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Disseminated Intravascular Coagulation

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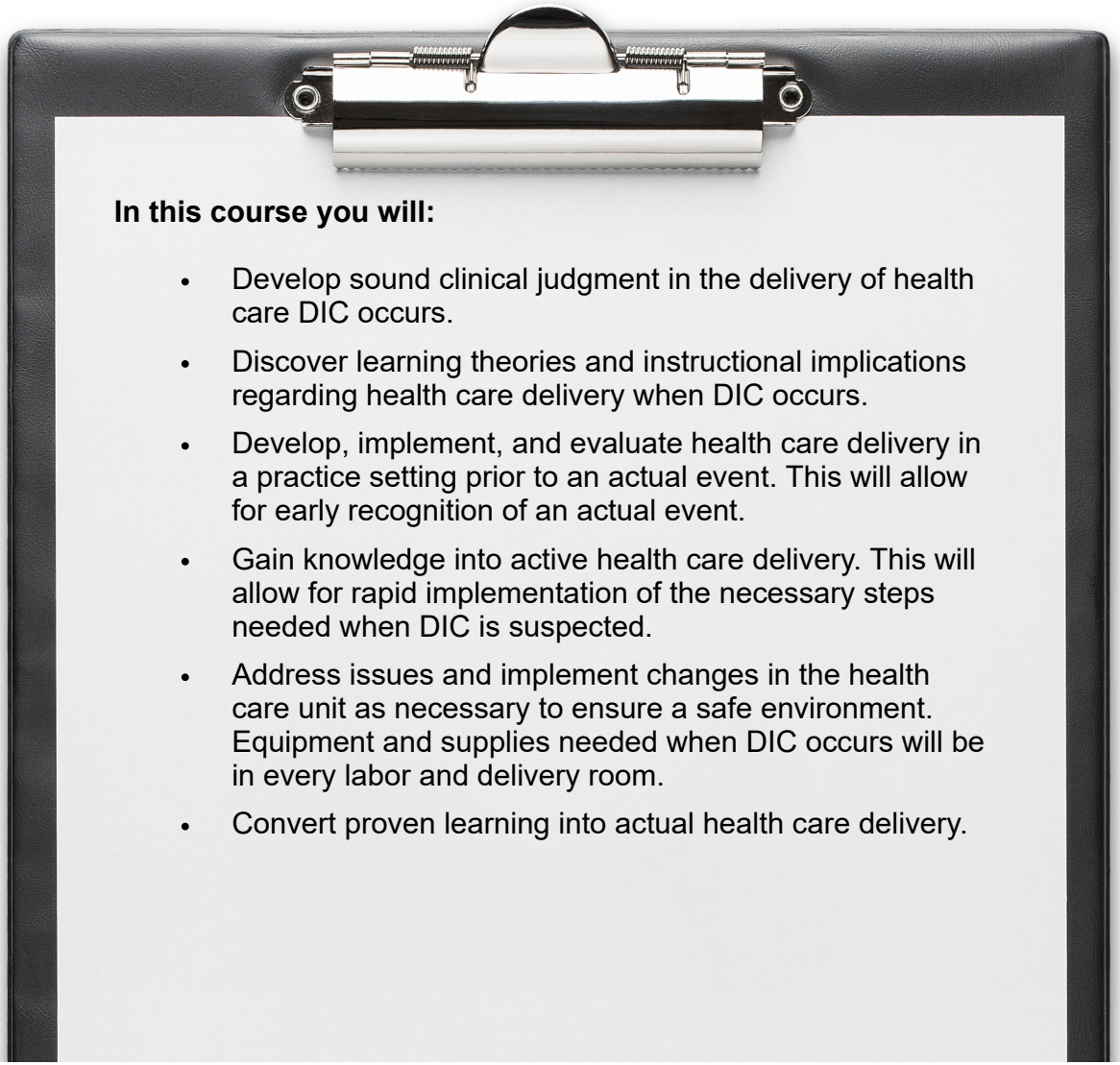
Course Description:

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

Click here to download a print version of this course.



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

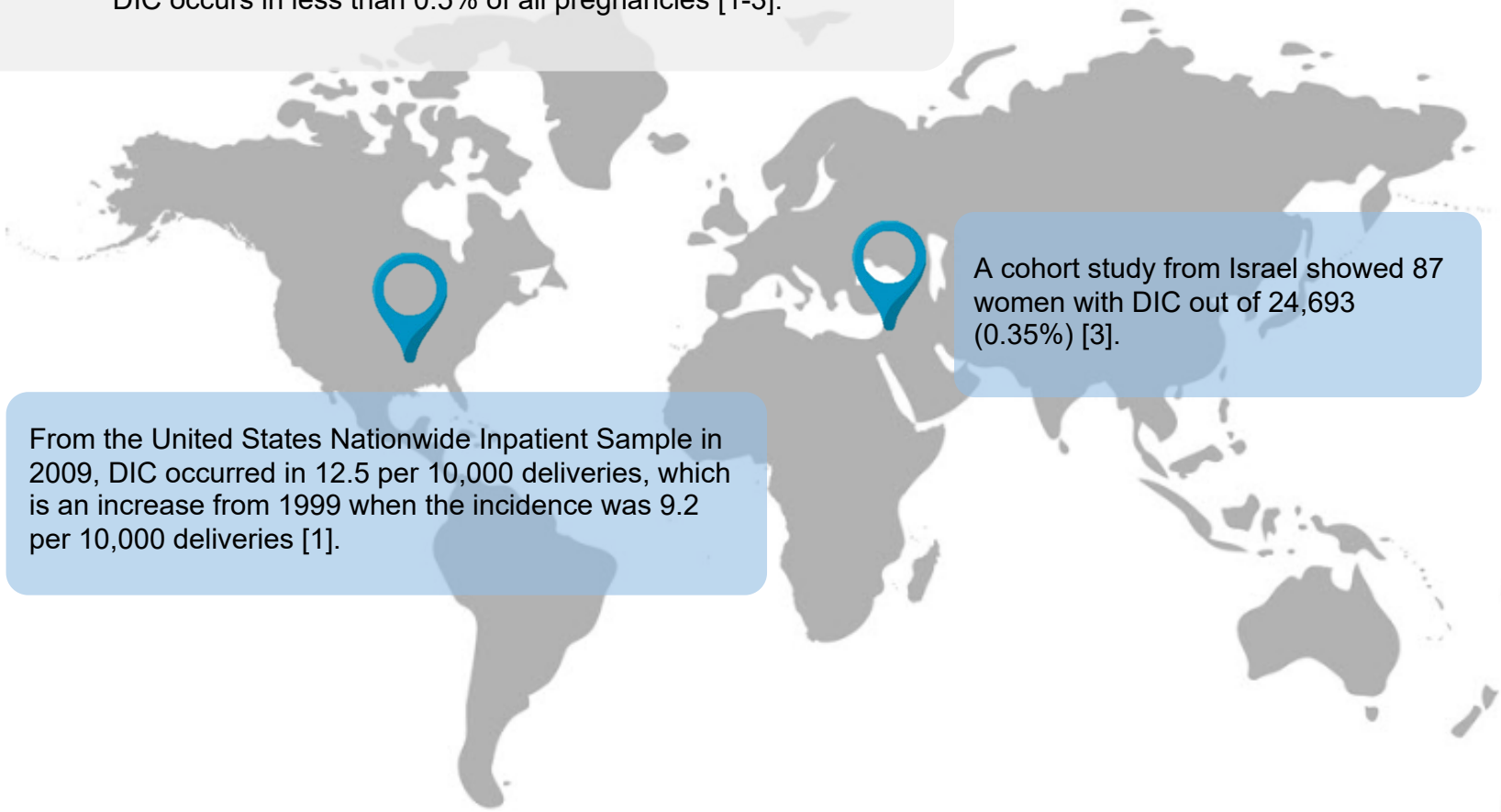
A pathologic disruption of the finely-coordinated process of hemostasis.

- Massive activation of the clotting cascade results in widespread thrombosis, which leads to depletion of platelets and coagulation factors and excessive thrombolysis.
  - This complication can result in massive hemorrhage, thrombosis, and/or multi-organ system failure.

