

12. Genetics of Thrombophilia

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Q1: "One of the list members recently reported that she was hetero and her brother was homo. I am new to FVLeiden and haven't grasped the genetics of it all as yet."

A1: Please see text and graphics below. The family fits graphic 3 or 5.

Q2: "If brother and sister are full-blood brother/sister, one could be hetero and the other not have it, but one can not be homo and the other hetero. There may be a mistake in the testing or information they received."

A2: This explanation is not correct. Graphic 3 shows how full-blood siblings can have very different genes: one sibling can be homozygous and another heterozygous (and yet another can not have factor V Leiden at all).

Q3: "Can factor V Leiden skip a generation?"

A3: In the strictest sense: no. In a wider sense: yes.

Parents (1st generation) who have factor V Leiden can have a child (2nd generation) that does not have factor V Leiden (see graphic 2 and 3). That 2nd generation child can obviously not pass any factor V Leiden on to his/her children (3rd generation), since he/she does not have any. Thus, in a strict sense, factor V Leiden cannot skip a generation and suddenly re-appear in the 3rd generation. However, if the 2nd generation child has a 3rd generation child with a partner who has factor V Leiden, the 3rd generation child can have factor V Leiden. Thus, factor V Leiden has "skipped a generation and reappeared".

Q4: "My brother & I are homozygous, 1 sister is hetero & 1 brother tested negative. My Dad has tested hetero. My mother was not tested since she died in the 1980's, but I was told that my mother had to have been hetero as well."

A4: The assumption that the mother was heterozygous is correct. The family fits graphic 3.

Q5: "You can have one parent hetero and one negative, and still be homozygous. That's what happened to me. It was explained to me that a single gene can mutate. I was told that it is rare but it does happen."

A5: While a factor V Leiden mutation may arise new in a person, this is extremely rare. It may occur roughly in 1 in a billion people.

Everybody carries 2 genes for each trait. We received one of these genes from our father, the other one from our mother. When we have a child ourselves, we pass one of our 2 genes on to our offspring; the offspring receives a second gene from our partner. For each of the various inherited abnormalities (factor V Leiden, prothrombin 20210 mutation, MTHFR, protein C deficiency, etc.), that increase the risk for blood clots, there are 3 possibly gene combinations:

1. we have 2 normal genes (i.e. we don't have the disorder);
2. we have one bad gene and 1 normal gene and (= we are heterozygous);
3. we have 2 bad genes (= we are homozygous).

The following scenarios are not possible:

1. Father or mother are known to be homozygous, and have a child that has normal genes.
2. The child is homozygous, but father and mother both have normal genes.

Not possible or extremely rare are the following scenarios:

1. The child is heterozygous, but father and mother both have normal genes.
2. The child is homozygous, and one parent is heterozygous and the other one has normal genes.

In these cases:

- a. either the test results are wrong,
- b. the information that the family received from the physicians is wrong,

- c. the father or mother are not the biological parent of the child (cases 1,2,3,4),
- d. The mutation may have arisen new in the child. This would be extremely rare, occurring in less than 1 in a billion people (cases 3 and 4).

The following graphics show the genetics of all thrombophilic disorders. There are always 4 gene combinations possible in the children, depending on which of the 2 genes the children get from their father and which of the 2 genes from their mother.

