



The Thrombophilias and Pregnancy

What are the thrombophilias?

The thrombophilias are a group of disorders that promote blood clotting. Individuals with a thrombophilia tend to form blood clots too easily, either because their bodies make too much of certain proteins, called blood clotting factors, or too little of anti-clotting proteins that limit clot formation. As many as 1 in 5 people in this country has a thrombophilia.

What are the symptoms of thrombophilia?

Most people with a thrombophilia do not know they have it because they have no symptoms. However, some will develop a blood clot where it does not belong. Often, blood clots form in the lower leg, causing swelling, redness and discomfort. This condition, called deep vein thrombosis, is often diagnosed with ultrasound or other imaging tests. Clots can become life-threatening if they break off and travel through the blood stream to vital organs (called venous thromboembolism or VTE). When the thromboembolism blocks blood vessels in the lungs, brain or heart, it can cause breathing difficulties (i.e., pulmonary embolus, a clot in the lungs), stroke or heart attack. A thrombophilia also may increase an individual's risk of coronary artery disease. Clots are more likely to develop when a person with a thrombophilia has other risk factors, including immobilization (due to a bone fracture, for example) or surgery. Pregnancy is another time when signs of thrombophilia are more common.

What are the risks of thrombophilia during pregnancy?

Most women with a thrombophilia have healthy pregnancies. However, the thrombophilias contribute to a number of pregnancy complications, including fetal losses that occur in late in the first trimester or in the second or third trimesters (i.e., stillbirths), placental abruption (when the placenta separates from the uterine wall, partially or completely, before delivery) and poor fetal growth. The thrombophilias also may cause a severe form of preeclampsia, a pregnancy-related disorder that can pose serious risks for mother and baby, that is characterized by high blood pressure and protein in the urine. Most of these problems are believed to result from blood clots in placental blood vessels that lead to placenta changes and reduced blood flow to the fetus.

Pregnant women with a thrombophilia are also at higher risk than other pregnant women of developing a VTE. However, even pregnant women without a thrombophilia are more likely than non-pregnant women to develop a VTE. This is due to normal pregnancy-related changes in blood clotting that limit blood loss during labor and delivery. Pulmonary embolus is now the leading cause of maternal death in the United States. Recent studies suggest that more than half of pregnant women who develop a pulmonary embolus or other VTE have an underlying thrombophilia.

What are the most common types of thrombophilia?

Most thrombophilias are inherited, though some can develop later in life. Two of the most common thrombophilias are factor V Leiden and prothrombin mutations. These occur in up to 5 to 9 percent and 2 to 3 percent, respectively, of Caucasians and are far less common in African-Americans and rare in Africans and Asians. Both are inherited in an autosomal dominant pattern, meaning that an affected person needs to inherit the gene from only one parent. Each child of an affected parent has a 50 percent chance of inheriting the thrombophilia. Another common thrombophilia, mild hyperhomocysteinemia (MTHFR), affects about 10 percent of people in the United States and is inherited in an autosomal recessive pattern. This means that an affected individual must inherit a copy of the abnormal gene from both parents. Some less common thrombophilias include antithrombin III deficiency (which is uncommon, but especially severe), protein C and protein S deficiencies.

Antiphospholipid syndrome (APS) is a thrombophilia that is not inherited but can develop later in

life. In APS, the body appears to develop antibodies against proteins that bind to certain fatty parts of cells called phospholipids. These antibodies may damage blood vessels, leading to blood clots. APS is considered an autoimmune disorder, like arthritis and systemic lupus erythematosus. SLE is a chronic inflammatory disease that affects many body systems including skin, joints, blood and kidneys, and early symptoms may include a facial rash and arthritis. Up to one-third of individuals with SLE have antiphospholipid antibodies in their blood, which may contribute to their increased risk of pregnancy complications. While most individuals with APS are otherwise healthy, the disorder is believed to contribute to up to 15 percent of repeated miscarriages.

Which pregnant women should be tested for thrombophilias?

All pregnant women who have had a blood clot should be offered testing, according to the American College of Obstetricians and Gynecologists. Many doctors also recommend testing if a woman has a family history of blood clots, pulmonary embolism or strokes that occurred prior to 60 years of age, or a history of pregnancy complications, including two or more miscarriages, stillbirth, early or severe preeclampsia, placental abruption or poor fetal growth due to undetermined causes.

How is thrombophilia treated during pregnancy?

Some pregnant women with a thrombophilia are treated with a blood-thinning drug called heparin (given by injection one or more times daily). This drug does not cross the placenta and is safe for the baby. In some cases, doctors may recommend low doses of aspirin along with heparin. Studies show that treatment helps prevent blood clots in the mother and appears to help improve pregnancy outcomes.

However, not all women with a thrombophilia need heparin treatment during pregnancy. A woman and her health care provider should discuss her individual risks of blood clots and pregnancy complications and the severity of her thrombophilia before deciding whether or not she needs treatment. Heparin treatment does pose some risk of side effects, including bone loss and potentially dangerous blood changes. Doctors often recommend a newer form of heparin, called low-molecular weight heparin, that appears to pose a lower risk of side effects than the standard form. Doctors continue to study which pregnant women with a thrombophilia can benefit from treatment and which treatment regimen is most effective.

Generally, treatment is not recommended for most pregnant women with one of the less severe thrombophilias (such as factor V Leiden or prothrombin mutation) and no history of blood clots or pregnancy complications. The risk of blood clots or pregnancy complications due to thrombophilia appears to be less than 1 percent in these women. However, some doctors may recommend about six weeks of treatment after birth (when risk of blood clots may be highest) if the woman has a strong family history of blood clots or if she has a cesarean delivery.

Heparin treatment is recommended throughout pregnancy and the postpartum period for women who have one of the more severe thrombophilias (such as antithrombin III deficiency) or more than one thrombophilia, even if they have not experienced any blood clots or pregnancy complications. Women with a thrombophilia who have a past history of blood clots are usually treated with heparin during pregnancy and the postpartum period.

Women with antiphospholipid syndrome usually are treated with heparin and low-dose aspirin. Studies suggest that the combination is more effective than either medication alone in preventing pregnancy loss.

Some doctors recommend low-dose heparin plus low-dose aspirin for women who have one of the milder thrombophilias and a history of pregnancy complications, but no history of blood clots.

Women with mild hyperhomocystinemia are usually treated with the B vitamins folic acid, B6 and B12. Studies suggest that women with this thrombophilia may not be at increased risk of blood

clots during pregnancy, but they may be at increased risk of pregnancy loss and placental abruption.

Some doctors recommend that women who have had three or more early miscarriages be tested for this thrombophilia and receive vitamin treatment, if needed. However, this recommendation is controversial.

After delivery, a blood-thinning drug called warfarin may be used in addition to, or instead of, heparin. This drug, which is taken orally, is safe during breastfeeding. It is not recommended during pregnancy because it can cause birth defects.