

Keynote: Rethinking protein

Ricardo Uauy

As we face the challenge of rethinking dietary protein requirements, we need to look at protein in a new light, applying functional definitions like growth and immunity, requirements of populations at risk for infection, and food insecurity, with more attention paid to protein quality. The current definition of protein requirement, according to the 2007 Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) report, is the lowest level of dietary protein intake that will balance the losses of nitrogen from the body and thus maintain the body's protein mass, in persons at energy balance with modest levels of physical activity [1]. In the case of children and pregnant or lactating women, intake should also fulfill the needs associated with the deposition of tissues or the secretion of milk at rates consistent with good health. It is acknowledged that this definition of the requirement in terms of nitrogen balance does not necessarily identify the optimal intake for health, which is less quantifiable. In addition, current requirements are specifically intended to meet the needs of healthy populations. How do the requirements change in the case of infection or energy deficit, such as the situation in many developing-country populations? What are the requirements for optimal health, and are they accurately represented by nitrogen balance? These unanswered questions should lead us to rethink protein and requirements in terms of at-risk populations, consider specific functional roles of some amino acids, or the specific needs for optimal growth and other functional outcomes in the context of the total diet.

Protein requirements and digestibility

Nitrogen balance studies have been used to estimate

Please address all inquiries to the author at: London School of Hygiene and Tropical Medicine, London, UK and the Institute of Nutrition (INTA), University of Chile, Santiago, El Libano 5524 Macul, Santiago de Chile; email: druauy@gmail.com.

the protein requirements of healthy adults. Measuring nitrogen balance requires collecting sweat, urine, fecal matter, hair, etc. The assessment of body cell mass is a technique that measures body protein content by assessing whole body potassium—an element found inside body cells and not present in body fat—making K40 an accurate index of total lean body mass and a potential biomarker of whole body protein status, provided we have age and gender population standards based on normal populations. The current Estimated Average Requirement (EAR) for protein for healthy adults is 0.66 g/kg, 10% higher than the value of 0.6 g/kg proposed by the 1985 Food and Agriculture Organization/World Health Organization/United Nations University (FAO/WHO/UNU) report [2]. The estimated Recommended Dietary Allowance (RDA) for protein, 0.83 g/kg, is also 10% higher than the 0.75 g/kg recommended in 1985. There is no firm evidence to suggest a distinction in requirements between men and women when values are expressed per unit of body mass. During growth, additional protein must be added in excess of the average maintenance requirement of 0.66 g/kg to meet the needs imposed by growth of lean body mass; this is how requirements are set for infants and children. Infants have higher protein needs in relation to body weight, with greatest demand during the last trimester of gestation and the first 2 years of life (**fig. 1**).

Protein requirements for children during catch-up growth are harder to determine at the population level, since recovery rates may vary. It may be important to provide more protein right away and less at later stages of recovery when lean mass growth slows down (**table 1**). If protein is the driver for growth, can we attain greater lean body mass growth by giving more protein? A faster turnover rate of protein allows for a faster rate of recovery; is this potentially better? The rates of protein synthesis are now considered in the evaluation of essential and conditionally essential amino acid needs, not just for protein synthesis but also for immune and specific organ function. These needs must be incorporated into protein requirements as we

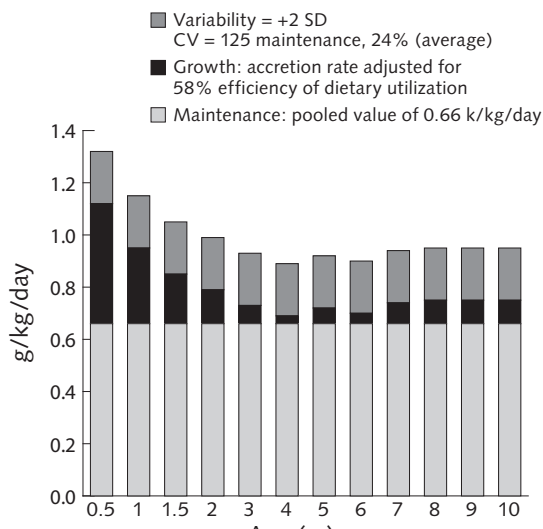


FIG. 1. Protein requirements for infants and young children: Maintenance plus growth and variability values. Source: FAO/WHO/UNU [1]

better define protein needs for specific body functions. In infants under 2 years of age, fat mass gain is more variable than lean mass gain during this time, and there is a need to analyze body composition in order to determine true energy and protein needs.

