MAYO CLINIC

Obstetric Hemorrhage & Beyond

Update on Postpartum Hemorrhage

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Disclosures

- None

Objectives

- Identify obstetric and maternal risk factors for postpartum hemorrhage
- Discuss published guidelines and acquire tools to create safety bundles for obstetric hemorrhage
- Identify appropriate circumstances for use of tranexamic acid and fibrinogen concentrate in maternal hemorrhage
- Assess when to activate a massive transfusion protocol and discuss how contemporary transfusion practices apply in the obstetric setting

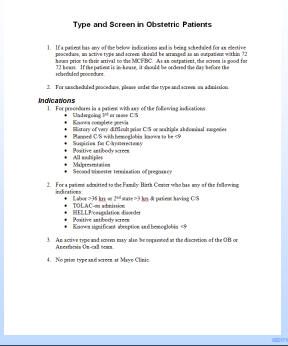
Background PPH

- Definition: >1000 ml blood loss after delivery
- Incidence: 2.9% births in United States
  - Increasing
- Leading cause maternal morbidity/mortality in US
- Common Causes
  - Uterine Atony (79%)
  - Placenta Accreta
  - Retained products
  - Trauma
  - Uterine Inversion

Bateman. Anes Analg 2010;110:1368-73

Risk Factors

- Multiple gestation
- Polyhydramnios
- Placenta Previa
- Abruption

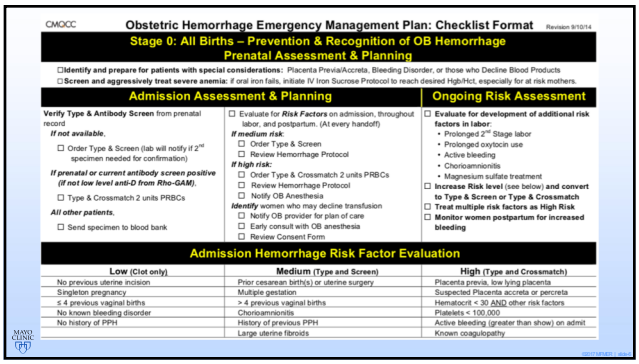


Type and Screen in Obstetric Patients

1. If a patient has any of the below indications and is being scheduled for an elective procedure, an active type and screen should be arranged as an outpatient within 72 hours prior to their arrival to the MCHSC. As an outpatient, the screen is good for 72 hours. If the patient is in-house, it should be ordered the day before the scheduled procedure.
2. For unscheduled procedure, please order the type and screen on admission.

Indications

1. For procedures in a patient with any of the following indications:
   - Undergoing 3rd or more C/S
   - Known complete previa
   - History of very difficult prior C/S or multiple abdominal surgeries
   - Planned C/S with hemoglobin known to be <9
   - Suspicion for C/hysterectomy
   - Positive antibody screen
   - All multiples
   - Malpresentation
   - Second trimester termination of pregnancy
2. For a patient admitted to the Family Birth Center who has any of the following indications:
   - Labor >34 hrs or 2nd stage >3 hrs & patient having C/S
   - TOLAC-on admission
   - HELLP/coagulation disorder
   - Positive antibody screen
   - Known significant abruption and hemoglobin <9
3. An active type and screen may also be requested at the discretion of the OB or Anesthesia On-call team.
4. No prior type and screen at Mayo Clinic.



CMOCC **Obstetric Hemorrhage Emergency Management Plan: Checklist Format** Revision 9/10/14

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

☐**Identify and prepare for patients with special considerations:** Placenta Previa/Accreta, Bleeding Disorder, or those who Decline Blood Products
☐**Screen and aggressively treat severe anemia:** if oral iron fails, initiate IV Iron Sucrose Protocol to reach desired Hgb/Hct, especially for at risk mothers.

Admission Assessment & Planning

Verify Type & Antibody Screen from prenatal record
If not available,
☐ Order Type & Screen (lab will notify if 2nd specimen needed for confirmation)
If prenatal or current antibody screen positive (If not low level anti-D from Rho-GAM),
☐ Type & Crossmatch 2 units PRBCs
All other patients,
☐ Send specimen to blood bank

☐ Evaluate for ***Risk Factors*** on admission, throughout labor, and postpartum. (At every handoff)
If medium risk:
☐ Order Type & Screen
☐ Review Hemorrhage Protocol
If high risk:
☐ Order Type & Crossmatch 2 units PRBCs
☐ Review Hemorrhage Protocol
☐ Notify OB Anesthesia
Identify women who may decline transfusion
☐ Notify OB provider for plan of care
☐ Early consult with OB anesthesia
☐ Review Consent Form