Incidence of Disseminated Intravascular Coagulation

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

DIC occurs in less than 0.5% of all pregnancies [1-3].

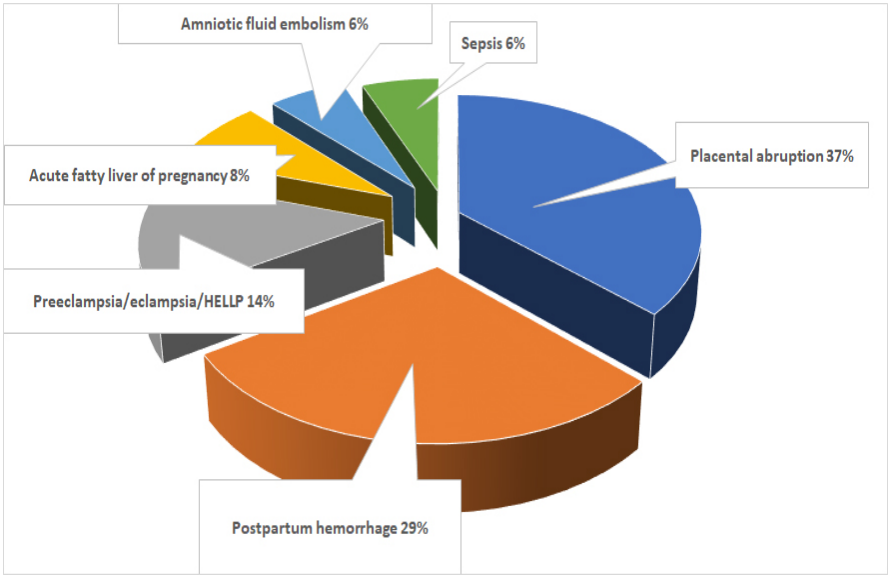


From the United States Nationwide Inpatient Sample in 2009, DIC occurred in 12.5 per 10,000 deliveries, which is an increase from 1999 when the incidence was 9.2 per 10,000 deliveries [1].

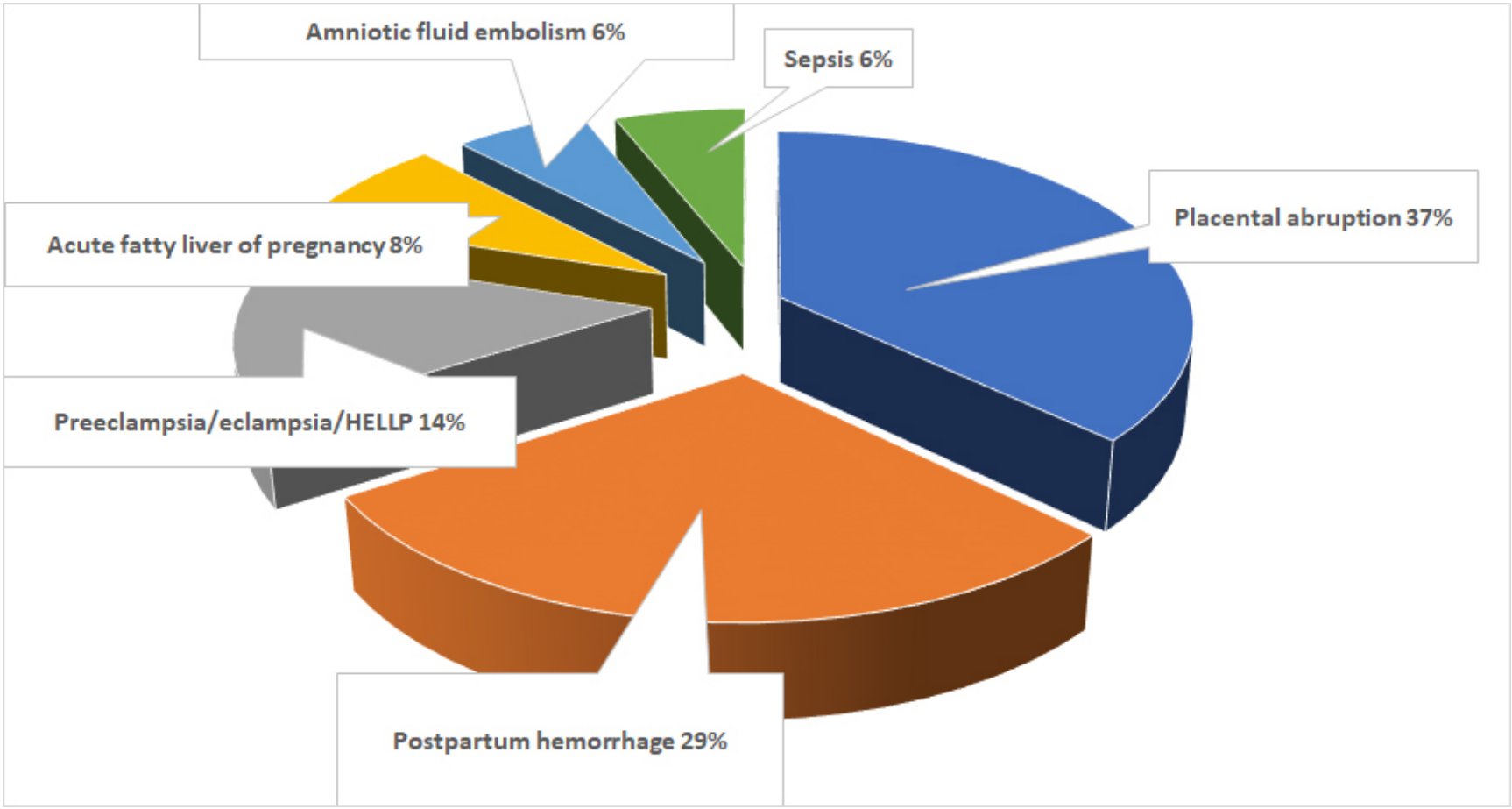
A cohort study from Israel showed 87 women with DIC out of 24,693 (0.35%) [3].

Risk Factors

- Pregnancy complications that may trigger and include the following [2]:
  - Placental abruption
  - Postpartum hemorrhage (PPH)
  - Preeclampsia/eclampsia/hemolysis, elevated liver enzymes, low platelets (HELLP)
  - Acute fatty liver of pregnancy (AFL)
  - Amniotic fluid embolism (AFE)
  - Sepsis



Click the chart to enlarge it.


Amniotic fluid embolism 6%
Sepsis 6%
Placental abruption 37%
Acute fatty liver of pregnancy 8%
Preeclampsia/eclampsia/HELLP 14%
Postpartum hemorrhage 29%

Risk Factors

- 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.
- 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 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 most common events that initiate DIC in the general population are sepsis, tissue trauma/destruction, and cancer (Events that Initiate DIC).

