



J: Postpartum Hemorrhage: Third Stage Emergency

(slide 1)

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Objectives

(slide 2) At the end of this lecture, participants will be able to:

1. List the important causes of postpartum hemorrhage.
2. Describe methods for preventing postpartum hemorrhage.
3. Demonstrate an awareness of the need for early recognizing and quick response.
4. Describe the initial approach to treating postpartum hemorrhage.

Epidemiology and Significance

(slide 3) Postpartum hemorrhage (PPH), traditionally defined as the loss of more than 500 milliliters of blood following delivery, occurs in up to 18 percent of births.^{1, 2} PPH is considered severe when blood loss exceeds 1000 milliliters or results in hemodynamic instability.³ Even with appropriate management, three percent of vaginal deliveries will result in severe PPH.⁴ PPH is the most common maternal morbidity in developed countries and a major cause of death worldwide.^{1, 3} Complications include orthostatic hypotension, anemia, and fatigue, making maternal care of the newborn more difficult. Postpartum anemia increases the risk for postpartum depression.⁵ Transfusion may be necessary and carries associated risks.⁶ In the most severe cases, hemorrhagic shock may lead to posterior pituitary ischemia with delay or failure of lactation (Sheehan's Syndrome).^{7, 8} Occult myocardial ischemia, dilutional coagulopathy, and deaths also occur.⁹

Risk Factors for Postpartum Hemorrhage

(slide 4) Risk factors include prolonged third stage, cesarean section, history of PPH, multiple pregnancy, fetal macrosomia and episiotomy.^{3, 9-12} However, postpartum hemorrhage occurs in women with no risk factors so providers must be prepared to treat it at every delivery.^{3, 4}

Prevention

(slides 5 to 10) The best preventive strategy is *active management of the third stage of labor (AMTSL)*. This involves 1) administering a uterotonic drug such as oxytocin with, or soon after, the delivery of the anterior shoulder and 2) controlled cord traction to deliver the placenta.¹³ Early cord clamping was included as a component of AMTSL in several trials in the Cochrane metaanalysis.¹³ However, recent trials have shown that a delay of about 60 seconds has benefits to the newborn without an increase in PPH or neonatal morbidity. These benefits include a decrease in anemia in preterm and term infants¹⁴⁻¹⁶ and decrease in intraventricular hemorrhage in the very preterm newborn.^{17, 18} International guidelines omit early cord clamping and substitute uterine massage following placental delivery as the third component of AMTSL.¹⁹

Active management decreases PPH and shortens the third stage of labor with no significant increase in cases of retained placenta.^{2, 13, 20} The incidence of PPH decreases by 60 percent (NNT=12 to prevent one case of PPH) when compared to expectant management, where the placenta is allowed to separate spontaneously, aided only by gravity or nipple stimulation.^{13, 21} A reduction in the incidence of PPH also occurs if oxytocin is given after placental delivery.^{2, 20} Despite good evidence that these prevention strategies work, they are underutilized.²² Hospital guidelines that encourage the use of active management result in significant reduction in the incidence of massive PPH.²³

Oxytocin is the preferred uterotonic agent for preventing PPH because it is at least as effective and has fewer side effects than the ergot alkaloids and prostaglandins.^{2, 24, 25} Misoprostol has a role in prevention of PPH because it is more effective than placebo²⁶ (NNT=18 to prevent one case of PPH) and has advantages over conventional uterotonics in resource-poor areas, i.e., it is inexpensive, heat and light stable, and can be administered without the use of syringes.^{27, 28} Misoprostol is not FDA approved for use in preventing postpartum hemorrhage but the US Pharmacopeia considered this indication an acceptable off-label use.¹⁸ A reasonable dose is 600 micrograms orally.^{27, 28} Women at risk for abnormal placentation, such as those with prior uterine surgery who have an anterior low-lying placenta, may benefit from an antenatal sonogram to look for invasive placenta. These patients, in addition to women with placenta previa, coagulopathy, or cervical pregnancy can be offered delivery at a center with



blood bank, anesthesia and surgical capabilities.²⁹⁻³¹ Consideration can also be given to prophylactic catheters for angiographic embolization prior to delivery in these patients.³² Other strategies for minimizing the impact of PPH include identifying and correcting anemia before delivery,³³ being aware of mother's beliefs about blood transfusions,³⁴ and eliminating routine episiotomy.^{10, 35} Re-examining the patient's vital signs and vaginal flow before leaving the delivery area may detect slow, steady bleeding.

