

SOAP

*Society for Obstetric
Anesthesia and Perinatology*



*Advancing the pregnancy-related health and outcomes
of pregnant women and their newborn.*

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Obstetric Hemorrhage

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Society for Obstetric Anesthesia and Perinatology

Learning Objective

- This presentation is part of a series of SOAP lectures for OB/GYN Residents, MFM Fellows, and practicing OB/GYNs and MFMs
- This lecture series covers topics that come up frequently on labor and delivery
- In this presentation, we review:
 - Best practices and society recommendations based on current evidence
 - Offers the OB Anesthesiologists perspective of these key topics

Outline

- Background
- Shock in Pregnancy
- General Principles of Management
- Massive Transfusion
- Disseminated Intravascular Coagulation
- Access
- Pitocin Dosing
- Tranexamic Acid
- Viscoelastic Coagulation Testing
- Key Points
- Resources
- About the Authors



Background - Postpartum Hemorrhage (PPH)



- Definition:
 - Varies by organization
 - ACOG: Cumulative EBL \geq 1000 mL or blood loss with signs and symptoms of hypovolemia regardless of route of delivery
 - WHO and the Royal College of OB/GYNs: Blood loss \geq 500 mL within 24 hours after birth. Severe PPH is \geq 1000 mL
 - Soc of OB/GYNs of Canada: Any blood loss that threatens hemodynamic stability or continues despite initial measures
 - California Maternal Quality Care Collaborative: Stage 0 = all women; Stage 1 \geq 500 mL after vaginal delivery or 1000 mL after cesarean delivery or vital sign changes; Stage 2 = Continued bleeding $<$ 1500 mL; Stage 3 = EBL \geq 1500 mL or $>$ 2 units PRBCs transfused, unstable vital signs, or DIC
- Incidence: Range of 1 -6 % reported in the United States
 - In a nationwide discharge database, the incidence was found to be 2.9%
- Uterine artery blood flow:
 - 500 – 700 mL/min
 - 15% of cardiac output
- Obstetric hemorrhage is the most common cause of maternal mortality worldwide and among the top 5 in the United States.

Pathogenesis of PPH



FOCAL OR DIFFUSE ATONY

- Most common cause
- Accounts for 75-79% of PPH
- 1 in 40 births affected
- Often respond to uterotonics and thus not the most common cause of massive transfusion
- Etiologies:
 - Retained tissue
 - Prolonged labor
 - Abnormal placentation
 - Placenta previa
 - Placental abruption
 - Uterine inversion
 - Drugs that cause uterine relaxation
 - Overdistended uterus
 - Macrosomia
 - Polyhydramnios
 - Multiple gestations

TRAUMA

- Lacerations
 - Cervical, vaginal, or higher up (spontaneous, episiotomy, Dührssen incision)
 - Potentially secondary to instrumented/operative deliveries
- Uterine rupture
- Surgical incisions/extensions