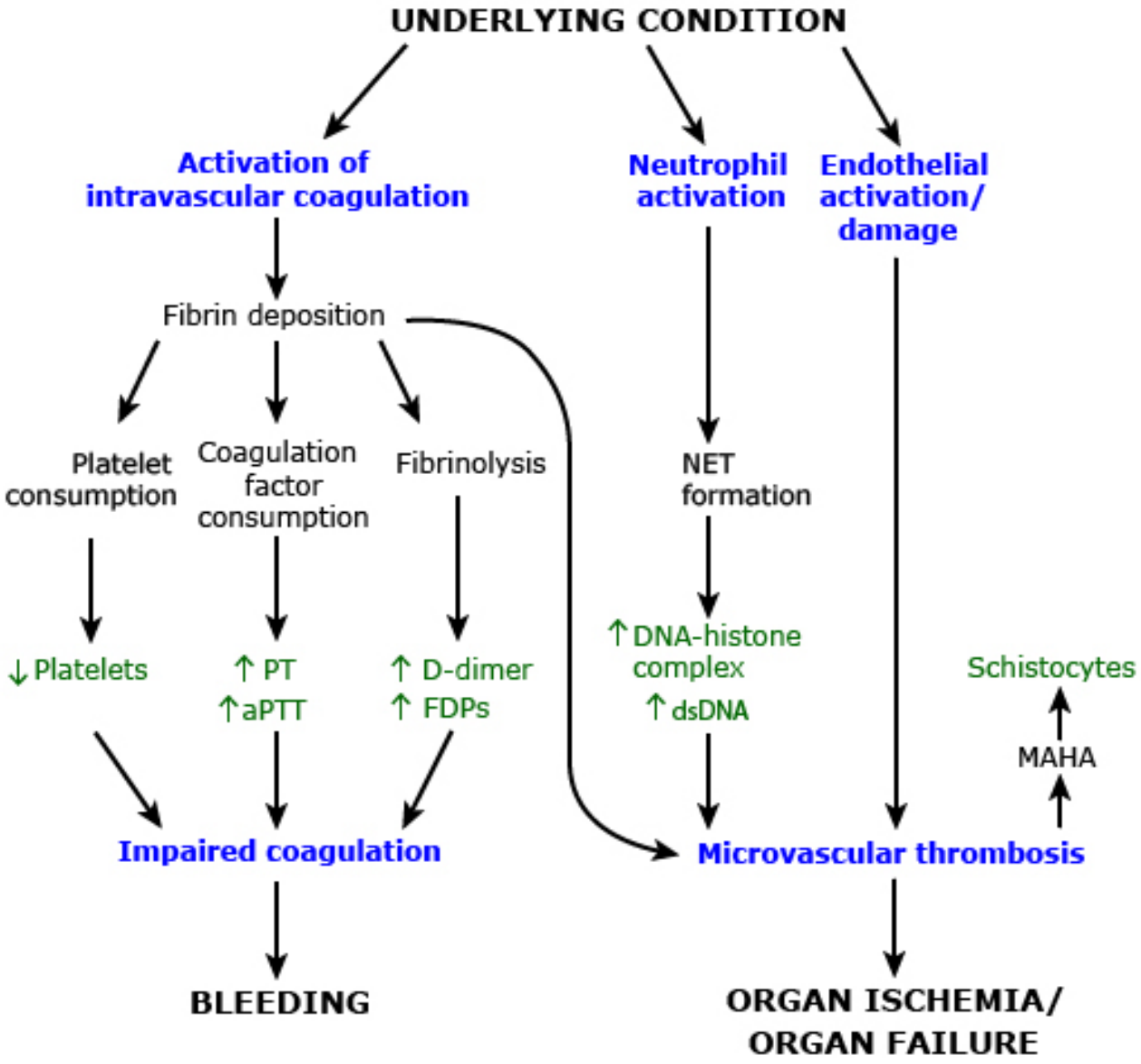
Click on the image to view a list of events that initiate DIC.

Events that Initiate DIC

- Septiciemia-Gram Negative and Gram Positive
- Cancer procoagulant (Trusseau's Syndrome)
- Burns
- Crush injury of complicated surgery
- Acute leukemia, especially promyelocytic
- Paroxysmal nocturnal hemoglobinuria
- Purpura fulminans
- Severe head injury
- Amphetamine overdose
- Snake of viper venoms
- Events that propagate and complicate DIC:
  - Shock
  - Complement pathway activation
- Abdominal aortic aneurysm
- Giant hemangioma (Kasaback-Merritt Syndrome)
- Liver disease:
  - Fulminant hepatic failure
  - Reperfusion after liver transplant
- Peritoneovenous shunt
- Acute hemolytic transfusion reaction (ABO incompatibility)
- Heat Stroke

Pathophysiology

- Several cases of DIC are caused by hemorrhage.
- As bleeding ensues, vasospasm occurs, which causes endothelial damage and initiation of DIC
- Because of bleeding, hypotension occurs, which causes decreased tissue perfusion leading to local hypoxia and tissue acidosis. This further exacerbates DIC by causing tissue release of cytokines.
- Following placental separation after delivery, fibrinogen is activated to become a fibrin mesh, which covers the placental site on the endometrium.
- DIC occurs when there is accelerated formation of fibrin clots with simultaneous breakdown of the clots. The body consumes the clotting factors faster then they can be produced.
- See **Figure 1**


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

Pathophysiology

- Events occurring in pregnancy such as preeclampsia, eclampsia and HELLP syndrome may contribute to endothelial damage.
- AFL 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 [12].
- Hemorrhage can lead to consumption of coagulation factors.
- 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.

Presentation of DIC

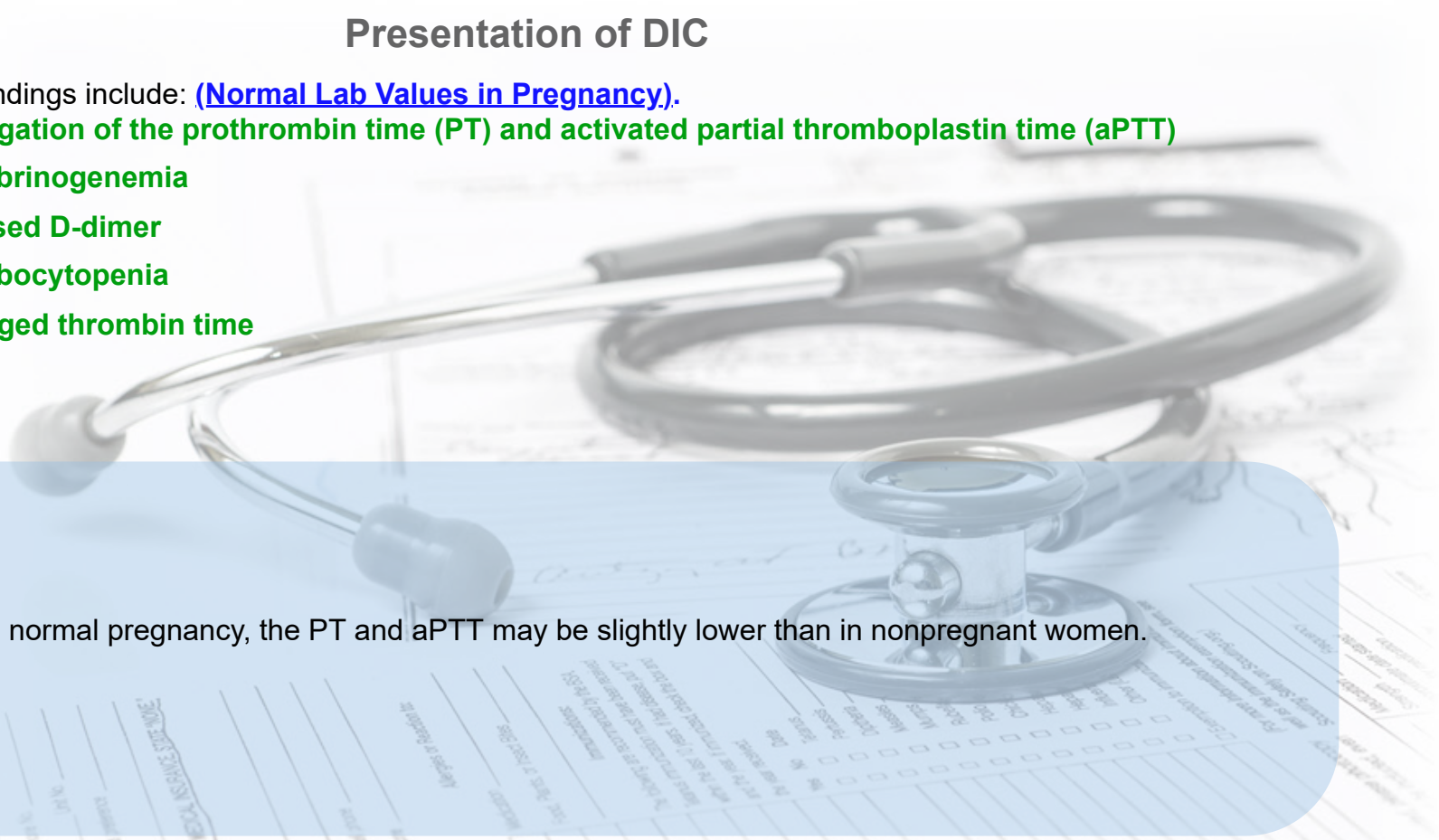
A presumptive diagnosis of DIC is usually made based on clinical presentation.

