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Venous Thromboembolic Disease

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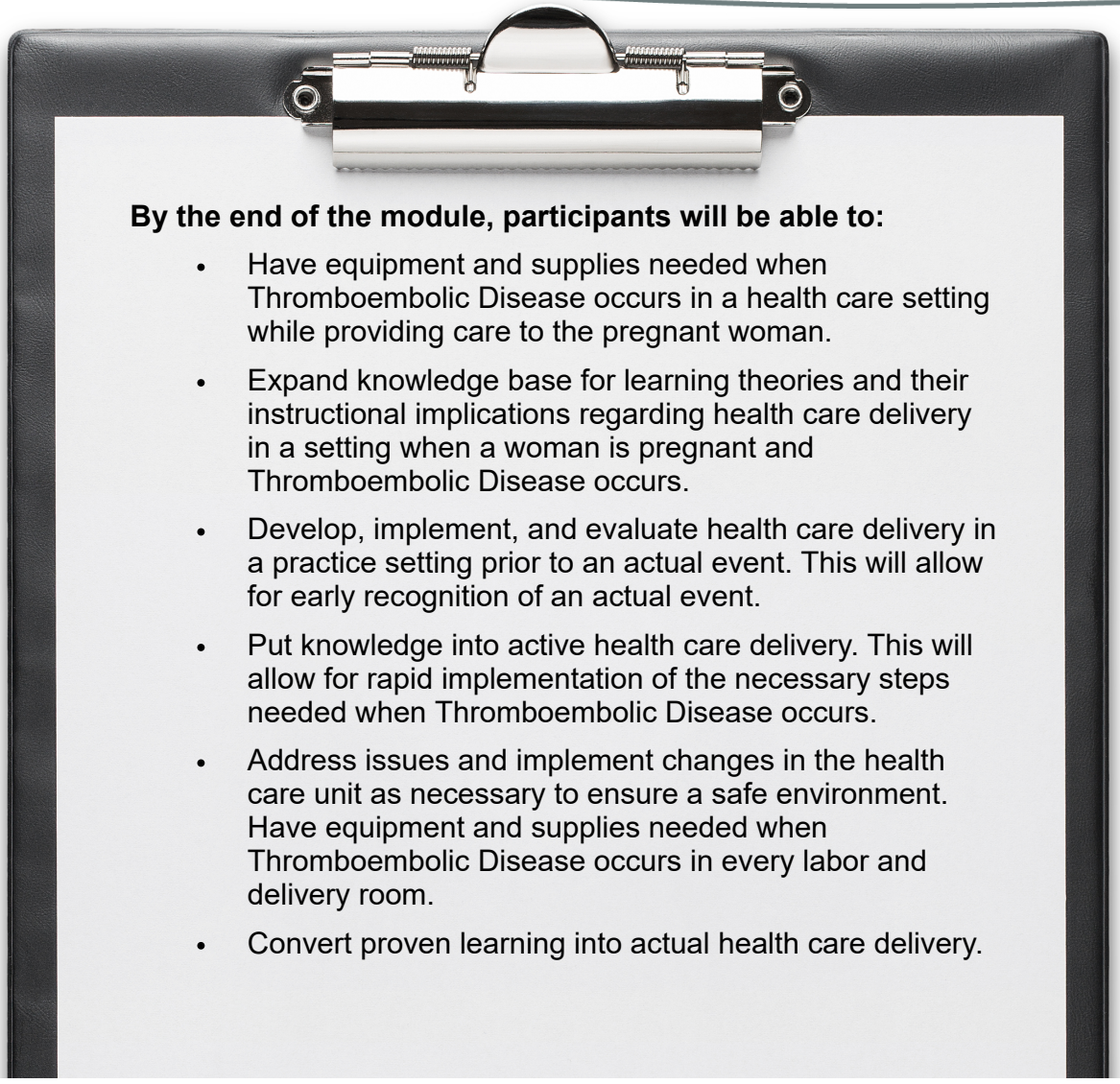
Course Description:

Venous thromboembolic (VTE) disease is a high acuity, low occurring process that when recognized can be managed. The course will help by giving understanding of the disease and its management. VTE is a detrimental disease process that is life threatening for the women it effects. The VTE course will provide knowledge for treatment of the pregnant woman while keeping the fetus safe.

Approximate Time to Complete: 70 minutes

Click here to download a print version of this course.



By the end of the module, participants will be able to:

- Have equipment and supplies needed when Thromboembolic Disease occurs in a health care setting while providing care to the pregnant woman.
- Expand knowledge base for learning theories and their instructional implications regarding health care delivery in a setting when a woman is pregnant and Thromboembolic Disease 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.
- Put knowledge into active health care delivery. This will allow for rapid implementation of the necessary steps needed when Thromboembolic Disease occurs.
- Address issues and implement changes in the health care unit as necessary to ensure a safe environment. Have equipment and supplies needed when Thromboembolic Disease occurs in every labor and delivery room.
- Convert proven learning into actual health care delivery.

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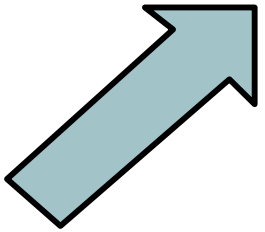


- The **Home** button will take you to the beginning of this course.
- The **Help** button will show you the features of this module
- The **X** will close this course

Venous Thromboembolic Disease

Collectively, deep venous thrombosis (DVT) and pulmonary embolism (PE) are referred to as venous thromboembolic disease (VTE).

Pregnancy is an established risk factor for VTE.

- The diagnosis of VTE occurs 1 in 500 - 2000 pregnancies within the United States [1-7].
- Compared to PE, DVT was three times more common [5].
- 75-80% of cases of VTE in pregnancy are caused by DVT, as compared to 20-25% of cases caused by PE. One half of cases occur in pregnancy and the other half postpartum [43].

Incidence

PE accounts for 9% of maternal deaths and is the seventh leading cause of maternal mortality [9-11].

- Black women have a three to four times higher pregnancy related mortality rate than white women.
  - Deaths from VTE are higher in black women and the reasons for this cannot be directly attributed to increased rates of VTE [8].

Carefully consider the risk assessment protocols available and adopt them in a systematic way to reduce the incidence of VTE in pregnancy and postpartum.

Click here to learn more about occurrence of VTE.

Incidence

From the late 1990's to early 2000, the incidence of VTE decreased, largely due to a decrease in postpartum VTE incidence [5, 12].

- This change could be due to the general increase in the use of thrombo-prophylaxis in the postpartum period.

However, VTE associated pregnancy hospitalizations between 1994 and 2009 demonstrates an increase of 14% with a concomitant increase in comorbid conditions such as obesity and hypertension among those admitted for VTE [13].

- When compared to non-pregnant women, there is 4-50x increased risk of VTE in pregnancy [1-6, 93].
- Further risk occurs in women with inherited thrombophilias.
- A personal history of thrombosis is the most important risk factor for VTE in pregnancy, increasing a woman's risk 3-4 fold [36].

- Compared to the nonpregnant population, the risk of VTE is higher in all stages of pregnancy, however, it is greatest in the postpartum period.
  - Equal distribution of VTE across trimesters of pregnancy is found in most studies [1, 2, 13-17].
  - However, there have been two large retrospective studies showing predominance in the first trimester (50% before 15 weeks) and third trimester (60%) [18, 19].
  - 50% of episodes of VTE occur in the postpartum period; the highest risk time period is within the first 6 weeks.

