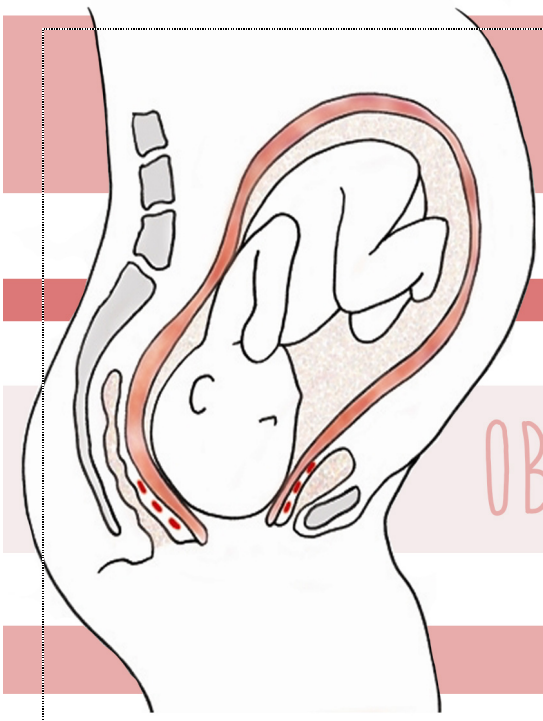


OBSTETRICS AND GYNECOLOGY

(Tutorial 7) Title: thromboembolic diseases in obstetrics and gynecology

Leader: Alanoud alyousef

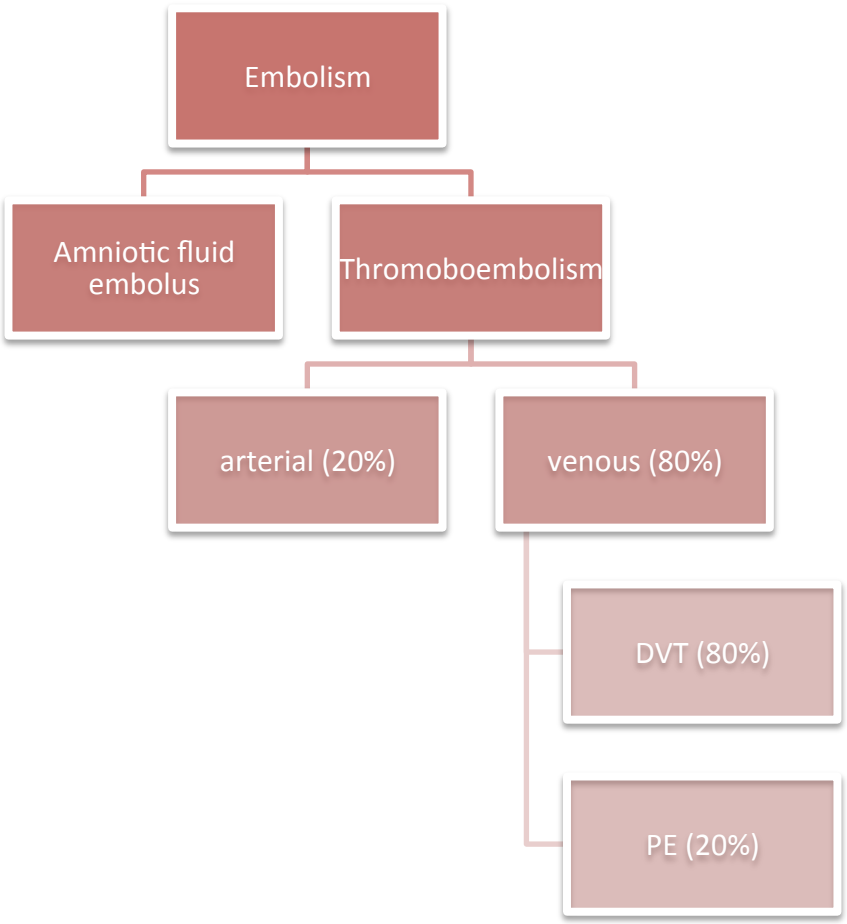
Sub-leader: Dana aldubaib

Done by: Norah Alnegheimish

Revised by: Razan Alshatwi

Doctor's note Team's note Not important Important

Objectives:

