MATERNAL911®

Disseminated Intravascular Coagulation (DIC)

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Course Description:

This course focuses on participants gaining a better understanding of Disseminated Intravascular Coagulation (DIC), and the issues it brings to health care organizations, while providing participants with a practice setting to examine and develop their own skills. Education is empowering. DIC is a detrimental disease process that is life threatening for the women it effects.

Approximate Time to Complete: 100 minutes

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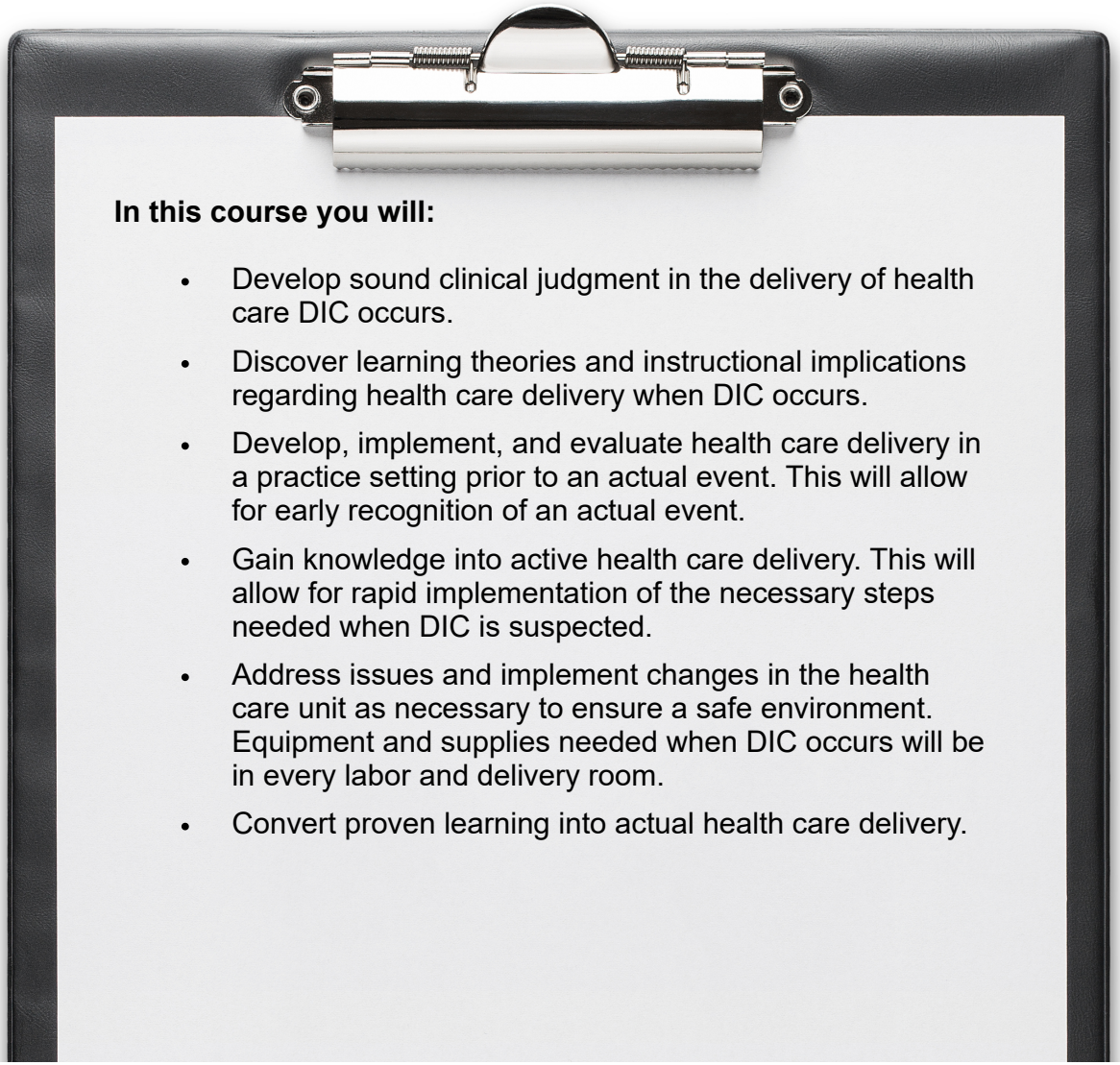

In this course you will:

- Develop sound clinical judgment in the delivery of health care DIC occurs.
- Discover learning theories and instructional implications regarding health care delivery when DIC occurs.
- Develop, implement, and evaluate health care delivery in a practice setting prior to an actual event. This will allow for early recognition of an actual event.
- Gain knowledge into active health care delivery. This will allow for rapid implementation of the necessary steps needed when DIC is suspected.
- Address issues and implement changes in the health care unit as necessary to ensure a safe environment. Equipment and supplies needed when DIC occurs will be in every labor and delivery room.
- Convert proven learning into actual health care delivery.

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Disseminated Intravascular Coagulation (DIC)

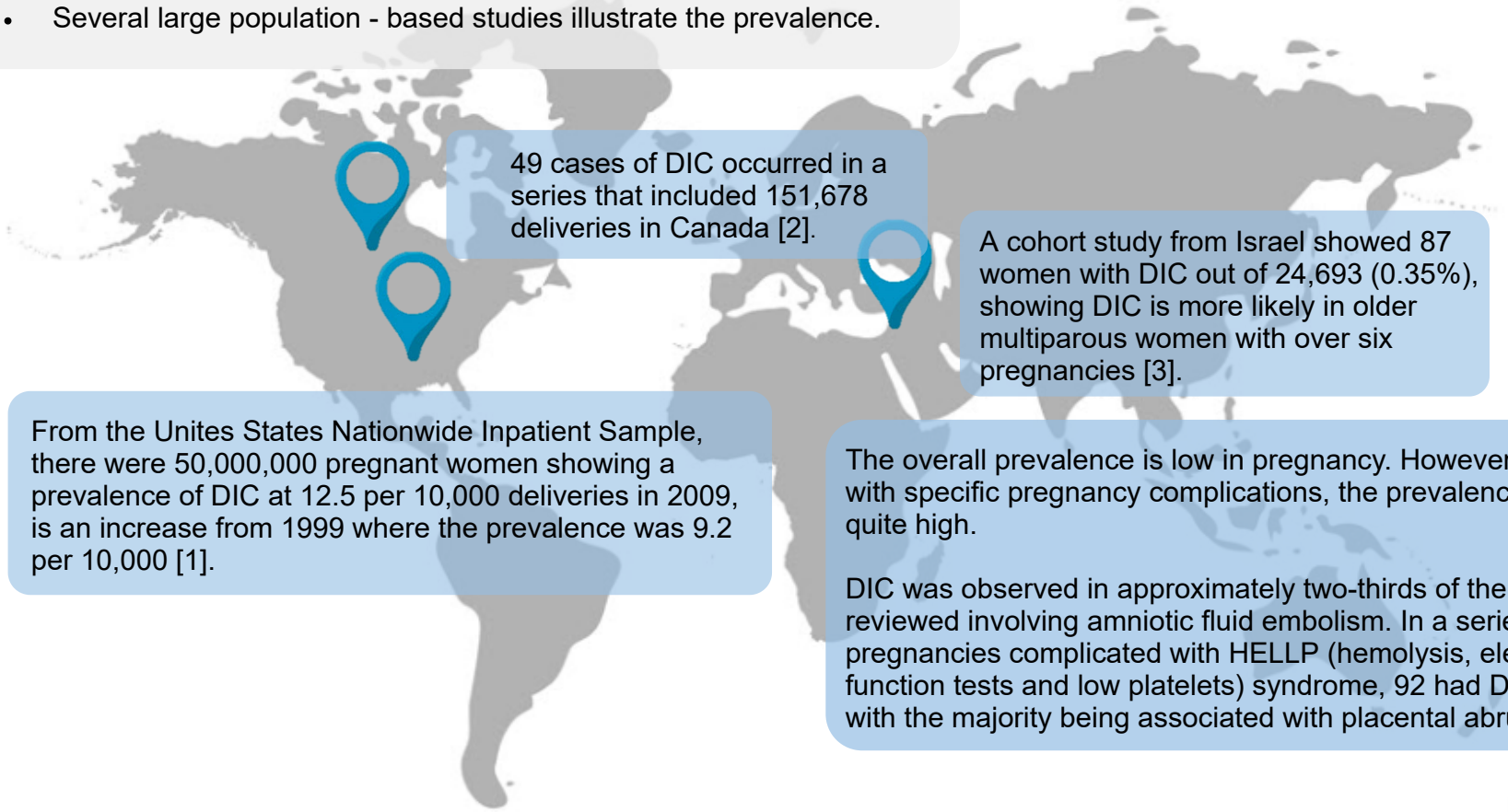
A pathologic disruption of the finely-coordinated process of hemostasis.

- Massive activation of the clotting cascade results in widespread thrombosis, which leads to depletion of platelets and coagulation factors and excessive thrombolysis.
    - This can result in hemorrhage, thrombosis, and/or multi-organ failure.
- A major medical challenge occurs when a woman presents with DIC and is further challenging when she is carrying a viable fetus.
- In the interest of the pregnant woman with DIC and heavy bleeding, performing an emergency cesarean delivery may not be appropriate. However, a category fetal heart rate (FHR) tracing and delaying delivery to transfuse the woman may not be in the best interest of the fetus.
- Labor and delivery of a fetal demise in a woman with DIC has the possibility for disastrous hemorrhage.

Occurrence of Disseminated Intravascular Coagulation (DIC)

- DIC in pregnancy has a prevalence of less than 0.5% [1-3].
- Several large population - based studies illustrate the prevalence.

Roll over each marker to learn about studies in different countries.



49 cases of DIC occurred in a series that included 151,678 deliveries in Canada [2].

A cohort study from Israel showed 87 women with DIC out of 24,693 (0.35%), showing DIC is more likely in older multiparous women with over six pregnancies [3].

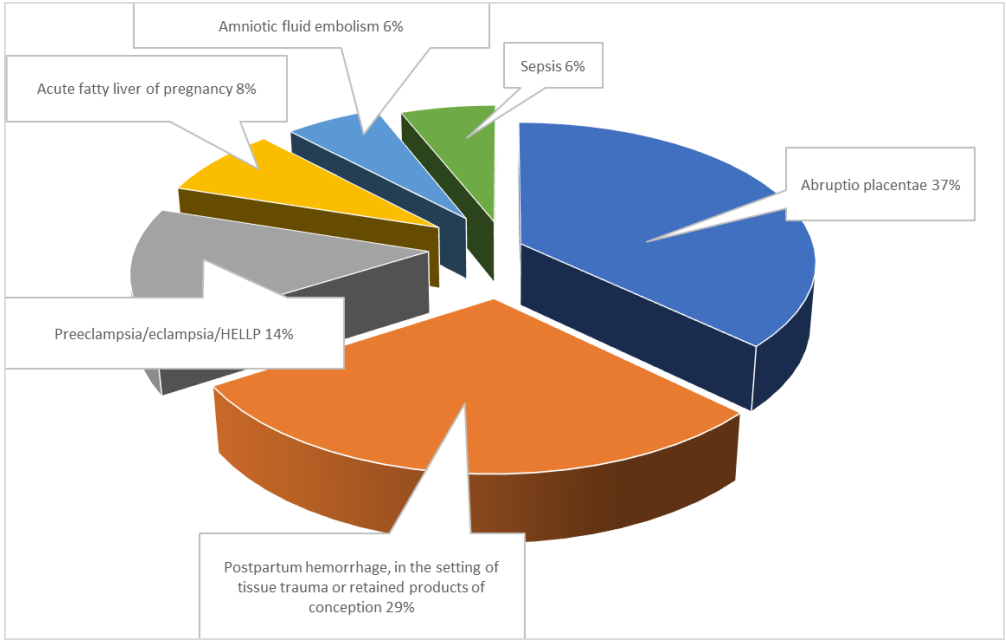
From the Unites States Nationwide Inpatient Sample, there were 50,000,000 pregnant women showing a prevalence of DIC at 12.5 per 10,000 deliveries in 2009, is an increase from 1999 where the prevalence was 9.2 per 10,000 [1].

The overall prevalence is low in pregnancy. However, in women with specific pregnancy complications, the prevalence can be quite high.

