

32. Factor 8, 9,11, and fibrinogen and blood clots

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Q1: "If you have too much factor 8 your blood likes to clot. There is some connection with estrogen: high factor 8 means that your estrogen level is high. Having excess factor 8 is quite rare."

A1: A high level of the clotting factor 8 is a risk factor for deep vein thrombosis and pulmonary embolism. Such high levels are not rare; they are very commonly seen in patients with venous thrombosis: 20 % of patients have elevated factor 8 levels. While estrogen does, indeed, increase factor 8 levels (high estrogen and factor 8 levels are found, for example, in pregnancy), high factor 8 levels do not necessarily mean that high estrogen levels are also present. There are also other reasons for high factor 8 levels.

Q2: "I have factor 8 and I was wondering if it is safe to take Prometrium® for ten days to jump start my period. The insert says that it causes clotting problems"

A2: Prometrium is a progestin preparation. Progestins used for contraceptive purposes do not increase the risk for thrombosis in the general population (see [Q/A 23](#)). However, progestins used for therapeutic purposes have been shown to lead to a slightly increased risk of venous blood clots. Since Prometrium contains higher doses of progestins than contraceptive pills, the risk for thrombosis with Prometrium is increased. High factor 8 levels further increase that risk. How high the risk is with this combination, is not known. However, it is known that women with high factor 8 levels who use combined oral contraceptives have a 10-fold increased risk of venous thrombosis (compared to women with normal factor VIII levels who do not take oral contraceptives): approximately 1 of 1,250 such women develops a thrombosis per year. The risk of thrombosis is likely less with Prometrium. Since Prometrium is only taken for a few days, the risk is likely quite low. However, I would need to know, what prompted testing of this patient's factor 8 level in the first place, how high her factor 8 level is, and what her other risk factors for DVT or PE are, before I could make a solid individual assessment and give recommendations.

Q3: "I am FVLeiden heterozygous and have a history of DVT. I just learned that my grandmother's sister died of factor XI complications. I know that I am obviously not a hemophiliac, but I was researching the internet and came across information regarding high levels of factor XI associated with blood clots. Anyone have any comments?"

A3: High levels of the clotting factor XI (factor 11) are a very mild risk factor for deep vein thrombosis and pulmonary embolism. Deficiency of factor XI causes a bleeding problem.

Increased levels of several of our clotting factors lead to an increased risk for deep vein thrombosis and pulmonary embolism. This is true for factor 8 (= factor VIII), factor 9 (= factor IX), factor 11 (= factor XI), and fibrinogen. The higher the factor level, the higher the risk for thrombosis. Compared to patients with low levels,

- patients with high factor VIII (8) levels have a 5-fold increased risk of venous thrombosis (ref. 1,2)
- patients with high fibrinogen levels have a 4-fold increased risk of venous thrombosis (ref. 3)
- patients with high factor IX levels (9) have a 2.5-fold increased risk of venous thrombosis (ref. 4)
- patients with high factor XI levels (11) have a 2-fold increased risk of venous thrombosis (ref. 5)

It is not clear why some people have higher levels than others. There appears to be an inherited component, but the high levels are not a straightforward heterozygous or homozygous condition. Since factor 8 and fibrinogen levels are often elevated when a patient is acutely sick (at a time of acute DVT or PE, infection, etc.) and decrease again when the patient has recovered, the levels should not be checked at the time of acute illness, but at baseline, i.e. 2 or 3 months after the acute illness. Since warfarin (= coumadin®) decreases factor 9 levels, obtaining factor 9 levels in patients on warfarin is not meaningful. There is no medication that can lower the levels of factor 8, factor 11, or fibrinogen. Since finding elevated levels does, at present, not influence the way these patients are managed, many physicians do not routinely test for these clotting factor levels in patients with DVT or PE. However, I often do, in the attempt to understand why a patient clotted.

References:

1. Koster T et al.: "Role of clotting factor VIII in effect of von Willebrand factor on occurrence of DVT". *Lancet* 1995;345:152-5.
2. Kamphuisen PW et al.: "High factor VIII antigen levels increase the risk of venous thrombosis but are not associated with polymorphisms in the von Willebrand factor and factor VIII gene". *British Journal of Haematology* 2001;115:156-8.
3. Koster T et al.: "Factor VII and fibrinogen levels as risk factors for venous thrombosis". *Thrombosis and Haemostasis* 1994;71:719-22.
4. van Hylckama VA et al.: High levels of factor IX increase the risk of venous thrombosis. *Blood* 2000;95:3678-82.
5. Meijers JCM et al.: "High levels of coagulation factor XI as a risk factor for venous thrombosis". *New England Journal of Medicine* 2000;342:696-701.