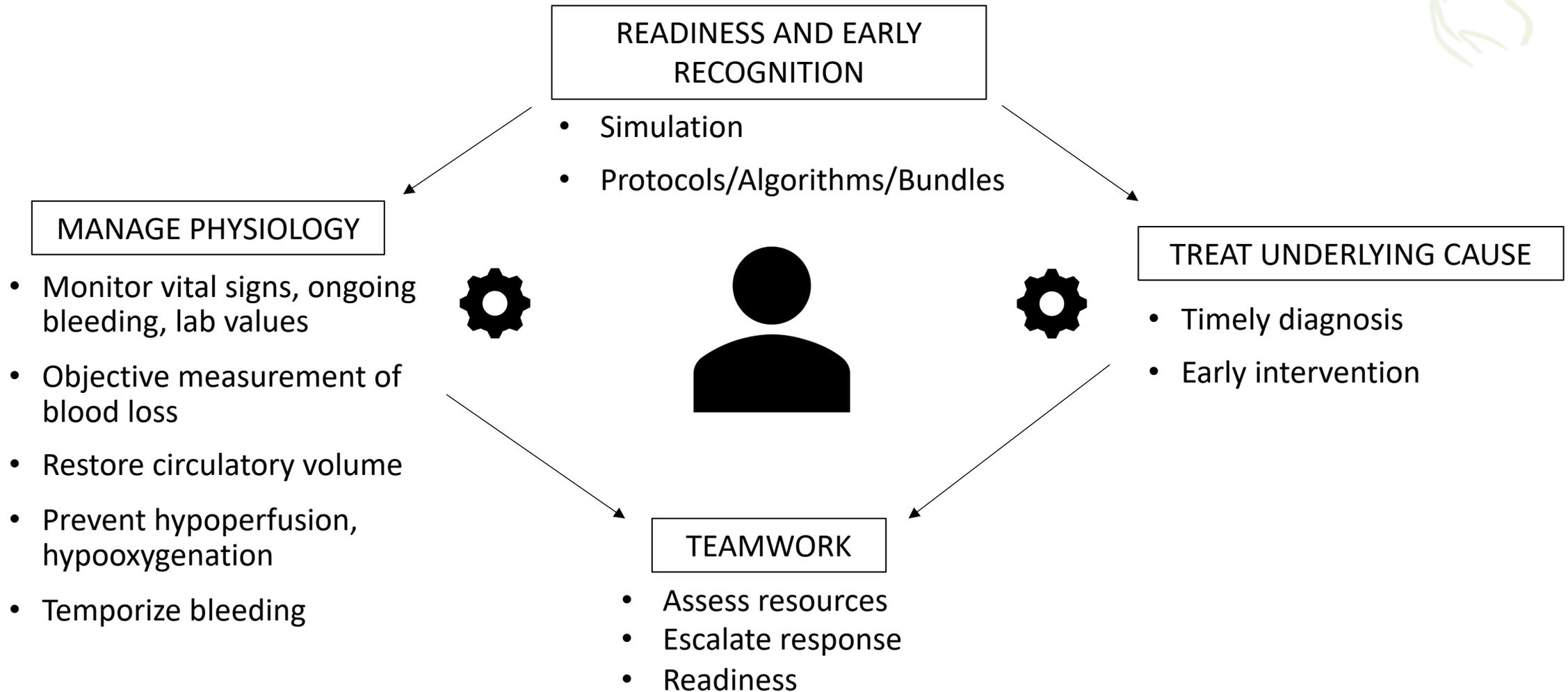
COAGULOPATHY

- Inherited
- Acquired from bleeding diathesis, amniotic fluid embolism, abruption, preeclampsia/HELLP syndrome

OTHER RISK FACTORS

- History of PPH
- Multiparity
- Obesity
- Chorioamnionitis
- Leiomyoma
- Couvelaire uterus
- Prolonged oxytocin use

General Principles of Management



Interventions for PPH



PHARMACOLOGIC INTERVENTIONS

MEDICATION	DOSE
Oxytocin (Pitocin)	10-40 units/500-1000 mL solution or 10U IM
Methylergonovine (Methergine)	0.2mg IM (may repeat q2h)
15-methyl PGF2a (Hemabate, Carboprost)	0.25 mg IM (may repeat q15min, max 8 doses)
Misoprostol (Cytotec)	800-1000 mcg PR, 600 mcg PO
Tranexamic Acid (TXA)	1g IV over 10 min, followed by additional 1g if ongoing bleeding 30 min later
Fibrinogen concentrate (Riastap, Fibryga)	70 mg/kg

SURGICAL INTERVENTIONS

- Laceration repair
- Curettage
- Bakri balloon
- B-Lynch suture
- O'Leary suture
- Uterine artery embolization
- Uterine tourniquet
- Hysterectomy
- Aortic compression
- Resuscitation endovascular balloon occlusion of the aorta (REBOA)
- Cell Salvage

Oxytocin (Pitocin)



- Synthetic preparation of endogenous oxytocin (produced in the posterior pituitary)
 - Endogenous oxytocin is similar to vasopressin (V_1 = vasoconstriction, increased systemic vascular resistance (SVR); V_2 = fluid reabsorption) and has cross-reactivity to ADH receptor in the kidney
- Mechanism:
 - Stimulation of oxytocin receptors in the uterine myometrium leads to myometrium contraction
 - Receptor concentration is upregulated with increased gestational age until ~ 34 weeks and with labor
- Indications:
 - Used to induce or augment labor
 - **First line agent** for both prophylaxis and treatment of PPH
 - A Cochrane review by Westhoff *et al.* comparing prophylactic administration of Pitocin in the 3rd stage to placebo showed that Pitocin reduced the rate of PPH greater than 500 mL by > 40%

Oxytocin (Pitocin)

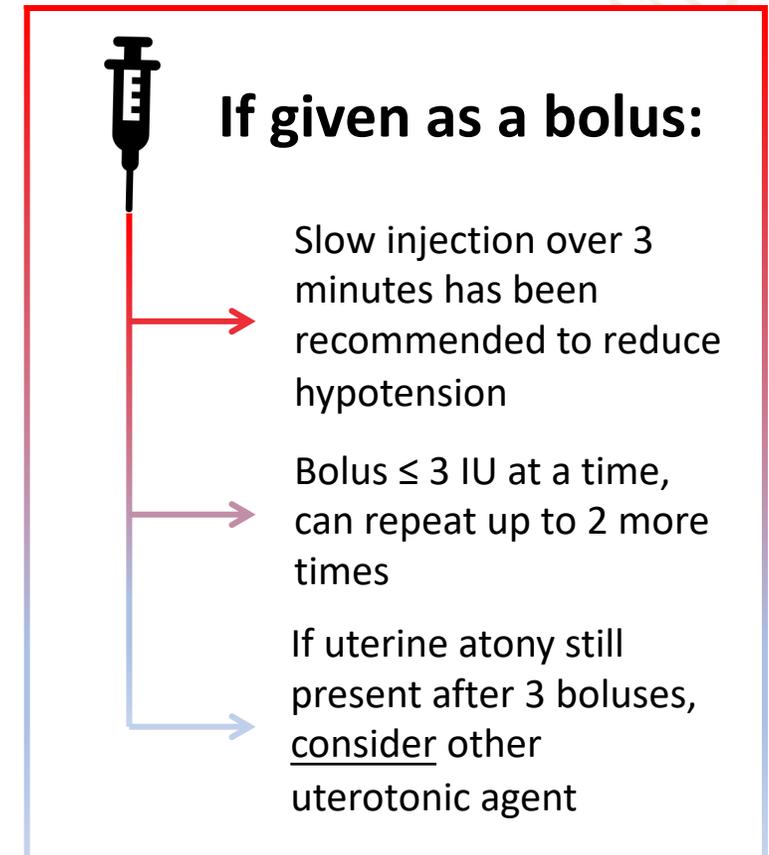
- Fast Onset:
 - ~1 minute when administered IV (IM onset of action: 3-7 minutes)
- Short half-life:
 - 1-6 minutes when administered IV
- Side effects:
 - Synthetic oxytocin can cause significant **hypotension** by decreasing SVR and a compensatory increase in heart rate and stroke volume (especially when given as a bolus)
 - Increases pulmonary vascular resistance
 - Can lead to free water retention due to cross-reactivity to ADH receptor in the kidney (resulting in **hyponatremia**)



Prolonged infusion of oxytocin for induction of labor is thought to result in **desensitization** of oxytocin receptors and a **decrease in receptor density** in the uterine myometrium

Oxytocin – What Dose?