DIC was observed in approximately two-thirds of the 53 cases reviewed involving amniotic fluid embolism. In a series of 442 pregnancies complicated with HELLP (hemolysis, elevated liver function tests and low platelets) syndrome, 92 had DIC (21%) with the majority being associated with placental abruption [4,5].

Risk Factors

- DIC does not occur in isolation.
- Pregnancy complications that may trigger and propagate DIC were evaluated in a review of 49 cases of DIC [2].
- Antecedent conditions included the following:
  - Abruptio placentae – 18 cases (37%)
  - Postpartum hemorrhage, in the setting of tissue trauma or retained products of conception – 14 cases (29%)
  - Preeclampsia/eclampsia/HELLP – 7 cases (14%)
  - Acute fatty liver of pregnancy – 4 cases (8%)
  - Amniotic fluid embolism – 3 cases (6%)
  - Sepsis – 3 cases (6%)
  - The fetus died in one-quarter of these cases



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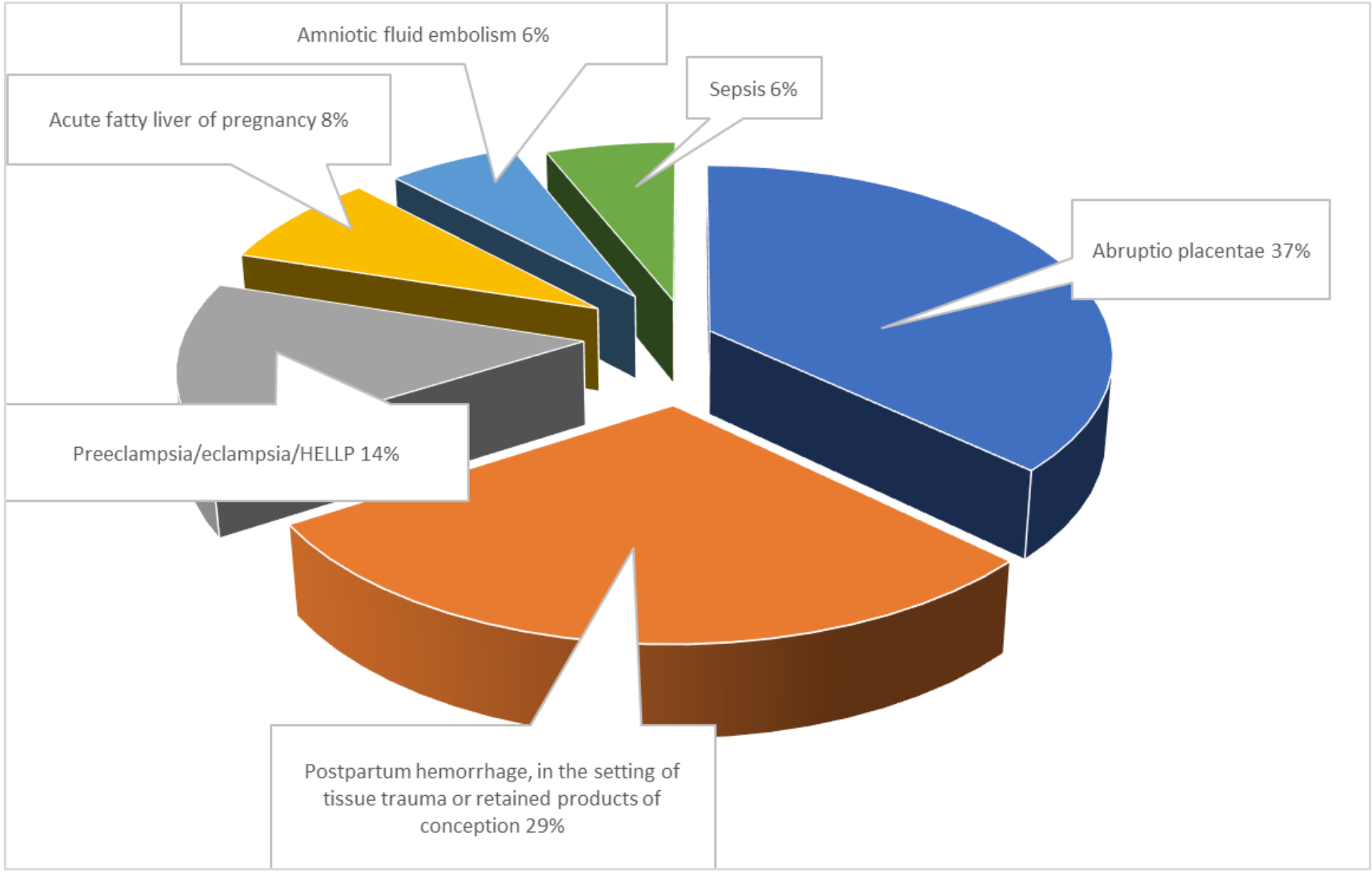

Amniotic fluid embolism 6%
Sepsis 6%
Acute fatty liver of pregnancy 8%
Abruptio placentae 37%
Preeclampsia/eclampsia/HELLP 14%
Postpartum hemorrhage, in the setting of tissue trauma or retained products of conception 29%

Continuing with Risk Factors

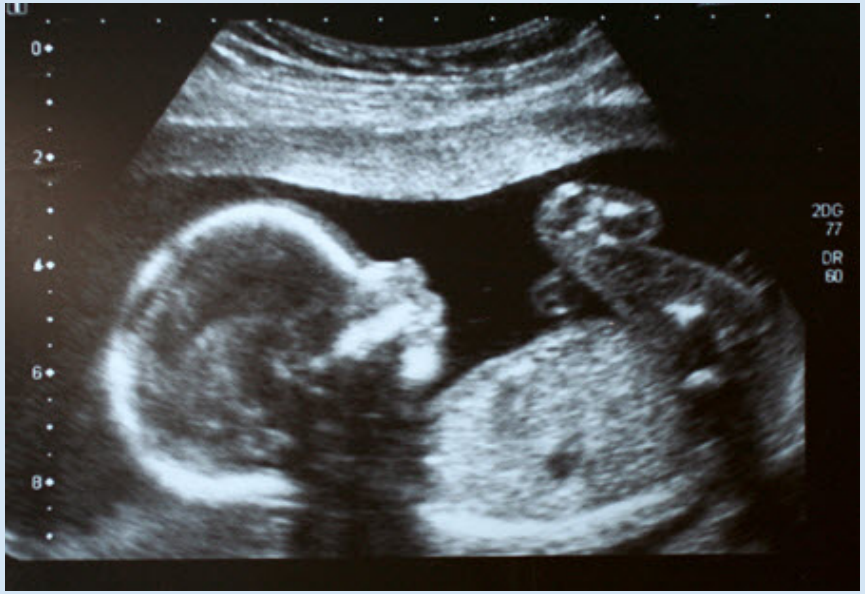
- Severe hemorrhage, itself, does not cause DIC, but severe postpartum hemorrhage can be associated with DIC.
- The loss of clotting factors and platelets plus the generation of large amounts of fibrinogen products interfere with fibrin clot formation and platelet aggregation causing the bleeding in DIC.
- When severe postpartum hemorrhage occurs rapidly, the depletion of clotting factors and platelets leads to consumptive coagulopathy; this is not DIC.
- When large amounts of tissue factor are released during severe postpartum hemorrhage, it can be accompanied by true DIC [6].
- Following separation of the membranes and placenta, uterine decidual-derived tissue factor is normally released into the maternal circulation, activates the coagulation cascade, and generates thrombin [7,8].
- There are various causes (i.e. large laceration, placenta accreta) of postpartum hemorrhage that are associated with large release of tissue factor, resulting in intense physiologic intravascular coagulation process initiated by placental separation occasionally leading to DIC.
- Approximately 1-5% of all DIC cases are attributed to obstetric hemostatic emergencies in high-resource countries and even higher percent in low-resource countries [9].
- The remaining cases are due to nonobstetric causes.
- Causes of DIC not specific to pregnancy should be considered, especially when an obvious pregnancy-associated cause is absent [10,11].
- The most common events that initiate DIC in the general population are sepsis, tissue trauma/destruction, and cancer (Table 1).

Click on the image to view Table 1.

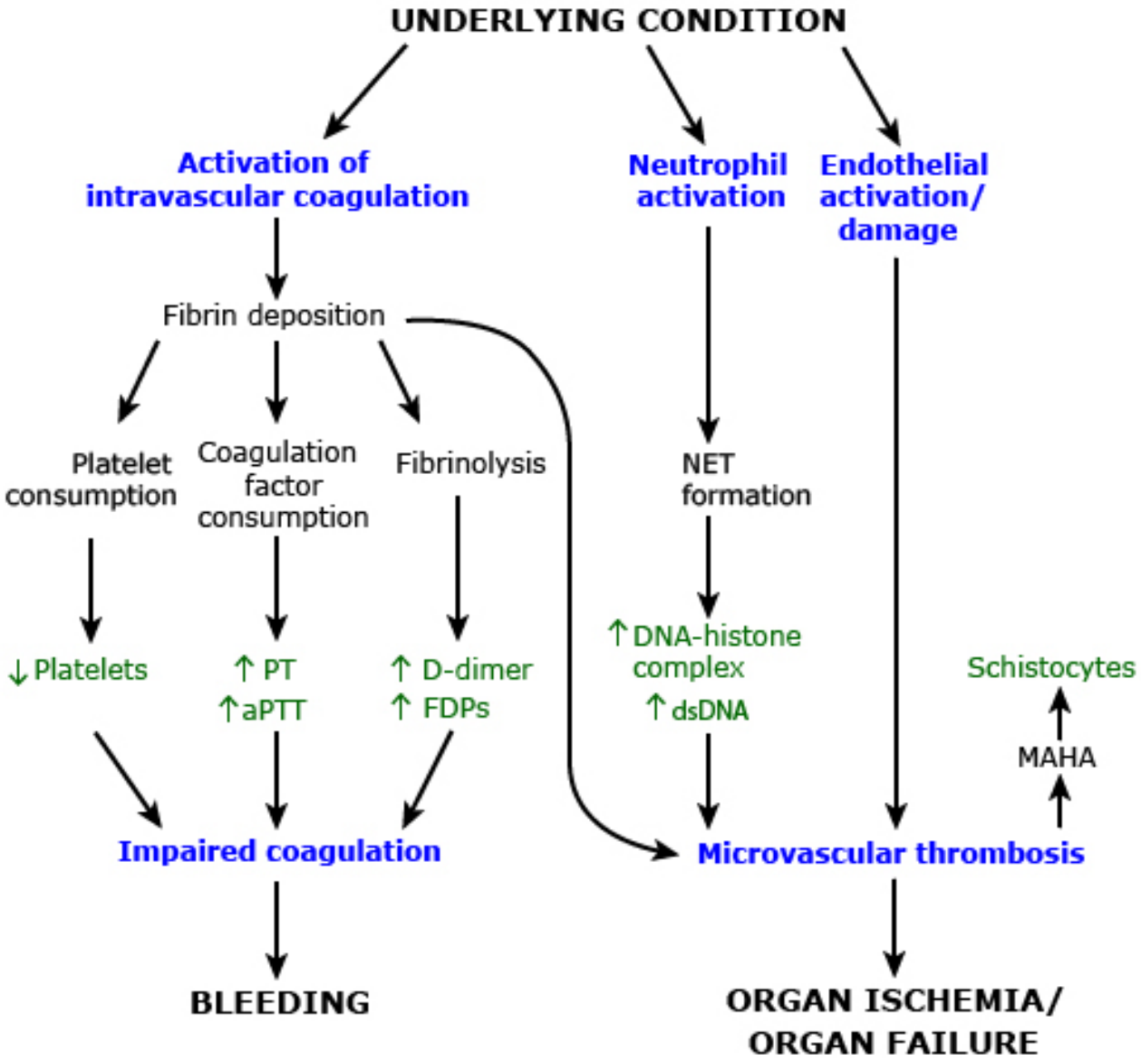
Table 1

Events that Initiate DIC				
Septiciemia-Gram Negative and Gram Positive	Crush injury or complicated surgery	Severe head injury	Abdominal aortic aneurysm	Peritoneovenous shunt
Cancer procoagulant (Trusseau's Syndrome)	Acute leukemia, especially promyelocytic	Amphetamine overdose	Giant hemangioma (Kasaback-Merritt Syndrome)	Acute hemolytic transfusion reaction (ABO incompatibility)
Complications of pregnancy: • Amniotic fluid embolism • Abruption • HELLP syndrome • Eclampsia and severe preeclampsia • Septic abortion	Paroxysmal nocturnal hemoglobinuria	Snake or viper venoms	Liver disease: • Fulminant hepatic failure • Reperfusion after liver transplant	Heat stroke
Burns	Pupurs fulminans	Events that propagate and complicate DIC: • Shock • Complement pathway activation		

