

Genetic testing for susceptibility to deep venous thrombosis

Background:

Deep venous thrombosis (DVT) and thromboembolism are common diseases in developed countries. Many risk factors are known, including prolonged bedrest, major surgery, trauma, malignancy, and smoking. Natural estrogens and their synthetic derivatives elevate the plasma levels of certain coagulation factors, thus, the risk of DVT is significantly increased during pregnancy, childbirth, oral contraceptive use. Being present in 50% of thromboembolic diseases, genetic causes are also important risk factors. About 20-30% of patients with DVT carry the Leiden mutation, and about 80% of familial thrombophilia is associated with this genetic defect. (The rest of the genetic factors, which are together involved in about 15% of inherited thrombotic cases, include mutations in the antithrombin, protein C, protein S genes.) Increased plasma homocystein levels also increase the risk of cardiovascular diseases, including DVT. The most common inherited causative factors of homocystein level elevation are a point mutation of the gene for the 5,10-methylene tetrahydrofolate reductase (MTHFR) enzyme. The most common mutation of the prothrombin (coagulation factor II) gene represents a mild risk factor of thrombosis by causing an increased prothrombin activity. As part of the diagnostic workup of thrombophilia, genetic testing may help set up the correct diagnosis; it allows the identification of a high-risk group for whom close surveillance, lifestyle change, perhaps preventive anticoagulant therapy are necessary; finally, it may indicate the need for family testing.

Indications for testing:

- venous thromboembolism (thrombophlebitis, pulmonary embolism)
- multiple thrombosis or thromboembolism in the family history
- thrombosis in an unusual location (mesentery, brain, retina)
- prior to pregnancy, oral contraceptive use, major surgery if there is a personal or family history of thrombosis
- recurrent pregnancy loss of unknown cause
- arteriosclerosis developing at a young age

Method:

A panel of mutations in the factor V gene (Leiden, Arg506Gln), prothrombin (factor II) gene (G20210A), and MTHFR gene (C677T) is tested by PCR, restriction digestion and lab-on-chip electrophoresis, or real-time PCR.

Sample requirement:

- buccal swab at room temperature *or*
- 2 ml blood in an EDTA (lavender top) tube, transported at +4 °C

References:

Shaw DM. Factor V Leiden: an overview. Clin Lab Sci. 2006 Fall;19(4):218-21.
De Stefano V, Rossi E, Paciaroni K, Leone G. Screening for inherited thrombophilia: indications and therapeutic implications. Haematologica. 2002 Oct;87(10):1095-108.
Kutteh WH, Triplett DA.
Thrombophilias and recurrent pregnancy loss.
Semin Reprod Med. 2006 Feb;24(1):54-66.