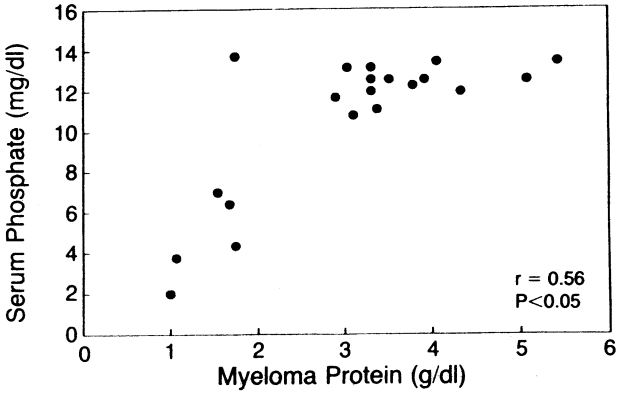


Figure 1. Correlation between the Concentration of Myeloma Protein and the Serum Phosphate Concentration in Patient 1 during the Course of the Disease.
Twenty serial measurements are shown.

*To the Editor:* Dr. Duffy described many of the problems in the diagnosis of myeloma. We would like to report a little-recognized condition in patients with myeloma — namely, the appearance of hyperphosphatemia in the absence of renal insufficiency. In 1991 we treated four patients with myeloma (Table 1).

Two patients had hyperphosphatemia. In these two patients, phosphate binding to a protein was demonstrated by ultrafiltration and dialysis of the serum. During the course of the disease, the therapy-induced fluctuations of the concentrations of the myeloma protein were closely correlated with the serum phosphate concentrations (Spearman rank-order correlation coefficient, 0.56; $P<0.05$) (Fig. 1). After the myeloma protein was isolated in Patient 1 by high-affinity chromatography,[1] the binding characteristics of the protein were investigated; a low-affinity ($K_d$, 23 mg per milliliter) and high-capacity (maximal binding capacity, 7.1 mg of phosphate per milligram of myeloma protein) saturable binding site was detected. It was calculated that in this patient 1 molecule of myeloma protein binds about 15 molecules of phosphate.

The fact that two of four consecutive patients with myeloma had hyperphosphatemia due to a phosphate-binding protein indicates that the incidence of this condition may be higher than previously recognized. We are aware of only one case report[2] describing the binding of phosphate to myeloma protein. Meticulous studies to estimate the incidence of this condition will be necessary; its occurrence may have been missed in the past because of the low affinity of the binding site and the wide physiologic range of serum phosphate. In addition, the pathophysiologic role of a phosphate-binding protein on the development of bone lesions remains to be defined. We suggest that myeloma should be considered in the differential diagnosis of patients with hyperphosphatemia.

Table 1. Clinical Characteristics of Four Consecutive Patients at the Time of the Diagnosis of Myeloma.

| Characteristic | Patient No. | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| Age (yr) | 59 | 64 | 72 | 77 |
| Sex | M | F | F | M |
| Type of paraprotein | IgGκ | IgAλ | IgGκ | IgGκ |
| Myeloma protein gradient (g/dl) | 3.3 | 3.8 | 2.5 | 2.8 |
| No. of bone lesions | 1 | 0 | 1 | 5 |
| Serum creatinine (mg/dl) | 0.8 | 1.2 | 0.9 | 1.1 |
| Serum phosphate (mg/dl) | 13.5 | 4.8 | 13.6 | 3.9 |
| Phosphate bound (% of total) | 84 | 44 | 87 | 18 |

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1. Akerström B, Brodin T, Reis K, Björck L. Protein G: a powerful tool for binding and detection of monoclonal and polyclonal antibodies. J Immunol 1985;135:2589-92.
2. Pettersson T, Hortling L, Teppo AM, Tötterman KJ, Fyhrquist F. Phosphate binding by a myeloma protein. Acta Med Scand 1987;222:89-91.

Dr. Duffy replies:

*To the Editor:* Anemia, a high erythrocyte sedimentation rate, rouleaux, and renal insufficiency constitute a quartet of findings that should suggest the diagnosis of myeloma; a high erythrocyte sedimentation rate is present in 90 percent of patients with this disorder.[1] Electrophoresis of serum and urinary protein will detect the myeloma in 98 to 99 percent of patients; this procedure, in our case, revealed a polyclonal hyperglobulinemia with a small light-chain spike. Drs. Grubb, Rouse, and Dalton are correct that immunoglobulin levels are normal or low in light-chain disease; in fact, a flat immunoglobulin curve is a clue to the presence of light-chain disease and calls for a urinary electrophoresis to look for the missing serum protein. Since approximately 90 percent of patients with light-chain disease have renal impairment at the time of diagnosis,[2] a small monoclonal serum spike is usually present in these patients. This was the case in our patient and permitted the diagnosis of light-chain myeloma to be made.

Dr. Rubins warns the clinician of the dangers of administering contrast medium in patients with myeloma[3]; the risk of such agents is real but exaggerated, and it pales when compared with the risk of hypercalcemia, infection, and dehydration as precipitants of renal failure in this disorder. Dr. De Geeter is correct that the bone scan gener-

ally is not normal in myeloma, although it commonly underestimates the number of osteolytic lesions; the recommendation stands that skeletal x-ray films are preferable to scanning in evaluating myeloma.[4] Hyperphosphatemia, like narrowed anion gaps, is a more recently described accompaniment of myeloma. All these comments highlight how instructive a discussion about diagnostic reasoning can be. Specimens from patients remain the clinician's clues to diagnosis.

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1. Kyle RA. Multiple myeloma: review of 869 cases. Mayo Clin Proc 1975;50: 29-40.
2. Buxbaum JN, Chuba JV, Hellman GC, Solomon A, Gallo GR. Monoclonal immunoglobulin deposition disease: light chain and light and heavy chain deposition diseases and their relation to light chain amyloidosis: clinical features, immunopathology, and molecular analysis. Ann Intern Med 1990; 112:455-64.
3. Cohen DJ, Sherman WH, Osserman EF, Appel GB. Acute renal failure in patients with multiple myeloma. Am J Med 1984;76:247-56.
4. Patton JT. Radiological investigations. In: Delamore IW, ed. Multiple myeloma and other paraproteinemias. London: Churchill Livingstone, 1986:103-14.