- Route of Administration:
 - IV route preferred to IM due to more precise dosing and onset of action
- Dose:
 - Bolus dose, infusion dose, and duration varies among institutions
 - Bolus:
 - 0.3 IU - 3 IU
 - For patients with labor arrest, the minimum effective dose was found to be closer to 3 IU compared to nonlaboring women who require a lower dose closer to 0.3-1 IU
 - Infusion:
 - Commonly, 10 to 40 IU in 500 to 1000 mL of NS, up to 500 mL/hr
 - Infusion rate adjusted for uterine tone and signs of PPH
 - Low dose infusion ~ 1 to 2.5 IU/hr
 - Higher doses have not demonstrated a clear clinical benefit
- Relative contraindications postpartum:
 - Hypersensitivity to oxytocin



If given as a bolus:

Slow injection over 3 minutes has been recommended to reduce hypotension

Bolus \leq 3 IU at a time, can repeat up to 2 more times

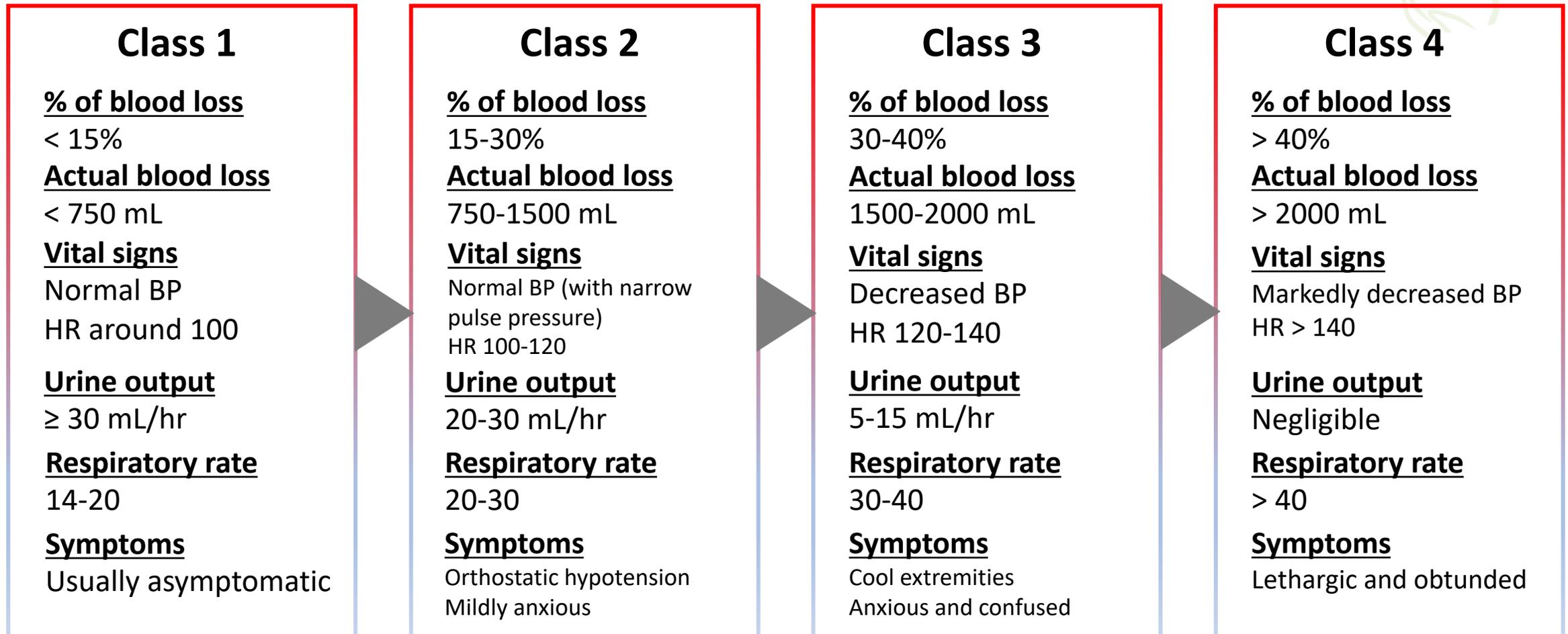
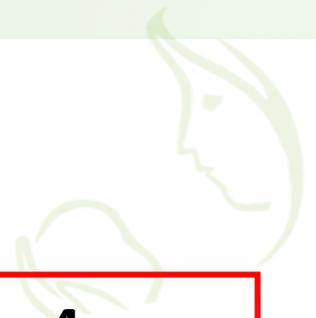
If uterine atony still present after 3 boluses, consider other uterotonic agent

