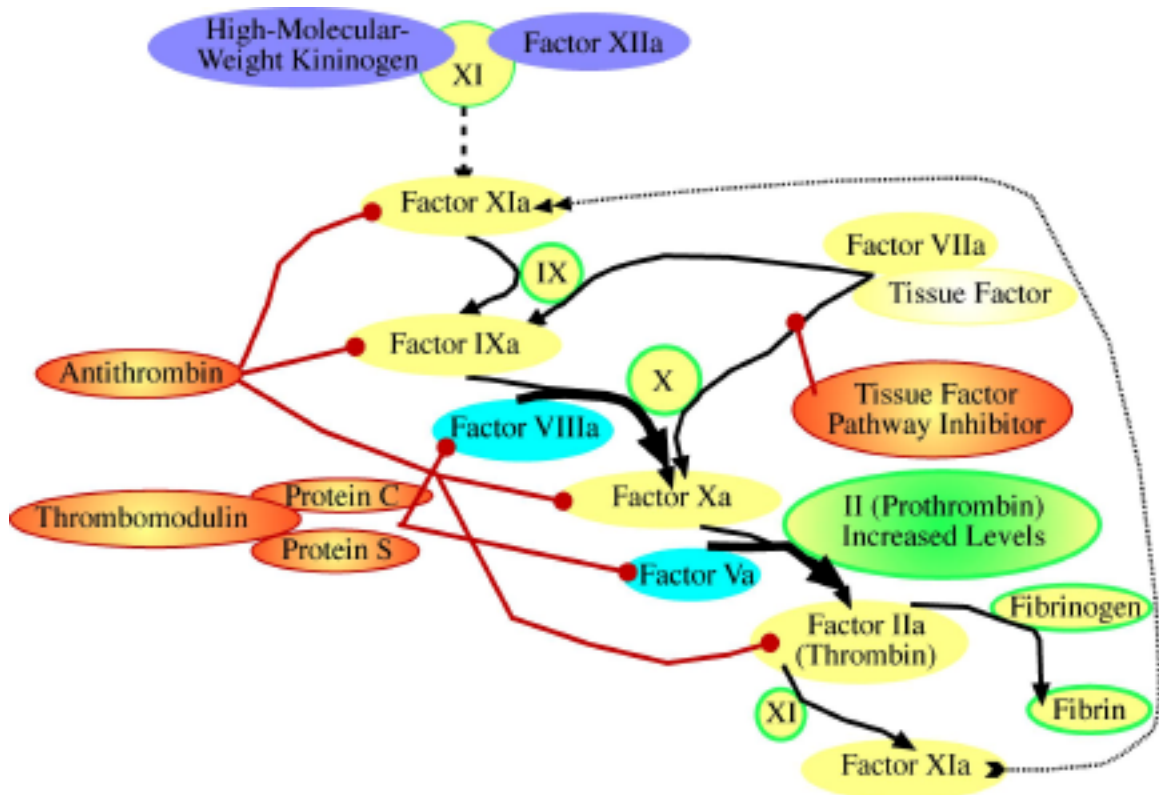


Prothrombin Gene Mutation 20210

The prothrombin gene mutation is a genetically acquired trait and was first described in 1996.

Mechanism of Action of Prothrombin Gene Mutation:



Prothrombin is the precursor to thrombin in the coagulation cascade (see the above diagram). Thrombin is required in order to convert fibrinogen into fibrin, which is the primary goal of the coagulation cascade. The gene has a mutation at position 20210, hence the disorder being referred to as prothrombin mutation 20210.

The mutation leads to an increased amount of thrombin circulating in the person's blood stream. The exact mechanism by which the prothrombin gene mutation results in a thrombophilic state is unclear. It is thought that the increased amount of circulating prothrombin provides a springboard upon which the clotting cascade can get started and that, in some circumstances, it may run out of control because of that springboard potential.

Epidemiology of the Prothrombin Gene Mutation:

In discussing any genetic mutation, including the prothrombin gene mutation, it is necessary to understand what is meant by the terms heterozygous and homozygous. To illustrate this, we will use the prothrombin gene mutation as an example. Normally, one has 2 copies of the prothrombin gene that are normal (PT/PT). When one is heterozygous for the prothrombin gene mutation, one copy is normal and the other has the prothrombin gene mutation (PT/PT20210). When one is homozygous for the prothrombin gene mutation, then both copies have the mutation (PT20210/PT20210).

