Laboratory Test for Prothrombin (Factor II) Gene Mutation (G20210A) Associated with Inherited Predisposition to Thrombosis

The UNC Molecular Genetics Laboratory tests for Prothrombin gene G20210A mutation which is responsible, in part, for inherited predisposition to venous thrombosis. Heterozygous mutation is quite prevalent in the general population (about 2%) and is associated with a 3-fold risk of venous thrombosis. Affected patients are candidates for antithrombotic prophylaxis.

Biology of the disease: Mutation in the prothrombin gene (a single G to A transition at position 20210) results in slightly elevated prothrombin levels and an associated risk of venous thrombosis. The prevalence of heterozygotes is 2% in healthy controls, 6% in venous thrombosis patients, and as high as 18% in selected thrombophilia patients with a positive family history. Most people with the mutation will not experience thrombotic events unless they have coexisting risk factors such as: oral contraceptive, pregnancy and perpeurium, perioperative state, immobilization, lupus anticoagulant, homocysteinemia, Factor V Leiden, or deficiency of selected coagulation factors such as protein S, protein C, or antithrombin III.

Clinical Indications for Prothrombin (Factor II) Gene Mutation testing:

1. History of recurrent venous thrombosis.
2. First venous thrombosis at <50 years of age in the presence of an acquired risk factor.
3. First venous thrombosis at any age and no associated acquired risk factor.
4. First venous thrombosis at an unusual anatomic site such as cerebral, mesenteric, portal, or hepatic vein.
5. First venous thrombosis in a subject with a first-degree family member who has had a venous thrombosis before age 50.
6. First venous thrombosis related to pregnancy, puerperium, oral contraceptive use, or hormone replacement therapy.
7. Women with unexplained pregnancy loss during the 2nd or 3rd trimester.
8. Asymptomatic individuals who merit testing include family members of a proband with a known prothrombin mutation, especially if there is a strong family history of thrombosis, or family members who are pregnant or considering oral contraceptive use or pregnancy.

Laboratory testing for Prothrombin Gene Mutation:

The preferred sample is 3 mL of blood in an ACD (yellow top) or EDTA (lavender-top), which may be refrigerated up to 48 hours. Molecular testing is performed using a TaqMan genotyping assay (Applied Biosystems). Genomic DNA is extracted from the blood sample, and targeted genomic regions are PCR amplified and detected by a TaqMan allelic discrimination assay.

Results are reported as heterozygous, homozygous, or normal genotype. Consider testing the same blood for Factor V Leiden which is also a risk factor for venous thrombosis.

References:

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3. Poort SR, et al. A Common Genetic Variation in the 3'-Untranslated Region of the Prothrombin Gene is Associated with Elevated Plasma Prothrombin Levels and an Increase in Venous Thrombosis. Blood 88:3698-3703, 1996.
4. Margaglione M, et al. Increased Risk for Venous Thrombosis in Carriers of the Prothrombin G -> A^{20210} Gene Variant. Ann Intern Med 129:89-93, 1998.
5. Seligsohn U, et al: Genetic susceptibility to venous thrombosis. NEJM 344:1222-1231, 2001.

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