The 2007 FAO/WHO/UNU protein and amino acid requirements were revised based on reevaluated nitrogen balance data plus new amino acid turnover

studies conducted using stable isotope techniques in adults. In the case of children, new values were based on factorial estimates incorporating adult maintenance requirements plus tissue composition for growth. Although total protein per unit of body weight required for maintenance is the same as that of adults, essential amino acid requirements per gram of protein (a measure of protein quality) have increased for children. This increase should lead to a reexamination of dietary protein quality, which should be based on how much of the amino acids in the protein we consume is absorbed and available for utilization. Based on more recent data, we now should consider that each amino acid has its own digestibility, and that in addition the effect of food processing may alter absorption of some amino acids and not that of others. Thus, before establishing recommendations, we will need to consider the digestibility of each individual amino acid from the specific food source or the mixed diet. This challenge requires that we go beyond traditional fecal sampling and collect samples from the ileum; alternatively, indirect methods based on metabolic responses may need to be developed. One reason for this is the need to incorporate amino acid production or modification by the microbiome and the potential colonic recycling of both essential and nonessential nitrogen, which modifies the amount of essential amino acids needed at various stages of life and in different situations. However, although ileal digestibility is now considered a more accurate measure of protein and amino acid

TABLE 1. Protein and energy needs for catch-up growth at varying rates of weight gain. Source: FAO/WHO/UNU [1]

Growth costs	Typical weight gain composition ^a			High rate of fat deposition ^b		
Net growth costs (kcal/g) ^c	3.29			5.12		
Gross growth costs (kcal/g) ^d	4.10			5.99		
Rate of gain (g/kg/day)	Dietary requirements			Dietary requirements		
	Protein ^e (g/kg/day)	Energy ^f (kcal/kg/day)	Protein/energy (%)	Protein ^g (g/kg/day)	Energy ^h (kcal/kg/day)	Protein/energy (%)
1	1.02	89	4.6	1.0	91	4.2
2	1.22	93	5.2	1.1	97	4.5
5	1.82	105	6.9	1.5	115	5.2
10	2.82	126	8.9	2.2	145	6.0
20	4.82	167	11.5	3.6	205	6.9

a. 73%–27% lean:fat equivalent to 14% protein and 27% fat.

b. 50:50% lean:fat equivalent to 9.6% protein and 50% fat.

c. Based on 5.65 kcal/g protein and 9.25 kcal/g fat.

d. Net costs adjusted for a 90% and 73% metabolic efficiency of fat and protein deposition, respectively, plus maintenance energy of additional nonutilized protein.

e. 14% deposited tissue adjusted for a 70% efficiency of utilization plus the safe level of maintenance at $1.24 \times 0.66 \text{ g/kg/day} = 0.82$ (see text).

f. Maintenance energy at 85 kcal/g (which includes maintenance protein energy) + gross energy costs at 4.10 kcal/g weight gain.

g. 9.7% deposited tissue adjusted for a 70% efficiency of utilization plus the safe level of maintenance at $1.24 \times 0.66 \text{ g/kg/day} = 0.82 \text{ g/kg/day}$ $1.27 \times .58 \text{ g/kg/day} = 0.737$.

h. As in f except that gross energy costs are 5.99 kcal/g weight gain.

digestibility, it will take time to collect human data, and thus it will be useful to find an appropriate animal model for human ileal digestibility.

Nutrition and growth

A major health problem we are facing today is stunting. Unfortunately, linear growth is age limited: we cannot grow in length after the metaphyseal growth plate fuses. The most critical periods for linear growth are from birth to 2 years of age and then during the pubertal growth stage typical of adolescence. Estimations of nitrogen balance do not answer the question of protein needs to achieve optimal linear growth. The question of what are the true measures of protein needs of children for optimal linear growth remains unanswered. Maintenance of whole body nitrogen balance as presently measured does not imply that nitrogen balance and amino acid needs for optimal organ and tissue function are being met.

As stated by Rand et al., “Other measures of both organ and whole-body protein adequacy are needed... and new approaches need to be exploited in the search for new paradigms for nutrient requirement studies in general” [3]. We need to look at health-related responses, both long and short term, growth and tissue repair, and functional roles of amino acids and proteins. Nutrition and infection have a synergistic effect on growth; several essential nutrients are critical to optimal immune function, including protein and amino acids. Infection commonly affects young children monthly or every other month. We need to focus research on how best to prevent and rapidly cure infection in children; this includes recovery of their length z-score to that prior to illness so that they achieve their full growth potential.