Presentation of DIC

- Clinical criteria
  - Bleeding from venipuncture and intravenous (IV) sites
  - Bleeding from incision sites and mucous membranes
  - Profuse vaginal bleeding
  - Shock
    - Tachycardia
    - Hypotension
    - Altered mental status
    - Weak pulses
    - Cool extremities
- Laboratory Criteria
  - Decreased fibrinogen
  - Increased D-dimer
  - Prolonged prothrombin time (PT)/INR
  - Prolonged activated partial thromboplastin time (aPTT)
  - Decreasing hemoglobin
  - Rising lactate dehydrogenase (LDH)
  - Rising bilirubin

Presentation of DIC

- Laboratory findings include: **(Normal Lab Values in Pregnancy)**.
  - **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
  - **Hypofibrinogenemia**
  - **Increased D-dimer**
  - **Thrombocytopenia**
  - **Prolonged thrombin time**



- In a normal pregnancy, the PT and aPTT may be slightly lower than in nonpregnant women.

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

Presentation of DIC

- Laboratory findings include: **(Normal Lab Values in Pregnancy).**
  - **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
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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 [13].
- Reduction in fibrinogen is the most specific test and one of the earliest findings in DIC [14].
- Fibrinogen levels <100mg/dL are generally associated with bleeding, prolongation of clotting times and indicative of severe disease.

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

Presentation of DIC

- Laboratory findings include: (Normal Lab Values in Pregnancy).
  - **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
  - **Hypofibrinogenemia**
  - **Increased D-dimer**
  - **Thrombocytopenia**
  - **Prolonged thrombin time**

- 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 [15].
- 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., DVT, PE, DIC).
- This finding can be seen in antepartum, postpartum, and postoperative patients.

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

Presentation of DIC

- Laboratory findings include: (Normal Lab Values in Pregnancy).
  - **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
  - **Hypofibrinogenemia**
  - **Increased D-dimer**
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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 [27].
- 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.

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

Presentation of DIC

- Laboratory findings include: **(Normal Lab Values in Pregnancy)**.
  - **Prolongation of the prothrombin time (PT) and activated partial thromboplastin time (aPTT)**
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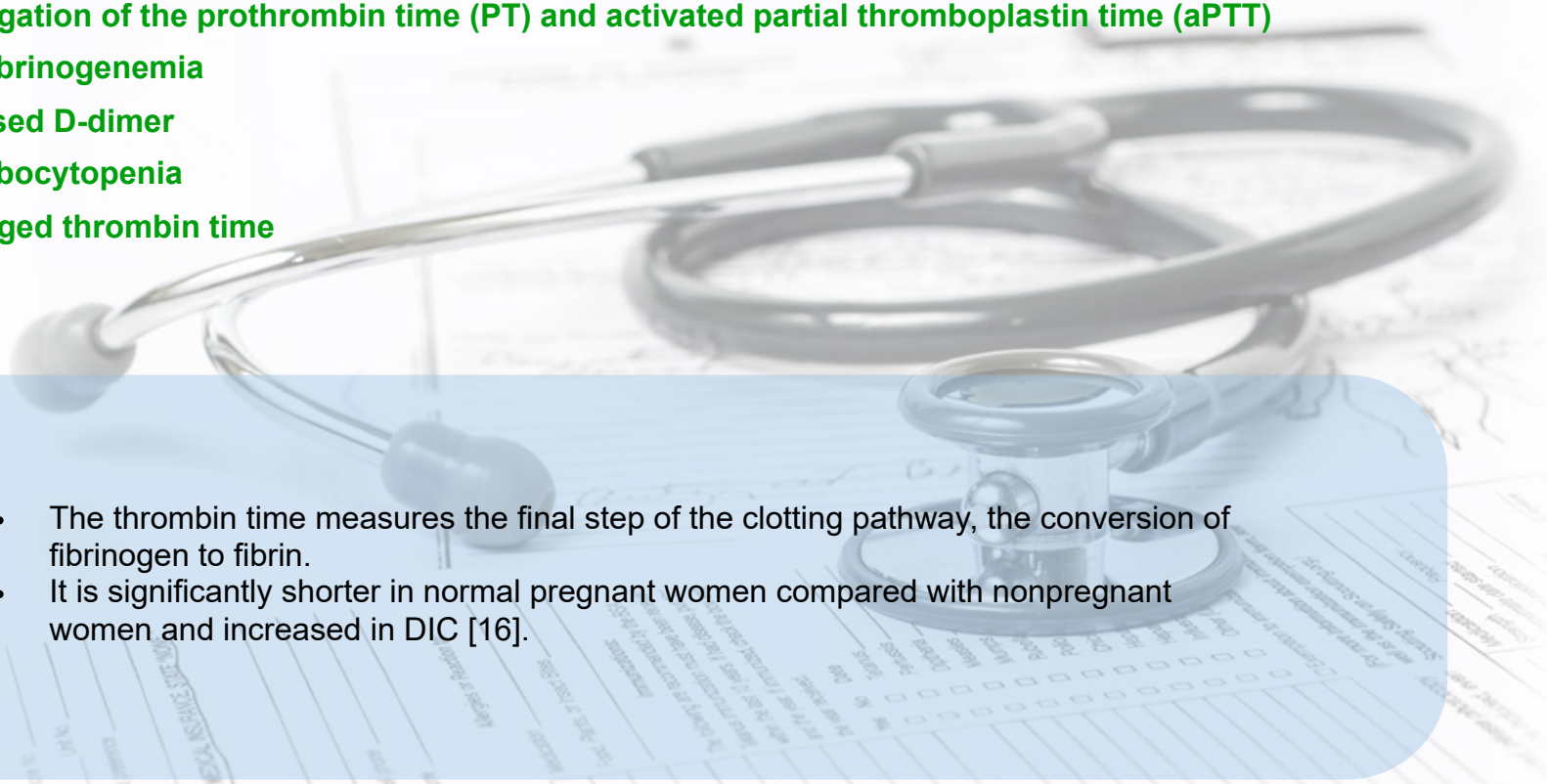

- The thrombin time measures the final step of the clotting pathway, the conversion of fibrinogen to fibrin.
- It is significantly shorter in normal pregnant women compared with nonpregnant women and increased in DIC [16].

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

Normal Lab Values in Pregnancy

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

- Laboratory testing includes the following:
  - Complete blood count (CBC)
  - Coagulation studies including PT, 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 culture should be performed in patients with suspected sepsis.

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 is 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.

Differential Diagnosis

- Transfusion reaction
- Primary thrombotic microangiopathy
- von Willebrand disease
- Antiphospholipid antibody syndrome
- Pulmonary embolism
- Heparin-induced thrombocytopenia

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 significantly reduced.

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 does not have an established diagnosis 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 Antibody Syndrome

- Antiphospholipid antibody 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

- Pulmonary embolism (PE) is the leading cause of death during pregnancy and postpartum. It 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 and is seen more commonly with heparin rather than low molecular weight heparin.
- 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.

Management of DIC

- Call for help.
- Notify staff that the following resources will likely be needed:
  - Anesthesia
  - Neonatology
  - Blood bank
  - Obstetrics
  - Maternal Fetal Medicine
  - Gynecologic Oncology
  - Interventional Radiology
  - General Surgery
  - Critical Care

Management of DIC

- Basic treatment for DIC is to treat the inciting event.
- While simultaneously treating the inciting event, IVF and blood products should be administered.
- Monitoring intake and output is critical in resuscitation efforts. Placement of a foley catheter is recommended.

Management of DIC

- 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.
- If the patient develops shock or requires CPR, intraosseous cannulation and peripheral venous access should be pursued simultaneously [3,4].
- 1-2 liters of crystalloid IV fluids should be bolused early in the course of DIC.

