Revised Reference Values for the Intake of Protein

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Keywords

Protein · Indispensable amino acids · Reference value · Protein requirement · Elderly

Abstract

Background: Following a timely update process, the nutrition societies of Germany, Austria, and Switzerland (D-A-CH) revised the reference values for the intake of protein in 2017. The Working Group conducted a structured literature search in PubMed considering newly published papers (2000–2017). **Summary:** For infants <4 months, the estimated values were set based on the protein intake via breast milk. Reference values for infants >4 months, children, adolescents, pregnant, and lactating women were calculated using the factorial method considering both requirement for growth and maintenance. For adults, reference values were derived from nitrogen balance studies; for seniors (>65 years), reports on metabolic and functional parameters under various protein intakes were additionally considered. Reference values (g protein/kg body weight per day) were set as follows: infants <4 months: 2.5–1.4, children: 1.3–0.8, adults <65 years:

0.8, adults >65 years: 1.0. **Key Messages:** The reference values for infants, children, adolescents, and adults <65 years are essentially unchanged compared to recently published values. Scientifically reliable data published between 2000 and 2017 guided the D-A-CH Working Group to set a higher estimated value for adults >65 years. Since the energy consumption continuously decreases with age, this new estimated protein intake value might be a challenge for the introduction of food-based nutrition concepts for older people.

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Introduction

The D-A-CH “reference values for nutrient intake” [1] are jointly issued by the nutrition societies of Germany, Austria, and Switzerland (the abbreviation D-A-CH arises from the initial letters of the common country identification: Germany [D], Austria [A], Switzerland [CH]) and are regularly revised according to a predefined protocol. Reference value is a collective term for recommended intake values, estimated values, and guiding val-

ues. A recommended intake value, according to its definition, meets the requirement of nearly any person (97.5%) of a defined group of metabolically healthy people. Estimated values are given when human requirements cannot be determined with desirable accuracy. Guiding values are stated in terms of aids to orientation [1].

Proteins, linear polymers of α -L-amino acids, are the dominant components of cell structures; about half of the dry weight of human cells is protein [2, 3]. Depending on age and gender, the human organism has an average protein content of approximately 7–13 kg [4, 5].

Endogenous protein is subject to constant formation and breakdown. Daily protein or amino acid turnover is approximately 300 g [6, 7], which is about 3–4 times greater than the mean intake in the general population [8]. Amino acids from exogenous sources (food) as well as from hydrolysis of endogenous proteins contribute to the intracellular amino acid pool [2, 9]. A quantitative breakdown of functional proteins (e.g., serum proteins, muscle proteins) to provide amino acids is associated with functional limitations [6].

Protein synthesis in the human body requires the intracellular availability of 20 different L-amino acids. Eleven of these so called “proteinogenic” amino acids can be endogenously synthesized in the human body (alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, proline, serine, and tyrosine; referred to as dispensable [formerly: nonessential] amino acids). Nine amino acids (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine; referred to as indispensable [formerly: essential] amino acids) require regular dietary intake. Except for lysine and threonine, metabolic needs for indispensable amino acids can also be covered through the intake of the corresponding keto acids, as they can be transaminated in the body to yield the respective amino acid [10]. The indispensability of histidine at present is only proven for infants [11]; whether this also applies to healthy adults needs still clarification [2, 12].

Depending on the number of amino groups in the amino acids, proteins have a characteristic percentage of nitrogen [2, 13, 14]. The nitrogen percentage of proteins in foods ranges from 15 to 24% [15]. For the calculation of the nitrogen content, a general nitrogen percentage of 16% is assumed. This results in a conversion factor of 6.25 g nitrogen per g protein. In addition to the elements forming the basic structure of proteins (carbon, hydrogen, and oxygen), they may also contain sulfur or selenium [2].

Strictly speaking, there is no requirement for protein, but for nitrogen and the 9 indispensable amino acids. Because protein is, indeed, the quantitatively most important source of nitrogen and amino acids in daily nutrition, reference values for daily protein intake were derived mainly for practical reasons. Since reference values are calculated on the basis of mean protein requirements adding a variation coefficient, it can be assumed that the requirements for all indispensable amino acids are covered by the consumption of mixed protein sources.

Following a timely update process, the D-A-CH reference values for protein and indispensable amino acids lastly published in 2000 [16] were revised and issued in German in September 2017 [1]. This paper summarizes the methodological concepts and most important results elaborated by the D-A-CH Protein Working Group.

