

Thrombophilia Laboratory Testing



FAST FACTS

Up to 60% of children and 40% of adults

with VTE have a laboratory thrombophilia.

Thrombosis risk increases with increasing numbers of risk factors for thrombosis.

Most individuals who are heterozygous for Factor V Leiden will never have a thrombosis.

Natural anticoagulant protein levels can be affected by acute thrombosis, anticoagulants or the age of the patient.

Homozygous heritable laboratory thrombophilias are a higher thrombosis risk than heterozygous.

If you have clinical questions or to discuss a patient, call the Physician Priority Link® at 513-636-7997 or 1-888-987-0135. To refer a patient directly, call the Thrombosis Program at 513-517-2234.

The incidence of venous thromboembolic disease (VTE) in children is increasing. Heritable thrombophilia is a predisposition to pathologic thrombosis. Thrombosis results from the interplay of genetic and acquired risk factors.

Identifying laboratory thrombophilia in unselected populations does not change medical management or improve outcomes. Thrombophilia testing has been identified by Choosing Wisely campaigns as an example of tests that should be ordered only in selected patients, where results would alter medical management. Even in families with an identified heritable thrombophilia, testing may not be necessary or helpful.

The most important and powerful action is to try to reduce or eliminate acquired thrombosis risk factors (such as immobility, obesity or exogenous estrogen). Counseling about a healthy lifestyle and diet, no smoking, and ambulating every two hours on long car or airplane trips is essential to any discussion about elevated thrombosis risk.

ASSESSMENT

In a young patient with **unprovoked thrombosis or a strong family history of thrombosis**, identifying all thrombosis risk factors, whether acquired or inherited, promotes an understanding of future thrombosis risk and guides medical management.

Prior to considering testing or a referral, perform an initial thrombophilia assessment.

- Does the patient have a history of **unprovoked** thrombosis?
- Is there a **strong family history** of thrombosis?
- Is there a **first degree** relative with thrombosis?
- Do you observe any clinical red flags?

HPE (HISTORY AND PHYSICAL EXAM) RED FLAGS

Situational History

Personal history of:

- Neonatal purpura fulminans
- Warfarin skin necrosis
- Unprovoked thrombosis (or weak thrombosis)
- Unusual site of thrombosis (ex. portal vein)
- Use of estrogen
- Obesity
- New immobility

Family History

First-degree family history of:

- Venous thrombosis at age <50 yrs, especially if unprovoked
- Family history of sudden death
- Family history of early stroke or MI <50 yrs
- Family history of recurrent miscarriages >3

WHEN TO REFER

- For concerns about a patient's thrombosis risk
- For management of pediatric thrombosis
- When thrombophilia testing is considered and you are uncertain about counseling for positive or negative results

If ordering tests prior to a referral, please refer to the table located on page two of this tool for the correct test names and the purpose of each test.

If you would like additional copies of this tool, or would like more information, please contact the Physician Outreach and Engagement team at Cincinnati Children's.

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ORDERABLE TEST (CONDITION)

Test name	Mechanism of thrombophilia	Genetic (G), developmental (D) or acquired (A)	Genetic prevalence estimate (white, general population)
Factor V Leiden (FVL)	Impaired natural anticoagulation	G	5% Heterozygote
Activated protein C resistance-functional test (FVL)	Impaired natural anticoagulation	G and A	Unknown
* Prothrombin gene (Factor II 20210)	Higher thrombin level	G	2% Heterozygote
* Protein C (deficiency)	Impaired natural anticoagulation	G, D, A	0.15% Heterozygote
* Protein S (deficiency)	Impaired natural anticoagulation	G, D, A	0.1% Heterozygote
* Antithrombin (deficiency)	Impaired natural anticoagulation	G, D, A	0.02% Heterozygote
* FVL and prothrombin gene (compound heterozygous)	Impaired natural anticoagulation/higher thrombin level	G	0.1% Heterozygote
Factor 8 (Factor VIII activity >90th percentile)	Promote prothrombotic state	G, A	Influenced by age, race, ethnicity, estrogen, stress, inflammation and other acquired factors
* + Anti-phospholipid profile (anti-phospholipid syndrome)	Promote prothrombotic state	A (very rarely G)	Unknown

* Literature supports an association with recurrent thrombosis risk

+ Anti-phospholipid profile includes: lupus anticoagulant, anti-beta 2 glycoprotein I IgG and IgM, anticardiolipin IgG and IgM. The diagnosis of antiphospholipid syndrome requires the presence of clinical criteria (blood clots or pregnancy morbidity) as well as a sustained positive antiphospholipid antibody at least 12 weeks after initial testing.

NOTE

Homocysteine levels should be assessed only in select circumstances. Mutational analysis for the relevant gene, methylene tetrahydrofolate reductase (MTHFR), should NOT be performed. Polymorphisms in *MTHFR* are very common and of uncertain relevance to thrombophilia. While elevated levels of homocysteine can be found in some adults with thrombosis, causality is unclear. In adult studies, lowering homocysteine levels with folic acid or a B-complex vitamin did not appear to reduce thrombosis risk.

For urgent issues, or to speak with the specialist on call 24/7, call the Physician Priority Link® at 1-888-987-7997.