Standardization of coagulation and fibrinolysis methods

Esbjerg, April 2000 Jörgen Jespersen,MD, DSc. Professor

Comprehensive biochemical research during the last 20-30 years has increased our insight in the composition and regulation of the systems of coagulation and fibrinolysis. It has become clear that these are basic biological systems, which are of main importance for a normal tissue repair, and therefore systems which are involved in the pathogenesis of major groups of diseases such as cardiovascular diseases, rheumatic diseases and cancer.

In the clinical laboratory information on the patient status regarding activity of coagulation and fibrinolysis was traditionally obtained with the use of complex biological measurement systems, but today most of the components involved in coagulation and fibrinolysis can be measured with so-called specific enzymatic and/or immunologic methods. It has been appreciated from clinical studies that measurement of coagulation and fibrinolysis proteins may give significant information with respect to e.g. risk stratification of patients with cardiovascular diseases, monitoring of antithrombotic treatment, identification of factor deficiency states, and in the monitoring of critically ill patients. Still, only a limited number of methods have been introduced wide spread in the clinical laboratory.

Why have the clinical laboratories hesitated to introduce new coagulation and fibrinolysis quantities in their standard repertoire? One central explanation is that there has not been a general standardization policy within this particular field of clinical biochemistry. Despite some national efforts (NCCLS; DIN) a comprehensive international standardization system has only succeeded for: Coagulation, tissue factor-induced; relative time (formerly prothrombin time), in which results are now expressed in terms of INR.

Also, the Standardization and Scientific Committee (SSC) within the International Society of Thrombosis and Haemostasis (ISTH) has been aware of the lack of a general standardization policy for coagulation and fibrinolysis proteins. This is the background why an ad hoc committee was established within SCC (Subcommittee of Fibrinolysis) dealing with standardization of methods. The work of this committee made it more and more clear that standardization issues could not be solved with EQUAS and with the use of common standards for a given analyte, because such an approach did not solve problems such as tremendous interlaboratory and between methods variation. It became clear that the most appropriate approach to standardization was the establishment of comprehensive standardization measurement systems known from clinical biochemistry.

Now the time had come to join forces with IFCC and contact between the Scientific Division and ISTH was established. In 1997 at the ISTH meeting in Florence a joint committee between ISTH and IFCC was formed. The aims of this new committee termed ACommittee - Standardization of Coagulation Test (C-SCT)@ were defined and agreed upon, and subsequently at the SSC meeting in Ljubljana in 1998 a basic discussion was started on defining standards on a molecular basis of a defined analyte instead of using activity- based arbitrary units. It was the opinion of the Committee members that it is essential in the future to assign

values to standards on the basis of highly specific and accurate methods when possible and not on the biological methods traditionally used within the field of coagulation and fibrinolysis. With establishment of C-SCT the exploratory work of the ad hoc committee under SSC has been brought to an end. The C-SCT included members who on one side are experienced within coagulation and fibrinolysis testing (ISTH) and on the other side are experienced with standardization of methods used widespread in the clinical laboratory (IFCC). Thus an important platform has been created, which in perspective will facilitate the widespread introduction of evidence-based clinically relevant coagulation and fibrinolysis methods in the laboratory.