Shock in Pregnancy



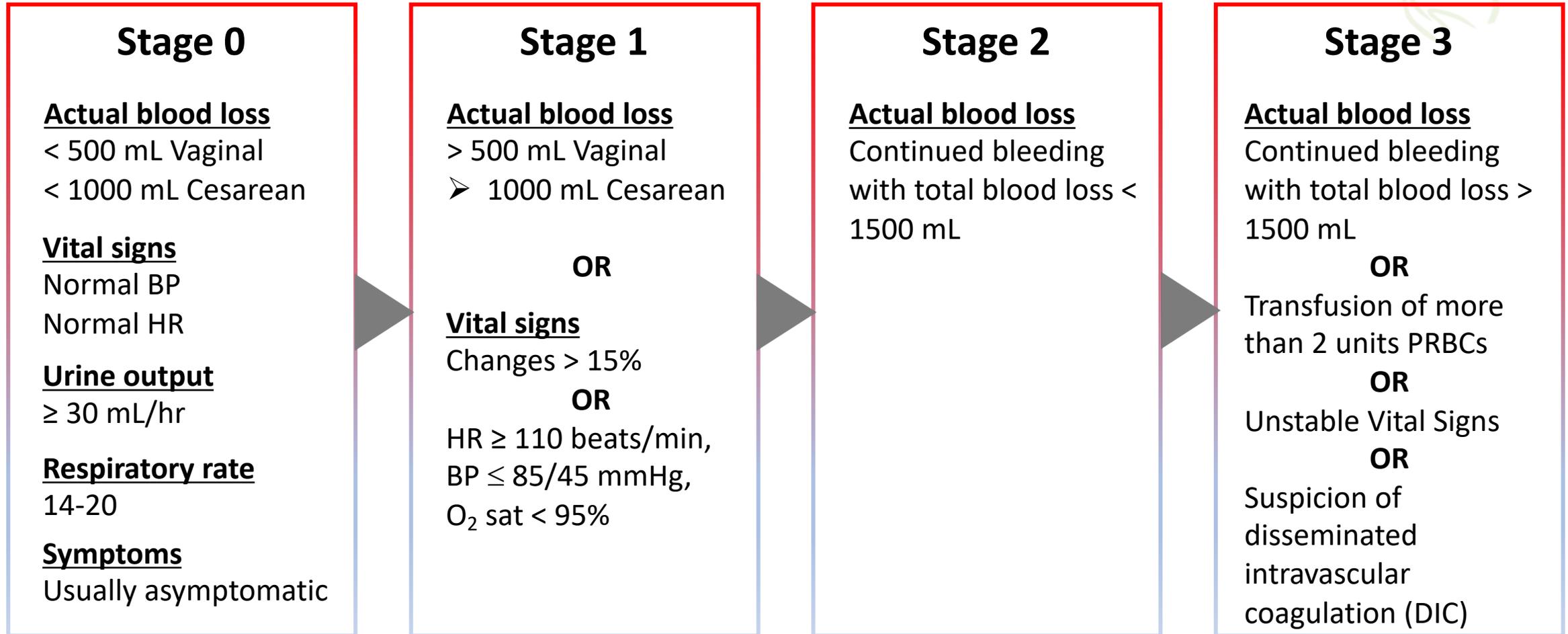
- Similarities to trauma or postsurgical patients, hemorrhagic shock secondary to postpartum hemorrhage can be classified into four stages developed by the American College of Surgeons in their Advanced Trauma Life Support (ATLS) program (next slide)
- The severity of hemorrhagic shock secondary to postpartum hemorrhage is often under-recognized by physicians and nurses
- Unrecognized or undertreated hemorrhagic shock will lead to compromised tissue perfusion, hypoxia, and end organ injury for both the mother and the fetus

Shock in Pregnancy: **ATLS Classes of Hemorrhagic Shock**



Shock in Pregnancy:

California Maternal Quality Care Collaborative Staging System



Shock in Pregnancy



However, it is important to note that the normal physiological changes that occur during pregnancy will often **obscure signs and symptoms of hemorrhagic shock** until it has become severe

- Increased cardiac output and heart rate of pregnancy will make identification of earlier stages of shock more difficult
- Increased respiratory volume and rates of pregnancy can mask underlying metabolic acidosis caused by significant hypovolemia
- Increased plasma and RBC volume of pregnancy will allow for greater degree of hemorrhage before significant symptoms and hematocrit drop will develop



Specifically, hypotension is a **LATE** sign of hemorrhagic shock in pregnancy, as the patient will usually have lost at least **30-35%** of her blood volume before presenting with hypotension



Therefore, do not wait for or rely on BP changes before initiating treatment for hemorrhagic shock in a pregnant patient!

Shock in Pregnancy



- Our patients can bleed (a lot!):
 - Often difficult to quantify: practice is shifting to quantification of blood loss (QBL) as a more objective measure than estimated blood loss (EBL)
 - Different than other patient populations (e.g. massive transfusion in **TRAUMA** patients)
- For the most part, our patients are young and healthy, so they are “sneaky”. They stay relatively stable until they have lost a lot of blood and then they collapse!

Shock in Pregnancy – Differential Diagnosis



- Other causes of shock can occur in the peripartum period, and should be maintained in the differential diagnosis
 - **Cardiogenic shock**
 - May be secondary to peripartum cardiomyopathy
 - Tachycardia, dyspnea, distended neck veins, and generalized edema
 - **Septic shock**
 - Fevers, chills, tachycardia, hypotension, altered mental status, and warm extremities
 - **Anaphylactic shock**
 - Latex, antibiotics, and nondepolarizing muscle relaxants are the most common in the ORs
 - Bronchospasm/hypoxia, tachycardia, hypotension, urticaria
 - **Obstructive shock**
 - May be secondary to a significant pulmonary embolism
 - Hypoxemia, tachycardia, hypotension, and right heart strain
 - **Amniotic fluid embolism**
 - Sudden cardiovascular collapse, coagulopathy, and respiratory failure/hypoxia
 - **Acute hemolytic transfusion reaction**
 - Hypotension, fever, dark urine, urticaria

