

# A Patient's Guide to Prevention of Blood Clots During Pregnancy: Use of Blood-Thinning Drugs to Prevent Abnormal Blood Clots in the Legs of Pregnant Women

## What Does Pregnancy Have to Do With Blood Clots in a Woman's Legs?

- ◆ A blood clot in a deep vein of the leg is called deep vein thrombosis (DVT). DVT can cause inflammation, swelling, and pain in the leg. It is of greater danger if the clot breaks loose and travels to the lungs. This is called pulmonary embolism (PE), and PE can cause serious illness or death. DVT is different from varicose veins, a condition affecting the surface veins of the leg. DVT and PE together are called venous thromboembolism (VTE).
- ◆ VTE in pregnancy can be caused by many factors, including thrombophilia, which is a tendency to form blood clots that are either inherited or develop during life. Other important factors include changes in the level and activity of the natural clotting factors of the body, injury to the veins, and decreased blood flow in the veins. The latter can be caused by hormonal changes and pressure on the veins by the uterus. The increased VTE risk requires special attention in a pregnant woman.

## What Can Be Done to Prevent VTE in Pregnant Women?

- ◆ Preventive measures are usually necessary only when a woman is at increased risk for VTE.
- ◆ Preventive measures can include early walking after delivery or surgery, or the use of compression stockings or blood thinning drugs.

## What Are Blood-Thinning Drugs?

- ◆ Blood-thinning (anticoagulant) drugs are medications given to prevent the blood from forming harmful blood clots or to treat blood clots that have already formed.
- ◆ Although clotting of blood is necessary to stop bleeding after injury, it can be harmful when it contributes to conditions such as VTE.
- ◆ A blood clot is formed by blood cells and non-cell blood components sticking together to form a solid mass—a clot. A clot can wholly or partially block a blood vessel.
- ◆ A harmful clot is sometimes called a thrombus.

## What Are the Blood-Thinning Drugs Used to Prevent or Treat VTE in Pregnant Women?

- ◆ The physician selects one or more blood-thinning drugs based on (1) the woman's risk for developing VTE, and (2) which drug or drugs will likely be most effective with the fewest side effects for the woman and her baby.
- ◆ Antiplatelet agents work by reducing the ability of platelets to stick together to form blood clots. Platelets are the blood cells that clump together to form a clot. Aspirin is the oldest and still most frequently used antiplatelet agent. Antiplatelet agents are given by mouth.
- ◆ Heparin reduces the ability of blood to clot, blocking the action of several clotting factors. It has some side effects that can be serious, but it can usually be used safely with close monitoring. Heparin is given by infusion or injection.
- ◆ Low-molecular-weight heparin (LMWH) is a subtype of heparin. It has fewer side effects than heparin. It is given by injection underneath the skin and does not usually require routine blood test monitoring.

- ◆ Factor Xa inhibitors block activity of a specific blood-clotting factor (factor Xa) in the blood. Factor Xa inhibitors can be given intravenously by injection or mouth. While the oral direct factor Xa inhibitors should not be used in pregnancy, there is some experience with the other factor Xa inhibitors during pregnancy.
- ◆ Vitamin K antagonists reduce the blood-clotting effect of clotting factors that depend on vitamin K for their activity. Warfarin (Coumadin) is an example of a vitamin K antagonist. Vitamin K antagonists can cause birth defects. These drugs should be used in pregnancy only when there is no alternative blood thinner that works as well. Vitamin K antagonists are given by mouth.

### **What Are the Side Effects and Complications of Blood-Thinning Drugs?**

- ◆ The risks to the mother from blood thinners used during pregnancy are the same as in non-pregnant women. A slightly increased risk of bleeding is the primary side effect of blood thinning drugs.
- ◆ Some blood-thinning drugs may have effects on a fetus (unborn child). A pregnant woman should discuss this with her physician if the use of blood-thinning drugs during the pregnancy is being considered.
- ◆ The woman and her physician should carefully consider the benefits and risks of blood-thinning drugs for prevention and treatment of VTE. When benefits outweigh the potential risks, the use of a blood thinner is justified. The values and preferences of the pregnant woman should also be considered.

### **Summary of Expert Guidelines for Some Specific Uses of Blood-Thinning Drugs to Prevent VTE in Pregnant Women**

Expert guidelines can be very useful when they are based on a review of reliable data by panels of experts. They are useful to physicians in making decisions affecting individual patients. The following sections of this guide summarize some expert guidelines covering a number of conditions in pregnancy for which blood-thinning drugs may be used.

- ◆ LMWH is recommended if treatment or prevention of VTE is required during pregnancy. A physician will determine if the drug is required and, if so, for how long and at what dose.
- ◆ The effect of the oral direct factor Xa inhibitors (apixaban and rivaroxaban) and direct thrombin inhibitors (dabigatran) on human fetal development is unknown. These drugs should not be used in pregnancy.
- ◆ Fondaparinux crosses the placenta in small amounts. Experience with this drug in pregnancy is limited. It is suggested that fondaparinux use during pregnancy be restricted to patients with severe allergic reactions to heparin (including heparin-induced thrombocytopenia) who cannot receive danaparoid.

### **For women who were receiving warfarin for VTE prevention before they became pregnant:**

- ◆ Warfarin is known to cross the placenta and may affect the fetus. LMWH should be substituted for warfarin in women receiving long-term warfarin for VTE prevention.