Diagnosis and Management

(slides 11 to 13) Preparation, early recognition and quick response to excessive blood loss will reduce morbidity associated with PPH. The diagnosis of PPH begins with recognition of excessive bleeding and methodical examination for its cause. The mnemonic, "The 4 Ts – Tone, Trauma, Tissue, and Thrombin" can be used to remember specific causes. (Table 2)

Table 2. Mnemonic for the specific causes of PPH – the Four Ts

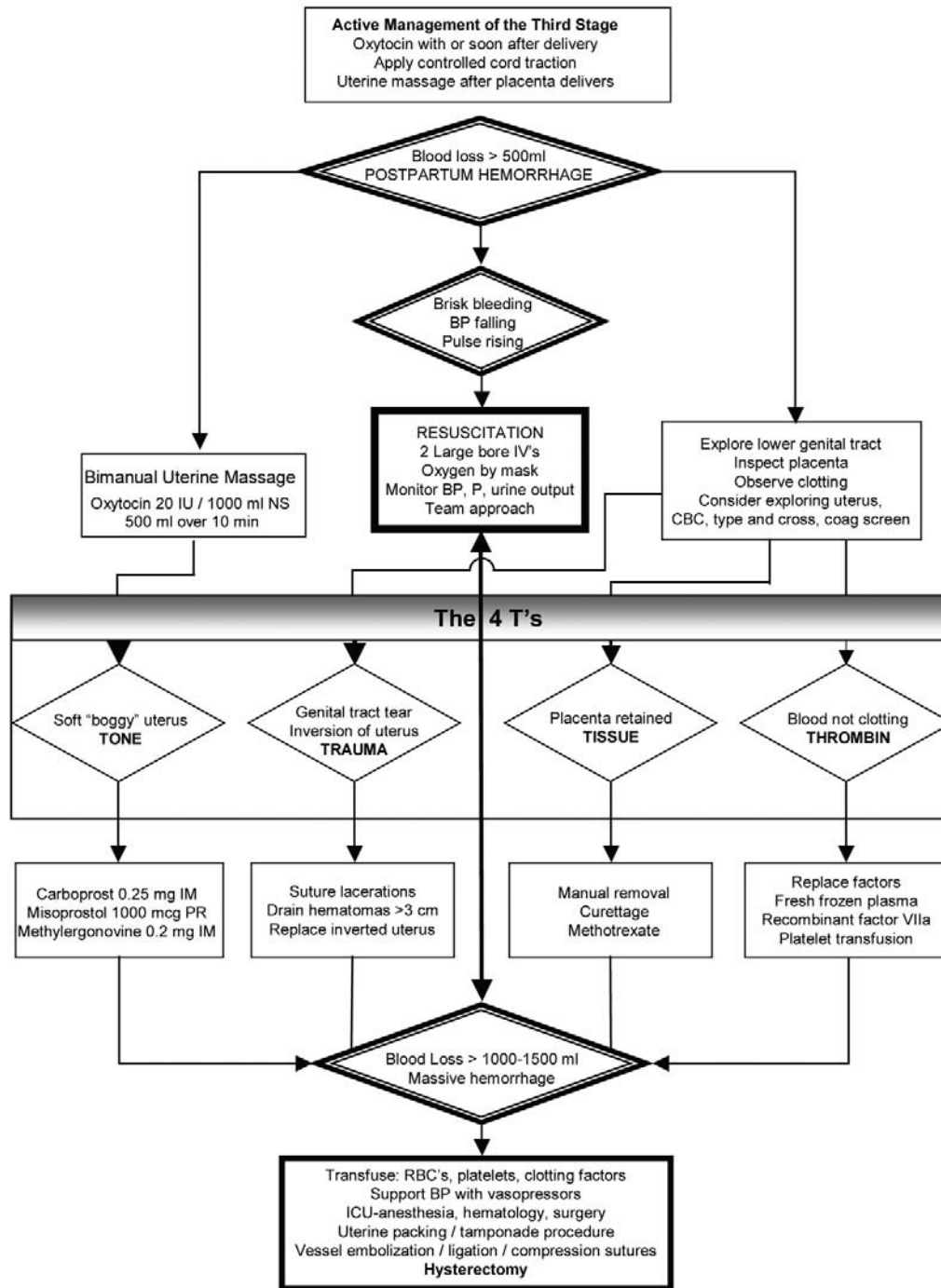
4 Ts	Specific Cause	Relative Frequency
<u>T</u> one	Atonic uterus	70 percent
<u>T</u> rauma	Lacerations, hematomas, inversion, rupture	20 percent
<u>T</u> issue	Retained tissue, invasive placenta	10 percent
<u>T</u> hrombin	Coagulopathies	1 percent

