formally contraindicated in most cases of clinical DIC. In conclusion, enhanced fibrinolysis plays an important role in preventing the development of organ failure in a model of TTF-induced DIC.

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Disorders of Hemostasis

Duplication of exon 13 causes one third of the cases of mild hemophilia A in northern Italy

A rearrangement of exon 13 in the factor VIII gene has been identified as the causative mutation in 32% of Northern Italian patients with mild hemophilia A. We have demonstrated that all share a common haplotype, thus suggesting that the mutation likely occurred in a single ancestor. To date, no predominant mutation has been identified in mild hemophilia A, therefore it would be extremely useful to carry out more extensive studies to ascertain whether the mutation is confined to northern Italy.

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Hemophilia A (HA) is an X-linked recessive disease, caused by wide-spread mutations in the factor VIII (FVIII) gene (http://europium.csc.mrc.ac.uk). Direct high performance liquid chromatography (DHPLC) screening detected a causative mutation in 9 of the 18 mild (FVIIIC ≥ 5%) HA patients examined among the families as well as the fact that about 50% of the cases were apparently sporadic, observed from the reported family history, are two features that seemingly contrast with these results. However, we must remember that most positive patients had a FVIII:C ≥ 8%, that they had been diagnosed in adulthood following trauma and/or surgical procedures, and that they could have had undiagnosed ancestors. Moreover, for the same reasons we were only able to examine the members of two generations. The body of information we obtained allows us to make some remarks. Firstly, conventional mutation screen-
Acquired hemophilia (AH) is a rare syndrome caused by inhibitors to factor VIII (rarely to factor IX), characterized by the sudden onset of bleeding, usually severe, in patients with no family or personal history of bleeding diatheses. It is a medical emergency, requires prompt treatment and is clinically and financially demanding. Various therapies can be used: human or porcine FVIII, DDAVP, immunoglobulins, activated prothrombin concentrate, immunoadsorption and recombinant activated factor VII (rFVIIa). The available data are from anecdotal case reports and retrospective studies with a limited number of patients; none of the available agents is effective in all the patients. rFVIIa, a systemic hemostatic agent with topical action, is beneficial in a variety of bleeding conditions: hemophiliacs with inhibitor, elective surgery (prostatectomy, hepatectomy, liver transplantation), hereditary platelet disorders, and severe bleeding secondary to oral anticoagulation and trauma.2,4

The multicenter study by Hay et al. on the use of the rFVIIa is the largest so far reported.1 Our study is a retrospective analysis of the patients reported to the Italian registry in 2001 (www.emonet.org) who were treated with rFVIIa. The following information was requested: primary condition, cause of bleeding or its spontaneous occurrence, site, severity evaluated by the hemoglobin level and by transfusion requirements, inhibitor titer, therapy, selection criteria and results. The clinical response was evaluated by the patient’s physician at 6, 12, 24 and >24 hours and was scored as very effective (complete cessation of bleeding), effective (residual minor bleeding), partially effective (reduced but still significant bleeding); ineffective. Any adverse event occurring within two months of the end of treatment was recorded. Twenty-eight new patients were registered, 15 of whom were treated with rFVIIa, 11 with other modalities, and 2 who did not require treatment (Table 1). rFVIIa was selected as first-line treatment in 19 bleeding episodes because of the severity of the episode and as salvage in one case. Bleeding was controlled in 90% of the patients, indicating the efficacy of rFVIIa in HA.

References