

## This Week's Citation Classic

**Merskey C, Johnson A J, Kleiner G J & Wohl H.** The defibrination syndrome: clinical features and laboratory diagnosis. *Brit J. Haematol.* 13:528-49, 1967.  
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**This paper demonstrates that nearly all cases of defibrination syndrome are associated with evidence of intravascular coagulation. Fibrinolysis is probably a secondary phenomenon as it cannot be shown by circulating plasmin or activator in the great majority of cases. Heparin therapy is occasionally beneficial. [The SCI® indicates that this paper has been cited over 230 times since 1967.]**

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May 10, 1978

"In the 1950s and early 1960s hypofibrinogenemia was attributed to circulating fibrinolysis. In the 1950s in Capetown, South Africa, I remember investigating a patient with such a syndrome, with Henriette Lackner, our local fibrinolysis expert, and being very puzzled by the lack of any evidence of lytic activity. Herbert Wohl and I encountered the same situation at the Bronx Municipal Hospital Center (BMHC) in 1961. At that time we consulted with Alan Johnson of New York University who had spent many years studying fibrinolysis and had available many different tests for fibrinolytic activity, including tests for many inhibitors. Again we drew a complete blank. He and Jack Newman recommended that we treat with human fibrinogen, the approved method of therapy at that time. This was infused, but it all disappeared overnight. Meanwhile all the clotting studies we had done suggested intravascular clotting, so with much trepidation we tried an anticoagulant, heparin. To our

surprise it worked, and the results of the clotting studies improved. When we stopped the heparin, to rule out coincidence, the patient deteriorated rapidly, showing symptoms suggestive of stroke. He improved when heparin therapy was resumed, convincing us that our new hypothesis was valid.

"At about this time, in John Sandson's immunology laboratory I found Joe de Vito measuring antigens with the Borden technic using formalinized, tanned red cell agglutination inhibition. I wondered whether it would work with fibrinogen as an antigen, and he thought it might. We tried it, to our joy, with success. Thus was born the tanned red cell hemagglutination inhibition immunoassay for fibrinolytic split products (TRCHII for short).

"George Kleiner and Wilma Marcus had a research laboratory in the labor ward of the BMHC, just one flight above our lab. They too were puzzled by the hypofibrinogenemia seen in obstetric patients. George visited James Pert's laboratory in Washington, DC, to learn the 'new' technic of immunoelectrophoresis. We were thus all set to study the many patients on the medical, surgical, and obstetrical services with similar disease syndromes, and the new technics at our disposal yielded positive and encouraging results.

"One day I heard from Rosemary Biggs that Gwyn MacFarlane, the doyen of the coagulation field in Great Britain, with whom I had spent an exciting two-year fellowship at the Radcliffe Infirmary, Oxford, was retiring. His colleagues were planning a *festschrift* in the *British journal of Haematology* in his honor. Her request for a suitable paper for this special number came at the right time. By then we were assembling all our data; what better place and better occasion to publish it? Subsequent studies by ourselves and others<sup>1</sup> led to much better understanding of this disease syndrome and thus to more rational therapy."

1. **Merskey C, Johnson A J, Harris J U & Wang M T.** Isolation of fibrinogen-fibrin related antigen (FR-antigen) by immunoaffinity chromatography from normal subjects and defibrinating patients and characterized by SDS-polyacrylamide gel electrophoresis and N-terminal analysis. *Clin. Res.* 26:555A, 1978.