Condition: Thrombophilia

Inheritance:

Genetically heterogeneous; most common autosomal dominant (with more severe manifestations in homozygote).

Genetic etiology:

Thrombophilias result from mutation in genes involved in limiting the extent of the blood clotting reaction. The most common form is due to mutation in the *F5* gene that encodes factor V, rendering the protein resistant to cleavage by activated protein C. The most common *F5* mutation is a G to AAC change at nucleotide 1691, referred to as Factor V Leiden. The second most common is a G to A change at position 20210 in the *F2* gene (encoding prothrombin). Less common causes involve mutations in genes for protein C or protein S.

Frequency:

Factor V Leiden: heterozygosity in 3-8% of individuals in Europe and USA; factor II: heterozygosity in 2-5%

Clinical features:

Thrombophilias present most often with venous thromboembolism, particularly in settings of prolonged inactivity, such as post-surgery. Heterozygotes for Factor V Leiden face a 4-8 increased relative risk of thrombosis, whereas homozygote risk is increased up to 80 fold. Risk is also increased in the presence of heterozygosity for mutations in *F5* and *F2*.

Management:

Avoidance of situations that would increase risk of thrombosis, if possible; anti-coagulation for thrombotic episodes.

Genetic counseling:

Transmitted as dominant traits with incomplete penetrance; both genetic and hematological testing available.

Human Genetics and Genomics, Fourth Edition. Bruce R. Korf and Mira B. Irons.