Risk Factors for VTE

- Personal history of thrombosis
- Personal history of thrombophilia
- Cesarean delivery
- Postpartum hemorrhage
- Postpartum infection [20]
- Obesity [21]
- Hypertension and Preeclampsia
- Autoimmune disease
- Advanced maternal age
- Heart Disease
- Sickle cell disease
- Multiple gestation [20]

- For the first six weeks postpartum, the risk is highest and slowly declines to rates approximate to that of the general population by 13-18 weeks [22].
- Commonly cited factors that increase the risk of VTE postpartum include the following [14,17,19, 20, 22-24]:
  - Cesarean delivery (a fourfold increase risk compared to vaginal birth) [68]
  - Medical comorbidities
    - Varicose veins
    - Cardiac disease
    - Inflammatory bowel disease
  - Body mass index (BMI) ≥25kg/m2
  - Young gestational age
    - Preterm delivery <36 weeks gestation
  - Obstetric hemorrhage
  - Stillbirth
  - Increased maternal age ≥35 years
  - Hypertension
  - Smoking
  - Eclampsia or preeclampsia
  - Postpartum infection

The majority of lower extremity DVT's occur on the left side in pregnancy and most commonly in the proximal veins (i.e. femoral). In addition, pelvic vein thrombosis is significantly higher during pregnancy and the puerperium.

There is no research describing an increased incidence of upper extremity DVT during pregnancy nor the puerperium.

Left Lower Extremity DVT

- DVT is predominantly left-sided in pregnancy (70 to 90%).
- In a retrospective study of 124 pregnant women with a DVT, the left leg was affected in 88% of the women [25].
- The left leg predominance has been attributed to increased venous stasis in the left leg related to compression of the left iliac vein, coupled with compression of the inferior vena cava by the gravid uterus [14, 26, 27].

Pelvic Vein DVT

- Pelvic vein DVT is more commonly diagnosed in pregnancy than in the general population.
- The true prevalence in pregnancy is unknown and may be due to poor sensitivity of compressing the proximal vein during ultrasound for the diagnosis of thrombosis in the pelvic veins [28].

The VTE risks are higher in pregnant women who have inherited thrombophilias [4, 29-35].

The thrombotic risk is three times higher for pregnant women with factor V Leiden, compared to the general population [29].

Low Risk Thrombophilia	High Risk Thrombophilia
Factor V Leiden heterozygous	Factor V Leiden homozygosity
Prothrombin gene mutation heterozygosity	Prothrombin gene mutation homozygosity
Protein C deficiency	Heterozygosity for Factor V Leiden and Prothrombin gene mutation
Protein S deficiency	Antithrombin III deficiency

Inherited Thrombophilias in Pregnancy

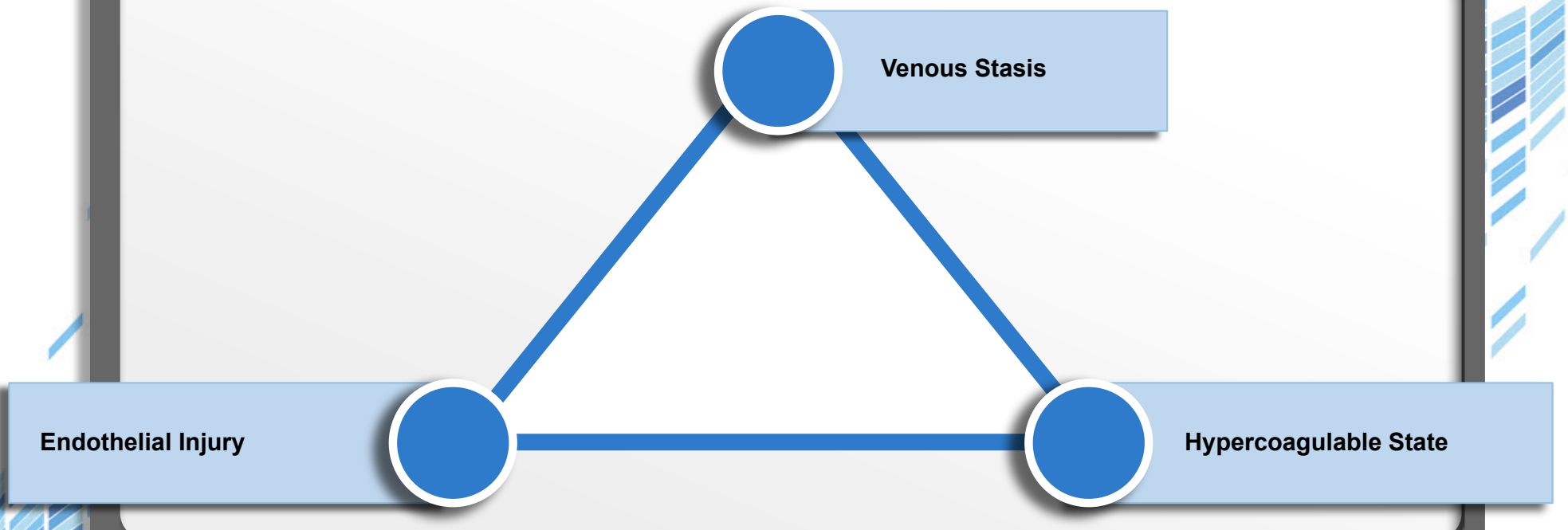
- The thrombotic risk is three times higher for pregnant women with factor V Leiden, compared to the general population [29].
- Pregnant women with an inheritable deficiency of antithrombin III, protein S, or protein C have an 8-fold increase risk of venous thrombosis in the antepartum and postpartum periods combined, compared to pregnant women without a known thrombophilia [30].
- One study described a 5% risk of thrombosis during pregnancy among women with known antiphospholipid syndrome [37].

Indications for VTE Prophylaxis

- VTE prophylaxis is recommended in pregnancy if the patient meets any of the following criteria:
  - Prior history of VTE (either DVT or PE)
  - Low risk thrombophilia with history of VTE
  - High risk thrombophilia without history of VTE
- If prophylatic anticoagulation is recommended, the treatment is Lovenox 40 mg daily if patient weight is <90 kg or Lovenox 40 mg BID if weight is >90 kg
- If the patient cannot tolerate lovenox, or if insurance does not cover the medication, Heparin can be used with dosing determined by trimester
  - 1st trimester - 5,000 units BID
  - 2nd trimester - 7,500 units BID
  - 3rd trimester - 10,000 units BID

Pathophysiology of VTE

Virchow's triad describes 3 factors that are known to be associated with VTE [2]:



All 3 risk factors are present in pregnancy, which likely contributes to the increased risk of VTE in pregnancy.

Pathophysiology of VTE

Two factors lead to venous stasis of the lower extremities during pregnancy:

- Pregnancy-associated changes in venous capacitance
- Compression of large veins by the gravid uterus.

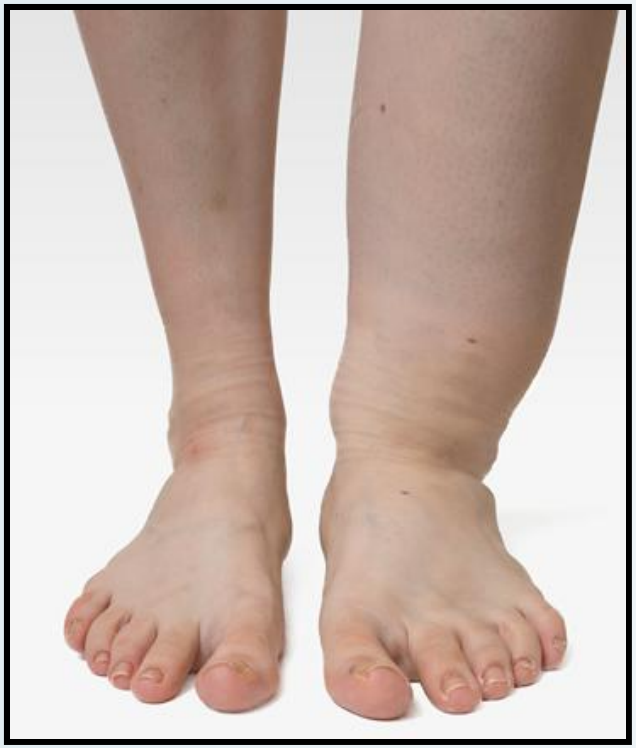
The increased venous stasis during pregnancy appears to occur even before the uterus has enlarged substantially.