Protein and energy

The protein requirement vis-à-vis the energy content and composition of the rest of the diet was the subject of a seminal paper by Dr. Nevin Scrimshaw in 1977, where he noted that in healthy, well-nourished populations, the requirement for protein is less than 6% of daily energy needs [4]. But this number is in fact highly dependent on the quality of protein: as protein quality decreases, the percentage of calories from protein needed to meet the requirement increases (fig. 2). Dr. Scrimshaw, using apparent consumption data, also showed that elasticity of demand is much higher for high-quality protein from

animal sources (0.42) than for energy (0.17) or total protein (0.18), according to data from Latin America. If the effect of household income on protein intake was considered, close to 40% of the population not only was getting less protein than required, but the intake was of lower quality (due to a marked effect of income on apparent consumption of animal protein). In a recent study by Ghosh et al., per capita protein available in the food supply was used to calculate the population risk of protein inadequacy based on average protein requirements. After adjustment for increased protein requirements during infection—as chronic infection affects a large portion of children in the developing world—many more people were at risk for inadequate protein than initially estimated [5]. Furthermore, using country-level data, a tight relationship between population risk of dietary protein inadequacy and prevalence of stunting was found, and protein quality remained significantly related to stunting rates after adjustment for energy, income, and prevalence of infection.

Conclusions

As we face the challenge of rethinking protein needs, we must look at protein in a new light; nitrogen balance

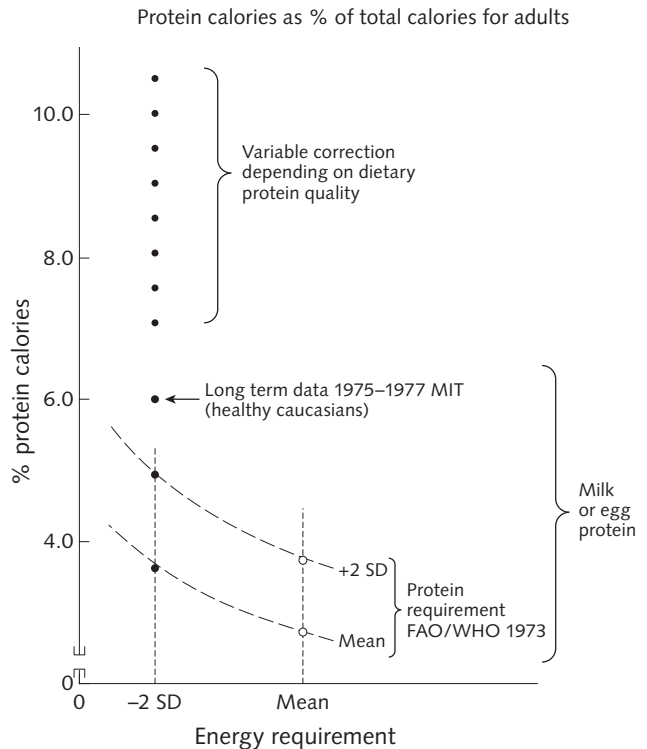


FIG. 2. Percentage of protein calories needed to meet daily protein requirements with different quality protein. Source: Scrimshaw [4]

is only the starting point and clearly not the final answer. Current requirements reflect the physiological needs obtained under ideal conditions; we should use them only if we are able to reproduce those conditions in daily life. Meeting the protein needs of developing-country populations must be based on the needs of children living under conditions of repeated infections, chronic energy deficit, poor environmental sanitation, and psychosocial stress, and not those of children living under conditions of a metabolic ward. This approach should also be used when judging protein quality of children's diets. We need to focus attention on vulnerable populations in developing countries where

stunting is prevalent. This should include providing not only sufficient energy and protein but also essential micronutrients necessary for optimal linear growth. Furthermore, criteria for sufficiency should be based not only on nitrogen balance or protein turnover but should also include relevant functional outcomes, such as achieving optimal muscle mass and linear growth. When feeding children from areas where stunting is prevalent, we need to assess dietary quality in terms of ability to promote and support normal length for age. This is our challenge going forward: this task is not an easy one, but this meeting is an excellent step in the right direction.

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