General Approach to a Woman with Postpartum Hemorrhage

(slides 11 to 12) Once excessive blood loss is suspected, treatment must be initiated quickly. As can be seen in Figure 1 (on the next page) many of the steps in diagnosis and management must be carried out simultaneously. When bleeding occurs prior to placental delivery attention is directed to its removal and inspection. If there is a delay in placental delivery or it is not intact, a manual removal may be required. Difficulty locating a plane between the placenta and the uterus may be due to a placenta accreta or one of its variants. After removal of the placenta, brisk bleeding will most often be due to uterine atony. The first maneuver to reduce bleeding is uterine massage. Oxytocin can be given next, via intramuscular or intravenous route. Uterine tone should improve with compression, massage, and oxytocin, but if the uterine muscle relaxes and bleeding resumes, a second oxytocic (carboprost or methylergonovine) can be administered. During this time, the lower genital tract can be explored and lacerations repaired. If uterine atony



Figure 1. Management of Postpartum Hemorrhage



Many of the steps involved in diagnosing and treating PPH can be undertaken simultaneously. While the steps in maternal resuscitation are consistent (center, bold) other actions taken may differ based on the actual cause. The 4Ts mnemonic: Tone Tissue Trauma Thrombin can help you remember the common causes of PPH.

Abbreviations: BP = blood pressure, IU = international units, NS = normal saline, ml = milliliters, min = minutes, P = pulse, Coag = Coagulation, mg = milligrams, IM = intramuscularly, "q" = every, cm = centimeter, RBC's = red blood cells, ICU = intensive care unit.

Coagulation screen includes platelet count, prothrombin time (INR), partial thromboplastin time, fibrinogen level, and fibrin split products (d-dimer).

has been treated and no lacerations or hematomas have been recognized, it is useful to explore the uterus to determine if retained placental fragments are responsible for continued bleeding. Uterine exploration will also allow detection of rupture or subtle uterine inversion. Hypotension or shock out of proportion to the amount of blood loss raises the suspicion for concealed hematomas, uterine rupture or partial inversion. Anaphylaxis and amniotic fluid or pulmonary embolism should also be considered. Persistent oozing or lack of clotting may signal a coagulopathy.