Transfusion goals



To provide adequate and early blood product replacement and to either prevent or correct DIC

Massive Transfusion Protocol Activation



- Consider the **Massive Transfusion Protocol (MTP)** in the presence of hemorrhage and
 - ❖ Systolic blood pressure ≤ 90 mmHg
 - ❖ Heart rate ≥ 120 beats per minute (bpm)
 - ❖ pH ≤ 7.24
- Consider MTP implementation if you anticipate transfusing ≥ 4 units of PRBCs over 1 hour or expected transfusion of ≥ 10 units over 24 hours (more than one total blood volume)
- If MTP: **minimize** crystalloid resuscitation to prevent dilutional coagulopathy
- **Fibrinogen:**
 - Being recognized as **crucial** in obstetric hemorrhage with targeted replacement (rather than FFP)
 - Found to be a biomarker of severity

Transfusion Ratio: controversies about MTP



ACOG

- 6 PRBC
- 4 FFP
- 1 Pack of platelets

Trauma Literature

- 1 PRBC
- 1 FFP
- 1 Pack of platelets

After the first 2 units of PRBC, early transfusion of FFP is correlated with improved survival after trauma.
So we are more and more aiming to **1:1 or 1:2 ratio for FFP:PRBC**

Transfusion Goals: Blood Products



- **PRBC:** aim to maintain Hg > 7.5-8 g/dL or Hct 21-24% and based on clinical signs and response
- **Platelet transfusions** indicated:
 - ❖ Surgical / obstetric patients with microvascular bleeding and PLT count <50,000
 - ❖ Any surgical patient with PLT count <20,000
- **FFP** (10-15 ml/kg) is indicated in the following situations:
 - ❖ Hemorrhage with elevated PT or PTT (> 1.5 times normal)
- **Fibrinogen concentrate (RiaSTAP)**
 - ❖ Weight based dosing = 70mg/kg
- **Cryoprecipitate** (1 or 2 pooled packs) should be administered in the following situations:
 - ❖ Hemorrhage with fibrinogen concentrations <100 mg/dL with goal to maintain > 150 mg/dL
 - ❖ Bleeding patients with von Willebrand's disease
 - ❖ If suspicion of severe abruption or AFE due to high risk of significant depletion



FUN FACT!

OR NOT... ABOUT BLOOD PRODUCTS

Fun Facts



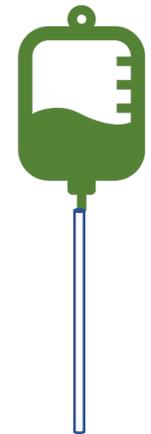
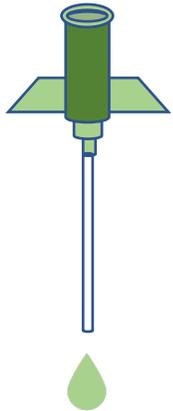
- Dilutional (acquired) coagulopathy occurs when 80% of blood volume has been replaced
- Platelets do **not** require cross-matching and are not always type specific. Rh negative platelets (at least those from whole blood) are preferentially given to patients with an Rh negative blood type because of the small risk of sensitization to the D-antigen
- Cryoprecipitate released from the Blood Bank is often in pools of 4-10 units. Each unit provides ≥ 150 mg of fibrinogen for a total of at least 1500 mg in a pool of 10 units (**from 10 separate donors!!!**) in a total small volume of approximately 80-100 cc
- Both PRBCs and FFP contain the anticoagulant citrate, which binds calcium. Calcium is necessary for adequate clotting and myocardial contraction, so it is critical to replace calcium
- Activity of clotting factors is significantly reduced ($> 50\%$ reduction) at a pH of 7.0 (as are the effects of vasopressors/inotropes), compared to a pH of 7.4
- Factor VII is a vitamin K-dependent serine protease. Each vial contains approximately 0.6 mg/mL (600 μ g/mL) **BUT** no consensus for OB hemorrhage (high risk of thrombosis)

What Kind of Access is Needed?

- IV Access

- If there is an increased risk for hemorrhage (including hematocrit < 30% or platelets < 100,000 ---place a 2nd large IV (18G or 16G))
- Short, large diameter catheters have good flow rates if large volume resuscitation is necessary

Color in the US	Gauge Size	Approximate Flow Rate	1000 mL Infusion Time	Uses
Blue	22 G	36 mL/min	27 min 46 sec	Small veins, slow infusions, pediatrics
Pink	20 G	60 mL/min	16 min 40 sec	Routine procedures, general IV infusions
Green	18 G	90 mL/min	11 min 6 sec	Rapid transfusions/large volumes, emergencies, high risk surgery
Grey	16 G	180 mL/min	5 min 33 sec	Rapid transfusions/large volumes, emergencies, high risk surgery
Orange	14 G	240 mL/min	4 min 10 sec	Rapid transfusions/large volumes, emergencies, high risk surgery

