Dear Sir,

Recently, Barton et al. [1] reported increased red blood cell (RBC) calcium content in patients with end-stage kidney disease. They did not refer to three other reports of erythrocyte calcium determination in chronic renal failure (CRF), utilizing atomic absorption spectroscopic techniques [2–4]. The results of the four studies can be compared if erythrocyte calcium content is expressed in the same units (table I). The variability in normal values is most likely due to the contaminating calcium present in the reagents used to extract calcium from intact or ashed cells and/or the effects of substances such as phosphate which interfere with calcium absorption. The techniques used in the two reports showing a lower calcium content address these problems [5,6], whereas the methods in the two older reports showing higher values were less well-defined. Given the difficulty of the measurement, the modest increase in red-cell calcium in renal failure patients (about 6 µmol/lRBC) noted by Barton et al. [1] and Udden et al. [2] must be interpreted cautiously.

Caution is also appropriate in the attribution of physiological significance to these results. The distribution of calcium among a heterogenous population of uremic RBC is not known. It is possible that much of the calcium is actually present in a small, potentially insignificant subpopulation of cells. In normal RBC most of the calcium exists in association with the membrane [7] and relatively little exists as a cytoplasmic ion (Ca++). It is not known whether the increased red-cell calcium content in CRF erythrocytes is membrane-associated or cytoplasmic. In sickle cell anemia the total RBC calcium is greatly increased, but evidence suggests that much of this is rendered inert by sequestration in intracytoplasmic vesicles [8]. Thus, an increase in total calcium does not always indicate biological activity. Also, some of the deleterious effects of calcium on red cells, such as membrane-protein cross-linking, occur at much higher levels than those obtained in CRF.

Anemia in CRF has been associated with decreased RBC deformability [9], increased magnesium content [10] and potassium content [11]. We described an association between RBC rigidity and increased calcium content but found no correlation between calcium content or deformability and the degree of anemia [2]. These studies do not show that changes in cation content are directly responsible for RBC dysfunction in uremia. In fact, the relationship between anemia and RBC magnesium and potassium content was similar to that found in anemic, but nonuremic, controls, suggesting that these changes reflect the young red cell age or some other epiphenomenon of CRF.
How calcium accumulates in red cells which possess an active Ca++ ATPase-associated Ca++
extrusion pump is also a mystery, although basal levels of this erythrocyte activity may be
decreased in CRF [12]. Parathyroid hormone, as noted by Barton et al., may also participate in
the accumulation of calcium by increasing erythrocyte calcium permeability. However,
parathyroid hormone also stimulates Ca++ ATPase activity [13] which suggests that other
factors must also be present to allow net calcium uptake.

However appealing the notion that RBC calcium is deleterious to red cells in renal failure may
be, the difficulty in demonstrating biological relevance of small changes in erythrocyte calcium
must be emphasized.

Table I. Summary of Four Studies reporting RBC calcium content in CRF

<table>
<thead>
<tr>
<th>Study</th>
<th>RBC calcium content reported values</th>
<th>values expressed in µmol/l</th>
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<tbody>
<tr>
<td></td>
<td>controls</td>
<td>patients</td>
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<td></td>
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<tr>
<td>a</td>
<td>Determined by AAS.</td>
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<tr>
<td>b</td>
<td>In calculating this value a mean red cell volume of 90 fl was assumed.</td>
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<tr>
<td>c</td>
<td>No standard deviation was reported.</td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>In calculating this value a specific gravity for RBC of 1.1 was assumed.</td>
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</tbody>
</table>

References


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