The venous pooling and valvular incompetence are due to hormonally induced dilation of veins decreasing the linear flow velocity in the lower extremities, although blood volume and total venous return are supra-normal in pregnancy [38].

Pathophysiology of VTE

- Pathogenesis for VTE in pregnancy is thought to involve endothelial injury. Delivery is associated with vascular injury and changes at the uteroplacental surface, likely contributing to the increased risk of VTE in the immediate postpartum period.
- Vascular intimal injury can be exaggerated by forceps, vacuum, or surgical delivery and amplify this phenomenon [1].

- During pregnancy, protein S decreases; however, there is a progressive increase in several coagulation factors including factors I, II, VII, VIII, IX, and X [1, 29, 38, 39].
- A resistance to activated protein C progressively increases in the second and third trimesters, which adds to the hypercoaguable state [41].



Clinical Features

- The clinical presentation of DVT in pregnancy is identical to a non-pregnant woman.
- When the proximal vein has a thrombus, the signs and symptoms to suggest this diagnosis are diffuse pain and swelling that may or may not be associated with erythema, warmth and tenderness of the lower extremity.
- Iliac vein thrombosis has symptoms including swelling of the entire leg with or without flank, lower abdomen, buttock or back pain [42].
- Typical symptoms include:
  - Unilateral leg pain
  - Unilateral edema
  - Unilateral lower extremity tenderness
  - Enlarged leg circumference

Laboratory Considerations

- Laboratory evaluation is not typically helpful in the diagnosis of VTE. D-dimer has limited diagnostic value in pregnant women due to elevated values regardless of presence of VTE
  - However, it does have a strong negative predictive value
  - When D-dimer is < 500ng/mL, DVT is unlikely [61].

- There are not established normal reference ranges during pregnancy, thus the altered levels of D-dimer throughout pregnancy and the puerperium are subject to misinterpretation.
  - False negative D-dimer's have been reported in pregnant women with DVT or PE [36].

Diagnosis of VTE

- Initial recommended test is compression ultrasound (CUS) of the proximal veins.
  - As opposed to non-pregnant patients in which DVT is most commonly distal, in pregnancy, DVT is commonly proximal.
  - 64% are ileofemoral, 17% are iliac
- In both pregnant and non-pregnant patients, the proximal vein CUS is highly sensitive and specific for the diagnosis of DVT.
- If results are negative or equivocal, and iliac vein thrombosis is suspected, additional imaging with Doppler ultrasound of the iliac vein, venography or MRI is recommended.
- DVT in pregnancy is most often diagnosed by demonstrating poor compressibility of the proximal veins on compressionultrasound (CUS).
- In both pregnant and non-pregnant patients, the proximal vein CUS is highly sensitive and specific diagnostic study for the diagnosis of DVT.
- CUS is less sensitive for pelvic vein thrombosis and distal lower extremity vein thrombosis [28].

Click the left and right arrows to see more.

Compression Ultrasonography (CUS)

- For diagnosing proximal vein thrombosis in pregnant patients poor compressibility of a thigh vein with ultrasound probe is highly sensitive (95%) and specific (>95%) [47].
- To assist in diagnosing isolated iliac vein thrombosis during pregnancy, patient positioning in the left lateral decubitus and the addition of doppler analysis for flow variation with respiration helps [43].
- Utilizing serial CUS can detect suspected distal lower extremity vein thrombosis that propagates proximally as progression of pregnancy occurs.

Click the left and right arrows to see more.

Serial Compression Ultrasonography

- Distal lower extremity vein thrombosis can propagate proximally in approximately 20% of cases in non-pregnant patients [45].
- In non-pregnant patients, performing day 3 and day 7 serial CUS has confirmed DVT in the setting of initially negative CUS [45, 46].
- Using this modality, of all patients with suspected DVT with initial negative CUS, only 2% are subsequently diagnosed with DVT [45].
- Similar findings have been demonstrated in limited studies on pregnant women.

Click the left and right arrows to see more.

Magnetic Resonance Venography

- A modality that can detect both thigh and pelvic vein DVT with a sensitivity approaching 100% in the non-pregnant population [48].
- Data is limited in pregnancy.
- Small case series of pregnant patients suggest this modality is useful for the diagnosis of pelvic and femoral vein thrombosis in situations where other non-invasive exams were equivocal [49, 50].
- MRI contrast cannot be utilized in pregnancy due to fetal risk.

Click the left and right arrows to see more.

Ascending Contrast Venography

- In the non-pregnant population, the gold standard for diagnosing lower extremity DVT is visualizing a filling defect by ascending contrast venography [52, 53].
- In pregnancy, venography is rarely performed due to concerns of exposure of ionizing radiation to the fetus, technical difficulties of femoral vein cannulation and decreased sensitivity for isolated ileofemoral thrombosis due to abdominal pelvic shielding [1, 44, 51].
- The alternative imaging test, CUS, approaches venography in diagnostic sensitivity and specificity without these risks, rendering contrast venography less useful for the diagnosis of DVT [1, 44, 51].

Pretest Probability

Predictive scoring systems (i.e. Wells score), the LEFt clinical prediction rule and D-dimer levels are clinical probability assessment tools for the diagnosis of suspected DVT.

Unfortunately, these tools have not been validated in large prospective trials and or in pregnancy; therefore, are not recommended.

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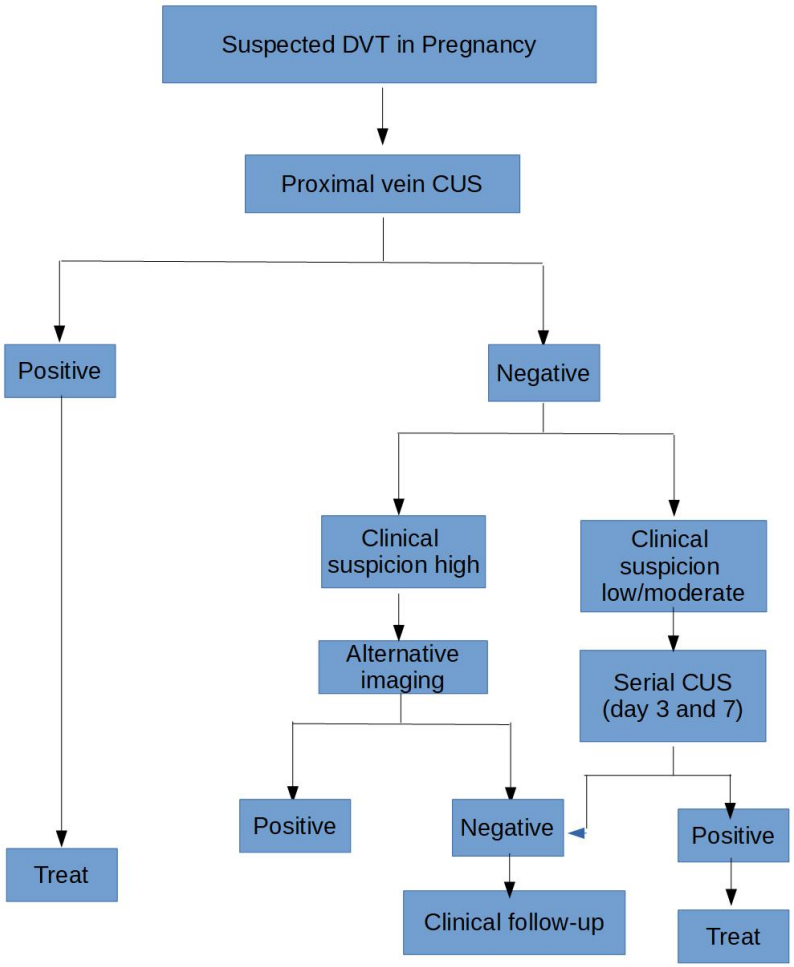
Diagnosis Algorithm for Suspected Deep Venous Thrombosis in Pregnancy



Diagnosis

- With concerning signs and symptoms (i.e. suspected iliac vein thrombosis with swelling of the entire leg and buttock), it may be warranted to obtain evaluation with doppler ultrasound directed at the iliac vein followed by magnetic resonance and then contrast venography, as needed.
- Emperic anticoagulation is suggested in these pregnant women.
- Preference to avoid unnecessary anticoagulation occurs when the risk of DVT is low.
    - Safety for withholding anticoagulation in this setting is assured from data with non-pregnant [48, 59, 64] and pregnant patients [50-52, 59, 61].
- Consider measuring D-dimer levels as an alternative if serial CUS is not feasible. When D-dimer is < 500ng/mL, DVT is unlikely [61].
- With ultrasound and magnetic resonance imaging, there is no measurable radiation exposure associated with these testing modalities.