Management of DIC

- Protocols can help standardize the management of patient's with DIC. Rapid establishment of venous access is the first priority [5].
  - In one study, a protocol was designed to limit the time spent in attempts to achieve peripheral and central venous catheterization [6].
  - Significant time to achieve improvement on venous access was found when a study followed rapid sequential steps. In this study, rapid sequential attempts at percutaneous femoral vein catheterization, saphenous vein cutdown, and intraosseous cannulation were initiated if 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 of DIC

- O-negative red blood cells, group AB fresh frozen plasma cryoprecipitate, and 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 (FFP) cryoprecipitate and cross-match compatible red blood cells (RBC).
- The goal with transfusions is to keep:
  - Hemoglobin ≥7g/dL
  - Platelet count ≥50,000/microL
  - Fibrinogen ≥200mg/dL
  - PT and aPTT <1.5 times control

Management of DIC

- Maintain oxygen saturation above 95%
- Maintain normal body temperature
  - This may require a warming blanket and/or an IVF warmer

Management of DIC

- As soon as DIC is suspected, order the following labs:
  - CBC
  - CMP
  - PT/INR
  - aPTT
  - Fibrinogen
- Additionally, draw 5 mL into a red top tube and observe for clot formation over 8-10 minutes.
- If there continues to be concern for DIC, labs should be followed every 1-2 hours until the condition is treated.

Management of DIC

- Assess fetal status (gestational age, fetal heart rate (FHR)).
- Assess maternal condition (blood loss, cervical status, hemodynamic stability, uterine contractions).
- Appropriate personnel, equipment, and supplies should be gathered for management.

Click the next arrow to continue with the lesson.

Management of DIC

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.
- In addition to delivery anesthesia, the anesthesiologist can also assist with IV access and placement of an arterial line and/or central venous access, if indicated.

Click each number in order to learn more.

Management of DIC

Notify the Blood Bank

- The blood bank should be notified of the potential need for massive transfusion.
- Cross matching of at least 2 units of PRBC should be initiated. If possible, the blood bank should also prepare 1 unit of fresh frozen plasma, 1 unit of cryoprecipitate and 1 pack of platelets.
- If necessary, emergency-release blood products can be made available.

Click each number in order to learn more.

Management of DIC

Establish IV Access and Begin Fluid Resuscitation

- Establish IV access peripherally with at least two IV catheters (≥18 gauge) and infuse crystalloid and blood products, when available, to support blood pressure (systolic ≥90mmHg or mean arterial pressure ≥65mmHg) and maintain urine output (≥0.5mL/kg/hour).
- 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.
- If blood products are available, fluid resuscitation should include 1-2 liters of LR. If LR is not available, normal saline is also acceptable.

Click each number in order to learn more.

Management of DIC

Recognize and Treat the Inciting Event

Click the terms and icons to see more information.

- The mainstay of treatment 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

- 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.
- Clinical symptoms, abnormal fetal heart tracing, fetal demise and/or DIC support the diagnosis of placental abruption.

Preeclampsia with Severe Features

- If seizures are present, the diagnosis is revised to eclampsia.
- Pre-eclampsia is a pregnancy complication that presents after 20 weeks gestation with hypertension accompanied by maternal symptoms and/or lab abnormalities.
- Pre-eclampsia with severe features and HELLP syndrome can result in DIC if delivery is not undertaken in a timely fashion.
- Typically, patients who progress to DIC in the setting of pre-eclampsia will have thrombocytopenia; however, this is not diagnostic of DIC unless clinical bleeding or other abnormal coagulation studies are present.

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Amniotic Fluid Embolism

AFE is an exceedingly rare complication that is characterized by sudden onset of hypotension due to cardiogenic shock, hypoxemia due to respiratory failure, and coma or seizures during labor or immediately postpartum.

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Acute Fatty Liver of Pregnancy

- AFL 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.
- AFL is a rare cause of DIC.

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Retained Fetal Demise

Retained fetal demise is diagnosed by ultrasound imaging that confirms the absence of the fetal heart rate.

If a demised fetus is retained for more than 2 weeks, there is risk of development of DIC.

If there is an unknown timeline for a fetal demise, a coagulation profile should be obtained at the time of diagnosis of demise.

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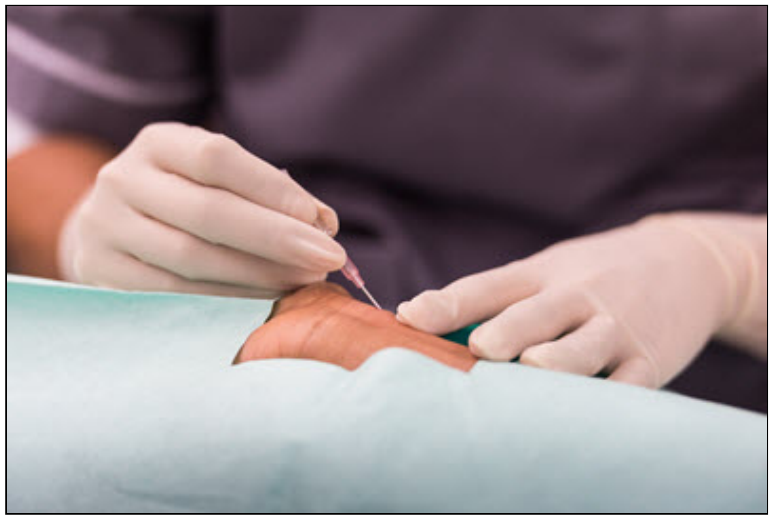
Septic Abortion

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.

Management of DIC



Insert an Arterial Line

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

Click each number in order to learn more.

Management of DIC

Blood Products

Obstetrical patients with DIC typically require blood products as part of resuscitation.

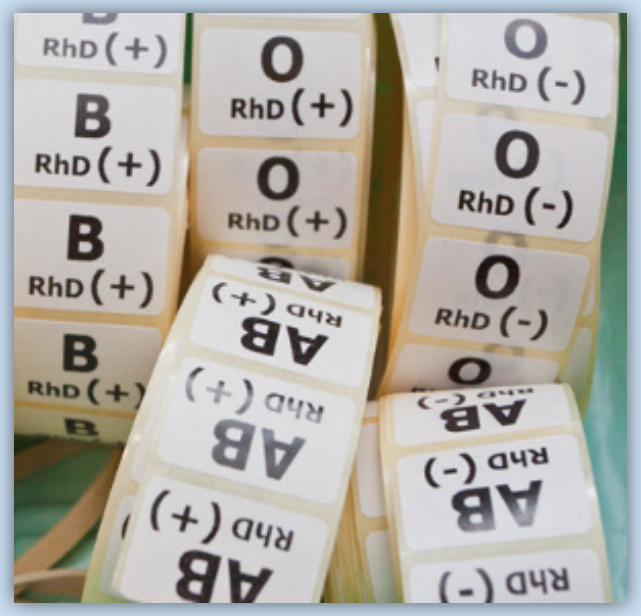
Transfusion

Massive Transfusion

Click the blue boxes to learn more about transfusions.

Management - Transfusion

- Fully typed and crossmatched RBCs requires at least 20 minutes to receive from the blood bank.
- Transfusion may begin immediately using type 0, Rh(D)-negative RBCs. When fully typed and crossmatched RBCs are available the patient should be switched to matched blood products.
- When transfusion is necessary prior to obtaining type specific FFP, type AB FFP, either Rh(D) positive or negative can be safely used.



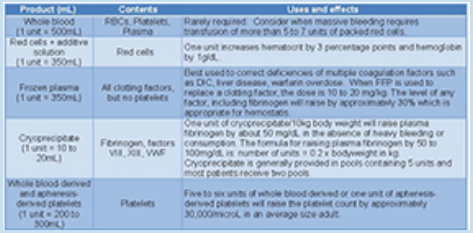
Management - Transfusion

- When ordering a massive transfusion protocol, it typically includes 4 units of pRBC, in addition to the following:
  - 4 units of FFP
- 1 pack of platelets, either:
  - A pool of 4 to 6 whole blood- derived platelet concentrates OR a single apheresis platelet unit.
  - 1 or 2 cryoprecipitate pools should also be requested for obstetric DIC.
    - A pool contains 5 individual units.
- Many massive transfusion protocols recommend transfusion of RBCs, FFP, and platelets in a ratio of 1:1:1.

Management - Transfusion

- Correcting 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 fibrinogen concentration below 100mg/dL is generally treated with 10 units of cryoprecipitate, which is two pools of 5 units (Table 3).
- Cryoprecipitate requires preparation by the blood bank, so if fibrinogen is <100 mg/dL, the blood bank should be alerted to start preparing this blood product.