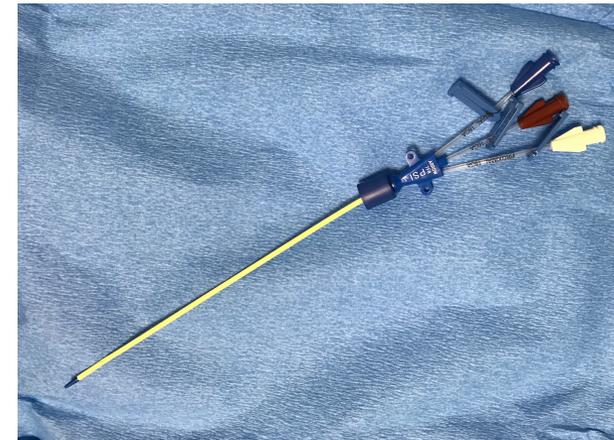


Central Venous Access

- Indications:
 - Poor/difficult peripheral IV access
 - Increased risk for hemorrhage with large-bore access needed
 - Peripherally caustic infusions
 - Hemodynamic monitoring
- Central line
 - Large-bore:
 - Introducer: 8.5Fr
 - Multi-lumen Access Catheters (MAC): 9 Fr lumen and 12 G side port
 - Great for large volumes and rapid infusion
 - Triple lumen: typically has one 16G lumen and two 18 G lumens, but a bit longer length, so slower infusion time
- Peripherally Inserted Central Catheter (PICC)
 - Small caliber, long length
 - Do not allow adequate flow rates for rapid, large volume resuscitation



Introducer: 8.5 Fr



Triple Lumen

Other Lines

- Intraosseous (IO) line
 - Infusion rate to gravity: 70-80 mL/min
 - Infusion rate under pressure: 150-160 mL/min
 - Equivalent to ~21 G IV
- Rapid Infusion Catheter (RIC)
 - Short, large-bore
 - Placed using a guidewire and dilator (similar to a central line)
 - 7Fr and 8.5Fr
 - Infusion rate ~ 600 mL/min



Rapid Infusion Catheter (RIC)
with dilator

Arterial Lines



- Indications
 - Continuous hemodynamic monitoring in unstable patients, hypertensive emergencies, patients requiring vasopressor therapy
 - Need for frequent blood draws and analysis (ABG, CBC, Coags)
- Examples where an A-line may be useful:
 - Ongoing hemorrhage requiring MTP
 - Any unstable patient
 - AFE requiring resuscitation
 - Severe preeclamptic patients requiring antihypertensive infusion

Intubation – When is it needed?

- Securing the Airway (Intubation) and providing oxygenation and ventilation may be needed in an emergency situation (like severe hemorrhage)
- Intubation is usually easier early rather than late in an emergency where airway edema may have worsened
- Examples when intubation may be needed:
 - Emergent C-section with no working neuraxial in place
 - Consider in known placenta Accreta/Increta/Percreta, depending on hospital practices
 - Unstable patient

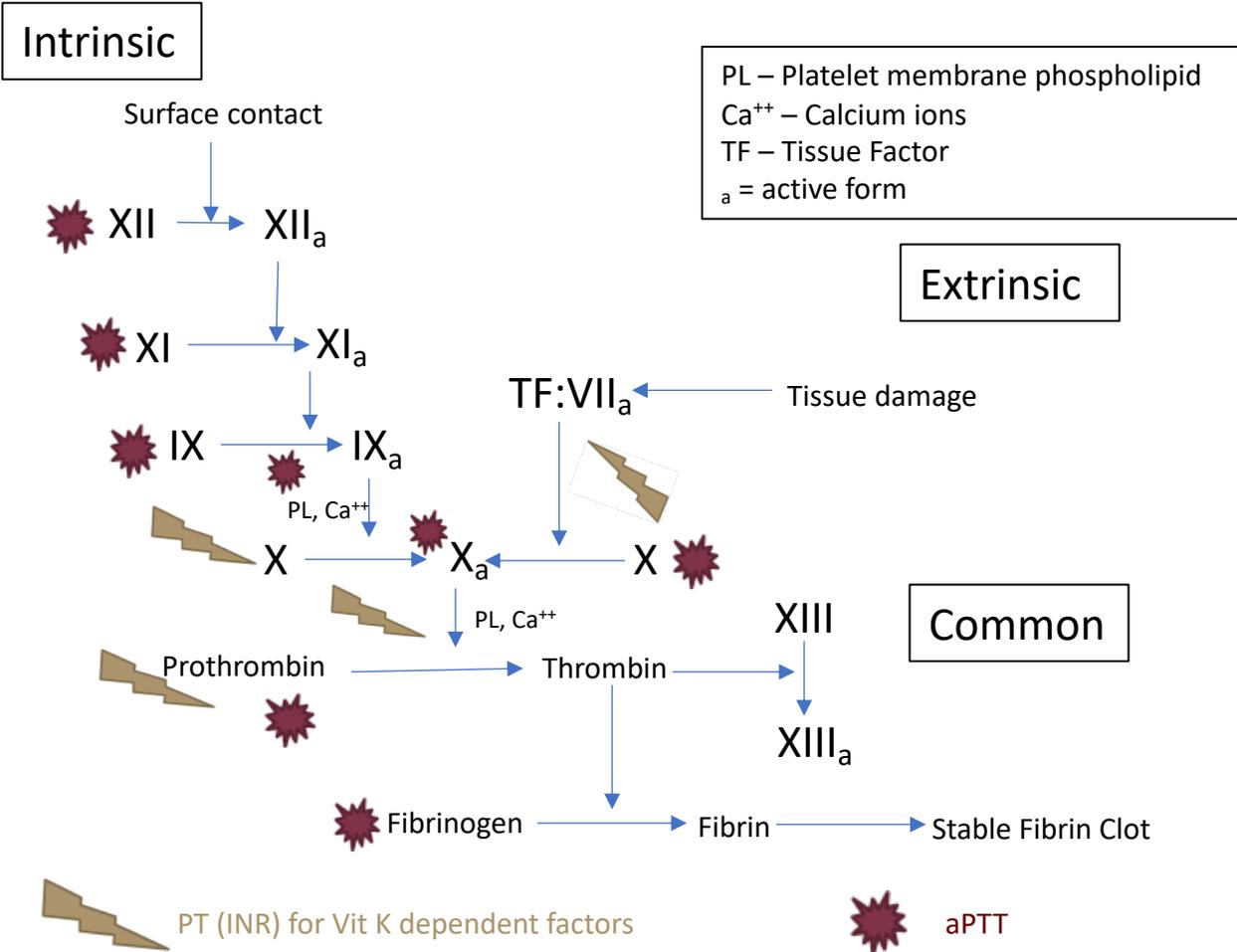
Disseminated Intravascular Coagulation (DIC)



