

This Week's Citation Classic®

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Karpatkin S & Siskind G W. In vitro detection of platelet antibody in patients with idiopathic thrombocytopenic purpura and systemic lupus erythematosus. *Blood* 33:795-812, 1969.

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This paper described two methods for the detection of serum antiplatelet IgG antibody (a platelet-factor-3 immuno-injury technique and a Dextran-agglutination technique) in patients with idiopathic thrombocytopenic purpura, a bleeding disorder with a disputed etiology. Proof was provided that the antiplatelet factor present in the serum of these individuals was an IgG immunoglobulin, providing evidence that this was an immunologic platelet disorder. [The SC[®] indicates that this paper has been cited in over 195 publications.]

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Gregory Siskind and I became good friends as intern and resident, respectively, on the NYU III Division medical house staff at Bellevue Hospital in 1960. By coincidence, we took fellowships at Washington University Medical School from 1961 to 1964. He furthered his immunologic interest by measuring antibody binding affinity with Herman Eisen in the Department of Microbiology, whereas I developed an interest in hematology, spending one year with William Harrington in the Division of Hematology and two years in biochemistry with Ernst Helmreich and Carl F. Cori. Harrington had earlier performed a heroic and dramatic experiment upon himself by infusing one unit of plasma into himself from a patient with the platelet bleeding disorder, idiopathic thrombocytopenic purpura (ITP), which promptly lowered his platelet count,¹ induced bleeding, and forced his immediate hospitalization. This, as well as other experiments, convinced him that ITP was an im-

munologic disorder due to the presence of circulating 7S IgG antibody, which coated platelets that were then phagocytosed by the reticuloendothelial system. However, the immunologic etiology of this disorder remained controversial, with many investigators criticizing Harrington's *in vitro* platelet agglutination studies of serum antiplatelet antibody reactivity.

After having completed our fellowships, Siskind and I again coincidentally obtained positions at New York University School of Medicine as instructors in the Department of Medicine, he in the Division of Immunology, I in the Division of Hematology. Having been students together and friends for many years, it was natural for us to discuss an area of overlapping interest: immunology as it relates to hematology. Out of these "social" discussions, the decision to collaborate on studying ITP arose. Using an indirect method for the detection of antiplatelet antibody, the platelet-factor-3 immuno-injury technique, but carefully controlling all experimental conditions, we proved that ITP was indeed an immunologic disorder due to the presence of 7S IgG antiplatelet antibody. The IgG could be adsorbed to platelets and it was established that the antiplatelet factor or agglutinin noted by others was neither thrombin nor residual prothrombin converted to thrombin, as had been proposed.²

Similar findings were obtained in patients with systemic lupus erythematosus. It is of interest that our paper, which has obviously become a classic citation, received considerable criticism from one reviewer who literally did not believe the data.

This work led to an extensive collaboration with Siskind that culminated in two important findings: (1) the spleen synthesizes a significant amount of antiplatelet antibody³ in this disorder (so that splenectomy not only removes phagocytic cells capable of destroying antibody-coated platelets, but also removes a source of antibody production) and (2) patients in "remission" have a compensated thrombocytolytic state.⁴ These studies also led to our suggestion that the word "idiopathic" in ITP be changed to "autoimmune" or ATP, a terminology that has been accepted by many investigators in the field.⁵

1. Harrington W J, Minnich V, Hollingsworth J W & Moore C V. Demonstration of a thrombocytopenic factor in the blood of patients with thrombocytopenic purpura. *J. Lab. Clin. Med.* 38:1-10, 1951. (Cited 255 times since 1955.)
2. Jackson D P, Schmid H J, Zieve P D, Levin J & Conley C L. Nature of a platelet-agglutinating factor in serum of patients with idiopathic thrombocytopenic purpura. *J. Clin. Invest.* 42:383-90, 1963. (Cited 35 times.)
3. Karpatkin S, Strick N & Siskind G W. Detection of splenic anti-platelet antibody synthesis in idiopathic autoimmune thrombocytopenic purpura (ATP). *Brit. J. Haematol.* 23:167-76, 1972. (Cited 80 times.)
4. Karpatkin S, Garg S K & Siskind G W. Autoimmune thrombocytopenic purpura and the compensated thrombocytolytic state. *Amer. J. Med.* 51:1-4, 1971. (Cited 120 times.)
5. Karpatkin S. Autoimmune thrombocytopenic purpura. *Semin. Hematol.* 22:260-88, 1985.