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# This Week's Citation Classic™

**Koller F, Loeliger A & Duckert F.** Experiments on a new clotting factor (Factor VII). *Acta Haematol.* **6**:1-18, 1951. [Department of Medicine, University of Zurich, Switzerland]

**Evidence for the existence of a factor in normal serum and plasma that accelerates thrombin formation is presented. It is not consumed during coagulation and is absorbed on barium sulfate. Its concentration is lowered very rapidly by oral anticoagulants. We designated it Factor VII. [The *SCI*® indicates that this paper has been cited in over 365 publications since 1955]**

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**"The starting point for the recognition of Factor VII as a new clotting factor was a contradiction: Owren declared in 1950 at the meeting of the European Society of Haematology in London that prothrombin was not consumed during normal blood coagulation but could be demonstrated in serum in high concentrations for weeks at a time.[1] This finding was in strict opposition to the classical coagulation theory and particularly to the work of Brinkhous (prothrombin utilisation test)[2] and Quick (prothrombin consumption test).[3] Obviously, Owren, on the one hand, and Brinkhous and Quick, on the other, were not referring to the same clotting factor. Loeliger, in our laboratory, therefore analysed both factors using the same assay methods as the authors mentioned, and Duckert isolated and purified Owren's factor using barium sulfate adsorption, elution with citrate, dialysis, and so on. With various concentrations of this purified factor (all other clotting factors being kept constant), they showed that the quantity of thrombin formed did not change, but that the velocity of its formation varied in proportion to the concentration. Owren's factor, which under normal conditions is present in about the same concentration in plasma as in serum, was therefore recognized as an accelerator of prothrombin conversion — as a new clotting factor that we designated Factor VII. Moreover, it could be demonstrated that the factor that is consumed during coagulation and therefore does not exist in normal serum (or only in traces) is the real precursor of thrombin and therefore has to be designated as prothrombin. Variations in its concentration correspond exactly to variations in the quantity of thrombin formed. The velocity of thrombin formation is, however, not influenced by this factor.**

**"Concerning terminology, we adopted the designation of clotting factors by Roman numerals inaugurated by Owren (Factor V). In 1954, an International Congress on Thrombosis and Embolism was held in Basel, Switzerland, where mutual understanding was almost impossible because of the many different names proposed for the same clotting factors. Therefore, on the initiative of Irving Wright in New York, a committee for the standardisation of the nomenclature of clotting factors was founded at the congress. Four years later, an agreement was reached: Roman numerals were recommended by the committee for the designation of all clotting factors, a proposal that has been almost universally accepted. Our designation of Factor VII therefore had important consequences.**

**"The reason this paper has been cited often is perhaps the thoroughness with which the characteristics of the new factor had already been studied in 1951 (purification, assay method, its role in thrombin formation, comparison with prothrombin, behaviour during anticoagulant treatment, and so on). The fact that Factor VII is lowered by anticoagulants more rapidly than any other vitamin K-dependent factor has practical implications in the beginning of anticoagulant therapy (sensitivity of thromboplastin to Factor VII in the Quick-test).**

**"For recent review articles on the present status of Factor VII, see references 4 and 5."**

1. **Owren P A**. Parahaemophilia: haemorrhagic diathesis due to absence of a previously unknown clotting factor. *Lancet* **1**:446-50. 1947. (Cited 85 times since 1955.)
2. **Brinkhous K M.** A study of the clotting defect in hemophilia: (he delayed formation of thrombin. *Amer. J Med. Sci.* **198**:509-16. 1939.
3. **Quick A J.** On the quantitative estimation of prothrombin. *Amer. J. Clin. Pathol.* **15**:560-6. 1945.(Cited 125 times since 1955.)
4. **Zur M & Nemerson Y.** Tissue factor pathways of blood coagulation. (Bloom A L & Thomas D P. eds.)*Haemostasis and thrombosis.* Edinburgh: Churchill Livingstone. 1981. p. 124-39.
5. **Rapaport S I**. The activation of Factor IX by the tissue factor pathway. (Menaché D. Surgenor D. Mac N & Anderson H D. eds ) *Haemophilia and haemostasis.* New York: Liss. 1981. p. 57-76.