Methods

Literature Research

The D-A-CH Working Group conducted a structured literature research in PubMed considering publications between 2000 and 2017. The research sought to identify all eligible English and German articles reporting results of original human studies, meta-analyses, and systematic reviews focusing on protein or amino acid requirements. The D-A-CH Protein Working Group selected the literature valid to be used for updating of the reference values for protein intake.

Data published on adult protein requirements were only included when measurements were performed using controlled human nitrogen balance studies; a linear relationship between nitrogen intake and nitrogen balance (linear model) was assumed. The minimum nitrogen intake that is sufficient to compensate the obligatory nitrogen losses (zero balance) was considered to meet the requirement. This minimum nitrogen intake was multiplied by a factor of 6.25 to receive protein quantities [17].

Derivation of Reference Values

The derivation of estimated values for protein intake for infants at the age of 0 to under 4 months is based on the nitrogen content in breast milk, which is considered to be the optimal diet for infants [18, 19]. The recommended protein intake for infants at the age of 4 months as well as for children and adolescents is derived by the factorial method using data from nitrogen balance studies in line with the approach of the WHO [12] and considered both, requirement for growth and maintenance. The recommended intake value for adults under 65 years of age is derived from the average requirement plus a 2-fold variation coefficient. Due to insufficient data for protein requirements based on balance studies in adults >65 years, the working group decided to consider additionally reports on metabolic and functional parameters under various protein intakes to derive an estimated value. Due to methodological problems, data on protein requirements during pregnancy and lactation are not available. Consequently, the reference values for protein intake are derived following a fac-

Table 1. Recommended intake values for protein

Age	Protein, g/kg body weight ^a /day		Reference weight, kg ^b		g/day	
	male	female	male	female	male	female
Infants						
0 to under 1 month ^c		2.5	3.3	3.2		8
1 to under 2 months ^c		1.8	4.5	4.2		8
2 to under 4 months ^c		1.4	6.0	5.5		8
4 to under 12 months		1.3	8.6	7.9		11
Children and adolescents						
1 to under 4 years		1.0	13.9	13.2		14
4 to under 7 years		0.9	20.2	20.1		18
7 to under 10 years		0.9	29.3	28.7		26
10 to under 13 years	0.9	0.9	41.0	42.1	37	38
13 to under 15 years	0.9	0.9	55.5	54.0	50	49
15 to under 19 years	0.9	0.8	69.2	59.5	62	48
Adults						
19 to under 25 years	0.8	0.8	70.8	60.5	57	48
25 to under 51 years	0.8	0.8	70.7	60.0	57	48
51 to under 65 years	0.8	0.8	68.7	58.2	55	47
65 years and older ^c	1.0	1.0	66.8	57.1	67	57
Pregnant women						
2nd trimester		0.9		64.6		55
3rd trimester		1.0		70.0		69
Lactating women						
		1.2		60.5		71

^a The information relates to normal weight; in case of overweight (body mass index (BMI) >25 kg/m² in adults), the calculation should be based on normal body weight.

^b [1].

^c Estimated values.

torial method: to the average protein requirement of nonpregnant women, additional amounts of protein needed for the maternal, and fetal protein deposition or for the milk production are considered.

Reference values for daily protein intake are presented in g/kg body weight and g, using the reference body weight for age and sex.

Results

Infants

A recent meta-analysis reported an average protein content in breast milk from mothers of term infants of 1.17 g/100 mL in the first month after birth and 1.0 g/100 mL in the second and third month after birth [20]. After correction for the nonprotein nitrogen (NPN, estimated to 25%), the average protein content in breast milk is 1.36 g/100 mL in the first month after birth and 1.17 g/100 mL in the second and third month after birth. Taking into account a daily average breast milk intake

[21] of 600 mL/day (0 to under 1 month), 694 mL/day (1 to under 2 months) and 723 mL/day (2 to under 4 months), respectively [22], the protein intake in all 3 age groups is 8 g/day. In consideration of the reference body weights, the estimated reference values (g/kg body weight per day) for protein intake are 2.5 for infants at the age of 0 to under 1 month, 1.8 for infants at the age of 1 to under 2 months, and 1.4 for infants at the age of 2 to under 4 months (Table 1). The reference value for infants at the age of 4 to under 12 months was derived by the factorial method (see children and adolescents).