- **DEFINITION:** pathologic condition associated with inappropriate activation of coagulation and fibrinolytic system → tendency towards hypercoagulability, but paradoxically results in severe bleeding.
- **INCIDENCE:** 1 in 500 deliveries for the severe type of DIC
- **PHYSIOPATHOLOGY:**
 - Intrinsic system: activates thrombin by sequential activation of factors XII, XI, IX, X, V, and II (prothrombin).
 - Extrinsic system: activated by tissue thromboplastin leading to sequential activation of factors VII, X, Vi and prothrombin 3.
 - Both pathways converge to activate factor X.
 - Factor X subsequently reacts with activated factor V in the presence of calcium and converts prothrombin to thrombin.
 - Thrombin then activates fibrinolytic system

IN DIC, THERE IS AN UNREGULATED EXPLOSIVE GENERATION OF THROMBIN DEPLETING CLOTTING FACTORS AND PLATELETS

Coagulation Changes in Pregnancy



Hemostatic parameters	Change at term pregnancy (% change)
Factor II and V	No change
Fibrinogen	Increases more than 100%
Factor VII	Up to 100% increase
Factors VIII, IX, X, XII and vWF	Increase more than 100%
Factor XI	Variable (usually decreases)
Protein C	No change
Protein S	Up to 50% decrease
D-Dimer	Up to 400% increase
Platelet count	Up to 20% decrease (unless other etiology associated)

Disseminated Intravascular Coagulation (DIC)



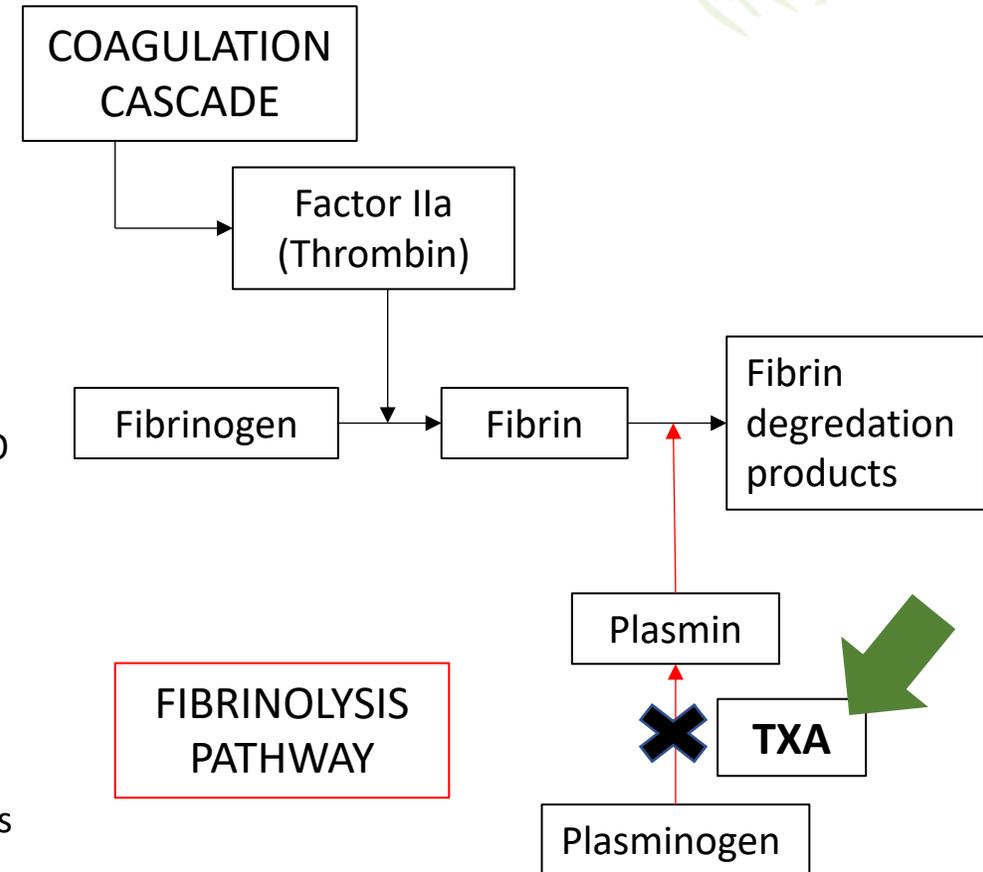
- DIAGNOSIS WHEN HIGH SUSPICION INDEX:
 - Prolonged PT and aPTT
 - Low platelet count
 - Elevated products of fibrin breakdown such as D-dimers
 - Low fibrinogen levels

DURING PREGNANCY, THOSE PARAMETERS CHANGE MIGHT NOT BE THAT OBVIOUS: TREND>>>THAN ABSOLUTE NUMBER

- TREATMENT:
 - Correct the underlying cause
 - Platelets when <50,000 and active bleeding
 - FFP (10-20 mL/kg) if active bleeding and prolonged PT/aPTT
 - Cryoprecipitate or Fibrinogen Concentrates if fibrinogen level too low (<1.5 g/L)