- (slide 11) Blood loss greater than 1000 milliliters is considered severe and requires quick action using an interdisciplinary team approach, including anesthesia and surgery. Massive hemorrhage requires immediate resuscitation measures: securing the airway, breathing, and circulation (ABC's); giving oxygen; starting two large bore IV's with normal saline or other crystalloid fluids; and obtaining stat labs (type & cross, complete blood count, coagulation studies). Heart rate and blood pressure should be monitored closely, and times of relevant events should be documented. While vital sign changes may be delayed even with significant hemorrhage, the earliest to occur is tachycardia and narrowing pulse pressure. In addition to rapid infusion of crystalloid, type-specific blood may be needed. If stat labs are unavailable, fresh frozen plasma should be given whenever more than five to ten units of packed red blood cells have been given acutely. A Foley catheter can be placed to empty the bladder and monitor urine output. Intractable hemorrhage may require uterine packing (plain or with vasopressin or carboprost), tamponade procedures (types include Foley catheter bulb, or hydrostatic), or hemostatic drugs such as recombinant factor VIIa.³² Compression of the aorta can be a temporizing measure.³⁶ Angiographic embolization or surgical ligation of arteries, and rarely, hysterectomy may be required.

Cause-Specific Approach to Postpartum Hemorrhage

Tone

- (slide 14) Uterine atony is the most common cause of PPH. Because hemostasis following placental separation depends on myometrial contraction, atony is treated initially by bimanual uterine massage followed by drugs that promote contraction of the uterus.

Uterine Massage

- (slide 10) Brisk flow of blood from the vagina after delivery of the placenta alerts the clinician to perform a bimanual examination of the uterus. If the uterus is soft, massage is performed by placing one hand in the vagina and pushing up against



the body of the uterus, while the other hand compresses the fundus from above through the abdominal wall. The anterior aspect of the uterus is massaged with the abdominal hand and the posterior aspect with the vaginal hand.

Uterotonic Agents

(slide 15) Uterotonic agents include oxytocin, ergot alkaloids, and prostaglandins (Table 3). Oxytocin (Pitocin®, Syntocinon®) stimulates the upper segment of the myometrium to contract rhythmically, constricting spiral arteries decreasing blood flow through the uterus.³⁷ Oxytocin is an effective first line treatment for PPH. The dose is 20 units (range 10 to 40 units) in one liter of normal saline, infused intravenously at 250 ml/hr. Five hundred milliliters can be infused over 10 minutes without complications. There is a long-held view that direct intravenous administration increases the risk of transient hypotension³⁸ but a randomized controlled trial found that a 10 unit IV bolus did not cause significant hypotension.³⁹

(slides 16 to 17) Prostaglandins are often used when other methods fail.²⁵ Prostaglandins enhance uterine contractility and cause vasoconstriction.⁴⁰ The prostaglandin most commonly used is 15-methyl prostaglandin F-2a, or carboprost (Hemabate®). Carboprost can be given either intramyometrially or intramuscularly in a dose of 0.25 mg, and can be repeated every fifteen minutes for a total dose of 2 mg. Carboprost has been shown to control hemorrhage in up to 87 percent of cases.⁴¹ In cases where it was not effective, chorioamnionitis or other risk factors for hemorrhage were often present.⁴¹ Hypersensitivity is the only absolute contraindication, but carboprost should be also be used with caution in patients with asthma or hypertension. Common side effects include nausea, vomiting and diarrhea.⁴⁰

(slide 18) Misoprostol (Cytotec®) is another prostaglandin that increases uterine tone and decreases bleeding postpartum.⁴² Misoprostol is effective in treatment of PPH but side effects may limit its use.^{43, 44} It can be administered by the sublingual, oral, vaginal, and rectal routes, sometimes in combination. Dosages range from 200 to 1000 mcg.⁴³⁻⁴⁵ Higher levels and larger doses are associated with more side effects including shivering, pyrexia, and diarrhea.^{43, 46} Despite being widely used, this indication is considered “off-label.”