Etiology

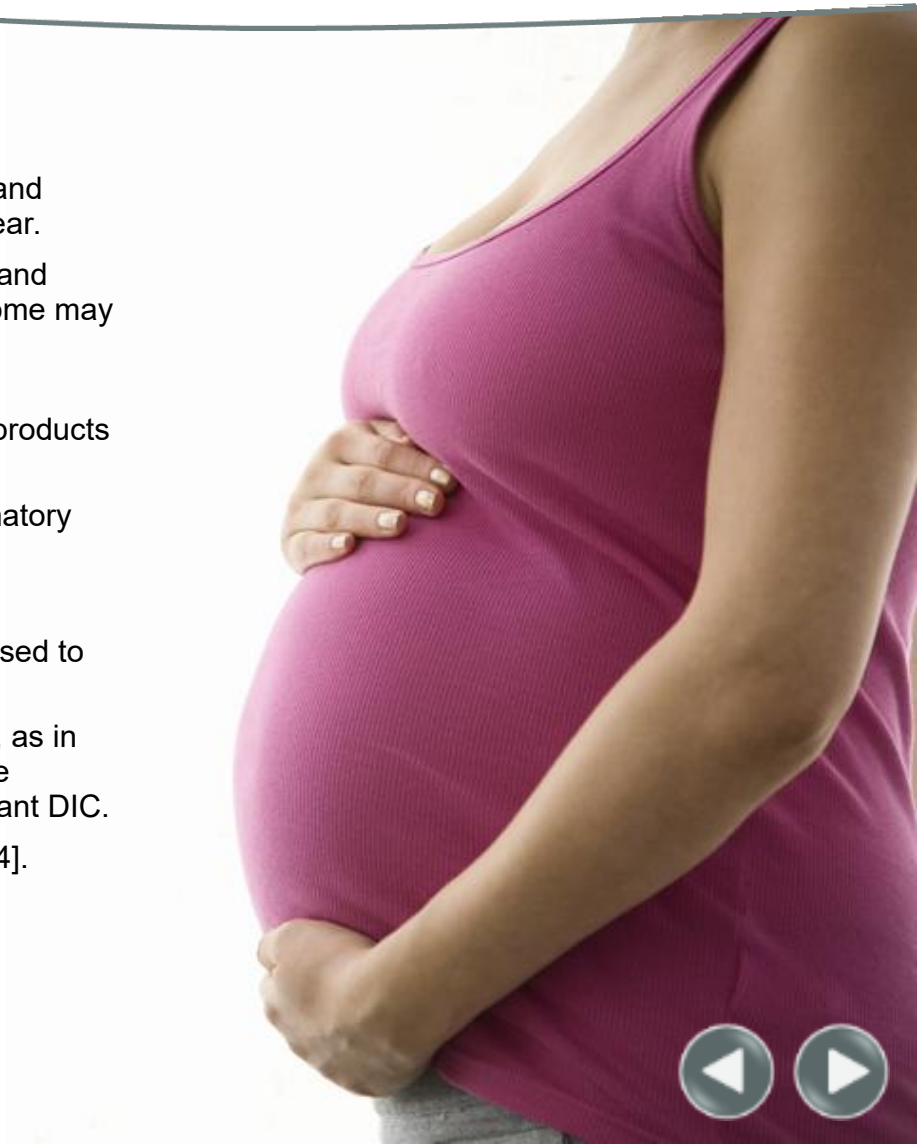


- Levels of some coagulation factors increase to prevent excessive peri-partum bleeding during pregnancy.
- In addition to systemic changes in coagulation factors, decidual cells lining the vascular bed of the placenta strongly express tissue factor, similar to other vascular endothelial cells [12,13].
- At the site of decidual trama the tissue factor is released to initiate the coagulation cascade, which generates thrombin and thus cross linked fibrin.
- Physiologic inhibitors of coagulation serve to prevent excessive fibrin generation.
- When DIC ensues, the excessive production of thrombin leads to widespread intravascular fibrin deposition and widespread fibrinolysis.
- The result is a depletion of coagulation factors and platelets along with the production of fibrin degradation products leading to profound bleeding diathesis (**Figure 1**).
- These changes overwhelm and incapacitate the physiologic regulatory mechanisms and lead to thrombin not being contained.
- The uncontrolled and ongoing fibrin deposition may lead to thrombosis, end organ damage and failure.


UNDERLYING CONDITION
Activation of intravascular coagulation
Neutrophil activation
Endothelial activation/ damage
Fibrin deposition
Platelet consumption
Coagulation factor consumption
Fibrinolysis
NET formation
↓ Platelets
↑ PT
↑ aPTT
↑ D-dimer
↑ FDPs
↑ DNA-histone complex
↑ dsDNA
Schistocytes
MAHA
Impaired coagulation
Microvascular thrombosis
BLEEDING
ORGAN ISCHEMIA/ ORGAN FAILURE

Etiology Continued

- DIC can be exacerbated by additional pregnancy complications and worsen hemostatic defects, although the mechanisms are not clear.
- Events occuring in pregnancy such as preeclampsia, eclampsia and HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome may contribute to endothelial damage.
- Acute fatty liver may impair the production of coagulation factors produced by the liver and impair clearance of fibrin degradation products and shock may reduce tissue perfusion.
- When sepsis occurs the interaction of DIC with systemic inflammatory response syndrome plays a role in the pathogenesis of DIC [15].
- Hemorrhage alone does not cause DIC.
- In the setting of shock, severe tissue hypoxemia has been proposed to result in the release of tissue factor from the damaged cells [14].
- When significant injury or necrosis of fetoplacental tissue occurs, as in abruptio placenta and retained fetal demise, this cascade may be initiated by release of procoagulant substances leading to fulminant DIC.
- Amniotic fluid is also rich in procoagulants and anticoagulants [14].



Issues Complicating DIC

- One of the following pregnancy complications may be present with DIC:
  - Abruptio placentae
  - Severe preeclampsia/eclampsia/HELLP syndrome
  - Amniotic fluid embolism (AFE)
  - Acute fatty liver of pregnancy
  - Septic abortion
  - Retained dead fetus
  - Massive hemorrhage
- Patients may present with severe bleeding (i.e. vaginal, intrauterine, intra-abdominal) and/or diffuse oozing of blood from skin (i.e. at intravenous sites) or mucosa (i.e. from a bladder catheter).
- Some patients have signs of shock:
  - Tachycardia
  - Hypotension
  - Weak peripheral pulses
  - Altered mental status
  - Cool extremities
  - Narrow pulse pressure (<25 mmHg)
  - Organ dysfunction
    - Acute renal failure
    - Hepatic dysfunction
    - Acute lung injury
    - Neurologic dysfunction

- Laboratory findings of DIC generally include prolongation of coagulation times and thrombocytopenia.
- These laboratory findings are interpreted for the pregnant woman which can be different from the nonpregnant woman **(Table 2).**
- **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
- **Hypofibrinogenemia**
- **Increased D-dimer**
- **Thrombocytopenia**
- **Prolonged thrombin time**

- DIC may cause an increase in the international normalized ration for the PT.
- In a normal pregnancy, the PT and PTT may be slightly lower than in nonpregnant women.

Roll over the bold green words aboves to learn more about each.

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- In a normal pregnancy, fibrinogen is >300mg/dL in the third trimester, a level that is significantly higher than in nonpregnant women [16].
- Reduction in fibrinogen is the least sensitive test and a late finding in DIC [17].
- Fibrinogen levels <100mg/dL are generally associated with bleeding and prolongation of clotting times.

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- In a normal pregnancy, D-dimer is 0.13 to 1.7mcg/mL in the third trimester, which is significantly higher than in nonpregnant women [18].
- Plasmin cleaves polymerized fibrin strands at multiple sites and releases fibrin degradation products (FDPs).
- One of the major FDPs is D-dimer.
- Since D-dimer is generated from cross-linked fibrin, but not from fibrinogen, an elevated plasma concentration of D-dimer indicates recent or ongoing intravascular blood coagulation (e.g., deep vein thrombosis, pulmonary embolism, DIC).
- This finding can be seen in antepartum, postpartum, and postoperative (cesarean delivery) patients.

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- In DIC the platelet count is generally mildly to moderately reduced. It is uncommon for the platelet count to be below 20,000/microL [34].
- The mean platelet count is slightly lower in a normal pregnancy than in a nonpregnant woman; however, it generally remains in the normal range.
- Thrombocytopenia is present in several pregnancy-related disorders, and is not specific for DIC.

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- The thrombin time measures the final step of the clotting pathway, the conversion of fibrinogen to fibrin.
- It is significantly shorter in normal pregnant women compared with nonpregnant women and increased in DIC [19].

Roll over the bold green words aboves to learn more about each.

Table 2

Test	Normal (reference) range		
	First trimester	Second trimester	Third trimester
Prothrombin time (seconds)	9.7 to 13.5	9.5 to 13.4	9.6 to 12.9
Activated partial thromboplastin time (seconds)	23.0 to 38.9	22.9 to 38.1	22.6 to 35.0
Platelet count ($x10^9$/L)	174 to 391	155 to 409	146 to 429
Fibrinogen (mg/dL)	244 to 510	291 to 538	301 to 696
D-dimer(µg/mL)	0.05 to 0.95	0.32 to 1.29	0.13 to 1.7

Clinical Evaluation

- When there is ongoing hemorrhage, shock, or fetal distress, the evaluation for DIC may need to occur concurrently with initial management of the specific disorder(s).
- Many pregnancy-associated causes of DIC are obvious from the history and physical examination.
- Additional findings of sepsis, malignancy, and liver failure should be sought, especially if the cause is not obviously apparent.
- Maternal vital signs are monitored closely.
- Fetal assessment as with every pregnant women.

- Laboratory testing includes the following:
  - Complete blood count (CBC) with platelet count
  - Coagulation studies including prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen level, and D-dimer.
  - BUN and creatinine
  - Liver function tests (LFT)
  - Urine output and blood loss should be monitored closely.
- Prior to the return of the first set of laboratory studies, a red top tube (i.e., no additives) containing 5mL of blood can be observed for clotting (Lee and White test).
  - At room temperature, if the blood in the tube clots within 8 to 10 minutes and the clot remains intact, the patient likely has adequate fibrinogen stores.
  - If the blood in the tube does not clot or an initial clot dissolves, it is likely that the patient is markedly deficient in key clotting factors.
- Although rarely necessary in the obstetric setting where DIC is typically fulminant, serial laboratory assessments over a few hours showing progressively prolonged coagulation times, decreasing platelet counts, increasing values for D-dimer and/or fibrin-degradation products, and falling fibrinogen levels can help distinguish mild DIC from normal pregnancy-related changes in these laboratory values.
- Blood and urine cultures should be performed in patients with suspected sepsis.
- In cases where intrauterine infection is suspected, amniotic fluid culture is appropriate.

Criteria for Diagnosis

- DIC is a clinical diagnosis.
- There is no single highly sensitive or specific test.
- The diagnosis of acute DIC is made in a pregnant woman when the clinical setting is appropriate, such as placenta abruption, AFE, or sepsis; and there is thrombocytopenia, prolonged PT, aPTT, low fibrinogen, and fibrinolysis (increased D-dimer) when another cause in not evident.
- When DIC is suspected, collaborating and consulting with specialists is recommended to confirm the diagnosis and to eliminate other possibly life-threatening causes of the findings such as thrombotic thrombocytopenic purpura (TTP).

Scoring Systems

- Scoring systems have been developed and have been used in research studies to diagnose DIC in nonpregnant women as there is no single diagnostic test to confirm or reject this diagnosis.
  - The scoring system usefulness in pregnancy in unknown.
- An important limitation for any DIC scoring system is that these systems are only intended to be used in the appropriate clinical setting.

Differential Diagnosis

- When considering the differential diagnosis, other causes of bleeding, thrombosis, and organ damage must be considered in the pregnant woman.
  - Bleeding, thrombosis, and/or organ damage can accompany DIC or contribute to DIC pathogenesis.
- Resolution of DIC may result with treatment for the underlying cause.

