factor deficiency. In a survey of 215 patients, only 13 were under twenty years of age and approximately half of the cases were associated with an immune disorder [1]. We also recently described a 14-year-old boy who had been treated with prednisone and cyclophosphamide for lupus nephritis, and developed an anti-F-VIII AAb despite no clinical or biological signs of lupus flare [3]. Moreover the cumulative frequency recently reported by Carter [4] in 241 cases published from 1980 to 1989 indicates a marked age dependency, with only 6% of the cases under twenty. This association was therefore probably not due to chance, and nephrosis might have favoured the onset of the AAb in our patient.

There have been considerable advances in identifying immune function defects in minimal-change nephrotic syndrome (MCNS) since the publication of the Shalhoub hypothesis [5], but the mechanism responsible for this disease remains elusive. Schnaper postulated that a chronic state of non-specific activation, leading to feedback to downregulate this activity, may be the primary abnormality in MCNS [2]. Under these circumstances, clones of B lymphocytes synthesizing anti-F-VIII:C inhibitor would have proliferated as part of the overall immune system dysregulation associated with nephrosis. However, the nephrotic syndrome is probably not directly involved in the occurrence of the anti-F-VIII AAb in our patient, since the presence or absence of proteinuria is not correlated with the titre of anti-F-VIII:C AAb. It seems more likely that this association of diseases is due to a common genetic defect leading to immune disorders enhanced by the initial immunosuppressive therapy.

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Update on phosphate binders

Sir,

In the review of alternative phosphate binders presented by professor Schaefer [1], the study of Clarkson [2] is cited as evidence of the importance of intestinal phosphate binding by calcium carbonate. In that study, phosphate absorption decreased in four of the five studied patients with chronic renal failure. It is, however, a misunderstanding to think that the inhibited absorption of phosphate brought about the declining plasma phosphate concentration observed in three of the five patients (the other two had unchanged concentrations), since phosphate balance was more positive in each of the five studied patients (and in the three normal controls, too). Hence the study [2], rather than forming a basis for the treatment of hyperparathyroidism, points to the divergence of phosphate balance and changes in plasma phosphate concentration, which is a consequence of the fact that only a minuscule part of the total body phosphorus is the non-esterified part measured in plasma. In a similar vein is our recent observation [3] that the difference in the serum phosphate concentration when changing from calcium carbonate to calcium acetate, though statistically significant, is definitely not related to the dietary intake of phosphorus.

In the study of Clarkson [2], calcium intake was increased by 8000 mg, yet this caused only an increased calcium absorption of 696 mg, or 9% in the patients. This indicates the deficiency of our understanding of calcium absorption as a combined result of an active, saturable, vitamin-D-dependent part and a passive, non-saturable part when high calcium loads are studied [4]. The assumption of 25% absorption of calcium from calcium carbonate may therefore well be too high, notwithstanding the effect of vitamin D, which is less important with a very high calcium intake [5].

The same phenomenon probably applies for phosphate, i.e. the importance of a vitamin D dependent, saturable mechanism decreases with increasing intake. Furthermore [6], the fact stressed by Schaefer [1] that net phosphorus absorbed was strictly linearly related to intake between 5 mg/kg/day and 40 mg/kg/day strongly indicates that with normal phosphate intake, only passive, non-saturable mechanisms need be invoked.

A recent study [7] supports an older report [8] indicating malabsorption of phosphate in renal failure. Both these studies, however, used a very low carrier dose of phosphorus, thereby probably exaggerating the importance of vitamin D depletion in these patients. Although not tested, it is likely that the phosphate absorption would increase in these patients following calcitrol. The suggestion by Schaefer [1] that animal experiments indicate that calcitrol considerably increases active intestinal absorption of phosphate is similarly conditional on the experimental circumstances.

Thus, although the experience that calcitrol may cause hyperparathyroidism is not to be questioned, the claim that increased intestinal absorption is the only possible mechanism lacks support. Similarly, hypercalcemia during treatment with calcium carbonate has been suggested not to be primarily due to gastrointestinal absorption [9].

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Dear Sir,

The problems raised in Dr Ring's letter are of interest although he misquoted my remarks concerning the studies by Clarkson et al. [1]. I stated that 'Clarkson et al. performed balance studies which documented that calcium carbonate reduces the elevated serum phosphate levels of patients with renal failure' [2]. It is evident from Clarkson's results that three of the five investigated patients showed a decrease of their serum phosphate, while the two remaining patients showed no significant change. However, it is of interest that their initial serum phosphate was already normal. In this context I advanced no speculations on the mechanisms possibly involved.

With regard to the effect of calcitriol on the intestinal uptake of phosphate I have similar problems with the comments by Dr Ring, as I did not claim in my paper 'that increased intestinal absorption is the only possible mechanism'. In my review it is stated that 'calcitriol considerably increases the active intestinal absorption of phosphate' [2].

It is always a little disappointing to realize that papers are not read with sufficient care. The purpose of my review was to give an overview of alternative phosphate binders, and not to hypothesize on unproven effects of commonly used calcium-containing phosphate binders.

Nevertheless the suggestions by Dr Ring are appreciated and welcome.

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