Inherited Thrombophilias:  Factor V Leiden (FVL), Factor II (Prothrombin) G20210A mutation, and methylene-tetrahydrofolate reductase (MTHFR C677T) mutation are the three most common inherited disorders of blood clotting that predispose individuals to venous thrombosis.  The Factor V Leiden (R506Q) mutation is associated with resistance to activated protein C.  Individuals who are heterozygous for FVL have a 2-8 fold risk of developing venous thrombosis.  When coupled with oral contraceptive use or estrogen therapy, heterozygotes have an estimated 30-fold risk of venous thrombosis.  Individuals who are homozygous for FVL have a 50-100 fold risk of developing venous thrombosis.  Up to 20% of individuals with venous thrombosis have FVL.  The frequency of heterozygous FVL in individuals of Caucasian descent is about 5% and about 1% in individuals of African-American descent.

The Prothrombin G20210A mutation is the second-most common cause of inherited thrombosis and results in elevated levels of prothrombin which mildly increases the risk of venous thrombosis.  An increased risk of cerebral vein thromboses and of myocardial infarctions in women less than 50 years of age may also be associated with this mutation, especially in conjunction with other environmental risk factors.  The G20210A mutation results in approximately 30% higher levels of prothrombin, which can cause a mild hypercoagulable condition associated with deep vein thrombosis.  Heterozygosity for the G20210A mutation results in a 3 to 10-fold higher risk of thrombosis.  Combined heterozygosity for Factor V Leiden and Prothrombin G20210A results in up to a 20-fold increased risk of thrombosis.  The population frequency of Prothrombin G20210A mutation is between 1% and 4% in Caucasians and about 0.2% in African-Americans.

The MTHFR C677T mutation lowers the levels of the functional enzyme MTHFR resulting in higher levels of homocysteine.  Hyperhomocysteinemia is associated with an increased risk of arterial and venous thrombosis.  Homozygosity of the C677T mutation results in elevated homocysteine levels and may mildly increase the risk of arterial and venous thrombosis.  Individuals with both the MTHFR C677T mutation and the Factor V Leiden mutation may be at a significantly greater risk of developing venous thrombosis than those with either mutation alone.  The homozygous MTHFR C677T mutation is quite common, occurring in about 5-15% of individuals of European, Middle Eastern and Asian descent.  The frequency of the homozygous mutation in individuals of African-American descent is approximately 1-2%.  Compound heterozygosity of C677T and A1298C is unlikely to be associated with increased risk for arterial and venous thrombosis.  Homozygosity of C677T and compound heterozygosity of C677T and A1298C result in a 2-3 fold risk of folate-sensitive neural tube defects.

Plasminogen activator inhibitor-1 (PAI-1) plays a critical role in blood coagulation.  Patients with the 4G/4G genotype have plasma PAI-1 levels that are 25% higher than those with the 5G/5G phenotype.  Elevated PAI-1 concentrations may be correlated with the progression of coronary artery syndrome, coronary thrombosis, and myocardial infarction.
INDICATIONS:
Evaluation of all patients with venous thrombosis, coronary artery disease, and/or stroke of unknown etiology.
Evaluation of asymptomatic individuals with a family history of venous thrombosis.
Evaluation of individuals with family members known to have Factor V Leiden, Prothrombin G20210A, MTHFR C677T, or MTHFR A1298C mutations.
Evaluation of women with recurrent pregnancy loss, unexplained severe pre-eclampsia, placental abruption, fetal growth retardation, stillbirth, or neural tube defects in offspring.

METHODOLOGY:
Allelic Discrimination TaqMan Assay (Applied Biosystems) is used to determine the genotype at each of the above loci. End-products are analyzed using the ABI 7500 Real-Time PCR System for genotype detection.
*Analysis of Factor V Leiden mutation is also offered as a single test.

SENSITIVITY:
This test methodology detects >99% of instances of these mutations.

SPECIMEN:
At least 2mLs whole blood in lavender top (EDTA) tube. Label tube with patient’s name, birth date, and date of collection. Phlebotomist must initial tube to verify patient’s identity.

TURN-AROUND TIME:
7 days.

COST:
Please call 1-866-450-4198 for institutional pricing or with any billing questions.

CPT CODES:
81240, 81241, 81291, 81400

RESULTS:
Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

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