Differential Diagnosis - Transfusion Reaction

- ABO incompatibility can cause severe transfusion reactions and can imitate or cause DIC.
- Severe transfusion reaction from ABO mismatch and DIC can cause anemia, thrombocytopenia, oozing from mucocutaneous sites, and bleeding.
- Transfusion reactions have a history of prior transfusion and many times are associated with a positive direct antiglobulin, Coombs test, unlike DIC.

Differential Diagnosis - Primary Thrombotic Microangiopathy

- Primary thrombotic microangiopathies such as TTP are rare during pregnancy.
  - Like DIC, patients may have anemia, thrombocytopenia, and organ damage. The physiologic stress of pregnancy may induce an underlying inherited or acquired condition.
  - Unlike DIC, in TTP the coagulation studies generally are normal and the ADAMTS13 activity is seriously reduced.
    - Cincinnati Children's Hospital Medical Center offers a test to measure activity levels of the protein called ADAMTS13 for TTP.

Differential Diagnosis - von Willebrand disease

- The most common inherited bleeding disorder is von Willebrand disease (VWD). Most pregnant women are already aware of this diagnosis.
- Pregnancy is generally well-tolerated in VWD due to the physiologic increases in von Willebrand factor (VWF) levels.
- A woman who has not had a prior hemostatic challenge may have moderate postpartum bleeding as the first manifestation of VWD. This is because VWF levels drop in the postpartum period.
- Thrombocytopenia and/or prolongation of the aPTT can be seen in some types of severe VWD as well as DIC.
- VWD does not cause prolongation of the PT, a low fibrinogen level, or elevated D-dimer; and patients with VWD will have low levels of factor VIII, VWF, and VWF activity (ristocetin cofactor activity) unlike DIC.

Differential Diagnosis - Antiphospholipid Syndrome

- Antiphospholipid syndrome (APS) is caused by autoantibodies to phospholipids that promote thrombosis. APS can occur with systemic lupus erythematosus or by itself.
- Patients with APS or DIC can have thrombosis, elevated D-dimer, and the aPTT is frequently prolonged.
- Patients with APS have a normal PT and bleeding generally does not occur, which is unlike DIC.

Differential Diagnosis - Pulmonary Embolism

- The leading cause of death during pregnancy and postpartum, pulmonary embolism (PE), is often not immediately recognized due to the vast array of presenting symptoms.
- Patients with DIC or PE may present with shock and elevated D-dimer.
- PE, unlike DIC, generally is not associated with bleeding, low fibrinogen, or prolongation of the clotting times.

Differential Diagnosis - Heparin-Induced Thrombocytopenia

- Heparin-induced thrombocytopenia (HIT) occurs when autoantibodies cause activation of platelets when heparin is present. HIT is a potentially life-threatening disorder.
- HIT is extremely rare in pregnancy.
- Like DIC, HIT can present with thrombocytopenia, thrombosis, and/or organ damage; and bleeding may be present due to the anticoagulant.
- Unlike DIC, HIT has a relationship of exposure to heparin.
- Patients with HIT do not have coagulation abnormalities, except for those due to their anticoagulant, but they will have positive testing for HIT antibodies.

There are numerous factors with the management of pregnant women with vaginal bleeding in the second and third trimesters including gestational age, the cause of bleeding, the severity and fetal status.

Management - Quick Overview

Notify staff and services that will or may be needed:

- Anesthesia
- Neonatology
- Blood bank
- Surgery
- Obstetrics
- Pelvic Surgery
- Maternal Fetal Medicine
- Gynecologic Oncology
- Interventional Radiology
- General Surgery

Management - Quick Overview

- Place at least two large bore (≥18 gauge) catheters.
- Peripheral venous access should be attempted before attempting other forms of vascular access if peripheral veins can be readily seen or palpated.
- Attempts at peripheral and central venous access in the head, neck, and chest should be limited during cardiopulmonary resuscitation (CPR) to avoid interruption of ventilation and chest compressions.
- During CPR or the treatment of severe shock, intraosseous cannulation and peripheral venous access should be pursued simultaneously [3,4].

Management - Quick Overview

- Protocols can help to facilitate the patient's care. Rapid establishment of venous access being a high priority [5].
  - In one study, for example, a protocol was designed to limit the time spent in futile attempts to achieve peripheral and central venous catheterization [6].
  - Significant improvement on venous access was found when a study revealed rapid sequential steps. In this study, rapid sequential attempts at percutaneous femoral vein catheterization, saphenous vein cutdown, and intraosseous cannulation were initiated if initial peripheral intravenous (IV) insertion failed after 90 seconds [6].
  - The study found resuscitations in compliance with the protocol achieved IV access more rapidly than did those deviating from the protocol when initiating percutaneous peripheral IV attempts failed [6].
  - Intraosseous cannulation had a high degree of success when other measures failed.

Management - Quick Overview

- Administer crystalloid with or without colloid, blood, and blood products, as needed.
- O-negative red blood cells, group AB fresh frozen plasma, and lyophilized fibrinogen can be given immediately and continued until the type and cross-match is complete, at which point the patient should be switched to type-specific fresh frozen plasma and cross-match compatible red blood cells.
- The goal with transfusions is to keep:
  - Hemoglobin greater than or equal to 7g/dL
  - Fibrinogen greater than or equal to 300mg/dL
  - Platelet count greater than or equal to 50,000/microL
  - PT and aPTT <1.5 times control

Management - Quick Overview

- Maintain oxygen saturation above 95%
- Keep the patient warm
- Identify and begin treatment of the triggering event

Management - Quick Overview

- Order laboratory panel to assess coagulation (PT, aPTT, fibrinogen); draw 5mL blood in a red top tube and observe clot formation over 8 to 10 minutes
- Order baseline laboratory panel: complete blood count (CBC), BUN, creatinine, liver function tests

Management - Quick Overview

- Assess fetal status (gestational age, FHR)
- Assess maternal condition (blood loss, cervical status, hemodynamic stability, uterine contractions)
- Appropriate personnel, equipment, and supplies (e.g., pelvic pack) should be available if hysterectomy is being considered

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Notify the Anesthesia Staff

- Notify the anesthesia staff for assistance with patient management and to provide anesthetic support for delivery if the patient is not already in the operating room.
- Placement of epidural and spinal anesthesia techniques is generally contraindicated in patients with a severe bleeding diathesis because of the risk of spinal epidural hematoma.

Click each number in order to learn more.

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Notify the Transfusion Service

- The transfusion service or blood bank should be notified of the pregnant patient regarding the potential need for blood products, including need for massive transfusion.
- Pretransfusion testing (crossmatching) can be initiated; if necessary, emergency-release blood products can be made available.

Click each number in order to learn more.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Establish IV Access and Begin Fluid Resuscitation

- Establish IV access peripherally with at least two IV catheters (≥18 gauge) and infuse crystalloid (with or without colloid) and blood products, when available, to support blood pressure (systolic ≥90mmHg or mean arterial pressure ≥65mmHg) and maintain urine output (≥0.5mL/kg/hour).
- The best approach to fluid resuscitation remains controversial.
- Initial fluid resuscitation for hemorrhagic shock with infusion of two to three liters of Lactated Ringer's (LR) is reasonable when blood and blood products are not available.

Click each number in order to learn more.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Recognize and Treat What Caused the Event

Click the terms and icons to see more information.

- The principle of therapy is to identify the underlying disorder leading to hemorrhage and initiate appropriate treatment for that condition.
- Obstetric causes of hemorrhage are generally readily identified by history, physical exam, and ultrasound findings.
- The pivotal element of treatment of all obstetric etiologies of DIC is delivery, because termination of pregnancy leads to resolution of the disorder that initiated the obstetric hemorrhage.

Abruption

Preeclampsia

Amniotic Fluid Embolism

Acute Fatty Liver of Pregnancy

Retained Fetal Demise

Septic Abortion

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Abruption

- Mild to moderate vaginal bleeding, abdominal pain, back pain, and uterine contractions are characteristics of placenta abruption.
- No vaginal bleeding may be present in concealed placental abruption.
- The woman may complain of uterine tenderness during and between contractions. The uterus will have increased tone and rigidity.
- Typical symptom; abnormalities of fetal heart rate (FHR) or fetal demise, and/or DIC support the clinical diagnosis of abruptio placentae.

Preeclampsia

Preeclampsia with severe features has hypertension associated with one or more signs or symptoms with increased maternal and fetal morbidity/mortality.

- The occurrence of a seizure upgrades the diagnosis to eclampsia.
- Women with HELLP syndrome often have many of the clinical findings associated with preeclampsia, as well as the laboratory findings that establish the syndrome.

Preeclampsia with Severe Features

Symptoms of central nervous system dysfunction:

- Altered mental status:
  - New onset cerebral or visual disturbance, such as:
    - Photopsia, scotomata, cortical blindness, retinal vasospasm
  - Severe headache (i.e. incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy
- Hepatic abnormality:
  - Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥ twice normal, or both
- Severe blood pressure elevation:
  - Systolic blood pressure ≥160mmHg or diastolic blood pressure ≥110mmHg on two occasions at least four hours apart while the patient is on bedrest (unless the patient is on antihypertensive therapy)
- Thrombocytopenia:
  - <100,000 platelets/microL
- Renal abnormality:
  - Progressive renal insufficiency (serum creatinine >1.1mg/dL or doubling of serum creatinine concentration in the absence of other renal disease)
- Pulmonary edema

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Amniotic Fluid Embolism

Amniotic fluid embolism (AFE) is characterized by the exceedingly sudden onset of hypotension due to cardiogenic shock, hypoxemia, respiratory failure, and coma or seizures during labor or immediately postpartum.

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Acute Fatty Liver of Pregnancy

- Acute fatty liver of pregnancy initially presents with nausea or vomiting (approximately 75% of patients), abdominal pain (50% epigastric region), anorexia, and jaundice.
- Approximately one-half of patients have signs of preeclampsia at presentation or at some time during the course of illness.

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Retained Fetal Demise

Retained fetal demise is diagnosed by ultrasound imaging that confirms the absence of the fetal heart rate, overlapping skull bones, gross distortion of fetal anatomy due to maceration, and soft tissue edema.

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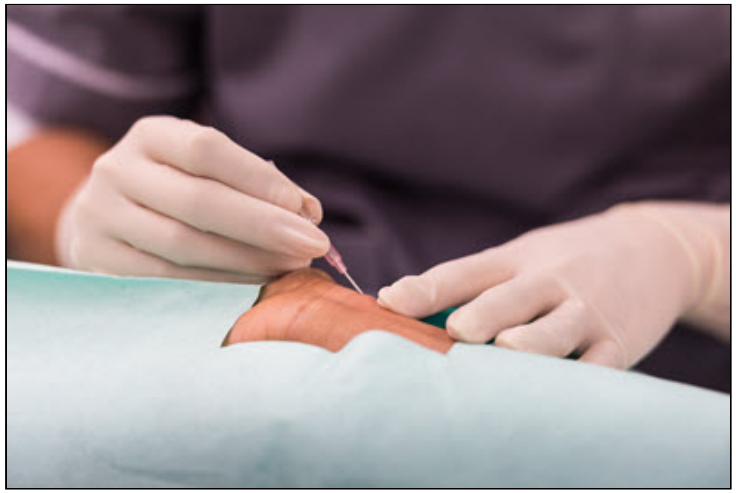
Septic Abortion

Septic abortion is characterized by abdominal and/or pelvic pain, malodorous vaginal discharge, fever and chills, bleeding or spotting, and uterine or adnexal tenderness after a spontaneous or induced abortion.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.



Insert an Arterial Line

An arterial line may be appropriate in the patient who needs continuous blood pressure monitoring, but the relative benefits versus risks depend on the severity of the hemorrhage.

Click each number in order to learn more.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Blood Products

Obstetrical patients have or are at a high risk for serious bleeding and thus have a high association to require an invasive procedure, often requiring transfusions.

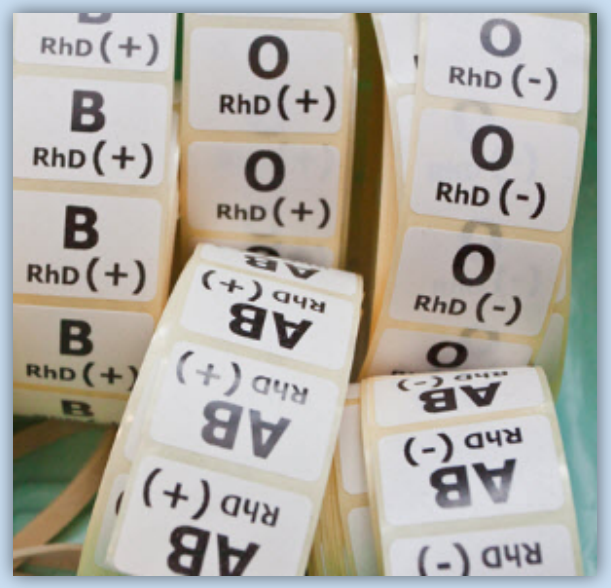
Transfusion

Massive Transfusion

Click the blue boxes to learn more about transfusions.

