

This Week's Citation Classic

Bachmann F, Duckert F & Koller F. The Stuart-Prower factor assay and its clinical significance. *Thrombos. Diath. Haemorrh.* 2:24-38, 1958. [Coagulation Lab., Dept. Medicine, Univ. Zürich, Switzerland]

A simple one-stage method is described for the assay of blood coagulation Factor X (Stuart-Prower-factor), using Seitz's filtered bovine plasma, Russell's viper venom, and cephalin as a source of lipid. Assay values of Factor X are not influenced by different concentrations of fibrinogen, prothrombin, or Factors V or VII. [The *SCI*[®] indicates that this paper has been cited over 390 times since 1961.]

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"During the early 1950s several new blood coagulation factors were discovered in rapid sequence. Their simultaneous discovery by several groups of investigators resulted in a profusion of nomenclature. Malicious critics maintained that the field of coagulation was but one unholy mess and that the main purpose of coagulationists at international meetings was to disagree. From 1951 to 1954, no less than four new coagulation factors were discovered (Proconvertin, SPCA, VII; Christmas factor, PTC, IX; PTA, XI; Hageman, XII).

"In 1955, Duckert et al.¹ postulated the existence of Factor X on the basis of *in vitro* experiments. Patients hitherto thought to suffer from Factor VII deficiency but whose coagulation defect resembled more closely that caused by the postulated Factor X were soon discovered independently in 1956 by Telfer et al.² (Prower-factor) in England, by Hougie³ (Stuart-factor) in the US, and in 1957 by our research group⁴ in Zurich,

Switzerland (Delia factor). During this exciting time I worked on my MD thesis in the lab of Koller, a physician who had early realized the importance of basic biochemistry in the field of hemostasis. His foresight led to the hiring of Duckert, a biochemist. The coagulation laboratory in Zurich initiated many physicians into the basic concepts of research work and the puzzling pedagogic tactics of Duckert. I remember how I was laboring to produce some fraction devoid of Factor X, trying various adsorption and salt precipitation methods, only to conclude, several weeks later, that all my attempts had been futile. At one point, Duckert smilingly observed: 'Don't continue along this line. It won't work. I too have tried all this without result.' To my astonished and dismayed question why he had not stopped me earlier, he calmly replied. You learn by your mistakes, not by your successes.'

"The observation of Hougie,³ that Russell's viper venom directly activates Factor X, i.e., acted like the combination of tissue thromboplastin plus Factor VII, led to the development of our assay. I was systematically exploring the optimal conditions for the preparation of the reactifs used in the assay, their optimal concentration and stability on storage at different temperatures, and the effect of surface contact. Rereading the article I realise that I have apparently succeeded in delineating all the possible pitfalls encountered in the preparation of the reagents and in revealing all the little tricks of the trade upon which the successful duplication of a method often depends.

"The paper had quite a success shortly after its publication and our 300 reprints were soon exhausted. Factor X was to be come a coagulation factor of crucial importance, because it takes a central position in the coagulation system, and its activated form, Factor Xa, is inhibited by small doses of heparin. This latter observation provided the basis for the successful and widely utilized low dose heparin prophylaxis in patients at risk to develop deep vein thrombosis."

1. Duckert F, Flückiger P, Matter M & Koller F. Clotting Factor X. Physiologic and physicochemical properties. *Proc. Soc. Exp. Biol. (NY)* 90:17-22, 1955.
2. Telfer T P, Denson K W & Wright D R. A 'new' coagulation defect. *Brit. J. Haematol.* 2:308-16, 1956.
3. Hougie C. The role of the Russell's viper venom on the Stuart clotting defect. *Proc. Soc. Exp. Biol.* 93:570-3, 1956.
4. Bachmann F, Duckert F, Geiger M, Baer P & Roller F. Differentiation of the Factor VII complex. Studies on the Stuart-Prower factor. *Thrombos. Diath. Haemorrh.* 1:169-94, 1957.