Ongoing Risk Assessment

☐ **Evaluate for development of additional risk factors in labor:**
- Prolonged 2nd Stage labor
- Prolonged oxytocin use
- Active bleeding
- Chorioamnionitis
- Magnesium sulfate treatment

☐ **Increase Risk level** (see below) **and convert to Type & Screen or Type & Crossmatch**
☐ **Treat multiple risk factors as High Risk**
☐ **Monitor women postpartum for increased bleeding**

Admission Hemorrhage Risk Factor Evaluation

Low (Clot only)	Medium (Type and Screen)	High (Type and Crossmatch)
No previous uterine incision	Prior cesarean birth(s) or uterine surgery	Placenta previa, low lying placenta
Singleton pregnancy	Multiple gestation	Suspected Placenta accreta or percreta
≤ 4 previous vaginal births	> 4 previous vaginal births	Hematocrit < 30 AND other risk factors
No known bleeding disorder	Chorioamnionitis	Platelets < 100,000
No history of PPH	History of previous PPH	Active bleeding (greater than show) on admit
	Large uterine fibroids	Known coagulopathy

The National Partnership for Maternal Safety

- www.safehealthcareforeverywoman.org
- OB Hemorrhage Bundle

- Readiness
- Recognition & Prevention
- Response
- Reporting/Systems Learning

OB Hemorrhage Bundle

COUNCIL ON PATIENT SAFETY IN WOMEN'S HEALTH CARE
safe health care for every woman

READINESS

Every unit

- Hemorrhage cart with supplies, checklist, and instruction cards for intrauterine balloons and compressions stitches
- Immediate access to hemorrhage medications (kit or equivalent)
- Establish a response team - who to call when help is needed (blood bank, advanced gynecologic surgery, other support and tertiary services)
- Establish massive and emergency release transfusion protocols (type-O negative/uncrossmatched)
- Unit education on protocols, unit-based drills (with post-drill debriefs)

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RECOGNITION & PREVENTION

Every patient

- Assessment of hemorrhage risk (prenatal, on admission, and at other appropriate times)
- Measurement of cumulative blood loss (formal, as quantitative as possible)
- Active management of the 3rd stage of labor (department-wide protocol)

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RESPONSE

Every hemorrhage

- Unit-standard, stage-based, obstetric hemorrhage emergency management plan with checklists
- Support program for patients, families, and staff for all significant hemorrhages

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REPORTING/SYSTEMS LEARNING

Every unit

- Establish a culture of huddles for high risk patients and post-event debriefs to identify successes and opportunities
- Multidisciplinary review of serious hemorrhages for systems issues
- Monitor outcomes and process metrics in perinatal quality improvement (QI) committee

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Review Article

Prophylactic tranexamic acid in parturients at low risk for post-partum haemorrhage: systematic review and meta-analysis

AOGS REVIEW ARTICLE

Tranexamic acid for preventing postpartum blood loss after cesarean delivery: a systematic review and meta-analysis of

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**

(review)

Novikova N, Hofmeyr GJ, Cluver C

of the Third Stage of Labor in Vaginal Delivery: A Randomized Controlled Study

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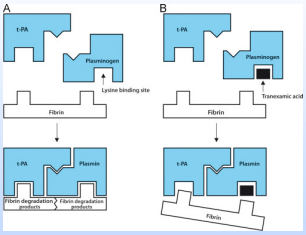
Mechanism of Action TXA

- Antifibrinolytic
- Lysine analog.
- Binds to receptors on plasminogen & plasmin
- Inhibits plasmin mediated fibrin degradation.



Relevant Data - TXA

- Half life 2 hours
- Clearance through the kidneys
- Crosses placenta
- Crosses into breastmilk
- No evidence of harm in fetus by placenta diffusion or breastfeeding

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*

- 20,060 women randomly assigned TXA (10,051) vs. placebo (10,009)
- Death due to bleeding in women with PPH reduced (RR 0.81, 95% CI 0.65-1; p=0.045)
  - If given within 3 hrs: (RR 0.69, 95% CI 0.52-0.91; p=0.008)

