Osmotic Fragility of Red Blood Cells, Secondary Hyperparathyroidism, and Uremia

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Dear Sir,

The papers of Docci et al., published in Nephron 41: 241 (1985) [1] and in Clinical Nephrology 25:68 (1985) [2], deal with the same issue and report that osmotic fragility of red blood cells in uremic and dialysis patients is increased, but this abnormality is not due to the state of secondary hyperparathyroidism. Although their data may allow such a conclusion, it is apparent that important facts and observations escaped these authors. Had they read the literature carefully and studied previous reports closely, they would not have concluded what they did.

The study of Bogin et al. [3] clearly demonstrated that parathyroid hormone (PTH) increases the osmotic fragility of human red blood cells in vitro and produces hemo-lysis. This effect reaches a maximum with 1 U of intact PTH per milliliter. We have previously assayed 1 U/ml of PTH and found it to be equal to 20 μ IEq/ml as measured by radioimmunoassay [4]; this value is only $\frac{1}{2}$ to 1 times higher than the blood levels of PTH in normal subjects. Thus, uremic patients with blood levels of PTH twice the normal value should display the maximum increase in osmotic fragility of red blood cells. Hence it is not surprising that all patients of Docci et al. [1], who had blood levels of PTH 7–14 times normal, had increased osmotic fragility of red blood cells and that no correlation was found between osmotic fragility and blood levels of PTH. It is equally not surprising that osmotic fragility did not normalize in these patients after parathyroidectomy, since the blood levels of PTH after surgery remained

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three to four times normal. We are also astonished that the authors claim that treatment with 1,25-(OH)₂D₃ was effective in controlling blood levels of PTH in their patients ; in fact their data show that blood levels of PTH were almost 14 times the normal values after treatment with this vitamin D metabolite. Two other reports clearly documented an effect of PTH on red blood cells in uremic patients. First, Saltissi and Carter [5] found a significant inverse relationship ($r = 0.67$, $p < 0.01$) between red blood cell survival, as measured by ⁵¹Cr, and the blood levels of PTH in 27 hemodialysis patients. Second, Akmal et al. [6] studied red blood survival with ⁵¹Cr in dogs with chronic renal failure and secondary hyperparathyroidism (group I) and in normocalcemic parathyroidectomized dogs with comparable degree and duration of chronic renal failure (group II). In group I, ⁵¹Cr red blood cell survival was shortened, and the values ranged between 16 and 20 (18.4 ± 0.65 ; SE) days, a value significantly ($p < 0.01$) lower than that in normal dogs (22–

35; 25.6 ± 1.9 days). In group II, ⁵¹Cr red blood cell survival ranged between 20 and 33 (25.2 ± 1.8) days, a value not different from that in normal dogs, but significantly higher ($p < 0.01$) than that in group I dogs; these data of Akmal et al. [6] demonstrate that excess blood levels of PTH and not other consequences of the uremic state are responsible for the shortened red blood survival in chronic renal failure.

The observations of Bogin et al. [3] in vitro, Saltissi and Carter [5] in humans, and of Akmal et al. [6] in dogs provide strong evidence for the role of PTH in the genesis of the hemolytic component of the anemia of uremia. The failure of Docci et al. [1, 2] to document the role of PTH lies in the design of their study and in the inappropriate interpretation of their data.

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References

Docci, D.; Turci, F.; Baldarti, L.: Lack of relation between secondary hyperparathyroidism and red blood cell osmotic fragility in chronic renal failure. *Nephron* 47:241–245 (1985). Docci, D.; Del Vecchio, C.; Salvi, P.; Turci, F.; Salvi, G.; Cenciotti, L.; Pretolani, E.: Osmotic fragility of erythrocytes, cell deformability and secondary hyperparathyroidism in uremic patients on maintenance hemodialysis. *Clin. Nephrol.* 25:68–73(1985).

Bogin, E.; Massry, S.G.; Levi, J.; Djaldeti, M.; Bristol, G.; Smith, J.: Effects of parathyroid hormone on osmotic fragility of human erythrocytes. *J. clin. Invest.* 69:1017–1025 (1982).

Meytes, D.; Bogin, E.; Ma, A.; Dukes, P.O.; Massry, S.G.: Effect of parathyroid hormone on erythropoiesis. *J. clin. Invest.* 67: 1263–1269 (1981).

Saltissi, D.; Carter, G.D.: Association of secondary hyperparathyroidism with red cell survival in chronic hemodialysis patients. *Clin. Sci.* 65:29–33 (1985).

Akmal, M.; Telfer, N.; Ansari, A.N.; Massry, S.G.: Erythrocyte survival in chronic renal failure: Role of secondary hyperparathyroidism. *J. clin. Invest.* 76:1695–1698 (1985).