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Editorial

Dietary protein and kidney function: when higher glomerular filtration rate is desirable[1,2]

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There is increasing focus on the optimal diet for preventing weight gain and obesity and particularly over the life span to maintain an optimal body composition with a sufficient amount of lean body mass and to avoid an excessive increase in body fat. Even within a normal BMI, the combination of low lean body mass and high body fat has become prevalent—i.e., so-called sarcopenic obesity (1); and with the changing demographic distribution with a rapidly increasing elderly population, the topic of achieving a "peak lean body mass" with particular emphasis on muscle and bone mass has become a priority.

Current evidence points to the importance of consuming a sufficient amount of dietary protein, calcium, and vitamin D in combination with physical training to build up and maintain strong bones and muscles to reach high peak mass and strength in adulthood, which, in turn, will serve as a reservoir that determines how many years of progressive loss can elapse before the situation becomes critical among the elderly. Research focuses currently on the optimal amount of nutrients and exercise to maintain bone and muscle strength and function among the elderly to prevent frailty and sarcopenia as long as possible. To help older persons (>65 y) maintain and regain lean body mass and function, the PROT-AGE study group recommends average daily intakes at least in the range of 1.0–1.2 g protein/kg body weight per day, and those who have acute or chronic diseases need even more dietary protein (1.2–1.5 g $\cdot$ kg body weight^{-1} $\cdot$ d^{-1}) (2). Only elderly persons with severe kidney disease [i.e., estimated glomerular filtration rate (GFR) <30 mL $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2}], but who are not undergoing dialysis, are an exception to this rule; these individuals may need to limit protein intake.

Although the sufficient amount of protein required for optimal health increases with aging, the age-related decline in GFR has drawn attention to the potential for high protein intakes to damage kidney function by increasing the risk of hyperfiltration and subsequent accelerated decline in GFR and risk of microalbuminuria. However, the potential for high protein intakes to cause kidney damage may be a misconception (3) that is not supported by strong scientific evidence. By contrast, recent studies suggest the opposite (4).

There is no doubt that protein intake influences kidney size and function, but most evidence suggests that these are reversible, physiologic adaptations. In a 6-mo randomized dietary intervention trial, Skov et al. (5) found in overweight subjects that a reduction in protein intake from 91 to 70 g/d decreased kidney volume by 6.2 cm^3 and GFR by 7.1 mL/min, whereas an increase in protein from 91 to 108 g/d increased kidney volume by 9.1 cm^3 and GFR by 5.2 mL/min, without any change in microalbuminuria. Jesudason et al. (6) failed to show any adverse effect of increasing protein intake in a randomized study in patients with type 2 diabetes with early-stage renal disease.

A novel way of achieving a higher lifetime GFR is suggested by an observational epigenetic study by Miliku et al. (7), which is reported in this issue of the Journal. The authors were inspired by animal studies that showed that low maternal protein intake during pregnancy leads to lower numbers of nephrons and a higher risk of renal disease and hypertension in the offspring. Hence, they studied a cohort of 3650 pregnant women and their children and assessed gestational maternal protein intake, and, at age 6 y, they measured the children's kidney volume and estimated GFR (eGFR) by serum creatinine and cystatin C concentrations. In parallel with previous reports in rats and sheep, they found that first-trimester maternal protein intake was positively associated with eGFR based on creatinine concentrations ($eGFR_{creat}$) in the offspring at 6 y of age, whereas maternal protein intake was not associated with childhood microalbuminuria.

The importance of the demonstrated ~4% increase in $eGFR_{creat}$ based on height and plasma creatinine (7) is difficult to assess. However, taken together with observational studies that suggest that maternal intake of nutrients, including protein, during pregnancy may contribute to increased lean body (8) and bone mass (9) in the offspring, the observations call for more randomized controlled dietary intervention studies in pregnant women to test if these associations follow a causal pathway. If they do, optimization of dietary intakes of protein to pregnant women could obtain a new importance by "programming" the offspring to higher GFR at birth and possibly a higher number of nephrons, which could be an important preventive effort against renal disease and sarcopenia in the elderly. However, as recently pointed out by Blumfield and Collins (10) in another editorial in a recent issue of the Journal, the relation between protein intake and optimal offspring health

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may be a quadratic (U-shaped) relation, so trials evaluating the optimal macronutrient ratio are required.

Study groups planning to follow this lead may need to address some methodologic issues first. It is remarkable that the present $eGFR_{creat}$ values (7) obtained in healthy 6-y-olds were generated by an algorithm originating from a clinical study in sick children with a variety of renal diseases and plasma creatinine concentrations 3-fold higher than those in the present cohort. Notably, the patients were also almost 11 y of (average) age and tended to have a higher BMI (11). Furthermore, the present authors chose the simplified "bedside" version rather than the original equation recommended by Schwartz et al. (11). Although these operational shortcuts may not have been detrimental to the present conclusions, future studies should strive toward optimization of early assessment of kidney glomerular and tubular damage by indexes based on conventional measurements and/or by new biomarkers (12, 13).

The 2 authors contributed equally to this editorial.

AA is consultant/member of advisory boards for Global Dairy Platform USA, McCain Foods Ltd USA, and McDonald's USA. He is member of the Collaboration Steering Committee of the Copenhagen University/Arla Foods Dairy Health and Nutrition Excellence Center. He gives numerous lectures in many countries each year for which travel expenses are typically covered by the meeting organizers, which are often supported by corporate sponsors. In the past 5 y he has received funding for research at his department from Danish Dairy Research Foundation, Arla Foods, Denmark, and Global Dairy Platform USA. PB declared no conflicts of interest.

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