Lancet. 2017 May 27;389(10084):2105-2116

WOMAN Trial Adverse Events

- Adverse events did not differ

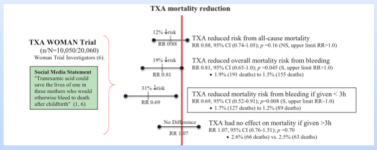
	Tranexamic acid group	Placebo group	RR (95% CI)	p value
Thromboembolic events*	10 033	9985	..	
Any event	30 (0·3%)	34 (0·3%)	0·88 (0·54–1·43)	0·603
Venous events	20 (0·2%)	25 (0·3%)	0·80 (0·44–1·43)	0·446
Deep vein thrombosis	3 (0·03%)	7 (0·07%)	0·43 (0·11–1·65)	0·203
Pulmonary embolism	17 (0·2%)	20 (0·2%)	0·85 (0·44–1·61)	0·611
Arterial events	10 (0·1%)	9 (0·09%)	1·11 (0·45–2·72)	0·827
Myocardial infarction	2 (0·02%)	3 (0·03%)	0·66 (0·11–3·97)	0·651
Stroke	8 (0·08%)	6 (0·06%)	1·33 (0·46–3·82)	0·599
Complications*	10 033	9985	..	
Renal failure	129 (1·3%)	118 (1·2%)	1·09 (0·85–1·39)	0·505
Cardiac failure	110 (1·1%)	115 (1·2%)	0·95 (0·73–1·23)	0·710
Respiratory failure	108 (1·1%)	124 (1·2%)	0·87 (0·67–1·12)	0·274
Hepatic failure	29 (0·3%)	30 (0·3%)	0·96 (0·58–1·60)	0·882
Sepsis	180 (1·8%)	185 (1·9%)	0·97 (0·79–1·19)	0·756
Seizure	33 (0·3%)	43 (0·4%)	0·76 (0·49–1·20)	0·242

Limitations

- Most women recruited in low resource countries with high MMR
  - Half recruited in Nigeria (814), Pakistan (178), Uganda (373)

Table 1 Maternal mortality rate (MMR) related to postpartum haemorrhage in three European countries and in the study by the WOMAN Trial Collaborators

Countries	MMR/100000 births
WOMAN Trial[1]	16 (tranexamic group) 19 (control group)
United Kingdom 2012–2014[2]	0.56
Netherlands 1993–2005[3]	0.7
France 2010–2012[4]	1.2



The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 183, OCTOBER 2017 *(Replaces Practice Bulletin Number 76, October 2006)*

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics in collaboration with Laurence E. Shields, MD; Dena Goffman, MD; and Aaron B. Caughey, MD, PhD.

Postpartum Hemorrhage

hemorrhage outside of the context of research. Although the generalizability of the WOMAN trial and the degree of effect in the United States is uncertain, given the mortality reduction findings, tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails. Earlier use is likely to be superior to delayed treatment, given that in the stratified analysis it appeared that the benefit was primarily in women treated sooner than 3 hours from the time of delivery. For those clinicians unfamiliar with tranexamic

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tranexamic Acid for the Prevention of Blood Loss after Vaginal Delivery

- TRAAP
- Primary Outcome: Postpartum Hemorrhage (>500ml)
- 4079 randomized → 3891 Vaginal Delivery
- TXA Group PPH 156/1921 women (8.1%)
- Placebo PPH 188/1918 (9.8%)
  - RR 0.83; 95% CI 0.68-1.01; P=0.07

NEJM 2018; 379:731-42

TRAAP Trial

- Conclusion: Among women with vaginal delivery who received prophylactic oxytocin, the use of TXA did not significantly lower risk of postpartum hemorrhage
- Should not be used routinely for prophylaxis

Table 4. Adverse Events (Modified Intention-to-Treat Population).

Event	Tranexamic Acid Group (N=1945)	Placebo Group (N=1946)	Relative Risk (95% CI)	P Value
In the delivery room				
Vomiting or nausea — no. (%)	136 (7.0)	63 (3.2)	2.16 (1.61–2.89)	<0.001
Nausea — no. (%)	103 (5.3)	49 (2.5)	2.10 (1.51–2.94)	<0.001
Vomiting — no. (%)	73 (3.8)	33 (1.7)	2.21 (1.47–3.32)	<0.001
Photopsia — no. (%)*	4 (0.2)	6 (0.3)	0.67 (0.19–2.36)	0.53
Dizziness — no. (%)	40 (2.1)	30 (1.5)	1.33 (0.83–2.13)	0.23
Blood pressure — no./total no. (%)				
Systolic ≥140 mm Hg	415/1597 (26.0)	378/1590 (23.8)	1.09 (0.97–1.23)	0.15
Diastolic ≥90 mm Hg	411/1594 (25.8)	406/1600 (25.4)	1.02 (0.90–1.14)	0.79
At 3 mo after delivery				
Completed interviews at 3 mo — no. (%)	1844 (94.8)	1849 (95.0)		
Thromboembolic event — no./total no. (%)				
Any†	1/1844 (0.1)	4/1849 (0.2)	0.25 (0.03–2.24)	0.37
Deep-vein thrombosis	0/1844	1/1849 (0.1)	—	—
Pulmonary embolism	0/1844	0/1849	—	—
Ovarian-vein thrombosis	0/1844	2/1849 (0.1)	—	—
Superficial-vein thrombosis	1/1844 (0.1)	1/1849 (0.1)	—	—
Seizure — no./total no. (%)‡	1/1844 (0.1)	0/1849	—	—
Readmission after discharge — no./total no. (%)	18/1844 (1.0)	16/1849 (0.9)	1.13 (0.58–2.21)	0.72
Anticoagulant therapy at and after discharge — no./total no. (%)	57/1830 (3.1)	56/1842 (3.0)	1.02 (0.71–1.47)	0.90