(slide 19) Methylergonovine (Methergine®) and ergometrine (Ergonovine®) are ergot alkaloids that cause generalized smooth muscle contraction, in which both the upper and lower segments of the uterus contract tetanically.⁴⁷ A typical dose is 0.2 mg IM, repeated every two to four hours. Because ergot alkaloid agents raise blood pressure, they are contraindicated in women with hypertension.⁴⁸ Other adverse effects include nausea and vomiting.⁴⁸



Table 3. Medications used for postpartum hemorrhage⁴⁸

Medication	Dose	Prevention	Treatment	Contraindications/ Cautions	Mechanism of Action	Side effects / Comments
Oxytocin (Pitocin [®] , Syntocinon [®])	10 IU IM 20 to 40 IU/liter NS infusion 500ml in 10 minutes then 250 ml/hour ⁴⁹ alternate route: IMM ³⁰	+	+	Contraindication: none Caution: Overdose or prolonged use can cause water intoxication	Stimulates the upper segment of the myometrium to contract rhythmically, constricting spiral arteries decreasing blood flow through the uterus. ³⁷	Rare
Carboprost (Hemabate [®]) Prostaglandin F-2_ analog	0.25 mg, IM or intramyometrially repeated q 15 to 90 minutes for a total dose of 2 mg alternate route: IMM	-	+	Contraindication: Active pulmonary, renal, hepatic, or cardiac disease Caution: History of asthma, hyper- hypotension, cardiovascular, renal, hepatic disease, anemia, jaundice, diabetes, or seizure disorder	Improves uterine contractility by increasing the number of oxytocin receptors and causes vasoconstriction ⁴⁰	Nausea, vomiting and diarrhea ²⁵
Misoprostol (Cytotec [®])* Prostaglandin E1 analog	Treatment: 1000 mcg rectally or 200 mcg oral with 400 mcg sublingual ^{43,} ^{44, 51} Prevention: 600mcg oral ^{27, 51}	+/- not as effective as other uterotonics	+	Contraindication: none Caution: Cardiovascular disease	Generalized smooth muscle contraction ²¹	Nausea, vomiting diarrhea, pyrexia, and shivering ²⁵
Methylergonovine (Methergine [®]) ————— Ergometrine (Ergonovine [®])	0.2 mg IM repeat q 2 to 4 hours ————— 0.5 mg IM alternate route: IMM ⁵⁰	+/-	+	Contraindication: Hypertension/ toxemia Caution: Sepsis, vascular, hepatic, or renal disease	Vasoconstriction and contracts smooth muscles upper and lower segments of the uterus tetanically ⁴⁰	Nausea, vomiting and Increased B/P

Table Footnotes:

Abbreviations: IM intramuscular, IMM intramyometrially, NS normal saline, Prostaglandin F-2_ 15-methyl prostaglandin F2_.

** Misoprostol is not approved by the U. S. Food and Drug Administration for use in postpartum hemorrhage.*

Trauma

(slide
20 to 21)

Lacerations and hematomas resulting from birth trauma can cause significant blood loss that can be lessened by hemostasis and timely repair. Sutures are placed if direct pressure does not stop the bleeding. Episiotomy increases blood loss^{10, 12} as well as the risk of anal sphincter tears³⁵ and should be avoided unless urgent delivery is necessary and the perineum is felt to be a limiting factor.⁴⁴



(slide 22) Hematomas can present as pain or as a change in vital signs out of proportion to the amount of blood loss observed. Small hematomas can be managed with close observation.⁵² Patients with persistent signs of volume loss despite fluid replacement, or with large or enlarging hematomas, require incision and evacuation of the clot.⁵² The involved area should be irrigated and the bleeding vessels ligated. Where there is diffuse oozing, a layered closure will help to secure hemostasis and eliminate dead space.

Uterine Inversion

(slide 23 to 26) Uterine inversion is rare, occurring in 0.05 percent of deliveries.⁴⁹ Active management of the third stage may reduce the incidence.⁵³ Fundal implantation of the placenta may lead to inversion; the role of fundal pressure and undue cord traction are uncertain.⁴⁹ The inverted uterus usually appears as a bluish-gray mass protruding from the vagina. Roughly half the time, the placenta is still attached and it should be left in place until after reduction.⁵³ Every attempt should be made to replace the uterus quickly. There are several methods for reduction. The Johnson method involves grasping the protruding fundus with palm of the hand, fingers directed toward the posterior fornix. The uterus is returned to position by lifting it up through the pelvis and into the abdomen with steady pressure towards the umbilicus.⁵⁴ Once the uterus is reverted, uterotonic agents should be given to promote uterine tone and prevent recurrence. If initial attempts to replace the uterus have failed or a cervical contraction ring develops, magnesium sulfate, terbutaline, nitroglycerin, or general anesthesia may allow sufficient uterine relaxation for manipulation. Failing that, the uterus will need to be replaced surgically.⁵³