Children and Adolescents

Based on 7 studies, the WHO sets the maintenance requirement in infants/children between 9 months and 14 years to 110 mg N/kg body weight per day. As this value is nearly identical with the maintenance requirement in adults (105 mg N/kg body weight per day; see below), the WHO assumes the maintenance requirement in children to be the same as in adults (0.66 g protein/kg

body weight per day; coefficient of variation 12%) [12]. The growth requirement is derived based on 2 studies on protein deposition during growth, a longitudinal study with children under 2 years of age [23], and a cross-sectional study with children at the age of 4–18 years [24]. After correction for the efficiency of protein turnover (58%) [12], an average requirement (sum of maintenance and growth requirement) of 1.12 g protein/kg body weight per day in infants at the age of 4 to under 12 months was calculated. The recommended intake is calculated from the average requirement plus twice the variation coefficient. In infants at the age of 4 to under 12 months, a reference value of 1.3 g/kg body weight per day was derived. Due to reduced growth rates, the average protein requirement continuously decreases with age (from 0.82 g/kg body weight per day at the age of 1 to under 4 years to 0.70 g/kg body weight per day [male] and 0.68 g/kg body weight [female] in adolescence). The recommended reference values calculated on the basis of the daily requirements are presented in Table 1.

Adults under 65 Years of Age

As outlined under methods section, the derivation of the reference value for protein intake for adults is based on the results of nitrogen balance studies.

Two recent meta-analyses [17, 25] of nitrogen balance studies indicated an average nitrogen requirement in adults of 105 mg N/kg body weight per day corresponding to 0.66 g protein/kg body weight per day. Since data on gender-specific differences of protein requirements are inconsistent [17, 25, 26], no different values for women and men were derived.

Considering a coefficient of variation of 12% (addition of 24%) [17], the recommended protein intake for men and women is 0.8 g protein/kg body weight per day corresponding to a recommended daily protein intake of 55–57 g protein for men and 47–48 g protein for women, respectively (Table 1).

Adults 65 Years of Age and Older

Two meta-analyses of nitrogen balance studies [17, 26] compared the nitrogen requirement of younger (≤ 55 or < 60 years) and older people (> 55 or ≥ 60 years). Differences in nitrogen requirement were reported but did not reach statistic significance. The authors calculated an average requirement of 0.66 g protein/kg body weight per day in metabolically healthy older as well as in younger and middle-aged adults. Two nitrogen balance studies in older persons (55–70 years [27], 77–99 years [28]) not considered in the meta-analyses due to methodological

limitations (no younger control group) indicate that the protein requirement may be slightly higher in older adults.

Metabolic studies indicate a reduced muscle protein synthesis in older age (≥ 60 vs. 18–31 years [29], 72 ± 2 vs. 25 ± 1 years [30], 60–74 vs. 19–38 years [31]). Experimental metabolic tests showed that older subjects (~ 71 vs. ~ 22 years [32], 68 ± 2 vs. 31 ± 2 years [33]) require larger quantities of amino acids for maximum muscle protein synthesis.

In a systematic review, the results of clinical studies on the influence of a single protein or amino acid administration on muscle protein synthesis in younger and older people are summarized (middle-aged persons ≥ 55 vs. 18–35 years). Eight of 21 studies showed significant differences between younger and older adults regarding the effects of protein or amino acid administration on muscle protein synthesis. The other 13 studies did not indicate a difference between younger and older subjects [34].

In one of the studies, older participants (~ 71 years) required 0.4 g protein/kg body weight for maximum stimulation of muscle protein synthesis, while in younger adults (~ 22 years), 0.24 g protein/kg body weight was sufficient [32]. This observation is explained by anabolic resistance [35–38], which implies that in older people, the production of endogenous proteins from dietary proteins is impaired, probably (among other reasons) due to reduced postprandial amino acid availability and decreased muscle blood flow [39–42].

Several prospective cohort studies [43–45] and a cross-sectional study [46] showed an association between protein intake and physical functionality or functional course, respectively. Subjects with a higher protein intake were compared with subjects with a lower average protein intake (≤ 0.8 vs. 0.81–1.19 vs. ≥ 1.2 g/kg body weight/day, age of the subjects: 65–72 years [43]; approximately 0.8 g/kg body weight/day vs. approximately 1.2 g/kg body weight/day, age of the subjects: ≥ 60 years [44]; 1.0 vs. 1.2 g/kg body weight/day, age of the subjects: 50–79 years [45]; 0.8–1.19 vs. ≥ 1.2 g/kg body weight/day, age of the subjects: 50–75 years [46]). Subjects with a higher protein intake showed better functional parameters regarding strength and mobility [43–46]. Over an observation period of several years, they also had a lower loss of specific function parameters (e.g., grip strength) [43–45]. However, after adjustment for fat mass, this was partially no longer statistically significant [43].