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/microL in an average size adult.

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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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/microL in an average size adult.

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 [17].
- 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 30-60 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 [18-20].

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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- Laboratory Testing
- Review of Massive Transfusion Protocol Events by Transfusion Services
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Click each blue term above to learn more.

- 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.

- Bedside Responsibilities
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Blood Bank Responsibilities

- Release two emergency O Neg RBCs if requested.
- Prepare 4 RBCs, 4 plasma, and 1 pack of platelets for adult MTP or 2 RBCs, 2 plasma, and ½ platelet apheresis for pediatric 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.

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

- 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.

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

Blood products are transfused to achieve the following minimum levels:

- Hemoglobin ≥7g/dL
- Platelet count ≥50,000/microL
- Fibrinogen greater than or equal to 200mg/dL
- PT and aPTT less than 1.5 times control

Click here to learn more.

Bedside Responsibilities
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Nursing Responsibilities
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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 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 in the setting of severe PPH or DIC [22,23].
- 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.
- 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 [21].
- Similar predictive data for platelet concentration are not available.

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- **Laboratory Testing**
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- Attending Physician, Surgeon, or Anesthesiologist Responsibilities

Click each blue term above to learn more.

- Laboratory studies are drawn initially every 30-60 minutes to guide blood product replacement.
- As the patient stabilizes, the laboratory testing interval can be extended.
- Some centers have found TEG useful in the setting of massive hemorrhage as it provides a "rapid global assessment" of hemostatic function [18-20].

- Bedside Responsibilities
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- Laboratory Testing
- **Review of Massive Transfusion Protocol Events by Transfusion Services**
- 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.

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

Click here to learn more.

- Determine if rFVIIa is required (see section below for guidelines).
- Monitor CBC, ABG, potassium, ionized calcium, and coag tests frequently.
- Determine when the protocol should be discontinued.
- Call the blood bank (this phone call may be delegated to another individual).
- Document discontinuation of massive transfusion protocol in the patient's chart.

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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.

Click each blue term above 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.

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.

Management of Vaginal Bleeding

Assess Blood Loss

- Quantifying blood loss [28]
- Closely monitor vital signs.
- 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.
- Signs of concealed abruption include maternal pain, rapid increase in fundal height, presence of hematoma on ultrasound, decreased urine output and decreasing hemoglobin.

Click each number in order to learn more.

Quantifying Blood Loss

- Visual estimation of blood loss can result in both over and underestimations.
- Quantified blood loss can be determined by weighing blood soaked items, subtracting the dry weight of the item and understanding that 1gm of weight equals 1mL of blood loss [28].
    - Additionally, quantifying blood loss can be performed by using measured suction containers or suction systems.
- Ongoing blood loss assessment should continue as long as active bleeding is present or if the patient is unstable [28].
- Quantifying the blood loss is an important part of evidence-based hemorrhage bundles [28].
    - Additional research is needed.
    - The clinical utility specific to the quantification approach remains unproven.
- Fluid and blood clots from the sterile or surgical drapes can be measured by volume and added to the weighed items for an accumulative quantification of blood loss.
    - Calibrated drapes have been proven to have an error rate less than 15% [29].

Management of DIC

Notify Neonatology Service

- To prepare for birth of a compromised or premature infant, the neonatology or pediatric department should be notified.
- If time allows, neonatology services may counsel the parents about newborn issues prior to the delivery.

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.
- Viability is the stage of maturity that would likely result in a chance of survival without severe deficits.
- Viability is determined by local practices; however, commonly is determined to be 23-24 weeks gestation. Recent data suggests there is also a chance of survival as early as 22 weeks.
- If the fetus is viable, measures should be taken to optimize the fetus prior to delivery. These measures typically include administration of antenatal corticosteroids, IV magnesium sulfate and Group B strep prophylaxis.

Click here to learn more about fetal assessment.

Management of DIC

Fetal Assessment Continued

- 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.
- In a pregnancy complicated by DIC, fetal heart rate tracings may demonstrate abnormalities due to poor placental perfusion and compromised fetal oxygenation.
- 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.
- If time allows, maternal and fetal risks related to immediate versus delayed delivery should be weighed; however, in an obstetric hemorrhage, immediate delivery is typically indicated, regardless of gestational age.

Click number 10 to continue learning about interventions.

Management of DIC

Management of Delivery

Mode of delivery is determined based on fetal viability, gestational age, fetal heart tracing, obstetric history and the acuity of the maternal presentation.

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 weeks, lethal or life threatening congenital anomaly).
- The trigger for DIC is removed upon delivery in many obstetrical cases, causing the myometrium to contract, thus removing both the major sources 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.
- The woman may require support with IVF as well as blood products during the course of delivery.
- Typically, if the fetus has demised or is not viable, efforts should be made to avoid cesarean section; however, if the patient has ongoing hemorrhage or is hemodynamically unstable, cesarean section may be required to expedite delivery.

Vaginal Delivery

- Although vaginal delivery carries the least morbidity; the patient and fetus may not tolerate the length of time required to achieve vaginal delivery.
- If there is ongoing hemorrhage, hemodynamic instability or other contraindication to vaginal delivery, C/S is recommended.

Cesarean Delivery

- If there is ongoing hemorrhage, hemodynamic instability or other contraindication to vaginal delivery, C/S is recommended.
- Not always possible, but desirable to correct and improve the clotting abnormality prior to cesarean delivery.
- If possible, begin blood product transfusion prior to beginning cesarean section in order to improve operative coagulation.
- Severe hypovolemia and DIC could prove fatal to the woman.
- With severe hypovolemia and DIC could prove fatal to the woman.
- When cesarean delivery is undertaken, 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 is helpful.
- If interventional radiology is available, request their assistance for potential uterine artery embolization.

Cesarean Delivery

- The surgical 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.
- Additionally, tranexamic acid (TXA), uterotonic medications and intrauterine balloon tamponade devices should be made available and administered if there are no contraindications.
    - Uterotonic medications include misoprostol, oxytocin, methylergonovine and carboprost

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 ongoing transfusion of blood products.
- 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 resuscitative measures, some patients will continue to decompensate, which is characterized by hypotension, hypothermia, coagulopathy and metabolic acidosis.
- Criteria associated with decompensation 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 [22].
- To stop the cycle, the bleeding area can be tightly packed using a pelvic pressure pack or lap sponges [23].
- The abdominal wound, including the fascia, can be left open and a pressure dressing is applied.
- Towel clips have been utilized to temporarily re-approximate the skin/subcutaneous tissue.

Management of DIC

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 [22].
- If there is concern for ongoing bleeding, as determined by abnormal vital signs, decreasing hemoglobin or abnormal physical exam, further surgical intervention or uterine artery embolization is likely required.
- If the patient's abdomen has been left open, definitive surgical closure should be attempted once the patient has stabilized.

Click each number in order to learn more.

Management of DIC

Hemostatic and Anticoagulant Therapies

- 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) [24].
- Pro-hemostatic treatment with tranexamic acid is recommended in the management of postpartum hemorrhage [26].

Click to learn more about tranexamic acid

Click each number in order to learn more.

Tranexamic Acid

- Intravenous 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 PPH [30].
- TXA is a competitive inhibitor of plasminogen activation and can reduce bleeding by inhibiting the breakdown of fibrinogen and fibrin clots.
- When administered within 3 hours of birth, maternal death from hemorrhage, regardless of cause, is reduced with no adverse maternal effects noted.

Tranexamic Acid

- 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 delay, with no benefit seen after 3 hours from birth.
- TXA should be initiated as soon as possible after the onset of bleeding and should be considered part of the standard PPH treatment package (i.e. uterotonics, non surgical and surgical interventions).
- Regardless of whether the postpartum 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 there is 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

- Known thromboembolic event in pregnancy
- History of coagulopathy
- Active intravascular clotting
- Known hypersensitivity to TXA
- Known subarachnoid hemorrhage

- DIC 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 [25].

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 data from the US Nationwide Inpatient Sample [1].
  - However, the majority of women with obstetric DIC survive.
- 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.
  - Uterine sparing surgical interventions for management of hemorrhage do not appear to adversely affect fertility.