Differential diagnosis of DVT

- Differential diagnosis in pregnancy is similar to non-pregnant patients
- Lower extremity edema
- Superficial thrombophlebitis
- Cellulitis
- Muscle strain
- Varicose veins

Differential diagnosis of VTE

- The diagnosis of PE is similar to that in non-pregnant women.
- Options include ventilation-perfusion scanning (VQ scan) or computed tomographic (CT) angiography.
  - Both types of studies are associated with low risk of radiation exposure to the fetus.
    - Fetal exposure from a VQ scan is 0.32-0.64 mGy.
    - Fetal exposure from CT angiography is 0.0033-0.1398, depending on the trimester in which it is performed.
  - Maternal radiation exposure is lower with VQ scanning.
  - The American Thoracic Society and Society of Thoracic Radiology clinical practice guidelines for evaluation of PE suggest a chest x-ray be used for initial evaluation.
    - Progression to VQ scan is recommended if the chest x-ray is normal.
    - Progression to CT angiography is recommended if the chest x-ray is abnormal.
    - This step-wise approach potentially limits radiation exposure to the pregnant woman.
    - However, the study that is initially performed relies on local availability and expertise. It is unclear which study is more accurate.

Management

- Empiric anticoagulation is indicated prior to diagnostic testing when there is a high suspicion for acute PE.
- Anticoagulant therapy is discontinued if VTE is excluded.
- If DVT or PE is diagnosed in pregnancy, the patient should be started on therapeutic Lovenox
  - Typical dosing is Lovenox 1 mg/kg BID.
  - Alternatively, the patient can be started on a Heparin drip.
- If anticoagulation is contraindicated, consideration should be given to placement of an IVC filter.

- Consider discussing prophylaxis if prior DVT or thromboembolic disease (i.e. Factor V Leiden) is present.
- Provide prophylaxis in pregnancy when indicated (i.e. compression stockings preop for cesarean).

The following approach is consistent with the 2012 American College of Chest Physicians (ACCP) guidelines on VTE and pregnancy [56].

Once anticoagulation is indicated, it should be initiated using subcutaneous low molecular weight Heparin (SC LMWH), or intravenous unfractionated Heparin (IV UFH) [54].

- **Subcutaneous LMWH**
- **IV UFH**
- **Warfarin**
- **Synthetic Heparin**
- **Subcutaneous Heparin**

Subcutaneous LMWH

- Subcutaneous LMWH is preferred over IV UFH or SC UFH because it has:
  - Fewer bleeding episodes
  - More predictable therapeutic response
  - Lower risk of heparin-induced thrombocytopenia
  - Longer half-life
  - Less bone mineral density loss
- SC LMWH decreased mortality and recurrent thrombosis.
- SC LMWH is more likely to reduce thrombus size and less likely to cause major hemorrhage [55].

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IV UFH

- IV UFH is preferred in patients with marked elevated risk of hemorrhage or persistent hypotension due to PE.
- IV UFH has a short half life and can potentially be reversed with protamine.
- Either IV UFH or SC UFH is preferred over SC LMWH when the pregnant woman has severe renal failure.
- IV UFH should be considered if delivery is imminent, surgery is planned or if thrombolysis is planned.

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Warfarin or direct oral anticoagulants

Contraindicated in pregnancy due to risk of teratogenicity. The only situation in which warfarin is considered in pregnancy is in the setting of a mechanical heart valve.

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- **Subcutaneous LMWH**
- **IV UFH**
- **Warfarin**
- **Synthetic Heparin**
- **Subcutaneous Heparin**

Synthetic Heparin

- Due to the lack of safety date, synthetic heparin pentasaccharides (i.e. fondaparinux, indraparinux) not recommended in pregnancy.

The following approach is consistent with the 2012 American College of Chest Physicians (ACCP) guidelines on VTE and pregnancy [56].

Once anticoagulation is indicated, it should be initiated using subcutaneous low molecular weight Heparin (SC LMWH), or intravenous unfractionated Heparin (IV UFH) [54].

- **Subcutaneous LMWH**
- **IV UFH**
- **Warfarin**
- **Synthetic Heparin**
- **Subcutaneous Heparin**

Subcutaneous Heparin

- Not recommended in the setting of active VTE due to difficulty in achieving reliable anticoagulation.
- If necessary to use, follow PTT levels. The level should be 1.5-2.5x the upper limit of normal 6 hours after an injection.

The following regimens are reasonable for the initial treatment of VTE during pregnancy or the puerperium.

- Regardless of the regimen, anticoagulant therapy should continue through the pregnancy.
  - **LMWH**
  - **IV UHF**
  - **SC UHF**

- Reasonable initial dosages of SC LMWH include [56, 57]:
- Dosing may require adjustment to maintain an anti-Xa level of 0.6-1.0iu/mL for [56, 58, 59].
- The anti-Xa level is first measured six hours after the third or fourth dose with every 12 hour dosing.
- Typical adjustments involve an increase or decrease by 10-25%.
- Some clinicians recheck the anti-Xa level every one to three months, once satisfactory levels are obtained; however, this is controversial because few women require dose adjustments [49].

Antifactor Xa levels are not required when LMWH is utilized for prophylactic anticoagulation because the optimal level has not been determined.

The following regimens are reasonable for the initial treatment of VTE during pregnancy or the puerperium.

- Regardless of the regimen, anticoagulant therapy should continue through the pregnancy.
  - **LMWH**
  - **IV UHF**
  - **SC UHF**

- IV UFH dosing consists of initial bolus of 80 units/kg followed by a continuous infusion of 18 units/kg per hour [55].
- Every four hours the infusion is titrated to achieve therapeutic activated partial thromboplastin time (aPTT).
- Each laboratory will have specified target ranges for the aPTT. Once this target level is reached, it should be rechecked once or twice daily.
- When long term or outpatient anticoagulant therapy is planned, the IV UFH should be transitioned to SC LMWH [56].

The following regimens are reasonable for the initial treatment of VTE during pregnancy or the puerperium.

- Regardless of the regimen, anticoagulant therapy should continue through the pregnancy.
  - **LMWH**
  - **IV UHF**
  - **SC UHF**

- A reasonable initial dose of SC UFH is 17,500 units every 12 hours.
- The SC UFH dose is then titrated to achieve therapeutic aPTT, where the aPTT level corresponds to an anti-Xa level of 0.3-0.7IU/mL [56].
- The target aPTT range is 1.5-2.5x the upper limit of normal, which varies depending on the lab.
- It is typical to have the first aPTT level measured six hours after the second dose then adjust by an increase or decrease of 10-30%.
- The aPTT may be measured after 3-4 days of treatment once a stable dose is achieved and then every few weeks.
- During the last 10 weeks of the pregnancy, more frequent monitoring is warranted.