A higher protein intake compared with a lower protein intake in older adults (1.2 vs. ≤ 0.8 g/kg body weight/day, age of the subjects: 65–72 years [47]; 1.6 vs. 0.8 g/kg body

weight/day, age of the subjects: 75 ± 3 years [48]; 1.3 vs. 0.9 g/kg body weight/day, age of the subjects: 67–84 years [49]; 1.2 vs. 0.8 g/kg body weight/day, age of the subjects: 70–79 years [50]) was also associated with greater fat-free mass or muscle mass, respectively, and partially with a lower loss [50] or even an increase [47, 48] of fat-free mass, body cell mass or muscle mass, respectively, over a period of several years. Data from the *NuAge study* showed a significant difference in men in fat-free body mass between the quartiles of protein intake at baseline (quartile 1: 0.86 g/kg body weight/day, quartile 4: 1.29 g/kg body weight/day, age of the subjects: 67–84 years) but no effect of protein intake on the loss of fat-free mass over 2 years. A cross-sectional study did not show any difference in muscle mass in subjects with higher protein intake compared with subjects with lower protein intake (≥ 1.2 vs. 0.8–1.19 g/kg body weight/day, age of the subjects: 50–75 years) [46].

Two prospective cohort studies showed a lower incidence of frailty or a reduced risk of frailty, respectively, at higher compared with lower protein intake over a period of about 3 years (quartile 1: men 31.6–82.9 g/day, women 26.9–68.0 g/day, quartile 4: men 115.8–218.4 g/day, women 95.7–181.3 g/day, age of the subjects: ≥ 60 years [51]; 1.2 vs. 1.0 g/kg body weight/day, age of the subjects: 65–79 years [52]).

Considering the results mentioned above, an estimated value is set at 1.0 g/kg body weight per day for both women and men above 65 years. In relation to reference body weight, the estimated value for adequate protein intake is 57 g/day for women and 67 g/day for men (Table 1).

Pregnancy

According to the WHO [53, 54], a body weight gain of 10–14 kg (mean 12 kg) is associated with optimal health of mother and fetus. With a body weight gain of 12 kg until birth of the child, 597 g protein is deposited [53, 55]. Body weight gain and protein deposition during pregnancy are not linear. Protein deposition distribution is approximately 1.3 g protein/day (20%) in the second trimester and 5.1 g protein/day (80%) in the third trimester. Body weight gain occurs to approximately 11% in the first, 47% in the second, and 42% in the third trimester [55]. To derive the protein requirement for protein deposition, it has to be corrected by the efficiency of protein turnover. For pregnant women, the efficiency of protein turnover is assumed to be the same as for nonpregnant women (47%) [56]. The protein requirement for the body weight gain during pregnancy, in relation to the average body weight gain in each trimester, has then to be added.

For the first trimester, an additional protein intake of 0.4 g per day was calculated; considering the recommended protein intake for women at the age of 19 to under 25 years of 48 g/day, this amount can be neglected (Table 1). For the second and third trimester of pregnancy, average additional protein requirements are considerably higher (5.5 g protein/day and 17.1 g protein/day, respectively). Consequently, considering a coefficient of variation of 12% (addition of 24%), the recommended additional protein intakes calculated to 7 and 21 g protein/day in the second and third trimester, respectively (Table 1).

To determine the recommended daily protein intake per kg body weight, the protein requirement for protein deposition is divided by total body weight. The total body weight is calculated from the average weight gain in each trimester and the reference body weight for women at the age of 19 to under 25 years. The resulting average additional protein requirement during pregnancy plus the protein requirement for nonpregnant women correspond to the average protein requirement for pregnant women. Thus, considering a coefficient of variation of 12% (addition of 24%), the recommended protein intake is 0.9 g protein/kg body weight/day in the second trimester and 1.0 g protein/kg body weight/day in the third trimester (Table 1).

Lactation

The protein content of human breast milk in various lactation periods was presented in detail above; in mature breast milk the average protein content is approximately 1.0 g/100 mL [20]. After correction for the NPN, the average protein content in breast milk is 1.17 g/100 mL in the first 3 months after birth. Assuming an average milk intake of the suckling of 750 mL/day, approximately 8.8 g protein/day is secreted [21]. Considering an efficiency of protein turnover similar to nonlactating women (47%) [56], the average additional protein requirement in lactating women is 18.6 g/day corresponding to an additional protein intake of 23 g/day (CV 12%). Based on the reference weight for women at the age of 19 to under 25 years, this corresponds to a recommended intake value of 1.2 g/kg body weight per day (0.8 g/kg body weight plus additional 0.4 g/kg body weight; Table 1).