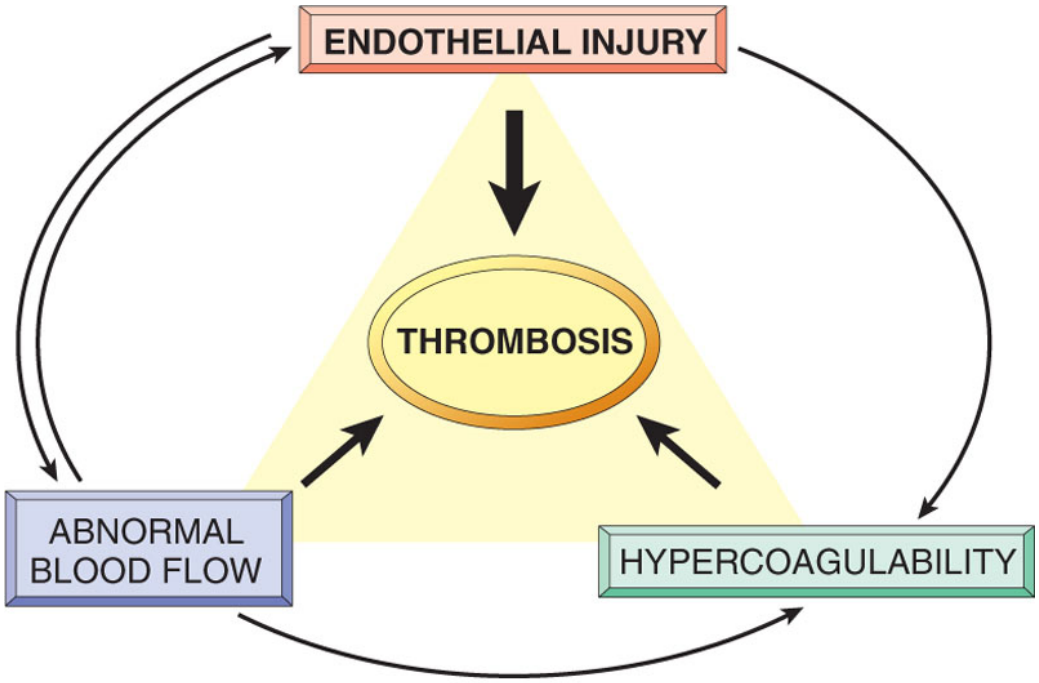

Embolism
Amniotic fluid embolus
Thromoboembolism
arterial (20%)
venous (80%)
DVT (80%)
PE (20%)

Pregnancy Associated Risk

Relative Risk: pregnant vs non-pregnant women

- Arterial thromboembolism (strokes and heart attacks) is increased 3- to 4-fold
- Venous thromboembolism (VTE) 4- to 5-fold increase
- 2 per 1000 deliveries: 20% of these events are arterial, and the other 80% are venous
- 80% of venous thromboembolic are DVT and 20% are pulmonary emboli.
- VTE accounts for 1.1 deaths per 100 000 deliveries (10% of all maternal deaths).
- Number 1 cause of maternal mortality in developed countries is thromboembolic disease
- 50% pregnancy-related pulmonary emboli occur after delivery
- Risk of venous thromboembolism increases postpartum and with cesarean section.

Pathophysiology



Virchow's triad of:

- Vascular injury, infection, and tissue trauma
- Hypercoagulability the triggering factors for DVT
- Venous stasis of pregnancy.

Pregnancy Hypercoagulability:

- Increased concentrations of factors VII, VIII, X, and von Willebrand factor and by pronounced increases in fibrinogen.
- Factors II, V, and IX are relatively unchanged
- ↑ Plasminogen; ↓ plasmin activity (increased plasminogen activator inhibitor levels)
- ↓ Free protein S (secondary to increased levels of its binding protein, the complement component C4b)
- ↑ fibrinopeptide A, b-thromboglobulin, platelet factor 4, fibrinogen
- Increase with conception decrease 8 weeks postpartum

Risk factors

1-The most important risk factor for VTE in pregnancy is a history of thrombosis.
The risk of recurrent VTE in pregnancy is also increased 3- to 4-fold. The rate of recurrent VTE in women who did not receive anticoagulation has been reported to range from 2.4% to 12.2%. In women who did receive anticoagulation, the rate of recurrent VTE has been reported to range from 0 to 2.4%.

2-Besides a history of thrombosis, the most important risk factor for VTE in pregnancy is thrombophilia. Thrombophilia is present in 20%

to 50% of women who experience VTE during pregnancy and the postpartum period. Both acquired and inherited thrombophilia increase the risk, e.g., factor V leiden, prothrombin G20210A, protein C and S deficiencies, antithrombin deficiency, antiphospholipid syndrome.

