Dear Sir,

It has long been known that in experimental and human hypertension occurs an increased vascular permeability which may be a major contributory factor, if not the cause of the development of the hypertensive vascular lesions [1]. When extreme and sufficiently sustained elevation of blood pressure (BP) occurs as in malignant hypertension (diastolic BP > 130 mm Hg) the increase in vascular permeability becomes easily apparent in the retinal vessels by fluoroangiography [2]. In this condition, proteinuria as well is frequently demonstrable by routine analysis, whereas in the benign phase of hypertension proteinuria is regularly absent. However, Parving et al. [3] using radioimmunological measurements, have found that patients with mild or moderate hypertension and without clinical proteinuria, nevertheless excrete more albumin in the urine than do normotensive controls. A decrease of proximal tubular protein reabsorption seemed to be ruled out in these patients on the basis of their normal daily excretion rate of β2-microglobulin. However, Mogensen et al. [4] have recently (1981) found an enhanced β2-microglobulin excretion in 7 patients with severe hypertension.

We have studied urinary excretion of albumin and β2-microglobulin in 26 normal subjects and 48 hyperten-

<table>
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<tr>
<th>Group</th>
<th>Sex</th>
<th>M</th>
<th>Mean Creatinine Clearance</th>
<th>Albumin Excretion</th>
<th>β2-Microglobulin Excretion</th>
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</thead>
<tbody>
<tr>
<td>Benign primary hyperten</td>
<td></td>
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<td>(range) ml/min × 1.73 m2/m</td>
<td>mg/24 h</td>
<td>µg/24 h</td>
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<tr>
<td>Malignant primary hyperten</td>
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Table 1. Comparison of results in patients with benign primary hypertension, accelerated or malignant primary hypertension, renal vascular disease and hypertension and controls (data are reported as MEAN ± SD)
A Benign primary hypertension
24 8 16 43 82 ± 24
(22–69) (53–139)
25.51 ± 62.73 (1.40–276.45)
239.84 ± 281.52 (18.82–1234.20)

14 11 3 44 66 ± 16
(36–56) (41–100)
10 4 6 43 78 ± 24
(34–58) (27–110)
26 11 15 30 87 ± 20
(17–46) (49–124)
69.30 ± 109.24 (1.35–336)
14.32 ± 12.91 (2.30–38.40)
8.97 ± 5.99 (1.43–29.87)
1054.36 ± 1603.31 (31.92–6000)
307.06 ± 443.30 (17.63–1482.94)
85.89 ± 48.56 (2.77–191.31)

Creatinine clearance: B vs. D p < 0.005; albumin excretion: B vs. D p < 0.05; β2-microglobulin
excretion: A vs. D p < 0.01; B vs. D p < 0.005; C vs. D p < 0.02.

SBP = Systolic blood pressure, mean of the group; DBP = diastolic blood pressure, mean of the

sive patients (table I). Criteria we used for accelerated hypertension were: retinal hemorrhages
and/or exudates and diastolic BP ≥ 130 mm Hg in several measurements during a day; for
malignant hypertension, the same criteria and papilledema [5,6]. In all hypertensive patients BP
measurements were taken 5 times a day, every 4 h during the waking cycle. Mean of BP values
of 3 days (5th to 7th) of observation was used to calculate mean BP of each group. All patients of
the first and third group were untreated. In the second group, 11 patients had taken small and
discontinuous doses generally of one drug. In none of these cases treatment included diuretics. In
all cases there was no detectable proteinuria, as tested by bromophenol strips (Albustix).

Differences between groups were analyzed by using Student’s t test for unpaired data. Results
are reported in table I. In the absence of clinical proteinuria, we have found a statistically
significant elevation of urinary albumin in patients with accelerated or malignant hypertension,
but not in those with benign hypertension or with renovascular hypertension. The urinary
excretion of β2-microglobulin was significantly increased in all hypertensive groups. Our results
are consistent with the hypothesis that sustained severe elevation of BP can cause increased
transglomerular escape of albumin. Whereas the increase of β2-microglobulin excretion may
have a similar origin, two other mechanisms may play a part: (1) with accelerating hypertension,
nephrosclerosis and glomerular damage regularly occur: it may be that the corresponding tubular
damage impedes reabsorption of microglobulin; (2) concerning benign hypertension, if the
reabsorption of β2-microglobulin may be considered partially mediated by sodium reabsorption,
the increased β2-microglobulin excretion may reflect an increased natriuresis (Na+, K+-ATPase
suppression? [7]). Increased β2-microglobulin excretion rate we observed in renovascular hypertension is explainable on the basis of a tubular damage due to ischemia.

The possible increase of urinary excretion of β2-microglobulin in hypertension, no matter of type and degree of disease, must be taken into account whenever the excretion of this protein is used as a tubular marker in conditions other than hypertension.

References