The prothrombin gene mutation is seen more commonly in the Caucasian population. About 1-2% of the general population is heterozygous for the prothrombin gene mutation. The prothrombin gene mutation is relatively uncommon in the native populations of India, Korea, Africa and North America. In contrast, in Spain rates of 6% have been reported.

Risks of the Prothrombin Gene Mutation:

The overall estimated incidence (annual occurrence) of deep venous thrombosis is 1 episode for every 1000 persons. This does not separate patients who had predisposing conditions from those who do not.

At this time, there is contradicting evidence regarding the role of the prothrombin gene mutation and arterial thrombosis (stroke, heart attack). Based on these data, for persons with the prothrombin gene mutation, the most important preventive steps for the purposes of arterial disease are controlling other risk factors including: smoking, hypertension (high blood pressure), hyperlipidemia (high cholesterol), obesity and a sedentary lifestyle (limited activity).

The role of the prothrombin gene mutation and venous thromboembolic events is illustrated in the table below. Relative risk is a numerical representation of the effects of a condition or treatment on an individual. If a condition or treatment has a relative risk of 1, patients with the condition have no additional risk or benefit from those without the condition. In the studies used below, a relative risk greater than 1 shows an increased risk. For the table below, a relative risk of 4 means that individuals with that condition are 4 times as likely as similar individuals without the same condition, to develop a venous thrombotic event. Despite the increased risk, it is important to remember that the relative risk is a statistical tool to help guide clinicians and scientists and that individual persons can have increased or decreased risks. Even with a very high relative risk, there is no guarantee that a venous thrombotic event will occur.

Thrombophilic Status	Relative Risk of Venous thrombosis
Normal	1
Oral contraceptive (birth control pill) use in a patient with otherwise normal clotting system	4
Factor V Leiden, <i>heterozygous</i>	5-7
Factor V Leiden, <i>heterozygous</i> combined with oral contraceptive use.	30-35
Factor V Leiden, <i>homozygous</i>	80
Factor V Leiden, <i>homozygous</i> combined with oral contraceptive use.	??? >100
Prothrombin Gene Mutation, <i>heterozygous</i>	3
Prothrombin Gene Mutation, <i>homozygous</i>	??? – venous thrombosis risk unknown. ??? - possible risk of arterial thrombosis.
Prothrombin Gene Mutation, <i>heterozygous</i> combined with oral contraceptive use.	16

Protein C deficiency, <i>heterozygous</i>	7
Protein C deficiency, <i>homozygous</i>	Severe thrombosis at birth
Protein S deficiency, <i>heterozygous</i>	6
Protein S deficiency, <i>homozygous</i>	Severe thrombosis at birth
Antithrombin deficiency, <i>heterozygous</i>	5
Antithrombin deficiency, <i>homozygous</i>	Thought to be lethal prior to birth
Hyperhomocysteinemia	2-4
Hyperhomocysteinemia combined with Factor V Leiden, <i>heterozygous</i>	20

Treatment of the Prothrombin Gene Mutation:

Treatment of the prothrombin gene mutation depends upon the individual patient’s risk of recurrent thromboembolic disease. When one has a venous clot, regardless of what thrombophilic state(s) one may have, that person will receive anticoagulation. This is accomplished by several different medications: 1) heparin, 2) warfarin and 3) low-molecular-weight heparins. These medications are generally used for 3-6 months. At this time, there are no long-term studies discussing the use of long-term anticoagulation in the prothrombin gene mutation. Studies have been done in patients with factor V Leiden (a disorder which has an increased risk of thrombosis relatively similar to the prothrombin gene mutation) and the risk of bleeding from anticoagulation outweighed the potential benefits of anticoagulation. Patients that have had multiple thromboembolic episodes or are at high risk of further episodes (for example, multiple deficiencies) may be started on long-term anticoagulation.

The use of long-term anticoagulation has risks associated with it (approximately a 3% chance per year of having a major hemorrhage, of which approximately 1/5 are fatal). Beginning long-term anticoagulation is influenced by the patient’s overall risk of recurrent thrombosis balanced against the risks associated with long-term anticoagulation on an individual basis.

Further Information:

For further information, please visit the University of Illinois – Urbana/Champaign and Carle Cancer Center webpages on coagulation disorders at: www-admin.med.uiuc.edu/hematology.

This information is provided as a resource to patients and health care providers. The information contained above represents common diagnostic and treatment modalities, but individual circumstances may require additional or different tests or medications. All medical decisions should be made with the advice and consultation of a physician or other health care provider.