Management - Transfusion

- Fully typed and crossmatched red blood cells (RBCs) requires at least 20 minutes.
- Transfusion may begin immediately using type 0, Rh(D)-negative RBCs. When fully typed and crossmatched RBCs are available switch to this type specific.
- When transfusion is necessary prior to obtaining type-specific fresh frozen plasma (FFP), type AB FFP, either Rh(D) positive or negative can be safely used.



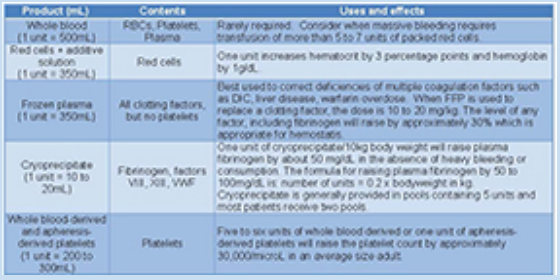
Management - Transfusion

- When making an initial order for transfusion products, the following should be ordered:
  - 6 units of FFP
  - 1 or 2 cryoprecipitate pools
    - A pool contains 5 individual units
- 1 dose of platelets, either:
  - A pool of 4 to 6 whole blood- derived platelet concentrates OR a single apheresis platelet unit.
- Many massive transfusion protocols recommend transfusion of RBCs, FFP, and platelets in a ratio of 1:1:1.

Management - Transfusion

- Correcting the low fibrinogen levels, which commonly occur in obstetrical hemorrhage, is important.
- FFP is generally given to correct hypovolemia and normalize coagulation in cases of obstetric hemorrhage.
- Cryoprecipitate is indicated when large amounts of fibrinogen must be administered in a low-volume product.
- A source of concentrated fibrinogen is cryoprecipitate, but takes time to be prepared for transfusion and brings risks of transmissible infections since it is a product that has pooled donors.
- Clinicians need to order cryoprecipitate with enough advanced planning to allow for this time.
- A fibrinogen concentration below 100mg/dL is generally treated with 10 units of cryoprecipitate, which is two pools of 5 units (table 3).

Click on Table 3 to view a larger version.



Product (mL)	Contents	Uses and effects
Whole blood (1 unit = 500mL)	RBCs, Platelets, Plasma	Rarely required. Consider when massive bleeding requires transfusion of more than 5 to 7 units of packed red cells.
Red cells + additive solution (1 unit = 350mL)	Red cells	One unit increases hematocrit by 3 percentage points and hemoglobin by 1g/dL.
Frozen plasma (1 unit = 350mL)	All clotting factors, but no platelets	Best used to correct deficiencies of multiple coagulation factors such as DIC, liver disease, warfarin overdose. When FFP is used to replace a clotting factor, the dose is 10 to 20 mg/kg. The level of any factor, including fibrinogen will raise by approximately 30% which is appropriate for hemostasis.
Cryoprecipitate (1 unit = 10 to 20mL)	Fibrinogen, factors VIII, XIII, VWF	One unit of cryoprecipitate/10kg body weight will raise plasma fibrinogen by about 50 mg/dL in the absence of heavy bleeding or consumption. The formula for raising plasma fibrinogen by 50 to 100mg/dL is: number of units = 0.2 x bodyweight in kg. Cryoprecipitate is generally provided in pools containing 5 units and most patients receive two pools.
Whole blood derived and apheresis-derived platelets (1 unit = 200 to 300mL)	Platelets	Five to six units of whole blood derived or one unit of apheresis-derived platelets will raise the platelet count by approximately 30,000/mcrcL in an average size adult.

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Management - Transfusion

- Lyphilized fibrinogen (RiaSTAP), a human fibrinogen concentrate, is very expensive but can be reconstituted immediately for use to correct low fibrinogen levels.
  - The use of purified, virally inactivated fibrinogen concentrate had a similar outcome as cryoprecipitate in resolving hypofibrinogenemia in an observational study of 77 cases of major obstetrical hemorrhage [22].
- The blood bank should be notified of the potential need for massive transfusion and a massive transfusion protocol initiated, if indicated and available.
- It is essential to have rapid restoration of blood components in massive hemorrhage to ensure adequate tissue perfusion, prevention of acidosis, coaguloapthy and hypothermia, which is often lethal.
- Laboratory studies every thirty minutes will help to guide blood product replacement. Then, as the clinical situation improves, the interval may be extended.
- Some centers have found thromboelastography (TEG) or rotational thromboelastometry (ROTEM), useful in the setting of massive hemorrhage as it provides a "rapid global assessment" of hemostatic function [23-25].

Bedside Responsibilities

Blood Bank Responsibilities

Nursing Responsibilities

Transfusion Targets

Laboratory Testing

Review of Massive Transfusion Protocol Events by Transfusion Services

Attending Physician, Surgeon, or Anesthesiologist Responsibilities

Click each blue term above to learn more.

Massive Transfusion Policy

- The massive transfusion protocol (MTP) is a multidisciplinary process whereby blood and blood components are obtained rapidly for an exsanguinating patient.
- The MTP is initiated as soon as possible reporting to the physician in charge of the transfusion service (TS MD) by the blood bank staff or patient care provider.
- The TS MD serves as a consultant in the evaluation and management of the patient's transfusion therapy during the massive transfusion episode.

Example Reasons for Initiation:

- Replacement of at least one blood volume (8 to 10 red blood cell units in a 70kg adult) within 24 hours or at least one half blood volume within 2 hours
- Life-threatening trauma presenting to the emergency department
- Unexpected or anticipated surgical blood emergencies
- Severe obstetrical hemorrhage

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- The massive transfusion protocol (MTP) is initiated by the patient's staff physician or the staff anesthesiologist by calling the blood bank (this phone call may be delegated to another individual).
- Clearly state to the blood bank: "Initiate the massive transfusion protocol." Indicate whether it is an adult MTP or pediatric MTP (for patient's less than 35kg).
- Give the patient's name and medical record number.
- Provide the patient's current location and a phone number that can be used to reach the patient's care team.
- Determine if patient requires emergency release of two uncrossmatched and untagged O Neg RBCs for immediate transfusion.

Note: Average time for first MTP set is 15 to 20 minutes

- Send a properly labeled specimen (3mL purple tube) to the blood bank for a type and screen if not done in last three days. The specimen label must contain the patient's name, medical record number, date, and the initials of the collector written on the tube.
- Record initiation of protocol in patient's chart.

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Blood Bank Responsibilities

- Release two emergency O Neg RBCs if requested.
- Prepare 4 RBCs, 4 plasma, and 1 dose of platelets for adult MTP.

Note: ***Group "O" uncrossmatched RBCs will be issued, if necessary, until type specific and later crossmatched becomes available.***

- Provide a cooler with ice for each set of RBC and plasma components.
- Notify the patient's care team when a set of components is ready for pickup.
- Notify physician on-call.
- Stay 1 MTP set ahead (prepare each set immediately following pickup of previous set).
- Continue process until notified to discontinue the protocol.

Click each blue term above to learn more.

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- Assign personnel to obtain the set of components from the blood bank.
- Blood bank will call when each set is ready for pickup.
- Send a completed release form with the personnel picking up the components.
- Order labs as directed by the team.
- Communicate the lab results to the team and the blood bank.

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Blood products are transfused to achieve the following minimum levels for delivery:

- Hemoglobin ≥7g/dL
- Platelet count ≥50,000/microL
- Fibrinogen greater than or equal to 300mg/dL
- PT and aPTT less than 1.5 times control

Click here to learn more.

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Hemoglobin Management

- Many factors need to be considered when determining the optimal hemoglobin concentration for a pregnant woman about to deliver. Factors include expected blood loss during delivery, the baseline hemoglobin, rate of blood loss, and if she has medical comorbidities.
- As the hemoglobin concentration decreases, the overall risk of mortality increases. Experts recommend the target hemoglobin for pregnant women be a minimum of 7g/dL when receiving massive transfusion and 8-10g/dL in women with severe postpartum hemorrhage (PPH) [29,30].
- Additional evidence to support transfusion targets in other settings is beyond the scope of this program.
- Maintaining the hemoglobin ≥7g/dL is a goal in massive transfusion due to pregnant women with DIC having ongoing blood loss, which further increases at the time of delivery and because equilibration generally results in a fall of hemoglobin.
- Following delivery with no active bleeding and hemodynamically stable, a lower hemoglobin level is acceptable.
- A fibrinogen level ≥100mg/dL is considered the minimum level necessary for adequate coagulation.
- An observational study demonstrated that 100% of postpartum women who developed severe hemorrhage had fibrinogen levels <200mg/dL, while 80% of those with fibrinogen >400mg/dL did not develop severe hemorrhage [27].
- Similar predictive data for platelet concentration are not available.

Click each blue term above to learn more.

Click here to view recommended uses of blood replacement products.

Table 3

Product (mL)	Contents	Uses and effects
Whole blood (1 unit = 500mL)	RBCs, Platelets, Plasma	Rarely required. Consider when massive bleeding requires transfusion of more than 5 to 7 units of packed red cells.
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Click each blue term above to learn more.

- Laboratory studies are drawn initially every 30 minutes to guide blood product replacement.
- As the woman stabilizes, the laboratory testing interval can be extended.
- Some centers have found thromboelastography (TEG) useful in the setting of massive hemorrhage as it provides a "rapid global assessment" of hemostatic function [23-25].

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- Attending Physician, Surgeon, or Anesthesiologist Responsibilities

- Each event is summarized by blood bank staff.
- Review is performed by blood bank supervisor and transfusion service physicians.
- The events are reported to the transfusion committee.

Click each blue term above to learn more.

- Bedside Responsibilities
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Click each blue term above to learn more.

Click here to learn more.

- Obtain baseline CBC and coagulation studies.
- Determine if rFVIIa is required (see section below for guidelines).
- Monitor CBC, ABG, potassium, ionized calcium, and coag tests frequently.
- If a coagulopathy is suspected measure the fibrinogen test and other coagulations studies.
- Determine when the protocol should be discontinued.
- Call the blood bank (this phone call may be delegated to another individual).
- Document discontinuation in the patient's chart.

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Click each blue term above to learn more.

Use of rFVIIa (Novo-Seven) in Surgery and Trauma
(not indicated in pregnancy; but may be utilized postpartum)

- Indication of the use of rFVIIa:
  - Active bleeding following administration of 6 to 8 units of red blood cells, 6 to 8 units of plasma, and one dose of platelets.
- Administer 10 units of cryoprecipitate if the fibrinogen is <100 mg/dL
- Contraindications for the use of rFVIIa:
  - pH <7.00
  - Immediately following cardiac arrest
  - Patient considered "unsalvageable" by staff surgeon
  - Pregnancy
  - Recent thrombotic event, MI, or stroke
- Dosing of rFVIIa:
  - If the patient has been on warfarin and arrives with an elevated INR and rapid bleeding, consider using one small vial of rFVII or 1.2mg. This is usually a 15 micrograms/kg dose for adults.
  - If the patient is not on warfarin, consider using 45 micrograms/kg as a half dose and repeat this dose in 30 to 60 minutes.
  - Always round down to the nearest full vial for doses of rFVIIa.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Maintain Oxygenation

Keep arterial oxygen saturation above 95%.

Avoid Hypothermia

- The patient should be kept warm with a forced-air warming system (e.g., Bair Hugger), which is the most effective method to maintain normothermia.
- Other interventions include the use of warmed blankets and fluid warmers, which should be used as needed.
- If large volumes of fluid and blood products are given, the infused fluids/blood products should be warmed so they are close to body temperature to prevent a significant drop in maternal core temperature.