Uterine Rupture

(slides 27 to 28) Although rare in an unscarred uterus, clinically significant uterine rupture complicates 0.6 to 0.7 percent of vaginal births after cesarean delivery (VBAC)^{18, 55, 56} The risk increases with previous classical incisions, use of prostaglandins for cervical ripening or induction, previous uterine surgeries and to a lesser extent with shorter intervals between pregnancies, and no previous vaginal delivery.^{18, 55, 57, 58} Compared to spontaneous labor, induction or augmentation increases the rate of uterine rupture, particularly if prostaglandins and oxytocin are used sequentially. However, the incidence of rupture is still low (one to 2.4 percent).⁵⁸ Misoprostol should not be used for cervical ripening or induction when attempting VBAC.⁵⁸

During labor, the main sign of uterine rupture is fetal bradycardia.⁵⁶ Tachycardia or late decelerations can also herald a uterine rupture, as can vaginal bleeding, abdominal tenderness, increasing abdominal girth, maternal tachycardia or



circulatory collapse.⁵⁷ Symptomatic uterine rupture requires surgical repair of the defect, or hysterectomy, but only one third of cases will have severe fetal or maternal health consequences.⁵⁶ Bloodless dehiscence or small, asymptomatic lower uterine segment defects discovered by postpartum urine exploration can be followed expectantly.⁵⁷

Tissue

Retained Placenta

(slide 29) A small gush of blood with lengthening of the cord and a slight rise of the uterus in the pelvis are the classic signs of placental separation. Most placentas separate from the uterine wall within one minute after the infant delivers.⁵⁹ Firm traction on the umbilical cord with one hand while the other applies suprapubic counter-pressure typically achieves placental delivery. (Brandt maneuver).⁶⁰ The mean time from delivery until placental expulsion is eight to nine minutes.⁴ A longer interval is associated with an increased risk of PPH, doubling after 10 minutes.⁴ Retained placenta, defined as the failure of the placenta to deliver within 30 minutes after birth, occurs in less than three percent of vaginal deliveries.⁶¹ One management option is to inject the umbilical vein with 20 ml of a 0.9 percent saline containing 10 to 20 units of oxytocin. This significantly reduces manual removal of the placenta compared with injecting saline alone.⁶²

(slides 30 to 32) Alternatively, one may proceed directly to manual removal of the placenta using appropriate analgesia. To manually remove the placenta:

1. Cease uterine massage and allow the uterus to relax. Subcutaneous terbutaline, intravenous nitroglycerin 50 micrograms, or general anesthesia may be required to relax the uterus. The patient can lose large amounts of blood as the uterus relaxes, so it becomes imperative to accomplish the removal rapidly and to be prepared to reverse the relaxation.
2. Identify the cleavage plane between the placenta and the uterine wall. Advance your fingertips in the plane until the entire placenta is free.
3. Cup the separated cotyledons into your palm. Deliver the placenta intact if possible.
4. After examining the uterine cavity and the placenta to ensure that the entire placenta and membranes have been removed, massage the uterus and give oxytocin.



If the cleavage plane cannot be identified or parts of the plane cannot be developed completely, prepare for surgical removal of the placenta:

1. Ensure that the patient has oxygen, two large bore intravenous catheters with replacement fluids running, adequate anesthesia started, proper surgical setup available, and appropriately trained providers present. Then, remove placental tissue either by vacuum or blunt curettage.
2. Curette the uterine cavity with a large blunt curette or large suction catheter. Take care to prevent perforating the soft, postpartum uterus.
3. Use ring forceps to grasp and remove placental tissue.
4. If the bleeding cannot be controlled with these measures, consider emergency hysterectomy.