Treatment

- Initiating LMWH is appropriate with low risk patients in an outpatient setting. Hospitalization may be warranted with the use of IV UFH when there is a large clot, maternal co-morbidities, or hemodynamic instability. A transition to LMWH may be started as the patient becomes hemodynamically stable [36, 40]

LABOR AND DELIVERY

When delivery is predicted (i.e. induction, scheduled cesarean), treating with SC LMWH should be discontinued 24 hours prior.

- This is particularly important for patients who desire neuraxial anesthesia. Neither spinal or epidural anesthesia is offered within 24 hours of a SC LMWH injection due to risk of spinal hematoma.

When the pregnant patient has a high risk for recurrent VTE (i.e. those with acute PE or proximal DVT developed in the past month), it may not be desirable to stop the anticoagulation therapy for 24-36 hours.

- These patients may benefit from having their anticoagulation switched to IV UFH.
- The IV UFH can be discontinued 4-6 hours prior to delivery [56].

Once the aPTT is in the normal range, a neuraxial catheter may be placed [60].

Immediately Post Partum

- Anticoagulation should be started twelve hours after cesarean delivery or six hours after a vaginal delivery, when significant bleeding has not occurred.
- Typically, patients are restarted on whichever anticoagulant was used during pregnancy.
- Long term anticoagulation therapy options include SC LMWH, SC UFH or an oral vitamin K antagonist (i.e. warfarin).
- When warfarin therapy is the chosen option, the patient should receive both warfarin and Heparin for at least five days due to a transient increased risk of VTE with initiation of warfarin.
- Once the international normalized ratio (INR) has been in the therapeutic range for two consecutive days, then the Heparin can be discontinued.
- Warfarin is safe during breastfeeding.[61].

Length of Therapy

The determination of length of anticoagulation should be individualized because the optimal duration is unknown.

Anticoagulation should occur for 3-6 months in women whose only risk for VTE were transient, such as pregnancy and cesarean delivery [56, 62-64].

Inferior Vena Cava Filters

Inferior vena cava (IVC) filters have been used during pregnancy with indications being the same in pregnant women as non-pregnant patients. Indications for use include the following [65, 66]:

- During active bleeding, following recent surgery or following a hemorrhagic stroke, when conventional anticoagulation is contraindicated.
- In women who develop new VTE despite being anticoagulated.
- When a complication occurs from anticoagulation, such as significant bleeding.
- In the setting of massive PE, particularly with right heart strain.
- Consideration may be given for IVC filter if VTE is diagnosed at term gestation when delivery is planned within a short period of time.
- Careful consideration must be given to IVC filter placement in pregnancy due to risk of migration or embedding into the vascular wall.

Thrombolysis and Thrombectomy

- Thrombolytic therapy should be reserved for pregnant patients with life-threatening acute PE [85].
- Teratogenicity due to thrombolytic agents has not been reported, but the risk of maternal hemorrhage is high.
- In a review of case reports and case series (172 pregnant women undergoing treatment with thrombolytic agents) shows the maternal mortality was one percent, the incidence of fetal loss was six percent and the incidence of maternal hemorrhagic complications was eight percent [67].
- Case studies of thrombectomy report its successful use as a life saving measure when other measures have failed [68, 69].

Heparin has several side effects, including bleeding, thrombocytopenia, skin necrosis, and osteoporosis. These adverse effects can occur even at prophylactic doses but are more likely with long term use.

Bleeding

Skin Necrosis

Osteoporosis

Thrombocytopenia

The bleeding management during heparin therapy depends upon:

- The location and severity of bleeding
- The risk of discontinuing the anticoagulant

In many cases, the heparin can be stopped and restarted after the bleeding is controlled.

Consideration to insert an inferior vena cava filter (IVC) should occur if the bleeding is severe enough to prohibit resumption of anticoagulation.

The anticoagulation therapy should not be resumed if the bleeding is related to a placenta previa or abruption. However, this recommendation is based on low quality evidence.

Click the side effects above to learn more.

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These adverse effects can occur even at prophylactic doses but are more likely with long term use.

Bleeding

Skin Necrosis

Osteoporosis

Thrombocytopenia

Skin Necrosis

Heparin-induced skin necrosis is a manifestation of Heparin Induced Thrombocytopenia (HIT) and may occur in the absence of thrombocytopenia.

Click the side effects above to learn more.

Heparin has several side effects, including bleeding, thrombocytopenia, skin necrosis, and osteoporosis.
These adverse effects can occur even at prophylactic doses but are more likely with long term use.

Bleeding

Skin Necrosis

Osteoporosis

Thrombocytopenia

Osteoporosis

Long term heparin therapy, longer than seven weeks, can reduce bone mineral density by reducing bone formation.

This effect appears more common with unfractionated heparin than low molecular weight heparin.

Click the side effects above to learn more.

Heparin has several side effects, including bleeding, thrombocytopenia, skin necrosis, and osteoporosis. These adverse effects can occur even at prophylactic doses but are more likely with long term use.

Bleeding

Skin Necrosis

Osteoporosis

Thrombocytopenia

Thrombocytopenia

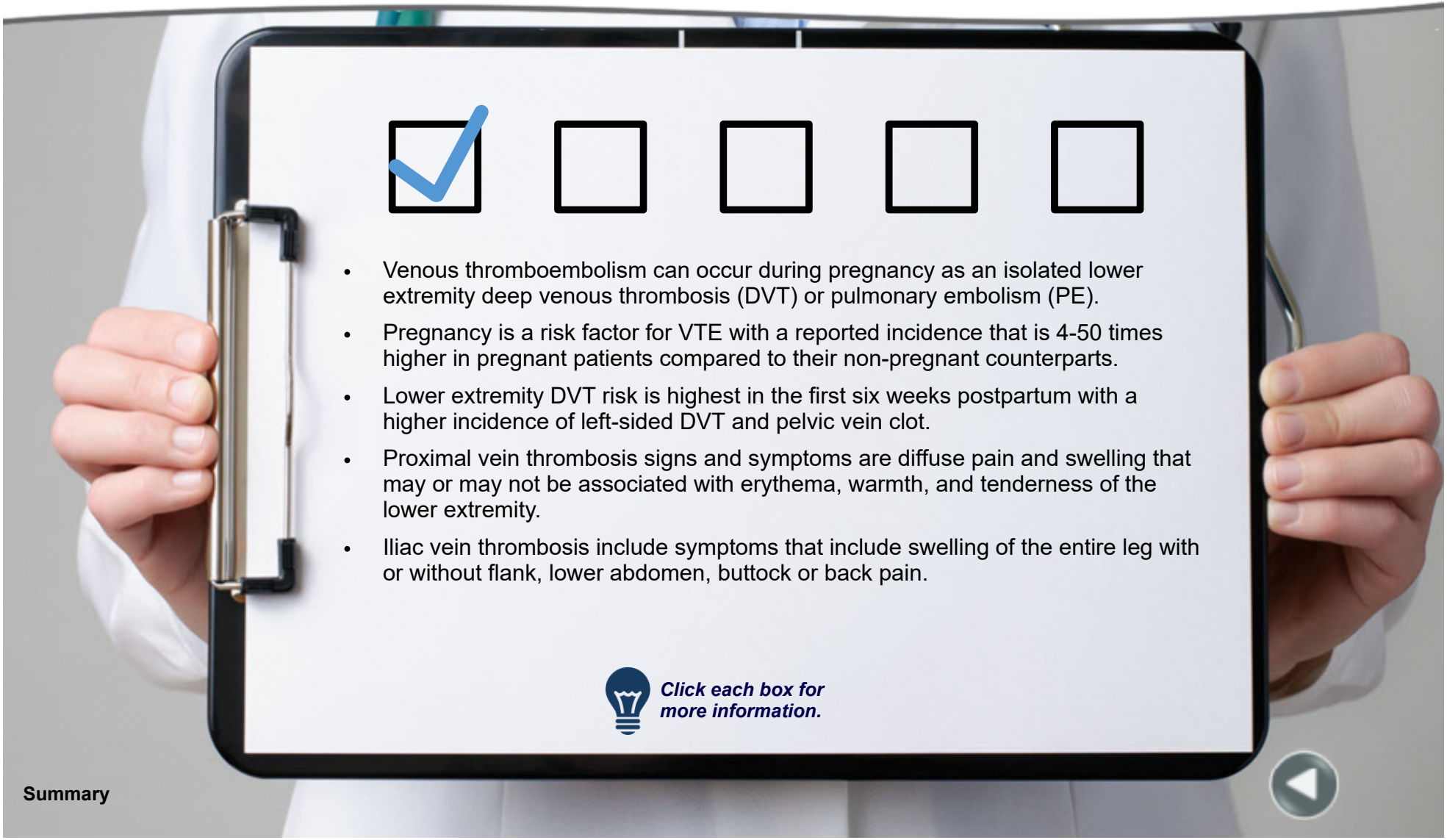
- Heparin-induced thrombocytopenia (HIT) is a potentially fatal complication of Heparin therapy.
- The risk of HIT in the obstetric population is <0.1%.
- Guidelines recommend obtaining platelet counts at the initiation of anticoagulation if the risk of HIT is >1%; therefore, platelet monitoring is not needed for most obstetric patients.