3-Other risk factors as summarized below:

Medical conditions	Complications of pregnancy and delivery
Heart disease	Multiple gestation
Sickle cell disease	Hyperemesis
Lupus	Fluid & electrolyte imbalance
Obesity	Antepartum hemorrhage
Anemia	Cesarean delivery
Diabetes	Postpartum infection
Hypertension	Postpartum hemorrhage
Smoking	Transfusion

Prevention

In most cases, the risks of anticoagulation (2% of bleeding with heparin or LMWH) outweigh its benefits.

Women who would benefit are those with a history of thrombosis.

Other women who may benefit from anticoagulation in pregnancy are women with inherited or acquired thrombophilia and a history of poor pregnancy outcome.

Choice of anticoagulants:

- Warfarin has harmful fetal effects. Warfarin taken during the critical period for organogenesis, the 4th to the 8th week after conception is associated with miscarriage and congenital anomalies such as nasal bony hypoplasia and nasal bridge depression. Some features can mimic chondrodysplasia punctata.

- The preferred agents for anticoagulation in pregnancy are heparin compounds. Neither heparin nor low-molecular-weight heparin crosses the placenta, and both are considered safe in pregnancy.
- Disadvantages of unfractionated heparin include heparin-induced thrombocytopenia (HIT) and osteoporosis.
- LMWH is mostly used due to its low side effects but switch to unfractionated heparin before delivery because it has an antidote (protamine sulfate can reverse the effects of heparin in a timely manner).
- In patients with metallic valves, warfarin is a better anticoagulant. Therefore, we use heparin in the first trimester and then switch to warfarin in the second trimester. 4 weeks prior to delivery, we switch back to heparin to reduce the risk of intracranial hemorrhage.

DVT and PE

DVT:

Symptoms: The two most common initial symptoms, present in more than 80% of women with pregnancy-related DVT, are pain and swelling in an extremity. In pregnancy DVT is much more common in the left leg than the right leg and it occurs in proximal vessels. While in the general population it's common in the right leg and distal.

Diagnosis: Compression US with Doppler flow studies is the initial and primary mode of diagnosis.

When results are equivocal or an iliac vein thrombosis is suspected, magnetic resonance venography (MRV) may be used.

The most reliable test for DVT is a venogram, but it is not generally performed due to radiation and risk of dye induced phlebitis.

D-dimer is sensitive and has a good negative predictive value, i.e. if it is negative, the patient is unlikely to have a DVT.

Treatment: when clinical diagnosis of DVT is made, anticoagulant therapy should be started pending the results of a diagnostic workup.

The treatment of a proven DVT in pregnancy is IV unfractionated

heparin or subcutaneous LMWH (enoxaparin). Intravenous anticoagulation should be maintained for at least 5 to 7 days, after which treatment is converted to subcutaneous heparin, which must be continued for the duration of pregnancy and 6 weeks postpartum (some sources say 6 months).

PE:

Symptoms: pleuritic chest pain, shortness of breath, palpitations, hemoptysis, syncopal episodes. Suggestive signs: tachycardia, tachypnea, low grade fever, pleural friction rub, and pulmonary rales.

Diagnosis: The diagnosis of new onset pulmonary embolism (PE) is similar to that in the nonpregnant individual. ECG can show sinus tachycardia. ABG may show oxygen tension less than 80 mm Hg. Pulmonary embolism is primarily a radiological diagnosis. Three algorithms may be used:

- If bilateral compression US of the lower extremities is positive for DVT, PE may be assumed in a symptomatic patient.
- Ventilation perfusion scan has minimal risk to the fetus, but cannot be used in those with an abnormal x-ray or in patients with asthma or COPD.
- Spiral CT: With an indeterminate study in a woman without a DVT, a confirmatory test, such as angiography or spiral computed tomography (spiral CT), is necessary to prevent the woman from unnecessary exposure to anticoagulation.
- Treatment: same as DVT.

