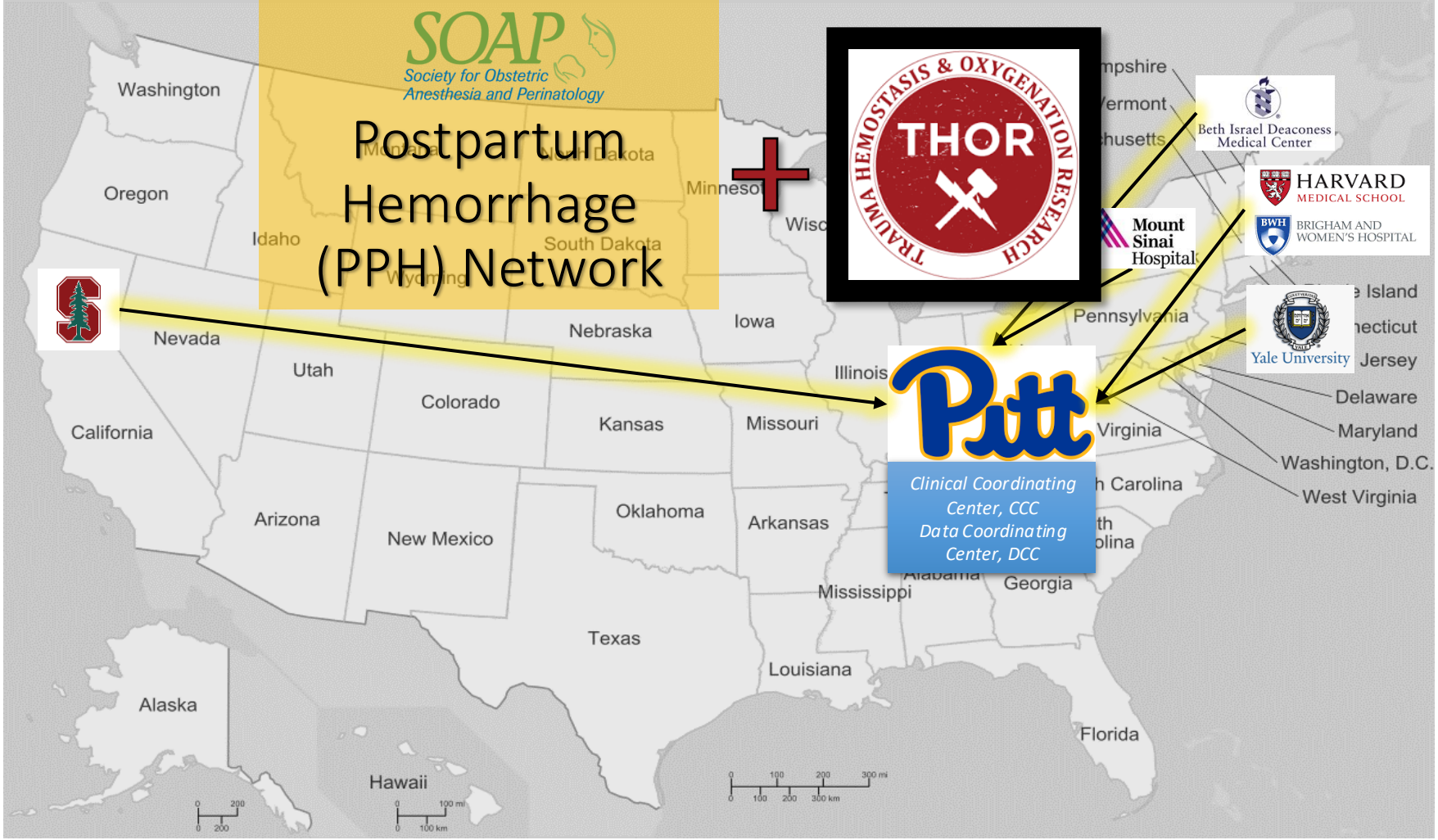
Values represent the mean ±SD or the median (IQR)

Bamberg C. Arch Gynecol Obstet. 2019 PMID: 30511192.

