

# This Week's Citation Classic

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Mielke C H, Jr., Kaneshiro M M, Maher I A, Weiner J M & Rapaport S I.

The standardized normal Ivy bleeding time and its prolongation by aspirin.  
*Blood* 34:204-15, 1969.

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Primary hemostasis is achieved through interaction of platelets with the vessel wall. Clinically, this can be monitored by the bleeding time, which is an *in vivo* measurement of platelet function. This paper describes a standardized technique to measure the bleeding time and its prolongation by aspirin. [The SCJ<sup>®</sup> indicates that this paper has been cited in over 410 publications since 1969.]

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"The bleeding time is an important clinical test which is used to identify patients who are at risk for bleeding. The concept was introduced in 1910<sup>1</sup> and underwent several modifications over the ensuing decades.<sup>2</sup> However, despite these changes, the test lacked sensitivity and was poorly reproducible. In fact, many physicians stopped using the test.

"My interest in the bleeding time began in 1968 when I was a clinical fellow in hematology at the University of Southern California in Los Angeles. A patient on the surgery service had a bleeding disorder which was suspected to be secondary to a qualitative platelet dysfunction. The house staff, clinical laboratory, and surgical and hematology residents had all performed bleeding times with conflicting results. Because of my position, I was asked to unravel the mystery and make a decision concerning whether or not this patient could go to surgery. I performed the bleeding time and, to my surprise and puzzlement, failed to clarify the hematolog-

ic picture for this patient. I was rather disturbed, and that evening I reconstructed the events of the day regarding this case. Several facts emerged. First, everyone had his own variation of the bleeding time technique. They used a wide variety of punctures or incisions and performed them on different sites. Secondly, there was no control of the length or depth of the measurements. Third, everyone was trying to equate these diverse measurements to the platelets' interaction with the vessel wall. I felt that if I could control these variables and develop a standardized methodology, it would be possible to improve the precision and reliability of the bleeding time so that useful clinical information could be obtained.

"Control of the length and depth of the incision appeared to be the most important. I tried to push a #11 Bard Parker blade through a sterile cork to control the depth. This was very difficult and I cut my finger in the process. The idea of a template was developed to control the length. A heavy cardboard template was created with a center slit. Working with Melvin Kaneshiro, we launched an uncontrolled clinical trial. A reproducible incision could be made, but the trial was short-lived because we couldn't get the blades through the corks in a reproducible fashion and the cardboard template couldn't hold the force of the blade. Thus, the length of the incision was again variable.

"The idea would have died then had it not been for polystyrene. I went to the university's machine shop and they agreed to make the polystyrene blade handle and template according to my design, as well as to mill a metal gauge<sup>3</sup> so that uniform control of blade depth could be achieved. We were then able to complete a clinical study to standardize the technique and at the same time to evaluate the influence of aspirin on primary hemostasis.<sup>3</sup>

"I believe the major reason this work has been cited so often is that it allowed the clinician a sensitive and reproducible technique to measure primary hemostasis.<sup>4</sup> Today the platelet is being intensively studied for its role in thrombosis and hemorrhagic diseases."

1. Duke W W. The relation of blood platelets to hemorrhagic disease. *J. Amer. Med. Assn.* 55:1185-92, 1910.
2. Ivy A C, Nelson D & Bucher G. The standardization of certain factors in the cutaneous "venostasis" bleeding time technique. *J. Lab. Clin. Med.* 26:1812-22, 1941.
3. Kaneshiro M M, Mielke C H, Jr., Kasper C K & Rapaport S I. The bleeding time after aspirin in disorders of intrinsic clotting. *N. Engl. J. Med.* 281:1039-42, 1969.
4. Mielke C H, Jr. & Rodvlen R. Bleeding time procedures. (Seligson D & Schmidt R M, eds.) *Clinical laboratory science, section I: hematology*. Boca Raton, FL: CRC Press; 1979. Vol. 1: p. 369-80.