Protein requirements: methodologic controversy amid a call for change\textsuperscript{1–3}

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The debate about whether and to what degree human protein requirements change with advancing age has existed for decades. Reports from the Institute of Medicine (1) and WHO/FAO/UNU (2) concurred that the Recommended Dietary Allowance (RDA)\textsuperscript{4} or safe amount of protein intake for both adult men and adult women is \(\sim 0.8\) g of good-quality protein per kilogram of body weight per day (g \(\cdot\) kg\(^{-1}\) \(\cdot\) d\(^{-1}\)) and that the Estimated Average Requirement (EAR) is 0.66 g \(\cdot\) kg\(^{-1}\) \(\cdot\) d\(^{-1}\) with an Acceptable Macronutrient Distribution Range for protein of 10–35% of energy.

In this issue of the Journal, Tang et al (3) used the indicator amino acid oxidation (IAAO) approach to determine the protein requirement of 6 white women aged 80–87 y and suggested that the current RDA and EAR for older women may be underestimated. Although it may be that, on average, octogenarian women should optimally consume a slightly higher amount of protein, especially if they are frail or their health is compromised by disease, the debate will continue for several reasons. First, data from short-term studies in small groups of volunteers do not unconvincingly support a need to change the EAR and RDA. This is especially so when there is limited, if any, information on long-term, clinically relevant outcomes related to different amounts of protein intake. Second, there has been and continues to be controversy about the use of the IAAO technique to estimate protein requirements in any age group.

Tang et al (3) argue that only when the quantity of the indicator amino acid (in this case, phenylalanine) is limiting, the “breakpoint” will be affected by the amount of phenylalanine available. Because their study design used phenylalanine in excess and sufficient for all 7 different amounts of protein tested, the authors conclude that the “breakpoint” would not be affected by a limiting amount of phenylalanine but rather by the amount of protein intake per se. On the other hand, Millward and Jackson (4) argue that the “breakpoint” in tracer oxidation under these circumstances coincided with the amino acid intake, which was balanced in terms of the content of the indicator amino acid, phenylalanine, in egg protein that was used in the meals. Consequently, the oxidation of the tracer would not “indicate” the oxidation of the rest of the dietary protein but only its own excess or limitation relative to the overall pattern of the demand for net postprandial protein synthesis. It is not likely that this difference of opinion will be easily resolved.

Historically, the nitrogen balance technique has been used to assess protein requirements and is often considered the “gold standard” (5). Recently, Conley et al (6) compared the nitrogen balance technique with the use of isotopically labeled leucine to estimate optimal protein intakes in young and older individuals. They concluded that both methods resulted in similar estimates of protein requirements and that the values were comparable between young and old adults. Age-related differences in protein metabolism are documented in the literature, but the authors concluded that “there are no compelling data that the dietary protein needs of old people are different than those of young people when expressed per kg body weight” (6).

Throughout the years, despite all of the efforts to refine the requirement of protein per se across the age span, the actual differences between the various studies are small. The estimates range from higher, lower, to the same as current recommendations (eg, references 6–10). Moreover, the values do not appear to differ significantly with advancing age, independent of co-morbid conditions. What is really needed are studies that show that incremental differences in amounts of protein intake make a difference, ie, that they do affect clinically important outcomes. We still do not know whether differences in intakes of \(\sim 0.5\) g \(\cdot\) kg\(^{-1}\) \(\cdot\) d\(^{-1}\) significantly affect human health and well-being. This suggests that new research paradigms are needed to enable an integrated systems evaluation of requirement. The availability of the present data in the literature may spawn collaborative studies that combine multiple approaches in the same individual or introduce novel new techniques to establish true requirements across the age span. Investigators will need to agree on the experimental design and outcomes for multicenter collaborative studies. Patients with specific conditions also need to be studied with standardized protocols to maximize the evaluation of the data to determine true requirements. In the present work, data from 2 volunteers with diabetes mellitus were excluded because their patterns of oxidation were not consistent with those of the other subjects.

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\textsuperscript{4}Abbreviations used: EAR, Estimated Average Requirement; IAAO, indicator amino acid oxidation; RDA, Recommended Dietary Allowance.

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Hence, it is clear that future work will require large numbers of volunteers and large resources, including possibly centralized laboratories for sample processing and analyses. Because the ultimate goal is to ensure that all populations have access to adequate nutritional intake that promotes health, it will be important to include relevant clinical and functional outcomes.

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REFERENCES