To the Editor:

The recent population-based study by Kyle et al., which was the first to provide precise epidemiologic information about primary systemic amyloidosis, reported the demonstration of a monoclonal (M)-protein in the serum or urine from 16 of 21 patients (76%) with amyloid of unequivocal Ig origin (AL).

However, the number of patients in whom free monoclonal Ig light chain (ie, Bence Jones [BJ] protein) represented the sole detectable M-protein was apparently lower than I would have expected to find in this disease. The frequency with which BJ proteinuria occurred in association with an intact M-protein in the serum is somewhat difficult to evaluate from the separate presentation of the results of the serum and urine investigations. All but one patient had the serum protein pattern analyzed by at least electrophoresis, with an intact M-protein in the serum from 47 to 79 years of age; median, 68 years) were recognized as having systemic deposition of AL without evidence of coexistent amyloid of unequivocal Ig origin (AL).

Light chain (ie, Bence Jones [BJ] protein) represented the sole detectable M-protein in 61% of the cases (Table I). BJ protein bands were also evident on serum electrophoresis of 5 patients, 4 of whom presented with serum creatinine levels greater than 177 μmol/L and with greater than 3 g of BJ protein excretion per day. Although most patients without an intact serum M-protein excreted BJ protein at amounts detectable by electrophoresis and immunofixation of unconcentrated or 100-fold concentrated urine, BJ protein would have been missed in almost one-third of the series by using such a degree of urine concentration.

These findings agree with our laboratory's experience in demonstrating that the results of screening for BJ protein depend not only on the application of immunofixation itself but also on the sensitivity of the electrophoretic method used, as well as the degree of urine concentration. In a series of 152 patients with IgG and IgA myeloma, BJ protein was detected in 78% of the urine concentrated up to 300-fold, whereas an overall incidence of 96% was obtained by using higher degrees of urine concentration. The finding of 85% of cases with an immunocytologic malignancy, including multiple myeloma and amyloidosis, among 13 patients who excreted less than 0.2 g/d of BJ protein without any intact M-protein detectable in their serum further stresses the clinical interest of demonstrating BJ proteinuria even when it occurs at such small concentrations that are likely to remain undetected by the routine procedures used in most hospital clinical chemistry laboratories.

The ability to confidently detect small amounts of urinary BJ protein would be of even more interest for the clinician in primary systemic amyloidosis, as the discovery of such an M-protein abnormality does often suggest appropriate investigation and diagnosis.

Table 1. Serum and Urine M-Proteins in 18 Patients With Primary Systemic Amyloidosis

<table>
<thead>
<tr>
<th>M-Protein</th>
<th>No. of Patients (%)</th>
<th>Serum BJ Protein No.</th>
<th>Total No.</th>
<th>Excretion (g/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact M-protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgG k</td>
<td>1 (6)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>IgG λ</td>
<td>4 (22)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>IgA λ</td>
<td>2 (11)</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>7 (39)*</td>
<td>0</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>BJ protein only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>λ</td>
<td>4 (22)</td>
<td>1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>λ</td>
<td>7 (39)</td>
<td>4</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>11 (61)</td>
<td>5</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>All M-proteins</td>
<td></td>
<td>18 (100)</td>
<td>5</td>
<td>16±</td>
</tr>
</tbody>
</table>

* Serum M-protein concentration (median, 1.4 g/dL; range, 0.5 to 3.5 g/dL).
1 Serum BJ protein concentration (median, 0.37 g/dL; range, 0.1 to 0.9 g/dL).
2 Urinary BJ protein excretion (median, 0.92 g/dL; range, 0.17 to 16.6 g/dL).

REFERENCES


ENZO PASCALI
Institute of General Clinical Medicine
University of Trieste
Trieste, Italy
Dr Pascali has correctly emphasized the importance of finding a monoclonal protein in the serum and urine of patients with primary amyloidosis (AL). As he pointed out, our study began in 1950, when immunoelectrophoresis and immunofixation were not available.

We found that 85% of the 710 AL patients we examined at the Mayo Clinic from 1982 through 1991 had a monoclonal protein in the serum or urine. When we examined the bone marrow for a monoclonal excess of plasma cells in patients without a monoclonal protein in the serum or urine, we found that 98% of patients with AL will have either a monoclonal protein in the serum or urine or a monoclonal excess of bone marrow plasma cells. Immunohistochemical staining of the amyloid is necessary in the remaining patients to differentiate AL from hereditary or senile systemic amyloidosis.

ROBERT A. KYLE
Hematology and Internal Medicine
Mayo Clinic
Rochester, MN

REFERENCE
Bence Jones protein in primary systemic amyloidosis [letter; comment]

E Pascali