Click each number in order to learn more.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Assess Blood Loss

- Concealed hemorrhages may occur in cases of severe abruption with the magnitude of blood loss being estimated and monitored using a combination fo parameters: hourly assessment of changes in fundal height, clot volume on ultrasound, urine output and serial hemoglobin/hematocrit assessment.
- Quantifying blood loss [35]
- Indirect assessment of blood loss can be accomplished with vital signs, knowing pregnant women can display changes in vitals later than nonpregnant women.
- Hemodynamic instability in non-anesthesthesized pregnant women may be suspected when:
  - Systolic blood pressure <100mmHg
  - Pulse >100bpm
  - Urine output <30mL per hour
- Other signs and symptoms of hemodynamic instability may be present, such as altered level of consciousness, shortness of breath, cold clammy skin, and pallor.

Click each number in order to learn more.

Quantifying Blood Loss

- Visual estimation of blood loss can result in both over and underestimations.
- Attempts to quantify the blood loss can occur with weighing the blood soaked items, subtracting the dry weight of the item and understanding that 1gm of weight equals 1ml of blood loss [35].
    - Validation with additional research is needed.
    - Artificial intelligence-based algorithms that use colorimetric analysis of pictures to quantify blood loss in real time do appear promising.
- Ongoing blood loss assessment should continue as long as active bleeding is present or if the patient is unstable [35].
- Quantifying the blood loss is an important part of evidence-based hemorrhage bundles [35].
    - Additional research is needed.
    - The clinical utility specific to the quantification approach remains unproven.
- Fluid and blood clots from the drapes can be measured by volume and added to the weighed items for an accumulative quantification of blood loss.
    - Calibrated drapes had an error rate less than 15% [36].

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Notify the Neonatology Service

- To prepare for birth of a compromised infant and/or prematurity, the neonatology service department should be notified.
- Neonatology services may counsel the parents about newborn issues prior to the actual event.

Fetal Assessment

- Management of the pregnant woman is impacted by fetal viability and gestational age.
- The focus is on the mother when there is an intrauterine fetal demise or the fetus is confirmed to be previable.
- By determining the limits of viability, desired futile interventions that are painful and costly may be avoided in the fetus or neonate that does not have a reasonable favorable outcome.
- Viability is the stage of maturity that would likely result in a chance of survival without severe deficits.

Click here to learn more about fetal assessment.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Fetal Assessment Continued

- Determining viability is desired to prevent interventions that are painful and costly in the fetus or neonate that does not have a favorable outcome.
- The age of viability is a challenge, especially those born at 23 to 24 weeks gestation. The decision lies upon a reasonable chance of survival without severe deficits.
- Determining the morbidity from prematurity, intensity of care and likelihood at various gestational ages is beyond the scope of this program.
- With a live fetus at a viable gestational age, a FHR typically shows a category III tracing in pregnancies complicated by major bleeding often resulting in poor placental perfusion and suboptimal fetal oxygenation.
- Weighing the outcomes between immediate delivery versus delaying delivery to optimize fetal outcome are considered when maternal hemorrhage occurs.
- In these cases, the maternal and fetal risks and benefits of immediate delivery for treatment of hemorrhage versus delaying delivery to optimize fetal outcomes need to be weighed.
- Involving the neonatology and anesthesia services can help when discussing these issues with the patient and her families.

Click number 10 to continue learning about interventions.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Management of Delivery

A key component to management is delivery, termination of pregnancy, which usually leads to resolution of the obstetrical disorder that initiated the hemorrhage.

Non-Viable Fetus | **Vaginal Delivery** | **Cesarean Delivery** | **Hysterectomy**

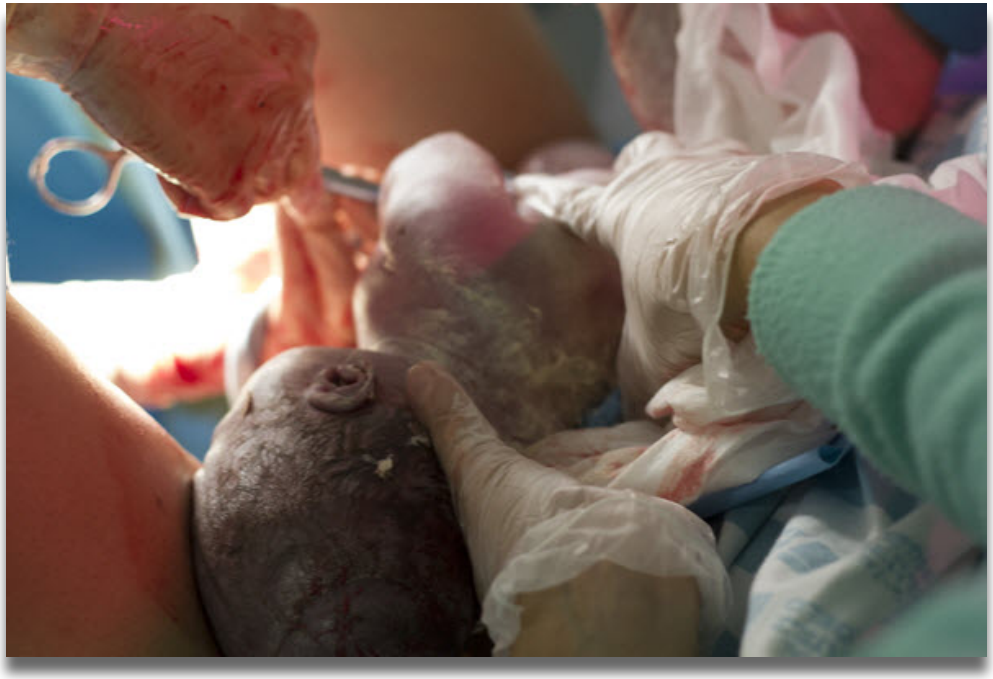
Click the blue boxes to learn more about delivery management.

Hemodynamically Stable Mother with Dead or Nonviable Fetus

- The goal is to minimize maternal morbidity and mortality risk when the fetus is dead or has a very poor prognosis (gestation is <23-24 weeks, lethal or life threatening congenital anomaly, preterminal FHR tracing).
- This often, but not always, means avoiding cesarean delivery due to the risk of uncontrollable hemorrhage from surgical incisions and lacerations.
- Delivery is initiated and the mother is supported with crystalloid, with or without colloids, and blood products.
- The trigger for DIC is removed upon delivery in many obstetrical cases, causing the myometrium to contract (involution of the uterus), thus removing both the major sources and site of hemorrhage.
- Dilation and extraction (D&E) is a good option in the second trimester for rapid uterine evacuation if the clinician is skilled in this procedure.
- Women able to labor should be induced if not already in labor or augmented if not progressing rapidly.
- When the cervix is not favorable, the use of either a mechanical method of ripening (balloon catheter or hygroscopic dilator) or a pharmacologic method of induction (misoprostol or oxytocin) is suggested.

Vaginal Delivery

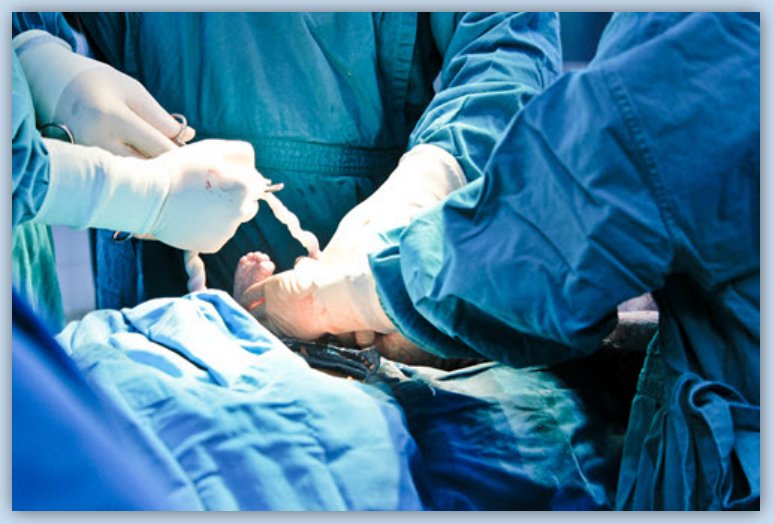
- The safest maternal option may not be vaginal delivery when hemodynamic instability from ongoing brisk uterine bleeding is occurring, nor if the mother would be endangered by vaginal delivery (for example, prior classical hysteretomy).
- In these cases, cesarean delivery is indicated to save the mother's life.
- Cesarean delivery is also indicated if prompt delivery has the potential to reduce fetal morbidity and mortality.



Cesarean Delivery

- Not always possible, but desirable to correct and improve the clotting abnormality prior to cesarean delivery.
- If there were a delay in operative intervention this could lead to worsening of coagulopathy, further blood loss, and potential fetal death.
- However, immediate operative intervention in a woman with severe hypovolemia and DIC could prove fatal to the woman.
- When cesarean delivery is imminent, then RBC's, FFP, platelets, and cryoprecipitate should be readily available in the operating room and administered if there is clinical or laboratory evidence of impaired coagulation. With cesarean birth, bleeding without clotting from the incision and needle sites is a clinical sign of coagulopathy.
- When bleeding is severe, there is no need to wait for laboratory studies, the FFP and cryoprecipitate should be given immediately.

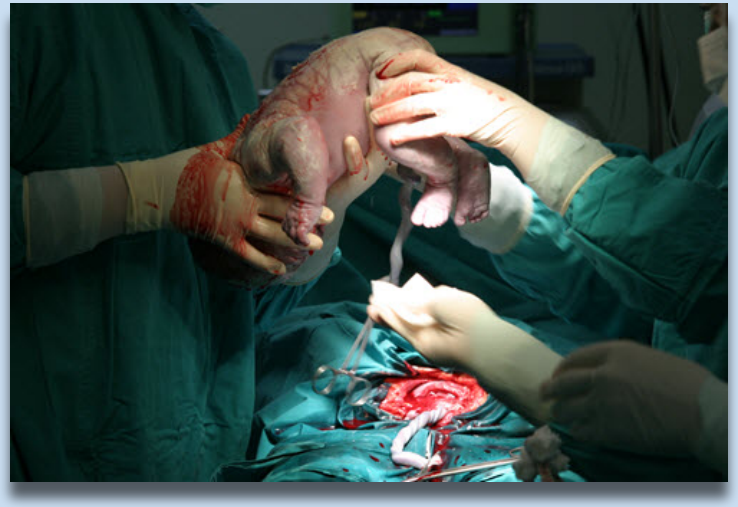
Cesarean Delivery



- Surgeons with experience in puerperal hysterectomy, pelvic surgery, and management of pelvic hemorrhage should be present.
- A GYN oncology surgeon, maternal fetal medicine specialist, obstetrician or general surgeon should be considered.
- Involvement of anesthesia, neonatology, and transfusion medicine service can be helpful for maternal and fetal outcome.
- Notifying the neonatal staff so they can prepare for resuscitation of a potentially compromised newborn will be helpful.
- When an interventional radiologist is available, notify them of their potential need.

Cesarean Delivery

- The surgical approach does not have data of randomized trials or controlled studies to recommend a certain surgical approach.
- The surgical approach decision is based on individual patient's characteristics and the clinical experience of the surgeon.
- Knowing the vertical infraumbilical incision is fast, provides excellent exposure and is less likely to be complicated by a rectus sheath hematoma, it makes this approach a good choice.
- Once the fetus is delivered, manual extraction of the placenta is important to perform to hasten involution of the uterus. It would also be diligent to have uterotonic drugs (such as oxytocin or methylergonovine) given and the hysterotomy incision closed promptly. All of these efforts are to curtail bleeding.



Cesarean Delivery

- Important points to communicate between the obstetrician, anesthesia and surgical team members may include the volume of blood loss, rate of blood loss, quality of clot formation and response to techniques used to control hemorrhage.
- When uterine bleeding remains brisk and maternal hemodynamic status deteriorates despite initial surgical intervention and blood component transfusion, consideration of a penrose drain or urinary catheter as a uterine tourniquet may be useful.
- When the Penrose drain or catheter is placed, place it as low as possible around the lower uterine segment without involving the urinary bladder. Once positioned, pull the two ends in the opposite directions as tightly as possible around the corpus to mechanically obstruct the vascular supply.
- A clamp may be used to hold the tourniquet in place.
- This technique decreases blood loss and allows the team to catch up with transfusion requirements.
- The tourniquet can be removed once the patient is hemodynamically stable. The surgery can then be completed and the abdomen closed in standard fashion.

