

## ***This Week's Citation Classic***

Brecher G, Schneiderman M & Cronkite E P. The reproducibility and constancy of the platelet count. *Amer. J. Clin. Pathol.* 23:15-26, 1953.

In blood diluted with 1% ammonium oxalate, platelets become easily recognizable by phase microscopy. The "phase" method, based on the unequivocal identification of platelets, is highly reproducible and reflects the platelet level in the circulation. [The *SCI*<sup>®</sup> indicates that this paper was cited 282 times in the period 1961-1977.]

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"The invention of the phase microscope by Zernicke enormously facilitated the examination of living cells by revealing cellular details without stains. In 1949, during explorations of the new tool, I noticed that platelets which are smooth, round discs in the circulation sent out filamentous projection *in vitro*, depending somewhat on the anticoagulant. With ammonium oxalate, the platelets appeared as dense black bodies easily distinguished from artifacts by their characteristic processes. Red cells were hemolyzed and became invisible, so they no longer interfered with counting platelets.

"The counting methods available in 1953 gave results that differed as much as twofold. We demonstrated that the entire variability of the platelet count with the new 'phase' method was accounted for by the statistical errors of counting cells in a

counting chamber. We argued that the method must, therefore, reflect the actual number of platelets in the sample because any bias would give an additional error. The argument was unconvincing to the editors of the *Journal of Laboratory and Clinical Medicine* who pointed to the many methods, some published in the *Journal of Laboratory and Clinical Medicine*, that had failed to provide reliable platelet counts. While it is pleasing that time proved our claim valid, the fact that 'phase' is still the reference method is regrettable. Our method has two drawbacks: The occasional clumping of platelets may vitiate the results and the method cannot be readily automated.

"To find oneself having written a 'Citation Classic' is pleasing to the ego. It is a sobering thought that a method paper may win these sweepstakes solely because of the frequency of the disease in which a particular measurement is useful. Thus, the frequency of citation of the phase method reflects the utility of accurate platelet counts. They are needed to quantify success of platelet transfusion and to discover mild degrees of bone marrow depression or excess platelet destruction. The physiologic message of the paper is seldom cited: platelet counts are constant for long periods in healthy individuals, but vary widely between them. The normal range is 150,000 to 450,000 platelets / mm<sup>3</sup>. A drop from 200,000 to 100,000 is known to be medically significant. May a drop from 300,000 to 200,000 have any value in predicting impending disease, given the normal constancy of platelet levels? Generally speaking, is it valuable to know an individual's 'own' level which is much narrower for many serum constituents than the 'range of normal'?<sup>1</sup> These puzzling questions are still unanswered "

1. Williams G Z. Clinical pathology tomorrow. *Amer. J. Clin. Pathol.* 32:121, 1962