Tranexamic Acid (TXA)

- Used in many surgical arenas to reduce blood loss (e.g. cardiac, orthopedic, pediatric, GU surgery)
- Increased fibrinolysis in PPH
- Mechanism:
 - antifibrinolytic agent that competitively inhibits plasminogen, preventing activation of plasmin and lysis of fibrin
- Indications:
 - Adjunctive therapy in PPH
 - Recommended use of TXA within 3 hours of birth for ongoing PPH – WHO Guidelines, 2017
- Side effects:
 - Allergic reaction, dizziness, hypotension, nausea/vomiting, diarrhea, muscle spasm, vision changes, thrombosis, and seizures.
- Relative contraindications:
 - Seizure disorder or conditions that lower the seizure threshold, such as preeclampsia
 - Hypersensitivity to TXA, acquired defective color vision, active thrombosis
 - Renal impairment



Tranexamic Acid (TXA)



- What's the dose?
 - Doses in studies range from 0.5g to 4g bolus with or without a subsequent 2nd bolus or infusion
- Notable Trials:

The World Maternal Antifibrinolytic (WOMAN) trial – Lancet 2017

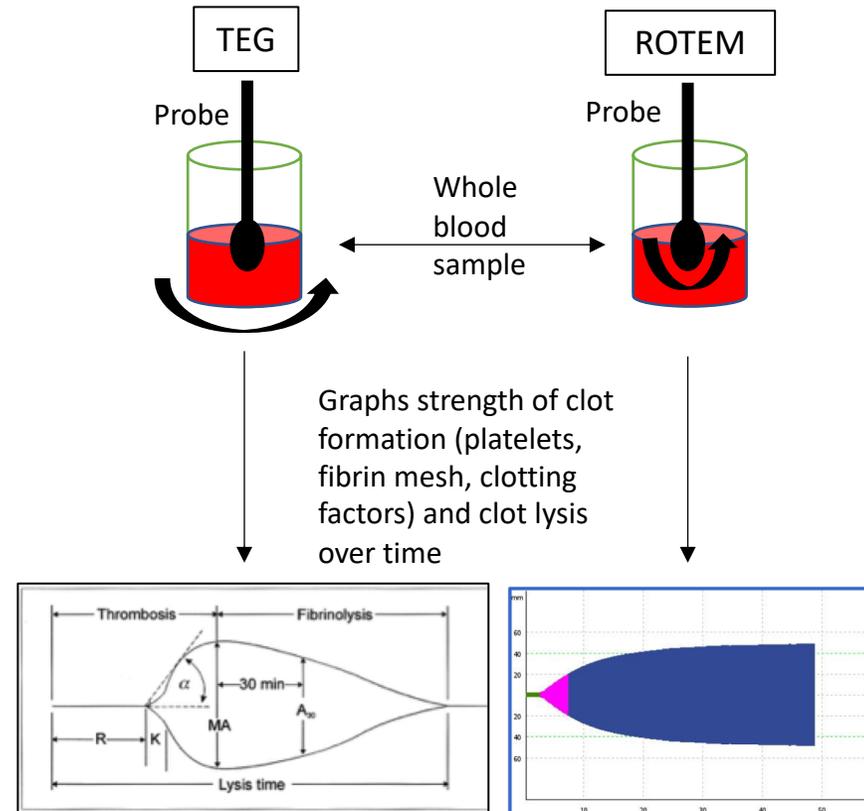
- Multi-country placebo-controlled randomized, double-blind trial
- n= 20,060 women with PPH
- Dose: TXA 1g IV over 10 minutes, repeated at 30 min for ongoing bleeding
- Results:
 - Fewer laparotomies by 36% (0.8 vs 1.3%, RR 0.64)
 - Did not reduce number of hysterectomies
 - Women who received TXA within 3 hours after birth had a 31% lower risk of death from bleeding (1.2 vs 1.7 %, RR 0.69)
 - Did not reduce all cause mortality
 - No increased risk of thromboembolic events

• French multicenter trial

- Randomized 152 women to either 4g of TXA over 1 hour followed by infusion of 1g/hr for 6 hours versus standard care without TXA
- Results:
 - Reduced EBL
 - Enhanced response to uterotonic agents
 - Less change in hemoglobin values
 - Lower number of blood products transfused
 - Trend toward fewer invasive surgical procedures

Viscoelastic Coagulation Testing

- Point-of-care test
- Two commercially available instruments
 - Thromboelastography (TEG)
 - Rotational Thromboelastometry (ROTEM)
- Detects specific deficiencies that can be specifically addressed
 - Early warning for fibrinogen replacement before replacement would have occurred based on standard coagulation studies
 - Potentially improved criteria for transfusion and decreased unnecessary transfusion with the associated risks
 - Promising technology, studied in trauma, cardiac surgery, liver transplant, but further studies need to be done to assess benefit (most studies are single center, observational studies)



Results yield information on:

- Thrombocytopenia/abnormal platelet function
- Low fibrinogen
- Hyperfibrinolysis
- Clotting factor deficiency
- Hypercoagulability

Key Points

- Significant drops in blood pressure are generally not manifested until substantial bleeding has occurred
- Fibrinogen replacement is crucial in obstetric hemorrhage with targeted replacement
- Multidisciplinary preparation and communication is critical
- Know your hospital's protocols and resources

Resources

- California Maternal Quality Care Collaborative (CMQCC.org)
- ACOG Safe Motherhood Initiative
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