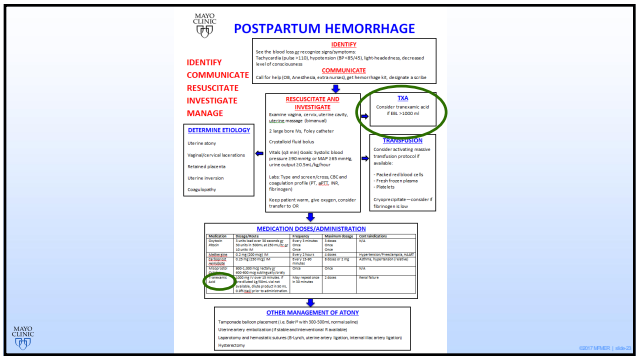
NEJM 2018; 379:731-42

Who Should Get TXA

- Uncontrolled hemorrhage
  - Within 3 hours of birth
- Jehovah's Witness approved

How to Administer TXA

- Give AFTER the cord is clamped
- 1000 mg IV infusion over 20 minutes
  - Approx 150 ml/hr
  - A pump is not required
- If bleeding continues 30 minutes after first dose, a second dose of 1000 mg may be given



Contraindications

- Active venous thromboembolism
- Significant renal disease
- Subarachnoid hemorrhage

Transfusion Strategy

Methods to Monitor Coagulopathy

- Clinical observation
- Standard laboratory testing
  - PT/PTT, fibrinogen, platelet count
- POC Viscoelastic Testing
  - ROTEM
  - TEG

Methods to Transfuse

- Fixed Ratio
- Goal Directed
- +/- Fibrinogen Concentrate

Fixed Ratio Transfusion 1:1:1

- Evidence in Non-pregnant adult major trauma
- Rate of transfusion in OB is low (0.9-2.3%)
  - Massive transfusion ≥ 10 pRBC
    - 6 in 10,000 deliveries
    - Abnormal placentation (27%)
- Massive Transfusion Protocol (MTP)
  - Shown to improve timeliness of blood transfusion
  - Improves communication/transport/availability

Mhyre. Obstet Gynecol 2013; 122:1288-1294

Fibrinogen & Pregnancy

- Normal Fibrinogen
  - Term Pregnancy: 4-6 g/L
  - Non-pregnant woman: 2-4 g/L
- Fibrinogen replacement is not required in PPH until < 2g/L

Fibrinogen Replacement

Product	Fibrinogen Content	Volume
1 unit pRBC	<100 mg	350 ml
1 unit FFP	400 mg	200-250 ml
1 6-pack platelets	80 mg x 6 = 480 mg	300 ml
1 unit apheresis platelets	300 mg	200-250 ml
1 10-pack cryoprecipitate	2500 mg	150 ml

Fibrinogen & PPH

- FFP contains 2 g/L fibrinogen
  - Ave fibrinogen w/ 1-2L blood loss is 4 g/L
  - Infusion FFP could reduce fibrinogen by dilution
- 18,501 women over 3 years
  - Women with PPH >1500 ml (n=456, 2.5%)
  - PT and aPTT remained normal until 4-5L
    - Infusion FFP unlikley to improve hemostasis
  - By 2 L blood loss, fibrinogen < 4 g/L
  - 4 L blood loss, fibrinogen < 2 g/L
- *Plasma fibrinogen is an important therapeutic target

Collins, IJOA 2018; ePub ahead of print

Fibrinogen Concentrate

- Not FDA approved for PPH
- Each vial: 900-1300 mg fibrinogen
- Average dose 2 g