Hysterectomy

- As a last resort in a woman desiring childbearing preservation, hysterectomy is performed, but should be initiated sooner than later when future pregnancy is not planned.
- Delaying hysterectomy increases blood loss and frequency of complications.
- Despite rescue measures, some patients will enter a lethal downward spiral characterized by hypothermia, coagulopathy and metabolic acidosis.
- Criteria proposed for this moribund state include pH <7.30, temperature <35 degrees Celsius, combined resuscitation and procedural time >90 minutes, non-mechanical bleeding, and transfusion requirement >10 units packed RBCs [29].
- To stop the cycle, the bleeding area can be tightly packed using a pelvic pressure pack or lap sponges [30].
- The abdominal wound, including the fascia, is left open and a pressure dressing is applied.
- Towel clips have been utilized to temporarily re-approximate the skin/subcutaneous tissue.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Post Delivery

- It is reasonable to transfer the patient to the intensive care unit (ICU) for continued monitoring, replacement of appropriate blood products, broad spectrum antibiotics and correcting physiologic derangements [29].
- When the patient continues to need two or more units of packed RBC's per hour for three hours, it is a sign she has ongoing bleeding and needs surgical intervention or arterial embolization by an interventional radiologist.
- Otherwise, when the patient is stable, she is returned to the operating room to undergo definitive surgical care.
- This approach halts the downward spiral and lessens the risk of abdominal compartment syndrome.

Click each number in order to learn more.

Many of the interventions will be appropriate in acutely ill patients, even if the etiology of hemorrhage is uncertain, and these can be initiated while the diagnostic evaluation is ongoing.

Hemostatic and Anticoagulant Therapies

- There is a lack of sufficient data on safety and efficacy in hemorrhaging pregnant women to make recommendations on hemostatic and antifibrinolytic drugs.
- There are no randomized clinical trials on the safety and efficacy of most hemostatic and antithrombogenic drugs or products in the treatment of the hemorrhage in women during pregnancy.
- These include heparin, danaparoid sodium, synthetic protease inhibitor, antithrombin, human recombinant activated protein C, recombinant human soluble thrombomodulin, recombinant tissue factor pathway inhibitor and recombinant activated factor VII (rFVIIa) [31].
- Pro-hemostatic treatment with tranexamic acid has been used for management of postpartum hemorrhage [33].

Click to learn more about tranexamic acid

Click each number in order to learn more.

Tranexamic Acid (TXA)

- Intravenous tranexamic acid (TXA) is recommended by the World Health Organization (WHO) to be used early, even within 3 hours, following vaginal birth or cesarean delivery in addition to standard care for women diagnosed with postpartum hemorrhage (PPH).
- TXA is a competitive inhibitor of plasminogen activation and can reduce bleeding by inhibiting the breakdown of fibrinogen and fibrin clots.
- By giving within 3 hours of birth, maternal death from hemorrhage, regardless of cause, and with no adverse maternal effects is noted.

Tranexamic Acid (TXA)

- TXA for PPH should not be utilized more than 3 hours after birth.
  - The benefits of TXA appear to decrease by 10% for every 15-minute dely, with no benefit seen after 3 hours from birth.
- TXA should be initiated as soon as possible after the onset of bleeding and within 3 hours of birth and should be considered part of the standard PPH treatment package (i.e. uterotonics, non surgical and surgical interventions).
- Regardless of whether the post part hemorrhage is from the genital tract trauma or other causes, TXA should be used in all cases.
- TXA administration involves a fixed dose of 1 gram in 10mL (100mg/mL) IV at 1mL per minute (administered over 10 minutes).
  - A second dose of 1g IV if bleeding continues after 30 minutes or if bleeding restarts within 24 hours of completing the first dose.
  - A bolus of TXA should be avoided due to a potential risk of transient lowering of blood pressure.
  - A decreased dose should be given when she has renal insufficiency.
  - TXA should not be given with solutions containing blood products, penicillin or mannitol.
- The half-life of TXA is 2 hours and antifribinolytic effect lasts for 7-8 hours.

Contraindications to TXA

Avoid in women with clear contraindications:

- Known thromboembolic event in pregnancy
- History of coagulopathy
- Active intravascular clotting
- Known hypersensitivity to TXA
- In patients with subarachnoid hemorrhage or DIC

- DIC, when pregnant, often leads to severe hemorrhage and the mortality depends on the ability to reverse the underlying cause as rapidly as possible.
- Most patients with DIC due to pregnancy-related complications rapidly improve with delivery and treatment of coagulopathy.
- In cases of acute fatty liver of pregnancy, however, resolution of DIC can take as long as 4 to 5 days postpartum because of ongoing liver dysfunction [32].

Maternal **Neonatal**

Click each button to learn more.

- Approximately one-quarter of maternal deaths between 1998-2009 were, at least in part, attributed to DIC from a study based on discharge coding data from the US Nationwide Inpatient Sample [1].
  - However, the majority of women with obstetric DIC survive.
  - This was demonstrated in a review of 49 cases of DIC, in which there were three maternal deaths (6%) [2].
- Hysterectomy rates in DIC vary.
  - In the series of 49 cases mentioned above, one-fifth required hysterectomy to control bleeding.
  - The risk of DIC recurrence in subsequent pregnancies is unknown, and depends on the underlying cause (e.g., risk of recurrent abruption is 5 to 15%).
  - Uterine sparing surgical interventions for management of hemorrhage do not appear to adversely affect fertility.

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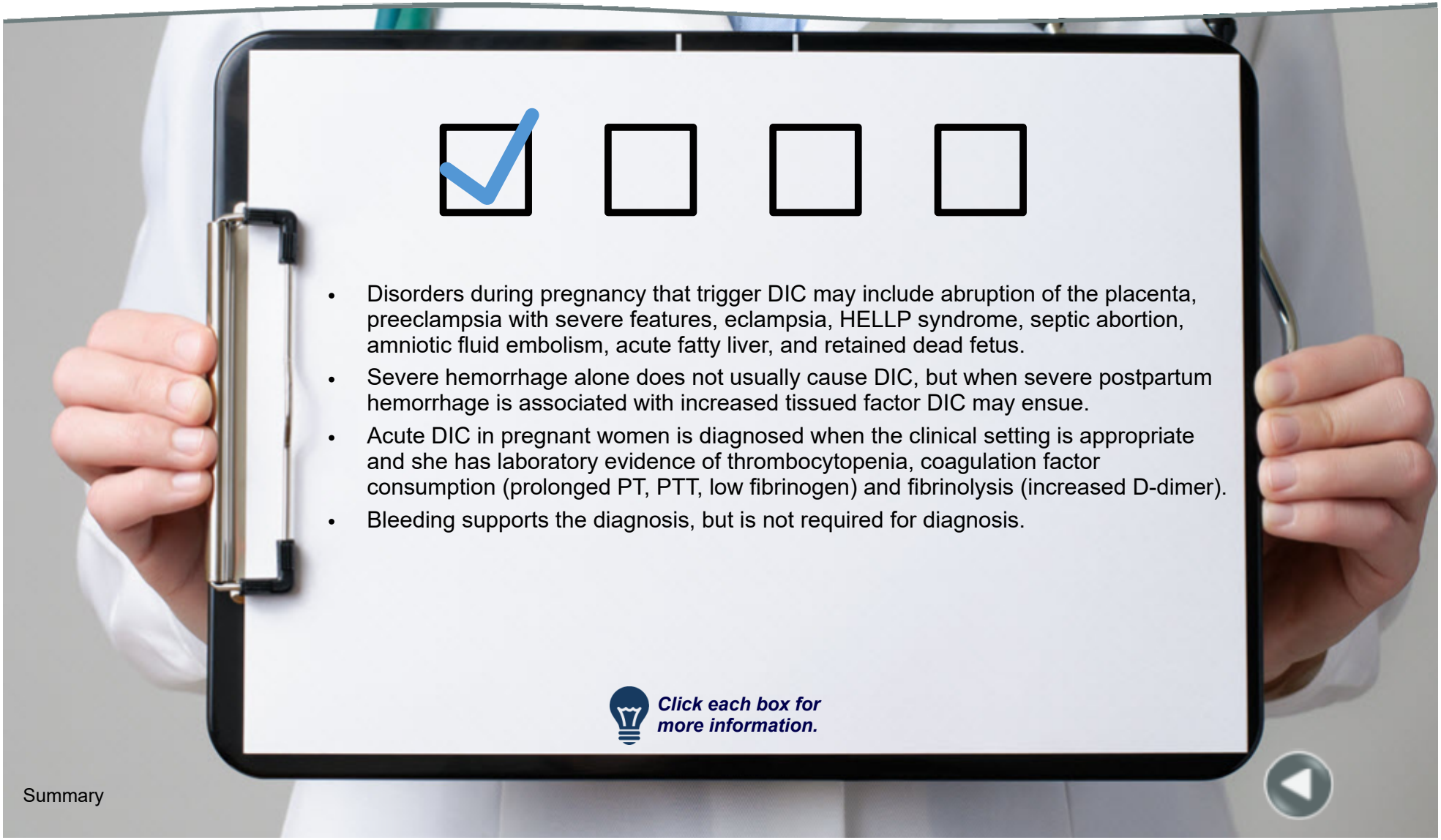
Maternal

Neonatal

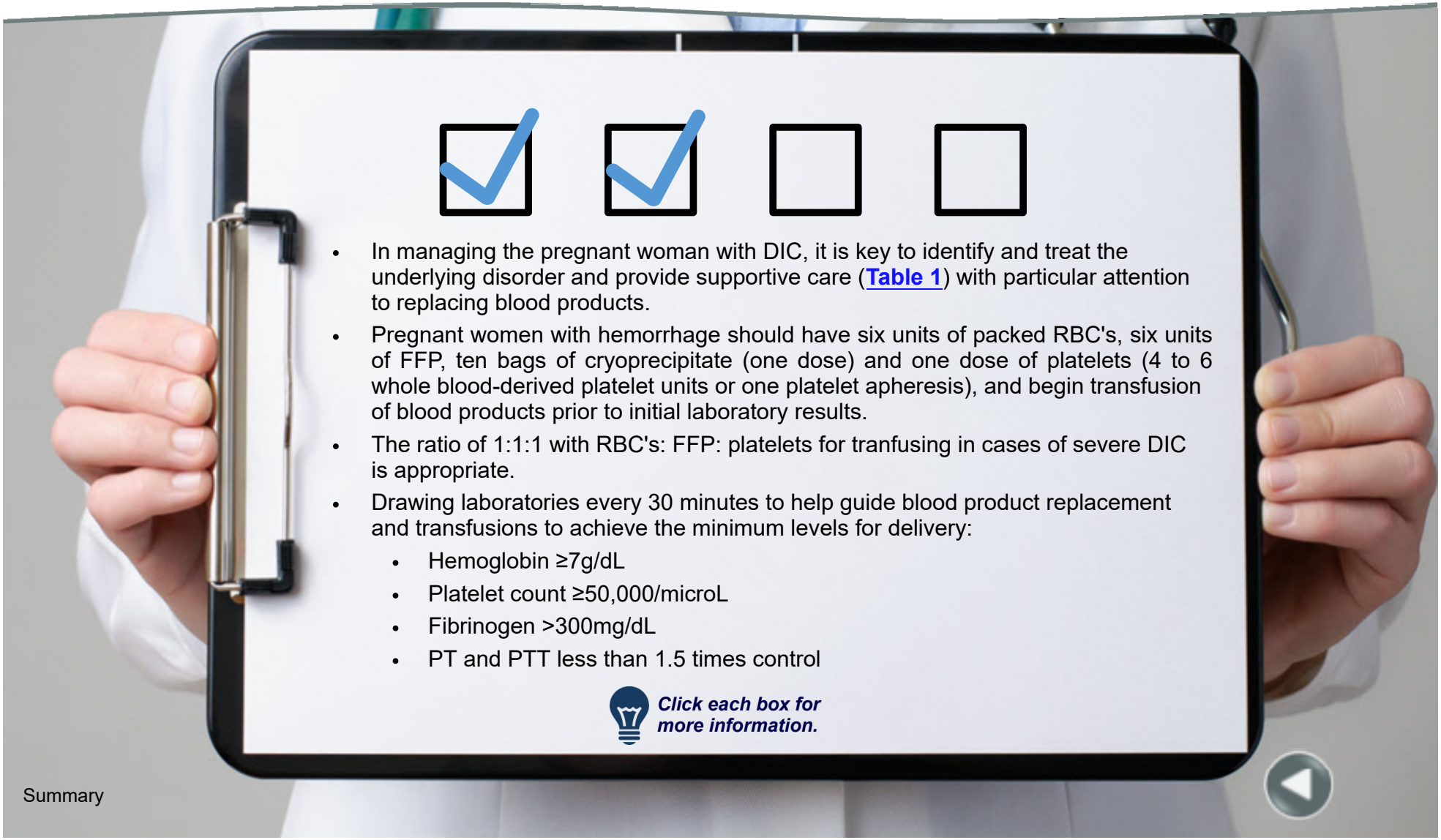
Click each button to learn more.

