Factor V Leiden mutation is associated with improved 30-day survival in patients with acute respiratory distress syndrome.


Abstract:
Researchers in Essen retrospectively examined 106 ICU patients with ARDS. Seven of the patients proved heterozygous for coagulation factor V Leiden (FVL), in which mutation glutamine replaces arginine in position 506 of the normal protein. The other 99 patients were homozygous for the normal factor. All of the FVL patients survived, while the genetically “normal” patients suffered 42% mortality at 30 days (p = .049) and 49% at 174 days (p = .014). No thrombotic complications were noted, but all patients were anticoagulated during ICU care with intravenous heparin or, in event of thrombocytopenia, hirudin.

Comments:
Coagulation factor V functions as cofactor for the conversion of prothrombin to thrombin by factor Xa. The FVL variant is fairly common (5% incidence of heterozygotes) and is resistant to inactivation by activated protein C, an enzyme that helps to prevent intravascular coagulation. Consequently, patients carrying FVL are at risk for thrombosis. It is surprising that this apparently deleterious genetic variation has a high incidence. Apparently, there are benefits in critical illness that weigh against the prothrombotic downside. Previous studies indicate that FVL is beneficial in clinical and experimental sepsis.

The FVL phenomenon is reminiscent of that of the sickle cell allele for hemoglobin. Though a double dose of the sickle cell allele is devastating, the incidence of the allele is kept high by natural selection because of benefit against malaria. Perhaps the incidence of otherwise deleterious FVL is kept high by benefits against severe illness.

The Essen group has previously determined that the so-called I allele (as opposed to the D allele) of angiotensin-converting enzyme reduces mortality from ARDS. That and the present observation indicate that genomics will have increasing prognostic value in critical care. Genomic observations may also lead to pharmacological therapies. Certainly, the coagulation and angiotensin systems are both subject to pharmacological manipulation.

The pharmacological implications of the present study are intriguing. The authors speculate that the benefit of FVL involves increased production of thrombin and concomitantly increased production of activated protein C. Yet, for fear of thrombosis, all of the patients were anticoagulated with heparin or hirudin. Those drugs are, of course, expected to oppose the proposed mechanism of benefit of FVL. Perhaps the anticoagulants had a detrimental effect on the ARDS process. That possibility poses a superb dilemma. Similarly, though aprotinin is clinically now in limbo, its inhibition of activated protein C could theoretically worsen ARDS in view of the Essen hypothesis. In any event, it is regrettable that FVL does not seem to prevent the onset of ARDS. Otherwise, there would be a lower incidence of FVL in these ARDS patients.