

# This Week's Citation Classic

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Salzman E W. Measurement of platelet adhesiveness: a simple in vitro technique demonstrating an abnormality in von Willebrand's disease.  
*J. Lab. Clin. Med.* 62:724-35, 1963.

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Passage of whole blood through a column of glass beads affords a simple measure of platelet adhesiveness, which is normal in disorders of blood coagulation and in patients receiving heparin but is deficient in thrombasthenia and in von Willebrand's disease. [The *SCI*<sup>®</sup> indicates that this paper has been cited over 590 times since 1963.]

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"Spurred by the key observation of Gaarder and associates<sup>1</sup> that adenosine diphosphate (ADP) was a powerful stimulus to platelet aggregation, laboratories began in the early-1960s to show increasing interest in the sticking of platelets to natural and artificial surfaces and to each other and in the importance of abnormal platelet function in bleeding and thrombosis.

"Techniques suitable for the study of these phenomena were badly needed. Hellem had described a method<sup>2</sup> in which anticoagulated blood was pumped slowly through a column of glass beads to measure 'platelet adhesiveness,' but the test was insensitive and did not correlate with the clinical state of patients who had hemorrhagic disorders. However, after the convenience and economy of evacuated blood collection tubes (Vacutainer<sup>®</sup>) were observed on hospital wards, it required only a simple modification of Hellem's technique to permit blood drawn by venipuncture to flow directly through a glass bead column into a Vacutainer tube containing an anticoagulant. The ratio of the platelet count in such a

blood sample to that in blood without glass bead contact was for simplicity termed 'platelet adhesiveness,' although retention of platelets in the column reflected platelet aggregation as well as adhesion of platelets to the glass surfaces.

"The test proved to be a convenient bedside method for assessment of a large number and variety of patients. It was quickly found that in diseases of blood coagulation (e.g., hemophilia), retention of platelets in the column was normal, but in acquired (e.g., uremia) or inherited (e.g., Glanzmann's thrombasthenia) disorders of platelet function, the values were grossly abnormal. This also proved to be the case in von Willebrand's disease, a congenital hemorrhagic state with a long bleeding time, a low plasma level of clotting Factor VIII, and at that time a dispute about whether a vascular malformation accounted for the long bleeding time. In many respects, platelets interact with glass beads as they do with subendothelial connective tissue in hemostasis, so the test is in a sense analogous to determination of the bleeding time. Since the glass bead test was performed *ex vivo*, however, an abnormal result had to be due to defective platelet function rather than to a vascular disorder. The fault in von Willebrand's disease is now known to lie in a component of the Factor VIII molecule required for normal platelet activity.

"Though not specific, the so-called platelet adhesiveness test proved useful for screening patients with hemorrhagic disorders and a long bleeding time and also helped to identify other platelet abnormalities, e.g., during cardiopulmonary bypass. It has now given way to more specific techniques for probing the intimate details of platelet physiology.<sup>3</sup> In its day the test's most important contribution was probably that, by providing a simple probe of the function of blood platelets, it helped to expand the ranks of investigators attracted to the study of these interesting cellular particles."

1. Gaarder A, Jonsen J, Laland S, Hellem A & Owren P A. Adenosine diphosphate in red cells as a factor in the adhesiveness of human blood platelets. *Nature* 192:531-2, 1961.

2. Hellem A J. The adhesiveness of human blood platelets in vitro. *Scand. J. Clin. Lab. Invest.* 12(Suppl.):1-117, 1960.

3. Gordon J L, ed. *Platelets in biology and pathology*. Amsterdam: Elsevier/North-Holland, 1981. Vol. 2.