



The city of Leiden, Netherlands



## PIC QUESTION OF THE WEEK: 11/12/07

Q: Are any medications contraindicated in patients with factor V Leiden?

A. Factor V plays a key role in the coagulation cascade. There exist two disorders associated with factor V and a clear understanding of their terminology and physiologic effects is necessary to distinguish their clinical characteristics. The conditions are referred to as factor V *deficiency* and factor V *Leiden*. Factor V deficiency is a very rare disorder (1:1 million people) in which the concentration of plasma coagulation factor V is low. This results in decreased efficiency of the clotting mechanism and increased risk of hemorrhage. Conversely, factor V *Leiden* (Dutch city in which the mutation was studied) is a thrombotic disorder associated with protein C resistance and occurs because of a mutation in the factor V gene. Protein C and its cofactor (protein S) maintain a normal coagulation profile by inactivating factors V and VIII and reducing the potential for clot development. The variant factor V in Leiden patients inhibits normal activity of the protein C pathway resulting in less inactivation of factors V and VIII, thus producing a pro-thrombotic state. Factor V Leiden is the most common inherited form of thrombophilia and occurs in both males and females. Approximately 3% to 8% of the Caucasian population is heterozygous for this genetic alteration while about 1 in 5,000 people is homozygous. Heterozygous individuals have a 4 to 8 fold greater risk of developing thrombosis than unaffected individuals while the risk in homozygous subjects may be approximately 80 times higher than that seen in the normal population. Plasma based coagulation tests are used in screening for factor V Leiden; however only DNA-based testing can provide confirmation. Women with the Leiden mutation who use oral contraceptives have a 30 to 50 fold greater risk for venous thrombosis than those without the condition, while those using hormone replacement therapy (HRT) have a 13 to 16 fold greater risk than those not receiving estrogen. Drugs that affect estrogen receptors also appear to increase the risk of venous thrombosis. Three cases of tamoxifen-associated venous thrombosis in women with factor V Leiden have been reported. Patients who develop deep vein thrombosis (DVT) or pulmonary emboli (PE) are initially treated with heparin or low-molecular weight heparin (LMWH) followed by warfarin (target INR of 2 to 3). Patients with factor V Leiden who have not suffered a thrombotic event usually do not require prophylactic anticoagulation; however, risk factors such as obesity, trauma, surgery, smoking, oral contraceptives, HRT, and pregnancy may warrant short term prophylaxis. The factor V Leiden mutation is recognized as a contributing factor for thrombosis in women. This risk is significantly increased if they use oral contraceptives or HRT.

### References:

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- Goodnight SH, Griffin JH. Hereditary thrombophilia. In: Beutler E, Lichtman MA, Coller BS, et al, eds. *Williams Hematology*. 6<sup>th</sup> ed. New York, NY: McGraw-Hill; 2001:1697-1714.

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