The human body normally maintains a careful balance between bleeding and clotting. Blood cells called platelets, proteins in the blood, and the cells lining the blood vessels are closely regulated, so that the body forms blood clots to stop bleeding resulting from injury, but it does not form an unwanted and harmful clot (also called thrombus or thrombosis) in our blood vessels. Thrombosis may cause heart attacks, strokes, and blood clots in the legs (called deep vein thrombosis) or in the lungs (called pulmonary embolism).

What Is Thrombophilia?
Thrombophilia is an inherited (genetic) or acquired tendency to develop thrombosis (Table 1). Thrombophils can cause thrombosis by manufacturing too much clotting protein, making abnormal clotting proteins that are resistant to breakdown, producing too little of proteins that prevent thrombosis, or damaging the walls of the blood vessel. Thrombophilias can cause thrombosis in arteries, veins, or both.

The most common thrombophilias include inherited abnormalities of clotting such as factor V Leiden and the prothrombin gene mutation and acquired proteins that cause thrombosis called antiphospholipid antibodies. Having multiple copies of abnormal thrombophilia genes, increasing levels of antiphospholipid antibodies, or a combination of thrombophilias multiplies the risk of thrombosis.

How Are Thrombophilias Diagnosed?
Thrombophilias are detected through blood tests. Some thrombophilia tests detect abnormal genes, whereas others measure levels of proteins in the blood. Some tests may not be accurate in the setting of a recent thrombosis or in the presence of blood thinners (also called anticoagulants) and may need to be performed at a later time.

How Does Thrombophilia Impact My Health?
All thrombophilias increase the risk of developing a first episode of thrombosis. However, only some thrombophilias increase the risk of recurrent thrombosis. Antiphospholipid antibodies are strongly associated with developing multiple episodes of thrombosis, especially if anticoagulation is not prescribed. The most frequent types of thrombosis caused by thrombophilias are deep vein thrombosis and pulmonary embolism. In addition to these blood clots in veins, antiphospholipid antibodies also increase the risk for heart attack and stroke.

Thrombophilias have important consequences for women's health. Thrombophilias increase the risk of thrombosis associated with birth control pills and hormone replacement therapy. In some women, thrombophilia may cause infertility and recurrent pregnancy losses. In pregnant women, thrombophilia may increase the risk of maternal thrombosis and certain pregnancy-related complications.

Should I Be Tested for Thrombophilia?
Healthcare providers will often test for thrombophilias in patients with thrombosis at a young age, multiple blood-clotting events, thrombosis in unusual sites, a strong family history of thrombosis, and recurrent miscarriages or difficulty conceiving a baby. Clinicians perform thrombophilia testing to determine the best blood thinner for a particular patient, how long a patient should take a blood thinner, risk of future thrombosis, risk of blood clots with hormonal therapies (such as birth control pills), and risk of family
members. Healthcare providers may also perform thrombophilia testing to uncover an explanation for unexpected or unprovoked thrombosis.

How Are Thrombophilias Treated?
The treatment of thrombophilias depends on the individual patient’s medical history. In patients with thrombosis who are diagnosed with thrombophilia, healthcare providers may recommend prolonged duration blood thinning to prevent future blood clots. For example, patients with antiphospholipid antibodies and thrombosis require long-term therapy with blood thinners to prevent miscarriage. Patients with thrombophilia and no history of thrombosis, preventive doses of blood thinners should be prescribed in situations that carry an increased risk for thrombosis, such as major surgery, trauma, immobility, or hospitalization for medical illness.

Women with thrombophilia should avoid contraceptives that are associated with an increased risk of thrombosis, including estrogen-containing birth control pills, vaginal rings, and patches. Alternative, safer contraceptives such as progestin-only pills (also called the minipill) and intrauterine devices should be considered. Estrogen replacement therapy should not be used to treat symptoms of menopause in women with thrombophilia. Some women with recurrent pregnancy loss and certain thrombophilias may benefit from low-dose blood thinners to prevent thrombosis that may cause miscarriage. Pregnant women with thrombophilia and a history of thrombosis are often treated with blood thinners during pregnancy and through the postpartum period to prevent serious complications such as deep vein thrombosis and pulmonary embolism.

Table 1. Major Types of Thrombophilias

<table>
<thead>
<tr>
<th>Category</th>
<th>Thrombophilia</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inherited</td>
<td>Factor V Leiden</td>
<td>Clotting factor becomes resistant to inactivation</td>
</tr>
<tr>
<td></td>
<td>Prothrombin gene mutation</td>
<td>Too much clotting protein is produced</td>
</tr>
<tr>
<td></td>
<td>Protein C deficiency</td>
<td>Not enough anticlotting protein</td>
</tr>
<tr>
<td></td>
<td>Protein S deficiency</td>
<td>Not enough anticlotting protein</td>
</tr>
<tr>
<td></td>
<td>Antithrombin deficiency</td>
<td>Not enough anticlotting protein</td>
</tr>
<tr>
<td>Acquired</td>
<td>Antiphospholipid antibodies</td>
<td>Proteins damage blood vessel walls</td>
</tr>
<tr>
<td></td>
<td>(anticardiolipin antibodies,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>lupus anticoagulant)</td>
<td></td>
</tr>
</tbody>
</table>

If I Have a Thrombophilia, What Can I Do to Prevent Blood Clots?
If diagnosed with thrombophilia, patients can take several steps to prevent thrombosis (Table 2). Patients should ensure that all of their healthcare providers are aware of the thrombophilia and should discuss whether treatment with blood thinners is appropriate, especially for high-risk situations such as major surgery. Patients should adopt a heart-healthy lifestyle by focusing on regular exercise, a diet low in saturated fat, cholesterol, and salt, losing weight if overweight or obese, and avoiding tobacco use.

Table 2. Tips for Reducing the Risk of Blood Clots Attributable to Thrombophilia

- Tell all of your healthcare providers that you have a tendency to develop blood clots.
- Talk to your healthcare provider about whether you should be taking a blood thinner to prevent blood clots.
- Ask your healthcare providers for protection against blood clots when you are most vulnerable, such as after major surgery, after traumatic injury, or when your mobility is limited.
- Avoid immobility.
- Adopt a heart-healthy lifestyle by exercising regularly, eating a diet low in saturated fat, cholesterol, and salt, losing weight if overweight or obese, and avoiding tobacco use.
- Make sure other medical problems such as kidney disease, lung disease, and heart disease are fully treated.

Further Information
For additional information, please consult the following resources:
- American Venous Forum (www.veinforum.org/patients/vein-handbook/chapter-3-clotting-disorders)
- National Heart, Lung, and Blood Institute (www.nhlbi.nih.gov/health/health-topics/topics/ebc/)
- North American Thrombosis Forum (www.natfonline.org)

Disclosures
None.
Thrombophilia and Hypercoagulability
Gregory Piazza

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