Click the side effects above to learn more.

Click the right arrow to go to the next page.

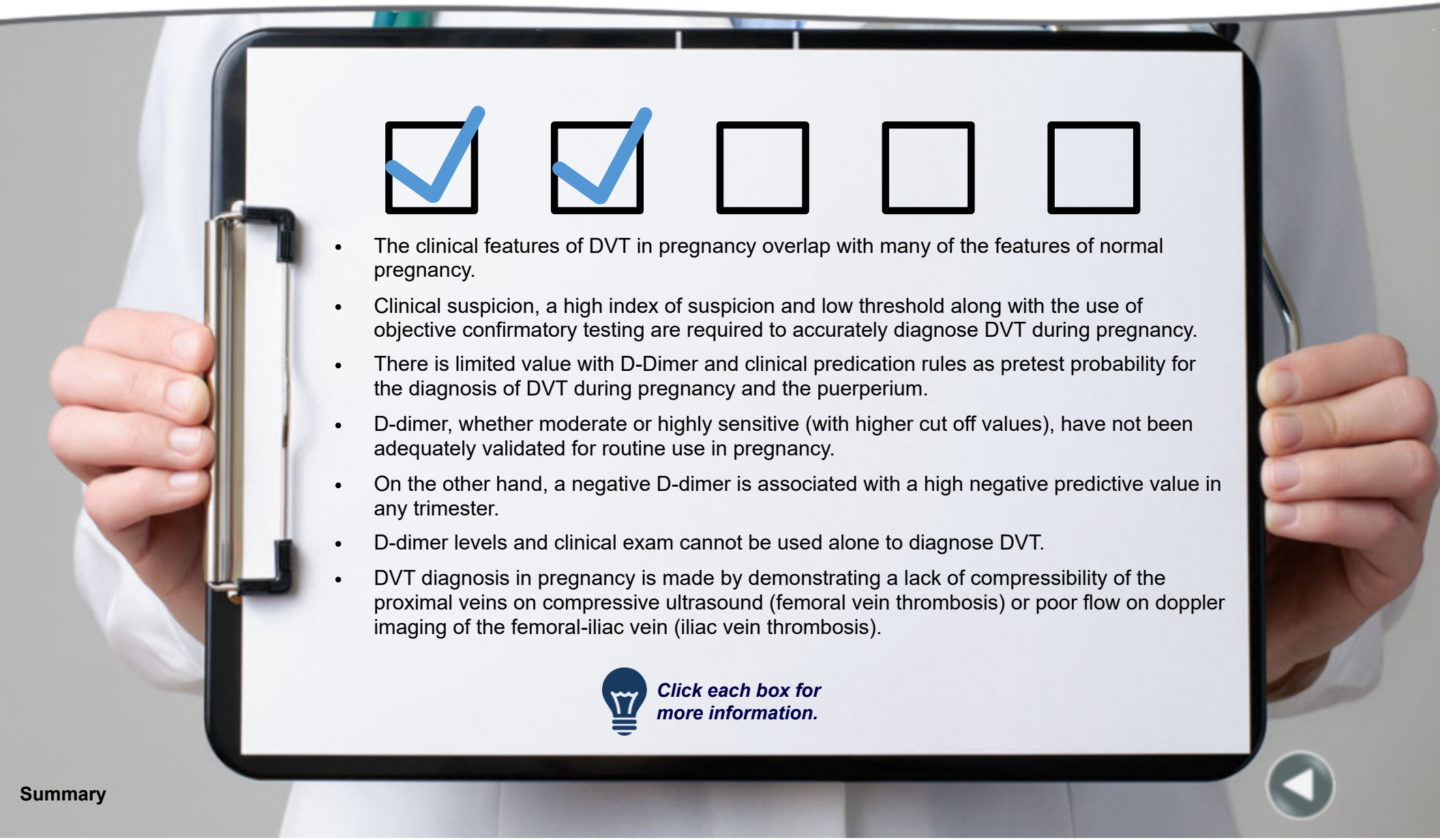
Clinical Scenario	Antepartum Management	Postpartum Management
No history of VTE, no thrombophilia	Surveillance* without anticoagulation therapy	Surveillance without anticoagulation therapy or postpartum prophylaxis anticoagulation therapy if the patient has multiple risk factors VT†
VTE diagnosed during pregnancy	Adjusted-dose LMWH/UFH	Adjusted-dose LMWH/UFH for a minimum of 6 weeks postpartum. Longer duration of therapy may be indicated depending on the timing of VTE during pregnancy, prior VTE history, or presence of thrombophilia. Oral anticoagulants may be considered postpartum based upon planned duration of therapy, lactation, and patient preference.
Single provoked VTE (precipitated by a single event such as surgery, trauma, or immobility) unrelated to estrogen or pregnancy due to a transient (resloved risk factor, non thrombophilia	Surveillance* without anticoagulation therapy	Surveillance without anticoagulation therapy or postpartum prophylactic anticoagulation therapy if the patient has additional risk factors †
History of single unprovoked VTE (no identified precipitating factor present; includes prior VTE in pregnancy or associated with hormonal contraception), not on long-term anticoagulation	Prophylactic, intermediate-dose, or adjusted-dose LMWH/UFH	Prophylactic, intermediate-dose, or adjusted-dose LMWH/UFH regimen for 6 weeks postpartum
Low risk thrombophilia‡ without previous VTE	Surveillance* without anticoagulation therapy	Surveillance without anticoagulation therapy or postpartum prophylactic anticoagulation therapy if the patient has additional risk factors‡
Low risk thrombophilia‡ with a family history (first-degree relative) of VTE	Surveillance* without anticoagulation therapy or prophylactic LMWH/UFH	Postpartum prophylactic anticoagulation therapy or intermediate-dose LMWH/UFH
Low risk thrombophilia‡ with a single previous episode of VTE--Not receiving long-term anticoagulation therapy	Prophylactic or intermediate-dose LMWH/UFH	Postpartum prophylactic anticoagulatioon therapy or intermediate-dose LMWH/UFH
High risk thrombophilia¥ without previous VTE	Prophylactic or intermediate-dose, or adjusted dose LMWH/UFH	Postpartum prophylactic anticoagulatioon therapy or intermediate-dose LMWH/UFH
High risk thrombophilia¥ with a single previous VTE or an affected first-degree relative--Not receiving long-term anticoagulation therapy	Prophylactic intermediate-dose or adjusted-dose LMWH/UFH	Postpartum prophylactic anticoagulatioon therapy or intermediate or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be equal to the selected antepartum treatment)
Two or more episodes of VTE--Not receiving long-term anticoagulation therapy (regardless of thrombophilia)	Intermediate-dose or adjusted-dose LMWH/UFH	Postpartum prophylactic anticoagulatioon therapy or intermediate or adjusted-dose LMWH/UFH for 6 weeks (therapy level should be equal to the selected antepartum treatment)
Two or more episodes of VTE--Not receiving long-term anticoagulation therapy (regardless of thrombophilia)	Adjusted-dose LMWH/UFH	Resumption of long-term anticoagulation therapy. Oral anticoagulants may be considered postpartum based upon planned duration of therapy, lactation, and patient preference.