(slides
33 to 34)

When the tissue plane between the uterine wall and placenta cannot be developed through blunt dissection with the edge of the gloved hand, the diagnosis of invasive placenta should be considered. Invasive placenta can be life threatening.⁶¹ The incidence has increased from 0.003 percent to 0.04 percent of deliveries since 1950's, likely related to the increase in cesarean section rates.⁶⁰ Classification is based on the depth of invasion. Placenta accreta adheres to the myometrium, placenta increta invades the myometrium, and placenta percreta penetrates the myometrium to or beyond the serosa.⁴⁹ Risk factors include: prior invasive placenta, previous cesarean delivery, placenta previa, (especially in combination with prior cesarean section/s, increasing to 67 percent with four or more), advanced maternal age, and high parity.⁶⁰ The usual treatment for invasive placenta is hysterectomy. For placenta percreta, however, conservative management is sometimes successful. This includes leaving the placenta in place or using weekly oral methotrexate⁶³ until beta HCG levels are zero.³¹ Women treated for a retained placenta must be observed for late sequelae, including infection and late postpartum bleeding.^{31, 63}

Thrombin

(slides
35 to 38)

Coagulation disorders, a rare cause of PPH, are unlikely to respond to the measures described above.⁴⁹ Most patients with coagulopathies are identified prior to delivery, allowing advanced planning to prevent PPH. Idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, von Willebrand's disease, and hemophilia are some of the disorders. Patients can also develop HELLP syndrome or disseminated intravascular coagulation (DIC). Obstetric conditions that can cause DIC include severe pre-eclampsia, amniotic fluid embolism, sepsis, placental abruption (often associated with cocaine use or hypertensive disorders)³² and prolonged retention of fetal demise.^{32, 64}



In addition, excessive bleeding can deplete coagulation factors and lead to a consumptive coagulopathy which promotes further bleeding. Coagulation defects should be suspected in those patients who have not responded to the usual measures to treat PPH, are not forming blood clots, or are oozing from puncture sites.

Evaluation should include a platelet count, prothrombin time (INR), partial thromboplastin time, fibrinogen level, and fibrin split products (d-dimer).

Management consists of treating the underlying disease process, serially evaluating the coagulation status, replacing appropriate blood components, and supporting intravascular volume.³²

Summary

(slide 39) Postpartum hemorrhage is unpredictable and can occur in women with no risk factors. Prevention strategies such as use of oxytocin and AMTSL are available and important, but are underutilized.²³ Uterine atony is responsible for the majority of PPH, and can be effectively managed by uterine massage, oxytocin, methylergonovine, and 15-methyl prostaglandin F_{2α}. The second most common cause of PPH, retained placenta, requires careful evaluation and anticipation of the rare cases with invasive placenta. Traumatic causes of postpartum hemorrhage require repair. For women with Thrombin-related causes, clotting factors need to be replaced. Early recognition, systematic evaluation and treatment, and prompt fluid resuscitation minimize the morbidity and mortality associated with postpartum hemorrhage, regardless of cause.

Summary of Recommendations

Strength of Recommendation – A

Active management of the third stage of labor should be utilized to decrease postpartum blood loss, length of third stage, and the incidence of PPH.¹³ (NNT 12)

There is no significant increase in the occurrence of retained placenta with active management of the third stage of labor.^{2, 13, 20}

Oxytocin remains the first choice for prevention of PPH because it is as, or more, effective² than ergot alkaloids or prostaglandins and has fewer side effects.^{24, 65}

Misoprostol has advantages **for prevention** in low-resource settings because it is effective (NNT 18), inexpensive, heat stable and simple to administer.^{27, 28}

Misoprostol is effective **for treatment** of postpartum hemorrhage but has more side effects than conventional uterotonic drugs.^{43, 44}

Acknowledgement

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