

11. Prothrombin 20210 mutation

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Q: "I am FVL hetero, factor II prothrombin, and have antiphospholipid antibodies. Should my baby get a vitamin K shot?"

A: This question can not be safely answered, because it is not clear what underlying disorders the patient has.

The patient is heterozygous for factor V Leiden and has antiphospholipid antibodies. However, it is not clear, whether she has

- the factor II 20210 mutation (= prothrombin 20210 mutation), which is a disorder that makes people clot more easily, or
- factor II deficiency (= prothrombin deficiency), which makes people bleed more easily.

"Prothrombin deficiency" and "prothrombin 20210 mutation" are two completely different disorders that are sometimes confused with one another; just the same way that "factor V deficiency" and "factor V Leiden" are often confused. Physicians and patients must be careful to use correct terminology to avoid misunderstanding, which may lead to inappropriate recommendations and treatment.

If the patient has the prothrombin 20210 mutation, then the baby should receive a vitamin K shot. The "American Academy of Pediatrics" recommends that all newborns should get a vitamin K shot. This is safe. The fact, that the mother has thrombophilic abnormalities (= abnormalities that makes one clot more easily) and the baby may have inherited some from the mother, should not influence this decision. Vitamin K supplementation does not pose a risk for thrombosis to a person, unless it is given to an individual who is taking coumadin® (= warfarin) because of previous thrombosis. However, if the patient has "prothrombin deficiency", then the baby may have inherited this bleeding disorder, and the vitamin K injection may lead to a hematoma (bleed into the skin or muscle) at the injection site.

Prothrombin deficiency

Prothrombin (= factor II) is one of the approximately 15 clotting proteins that is needed to stop us from bleeding. If you are low in prothrombin, you have a tendency to bleed. The diagnosis is made by finding low factor II activity levels in the blood. Prothrombin deficiency (= factor II deficiency) can either be inherited or acquired. The inherited form is very rare. There is typically a family history of bleeding. The acquired form is also uncommon, but can occur together with a lupus anticoagulant (which is one type of the antiphospholipid antibodies). It is then called "hypoprothrombinemia-lupus anticoagulant syndrome". Not everybody with antiphospholipid antibodies or lupus anticoagulant also has hypoprothrombinemia; very few patients do. If patients have a lupus anticoagulant and hypoprothrombinemia, they may either bleed, due to their low factor II levels, or clot, due to their lupus anticoagulant. Sometimes they do both. Prothrombin deficiency together with deficiencies of other clotting proteins is furthermore seen in the following situations:

- vitamin K deficiency
- coumadin (= warfarin) therapy
- liver disease
- rat poison ingestion

Prothrombin 20210 mutation

The prothrombin 20210 mutation (= factor II 20210 mutation) is a very common mutation and is a mild risk factor for deep vein thrombosis (= DVT) and pulmonary embolism (= PE). It is also called prothrombin 20210A mutation. It occurs in approximately 2 % of the U.S. American population. Because it is a mutation that arose in Europe in the Caucasian population, it is not found in native Americans, native Africans, native Asians, and Australian aborigines. Due to the mixture of races in the U.S., it is found in 0.2 % of the Afro-American population. Individuals can either be

- heterozygous (i.e. have 1 mutated gene), or
- homozygous (i.e. have 2 mutated genes).

The mutation was discovered in 1996. It is tested for by a genetic test (PCR = polymerase chain reaction). While factor II activity levels in blood are slightly higher in individuals with the prothrombin 20210 mutation, this test is not helpful in making a diagnosis. The genetic test is the gold-standard. However, the factor II activity test is sometimes ordered by physicians. Sometimes this is done by mistake and because the physician is unfamiliar with the prothrombin 20210 mutation. Some physicians may also use the factor II activity level as a less expensive screening test; only if the factor II level is above 100 % do they obtain the genetic test. There are some pitfalls to this approach, since factor II levels are low and therefore unreliable in patients on coumadin, in patients with vitamin K deficiency, and in patients with liver disease.

Some numbers:

- 1 in 50 U.S. Americans is heterozygous for the prothrombin 20210 mutation, i.e. a total of 5.6 million people in the U.S.;
- 1 in 10,000 Americans is homozygous for the prothrombin 20210 mutation, i.e. a total of 28,000 people in the U.S.;
- A person can have both, factor V Leiden and the prothrombin 20210 mutation: 1 in 4,000 Americans is heterozygous for factor V Leiden plus heterozygous for the prothrombin 20210 mutation; that makes a total of 70,000 people in the U.S.