Letters and Replies

High-protein diets are not hazardous for the healthy kidneys

Sir,

The recent letter by Luyckx and Mardigan [1] has a somewhat misleading title, as there is certainly no scientific evidence that the high-protein diets are hazardous for healthy kidneys. Furthermore, real world examples support this contention since protein-related kidney problems are essentially non-existent in the body-building community in which extremely high-protein intake has been the norm for over half a century [2]. Also, men in the famous Lewis and Clark expedition across America reportedly ate as much as nine pounds of buffalo meat each day with no ill effects [3]. That is well over 600 g of protein as a daily minimum.

Nevertheless, Anderson and Brenner suggested that high-protein intake played a central role in the decline of renal function with age and that protein restriction might prevent this decline [4]. However, as discussed by Walser [5], this recommendation cannot be supported for a number of reasons: (i) caloric restriction is more effective in rats than is protein restriction in retarding age-associated decline in renal function; (ii) protein restriction tends to lower glomerular filtration rate rather than increase it; and (iii) there is certainly no evidence suggesting that a high intake of protein causes progressive reduction in renal function. Thus, Walser concluded that it is clear that protein restriction does not prevent decline in renal function with age, and, in fact, is the major cause of that decline [5]. According to Walser [5], a better way to prevent the decline would be to increase protein intake.

More recently, the study by Poortmans and Dellalieux [6] investigated body-builders and other well-trained athletes with high- and medium-protein intake, respectively. The athletes underwent a 7-day nutrition record analysis as well as blood sample and urine collection to determine the potential renal consequences of a high protein intake. The data revealed that despite higher plasma concentration of uric acid and calcium, body-builders had renal clearances of creatinine, urea, and albumin that were within the normal range. To conclude, it appears, at least in the short term, that protein intake under 2.8 g/kg does not impair renal function in well-trained athletes.

More recently, Knight et al. [7] determined whether protein intake influences the rate of renal function change in women over an 11-year period. 1624 women enrolled in the Nurses’ Health Study who were 42–68 years of age in 1980 and gave blood samples in 1989 and 2000. Ninety-eight percent of women were white, and 1% was African American. In multivariate linear regression analyses, high protein intake was not significantly associated with change in estimated glomerular filtration rate (GFR) in women with normal renal function (defined as an estimated GFR ≥80 ml/min per 1.73 m²). Thus, the authors concluded that high protein intake does not seem to be associated with renal function decline in women with normal renal function. As pointed out by Lentine and Wrone, the generalizability of these findings is limited by sampling characteristics to white mid-adulthood, but this limitation is overshadowed by strong internal validity based in a large sample size, prospective outcomes ascertainment, and adjustment for multiple covariates [8].

Finally, Pons et al. [9] examined the effect of a protein-rich diet on cyclosporin A (CsA)-induced acute nephrotoxicity in rodents using markers of tubular damage. Interestingly enough, they concluded that a protective effect of high-casein diet against CsA-induced proximal tubular damage was observed in Sprague–Dawley rats. Lacroix et al. [10] studied the effects of a very-high-protein diet in rats over a period of 6 months. Forty-eight Wistar rats received either a normal-protein diet (14% protein) or a very-high-protein diet (50% protein). No nephrocalcinosis, no area of collagenous sclerosis, and no hypercellularity were detectable. Also, endothelial and mesangial cells were normal and so were surrounding tubules.

In summary, for individuals with normal renal function, the risks of high-protein weight loss diets are minimal and must be balanced against the real and established risk of continued obesity [11,12].

Conflict of interest statement. None declared.

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1. Luyckx VA, Mardigan TA. High-protein diets may be hazardous for the kidneys. Nephrol Dial Transplant 2004; 19: 2678
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**Reply**

Sir,

Our intention was to raise awareness of the potentially deleterious effect of a high-protein diet on progression in patients with renal disease. The impact of a high protein diet on normal kidneys, however, is not necessarily as clear-cut as put forward by Dr Manninen. The statement that a high protein diet should be used to ‘prevent’ renal functional decline is incorrect. In the short term, a high protein diet does lead to an increase in renal blood flow and an increase in glomerular filtration rate (GFR) [1,2]. This increase, however, termed hyperfiltration, does not represent a true sustained ‘improvement’ in renal function, but rather reflects a physiologic recruitment of renal functional reserve to offload the increased metabolic burden posed by a high-protein diet [1].

Conversely, hyperfiltration in the setting of renal ablation in rats may be attenuated by a low-protein diet, and renal disease progression halted or delayed [1,3,4]. The increase in single nephron GFR occurring after a high-protein meal is associated with glomerular hypertension, a pivotal factor in the final common pathway of progressive renal failure [4,5]. In contrast to the finding of Lacroix et al. [6], Hostetter et al. [2], did find evidence of increased glomerulosclerosis and proteinuria in normal rats fed a high-protein diet for 4 and 8 months. In addition, in rats with increasing degrees of renal mass ablation, a high protein diet resulted in progressive, several-fold increases in proteinuria and glomerulosclerosis, which worsened over time [2]. In all groups, rats on a high-protein diet had a higher GFR compared to those on a normal protein diet reflecting the hyperfiltration [2]. Differences in animal strain may account for these authors’ conflicting observations, which should raise further caution in extrapolation to humans. Interestingly, in both studies the high- and low-protein diets were isocaloric, a factor that may not always be the case in humans. People tend to take popular dietary advice to the extreme and may feel it is acceptable to consume protein ad libitum, regardless of calorie intake, as long as carbohydrates are avoided.

Although data in humans are not highly conclusive, Knight et al. [7] also found that in women with mild renal insufficiency a higher protein diet may accelerate loss of renal function. The human studies reporting lack of gross harm of high-protein diets cited by Dr Manninen should be regarded with a healthy skepticism, as the ability to detect renal dysfunction in the early 1800s, or a study of 7 days duration, cannot address long-term effects on renal function. It should be noted too that these reports included subjects with high-protein intake in the setting of high caloric expenditure (early explorers and body builders), which may offset a potentially negative impact of a high-protein diet on the kidney. Calorie restriction itself has been demonstrated to play a role in attenuating renal disease progression [8]. Manninen’s letter does not fit the demographic we wish to target. Many people desperate for weight loss are often obese, diabetic, hypertensive and have, or are at high risk for, renal disease. These people tend to be sedentary. As we stated previously [9], the potential metabolic benefits in terms of weight loss, glucose and lipid control may outweigh the potential renal hazards of a high protein diet, but this remains to be demonstrated in clinical trials. In the interim, we strongly suggest that patients with renal dysfunction follow such high-protein, low-carbohydrate diets under close supervision of a dietician for guidance in appropriate food choices, attention to caloric intake and a healthy exercise programme.

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**Serum albumin: a late-reacting negative acute-phase protein in clinically evident inflammation in dialysis patients**

Sir,

In their interesting study, Nascimento et al. [1] found that baseline C-reactive (CRP) was not correlated with serum