



Dr
Yesim
Dargaud

I am in my final year of residency at Edouard Herriot University Hospital, Lyon, France, and expect to obtain my MD degree in April 2004. My particular area of interest is hemostasis and hemophilia and I plan to continue my clinical training in this field to become an expert in coagulation disorders.

Under the mentorship of Professor Claude Negrier my training will cover three main topics:

- 1) Extend my participation in the Hemophilia Comprehensive Care Centre
- 2) Continue my PhD project on factor VIII and factor IX expression in human hematopoietic CD34+ cells
- 3) Conduct a research project on the utility of the Thrombin Generation Test (TGT) in hemophilia patients and especially in the follow-up of treatments given to inhibitor-developing hemophiliacs.

Approximately 30% of severe hemophilia A and 5% of severe hemophilia B patients develop an inhibitor to coagulation factor concentrates within the first 50 days of exposure. In

Thrombin generation test in the monitoring of by-passing agents in patients with inhibitors

these patients, classical FVIII/FIX replacement treatment may become inefficient, necessitating the use of bypassing agents such as rFVIIa and APCCs. These agents have complex modes of action but all limit bleeding by triggering thrombin generation without any influence on the plasmatic level of FVIII/FIX. A major limitation is that no routine test is available to predict or to monitor the hemostatic potential of these bypassing agents. Moreover, the optimal dose to use in various clinical situations is not clearly established.

Two major risks associated with surgery in inhibitor-developing patients are excessive bleeding and disseminated intravascular coagulation/thromboembolism. Available routine laboratory tests have a poor capacity for the early detection of these complications and permit very limited correlation with clinical efficacy of bypassing agents. As the final product generated by bypassing agents is thrombin, it is worthwhile to test thrombin generation for the monitoring of the bypassing agents in inhibitor-developing hemophiliacs. TGT permits a real-time measurement of the thrombin concentration generated in plasma. It can thus give objective, ex vivo information on the hypo- or hypercoagulability state of the coagulation system. Recently published data on a limited population showed that the TGT might enable the monitoring of the thrombin generating capacity induced by the bypassing agents. Some preliminary work has been done in our centre, and I recently had the opportunity to undergo training on TGT in Maastricht,

under the supervision of Professor HC.Hemker and Professor S.Beguin. We have subsequently planned a scientific collaboration on this topic.

The Haemostasis Department at Edouard Herriot University Hospital provides a provincial resource for specialized hemostasis. Approximately 4500 hemostasis consultations are performed annually and there is a highly specialized hemostasis laboratory with specifically trained technicians. As a recognized reference centre in France, the Lyon Haemophilia Centre with the support of the coagulation laboratory and the preclinical research structure would, in combination with the Bayer Clinical Scholarship Award Program, provide the best possible opportunity to develop my skills in the field of hemostasis and thrombosis.

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