Discussion

Per definition, D-A-CH reference values for nutrients are used to plan health-maintaining diets and to evaluate actual nutrient intakes of healthy people [1]. Per defini-

tion, intakes according to reference values cover nutrient requirements in 97.5% of the population; thus, risks for symptoms of nutrient deprivation and associated metabolic disorders are minimized. In general, the recommended reference value for adults is derived from the average nutrient requirement plus a coefficient of variation. This surplus should ensure that a protein intake following the recommendations should provide all indispensable amino acids in sufficient quantities independent of the specific biological value of the protein mixture consumed individually, at least when considering typical dietary patterns and food choices in developed countries.

Obviously, the scientific reliability of the reference values strictly depends on the confidential assessment of the respective average requirements. In accordance with the strategy of other international Nutrition Societies [12, 56], the Working Group decided to use age- and sex-specific protein requirements only when they were determined in controlled nitrogen balance studies. Within the last years, the indicator amino acid oxidation (IAAO) method was proposed as an alternative, probably more precise technology to estimate the protein requirements [57, 58]. Until today, the IAAO method has been only occasionally used to determine protein requirement in children [59], young adults [60–62], older people [63, 64], and pregnant women [65]. Compared to earlier data from nitrogen balance studies, protein requirements assessed with IAAO tend to be generally higher (+15–73%). Due to limited data, final conclusions with respect to the “true” values are currently not possible; initial discussions about the true value are controversial [66–68].

Due to the lack of age-specific data, derivation of D-A-CH reference values lastly published in 2000 could not reliably consider distinct age groups in adulthood [16]. Reliable knowledge of adult protein requirements is still poor today; however, numerous recent human studies focusing on functional and/or metabolic outcomes strongly suggest that adults >65 years may benefit from a protein intake higher than 0.8 g/kg body weight/day as recommended for adults aged 18–65 years [43–52]. Consequently, the Working Group decided to consider these current data in addition to results of nitrogen balance studies and to define an estimated value of 1.0 g/kg body weight/day for older adults (Table 1). This is in line with the statements of the PROT-AGE Study Group [39], the European Society for Clinical Nutrition and Metabolism [40], and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis [69] recommending a protein intake of 1.0–1.2 g/kg body weight per

day for adults above 65 years of age [39, 40] or between 50 and 70 years [69] to maintain functional integrity. In contrast, the EFSA [56], the IOM [70], and the WHO [12] do not recommend other protein intake quantities for older adults (≥ 60 years [56], ≥ 51 years [70]) than for younger adults.

The calculation of D-A-CH reference values consider age- and sex-dependent reference body weights and are also valid in physically active adults (30 min 4–5 times a week) [71–73]. Whether increased physical activities (strengths/resistance training) or even competitive sports (athletes) may lead to a considerable higher protein demand is still under debate. Presently, a newly installed D-A-CH Working Group on Sports Nutrition is dealing with that topic and will publish specific recommendations in due time.

As outlined above, reference values are scientifically valid for healthy subjects; disease-specific alterations in protein/amino acid metabolism are not taken into account. Nevertheless, reference values for healthy subjects are frequently used to establish dietetic concepts in clinical nutrition by simply adding a surcharge to cover a potential higher requirement. Indeed, higher protein/amino acid demands are assumed in various diseases; reliable data are, however, not available. The protein reference values do also not consider potential preventive effects of protein consumption.

Conclusion

The present revision of the D-A-CH reference values lastly published in 2000 in the light of newly data published has led to one important change: a specific estimated value for adults >65 years has been set. Since the energy consumption continuously decreases with age, this new estimated protein intake value might be a challenge for the introduction of food-based nutrition concepts for older adults. The process for the derivation of reference values for pregnant and lactating women is now specified in detail; reference values for infants, children, adolescents, and adults <65 years are essentially unchanged.

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Ethics Statement

The authors have no ethical conflicts to disclose.

Disclosure Statement

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Author Contributions

P.S. and M.R.: conducted the literature research and drafted the manuscript. K.B., J.M.B., I.E., H.H., E.L.-B., G.S., and D.V.: revised the draft critically. All authors contributed to the conception of the manuscript and interpreted the data. All authors read and approved the final manuscript.

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