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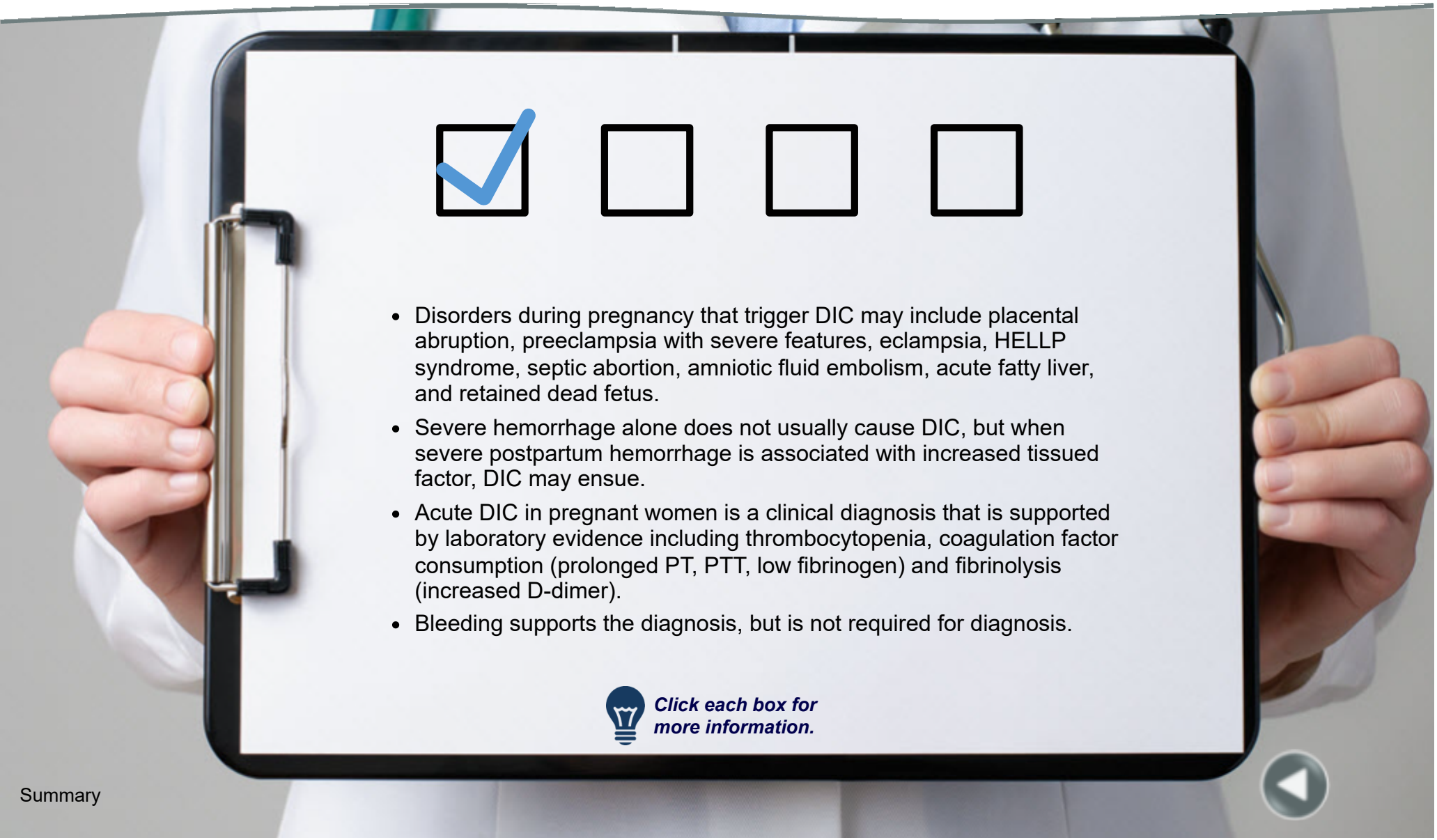
Maternal

Neonatal

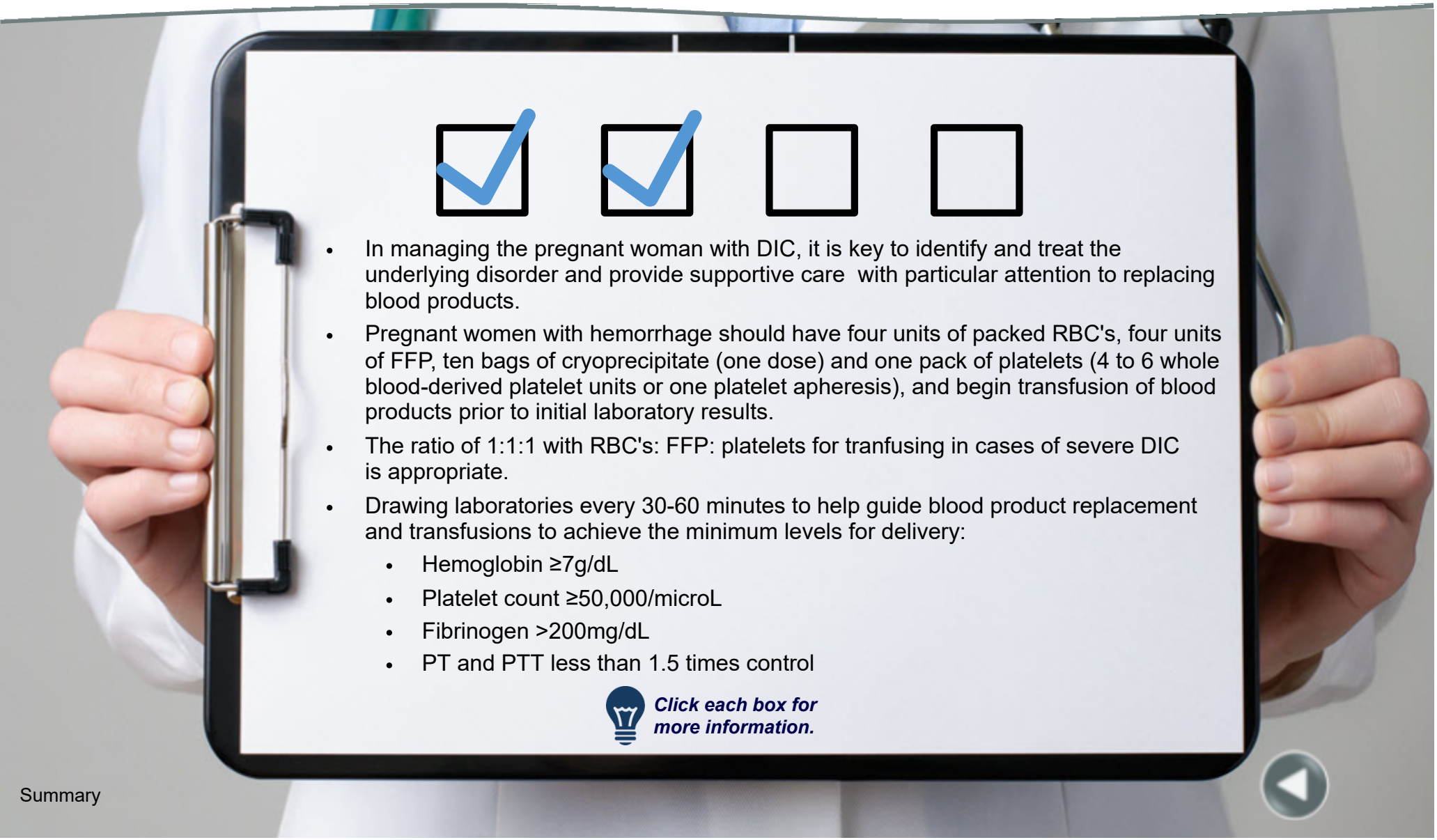
Click each button to learn more.

- Neonatal survival depends on the gestational age at the time of delivery and the underlying etiology of DIC.
- 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 placental abruption, 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 a clinical diagnosis that is supported by laboratory evidence including 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 with particular attention to replacing blood products.
- Pregnant women with hemorrhage should have four units of packed RBC's, four units of FFP, ten bags of cryoprecipitate (one dose) and one pack 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 30-60 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 >200mg/dL
  - PT and PTT less than 1.5 times control

Click each box for more information.