Abbreviations: LMWH, low molecular weight heparin, UFH, unfractionated heparin; VTE, venous thromboembolism
*VTE risk assessment should be performed prepregnancy or early in pregnancy and repeated if complications develop, particularly those necessitating hospitalization or prolonged immobility.
†First-degree relative with a history of thrombotic episode, or other major thrombotic risk factors (eg, obesity, prolonged immobility, cesarean delivery).
‡Low-risk thrombophilia: Factor V leiden heterozygote; prothrombin G20210A mutation heterozygote; protein C or protein S deficiency, antiphospholipid antibody.
¥High-risk thrombophilias include Factor V leiden homozygosity prothrombin G20210A mutation homozygosity, heterozygosity for factor V Leiden and prothrombin G20210A mutation, or antithrombin deficiency.



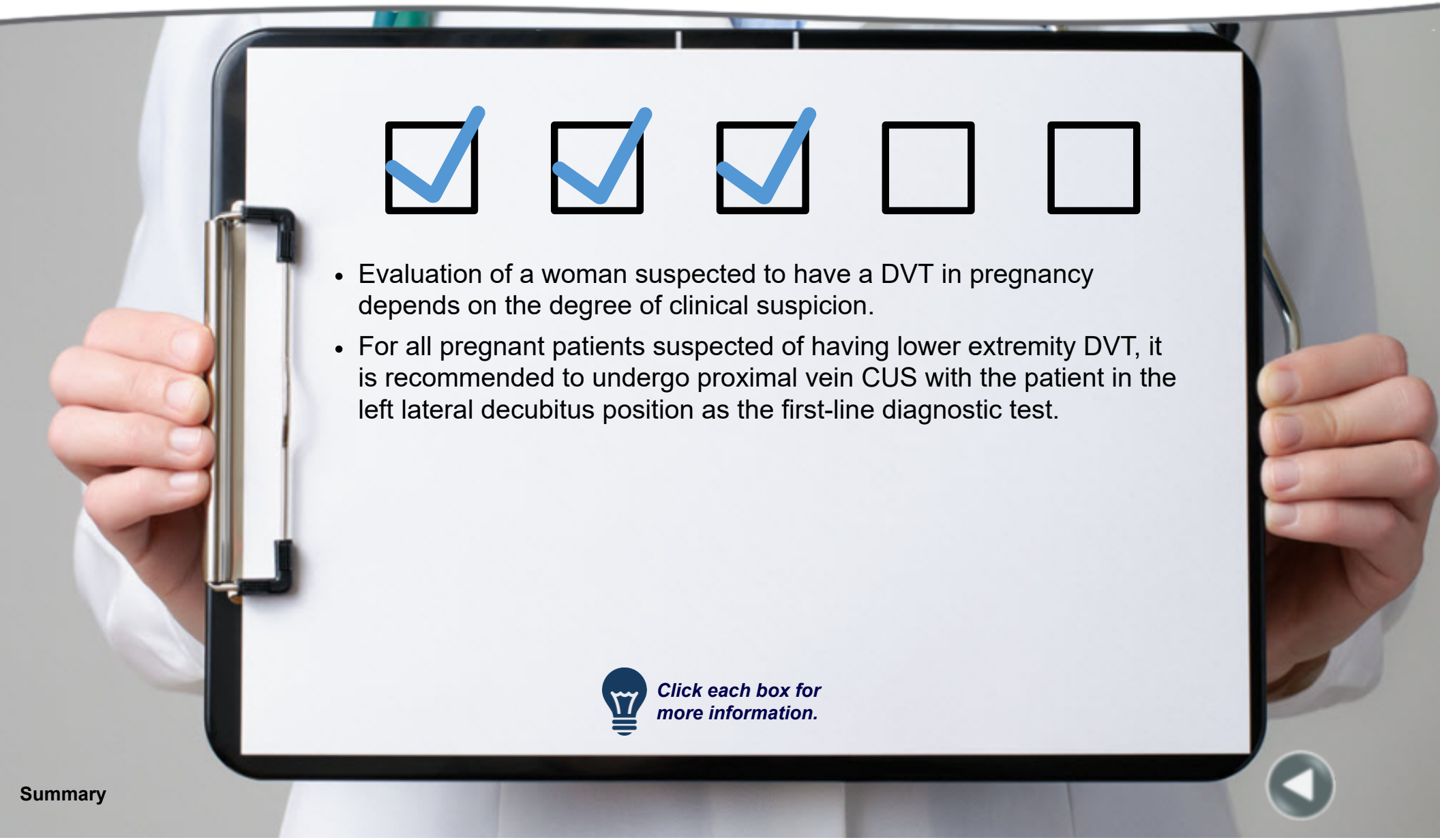
- Venous thromboembolism can occur during pregnancy as an isolated lower extremity deep venous thrombosis (DVT) or pulmonary embolism (PE).
- Pregnancy is a risk factor for VTE with a reported incidence that is 4-50 times higher in pregnant patients compared to their non-pregnant counterparts.
- Lower extremity DVT risk is highest in the first six weeks postpartum with a higher incidence of left-sided DVT and pelvic vein clot.
- Proximal vein thrombosis signs and symptoms are diffuse pain and swelling that may or may not be associated with erythema, warmth, and tenderness of the lower extremity.
- Iliac vein thrombosis include symptoms that include swelling of the entire leg with or without flank, lower abdomen, buttock or back pain.

Click each box for more information.