Grace's Gaps in Current Knowledge

- Unresolved Issues:
  - Optimal fibrinogen threshold for intervention
  - Role of dysfibrinogenemia in treatment failure
  - Lack of rapid, point-of-care dysfibrinogenemia assays
  - What exactly is driving coagulopathy during most severe PPH?
- Controversies:
  - Timing of TXA in non-hyperfibrinolytic PPH
  - FFP vs. factor concentrates for factor replacement

Hofer S. Eur J Anaesthesiol. 2023. PMID: 36131564
de Lloyd L. J Thromb Haemost. 2023. PMID: 36696216
Massoth C. Curr Opin Anaesthesiol. 2023. PMID: 36815533
Bonnet MP. F1000Res. 2016. PMID 27408694
Liu LY. Int J Womens Health. 2023. PMID: 37283995



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Postpartum Hemorrhage (PPH) Network

- Status: Recruiting
- Purpose: To understand coagulopathy in severe PPH, to provide optimal treatment and improve outcomes
- The data will inform a multicenter trial protocol to test effectiveness of therapeutic interventions in PPH
- The **objective** is to characterize patterns of coagulopathy in severe PPH using the TEG-6 and ROTEM sigma and standard central lab blood analyses

werfen

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Thromboelastographic and Thromboelastometric Profiles in Severe PPH

Aim 1: Prove Network feasibility for prospective trial
Aim 2: Describe VET patterns in severe PPH

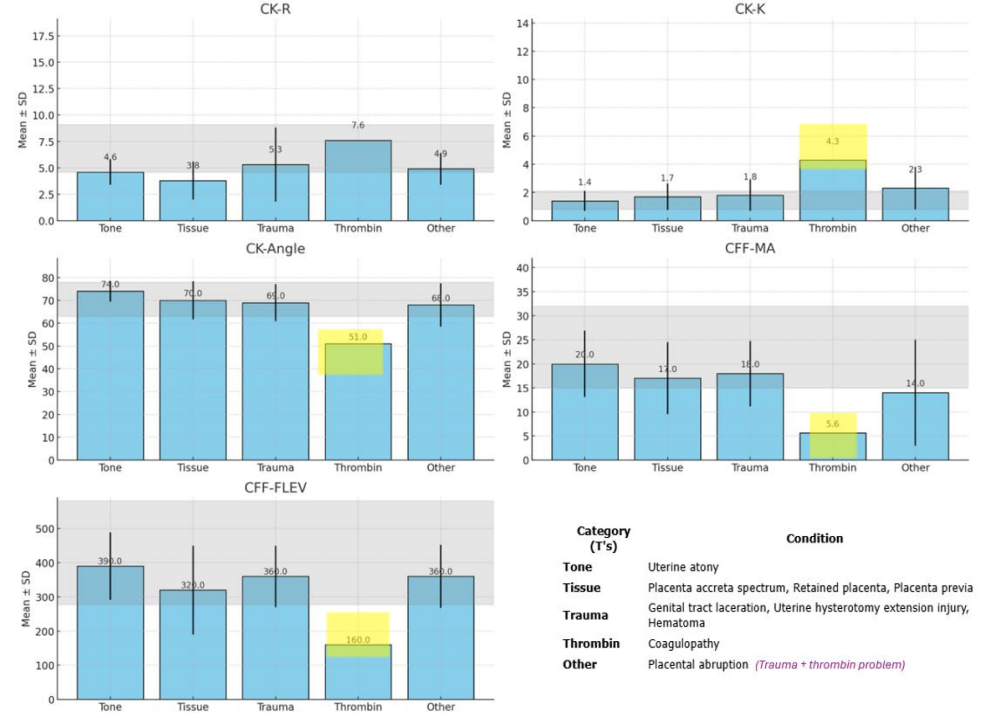
- IRB Approved STUDY22120014
- Target N=100
- Inclusion
  - Postpartum, on Labor & Delivery Unit
  - Severe PPH defined as:
  - Transfusion of 2 or more PRBC units or Use of cell salvage
- Exclusion
  - Known inherited coagulopathy
  - Exposed to anticoagulants within 5 half-lives of respective agent

Category (T's)	Condition
Tone	Uterine atony
Tissue	Placenta accreta spectrum, Retained placenta, Placenta previa
Trauma	Genital tract laceration, Uterine hysterotomy extension injury, Hematoma
Thrombin	Coagulopathy
Other	Placental abruption

RBC Transfusion Chunking, based on data distribution alone:
Low RBC transfusion 0-2
Moderate RBC transfusion 3-4
High RBC transfusion >4