- Neonatal survival depends on the stage of pregnancy and placental function.
- In a series of 91 cases of DIC, there were 40 neonatal deaths (44%); 28 occurred antepartum, three intrapartum, and nine postpartum [3].



- Disorders during pregnancy that trigger DIC may include abruption of the placenta, preeclampsia with severe features, eclampsia, HELLP syndrome, septic abortion, amniotic fluid embolism, acute fatty liver, and retained dead fetus.
- Severe hemorrhage alone does not usually cause DIC, but when severe postpartum hemorrhage is associated with increased tissued factor DIC may ensue.
- Acute DIC in pregnant women is diagnosed when the clinical setting is appropriate and she has laboratory evidence of thrombocytopenia, coagulation factor consumption (prolonged PT, PTT, low fibrinogen) and fibrinolysis (increased D-dimer).
- Bleeding supports the diagnosis, but is not required for diagnosis.

Click each box for more information.

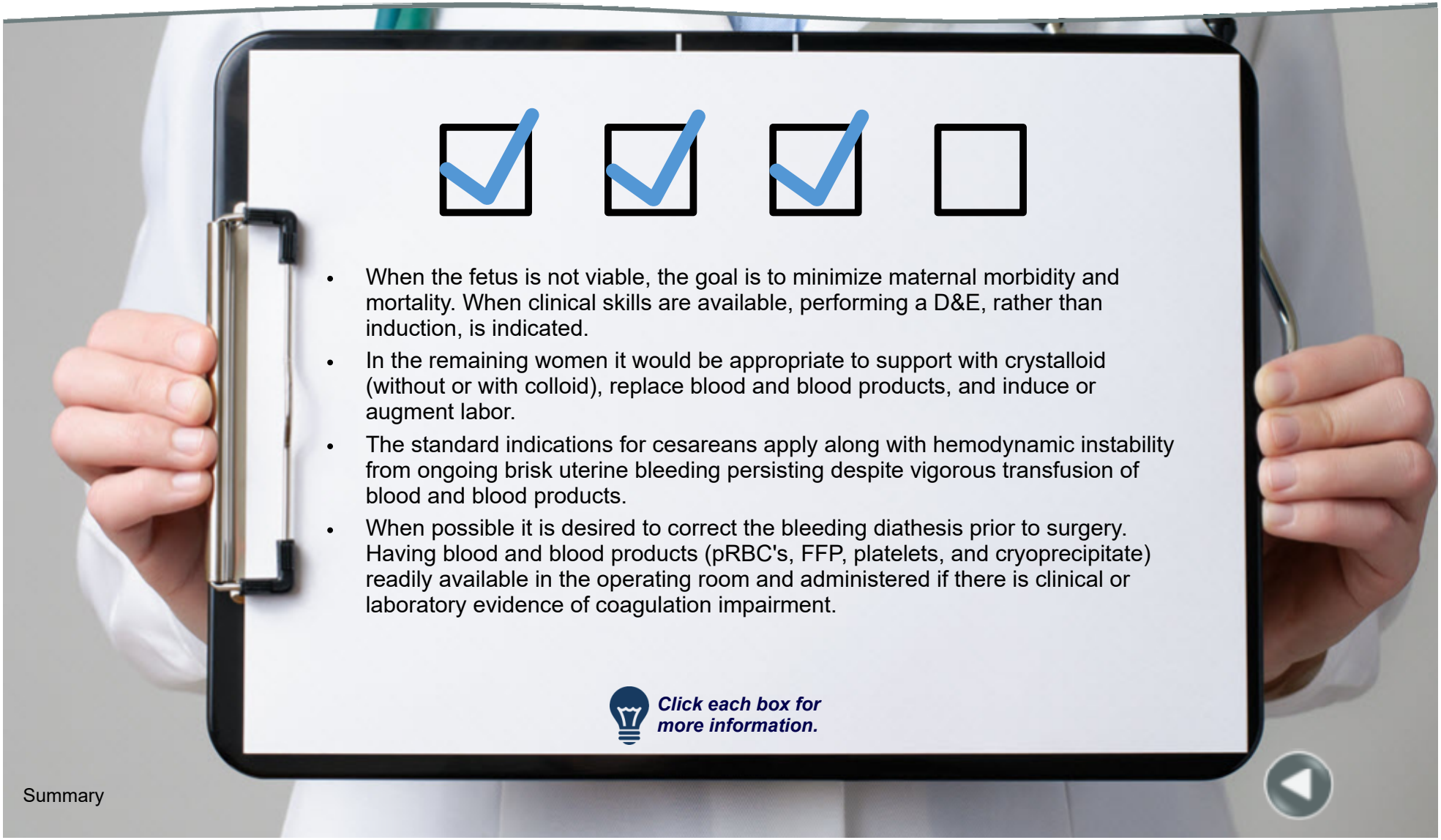


- In managing the pregnant woman with DIC, it is key to identify and treat the underlying disorder and provide supportive care (Table 1) with particular attention to replacing blood products.
- Pregnant women with hemorrhage should have six units of packed RBC's, six units of FFP, ten bags of cryoprecipitate (one dose) and one dose of platelets (4 to 6 whole blood-derived platelet units or one platelet apheresis), and begin transfusion of blood products prior to initial laboratory results.
- The ratio of 1:1:1 with RBC's: FFP: platelets for tranfusing in cases of severe DIC is appropriate.
- Drawing laboratories every 30 minutes to help guide blood product replacement and transfusions to achieve the minimum levels for delivery:
  - Hemoglobin ≥7g/dL
  - Platelet count ≥50,000/microL
  - Fibrinogen >300mg/dL
  - PT and PTT less than 1.5 times control

Click each box for more information.

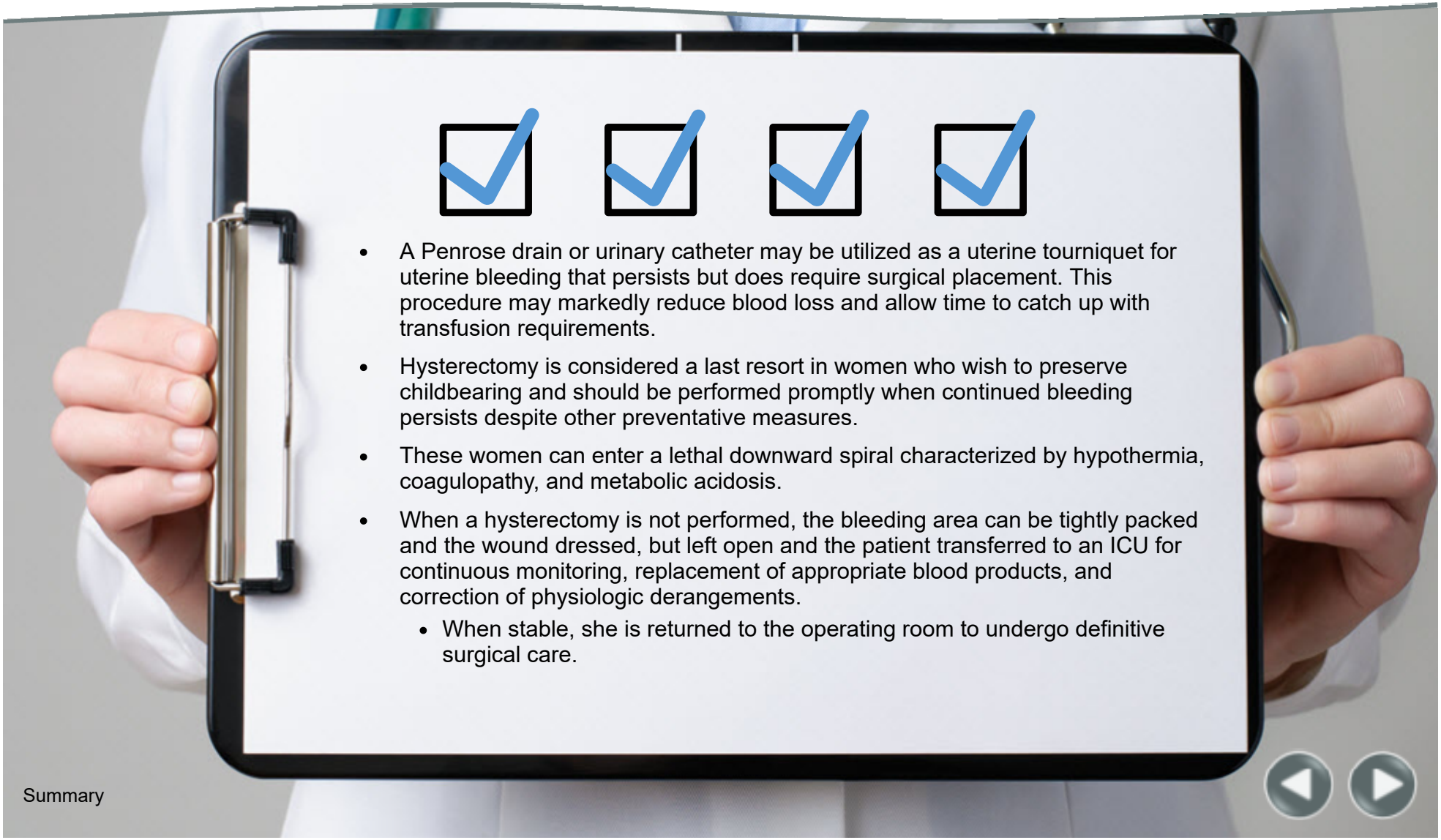
Table 1

Events that Initiate DIC				
Septiciemia-Gram Negative and Gram Positive	Crush injury or complicated surgery	Severe head injury	Abdominal aortic aneurysm	Peritoneovenous shunt
Cancer procoagulant (Trusseau's Syndrome)	Acute leukemia, especially promyelocytic	Amphetamine overdose	Giant hemangioma (Kasaback-Merritt Syndrome)	Acute hemolytic transfusion reaction (ABO incompatibility)
Complications of pregnancy: • Amniotic fluid embolism • Abruption • HELLP syndrome • Eclampsia and severe preeclampsia • Septic abortion	Paroxysmal nocturnal hemoglobinuria	Snake or viper venoms	Liver disease: Fulminant hepatic failure Reperfusion after liver transplant	Heat stroke
Burns	Pupurs fulminans	Events that propagate and complicate DIC: • Shock • Complement pathway activation		



- When the fetus is not viable, the goal is to minimize maternal morbidity and mortality. When clinical skills are available, performing a D&E, rather than induction, is indicated.
- In the remaining women it would be appropriate to support with crystalloid (without or with colloid), replace blood and blood products, and induce or augment labor.
- The standard indications for cesareans apply along with hemodynamic instability from ongoing brisk uterine bleeding persisting despite vigorous transfusion of blood and blood products.
- When possible it is desired to correct the bleeding diathesis prior to surgery. Having blood and blood products (pRBC's, FFP, platelets, and cryoprecipitate) readily available in the operating room and administered if there is clinical or laboratory evidence of coagulation impairment.

Click each box for more information.



- A Penrose drain or urinary catheter may be utilized as a uterine tourniquet for uterine bleeding that persists but does require surgical placement. This procedure may markedly reduce blood loss and allow time to catch up with transfusion requirements.
- Hysterectomy is considered a last resort in women who wish to preserve childbearing and should be performed promptly when continued bleeding persists despite other preventative measures.
- These women can enter a lethal downward spiral characterized by hypothermia, coagulopathy, and metabolic acidosis.
- When a hysterectomy is not performed, the bleeding area can be tightly packed and the wound dressed, but left open and the patient transferred to an ICU for continuous monitoring, replacement of appropriate blood products, and correction of physiologic derangements.
  - When stable, she is returned to the operating room to undergo definitive surgical care.

MATERNAL911

Congratulations!

You have successfully completed this module.

Click on the above 'X' to take the post-test for this course.
If you do not attain a passing score after two attempts at the post-test the entire program must be repurchased.

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