To the editor:

**Factor V Leiden and intracranial hemorrhage**

The prevalence of factor V Leiden (FVL) in people of northern and central European descent suggests that FVL bestowed a survival advantage on those populations. In the study by Corral et al., the presence of FVL reduced the risk of spontaneous intracranial hemorrhage by 5-fold. Specifically, FVL protected against hemorrhagic transformation of ischemic events associated with arteriosclerotic cerebrovascular disease in subjects with a mean age of 66.4 years. Although this finding is of interest, it seems unlikely that this advantage led to the persistence of FVL in European populations. There is no apparent survival advantage, biologically speaking, to protecting elders from hemorrhagic stroke. It is more plausible that this allele protected those of childbearing potential. Today, acquired hemorrhagic disease is uncommon in young people. However, it is likely that hemorrhagic disease of the newborn (HDN) was prevalent thousands of years ago, contributing significantly to neonatal mortality. HDN is caused by vitamin K deficiency, a common condition in neonates even today, and can result in life-threatening intracranial hemorrhage. Therefore, one could hypothesize that FVL is prevalent in certain populations because it lessens the severity of HDN. It is possible that clinically significant vitamin K deficiency was more common thousands of years ago because food sources rich in vitamin K were not available year-round and breast-feeding, which is a significant risk factor for HDN, was more common.

The hemostatic system of the neonate is such that the presence of FVL could result in enhanced thrombin generation because of the limited capacity of both the antithrombin and the protein C pathways. Significant vitamin K deficiency could further enhance this effect. In the neonate, levels of procoagulant and anticoagulant vitamin K–dependent proteins are low. In the healthy neonate, a balance is maintained, making bleeding and thrombotic complications uncommon. With worsening vitamin K deficiency, this balance is lost in favor of bleeding. The presence of factor V Leiden could prevent the loss of this fine balance by attenuating the protein C pathway.

The study by Corral et al. is important in that it lends evidence to the notion that there is benefit to having factor V Leiden. However, for a polymorphism associated with disease to persist in a population, the net effect must favor survival of those most likely to procreate. Nonetheless, the hypothesis that FVL protects against fatal intracranial hemorrhage in neonates with HDN would be difficult to prove; therefore, the elder population with cerebrovascular disease will have to suffice as an acceptable experimental model.

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**References**


To the editor:

**Short-course corticosteroid-induced pulmonary and apparent cerebral aspergillosis in a patient with idiopathic thrombocytopenic purpura**

In a recent report on adults with idiopathic thrombocytopenic purpura (ITP), Portielje et al. presented limited data on the morbidity and mortality attributed to the systemic effects of short-course corticosteroids in the context of initial treatment of ITP. Certain patients may be at high risk for unusual opportunistic infections.

In this letter we present a patient with ITP and no occupational hazard or apparent underlying disease who, during the course of treatment with oral methylprednisolone (MP), developed invasive bilateral pulmonary aspergillosis and multiple intracerebral lesions, presumably due to aspergillosis. We believe that this is the first reported case of cerebral aspergillosis after short-course corticosteroid treatment in an otherwise immunocompetent host with ITP.

A 52-year-old man was admitted to our department with asymptomatic severe thrombocytopenia (18 × 10^9/L), found on a routine full blood count (FBC). Clinical examination was unremarkable. Routine blood chemical values were normal, and tumor markers were negative. Serological tests for hepatitis B and C viruses, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, herpes zoster virus, and human immunodeficiency virus (HIV) were negative. The patient had no clinical or laboratory evidence of autoimmune or immunodeficiency syndromes. Findings on chest radiograph and computed tomography (CT) scans of the chest, abdomen, and pelvis were normal. A bone marrow smear revealed normal numbers of megakaryocytes in an otherwise normal bone marrow, while antiplatelet IgG and IgM antibodies were positive. Treatment was initiated with 1 mg/kg oral MP daily, and 3 days later the patient was discharged after a prompt recovery of the platelet (PTL) count (70 × 10^9/L). The patient was followed up at the outpatient clinic, and tapering of MP was initiated after 4 weeks of treatment, while corticosteroid-induced type 2 diabetes mellitus developed. Eight weeks later, while on 24 mg MP daily, the patient was readmitted, afebrile and with a 3-day history of fatigue and palpitation. The FBC revealed a normal hemoglobin level and
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