### **For women who are breast-feeding:**

- ◆ Warfarin, heparin, LMWH, danaparoid, and r-hirudin are acceptable for use during breast-feeding. Blood-thinning drugs that **should not be used by a breast-feeding woman** are oral direct factor Xa inhibitors such as apixaban and rivaroxaban, and oral direct thrombin inhibitors such as dabigatran. The use of alternative blood thinners is suggested in breast-feeding women receiving fondaparinux.

### **For women using assisted reproductive technology to become pregnant:**

- ◆ Routine VTE prevention with blood-thinning drugs is not recommended in these women.
- ◆ Women who develop severe ovarian hyperstimulation syndrome may benefit from preventative LMWH for 3 months following resolution of hyperstimulation.

### **For women who had cesarean section for delivery:**

- ◆ Early mobilization (walking) is the only VTE prevention recommended for healthy women with no additional VTE risk factors.
- ◆ For women considered at moderate to high risk for VTE because of the presence of additional risk factors, the use of LMWH or the use of antiembolism stockings or compression cuffs is suggested.
- ◆ For women whose high risk for VTE persists after delivery, VTE prevention may be considered for up to 6 weeks after discharge from the hospital.

### **For women who develop VTE during pregnancy:**

- ◆ Treatment with full-dose LMWH is recommended, continuing for a total of least 3 months, including at least 6 weeks after delivery.
- ◆ Treatment with LMWH should be stopped at least 24 hours before induction of labor or cesarean section.

### **For pregnant women who had VTE during a previous pregnancy:**

- ◆ For all pregnant women with previous VTE who are not receiving long-term blood thinners, 6 weeks of LMWH or warfarin after delivery is suggested.
- ◆ For pregnant women thought to be at low risk of another VTE because they had one previous VTE that occurred after surgery, leg casting, or admission to the hospital, no blood-thinning therapy is recommended before delivery. However, close monitoring for signs or symptoms of VTE is suggested.
- ◆ For pregnant women at moderate to high risk of another VTE because a previous VTE was unexplained or occurred with pregnancy or estrogen therapy, LMWH before delivery as well as after delivery is suggested.
- ◆ For pregnant women who are on long-term therapy with warfarin or another vitamin K antagonist, replacement of the vitamin K antagonist with LMWH prior to or early in pregnancy (before 6 weeks) is recommended.

### **For pregnant women with the tendency to form blood clots (thrombophilia) but who never had a VTE:**

- ◆ Consultation with a physician is advised. The need for VTE prevention therapy should be guided by the type of thrombophilia and a patient's family history of thrombosis. Generally, blood thinners before delivery are suggested only for women with a family history who have the highest-risk thrombophilias (homozygosity for the factor V Leiden or prothrombin gene mutation).
- ◆ Blood thinners are suggested for 6 weeks following delivery in all women with thrombophilia who have a family history of thrombosis, as well as women with the highest-risk thrombophilias who do not have a family history of thrombosis.

### **For women with thrombophilia and pregnancy complications:**

- ◆ A type of acquired thrombophilia called antiphospholipid antibody syndrome has been linked with an increased risk of miscarriage. For women with this condition and a history of three or more pregnancy losses, a combination of low dose aspirin and either heparin or LMWH is recommended.
- ◆ There is no good data to support blood-thinning therapy in women with other thrombophilias or other pregnancy complications. Women should discuss the pros and cons of different types of prevention therapy with their doctor.

### **For pregnant women who do not have thrombophilia but who had high blood pressure (preeclampsia) or miscarriage in a previous pregnancy:**

- ◆ Pregnant women with preeclampsia may experience a rise in blood pressure, fluid retention (edema), headache, and visual impairment. If convulsions occur, preeclampsia has progressed to eclampsia. Preeclampsia increases risk for pregnancy loss, premature delivery, placental abruption (separation of the placenta), and maternal death.
- ◆ The cause of preeclampsia is unknown, although it is associated with abnormal blood clotting, even in women without thrombophilia.
- ◆ For women at risk for preeclampsia, low-dose aspirin beginning in the second trimester of pregnancy is recommended.
- ◆ Two large studies have shown that blood thinners are not helpful in preventing recurrent pregnancy loss in women without thrombophilia who have a history of miscarriages. Therefore, preventative blood thinners are not recommended in these patients.

### **For pregnant women who have mechanical heart valves:**

- ◆ All people with mechanical heart valves must take blood-thinning drugs. The drugs prevent formation of harmful blood clots around the valves, as well as stroke.
- ◆ It is not known which blood-thinning drug to use in pregnant women with mechanical heart valves. All of the available drugs have limitations. Vitamin K antagonists appear to be better at preventing stroke but have risks to the fetus. Although LMWH is safe for the fetus, it may not be as good at preventing clots as vitamin K antagonists in this situation.
- ◆ Given these problems, several drug choices are available, and women with mechanical heart valves should discuss the pros and cons of each of these options with their physician before becoming pregnant.



**American College of Chest Physicians**

[www.chestnet.org](http://www.chestnet.org)

**CHEST Journal**

<http://chestjournal.chestpubs.org>

These materials are for informational and educational purposes only. They are not intended to replace the medical advice of a qualified health-care provider. Please see your doctor if you are having medical problems associated with the health issues described in this guide.

*American College of Chest Physicians © 2012*