Preliminary Results by Hemorrhage Etiology *(study complete August 2025)*

N=48 of 100



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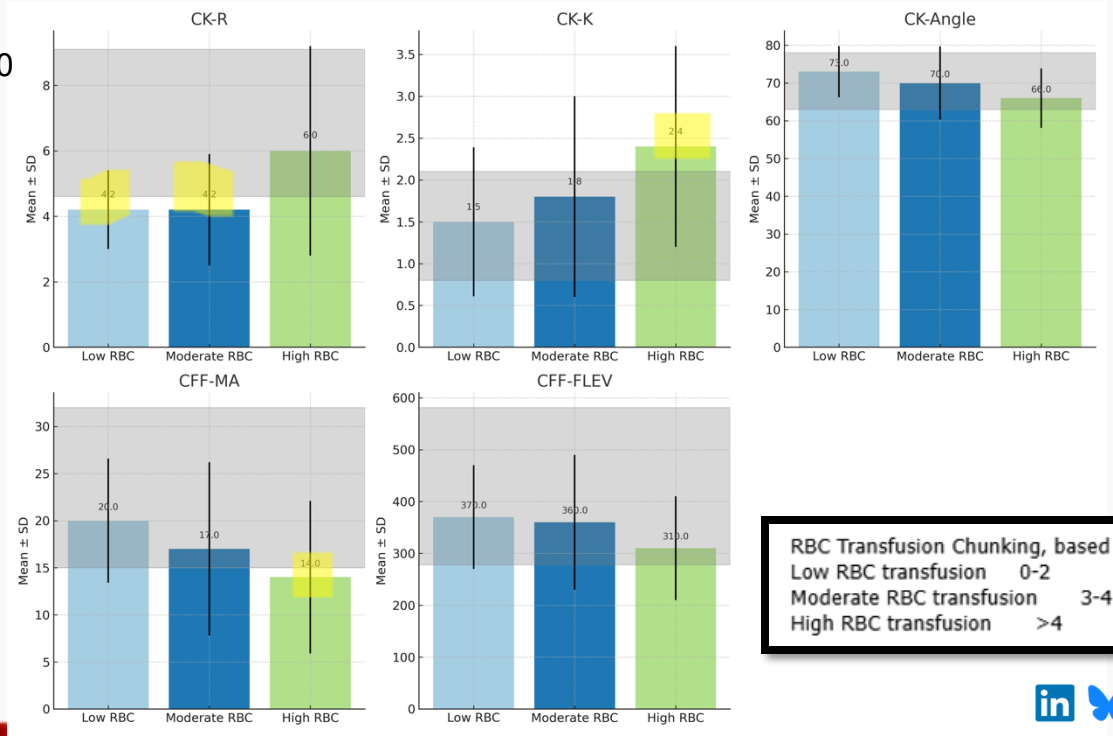
Tissue	Placenta accreta spectrum, Retained placenta, Placenta previa
Trauma	Genital tract laceration, Uterine hysterotomy extension injury, Hematoma
Thrombin	Coagulopathy
Other	Placental abruption *(Trauma + thrombin problem)*

Patients with AOC may be most interesting for precision interventions (fibrinogen, platelets)

Preliminary Results by Transfusion Volume *(study complete August 2025)*

N=48 of 100



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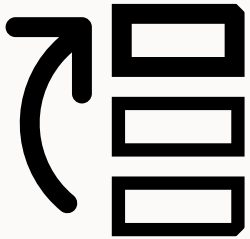
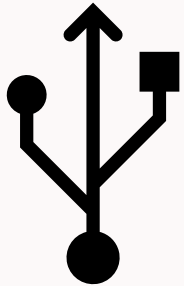
Future Directions



Research Priorities

Validate biomarkers for early AOC detection; Develop pregnancy-specific transfusion algorithms; Large, pragmatic trials to identify who/what/when/where for therapies



Technological advances

Portable viscoelastic testing for resource-limited settings; Precision therapies and dosing given evolving information (balance risks, harms)

Summary & Key Takeaways

Postpartum Hemorrhage is Distinct

AOC is fibrinogen-centric with hyperfibrinolysis, distinct from TIC
TXA and fibrinogen replacement are cornerstones of treatment

Emphasis on Individualized Therapies

Personalized, viscoelastic-guided protocols improve outcomes

Research Needs

Prioritize research on dysfibrinogenemia diagnostics and pregnancy-specific guidelines (*pursuing pragmatic clinical trials*)

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Thank you

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