EDITORIAL

Why Has the Autohemolysis Test Not Gone the Way of the Cephalin Flocculation Test?

By E. Beutler

MEDICINE CHANGES. Twenty-five years ago, a battery of liver function studies included the cephalin flocculation and thymol turbidity tests; today’s house officers have never heard of these procedures because they have been supplanted by more specific and more quantitative tests. Nowadays a comment about the “NPN” is greeted with blank stares; no young physician has ever heard of a nonprotein nitrogen determination as a test of renal function. The ballistocardiogram saw its heyday some 15 yr ago, but we rarely hear of it today. However, the autohemolysis test seems to live on.

In 1954, Selwyn and Dacie, studying a relatively recently recognized group of hemolytic disorders, the hereditary nonspherocytic hemolytic anemias, noted that when sterile blood from these patients was incubated for 24 or 48 hr, more hemolysis than normal occurred. Investigating four such patients, they observed that in two patients autohemolysis was relatively modest and was partially corrected by glucose, while in two cases hemolysis was more severe and was not corrected by glucose.

Studies were also carried out with adenosinetriphosphate (ATP) in the suspending medium, a strange addition since ATP does not penetrate the red cell membrane. The fact that an effect on hemolysis was observed was most likely due to the effect of ATP on pH, since it is very acid, and on osmolarity, since very high concentrations were used. The phenomenon of “autohemolysis” is undoubtedly a very complex one, and within the context of the modern views of red cell structure and metabolism it is difficult to see how useful information could be obtained from such a crude procedure. Nonetheless, use of the autohemolysis test led, more or less accidentally, to some important advances in the understanding of nonspherocytic hemolytic anemia. De Gruchy et al. speculated that the red cells of patients with type II autohemolysis had a lesion in glycolysis with impairment of energy production, and indeed, some of these patients were subsequently discovered to have a hereditary defect in the activity of pyruvate kinase.

As information accumulated about the autohemolysis test and about defects in red cell metabolism, it became increasingly clear that the information provided by the autohemolysis test was not specific, and that its usefulness with respect to diagnosis of the site of the metabolic defect or to predicting response to treatment was at best very limited. Although many clinicians assumed that the type II autohemolysis pattern was characteristic of pyruvate kinase defi-
ciency, type I, normal, or mixed patterns were frequently found. Indeed, in 14 patients studied by Miwa and Nishina, only 6 were interpreted as having type II autohemolysis. In several of these, furthermore, the degree of autohemolysis was minimal, and it was questionable whether the classic criteria of type II autohemolysis were met. If the autohemolysis test has any utility, it would seem to be limited to confirmation of the diagnosis of hereditary spherocytosis in mild or atypical cases. Characteristically, there is marked autohemolysis in this disorder and almost complete correction by the addition of glucose.

Why then has the autohemolysis test survived for so many years? Fifteen years ago, Dr. Dacie, the cooriginator of the test, wisely wrote: "The terms 'Type I' and 'Type II' introduced by Selwyn and myself in 1954 have clearly outlived their usefulness and I am keen to discard them." Frankly, the reason why an essentially useless test continues to be performed eludes me. It might be easier to understand if it were very simple to carry out. However, it requires use of sterile blood and sterile glassware and is therefore more time consuming than many useful procedures that are carried out in the hematology laboratory. Certainly the available screening tests for glucose-6-phosphate dehydrogenase, pyruvate kinase, glucosephosphate isomerase and triose phosphate isomerase deficiencies are much simpler to perform and yield more valuable information.

It may be that hematologists feel comfortable with the autohemolysis test because the results of the test are easy to read and because the hemolysis observed in vitro resembles superficially the clinical state that is being studied. Perhaps the test has some hidden value apparent to those who use it regularly that is inapparent to me. If so, I hope they will document its value in the literature. If not, perhaps this test will go the way of the cephalin flocculation, the thymol turbidity, the NPN, and the dinosaur.

REFERENCES


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