

## References

1. Denniston GC, Pfenninger JL. Vasectomy. In: Procedures for primary care physicians (Pfenninger JL, Fowler GC, editors). St. Louis: Mosby; 1994. p. 520–40.

### Excess Factor VIII and Hypercoagulability

*To the Editor:* The author of this article<sup>1</sup> states that “This is a report of 3 cases of thromboembolism not associated with conventional risk factors (trauma, cancer, or immobility). The patients were found to have elevated factor VIII activity without other evidence of a hypercoagulable state.”

I would respectfully disagree that the patients show no evidence of any other hypercoagulable state. The anti-thrombin level was low in all 3 patients and could constitute a prothrombotic risk factor. In addition, the known risk factors, factor V Leiden and the prothrombin gene mutation, were not evaluated. Thus, we do not know whether the patients had these common risk factors.

The author also quotes sources to support the contention that “Elevated factor VIII levels have been found to persist over time and to be independent of the acute phase response.”

This statement is a little misleading in the context of the current report. Previous studies found that even though factor VIII (FVIII) is an acute phase reactant, elevated FVIII levels persisted in some patients with thrombosis after an acute inflammatory stimulus had resolved. In addition, those authors compared FVIII levels with other acute phase reactants (ie, fibrinogen and C-reactive protein [CRP]) to determine whether there was evidence of concurrent acute inflammation. They only considered FVIII level to be an independent (not inflammation-related) risk factor for thrombosis when levels of other acute phase reactants were not elevated. The current study did not verify, by measuring CRP or fibrinogen levels, that the patients did not suffer from an inflammatory state that could have elevated FVIII levels.

Thus, it would have been very useful to know the CRP and fibrinogen levels for the patients reviewed in this report. This would allow firm conclusions to be drawn about whether the FVIII elevation was or was not related to a concurrent inflammatory state. The presence of an inflammatory state might suggest the presence of other factors predisposing to thrombosis. Thus, I do not believe that the author has clearly ruled out other risk factors for thrombosis in his patients and thus cannot attribute their thrombotic tendency to elevated FVIII levels.

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## References

1. Bobrow RS. Excess factor VIII: a common cause of hypercoagulability. *J Am Board Fam Pract* 2005;18:147–9.

### Author's Reply

*To the Editor:* In her critique of our article, Dr Hoffman states that factor V Leiden and the prothrombin gene mutation were not evaluated in the three patients. They were. The “NP” in the table means “not present” (see key under table).

That factor VIII can be an acute phase reactant seems to be common knowledge. However, I listed 3 references<sup>1–3</sup> that specifically examined this in patients with venous thromboembolism (VTE) and concluded that the increase in factor VIII was “persistent and independent of the acute phase response.” O’Donnell et al<sup>1</sup> use that specific phrase in their title and find 94% of 35 VTE patients with elevated FVIII to have a persistent increase, independent of CRP and fibrinogen. O’Donnell et al<sup>2</sup> found elevated FVIII to be the single most common risk factor in 260 VTE patients and also stated that it did not correlate with CRP or fibrinogen. Kamphuisen et al<sup>3</sup> reached the same conclusion. (“Increased levels of FVIII and fibrinogen in patients with VTE are not caused by acute phase reactions.”)

I would have liked to have had CRP and fibrinogen levels on my patients, but this was a retrospective study and none were done.

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## References

1. O’Donnell J, Mumford AD, Manning RA, Laffan M. Elevation of FVIII: C in venous thromboembolism is persistent and independent of the acute phase reaction. *Thromb Haemost* 2000;83:10–3.
2. O’Donnell J, Tuddenham EG, Manning R, Kembell-Cook G, Johnson D, Laffan M. High prevalence of elevated factor VIII levels in patients referred for thrombophilia screening: role of increased synthesis and relationship to the acute phase reaction. *Thromb Haemost* 1997;77:825–8.
3. Kamphuisen PW, Eikenboom JC, Vos HL, et al. Increased levels of factor VIII and fibrinogen in patients with venous thromboembolism are not caused by acute phase reactions. *Thromb Haemost* 1999;81:680–3.