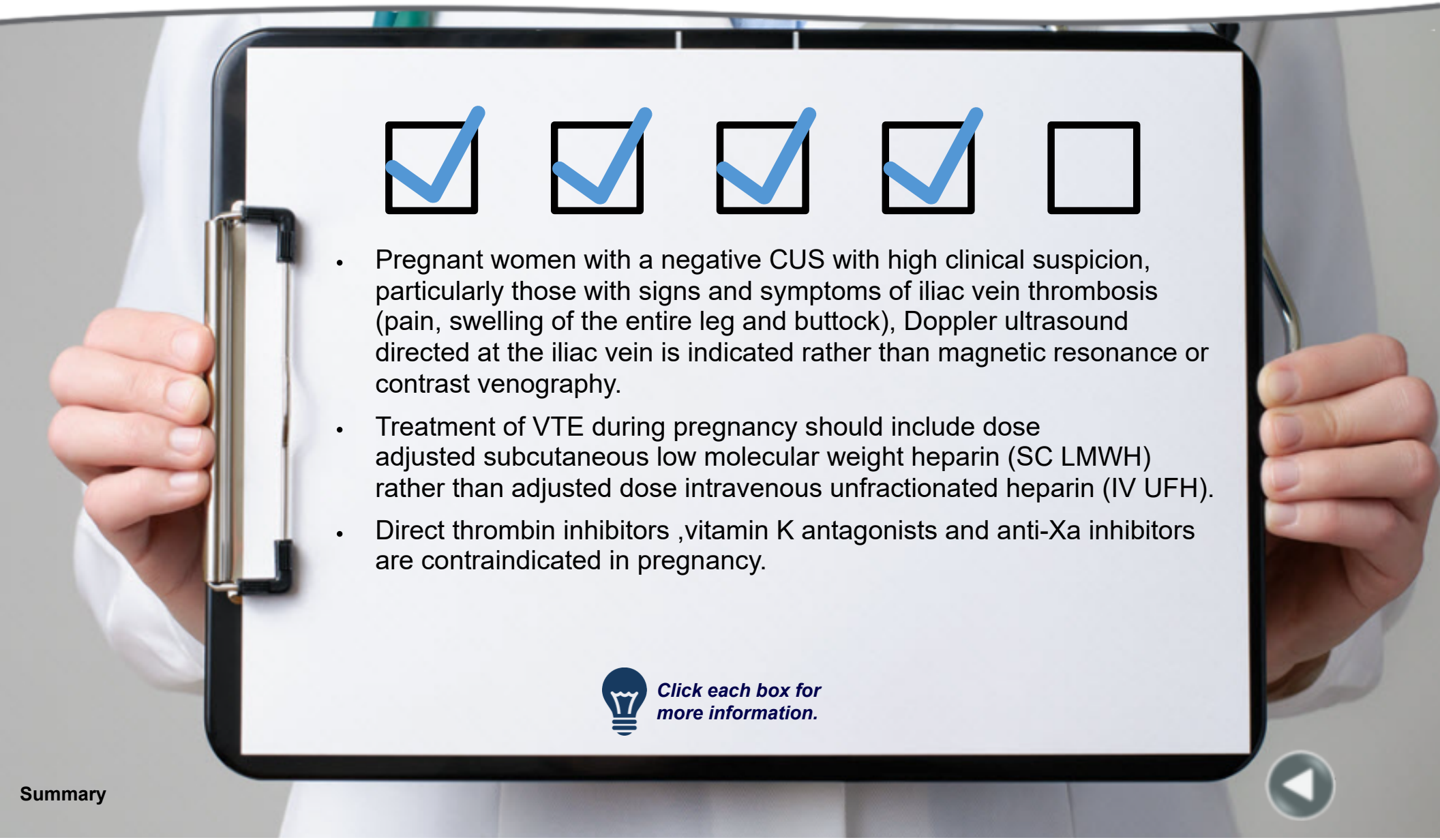
- The clinical features of DVT in pregnancy overlap with many of the features of normal pregnancy.
- Clinical suspicion, a high index of suspicion and low threshold along with the use of objective confirmatory testing are required to accurately diagnose DVT during pregnancy.
- There is limited value with D-Dimer and clinical predication rules as pretest probability for the diagnosis of DVT during pregnancy and the puerperium.
- D-dimer, whether moderate or highly sensitive (with higher cut off values), have not been adequately validated for routine use in pregnancy.
- On the other hand, a negative D-dimer is associated with a high negative predictive value in any trimester.
- D-dimer levels and clinical exam cannot be used alone to diagnose DVT.
- DVT diagnosis in pregnancy is made by demonstrating a lack of compressibility of the proximal veins on compressive ultrasound (femoral vein thrombosis) or poor flow on doppler imaging of the femoral-iliac vein (iliac vein thrombosis).

Click each box for more information.



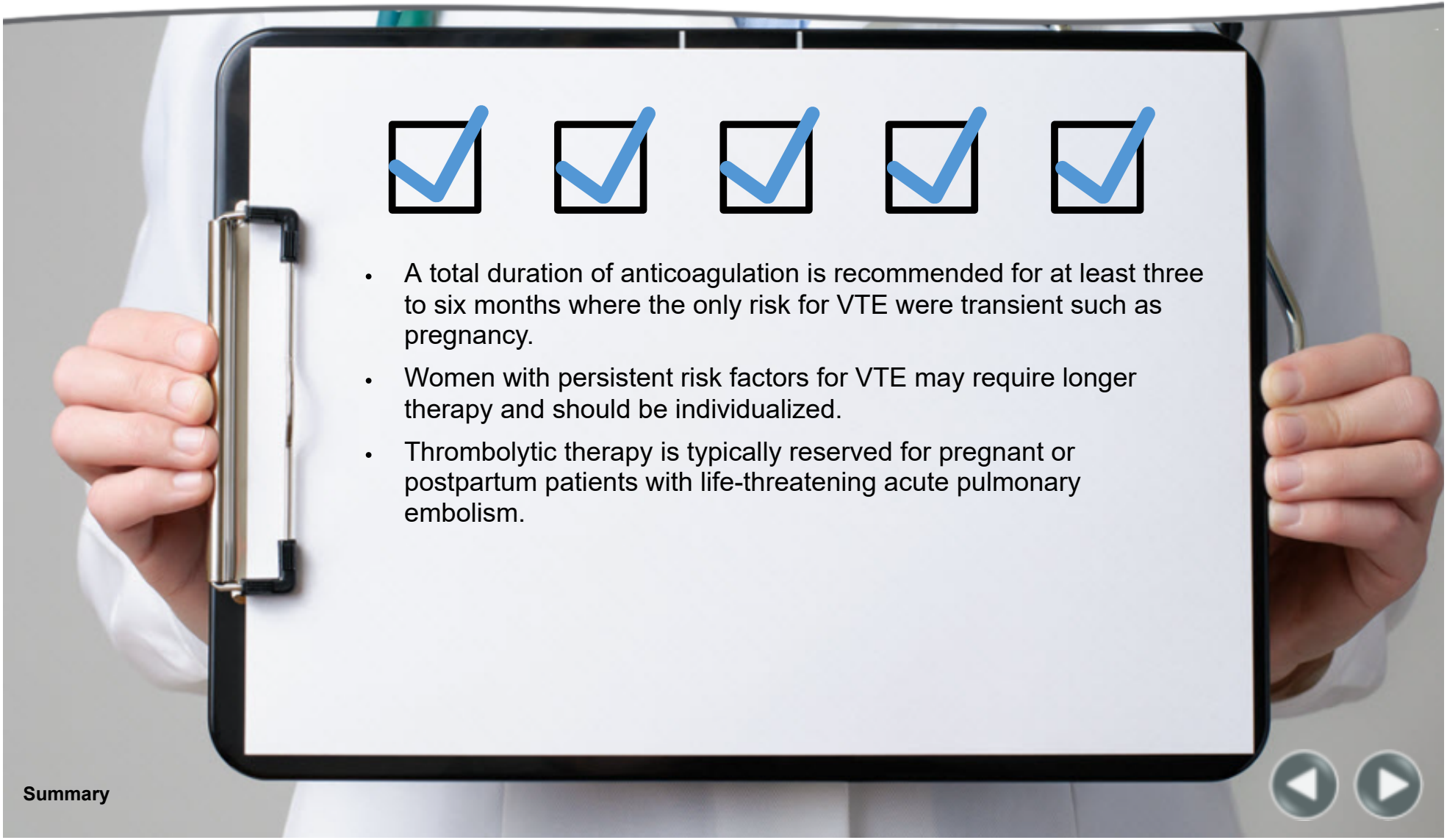
- Evaluation of a woman suspected to have a DVT in pregnancy depends on the degree of clinical suspicion.
- For all pregnant patients suspected of having lower extremity DVT, it is recommended to undergo proximal vein CUS with the patient in the left lateral decubitus position as the first-line diagnostic test.

Click each box for more information.



- Pregnant women with a negative CUS with high clinical suspicion, particularly those with signs and symptoms of iliac vein thrombosis (pain, swelling of the entire leg and buttock), Doppler ultrasound directed at the iliac vein is indicated rather than magnetic resonance or contrast venography.
- Treatment of VTE during pregnancy should include dose adjusted subcutaneous low molecular weight heparin (SC LMWH) rather than adjusted dose intravenous unfractionated heparin (IV UFH).
- Direct thrombin inhibitors ,vitamin K antagonists and anti-Xa inhibitors are contraindicated in pregnancy.

Click each box for more information.



- A total duration of anticoagulation is recommended for at least three to six months where the only risk for VTE were transient such as pregnancy.
- Women with persistent risk factors for VTE may require longer therapy and should be individualized.
- Thrombolytic therapy is typically reserved for pregnant or postpartum patients with life-threatening acute pulmonary embolism.

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