Effect of Urine Chemistry on Red Cells

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Dear Sir,

We wish to comment on two recent studies that appeared in Nephron on the influence of urine chemistry on the size and shape of red cells [1, 2]. Turitzen et al. [1] reported that urinary osmolality below 210 led to hemolysis of red cells with very low values for the mean corpuscular volume (MCV) of the resultant red cell ghost population. The results of Turitzen et al. [1] are compatible with our own observation that red cell ghosts, induced by incubation of red cells in distilled water, have extremely low MCV values [3]. (Ghosts actually have normal volume, but appear smaller when sized electrically, because of their lower electrical resistance [4].) We feel, however, that it is more physiologically appropriate to relate hemolysis to the medium's tonicity (crudely estimated as twice the sum of sodium and potassium concentration) rather than to its osmolality. In particular, urea is irrelevant to red cell volume [5,6]. In saline solutions, the threshold for 50% hemolysis occurs rather steeply at approximately 140 mosm/l [7]. Parpart et al. [8] showed, in 1947, that the hemolytic threshold in a buffered electrolyte solution is approximately 140 mosm/l at pH 7.4, but is above 140 if the medium is more acidic. Thus, acidity reduces red cell resistance to hypotonicity. The explanation is probably that red cells swell in acidic media [9]. We have found that urine pH is the most important determinant of the MCV of nonglomerular hematuria and it exerts a modest effect on the MCV of glomerular hematuria [10].

We also believe that hemolysis of a subset of nonglomerular red cells, due to a combination of hypotonicity and acidity, probably accounts for the 'mixed' red cell size histogram pattern that has been observed by us and others in nonglomerular hematuria [10–13]. It would be interesting to reanalyze the hemolysis data of Turitzen et al. [1] in light of the interaction between tonicity and pH.

We were very interested in the in vitro model of glomerular hematuria of Briner and Reinhart [2] and their excellent discussion of the mechanism of hemolysis. They concluded that to generate dysmorphism, both physical stress (filtration of red cells through 3- μ m pores under pressure) and chemical stress (e.g. hypoosmolal urine) were necessary. The model was more effective when the stresses were applied simultaneously than when applied sequentially, although the latter more closely simulates in vivo conditions. Their conclusion is in accord with our recent conclusion, based on studying urinary MCV during a furosemide-induced diuresis, that both glomerular and

tubular injuries to red cells are necessary to explain the full degree of microcytosis of glomerular hematuria [10].

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