OCP

Estrogen (prothrombotic state):

- Increased levels of factors II, VII, VIII, and X and fibrinogen, decreased levels of antithrombin and protein S and acquired resistance to activated protein C.
- 3-6 fold increased risk compare to non users
- 2-fold, lower risk for oral contraceptives containing 30 mg ethinylestradiol than for those with 50 mg ethinylestradiol

- Third generation OCPs are worse than 2nd generation OCPs. The progesterone in third generation OCPs cannot counteract the effects of estrogen.
- The risk was not cumulative with longer use, i.e. the risk brought about by oral contraceptives was immediate and only lasted as long as oral contraceptives were taken.
- The risk of VTE is highest in the 4 months, the risk reduces and remains stable thereafter
- No increased risk of thrombosis with progestogen-only methods
- DO NOT PRESCRIBE OCPs WITHOUT TAKING PROPER HISTORY. Ask about risk factors.
- DO NOT PRESCRIBE OCPS FOR:
    - PATIENTS WITH PREVIOUS THROMBOEMBOLISM.
    - SMOKERS who are >35 YEARS OLD= ABSOLUTE CONTRAINDICATION
    - patients who are undergoing major surgery with prolonged immobilization, SLE patients with antiphospholipid syndrome, and those with known thrombogenic mutations e.g. factor V leiden, prothrombin mutation, protein C, S, or antithrombin deficiency.

Pregnancy puts the patient in a greater risk than taking OCP so be sure to start the patient with another contraceptive method.

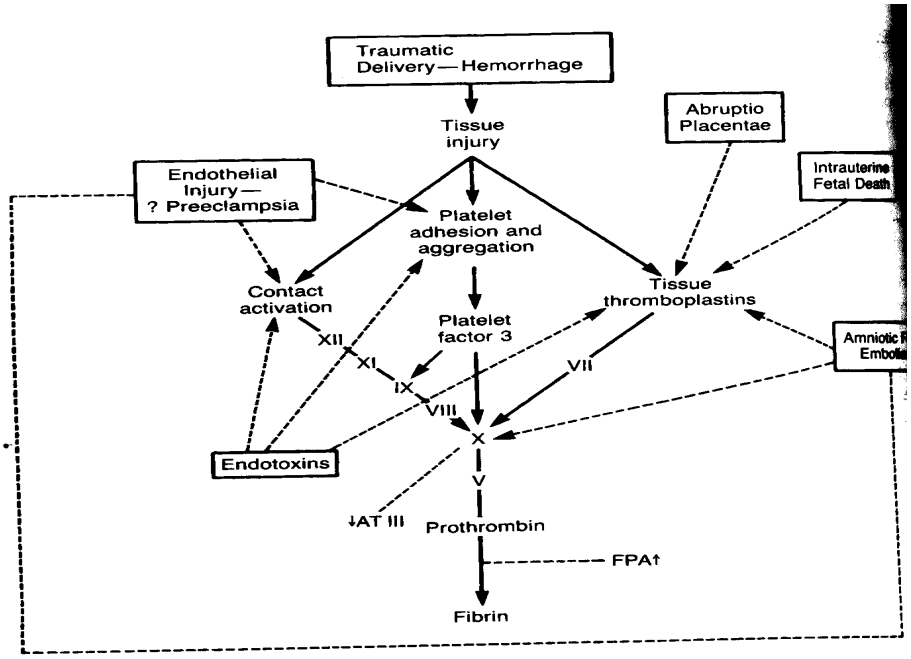
Doctor didn't go through the rest

Consumptive Coagulopathy (DIC)

Significance:

- Bleeding
- Circulatory obstruction→organ hypoperfusion and ischemic tissue damage
- Renal failure, ARDS
- Microangiopathic hemolysis

Pathogenesis:



Etiology:

- Placental abruption (most common cause in obstetrics)
- Sever Hemorrhage (Postpartum hge): severe tissue hypoxia in the setting of shock has been proposed to result in release of tissue factor from damaged cells
- Fetal Death and Delayed Delivery >2wks: see below
- Amniotic Fluid Embolus: see below
- Septicemia: see below
- Acute fatty liver syndrome: acute fatty liver may impair hepatic production of coagulation factors and clearance of fibrin degradation products.