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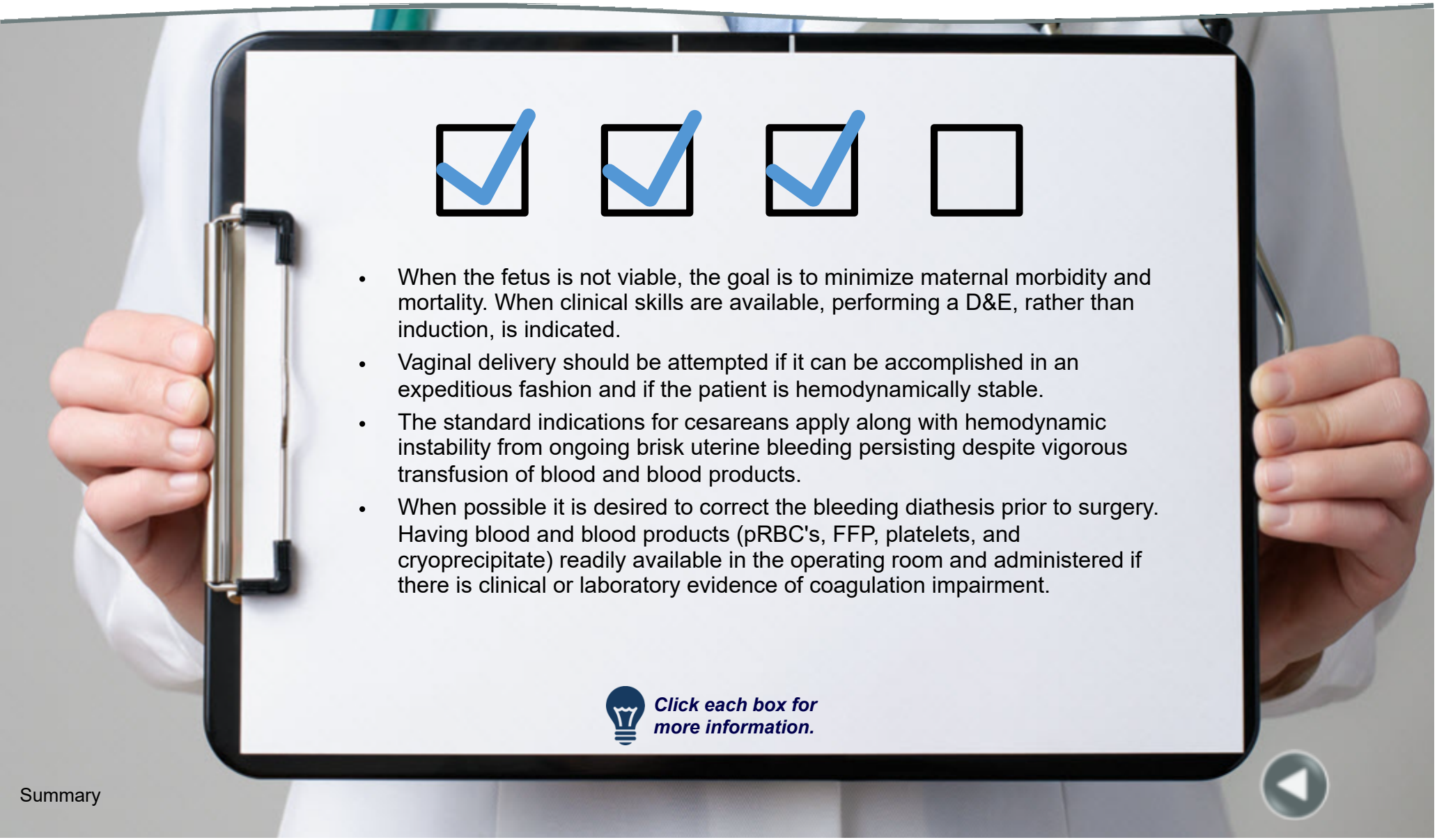
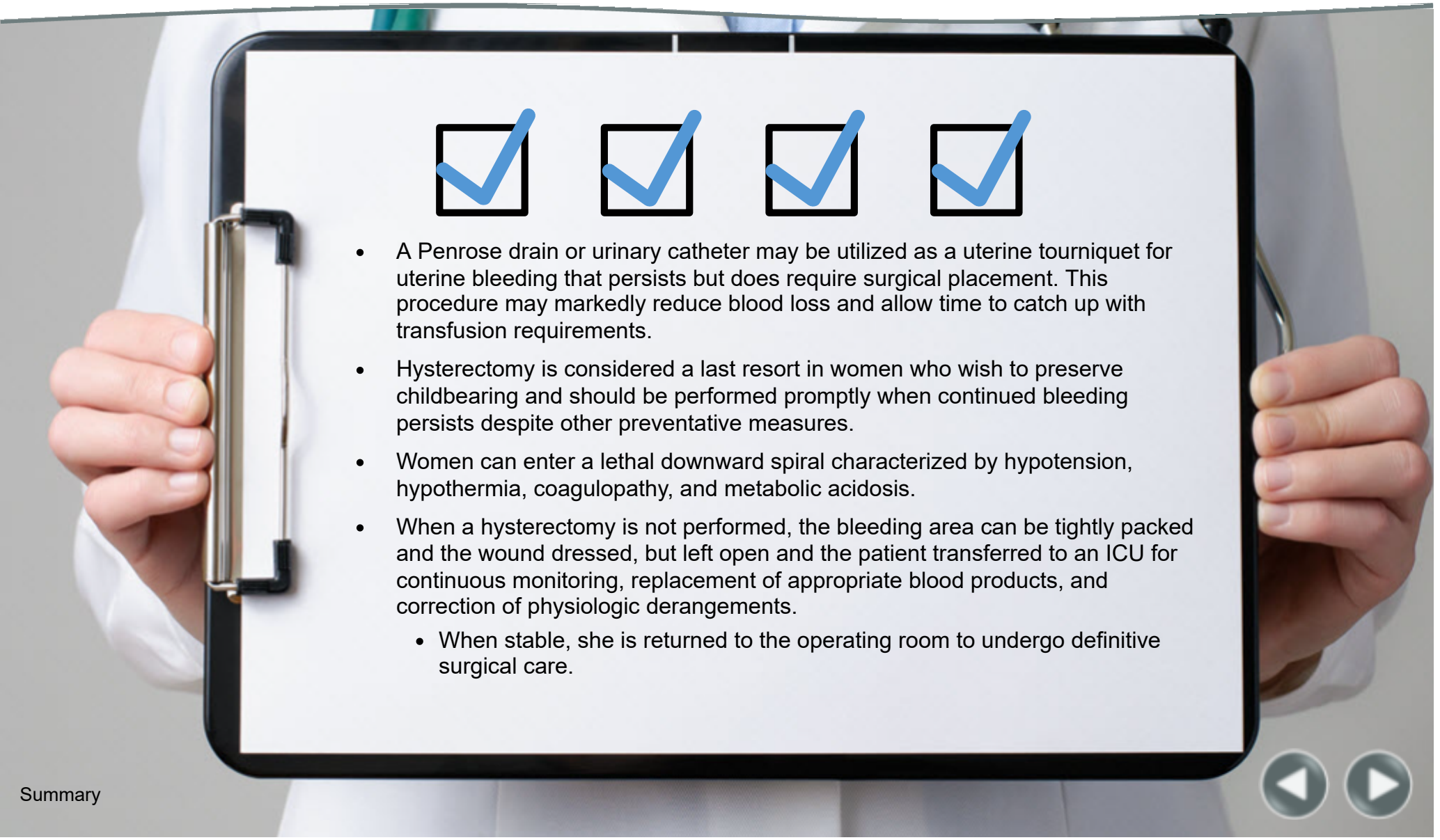


- When the fetus is not viable, the goal is to minimize maternal morbidity and mortality. When clinical skills are available, performing a D&E, rather than induction, is indicated.
- Vaginal delivery should be attempted if it can be accomplished in an expeditious fashion and if the patient is hemodynamically stable.
- 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.
- Women can enter a lethal downward spiral characterized by hypotension, 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.

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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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