

# This Week's Citation Classic

**Hardisty R M & Macpherson J C.** A one-stage factor VIII (antihæmophilic globulin) assay and its use on venous and capillary plasma. With a note on the calculation of confidence limits by G.I.C. Ingram. *Thromb. Diath. Haemorrhag.* 7:215-29, 1962. [Department of Haematology, Hospital for Sick Children, London, England]

The paper describes a one-stage method for the assay of factor VIII, in which contact activation is controlled by the addition of kaolin to the system. Normal range, confidence limits, and correlation with the results of a two-stage method are given. [The *SCI*<sup>®</sup> indicates that this paper has been cited over 280 times since 1962.]

R.M. Hardisty  
Department of Haematology  
Hospital for Sick Children  
London WC1N 3JH  
England

April 13, 1981

"There is nothing particularly revolutionary, or even original, about this paper. It is simply a detailed description of a method which has subsequently been widely adopted in a rapidly developing field, and has evidently stood the test of time — a contribution to technology rather than a major conceptual development. No doubt most of the citations appear in the methods section of subsequent papers: a prosaic, if honourable, way to 'classical' status.

"In the late 1950s, factor VIII (the antihæmophilic factor in plasma) was usually assayed either by two-stage methods based on the thromboplastin generation test or by one-stage methods based on the partial thrombo-plastin time. The latter methods,

though simpler to perform, were in general less accurate and reproducible than the former. Margolis had already shown that the chief source of variability in such methods was the nature and amount of surface to which the plasma was exposed, and had devised a simple screening test for blood coagulation defects in which these were controlled by the addition of a standard amount of kaolin suspension to the test system.<sup>1</sup>

"The first step in the activation of the blood coagulation mechanism by such foreign surfaces had been shown to concern the Hageman factor (now called factor XII). It is therefore perhaps not surprising that the first people to adapt Margolis's test as a specific assay method should be Oscar Ratnoff (who first described Hageman and his clotting defect) and myself (who discovered the first British case of Hageman trait, and had worked with Margolis on the role of the Hageman factor in blood coagulation). Breckenridge and Ratnoff, in fact, independently arrived at a factor-VIII assay method which was almost identical to ours in every detail, and published it three months later.<sup>2</sup>

"Why, then, should our paper have been the one to become a *Citation Classic*? Ratnoff was kind enough to concede that our job was more thorough than theirs, thanks largely to the careful statistical evaluation carried out on our data by Ilsley Ingram. Another probable reason is that Breckenridge and Ratnoff buried their method in a paper about factor-VIII inhibitors, while the description and evaluation of the technique was the chief *raison d'être* of our paper."

1. **Margolis J.** The kaolin clotting time. A rapid one-stage method for diagnosis of coagulation defects. *J. Clin. Pathol.* 11:406-9, 1958.
2. **Breckenridge R T & Ratnoff O D.** Studies on the nature of the circulating anticoagulant directed against antihæmophilic factor: with notes on an assay for antihæmophilic factor. *Blood* 20:137-49, 1962.