Treatment:

- Identify and treat source of coagulopathy
- Correct coagulopathy: FFP, cryoprecipitate, platelet

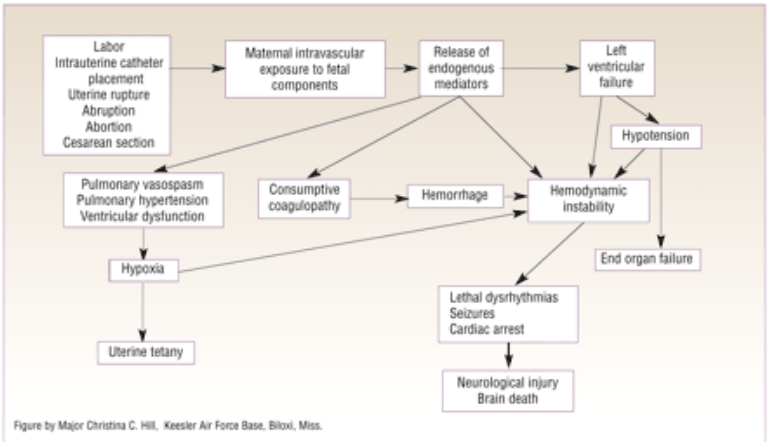
Fetal Death and Delayed Delivery

- Spontaneous labor usually in 2 weeks post fetal death
- Maternal coagulation problems < 1 month post fetal death
- If retained longer, develop coagulopathy
- Consumptive coagulopathy mediated by thromboplastic from dead fetus
- tx: correct coagulation defects and delivery

Amniotic Fluid Embolus

This syndrome is characterized by a fulminating consumption coagulopathy, intense bronchospasm and hypoxia, and vasomotor collapse (hypotension). Now known as anaphylactoid syndrome of pregnancy.

1 in 8000 to 1 in 30 000 pregnancies (rare)



Pathophysiology: brief pulmonary and systemic hypertension→transient, profound oxygen desaturation (neurological injury in survivors) → secondary phase: lung injury and coagulopathy

Diagnosis is clinical

Treatment: supportive

Prognosis:

- 60% maternal mortality; profound neurological impairment is the rule in survivors

- fetal: outcome poor; related to arrest-to-delivery time interval; 70% neonatal survival; with half of survivors having neurological impairment

Sepsis and Septic Abortion

Sepsis:

- Due to septic abortion, antepartum pyelonephritis, puerperal infection
- Endotoxin activates extrinsic clotting mechanism through TNF (tumor necrosis factor)
- Treat cause

Septic abortion:

Coagulation defects from:

- Sepsis (*Clostridium perfringens* highest at Parkland) during instrumental termination of pregnancy
- Thromboplastin released from placenta, fetus, decidua or all three (prolonged retention of dead fetus)

Summery

Thromboembolic disease is the number 1 cause of mortality in developed countries. (The second cause in SA after hemorrhage) Pregnant women are at an increased risk of thromboembolism. Most cases are venous (80%). The most important risk factor is a history of thrombosis, followed by thrombophilia.

DVT manifests as a unilateral pain and swelling in an extremity. Diagnosis is based on compression US with Doppler flow. Treatment is with heparin.

OCPs, due to their estrogenic effects, are associated with an increased risk of thromboembolism. The risk is greatest in the first months. DO NOT PRESCRIBE OCPs WITHOUT TAKING PROPER HISTORY.

Disseminated intravascular coagulation in obstetrics is caused mostly by placental abruption.

References:

http://atvb.ahajournals.org/content/29/3/326.full

Essentials of Obstetrics and Gynecology by Hacker and Moore's. Fifth edition.

http://www.uptodate.com/contents/disseminated-intravascular-coagulation-during-pregnancy

http://ccn.aacnjournals.org/content/23/6/42.full

MCQ's :

1. A 24-year-old woman appears at 8 weeks of pregnancy and reveals a history of pulmonary embolism 7 years ago during her first pregnancy. She was treated with intravenous heparin followed by several months of oral warfarin (Coumadin) and has had no further evidence of thromboembolic disease for over 6 years. Which of the following statements about her current condition is true?

a. Having no evidence of disease for over 5 years means that the risk of thromboembolism is not greater than normal
b. Impedance plethysmography is not a useful study to evaluate for deep venous thrombosis in pregnancy
c. Doppler ultrasonography is not a useful technique to evaluate for deep venous thrombosis in pregnancy
d. The patient should be placed on low-dose heparin therapy throughout pregnancy and puerperium
e. The patient is at highest risk for recurrent thromboembolism during the second trimester of pregnancy

2. Which of the following is an absolute contraindication to the use of combination oral contraceptive pills?

a. Varicose veins
b. Tension headache
c. Seizure disorders
d. Obesity and smoking in women over 35 years of age
e. Mild essential hypertension

For mistakes or feedback

Obgynteam432@gmail.com

Answers 1-d. 2-d