Factor V Leiden

Since its discovery, factor V Leiden has become the most recognized cause of inherited thrombophilia. Factor V Leiden is present in:

- ~ 20% of all people with their first idiopathic VTE.
- ~ 40% of all individuals under the age of 50 at the time of their first idiopathic VTE
- ~ 60% of venous thrombosis cases in pregnant woman

PREVALENCE OF FACTOR V LEIDEN BY RACE	
Caucasian	5.0%
Hispanic American	2.2%
African American	1.2%
Native American	1.2%
Asian American	0.5%

INCIDENCE OF A THROMBOTIC EVENT

Heterozygotes

- Annual incidence of a thrombotic event is ~ 0.3 to 0.5%
- Lifetime risk for VTE approximately 10%
- Recurrence risk is 40 to 50%

Homozygotes

- Annual incidence of a thrombotic event under age 50 is approximately 1%
- Annual incidence of a thrombotic event at age 50 and older is 2%
- Lifetime risk between 50 and 60%

RISK OF VENOUS THROMBOSIS BASED ON INHERITANCE OF FACTOR V LEIDEN

Inherited and/or Environmental Risk Factors	Relative Risk
Single FVL	4-7
Single FVL and pregnancy/postpartum period	7-16
Single FVL and hormone replacement therapy	13-15
Both FVL and prothrombin G20210A	20
Single FVL and hyperhomocysteinemia	20
Single FVL and oral contraceptives	30-35
Two FVL and pregnancy/postpartum period	40
Two FVL (homozygote)	50-80
Single FVL and either protein C, S or antithrombin III deficiency	72-93
Both FVL and prothrombin G20210A, and preg/postpartum period	100
Two FVL mutations (homozygote) and oral contraceptives	100

Williams, et al. (2004) www.advanceweb.com 13(5):68

Factor V Leiden

Function and Risk of VTEs

Factor V Leiden refers to a single amino acid substitution (G1691A) present in the gene coding for factor V.
Factor V Leiden results in a resistance to activated protein C (APC)
Factor V Leiden is present in approximately 95% of the people with APC resistance
The 5% of patients with APC resistance that do not have a factor V Leiden mutation still have the same increased risk for VTE's.

Testing for Factor V Leiden

Consensus statements regarding factor V Leiden genetic testing published by the American College of Medical Genetics (ACMG) and the College of American Pathologists (CAP) do not favor a specific assay for factor V Leiden testing. Therefore, **physicians may chose** whether they prefer to use the **functional assay for APC resistance** or the **PCR-based DNA analysis**.

- Functional Assay for APC Resistance

  Advantages:
  - Can identify 100% of individuals with APC resistance, including the 5% of patients with APC resistance not caused by factor V Leiden.
  - Can be used for individuals receiving anticoagulation therapy, during acute thrombosis, or during pregnancy if these factors are appropriately considered
  - Specificity and sensitivity approaches 100%

  Disadvantage:
  - Must perform follow-up DNA analysis to ascertain who has factor V Leiden

- PCR-Based DNA Analysis

  Advantages:
  - Polymorphism is known which facilitates the evaluation of family members
  - Can be used for individuals receiving anticoagulation therapy, during acute thrombosis, or during pregnancy without having the account for these factors
  - Sensitivity 100% for individuals carrying a G to A substitution at nucleotide 1691 in the *F5* gene

  Disadvantage:
  - Cannot detect the 5% of individuals that are APC resistant, who do not have factor V Leiden